



ciber

Centro de Investigación Biomédica en Red

ANNUAL REPORT 2020







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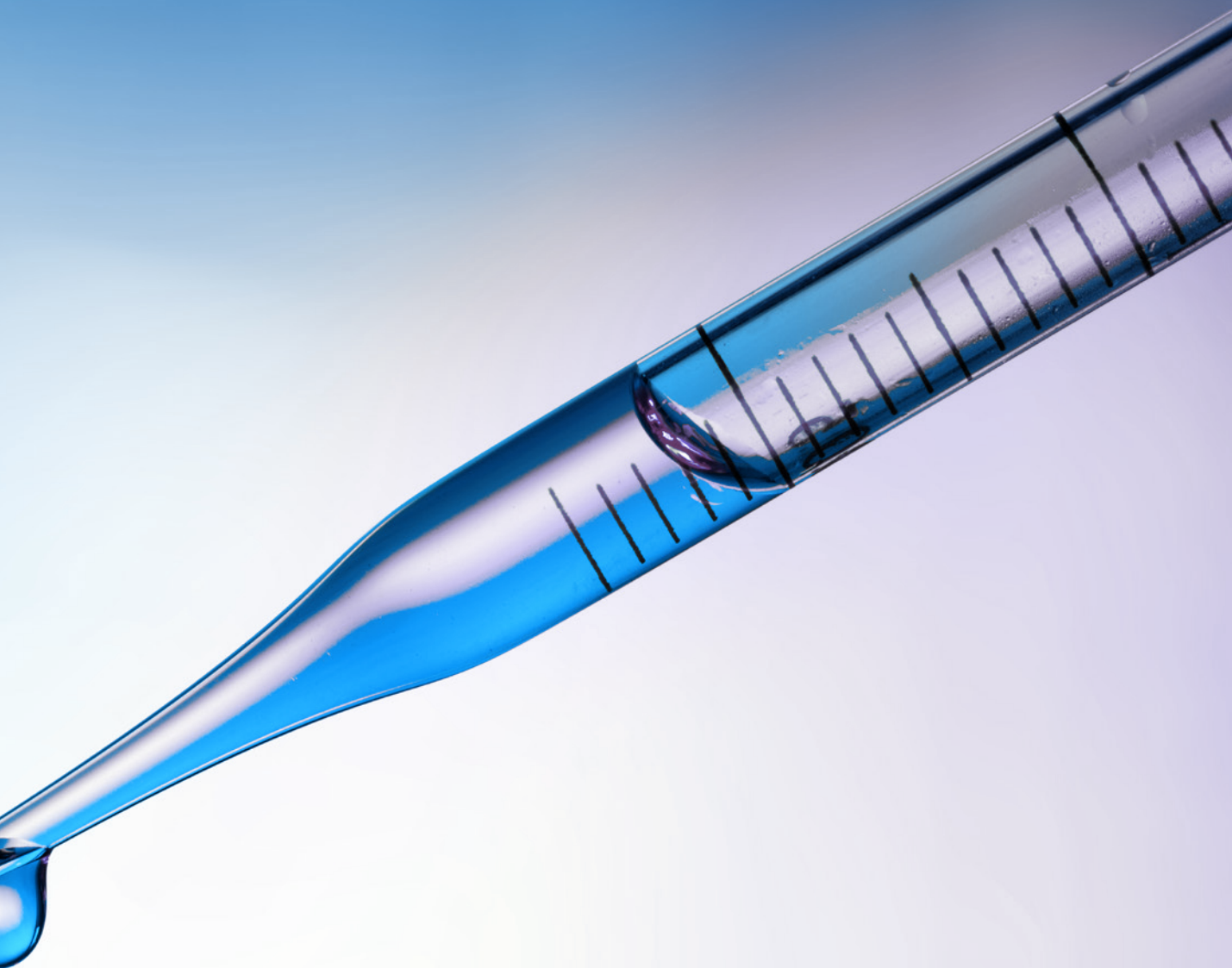
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**CENTRO DE
INVESTIGACIÓN
BIOMÉDICA EN RED
CONSORTIUM**



WELCOME FROM CIBER'S MANAGING DIRECTOR

Manuel Sánchez Delgado



2020 has been one of the most difficult years of the last decades, and this is also true for the CIBER Consortium. Nevertheless, despite the healthcare crisis we are witnessing, the work that we have been carrying out from the various research centers has been increasingly valued.

I would like to take the opportunity here to first of all convey my deepest gratitude for the efforts made during this difficult year not only at the level of healthcare, of course, but also in the field of research which has gone to great lengths endeavouring to provide prompt solutions to healthcare emergencies. At the management level, a great effort has also been made to ensure that extra resources reach the laboratories to be able to give urgent response to the pandemic situation.

The CIBER network research model, unique in our country, has about 6000 researchers (contracted and attached) in more than 420 research groups distributed throughout the Spanish geography and working in 11 thematic research areas.

During 2020, despite the circumstances, the CIBER Consortium, at an organizational level, has responded quickly to the needs of teleworking, providing satisfactory results and clearly showing the opportunities offered by our network structure. The research staff has continued their work, geared towards the understanding, diagnosis and treatment of multiple diseases including, of course, COVID-19, and always with the aim of improving our National Health System and the health of all citizens.

I would like to highlight the increase in projects that have been awarded in this period, with a fundraising of more than 30 million Euros, through 28 national projects and 5 European concessions. These figures are much higher than in previous periods and with excellent results, placing our Consortium at its best levels of competitiveness in recent years. Among other major milestones, I highlight the relevance for CIBER of the coordination of the Predictive Medicine (CIBERESP) and Genomic Medicine (CIBERER) programs of the IMPaCT Infrastructure; and the emergency aid received from the COVID-19 Fund of the Instituto de Salud Carlos III, with an amount of close to 2.5 million Euros to support three projects aimed at the study of COVID-19.

During 2020, collaboration and synergies between the groups and between the different thematic areas of the CIBER have become more necessary than ever and despite the difficulty of holding events in person to share knowledge, the work of the Scientific Directorate has been noteworthy in their efforts to adapt to the circumstances by organizing its meetings and annual conferences in virtual format.

The pandemic situation has not slowed down the scientific results of the groups, on the contrary, the number of papers in 2020 has increased in most of the CIBER areas, reaching nearly 8,000 publications, 60% in the first quartile and about 25% in the first decile. The number of publications in collaboration between the areas has remained at very high levels, similar to previous years. In addition, during the 2020 period, 20 new priority patent applications were submitted, 1 software was developed, 3 orphan drug designations were made, and 6 license agreements were signed.

The CIBER continued with the commitment to make the results of its research groups reach society through its Scientific Culture and Innovation Unit (UCC + I). In 2020, about 180 press releases were disseminated and other informative pieces were organized coinciding with special days, accounting for more than 11,000 impacts in the media. Once again, collaboration with institutions in terms of communication has been key to reaching these results.

The CIBER once again joined in the activities of the International Day of Women and Girls in Science and the Science Week, organizing for the latter the #Quesigalaciencia video contest, and presented the three winning works through online meetings with researchers. This type of initiative will continue to be promoted from our center in the coming years.

