Annual report '22

ciber
CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED

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BIOMEDICAL RESEARCH NETWORKING CENTER CONSORTIUM (CIBER)

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Welcome from the President of CIBER'S Governing Board

Cristóbal Belda

At present, the CIBER Consortium has 518 research groups of excellence in 104 institutions, a staff of 881 contracted people and around 600 researchers as assigned personnel, integrated within the 13 thematic areas of research. These data are the result of several actions that have taken place during 2022 and that have set a new milestone in the history of our Consortium.

On the one hand, the merger of the CIBER of Neurodegenerative Diseases (CIBERNED) involves the integration of 55 groups for the study of Parkinson's disease, Alzheimer's, ALS and Multiple Sclerosis, among others. The fight against these diseases is a vitally important challenge for our society, both because of the consequences in terms of loss of health for the people who suffer from them and their families, and because of the socio-economic impact derived from their symptoms and the necessary clinical and social support they require. I am confident that the integration of CIBERNED will result in increased collaboration with the other areas of the consortium and with patients and their families.

At the same time, the incorporation, through the Strategic Action in Health (Acción Estratégica en Salud-AES), of the CIBER area of Infectious Diseases (CIBERINFEC), with 46 research groups, has represented an important challenge for the management and organization of resources during this period, obtaining highly satisfactory results. The Infectious Diseases area, directed by Prof. Jesús Oteo, researcher at the National Microbiology Center of the ISCIII, is working both to respond to the new questions raised by the COVID-19 pandemic and to investigate other major health problems such as antimicrobial resistance, HIV infection, neglected tropical diseases and global health, among others. This is the culmination of a stage in the strengthening of the CIBER model, promoted by the Instituto de Salud Carlos III to promote collaborative research of excellence in biomedicine with a strong commitment to patients and their families.

From the point of view of research results, CIBER has played an essential role in the international positioning of all the entities attached to the ISCIII, which has recently been considered one of the 20 organizations with the greatest impact on health worldwide. Here it is necessary to emphasize once again the great research efficiency of the groups and of the CIBER entry and exit mechanism. This mechanism, based on continuous evaluation, allows the groups with the greatest excellence to enter while discarding those that are not able to keep up with the frenetic scientific pace of the whole. In other words, scientific excellence at its most competitive edge. This system seeks to improve the quality of research, favor synergies, avoid duplication in the Science and Innovation System and optimize resources. All this allows, through the collaboration of the CIBER groups, the results of research to more efficiently reach those afflicted, the public, the health industry and, in short, the entire National Health System.

The main indicators of scientific publications of the groups reveal a total of more than 8,900 scientific articles, of which more than 60% have been published in highly competitive journals.

Many of these studies have changed clinical practice and have revealed new diagnostic and therapeutic options for different types of diseases. During this period, 16 new priority patent applications and 8 other inventions (software, trademarks

and other industrial property assets were filed, and 7 licenses were signed. In addition, 19 ownership contracts, 4 scientific cooperation agreements and more than 30 other contracts including material transfer agreements (MTAs) and confidentiality agreements (CDAs) were signed.

However, the position of the CIBER groups is no more than a reflection of the excellence of the research personnel that comprise these groups. As a reflection of this, three researchers attached to the CIBER, Miguel Ángel Martínez, Mariano Barbacid and Ana Martínez Gil, won different categories of the National Research Awards. In addition, Arkaitz Carracedo and María Victoria Llorens Martín, were awarded in the new category of the National Research Awards for Young People. Also worth noting is that the researcher Rosa Faner obtained a Consolidator Grant to study COPD and gene-environment interactions in childhood.

The CIBER has obtained very significant funding which, complemented by the nominative subsidy of more than 40 million euros allocated annually from the ISCIII budget, has allowed the implementation of research projects with a high impact on health. I would like to highlight, without being exhaustive, some of the proposals funded through the Personalized Precision Medicine call of the Strategic Action in Health 2021-2023, such as the MePRAM project, which proposes an integral and comprehensive approach to antimicrobial resistance by incorporating new omics technologies in the detection and early diagnosis of multi-resistant microorganisms; or the Immune4ALL project, which explores the feasibility of predictive and pharmacodynamic biomarkers of immunotherapy in solid tumors. These are just two examples of the projects being developed at the CIBER and which I have no doubt will provide interesting results in tackling these specific health problems.

Similarly, I would like to highlight the implementation during 2022 of the CIBER Technological Development Platform. This initiative, promoted by the CIBER technology transfer office, focuses its activity on three fundamental axes: to promote the capabilities of the consortium in terms of technological development; to improve the processes of valorization, transfer and commercialization of technologies in the CIBER; and to establish alliances with strategic agents that can help us to develop these technologies.

2022 has also been an important period for communication and visibility activities of the CIBER Consortium. The integration of the two previously mentioned areas (CIBERNED and infectious diseases) has promoted a redefinition of the communication strategy including actions to strengthen institutional and internal communication within the CIBER. In this sense, the corporate identity of the Consortium was updated and a new institutional video was made in which the center's own staff informs about the research areas. In coordination with the above, the Scientific Culture and Innovation Unit of the CIBER has continued in 2022 its work of communicating research results to the public. During this period, research personnel have been incorporated to join forces and expertise in scientific dissemination. This group has collaborated in the development of some of the outreach activities carried out in 2022, such as the one on the occasion of the International Day of Women and Girls in Science, on February 11, or the IMPROCIENCIA activity, during the Madrid Science Week, which brought together more than 300 teenagers at the Instituto de Salud Carlos III. MENTESCOPIA, an outreach program with a clear purpose: to end the stigma of mental health among the young population, is also aimed at this audience.

In addition to these activities, the CIBER Consortium disseminated almost 1350 news items on scientific results and continued to add followers in the different social networks, reaching a total of more than 67,000 people through these channels.

Finally, I would not like to end without mentioning some conferences of special interest held in 2022 such as the one held jointly by CIBER-ASEBIO: "Advanced Therapies from academia to industry", the conference for patients in Rare Diseases "Research is Progress" or the meeting aimed at patients in the Mental Health area. Similarly, in 2022, meetings were held for young research personnel shared among various thematic areas.

Internal Organization

El Consorcio Centro de Investigación Bio- médica en Red, M.P, CIBER (Biomedical Research Networking Center Consortium), a public research consortium created at the initiative of the Instituto de Salud Carlos III (ISCIII) , promotes research of excellence in Biomedicine and Health Sciences that is carried out in the National Health System and in the Science and Technology System.

The scientific program of the CIBER is organized around the following **thematic areas** of research:

- **Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)**
- **Cardiovascular Diseases (CIBERCV)**
- **Diabetes and Associated Metabolic Diseases (CIBERDEM)**
- **Liver and Digestive Diseases (CIBEREHD)**
- **Rare Diseases (CIBERER)**
- **Respiratory Diseases (CIBERES)**
- **Epidemiology and Public Health (CIBERESP)**
- **Frailty and Healthy Ageing (CIBERFES)**
- **Infectious Diseases (CIBERINFEC)**
- **Neurodegenerative Diseases (CIBERNED)**
- **Physiopathology of Obesity and Nutrition (CIBEROBN)**
- **Cancer (CIBERONC)**
- **Mental Health (CIBERSAM)**

The CIBER currently has a staff of 881 people and 5.654 attached researchers, integrated within over 500 research groups, working in different locations, linked to over 100 consortium institutions, belonging to different Administrations, Institutions and Autonomous Communities, of the public and private sector.

The governing, management and administrative bodies are as follows:

GOVERNING BOARD AND PERMANENT COMMISSION

The **Governing Board**, presided over by the president of the ISCIII, is made up of three representatives of the ISCIII and an institutional representative of each of the institutions in the consortium appointed by their senior authorities. It meets every six months.

The **Permanent Commission** constitutes a delegated commission formed by the ISCIII and 8 members of the Governing Council, which can by be renewed annually. Both the operation and the purposes of the governing, support and advisory bodies are established in the CIBER statutes.

MANAGEMENT COMMITTE AND Y ADVISORY COMMITTEES

In each area of the CIBER there is a Management Committee and an External Scientific Advisory Committee.

The **Management Committee** is made up of the Scientific Management of each area, the program Coordinators and the Managing Director of the CIBER, as well as a representative of the Instituto de Salud Carlos III.

The **External Scientific Advisory Committee** is a body providing scientific assessment and support, made up of relevant personalities in the field of health sciences distinguished by their professional or scientific career in line with the objectives of the center. This is the body in charge of carrying out the annual evaluation of the activity of the areas and their research groups.

SCIENTIFIC DIRECTORS

The Scientific Directors of the CIBER represent each of the thematic areas and preside over the Management Committees. In 2022, they were the following:

CIBER-BBN	**Dr. Ramón Martínez Máñez**
CIBERCV	**Dr. Francisco Fernández-Avilés**
CIBERDEM	**Dr. Eduard Montanya Mías**
CIBEREHD	**Dr. Rafael Bañares Cañizares**
CIBERER	**Dr. Pablo Lapunzina Badía**
CIBERES	**Dr. Ferran Barbé Illa**
CIBERESP	**Dra. Marina Pollán Santamaría**
CIBERFES	**Dr. Leocadio Rodríguez Mañas**
CIBERINFEC	**Dr. Jesús Oteo Iglesias**
CIBERNED	**Dr. Adolfo López de Munain**
CIBEROBN	**Dr. Carlos Diéguez González**
CIBERONC	**Dr. Anna Bigas Salvans**
CIBERSAM	**Dr. Eduard Vieta Pascual**

CODE OF ETHICS

The purpose of the CIBER Code of Ethics is to establish the general regulations and principles governing the behavior of all persons involved in CIBER activities, in order to ensure that their behavior not only complies with current legislation, but also with high standards of integrity, professionalism and responsibility. Both the governing and management bodies of the consortium and all CIBER employees, regardless of their hierarchical level, functional location or legal relationship with the consortium (whether it is through employment, training, contractual, or of any other similar nature), must comply with the rules and principles established in this code of ethics.

It is important to emphasize that the code of ethics functions as a complement to the statutes and regulations in force applicable to the consortium, and not as a substitute.

The CIBER code of ethics is based on the following general ethical principles:

- **Respect for all persons**
- **Non- discrimination and equal opportunity**
- **Respect for privacy**
- **Work-life balance**
- **Environmental Protection**
- **Prevention of occupational hazards**
- **Collective Rights**

As regards the general conduct guidelines, the following are taken into account:

- > Compliance with the law
- > Committment to CIBER
- > Professionalism
- > Responsibility
- > Gifts, courtesies & gratuities
- > Conflict of interests
- > Relations with suppliers
- > Relations with other institutions
- > Selection process
- > Dissemination of information
- > Confidential and restricted information
- > Protection of personal data
- > Performance of other activities
- > Use of resources and means for the development of ones professional activity
- > Care of facilities, equipment, spaces and rational use of resources
- > Protection of assets

For more information, the latest versión of the CIBER code of ethics can be consulted at: https://www.ciberisciii.es/media/3101942/codigo-etico-ciber-v0.pdf

Ciber in figures

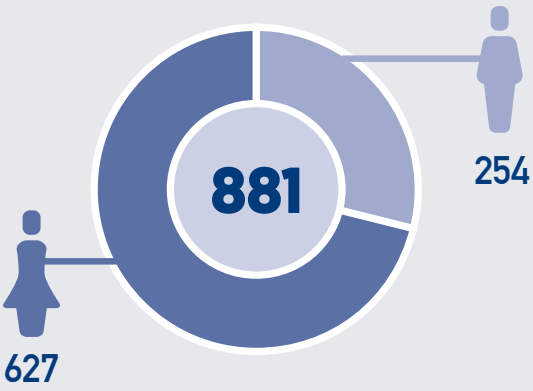
Economic Data

TOTAL INCOME 2022

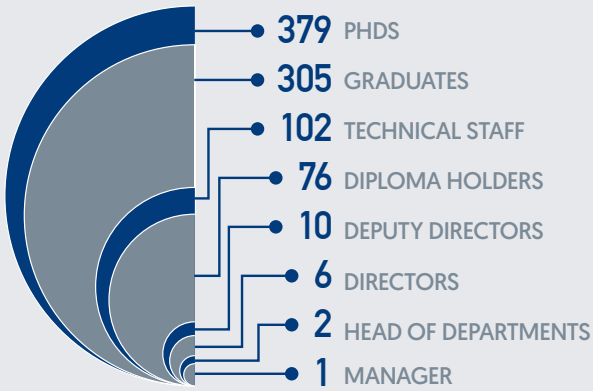
41.754.950,00 €

Personnel Data

TOTAL BY GENDER



TOTAL BY CATEGORY

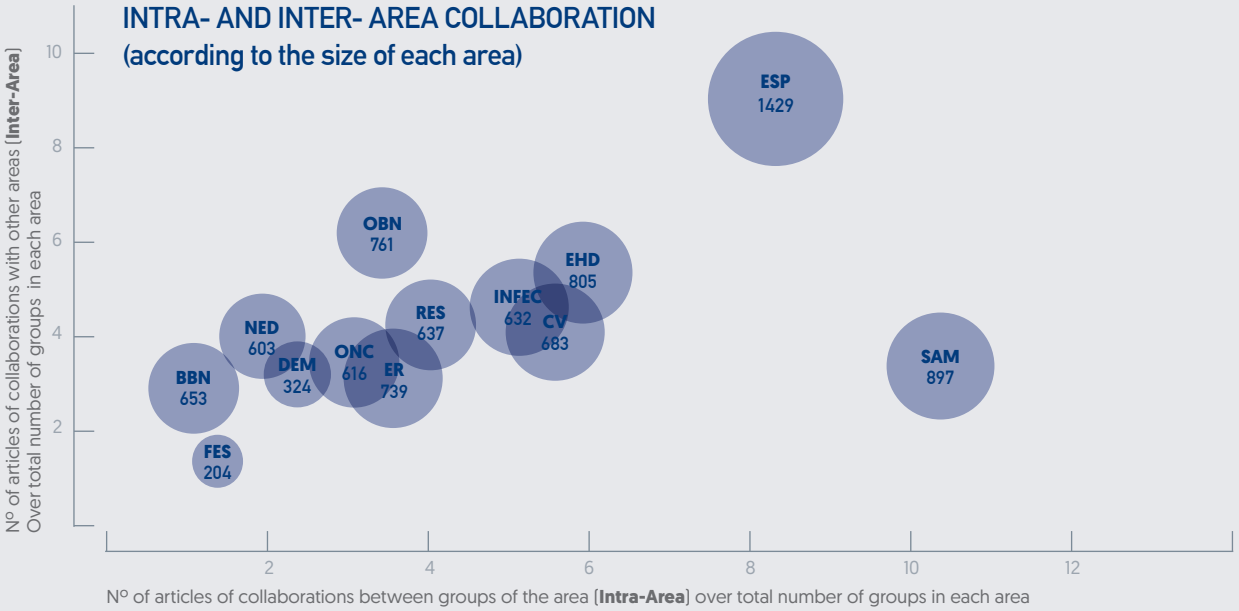


Productivity Data

TOTAL PUBLICATIONS 2022

8.983

INTRA- AND INTER- AREA COLLABORATION
(according to the size of each area)



Projects Data

National International

PROJECTS OBTAINED	15	27	42
APPLICATIONS SUBMITTED	46	106	152
FUNDS OBTAINED	10.101.102,77 €	34.320.990,79 €	44.422.093,56 €

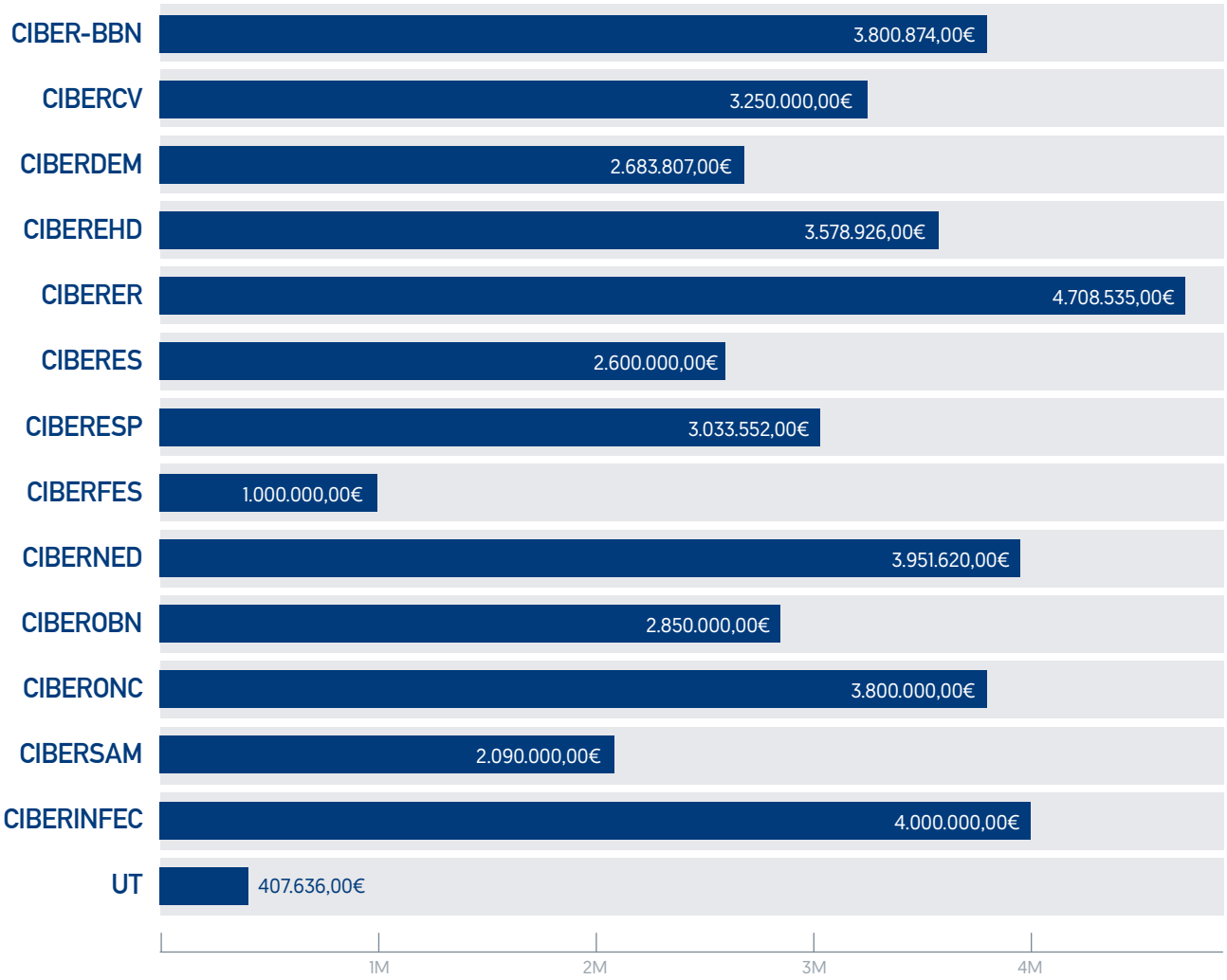
Transfer Data

Communication Data

- Press Releases **243**
- Media Impacts **15.561**
  - Digital **14.273**
  - Press **1.255**
  - Radio and Tv **33**
- News **1349**
- Agenda Events **586**
- Websitevisits **1.467.554**
- Website users **307.436**
- Youtube Suscribers **810**
- Twitter Accounts **14** /Followers **67.140**

Economic Data

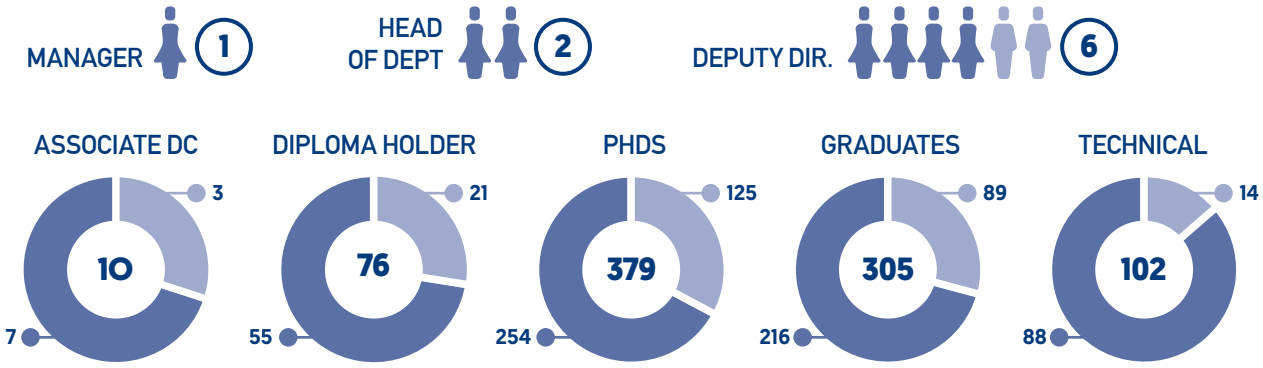
Resources obtained by area in 2022



Personnel

Contracted personnel by area and gender

Contracted personnel by category and gender



Transfer

One of the main objectives of the CIBER is to transfer the knowledge generated by its research groups to society. Thus, research results are developed in protocols, services and products for the improvement of clinical practice and quality of life of the population. To this end, the Knowledge Transfer area of the CIBER serves as a link between our researchers and companies, private entities, public research centers and other agents of the system to make cooperation with them effective so that the research results can be applied.

Throughout 2022 in the CIBER, 16 new priority patent applications were filed and another 8 developments were undertaken ranging from software, orphan drug designations and trademarks. In addition, 7 license and license option contracts were signed, among other indicators summarized in the following table:

PRIORITY PATENT APPLICATIONS	SIGNED LICENSES/ LICENSE OPTIONS	OTHER IPRS	SIGNED CO-OWNERSHIP CONTRACTS	SIGNED CDAS	SIGNED MTAS *	SCIENTIFIC COOPERATION CONTRACTS
16	7	8	19	10	21	4

*This does not include the MTAs/DTAs of the IMPaCT Genome Project, which number in the dozens.

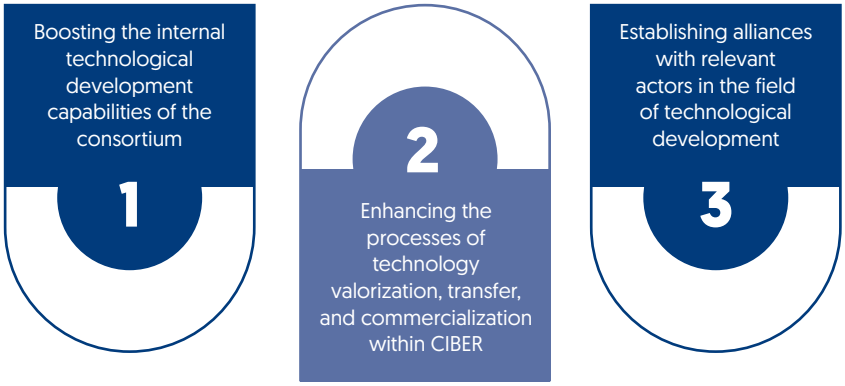
In addition, we have continued to work on supporting the creations of spin-offs, commercialization, attendance at science fairs, organization of events, dissemination and outreach, among other activities. We have also taken on the management of CIBER's data protection.

CREATION OF THE CIBER TECHNOLOGICAL DEVELOPMENT PLATFORM:

In particular, we highlight as one of the major achievements of 2022 the development of the Technological Development Platform which has as its main objective the early accompaniment and support to CIBER research projects to ensure a better translational ratio throughout the course of their development.

It is an inter-area, multidisciplinary structure that draws on the CIBER network structure for a better valorization of our products and capabilities.

Its activity is structured around the following axes:



The activity of the Platform will be coordinated together with CIBER's Knowledge Transfer Office (OTC) sharing resources and equipment.

Gender Equality Plan

The CIBER Gender Equality Plan seeks to implement the universal legal principle of equality between women and men which is recognized in various international human rights texts. To achieve this objective, general and specific goals have been defined, as well as specific actions included in the plan.

This plan is framed within the current legislation, in particular, in the Organic Law 3/2007, of March 22, for the Effective Equality of Women and Men and the Royal Decree Law 6/2019, of March 1, on urgent measures to guarantee equal treatment and opportunities between women and men in employment and occupation.

According to Article 46 of the Organic Law 3/2007, equality plans are a set of ordered measures adopted after a diagnosis of the situation, with the aim of achieving equal treatment and opportunities between women and men in the workplace, and eliminating discrimination based on gender. These plans establish specific equality objectives, strategies and practices for their achievement and monitoring and evaluation systems.

Among the issues covered by the equality plans are female under-representation, access to employment, professional classification, vocational training and promotion, remuneration, reconciliation of personal, working and family life, working conditions and the prevention of sexual harassment and gender-based harassment.

According to Article 3 of the Organic Law 3/2007, the principle of equal treatment between women and men implies the absence of any direct or indirect discrimination based on gender, and especially those derived from maternity, the assumption of family obligations and marital status.

With this Equality Plan, CIBER hopes to continue working on the integration of the principle of equal opportunities and treatment in the management of its personnel, in order to improve the working environment and labor relations, the personal satisfaction of the staff, their quality of life and occupational health.

For more information, the CIBER Equality Plan 2022-2026 can be found at:
https://www.ciberisciii.es/media/3072366/plan-igualdad-ciber.pdf

Communication

12 RELEVANT CIBER NEWS IN 2022:

https://twitter.com/CIBER_ISCIII/status/1608788285157171202?s=20 Dissemination activities of the Scientific Culture Unit

1 In January the new CIBER area of infectious diseases CIBERINFEC was created and the CIBERNED area was integrated into the Consortium, at the same time as Margarita Blázquez took over management. A challenge for the structure and a source of great satisfaction to continue growing.

2 On Feb. 11, we started the #ConversationswithWomenScientists series.
We have thoroughly enjoyed sharing experiences beyond science.

3 In March, the CIBERESP Conference was held at the EASPsalud where CIBER-BBN and CIBERINFEC also participated.

4 EIn April, the groups of the CIBERFES area met during the SEMEG congress.
We also announced the renewal of the accreditation of Nanbiosis CIBERBBN as #ICTS.

5 At the end of May, the annual CIBERER meeting was held in Castelldefels where 70+ projects were presented.

6 And in June, #Neuro2022, an internationally prestigious meeting organized by the Queen Sofia Foundation, CIEN Foundation and CIBERNED in Salamanca.

7 In July, Presentation of #CI BERpostcovid results with CIBERESP and CIBERES.

8 In August we were preparing for the #GladiatorRace in A Coruña where #IMPaCT-Genómica was also presented.

9 In September, Alcala de Henares hosted the first meeting of the CIBERESP #CohorteIMPaCT to study and improve the health of the Spanish population.

10 In October, together with AseBio una, we held a conference to promote the potential of Advanced Therapies and to connect Academia & Industry.

11 In November we were back with #Improcien cia in SaludISCIII during # MadrimasdScienceWeek and CIBEROBN, CIBEREHD, CIBER-BBN and CIBERDEM conferences were also held.

12 We closed the year with record external funding of almost 43M€ for research and health projects and the incorporation of 13 groups to the consortium.
Thus, 2023 will be full of enthusiasm and hard work (and novelties). Research is progress.

NEW CORPORATE IMAGE AND INSTITUTIONAL VIDEO

In 2022 the CIBER developed its **new communication plan** which incorporates the strategy to be followed by the Consortium geared towards its strategic objectives and audiences. It is a set of common bases that will regulate the center's communication with a commitment to internal and institutional communication, in addition to the tasks of scientific communication, which will be centered more at the Scientific Culture Unit. In this sense, as part of a strengthening of the institutional image of the Consortium, the logos and corporate image for all the thematic areas were updated, something that will contribute to a better positioning of the CIBER and its areas in the eyes of external audiences. Similarly, in 2022, a **new institutional presentation video** was produced in which CIBER staff present the objectives and the 13 research areas.

Both research and management staff participated in the making of the video and we would like to thank them for their contribution: Empar Lurbe, Eli Prats, Marina Po- llán, Gemma Moreno, David Martínez, Jesús Oteo, Pablo Lapunzina, Alejandro de la Torre y Carmen Fariñas, Julián Isla, Juan Luque, Adriana Reatigui, Sara Téllez, Pablo Casadejús, Mónica López and Natalia Jarillo..

OUTREACH ACTIVITIES OF THE CIBER SCIENTIFIC CULTURE UNIT (UCC+I)

CONVERSATIONS WITH WOMEN SCIENTISTS

On the occasion of the "International Day of Women and Girls in Science" on February 11, the CIBER launched a series of "Conversations with women scientists". These 6 videos, of approximately 12 minutes, and with participation from all areas, could be seen throughout 2022 coinciding with other important occasions. The researchers talked about science and also about their personal interests in order to bring women scientists into the limelight and attract new scientific vocations. The videos were disseminated through the CIBER channels (web pages, Twitter and YouTube) and already add up to more than 700 views on YouTube and more than 2.700 on Twitter.

Links to the series:

- Feb 11. International Day of Women and Girls in Science: Lina Badimon y Esther Pueyo
- March 8. International Women's Day. Karmele Valencia and Rosario Perona
- April 23. World Book Day: Dolores Corella and Sofía Pérez del Pulgar
- May 18. International Museum Day: Deborah Burks and Mª Ángeles Bonmatí
- June 20. Yellow Day: María Llorens and Gisela Mezquida'
- November 10. International Week of Science and Peace: Cristina Calvo, Jéssica González and Vicky Serra

CIBER ACTIVITY AT THE MADRID SCIENCE WEEK

In its fourth edition, **#ImproCiencia**, the CIBER's traditional science outreach event, once again united science and theatrical improvisation to explain, in an entertaining way, the biomedical research carried out by the CIBER to 300 students of secondary school, high school and vocational training. After the theatrical improvisation the students participated in workshops on healthy habits. The activity, part of the Madrid Science Week, took place on Tuesday, November 8, 2022 at the Instituto de Salud Carlos III.

The company Impro Impar prepared **theatrical improvisations** to enliven the different research projects:

- INFECTIOUS DISEASES. Are dogs man's best friend? Ana Méndez.
- RARE DISEASES. Spread your wings. Butterfly skin. Sara Guerrero.
- NEURODEGENERATIVE DISEASES. Not everything in the brain are neurons. José Ángel Morales.

Los following Healthy Habits workshops were presented:

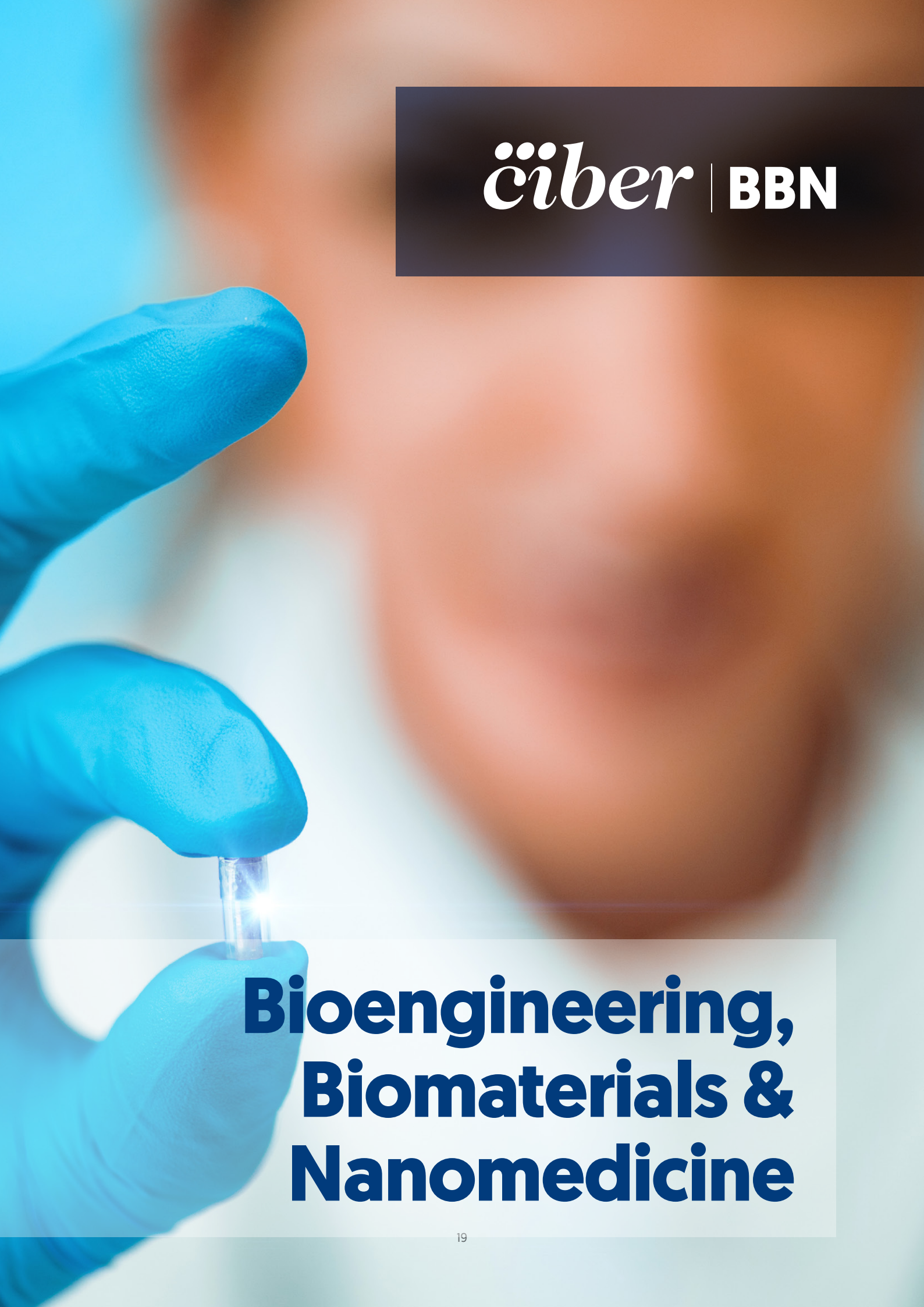
- MENTAL HEALTH. MenteScopia a Project for Mental Health.
- NUTRITION. Chocolate sampling. Josep Tur, Catalina Mª Mascaró and Cristina Bouzas.
- EXERCISE. From adolescence to aging. Ignacio Ara and Irene Rodríguez.
- SLEEP. Avoid depriving yourself of sleep Elvira Casado and Mariángeles Bonmatí.

Youtube recording links:

https://www.youtube.com/watch?v=1gEH1hCciX0

https://www.youtube.com/watch?v=3-s_-kMrTyk

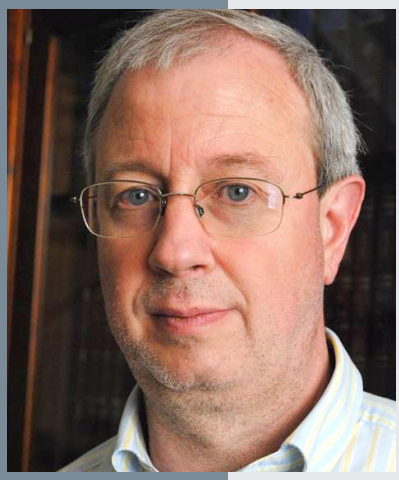
Thematic Areas of Research



ciber | BBN

Bioengineering, Biomaterials & Nanomedicine

Welcome from the scientific director



Ramón Martínez Máñez

Dear friends,

I am very pleased to summarize in this letter the highlights of CIBER-BBN during 2022, the year in which the Covid-19 pandemic, which has so intensely marked our lives, gradually gave way to the usual routines prior to 2020. One example was the recovery of the conference in La Coruña, in a long-awaited reunion of the entire CIBER-BBN research staff, as well as the joint celebration of a conference for young researchers with CIBERESP in Barcelona.

The Steering Committee has endeavored to promote and encourage research in collaboration with other areas, the main objective of the CIBER consortium. For the first time, more than half of the intramural research that has been active has been in cooperation with other areas. In addition, we have collaborative links with all areas, including CIBERNED and CIBERINFEC, which have been the most recent additions to the consortium. As for specific actions involving funding, two calls for seed projects have been launched with CIBERESP, in which funding has been granted to five projects, and one with CIBEREHD, with funding obtained for two projects.

At the beginning of the year, 14 Early Stage projects were presented, which in this edition were open to collaboration with other areas. This has also served to stimulate interaction outside BBN among the more senior contracted researchers.

In view of the success of this initiative, at the end of the year a new call was launched, this time with funding, collecting funds initially earmarked for other actions but which had not yet been committed to. As a result, at the end of 2022, seven Early Stage projects were awarded, all of them collaborative, (three intra BNN and four inter-area) led, at the PI and CO-PI level, by contracted PhDs. In addition, in the call for valorization, highly valued by the groups, 4 projects have been initiated which have received funds to increase their TRL.

Scientific production has decreased 15%, reaching the level of 2019 as regards the total number of publications. In terms of quality, 68% are Q1 publications and 25% are D1 publications.

Nevertheless, the greatest achievement of the previous year has undoubtedly been the ARISTOS project within the COFUND Marie Skłodowska-Curie program. ARISTOS is an excellence training program aimed at postdoctoral researchers that contemplates the hiring of 27 postdocs to be distributed across all CIBER areas. This initiative will be the first major strategic action on a consortium-wide level and represents a unique opportunity to position the CIBER within the international research excellence framework.

Regarding NANBIOSIS, its designation as a singular scientific-technical infrastructure has been revalidated by the Ministry in the new configuration of the ICTS map after the four-year evaluation process.

Finally, I would not like to end this communication without paying special tribute to Manuel Sánchez, who left us at the beginning of 2022, a key member of the consortium and to whom we owe the configuration of CIBER as it is today.

For yet another year, I would like to thank the CIBER-BBN community for its commitment and dedication to collaborative research.

Warmest regards to all,

Programs

Bioengineering and medical imaging

Raimon Jané

COORDINATOR

In 2022, seven new proposals for intramural collaborations have been presented in this research program (5 of them in collaboration with other areas), in addition to the ongoing active collaborations from previous years.

- Development of non-invasive elec- trodes for long-term electroen- cephalography (EEG) recording with application in brain-computer interfaces (Roberto Hornero)
- Genetic analysis of sepsis and intraoperative neuromonitoring for the assessment of postoperative behavioral changes in children (Roberto Hornero)
- COVID-Cough, Early identification of severity in patients with COVID19 using acoustic cough analysis with smartphones (Raimon Jané)
- CASA-DP, Cancer Stroma Assessment through Digital Pathology (María Jesús Ledesma)
- LIP, Image based biomarkers for Immunotherapy response prediction in Lung cancer (María Jesús Ledesma)
- LPIR, Lung parenchymal lesion characterization for the study of respiratory diseases (María Jesús Ledesma)
- Validation of quantitative susceptibility mapping for cortical iron deposits quantification in Parkinson's disease (Raúl Tudela)

The clinical areas addressed by these new proposals are infectious diseases (2), neurological diseases (2), cancer (2) and respiratory diseases (1).

As regards seed projects with other CIBER areas, the following projects have been initiated in the 2022 call with CIBERESP:

- ALEVINT Platform (ALimentación, EValuación, INvestigación y Tanslación), (Antonio Cobo)
- M&M, mHealth methods in mental health research: designing an objective tool to assess mental health in epidemiologic and clinical studies (Jordi Aguiló)

Within the framework of the Early Stage 2022 call, which aims to promote collaborations in which contracted CIBER-BBN PhDs participate as coordinators (PIs o Co-PIs), the following projects have been initiated:

- ANÍMATE_2, A scalable and configurable mHealth platform to improve people's adherence to treatment with data-driven personalized motivational strategies (Antonio Cobo y Eugenia Mato)
- TinyHeart, ECG-based biomarkers of pediatric sleep apnea: pre and post treatment evaluation (Gonzalo Gutiérrez, Pablo Laguna)

The results of three intramural collaborations in the bioengineering program at the annual conference held in La Coruña:

- M4Health, Multimodal mHealth tools for improving monitoring of Obstructive Sleep Apnea patients (Yolanda Castillo Escario)
- Quantification of SPECT images in Parkinson's disease and degenerative parkinsonisms (Aida Niñerola)

- Sudden cardiac death prediction in Congestive Heart Failure patients from the ECG (Pablo Laguna)

During the conference, awards for Young researchers were presented for the best articles published in 2021. Two publications of the bioengineering program from the group led by Roberto Hornero were distinguished, awarding prizes to Fernando Vaquerizo-Villar and Pablo Núñez for their papers A convolutional neural network architecture to enhance oximetry ability to diagnose pediatric obstructive sleep apnea and Abnormal meta-state activation of dynamic brain networks across the Alzheimer spectrum, respectively.

The poster Graphene microtransistors for multimodal electro-physiology recording (Eduardo Fernández, R. Villa's group) was also awarded a prize at the conference for young researchers in collaboration with CIBERESP held in November 2022.

CIBER-BBN has continued its collaboration with CIBERONC, through the Living Labs Strategic Actions of this area. In the Cancer Stroma Assessment through Digital Pathology (CASA-DP) project, coordinated by Nuria Malats from CIBERONC, researcher María Jesús Ledesma from the group led by Andrés Santos participates in activities related to digital pathology analysis.

Biomaterials and advanced therapies

José L. Gómez Ribelles

COORDINATOR

The scientific activity of the program has been structured around 41 active iintramural collaborations, 34 presented in the preceding years, and seven new proposals initiated in 2022:

- Chemically crosslinked hyaluronic acid-chitosan scaffolds for potential application on tissue regeneration (Luis García Fernández)
- Nanococo, Protein-functionalized nanoparticles as serotype-independent pneumococcal vaccines (María Rosa Aguilar)
- Preclinical application of carbosilane dendrimer systems for the prevention and treatment of bacterial infections in skin wounds (María Gemma Pascual)
- Mesenchymal stem cells as a next generation drug delivery system for ocular surface diseases (Margarita Calonge)
- BRAV3, Computational biomechanics and bioengineering 3D printing to develop a personalised regenerative biological ventricular assist device to provide lasting functional support to damaged hearts (Manuel Doblaré, Esther Pueyo, Nuria Montserrat)
- CARDIOPRINT, Advanced multifunction 3D biofabrication for the generation of computationally modelled human-scale therapeutic cardiac tissues (Manuel Doblaré, Esther Pueyo, Nuria Montserrat)
- In vitro cell culture platforms based on injectable hydrogels with affinity to growth factors for hepatotoxicity studies (Mercedes Santos)

The clinical areas addressed by the new proposals were infectious diseases (2), cardiovascular diseases (2), hepatic diseases (1), ophthalmic diseases (1) and musculoskeletal diseases (1).

Within the framework of the Early Stage 2022 call, which aims to promote collaborations in which contracted CIBER-BBN PhDs participate as coordinators (PIs o Co-PIs), the following projects have been initiated:

- ALS-REPAIR, Boron-loaded alginate hydrogels for muscle recovery of amyotrophic lateral sclerosis –ALS– (Patricia Rico)
- Microskin, New skin on chip model: integration of microbiota in microfluidic skin model and study of its effect (Jesús Ciriza)
- NANOCu4BONE, Design of multifunctional copper-containing nanoparticles for the treatment of bone infections (Carla Jiménez)
- TAMS, Typing amyloidosis by mass spectrometry (Tamara Hermida)

The results of three intramural collaborations in the biomaterials program were presented at the annual conference held in La Coruña:

- Functionalization of polymer coatings using antimicrobial agents for prevention of mesh infection following hernia surgery (Bárbara Pérez)
- 3D culture medium for multiple myeloma cells (José Luis Gómez Ribelles)

- Mechanobiology of colorectal cancer tumor organoids (Xavier Trepat)

The prize for the best young researcher publication in the biomaterials program awarded during the annual conference went to Javier Plou, a researcher in the group led by Luis Liz-Marzán, for his work Preventing Memory Effects in Surface-Enhanced Raman Scattering Substrates by Polymer Coating and Laser-Activated Deprotection.

As regards the development of innovative drugs, such as advanced therapies, CIBER-BBN has continued its participation as a stakeholder of the AEMPS European STARS-CSA project.

Specifically, CIBER-BNN attended the STARS Global Conference 'Excellence in Regulatory Science', an event co-organized by the European Medicines Agency (EMA) held in-person in Brussels in May 2022.

Nanomedicine

M. Pilar Marco Colás

COORDINATOR

In 2022, eight new proposals for intramural collaborations were submitted, adding to the 63 already in progress, bringing the total number of active collaborations in 2022 to 71.

- MEMPHYS, Membrane biophysics in lysosomal storage disorders for improved therapies (Pau Gorostiza)
- Development of monoclonal antibodies against C99 fragment of APP protein and study of its therapeutic properties for the Alzheimer's disease treatment (María Pilar Marco, Núria Pascual)
- Development of systems based on gated materials for assessing the risk to suffer cardiotoxicity associated to anthracycline treatment (Ramón Martínez-Máñez)
- Biomedical nanomotors for the treatment of fungal infections (Ramón Martínez-Máñez)
- Development of new senolytic strategies for the detection and treatment of metabolic associated fatty liver disease (Ramón Martínez-Máñez)
- Development of a non-viral genome-editing platform based on CRISPR/Cas9 and autoassembled lipid nanoparticles to correct genetic mutations in rare diseases (Gustavo Puras)
- Development and optimization of anti-inflammatory nanotherapies in inherited retinal dystrophies (Gustavo Puras)
- Nano4Infection, Design of nanoantibiotics against bone infection (Isabel Izquierdo)

The clinical areas addressed by these new proposals were rare diseases (2), infectious diseases (1), cardiovascular diseases (1), neurodegenerative diseases (1), hepatic diseases (1), ophthalmic diseases (1) and bone diseases (1).

Throughout 2022, eight projects of the Early Stage 2022 call have remained active, coordinated by contracted PhDs:

- DIVITRI, Diagnosis of virus by triplex formation (Anna Aviñó)
- ADIPONP, Optimization of a new siRNA delivery system for in vivo specific adipocyte gene knockdown in long term experiments (Marina Giannotti)
- miNANO, microRNA nanosensors for early diagnosis of breast cancer (Antoni Llopis)
- Phage-CSC, Phage display identification of peptide ligands selective for breast cancer stem cells (Daniel Pulido)
- RESTORE-COL6, Smarty nanovesicle platform to restore functional collagen VI in congenital muscular dystrophy (Mariana Köber)
- DUALNANOBRAIN_II, Dual-targeting shuttle nanocarriers for alzheimer's therapy (Santiago Grijalvo)
- BBBonchip-4AD, Microphysiological model of the blood-brain barrier (BBB)–hippocampus for the in vitro evaluation of the permeability and efficacy of poly(lactic-co-glycolic acid) (PLGA)-based nanocarriers against Alzheimer disease (Anna Lagunas y Mónica Mir)
- I-QS, Improved quorum sensing immunoassays for S. aureus detection (Pablo Salvador)

As for collaborative projects with other areas, the following seed projects have been financed and developed:

CIBEREHD-BBN 2021:

- PyLOC, Advanced point-of-care nanobiosensor for the specific identification of H. pylori infections (M. Carmen Estevez)
- OTHELLO, Liver organoids: a tool to optimize the transfer of therapeutic nanoparticles in hepatocellular carcinoma therapy (Jesús Santamaría)

CIBEREHD-BBN 2022:

- LIVERSEN, Development of senolytic strategies for the treatment of metabolic associated fatty liver disease (Ramón Martínez-Máñez)

- PhotoENS, Modulation of the enteric nervous system by photoswitchable drugs (Pau Gorostiza)

Four intramural collaborations in the nanomedicine program presented their results at the annual conference held in La Coruña:

- QS-profile, Immunochemical diagnostic strategies based on the quorum sensing system (Pilar Marco)
- ORDECA2, Radical dendrimers to improve the Magnetic Resonance Imaging (José Vidal)
- NANOLINK, Site-directed conjugation of multivalent protein nanomaterials for precision medicine of cancer (Ugutz Unzueta)
- Tailored nanopatterning scaffolds for musculoskeletal tissue regeneration (Josep Samitier)

LThe publications distinguished in the nanomedicine program for the best articles by young authors were Label-Free Plasmonic Biosensor for Rapid, Quantitative, and Highly Sensitive COVID-19 Serology: Implementation and Clinical Validation (Olalla Calvo) and Targeted-lung delivery of dexamethasone using gated mesoporous silica nanoparticles. A new therapeutic approach for acute lung injury treatment (Alba Garcia-Fernández).

The presentation of the paper Customized DNA origami for delivery of therapeutic cargoes by Natalia Navarro (R. Eritja's group) received the Best Oral Presentation Award at the Young Researchers Conference in collaboration with CIBERESP. The poster by Isabel Caballos (Martínez-Máñez group) entitled Nanoporous anodic alumina gated material as a diagnostic tool for the rapid and accurate detection of SARS-CoV-2 spike protein was also awarded.

In collaboration with CIBERONC within its Living Labs Strategic Actions, Bárbara Blanco and Judith Guasch have continued their involvement in the project Patient Derived Organoids 2.0: Recapitulating stromal and immune microenvironment in annotated organoid platforms for advancing towards personalized cancer treatment, coordinated by Patricia Pérez Galán (CIBERONC).

Training

Rosa Villa Sanz

COORDINATOR

Throughout 2022 we have continued with the mobility actions that finance researcher stays in other research groups, both from the CIBER consortium as well as external.

Mobility between research groups is considered by CIBER-BBN as an essential element to enhance the training of group members in priority lines of research based on the needs of development and implementation of new techniques in the CIBER.

The aim of this initiative is to promote short-term stays in other research groups to facilitate the transfer of experience and technology, and to enhance collaboration between the different CIBER groups. Stays in external groups (national or international) are also considered, as long as the stay is framed within the priority and strategic lines of work of the CIBER-BBN thematic areas.

Mobility Actions in 2022

Also within the framework of the Training program the I Young Researchers Meeting CIBER-ESP-BBN was organized in collaboration with CIBERESP, which took place on November 21 and 22 at the CosmoCaixa Science Museum in Barcelona, in an exclusively in-person mode, with an attendance of over 80 young researchers from both areas.

The program consisted in nine sessions covering a wide range of issues such as chronic diseases, genetics and multiomics, oncology and other topics. In addition, the program culminated with two round tables. The first was Artificial intelligence in precision medicine: believing in data with the participation of Karim Lekadir, María Aragón and Miguel Luengo. The second, on the subject of mental health, Mental health before, during and after PhD: How can we survive? included the participation of Amaia Ayala-García, Ramón Nogueras and Elvira Reche.

The event was organized for and by young researchers. CIBER-BBN collaborated with the following research staff for the scientific and logistical organization of the event: José Tapia, Alba Martín, Inmaculada García, Miguel Ángel Lerma, Alejandra Estepa and Javier Plou.

Platforms

Nanbiosis ICTS

In 2022, the Proteomics Unit 30, belonging to the CIBER node and located at the institute for Biomedical Research of A Coruña, was incorporated into NANBIOSIS.

In 2022, The Ministry of Science and Innovation concluded the four-yearly evaluation process of the ICTS and NANBIOSIS was included in the new configuration of the national ICTS map. Throughout 2022, a revision process of the open and competitive access system to NANBIOSIS has been designed to prioritize access requests based on criteria of scientific quality and singularity in two annual calls. This revision has been necessary to comply with the new guidelines for all ICTS.

As for dissemination and synergy-seeking activities carried out during this period, we highlight the Researchers Forum together with the CSIC Connection-Nanomedicine Network held on June 30 and July 1 in Barcelona which focused on nanomedicine. The event was of a hybrid nature: face-to-face and online, with a total of 130 registered participants. The event included 20 presentations that generated a lot of interest and participation from the audience. A subsequent survey showed that the meeting proved to be highly positive in terms of attendees' satisfaction, its usefulness for learning about new lines of work in other groups and in building synergies.

The equipment upgrade actions financed through the Next Generation EU call of 2021 with more than 1,8 M€ have been implemented throughout the year 2022.

In terms of scientific activities and results, worth highlighting is a new method for detecting RNA viruses based on the technology of using triplex structure-forming probes, an innovative methodology that opens up new options for detecting viruses such as SARS-CoV-2, influenza A virus (H1N1) or respiratory syncytial virus (RSV). NANBIOSIS units U2, U3, U29 y U1 have played an important role in these results.

Another example of results obtained from the collaboration between several units (U2 and U3 in this case) has been the development of an ELISA based on microplates that shows great analytical potential for diagnosing and stratifying Staphylococcus aureus infections.

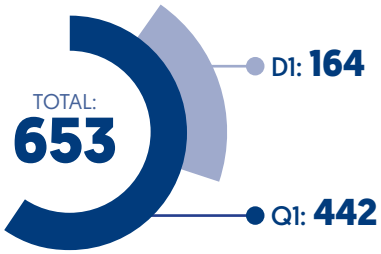
Regarding the European SAFE-N-MEDTECH project, in which NANBIOSIS holds a very relevant participation, the results of the Project have resulted in the creation of a non-profit organization, called OITB-Pathway, to make the experience of the project and its members available to the scientific community offering a comprehensive service throughout the life cycle of a product consisting of: early advisory services, prototype production, regulatory advice and health technology assessment.

NANBIOSIS participated in the ICTS Annual Conference held in Seville in September, where it presented its strategy and dissemination activity.