In short, these are just some examples of the results that have been obtained in the CIBER consortium during an exceptional year, in every sense. Throughout this report, many other milestones of our center will be made shared. Once again, I would like to acknowledge the exceptional effort made by the research staff in the fight against COVID-19 and give my sincere appreciation for all the work carried out.



INTERNAL ORGANIZATION

The Centro de Investigación Biomédica en Red, M.P, **CIBER**, a public research consortium set up by the Instituto de Salud Carlos III (ISCIII), furthers excellence research in Biomedicine and Health Sciences carried out within the National Health System and the Science and Technology System.

The CIBER's scientific programme is based on the following thematic Research areas:

- » **Bioengineering, Biomateriales 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)**
- » **Physiopathology of Obesity and Nutrition (CIBEROBN)**
- » **Cancer (CIBERONC)**
- » **Mental Health (CIBERSAM)**

At the present time, the Ciber has a staff of 804 persons and around 6.000 attached researchers integrated in over 420 research groups working in separate locations, associated with 99 institutions in the consortium and belonging to administrations and public and private sector institutions of Spain's different regional "Autonomous Communities".

Its governing, management and administrative bodies are as follows:

GOVERNING BOARD AND PERMANENT COMMISSION

The **Governing Board**, presided over by the Director 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** is a delegated commission made up of the ISCIII and 8 members of the Governing Board, which can be renewed annually. Its operation and the support and assessment functions of the governing bodies are all established in the statutes of the CIBER.

STEERING COMMITTEE AND ADVISORY BOARDS

In each CIBER area there is **Management Committee** and an External Scientific **Advisory Committee**.

The Management Committee is made up of the Scientific Director 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 renowned for their professional or scientific careers in line with the objectives of the center. This body is in charge of carrying out the annual assessment 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 2020 the following persons held this office:

- » CIBER-BBN Scientific Director: **Dr. Ramón Martínez Máñez**
- » CIBERCV Scientific Director: **Dr. Francisco Fernández-Avilés**
- » CIBERDEM Scientific Director: **Dr. Eduard Montanya Mias**
- » CIBEREHD Scientific Director: **Dr. Rafael Bañares Cañizares**
- » CIBERER Scientific Director: **Dr. Pablo Lapunzina Badía**
- » CIBERES Scientific Director: **Dr. Ferran Barbé Illa**
- » CIBERESP Scientific Director: **Dra. Marina Pollán Santamaría**
- » CIBERFES Scientific Director: **Dr. Leocadio Rodríguez Mañas**
- » CIBEROBN Scientific Director: **Dr. Carlos Diéguez González**
- » CIBERONC Scientific Director: **Dr. Anna Bigas Salvans**
- » CIBERSAM Scientific Director: **Dr. Eduard Vieta Pascual**



ECONOMIC DATA

CIBER

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|----------------------------|---------------------------|------------------------------|---------------------|----------------------|
| | 26.303.330,00 | 30.625.695,37 | 2.248.015,59 | 2.206.305,83 | 61.383.346,79 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|----------------------|---|----------------------|----------------------|
| Scientific Management, Scientific Secretary, Communication | 5.379,49 | 253.620,90 | 566.223,61 | 825.224,00 |
| Groups | 1.387.993,21 | 3.832.732,64 | 19.115.060,73 | 24.335.786,58 |
| Training | 306,00 | 85.030,12 | 1.753.180,99 | 1.838.517,11 |
| Programmes | 4.305,73 | 126.583,50 | 250.800,33 | 381.689,56 |
| Platforms | 196.719,24 | 193.145,22 | 388.540,36 | 778.404,82 |
| Transference | 16.302,17 | 318.872,98 | 229.848,79 | 565.023,94 |
| Intramural Projects | 105.058,08 | 1.076.158,21 | 145.681,91 | 1.326.898,20 |
| External Projects | 239.412,86 | 2.223.645,56 | 2.628.793,56 | 5.091.851,98 |
| Financial Resources Technical Unit (UT) | 6.640,45 | 599.201,15 | - | 605.841,60 |
| Human Resources (UT) | - | 1.494,15 | 1.492.124,88 | 1.493.619,03 |
| Prevention of Occupational Hazards (UT) | - | 72.217,40 | - | 72.217,40 |
| Communication (UT) | - | 85.591,80 | - | 85.591,80 |
| TOTAL CIBER | 1.962.117,23 | 8.868.293,63 | 26.570.255,16 | 37.400.666,02 |

CIBER-BBN

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 3.054.405,40 | 1.225.455,02 | 207.710,82 | - | 4.487.571,24 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 3.776,99 | 67.815,82 | 71.592,81 |
| Groups | 271.651,66 | 276.487,60 | 940.623,00 | 1.488.762,26 |
| Training | 306,00 | 11.791,38 | 1.550.655,98 | 1.562.753,36 |
| Programmes | - | 477,50 | 61.435,07 | 61.912,57 |
| Platforms | 158.734,00 | 31.257,23 | 41.885,06 | 231.876,29 |
| Transference | 1.415,48 | 53.986,05 | 75.710,87 | 131.112,40 |
| Intramural Projects | 39.265,09 | 104.076,76 | - | 143.341,85 |
| External Projects | 45.018,10 | 397.849,31 | 807.473,40 | 1.250.340,81 |
| TOTAL CIBER-BBN | 516.390,33 | 879.702,82 | 3.545.599,20 | 4.941.692,35 |

(*) The difference between expenditure and income for the period is covered with remainders from previous years.

CIBERCV

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 2.533.665,75 | 1.570.404,41 | - | 69.003,00 | 4.173.073,16 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 3.435,66 | 38.968,86 | 42.404,52 |
| Groups | 190.711,25 | 589.395,10 | 1.870.597,11 | 2.650.703,46 |
| Training | - | 3.755,58 | 140.639,39 | 144.394,97 |
| Programmes | - | 7.980,72 | - | 7.980,72 |
| Transference | - | 11.119,90 | - | 11.119,90 |
| Intramural Projects | - | 26.000,91 | 69.563,93 | 95.564,84 |
| External Projects | - | 10.290,81 | 98.143,51 | 108.434,32 |
| TOTAL CIBERCV | 190.711,25 | 651.978,68 | 2.217.912,80 | 3.060.602,73 |

CIBERDEM

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 2.156.724,16 | 314.432,56 | 22.990,00 | - | 2.494.146,72 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 3.513,41 | 52.238,22 | 55.751,63 |
| Groups | 984,21 | 80.382,41 | 2.296.381,51 | 2.377.748,13 |
| Transference | - | 4.162,31 | - | 4.162,31 |
| Platforms | 33.710,48 | 79.337,86 | - | 113.048,34 |
| Intramural Projects | - | 33.988,93 | - | 33.988,93 |
| External Projects | - | 58.419,46 | 9.919,84 | 68.339,30 |
| TOTAL CIBERDEM | 34.694,69 | 259.804,38 | 2.358.539,57 | 2.653.038,64 |

(*) The difference between expenditure and income for the period is covered with remainders from previous years.