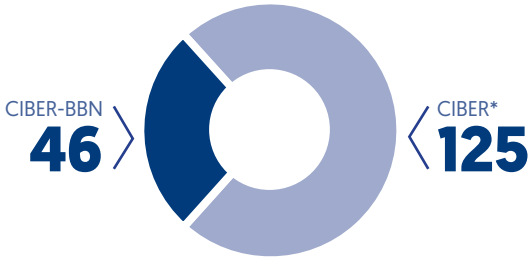
Scientific production

Publications

No. of publications in 2022

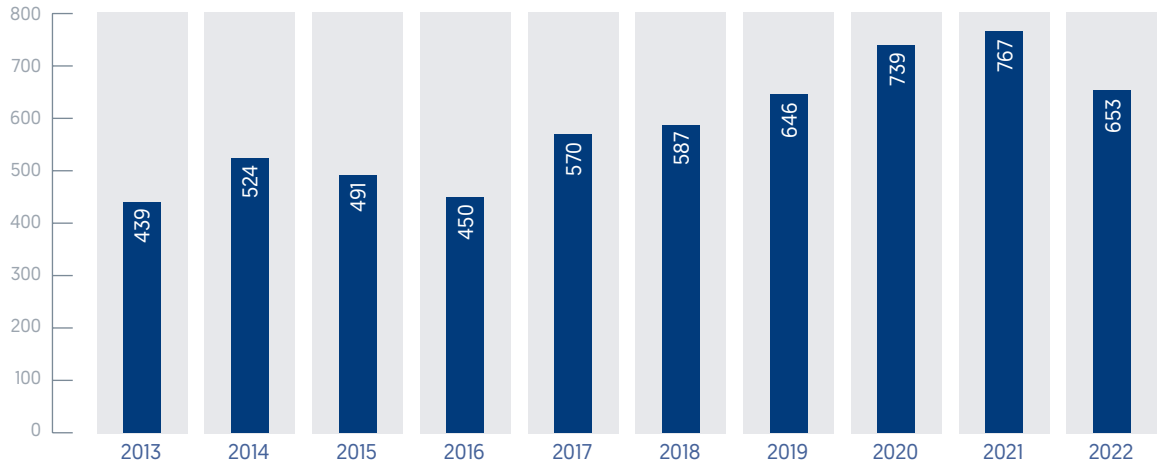


Collaborations



*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
87,244	Mila-Aloma M., Ashton N.J., Shekari M., Salvado G., Ortiz-Romero P., Montoliu-Gaya L. et al. Plasma p-tau231 and p-tau217 as state markers of amyloid-β pathology in preclinical Alzheimer's disease. Nature Medicine. 2022;28(9):1797-1801.
72,087	Sharma A., Kumar A., De La Torre B.G., Albericio F.. Liquid-Phase Peptide Synthesis (LPPS): A Third Wave for the Preparation of Peptides. Chemical Reviews. 2022;122(16):13516-13546.
72,087	Monta-Gonzalez G., Sancenon F., Martínez-Manez R., Marti-Centelles V.. Purely Covalent Molecular Cages and Containers for Guest Encapsulation. Chemical Reviews. 2022;122(16):13636-13708.
69,504	A saturated map of common genetic variants associated with human height. Nature. 2022.
69,504	Canellas-Socias A., Cortina C., Hernando-Momblona X., Palomo-Ponce S., Mulholland E.J., Turon G. et al. Metastatic recurrence in colorectal cancer arises from residual EMP1+ cells. Nature. 2022;611(7936):603-613.
66,85	Batlle D., Monteil V., Garreta E., Hassler L., Wysocki J., Chandar V. et al. Evidence in favor of the essentiality of human cell membrane-bound ACE2 and against soluble ACE2 for SARS-CoV-2 infectivity. Cell. 2022;185(11):1837-1839.
63,832	Orive G., Lertxundi U., Brodin T., Manning P.. Greening the pharmacy. Science. 2022;377(6603):259-260.
60,615	Quintanilla M., Henriksen-Lacey M., Renero-Lecuna C., Liz-Marzan L.M.. Challenges for optical nanothermometry in biological environments. Chemical Society Reviews. 2022;51(11):4223-4242.
60,615	Vallet-Regi M., Schuth F., Lozano D., Colilla M., Manzano M.. Engineering mesoporous silica nanoparticles for drug delivery: where are we after two decades?. Chemical Society Reviews. 2022;51(13):5365-5451.
60,615	Garcia-Peiro J.I., Bonet-Aleta J., Santamaria J., Hueso J.L.. Platinum nanoplatforms: classic catalysts claiming a prominent role in cancer therapy. Chemical Society Reviews. 2022.

CIBER-BBN Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Abasolo Olaortua, Ibane	8	7	2	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Aguilar de Armas, Mª Rosa	11	10	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Albericio Palomera, Fernando	34	20	2	Universidad de Barcelona	Barcelona
Arcos Navarrete, Daniel	20	18	2	Universidad Complutense de Madrid	Madrid
Arús Caralto, Carles	9	6	1	Universidad Autónoma de Barcelona	Barcelona
Becerra Ratia, José	10	5	-	Universidad de Málaga	Málaga
Calonge Cano, Margarita	16	5	2	Universidad de Valladolid	Valladolid
Corcoy Pla, Rosa	15	6	2	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Engel López, Elisabeth	4	3	2	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Eritja Casadellà, Ramon	4	2	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Fernández Jover, Eduardo	6	4	1	Universidad Miguel Hernández	Alicante
Franco Puntes, Victor	1	1	-	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Gallego Ferrer, Gloria	19	13	3	Universidad Politécnica de Valencia	Valencia
Gómez Ramírez, Rafael	16	12	2	Universidad de Alcalá	Madrid
González Martín, Mª Luisa	9	5	2	Universidad de Extremadura	Badajoz
Gorostiza Langa, Pau	13	12	8	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Hernando Pérez, Mª Elena	31	11	4	Universidad Politécnica de Madrid	Madrid
Hornero Sánchez, Roberto	18	10	5	Universidad de Valladolid	Valladolid
Jané Campos, Raimon	13	8	5	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Laguna Lasaosa, Pablo	28	18	6	Universidad de Zaragoza	Zaragoza
Lechuga Gómez, Laura María	7	6	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Liz Marzán, Luis Manuel	29	25	14	CIC biomaGUNE	Guipúzcoa
López Higuera, José Miguel	14	6	-	Universidad de Cantabria	Cantabria
Mangues Bafalluy, Ramon	26	20	9	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Marco Colás, María Pilar	15	15	5	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Martínez Barca, Miguel Ángel	17	9	1	Universidad de Zaragoza	Zaragoza
Martínez De La Fuente, Jesús	21	17	7	Agencia Estatal Consejo Superior de Investigaciones Científicas	Zaragoza
Martínez Mañez, Ramón	26	20	7	Universidad Politécnica de Valencia	Valencia
Pascual González, Mª Gemma	8	3	2	Universidad de Alcalá	Madrid
Pedraz Muñoz, José Luis	34	27	8	Universidad del País Vasco	Álava
Raya Chamorro, Ángel	8	8	7	Fundación IDIBELL	Barcelona
Rodríguez Abreu, Carlos	9	3	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Rodríguez Cabello, José Carlos	17	15	7	Universidad de Valladolid	Valladolid
Ruiz Romero, Cristina	7	5	1	Servicio Gallego de Salud	Coruña, A

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Samitier Martí, Josep	25	20	9	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Santamaría Ramiro, Jesús	36	30	9	Universidad de Zaragoza	Zaragoza
Santos Lleó, Andrés	18	11	4	Universidad Politécnica de Madrid	Madrid
Setoain Peregó, Xavier	44	23	14	Universidad de Barcelona	Barcelona
Trepat Guixer, Xavier	9	7	6	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Ventosa Rull, Leonor	13	11	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Vilaboa Díaz, Núria	2	1	-	Servicio Madrileño de Salud	Madrid
Villa Sanz, Rosa	12	8	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Villaverde Corrales, Antonio	25	24	11	Universidad Autónoma de Barcelona	Barcelona

Clinical Guidelines 2022

- Matriz Urgencias: APENDICITIS AGUDA COMPLICADA K81. Francisca García-Moreno Nisa.

- Toward Universal Eye Health Coverage—Key Outcomes of the World Health Organization Package of Eye Care Interventions. Margarita Calonge.

- Gastrointestinal stromal tumors: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. Antonio López Pousa.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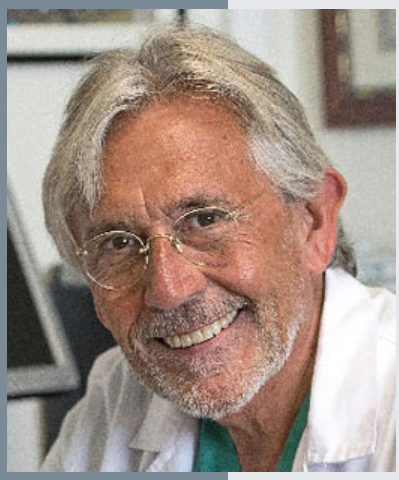
Cardiovascular
Diseases

Welcome from the scientific director



Francisco Fernández-Avilés

Dear colleagues of the CIBER's thematic area of Cardiovascular Diseases [CIBERCV], personally and on behalf of the Steering Committee I would like to thank you all for the enormous dedication you have shown in 2022 and for your ongoing commitment. The sixth year of our thematic area has without a doubt been very satisfactory, both in terms of the achievements and the enormous involvement of all the groups, which have surmounted no small number of difficulties.

In 2022, our area has published more than 700 articles in high-ranking scientific journals. In the field of communication, CIBERCV has had over 900 press appearances both online and in print media. Our CIBERCV is currently involved in several European projects, as well as in two multicenter projects of the Call for Independent Clinical Research Projects of the ISCIII. In addition, in 2022, we have obtained funding through the Call for Personalized and Precision Medicine for the development of the Spanish Project, a multicenter study to evaluate the non-inferiority of a personalized precision strategy for the prevention of sudden death in patients with non-ischemic dilated cardiomyopathy, in which 21 research groups from our area will participate.

We have successfully undergone the fourth evaluation by the External Scientific Advisory Board, with a favorable report on our performance and very useful recommendations for improvement that include the need to: [1] strengthen internationalization and excellence, [2] identify, attract and retain young talent, [3] focus on key areas, promoting the main technological capabilities, [4] promote and reward multidisciplinarity and [5] take advantage of and strengthen the great capabilities of the national health system, particularly with regard to data and registry management.

We have been grappling with a widespread shortage of resources against the enormous bureaucratic difficulties of the National State Administration. Nevertheless, and more optimistically, we are aware that science managers are also committed to this battle and we believe that the Consortium that hosts us is an unparalleled venue of excellence that ensures a stable budget, even if it is chronically poor and severely affected by the current political instability. All this is allowing us to place Spanish cooperative cardiovascular research at the highest national and international level of competitiveness. Thanks to all of you.

To conclude, during 2022, the CIBERCV has continued to face its challenges with motivation and strong commitment to the CIBER consortium, which has resulted in cooperative scientific activity of the highest level. This is all thanks to the efforts of the people involved and the framework of stability offered by the CIBER. We consider this to be essential to promote cooperative research of excellence in Spain, with the aim of contributing to reducing the impact of cardiovascular diseases in our environment and generating prosperity through leading research, innovation and training in this discipline within the national and international framework.

Programs

Myocardial Damage and its consequences

Francisco Fernández-Avilés

COORDINATOR

Juan Delgado Jiménez

COORDINATOR

Program 1 has generated important advances aimed at understanding and treating myocardial damage and its associated consequences, both of genetic origin and due to acquired disorders of the heart muscle.

This line of research dedicated to myocardial healing and remodeling has undertaken a major effort designing a series of collaborative translational research projects from a number of international calls. The ARTIST multicenter clinical trial with 3 clinical groups (PI: Ángel Arenal Maíz) is testing the clinical efficacy of a novel strategy to target ablation of atrial fibrillation. Also noteworthy is the MEDIMACS clinical trial, and international project financed by the EC, a collaborative project testing the impact of the Mediterranean Diet on the remodeling of atherosclerotic plaques after acute coronary syndrome. A further highlight is the CIBER bB-Echo, a large muticenter clinical trial within the CIBER Consortium (involving CIBER-CV, CIBER-ONC, CIBERHD, and CIBER-DEM thematic areas) that will test the potential of acute beta-blockers to reduce biological variability in the assessment of LV systolic function.

Arterial disease, myocardial ischemia and structural damage

Borja Ibáñez Cabeza

COORDINATOR

Alberto San Román Calvar

COORDINATOR

Within Program 2, important work has been carried out on the study and treatment of cardiovascular disorders that can cause premature death and disability, linked to myocardial ischemia and structural pathologies of the heart and arteries.

The highlights of this program in 2022 are related to acute myocardial damage, mainly secondary to myocardial ischemia/reperfusion (acute myocardial infarction), but also from other types of injury, such as myocarditis and cardiotoxicity related to cancer treatment. Within this research line, the underlying process responsible for acute myocardial infarction (i.e., atherothrombosis) has been very active for this line, as reflected in high impact papers resulting from collaborative efforts, as well as the initiation of grants funded by the European Commission coordinated by members attached to this research line with other participating groups as partners.

Cardiovascular Epidemiology and risk factors

Jaume Marrugat de la Iglesia

COORDINATOR

Program 3 has continued to promote research into the mechanism linking cardiovascular risk factors with the serious diseases they entail, with the ultimate aim of preventing and reducing the high impact of cardiovascular diseases on society. Of particular note this year is the project: Discrimination of COVID-19 severity with a genetic risk score. A set of genetic variants of coronary heart disease, thrombosis, inflammation and virus, infectivity, and their ability individually and in a polygenic score to discriminate patients according to the severity of COVID-19, a project involving three groups of CIBERCV, one of CIBERESP and REDIAP coordinated by the REGICOR group of Program 3a, who have conducted a study with 1800 cases of COVID-19 with hospitalization and 700 controls of patients with COVID-19 treated at home. Ten variants were significantly associated and a score was designed with the minimum necessary number of variants. Each increase of one risk allele in the score represented a 6% increase in the probability of severe COVID-19, and a 3% improvement in discriminatory ability, versus a model with clinical variables. A significant interaction with age was identified, indicating that prediction is especially important in younger patients. A patent has been filed and the article has been submitted for publication.

Molecular and imaging biomarkers, and precision cardiovascular medicine

Javier Díez Martínez

COORDINATOR

Program 4 has generated important advances in the field of biomarkers in relation to cardiovascular diseases, most notably the study "Clonal hematopoiesis and risk of progression of heart failure with reduced left ejection fraction", projects developed by the CiberCV groups of the Hospital Virgen de la Arrixaca in Murcia, Hospital German Trias y Pujol in Barcelona, the CNIC in Madrid and the CIMA in Pamplona. This study opens up a new way of understanding the association of age with heart failure through clonal hematopoiesis. In particular, their work highlights the role of somatic mutations in DNMT3A or TET2 in the progression of HF with reduced ejection fraction (HFrEF) of ischemia and non-ischemic etiology, in terms of HF-related mortality and hospitalization for acute decompensated HF disease. This work incorporates specific somatic mutations as new biomarkers potentially useful to increase prognostic accuracy in HFrEF and to design personalized preventive and therapeutic strategies.

Training

José A. Barrabés Riu

COORDINATOR

The main objective of the CIBERCV Training and Mobility Program is to train young people to become cardiovascular researchers of the future in order to improve the cardiovascular health of society. In addition, this program promotes the organization of specific workshops and courses in order to share the valuable advances and knowledge acquired by CIBERCV researchers.

In 2022, 5 mobility grants were awarded to CIBERCV researchers for stays in Spanish and foreign research centers.

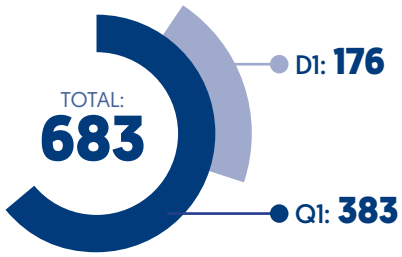
Of particular note is the organization of courses on different topics in the field of cardiovascular research such as Atrial Fibrillation, Cardiac Amyloidosis, Heart Failure, Atherosclerosis, Arrhythmias, Cardiac Transplantation, Cardiological applications of 3D printing, and other advances in basic science and clinical excellence.

Within the CIBERCV this program continues to be the main training initiative and in 2022 it has contributed to the strengthening of translational quality research, promoting collaboration between the groups in the CV area and other thematic areas of the CIBER.

Scientific production

Publications

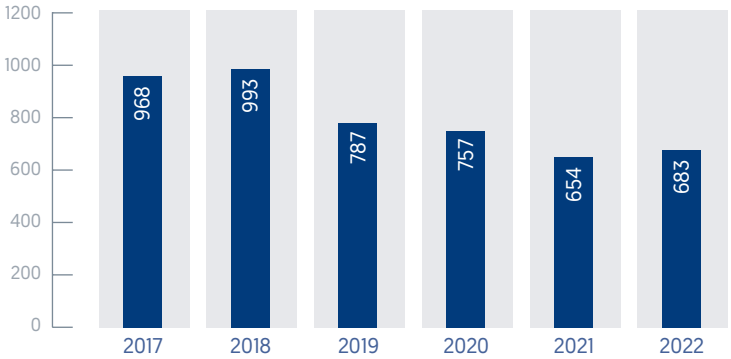
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

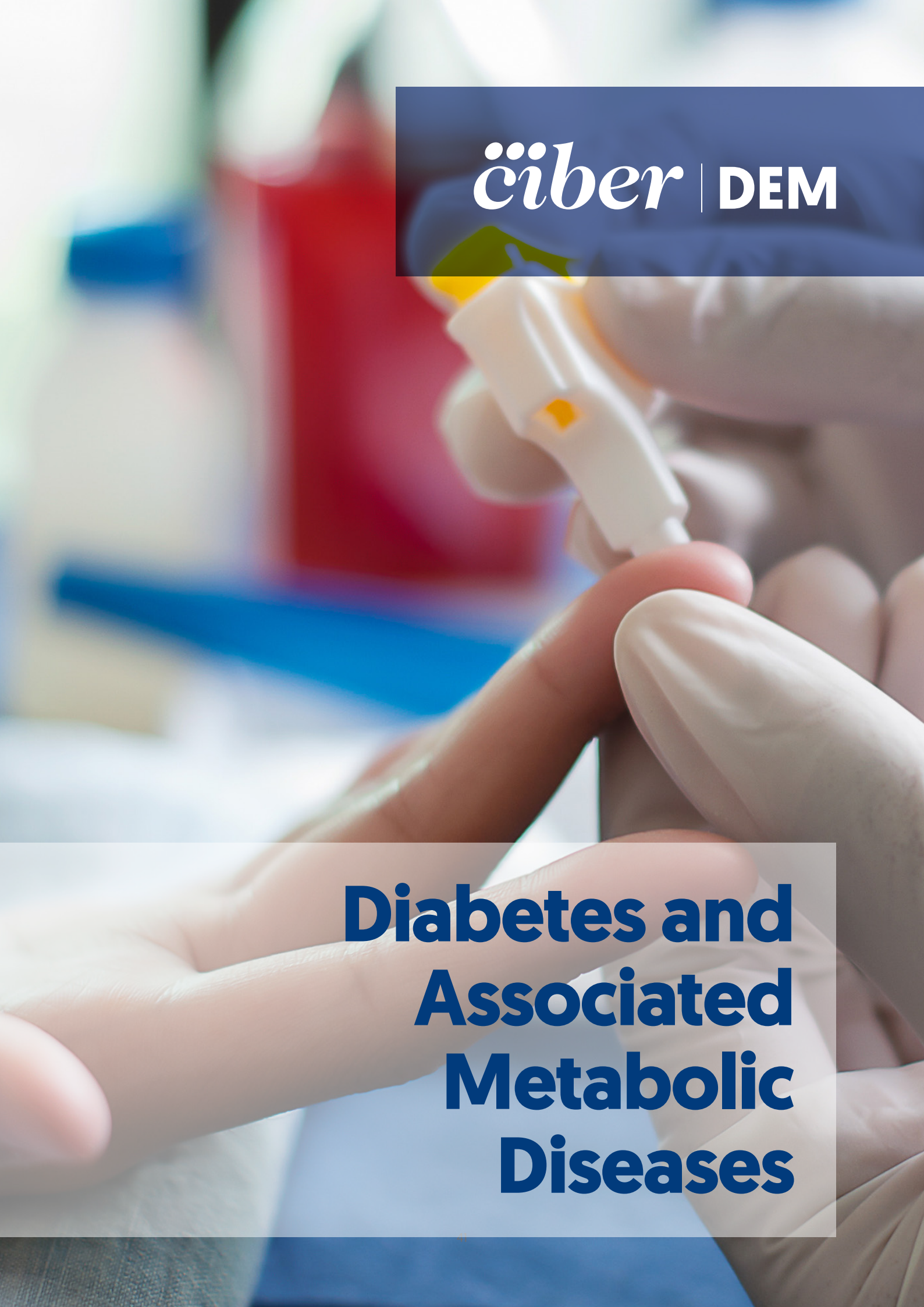
IF	PUBLICATION
69,5040	Senescence atlas reveals an aged-like inflamed niche that blunts muscle regeneration
28,2130	Caveolin-1 dolines form a distinct and rapid caveolae-independent mechanoadaptation system
27,2060	Phase 2 Study of Aficamten in Patients With Obstructive Hypertrophic Cardiomyopathy
27,2060	Infective Endocarditis After Transcatheter Aortic Valve Replacement: JACC State-of-the-Art Review
23,2180	RyR2 Serine-2030 PKA Site Governs Ca2+Release Termination and Ca2+Alternans
18,9980	A prespecified exploratory analysis from FIDELITY examined finerenone use and kidney outcomes in patients with chronic kidney disease and type 2 diabetes
18,1740	Biomarkers of inflammation in heart failure: from risk prediction to possible treatment targets
18,1740	Mavacamten in obstructive hypertrophic cardiomyopathy – Are beta-blockers blocking part of its shine?
13,9340	Revisiting skeletal myopathy and exercise training in heart failure: Emerging role of myokines
13,5690	Donor heart selection: Evidence-based guidelines for providers

CIBERCV Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Andres Garcia, Vicente	8	4	0	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Badimon Maestro, Lina	25	15	8	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Barrabes Riu, Jose Antonio	47	32	13	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Bayes Genis, Antonio	69	38	25	Fundación Instituto de Investigacion Germans Trias i Pujol	Barcelona
Blanco Colio, Luis Miguel	8	1	1	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Bosca Gomar, Lisardo	7	5	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Brugada Terradellas, Ramon	19	8	7	Fundación Instituto de Investigacion Biomédica de Girona	Girona
Chorro Gasco, Francisco Javier	17	8	2	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia
Civeira Murillo, Fernando	18	10	3	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Crespo Leiro, Maria Generosa	40	26	10	Servicio Gallego de Salud	Coruña, A
de la Pompa Mínguez, José Luis	7	6	4	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	Madrid
Delgado Jiménez, Juan Francisco	56	34	21	Servicio Madrileño de Salud	Madrid
Delpon Mosquera, Maria Eva	9	1	2	Universidad Complutense de Madrid	Madrid
Díez Martínez, Domingo Francisco Javier	13	10	7	Fundación para la Investigación Médica Aplicada	Navarra
Elosua Llanos, Roberto	9	1	3	Consorci Mar Parc Salut de Barcelona	Barcelona
Fernández-Aviles Díaz, Francisco	41	21	11	Servicio Madrileño de Salud	Madrid
García Pavia, Pablo	33	1	12	Servicio Madrileño de Salud	Madrid
González Juanatey, Jose Ramon	69	34	8	Servicio Gallego de Salud	Coruña, A
Guerra Ramos, Jose Maria	31	18	6	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Ibáñez Cabeza, Borja	38	27	19	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Jiménez Navarro, Manuel Francisco	42	26	9	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	Malaga
Marin Ortuño, Francisco	56	31	6	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	Murcia
Marrugat de La Iglesia, Jaume	7	4	0	Consorci Mar Parc Salut de Barcelona	Barcelona
Martínez Dolz, Luis	49	16	6	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	Valencia
Martínez González, José	10	1	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Mayor Menéndez, Federico	3	0	0	Universidad Autónoma de Madrid	Madrid
Mont Girbau, Josep Lluis	27	10	7	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Pérez-Villacastín Domínguez, Julián	4	1	0	Servicio Madrileño de Salud	Madrid
Redondo Moya, Juan Miguel	13	8	6	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Salaices Sánchez, Mercedes	3	3	0	Universidad Autónoma de Madrid	Madrid
San Roman Calvar, José Alberto	44	26	7	Hospital Clínico Universitario de Valladolid	Valladolid

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Sánchez Fernández, Pedro Luis	30	20	5	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	Salamanca
Sánchez Madrid, Francisco	36	20	6	Universidad Autónoma de Madrid	Madrid
Sánchez Margallo, Francisco Miguel	3	1	1	Fundación Centro de Cirugía de Mínima Invasión Jesús Usón	Caceres
Sanchís Fores, Juan	54	24	11	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia
Vázquez, Cobos Jesús Maria	13	12	8	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Zamorano Gómez, José Luis	15	7	3	Servicio Madrileño de Salud	Madrid



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Diabetes and Associated Metabolic Diseases

Welcome from the scientific director

Eduard Montanya Mías

CIBERDEM has maintained throughout 2022 an outstanding and high-quality scientific production, with 24% of publications in the first decile and 61% in the first quartile. The publications show the high collaborative activity both within CIBER and internationally, with 52% and 36% of collaborative publications, respectively. Our web page contains a detailed list of the most relevant publications of each group and the main achievements of each research program in 2022 are detailed in the Annual Report.

In the area of collaborative activity, worth mentioning is the participation in CIBER collaborative projects, such as the ARISTOS project, the IMPACT and Independent Clinical Research projects, as well as the participation of CIBERDEM researchers in European collaborative projects (RECOGNISED, CARDIATEAM).

As part of the collaboration with other areas, at an institutional level we have participated in the CIBER-BBN annual meeting and in the Inter-area round table of the XVIII National Congress of the Spanish Society for the Study of Obesity (SEEDO) together with CIBEROBN and CIBEREHD. In collaboration with CIBERFES and CIBEREHD, the First Congress of the Spanish Metabolomics Society was organized. CIBERDEM's internal collaborative activities include the call for intramural projects 2022, especially aimed at enhancing the competitiveness of young CIBERDEM researchers, and the mobility actions that have allowed the organization of stays in CIBER and international groups. This year, both the Meeting of Young Researchers and the Annual Meeting were held in a face-to-face format, allowing researchers to meet up once again whilst strengthening the cohesion of the area.

In terms of translation and transfer, CIBERDEM members have actively participated in the preparation of clinical guidelines and consensus documents in multiple areas relevant to diabetes (primary care, children and adolescents, the elderly or frail, cardiovascular risk) and a significant boost has been given to the development of a CIBER patent on computational tools in metabolomics, which has been awarded a Special Mention in the Best Patent Category of the Spanish Patent and Trademark Office.

As regards technological platforms, it is worth mentioning that the coordination of the Metabolomics platform has led the creation of the Spanish Metabolomics Society (SESMet).

For more detailed information on CIBERDEM's activities and achievements in 2022, please check out the Scientific Report and also visit our website (www.ciberdem.org), as well as follow us on Twitter (@ciberdem).

Programs

Epidemiology, genetics and epigenetics of diabetes mellitus. Chronic complications and comorbilities

Ángela Martínez Valverde

COORDINATOR

1. Epidemiology of diabetes mellitus, its chronic complications and comorbilities

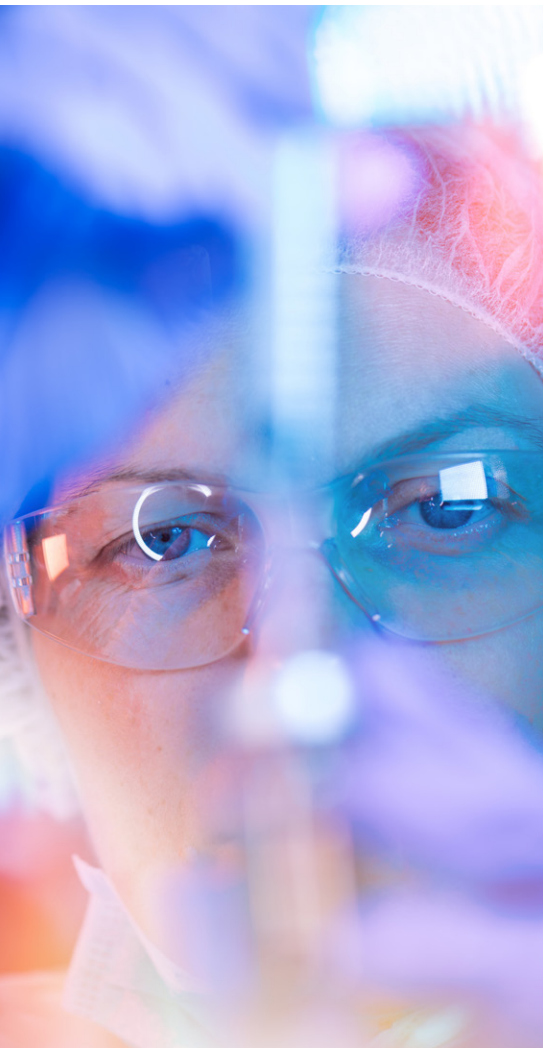
Within the study di@bet.es a relationship has been found between the fatty acid composition of red blood cells and alterations in glucose metabolism (Chiva-Blanch et al., Nutrients 2022,14:1368) and the role of VEGF-b in the incidence of metabolic syndrome in the general population has been evidenced (Lago-Sampedro et al., Int J Obes 2022), as well as other risk factors for metabolic diseases (Valdes et al., Environ Health. 2022).

CIBERDEM has participated in the elaboration of the ISPAD International Clinical Guidelines on Monogenic Diabetes (Greeley et al., Pediatr Diabetes 2022).

2. Genetics, epigenetics and environmental factors in the development of diabetes and its complications

The rs1801260 variant has been reported to have a protective effect against morbid obesity, whereas the TT genotype of the rs3749474 variant has been found to be associated with this pathology. Both variants showed a significant association with long-term weight loss and weight regain after bariatric surgery, irrespective of the patient profile before surgery (Torrego-Ellacuria et al., Nutrients 2022).

The analysis of more than 110 SNPs has identified genetic variants associated with the regulation of glucose homeostasis for the prediction of gestational diabetes, as well as its modulation through a nutritional intervention based on the Mediterranean diet. These data are the basis for designing a genetic risk questionnaire (Ramos-Levi et al. Front. Endocrinol. 2022).



3. Molecular mechanisms associated with the appearance and progression of chronic complications of diabetes: therapeutic strategies

People with diabetes and macrovascular complications admitted to hospitals for COVID-19 have been found to have an increased risk of mortality. However, these same patients are often less frequently treated with invasive mechanical ventilation and admitted to intensive care units (Llauradó et al., Cardiovasc Diabetol. 2022).

In the context of macrovascular complications of diabetes, the vasoprotective effect of a synthetic flavonoid has been described in preclinical models of DT1 and DT2 improving endothelial dysfunction, inflammation, oxidative stress and cellular senescence in the aorta and reducing the size of atheromatous plaques (Jimenez-Castilla et al., Antioxidants 2022).

An association of elevated circulating α-klotho concentration with subclinical atherosclerosis in the absence of renal failure has been demonstrated in patients with DT1 (Castel-Blanco et al., Cardiovasc Diabetol. 2022).

Triglyceride-rich glycoproteins and lipoproteins determined by 1H-NMR have been used to detect hepatic steatosis (Moreno-Vedia et al., Front Endocrinol 2022).

We have conducted the LIRALUNG clinical trial in which CIBEROBN and CIBERES have collaborated, demonstrating that liraglutide improves respiratory function in patients with DT2 (López-Cano 2022, Diabetes).

Epigenetic regulators associated with advanced stages of diabetic nephropathy have been reported (Opazo-Rios et al., Front Pharmacol 2022)..

4. Nutritional and lifestyle aspects in the development and prevention of diabetes.

Nutritional intervention based on the Mediterranean diet is associated with an overexpression of miR-222 and miR-103 that correlates with improved insulin sensitivity and proinflammatory cytokine profile during pregnancy and postpartum (Valerio et al., Nutrients 2022).

Molecular and cellular determinants of islets pancreatic function, damage and protection. Regenerative medicine and advanced therapies

Franz Martín Bermudo

COORDINATOR

1. Pancreatic islet funtion and regulation: molecular, and cellular basis and therapeutic targets

The endocrine disruptor bisphenol A alters the protection against apoptosis exerted by estrogen receptors ERα and ERβ on beta cells by activating the G protein-coupled estrogen receptor (Babiloni-Chust et al., Environ Int 2022).

The effect of different endocrine disruptors on the function and viability of animal and human pancreatic beta cells has been evaluated in various in vitro models (Al-Abdulla et al., Int J Mol Sci 2022; Dos Santos et al., Int J Mol Sci 2022).

The anti-diabetic and beta-cell survival enhancing effect of the agonist BL001 has been described to occur via activation of the LRH1/NR5A2 receptor, which takes place through the PTGS2/PGE2/PTGER1 signaling pathway (Cobo-Vuilleumier et al., iScience 2022).

The regulation of diurnal oscillations of energy expenditure, necessary for the maintenance of metabolic homeostasis, has been found to require priming of the suprachiasmatic nucleus by retinohypothalamic terminals and dopaminergic innervation of the basal nuclei (Fernández-Pérez et al., Cell Reports 2022).

Chronic treatment with the antipsychotic aripiprazole has been reported to alter glucose homeostasis and decrease insulin secretion due to increased serotonin levels in pancreatic islets (Grajales et al., Diabetologia 2022).

In animals with type 2 diabetes mellitus (DM2), ingestion of a mixture of cocoa and al- garroba, rich in flavonols, improves beta-cell function, insulin resistance and protects the heart from the onset of diabetic cardiomyopathy (García-Díez et al., Antioxidants 2022).

Treatment with EV-miRNAs induced by obesity and exercise improves insulin sensitivity and glycemia in obese mice (Castaño et al., Int J Mol Sci 2022).

The mechanisms responsible for weight loss in DM2 patients of the GLP-1 receptor agonist semaglutide have been described (Meier et al., Diabetes Obes Metab 2022)..

2. Preventive and therapeutic strategies in regenerative medicine, cell therapy and gene therapy

A new type of transcriptional regulator has been identified that acts as a rheostat of HNF1A, a key gene for monogenic diabetes and DM2 (Beucher et al., Nat Cell Biol 2022).

Mutations of a single transcriptional enhancer disrupt pancreatic differentiation processes and cause a Mendelian diabetic phenotype (Escalada et al., Dev Cell 2022).

A single administration with liver-targeted AAV-BMP7 vectors in obese mice has been described to induce browning of white adipose tissue and its thermo-gene activation. It also decreases adipose tissue hypertrophy and inflammation, steatosis and steatohepatitis, insulin resistance and obesity (Casana et al., Mol Ther Methods Clin Dev 2022).

3. Application of new technologies to the treatment of diabetes

An automated detection system for the artificial pancreas without meal announcement has been evaluated with clinical data (Sala-Faccioli et al., Comput Methods Programs Biomed 2022).

A control module has been designed module for the elimination of meal and exercise announcements in hybrid artificial pancreas systems, with no need for retuning (Sala-Mira et al., Comput Methods Programs Biomed 2022).

A simulator with realistic scenarios has been developed for evaluations of continuous subcutaneous insulin infusion therapy and multiple daily injections (Estremera et al., J Biomed Inform, 2022).

Cellular and molecular mechanisms involved in the development and progression of type 2 diabetes & identification of new therapeutic targets

Antonio Zorzano Olarte

COORDINATOR

1. Inflammation as a pathogenic process in diabetes mellitus.

Determinants of the development of inflammation in aging have been identified in skeletal muscle (Irazoki et al., Aging Cell 2022).

It has been shown that during proinflammatory activation there is a transfer of polyunsaturated fatty acids (PUFA) from lipid droplets to membranes in order to replenish PUFA levels that have been depleted in the membrane compartment (Ber- múdez et al., Biomolecules 2022).

It has also been shown that the intestinal microbiota is a relevant source of circulating succinate, and contributes to the metabolic and inflammatory dysfunction observed in obesity and type 2 diabetes. These studies have also allowed the identification and in vivo validation of specific bacteria that, when administered orally, are able to consume intestinal succinate, thus causing a reduction of circulating succinate with subsequent metabolic and inflammatory improvement (Huber-Ruano et al., Microbiome. 2022).

2. Identification of molecular mechanisms and new therapeutic targets for the development of personalized early interventions.

It has been determined that resveratrol decreases the formation of toxic aggregates of human amylin in pancreatic beta cells, altering the formation of extracellular vesicles carrying human amylin, as well as the deleterious effects produced in neuronal cells (submitted for publication).

Transcription factor ATF4 and the mTOR-CRTC2 axis have been documented to be involved in the reduction of PGC-1α coactivator levels under conditions of endoplasmic reticulum stress in skeletal muscle. Inhibition of these pathways could be a potential therapeutic target for the treatment of insulin resistance (Montori-Grau et al., Cell Commun Signal 2022).

Targeted deletion of insulin-degrading enzyme (IDE) in pancreatic α cells has been shown to lead to α-synuclein aggregation, which may contribute to impaired glucagon secretion through cytoskeleton dysfunction. In addition, IDE deficiency triggers alterations in cilia formation, which induces α cell hyperplasia (Merino et al., Diabetologia 2022).

A new molecular explanation for the understanding of the contribution of autophagy in the energy metabolism of brown adipose tissue has been identified (Sabaté-Pérez et al., Autophagy 2022), which may facilitate the design of therapeutic strategies (Sabaté-Pérez et al., Autophagy 2022).

3. Identification of biomarkers of risk for diabetes progression.

The current position on the role of metabolomics in biomarker identification has been revised (Giera et al., Cell Metab. 2022).

Serum concentrations of bone morphogenic protein-8B (BMP8B), an adipokine produced Training by brown adipose tissue (BAT), are elevated at birth and decrease in the first year of life, remaining above adult values. Changes in BMP8B reflect changes in BAT activity in early stages of development (García-Beltran et al., Front. Pediatr. 2022).

Growth and differentiation factor-15 (GDF15) reduces intake and body weight. In prepubertal girls, prolonged treatment with metformin, an exogenous GDF15 secretagogue, increases GFD15 and reduces central adiposity and insulin resistance. GDF15 could mediate these long-term effects (Diaz et al., Pediatr. Res. 2022).

One out of four women with type 1 diabetes have been reported to present with hyperandrogenic disorders including polycystic ovary syndrome (Bayona et al., Hum Reprod. Update 2022).

Training

Ángel Nadal Navajas

COORDINATOR

The main objectives of the CIBERDEM Training Program are to boost the competitiveness of its young researchers and to promote cohesion and collaboration among the research groups in the area. The main actions are detailed below.

A new call for intramural projects for young people has been carried out, which has granted funding to 3 intramural projects, with the participation of 6 CIBERDEM groups, and the three intramural projects awarded in the previous call have been completed. The impact of the granting of intramural projects on the professional development of young researchers has been assessed, with a very positive evaluation on the part of the researchers.

The Mobility Actions have financed stays in CIBER and international groups, with a total of 4 actions granted.

The XIII Annual CIBERDEM Meeting in face-to-face format was held on November 10 and 11, with the attendance of more than 130 researchers, who shared the most innovative aspects of diabetes research carried out in CIBERDEM, in addition to having served as an important element of cohesion.

The third Meeting of Young Researchers took place on November 9, with the participation of more than 80 young researchers.

CIBERDEM has organized for the fifth consecutive year the joint SED-CIBERDEM Symposium at the XXXIII National Congress of the Spanish Diabetes Society (April 28). The Symposium focused on strategies for beta cell protection, key factors in embryonic development and beta cell function, and new methods for the diagnosis and monitoring of cognitive impairment in type 2 diabetes.

CIBERDEM has developed and completed the fourth edition of the Postgraduate Expert Course of the University of Barcelona 2021-2022 “Chronic Complications of Diabetes Mellitus,” which awards 15 European ECTS credits.

Based on the institutional links established with the German Center for Diabetes Research (DZD), CIBEDEM has facilitated the participation of young researchers in the DZD Diabetes Research School in Stockholm.

Finally, it is important to note that it is impossible to detail in the Report the many training activities organized individually by CIBERDEM groups.

Communication and dissemination to society

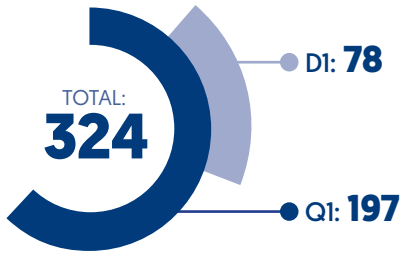
CIBERDEM maintains its commitment to bringing research results closer to society, participating in dissemination actions and collaborating with various initiatives of patient associations such as the Spanish Diabetes Federation (FEDE), DiabetesCero, the Catalan Diabetes Association and Canal Diabetes.

In terms of institutional presence in scientific societies, CIBERDEM participated in the Congress of the Spanish Diabetes Society.

Scientific production

Publications

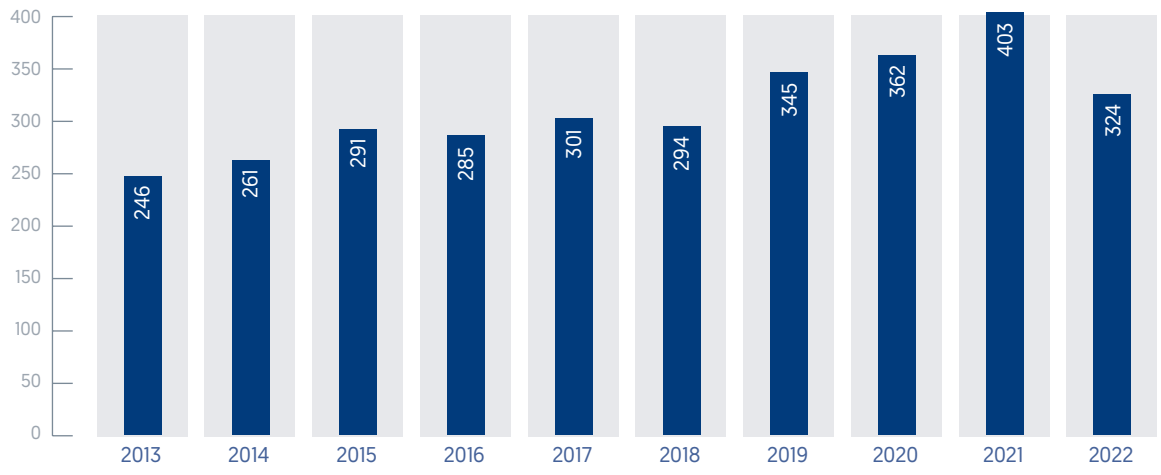
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
68,164	Balboa D., Barsby T., Lithovius V., Saarimaki-Vire J., Omar-Hmeadi M., Dyachok O. et al. Functional, metabolic and transcriptional maturation of human pancreatic islets derived from stem cells. Nature Biotechnology. 2022;40(7):1042-1055.
44,867	Magliano DJ, Chen L, Carstensen B, Gregg EW, Pavkov ME, Salim A et al. Trends in all-cause mortality among people with diagnosed diabetes in high-income settings: a multicountry analysis of aggregate data. The Lancet. Diabetes & Endocrinology. 2022;10(2):112-119.
44,867	Tomic D., Morton J.I., Chen L., Salim A., Gregg E.W., Pavkov M.E. et al. Lifetime risk, life expectancy, and years of life lost to type 2 diabetes in 23 high-income jurisdictions: a multinational, population-based study. The Lancet Diabetes & Endocrinology. 2022;10(11):795-803.
41,376	Mahajan A., Spracklen C.N., Zhang W., Ng M.C.Y., Petty L.E., Kitajima H. et al. Multi-ancestry genetic study of type 2 diabetes highlights the power of diverse populations for discovery and translation. Nature Genetics. 2022;54(5):560-572.
39,922	Dijk W., Di Filippo M., Kooijman S., Van Eenige R., Rimbert A., Caillaud A. et al. Identification of a Gain-of-Function LIPC Variant as a Novel Cause of Familial Combined Hypocholesterolemia. Circulation. 2022;146(10):724-739.
31,373	Giera M., Yanes O., Siuzdak G. Metabolite discovery: Biochemistry's scientific driver. Cell Metabolism. 2022;34(1):21-34.
28,213	Beucher A., Miguel-Escalada I., Balboa D., De Vas M.G., Maestro M.A., Garcia-Hurtado J. et al. The HASTER lncRNA promoter is a cis-acting transcriptional stabilizer of HNF1A. Nature Cell Biology. 2022;24(10):1528-1540.
18,361	Zaugg J.B., Sahlen P., Andersson R., Alberich-Jorda M., de Laat W., Deplancke B. et al. Current challenges in understanding the role of enhancers in disease. Nature Structural and Molecular Biology. 2022;29(12):1148-1158.
18,01	Atla G., Bonas-Guarch S., Cuenca-Ardura M., Beucher A., Crouch D.J.M., Garcia-Hurtado J. et al. Genetic regulation of RNA splicing in human pancreatic islets. Genome Biology. 2022;23(1):196.
17,694	Moreau F., Kirk N.S., Zhang F., Gelfanov V., List E.O., Chrudinova M. et al. Interaction of a viral insulin-like peptide with the IGF-1 receptor produces a natural antagonist. Nature Communications. 2022;13(1):6700.

CIBERDEM Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Balsinde Rodríguez, Jesús	8	4	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	Valladolid
Blanco Vaca, Francisco	40	25	13	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Bondia , Jorge	14	8	2	Universidad Politécnica de Valencia	Valencia
Bosch Tubert, Fàtima	4	3	2	Universidad Autónoma de Barcelona	Barcelona
Burks , Deborah	2	1	0	Fundación Centro de Investigación Príncipe Felipe	Valencia
Calle Pascual, Alfonso	8	6	1	Servicio Madrileño de Salud	Madrid

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Castaño González, Luis	15	10	3	Asociación Instituto de Investigación Sanitaria de Biocruces	Vizcaya
Correig Blanchart, Francesc	26	17	12	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona
Egido de los Rios, Jesús	13	9	4	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Escobar Morreale, Héctor	10	2	1	Servicio Madrileño de Salud	Madrid
Ferrer Marrades, Jorge	7	7	7	Fundación Centro de Regulación Genómica	Barcelona
Guillén Viejo, Carlos	3	1	0	Universidad Complutense de Madrid	Madrid
Ibáñez Toda, Lourdes	7	5	0	Fundación para la Investigación y Docencia Sant Joan de Deu	Barcelona
Martín Arribas, Maria Angeles	6	5	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Martín Bermudo, Francisco	9	8	2	Universidad Pablo de Olavide	Sevilla
Martínez Valverde, Ángela María	12	8	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Mauricio Puente, Diego	62	33	11	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Montanya Mias, Eduard	5	3	1	Fundación IDIBELL	Barcelona
Nadal Navajas, Ángel	9	8	4	Universidad Miguel Hernández	Alicante
Novials Sardà, Anna Maria	6	5	2	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Real Collado, José Tomas	18	9	2	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia
Ribalta Vives, Josep	18	5	0	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona
Rojo Martínez, Gemma	18	12	2	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	Malaga
Simó Canonge, Rafael	35	17	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Vallejo Fernández de la Reguera, Mario	2	2	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Vázquez Carrera, Manuel	5	4	1	Universidad de Barcelona	Barcelona
Vendrell Ortega, Joan	18	14	8	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona
Vidal Cortada, Josep	21	15	6	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Zorzano Olarte, Antonio	9	6	3	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelon

Clinical Guidelines 2022

- 2022 update to the position statement by Primary Care Diabetes Europe: a disease state approach to the pharmacological management of type 2 diabetes in primary care. Prim Care Diabetes 2022, 16(2):223-244. Primary Care Diabetes Europe.

- ISPAD Clinical Practice Consensus Guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents. Pediatr Diabetes 2022, 23(8):1188-1211 International Society for Pediatric and Adolescent Diabetes.

- Comprehensive approach to people with type 2 diabetes. Diabetes Knowledge Area of the Spanish Society of Endocrinology and Nutrition. Endocrinol Diabetes Nutr 2022, doi. org/10.1016/j.endinu.2022.07.006. Spanish Society of Endocrinology and Nutrition (SEEN).

- Executive summary on the management of type 2 diabetes mellitus in the elderly or frail. Update 2022 of the 2018 comsensus document «Treatment of type 2 diabetes mellitus in the elderly patient». Revista Clínica Española 2022, 222:496-49. Spanish Society of Diabetes (SED), Spanish Society of Endrocrinology and Nutrition, SPanish Society of Family and Community Medicine (semFYC), Spanish Society of General and Family Physicians (SEMG), Spanish Society of Primary Care Physicians (SEMERGEN) and Spanish Society of Internal Medicine (SEMI).

- Recommendations for the diagnosis and treatment of hypoglycaemia after bariatric surgery. Endocrinol Diabetes Nutr (Engl Ed) 2022, 69(9):723-731. Obesity Group of the Spanish Society of Endocrinology and Nutrition (GOSEEN).

- SEA 2022 standards for the comprehensive control of cardiovascular risk. Clin Investig Arterioscler (Engl Ed) 2022, 34:130-179. Sociedad Española de Arteriosclerosis (SEA).

- Treatment of hypertriglyceridemia with ethyl icosapent in patients at high/very high cardiovascular risk. Consensus document of the Spanish Society of Cardiology and Spanish Society of Diabetes. Endocrinol Diabetes Nutr 2022, doi. org/10.1016/j. endinu.2022.03.004. Spanish Society of Cardiology and Spanish Society of Diabetes

- Decision tree for pharmacological treatment of chronic heart failure with ejection fraction < 50 % of the redGDPS. Diabetes práctica 2022, 13(01):1-52. Network of Diabetes Study Groups in Primary Health Care.

- Clinical Guidelines on the management of dyslipidemia for the prevention of cardiovascular diseases. Network of Lipid and Arteriosclerosis Units of Catalonia.

- Executive Summary of the SEQCML/ SEEN/ SEEP position paper. Recommendations for sex steroid measurement in clinical practice. Endocrinol Diabetes Nutr 2022, doi.org/10.1016/j. endi- nu.2022.11.004 Spanish Society for Laboratory Medicine (SEQCLM), Spanish Society of Endocrinology and Nutrition and Spanish Society of Pediatric Endocrinology (SEEP).

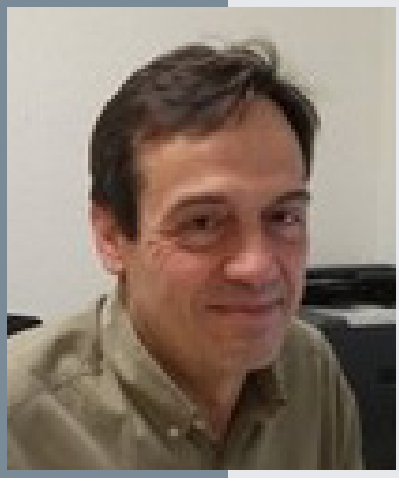
- Executive Summary of the SEEN-SEGO consensus document on the management of thyroid dysfunction during pregnancy. Endocrinol Diabetes Nutr 2022, doi.org/10.1016/j. endinu.2022.03.00. SEEN and the Spanish Society of Gynecology and Obstetrics.

- Clinical practice guidelines for transsexual, transgender and gender diverse minors. Anales de Pediatría 2022, 96:349. e1-340.e11. Spanish Association of Pediatrics.

ciber | EHD

Liver and Digestive Diseases

Welcome from the scientific director



Rafael Bañares Cañizares

Throughout the year 2022, the area of liver and digestive diseases (CIBEREHD), has maintained its research development in the field of liver and gastrointestinal tract diseases, globally characterized by their high prevalence, by their marked negative influence on the quality of life of patients and by their not insignificant mortality. In fact, liver diseases represent one of the main causes of mortality in the world, with an increasing trend.

The research activity of CIBEREHD has maintained its structure around three major programs i) Mechanisms of liver damage, progression to advanced cirrhosis and transplantation ii) Gastrointestinal pathophysiology: inflammatory disease and motility disorders and iii) Hepatic and digestive oncology. Each program has clinical and translational research groups, which allows for a multidisciplinary approach that is strongly promoted by the area's scientific policy.

The scientific quality of CIBEREHD has traditionally been evidenced by the high quantity and quality of its scientific production. In 2022, it has reached the record number of publications in the area while maintaining strong international leadership, as well as a marked activity in the generation of clinical practice documents of great value for society. Notably, the number of publications involving other areas of the CIBER has increased significantly.

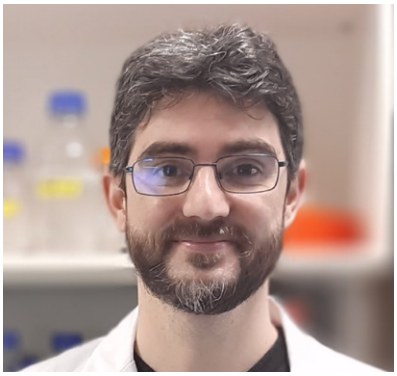
This year CIBEREHD has maintained its global strategy aimed at training researchers with a focus on generational renewal. For this reason, during the year 2022 the pre-doctoral training program(Jaume Bosch contract) has continued, aimed at promoting the collaborative activity of translational groups. On the other hand, the bioinformatics course and the workshops for young researchers have been consolidated, as has the CIBEREHD Research School, the second edition of which has been dedicated to knowledge of omics platforms.

The 2022 meetings of the area, which were fortunately held in person, made it possible to renew relations between the groups and to structure the collective research project, the definitive version of which is planned for 2023.

The area will undoubtedly face important challenges in the coming years: the adaptation of its strategy to the changing context of the diseases in the area (especially fatty metabolic liver disease, inflammatory bowel disease, hepatocarcinoma or colon cancer), the need to increase its funding, the definitive incorporation of the voice of patients, as well as clearly communicating the results obtained to society. Our commitment is to rise to the challenges posed in order to provide society with the necessary return of our research activity.

Programs

Mechanism of liver damage, evolution and progression of cirrhosis and liver transplantation.



Jordi Gracia Sancho

COORDINATOR

Javier Ampuero Herrojo

COORDINATOR

Manuel Luis Rodríguez Perálvarez

COORDINATOR

During the year 2022, studies of great impact have been published in the program Mechanism of liver damage, evolution and progression of cirrhosis and liver transplantation. In the area of liver transplantation, a national study on normothermic regional perfusion has been carried out, which has consolidated the success of asystole donation as a strategy to expand the donor pool (PMID: 34856070). In addition, a new waiting list prioritization model called GEMA has been developed and externally validated, capable of reducing mortality on the waiting list and correcting existing gender disparities in access to liver transplantation (PMID: 36528041). Furthermore, high-impact multicenter studies have been carried out on transplantation in chronic veno-occlusive disease (PMID: 36479977) or post-transplant cancer (PMID: 35286761), including a consensus document developed by the Spanish Society of Liver Transplantation (SETH) and the International Liver Transplant Society (ILTS) on the approach to malignant pathology in transplantation.