CIBEREHD

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 2.817.945,36 | 133.100,00 | 163.659,09 | 109.885,97 | 3.224.590,42 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 45.445,03 | 494,68 | 45.939,71 |
| Groups | 140.473,71 | 297.407,37 | 2.490.392,00 | 2.928.273,08 |
| Training | - | 12.149,09 | - | 12.149,09 |
| Platform | - | 1.099,02 | 88.275,05 | 89.374,07 |
| Transference | - | 7.628,86 | - | 7.628,86 |
| Intramural Projects | 4.400,37 | 177.132,75 | 1.517,07 | 183.050,19 |
| External Projects | - | 70.413,25 | 280.054,50 | 350.467,75 |
| Total CIBEREHD | 144.874,08 | 611.275,37 | 2.860.733,30 | 3.616.882,75 |

(*) The difference between expenditure and income for the period is covered with remainders from previous years.

CIBERER

» Total Resources

| INCOME 2020 | ISCI Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|------------------|-------------------|----------------------|--------------|----------------------|
| | 3.783.808,05 | 8.375.808,13 | 857.120,98 | 97.523,50 | 13.114.260,66 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | 2.022,72 | 58.519,92 | 133.021,15 | 193.563,79 |
| Groups | 40.265,50 | 130.302,00 | 2.995.434,63 | 3.166.002,13 |
| Training | - | 1.246,38 | 20.262,88 | 21.509,26 |
| Platforms | 234,19 | 12.350,69 | 147.898,20 | 160.483,08 |
| Transference | 14.886,69 | 238.218,36 | 63.037,92 | 316.142,97 |
| Intramural Projects | 27.446,36 | 332.025,94 | 3.307,65 | 362.779,95 |
| External Projects | 21.364,68 | 528.475,50 | 399.102,97 | 948.943,15 |
| Total CIBERER | 106.220,14 | 1.301.138,79 | 3.762.065,40 | 5.169.424,33 |

CIBERES

» Total Resources

| INCOME 2020 | ISCI Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|------------------|-------------------|----------------------|--------------|---------------------|
| | 2.030.341,67 | 2.605.514,08 | 93.150,00 | 88.638,73 | 4.817.644,48 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 30.000,00 | 36.704,75 | 66.704,75 |
| Groups | 248.620,73 | 391.274,31 | 1.349.046,34 | 1.988.941,38 |
| Training | - | 8.224,14 | - | 8.224,14 |
| Programmes | - | 2.683,45 | - | 2.683,45 |
| Platforms | 645,57 | 1.336,28 | 85.146,29 | 87.128,14 |
| Transference | - | 6.630,72 | 91.100,00 | 97.730,72 |
| Intramural Projects | 5.584,26 | 28.149,81 | 38.218,86 | 71.952,93 |
| External Projects | 111.451,21 | 681.997,70 | 500.155,09 | 1.293.604,00 |
| TOTAL CIBERES | 366.301,77 | 1.150.296,41 | 2.100.371,33 | 3.616.969,51 |

CIBERESP

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|----------------------|
| | 2.249.571,24 | 14.283.253,60 | 6.776,00 | 12.940,00 | 16.552.540,84 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 6.459,35 | 36.391,39 | 42.850,74 |
| Goups | 110.490,93 | 414.582,71 | 1.732.370,85 | 2.257.444,49 |
| Training | - | 3.000,00 | - | 3.000,00 |
| Intramural Projects | 1.246,84 | 30.884,96 | - | 32.131,80 |
| Programmes | 1.465,95 | 81.780,97 | 129.446,28 | 212.693,20 |
| External Projects | 6.215,28 | 50.649,42 | 29.224,93 | 86.089,63 |
| TOTAL CIBERESP | 119.419,00 | 587.357,41 | 1.927.433,45 | 2.634.209,86 |

CIBERFES

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 601.601,00 | 813.834,08 | 16.251,18 | 4.611,05 | 1.436.297,31 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|------------------|---|-------------------|-------------------|
| Scientific Management, Scientific Secretary, Communication | - | 2.237,36 | 70.525,49 | 72.762,85 |
| Groups | 37.883,67 | 110.767,99 | 400.056,62 | 548.708,28 |
| Programmes | - | - | 51.856,94 | 51.856,94 |
| Training | - | 14,35 | - | 14,35 |
| External Projects | - | 20.065,42 | 15.712,71 | 35.778,13 |
| TOTAL CIBERFES | 37.883,67 | 133.085,12 | 538.151,76 | 709.120,55 |

CIBEROBN

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 2.226.872,37 | 854.888,52 | 216.049,08 | 8.470,00 | 3.306.279,97 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | 1.513,23 | 21.793,25 | 47.862,70 | 71.169,18 |
| Groups | 123.709,63 | 420.478,35 | 1.551.480,92 | 2.095.668,90 |
| Training | - | 9.619,27 | - | 9.619,27 |
| Programmes | 2.839,78 | 7.684,48 | - | 10.524,26 |
| Platforms | 3.395,00 | 30.637,90 | 25.335,76 | 59.368,66 |
| Transference | - | 1.289,09 | - | 1.289,09 |
| Intramural Projects | 19.222,17 | 201.261,79 | 33.074,40 | 253.558,36 |
| External Projects | 27.619,04 | 221.000,94 | 235.510,56 | 484.130,54 |
| TOTAL CIBEROBN | 178.298,85 | 913.765,07 | 1.893.264,34 | 2.985.328,26 |

CIBERONC

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|------------------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 2.880.743,25 | 71.250,01 | 131.750,68 | 5.000,00 | 3.088.743,94 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | - | 48.378,98 | 15.829,75 | 64.208,73 |
| Groups | 92.067,16 | 785.911,99 | 2.041.797,28 | 2.919.776,43 |
| Training | - | 20.431,66 | 41.622,74 | 62.054,40 |
| Programmes | - | 19.116,04 | - | 19.116,04 |
| Intramural Projects | 4.022,99 | 100.122,54 | - | 104.145,53 |
| External Projects | - | 44.296,55 | 92.898,26 | 137.194,81 |
| TOTAL CIBERONC | 96.090,15 | 1.018.257,76 | 2.192.148,03 | 3.306.495,94 |

(*) The difference between expenditure and income for the period is covered with remainders from previous years.

CIBERSAM

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|----------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 1.696.198,59 | 221.638,16 | 532.557,76 | 15.100,00 | 2.465.494,51 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|--|-------------------|---|---------------------|---------------------|
| Scientific Management, Scientific Secretary, Communication | 1.843,54 | 30.060,95 | 66.370,80 | 98.275,29 |
| Groups | 131.134,76 | 335.742,81 | 1.446.880,47 | 1.913.758,04 |
| Training | - | 10.635,96 | - | 10.635,96 |
| Programmes | - | 6.860,34 | 8.062,04 | 14.922,38 |
| Platforms | - | 37.126,24 | - | 37.126,24 |
| Intramural Projects | 3.870,00 | 42.513,82 | - | 46.383,82 |
| External Projects | 27.744,55 | 140.187,20 | 160.597,79 | 328.529,54 |
| TOTAL CIBERSAM | 164.592,85 | 603.127,32 | 1.681.911,10 | 2.449.631,27 |

UT EXPENSES

» Total Resources

| INCOME 2020 | ISCIII Transfer | Project Grants | Rendered services | Other income | TOTAL |
|----------------|--------------------|-------------------|----------------------|--------------|---------------------|
| | 271.453,16 | 156.116,80 | - | 1.795.133,58 | 2.222.703,54 |

» Total expenses

| PROJECT | Inventoriable | Provisions and other activity expenses | Personnel | Total expense |
|---------------------------------------|-----------------|---|---------------------|---------------------|
| Economic Resources | 6.640,45 | 599.201,15 | - | 605.841,60 |
| Human Resources | - | 1.494,15 | 1.492.124,88 | 1.493.619,03 |
| Prevention of occupational Hazards | - | 72.217,40 | - | 72.217,40 |
| Communication | - | 85.591,80 | - | 85.591,80 |
| TOTAL UT | 6.640,45 | 758.504,50 | 1.492.124,88 | 2.257.269,83 |

(*)The difference between expenditure and income for the period is covered with remainders from previous years.



PERSONNEL

» Distribution of contracted personnel by areas, categories and gender

| | MEN | WOMEN | OVERALL TOTAL |
|------------------|-----------|-----------|---------------|
| CIBER-BBN | 32 | 69 | 101 |
| Dip. holders | 1 | 4 | 5 |
| Doctors | 22 | 44 | 66 |
| Graduates | 9 | 16 | 25 |
| Technical staff | - | 5 | 5 |
| CIBERCV | 20 | 43 | 63 |
| Dip. holders | 1 | 3 | 4 |
| Doctors | 12 | 21 | 33 |
| Graduates | 7 | 13 | 20 |
| Technical staff | - | 6 | 6 |
| CIBERDEM | 16 | 54 | 70 |
| Dip. holders | - | 1 | 1 |
| Doctors | 11 | 32 | 43 |
| Graduates | 2 | 13 | 15 |
| Technical staff | 3 | 8 | 11 |
| CIBEREHD | 27 | 62 | 89 |
| Dip. holders | 1 | 5 | 6 |
| Doctors | 13 | 28 | 41 |
| Graduates | 10 | 19 | 29 |
| Technical staff | 3 | 10 | 13 |

| | MEN | WOMEN | OVERALL TOTAL |
|-----------------|-----------|-----------|---------------|
| CIBERER | 29 | 76 | 105 |
| Dip. holders | - | 2 | 2 |
| Doctors | 21 | 47 | 68 |
| Graduates | 8 | 16 | 24 |
| Technical staff | - | 11 | 11 |
| CIBERES | 12 | 73 | 85 |
| Dip. holders | - | 14 | 14 |
| Doctors | 4 | 21 | 25 |
| Graduates | 8 | 27 | 35 |
| Technical staff | - | 11 | 11 |
| CIBERESP | 15 | 44 | 59 |
| Dip. holders | 2 | 8 | 10 |
| Doctors | 6 | 19 | 25 |
| Graduates | 6 | 16 | 22 |
| Technical staff | 1 | 1 | 2 |
| CIBERFES | 6 | 11 | 17 |
| Doctors | 4 | 4 | 8 |
| Graduates | 2 | 6 | 8 |
| Technical staff | - | 1 | 1 |

| | MEN | WOMEN | OVERALL TOTAL |
|-----------------|-----------|-----------|---------------|
| CIBEROBN | 11 | 49 | 60 |
| Dip. holders | 1 | 4 | 5 |
| Doctors | 5 | 14 | 19 |
| Graduates | 4 | 22 | 26 |
| Technical staff | 1 | 9 | 10 |
| CIBERONC | 18 | 46 | 64 |
| Dip. holders | 2 | 10 | 12 |
| Doctors | 12 | 21 | 33 |
| Graduates | 4 | 15 | 19 |

| | MEN | WOMEN | OVERALL TOTAL |
|-----------------|-----------|-----------|---------------|
| CIBERSAM | 14 | 38 | 52 |
| Dip. holders | 1 | 5 | 6 |
| Doctors | 9 | 13 | 22 |
| Graduates | 4 | 16 | 20 |
| Technical staff | | 4 | 4 |
| CIBERUT | 12 | 27 | 39 |
| Doctors | 2 | 1 | 3 |
| Graduates | 9 | 23 | 32 |
| Technical staff | 1 | 3 | 4 |

| | MEN | WOMEN | OVERALL TOTAL |
|----------------------|------------|------------|---------------|
| OVERALL TOTAL | 212 | 592 | 804 |



ACTIVITY HIGHLIGHTS

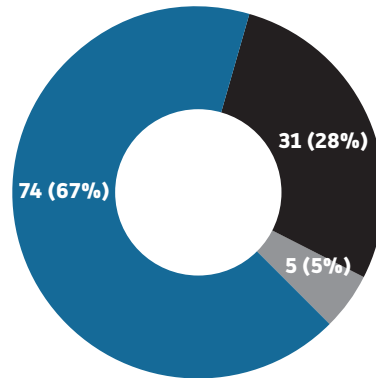
PROJECTS

Number of projects underway in 2020 resulting from competitive grants:

| Body / Grant | Grants 2020 | BBN | CV | DEM | EHD | ER | ES | ESP | FES | OBN | ONC | SAM |
|---|-------------|-----------|----------|----------|----------|-----------|-----------|----------|----------|----------|----------|----------|
| European | 31 | 9 | 3 | 1 | - | 4 | 3 | - | 1 | 6 | 2 | 2 |
| United States | 5 | - | - | - | - | 3 | - | - | - | 1 | - | 1 |
| National | 74 | 15 | 2 | 4 | 2 | 13 | 14 | 6 | 1 | 7 | 4 | 6 |
| ISCIII - FIS | 30 | 1 | 1 | 2 | 1 | 6 | 5 | 4 | 1 | 2 | 2 | 5 |
| ISCIII - Others | 10 | 2 | - | - | - | 2 | 5 | 1 | - | - | - | - |
| MECD | 2 | 1 | - | - | - | - | - | - | - | - | - | 1 |
| MINECO | 17 | 11 | - | 2 | - | 1 | 3 | - | - | - | - | - |
| Private Foundations | 9 | - | 1 | - | 1 | 4 | - | 1 | - | 1 | 1 | - |
| Other public grants (Valencia and Aragón regional governments) | 6 | - | - | - | - | - | 1 | - | - | 4 | 1 | - |