As regards the program's clinical groups, two multicenter studies have been published that address the risk of hepatocarcinoma in hepatitis C, with the aim of determining which patients should be followed up after cure (PMID: 34817975; PMID: 34856322). In addition, through a meta-analysis of competing risks, the use of carvedilol has been confirmed to

reduce the probability of decompensation in patients with cirrhosis withportal hypertension (PMID: 3566171713). Furthermore, a scale has been developed for the diagnosis of hepatotoxicity due to drugs called RECAM, which makes it possible to determine the drug responsible (PMID: 35014066). New biomarkers for the diagnosis of autoimmune hepatitis have also been identified in an international multicenter study (PMID: 34473365).

The program's pre-clinical research has resulted in the publication of a study demonstrating the role of intrahepatic vascular angiogenesis during the ductular reaction to acute and chronic liver injury (PMID: 34490644). In addition, a study in the field of metabolic liver disease demonstrated how hepatic mitochondrial function is key to the prevention and treatment of steatohepatitis, showing the importance of the liver axis (PMID: 35563780).

Gastrointestinal pathophysiology: inflammatory disease and motility disorders

Pere Clavé Civit

COORDINATOR

The CIBEREHD Gastrointestinal Pathophysiology program includes groups that develop their studies around three main lines of research: a) esophago-gastroduodenal acid peptic disease and Helicobacter Pylori (HP); b) Inflammatory Bowel Disease (IBD), celiac disease (CD) and eosinophilic esophagitis (EoE); and c) Functional digestive disorders and neuro-gastroenterology. The program's studies focus on the epidemiology, pathophysiology, diagnosis, prevention and treatment of these diseases through cooperative research, very often international and multidisciplinary, clinical and basic; and with a high level of clinical translation thanks to the high participation in consensus documents and national and international clinical practice guidelines. The high level of cooperation is also justified by the participation of the groups of the area, especially those dedicated to IBD, in other stable research structures promoted by Scientific Societies or national and international working groups (AEG, GETECCU, etc.). The year 2022 has brought the incorporation of new groups into the area and the successful overcoming of the COVID-19 period which was a major disruptive element in the scientific activity of the group. The most relevant milestones of the program in 2022 are:

a) Esophago-gastroduodenal acid peptic disease and Helicobacter Pylori (HP).

The main advances focus on improving the treatment of infection and understanding the pathophysiology of HP-associated carcinogenesis. A study derived from the European registry (Hp-EuReg) showed that empirical salvage treatment when initial treatments do not work does not achieve the necessary effectiveness in Europe. Several CIBEREHD investigators participated in the international consensus of the European Helicobacter and Microbiota Study Group (EHMSG) to identify the different clinical scenarios, the most appropriate tests and the therapeutic measures to be adopted to obtain the greatest efficacy, in order to cure gastritis and peptic ulcer, as well as to prevent gastric cancer. Finally, gene expression studies in samples of dyspeptic patients have made it possible to describe patterns of correlation between genes, to group them into co-expression modules and to associate them with steps ranging from atrophy, intestinal metaplasia, dysplasia and finally gastric cancer.

b) Inflammatory Bowel Disease (IBD), celiac disease (CD) and eosinophilic esophagitis (EoE).

It is not easy to summarize the activity of this area, one of the most active of the CIBEREHD, which includes the publication in The Lancet Gastroenterology and Hepatology of a study by the CIBEREHD group of the Hospital Universitario Mutua de Tarrasa, which demonstrates that endoscopic balloon dilatation (EBD) is the endoscopic treatment of choice for the management of fibrous strictures in patients with Crohn's disease. This is the only randomized clinical trial published worldwide on the endoscopic treatment of strictures in this pathol-

ogy. Also noteworthy is the launch of the EoE CONNECT registry, the European Registry of Clinical, Environmental, and Genetic Determinants in Eosinophilic Esophagitis in which various CIBEREHD groups are participating. Finally, researchers from CIBERSAM and CIBEREHD have discovered a mechanism by which psychological stress contributes to colonic inflammation, which could expand the pharmacological tools available for IBD.

c) Functional digestive disorders and neurogastroenterology.

One of the milestones of the year 2022 has been the visit of Dr. David Julius to CIBEREHD. Julius, chair of the Department of Physiology at the University of California San Francisco received the Nobel Prize in Physiology/Medicine 2021 for the discovery of the TRP receptor family (TRPV1, TRPA1, TRPM8), which allowed us to understand how we perceive, among other stimuli, pungency and pain. During his visit and the webinar, which was attended by nearly 300 people, Dr. Julius explained his discovery and the CIBEREHD group of the Consorci Sanitari del Maresme presented their experience in the use of the TRPV1, TRPA1 and TRPM8 receptors as therapeutic targets for the active treatment of pharyngeal sensitivity disorders in the elderly or neurological patients with oropharyngeal dysphagia.

Hepatic and digestive oncology

María Reig Monzón

COORDINATOR

The scientific activity in Liver and Digestive Oncology has maintained its high level of quality and the advancement of knowledge has been transferred to society through clinical practice guidelines (PMID: 34801630).

Currently, CIBEREHD researchers lead an extensive international network of collaborative research and the projects we have carried out have been mostly collaborative both within CIBEREHD and between CIBER groups.

Translational contributions have been made in the field of the role of NADPH oxidases in hepatocellular carcinoma (HCC), particularly in the molecular mechanism regulated by NOX4 (PMID: 35920301). New diagnostic strategies have also been developed, such as the first prospective study on liquid biopsy in bile using a commercial NGS panel to detect mutations that aid in the diagnosis of cancer in patients with suspected malignant biliary strictures (PMID: 34285068). In the clinical field, we have contributed knowledge in the field of immunotherapy, as despite not achieving the main objective of demonstrating a significant improvement in overall survival, the superior tolerance of immunotherapy was confirmed and it showed better long-term survival, laying the foundations for the development of drug combinations (PMID: 34914889). Additionally, in the field of loco-regional treatment innovation (PMID: 35351630) we have demonstrated the applicability of new doxorubicin-loaded spheres for the treatment of HCC (PMID: 35351630).

In the field of digestive cancer, worth mentioning are the publications related to hereditary and familial forms of colorectal cancer (PMID: 34607378), diagnostic strategies based on metabolite detection that can complement and improve the detection of advanced adenomas (PMID: 35736483), or the molecular mechanisms involved in the development, progression and resistance to treatment in colorectal and pancreatic cancer (PMID: 35066875). In addition, we have made contributions in the field of molecular epidemiology of colorectal cancer and analysis of population-based screening strategies (PMID: 35247318), in the field of diagnostic and therapeutic endoscopy, and in the field of minimally invasive surgery in gastrointestinal and pancreatic oncology (PMID: 34086597).

The most relevant publications of the groups involved in the area of liver and gastrointestinal cancer are listed below according to date of publication.

- Yau T et al. Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a randomised, multicentre, open-label, phase 3 trial. Lancet Oncol. 2022 Jan 23(1):77-90.
- Lahoz S et al. Copy-number intratumor heterogeneity increases the risk of relapse in chemotherapy-naive stage II colon cancer. J Pathol. 2022 257(1):68-81.
- Reig M et al. BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. J Hepatol. 2022 Mar 76(3):681-693.
- Houwen B.B.S.L et al. Linked Colour imaging for the detection of polyps in patients

with Lynch syndrome: A multicentre, parallel randomised controlled trial. Gut 2022 71(3):553-560.

- Arechederra M et al. Next-generation sequencing of bile cell-free DNA for the early detection of patients with malignant biliary strictures. Gut 2022 71(6):1141-1151.
- Carballal S et al. Prevalence of adenomatous polyposis in a fecal immunochemical test-based colorectal cancer screening program and risk of advanced neoplasia during follow-up. Endoscopy 2022 54(7):688-697.
- Marin JJG et al. Expression of chemoresistance-associated ABC proteins in hepatobiliary, pancreatic and gastrointestinal cancers. Cancers (Basel) 2022 14(14):3524.
- Marin JJG et al. Impact of Alternative Splicing Variants on Liver Cancer Biology. Cancers (Basel) 2022 14(1):18.
- Garcia-Etxebarria K et al. A survey of functional dyspepsia in 361,360 individuals:Phenotypic and genetic cross-disease analyses. Neurogastroenterol Motil. 2022 34(6):e14236.
- Telleria O et al. A Comprehensive Metabolomics Analysis of Fecal Samples from Advanced Adenoma and Colorectal Cancer Patients. Metabolites 2022 15;12(6):550.
- Malagari K et al. Polyethylene Glycol Drug-Eluting Embolic Microspheres Loaded with Doxorubicin for the Treatment of Hepatocellular Carcinoma: Feasibility, Safety, and Pharmacokinetic Study. J Vasc Interv Radiol. 2022 33(7):752-761.
- de-Madaria E et al. The present and future of gastroenterology and hepatology: an international SWOT analysis (the GASTROSWOT project). Lancet Gastroenterol Hepatol. 2022 7(5):485-494.
- Lazcanoiturburu N et al. A. Lack of EGFR catalytic activity in hepatocytes improves liver regeneration following DDC-induced cholestatic injury by promoting a pro-restorative inflammatory response. J Pathol. 2022 258(3):312-324.

Training

Sofía Pérez del Pulgar Gallart

COORDINATORA

2nd Predoctoral Training Action "Jaume Bosch" CIBEREHD 2022

With the aim of promoting the training of young researchers, the second call for the "Jaume Bosch" Predoctoral Training Action has been resolved. Once again this year, we have selected the best scientific and training proposal for a CIBEREHD research group to hire a researcher to carry out a doctoral thesis in basic/translational research within the framework of a collaborative project between two or more groups in the area.

Call deadline: Octobre 13 to November 15, 2021

Date of resolution: January 24, 2022

Selected project: Molecular mechanisms and novel biomarkers in drug-induced liver injury using patient-derived dermal fibroblasts and keratinocytes

PIs: María Isabel Lucena (Coordinator) and Pau Sancho Predoctoral researcher under contract: Antonio Segovia

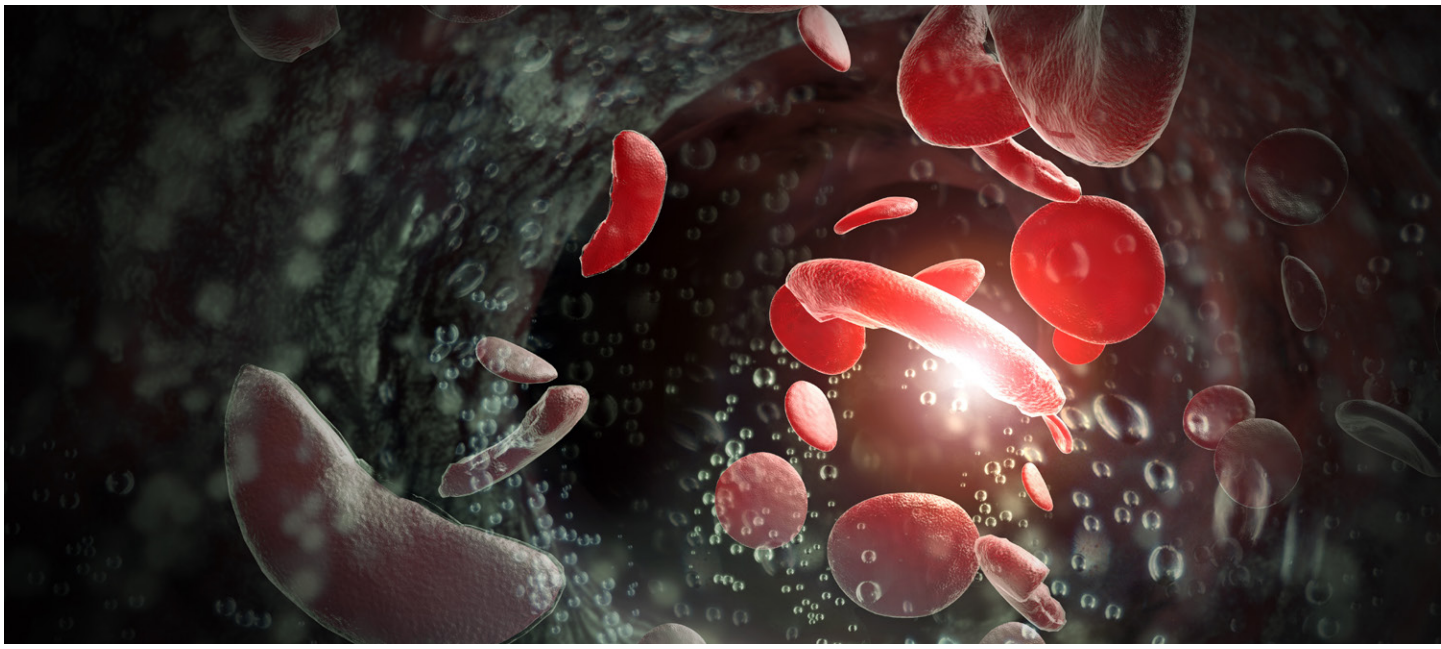
2nd CIBEREHD Bioinformatics Course

Coordinators: Ana Corraliza and Juanjo Lozano.

Date: Octubre 17, 19 and 21 (online); November 15 and 24 (in person).

Methodology: 3 theoretical sessions (Introduction to R and Rstudio; Introduction statistics in R; Transcriptomics - RNA sequencing. 6 hours) and 1 practical session in small groups (from transcriptomics data collection to final results: Resolving of actual cases. 4 hours).

Number of registered participants: 44 people



• 2ª CIBEREHD Research School: Omics in the study of liver and digestive diseases

The CIBEREHD Research School aims to promote the training of the area researchers in the different fields of health research (basic, translational and clinical), as well as to foster interactions between the different CIBEREHD groups. For this reason, this training action is especially aimed at young researchers and each year it is organized by a different group, offering a topic in line with their experience.

Coordinators: Malu Martínez-Chantar and Ana María Aransay

Date and venue: October 5 and 6, 2022; CICbioGUNE, Derio

Methodology: On the first day, the main protocols of the metabolomics, proteomics, electron microscopy, NMR, genomics and Seahorse platforms were presented and visits to the platforms were made. The second day continued with the presentations and the course closed with a keynote lecture by Urko Martínez Marigorta.

Number of participants: 32 people..

• Young Researchers Workshop - XVI CIBEREHD Scientific Conference, November 15, 2022

In its 3rd edition, this activity aimed at young researchers consisted of three parts: the colloquium "Bringing the patient's vision closer to young researchers" with the participation of Dr. Sabela Lens and a patient of hers who was cured after receiving treatment for hepatitis C, the presentation of two successful cases of mobility actions and the presentation of the four best posters selected by an evaluation committee made up of CIBEREHD researchers.

Mobility Actions: Gemma Iserte (Group led by María Reig, Hospital Clínic, Barcelona) explained her experience during her stay at the Mayo Clinic (Rochester, USA). Beatriz Pacín (Group led by María Buti, Vall d'Hebron Hospital, Barcelona) presented the experimental work carried out during her stay at CIMA (University of Navarra) under the supervision of Dr. Gloria González Aseguinolaza.

Best Poster Awards: Laia Abad (Liver Vascular Biology Research Group, IDIBAPS), Álvaro del Río-Álvarez (Childhood Liver Oncology Group, IGTP).

Marco Sanduzzi (BCLC Group, Hospital Clí- nic de Barcelona, IDIBAPS), Nicolau Guan- yabens (Gastrointestinal Physiology Lab, Hospital de Mataró).

.

• Other training actions

Participation in courses/workshops/seminars: 18 national and 6 international actions.

Organization of seminars/symposia: 17 actions endorsed by CIBEREHD, 4 of them developed at the international level: "OGiP Seminars" organized by Sergi Castellví, "The BCLC 2022 update" organized by María Reig and Jordi Bruix, "Consensus conference on drug-induced autoimmune hepatitis (DI-AIH)" chaired by Raúl Andrade and "Liver Seminars" (https://liverseminars.eu/), an initiative led by Jordi Gracia and Rafael Bañares.

Mobility Actions 2022: Gemma Iserte (Group: María Reig) completed an international stay at the Mayo Clinic (Rochester, USA, 2 months) and Miriam Tarrado at The Francis Crick Institute (London, UK, 3 months). Beatriz Pacín (Group: María Buti) completed a national stay at CIMA (Navarra, Navarra, 1 week), María Luque (Group: Paloma Martín) at CICbioGUNE (Derio, 1 week) and Elisa Melón (Group: Azucena Salas) at CIB Margarita Salas, CSIC (Madrid, 2 weeks).

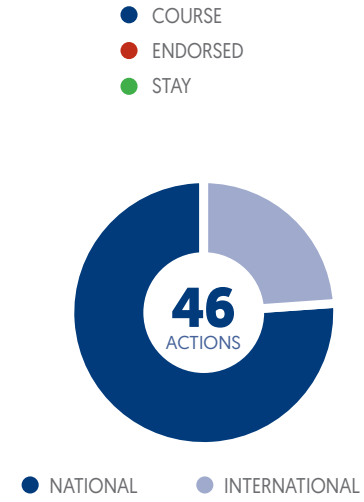
The following tables show the different training actions carried out:

HEPATOLOGY	
PI	**ACTIONS**
A. Albillos	
R. Andrade	●●
R. Bañares	●
M. Berenguer	
M. Buti	●●●●
J.V. Castell	
J.I. Esteban	●
J.C. Fernández-Checa	●●
R. Francés	●
C. Fondevila	
X. Forns	●
C. García Monzón	
J.C. García Pagán	●●●
J. García-Samaniego	
J. Genescà	
P. Ginés	
J. Gómez	
J. González Gallego	●
C. Guarner	●●
R .Jover	●
P. Martín Sanz	●
M. de la Mata	
J.M. Mato	
A. Parés	
M. Romero	●●

GASTROENTEROLOGY	
PI	**ACTIONS**
F. Azpiroz	●
X. Calvet	
P. Clavé	●
E. Domenech	●
J.V. Esplugues	
M. Esteve	
A. Lanas	
A. Salas	●●
J. Pérez Gisbert	●●●●●●
F. Sánchez de Medina	

LINKED GROUPS	
PI	**ACTIONS**
L. Caballería	
J.L. Calleja	
J. Crespo	
J. Cubiella	●
C. García	
J. Molina	
F.J. Padillo	

ONCOLOGY	
PI	**ACTIONS**
C. Armengol	
M. Reig	●●●●
L. Bujanda	
M. Cascante	●
A. Castells	●●
I. Fabregat	●●
J.J. García Marín	
M. Pastor	
B. Sangro	●●●



Platforms

Bioinformatics

The Bioinformatics platform continues to collaborate actively in the operation of CIBEREHD and CIBER, with a productive year in 2022, as reflected in the number of publications resulting from its support.

The 2nd CIBEREHD Bioinformatics Course has been organized and coordinated together with Dr. Sofia Pérez del Pulgar. The satisfaction questionnaire shows that it was favorably evaluated by the students with very high acceptance. This was an improvement on the previous year's evaluation.

A collaboration established with the group led by Dr. Castells has generated a very relevant publication with the discovery that the methylation of a biomarker (HLA-F) is related to the appearance of Serrated Polyposis. The platform performed the entire bioinformatics analysis including data processing and data analysis from massive methylation.

> Jung G, Hernández-Illán E, Lozano JJ, Sidorova J, Muñoz J, Okada Y, Quintero E, Hernandez G, Jover R, Carballal S, Cuatrecasas M, Moreno L, Diaz M, Ocaña T, Sánchez A, Rivero L, Ortiz O, Llach J, Castells A, Pellisé M, Goel A, Batlle E, Balaguer F. Epigenome-Wide DNA Methylation Profiling of Normal Mucosa Reveals HLA-F Hypermethylation as a Biomarker Candidate for Serrated Polyposis Syndrome. J Mol Diagn. 2022 Jun;24(6):674-686. PMID: 35447336. DOI: 10.1016/j.jmoldx.2022.03.010

Another excellent collaboration, with the same group, has been reflected in a high impact publication that concludes that ulcerative colitis and sporadic colorectal cancer have microRNA expression patterns and that some of them are related to early neoplastic progression.

> Quintanilla I, Jung G, Jimeno M, Lozano JJ, Sidorova J, Camps J, Carballal S, Bujanda L, Vera MI, Quintero E, Carrillo-Palau M, Cuatrecasas M, Castells A, Panés J, Ricart E, Moreira L, Balaguer F, Pellisé M. Differentially Deregulated MicroRNAs as Novel Biomarkers for Neoplastic Progression in Ulcerative Colitis. Clin Transl Gastroenterol. 2022 Jul 1;13(7):e00489. PMID: 35404333. DOI: 10.14309/ctg.0000000000000489

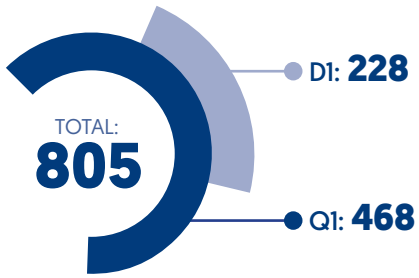
Continuing with the fruitful relationship established years ago with Dr. Joan Clarià, and forming part of a team of international researchers -including the CIBEREHD-, coordinated and led from Barcelona by the European Foundation for the Study of Chronic Liver Failure (EF Clif), a number of high-impact publications have been published, such as:

> Zhang IW, Curto A, López-Vicario C, Casulleras M, Duran-Güell M, Flores-Costa R, Colsch B, Aguilar F, Aransay AM, Lozano JJ, Hernández-Tejero M, Toapanta D, Fernández J, Arroyo V, Clària J. Mitochondrial dysfunction governs immunometabolism in leukocytes of patients with acute-on-chronic liver failure. J Hepatol. 2022 Jan;76(1):93-106. PMID: 34450236. DOI: 10.1016/j.jhep.2021.08.009

Scientific production

Publications

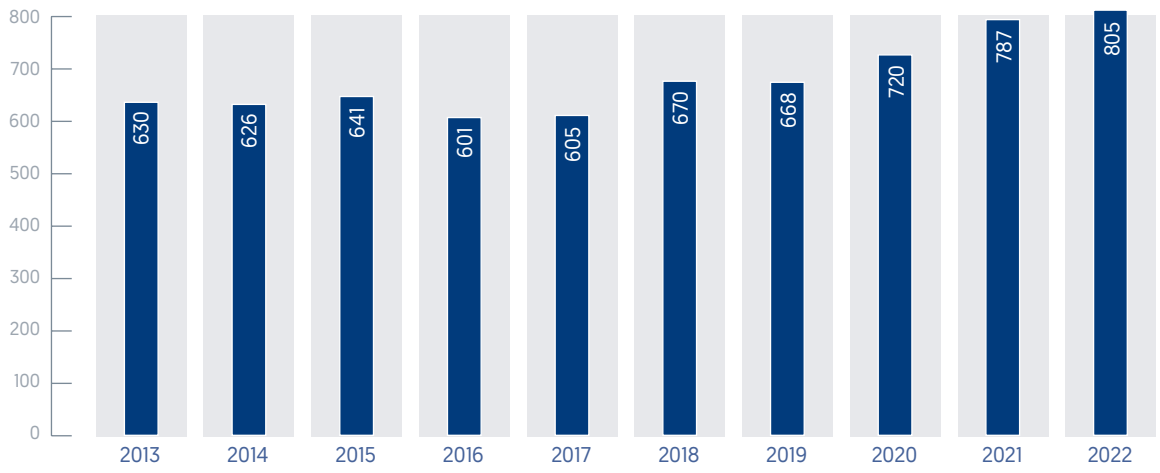
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
73,082	Lazarus J.V., Mark H.E., Anstee Q.M., Arab J.P., Batterham R.L., Castera L. et al. Advancing the global public health agenda for NAFLD: a consensus statement. Nature Reviews Gastroenterology and Hepatology. 2022 Jan;19(1):60-78.
54,433	Yau T, Park JW, Finn RS, Cheng AL, Mathurin P, Edeline J et al. Nivolumab versus sorafenib in advanced hepatocellular carcinoma (CheckMate 459): a randomised, multicentre, open-label, phase 3 trial. The Lancet. Oncology. 2022 Jan;23(1):77-90.
31,795	Kartal E., Schmidt T.S.B., Molina-Montes E., Rodriguez-Perales S., Wirbel J., Maistrenko O.M. et al. A faecal microbiota signature with high specificity for pancreatic cancer. Gut. 2022 Jul;71(7):1359-1372.
31,795	Ventura-Cots M, Argemi J, Jones PD, Lackner C, El Hag M, Abraldes JG et al. Clinical, histological and molecular profiling of different stages of alcohol-related liver disease. Gut. 2022 Sep;71(9):1856-1866.
31,795	Fromme M., Schneider C.V., Pereira V., Hamesch K., Pons M., Reichert M.C. et al. Hepatobiliary phenotypes of adults with alpha-1 antitrypsin deficiency. Gut. 2022;71(2):415-423.
31,373	Ramirez S., Haddad-Tovolli R., Radosevic M., Toledo M., Pane A., Alcolea D. et al. Hypothalamic pregnenolone mediates recognition memory in the context of metabolic disorders. Cell Metabolism. 2022;34(2):269-284.e9.
30,083	da Silva Lima N., Fondevila M.F., Novoa E., Buque X., Mercado-Gómez M., Gallet S. et al. Inhibition of ATG3 ameliorates liver steatosis by increasing mitochondrial function. Journal of Hepatology. 2022 Jan;76(1):11-24.
30,083	Montano-Loza AJ, Ronca V, Ebadi M, Hansen BE, Hirschfield G, Elwir S et al. Risk factors and outcomes associated with recurrent autoimmune hepatitis following liver transplantation. Journal of hepatology. 2022 Jul;77(1):84-97.
30,083	Fondevila MF, Fernández U, Heras V, Parracho T, Gonzalez-Rellan MJ, Novoa E et al. Inhibition of carnitine palmitoyl-transferase 1A in hepatic stellate cells protects against fibrosis. Journal of hepatology. 2022 Jul;77(1):15-28.
30,083	Semmler G., Lens S., Meyer E.L., Baiges A., Alvardo-Tapias E., Llop E. et al. Non-invasive tests for clinically significant portal hypertension after HCV cure. Journal of Hepatology. 2022;77(6):1573-1585.

CIBEREHD Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Albillos Martínez, Agustín	63	31	16	Universidad de Alcalá	Madrid
Andrade, Raúl	28	18	10	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	Malaga
Armengol Niell, Carolina	15	11	4	Fundación Instituto de Investigacion Germans Trias i Pujol	Barcelona
Azpiroz Vidaur, Fernando	35	12	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Bañares Cañizares, Rafael	39	30	20	Servicio Madrileño de Salud	Madrid
Berenguer Haym, Marina	31	19	10	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Bujanda Fernández de Pierola, Luis	54	32	18	Asociación Instituto Biodonostia	Guipuzcoa
Buti Ferrer, María Asunción	39	20	9	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Calvet Calvo, Xavier	23	8	5	Corporación Sanitaria Parc Taulí	Barcelona
Cascante Serratosa, Marta	9	7	2	Universidad de Barcelona	Barcelona
Castells Garangou, Antoni	61	34	16	Hospital Clínico y Provincial de Barcelona	Barcelona
Clave Civit, Pere	23	10	3	Fundación Privada Salud del Consorcio Sanitario del Maresme	Barcelona
Domenech Morral, Eugeni	23	10	3	Fundación Instituto de Investigacion Germans Trias i Pujol	Barcelona
Esplugues Mota, Juan Vicente	16	9	5	Universidad de Valencia	Valencia
Esteban Mur, Juan Ignacio	28	14	7	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Esteve Comas, María	35	9	3	Fundación Mutua Terrassa	Barcelona
Fabregat Romero, Mª Isabel	13	8	5	Fundación IDIBELL	Barcelona
Fernández-Checa Torres, José Carlos	12	9	6	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Fondevila Campo, Constantino	52	33	16	Servicio Madrileño de Salud	Madrid
Forns Bernhardt, Xavier	35	21	17	Hospital Clínico y Provincial de Barcelona	Barcelona
Francés Guarinos, Rubén	19	12	6	Instituto de Investigación Sanitaria y Biomédica de Alicante	Alicante
García Marín, José Juan	19	15	10	Universidad de Salamanca	Salamanca
García Pagán, Juan Carlos	34	27	23	Hospital Clínico y Provincial de Barcelona	Barcelona
García-Samaniego Rey, Javier	2	2	2	Servicio Madrileño de Salud	Madrid
Genesca Ferrer, Joan	44	28	17	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Gines Gibert, Pere	45	27	19	Hospital Clínico y Provincial de Barcelona	Barcelona
Gómez Castilla, Jordi	8	6	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Granada
González Gallego, Javier	9	7	2	Universidad de León	Leon
Guarner Aguilar, Carlos	15	10	8	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Jover Atienza, Ramiro	17	12	3	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Lanas Arbeloa, Ángel	44	17	8	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Martín Sanz, Paloma	9	7	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Mata García, Manuel de la	15	9	5	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Mato de la Paz, José María	40	27	17	CIC BIOGUNE	Vizcaya
Pares Darnaculleta, Albert	9	6	5	Hospital Clínico y Provincial de Barcelona	Barcelona
Pastor Anglada, Marçal	3	3	0	Universidad de Barcelona	Barcelona
Pérez Gisbert, Javier	68	30	11	Servicio Madrileño de Salud	Madrid
Reig Monzón, María Elisa	32	23	13	Hospital Clínico y Provincial de Barcelona	Barcelona
Romero Gómez, Manuel	40	26	17	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Salas Martínez, Azucena	41	20	11	Hospital Clínico y Provincial de Barcelona	Barcelona
Sánchez de Medina López Huertas, Fermín	11	9	3	Universidad de Granada	Granada
Sangro Gómez-Acebo, Bruno Carlos	62	45	27	Universidad de Navarra	Navarra

Linked clinical groups

GROUP LEADER	INSTITUTION - CENTER	PROV. CENTER
Caballería Rovira, Llorenç	Universidad Autónoma de Barcelona	Barcelona
Calleja Panero, Jose Luis	Servicio Madrileño de Salud	Madrid
Crespo Garcia, Javier	Instituto de Investigación Marques de Valdecilla	Cantabria
Cubiella Fernández, Joaquín	Servicio Gallego de Salud	Coruña, A
García Monzón, Carmelo	Servicio Madrileño de Salud	Madrid
Molina Infante, Javier	Fundación para la Formacion y la Investigación de los Profesionales de la Salud (FUNDESALUD)	Caceres
Padillo Ruiz, Francisco Javier	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla

Clinical Guidelines 2022

- Baveno VII - Renewing consensus in portal hypertension.
- BCLC strategy for prognosis prediction and treatment recommendation Barcelona Clinic Liver Cancer (BCLC) staging system. The 2022 update.
- Chronic pancreatitis for the clinician. Part 1: Etiology and diagnosis. Interdisciplinary position paper of the Societat Catalana de Digestologia and the Societat Catalana de Pàncrees.
- Chronic pancreatitis for the clinician. Part 2: Treatment and follow-up. Interdiscipli-nary Position Paper of the Societat Catalana de Digestologia and the Societat Catalana de Pàncrees.
- Consensus Statement on Hemostatic Management, Anticoagulation, and Antiplatelet Therapy in Liver Transplantation.
- De Novo Malignancy After Liver Transplantation: Risk Assessment, Prevention, and Management-Guidelines From the ILTS-SETH Consensus Conference.
- Documento de posicionamiento de la Societat Catalana de Digestologia sobre elastografía hepática 2022.
- Documento de posicionamiento. Recomendaciones del grupo español de trabajo en enfermedad de Crohn y colitis ulcerosa (GETECCU) sobre el tratamiento de la estenosis en la enfermedad de Crohn.
- EASL Clinical Practice Guidelines on prevention and management of bleeding and thrombosis in patients with cirrhosis.
- EASL Clinical Practice Guidelines on the management of hepatic encephalopathy.
- ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment.
- ECCO Guidelines on Therapeutics in Ulcerative Colitis: Surgical Treatment.
- Endoscopic Diagnosis and Management of Esophago-Gastric Variceal Hemorrhage (EGVH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline.
- Endoscopic management of subepithelial lesions including neuroendocrine neoplasms: European Society of Gastrointestinal Endoscopy (ESGE).
- European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations".
- Evaluation and Management of Liver Transplant Candidates With Prior Nonhepatic Cancer: Guidelines From the ILTS/SETH Consensus Conference.
- Executive Summary of the KDIGO 2022 Clinical Practice Guideline for the Prevention, Diagnosis, Evaluation, and Treatment of Hepatitis C in Chronic Kidney Disease.
- Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility.
- Impact of COVID-19 on the liver and on the care of patients with chronic liver disease, hepatobiliary cancer, and liver transplantation: An updated EASL position paper.
- Indicaciones y evaluación del riesgo de las exploraciones endoscópicas en personas de edad avanzada o frágiles. Documento de posicionamiento de la Societat Catalana de Digestologia, la Societat Catalana de Geriatria i Gerontologia y la Societat Catalana de Medicina de Família i Comunitària.
- Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report.
- Nonhepatic Cancer in the Pediatric Liver Transplant Population: Guidelines From the ILTS-SETH Consensus Conference.
- Prevention and Management of Donor-transmitted Cancer After Liver Transplantation: Guidelines From the ILTS-SETH Consensus Conference.
- Recommendations of the Spanish Working Group on Crohn's disease and Ulcerative Colitis on the importance, screening and vaccination in patients with IBD.
- Thromboprophylaxis for venous thromboembolism prevention in hospitalised patients with cirrhosis: Guidance from the SSC of the ISTH.
- V Conferencia Española de Consenso sobre el tratamiento de la infección por Helicobacter pylor [V Spanish Consensus Conference on Helicobacter pylori infection treatment].

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Rare Diseases

Welcome from the scientific director

Pablo Lapunzina Badía

With this Scientific Report I am pleased to present the scientific contributions of the groups that make up the area of Rare Diseases, which are a testimony to the effort and dedication of all those involved, as well as the intense collaborative work that makes it possible for us to achieve our objectives for the development of new therapies and the rapid diagnosis of rare diseases.

Ultimately, our aim is the patients, who suffer from low prevalence diseases, many of them unknown to a large part of society but nevertheless no less important.

Many of these diseases present symptoms and consequences that are generally devastating and have no effective treatments to date. Therefore, every result, from basic to clinical research, every advance in the field of rare diseases that is made, is crucial for the lives of these patients.

The dissemination, communication and sharing of scientific findings of each of the 76 groups that make up the CIBERER contribute to cross-disciplinary knowledge between seemingly very different disciplines and pathologies. As part of the CIBERER, we work as a multidisciplinary team, where each group is important, from those searching for therapeutic targets in cellular, animal or bioinformatics models, to those involved in the designation of orphan drugs, in clinical trials with cell or gene therapies.

We are generators of hope for patients and their families, so that their quality of life improves, so that the pain they suffer is more bearable, while we, from the predoctoral student to the most senior researcher, continue to work to provide a cure for these diseases.

Programs

Translational genomic medicine

Ángel Carracedo

COORDINATOR

In 2022, the IMPACT-Genomics program of the Precision Medicine Infrastructure associated with Science and Technology (IMPaCT) of the ISCIII continued to promote the establishment of a cooperative infrastructure for the performance of highly complex genetic studies, with the aim of accelerating R&D&I transfer and improving efficiency in the use of National Health System resources. Within the framework of the project, the following, among others, deserve special mention:

- The organization of a training day to present the IMPaCT program and the milestones achieved as well as future actions.
- Ángel Carracedo received the Rare Diseases Protagonist of the Year Award from the Weber Foundation and newsRare journal, for his work in the program.
- Co-organization of a race together with the Art for Dent association, to present the work in the diagnosis of rare diseases and providing them with greater visibility.

Among the milestones of 2022 we highlight the following:

- Ángel Carracedo's group has published a series of papers that study the relationship between DNA methylation and gene expression in children and newborns, to aid in the interpretation of epigenomic studies, as well as a systematic analysis that relates obesity to altered metabolic plasticity in adipose tissue.
- The study published in Briefings in Bioinformatics by Miguel Angel Medina's group that allowed us to determine some of the molecular mechanisms involved in angiogenesis-dependent rare diseases. This group has also identified compounds with therapeutic potential.
- The work of the Bioinformatics Working Group coordinated by Beatriz Morte in the organization of outreach activities, such as the annual conference or the workshop to present bioinformatics tools based on systems biology to study rare diseases. Among the more than 20 CIBERER groups that make up this group are those of Joaquín Dopazo and Miguel Ángel Medina.
- The identification of a retinitis pigmentosa candidate gene with a whole genome analysis strategy, work published in npj Genomic Medicine by Salud Borrego's group, which also proposes a strategy for the prioritization of whole genome sequencing variants transferable to other rare diseases.
- The work published in Nature Communications by Santiago Rodríguez de Córdoba's group describes how two key proteins interact and are recognized in the fight against infections, a finding that could contribute to the development of strategies against inflammatory autoimmune diseases.
- The publication in Anal Chem by Mario Fernández Fraga's group, which highlights the potential of FokI-mediated signal amplification as a sensor mechanism for the detection of human pathogens. The proof of concept performed with SARS-CoV-2 has shown good results with respect to conventional approaches.

Lastly, we would like to highlight the participation of the groups of the research program in eight proposals in the ACCI 2021 Call, in which three obtained funding, one of them coordinated by Javier Pérez Florido.

Mitochondrial and inherited metabolic medicine

Rafael Artuch

COORDINATOR

There have been changes in 2022 in the leadership of the CIBERER units: Glòria Garrabou replaces Josep Maria Grau/ Francesc Cardellach and Carlos Santos Ocaña replaces Plácido Navas. These researchers continue to participate actively and have contributed significantly to the progress of the program. Also noteworthy is the merging of 2 groups led by Raúl Estévez and Manual Palacín, which will increase knowledge in the study of new disease genes or new mutations in membrane proteins.

The following are some examples of scientific advances:

Diagnostics:

- Progress is being made in the funtional genomics study to conclude the diagnostics and complete the description of rare pathologies. Belén Pérez, and Santiago Ramón-Maiques (Alberto Marina) -PMID:36564894.
- A gene causing a new neurological and bone syndrome has been identified. Aurora Pujol - PMID: 35325049.
- A standardized protocol for the diagnosis of defects in the mitochondrial respiratory chain has been proposed. Glòria Garrabou, Eduardo Ruiz-Pesini, Miguel Ángel Martin, Elena Garcia-Arumi (Ramon Marti), Laura Gort (Antònia Ribes) - PMID: 35453428.
- A new demyelinating neuropathy of mitochondrial origin due to genetic lesions in the TMRT5 gene has been defined. Clara Marco Marín - PMID: 35342985.
- New clinical variants combining multiple omics techniques to complete the diagnosis of HMD have been defined. Belén Pérez - PMID: 36361642.
- The diagnostic contribution of RNAseq in an adult patient with PEX1 mutations has been described. Antònia Ribes - PMID: 36293220.
- Improved identification of genetic variants responsable for disease through exome reanalysis. Rafael Artuch, Glòria Garrabou, Daniel Grinberg, Ramón Martí, Aurora Pujol, Alfons Macaya, Antònia Ribes - PMID 35569879.

Therapies:

- Promising results with gene therapy to combat muscular dystrophy have been described. Cecilia Jiménez-Mallebrera (Rafael Artuch) PMID: 35886995.
- Contributions have been made to improve molecular therapies for primary hyperoxalurias. Eduardo Salido - PMID: 36113265.
- New treatments for autism in a KO zebrafish model for YWHAZ have been tested. Susanna Balcells - PMID: 35501409.
- Progress has been made in the use of pharmacochaperones in the most common glycosylation defect using the structure of the molecular target as well as proposing a functional platform. Belén Pérez, Santiago Ramón-Maiques (Alberto Marina) - PMID: 34859900 y 35789514.

Other milestones:

- Advances have been made in the understanding of the pathogenetic causes of Leber's hereditary optic neuropathy. Julio Montoya, Eduardo Ruiz-Pesini - PMID: 35808913.
- New aspects of the pathophysiology of Megalencephalic leukoencephalopathy with subcortical cysts have been described. Ekaitz Errasti-Murugarren, Raúl Estévez (Manuel Palacin) - PMID: 35628339.
- More than 100 mitochondrial genoma alterations in the human brain have been found. Glòria Garrabou - PMID: 35085849.
- Discovery of the effects of caloric restriction that reduces mitochondrial defects associated with Coenzyme Q deficiency. Plácido Navas, Antònia Ribes and Rafael Artuch PMID: 35936917.
- New findings that could have therapeutic implications in MELAS syndrome have been described. Miguel Ángel Martín Casanueva PMID: 35088140.
- It has been demonstrated that mitochondria are a target for the treatment of lung cancer. José M. Cuezva PMID: 35534478.
- Publication of the first clinical guide for children affected by Schaaf-Yang syndrome (Roser Urreizti, Susanna Balcells, Rafael Artuch, etc. doi:10.1136/jmedgenet-2022-108690).
- Participation in the international reference treatise (Àngels García-Cazorla, Rafael Artuch, Vicente Rubio) and the international reference guide for physicians (Vicente Rubio, Antònia Ribes, Manuel Palacín, Frederic Tort and Rafael Artuch), both documents on HMD.

Neurological disorders

Pia Gallano

COORDINATOR

This Research Program is made up of 7 groups from different fields, ranging from clinical, genetic and pathophysiological research in neurological pathologies, both of genetic and acquired origin.

At the scientific level, several publications stand out, for example, the work published in the Annals of Clinical and Translational Neurology, coordinated by Eduard Gallardo and Elena Cortés-Vicente, with the participation of Teresa Sevilla, which consists of the analysis of clinical data from 15 national hospitals included in the myasthenia gravis registry.

Luis Querol (Eduard Gallardo's unit) and Josep Dalmau propose the use of a blood biomarker of neuronal damage that will allow the precise and non-invasive identification of whether the origin of the psychotic break is autoimmune or psychiatric, in a study published in Neurology.

The article published in Annals of Neurology led by Juan Jesús Vílchez (Teresa Sevilla's unit), in collaboration with Pia Gallano and Lidia González-Quereda, consists of a Spanish multicenter study that has deepened the understanding of the forms of expression of a rare mutation of the dystrophin gene, which is responsible for Duchenne and Becker muscular dystrophies.

The unit led by Pascual Sanz has published in Molecular Neurobiology the benefits of drugs modulating glutamatergic transmission in preclinical models of Lafora disease.

In terms of project activity, of particular note is the launch of the CANVAS registry within the Registry of genetic and low prevalence diseases (GenRaRe), the result of an intramural project led by Lidia González-Quereda (Pia Gallano's unit), with the participation of Pilar González-Cabo, Luis Querol and Teresa Sevilla, together with Carmen Aguado (CIBERER-Biobank).

It has been a fruitful year for the groups that make up this program, as all of them have received funding in some of the current intramural calls. In the 2020 Call for Cooperative and Complementary Intramural Actions (ACCI), of the 9 projects awarded, two are coordinated by researchers of the program (Lidia González-Quereda and Marina Sánchez/ José Serratosa's Unit), with the participation of 6 groups from the program.

Furthermore, in the 2021 Call for proposals, a project has been financed on new serological markers in patients with rare neuroimmune diseases, led by Luis Querol with the participation of Josep Dalmau. In addition, there is the project consisting of the first methylation data repository from the Spanish reference population and improvements in the epigenetic study in patients with undiagnosed rare diseases (Epi-ENoD), with the participation of José Luis García-Giménez (Federico Pallardó's unit).

This Research Program also stands out for its great harmony with patient associations. For example, Carlos Romá (Federico Pallardó's unit) has undertaken a collaboration with the Dravet Syndrome Foundation with the aim of promoting the development of advanced therapies for this rare childhood epilepsy, which is usually drug-resistant. Also, Clara Serra (Pía Gallano's unit) has collaborated in the writing of the "CuadERno de investigación" ("REsearch Notebook") of the FEDER Foundation, which explains the usefulness of genetic counseling to the group of people affected by rare diseases.

Pediatric and developmental medicine

Cristina Fillat

COORDINATOR

Among the objectives of promoting the development of genomic diagnostic tools and exploring therapies for the diseases of interest to the Program, we highlight the following:

- Identification of a specific methylomic signature that expands the phenotypic spectrum and explains the missense variants in Au-Kline syndrome and the relationship of several variants with neurodevelopmental disorders, from the group coordinated by Pablo Lapunzina;
- Identification of a new cell phenotype in neurogenetic diseases such as Charcot-Marie Tooth from mitochondria-lysosome contacts, from the group coordinated by Francesc Palau;
- Identification of the principles of gene regulation of fusion oncogenes in Ewing sarcoma using a multiomic approach, from the group led by Javier Alonso;
- Participation in the identification of a new treatment for Williams-Beuren syndrome, from the group coordinated by Luis Pérez Jurado;
- Description of alterations in the glial cells of a DYRK1A haploinsuficiency model, and the identification of lamivudine in the improvement of neurological phenotypes in Down syndrome models from the group coordinated by Cristina Fillat.

The groups of Pablo Lapunzina and Víctor Luis Ruiz-Pérez have jointly identified a new genetic cause of orofaciodigital syndrome.

Furthermore, there are numerous individual publications of the groups within this research line, described in more detail in the specific section devoted to each group.

Also worth mentioning are the 2 intramural projects granted during 2022 coordinated by groups from other CIBERER Research Programs in which the groups led by Luis Pérez Jurado and Pablo Lapunzina participate.

Together with FEDER, several researchers have collaborated in the creation of a "research notebook" on diagnostic genetic techniques and in the awareness program for young people "Take on a rare challenge".

Sensorineural pathology

Lluís Montoliu

COORDINATOR

In 2022, the 7 groups that make up the Research Program obtained important results in the areas of science, dissemination and collaboration with patient associations, both independently and in collaboration with other CIBERER groups.

It has been a fruitful year for the groups that make up this program, as all of them have received funding in one or other of the current intramural calls for proposals.

The actions of the Working Groups granted in 2021 have been developed, 4 of which are coordinated by groups from the Research Program: Matías Morín, Almudena Fernández, José María Millán and Silvia Murillo, with the participation of 6 groups from the program.

In the 2021 Call for Complementary Intramural Cooperative Actions, of the 13 projects awarded, 3 are led by Program researchers: Almudena Fernández, Lluís Montoliu and Serena Mirra, and 5 involve the participation of PoI groups: Gemma Marfany, Carmen Ayuso, José María Millán and Miguel Ángel Moreno.

The projects awarded in the Call for New Experimental Models for Rare Diseases, in which Paola Bovolenta and Almudena Fernández participate, have been carried out.

Work has been carried out on the Translational Research Project, led by the Linked Clinical Group coordinated by José Antonio López Escámez, with the participation of Carmen Ayuso, Joaquín Dopazo, Miguel Ángel Moreno Pelayo and José María Millán.

Additionally, work has been carried out in the CIBER unit incorporated into the Biobanks and Biomodels Platform (2021-2023) of the Instituto de Salud Carlos III, with the participation of Isabel Varela and Lluís Montoliu.

Events organized by groups of the Research Program:

- XVII Conference on Translational Research and Precision Medicine: "Precision Medicine, beyond the genome", February 3, coordinated by Carmen Ayuso.
- "The importance of hearing health, damage caused by noise exposure and recent advances in hypoacusis research", March 28, within the framework of World Hearing Day, coordinated by Isabel Varela.
- Course: "Advances in Research with Experimental Models: the future of the 3Rs", March 30 to April 1, organized by Isabel Varela-Nieto and Silvia Murillo.
- V "Genomic editing and gene therapy" course, July 8, coordinated by Lluís Montoliu and Almudena Fernández.
- V "Course on Bioinformatics Analysis of massive sequencing data applied to genetic diagnosis and translational research", November 14-23, coordinated by Miguel Ángel Moreno and Matías Morín.

Awards and appointments granted to members of the Research Program:

- Paola Bovolenta, member of the European Academy.
- Carmen Ayuso and Pablo Mínguez, academicians of the Spanish Royal National Academy of Medicine, for "Human Genetics" and "Health Bioinformatics".
- José María Millán, finalist in the Spanish Association of Orphan and Ultra-Orphan Drug Laboratories Awards (AELMHU).
- Lluís Montoliu, COSCE Award for the Dissemination of Science.
- Isabel Varela-Nieto, member of the International Science Council and Plaque of Honor of the Spanish Association of Scientists.
- José Manuel Zubeldia, permanent member of the European Medicines Agency.

Endocrine medicine

Susan Webb

COORDINATOR

This Research Program consists of only two full-fledged research groups and a third associated group, hence the importance of incorporating the additional strength of the Linked Clinical Groups.

During 2022, two researchers linked to this program have obtained respective awards. Joan Gil, from the group led by Susan Webb, was awarded by the Spanish Society of Endocrinology and Nutrition at its 63rd congress for his oral communication on biomarkers in non-functioning pituitary tumors, and a study on the application of a genetic panel for the diagnosis of primary ciliary dyskinesia, coordinated by Antonio Moreno's group, was awarded by the journal Archivos de Bronconeumología.

The most relevant work on Cushing's syndrome is the result of research in the group led by Susan Webb. In 2022, to be highlighted is the outcome of the Endo-ERN network on the practical clinical management of thromboprophylaxis in Cushing's syndrome published in the Orphanet Journal of Rare Diseases (DOI: 10. 1186/s13023-022-02320-x) and the study on progression of corticotropic tumors after bilateral suparenalectomy, from the ERCUSYN consortium (European registry of Cushing's syndrome) led by Elena Valassi in Endocrine Related Cancer (DOI: 10. 1530/ERC-22-0074), as well as different studies related to acromegaly with the participation of several linked clinical groups of the CIBERER on Data mining applied to precision medicine in Scientific Reports (Doi: 10.1038/s41598-022-12955-2), and the effect of mindfulness therapy published in Clinical Endocrinology (DOI: 10.1111/cen.14844).

From the group led by Luis Castaño worth mentioning are the clinical guidelines published by ISPAD on the diagnosis and management of monogenic diabetes in infants and adolescents published in Pediatric Diabetes (DOI: 10.1111/pedi.13426), as well as the identification of candidate biomarkers for the prediction and monitoring of partial remission in pediatric type 1 diabetes published in Frontiers in Immunology (DOI: 10.3389/fimmu.2022.825426).

Inherited cancer, haematologic and dermatological diseases

Juan Antonio Bueren

COORDINATOR

This research Program has reached very relevant scientific, translational and collaborative milestones during the year 2022:

Advances in the knowledge of the molecular basis of disease

- Javier Corral's work on the characterization of molecular mechanisms of antithrombin deficiency, FXI deficiency and hereditary thrombocytopenia.
- Marcela del Río's studies on the clinical relevance of the ex- pression of antifibrotic factors and autoantibodies in the progression of epidermolysis bullosa.
- The identification of a molecule that increases DNA repair by Rosario Perona's group.
- Víctor Mulero's group has focused on the mechanisms of regulation of hematopoiesis by the inflammasome and the RNA component of telomerase, using zebrafish and iPS cells from patients with DC.
- Jordi Surrallés' study on genetic characterization of head and neck tumors in Fanconi Anemia (FA) patients.
- Mercedes Robledo's studies on tumor localization and mutational status in patients with pheochromocytoma/paraganglioma.
- Eduardo Lopez's group has characterized in SARS-CoV-2 infection the multisystemic inflammatory response in children and the immune response in immunodeficiencies.

Development of diagnostic/prognostic tools

- Teresa Caballero's group's development of guidelines for classification and treatment of angioedema.
- The international multidisciplinary work for the diagnosis of HHT published by Luisa Botella's group.
- Mercedes Robledo's group has identified possible biomarkers for the follow-up of patients with pheochromocytoma/paraganglioma.
- The development of third-generation sequencing for the diagnosis of RDs by Javier Corral's group.
- Marcela del Río's group has developed an in vitro system for the analysis of dermo-epidermal adhesion.
- Eduardo López's group has developed strategies for functional validation of variants in inborn errors of the immune response including the use of gene editing tools.

Therapeutic advances

- The identification of propranolol as a potential drug for Von Hippel Lindau disease by Maria Luisa Botella's group.
- The results of phase I/II of the clinical trial of FA gene therapy led by Juan A. Bueren and Julián Sevilla have allowed the development of a global phase II clinical trial with promising results.
- Initiation of a clinical trial with mesenchymal cells for graft-versus-host disease based on the work of Rosa Yáñez.
- Clinical trial on the use of metformin in FA led by Jordi Surrallés.
- Preclinical studies by Marina Garín have demonstrated therapeutic efficacy of mesenchymal cells for inflammatory bowel disease.
- Marta Carretero's studies on the efficacy of Aptamers in wound healing.
- The clinical finding of María José Escámez on the therapeutic potential of TRIDs for epidermolysis bullosa.
- Fernando Larcher's results on genome editing for genodermatosis.

Linked clinical groups: we highlight the clinical trials of Julián Sevilla for pyruvate kinase deficiency, type I leukocyte adhesion defect and the use of eltrombopag as an adjuvant in FA..

Training

Luis Pérez Jurado

COORDINATOR

The CIBERER Training Program has developed its key actions in 2022 along two general lines:

- Courses: Organization and calls for attendance grants.
- Mobility grants.

Organization of courses and seminars

The following courses and seminars were organized or co-organized:

- EURORDIS SUMMER SCHOOL, 6th Edition. Held in hybrid format.
- Advances in research with animal models: the future of the 3Rs.
- Workshops on EGA/Beacons; tools and applications based on systems biology for the study of Rare Diseases.
- Orphan drug designation, development and access.
- V Young Researchers Meeting, in collaboration with CIBERONC.
- Refresher course on the complement system in pathology.
- UB-CIBERER Mini Symposium on Genetic Rare Diseases.

Call for attendance grants

Grants were also offered to attend the following courses and congresses:

- Advances in research with animal models: the future of the 3Rs. 7 grants.
- REDTRANSFER course: Valorization of R+D results and technologies for research personnel. 3 grants.
- V Young Researchers Meeting. 10 grants.
- Course on Bioinformatics Analysis of massive sequencing data applied to genetic diagnosis and translational research. 5th edition. 12 grants.