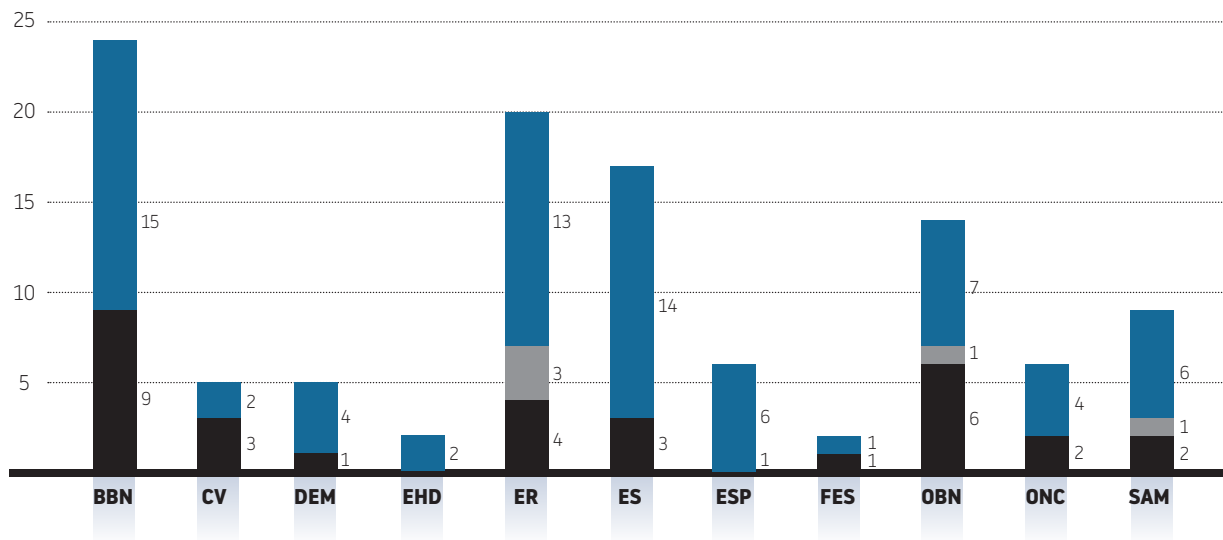
COMPETITIVE PROJECTS UNDER WAY ACCORDING TO FUNDING SOURCE

■ NATIONAL ■ EUROPEAN ■ UNITED STATES



COMPETITIVE PROJECTS UNDERWAY ACCORDING TO THEMATIC AREA AND FUNDING SOURCE

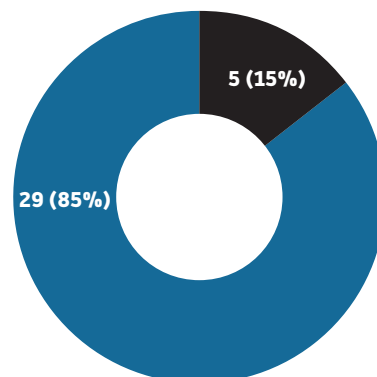
■ NATIONAL ■ EUROPEAN ■ UNITED STATES



In 2020, CIBER obtained the following grants from competitive calls.

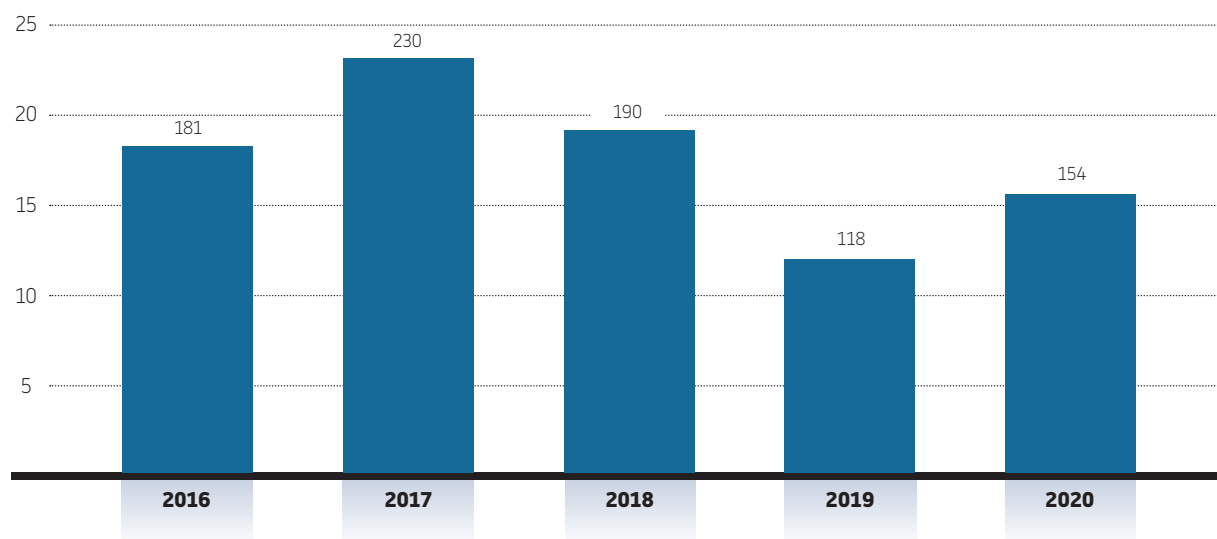
COMPETITIVE PROJECTS AWARDED IN 2020

■ NATIONAL ■ EUROPEAN



The number of applications in 2020 for competitive projects with external funding has been 154.

SUBMITTED APPLICATIONS TO COMPETITIVE GRANTS



TRANSFERENCE

One of the CIBER's main objectives is the transfer of the knowledge generated by its researchers in such a way that the results of research are implemented in protocols, services and products for the improvement of clinical practice and the quality of life of the population at large. To this end, the Technology Transfer area of the CIBER works as a liaison between our researchers and companies, private organisations, public research centers and other innovation agents to put the cooperation between them into practice, and ensure that the results of research can finally be applied.

Throughout 2020, despite the pandemic, 20 new priority patent applications were submitted at the CIBER. In addition, 1 software was developed, as well as 3 orphan drug designations and a development which was able to obtain a trade secret licence agreement. Finally, 6 licence contracts were signed.

| THEMATIC AREA | Priority patent applications | Other IPRs and software | Licences and licence options |
|---------------|------------------------------|-------------------------|------------------------------|
| CIBER-BBN | 10 | 1 | 3 |
| CIBERDEM | 2 | - | - |
| CIBEREHD | 2 | - | 1 |
| CIBERER | 4 | 3 | 1 |
| CIBERES | 1 | - | 1 |
| CIBERESP | - | - | - |

| THEMATIC AREA | Priority patent applications | Other IPRs and software | Licences and licence options |
|---------------|------------------------------|-------------------------|------------------------------|
| CIBEROBN | 1 | - | - |
| CIBERSAM | - | 1 | - |
| CIBERCV | - | - | - |
| CIBERONC | - | - | - |
| CIBERFES | - | - | - |

Throughout 2020, the following activities and procedures were carried out, among others:

- » Dozens of CDAs (20) and MTAs (22) and joint ownership agreements (27) were managed.
- » Support was given to the CIBER spin-off in achieving a capital increase.
- » Various ongoing commercialization and technology dissemination activities have been maintained.
- » Online partnering events were attended such as: BioEurope, Medtech Summit 2020, biomedica on the move 2020, EEN Matchmaking Event, virtual, Medica, EEN Matchmaking Event, y Asebio Investors day, among others.
- » Various departments of the CIBER Central Technical Unit were supported in reviewing contracts, proposals and other issues.
- » Organization of training and dissemination conferences and events:
 - The CIBERER area organized the Conference on the designation, development and access to orphan drugs on October 28, 2020.
 - The CIBERBBN organized the Webinar “Introduction to regulatory aspects of in vitro diagnostic medical devices” (IVD), online, November 25, 2020.
- » Calls for internal projects:
 - The CIBER-BBN area launched the third call for valorisation projects. 4 project proposals were presented and 4 have been financed. The main objective of these projects is to help increase the TRL (Technology Readiness Level) of their technologies, in a move towards their exploitation. and commercialization (minimum TRL = 3). In addition, in December 2020 a new call for transfer projects was published that will be resolved in 2021. The main objective of these projects is to support those specially geared towards technology transfer, in order to bring them closer to the final product and to be able to identify companies willing to get involved in the project with their own financial contribution in addition to the financing provided by the CIBER-BBN.
 - The CIBERER area published their intramural call for cooperative and complementary actions, seeking projects with great translational potential.
- » Lastly, the CIBER-BBN area continues to participate together with the AEMPS (Spanish Agency for Medicines and Health Products) in the STARS-CSA project: *Strengthening Training of Academia in Regulatory Science*.

COMMUNICATION

PRESS RELEASES

In 2020, 179 press releases were issued concerning the research results of the groups. These include press releases sent from the institutions in the consortium that were prepared in collaboration with the CIBER.

| CIBER Area | CIBER Press Releases 2020 |
|----------------|---------------------------|
| CIBEROBN | 29 |
| CIBERONC | 22 |
| CIBERDEM | 21 |
| CIBERER | 15 |
| CIBERCV | 13 |
| CIBER-BBN | 13 |
| CIBERESP | 13 |
| CIBERSAM | 11 |
| CIBEREHD | 9 |
| CIBERES | 9 |
| CIBERFES | 7 |
| CIBER | 3 |
| SEVERAL AREAS* | 14 |
| TOTAL | 179 |

NEWSLETTERS

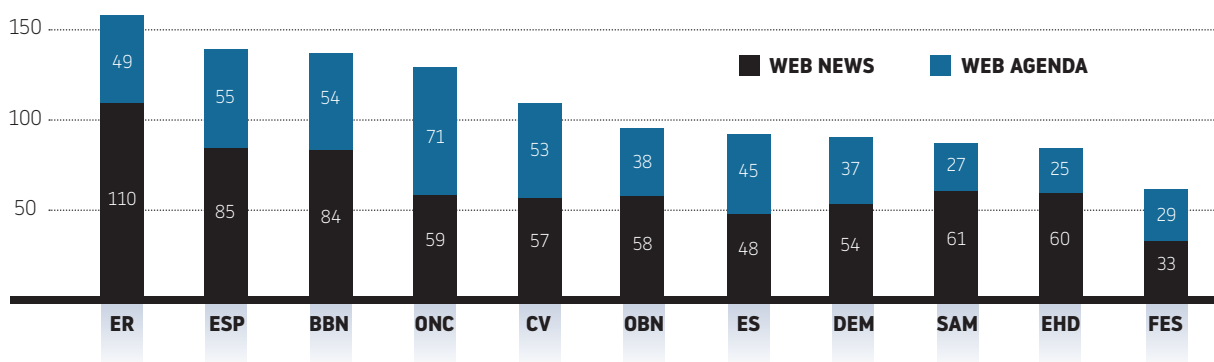
In 2020, 5 CIBER newsletters have been prepared and disseminated which include relevant content from the eleven thematic areas. The newsletter is sent quarterly, through the Mailchimp platform.

<http://www.ciberisciii.es/comunicacion/boletines>

The CIBERER has also distributed **7 social** and **10 scientific newsletters**.

WEB PAGES

1078 news items and **601 agenda events** were disseminated on the websites of the different areas.

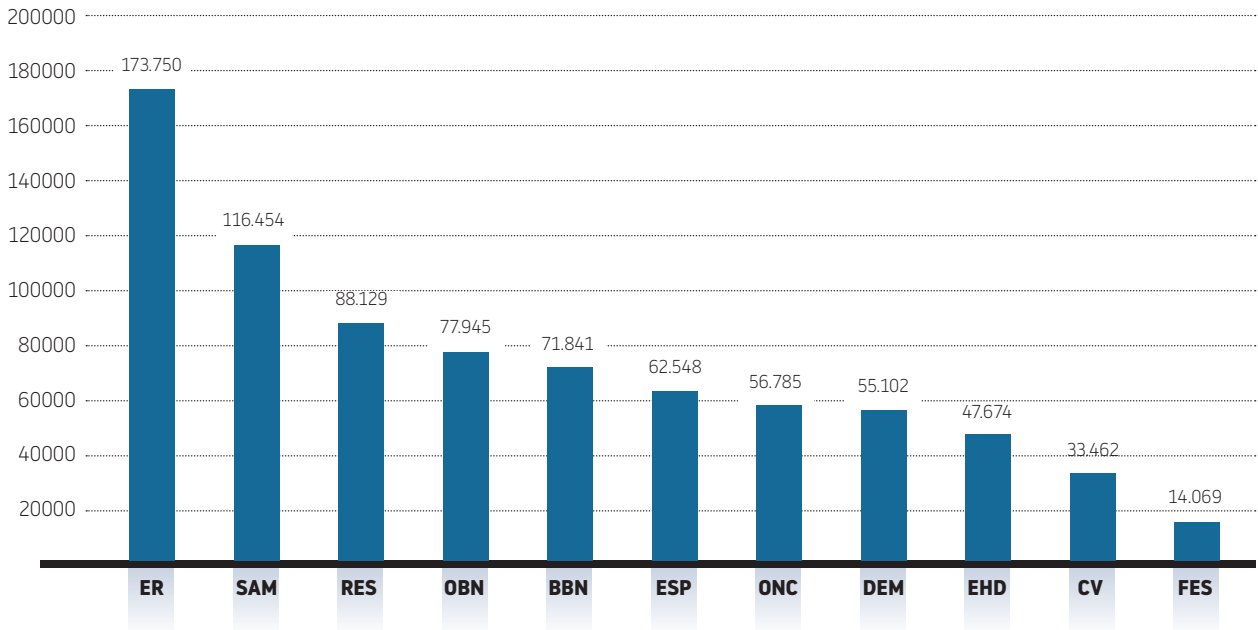


CIBER WEB VISITS

During 2020, the CIBER web pages and its areas had more than 470,000 users who visited more than 1,200 web pages of the center.