Mobility grants

In 2022, mobility grants continued to be open to internal and external, national and international mobility, with the former being provided preferentially. Thus, several researchers were able to benefit from this program to broaden their training and advance the projects in which they were involved.

The following table shows the mobilities carried out in 2022:

BENEFICIARY	ISSUING GROUP	RECEIVING GROUP
Mariví Cascajo Almenara	PI: Carlos Ocaña	PI: Francisco Javier Alonso
Maria Teresa Rubio López	PI: Pascual Sanz Bigorra	Lund Stem Cell Center, Universidad de Lund (Lund, Suecia)
Alba Escalera Balsera	PI: José Antonio López Escámez	Welcome Centre for Human Genetics (Oxford, Reino Unido)
Laura Sánchez Bellver	PI: Gemma Marfany Nadal	PI: Víctor Luis Ruiz Pérez

Platforms

Biobank

The activity of the CIBERER Biobank (CBK) can be summarized in the following points:

The number of biological samples in the Biobank system is 1080, from 84 different pathologies that can be consulted in the online catalog (http://www.ciberer-bio-bank.es/Catalogo/). Samples have been received from 143 new donors. One of the main activities of the CBK is the transfer of samples, with 110 biological samples being transferred to 4 research projects.

The provision of services to CIBERER/CIBER researchers has been continued and the offer has meant that the number of processing services has been maintained, with a total of 171 in 2022. Part of the services are for external groups and biotech companies, which generated a turnover of 1,411 €.

The CBK continues to collaborate with Biobank networks: in the Valencian Biobank Network, the CBK is responsible for managing applications for prospective RD collections in the Valencian Community; in the ISCIII National Biobank and Biomodel Network Platform and also in the Eurobiobank. The collaboration agreements with IBSP-CV/FISABIO and the National DNA Bank are still in force and the sample deposit agreement with INCLIVA for the creation of a collection of fibroblasts from control donors has been maintained. We are also collaborating with the patient associations listed below:

- ENACH Association (Neurodegenerative disease due to brain iron accumulation),
- AFASW, Alliance of families affected by Wolfram Syndrome
- DDX3X Association Spain

As regards agreements with the industry, collaboration agreements have been maintained with EpiDisease SL in two projects TEST ScoliPro® and TESTIVDEIA, and a Know-how license with Seqplexing SL (development of a kit for the detection of SARS-Cov-2 in cell lines).

The CBK has participated in several research projects, namely: i) ISCIII Biobanks Platform (Strategic Action in Health PT20/00118) and ii) CIBERER ACCI Call 2020. It has also participated in the CIBERER Organoids Working Group. Furthermore, it has been included in 3 additional projects; i) 2 projects in the CIBERERER ACCI call 2021 and ii) 1 project together with three CIBERER groups in the EJP RD call. These projects have allowed obtaining additional funding for the CBK. The biobank team has attended and participated in ten different events where the CBK activity has been disseminated.

Publications: as a result of the management of the biobank, there have been four new publications:

- Parrado, A., et al. Glycobiology. Mar 19;32(2):84-100. doi: 10.1093/glycob/cwab087.
- Luque, J., et al. . May. 201(5-6):481-493. doi: 10.1111/cge.14113. Epub 2022 Feb 4.
- Tosco-Herrera, E. et al.. Hum Mutat. Dec;43(12):2010-2020. doi: 10.1002/humu.24459. Epub 2022 Sep 12.
- García Giménez, J.L., et al. Orphanet J Rare Dis. Dec 27;17(1):450. doi: 10.1186/s13023-022-02603-3.

Bioinformatics for rare diseases (BIER)

One of the main activities of BiER is its dedication to the ENoD project in which it not only looks for SNP-type variants or small indels in patient sequencing data, but also for more complex variants such as structural variants or triplet expansions.

It is important to note that the high confidence variant detection rate (STRONG) is 23%, almost double that reported in the literature for reanalysis of undiagnosed cases. Although we did not receive feedback from all, in general the feedback we received was confirmatory. Collaborations have also been extended to more groups, among them the group led by A. Moreno from VHIR and V. Mulero from the Biomedical Research Institute of Murcia.

Following the pattern of previous years, the ENoD data are used to increase and make more precise the genetic variability database of the Spanish population, CSVS, (http://csvs.babelomics.org/), which has continued to prove useful for filtering local polymorphic variants in numerous studies, as well as for putting different researchers in contact with each other, thus making the samples it contains discoverable.

Aware of the importance of taking into account other types of mutations not clearly detectable with conventional exome prioritization, a bioinformatics tool, MIGNON, has been developed for the analysis of gene expression data.

Another tool developed is SPACNACS, a collaborative web server that allows us to know the population frequency of CNVs in the Spanish population, opening up the possibility of discovering new CNV-type variants that may be causative or modifying in human diseases. Additional studies on the local impact of CNVs in some phenotypes and on pharmacogenomic variants have also been carried out.

It is freely available at: : http://csvs.clinbioinfosspa.es/spacnacs/

Resource map for rare diseases (MAPER)

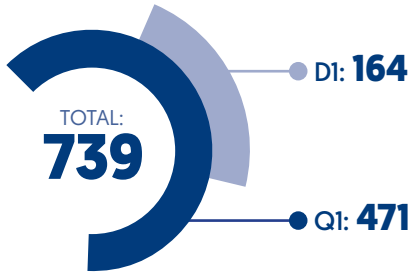
In 2022, information continued to be collected for the MAPER database. The data on research projects and clinical trials accessible through the MAPER website are as follows:

- 1258 biomedical research projects and 797 clinical trials.
- 896 Principal Investigators with at least one Project or trial are included in the database.

Scientific production

Publications

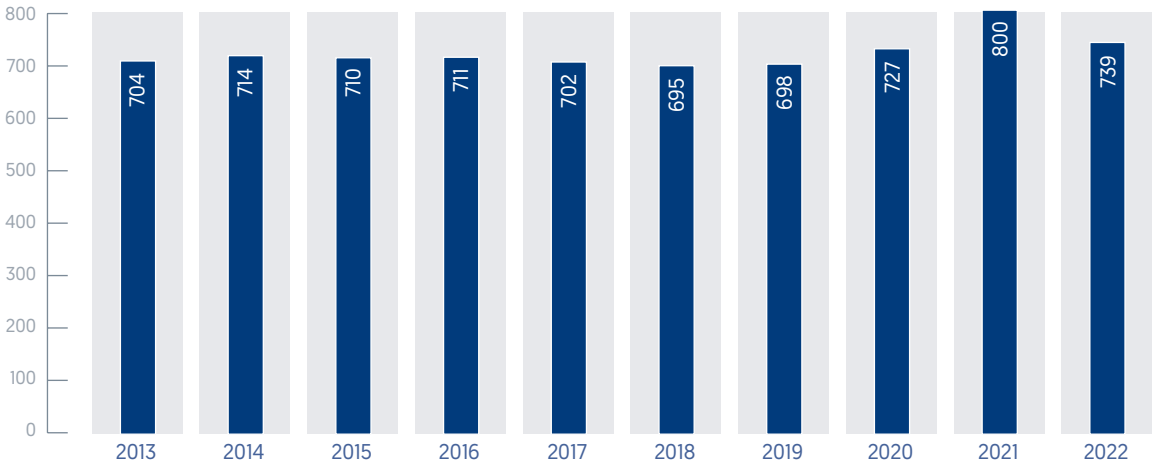
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
202.731	Borobia AM, Carcas AJ, Pérez-Olmeda M, et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial [published correction appears in Lancet. 2021 Aug 14;398(10300):582]. Lancet. 2021;398(10295):121-130. doi:10.1016/S0140-6736(21)01420-3
176.082	Breast Cancer Association Consortium, Dorling L, Carvalho S, et al. Breast Cancer Risk Genes - Association Analysis in More than 113,000 Women. N Engl J Med. 2021;384(5):428-439. doi:10.1056/NEJMoa1913948
157.375	Crovetto F, Crispi F, Casas R, et al. Effects of Mediterranean Diet or Mindfulness-Based Stress Reduction on Prevention of Small-for-Gestational Age Birth Weights in Newborns Born to At-Risk Pregnant Individuals: The IMPACT BCN Randomized Clinical Trial. JAMA. 2021;326(21):2150-2160. doi:10.1001/jama.2021.20178
157.375	Crovetto F, Crispi F, Gratacós E. Mediterranean Diet or Mindfulness-Based Stress Reduction and Prevention of Small-for-Gestational-Age Birth Weights in Newborns-Reply. JAMA. 2022;327(13):1293-1294. doi:10.1001/jama.2022.2167
87.244	Brodin P, Casari G, Townsend L, et al. Studying severe long COVID to understand post-infectious disorders beyond COVID-19. Nat Med. 2022;28(5):879-882. doi:10.1038/s41591-022-01766-7
69.504	Webster ALH, Sanders MA, Patel K, et al. Genomic signature of Fanconi anaemia DNA repair pathway deficiency in cancer. Nature. 2022;612(7940):495-502. doi:10.1038/s41586-022-05253-4
69.504	Zhang Q, Bastard P; COVID Human Genetic Effort, Cobat A, Casanova JL. Human genetic and immunological determinants of critical COVID-19 pneumonia. Nature. 2022;603(7902):587-598. doi:10.1038/s41586-022-04447-0
63.832	Michel M, Benítez-Buelga C, Calvo PA, et al. Small-molecule activation of OGG1 increases oxidative DNA damage repair by gaining a new function. Science. 2022;376(6600):1471-1476. doi:10.1126/science.abf8980
63.798	Lee D, Le Pen J, Yatim A, et al. Inborn errors of OAS-RNase L in SARS-CoV-2-related multisystem inflammatory syndrome in children. Science. 2023;379(6632):eabo3627. doi:10.1126/science.abo3627
59.935	Mercuri E, Deconinck N, Mazzone ES, et al. Safety and efficacy of once-daily risdiplam in type 2 and non-ambulant type 3 spinal muscular atrophy (SUNFISH part 2): a phase 3, double-blind, randomised, placebo-controlled trial. Lancet Neurol. 2022;21(1):42-52. doi:10.1016/S1474-4422(21)00367-7

CIBERER Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alonso García de La Rosa, Francisco Javier	14	6	1	Instituto de Salud Carlos III	Madrid
Artuch Iriberri, Rafael	41	23	5	Fundación para la Investigación y Docencia Sant Joan de Déu	Barcelona
Ayuso, Carmen	25	11	3	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Balcells Comas, Susanna	23	13	8	Universidad de Barcelona	Barcelona
Borrego López, Salud	5	3	0	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Botella Cubells, Luisa María	7	6	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Bovolenta, Paola	2	0	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Bueren, Juan Antonio	20	13	7	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	Madrid
Caballero Molina, María Teresa	14	7	3	Servicio Madrileño de Salud	Madrid
Carracedo, Ángel	22	16	0	Universidad de Santiago de Compostela	A Coruña
Castaño González, Luis	18	13	1	Asociación Instituto de Investigación Sanitaria de Biocruces	Vizcaya
Corral de La Calle, Javier	28	17	6	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	Murcia
Cuezva, José Manuel	8	6	0	Universidad Autónoma de Madrid	Madrid
Dalmau Obrador, Josep	7	7	5	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Del Río Nechaevsky, Marcela	13	9	6	Universidad Carlos III	Madrid
Dopazo Blázquez, Joaquín	7	5	0	Fundación Pública Andaluza Progreso y Salud	Sevilla
Fernández Fraga, Mario	9	8	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Asturias
Fillat, Cristina	15	8	2	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Gallano Petit, María Pia	13	11	2	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Gallardo Vigo, Eduardo	24	16	8	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Garrabou Tornos, Glòria	20	18	7	Universidad de Barcelona	Barcelona
Gratacos, Eduard	38	24	15	Hospital Clínico y Provincial de Barcelona	Barcelona
Lapunzina Badía, Pablo Daniel	44	18	0	Servicio Madrileño de Salud	Madrid
López Granados, Eduardo	8	3	2	Servicio Madrileño de Salud	Madrid
Marfany Nadal, Gemma	7	5	0	Universidad de Barcelona	Barcelona
Marina Moreno, Alberto	21	17	5	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Martí Seves, Ramón	17	14	4	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Martín Casanueva, Miguel Ángel	17	10	0	Servicio Madrileño de Salud	Madrid
Medina Torres, Miguel Ángel	13	9	5	Universidad de Málaga	Málaga

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Millán Salvador, José María	14	7	2	Fundación para la Investigación del Hospital Universitario y Politécnico La Fe de la Comunidad Valenciana	Valencia
Montoliu José, Lluís	3	3	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Moreno Galdó, Antonio José	20	11	0	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Moreno Pelayo, Miguel Ángel	9	5	0	Servicio Madrileño de Salud	Madrid
Mulero Méndez, Victoriano	8	8	5	Universidad de Murcia	Murcia
Nieto Toledano, María Ángela	0	0	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Alicante
Palacín, Manuel	8	5	1	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Palau Martínez, Francesc	10	5	0	Fundación para la Investigación y Docencia Sant Joan de Déu	Barcelona
Pallardó Calatayud, Federico	13	10	1	Universidad de Valencia	Valencia
Pérez González, María Belén	14	7	2	Universidad Autónoma de Madrid	Madrid
Pérez Jurado, Luis	17	15	8	Universidad Pompeu Fabra	Barcelona
Perona Abellón, Rosario	6	6	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Puig Sardá, Susana	46	30	11	Hospital Clínico y Provincial de Barcelona	Barcelona
Pujol Onofre, Aurora	32	28	19	Fundación IDIBELL	Barcelona
Ribes, Antonia	14	9	5	Hospital Clínico y Provincial de Barcelona	Barcelona
Robledo Batanero, Mercedes	25	17	3	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid
Rodríguez de Córdoba, Santiago	7	6	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Ruíz Pérez, Víctor Luis	12	9	5	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Ruíz Pesini, Eduardo	9	5	1	Universidad de Zaragoza	Zaragoza
Salido, Eduardo	10	5	1	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	Santa Cruz De Tenerife
Santos Ocaña, Carlos	18	8	3	Universidad Pablo de Olavide	Sevilla
Sanz, Pascual	3	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Serratosa, José	1	1	0	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Sevilla Mantecón, María Teresa	17	14	3	Fundación para la Investigación del Hospital Universitario y Politécnico La Fe de la Comunidad Valenciana	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Surrallés, Jordi	8	6	4	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Varela Nieto, Isabel	24	12	5	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Webb, Susan	17	11	0	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona

Clinical Guidelines 2022

- ISPAD Clinical Practice Consensus Guidelines 2022: The diagnosis and management of monogenic diabetes in children and adolescents.
- Indications for Digital Monitoring of Patients With Multiple Nevi: Recommendations from the International Dermoscopy Society.
- Executive summary of the SEEN [Sociedad Española de Endocrinología y Nutrición [Spanish Society of Endocrinology and Nutrition]]-SEGO [Sociedad Española de Ginecología y Obstetricia [Spanish Society of Gynaecology and Obstetrics]] consensus document on the management of thyroid dysfunction during pregnancy.
- Systematic Review of the Therapeutic Role of Apoptotic Inhibitors in Neurodegeneration and Their Potential Use in Schizophrenia.
- Consensus guide on prophylactic gonadectomy in different sex development.
- Classification and Treatment of Angioedema without Wheals: A Spanish Delphi Consensus.
- Genetic counselling and testing in pulmonary arterial hypertension -A consensus statement on behalf of the International Consortium for Genetic Studies in PAH.
- Efficacy and safety of high doses of irinotecan in patients with metastatic colorectal cancer treated with the FOLFIRI regimen based on the UGT1A1 genotype: A systematic review.
- Genome-wide meta-analysis for Alzheimer's disease cerebrospinal fluid biomarkers.
- Systematic Literature Review of Hearing Preservation Rates in Cochlear Implantation Associated With Medium- and Longer-Length Flexible Lateral Wall Electrode Arrays.
- Management of early treated adolescents and young adults with phenylketonuria: Development of international consensus recommendations using a modified Delphi approach.
- European Neuromuscular Centre consensus statement on anaesthesia in patients with neuromuscular disorders.
- Diagnosis and management of hypertension in patients with Cushing's syndrome: a position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension.
- Meta-analysis of epigenome-wide association studies in newborns and children show widespread sex differences in blood DNA methylation.
- Clinical practice guidelines for transsexual, transgender and gender diverse minors.
- The international WAO/EAACI guideline for the management of hereditary angioedema - The 2021 revision and update.
- SEOM-GEMCAD-TTD clinical guidelines for localized rectal cancer (2021).
- Delphi consensus on recommendations for the treatment of spinal muscular atrophy in Spain (RET-AME consensus).
- Current status of precision medicine in pediatric oncology in Spain: a consensus report by the Spanish Society of Paediatric Haematology and Oncology (SEHOP).
- Comprehensive summary of mitochondrial DNA alterations in the postmortem human brain: A systematic review.
- Diagnostic delay in rare diseases: systematic review.
- Position paper on a simplified histopathological classification of basal cell carcinoma: results of the European Consensus Project.
- A systematic study and literature review of parental somatic mosaicism of FBN1 pathogenic variants in Marfan syndrome.

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Respiratory Diseases

Welcome from the scientific director

Ferran Barbé Illa

Dear friends:

Once again this year we present in the following report the most relevant data of the CIBERES scientific activity of 2022.

First of all, allow me to welcome Dr. María Molina Molina and Dr. Federico Martinón Torres, PIs of the two new groups that joined CIBERES at the beginning of 2022. I am sure that their contribution to the area will be of great importance in the coming years, as is endorsed by the research trajectory that has brought them here.

2022 was the year in which we left behind the main consequences of the COVID-19 pandemic. However, we have continued and will continue to work on this disease and its sequelae. Thus, CIBERES in collaboration with CIBERESP presented in mid-2022 the results of the study on persistent COVID: operational definition and conclusions for further research, which lays the groundwork for further study of this syndrome that is significantly affecting many patients.

It is precisely in order to guarantee continuity in this field that the CIBERES Steering Committee approved the launch of a new Research Program on COVID-19 and other respiratory viruses, and in the coming months the new lines of research that will nourish the program will be organized and from which we hope to obtain very relevant results for society.

Another important decision of the Steering Committee was to strongly support the training and international projection of young researchers of the area. Thus, the authors of the best communications presented during the Teaching Conferences received grants to participate and present their work at the American Thoracic Society congress. Our intention is to maintain, or even expand, this line of action in the future by opening it up to the European Respiratory Society congress.

I would especially like to point out that last year CIBERES submitted the results and new projects of its lines of research to external evaluation. The evaluators' assessments were very positive and all the lines evaluated amply met the quality standards required to carry out their activities.

I would like to once again encourage you to review the news published on our web site that attest, with concrete results, to the excellence of the work of our CIBER area.

Allow me to end with a few words of recognition and thanks to Dr. Eduard Monsó, who retired in 2022, for his enormous contribution to CIBERES since its inception.

My best wishes and best regards to all of you.

Programs

Chronic respiratory diseases

José Luis López Campos

COORDINATOR

In 2022, the CIBERES chronic respiratory diseases program continued with its planned objectives.

The COPD strategic line continued with the development of each of the work packages of the strategic project. The corporate project From disease activity to lung function trajectories 2019-21 (ATRACTIVE 19-21) ended meeting the anticipated milestones and with an excellent rating obtaining 14.5 pointsover a maximum of 15 and with the publication of numerous contributions in first quartile journals. From this point on, during 2022, the continuation of the strategic COPD research program for the following three-year period 2023-2025 has been planned with a new research project called Insights of Novel Trends Evaluation of lung Growth Routes, Airway disease and Lung Cancer (INTEGRAL). INTEGRAL aims to investigate the determinants of trajectory and associated morbidity, including lung cancer, over the course of a lifetime, based on (1) clinical, phenotypic, microbiological and molecular characterization of pre-COPD, young-COPD and older-COPD individuals throughout the progression of COPD and (2) collaboration with the CIBERES lung cancer program to jointly explore associations between COPD and lung cancer.

In the sleep line, work has continued on the key objectives of its proposal combining experimental and clinical research: (1) characterization of the phenotypes of sleep disordered breathing by using biomarkers; (2) study of the impact of sleep disordered breathing on the systemic level and comorbidities; and (3) relationship between sleep disorders and chronicity. This activity has resulted in several publications, among which we highlight the evaluation of inflammasome activation in sleep apnea (Díaz-García E, et al. AJRCCM 2022), the relationship between tumor dissemination and mechanical ventilation (López-Alonso I, et al. Eur Respir J 2022). Similarly, the sleep group has continued to advance in the study of hypoventilation-obesity syndrome and has participated in the development of the current SEPAR obstructive sleep apnea guidelines.

The Asthma line continues to maintain two large databases, one of 500 patients with asthma of varying severity and the other of 540 patients with severe asthma with and without nasal polyposis treated with biologics. Multiple analyses of both databases have been performed. Analyses have included patient overview, exacerbation analysis, influence of treatable traits, cluster phenotyping, biomarkers in blood and induced sputum, and efficacy of biologics on olfaction in patients with nasal polyposis. These data have resulted in a total of 8 publications in 2022, six of them in Q1 journals. Moreover, studies have also been carried out mainly in the area of mRNA, gene expression and characterization of eosinophils in asthmatic patients. These have resulted in 5 publications.

Infectious respiratory diseases

Antoni Torres Martí

COORDINATOR

Tuberculosis

54 publications: new models in the study of tuberculosis (Galleria mellonella, Drosophila melanogaster, microfluidic); point-of-care diagnostics; genomic analysis of outbreaks, mutation rates, MDR strains, IS6110-based analysis; stimulation of the innate immune response, immune profiling for tuberculosis monitoring; mechanisms of resistance to oxidative stress; dormancy; new compounds, and treatments against mycobacteria, including nanoparticles; impact of BCG tuberculosis vaccine on bladder cancer and COVID-19; impact of exposure to tobacco smoke; impact of cAMP on safety and efficacy of tuberculosis vaccines. Publications on other respiratory pathogens (SARS-CoV-2, Pseudomonas aeruginosa, Klebsiella pneumoniae, Staphylococcus aureus).

4 new research projects including the coordination of a European project on improvements in the diagnosis and treatment of tuberculosis.

2 New clinical trials: efficacy, safety and inmunogenicity of MTBVAC in newborns, and efficacy and safety of RUTI.

3 Doctoral theses: macrophage-TB interactions, betalactams for TB treatment, innate immune response.

Host-pathogen Interactions

23 publications, 43 communications (congresses and dissemination actions to society). 3 doctoral theses

MILESTONES:

Demonstration, using MRI, of the binding of the SARS-CoV-2 glycoprotein Spike to sialic acid in its variants α2,3 y α2,6 sialil N-acetillactosamina; the sialic acid binding site is in the Spike N-terminal domain. Thus, glycoconjugates containing sialic acid on the host cell surface may be binding factors or helper co-receptors.

Prolonged azithromycin therapy in COPD patients causes macrolide resistance and induces genetic changes that favor pathoadaptation during persistent respiratory colonization.

Identification of the molecular basis of the production and secretion of the second messenger c-di-AMP in attenuated vaccines against Mycobacterium tuberculosis, and its role in their attenuation and protection.

Characterization of Staphylococcus aureus-Pseudomonas aeruginosa interaction simultaneously isolated in respiratory samples.

PCV vaccines and the SARS-CoV-2 pandemic are associated with an increase in Streptococcus pneumoniae strains, serotypes 11A, 24F, and 23B, with reduced susceptibility to β-lactams and erythromycin.

Pneumonia

136 publications and more than 80 communications at congresses. 1 thesis directed.

MILESTONES:

New diagnostic tools (antigenemia) to identify COVID-19 patients at risk of poor evolution - patent application.

Anti-S SARS-CoV-2 antibody levels are important in the prediction of mortality, dissemination in patients with COVID-19 in critical care units, in institutionalized and immunosuppressed patients.

Increase in Staphylococcus aureus as a cause of community-acquired pneumonia in children after vaccination with PCV13.

Microbiological diagnostic testing has a positive effect on the de-escalation of antibiotic treatment and on the outcome of patients with community-acquired pneumonia.

Description of the genetic characteristics of the main emerging pneumococcal serotypes causing invasive disease in Spain.

The SARS-CoV-2 pandemic has had an impact on the incidence of pneumococcal disease and antibiotic resistance.

Diffuse respiratory diseases

Francisco Pérez Vizcaino

COORDINATOR

The main results of the CIBERESUCICOVID study have been published, a multicenter, observational, prospective/retrospective strategic study led by CIBERES that has followed a cohort of more than 8000 patients with COVID-19 in 55 ICUs followed at 3, 6 months and one year which ended in December 2021. It has collected thousands of biological samples. Hundreds of publications in epidemiology: incidence, mortality, risk factors, prognostic implications of comorbidities, radiological characteristics, pulmonary function, risk stratification. Biomarker analysis, microRNAs, antibodies, transcriptomic analysis, identification of genetic and epigenetic polymorphisms associated with mortality, mitochondrial haplogroups. Efficacy of antiviral and immunotherapeutic treatments. Persistent Covid..

Other program milestones

- Mechanisms involved in mechanical ventilation and tumor dissemination.
- Regional lung ventilation using PET and radiofluorinated gases.
- Animal model guidelines in acute lung injury (American Thoracic Society).
- Clinical Guidelines for Idiopathic Pulmonary Fibrosis and Progressive Pulmonary Fibrosis (ATS/ ERS/JRS/ALAT).
- Efficacy of pirfenidone in Interstitial lung disease.
- Identification of new loci associated with idiopathic pulmonary fibrosis.
- Metabolomic analysis in idiopathic pulmonary fibrosis.
- Characterization of mesenchymal stem cells in patients with idiopathic pulmonary fibrosis.
- Identification of new genetic variants in idiopathic pulmonary fibrosis.
- Characterization of the endothelial metabolic profile in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension.
- Protein network analysis in chronic thromboembolic pulmonary hypertension.
- Exercise capacity in different forms of pulmonary hypertension.
- Cohort study of patients with pulmonary arterial hypertension to identify responders and non-responders to physical training.
- Alterations of pulmonary circulation in vitamin D receptor knockout models.
- Vitamin D deficiency aggravates right ventricular function in rats genetically deficient in BMPR2.
- Development of 18F-CF4 for improved PET ventilation imaging.
- Heteroplasmy in pulmonary hypertension.
- Development of a Biobank of tissues from animal models of pulmonary hypertension.
- Development of a Biobank of tissues of pulmonary hypertension associated with respiratory diseases.
- Co-exposure to Schistosoma and HIV as a model of pulmonary vascular dysfunction.
- Efficacy of a beta3-adrenergic agonist in pulmonary hypertension associated with heart failure.
- Role of IL11 in pulmonary hypertension.
- 6th Pulmonary Hypertension Research Meeting (CIBERES) was held on-line in March 2022.

Training

Laura Amado

COORDINATOR

In 2022, the actions of the CIBERES Training Program were once again face-to-face.

In the mobility subprogram, 4 grants were awarded for Intra-area stays and 6 grants for international stays in accordance with the standard regulations for all CIBER areas. In addition, 3 grants were awarded for training courses of interest to CIBERES research personnel, and 5 grants for attendance to congresses for the presentation of CIBER project results.

On November 24 and 25, 2022, the XV CIBERES Training Conference was held in Madrid with a hundred participants and 51 research papers received. The program of the Conference is available at: https://webinar.cientifis.com/c-jornadasfor- macionciberes/

The aim of the Conference was, once again this year, to present the lines of research, the research activity and the resources available in the different CIBERES groups, as well as to promote interaction between young researchers, and between clinical and basic profiles. A presentation of the CIBER Internationalization Platform was given by Cristina Rodríguez, coordinator of this department.

Twenty-seven oral communications were presented. The papers were varied and focused on the lines of research in the area of Respiratory Diseases. A round table was also organized ("Scientific career in biomedicine: different trajectories towards a common objective"), in which six speakers offered different perspectives on the professional opportunities offered by the biomedical research sector. The round table, which included Ángeles Heras, Professor of Physical Chemistry at the Universidad Complutense of Madrid, as a guest of honor from outside CIBER, was very well received by the attendees, most of whom were in predoctoral stages.

In addition, 20 posters were exhibited.

As in previous years, all papers presented have been published in a special issue of the journal Archivos de Bronconeumología, available at the following link: https://www.archbronconeumol.org/en-vol-59-num-sc1-sumario-X0300289623X00C10

The CIBERES Training Program also carried out the ATS/ERS Training Action 2023, with an endowment of 40,000 euros, for the dissemination of the results of CIBERES researchers at an international scientific meeting (American Thoracic Society International Conference or European Respiratory Society International Congress) in 2023. The scientific quality of the abstracts is evaluated by peers before being accepted for presentation at the Conference, while clarity of exposition and ability for discussion are evaluated during the Conference by the members of the Training Committee. The 20 papers with the best final evaluation have been nominated to receive these grants. Recipients must commit to present their results at the aforementioned scientific meetings, in accordance with the terms and conditions of the ATS/ERS 2023 Training Action.

The results of the requests for endorsements for face-to-face events (17) are summarized in the following table.

Number of requests for endorsements

Reasons for exclusion:
Panel of organizers and speakers unbalanced (<25% women)

Platforms

Pulmonary Biobank

Cristina Villena

COORDINATOR

Nearly 135,000 samples have been collected from 4,400 donations for the support of projects, collaboration has been initiated in several multicenter projects (HYPNOSA, ISAAC, IMPACT), and we have participated in:

1. Scientific events

- Cristina Villena: "Impact of the collaborative work of the Biobanks Platform: COVID19 sample collection in research". Invited lecture in "From Biological Samples to Precision Medicine" of the International Precision Medicine Forum May 23-31, 2022. Organized by the MARQUÉS DE VALDECILLAIDIVAL RESEARCH INSTITUTE FOUNDATION.
- Cristina Villena: "Sample and data harmonisation: Spanish Biobank Network-ISCIII, Pulmonary Biobank Consortium". Invited speaker in Module 4 "Basis of Translational Research and Biobanks" of the Official Master's Degree in Translational Medicine (2022 edition). Organized by: University of Barcelona. Online.
- Cristina Villena "The acquisition and use of biological samples in research: legal, ethical and scientific bases" Invited lecture at the Round Table Lecture Series of the Germans Trias i Pujol Health Sciences Research Institute (IGTP). Organized by: Josep Carreras Leukemia Research Institute (IJC). Online.
- Cristina Villena "Management of biological samples. Traceability." Invited lecture at the V TRAINING CONFERENCE CEI-IB. Organized by: CEI-IB, IdISBa and Dirección General de Acreditación, Docencia e Investigación en Salud CAIB. Mallorca.
- Cristina Villena "Utility of biobanks of human, animal and bioimaging samples." Invited lecture at Advances in Research with Experimental Models: the future of the 3Rs. CIBERER training courses in phenotyping. Tenth Edition. Organized by: CIBERER and the Official College of Veterinarians of Madrid. Madrid.
- Cristina Villena. I IMPaCT Cohort Workshop: start-up. "Collection of biological samples". Invited lecture. Organizing entity: ISCIII. Madrid. September 19, 2022.

At the 1st Meeting of the ISCIII Platform for Biobanks and Biomodels, Santander, October 27-28, 2022, the following presentations were made:

- Cristina Villena, Carmen Aguado, Almudena Fernández, Julia Fernández, Luzma Garcia, Beatriz Gómez, Fernando Gómez, Miguel López de Heredia, Juan Luque, Salvador Martí, Ingrid Mendes, Lluís Montoliu, Silvia Murillo-Cuesta, Isabel Varela-Nieto. ""CATALOG OF BIORESOURCES IN CYBER-ISCIII INCLUDED IN THE PT-20 BIOBANKS AND BIOMODELS PLATFORM. " Oral poster.
- Fernando Gómez, et al. "Semantic interoperability in Biobanks: creation of a set of SNOMED CT concepts for specific use in biobanks at national and international level." Oral poster.
- Fernando Gómez, et al. "Proposal of minimum datasets associated with biobank collections. Approach by pathology type." Oral poster.

2. Research Projects

Biobanks and Biomodels Platform (PT20). ISCIII platforms to support R&D&I in Bio-medicine and Health Sciences of the Strategic Action in Health 2017-2020. PT20/00118. FIS (ISCIII). 2021-2023. PI: Cristina Villena. Granted: 132.825€.

Coordination of the Work Package 4 Definition of procedures for handling biological samples and biobank of the IMPaCT Predictive Medicine Program Cohort. IMP/00021. 2021-2023. PI: Marina Pollán Santamaría (CIBERESP). Granted: 14.000.000€. And participation in the Steering group for the start of participant recruitment.

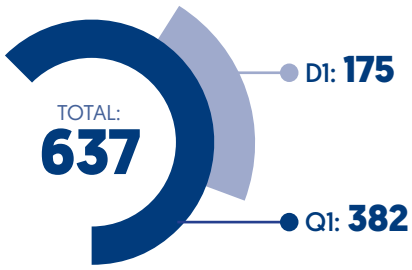
3. Extraordinary Activities

CIBER transversal action, coordinated by Cristina Villena, made up of teams from the 4 thematic areas CIBERES, CIBERER, CIBER-BBN and CIBERONC, for the creation of a CIBER catalog of bioresources available in R+D+I.

Scientific production

Publications

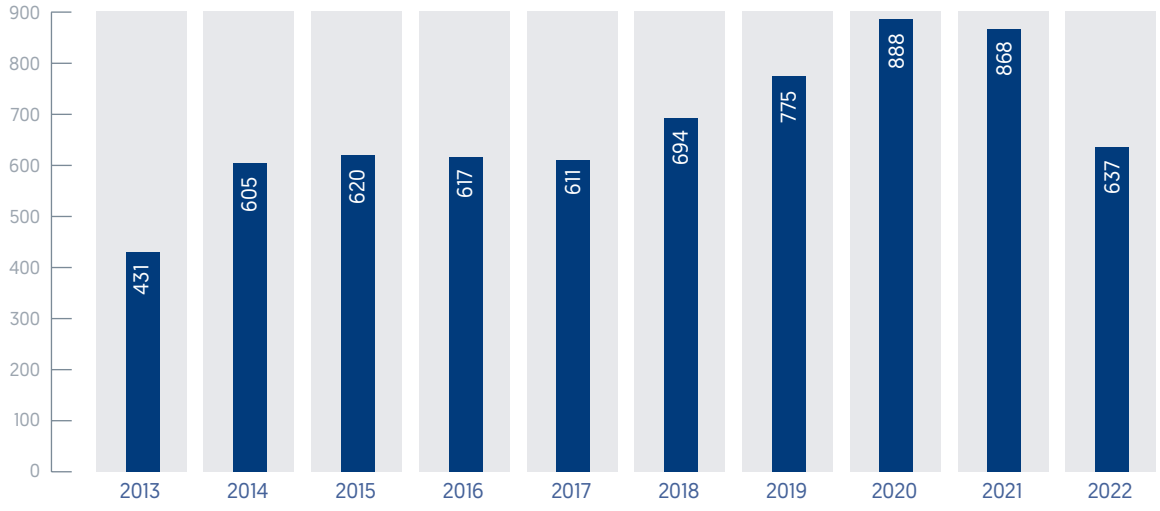
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
102,642.	Agusti A., Melen E., DeMeo D.L., Breyer-Kohansal R., Faner R.. Pathogenesis of chronic obstructive pulmonary disease: understanding the contributions of gene–environment interactions across the lifespan. The Lancet Respiratory Medicine. 2022;10(5):512-524.
102,642	Agusti A., Vogelmeier C.F., Halpin D.M.G.. Tackling the global burden of lung disease through prevention and early diagnosis. The Lancet Respiratory Medicine. 2022;10(11):1013-1015.
86,208	Sempere J, Llamosí M, López Ruiz B, Del Río I, Pérez-García C, Lago D et al. Effect of pneumococcal conjugate vaccines and SARS-CoV-2 on antimicrobial resistance and the emergence of Streptococcus pneumoniae serotypes with reduced susceptibility in Spain, 2004-20: a national surveillance study.The Lancet. Microbe. 2022;3(10).
71,421	Soriano J.B., Murthy S., Marshall J.C., Relan P., Diaz J.V.. A clinical case definition of post-COVID-19 condition by a Delphi consensus. The Lancet Infectious Diseases. 2022;22(4):e102-e107.
41,787	Ranzani O.T., Niederman M.S., Torres A.. Ventilator-associated pneumonia. Intensive Care Medicine. 2022.
41,787	Martin-Loeches I., Chastre J., Wunderink R.G.. Bronchoscopy for diagnosis of ventilator-associated pneumonia. Intensive Care Medicine. 2022.
41,787	Ceccato A., Pérez-Arnal R., Motos A., Barbe F., Torres A., Saera M.B. et al. One-year mortality after ICU admission due to COVID-19 infection. Intensive Care Medicine. 2022;48(3):366-368.
41,787	De Waele J.J., Girardis M., Martin-Loeches I.. Source control in the management of sepsis and septic shock. Intensive Care Medicine. 2022;48(12):1799-1802.
41,787	Hernandez G., Paredes I., Moran F., Buj M., Colinas L., Rodriguez M.L. et al. Effect of postextubation noninvasive ventilation with active humidification vs high-flow nasal cannula on reintubation in patients at very high risk for extubation failure: a randomized trial. Intensive Care Medicine. 2022;48(12):1751-1759.
33,801	Farre R.. Measuring intra-subject changes in respiratory mechanics by oscillometry: impedance versus admittance. European Respiratory Journal. 2022;60(4).

CIBERES Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Agusti García Navarro, Alvar	46	30	16	Hospital Clínico y Provincial de Barcelona	Barcelona
Almendros López, Isaac	15	10	4	Universidad de Barcelona	Barcelona
Ardanuy Tisaire, María Carmen	11	6	4	Fundación IDIBELL	Barcelona
Barbé Illa, Ferrán	36	22	8	Instituto de Investigacion Biomédica de Lleida. Fundación Dr. Pifarre	Lleida
Barberá Mir, Joan Albert	20	12	9	Hospital Clínico y Provincial de Barcelona	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Barreiro Portela, Esther	11	5	2	Consorci Mar Parc Salut de Barcelona	Barcelona
Blanch Torra, Lluis	37	22	9	Corporación Sanitaria Parc Taulí	Barcelona
Cardona Iglesias, Pere Joan	10	6	3	Fundación Instituto de Investigacion Germans Trias i Pujol	Barcelona
Corral Peñafiel, Jaime	7	3	1	Fundación para la Formacion y la Investigación de los Profesionales de la Salud (FUNDESALUD)	Caceres
Cortijo Gimeno, Julio	7	6	2	Universidad de Valencia	Valencia
Fernández Muñoz, Angel Esteve	25	14	7	Fundación IDIBELL	Barcelona
García Río, Francisco José	34	19	6	Servicio Madrileño de Salud	Madrid
Garmendia García, Juncal	12	9	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Jimenez Castro, David	24	21	16	Servicio Madrileño de Salud	Madrid
López-Campos Bodineau, Jose Luis	48	24	11	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Lorente Balanza, José Ángel	17	10	6	Servicio Madrileño de Salud	Madrid
Martín Montañés, Carlos	10	5	1	Universidad de Zaragoza	Zaragoza
Martinon Torres, Federico	16	9	5	Servicio Gallego de Salud	Coruña, A
Molina Molina, María	8	4	3	Fundación IDIBELL	Barcelona
Monsó Molas, Eduard	18	10	3	Corporación Sanitaria Parc Taulí	Barcelona
Mullol Miret, Joaquim	35	20	8	Hospital Clínico y Provincial de Barcelona	Barcelona
Muñiz Albaiceta, Guillermo	19	10	4	Fundación para la Investigación e Innovacion Biosanitaria en el Principado de Asturias (FINBA)	Asturias
Muñoz Gall, Xavier	65	36	16	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Muñoz García, Patricia	49	32	12	Servicio Madrileño de Salud	Madrid
Peces Barba Romero, Germán	17	10	4	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Pérez Vizcaíno, Francisco	2	2	0	Universidad Complutense de Madrid	Madrid
Pozo Abejón, María Victoria Del	29	24	7	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Relló Condomines, Jordi	46	31	14	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Ruiz Cabello Osuna, Jesús	3	1	1	CIC biomaGUNE	Guipuzcoa
Torres Martí, Antoni	59	39	18	Hospital Clínico y Provincial de Barcelona	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Villar Hernández, Jesús	30	21	11	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	Palmas, Las
Yuste Lobo, José Enrique	9	7	4	Instituto de Salud Carlos III	Madrid

Clinical Guidelines 2022

- Multidisciplinary consensus on sputum induction biosafety during the COVID-19 pandemic
- Central venous catheter insertion: Review of recent evidence
- Summary of Recommendations and Key Points of the Consensus of Spanish Scientific [SEPAR, SEMICYUC, SEMES; SECIP, SENEO, SEDAR, SENP] on the Use of Non-Invasive Ventilation and High-Flow Oxygen Therapy with Nasal Cannulas in Adult, Pediatric, and Neonatal Patients With Severe Acute Respiratory Failure
- International Consensus Document on Obstructive Sleep Apnea Documento internacional de consenso sobre apnea obstructiva del sueño
- Forum COPD Working Group Consensus on the Diagnosis, Treatment and Follow-Up of COPD Consenso sobre el diagnóstico, tratamiento y seguimiento de la EPOC: Grupo de trabajo EPOC Forum
- SEPAR recommendations and new challenges on COVID-19 vaccine in respiratory diseases Recomendaciones SEPAR y nuevos retos sobre la vacuna contra la COVID-19 en las enfermedades respiratorias
- Management and outcomes in critically ill nonagenarian versus octogenarian patients
- Early evaluation of organ failure using MELD-XI in critically ill elderly COVID-19 patients
- Acute respiratory distress syndrome subphenotypes and therapy responsive traits among preclinical models: protocol for a systematic review and meta-analysis
- Development and characterization of a new swine model of invasive pneumococcal pneumonia
- Steroid use in elderly critically ill COVID-19 patients
- Awake Proning as an Adjunctive Therapy for Refractory Hypoxemia in Non-Intubated Patients with COVID-19 Acute Respiratory Failure: Guidance from an International Group of Healthcare Workers
- Use of Biomarkers to Identify Acute Kidney Injury to Help Detect Sepsis in Patients With Infection
- Precision medicine in acute respiratory distress syndrome: workshop report and recommendations for future research
- INHALEd nebulised unfractionated HEParin for the treatment of hospitalised patients with COVID-19 [INHALE-HEP]: Protocol and statistical analysis plan for an investigator-initiated international metatrial of randomised studies
- [ISAR Score [Identification of Seniors At Risk] predicts mortality in patients older than 75 years admitted in Intensive Care]
- Cardiopulmonary coupling indices to assess weaning readiness from mechanical ventilation
- Automated detection and quantification of reverse triggering effort under mechanical ventilation

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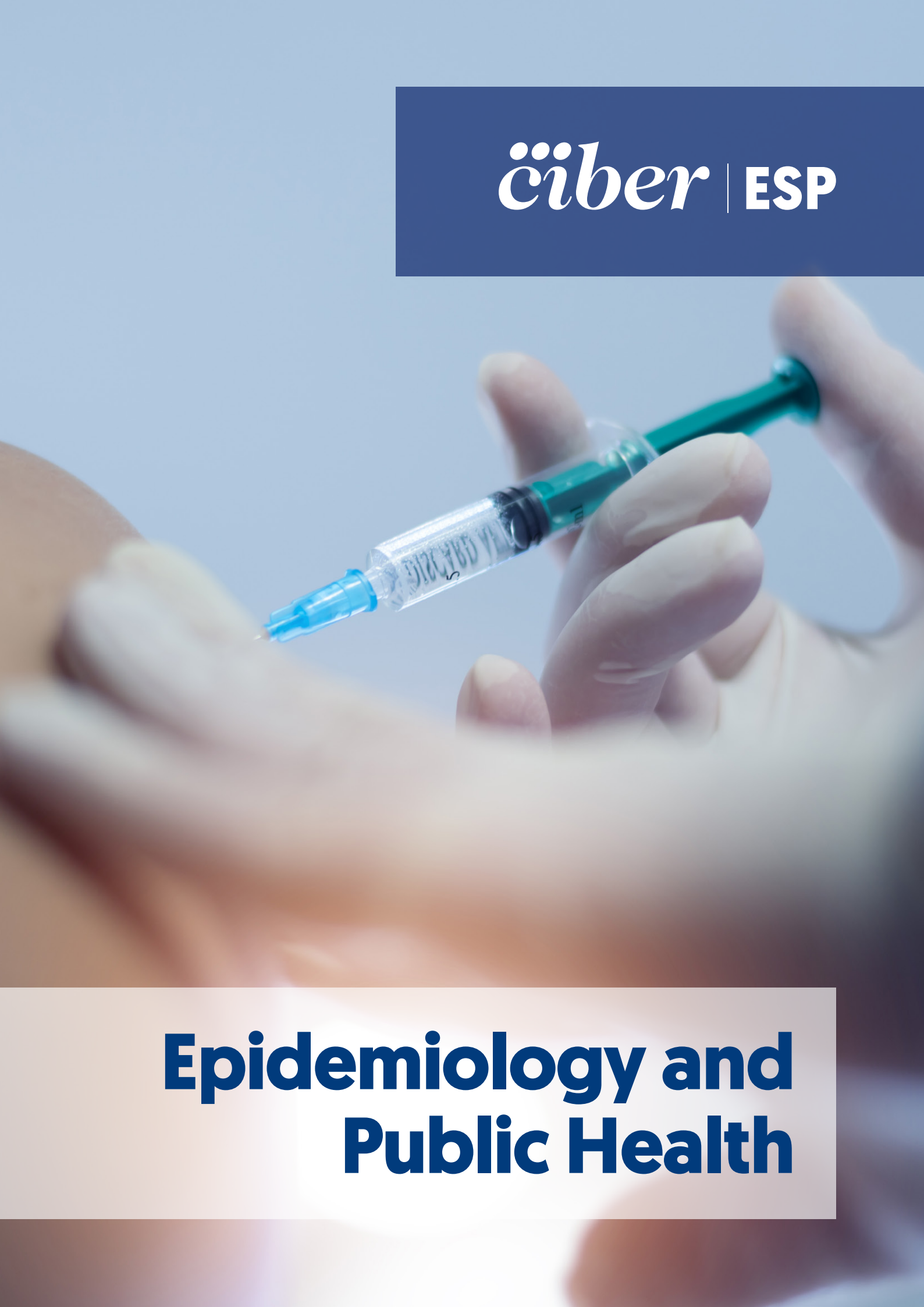

Epidemiology and Public Health

Welcome from the scientific director

Marina Pollán Santamaría

Throughout 2022, CIBERESP has intensified its collaborative activity, occupying the first place in the CIBER areas in number of collaborative articles. Regarding strategic projects, we lead the IMPaCT cohort of the Infrastructure for Precision Medicine associated with Science and Technology. Thanks to the involvement of researchers and professionals from all CIBER areas and regional health services, in 2022 we have developed the protocols that a study of this magnitude requires for its implementation, initially tested in a pilot study with volunteers. We have worked with CIBERES to carry out the first working package of the CIBERPOSCOVID project, providing a consensus definition of persistent COVID in which professionals and patient associations participated. Finally, in

coordination with CIBERINFEC, in the Monkeypox project we are developing several epidemiological studies on this disease. In 2022 we continued to promote the collaboration and leadership of young researchers through the call for CIBERESP projects. We launched a new call for seed projects with CIBER-BBN in which 3 projects have been selected and will be launched soon. In addition, one of the projects from the previous joint call for projects has obtained funding in the national call for projects of the Strategic Action in Health (Acción Estratégica en Salud).

Through the training program, we have promoted the annual mobility grants that allow the exchange between groups and the stay of CIBERESP researchers in centers in other countries, the traditional meeting of excellence between young people working on their doctoral thesis with established researchers, meeting this year in Santiago de Compostela, and we organized the CIBERESP round table at the joint congress of the Spanish and Portuguese Epidemiology Societies in San Sebastian, presenting the best collaborative communications between groups in our area. In addition to our annual scientific conference, held this year in Granada, we have held the first scientific meeting of young CIBERESP and CIBER-BBN reserachers in Barcelona, promoting knowledge, collaboration and a sense of belonging of the youngest members of the network. We invite interested readers to review all the collaborative work of the CIBERESP programs and the results reported by their coordinators.

In conclusion, after the difficult period that the pandemic has meant for an area dedicated to public health, the results of 2022 consolidate and strengthen the work of CIBERESP in its mission to provide relevant information on the main health problems and their determinants. We hope that our results will be useful and help to guide policies aimed at protecting and improving the health of our population.

Programs

Epidemiology and control of chronic diseases

Mª José Sánchez Pérez

COORDINATOR

MCC-Spain

The MCC-Spain project, led by M. Kogevinas and M. Pollán, is being used as a study of prognostic factors for colorectal, breast or prostate cancer.

Controls were recontacted in the framework of the CONTENT project, focusing on the possible mental health and socio-economic effects of COVID, as well as on the analysis of Long COVID.

In 2022, 16 articles were published, 7 of them in the SToP (stomach cancer) and PRACTICAL (prostate cancer) consortia, in addition to 2 articles of the CONTENT/COVICAT project

Gen-risk

The Genrisk project, led by V. Moreno, relies heavily on MCC-Spain.

In 2022, the preparation of genotyping data was completed, with quality controls and SNP imputation was performed, using TOPMed and 1000 Genomes as reference, obtaining more than 15 million SNPs with sufficient quality to perform genetic analysis.

Collaborations have been established with researchers from CIBERONC and CIBER-BBN, and 2 international collaborative projects have been awarded in Horizon Europe: DISCERN (HORIZON-MISS-2021-CANCER-02-03, WP-1) and TANGERINE (JTC 2021. TRANSCAN-3 ERA-NET; IP: V. Moreno).

In addition, the remote computing and analytical platform was upgraded to facilitate genetic and statistical analysis.

Samples are ready to start metabolomics analysis.

Epidemiological Surveillance of Cancer (VICA)

The VICA subprogram, coordinated by M.J. Sánchez and P. Fernández, is making progress in the development of the Epidemiological Information System on Cancer in Spain (SIEC), in collaboration with the Spanish Network of Cancer Registries, having developed the data management modules and scripts necessary for the processing of information and the SIEC web portal, as well as its content, using RShiny.

A study has been carried out analyzing the spatial distribution of municipal mortality due to colorectal cancer in Spain stratified by sex and age groups, implementing a new methodological approach for the combined smoothing of all the strata evaluated. Life expectancy by socioeconomic level in Spain has been analyzed for the first time, with great media repercussion.

An international collaboration has been established with the Instituto Nacional de Saúde Doutor Ricardo Jorge (Lisbon, Portugal) to update the Municipal Cancer Mortality Atlas in Spain and Portugal (AMOCAPE) and to study the influence of socioeconomic factors on spatial patterns.

A face-to-face methodological workshop was held on cancer incidence estimates in Granada.

Three collaborative scientific articles were published in Q1 indexed journals and one article is currently under review. 4 communications have been presented at scientific congresses (5 national and 2 international).

European Prospective Investigation into Cancer and Nutrition (EPIC)

In the EPIC-Spain cohort, ISCIII funding has been obtained for two multicenter projects: 1) Impact of Covid-19 pandemic on health-related lifestyle and quality of life in the elderly and older adults in Spain, y 2) Co-exposure to heavy metals and metaloids, associated genetic susceptibility and can- cer risk in the EPIC prospective cohort: the MixMET Project, which had been funded as an intramural CIBERESP project.

Forty-three scientific articles were published in D1 y Q1 indexed journals

Prevention, surveillance and control of communicable diseases (PREVICET)

Pere Godoy García

COORDINATOR

Flu and respiratory viruses subprogram

The groups of Ángela Domínguez and Cristina Rius have characterized patients hospitalized with influenza in the season 2017-18 in Catalonia (Int.J.Environ.Res.Public.Health.19:14793, PLoS One.17:e0270740 and J.Med.Virol.94:4417) and have worked on collaborative projects on: a) effectiveness of influenza and pneumococcal vaccination (PI19/00354), b) SARS-CoV-2 transmission among household contacts (PI21/01883), in vulnerable population (PLoSONE doi:10.1371/journal.pone.0280614;doi: 10.1371/journal.pone.0269639) and c) an intramural project (ESP22PI01).

The groups of Juan E. Echevarría and Amparo Larrauri have evaluated the effectiveness of COVID-19 and influenza vaccine versus hospitalization based on surveillance data (Influenza Other. Respir. Viruses.16:1014-2, Lancet.Infect.Dis.22:1313-20, CID. doi: 10.1093/cid/ciac429) within the framework of national and international studies (VEBIS ECDC/2021/016. 2021-2025 and ECDC/2021/019. 2021-2025).

Vaccine preventable diseases subprogram

The groups of Juan E. Echevarría and Amparo Larrauri have characterized mumps virus genotypes (JID227:151-160) and the causes of vaccine failure in measles, mumps and varicella.

An editorial on pertussis vaccine in pregnant women (Enferm.Infecc.Microbiol.Clin.40:467) and 5 articles on invasive pneumococcal disease and pertussis (Emerg.Infect.Di.2:2231; Emerg.Infect.Dis;28:127; Vaccine;40:637; BM- JOpen.12:e058003; Ann.Pediatr.96:501) have been published.

Viral hepatitis subprogram

The spatio-temporal distribution of hepatitis A in Spain during the 2016-2017 European outbreak has been analyzed (Int.J.Environ.Res.PublicHealth.19:16775) and the studies (TrazHE project) on hepatitis E have continued (EuroSurveill.27(23):2100542).

Tuberculosis subprogram

The risk factors for tuberculosis in contacts of patients with pulmonary tuberculosis have been analyzed (PI18/01751), an article on the impact of COVID-19 in the study of contacts has been published (Eur.J.Public Health.32:643.) and the inclusion of patients on video (TDO) has been completed (Eur.J.Public Health.32:643).

Epidemic outbreaks subprogram

The thesis "Epidemiology of gastroenteritis outbreaks of viral etiology in closed and semi-closed institutions" (Epidemiol.Infect.147:e225; Viruses.13:1100; Sci. Rep.11:23218; Viruses.12:1392 and Microbiol.Spectr.10:e0011922) was presented as a result of project PI16/02005.

Emerging and re-emerging diseases subprogram

The groups of Ángela Domínguez and Cristina Rius are working on Subproject 3.2. "Epidemiological investigation of Monkeypox cases and their contacts". (CIBER Strategic Action MONKPOX-ESP22).

Jordi Figuerola's group together with other CIBER groups have characterized epidemiological aspects of the Monkeypox outbreak in Madrid. They have also characterized the epidemic outbreak of WNV in Andalusia in 2020 (Emerg.Microb.Infect.11:2570-2578); they have characterized new zoonotic phleboviruses in Algeria (Viruses14:1796) and a new lineage of Usutu virus circulating in Spain (Transbound.Emerg.Dis.2022).

The group of Jordi Figuerola and Cristina Rius have proposed actions to improve zoonosis management in Barcelona (STOTEN 845, 157192; Pathogens 11:423) and worked on the intramural project on WNV involving four PREVICET groups.

Juan E. Echevarría's group has characterized the rabies outbreak in Melilla and Jordi Figuerola's group has searched for and characterized potentially emerging viruses in Iberian bats (VIROBAT and NEXTHREAT projects).

The groups of Carmen Muñoz, Juan E. Echevarría and Amparo Larrauri have worked on an intramural project to improve the diagnosis and epidemiological characterization of meningoencephalitis.

Biological and behavioural determinants in the contraction and spread of communicable diseases in vulnerable populations (DAPET program)

Juan Carlos Galán Montemayor

COORDINATOR

Program Actions

In 2022, two international emergencies of social impact attracted the attention of this program.

1) **The evolution of the COVID-19 epidemic.** The European RELECOV project for epidemiological surveillance of SARS-CoV-2 coordinated by the ISCIII and with the participation of 4 groups of this program ended in September 2022. This project has been continued with RELECOV-2 for the consolidation of this network, with the participation of the groups of Andrés Moya, Jordi Casabona and Juan C. Galán. Dr. Moya's group, in collaboration with Dr. Casabona's group, published a paper on epidemiological analysis of SARS-CoV-2 in Catalonia (mSphere. 2022. doi: 10.1128/msphere.00346-22). E. Calderón's group collaborated in a network on severe COVID (Hum Mol Genet. 2022 doi: 10.1093/hmg/ddac158) with other CIBER groups.

2) **The outbreak of mpox** whose epicenter has been Europe, Spain being one of the main countries in the communication of cases, generated a collaborative project between CIBERINFEC and CIBERESP to analyze this emergency. On the other hand, simultaneous collaborations arose with other CIBER groups to describe clinical and/or epidemiological characteristics. Dr. Casabona's group participated in a collaborative work on viral dynamics in monkeypox patients (Lancet Infect Dis. 2022 doi: 10.1016/S1473-3099(22)00794-0) in collaboration with other CIBER groups.

Actions of the Communicable infections through organic fluids Subprogram

Drs. Casabona and Galán jointly published an editorial "A challenging future in the sexually transmitted infection diagnostics landscape: Chlamydia trachomatis as model" Enfer Infecc Microbiol Clin (Engl Ed). 2022 doi: 10.1016/j.eimce.2022.03.015, on the need for a paradigm shift in STI screening systems.

Dr. Laia Alemany's group, evaluated the implementation of cervical cancer programs in 202 countries (Lancet Glob Health. 2022. doi: 10.1016/S2214-109X (22)00241-8.). Dr. Casabona's group published on the prevalence of HPV in lung cancer (Sci Rep. 2022. doi: 10.1038/s41598-022-17237-5.) and Dr. Galán's group, the first autonomic study on the population-based implementation of HPV in cervical cancer screening Enferm Infecc Microbiol Clin 2022. doi: 10.1016/j.eimce.2022.08.001.).

Dr. Moya's group led a project on syphilis epidemiology Mol Biol Evol. 2022 doi: 10.1093/molbev/msab318. The program also featured a spontaneous panel on syphilis entitled "The syphilis epidemic, a silent reemergence" that highlighted the public health problem of STIs.

Actions of the Antimicrobial resistance Subprogram

This subprogram has organized a meeting for visualizing antibiotic resistance as a public health problem, with the participation of several CIBER groups. Juan C. Galán's group published a paper on the intra-patient evolution of antibiotic resistance plasmids in Nat Ecol Evol. 2022. doi: 10.1038/s41559-022-01908-7 in collaboration with CIBERINFEC researchers. This same group has participated in the development of new molecules for multidrug-resistant bacteria in Nat Chem. 2022 doi: 10.1038/s41557-021-00831-x.

A. Moya's group worked on the transmission of drug-resistant mycobacterium tuberculosis in Microb Genom. 2022 Jul;8(7): mgen000844. doi: 10.1099/mgen.0.000844 with other CIBERINFEC groups.

Social determinants of health

Mª José López Medina

COORDINATOR

In 2022, two subprograms have been launched in which all the groups of the Social Determinants of Health Program participate: The **subprogram on Social Inequalities in the Health of Young People in Spain**, and the **subprogram on Inequalities in Health and COVID-19**. During the course of this year, the data to be used and the lines of work to be promoted by both subprograms have been defined. In addition, the first version of the "Atlas of the Social Determinants of Health in Spain 2022: Evolution and variability between Autonomous Communities" has been published, which compiles and shows a set of the main indicators of the social determinants of health for which information is available for the different Spanish Autonomous Communities (http://www.easp.es/atlasdss/). This atlas has been led by Antonio Daponte's group and Marc Sáez's group, with the participation of the 6 groups of the Program.

Worth mentioning is the participation of the Program groups in several European projects in collaboration with other CIBER groups, among them the project "INIA: Intersex-New Interdisciplinary Approaches" (Antonio Daponte's group), which aims to generate knowledge that supports the wellbeing of intersex people or people with variations in sexual characteristics, or the project "Pan-European Response to the Impacts of COVID-19 and future Pandemics and Epidemics (PERISCOPE)" (Mª José López's group), which aims to estimate the impact of the pandemic. In 2022, the European project "PARC: European partnership to improve chemical risk assessment" has also been launched, in which Isabel Ruiz's group participates, and which aims to develop a chemical risk assessment, incorporating both human health and the environment. Other collaborations at the European level, such as the Joint Action for Equity in Health in Europe, in which Carme Borrell's group participated, ended this year, resulting in the publication of several scientific articles on the monitoring of health inequalities.

Furthermore, competitive funding has been obtained for various national projects of the Ministry of Science and Innovation, such as the project "Environmental Determinants of

Health: multicenter project based on Population Health Surveys (DAS-EP project)" (Antonio Daponte's group) or the project "Characterization of the use of pornography and its association with affective sexual health and sexual violence" (Mª José Belza's group).

Regarding the translation and dissemination of results beyond scientific articles, worth mentioning is the participation of several researchers from different groups of the Program (groups led by Isabel Ruiz, Mª José Belza and Carme Borrell) in the "Health and Gender Report 2022. Multidisciplinary approach to the COVID-19 pandemic", of the Ministry of Health, as well as the dissemination of the results of the European project "Adapting schools to Climate Change with green, blue, and grey measures" (Mª José López's group), with various events to transfer the results both to the school population and at the political level.

Epidemiology and prevention in environmental and occupational health

Marieta Fernández Cabrera

COORDINATOR

The program has continued with its scientific activity.

Sunyer's group has led (participated in) the international projects: HYPAXE, IGRO, PRESSURE, MOODCOVID, ALTER, in metabolomics, transcriptomics, neonatal microbiota and exposome; and worked with CIBERESP groups in the COVID-sentinel schools report and the SAMID network, and with other CIBERs CIBER [CIBERES: TO-LIFE project: artificial intelligence-COPD; CIBEROBN: STOP-childhood obesity]. The following transfer products deserve special mention: 'Misinformation in science news', 'Healthy lungs for life in schools' and 'How can we think together the city of the future?'.

Vioque's group continues to study the role of dietary, environmental and social factors in cardiometabolic risk and mortality in the adult population (PREDIMED PLUS and Nutrition & Health Survey, Autonomous Community of Valencia); and in cancer risk (StoP international consortium, with the participation of Tardón's group).

Outstanding publications of López-Espinosa's group include: thyroid function, hypertension and preeclampsia (Toloza et al., 2022), respiratory diseases (Pinot de Moira et al., 2022; Herrera-Luis et al., 2022), cancer (Pinot de Moira et al., 2022; Hernández García et al., 2022), exposure to pollutants (Abellan et al., 2022; Lozano et al., 2022; Binter et al., 2022; Whitworth et al., 2022) and climate-mortality (Mistry et al., 2022), supported by 13 collaborative projects.

Also noteworthy are the collaborations of Martí-Puig's group to identify molecular biomarkers in rare diseases, with CIBERESP groups (environmental exposure, epi- genetics and age acceleration), CIBERNED (diagnostic strategies in prion and triplet expansion diseases) and CIBERER (genomic analysis).

Of interest are also the international collaborations of Olea's group [School of Public Health-Harvard, HEEDS/USA consortium; School of Public Health/FIOCRUZ, Universidade Federal da Bahia-Brazil; different European groups]. Noteworthy cross-cutting activities: validation and implementation of biomarkers of effect (early damage), non-persistent pesticides, precocious puberty and hormonal alterations (children and adolescents), women's health (endometriosis) and pregnancy intervention (reduction of chemical exposure, mother and offspring). COVID-19 and its relationship with environmental and health factors have also been the subject of collaborative work.

Several intramural projects have been led (participated in): MENTABIOTA, EPIDATA, EMBA, APBO, among others; state and international funding, human resources and several doctoral theses have been obtained.

INMA Subprogram

Collaborations are also key pillars in INMA. There are 35 active projects [involving 16 CIBERESP groups, and other CIBER groups/Networks (CIBEROBNx2, CIBERDEM, CIBERES, CIBERSAMx2, CIBERFES), RedSAMID, Red-Grimalt, REDISSEC], and several intramural projects. INMA also serves as a platform for COVID projects and collaborates in health crisis management.

We have participated in international consortia (EGG/EAGLE, PACE, NCD-RisC, HBM4EU, PARC, Consortium thyroid & pregnancy), and approved 21 collaborative and 19 external proposals.

Strategic achievements related to the new growth stage of the participants: "adolescence" (sexual development, sleep problems, stress, mental health, physical activity-sedentarism, obesity, cardiometabolic health, inflammation markers, internal-external exposures (exposome), microbiome, metabolomics). The collection of data (uniformity in the design of visits and questionnaires) and biological samples is ongoing.

The visits of 14-16 year-olds in 2 INMA cohorts have been completed. The next follow-up begins in INMA-Menorca (25 years) and INMA-Sabadell (18 years) (2023).

We highlight the scientific excellence: 43 CIBERESP collaborative articles, Q1 (88.4%), D1 (32.6%).

Research in health services in clinical practice

Antoni Serrano Blanco

COORDINATOR

As a transversal program we work with CIBERESP, CIBERES, CIBERSAM, CIBERBBN, CIBERCV, RICAPPS and other organizations. We continue to work on COVID-19 projects, increasing the MAPAC commissions network, updating DianaSalud, exploiting the WORKss cohort and expanding the ECONOS database.

Efficiency and equity of the health system (EYESS)

The **CIBERPOSTCOVID** Project led by Victoria Serra and Antoni Serrano, with the participation of all Program 6 groups and others from Program 1, has defined persistent COVID in Spain (https://www.ciberisciii.es/me-dia/3049157/informe-ciberpostcovid -castellano.pdf).

Other ongoing collaborative projects:

1) The Measurement of Mental Well-being as an Indicator for Population Health Monitoring (**WEMWEBS**) led by Gemma Vilagut with CIBERESP and CIBERSAM groups; 2) **Mental-GPS**. "Promoting International Comparability of Mental Health Indicators in General Population Surveys". CIBERESP 2021-23 (PI: Jorge Arias, co-PI: Gemma Vilagut; with CIBERESP and CIBERSAM groups); 3) "Evaluation of **Adherence to Antipsychotics** from Real Clinical Practice Data" PI Antoni Serrano, with participation of Victoria Serra's group; 4) "The impact of the COVID-19 pandemic and its restrictions on the chronification of benzodiazepine (**B-long**) use", led by Ignacio Aznar and Lucy Parker, with participation of 4 CIBERESP groups and one CIBERSAM group; and 5) "The health and social costs of strokes", PI Aida Ribera, with the participation of 3 CIBERESP groups.

ECONOS (https://costesunitariosprisma.org) already includes≥70.000 affordable rates of Spanish health services, with free access to CIBER.

Health and social burden of disease

We have started the **M&M** project "Designing an Objective Tool to Assess Mental Health in Epidemiologic and Clinical Studies" led by Jordi Alonso (CIBERESP) and Jordi Aguiló (CIBER-BBN) and we expect results in 2023.

We continue working on the following: 1) **MINDCOVID**; Mental health Impact and NeeDs associated with COVID-19 (https://mindcovid.org), led by Jordi Alonso, involving 6 CIBERESP groups and 7 CIBERSAM; 2) the **WORKss platform** (http://www.cisal.upf.edu/workss/esp) and the Continuous Sample of Working Lives (MCVL) focusing on the analysis of return to work after cancer; and 3) we have collaborated with several hospitals in the study of COVID affectation in health professionals.

Blanca Lumbreras' group has participated in the edition of the **SESPAS Report 2022**: "Public Health and the Health Administration in the face of the COVID-19 pandemic".

Clinical adequacy, knowledge synthesis and transfer

We have consolidated the **MAPAC Commissions** network in 13 Spanish hospitals by holding 9 coordination meetings and developing 5 multicenter projects.

The project "Comparative research on the **effectiveness for shared decision making** in the treatment of localized prostate cancer with new and traditional modalities" led by Montse Ferrer and with the participation of Ignacio Ferreira and Xavier Bonfil's group, has started.

We have held the "Conference on the **Cochrane Library** health evidence ecosystem", at the Ministry of Health and the "XVIII Meeting of the Iberoamerican Cochrane Network", led by Xavier Bonfill's group.

Xavier Bonfill's and Javier Zamora's groups have initiated the **European guidelines for colon cancer prevention and screening** and updated the **breast cancer guidelines**.

Training

Mònica Guxens Junyent

COORDINATOR

In 2022, the Training Program has continued to maintain the two basic lines of action of its programming: mobility actions, aimed at facilitating contact and work with other national or international groups; and further training actions, aimed at enhancing the quality of scientific work and its dissemination in Public Health forums.

In 2022, **mobility actions** have been promoted by means of a document agreed among all the training programs of the CIBER areas. At the **national level**, 1 short stay between CIBERESP groups has been financed. **International mobility** has also been promoted with the financing of 5 short stays of between one month and three months in international research centers of excellence. These actions have made it possible to promote the professional development of our own research personnel and, in one case, to obtain an international doctorate degree.

As part of the further training actions, **the Meeting for Excellence in Public Health Research was held in Santiago de Compostela**. The objective of this action is to promote quality research in Public Health. This year's edition was attended by 8 young CIBERESP researchers, 2 senior CIBERESP panelists and a member of the CIBERESP Steering Committee.

Once again, the collaboration of CIBERESP with the Spanish Society of Epidemiology has continued with the financing of the **Awards for the 10 best communications** presented by young researchers at the Annual Meeting of the Spanish Society of Epidemiology, which was held in conjunction with the Congress of the Portuguese Association of Epidemiology. The award includes a diploma and covers the cost of registration for the following year's meeting. The SEE meeting also included the CIBERESP spontaneous round table, which, through the **Award for the best papers presented at the CIBERESP** round table, financed the registration of the 6 best papers selected for presentation.

The Training Program also promotes that the training or scientific activities carried out by other entities establish special conditions for CIBERESP members, favoring their participation in these activities.

Platforms

BiblioPRO

BibioPRO is a virtual repository of Patient Perceived Outcomes (PROs). Its mission is to promote their measurement through: **exhaustive inclusion** of information of instruments in Spanish by means of **systematic reviews; scientific evaluations and training**. The BiblioPRO Scientific Committee includes **17 researchers** from **15 institutions (CIBERESP, CIBERSAM, CIBERNED and REDISSEC)**.

Repository (2022)

- **Registered users:** 3.079 new users, reaching 28.000 accumulated users, an increase of 12%.
- **Annual Website Visits:** 57.671 in 2022, increasing 13% over 2021.
- **Instruments:** 133 new instruments, reaching 2.402 in 2022, an increase of 6%.
- **Sublicences:** 409 sublicences have been processed in 2022.
- **Sytematic Review of Instruments:** development of a search algorithm using natural language processing (NPL).

BiblioPRO International

- 130 instruments are available at BiblioPRO International, doubling the number of instruments in 2021. (www.biblioprointernational.org)

Evaluations with the EMPRO online tool (https://empro imim.es)

- Ischemic heart disease.
- Oral health in older adults.
- Vocal health.
- Quality of health in mental health.
- DUKE instrument for social support

Competitive Research Projects

- **ISCIII cofinanciado por EU PI21/00026.** "Implementation of PROMs and PREMs in routine clinical care: evaluation of their requirements and impact 2022-2024". Groups: Alonso Caballero, Jordi and Ferreira González, Ignacio.
- **ISCIII PI22/00845.** "Evaluation of person-centered outcomes and experiences of comprehensive geriatric hospital at home: need for a multipurpose toolkit (RECEP-HAD) 2022-2024". Groups: Alonso Caballero, Jordi and Ferreira González, Ignacio.
- **IMI-Project: 945052.SISAQOL-IMI (EUROPEAN).** "International Standard in Analysing Patient-Reported Outcomes and Quality of Life endpoints".
- **HORIZON EUROPE 2022/10591/I.** "Quality of Life in Oncology: measuring what matters for cancer patients and survivors in Europe 2023-2026". Group: Alonso Caballero, Jordi.

Training and research support activities

- **International Webinar** (July-2022): "PROMIS- Patient-Reported Outcomes Measures. Fixed instruments vs adaptative forms: which ones to choose?" 140 attendees via streaming, 47 views https://www.youtube.com/watch?v=ydL9fIVCYgk.
- **PROMs/PREMs Workshop**. Association of Medicine of the pharmaceutical industry (AMIFE), April 29, 2022.
- **Plenary guest speaker**: "Use of PROMs/PREMs in health sciences research. An approach for young researchers". II Doctoral Meeting in Health Sciences. Málaga, December-2022.
- VIII Primary Care Research meeting of Mallorca. Primary care management. Mallorca. June-2022.
- **Advisory:**

  IMPACT (Call for precisión medicine infrastructure associated with science and technology) Coordinator: ISCIII.

  Naveta: Telepharmacy plataforma with PROMs/PREMs. Coordinator: FARUPEIB

  Electronic Health Record (HES). Coordinator: Department of Health of the Catalan Government.

  H2O Project. Coordinator: University of Vienna

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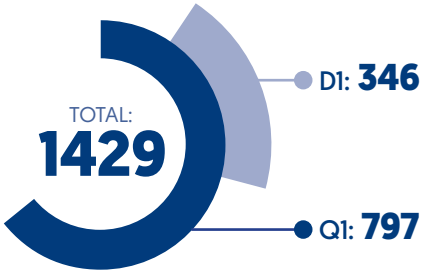
Publications in 2022

- Pardo Y et al. "Patient-centered care in Coronary Heart Disease: what do you want to measure? A systematic review of reviews on patient-reported outcome measures". Qual Life Res. 2022. Groups: Alonso Caballero, Jordi y Ferreira González, Ignacio.
- Zaror C, et al. "Impact of early childhood caries on oral health-related quality of life: A systematic review". Int J Dent Hyg. 2022. Groups: Alonso Caballero, Jordi y Bonfill Cosp, Xavier.
- Mayoral K, et al. "Measurement properties of the EQ-5D-Y administered through a smartphone app in children with asthma". Health Qual Life Outcomes. 2022. Groups: Alonso Caballero, Jordi y Serra Sutton, Victoria.

Scientific production

Publications

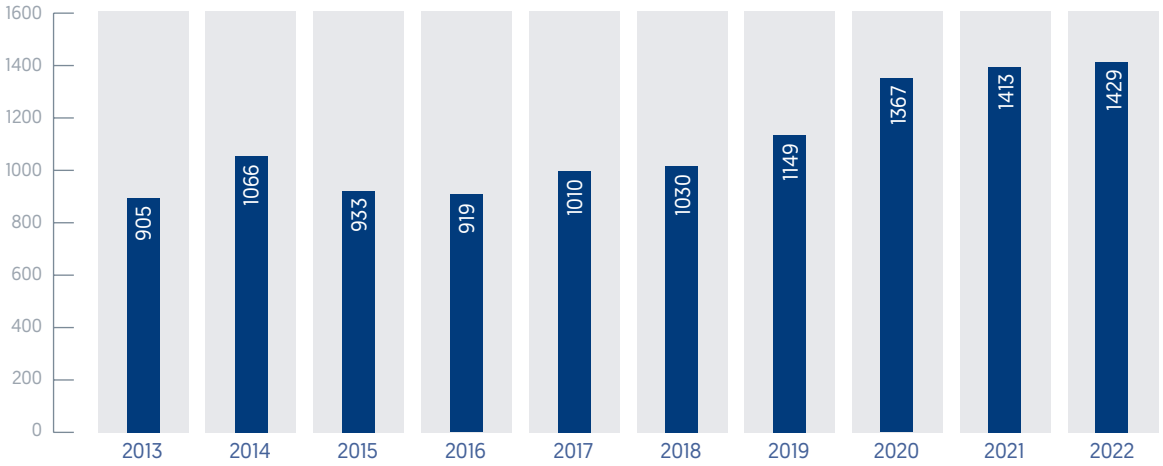
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
96,216	Paytubi S., Benavente Y., Montoliu A., Binefa G., Brotons M., Ibanez R. et al. Everything causes cancer? Beliefs and attitudes towards cancer prevention among anti-vaxxers, flat earthers, and reptilian conspiracists: online cross sectional survey. BMJ (Clinical research ed.). 2022;379:e072561.
38,927	Guinovart C., Sigauque B., Bassat Q., Loscertales M.P., Nhampossa T., Acacio S. et al. The epidemiology of severe malaria at Manhiça District Hospital, Mozambique: a retrospective analysis of 20 years of malaria admissions surveillance data. The Lancet Global Health. 2022;10(6):e873-e881.
30,528	Guerra S, Ledford JG, Melén E, Lavi I, Carsin AE, Stern DA et al. Creatine Kinase is Decreased in Childhood Asthma. American journal of respiratory and critical care medicine. 2022.
28,75	O'Callaghan-Gordo C., Arjona L., Brocal F., Caplin B., Espinosa A., Garcia R. et al. Heat stress and incidence of acute kidney injury among agricultural workers in Spain. The Lancet. Planetary health. 2022;6:S16.
21,286	Garcia-Garcia D., Herranz-Hernandez R., Rojas-Benedicto A., Leon-Gómez I., Larrauri A., Penuelas M. et al. Assessing the effect of non-pharmaceutical interventions on COVID-19 transmission in Spain, 30 August 2020 to 31 January 2021. Eurosurveillance. 2022;27(19).
21,286	Martínez-Baz I., Casado I., Miqueleiz A., Navascues A., Pozo F., Trobajo-Sanmartin C. et al. Effectiveness of influenza vaccination in preventing influenza in primary care, Navarre, Spain, 2021/22. Eurosurveillance. 2022;27(26).
21,286	Munoz-Chimeno M., Barturen S., Garcia-Lugo M.A., Morago L., Rodriguez A., Galan J.C. et al. Hepatitis E virus genotype 3 microbiological surveillance by the Spanish Reference Laboratory: geographic distribution and phylogenetic analysis of subtypes from 2009 to 2019. Eurosurveillance. 2022;27(3).
20,693	Soldevila N., Basile L., Martínez A., Torner N., Marcos M.A., Mosquera M.D.M. et al. Surveillance of influenza B severe hospitalized cases during 10 seasons in Catalonia: Does the lineage make a difference?. Journal of Medical Virology. 2022;94(9):4417-4424.
17,694	Maitre L., Bustamante M., Hernandez-Ferrer C., Thiel D., Lau C.-H.E., Siskos A.P. et al. Multi-omics signatures of the human early life exposome. Nature Communications. 2022;13(1).
16,876	Madhvani K., Garcia S.F., Fernández-Felix B.M., Zamora J., Carpenter T., Khan K.S.. Predicting major complications in patients undergoing laparoscopic and open hysterectomy for benign indications. CMAJ. Canadian Medical Association Journal. 2022;194(38):E1306-E1317.

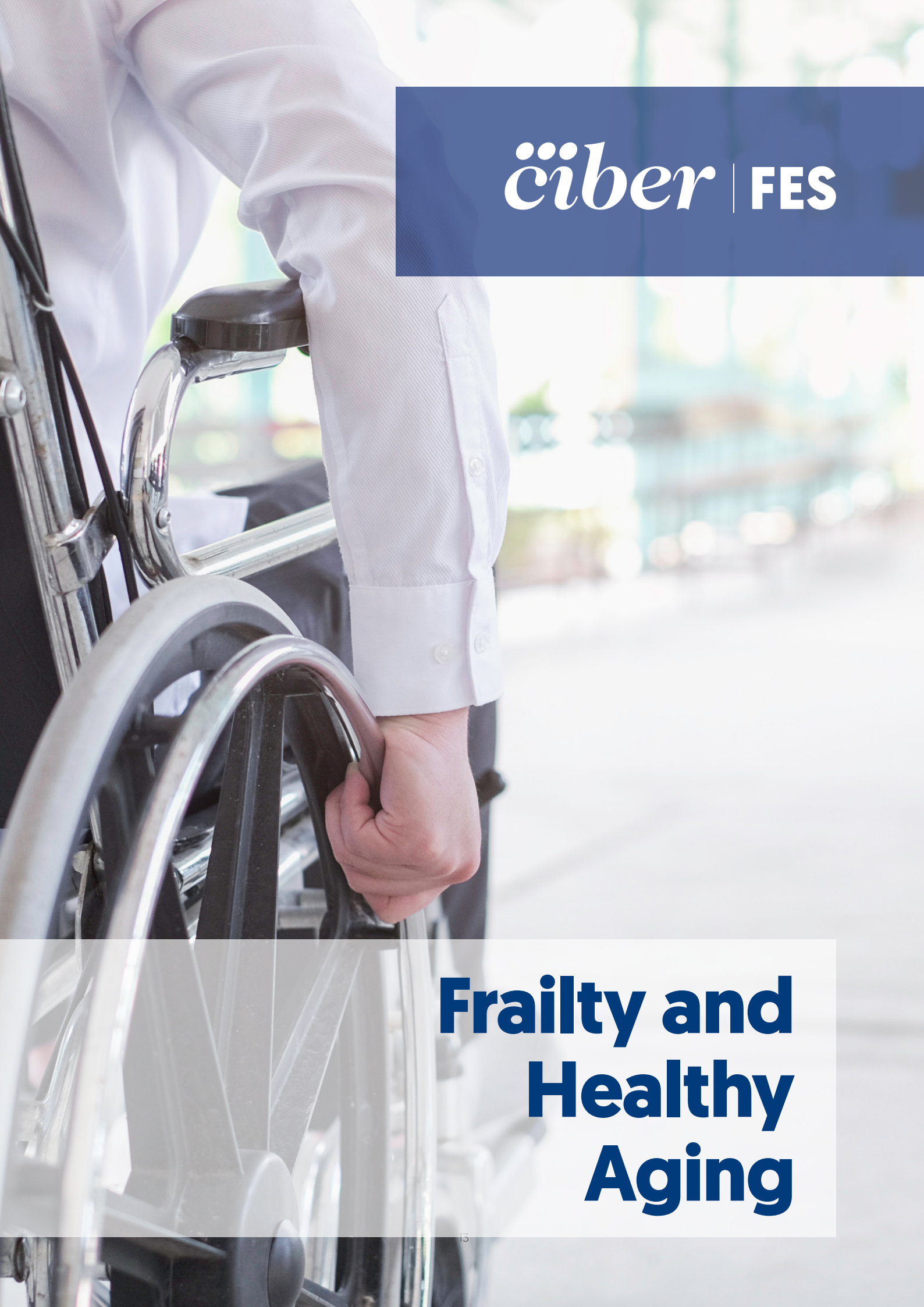
CIBERESP Groups. Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alemany Vilches, María Eulalia	26	13	5	Instituto Catalán de Oncología	Barcelona
Alonso Caballero, Jordi	41	18	7	Consorci Mar Parc Salut de Barcelona	Barcelona
Belza Egozcue, María José	39	11	4	Instituto de Salud Carlos III	Madrid
Bonfill Cosp, Xavier	70	30	14	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Borrell Thio, Carme	56	21	4	Agencia de Salud Pública de Barcelona	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Bueno Cavanillas, Aurora	87	44	8	Universidad de Granada	Granada
Calderón Sandubete, Enrique José	19	12	3	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Casabona Barbara, Jordi	38	10	4	Fundación Instituto de Investigación Germans Trias i Pujol	Barcelona
Castilla Catalán, Jesús	77	47	20	Instituto de Salud Pública de Navarra	Navarra
Chirlaque López, María Dolores	81	45	19	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	Murcia
Daponte Codina, Antonio	11	5	2	Escuela Andaluza de Salud Pública	Granada
Delgado Rodríguez, Miguel	51	31	6	Universidad de Jaén	Jaen
Domínguez García, Ángela	33	7	4	Universidad de Barcelona	Barcelona
Echevarría Mayo, Juan Emilio	26	15	10	Instituto de Salud Carlos III	Madrid
Ferreira González, Ignacio	27	13	6	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Figueiras Guzmán, Adolfo	62	29	8	Universidad de Santiago de Compostela	Coruña, A
Figuerola Borrás, Jordi	21	10	7	Agencia Estatal Consejo Superior de Investigaciones Científicas	Sevilla
Galán Montemayor, Juan Carlos	42	31	10	Servicio Madrileño de Salud	Madrid
Ibarluzea Maurolagoitia, Jesús	75	55	23	Asociación Instituto Biodonostia	Guipúzcoa
Lacasaña Navarro, Marina[1]	26	10	4	Escuela Andaluza de Salud Pública	Granada
Larrauri Cámara, Amparo	29	18	11	Instituto de Salud Carlos III	Madrid
López Espinosa, María José	53	35	15	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	Valencia
López Medina, María José	15	6	2	Agencia de Salud Pública de Barcelona	Barcelona
Lumbreras Lacarra, Blanca	30	13	2	Universidad Miguel Hernández	Alicante
Martí Puig, Eulalia	14	13	9	Universidad de Barcelona	Barcelona
Menéndez Santos, Clara	25	16	8	Hospital Clínico y Provincial de Barcelona	Barcelona
Morales Suárez-Varela, María Manuela	28	13	2	Universidad de Valencia	Valencia
Moreno Aguado, Víctor	55	35	12	Instituto Catalán de Oncología	Barcelona
Moya Simarro, Andrés	66	52	27	Universidad de Valencia	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Muñoz Almagro, María Carmen	59	28	13	Fundación Privada para la Investigación y Docencia Sant Joan de Déu	Barcelona
Olea Serrano, Nicolás	37	28	12	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO)	Granada
Pollan Santamaría, Marina	50	31	13	Instituto de Salud Carlos III	Madrid
Porta Serra, Miquel	18	13	4	Consorci Mar Parc Salut de Barcelona	Barcelona
Rius Gibert, Cristina	29	17	11	Agencia de Salud Pública de Barcelona	Barcelona
Rodríguez Artalejo, Fernando	56	36	16	Universidad Autónoma de Madrid	Madrid
Sáez Zafra, Marc	35	20	7	Universidad de Gerona	Girona
Sánchez Pérez, María José	87	56	17	Escuela Andaluza de Salud Pública	Granada
Schröder, Helmut	24	12	2	Consorci Mar Parc Salut de Barcelona	Barcelona
Serra Pujadas, Consol[2]	41	19	6	Universidad Pompeu Fabra	Barcelona
Serra Sutton, Victoria	11	6	3	Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS)	Barcelona
Serrano Blanco, Antonio	18	4	2	Fundación Privada para la Investigación y Docencia Sant Joan de Déu	Barcelona
Sunyer Deu, Jordi	128	99	59	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	Barcelona
Tardón García, Adonina	68	38	14	Universidad de Oviedo	Asturias
Villanueva Belmonte, Cristina	117	99	60	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	Barcelona
Vioque López, Jesús	59	36	7	Universidad Miguel Hernández	Alicante
Zamora Romero, Javier	70	35	21	Servicio Madrileño de Salud	Madrid

1. Up to 11/30/2022 Isabel Ruiz Pérez
2. Up to 11/30/2022 Fernando García Benavides



ciber | FES

Frailty and Healthy Aging

Welcome from the scientific director

Leocadio Rodríguez-Mañas

During the past year 2022, CIBERFES reached several significant milestones, notably strengthening both the collaborations between the groups in our area and the collaborations of CIBERFES groups with other CIBER areas. In this regard, worth mentioning is the MI- RATAR-IMMAGE project, which, with the participation of 2 FES groups, was funded in the 2022 call for personalized medicine projects of the ISCIII. Also worth highlighting are the collaborations for the preparation of several European proposals, such as MYOLD, which, with the participation of 3 FES groups and a NIA-NIH group, was submitted to last year's ERC Synergy Grants call, or the proposal to the Horizon Europe program, which, under the coordination of CIBERFES, includes the participation of 2 CIBER-BBN groups and will compete in the call "The Silver Deal - Person-centred health and care in European regions".

Similarly, at the European level, in 2022 the extension of the European Horizon 2020 DIABFRAIL-LATAM project was obtained, coordinated by CIBERFES and with the participation of 4 groups from our area, which will allow the scaling up of the intervention contemplated in this project to be carried out satisfactorily. This project will be carried out by the Pan American Health Organization under the coordination of CIBERFES.

Other notable collaborations include the collaboration with CIBEREHD in the design of a study on gastrointestinal pathology frequently found in the elderly, and of course the participation of 3 CIBERFES groups together with 1 CIBERESP group in the aging program of the WHO "Clinical Consortium of Healthy Aging-CCHA", where these groups participate in the validation of different aspects of the WHO ICOPE program.

In addition, in 2022, the project 'Clinical and biological factors involved in the trajectories of rapid progression to frailty', coordinated by Francesc Xavier Nogués, head of the CIBERFES group at IMIM, obtained one of the grants awarded by the Soria Melguizo Foundation in 2022.

In 2022, CIBERFES researchers also obtained important individual awards, such as the XVI Scientific Career Award granted by the Francisco Cobos Foundation to José Antonio Enríquez, PI of the CIBERFES group at the CNIC, or the Castilla and León Award for Scientific and Technical Research and Innovation granted to Juan Pedro Bolaños, PI of the CIBERFES group at the University of Salamanca.

In the area of dissemination, we highlight the reinforcement of CIBERFES visibility activities through the collaboration agreement signed with the training and learning platform Senior Channel, in order to publicize the activities of our area, and raise awareness of the problems which the research carried out by the CIBERFES groups aims to address.

2022 was also the year of important advances from the point of view of training actions, with the consolidation of the Guillén Llera training seminars. The success of these seminars has led CIBERFES to redouble its commitment to them with the plan to include, in future editions, the participation of external international speakers of renowned prestige.

Programs

Basic, clinical and environmental mechanisms associated with the development of frailty. Impact on healthcare systems

José Viña Ribes

COORDINATOR

The groups have had an intense research activity, with special mention of the collaboration in carrying out the DIABFRAIL- LATAM project led by Dr. Rodríguez Mañas' group with the collaboration of Dr. Olga Laosa. We are also grateful for the important activity of Mr. FJ Mansoa in the coordination of the Scientific Directorate, CIBERFES.

Dr. Mª Ángeles Rol has created the Gomarco Chair of Sleep, and an intellectual property registry (the "4-stroke test"). They have collaborated in the dissemination of CIBER, for example: #ImproCiencia or in The conversation.

Dr. Manuel Muñoz's group has characterized new pathogenic variants of the ALPL gene in patients with hypophosphatasia, a rare entity associated with frailty (Frontiers in Endocrinology, 2022).

Dr Juan P Bolaños' group has published a paper in Nature Communications (doi: 10.1038/s41467-022-28191-1), where they identified the aberrant upregulation of a glucose metabolism protein in neurons of neurodegenerative Batten disease.

Dr. Mikel Izquierdo's group has published 35 papers in international journals. Among them, the Effect of an Exercise Intervention on Functional Decline in Very Old Patients During Acute Hospitalizations JAMA Intern Med 2022 Mar 1;182(3):345-347.

Dr. Juan Antonio Enriquez has been elected a Member of the European Molecular Biology Organization (EMBO) and has been awarded the 7th Lifetime Achievement Award for the best biomedical publication of the year.

Dr. Ara, and his group in coordination with the Toledo Hospital Complex, the University Hospital of Getafe and the Hospital Donostia have obtained funding for a project related to the "Identification and validation of Biomarkers of frailty" in the CIBERFES intramural call.

Dr. Viña's group has published the favorable results of a clinical trial to delay the onset of dementia in patients with prodromal Alzheimer's disease: Genistein effect on cognition in prodromal Alzheimer's disease patients. Alzheimers Res Ther. 2022 Nov 4;14(1):164.

In addition, in collaboration with Dr. Muñoz Cánovas, Dr. Gómez-Cabrera has studied the mechanisms of muscle repair. Muscle repair after physiological damage relies on nuclear migration for cellular reconstruction. Science. 2021 Oct 15;374(6565):355-359.

Dr. Escames' group, together with Prof. Yang's group at Northwest University in X'ian, China, identified several functions of clock genes related to aging in general, and established clock genes as emerging therapeutic targets against aging. (Aging Res Rev 202; https://doi.org/10.1016/j.arr.2022.101725.

Dr. Arevalo has described that high-fat diet induces anxiety, alterations in gut microbiota and neuroinflammation in wild-type and TgAPP mice, with the exception of female TgAPP mice. They have also elaborated: "Guidelines for the use and interpretation of assays for monitoring autophagy".

Dr. Andrés-Lacueva's group is working on the project "FOOD4BRAIN-Study of dietary patterns based on metabotypes associated with brain health", and has also published the importance of an intervention with a dietary pattern rich in polyphenols in the elderly, which highlights the positive modification of the composition of the microbiota affecting the excretion of metabolites such as urolithins or indole-3 propionic acid and its effects on intestinal permeability.

Tackling frailty. Detection, screening, diagnosis and treatment. Healthcare models

Xavier Nogués Solan

COORDINATOR

Translational clinical research in frailty in program 2 of CIBERFES is mainly composed of clinicians, and despite the " aftermath" of the pandemic, it has managed to carry out its research activity more efficiently than in the previous two years. We highlight the following:

From Dr. Oriol Grau's Barcelonabeta Brain Research Center group, the demonstration of the use of biomarkers in blood of phosphorylated tau for the detection of brain amyloid in the preclinical phase of Alzheimer's disease (Mila-Alomà et al, 2022 Nat Med).

Dr. Manuel Muñoz, from the Foundation for Biosanitary Research in Eastern Andalusia, has published relevant studies on cardiorespiratory fitness and bone turnover markers in adults with metabolic syndrome (Int J Sport Nutr Exerc Metab, 2022) or the role of undercarboxylated osteocalcin as an early biomarker of cardiovascular disease (Nutrients, 2022).

Dr. Andrés Lacueva's group has shown that alterations in neurogenesis are modulated by metabolomic and lipidomic biomarkers, suggesting that diet could play an important role in the regulation of the neurogenic process in humans, mainly in relation to late depressive symptomatology. [https://www.nature.com/articles/s41380-022-01644-1]

Dr Feliciano Priego's group at the Foundation for Biomedical Research of Cordoba FIBICO has developed a new analytical method for the determination of vitamin D3 metabolites including glucuronide and sulfate derivatives.

Dr. Angeles Rol's group at the University of Murcia has created the Gomarco Chair of Sleep, and an intellectual property registration for the "4-stroke test" (08/2022/508; Date:09/09/2022).

Dr Pedro Abizanda's group at SESCAM Hospital de Albacete has published more results from the FRADEA study on depression and hospitalization (Geriatr Nurs. 2022) and the use of technology in the care of frail people. Stud Health Technol Inform. 2022.

Dr. José Antonio Serra's group at the Hospital Gregorio Marañón has published more than 20 scientific articles, with several inter- and intra-area collaborations. It also highlights the successful completion of two projects on exercise interventions for the prevention of func-

tional deterioration associated with hospitalization, and as an element in the pre- and rehabilitation of elderly patients with colorectal cancer, respectively.

Dr. Ander Matheu's Biodonostia group has identified the relevant role of senescence in the pathophysiology of myotonic dystrophy type 1 and on the physiological and pathological role of chaperone-mediated autophagy in brain aging (Insight. 2022 and Cancer Res. 2022)

Dr. Mikel Izquierdo's group at the Public University of Navarra-Navarrabiomed, focused on research on Physical Exercise, Health and Quality of Life, has published 35 articles including the Effect of an Exercise Intervention on Functional Decline in Very Old Patients During Acute Hospitalizations: Results of a Multicenter, Randomized Clinical Trial. JAMA Intern Med 2022;182:345-347.

In addition to their publications on osteoporosis, Dr. Xavier Nogués' IMIM group in Barcelona has restarted the coordination of the COHORFES project, postponed due to COVID-19, and has received a grant from the Soria Melguizo Foundation for research in the cohort using proteomic techniques.

Training

Pedro Abizanda Soler

COORDINATOR

In 2022, face-to-face training activities were resumed in CIBERFES, which had been interrupted in 2020-2021 due to the pandemic. The main event was the "Third Guillén Llera Seminar" held in Albacete on April 1, coinciding with the 9th National Meeting of the Spanish Society of Geriatric Medicine (SEMEG). CIBERFES participants were invited to participate in all the activities of the Congress, under the slogan "Geriatric Medicine: The Science of Function", in complete alignment with CIBERFES objectives.

In this Third Seminar there were two round tables with oral presentations and three round tables with poster presentations. The moderators were Dr. José Viña (University of Valencia. Coordinator of CIBERFES Program 1), Dr. Xavier Nogués (Hospital del Mar. Barcelona. Coordinator of CIBERFES Program 2), Dr. Consuelo Borrás (University of Valencia), Dr. José Antonio Serra (Hospital Universitario Gregorio Marañón. Madrid) and Dr. Ignacio Ara (University of Castilla-La Mancha). Relevant topics for CIBERFES were addressed, such as "New mechanism of muscle repair after physiological damage. Importance in aging" by Dr. María del Carmen Gómez-Cabrera (University of Valencia), "Oxidative stress, sarcopenia and fragility" by Dr. Ana Coto (University of Oviedo), "Mitochondria and mtDNA in healthy aging" by Dr. José Antonio Enríquez (CNIC. Madrid), "ICT solutions and improvement of the quality of life of the elderly" by Dr. Rodrigo Pérez-Rodríguez (Fundación Investigación Biomédica de Getafe. Madrid), and the "DIABFRAIL-LATAM Project" by Dr. Leocadio Rodríguez-Mañas (Hospital Universitario de Getafe. Scientific Director CIBERFES). A total of 193 posters were presented at the Congress.

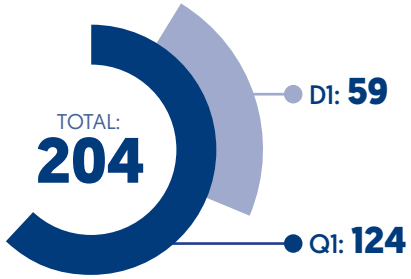
As regards specific group training activities, a stay was made at the University of Alberta, at The Metabolomic Innovation Center (TMIC), research seminars were held with Early Career Scientists within the framework of the European project of the Joint Programme Initiative HEalthy Diet for a HEalthy Life (INTIMIC), and we have participated in the Cajal School "Brain for Brain Function (BBF)", of the Bordeaux School of Neuroscience, held in Bordeaux (France) and in the 4th ISN-JNC Flagship School "Brain Metabolism in Health and Disease", held in Schmerlenbach (Germany). There has also been collaboration with the National Agency for Research and Development, Chilean Ministry of Science, Technology, Knowledge and Innovation in the "Strengthening of the International Network on Fragility Syndrome and Cardiovascular Risk in the Elderly". We have participated in the CIBERFES mobility program with international funding to support the work being done with Dr. Rafael de Cabo in Baltimore (NIA). Some groups have carried out Intra-area training stays. All the groups have carried out training activities in their work centers, have tutored doctoral theses, Master's theses and dissertations, have given national and international courses, have made presentations at national and international congresses and have participated in Master's degrees related to CIBERFES objectives.

The next CIBERFES face-to-face meeting will be held in Donostia on October 19-20, 2023, coordinated by Dr. Ander Matheu's group.

Scientific production

Publications

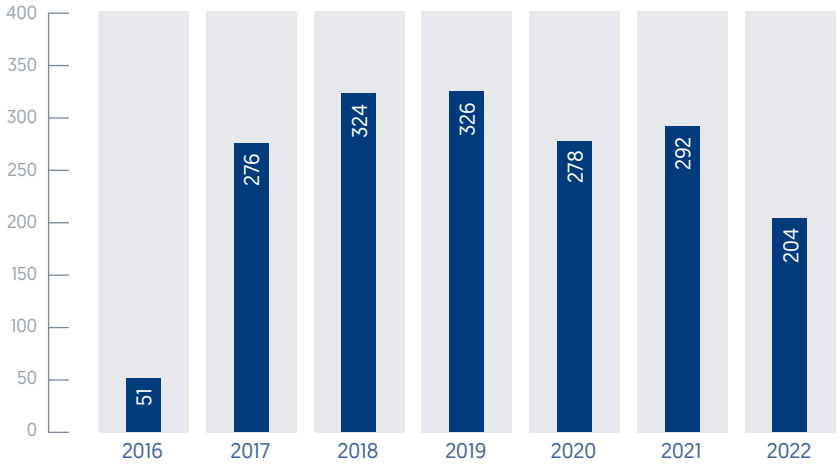
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
13,934	Revisiting skeletal myopathy and exercise training in heart failure: Emerging role of myokines
13,36	Analysis of Psychological Symptoms Following Disclosure of Amyloid-Positron Emission Tomography Imaging Results to Adults With Subjective Cognitive Decline
8,101	Metabolomic patterns, redox-related genes and metals, and bone fragility endpoints in the Hortega Study
7,802	Predictors of Maintained Transitions Between Robustness and Prefrailty in Community-Dwelling Older Spaniards
7,419	Plasma anthocyanins and their metabolites reduce in vitro migration of pancreatic cancer cells, PANC-1, in a FAK- and NF-kB dependent manner: Results from the ATTACH-study a randomized, controlled, crossover trial in healthy subjects
6,315	Insulin resistance in Alzheimer's disease: The genetics and metabolomics links
6,117	A mixture of four dietary fibres ameliorates adiposity and improves metabolic profile and intestinal health in cafeteria-fed obese rats: an integrative multi-omics approach
5,285	Dance as an Intervention to Improve Physical and Cognitive Functioning in Older Adults
4,638	Primary head and neck cancer cell cultures are susceptible to proliferation of Epstein-Barr virus infected lymphocytes
4,428	Alternative respiratory oxidases to study the animal electron transport chain

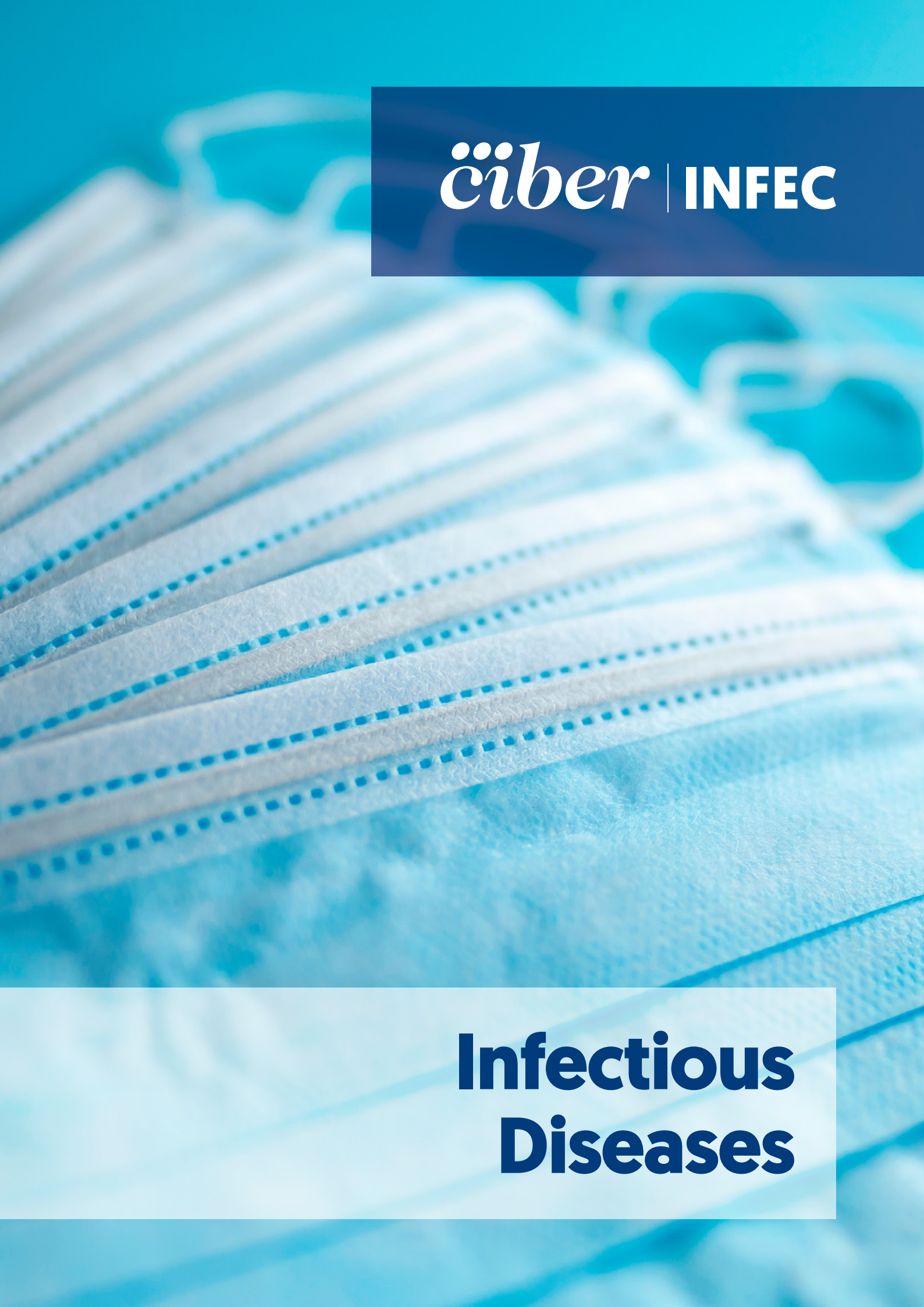
CIBERFES Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Abizanda Soler, Pedro	7	4	4	Servicio de Salud de Castilla-La Mancha	Albacete
Escames Rosa, Germaine	7	7	4	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO)	Granada
Andrés Lacueva, María Cristina	9	6	3	Universidad de Barcelona	Barcelona
Ara Royo, Ignacio	22	14	1	Universidad de Castilla-La Mancha	Ciudad real
Bolaños Hernández, Juan Pedro	4	2	2	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	Salamanca
Nogués Solan, Francesc Xavier	12	1	0	Consorci Mar Parc Salut de Barcelona	Barcelona
Enríquez Domínguez, José Antonio	11	8	6	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Arévalo Arévalo, María Angeles	5	4	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Garcia García, Francisco José	10	7	3	Fundación del Hospital Nacional de Parapléjicos	Toledo

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Izquierdo Redin, Mikel	35	20	11	Universidad Pública de Navarra	Navarra
Rol de Lama, María Ángeles	2	0	0	Universidad de Murcia	Murcia
Matheu Fernández, Ander	8	7	2	Asociación Instituto Biodonostia	Guipúzcoa
Grau Rivera, Oriol	18	12	12	Fundación Barcelonabeta Brain Research Center	Barcelona
Moreno Casbas, Teresa	6	2	0	Instituto de Salud Carlos III	Madrid
Muñoz Torres, Manuel	3	3	0	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO)	Granada
Priego Capote, Feliciano	3	2	1	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Rodríguez Mañas, Leocadio	18	12	6	Servicio Madrileño de Salud	Madrid
Serra Rexach, José Antonio	17	12	4	Servicio Madrileño de Salud	Madrid
Viña Ribes, José	21	15	4	Fundación Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia

Clinical Guidelines 2022

- Executive summary clinical practice guideline of postmenopausal, gluco-corticoid-induced, and male osteopo-rosis (2022 update)



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Infectious Diseases

Welcome from the scientific director

Jesús Oteo Iglesias

Dear friends, 2022 was the year in which the Center for Biomedical Research in Infectious Diseases Network (CIBERINFEC) was launched. This is an exciting initiative that promotes collaborative research of excellence in infectious diseases (ID), bringing together more than 550 scientists belonging to 46 research groups distributed throughout Spain.

Infectious diseases are one of the main health threats worldwide, and pose a great challenge to health systems. Every person suffers some infection during his or her lifetime; infections such as tuberculosis, AIDS, malaria, among many others, generate large epidemics; the increase in resistance to antimicrobials makes it difficult to treat infections that not long ago were easily cured; and the appearance of variants of known microorganisms means that some infections preventable by vaccination can re-emerge. The peculiarity of IDs is that they are produced by microorganisms, by beings capable of reproducing, adapting to the environment and evolving, and sometimes they are capable of doing so much faster than "higher" living beings, which gives them a characteristic of unpredictability for which we must be prepared. The COVID-19 pandemic is a clear example, as well as a stark reminder, of all this.

The creation of CIBERINFEC is therefore established as a necessary tool in the fight against these threats.

In this first year, CIBERINFEC has devoted a large part of its activity to generating structures, drawing up procedures and establishing the rules of operation and coordination. The research activity has been organized into four Scientific Programs that address the main health problems related to IDs such as global health, emerging and re-emerging infections (Program 1), antimicrobial resistance (Program 2), HIV/AIDS and sexually transmitted infections (Program 3), and infections in immunocompromised non-HIV patients and healthcare-associated infections (Program 4). In addition, a cross-cutting Training Program has been created.