Web www.ciberisciii.es > **1.289.958** visits in 2020

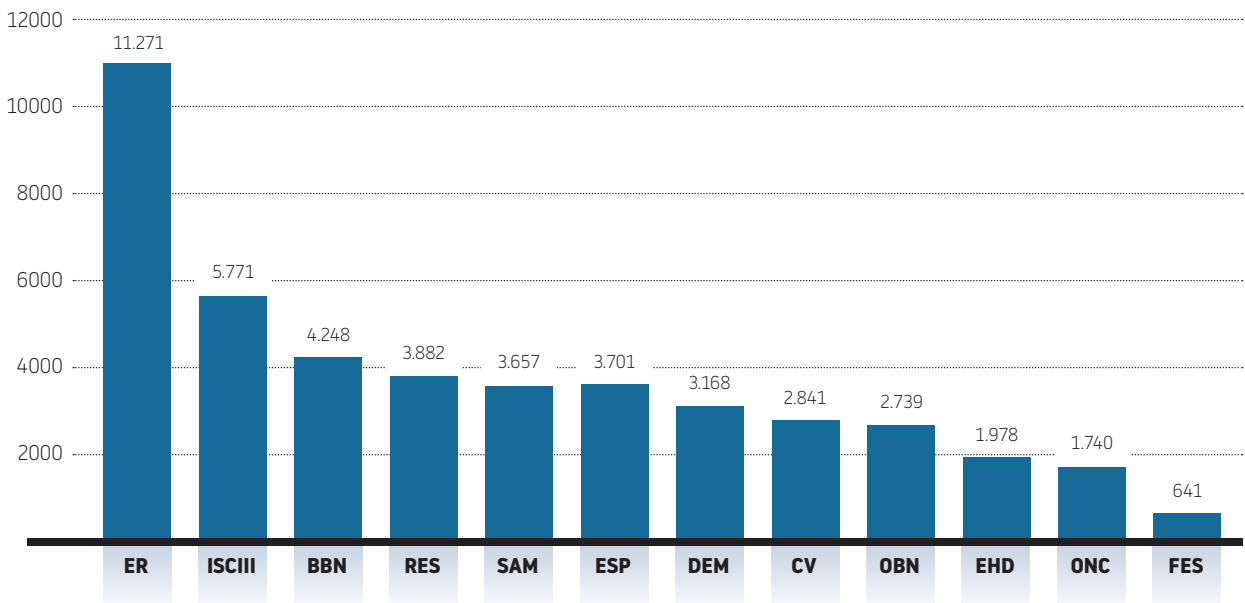
» Website visits per CIBER area in 2020



SOCIAL NETWORKS

Followers in the different CIBER profiles on Twitter:

» Twitter: followers as of 31/12/20



CIBER ACTIVITY AT THE MADRID SCIENCE WEEK

In 2020, the CIBER activity was carried out for the #QueSigaLaCiencia Science Week, a campaign on social networks that aimed to convey to society, from an optimistic point of view, the importance of research and the work carried out by the CIBER research staff.


The call- linked to the campaign- had a high participation of the groups, who presented a total of 69 videos of all the thematic areas. The research staff took on the challenge of sharing their research in one minute, giving free rein to their imagination and using different formats. The jury was made up of 4 people from the CIBER Technical Office and a representative from each CIBER area.

During the Science Week, [5 digital meetings](#) were held with researchers who made their daily work known and debated different aspects of social interest through YouTube.

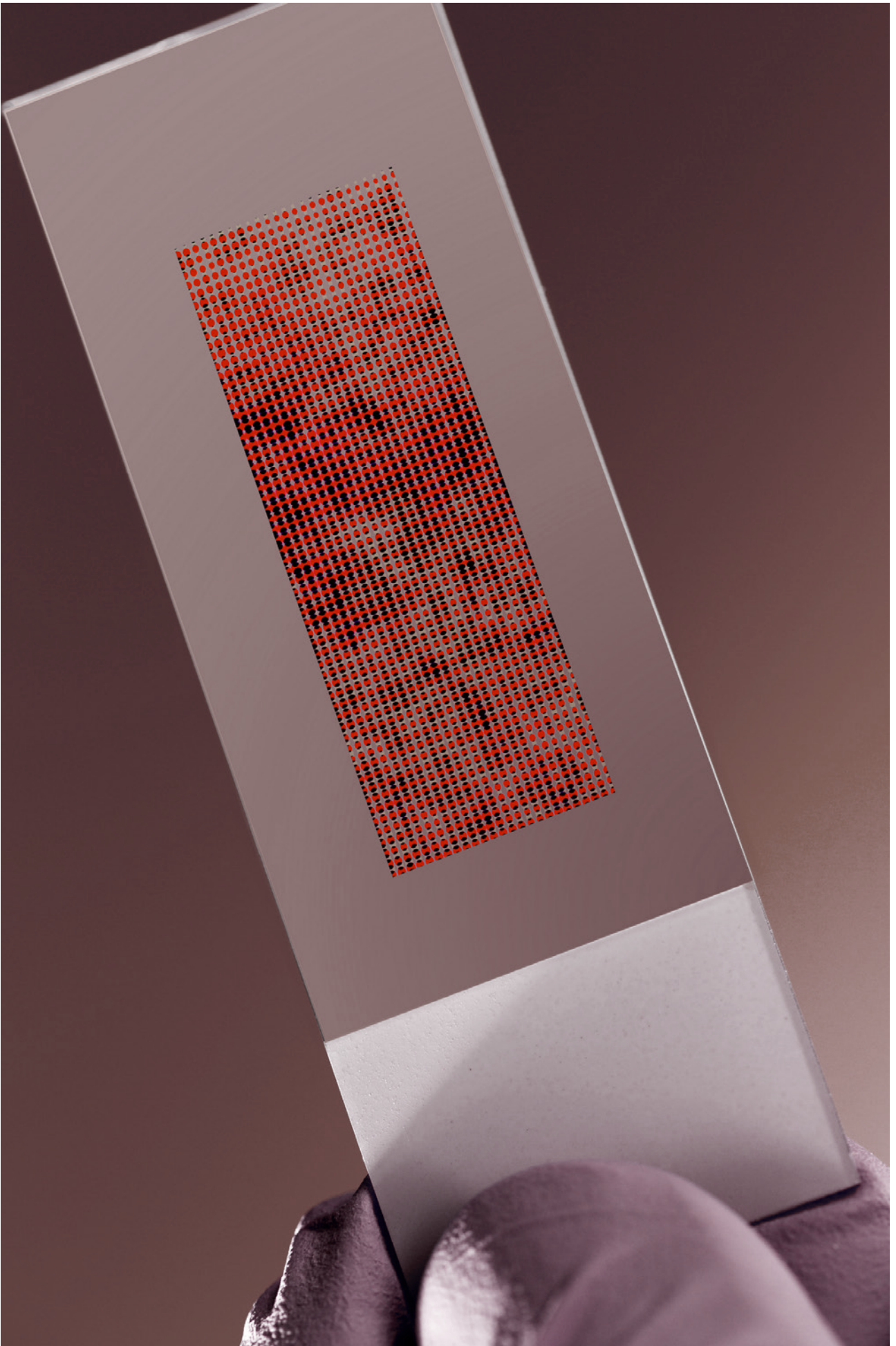
- » **Youtube:** 1625 views of the [meetings](#) with CIBER researchers. +73 subscribers, 7165 views (videos + meetings)
- » **Twitter:** 464.7K impressions, 5.8K likes, +93 followers
- » [3 researcher prizes](#) were awarded by the jury and 1 additional prize was awarded by the public (on social networks)



cyber-bbn



**BIOENGINEERING,
BIOMATERIALS &
NANOMEDICINE**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Ramón Martínez Máñez

The year 2020 has undoubtedly been a year marked by the Covid-19 pandemic, which has had a strong impact on our personal circumstances and on our professional development. Unexpectedly and urgently, we had to reorganize our work, in many cases absent ourselves from the laboratories and try to continue our scientific activity in the best possible way. Many of the CIBER-BBN groups (both from CIBER and from their institutions of origin), like so many scientists worldwide, have adapted their lines of work and have tried to contribute their scientific knowledge and efforts to give support to the eradication of the pandemic and its effects.

2020 has certainly been an unusual year, hopefully the most unusual that we will ever have to live, but despite this CIBER-BBN has maintained its scientific activity and in the next pages you will find a summary of the activity carried out and the accomplishments achieved.

Our basic scientific activities as regards internal projects (intramural collaborations and Early Stage projects for contracted doctors) have continued, increasing the number of collaborations as well as the interaction with other thematic areas. The call for valorisation projects, funded to increase the TRL level of our technologies, has also been maintained and four new projects have been started.