Despite having had only a short time to develop, CIBERINFEC has also promoted different cross-cutting initiatives to support cooperative research during 2022. With barely six months under its belt, the first call for intramural projects was held, supporting seven collaborative projects with a total of 31 participating groups representing the four Scientific Programs. The general objective of the call was to foster cooperative research projects between translational researchers and clinical researchers from at least three CIBER research groups, as well as to promote the participation of young researchers.

In the spring of 2022, the WHO established the Monkeypox outbreak as an international public health emergency. In this context, CIBERINFEC initiated a specific transversal inter-program strategic action for an integrated and multidisciplinary approach to Monkeypox research in Spain. This is a CIBERINFEC initiative (15 participating groups), in collaboration with CIBERESP (seven groups), which establishes synergies with the Spanish Society of Infectious Diseases and Clinical Microbiology. It has been structured into five working packages: WP 1. Coordination, dissemination and translation; WP 2. Clinical research: WP 3. Epidemiological research; WP 4. Virological research; WP5. Harmonization of detection procedures.

CIBERINFEC approved a second cross-cutting strategic action during 2022 to conduct a pilot study on invasive Streptococcus pyogenes infections in children. This initiative was motivatedby the alert about the unusual increase of these infections in the United Kingdom, and the observation of a similar apparent trend in Spain.

At CIBERINFEC we want to contribute as much as possible to improving people's quality of life through excellent and practical cooperative research, and this is only possible with a comprehensive and multi-

disciplinary approach that promotes both personalized and precision medicine, as well as the integration of new technologies. With this strategy, in 2022 CIBERINFEC submitted a transversal proposal to the Call for Personalized Medicine Research Projects of the ISCIII with the participation of 31 research groups (29 from CIBER and 26 from CIBERINFEC) and representation of the four scientific programs of this thematic area. This proposal, entitled "Precision medicine against anti-microbial resistance: MePRAM Project", has been funded and its execution has already begun. The general objective of MePRAM is an integral and comprehensive approach to AMR aimed at integrating genomic technologies in the diagnosis of multidrug-resistant microorganisms, in order to optimize and personalize the clinical management and treatment of patients

Transversality in this type of initiative becomes a key element, as well as collaboration with other thematic areas of CIBER, but also with other public and private institutions and scientific societies as the only way to effectively fight against IDs. These collaborations have begun to be developed since the beginning of CIBERINFEC.

Finally, I would like to highlight CIBERINFEC's commitment to the dissemination of knowledge and the bridging of research with society. The involvement of society in science and research is simply indispensable. Science is not only part of society, but must also be directed primarily towards improving its conditions. We are all participants in science, and this is especially true and transcendent in the field of health.

Programs

Global Health, emerging and re-emerging infections

Agustín Benito Llanes

COORDINATOR

Cristina Calvo Rey

COORDINATOR

This program includes the participation of 31 of the 46 CIBERINFEC groups. Twelve of the groups were already working in collaboration as part of the former RICET network (Collaborative Research Network in Tropical Diseases) and therefore their synergies have been maintained. During 2022, the REDIVI network (Network of Hospital Units for the care of immigrants and travelers) continued its activities within CIBER, collecting information on the impact of infectious pathology imported into our country as a result of migration and international travel, and the National Registry of Leishmaniasis (ReNLeish) has been created, which reports its information to the World Health Organization (WHO); and has been included on its web page (https://leishinfowho-cc55.es/).

This Program has initiated different collaborative lines of research in different areas during 2022 such as:

- The development of rapid methods for bedside diagnosis of tuberculosis.
- The search for clinical or biological markers of severe COVID-19 infection or persistent COVID.
- Surveillance of arboviruses and their vectors which has led, for example, to the detection of the Aedes aegypti mosquito in the Canary Islands.

In addition, research groups of this Program have actively participated in the cross-cutting strategic action on the "Clinical and microbiological impact of the monkeypox virus outbreak in patients in Spain", coordinated by Mª Paz Sánchez Seco (National Microbiology Center).

Among the main scientific achievements of this Program in 2022 are:

- The use of nanoparticles loaded with a statin, pitavastatin, as a novel and effective therapeutic strategy for the treatment of keratitis caused by the amoeba Acanthamoeba.
- The usefulness of benznidazole to treat chronic Chagas disease in children; a strategy that, however, shows little effect in adults.
- The appearance of zoonoses and emerging infections, such as the discovery of Ortho- hepevirus C, which causes 2% of acute hepatitis of unknown origin.
- The characterization of the evolutionary bases of Fascioliasis, a zoonotic parasitic disease included by WHO in the list of priority neglected diseases, as well as its dissemination mechanisms.
- The impact of the basal state of the immune system on the response to the malaria vaccine, which has important implications for the implementation of the vaccine.
- The discovery of new biomarkers that explain the abnormal response of the immune system in children with bronchiolitis and wheezing triggered by respiratory viruses, in a collaboration between CIBERINFEC and CIBERES.
- A very important area for some of the groups of this program has been research related to SARS-CoV-2 infections. Some of the main contributions, among many others, of this program in this area have been:
  - The success of virus detection in wastewater for the prediction of successive pandemic waves in Galicia.
  - The characterization of the ACE2 protein in saliva as an indicator of poor prognosis of COVID, increased probability of infection and increased risk of severe disease in children and adults.

Our main objectives and what our research will focus on in the coming months will be mainly the study of the impact of tropical infections in Spain and worldwide, through our platforms abroad (Africa and Latin America) as well as the early detection of emerging viral or bacterial infections. Of course, we will also be studying biomarkers of infectious diseases, as well as the development of therapeutic targets for neglected tropical diseases or vaccines through our groups.

Antimicrobial Resistance

Jesús Rodríguez Baño

COORDINATOR

Rafael Cantón Moreno

COORDINATOR

In Program 2 of CIBERINFEC, Antimicrobial Resistance, 21 groups participate, 13 of them as a priority program and 8 as non-priority. Many of these groups were already working together in the former REIPI network (Spanish Network for Research in Infectious Pathology), thus maintaining the synergies established in the past and strengthened by the incorporation of new participants..

The program, with seven lines of work (https://www.ciberinfec.es/programas-de-investigacion/resistencia-a-antimicrobianos), has developed projects and obtained different scientific achievements which are summarized below::

- Participation in resistance surveillance programs at the national and international level, with the application of whole genome sequencing techniques, from state-of-the-

art platforms and bioinformatics programs with the description and monitoring of emerging resistance mechanisms in bacteria and fungi, the expression of resistance genes and their phenotypic recognition.

- Coordination and participation in the National Network of laboratories for the surveillance of resistant microorganisms (RedLabRA) for the integration of genomic sequencing in surveillance in collaboration with AEMPS.
- Securing private and foundation funding for projects with a OneHealth approach to resistance focused on the participation of the hospital environment and its relationship with infections caused by multiresistant bacteria.
- Development of antimicrobial use improvement programs in units with high antimicrobial use, long-stay centers, community infections. Antimicrobial prescribing performance programs from the patient perspective.
- Clinical transfer with the coordination of clinical guidelines:
  - European (ESCMID): for the treatment of multidrug-resistant Gram-negative bacilli infections (doi:10.1016/j.cmi.2021.11.025).
  - Spanish (SEIMC): on the diagnosis and treatment of Carbapenem-resistant Gram-negative microorganisms (doi:10.1016/j.eimce.2022.06.014).
- Internationalization with participation in proposals and development of projects funded by European agencies:
  - Joint programming initiative on Antimicrobial resistance (JPI-AMR) focused on the analysis of reservoirs and involvement of vehicles in the transmission of ESBL-producing enterobacteria, relevance of abiotic surfaces and hospital effluent in the transmission of carbapenemase-producing enterobacteria.
  - Innovative Medicines Initiative (IMI). Impact of the use of monoclonal antibodies and vaccines on resistance.
  - ERA-NET. Development of new surveillance strategies.
  - Horizon H2020. Identification of best practices, development and validation of interventions, infection prevention and clinical management plans against resistant bacterial infections in high prevalence settings.
- Participation in pre-commercial public procurement programs related to the diagnosis of multiresistant microorganisms.
- Development of new strategies in the modulation of the microbiota and use of vaccines against multidrug-resistant microorganisms, including M. tuberculosis.
- Participation in clinical trials of new antimicrobials and strategies for the use of known antimicrobials against multidrug-resistant bacteria.
- Leadership in clinical trials of diagnostic tests to improve the diagnosis of multidrug-resistant microorganisms.
- Development of vehicles in the treatment of opportunistic pathogens resistant to antimicrobial treatments.
- Development of artificial intelligence algorithms to interpret results in diagnostic systems.
- Development of alternative laboratory models (organoids, Galleria, hollow-fiber) for the study of infections caused by multidrug-resistant microorganisms.
- Development of sensors for the detection of multidrug-resistant microorganisms.

HIV/AIDS and sexually transmitted infections (HIV/AIDS and STIs)

Santiago Moreno Guillén

COORDINATOR

José Mª Miró Meda

COORDINATOR

The program committee has held five meetings during 2022, three via videoconference (March 24, June 30 and October 27) and two in person, one at the CIBERINFEC meeting on September 20 and the other at the GESIDA congress on November 29.

During these meetings, work has been done on the elaboration and approval of the strategic lines of P3, which are described below and to which the research groups must send their proposals for participation during the first quarter of 2023:

A) Structures; maintenance and development of structures to integrate clinical and epidemiological data.

In this line, the CoRIS cohort has been consolidated in CIBERINFEC. This cohort, which also has biological samples associated with clinical data in the Biobank of the Hospital General Universitario Gregorio Marañón in Madrid, has been included in a CIBERINFEC platform and will be called CoRIS-CIBERINFEC. This strategic action is of vital importance to maintain thescientific activity of CoRIS and the collaboration of the 22 associated clinical groups..

B) Epidemiology and Public Health.

Characteristics of the HIV epidemic, improvement of management and treatment, quality of life. This line is structured along the following work packages.

WP1. Epidemiological Studies.

WP2. Public Health Interventions.

WP3. Quality of life.

WP4. Evolution of infection according to different treatments.

WP5. Special groups: Pediatrics, adolescents, Trans patients, patients with high degree of frailty, patients with social exclusion.

C) Senescence and co-morbidities.

This line addresses issues such as the early development of pathology associated with aging and comorbidities (cardiovascular disease, cancer, fatty liver, others). As an example, a specific collaborative project initiated in 2022 is the development of a predictive model of fatty liver disease progression in HIV-infected patients.

WP1. Epidemiological.

WP2. Clinical. Associated diseases and co-morbidities.

WP3. Biomarkers.

WP4. Pathogenic mechanisms.

WP5. Senolytic treatments.

D) Co-infections and new infections.

This line includes aspects such as the COVID observatory and immunosuppressed patients and HIV-hepatitis virus co-infection. In addition, this program has actively participated in the cross-cutting strategic action on Monkeypox in coordination with WP1 with the researchers José Luis Blanco (Hospital Clínic de Barcelona) and Vicente Estrada (Hospital Clínico San Carlos de Madrid).

E) PREP and sexually transmitted infections. PREP implementation and consequences.

This strategic line is structured along the following work packages:

WP1. Creation and analysis of PREP cohorts.

WP2. Epidemiology. Impact on new cases and evolution of the epidemic. WP3. Virological studies in PREP escape/failure.

F) Cure.

Control of HIV replication, reservoirs and treatment strategies. The groups of this CIBERINFEC Program have LTNP and EC cohorts of high biological value that can be exploited at different levels.

WP1. Description and analysis of the EC and LTNP cohorts.

WP2. Clinical evolution. Studies on loss of control.

WP3. Virological mechanisms of infection persistance.

WP4. Immunological studies.

WP5. Clinical trials. Therapeutic vaccines, immuno- modulating treatments.

G) Preventive vaccines.

This line is structured along the following work packages.

WP1. Experimental models.

WP2. New prototypes.

WP3. Immunological and virological techniques for vaccine evaluation.

WP4. Clinical trials.

Infections in non-HIV immunosuppressed patients and healthcare-associated infections

José Mª Aguado García

COORDINATOR

Jordi Carratalá Fernández

COORDINATOR

This Program consists of two basic lines of research: a) Infections in immunocompromised non-VIH patients: solid organ transplantation, hematopoietic progenitor transplantation, onco-hematological patients, invasive fungal infection and immunocompromised pediatric patients and b) Healthcare-associated infections.

Among the main scientific achievements of this Program in 2022 are:

- Development of different biomarkers that allow the diagnosis of latent infection with Leishmania spp. of special interest in the immunocompromised patient.
- Role of Torque tenovirus as a marker of immunosuppression in children and adults.
- Studies on the importance of infection by multidrug-resistant bac-

teria focused on oncohematological patients and multinational intervention studies on SARS-CoV-2 infection.

- Contributions on the role of antibodies against type I interferons, not only in the control of SARS-CoV-2 infection, but also in the control of influenza virus infection. In addition, other relevant contributions have been made regarding the impact of RNAemia in COVID-19.
- Management of bacteremic osteoarticular infection caused by Staphylococcus aureus.
- Evolution of transplanted patients with COVID-19 and the immunological response of these patients.
- Role of different biomaterials and nanosystems in osteoarticular infection and in studies aimed at counteracting the action of biofilm and the antimicrobial effect of these materials.
- Trials aimed at improving the management of infection in transplant patients by monitoring cellular response. As well as the study of infection by multidrug-resistant bacteria in solid organ transplant recipients.
- Relevant contributions in the field of Streptococcus pyogenes infection.
- Studies on gliatoxin production in different fungi that open the door to new diagnostic and therapeutic targets for invasive fungal infection in immunocompromised patients.
- Defining a series of specific immune signatures to differentiate COVID19 from other infections that allow predicting the severity of the disease and the risk of death.
- Understanding the role of certain substances, such as hypochlorite, and physical measures, such as hyperthermia, on biofilm development and response to infection in animal models.
- Treatment of invasive aspergillosis in the solid organ transplant patient, as well as on different aspects of genetic risk (SNP polymorphisms) of various viral infections (CMV, BK virus, Torque tenovirus) and development of bio-markers to define the risk of infection and rejection in transplant recipients.
- Multicenter study on the consequences of infection by nontuberculous mycobacteria in solid organ transplant patients.
- Development of azole resistance both in Candida (especially related to Candida parapsilosis) and Aspergillus and in the analysis of genetic aspects that measure the risk of developing invasive infection by Aspergillus in immunocompromised population.
- Contributions in the field of epidemiology and genetics of bacterial resistance. Improved knowledge of Aspergillus spp infection in patients with solid organ transplantation.
- Behavior of infectious endocarditis in different situations (patients with multivalvular disease, elderly patients, children, etc.).
- Role of oxidative stress and lipid peroxidation in sepsis and the usefulness of different biomarkers. In addition, the role of genetic variants in the risk of sepsis was evaluated.

Strategic actions and intramural projects

Antonio Oliver

COORDINATOR

1. Strategic actions

a) Monkeypox Strategic Action (MPXV). Clinical and microbiological impact of the monkeypox virus outbreak in patients in Spain (2022).

This action arose as a result of a case of MPXV infection from Nigeria in the United Kingdom, and the subsequent significant increase in the notification of cases in Spain. The situation experienced since the first detection in our country prompted hospitals and/or laboratories of different health institutions to develop working protocols and methods for screening patients and detecting the virus in order to diagnose, treat and implement control measures to contain the spread of the infection.

Consequently, CIBERINFEC considered the need to provide knowledge on aspects related to the response of the infected patient, the evolution and adaptation of the virus in its new environment and the methodology to be used to fight it. This objective is in line with CIBERINFEC's mission, which is to contribute to improving the health of society by reducing the negative impact of infectious diseases on the individual health of people and on the general health status of the population.

b) Strategic action *Streptococcus pyogenes*. Pilot study on severe invasive *S. pyogenes* infections in children.

In the United Kingdom, there was an unusual overall increase in S. pyogenes infections in the autumn-winter of 2022, from 186 to 851 cases in the same period, with a predominance of the usual non-invasive upper airway infections. However, at the same time, an increase in invasive infections by this bacterium was observed in children under 10 years of age.

The increase in invasive infections could be due to several causes, such as the increased circulation of more virulent strains, influenza and RSV epidemics that coincided in the same time period, which could favor bacterial superinfection, or simply to the increase in cases of non-invasive S. pyogenes infection, with the consequent increase in severe cases. The latter could be related to a special susceptibility of the host to a new strain (immunological or genetic) or to a decrease in herd immunity, perhaps due to distancing and isolation measures.

Therefore, the objective of this strategic action has been to provide an agile response by identifying the cases of invasive S. pyogenes infection in our country, comparing it with the incidence and clinical severity of previous years, characterizing the strains involved, and analyzing the host immune response.

2. Intramural Projects

In 2022, the first year of CIBERINFEC, the first call for intra- mural projects was made through which seven collaborative projects have been funded with a total of 31 participating groups. The general objective was to promote collaborative research projects between translational researchers and clinical researchers from at least three CIBER research groups; as well as to promote the participation of young researchers.

The projects funded were the following:

a) Study of the mechanism of action of cyclic peptides (CP1 and CP3) as potential inhibitors of active efflux pumps in *Pseudomonas aeruginosa*.

We will study the efficacy of two cyclic peptides as potential inhibitors of active expulsion pumps in multidrug-resistant *Pseudomonas aeruginosa* strains.

b) Biomarkers and underlying immunopathological mechanisms of post COVID-19 condition.

We aim to identify biomarkers of Post-COVID to improve diagnosis and provide com- prehension about the underlying mechanisms of this condition, with the ultimate goal of targeting treatment goals and interventions to improve patient management and quality of life.

c) Surveillance of emerging vectors and arboviruses in an insular system.

Monitoring of the possible introduction of invasive mosquitoes in an insular system in order to study vectors transmitting viral diseases.

d) Impact of multi-resistance to antibiotics in Intensive Care Units: MURAN-ICU Project.

Prospective, multicenter, multidisciplinary study in 7 hospitals to evaluate the prevalence and clinical impact of multi-resistant bacteria to antibiotics in ICU patients and environment. The study will focus on carbapenemase-producing Enterobacteriaceae, ESBL-producing Klebsiela pneumoniae, and carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter spp.* according to WHO priorities.

e) Development of a predictive model of fatty liver disease progression in HIV-infected patients.

The aim is to develop a predictive model that identifies people living with HIV (PLWHIV) with a higher probability of progressing to steatohepatitis with a risk of clinical progression.

f) Validation in immunosuppressed patients of clinical phenotypes with prognostic value of COVID-19. Its association with the presence of viremia and immune response in the first evaluation of patients.

Study the incidence of COVID-19 in patients with hematologic and solid malignancies receiving chemotherapy or CAR-T therapy, and in solid organ or hematopoietic stem cell transplant recipients, determine its impact on the clinical outcome of these patients, and validate in these patients the usefulness of clinical phenotypes already validated in the general population.

g) Exploring new point of care methods for the diagnosis of tuberculosis. A combination approach.

Development of an algorithm for improved diagnosis by combining rapid molecular techniques with classical ones in low and high prevalence tuberculosis settings.

Training

Mª del Carmen Fariñas Álvarez

COORDINATOR

The main objective of the CIBERINFEC Training program in 2022 has been to promote training in the field of infectious diseases, especially aimed at young researchers with the aim of training future scientific leaders in this field.

During this first year, the bases and forms for the application, evaluation and awarding of training grants have been prepared. In addition, the CIBERINFEC scientific sponsorship regulations have also been established.

Eight sponsorships have been granted for scientific activities, proposed by one or several CIBERINFEC groups and financed by public or private entities, with the aim of favoring the dissemination of scientific progress in infectious diseases and microbiology.

The training grants have been developed along three general lines:

A. Mobility grants, financing short-term stays (between 1 and 6 months) outside the place of residence, for learning techniques or planning and carrying out projects in collaboration with other national or international groups.
B. Registration or enrollment in courses or training activities (except for congresses, presentation sessions or other similar events).
C. Travel grants to attend courses or training activities outside the usual place of residence.

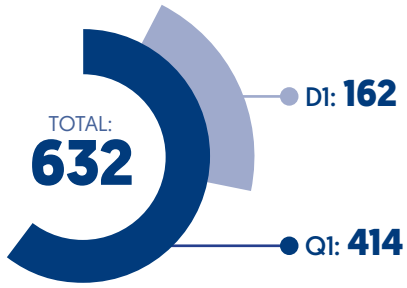
Seven mobility grants were financed (Ohio University, Queen's University, Leiden University, Rotterdam University, University of the Republic of Uruguay), five course registrations and one travel grant to attend a face-to-face course.

Finally, work has been carried out in collaboration with CIBERES on the design of a joint conference for young researchers to be held in 2023.

Scientific production

Publications

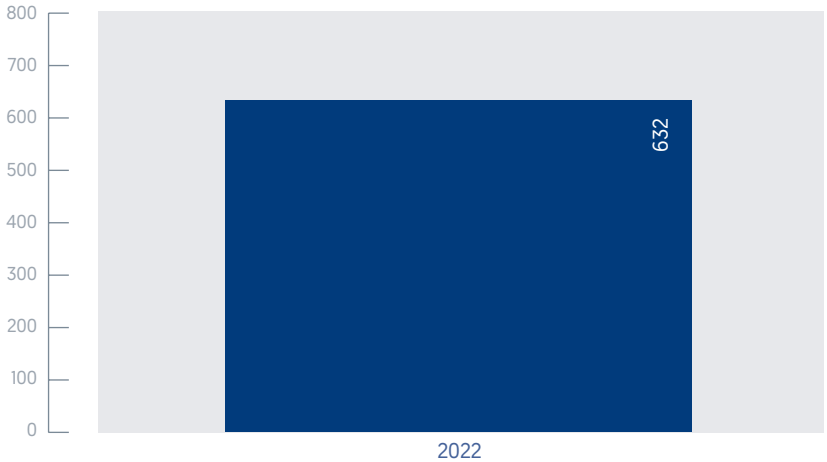
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
202,731	Thornhill J.P., Palich R., Ghosn J., Walmsley S., Moschese D., Cortes C.P. et al. Human monkeypox virus infection in women and non-binary individuals during the 2022 outbreaks: a global case series. The Lancet. 2022;400(10367):1953-1965.
176,082	Thornhill J.P., Barkati S., Walmsley S., Rockstroh J., Antinori A., Harrison L.B. et al. Monkeypox Virus Infection in Humans across 16 Countries - April-June 2022. New England Journal of Medicine. 2022;387(8):679-691.
87,244	Gunst J.D., Pahus M.H., Rosas-Umbert M., Lu I.-N., Benfield T., Nielsen H. et al. Early intervention with 3BNC117 and romidepsin at antiretroviral treatment initiation in people with HIV-1: a phase 1b/2a, randomized trial. Nature Medicine. 2022;:-.
87,244	Bailon L., Llano A., Cedeno S., Escriba T., Rosas-Umbert M., Parera M. et al. Safety, immunogenicity and effect on viral rebound of HTI vaccines in early treated HIV-1 infection: a randomized, placebo-controlled phase 1 trial. Nature Medicine. 2022;:-.
86,208	Hernaez B, Muñoz-Gómez A, Sanchiz A, Orviz E, Valls-Carbo A, Sagastagoitia I et al. Monitoring monkeypox virus in saliva and air samples in Spain: a cross-sectional study.The Lancet. Microbe. 2022;:-.
73,082	Calleja J.L., Aguilera A., Buti M., Crespo J., Garcia F., Jorquera F. et al. Ten steps to eliminating hepatitis C in hospitals. Nature Reviews Gastroenterology and Hepatology. 2022;19(8):481-483.
71,421	Monge S., Rojas-Benedicto A., Olmedo C., Mazagatos C., Jose Sierra M., Limia A. et al. Effectiveness of mRNA vaccine boosters against infection with the SARS-CoV-2 omicron (B.1.1.529) variant in Spain: a nationwide cohort study. The Lancet Infectious Diseases. 2022;22(9):1313-1320.
71,421	Daubenberger C.A., Moncunill G.. Next-generation malaria subunit vaccines to reduce disease burden in African children. The Lancet Infectious Diseases. 2022;22(12):1655-1656.
69,504	Zhang Q., Bastard P., Karbuz A., Gervais A., Tayoun A.A., Aiuti A. et al. Human genetic and immunological determinants of critical COVID-19 pneumonia. Nature. 2022;603(7902):587-598.
68,164	Schwarz M., Torre D., Lozano-Ojalvo D., Tan A.T., Tabaglio T., Mzoughi S. et al. Rapid, scalable assessment of SARS-CoV-2 cellular immunity by whole-blood PCR. Nature Biotechnology. 2022;40(11):1680-1689.

CIBERINFEC Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Aguado Garcia, José María	29	18	6	Servicio Madrileño de Salud	Madrid
Alcami Pertejo, José	20	15	4	Instituto de Salud Carlos III	Madrid
Almirante Gragera, Benito	34	19	10	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Arribas López, José Ramon	39	24	16	Servicio Madrileño de Salud	Madrid
Bargues Castelló, María Dolores	6	3	1	Universidad de Valencia	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Benito Llanes, Agustín	9	6	3	Instituto de Salud Carlos III	Madrid
Bou Arevalo, Germán	11	10	1	Servicio Gallego de Salud	Coruña, A
Calvo Rey, Cristina	43	27	8	Servicio Madrileño de Salud	Madrid
Cantón Moreno, Rafael	51	35	9	Servicio Madrileño de Salud	Madrid
Carratala Fernández, Jordi	50	20	8	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	Barcelona
Castilla Castrillón, Joaquin	3	3	0	Asociación Centro de Investigación Cooperativa en Biociencias, CIC BIOGUNE	Vizcaya
Cisneros Herreros, José Miguel	22	14	7	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
De Los Santos Gil, Ignacio	9	6	3	Servicio Madrileño de Salud	Madrid
Dobaño Lazaro, Carlota	30	20	7	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	Barcelona
Esteban Moreno, Jaime	22	16	3	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Estrada Pérez, Vicente	6	4	3	Servicio Madrileño de Salud	Madrid
Fariñas Álvarez, María del Carmen	19	6	2	Instituto de Investigación Marques de Valdecilla	Cantabria
Gabaldón Estevan, Juan Antonio	11	8	3	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Garcia Garcia, Federico	15	11	6	Fundación Pública Andaluza para la Investigación Biosanitaria de Andalucía Oriental – Alejandro Otero (FIBAO)	Granada
Gascon Brustenga, Joaquim	13	9	4	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	Barcelona
Gómez Rodriguez, Carmen Elena	10	9	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Gutierrez Rodero, Felix	10	7	3	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	Alicante
Horcajada Gallego, Juan Pablo	14	8	2	Consorci Mar Parc Salut de Barcelona	Barcelona
Jarrin Vera, Inmaculada	21	7	6	Instituto de Salud Carlos III	Madrid
Llor Vila, Carles	5	1	1	IDIAP Jordi Gol	Barcelona
Lorenzo Morales, Jacob	14	10	3	Universidad de La Laguna	Santa Cruz De Tenerife
Martínez Picado, Javier	39	31	13	Fundación Instituto de Investigacion Germans Trias i Pujol	Barcelona
Mellado Terrado, Emilia	5	4	1	Instituto de Salud Carlos III	Madrid
Miró Meda, José María	20	10	5	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Molina Romero, Israel	14	9	5	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Moreno Guillén, Santiago	28	22	8	Servicio Madrileño de Salud	Madrid
Moreno Nuncio, Francisco Javier	12	6	4	Instituto de Salud Carlos III	Madrid
Navarro Gómez, María Luisa	35	22	5	Servicio Madrileño de Salud	Madrid
Oliver Palomo, Antonio	27	20	4	Fundación Instituto de Investigación Sanitaria Illes Baleares (IdISBa)	Illes Balears
Oteo Iglesias, Jesús	9	8	4	Instituto de Salud Carlos III	Madrid
Pardo Jimeno, Julian	11	8	1	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Peraire Forner, José Joaquín	9	7	1	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona
Pérez Molina, José Antonio	6	6	4	Servicio Madrileño de Salud	Madrid
Pineda Vergara, Juan Antonio	12	8	6	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Resino García, Salvador	30	21	11	Instituto de Salud Carlos III	Madrid
Rivero Roman, Antonio	32	26	19	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Rodríguez Baño, Jesús	34	18	9	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Sánchez-Seco Fariñas, Maria Paz	10	6	5	Instituto de Salud Carlos III	Madrid
Tamayo Gómez, Eduardo	17	10	2	Hospital Clínico Universitario de Valladolid	Valladolid
Torre Cisneros, Julián Carlos	26	16	2	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Vila Estapé, Jordi	12	7	3	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	Barcelona

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Neurodegenerative Diseases

Welcome from the scientific director

Adolfo López de Munain Arregui

Dear colleagues,

At the end of 2022 and with COVID beginning to be a bad distant memory, it is time to take stock of a year which we can consider a year of transition for CIBERNED since it is our first year integrated into the CIBER structure. Changes always pose difficulties that we have tried to resolve to the best of our ability and we cannot fall into the complacency of believing that the whole transition has been carried out perfectly. We have regulations such as the labor legislation that binds us and adds to the usual administrative-bureaucratic nightmares typical of the Spanish administration and which we cannot avoid. Surely in 2023, with budgets in line with a way of spending in accordance with current regulations and the ways and practices of CIBER, we hope that the number of incidents will be lower

From a scientific point of view, the postponed Global Summit was held in Salamanca and was a scientific and social success with a great media impact in the city that made it worth the wait. Thanks to all those who in the previous years helped to build this forum, which was possible in the midst of many difficulties. It is now time to prepare the new path of CIBERNED and plan how our own meetings will work, keeping some traditions such as the online seminars that we began during the pandemic and that Teresa Iglesias continues to organize with exemplary dedication. We are currently setting up together with the CIEN Foundation and the Spanish Society of Neurology an attractive scientific program for September 19-22 in Malaga.

As an institution, CIBERNED closes 2022 with more than commendable numbers that attest to its scientific trajectory and which are reflected in this report.

In relation to the objectives for 2023, we will strengthen our relationship with clinical institutions and patient associations through agreements in order to comply with one of the requests of the Instituto de Salud Carlos III to increase the visibility of research.

2022 was also a year of farewells and welcomes. We bid farewell to Pura Muñoz who is moving to a prestigious laboratory on aging in the United States and to Isidre Ferrer due to retirement. Our eternal gratitude for their contributions over many years to CIBERNED and to Spanish science. The doors of our center and its meetings will always be open to you.

We also welcome the arrival of Tomas Sobrino to Program 1 and the group of researchers who form a transversal line around program 4 on Neuroinflammation and Neurodegeneration, namely David Otaegui, Manel Comabella and Diego Clemente. We look forward to all of your valuable contributions from novel scientific angles that will enrich the scientific wealth of our Institution.

I would like to end by congratulating all the CIBERNED researchers who received awards and distinctions from different organizations over the past year and who contribute to making the work of the center more visible. I hope that 2023 will be full of new triumphs, good luck and see you in Malaga!

Programs

Alzheimer's Disease and other degenerative dementias

Alberto Lleó

COORDINATOR

Eva Carro

COORDINATOR

In 2022, important scientific work has been carried out in this program focused on improving the diagnosis and treatment of patients with Alzheimer's disease and other dementias. Progress has also been made in the identification of new genetic risk factors associated with Alzheimer's disease through international multicenter projects. These advances have also made it possible to identify new therapeutic strategies.

The importance of the early diagnosis of Alzheimer's disease was also highlighted at the Global Summit.

NEURO 2020-22 was held in Salamanca and was chaired by Queen Sofia and attended by Queen Silvia of Sweden, as well as by relevant international researchers in the field of neurodegenerative diseases, such as Prof. Thomas C. Sudhof, Nobel Laureate in Medicine in 2013.

It should also be noted that Dr. Pura Muñoz-Cánoves, principal investigator of CIBERNED, has been awarded the Santiago Ramón y Cajal National Prize in the area of Biology, granted by the Ministry of Science and Innovation in recognition of her scientific contributions in the field of tissue regeneration. Dr. María Llorens Martín, principal investigator of CIBERNED at the "Severo Ochoa" Molecular Biology Center (CBMSO) was awarded the Pfizer Scientific Innovation Award in the basic research category and the Translational Medical Research Award of the Royal National Academy of Medicine 2022 for her research entitled "Impact of neurodegenerative diseases on human adult hippocampal neurogenesis".

In summary, the program has obtained outstanding results in the basic, translational and clinical areas, with discoveries that have great potential for clinical application.

Parkinson's Disease and other neurodegenerative movement disorders

José Javier Lucas

COORDINATOR

José Ángel Obeso*

COORDINATOR

The most relevant results and milestones of the program during 2022 have resulted in high impact publications and patents, and in the participation in and promotion of clinical trials.

Regarding Parkinson's disease, a study was conducted at HM-CINAC in a cohort with focal motor signs and scarce symptomatology, demonstrating focal onset of striatal dopaminergic denervation in the posterior and central region of the putamen, corresponding to the somatotopic representation of the upper extremity, where motor symptoms were initiated in 80% of the patients studied (Pineda-Pardo et al 2022). Another study described that the application of magnetic stimulation (TMS) on the pre-supplementary area improves the inhibitory response to sexual stimulation in the group with impulsivity in the form of hypersexuality associated with dopaminergic drugs. This work describes a cortico-basal ganglia network associated with hypersexuality in Parkinson's disease and outlines possible non-pharmacological therapeutic applications (Mata-Marín et al 2022). In addition, an MR tractography study of the subthalamic nucleus (STN) describes, for the first time in humans, the somatotopic organization of the motor region of the STN, distinguishing the connection between primary motor area and supplementary motor area. Finally, a correlation between clinical response to subthalamotomy and the functional anatomy of the nucleus has been described (Rodriguez-Rojas et al 2022). A new study describes a compound that inhibits the interaction between transcription factor NRF2, master regulator of multiple neuroprotective processes, and its repressor beta-TrCP, with the aim of developing a medicinal chemistry program that allows the use of a compound optimized therefrom for the treatment of Parkinson's disease (Fernández-Ginés et al 2022). In order to predict the risk of developing impulse control disorders (ICD) in Parkinson's disease, it was shown that, in the absence of an established ICD, patients who develop them in the future already present a different neurophysiological activity beforehand, with the extent of this component being a clear risk marker (Marín-Lahoz et al 2022).

In a collaborative study in which extracts of synuclein-positive glial cytoplasmic glial inclusions from the brains of patients with Multiple System Atrophy were injected into the striatum of experimental primates, it was found that, after 2 years, there was nigrostriatal loss, reduced oligodendrocyte activity and striatal inflammation. This study demonstrates for the first time the generation of pathology with features similar to multisystem atrophy in primates. (Teil et al 2022).

As for Huntington's disease (HD), while the structural changes accompanying progression are well known, the architecture of neuronal networks and their disruption is less well known in this disease. One study showed that HD associates a progressive alteration of connectivity between certain nodes of the default neural network and the salience network, these parameters being clearly related to the pathological burden of the disease. In turn, it was shown that certain parameters such as inter-network variability is already decreased during the pre-symptomatic phase before there is structural damage (Aracil-Bolaños et al 2022).

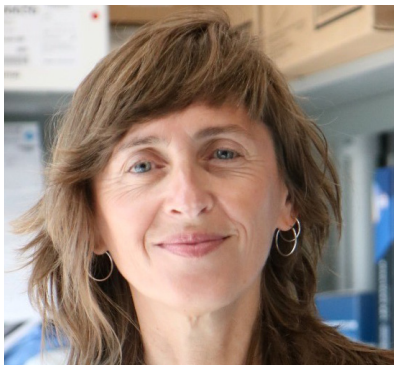
Furthermore, a study on the mechanisms of cellular oxygen sensitivity showed that the integrity of the mitochondrial electron transport chain (ETC) is essential for the process of O2 regulation of breathing and described the way in which the lack of O2 stimulates the respiratory center. It is also shown that the ETC of glomus cell mitochondria can use alternative electron acceptors to O2, which explains their resilience to hypoxia (Cabello-Rivera et al 2022).

- Aracil-Bolaños I, Martínez-Horta S, González-de-Echávarri JM, Sampedro F, Pérez-Pérez J, et al. 2022. Structure and Dynamics of Large-Scale Cognitive Networks in Huntington's Disease. Mov Disord 37: 343-53

* Until May 31 and replaced by Dr. Pablo Mir on July 5

- Cabello-Rivera D, Ortega-Sáenz P, Gao L, Muñoz-Cabello AM, Bonilla-Henao V, et al. 2022. Oxygen regulation of breathing is abolished in mitochondrial complex III-deficient arterial chemoreceptors. Proc Natl Acad Sci U S A 119: e2202178119
- Fernández-Ginés R, Encinar JA, Hayes JD, Oliva B, Rodríguez-Franco MI, et al. 2022. An inhibitor of interaction between the transcription factor NRF2 and the E3 ubiquitin ligase adapter β-TrCP delivers anti-inflammatory responses in mouse liver. Redox Biol 55: 102396
- Marín-Lahoz J, Martínez-Horta S, Pagonabarraga J, Horta-Barba A, Aracil-Bolaños I, et al. 2022. Predicting Impulse Control Disorders in Parkinson Disease through Incentive Biomarkers. Ann Neurol 92: 974-84
- Mata-Marín D, Pineda-Pardo J, Michiels M, Pagge C, Ammann C, et al. 2022. A circuit-based approach to modulate hypersexuality in Parkinson's disease. Psychiatry Clin Neurosci
- Pineda-Pardo JA, Sánchez-Ferro Á, Monje MHG, Pavese N, Obeso JA. 2022. Onset pattern of nigrostriatal denervation in early Parkinson's disease. Brain 145: 1018-28
- Rodriguez-Rojas R, Pineda-Pardo JA, Mañez-Miro J, Sánchez-Turel A, Martínez-Fernández R, et al. 2022. Functional Topography of the Human Subthalamic Nucleus: Relevance for Subthalamotomy in Parkinson's Disease. Mov Disord 37: 279-90
- Teil M, Dovero S, Bourdenx M, Arotcarena ML, Camus S, et al. 2022. Brain injections of glial cytoplasmic inclusions induce a multiple system atrophy-like pathology. Brain 145: 1001-17.

ALS and other neuromuscular disorders



Rafael Fernández Chacón

COORDINATOR

Carmen Paradas

COORDINATOR

The "Neuroplasticity and Regeneration" group at the Autonomous University of Barcelona (UAB) has continued its research activity in the areas of neuroprotection, motor neuron diseases, neuropathies, nerve regeneration and neural trauma. Among the results obtained, of note are the gene therapy trials to over-express klotho in the animal model of ALS, and the studies of new sigma1 receptor ligands to prevent motor neuron death and promote axonal regeneration, which have resulted in two patents. Other significant research has been on the contribution of the inflammatory response in platinum-induced neuropathy, the activity of regulators of the inflammatory response in neural trauma and demyelinating diseases, and the use of decellularized grafts to repair clinically applicable nerve lesions.

Dr. Carmen Paradas' group at the Biomedicine Institute of Seville has been involved in the clinical analysis of different forms of ALS, specifically in the characterization of the cohort of patients with familial ALS associated with mutations in the SOD1 gene in Spain, analyzing the impact of different phenotypic and genotypic features on the natural history of the disease (Vazquez-Costa et al, European Journal of Neurology 2023), as well as a form of sporadic FUSopathy (García-Roldán et al. BMC Neurology 2023). Through participation in the largest natural history study in muscular dystrophies, follow-up data in key dysferlinopathies have been established for the development of future clinical trials (Moore et al, Neuromuscular Disorders 2023; Moore et al, Muscle&Nerve 2022; Moore et al. Journal of cachexia, sarcopenia and muscle, 2022). As part of the multicenter follow-up of patients with mitochondrial myopathy due to thymidine kinase-2 deficiency, the group has led the description of the

muscle MRI pattern, useful as a diagnostic and follow-up tool in these patients (Domínguez-González et al, Journal of Neurology. 2022).

In 2022, three doctoral theses directed by Dr. Paradas have been defended in the field of ALS (Dr. Yolanda Morgado), muscular dystrophies (Dr. Pilar Carbonell) and neuropathology (Dr. Rainiero Ávila).

The most relevant results and milestones of the program of the group led by Dr. López de Munain during 2022 have been translated into high impact publications, patent extension, and the participation and promotion of clinical trials. The molecular mechanisms underlying the phenotypes associated with myotonic dystrophy type 1 (DM1) remain largely unknown. Along these lines, Garcia-Puga's study, JCI Insight 2022, has identified the accumulation of cellular senescence as part of the pathophysiology of DM1 and has linked this fact to the efficacy of senolytic compounds in the preclinical setting. Specifically, the study demonstrates that the compounds Quercetin, Dasatinib and Navitoclax selectively eliminate senescent cells, decrease the expression of senescence-related factors and reverse the accelerated aging phenotype in both DM1 fibroblasts in vitro and in Drosophila in vivo. Also in relation to DM1, Garcia-Puga's review, Int J Mol Sci 2022, links metformin to an improvement in the disease phenotype, with promising preclinical and clinical results and an ongoing phase III clinical trial. Metformin is a widely used compound in patients with type 2 diabetes mellitus (T2DM) without serious adverse effects. However, metformin exerts benefits beyond T2DM, being able to reverse defects in alternative splicing in DM1 samples in vitro and in vivo and is able to reduce the risk of developing cancer in patients with DM1, as well as increase the functionality and mobility of patients with DM1.

Regarding calpain-3-related limb-girdle muscular dystrophy R1 (LGMDR1), the possible contribution of the ubiquitin-proteosome pathway to increased SERCA degradation has been investigated (Lasa-Elgarresta, Front CellDevBiol 2022). Consistent with previous results, human CAPN3-deficient myotubes were observed to exhibit reduced levels of SERCA protein and high cytosolic calcium concentration. Treatment with the proteosome inhibitor bortezomib (Velcade) increased SERCA2 protein levels and normalized intracellular calcium levels in CAPN3-deficient myotubes. Knock-out mice for CAPN3 (C3KO) were observed to exhibit SERCA deficits in skeletal muscle early in the disease, prior to the manifestation of muscle deficits. Overall, the results of this study lay the groundwork for exploring inhibition of the ubiquitin-proteosome pathway as a novel therapeutic target to treat patients with LGMDR1.

Moreover, the group led by Dr. Rosario Osta has described for the first time that the reduction of the levels, but not the absence, of Granzyme A (gzmA), a serine protease involved in the modulation of the inflammatory immune response and increased in serum of ALS patients, could improve disease progression in the animal model SOD1G93A (Moreno-Martínez et al., Int J Mol Sci, 2022). In addition, they coordinated the meeting on "Non-coding RNAs in MND/ALS" at ENCALS 2022 and their use as diagnostic and prognostic biomarkers in ALS patients.

Similarly, Rafael Fernández Chacón's group, focused on the molecular mechanisms of nerve terminal maintenance, has generated genetically modified mice that recapitulate key pathological features of a devastating neurodegenerative disease, Kufs disease, or CLN4, which is an adult autosomal dominant neuronal ceroid lipofuscinosis. These new models have opened perspectives for understanding the molecular mechanisms of the disease and could be used in the context of therapeutic strategies for the reversal of the pathology found.

Throughout 2022, Dr. Ana Martinez's group has continued to work on modulating TDP-43 as a therapeutic strategy for ALS and other TDP-43-pathologies (frontotemporal dementia and Alzheimer's disease, predominantly) (Nozal V, J Med Chem. 2022; Cuevas EP, Biomedicines. 2022; Maestro I, Int J Mol Sci. 2022; Lastres-Becker I, Biomolecules 2022; Martín-Cámara O, J Med Chem. 2022). They have thus demonstrated the recovery of functional homeostasis of TDP-43 in cellular and animal models after treatment with tau and tubulin quinase 1 (TTBK1) inhibitors. They have also described the pathology of TDP-43 in samples of Alzheimer's patients, with a severity directly proportional to the loss of cognitive abilities in the patient, and the prion-like behavior of TDP-43 in these samples with the consequent cell-to-cell spread of the disease. In addition, they have developed mitophagy modulators that have a neuroprotective role in several ALS models and can be used in different familial variants of this pathology. In collaboration with another CIBERNED group, they have also defined the role of NRf2 in ALS and FTD, as well as the therapeutic role of fasudil derivatives with NRf2 activity.

Dr. Abraham Acevedo's group has continued working on the generation of mouse strains as close as possible to human ALS pathology, generating new strains of genomically humanized mice that carry pathogenic knock-in (KI) mutations in TDP-43. These are the first mice worldwide that express only human TDP-43 with pathogenic mutations, without expressing the endogenous mouse TDP-43 gene, allowing us for the first time to study the functional consequences of human mutations, and in particular the possible involvement of mutations in the loss of TDP-43 function, in the context of an animal model.

Finally, in 2022, the group led by Dr. Jon Infante has characterized early vs. late-onset ALS patients within their region over the last 30 years by identifying new prognostic factors. Also, through an ALSGESCO collaboration, they have participated in the genotypic-phenotypic description of the ALS spectrum secondary to SOD1 mutations in our country. In the context of the international ESMI Consortium, they have carried out a longitudinal follow-up of a cohort of 243 patients with SCA3 contributing to the identification of clinical and molecular biomarkers. In addition, they have contributed to the characterization of the phenotypic spectrum of CANVAS syndrome associated with expansions in the RFC1 gene. Furthermore, they have continued working on the identification of biomarkers of premotor stages of Parkinson's disease associated with mutations in LRRK2, having identified subclinical gait and oculomotor alterations. In the line of genetics of dementias, participating in national (DEGESCO) and international (IGAP) consortia, they have contributed with several high impact publications during 2022. Additionally, in the context of the study of Alzheimer's disease in preclinical and prodromal phases "Valdecilla Cohort for the study of memory and brain aging" they have identified retinal alterations in the preclinical phase.

Training

Teresa Iglesias Vacas

COORDINATOR

The CIBERNED Training Program has continued its activities during the year 2022, which is currently organized around three main axes: the virtual Scientific Sessions "CIBERNED Webinar Series", the Training and Mobility Grants Plan, and the annual Scientific Forum.

The Webinars were initiated in 2021 with the aim of disseminating the latest discoveries of the different groups and fostering collaborations, in addition to achieving a high impact and educational value. This year they have continued to be held every two weeks with a high level of acceptance and participation. We know that the audience includes numerous predoctoral students to whom we have given attendance certificates that can be validated as a scientific activity in their University Doctorate Programs. A total of twenty-two seminars have been broadcasted throughout 2022, mainly given by predoctoral (13) and postdoctoral (4) researchers from the different programs, although senior researchers from the area (6) and some external collaborators (2) have also participated as speakers. The videos of most of the presentations are available on YouTube through the CIBER web page, with the express consent of the speaker. This activity is highly educational, especially for PhD students who have the opportunity to present their results and discuss them with an audience of experts in a more personal setting.

Within the Training and Mobility Grants plan, we have contributed to finance a total of eight activities to applicants of the 7th and 8th call. The stays have been both international and national, and within the latter, there have been some intra- and inter-area stays. At the end of this year we resolved the 9th call with grants for stays and courses that will run until June 2023.

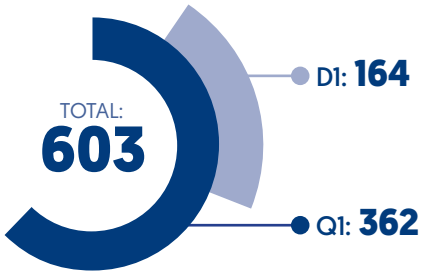
Our Scientific Forum, also organized this year together with the CIEN Foundation, has been of great relevance within the framework of an event of exceptional interest "Neurodegenerative Diseases 2020. International Year of Research and Innovation", at the international summit "Global Summit on Neurodegenerative Diseases NEURO 2020/2022" held in Salamanca from June 21 to 24. The opening of the event took place on June 21, World Amyotrophic Lateral Sclerosis (ALS) Day, was chaired by H.M. Queen Sofia and featured a keynote lecture by the 2013 Nobel Laureate in Medicine, Dr. Thomas C. Sudhof of Stanford University (California, USA). The scientific program included a very prominent participation of CIBERNED researchers, along with other prestigious national and international invited researchers. Worthy of note was the presentation of a large number of posters, among which the ten best among the different programs were selected for a special session of "Flash Talks", starring young researchers. Finally, we presented the Young Researcher Award to Julia Terreros Roncal, from Dr. María Llorens Martín's group, for her publication "Impact of neurodegenerative diseases on human adult hippocampal neurogenesis, Science, 2021)" presented at session XI of the annual Scientific Forum.

We are designing activities for the creation of new axes, which will expand the training program, in addition to increasing its quality, scope and interest for all members of the different research groups in our area and CIBER inter-areas.

Scientific production

Publications

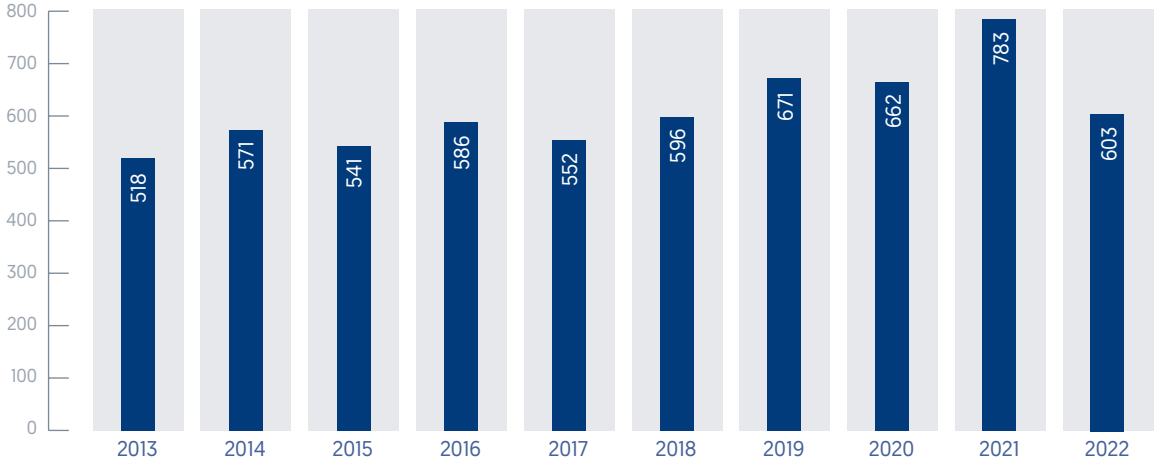
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
176,082	Devos D., Labreuche J., Rascol O., Corvol J.-C., Duhamel A., Delannoy P.G. et al. Trial of Deferiprone in Parkinson's Disease. New England Journal of Medicine. 2022;387(22):2045-2055.
113,915	Sousa-Victor P., Garcia-Prat L., Munoz-Canoves P.. Control of satellite cell function in muscle regeneration and its disruption in ageing. Nature Reviews Molecular Cell Biology. 2022;23(3):204-226.
69,504	Kousathanas A, Pairo-Castineira E, Rawlik K, Stuckey A, Odhams CA, Walker S, Russell CD, Malinauskas T, Wu Y, Millar J, Shen X. Whole-genome sequencing reveals host factors underlying critical COVID-19. Nature. 2022 Jul 7;607(7917):97-103.
69,504	Han L., Wei X., Liu C., Volpe G., Zhuang Z., Zou X. et al. Cell transcriptomic atlas of the non-human primate Macaca fascicularis. Nature. 2022;604(7907):723-731.
69,504	Moiseeva V., Cisneros A., Sica V., Deryagin O., Lai Y., Jung S. et al. Senescence atlas reveals an aged-like inflamed niche that blunts muscle regeneration. Nature. 2023;613(7942):169-178.
66,850	Crouch E.E., Bhaduri A., Andrews M.G., Cebrian-Silla A., Diafos L.N., Birrueta J.O. et al. Ensembles of endothelial and mural cells promote angiogenesis in prenatal human brain. Cell. 2022;185(20):3753-3769.e18.
66,850	Akkermans O., Delloye-Bourgeois C., Peregrina C., Carrasquero-Ordaz M., Kokolaki M., Berbeira-Santana M. et al. GPC3-Unc5 receptor complex structure and role in cell migration. Cell. 2022;185(21):3931-3949.e26.
66,850	Chen A., Liao S., Cheng M., Ma K., Wu L., Lai Y. et al. Spatiotemporal transcriptomic atlas of mouse organogenesis using DNA nanoball-patterned arrays. Cell. 2022;185(10):1777-1792.e21.
63,832	Lee D, Le Pen J, Yatim A, Dong B, Aquino Y, Ogishi M et al. Inborn errors of OAS-RNase L in SARS-CoV-2-related multisystem inflammatory syndrome in children.Science (New York, N.Y.). 2022.
63,832	Alvarez-Buylla A., Cebrian-Silla A., Sorrells S.F., Nascimento M.A., Paredes M.F., Garcia-Verdugo J.M. et al. Comment on "Impact of neurodegenerative diseases on human adult hippocampal neurogenesis. Science. 2022;376(6590).

CIBERNED Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Acevedo Arozena, Abraham	1	1	0	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	Santa Cruz de Tenerife
Alberch Vié, Jordi	15	11	5	Universidad de Barcelona	Barcelona
Boada Rovira, Mercè	34	22	18	Fundació ACE, Institut Català de Neurociències Aplicades	Barcelona
Bullido Gómez-Heras, María Jesús	4	3	2	Universidad Autónoma de Madrid	Madrid
Calero Lara, Miguel	32	11	4	Instituto de Salud Carlos III	Madrid
Camins Espuny, Antonio	23	17	6	Universidad de Barcelona	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Cantero Lorente, José Luis	6	5	1	Universidad Pablo de Olavide	Sevilla
Carro Díaz, Eva María	42	14	2	Instituto de Salud Carlos III	Madrid
Ceña Callejo, Valentín	4	3	0	Universidad de Castilla la Mancha	Albacete
Comella Carnice, Joan Xavier	4	4	0	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Cuadrado Pastor, Antonio	15	13	6	Universidad Autónoma de Madrid	Madrid
De Felipe Oroquieta, Javier	3	1	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Del Río Fernández, José Antonio	15	11	1	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Fariñas Gómez, Isabel	2	2	0	Universidad de Valencia	Valencia
Fernández Chacón, Rafael	1	0	0	Universidad de Sevilla	Sevilla
Fernández Ruiz, Javier	7	5	3	Universidad Complutense de Madrid	Madrid
Ferrer Abizanda, Isidro	31	22	4	Fundación IDIBELL	Barcelona
Franco Fernández, Rafael	13	10	0	Universidad de Barcelona	Barcelona
Fuentes Rodríguez, José Manuel	12	4	2	Fundación para la Formacion y la Investigación de los Profesionales de la Salud (FUNDESALUD)	Caceres
García Verdugo, José Manuel	10	6	4	Universidad de Valencia	Valencia
Gutiérrez Pérez, Antonia	14	12	2	Universidad de Málaga	Malaga
Guzmán Pastor, Manuel	3	3	1	Universidad Complutense de Madrid	Madrid
Iglesias Vacas, Teresa	2	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Infante Ceberio, Jon	43	28	16	Instituto de Investigación Marques de Valdecilla	Cantabria
Kulisevsky Bojarski, Jaime	35	10	8	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Labandeira García, José Luis	11	7	4	Universidad de Santiago de Compostela	Coruña, A
Lanciego Pérez, José Luis	5	2	2	Fundación para la Investigación Médica Aplicada	Navarra
Lleó Bisa, Alberto	52	35	27	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Llorens Martín, María Victoria	17	8	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
López Barneo, José	9	5	3	Universidad de Sevilla	Sevilla
López de Munain Arregui, Adolfo	39	23	8	Asociación Instituto Biodonostia	Guipuzcoa

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Lucas Lozano, José Javier	1	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Martí Doménech, María José	56	28	22	Hospital Clínico y Provincial de Barcelona	Barcelona
Martínez Gil, Ana	15	10	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Matute Almau, Carlos	16	13	4	Universidad del País Vasco	Vizcaya
Mir Rivera, Pablo	25	14	9	Universidad de Sevilla	Sevilla
Moratalla Villalba, Rosario	2	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Muñoz Cánoves, Pura	13	10	10	Universidad Pompeu Fabra	Barcelona
Naranjo Orovio, José Ramón	6	5	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Navarro Acebes, Xavier	29	13	4	Universidad Autónoma de Barcelona	Barcelona
Obeso Inchausti, José Ángel	23	15	11	Fundación HM Hospitales Madrid	Madrid
Osta Pinzolas, Rosario	6	5	2	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Paradas López, Carmen	7	7	3	Universidad de Sevilla	Sevilla
Pérez Castillo, Ana María	5	4	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Pérez Tur, Jordi	7	6	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	Valencia
Rodríguez Álvarez, José	6	4	1	Universidad Autónoma de Barcelona	Barcelona
Rodríguez Díaz, Manuel	1	1	0	Universidad de La Laguna	Santa Cruz De Tenerife
Sáez Valero, Javier	4	3	1	Universidad Miguel Hernández	Alicante
Soriano García, Eduardo	7	2	0	Universidad de Barcelona	Barcelona
Torres Alemán, Ignacio	5	4	1	Achucarro Basque Center for Neuroscience	Vizcaya
Trullás Oliva, Ramón	17	11	6	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Vicario Abejón, Carlos	3	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Vila Bover, Miquel	11	6	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Vitorica Ferrández, Francisco Javier	4	4	1	Universidad de Sevilla	Sevilla
Wandosell Jurado, Francisco	3	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid

Clinical Guidelines 2022

- Toscano Prat, C.; Pérez Pérez, J.; Carmona Abellán, M.; Blázquez Estrada, M.; Suárez San Martín, E.; García Fernández, C. Urgencias en trastornos del movimiento. En: Manual del grupo español de trastornos del movimiento. (pp.: 115-35). 2022.

- Pascual, B.; Campolongo, A.; Bueno, A. Enfermedad de Parkinson: manejo ante diferentes escenarios quirúrgicos. 2022.

- Maestre, SJ.; Mir Rivera, P. Escalas de evaluación recomendadas en el diagnóstico y seguimiento. En: Recomendaciones de Práctica Clínica en la Enfermedad de Parkinson. (pp.: 87-102). 2022. ISBN: 978–84-7429–765-2.

- Deuschl G, Antonini A, Costa J, Śmiłowska K, Berg D, Corvol JC, Fabbrini G, Ferreira J, Foltynie T, Mir P, Schrag A. European Academy of Neurology/Movement Disorder Society-European Section guideline on the treatment of Parkinson's disease: I. Invasive therapies. European Journal of Neurology. 2022 Sep;29(9):2580-95.

- De Fàbregues-Boixar, O.; Compta, Y.; Pascual, B.; Gerència del Medicament del CatSalut: Montoya, A.; Vives, R.; Pontes, C. Levodopa inhalada para el tratamiento de la enfermedad de Parkinson. Barcelona: Servei Català de la Salut. Departament de Salut. Generalitat de Catalunya; 2022.

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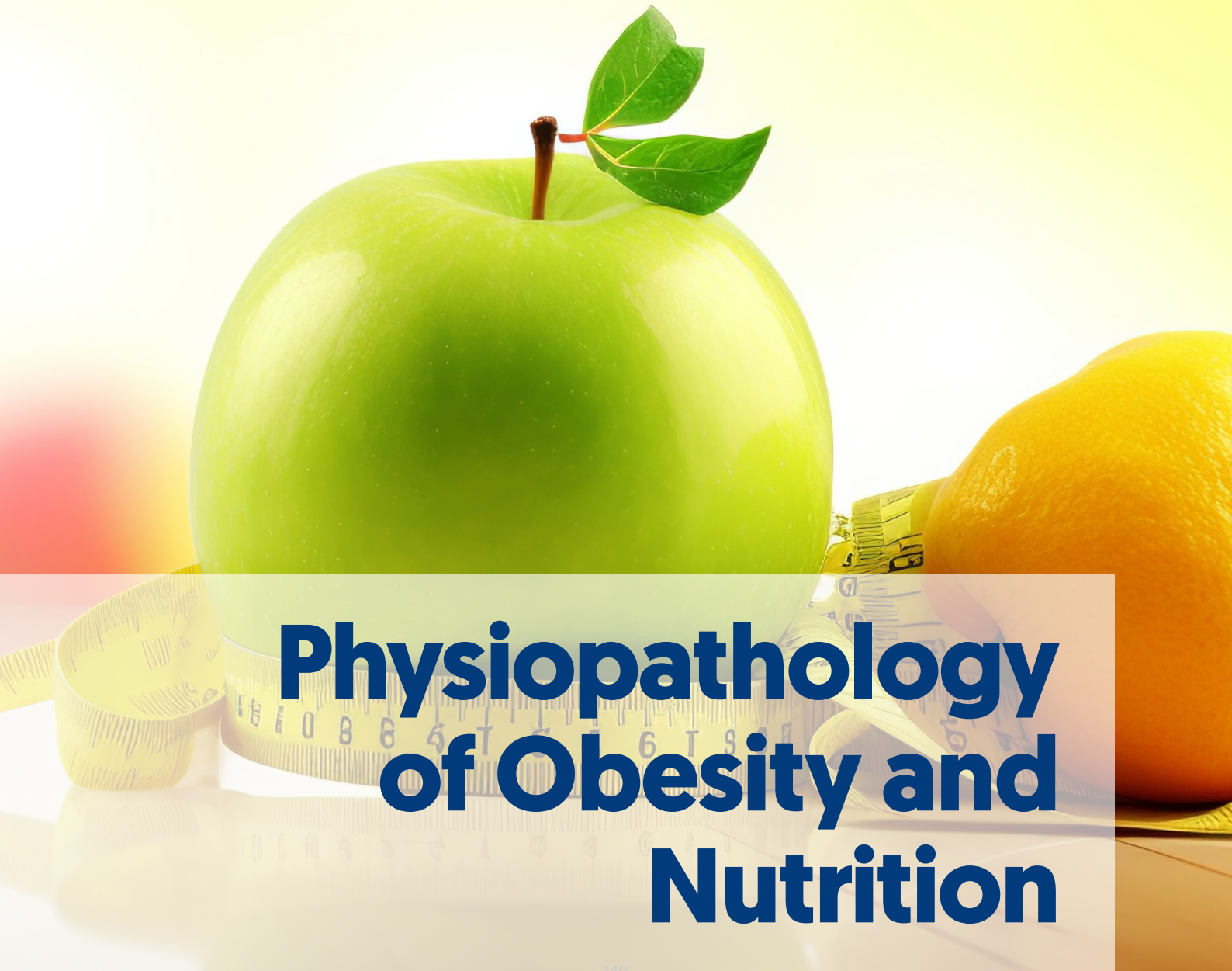


Physiopathology of Obesity and Nutrition

Welcome from the scientific director

Carlos Diéguez González

The most significant aspect of 2022 has been the return to normality after the COVID-19 pandemic, although it is true that this was only achieved in the second part of the year. This allowed us to resume face-to-face activities, highlighting the annual PIs meeting and the annual CIBEROBN symposium in Barcelona, where we also carried out a joint scientific activity with the Spanish Obesity Society. This allowed us to discuss new scientific challenges and to seek organizational improvements.

One of the most significant novelties of 2022 was the call, through the Spanish Obesity Society (AES), for the incorporation in 2023, of two new groups. The two selected, Jonathan Ruiz and José María Ordovás, will come to reinforce two particularly strategic areas such as physical exercise and big data, artificial intelligence, obesity and nutrition.

What we can be absolutely certain of is that we continue to pursue the consolidation and scientific growth of the CIBEROBN. This is reflected in the number of publications in high quality journals (e.g. 157 in D1), researcher training (91 doctoral theses, 36 of them international) or the securing of international projects.

The relevance of our Scientific Program has been highlighted in several prestigious international forums. At the end of 2022, Nature Medicine published an article analyzing and highlighting the eleven most relevant clinical trials in biomedical research at the present time. The fact that one of those chosen was PredimedPlus illustrates the expectations for this project worldwide. In this regard, it should be noted that 2022 marked the end of the intervention phase. The fact that this milestone has been reached, given the complexity of the study and the COVID pandemic that occurred during its development, can only be understood by acknowledging the professionalism and involvement of all the researchers participating in this project. Another recognition similar to the previous one is related to the CORDIOPREV study, published in The Lancet, which was selected by the European Society of Cardiology as one of the ten most relevant studies worldwide in 2022 on the subject of dyslipidemia.

In the context of international projects, worth highlighting is the presentation of an ambitious project to the European Union call for proposals on the subject of obesity. The proposal, coordinated by CIBEROBN and involving researchers from eight different countries, was selected for funding, with funding of close to 10 million Euros, and will be launched in the first half of 2023 for a duration of five years. This will undoubtedly help to boost the internationalization of CIBEROBN.

In summary, 2022 has been a year full of good news with regards to the scientific activity of CIBEROBN, all of them in line with our mission: to improve the health of the population, both at the level of primary prevention and on the basis of basic and translational research. This has all been possible largely due to the very high integration of different CIBEROBN Groups/Researchers, as well as other CIBER thematic areas. This illustrates the need for cooperative structures such as the CIBER to carry out ambitious studies with a high impact on the health of the population as well as beyond our national borders.

Programs

Nutrition

Jordi Salas-Salvadó

COORDINATOR

The Nutrition program is one of the two CIBEROBN programs (Nutrition and Obesity) that includes epidemiological research in obesity and nutrition for which important milestones have been achieved in terms of recruitment, follow-up and/or publication of results, as well as national and international collaborations. We highlight the advances in follow-up and interventions and publications in the PREDIMED Plus study -a randomized controlled clinical trial with intensive lifestyle intervention with an energy restricted Mediterranean diet, increased physical activity and behavioral support compared to a control group to assess its effects on weight loss and reduction of cardiovascular events.

By the end of 2022, the intervention of the more than 6800 randomized participants was completed and the 2-year follow-up of the non-intervention cohort began. In December 2022, the journal Nature Medicine selected PREDIMED-Plus as one of 11 studies worldwide that are expected to change the history of medicine. Other milestones are publications derived from the PREDIMED Plus study, including the effect of the pandemic on the participants' interventions and body weight, as well as the follow-up and publications of the " University of Navarra Follow-up" cohort (n=23,000). There have also been milestones in the publications of the CORDIOPREV study, a randomized controlled trial with lifestyle intervention with a Mediterranean diet in secondary cardiovascular prevention, which has been successfully completed and the effect of the interventions on cardiovascular disease has been published in the Lancet with a high media impact. Other milestones are the advances in recruitment, follow-up and publication of results of studies initiated, many of them in collaboration with different CIBER groups or outside CIBER: PREDI-DEP (Prevention of recurrent depression with a Mediterranean diet. PREDI-DEP), PREDIMAR (PREVENTION with a Mediterranean Diet of Recurrent Arrhythmias in patients with atrial fibrillation, n=720), MEDICAR (In collaboration with SEAT, study in 14,000 workers assessing lifestyle and health), CORALS (cohort of children to assess obesity risk factors, n=1570), which has published the first results in the Journal of Pediatrics, LifeBreast (Lifestyles and breast cancer) and the European H2020 STOP studies "Science and Technology in Childhood Obesity Prevention", on policies for preventing and tackling childhood obesity, SWEET "Sweeteners and sweetness enhancers: Impact on health, obesity, safety and sustainability", and PRIME "Prevention and Remediation of Insulin Multimorbidity in Europe", among others. In addition, other projects have continued, such as the EU-Project (H2020), entitled: Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviors. Eat2beNICE, the JPI HDHL Identification and validation of integrative biomarkers of physical activity level and Health in children and adolescents, the JPI DEAL Metabolite markers of dietary intake and the NIH projects within the PREDIMED Plus study: "Effect of an Intensive Lifestyle Intervention on the Atrial Fibrillation Substrate; 2018-2022" and PREDIMED: "Mediterranean diet, metabolomics and cardiovascular disease". In addition, different projects have been initiated: 3 on personalized medicine from ISCIII, a PROMETEO-HG Project, several European projects (Vegan screener), a new NIH Project on multi-fluid-metabolomics and a Soria Melguizo Foundation project on COVID in PREDIMED and PREDIMED-plus respectively.

In 2022, dozens of publications have been published in high-impact international journals, among them:

- Relationship of Circulating Vegetable Omega-3 to Prognosis in Patients With Heart Failure. J Am Coll Cardiol. 2022 Nov 1;80(18):1751-1758. PMID: 36302588.
- Long-term secondary prevention of cardiovascular disease with a Mediterranean diet and a low-fat diet (CORDIOPREV): a randomised controlled trial. Lancet 2022; 399(10338):1876-1885. PMID: 35525255.

- Effects of Supplemented Mediterranean Diets on Plasma-Phospholipid Fatty Acid Profiles and Risk of Cardiovascular Disease after 1 Year of Intervention in the PREDIMED Trial. Clin Chem. 2023 Jan 23:hvac221. PMID: 36683466.
- Effectiveness and safety of ustekinumab in elderly patients with Crohn's disease: Real world evidence from the ENEIDA registry. Journal of Crohn's and Colitis. 2022.
- Host and gut microbial tryptophan metabolism and type 2 diabetes: an integrative analysis of host genetics, diet, gut microbiome and circulating metabolites in cohort studies. Gut. 2022 Jun;71(6):1095-1105 PMID: 34127525.

Obesity

Fernando Fernández-Aranda

COORDINATOR

In 2022, the subprograms of the Obesity Program have continued to strengthen the collaboration ties between the different groups, collaborations between the Obesity and Nutrition Program, and with international groups. Actions in this sense have crystallized in leading publications both in the field of basic research, with preclinical models, and in clinical and translational work, as well as in obtaining European research resources and leadership at the international level. The main achievements, grouping all the subprograms together, are described below.

Publicaciones Internacionales Relevantes

In terms of production, the following publications deserve special mention as examples of intra- and inter-area and international collaborations:

Publications in first-decile journals, leading journals in the area, such as: Gut (PMID: 35580962), J Hepatol (PMID: 34555423), Metabolism (PMID: 35985506), Obes Rev. (PMID: 35362662), Lancet Diabetes Endocrinol. (PMID: 36356613), Nat Commun. (PMID: 35945211 & PMID: 36097264), Diabetes Care (PMID: 36044664), Eur Heart J (PMID: 35896123), Nat Rev Endocrinol Cell Metab. (PMID: 35986176), Cell Host Microbe. (PMID: 35176247), Cell Metab. (PMID: 35508109), Mol. Ther.Nucl. Acids. (PMID: 35141047), EBioMedicine. (PMID: 36206624), Nat Metab. (PMID: 35879461), J Adv Res. (PMID: 35024196), BMC Med. (PMID: 36289459), Nat Rev Dis Primers. (PMID: 35301358), Biol Psychiatry (PMID: 34861974), Psychol Med (PMID: 32698931).

International Projects

In terms of international resources secured, in which members of the CIBEROBN obesity program participate as PIs and/or coordinators, the following projects deserve special mention: 1) Prevention and Remediation of Insulin Multimorbidity in Europe (PRIME). (Horizon2020) (2020-2024) (Ref.847879), in collaboration with the nutrition program. PIs: J. Salas-Salvado/F. Fernández-Aranda. 2) Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviors (Eat2beNICE). (Horizon2020) (2017-2023) (Ref. 728018) in collaboration with the nutrition program. PIs: F. Fernández-Aranda/J.Salas-Salvado. 3) Identification and validation of integrative biomarkers of physical activity level and Health in children and adolescents (INTEGRActiv) (JPI HDHL) (2022-2025) (Ref. in ISCII: AC21_2/00033), Coordinator: Catalina Picó/PI: E Lurbe. 4) Stratification of Obese Phenotypes to Optimize Future Obesity Therapy (SOPHIA) (Ho- rizon2020) (2020-2025) (Ref.: 875534-2) PIs: G Frühbeck/ JM Fernández-Real. 5) Network for blood pressure research in children and adolescents (HyperChildNET). (COST Action) (2020-2025) (Ref. CA 19115). Coordinator E. Lurbe/ PI: F. Fernandez-Aranda. 6) Gut-bra- in-axis: Targets for improvement of cognition in the elderly (SMARTAGE) International Training Network (Marie Curie-H2020) (2020-24) (Ref. 859890). PI JM Fernández-Real. 7) Personalized prediction of cognition through the human microbiota. (ThinkGut) (Interreg-POCTEFA - Horizon 2020) (2019-2022) (Ref EFA345/195), Coordinator: JM Fernández-Real. Special mention, as it is coordinated by CIBERobn and starting in 2023: 8) Preventing lifetime obesity by early risk-factor identification, prognosis and intervention (eprObes) (Horizon Europe) (2023-2028) (Ref 101080219-2); Coordinators: M. Tena/E. Lurbe/F.Fernández-Aranda.

National Projects

1) Neurocognition, Neuronal Activity and Biomarkers in Patients with Extreme Weight Conditions: Prospective Study on Response to Treatment (PI20/00132), funded by ISCI-II (2021-2023), PI: F. Fernández-Aranda. 2) Impact of birth weight and growth pattern on cardiometabolic risk factors in postpubertal adolescents: clinical and molecular approach (PI20/00269) funded by ISCIII (2021-2023), PI: E. Lurbe. 3) Therapy in your Pocket: Effectiveness of Serious Games in Behavioral Addictions (GAME4HEALTH) (Ref. 347/21), funded by Institut d'Investigació Biomèdica de Bellvitge (IDIBELL) / PECT-II-IDIBELL Inter- nal call for innovation projects (2022), PI: S. Jiménez-Murcia. 4) Psychoneuroendocrine substrates in gambling disorder and their association with treatment outcome: usefulness of gamification in the rehabilitation process (Ref: 2021I031), Funded by the Ministry of Health / Call for grants for the development of research projects on addictions 2021 (2022-2024), PI: S. Jiménez-Murcia. 5) DTG/3TC vs. BIC/FTC/TAF Maintenance Therapy in People Living With HIV: (PASO-DOBLE), substudy: "Change in subcutaneous and visceral fat" (2020-003686-18), funded by Fundacion SEIMC-GESIDA (2021-2024), PI: F. Villarroya. 6) Paternal RNA-mediated epigenetic inheritance of metabolic disorders: impact of weight loss on the human sperm (HEROS) (AC18/00012), funded by JPI-HDL/ ISCIII (2019-2023). PI: J.M. Fernández-Real (work-package leader). 7) Therapeutic targets and biomarkers from precision medicine in MAFLD (PreMed-MAFLD). Precision Personalized Medicine of the Strategic Health Action project (PMP21/00072). (2022-2025). 8) Astrocytes, exomes and Mirnas in the differential response of males and Females to specific fatty acids. 9) INNOHEALTHFOOD: Personalized nutrition platform to support the food sector for the development of products with high added value for health use adapted to population needs.10) EMANATE Project: Patients with obesity and Heterozygous variants in POMC, LEPR, NCOA1, and SH2B1. 11) DIVERSE - Disentangling the Interplay between behaViours and biomarkERS across the lifEspan. 12)MEDKIDS New food products for the development of a healthy food product with high added value for health use adapted to population needs. 13)Gene expression in adipose tissue of participants from all FatBank nodes using the whole transcriptome. 14)Involvement of the gut microbiota-brain cross talk in the loss of eating control (GMBCrossTalk-Food - HR22- 00737) (2022-2025) Funded by Fund.Bancaria "LA CAIXA". PI: JM. Fernández-Real Lemos 14) Control strategies and drug-genetic study for personalized treatment of fatty liver associated with metabolic dysfunction in patients with prediabetes: PROMETEO-HG study. 15) To analyze the role of epigenetic mechanisms (DNA methylation, lncRNAs and miRNAs) in the development of obesity-associated diseases such as type 2 diabetes mellitus. 16) Game4mental-health: Integration of therapeutic approaches based on new technologies (DTS22/00072). (2023-2025) PI: S. Jiménez-Murcia.

Participation in international Guidelines

In addition to our intense scientific activity, we also participated in the preparation of the following international clinical guidelines of the European Society of Hypertension:

- de Simone G, Mancusi C, Hanssen H, Genovesi S, Lurbe E, Parati G, Sendzikaite S, Valerio G, Di Bonito P, Di Salvo G, Ferrini M, Leeson P, Moons P, Weismann CG, Williams B. Hypertension in children and adolescents. Eur Heart J 2022 Sep 14;43(35):3290-3301. doi: 10.1093/eurheartj/ehac328. PMID: 35896123.
- A otro nivel, se participó activamente en State of the art y consenso internacional de Trastorno por Atracón en revista de alto prestigio: Giel KE, Bulik CM, Fernández-Aranda F, Hay P, Keski-Rahkonen A, Schag K, Schmidt U, Zipfel S. Binge eating disorder. Nat Rev Dis Primers. 2022 Mar 17;8(1):16. doi: 10.1038/s41572-022-00344-y. PMID: 35301358; PMCID: PMC9793802.

Dissemination

In the field of internationalization, the CIBEROBN Obesity program and its members have maintained their usual activity in the organization of specific workshops and symposiums related to obesity and nutrition, within the European Society for Clinical Investigation (ESCI), European Congress on Obesity (ECO) and European Society of Endocrinology (ESE).

The COST-Hyperchildnet Group has led a special issue in the journal Frontiers in Cardiovascular Medicine on Blood Pressure in Children and Adolescents: Moving Forward https://www.frontiersin.org/research-topics/35719/blood-pressure-in-children-and-adolescents-moving- forward; Guess editors: Empar Lurbe, Elke Wuhl and Fernando Fernández-Aranda.

Regarding social dissemination and promotion of a scientific mindset among young people, in 2022 we continued to organize the annual Crazy about Nutrition course (Locos por la Nutrición) (sponsored by the Pedrera Foundation) at the Hospital de Bellvitge.

Participation/creation of specific Networks

Several members of the subprograms participate in international associations, which allows for synergies with other groups with a high potential for research, design of specific projects in the area and dissemination throughout the scientific community. Among these we highlight the following: Academy of Eating Disorders (AED); Eating Disorders Research Society (EDRS); International Neuropsychological Society; International Society of Addiction Medicine; European Endocrinology Society; International Society for the Study of Behavioral Addictions; European Association for the Study of Obesity (EASO), which collaborates closely with the Spanish Society for the Study of Obesity (SEEDO).

Members of the "European College of Neuropsychopharmacology Nutrition Network (BrainFood)" which includes other members from the Netherlands, Sweden, Italy, Ireland, United Kingdom, France, Estonia, Germany, Switzerland.

Adipoplast- Thematic network on adipose plasticity and its pathologies (http:// adipoplast.org/), corresponds to a network of excellence in adipose tissue research funded by the Ministry of Science, Innovation and Universities, led by CIBEROBN and involving relevant CIBEROBN groups.

Members of the "Value of Treatment" Work- group of the European Brain Council/European Psychiatric Association.

Training

Manuel Tena-Sempere

COORDINATOR

As in previous years, the main focus of the CIBEROBN Training Program has been on the youngest members of the groups, with measures aimed at promoting training stays in intra- and inter-area groups, as well as the development of training activities, with special attention to the holding of the annual conferences of our CIBER area, which returned to their face-to-face format after two years of being organized online due to the pandemic.

It is important to recognize that, despite the lifting, throughout 2022, of most of the restrictions derived from the health measures to combat the COVID-19 pandemic, and the sustained commitment of the CIBEROBN training program to support mobility actions of its junior members, the extent of the use of this mobility program has been reduced, due to a lower demand by the groups, as well as to the needs of adapting to the new CIBER training program, which was finally put into place in the course of 2022. This new program essentially maintains the mobility activities of CIBER members, although it includes a more regulated structure and procedure to apply for these activities, which became effective in 2022 and necessarily requires a period of adjustment on behalf of the applicant groups.

In fact, the process of adapting and improving the CIBER training program, implemented during 2022, continues, in a process that contemplates the development of other transversal training actions, which are expected to materialize throughout 2023, in order to extend the training offer to the members of the groups, and particularly to the personnel hired by CIBER, as a key tool in their ongoing training processes. This process, which is being coordinated from the Instituto de Salud Carlos III, aims to multiply and homogenize the training offer of the CIBER as a whole. It is expected that, after a short pause in some of the activities due to the renewal of the program, the definition of new contents and procedures will make it possible to increase CIBER training activities throughout 2023.

In addition, the CIBEROBN training program has been able to implement in 2022 some of the training activities and scientific events, in which our CIBER participated, which had suffered delays due to the pandemic. For example, the Workshop "Fat sensing and the brain control of puberty", organized by the International University of Andalusia, with active participation of our CIBER area, which was postponed in 2020 and 2021, has finally been held in 2022, with the participation of 15 speakers (two of them from CIBEROBN), with full attendance, including several members of our CIBER.

Similarly, the annual meeting of our CIBER area, entitled "Obesity and Nutrition in the 21st Century", organized under the coordination of the Training area, has finally been able to be held in a face-to-face format, leaving behind the virtual format that had to be adopted in 2020 and 2021. Given that this annual meeting is considered a priority element in the CIBEROBN training program, the holding of this conference in Barcelona on November 15 and 16 was a necessary return to normality, making it possible not only to attend high-level scientific sessions, with speakers from CIBEROBN, other CIBER areas and external speakers, but also to hold work meetings of the groups and the Nutrition and Obesity programs.

Strategically, the annual CIBER conferences were held the days immediately prior to the annual congress of the Spanish Society for the Study of Obesity (SEEDO; Barcelona, November 16-18), also held in Barcelona, in order to promote synergies and favor joint activities. In fact, the pre-SEEDO course, which preceded the formal start of the society's congress on the afternoon of November 16, was organized jointly by SEEDO and the training area of CIBEROBN, and was attended by numerous speakers from our CIBER area, who disseminated the activities of their groups in the forum provided by the annual SEEDO meeting. Given the success of this initiative and the need to seek new formulas with which to expand the training offer of our CIBER, we plan to extend these joint activities in the coming years.

Finally, and as a training element of major importance, we would like to highlight in this section that in 2022 a total of 91 Doctoral Theses have been completed (36 of them international), which represents the consolidation of a growing trend in this important training activity.

Platforms

Fatbank-Biobank

The milestones achieved in the FATBANK Platform in 2022 have been:

- Introduction of 122 new cases, reaching 2256 cumulative cases.
- Introduction of 2171 samples (serum, plasma, buffy coat, stool and adipose tissue), reaching 69011 cumulative samples available to the scientific community.
- Transfer of 341 samples of visceral tissue and subcutaneous tissue for research projects.
- Published articles where samples from the platform were used and where the platform is mentioned.

  - Latorre, J., Mayneris-Perxachs, J., Oliveras-Cañellas, N., Ortega, F., Comas, F., Fernández-Real, J. M., & Moreno-Navarrete, J. M. (2022). Adipose tissue cysteine dioxygenase type 1 is associated with an anti-inflammatory profile, impacting on systemic metabolic traits. EBioMedicine, 85, 104302.

  - Latorre, J., Martínez, C., Ortega, F., Oliveras-Cañellas, N., Díaz-Sáez, F., Aragonés, J., ... & Moreno-Navarrete, J. M. (2022). The relevance of EGFR, ErbB receptors and neuregulins in human adipocytes and adipose tissue in obesity. Biomedicine & Pharmacotherapy, 156, 113972.

  - Martínez, C., Latorre, J., Ortega, F., Arnoriaga-Rodríguez, M., Lluch, A., Oliveras-Cañellas, N., ... & Moreno-Navarrete, J. M. (2022). Serum neuregulin 4 is negatively correlated with insulin sensitivity in humans and impairs mitochondrial respiration in HepG2 cells. Frontiers in Physiology, 1989.

  - Rodríguez-Barrueco, R., Latorre, J., Devis-Jáuregui, L., Lluch, A., Bonifaci, N., Llobet, F. J., ... & Llobet-Navas, D. (2022). A microRNA cluster controls fat cell differentiation and adipose tissue expansion by regulating SNCG. Advanced Science, 9(4), 2104759.

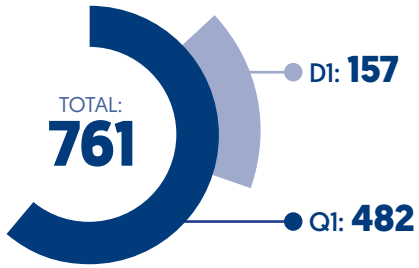
  - Pellegrinelli, V., Rodriguez-Cuenca, S., Rouault, C., Figueroa-Juarez, E., Schilbert, H., Virtue, S., ... & Vidal-Puig, A. (2022). Dysregulation of macrophage PEPD in obesity determines adipose tissue fibro-inflammation and insulin resistance. Nature Metabolism, 4(4), 476-494.

  - Luque, J., Mendes, I., Gómez, B., Morte, B., López de Heredia, M., Herreras, E., ... & García-Redondo, A. (2022). CIBERER: Spanish national network for research on rare diseases: A highly productive collaborative initiative. Clinical Genetics, 101(5-6), 481-493.
- OUTBRAT Project: Sample transfer, progress in the implementation and analysis of Project results, in collaboration with all nodes of the platform.
- Approval of "Regulations for the use and authorship of the FATBANK Platform", an internal agreement that regulates the functioning of the FATBANK Steering Committee, the management of the database, the use of samples and/or data and authorship in publications.

Scientific production

Publications

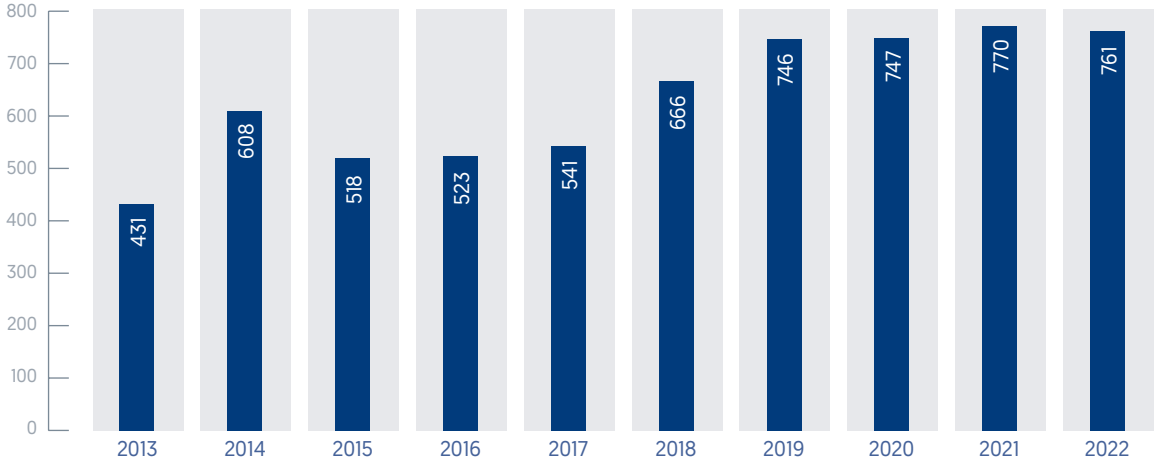
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
65,038	Binge eating disorder
63,832	GnRH replacement rescues cognition in Down syndrome
47,564	An updated view on human neonatal thermogenesis
47,564	The role of iron in host–microbiota crosstalk and its effects on systemic glucose metabolism
44,867	Efficacy and safety of setmelanotide, a melanocortin-4 receptor agonist, in patients with Bardet-Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial with an open-label period
35,855	Ultra-processed food consumption and disease: The jury is still out
31,795	Hepatic p63 regulates glucose metabolism by repressing SIRT1
31,373	Hypothalamic pregnenolone mediates recognition memory in the context of metabolic disorders
31,373	Microbiota alterations in proline metabolism impact depression
31,373	A diabetic milieu increases ACE2 expression and cellular susceptibility to SARS-CoV-2 infections in human kidney organoids and patient cells

CIBEROBN Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Argente Oliver, Jesús	35	23	3	Servicio Madrileño de Salud	Madrid
Baños, Rosa María	55	32	32	Universidad de Valencia	Valencia
Corella Piqué, Dolores	56	39	18	Universidad de Valencia	Valencia
Dieguez, Carlos	30	29	15	Universidad de Santiago de Compostela	Coruña, A
Estruch Riba, Ramón	54	36	13	Hospital Clínico y Provincial de Barcelona	Barcelona
Fernández Aranda, Fernando	44	30	3	Fundación IDIBELL	Barcelona
Fernández Real, José Manuel	19	15	7	Fundación Instituto de Investigacion Biomédica de Girona	Girona
Fito Colomer, Monserrat	79	51	18	Consorci Mar Parc Salut de Barcelona	Barcelona
Frühbeck Martínez, Gema	33	20	3	Universidad de Navarra	Navarra
Gil Campos, Mercedes	25	19	3	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Herrero, Laura	20	16	4	Universidad de Barcelona	Barcelona

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Lamuela, Rosa Maria	25	19	13	Universidad de Barcelona	Barcelona
Lasunción Ripa, Miguel Angel	27	20	7	Servicio Madrileño de Salud	Madrid
López Miranda, José	52	37	15	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Lurbe Ferrer, Empar	17	8	3	Consorcio Hospital General Universitario Valencia	Valencia
Martínez González, Miguel Ángel	96	59	26	Universidad de Navarra	Navarra
Moreno Aliaga, Maria Jesús	78	55	14	Universidad de Navarra	Navarra
Moreno Aznar, Luis Alberto	54	37	11	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Ortega, Emilio	64	38	12	Hospital Clínico y Provincial de Barcelona	Barcelona
Osada, Jesús	18	13	2	Universidad de Zaragoza	Zaragoza
Palou Oliver, Andreu	16	15	4	Universidad de las Islas Baleares	Illes Balears
Pintó Salas, Xavier	41	31	10	Fundación IDIBELL	Barcelona
Portillo Baquedano, Maria Del Pui	19	13	3	Universidad del País Vasco	Alava
Romaguera Bosch, M Adoracion	50	36	15	Fundación Instituto de Investigación Sanitaria Illes Baleares (IdISBa)	Illes Balears
Salas Salvadó, Jordi	83	62	23	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona
Santos Lozano, José M	30	21	7	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Seoane Camino, Luisa Maria	18	12	5	Servicio Gallego de Salud	Coruña, A
Serra Majem, Lluis	49	36	15	Universidad de las Palmas de Gran Canaria	Palmas, Las
Tena Sempere, Manuel	33	25	10	Universidad de Córdoba	Cordoba
Tinahones Madueño, Francisco José	69	52	15	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	Malaga
Tur Mari, Josep A	107	74	24	Universidad de las Islas Baleares	Illes Balears
Villarroya Gombau, Francesc	20	14	7	Universidad de Barcelona	Barcelona

Clinical Guidelines 2022

- A Guide to Performing and Interpreting Precision Nutrition Epigenome-Wide Association Studies
- Advances in omics and computation applied to chronobiology: A guide for their integration in precision health
- Healthy early childhood nutrition
- Clinical recommendations for the practice of sports_seen in people with diabetes mellitus
- How to make healthier dishes
- Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement
- Vegetarian Diet: What do I need to know?
- Dietary and Lifestyle Patterns and the Risk of Female Breast Cancer in Adulthood: World Cancer Research Fund Systematic Literature Review
- Consensus Document on Health and Emotional Wellbeing in Universities
- Effect of Physical Activity, Smoking, and Sleep on Telomere Length: A Systematic Review of Observational and Intervention Studies
- Eligibility criteria for Menopausal Hormone Therapy (MHT): a position statement from a consortium of scientific societies for the use of MHT in women with medical conditions. MHT Eligibility Criteria Group
- SEA 2022 standards for global control of cardiovascular risk
- Executive Summary from Expert consensus on effectiveness and safety of iDPP-4 in the treatment of patients with diabetes and COVID-19
- Executive summary of the consensus statement of: Clinical recommendations for sport practice in people with diabetes (RECORD Guide). Update 2021. Diabetes Mellitus Area of the Spanish Society of Endocrinology and Nutrition (SEEN)
- Executive summary of the consensus statement of: Clinical recommendations for sport practice in people with diabetes (RECORD Guide). Update 2021. Diabetes Mellitus Area of the Spanish Society of Endocrinology and Nutrition (SEEN)
- Executive summary on the treatment of type 2 diabetes mellitus in elderly or frail individuals. 2022 update of the 2018 consensus document Treatment of type 2 diabetes mellitus in the elderly
- Executive summary on the treatment of type 2 diabetes mellitus in elderly or frail individuals. 2022 update of the 2018 consensus document Treatment of type 2 diabetes mellitus in the elderly
- Expert Panel Guidance and Narrative Review of Treatment Simplification of Complex Insulin Regimens to Improve Outcomes in Type 2 Diabetes
- Expert recommendations for using time-in-range and other continuous glucose monitoring metrics to achieve patients centered glycemic control in people with diabetes
- Clinical guidelines on the management of dyslipidemias for cardio-vascular prevention
- Fair Trade and Responsible Consumption Guide
- Multidisciplinary guide to childhood and juvenile epilespy
- Guideline for the assessment of disability in rare diseases
- Guide and advances on childhood obesity determinants: Setting the research agenda
- Hypertension in children and adolescents
- International consensus document on obstructive sleep apnea
- Manual of Endocrinology and Nutrition of the Spanish Society of Endocri- nology and Nutrition. Area IV. Lipids and cardiovascular risk. 142. Treatment of dyslipidemias.
- Menopause and obesity
- Obesity and fertility. Position statement
- 'Obesities': Position statement on a complex disease entity with multifaceted drivers
- Taste perception and flavor preferences: A guide to their measurement and evaluation of associated pathologies
- Position guidelines and evidence base concerning determinants of childhood obesity with a European perspective
- Prevention of Cardiorenal Complications with Sodium–Glucose Cotransporter Type 2 Inhibitors: A Narrative Review
- Recommendations for the diagnosis and treatment of hypoglycaemia after bariatric surgery
- Answers to doubts and false beliefs about nutrition

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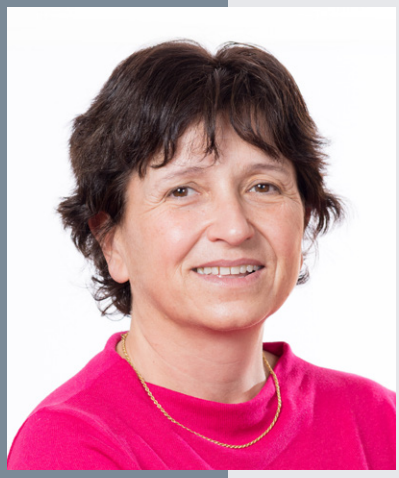
Cancer

Welcome from the scientific director



Anna Bigas Salvans

Dear friends and colleagues,

I am pleased to present to you CIBERONC's annual report for the year 2022. This has been a very important year for us, as we have achieved important advances in cancer research thanks to the commitment and dedication of all of you. So, first and foremost, as always, thank you.

During 2022, we have continued to work on innovative research projects in all the oncological pathologies that we cover in CIBERONC, from prevention to treatment and patient care. We have established new collaborations and strengthened our alliances with other research centers and other CIBER areas, resulting in the projects awarded in 2022, including the following:

- Personalized Clinical Management of Endometrial Cancer using Liquid Biopsy, Genomics and Artificial Intelligence (ECLAI) – ERA PerMed JTC2021 – PI: Dr. Gema Moreno. Awarded budget: 224.027€
- Circulating tumour microenvironment components as Urothelial Cancer Immunotherapy Response Predictors (UCIPredict) – TRASCAN-3 – PI: Dr. Marta Dueñas. Awarded budget: 248.050€
- Immune4ALL: Exploring the Feasibility of predictive and pharmacodynamics biomarkers of immunotherapy in solid tumors - national call. PI: Dr. Enrique de Álava. Awarded Budget: 4.992.900€

Internationally, CIBERONC continues with its relevant role in the 4.UNCAN. eu project, which aims to define the scientific priorities of the Cancer Mission and cancer research until 2027, as well as with its participation in the JANE project, which aims to study the current cancer research networks and prepare everything, based on current knowledge, to launch 7 Networks of Expertise at European level in the following areas: personalized primary prevention; survival; palliative care; omics technologies; high-tech medical resources; complex and poor prognosis cancers and, finally, adolescents and young adults with cancer.

In terms of face-to-face interactions, several in-person meetings have taken place this year. On the one hand, the Work Modules meetings in Badalona, Madrid and Pamplona, respectively, have attracted a total of 175 researchers to these events, with a strong collaborative approach and aimed at young researchers in the network. In addition, the 2022 annual meeting, in virtual format, brought together 298 attendees to listen to 26 guests and was the setting for the presentation of the award for the most collaborative researcher to Dr. Bruno Paiva.

Finally, the Young Researchers meeting brought together more than 100 junior CIBERONC researchers in Santiago de Compostela, in an event in which more than 65 abstracts were presented and where the program was developed in collaboration with the CIBER of Rare Diseases (CIBERER).

This year, in which the pandemic has enabled the recovery, at least partially, of face-to-face events, has been a positive year in terms of the renewal of in-person meetings among researchers. We hope that this will be the first year of many more such future meetings that will stimulate collaborative and translational research by CIBERONC researchers.

Programs

Digestive Tract Tumors

Gabriel Capellà Munar

COORDINATOR

The main milestones of the Digestive Tract Tumors program in 2022 have been the following:

1. Creation of the SPADA database

Based on two different registries created by program groups, a national registry of genetic variants in genes mainly involved in gastrointestinal cancer predisposition has been created. The ultimate aim of SPADA is to offer a useful resource to the research community and clinical genetics laboratories to improve knowledge of the genetic basis of hereditary cancer and, therefore, to improve diagnosis, risk assessment, prevention and treatment of cancer in carriers and their families.

SPADA, the SPAnish variant DAtabase for hereditary cancer, is coordinated by C. Lázaro and G. Capellá and is a tool for storing and sharing VCF files and related minimal clinical information from diagnostic laboratories as well as specific initiatives such as PANGENFAM. The database is hosted by CIBER and is intended to be the seed for more ambitious data sharing initiatives.

Organizationally, three committees (advisory, executive, and administrative) have been created to deal with SPADA. The Executive Committee will include representatives of the relevant National Societies (SEOM, AEGH) as well as CIBERONC. The creation of working groups led by key Investigators based on research interests is foreseen. The registry portal will have a space dedicated to research where projects based on the registry will be openly shared with the aim of promoting new collaborative studies.

2. ALIPANC

Four program members interested in pancreatic cancer (A. Carrato; J. Feliu, N. Malats and F.X. Real) are core members of ALIPANC, the Alliance for Pancreatic Cancer Research (https://alipanc.org/), an initiative that brings together more than 40 groups interested in clinical and translational pancreatic research. J Tabernero and A Cervantes have also joined the effort. CIBERONC investigators have committed to deepen the relationship of ALIPANC with CIBER. The formalization of a general collaboration protocol between CIBERONC and ALIPANC is underway.

3. MET-CRC-BIORESOURCE

Three years ago, under the leadership of A Cervantes, the program set out to explore the clinical utility of metastatic colorectal cancer (CRC) transcriptomic signatures with the collaboration of 5 groups of the program: E. Aranda, E. Batlle, A. Carrato, J. Feliu, J. Tabernero. A total of 134 cases were identified as candidates for participation in the study for which paired samples of primary CRC tumor and hepatic metastases were available. Of these, 100 passed the pre-established quality filters. However, this quality has not been reflected in obtaining reproducible signatures. This activity is being redefined based on the premise that the biorepository is of high added value and that it allows relevant questions to be answered.

Breast Cancer

Joaquín Arribas López

COORDINATOR

The main milestones of the Breast Cancer Program in 2022 have been the following:

Three groups of the program, those led by E. Alba, G. Moreno and J. Arribas, participate in the Immune4all project (Exploring the Feasibility of predictive and pharmacodynamics biomarkers of immunotherapy in solid tumors), recently endowed with over 4,000,000 €, to find biomarkers of response/resistance to immunological therapies. In fact, Drs. J. Arribas and G. Moreno coordinate objective 1 (Breast Cancer) with a funding of 925,400 €. This project is coordinated by Dr. Enrique de Alava (Low Prevalence Tumors Program) and the projects represent a model of the collaborative efforts of CIBERONC.

Two groups from the Breast Cancer program, those led by Drs. J. Albanell and J. Arribas, will participate in a phase I clinical trial to test the safety and efficacy of CAR T cells directed against a HER2-positive breast cancer subtype (Design and implementation of a phase 1, open-label, dose escalation clinical trial using p95HER2 CAR HER2 BiTE T cells in patients with advanced solid tumors positive for p95HER2). The proposal received a funding of €1,400,000.

During 2022 the program held two meetings, one online (held on March 24) and one face-to-face (held in Barcelona on October 19). Both meetings were very successful and were attended by several members of all the groups. These meetings served to establish the collaborations evidenced in the published papers and proposals funded in 2022 for groups within the program.

Respiratory tract tumors

Luis Montuenga Badía

COORDINATOR

The main milestones of the Respiratory Tract Tumors Program in 2022 have been the following:

Leadership, development and active participation of multiple program groups in the INGENIO project (Integrative genomic, digital imaging and clinical information towards precision oncology optimization). The groups participating in the program are led by Dr. Paz-Ares, Dr. Montuenga and Dr. Camps. This project also involves the participation of other CIBERONC groups (Dr. Palacios, Dr. De Álava, Dr. Cervantes, Dr. Tabernero, Dr. López, Dr. Capellà. Dr. Matias-Guiu, Dr. Albanell, Dr. Ramón y Cajal, Dr. Malats, Dr. Bigas, Dr. Noguera) and groups from the CIBER areas of BBN (Dr. Ledesma) and RD (Dr. Dopazo).

This project, presented in the PMP21 call for proposals and awarded €3,196,600, has as its main objective to implement precision oncology in lung cancer patients, creating a federated database that encompasses clinical data, imaging and genomic information.

Digital Spatial Profiling (DSP) technology to evaluate in situ transcriptomic/proteomic data has been successfully established in the program. A strategic project from the Spanish Ministry of Research and Technology (Strategic Lines Program, Next Generation EU) has been awarded to researchers from the groups of L. Montuenga and L. Paz- Ares to implement this technology in the context of the project: "Use of MYC inhibition to overcome resistance to immunotherapy in KRAS-driven NSCLC with differential mutational profile-MYCOMBIO".

The program has established a general action protocol with the Spanish Association of Patients and Families Affected by Lung Cancer (AEACaP) for the joint development and mutual support in research tasks.

The Community of Madrid, through its call "Programs for R&D Activities in Biomedicine 2022 (PAIDIR 2022)" has financed a Lung Cancer Research Program: iLUNG2.0 (REF: 2022/BMD-7437; 894,000 €; 4 years) to the CIBERONC groups of L. Paz-Ares and M. Barbacid, in collaboration with those of J. Tamayo (INM-CSIC), M. Malumbres (CNIO) and F. López-Ríos (FIBH12O).

In addition, researchers of the program have been very active in two strategic collaborative projects between CIBERONC and CIBERBBN in the project: Patient-derived organoids 2.0: Recapitulation of the stromal and immune microenvironment in annotated organoid platforms to advance towards personalized cancer treatment and the project CASA-Digital Pathology: Assessment of tumor stroma by digital pathology. The first project involves 24 CIBERONC groups (including 4 from the respiratory tract tumor program) and 5 CIBER-BBN groups. The second project involves 5 CIBERONC groups (including one from this program) and 1 CIBER-BBN group.

Hematological Tumors

Dolors Colomer Pujol

COORDINATOR

The main milestones of the Hematological Tumors Program in 2022 have been the following:

Characterization of Richter transformation in chronic lymphocytic leukemia (among others).

Richter transformation (RT) is a paradigmatic evolution of chronic lymphocytic leukemia (CLL) into a very aggressive large B-cell lymphoma that confers a dismal prognosis. The mechanisms driving RT were largely unknown until this work.

Collaborative work between many centers (5 CIBERONC) characterized the entire genome, epigenome and transcriptome, combined with single-cell DNA/RNA sequencing analyses and functional experiments. Only with a collaborative effort it is possible to collect 19 cases with 54 longitudinal samples over 19 years of evolution. Already at the time of CLL diagnosis, several tiny subclones with genomic, immunogenetic and transcriptomic features of RT cells, which had remained latent for up to 19 years prior to transformation, were observed. These findings demonstrated the early presence of subclones leading to advanced stages of cancer progression, as well as the identification of potential therapeutic targets for RT (PMID: 35953718).

Several new tools have been developed and are now available to assist clinical investigators. Among them:

- An NGS panel for the molecular karyotyping of multiple myeloma (MM)
- A flow cytometry method to assess circulating tumor cells in MM.
- Mass spectrometry is now applicable in MM.
- A machine learning tool is being used in the evaluation of MM.
- The genomics of T-cell acute lymphoblastic leukemia is better understood with this work.
- There is a sample centralization network in Acute Lymphoblastic Leukemia with t (9;22).
- The PETHEMA group has a registry of acute myeloid leukemia and its genetic anomalies.
- A score has been developed to predict early severe infections in MM.
- New prognostic tools for chronic lymphocytic leukemia are now available.
- An interlaboratory analytical validation of NGS clonotypic assessment and MRD monitoring in MM has been performed.

Several clinical trials have been promoted by CIBERONC investigators with the support of CIBERONC laboratories:

- Ibrutinib and Rituximab for Indolent Clinical Forms of Mantle Cell Lymphoma. PMID:35030036. Two PIs from CIBERONC centers. Collaboration of five CIBERONC centers.

- Ponatinib, chemotherapy and transplantation in adults with Philadelphia chromosome positive acute lymphoblastic leukemia. PMID: 35675590; Collaboration of six CIBERONC centers. The centralizing laboratory is a CIBERONC center.
- BRESELIBET Phase III trial to evaluate the use of BV in patients with RRHL who present a challenge to the use of transplantation. Ongoing trial: Collaboration of at least five CIBERONC centers. Centralization of samples in a CIBERONC center.
- Clinical trial with humanized CART directed against BCMA [ARI0002h] in patients with relapsed/refractory multiple myeloma. Ongoing trial: Collaboration of at least four CIBERONC centers.
- Teclistamab in Relapsed or Refractory Multiple Myeloma. PMID:35661166. Collaboration of at least four CIBERONC centers.

Low prevalence tumors

Enrique de Álava Casado

COORDINATOR

The main milestones of the Low Prevalence Tumors Program in 2022 have been the following:

The cooperative projects on the immune landscape of uterine sarcomas and uveal melanomas have been completed. The results of these projects have been published as follows: PMID: 36467415.

A new Scientific Program was designed and approved in June 2022 for the next 4 years, to be implemented on 01/01/2023.

A cooperative project has been designed to cover the activities of the Scientific Program. The project was submitted to an important National competitive call on Personalized Medicine and was selected to be funded. This project entitled Immune4ALL is led by the coordinator of this program and involves 24 CIBERONC groups and several CIBEREHD and non-CIBER groups.

The project, funded with almost 5M€, is structured around several pilot studies that include the development and/or validation of predictive and pharmacodynamic biomarkers for immunotherapy and the generation of a computational framework for data processing, analysis, filtering, visualization and clinical decision support aligned with IMPaCT. We have chosen several robust tumor entities that cause high mortality, specifically in women, such as breast, ovarian and cervical carcinoma, or in both sexes, such as hepatocellular carcinoma, bile duct carcinoma, neuroendocrine tumors of the GI tract and colorectal carcinoma. In addition, the project has two General Objectives dedicated to social and economic aspects [creation of shared decision-making spaces with patients and generation of cost-effective evidence] and to training activities with patients and professionals in the field of precision medicine. The strategy of our Program for 2023 is to integrate leading groups with outstanding experience in clinical, translational and technological research in the development and validation of immuno-oncological biomarkers [including Digital Pathology/ Artificial Intelligence, liquid biopsies and experimental models] and in the development of personalized immunotherapies working in recognized Research Institutions throughout the country, under the umbrella of the CIBER.

Molecular mechanisms of cancer

Xosé R. García Bustelo

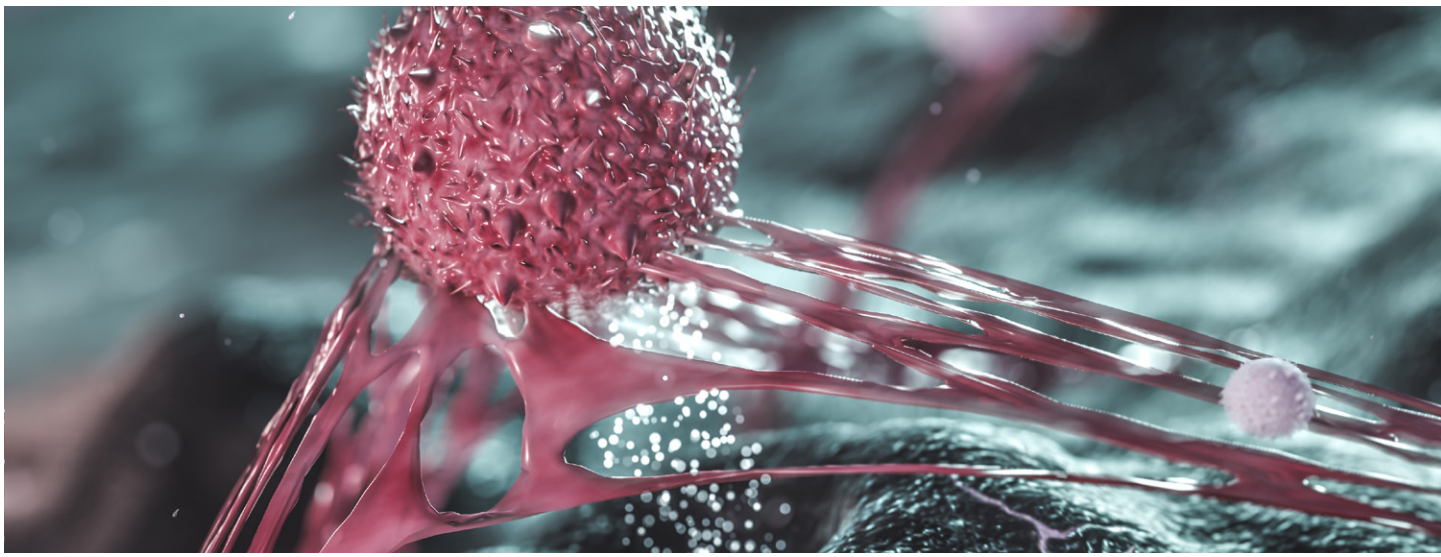
COORDINATOR

Following the reorganization of scientific activities that took place at CIBERONC this year, the Tumor Progression Mechanisms Program has become more transversal in nature in order to foster better cooperative research within this area of CIBER. To this end, in addition to its own research project, the Program also has among its medium-term strategic objectives bi-directional scientific collaboration with the other CIBERONC programs and the coordination of the bioinformatics analysis section of this CIBER area. To emphasize this more transversal character, the Program has changed its name to a more general one that better reflects our scientific mission: Molecular Mechanisms of Cancer. With these changes, we believe that our Program acquires greater added value within the CIBER and, above all, that it will play a more active role in the translation of advances in cancer knowledge to the clinical setting.

From the scientific point of view, during this year we have made significant progress in all the objectives of our joint research project. Major milestones have been the validation and mechanistic dissection of new oncogenic drivers identified in cancer (e.g., publications with PMIDs 35294890, 36476833, 35895495 and 35927489) which, in turn, has allowed us to: (i) identify molecular signatures of interest for both classification and diagnosis of specific tumors; (ii) identify therapeutic vulnerabilities associated with the molecular alterations under study. We have also made significant progress in the development of new antitumor pharmacological strategies (PMIDs 36056964, 35584009, 35921760 and 35915983) which, in some cases, have already entered the initial phases of clinical trials. Simultaneously, a new bioinformatics tool has been developed that enables reliable correlations to be established between gene copy number changes and gene expression using public data from Pan-Cancer projects (PMID 36290315). As validation, this study allowed the identification of new oncogenes and tumor suppressor genes potentially involved in glioblastoma (PMID 36290315). From now on, this tool will be important for all other CIBERONC programs.

We have also been successful in attracting extramural funding from international (5 projects) and national (2 projects) sources, which together have reached an overall funding of 45M euros.

Finally, worth highlighting is that the Program has held several scientific meetings aimed specifically at group leaders, predoctoral and postdoctoral researchers in order to promote the exchange of data and the sense of belonging of the researchers to the Program. Within this section, the first retreat of our Program was held for the first time within CIBERONC, which took place in November 2022 in Santiago de Compostela. This meeting allowed us to discuss progress and plan future strategies within our Program as well as to establish possible ways of collaboration with other scientific programs of CIBERONC and CIBEROBN.



Training

Gema Moreno Bueno

COORDINATOR

The main milestones of the Training and Mobility Program in 2022 have been the following:

1. Training Program

This specific action provides young researchers with a training opportunity in highly specialized courses. In addition, this activity also contributes to the scientific activity of the CIBERONC consortium by sponsoring the organization of national and international training courses as well as specialized symposia.

During 2022, the program opened two calls for proposals and funded a total of 27 actions to attend national and international training courses (out of 47 requested) and three others to organize or sponsor national and international training courses.

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2. Mobility Program

The mobility call finances stays between different CIBERONC groups (activity called intramural); those carried out in laboratories outside the CIBER (called extramural) and finally those carried out within other CIBER laboratories (called interdisciplinary) which aim to improve multidisciplinary training in different fields of specialization.

These are carried out through scientific stays of young CIBERONC researchers in different laboratories to improve their training in specific methodologies and reinforce national and international collaborations between scientific groups.

In 2022, the program had two calls and awarded a total of 14 actions (out of 16 applications): 4 intramural actions, 7 extramural actions (national or international) and 3 interdisciplinary actions (national).

3. Contracts for initiation to research in Oncology

EThis action aims to introduce graduate students to translational oncology research by hiring them for a contract period of up to 6 months in a selected CIBERONC group before starting an official PhD program. To apply for one of these contracts, the interested Group must propose a scientific project to be carried out by the selected candidate for the duration of the contract.

In 2022, the program funded 3 initiation contracts (out of 5 applications received).

4. Promotion of Young Researchers: V Meeting of Young CIBERONC Researchers

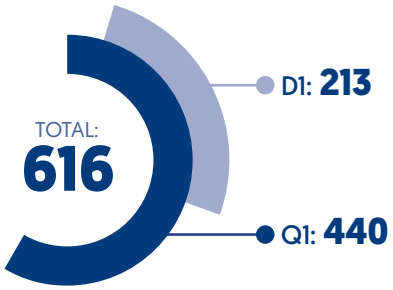
This action is considered an important training and scientific activity for young CIBERONC researchers. This meeting is organized entirely by PhD students and junior postdoctoral fellows (who make up the organizing scientific committee) selected in an open call. This event offers an excellent opportunity for young researchers to be trained in all aspects involved in the organization of a scientific meeting. At the same time, it hosts the scientific forum where students present their own data to their colleagues and invited scientists. Since 2021, this meeting is organized in collaboration with other CIBERs with the aim of improving multidisciplinary training and enhancing cross-disciplinary scientific networks among young researchers.

In 2022, the V Meeting of Young Researchers took place on November 14 and 15 in Santiago de Compostela. In this edition, the meeting was organized in collaboration with CIBERER (rare diseases) with over 100 participants, 69 abstracts presented and 12 presentations by CIBERONC and CIBERER, two plenary lectures and two round tables.

Scientific production

Publications

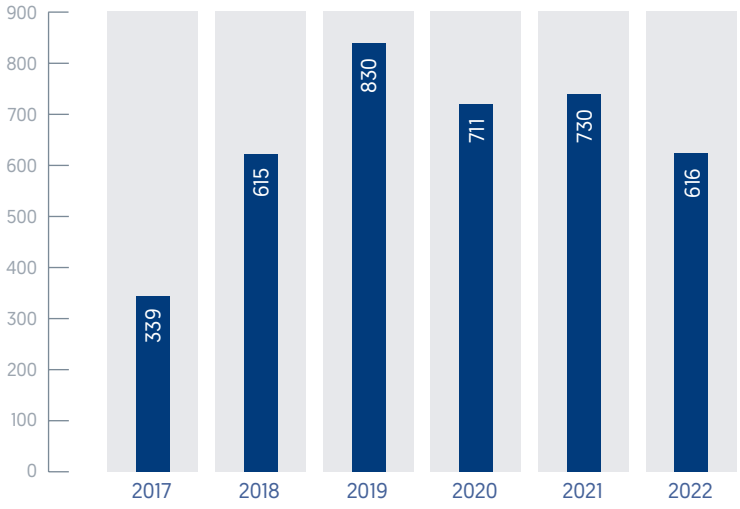
No. of publications in 2022



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

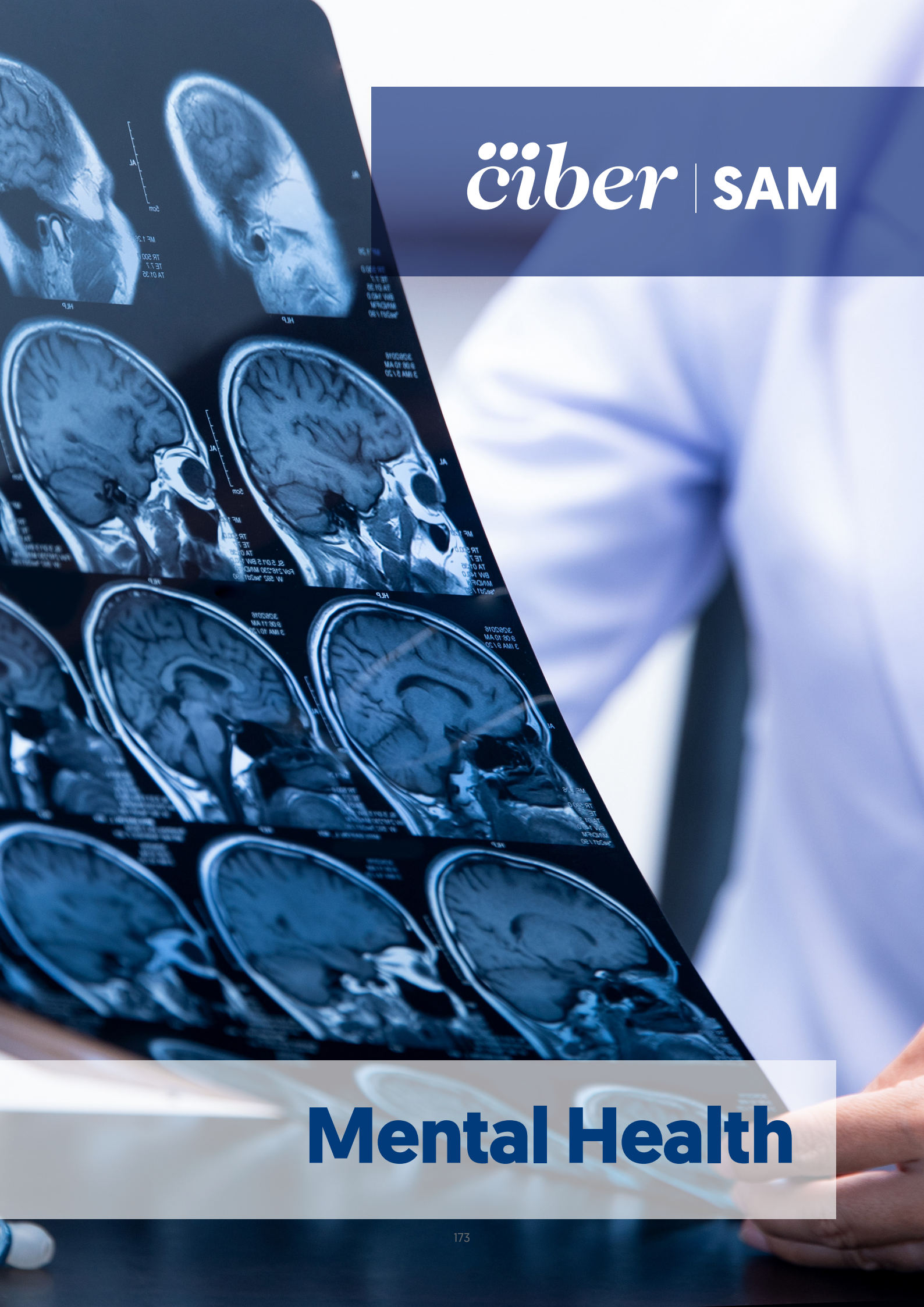
IF	PUBLICATION
87,24	Atezolizumab with enzalutamide versus enzalutamide alone in metastatic castration-resistant prostate cancer: a randomized phase 3 trial
87,24	Pan-cancer efficacy of pralsetinib in patients with RET fusion–positive solid tumors from the phase 1/2 ARROW trial
87,24	Detection of early seeding of Richter transformation in chronic lymphocytic leukemia
87,24	RNF43 mutations predict response to anti-BRAF/EGFR combinatory therapies in BRAF V600E metastatic colorectal cancer
87,24	Clinical and molecular response to tebentafusp in previously treated patients with metastatic uveal melanoma: a phase 2 trial
69,50	Behavioural immune landscapes of inflammation
69,50	Signatures of TOP1 transcription-associated mutagenesis in cancer and germline
69,50	Metastatic recurrence in colorectal cancer arises from residual EMP1+ cells
65,04	Small round cell sarcomas
54,43	Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial

CIBERONC Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alava Casado, Enrique de	9	8	5	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Alba Conejo, Emilio	19	12	6	Universidad de Málaga	Malaga
Albanell Mestres, Joan	22	14	8	Consorci Mar Parc Salut de Barcelona	Barcelona
Aranda Aguilar, Enrique	4	3	-	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	Cordoba
Arribas López, Joaquín	13	9	7	Consorci Mar Parc Salut de Barcelona	Barcelona
Barbacid Montalbán, Mariano	-	-	-	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Oncológicas Carlos III	Madrid
Batlle Gómez, Eduard	8	8	8	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Bigas Salvans, Anna	17	14	6	Consorci Mar Parc Salut de Barcelona	Barcelona
Campo Guerri, Elías	26	19	12	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Camps Herrero, Carlos	17	8	1	Consorcio Hospital General Universitario Valencia	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Capella Munar, Gabriel	21	15	3	Fundación IDIBELL	Barcelona
Carnero Moya, Amancio	11	7	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Sevilla
Carracedo Pérez, Arkaitz	11	10	9	CIC BIOGUNE	Vizcaya
Carrato Mena, Alfredo	20	13	7	Servicio Madrileño de Salud	Madrid
Cervantes RuiPérez, Andres	15	10	7	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia
Colomer Pujol, Dolors	17	12	8	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Crespo Baraja, Pedro	4	3	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	Cantabria
Esteller Badosa, Manel	20	18	9	Fundación Instituto de Investigación contra la Leucemia Josep Carreras	Barcelona
Feliú Batlle, Jaime	13	8	5	Servicio Madrileño de Salud	Madrid
Garcia Bustelo, Xose Ramon	6	5	3	Fundación de Investigación del Cáncer de la Universidad de Salamanca	Salamanca
García Sanz, Ramón	70	49	28	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	Salamanca
López Bigas, Nuria	1	1	1	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
López López, Rafael	27	18	6	Servicio Gallego de Salud	Coruña, A
López Otin, Carlos	6	6	4	Universidad de Oviedo	Asturias
Malats Riera, Nuria	7	7	6	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid
Martin Jimenez, Miguel	2	-	-	Servicio Madrileño de Salud	Madrid
Matias-Guiu Guia, Francisco Javier	25	20	11	Instituto de Investigacion Biomédica de Lleida. Fundación Dr. Pifarre	Lleida
Melero Bermejo, Ignacio	28	24	13	Universidad de Navarra	Navarra
Montuenga Badia, Luis	24	21	11	Fundación para la Investigación Médica Aplicada	Navarra
Moreno Bueno, Gema	5	5	3	Universidad Autónoma de Madrid	Madrid
Muñoz Terol, Alberto	5	4	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Noguera Salva, Rosa	2	1	1	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	Valencia
Orfao de Matos Correia e Vale, Jose Alberto	2	2	2	Fundación de Investigación del Cáncer de la Universidad de Salamanca	Salamanca
Palacios Calvo, Jose	8	4	1	Servicio Madrileño de Salud	Madrid
Pandiella Alonso, Atanasio	7	4	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Paramio Gonzalez, Jesús Maria	29	24	8	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	Madrid
Paz-Ares Rodriguez, Luis	16	12	5	Servicio Madrileño de Salud	Madrid
Piris Pinilla, Miguel Angel	13	11	9	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Prosper Cardoso, Felipe	28	26	13	Fundación para la Investigación Médica Aplicada	Navarra
Ramon Y Cajal Agüeras, Santiago	18	15	10	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Real Arribas, Francisco Xavier	4	3	2	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid
Rodrigo Tapia, Juan Pablo	14	6	1	Fundación para la Investigación e Innovacion Biosanitaria en el Principado de Asturias (FINBA)	Asturias
San Miguel Izquierdo, Jesús Fernando	33	26	17	Universidad de Navarra	Navarra
Santisteban Sanz, María del Pilar	8	5	-	Agencia Estatal Consejo Superior de Investigaciones Científicas	Madrid
Santos de Dios, Eugenio	-	-	-	Fundación de Investigación del Cáncer de la Universidad de Salamanca	Salamanca
Sanz Santillana, Guillermo	27	14	6	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	Valencia
Seoane Suarez, Joan	6	5	3	Fundación Privada Instituto de Investigación Oncológica Valle de Hébron-VHIO	Barcelona
Tabernero Caturla, José María	17	13	8	Fundación Privada Instituto de Investigación Oncológica Valle de Hébron-VHIO	Barcelona



ciber | SAM

Mental Health

Welcome from the scientific director

Eduard Vieta Pascual

The year 2022 has been the year of the end of the pandemic, but also the year of the war in Ukraine and the aftermath of the mental health repercussions resulting from these extraordinary global circumstances. True to its mission, CIBERSAM has promoted collaborative translational research through its programs and interaction with other Ciber areas, leading advances in the treatment of psychosis and affective disorders in children and adolescents (a growing topic also due to the impact of the pandemic), suicide prevention through the "Survive" macro-study, or, among others, the perspective of the patient with bipolar disorder. CIBERSAM has achieved this year the identification and characterization of a population of immature excitatory neurons in the neocortex of adult humans, and the development of lipid nanoparticles with antisense oligonucleotides to modulate the neuroinflammatory control of perivascular macrophages of the blood-brain barrier in models of psychiatric pathologies. Also noteworthy in 2022 are the advances in the treatment of autism and attention deficit hyperactivity disorder led by CIBERSAM, as well as the usual contributions derived from participation in international consortia in genetics, neuroimaging, and biomarkers, in line with the general framework of Precision Psychiatry, which is central to the mission and strategy of our area.

Beyond the important scientific advances, the mental health area of CIBERSAM stands out for its activity in teaching and training of researchers through its Interuniversity Master, the supervision of doctoral theses, and its courses (finally in person again!) in Neurosciences, Laboratory of Ideas and the Instruments Bank. CIBERSAM has also played an outstanding role in the elaboration of international therapeutic guidelines (32 this year), in the participation and leadership in clinical trials, and in science dissemination activities such as the Mentescopia project, among others. This year has also been particularly prolific in terms of awards granted to CIBERSAM researchers.

In line with Ciber's new strategic plan, which in the coming years will frame the progression of research and innovation generated by the center, as well as its governance, we leave behind an extraordinary 2022 filled with hope stemming from the recovery from the Covid-19 pandemic and the availability of more expansive budgets in science and innovation. May this report serve to honor the hard work, under difficult conditions, of all those who work for the advancement of science applied to mental health in our country.

Programs

Depression and suicide prevention

Diego Palao Vidal

COORDINATOR

The COVID-19 pandemic has had a considerable impact on the mental health of the population. Many of the factors associated with suicide risk persist (increase in the incidence of depression by more than 25%, economic impact or limited access to health and social services). The social gradient, gender and age differences or the impact on different populations have been highlighted in some of the epidemiological studies carried out with the participation of researchers from the program.

Suicide is also associated with other mental illnesses and has been the subject of cross-cutting research for CIBERSAM. During 2022, more than 340 articles on depression and more than 90 on suicide have been published in collaboration with other CIBERs and international research groups in epidemiology, neurobiology and prevention. The 5 groups of the Program have published several articles in top quality journals such as JAMA Psychiatry, Nature Communications, Nature Metabolism, Lancet Psychiatry, Biological Psychiatry..., 17 doctoral theses have been presented and competitive funding has been obtained for 27 national and international projects as well as 11 contracts.

The SURVIVE cohort project (8 groups involved) is concluding the trial of suicide prevention interventions (one in adolescents) and is beginning to disseminate results of the monitoring of suicidal behaviors in Spain.

The participation in regional, national and international working groups and consortiums on resistant depression, electroconvulsive therapy (GenECT) and neuroimaging (GEMRIC, ENIGMA) deserve special mention. Papers have been published that have deepened the study of the mechanism of action of ECT and the neurobiology of depression, as well as the knowledge of various factors associated with depression (aging, loneliness, lifestyles and pain). In addition, the groups continue to investigate the development and evaluation of possible diagnostic and prognostic biomarkers in neuroimaging, neurocognition, neurophysiology, immunometabolism and genetics.

Some examples are the translational studies on the polymorphism of the PACAP-PAC1R (pituitary adenylate cyclase-activating polypeptide) system associated with the risk of suffering post-traumatic stress in women through hippocampal modulation to stressful stimuli and its replication in animal models, results that could open up new targets for therapeutic intervention. Also, the studies to identify altered miRNAs in the cingulate cortex of subjects with depression, validate their potential as peripheral biomarkers of antidepressant effects and develop new nanotherapies.

In the lines of molecular basis and evaluation of new drugs and therapeutic targets in depression, research continues on the glutamatergic pathway, the antidepressant effects of oligonucleotides in animal models and several clinical trials on new therapeutic targets for treatment resistant depression, which affects one third of the people affected.

During this year, researchers from the program have been leaders in scientific dissemination in depression and suicide prevention in various forums. In addition, they have been involved in the discussion with health policy managers at the national (e.g., suicide prevention conference in the Congress of Deputies) and regional (e.g., coordinating the implementation of the Catalan suicide prevention plan) levels).

Schizophrenia

Edith Pomarol-Clotet

COORDINATOR

The CIBERSAM Schizophrenia Program is the largest CIBERSAM program (11 research groups + 2 linked clinical groups) and the most fruitful in terms of publications and funded competitive projects.

This year 2022 has been an excellent year in terms of high-level publications with 105 publications in the first decile, 120 in the first quartile in collaboration with other CIBERSAM groups, 31 with other CIBER consortia, as well as 162 in international collaborations. Also noteworthy are 40 systematic reviews and meta-analyses.

Among these publications, the following stand out for their high level of impact and/or collaboration: Schizophrenia published in Lancet; Mapping genomic loci implicates genes and synaptic biology in schizophrenia in Nature; Fingerprints as Predictors of Schizophrenia: A Deep Learning Study published in Schizophrenia Bulletin; Effect of polygenic risk score, family load of schizophrenia andexposome risk score, and their interactions, on the long-term outcome of first-episode psychosis in Psychological Medicine.

In addition, 41 new clinical trials, epidemiological studies or community interventions were developed in 2022, doubling the number achieved the previous year. We would also like to highlight the elaboration of 16 new clinical guidelines.

In terms of program activities, two annual follow-up meetings and a scientific conference on "Neuroimaging and genetics" have been held with a high level of participation. These activities have promoted the implementation of new collaborative projects. In addition, worth mentioning are the funding of the AGES-CM consortium (Environment and Genes in Schizophrenia); Applied pharmacogenetics to predict response to treatment in the first psychotic episodes; Microbiome-gut-brain axis and related inflammatory markers in patients with schizophrenia; Personalized metacognitive interventions and study of a screening tool for patients with a psychiatric neurodevelopmental disorder: 22q11.2 deletion syndrome as a model.

We also highlight the completion of more than 10 doctoral theses, among these: Constitutive activity and drug funtional selectivity of 5-HT2A receptors in post-mortem brain of subjects with schizophrenia; Metabolic Syndrome in Antipsychotic Naïve Patients with First-Episode Psychosis and Determination of brain flow by transcranial ultrasound in patients with schizophrenia and healthy controls.

In addition, of note is the successful organization of the Schizophrenia Track in the 2022 National Congress of Psychiatry (CNP) which has boosted the visibility of CIBERSAM, as well as the media dissemination of news such as the study on the involvement of the brain area of social cognition in delusions; identification of the relationship between schizophrenia and loneliness through the analysis of its genetic bases; analysis of the genetic variability of people with schizophrenia and healthy people of the DISC1 gene; identification of 119 new genes related to schizophrenia; and new pharmacological approaches to schizophrenia in an animal model. Also noteworthy is MenteScopia, a multimedia project to disseminate information on mental illnesses and their prevention.

Finally, we would like to mention the achievement of the Dr. Carles Vallbona i Calbó Award and the Vila Saborit Award for Best Publication 2021 from the Societat Catalana de Psiquiatria i Salut Mental (Catalan Society of Psychiatry and Mental Health).

Bipolar disorder

Vicent Balanzá-Martínez

COORDINATOR

In 2022 the groups of the program have published research results in high impact journals such as Lancet, World Psychiatry, JAMA Psychiatry, Translational Psychiatry, or Biological Psychiatry, among others. Most of the articles are collaborative with groups from the program, other CIBERSAM groups and other CIBERs. A considerable percentage are publications participating in international consortia, such as GBD and ENIGMA.

During 2022, we have continued to contribute to the advancement of knowledge on the impact of the COVID-19 pandemic on mental health, in terms of depression and suicide. The groups continue to investigate the identification of potential biomarkers (neuroimaging, neurocognitive, genetic) for accurate diagnosis and prognosis of bipolar disorder. The subject matter of the projects encompasses such broad aspects as neurocognitive improvement in older adults with bipolar disorder, pharmacogenomics and pharmacogenetics, multimorbidity, lifestyle, and the role of the microbiome-gut-brain axis and the retina in the disease. Currently, a group of the program is leading an intramural CIBERSAM project.

Relevant scientific achievements include participation in an extensive GWAS study identifying a risk locus that contributes significantly to suicide attempt in bipolar disorder. In addition, three members of the program have been appointed by WHO to conduct reports on mental health at the workplace in Europe and on the impact of COVID-19 on mental health.

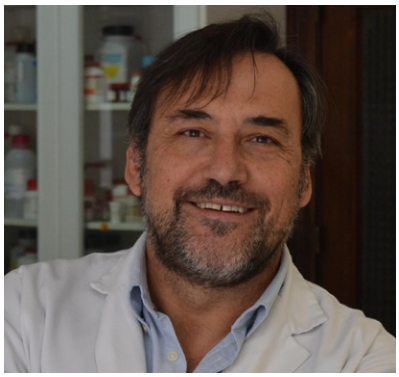
Competitive funding has been obtained for numerous clinical trials, projects and contracts from state and regional public bodies (ISCIII-FIS, MCINN, Generalitat Valenciana, Fundación de Investigación Biosanitaria del Principado de Asturias, Instituto de Investigación Sanitaria Bioaraba); the European Union; foundations (La Marató TV3) and various pharmaceutical companies.

Researchers from the program have obtained awards and distinctions, such as Honorary Member of the Royal Academy of Catalan Medicine or the Santiago Reig 2022 Award for Best Publication 2021 from CIBERSAM. The groups of the program have participated in numerous national and international scientific meetings, most notably the organization of the "ECNP Workshop on Clinical Research Methods", the Symposium on Bipolar and Depressive Disorders, the Course on Psychopharmacology and Neuroscience or the CIBERSAM International Forum on Research in Psychiatry.

The program has also played a leading role in the media and other public arenas of scientific interest with diverse topics, such as mental health and neuroscience, the evolution of suicide mortality data in our country (2000-2021) or "Edad con Salud" (Healthy Aging), a decade of studies on health and wellbeing in the Spanish adult population.

Activities aimed at the general public have been developed, such as the organization of the "Citizens' Convention for the future Valencian mental health plan", the participation in various forums during the "Combat Depression" and "Mental Health" world days, as well as in meetings with associations of families and patients with bipolar disorder. Finally, we highlight the growing participation of the groups in the dissemination of scientific news through websites and social networks.

Therapeutic innovation



Juan Carlos Leza

COORDINATOR

The groups that make up the program have maintained an extensive and solid research activity in terms of publications, especially original basic-clinical research, most of which are collaborative between groups in the program and others in the CIBER consortium and, in a significant number, the result of consolidated relationships with international groups. Among them are original publications (more than 400 in total). They have also participated as authors in systematic reviews or as editors of special issues or volumes by invitation.

The activity of the program's researchers has also been reflected in their participation in 26 consensus clinical guidelines published on various aspects: evaluation of neurocognitive disorders, clinical and pharmacological management in patients with treatment-resistant schizophrenia or depression, clinical management in electroconvulsive therapy, and interventions in patients with borderline personality disorder and ASD. In 2022, 32 clinical trials have been opened with new antidepressant and antipsychotic drugs and other treatment strategies, including virtual reality and neurocognitive stimulation techniques.

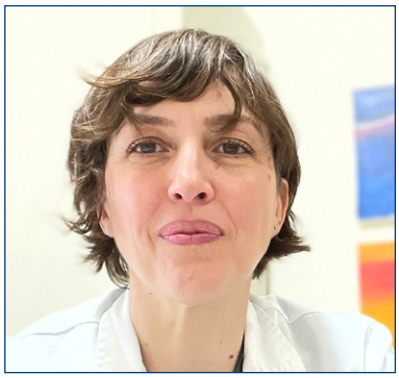
In addition to the numerous competitive projects, several groups in the program have signed contracts with companies on topics related to innovation: use of conjugated miRNAs in models of neuropsychiatric pathologies, brain image reconstruction systems, among others. Also, in innovation in Neuropharmacology training. Other innovation projects include the development of a metabolic risk algorithm in schizophrenia, the app "Psychopharmacological dose calculator" eDOSE and others that use AI for the prediction of drug response.

Members of the program have coordinated, participated or been invited to participate in numerous national and international scientific forums. They have also participated in dissemination events in the press, radio and television, events with patient associations, etc... In addition, many groups maintain very active social media accounts and web pages for the dissemination of scientific news.

Below are some examples of the most important scientific achievements published by the groups in the program in 2022:

- Identification of mechanisms that would explain differences in predisposition to opiate abuse.
- Identification and characterization of a population of immature excitatory neurons in adult human neocortex.
- Description of the neurobiological mechanisms of the acute effects of psilocybin.
- Development of a preclinical model to study depressive symptomatology of Parkinson's disease.
- Identification of changes in the plasticity of the locus coeruleus over time and its relationship with co-morbid chronic pain and depression.
- Identification of a genetic variation of the PACAP receptor and its role in the extinction of conditioned fear in women with a history of traumatic stress.
- Design and development of the Mental Health module incorporated into the Guttman Neuropersonal Trainer (GNPT®) cognitive telerehabilitation platform to personalize the therapeutic sessions for each patient.
- Design of a tool to assess whether MRI is able to detect patients at high risk of relapse after the first psychotic break with AI methods.
- Development of lipid nanoparticles with antisense oligonucleotides to modulate the neuroinflammatory control of perivascular macrophages of the BBB in models of psychiatric pathologies.

Mental disorders of the child and adolescent



Carmen Moreno Ruíz

COORDINATOR

This program, made up of seven clinical and basic groups, develops national and international collaborative research on childhood- and adolescent-onset mental disorders.

In 2022, projects have been developed on the gene-environment interaction in the trajectories of mental health problems, the long-term effects of pregnancy on the human brain, the role of intrauterine stress and cognitive reserve in children and adolescents at risk of psychosis, the design of genetic diagnostic algorithms in autism, and predictors of intergenerational transmission of mental illness.

The results of these works have been published mainly in journals indexed in the first quartile such as Nature, World Psychiatry, Lancet Psychiatry, Nature Genetics, Gut, Nature Neuroscience, Brain Behavior and Immunity, Nature Communications, Molecular Psychiatry or Journal of the American Academy of Child and Adolescent Psychiatry.

Among the main results published are the first clinical trial demonstrating the efficacy of agomelatine for the treatment of adolescents with major depression and the first meta-analysis to evaluate a wide range of pharmacological interventions for irritability and emotional dysregulation in autism, which found short-term efficacy of risperidone and aripiprazole. Also in autism, a systematic review found no biomarker of response that could be used in clinical trials, suggesting the need to implement methodological improvements in research in this field, and another systematic review and meta-analysis concluded that people with autism or ADHD had higher mortality rates than the general population.

In a study of patients (12-60 years old) with anti-NMDA encephalitis, schizophrenia and controls, only participants with anti-NMDAR encephalitis progressively improved. Another study found that cognition-based stratification may help elucidate the biological underpinnings of cognitive heterogeneity in youth at familial risk for schizophrenia and bipolar disorder. In early-onset OCD, we found evidence of monocyte dysregulation, suggesting a proinflammatory predisposition. Furthermore, in an animal model of induced neurodevelopmental disturbance, a negative relationship was found between glucocorticoid receptor signaling and serotonin 5-HT2AR receptor expression in the frontal cortex, which may have implications for the pathophysiology of neurodevelopmental disorders.

Finally, several studies have found that parenthood is a period of increased brain plasticity within critical areas of the brain for cognitive and social processing. One found evidence of cortical structural changes in parents, suggesting that the experience of transition to parenthood is a window of brain neuroplasticity.

This year, members of the program have received, among others, the Dr. Carles Vallbona i Calbó Award, Best Poster Award at the IRSJD Debates Meeting, Best Oral Communication Award Aepnya Congress, Research Assistance Award AEPNyA, SIRS Early Career Award, ECNP Excellence Award, SEPSM Award to Young Accredited Researchers and Recognition to Outstanding Person XXV edition “Recognition of Childhood” Awards of the Community of Madrid.

Psychosomatic, anxiety and impulse control disorders

Virginia Soria

COORDINATOR

During 2022, results of the research conducted in the Psychosomatic, Anxiety and Impulse Control Disorders Program have been reported in publications in prestigious scientific journals providing evidence for the application of functional neuroimaging in neurobiological models of overeating and binge eating disorder, on the efficacy and acceptability of various psychotherapies in borderline personality disorder (BPD) showing how dialectical-behavioral therapy reduces polypharmacy. New data have been provided on the association of neurohormonal receptor biomarkers with cognitive aspects in BPD and the involvement of inflammatory biomarkers related to clinical profiles in eating disorders. Right prefrontal cortical thickness has been identified as a marker of response to cognitive-behavioral therapy in children with obsessive-compulsive disorder (OCD) and the long-term efficacy and safety of deep brain stimulation in severe resistant OCD has been confirmed. Preliminary data support the use of deep brain stimulation in refractory anorexia nervosa.

Mention should be made of the active participation of program researchers in the media and scientific dissemination projects addressing the destigmatization of mental illnesses, mental health education, prevention and treatment based on the advances developed in the field of neurosciences.

Reviews, guidelines and consensus recommendations have been prepared on the management of neurocognitive disorders, self-injury in adolescence, problematic use of the Internet, the role of serious video games in attention deficit hyperactivity disorder (ADHD) and we have participated in international guidelines for the treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders.

Funding has been obtained for projects that will provide evidence on the efficacy and clinical applicability of artificial intelligence in diseases prevalent in aging, psychotherapies in disorders related to work-related stress, psychological trauma, eating disorders and autism spectrum, combined treatments such as lifestyle modification with metacognitive training, neuro-hormonal treatments plus self-compassion in BPD, perinatal depression, advanced therapies in OCD, as well as to further address the impact of COVID19. Funding has also been obtained to maintain the long-term prospective study of several cohorts of patients, such as the OCD Barcelona cohort and the SURVIVE cohort for the study of the prevention of suicidal behavior and intervention using digital tools.

We have continued to participate extensively in international platforms and consortia such as COSMIC, ENIGMA, EMPOWER, IMI EU-PEARL and the Psychiatric Genomics Consortium, with outstanding leadership in healthy aging, OCD and ADHD. Also noteworthy is the establishment of contracts with companies for the evaluation of pre- and probiotic compounds in pre-clinical models of neuropsychiatric disorders.

The program's commitment to the development of research talent, supported by doctoral theses with honorable mentions, is also noteworthy. We would also like to highlight the awarding of the Spanish Society of Psychiatry and Mental Health Award for "Professional Career in Psychiatry" to Professor Antonio Lobo, a leading figure in Psychosomatic Psychiatry.

Training

Esther Berrocoso

COORDINATOR

During 2022, the Transversal Training Program has financed a total of 34 actions. As regards training aimed directly at human resources training, 3 researcher training stays stand out, two international and one national. In addition, a significant number of actions were carried out for registration to courses, congresses and research seminars, 6 activities were with "on-line" participation and 28 in person, in various events with the presence of CIBERSAM. Among the courses or events where CIBERSAM has participated or has lent its support, we highlight the following: 9th edition of the CIBERSAM Laboratory of Ideas, which this year was held in Vitoria-Gasteiz, May 26-27, 2022. This course has offered an opportunity for young researchers who are part of any CIBER or RETIC to raise and discuss their scientific advances and had as its motto "The road to translation and venture". The XIX CIBERSAM Intensive Course on Introduction to Neuroscience Research, Barcelona, September 9, 2022, which focused on mental health and human neurodevelopment, and how various environmental factors can influence it, was also held, in person, in Barcelona. In addition, the XI Workshop of the CIBERSAM Bank of Instruments, September 20, 2022, was also held in Barcelona.

Other courses in which CIBERSAM has participated or has lent its support:

- XXIII Symposium on Bipolar and Depressive Disorders, Barcelona, March 11, 2022.
- XXVII Theoretical-Practical Course on Electroconvulsive Therapy. L'Hospitalet de Llobregat, May 23-27, 2022.
- Statistics for Health Sciences. Barcelona, June 3-17, 2022.
- Clinical and Translational Research towards Precision Medicine in Mental Health. Santander, June 6-17, 2022.
- Mental Health Research. Translation is born from integration. Valencia, October 6, 2022.
- Course on Resistant Pathologies, Barcelona, October 6-7, 2022.
- 24th Congress of Dual Pathology. Madrid, October 24-29, 2022.
- XXV National Congress of Psychiatry 2022. Santiago de Compostela, November 17-19, 2022.
- #ImproScience. CIBER Activity. Madrid Science Week, November 8, 2022.
- VIII Meeting between mental health researchers, patients and relatives. Madrid, December 13, 2022.

Another of the basic pillars of the Training axis is the Interuniversity Master's Degree in Initiation to Research in Mental Health [https://www.mastersaludmental.unican.es/], with 57 registrations for the 2022 edition. The number of students enrolled in the type A and B stays was 39, and a total of 31 Master's theses were presented.

Finally, the Training Program has participated, together with other CIBERs, in the transversal training plan regarding the homogenization of the CIBER training plan, and has updated the regulations and documentation associated with the training actions. In addition, the management staff associated with Training and Interuniversity Masters has been consolidated, which will contribute to the long-term projection of this Program.

Platforms

Susana Carmona

COORDINATOR

Official CIBERSAM Platforms:

- Instruments Library
- DNA collections and biological samples
- Neuroimaging

CIBERSAM's own three platforms and the linked external platform have continued acting as support instruments for projects and activities. The respective indicators, both of their own activity and productivity (publications, etc...) guarantee a sustained trajectory over time

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	INSTRUMENTS LIBRARY	DNA COLLECTIONS AND SAMPLES	NEUROIMAGING
Existing Instruments	342		
Added instruments	9 + 2 updates		
Consultations or requests for use	15		8
Financed publications	101		
Training activities	1		
Stored images			24912
Contributing groups		10	3
User groups		4	1
Patients included		18491	
New patients		294	

The activity of the external platform is reflected in the following indicators:

	BRAIN COLLECTION
Number of existing samples (different subjects)	1427
Number of new samples added (different subjects)	56
Number of groups using samples	6
Number of consultations made	8
Training activities	1

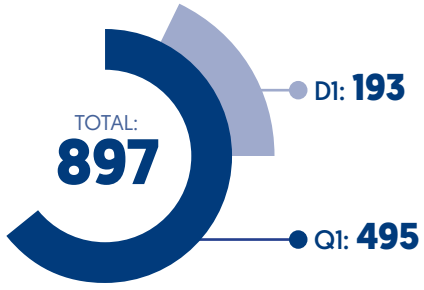
Furthermore, the scientific productivity generated as a result of the use and exploitation of the CIBERSAM platforms in 2022 and the comparison with the data from 2018 is reflected in the following table::

USE OF CIBERSAM PLATFORMS BY INTRA-AREA OR EXTERNAL GROUPS	2019	2020	2021	2022
Total no. of Publications	**37**	**37**	**75**	**96**
GRIDSAM Publications	11	15	25	37
DNA Publications	10	10	11	39
Neuroimaging Publications	7	10	8	8
Instruments Publications	8	6	39	53
Brains Publications	8	6	7	3
Total no. of Clinical Trials	**1**	**1**	**0**	**5**
Instruments Trials	1	1	-	4
GRIDSAM	-	-	-	1
Total no. of Patents	**1**	**0**	**0**	**0**
Brain Patents	1	-	-	0
Total no. of Clinical Guidelines	**1**	**0**	**0**	**1**
Instruments Clinical Guidelines	1	-	-	1

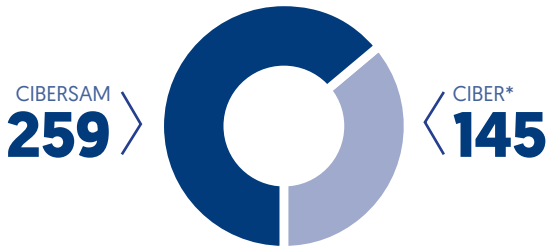
Scientific production

Publications

No. of publications in 2022

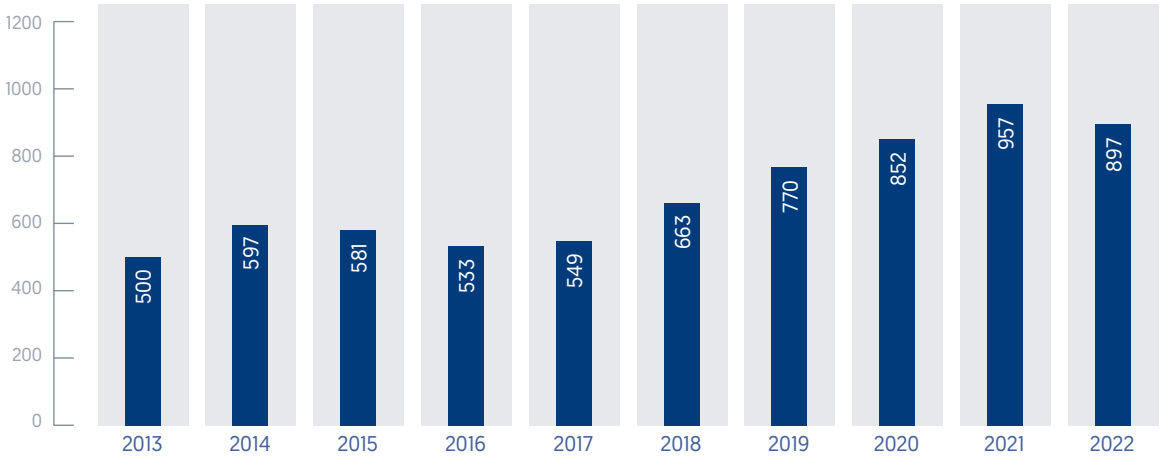


Collaborations



*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
202,731	Jauhar S, Johnstone M, McKenna PJ. Schizophrenia. Lancet. 2022 Jan 29;399(10323):473-486. doi: 10.1016/S0140-6736(21)01730-X. PMID: 35093231.
202,731	GBD 2020 Alcohol Collaborators. Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020. Lancet. 2022 Jul 16;400(10347):185-235. doi: 10.1016/S0140-6736(22)00847-9. PMID: 35843246.
202,731	GBD 2019 Cancer Risk Factors Collaborators. The global burden of cancer attributable to risk factors, 2010-19: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022 Aug 20;400(10352):563-591. doi: 10.1016/S0140-6736(22)01438-6. PMID: 35988567.
79,683	Fusar-Poli P, Estradé A, Stanghellini G, Venables J, Onwumere J, Messas G, Gilardi L, Nelson B, Patel V, Bonoldi I, Aragona M, Cabrera A, Rico J, Hoque A, Otaiku J, Hunter N, Tamelini MG, Maschião LF, Puchivailo MC, Piedade VL, Kéri P, Kpodo L, Sunkel C, Bao J, Shiers D, Kuipers E, Arango C, Maj M. The lived experience of psychosis: a bottom-up review co-written by experts by experience and academics. World Psychiatry. 2022 Jun;21(2):168-188. doi: 10.1002/wps.20959. PMID: 35524616.
79,683	Kessler RC, Kazdin AE, Aguilar-Gaxiola S, Al-Hamzawi A, Alonso J, Altwaijri YA, Andrade LH, Benjet C, Bharat C, Borges G, Bruffaerts R, Bunting B, de Almeida JMC, Cardoso G, Chiu WT, Cía A, Ciutan M, Degenhardt L, de Girolamo G, de Jonge P, de Vries YA, Florescu S, Gureje O, Haro JM, Harris MG, Hu C, Karam AN, Karam EG, Karam G, Kawakami N, Kiejna A, Kovess-Masfety V, Lee S, Makanjuola V, McGrath JJ, Medina-Mora ME, Moskalewicz J, Navarro-Mateu F, Nierenberg AA, Nishi D, Ojagbemi A, Oladeji BD, O'Neill S, Posada-Villa J, Puac-Polanco V, Rapsey C, Ruscio AM, Sampson NA, Scott KM, Slade T, Stagnaro JC, Stein DJ, Tachimori H, Ten Have M, Torres Y, Viana MC, Vigo DV, Williams DR, Wojtyniak B, Xavier M, Zarkov Z, Ziobrowski HN; WHO World Mental Health Survey collaborators. Patterns and correlates of patient-reported helpfulness of treatment for common mental and substance use disorders in the WHO World Mental Health Surveys. World Psychiatry. 2022 Jun;21(2):272-286. doi: 10.1002/wps.20971. PMID: 35524618.
79,683	McIntyre RS, Alda M, Baldessarini RJ, Bauer M, Berk M, Correll CU, Fagiolini A, Fountoulakis K, Frye MA, Grunze H, Kessing LV, Miklowitz DJ, Parker G, Post RM, Swann AC, Suppes T, Vieta E, Young A, Maj M. The clinical characterization of the adult patient with bipolar disorder aimed at personalization of management. World Psychiatry. 2022 Oct;21(3):364-387. doi: 10.1002/wps.20997. PMID: 36073706.
77,056	Bugarski-Kirola D, Arango C, Fava M, Nasrallah H, Liu IY, Abbs B, Stankovic S. Pimavanserin for negative symptoms of schizophrenia: results from the ADVANCE phase 2 randomised, placebo-controlled trial in North America and Europe. Lancet Psychiatry. 2022 Jan;9(1):46-58. doi: 10.1016/S2215-0366(21)00386-2. Epub 2021 Nov 30. PMID: 34861170.
77,056	Fusar-Poli P, Salazar de Pablo G, Rajkumar RP, López-Díaz Á, Malhotra S, Heckers S, Lawrie SM, Pillmann F. Diagnosis, prognosis, and treatment of brief psychotic episodes: a review and research agenda. Lancet Psychiatry. 2022 Jan;9(1):72-83. doi: 10.1016/S2215-0366(21)00121-8. Epub 2021 Nov 29. PMID: 34856200.
77,056	Arango C, Buitelaar JK, Fegert JM, Olivier V, Pénélaud PF, Marx U, Chimits D, Falissard B; study investigators. Safety and efficacy of agomelatine in children and adolescents with major depressive disorder receiving psychosocial counselling: a double-blind, randomised, controlled, phase 3 trial in nine countries. Lancet Psychiatry. 2022 Feb;9(2):113-124. doi: 10.1016/S2215-0366(21)00390-4. Epub 2021 Dec 14. Erratum in: Lancet Psychiatry. 2022 Mar;9(3):e10. PMID: 34919834.
77,056	Crossley NA, Alliende LM, Czepielewski LS, Aceituno D, Castañeda CP, Diaz C, Iruretagoyena B, Mena C, Mena C, Ramirez-Mahaluf JP, Tepper A, Vasquez J, Fonseca L, Machado V, Hernández CE, Vargas-Upegui C, Gómez-Cruz G, Kobayashi-Romero LF, Moncada-Habib T, Arango C, Barch DM, Carter C, Correll CU, Freimer NB, McGuire P, Evans-Lacko S, Undurraga E, Bressan R, Gama CS, López-Jaramillo C, de la Fuente-Sandoval C, Gonzalez-Valderrama A, Undurraga J, Gadelha A. The enduring gap in educational attainment in schizophrenia according to the past 50 years of published research: a systematic review and meta-analysis. Lancet Psychiatry. 2022 Jul;9(7):565-573. doi: 10.1016/S2215-0366(22)00121-3. PMID: 35717966.

CIBERSAM Groups, Publications in 2022

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Arango López, Celso	105	74	37	Servicio Madrileño de Salud	Madrid
Ayuso Mateos, José Luis	56	31	17	Universidad Autónoma de Madrid	Madrid
Baeza Pertegaz, María Inmaculada	95	61	26	Hospital Clínico y Provincial de Barcelona	Barcelona
Berrocoso Domínguez, Esther	17	10	2	Universidad de Cádiz	Cadiz
Bortolozzi Biasoni, Analia	11	8	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	Barcelona
Crespo Facorro, Benedicto	62	39	17	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla
Desco Menéndez, Manuel	22	13	4	Servicio Madrileño de Salud	Madrid
Fañanas Saura, Lourdes	38	25	12	Universidad de Barcelona	Barcelona
González Pinto Arrillaga, Ana	56	31	9	Asociación Instituto de Investigación Sanitaria BIOARABA	Alava
Haro Abad, Josep Maria	202	106	53	Fundación para la Investigación y Docencia Sant Joan de Deu	Barcelona
Ibáñez Cuadrado, Ángela	71	22	7	Servicio Madrileño de Salud	Madrid
Leza Cerro, Juan Carlos	56	24	8	Universidad Complutense de Madrid	Madrid
Meana Martínez, José Javier	31	18	7	Universidad del País Vasco	Vizcaya
Menchón Magriña, José Manuel	67	34	12	Fundación IDIBELL	Barcelona
Nacher Rosello, Juan Salvador	51	28	11	Universidad de Valencia	Valencia
Olivares Diez, José Manuel	12	9	1	Servicio Gallego de Salud	Pontevedra
Palao Vidal, Diego Jose	41	20	7	Fundación Instituto de Investigación e innovación Parc Taulí	Barcelona
Pérez Sola, Víctor	89	48	12	Consorci Mar Parc Salut de Barcelona	Barcelona
Pomarol Clotet, Edith	53	27	10	Fundación para la Investigacion y Docencia Maria Angustias Gimenez (FIDMAG)	Barcelona
Ramos Quiroga, José Antonio	61	31	12	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Rodríguez-Jiménez, Roberto	61	29	6	Servicio Madrileño de Salud	Madrid
Sáiz Martínez, Pilar Alejandra	48	29	13	Universidad de Oviedo	Asturias
Tabarés Seisdedos, Rafael	52	35	19	Universidad de Valencia	Valencia

GROUP LEADER	PUBLICATIONS	Q1	D1	INSTITUTION - CENTER	PROVINCE
Vieta Pascual, Eduard	137	102	36	Hospital Clínico y Provincial de Barcelona	Barcelona
Vilella Cuadrada, Elisabet	24	9	6	Fundación Instituto de Investigacion Sanitaria Pere Virgili	Tarragona

Clinical Guidelines 2022

- A Guideline and Checklist for Initiating and Managing Clozapine Treatment in Patients with Treatment-Resistant Schizophrenia.
- A normative chart for cognitive development in a genetically selected population.
- Advances in problematic usage of the internet research - A narrative review by experts from the European network for problematic usage of the internet.
- An International Adult Guideline for Making Clozapine Titration Safer by Using Six Ancestry-Based Personalized Dosing Titrations, CRP, and Clozapine Levels.
- An international clozapine titration guideline to increase its safety and move forward on the route started by German-speaking psychiatrists in the 1960s.
- An international guideline with six personalised titration schedules for preventing myocarditis and pneumonia associated with clozapine.
- Aripiprazole for the treatment of schizophrenia: Recommendations of a panel of Spanish experts on its use in clinical practice.
- Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) recommendations for the management of patients with bipolar disorder with mixed presentations.
- Clinical management of adult patients with serious mental disorder and comorbid diagnosis of substance use disorder.
- Cultural adaptation to Spanish of the "Patient Satisfaction Survey" to assess satisfaction with electroconvulsive therapy (ECT).
- Ethical considerations for precision psychiatry: A roadmap for research and clinical practice.
- Expert consensus recommendations on the use of randomized clinical trials for drug approval in psychiatry- comparing trial designs.
- Clinical guidelines for the therapeutic management of difficult-to-treat depression.
- Guide to psychological interventions in schizophrenia.
- Guía de Práctica Clínica para el tratamiento farmacológico y psicológico de los pacientes adultos con un trastorno mental grave y un trastorno por uso de sustancias.
- Guidelines on the management of Emergencies in Primary Care.
- Clinical significance of vitamin B12 deficiency. Beyond megaloblastic anemia.
- Leadership, management, quality, and innovation in organ donation: 2019 Kunming recommendations for One Belt & One Road countries.
- Mental Health and COVID-19: Early evidence of the pandemic's impact
- Pharmacological Treatment of Early-Onset Schizophrenia: A Critical Review, Evidence-Based Clinical Guidance and Unmet Needs.
- Problematic use of the internet during the COVID-19 pandemic: Good practices and mental health recommendations.
- Electroconvulsive Therapy Clinical Protoco.
- Assertive Community Treatment Team (ACT) Action Protocol.
- Protocol for early Detection and Intervention in Emotional Instability and Borderline Personality Disorder.
- Protocol for the detection, diagnosis and intervention in Autism Spectrum Disorder from a Mental Health perspective..
- The transition from adolescence to adulthood in patients with schizophrenia: Challenges, opportunities and recommendations.

- Tobacco Use Disorder (TUD) and Dual Diagnosis. Joint statement by the Spanish Psychiatry Society and the Spanish Dual Disorders Society.

- Treatment Approaches for First Episode and Early-Phase Schizophrenia in Adolescents and Young Adults: A Delphi Consensus Report from Europe.

- Male violence. Proposals for its approach in Mental Health and Addiction Centers.

- WHO guidelines on mental health at work.

- World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders - Version 3. Part I: Anxiety disorders.

- World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders - Version 3. Part II: OCD and PTSD.

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