At the international level, our ICTS NANBIOSIS has continued to be involved in the European SAFE-N-MEDTECH project and the SMART4FABRY project, coordinated by CIBER, has culminated successfully, being rewarded at the beginning of 2021 with an orphan drug designation by the EMA. We have also repeated the effort made in 2019 to present a proposal to the COFUND program (MSCA-H2020) to attract postdoctoral researchers to all CIBER areas.

Participation in international partnering events has not been possible, but the search for opportunities to license our technologies and attract strategic industrial partners has continued through virtual events.

In this year of online events, we highlight the adaptation of our Annual Conferences to the virtual format, with the presence of interesting keynote presentations and a review of collaborative results.

Making use of virtual communication tools, the webinar “*Introduction to regulatory aspects of in vitro diagnostic (IVD) medical devices*” was organized, which was very well received among the attending researchers.

We have witnessed an increase in publications during this year of confinement of around 15%, with the quality being maintained, approaching 70% in Q1 and 25% in D1 .

It has been precisely in a year like this that the need for a robust science system has been valued, which can provide answers to the current healthcare system and which can contribute, from our field of biomedical research, to the improvement of health surveillance systems and the development of new diagnostic tools and novel therapeutic strategies.

This year in particular I want to thank all the researchers that make up the CIBER-BBN community for all their work and also acknowledge the effort of the CIBER professionals who have faced the virus from their healthcare positions. I would also like to send a warm embrace to all those who have been hardly hit by the pandemic.



PROGRAMMES

BIOENGINEERING AND MEDICAL IMAGING

Coordinator: **Jordi Aguiló Llobet**

This programme has been very active during 2020 with the presentation of five new proposals for intramural collaborations with a time horizon of two years (2020-2021). To these proposals must be added those submitted in previous years, eight presented in 2019 and 28 proposals in 2018 that have remained active in 2020. Of these new proposals, one is in collaboration with CIBERCV. The proposals and coordinators have been:

- >> *Analysis of overnight heart rate variability to help in sleep apnea-hypopnea syndrome characterization and diagnosis, coordinated by Roberto Hornero.*
- >> *Explanatory and predictive models of failure in Transcatheter Aortic Valve Implantation (TAVI) using Big Data analysis techniques, coordinated by Roberto Hornero.*
- >> *Neural connectivity analysis pre- and post-transcranial magnetic stimulation in patients with neurological diseases, coordinated by Roberto Hornero.*
- >> *Electrophysiological signal processing for the assessment of disabling neurological diseases, coordinated by Joan F. Alonso López.*

The most frequently addressed pathologies have been cardiovascular diseases with three proposals and neurological diseases with two proposals.

In addition, during the month of July 2020, the Early Stage 2018 call ended, and a total of 26 project reports were received, four of these belong to the field of Bioengineering and Medical Imaging:

- >> *CARDIOGRAFET II Disposable sensing platform based on graphene-SGFET to monitor biomarkers for cardiac diseases II, coordinated by Elisabet Prats in collaboration with the Hospital Clinic and resulting in a publication.*
- >> *Nano-Mea, Nanoparticle drug delivery systems for the improvement of the chronically implanted microelectrode-array viability, coordinated by Cristina Soto.*

- >> *NANORASI, Optogenetic approach to visual rehabilitation using nanoparticle vectors, coordinated by Lawrence Humphreys.*
- >> *Lyfe4AD, Comprehensive approach of non-adherent patients through an mHealth environment in people with endocrine disease, coordinated by Carmen Pérez Gandía.*

Furthermore, continuing with the favorable reception of this call, the call for Early Stage 2020 projects with the same characteristics was published at the beginning of this year. 17 proposals were received, one of them belonging to this programme:

- >> *ANÍMATE, Personalized motivation through mHealth strategies, for improving the patient empowerment and to enhance their Adherence, coordinated by Carmen Pérez Gandía.*

During the CIBER-BBN Annual Conference, held virtually in November, several sessions were devoted to the presentation of a selection of the Intramural Collaborations that are currently being developed. Specifically, three that belong to this programme were shown:

- >> *Hybrid PET and T1 MRI agents for atherosclerosis detection, presented by Lucía Gutierrez and Fernando Herranz.*
- >> *Automatic electrogram signal analysis for reentrant circuit mapping on scar-related ventricular arrhythmia patients, presented by Alejandro Alcaine.*
- >> *Neurological mechanisms of resilience to Alzheimer's Disease, presented by Juan Domingo Gisbert.*
- >> *New gene therapy approaches for retinal degenerations based on smart non-viral vectors, presented by Gema Martínez Navarrete.*
- >> *Artificial BioPancreas: Novel macro and micro encapsulation of pancreatic β -cells for diabetes type 1 therapy, presented by Mar Alvarez and Laura Saenz del Burgo.*

As regards the activity at the national level, we highlight the granting of an AES 2020 Health Research Project as coordinator to the researcher Margarita Julià, from the group led by Carles Arús.

BIOMATERIALS AND ADVANCED THERAPIES

Coordinator: **José Luis Gómez Ribelles**

José Luis Gómez Ribelles replaced Julio San Román as coordinator of the programme in 2020. The scientific activity of the programme was mainly structured around 35 Intramural collaborations submitted during the previous two years and to which three new ones were added:

- >> *Smart biomaterials for controlled release of growth factors for bone tissue engineering, coordinated by Gustavo Rico.*
- >> *Abdominal prostheses and fixation mechanisms to improve adaptation to host tissue properties in hernia repair, coordinated by Gemma Pascual.*
- >> *Mechanical variables driving mechanosensing, coordinated by Xavier Trepal.*

Cancer was the topic most frequently addressed by these collaborations, followed by regenerative medicine and infectious and cardiovascular diseases. In addition, out of a total of 13 collaborations with groups from other thematic areas, those with the greatest participation were CIBERONC, CIBERCV, CIBERES and CIBERER.

Of all the intramural collaborations of the programme, two stand out that resulted in joint publications, the results of which were presented at the Annual Conference:

- >> *Mechanical regulation of cell division and polyploidy in the zebrafish epicardium, coordinated by Ángel Raya.*
- >> *NIR-responsive scaffolds for biomedical applications, coordinated by Nuria Vilaboa.*

CIBER contracted staff in programme groups have participated in eight Early Stage projects completed in July 2020: COAT-EBM by Leonor Santos, OCUSySTEM by Teresa Nieto, SMEW by Soledad Pérez-Amodio, 3DHEPPEG by Miguel Ángel Mateos, HYDROREG by Patricia Rico, tMELANO by Sara Oliván, BONESCAFF by Alessandra Girotti and CADHForce by Raimon Sunyer. In addition, four new Early Stage projects of the 2020 call were started:

- >> *HydroCartReg: Chemically crosslinked hyaluronic acid-chitosan scaffolds for potential application on cartilage regeneration after microfracture procedure, coordinated by Luis García-Fernández.*
- >> *OCUSySTEM-II: Mesenchymal stem cells as a next generation drug delivery system for ocular surface diseases, coordinated by Teresa Nieto.*
- >> *SCIELR: A new biomaterial platform for spinal cord recovery, coordinated by Alessandra Girotti.*
- >> *MYORESTORE: Biomaterial systems to synergistically induce muscle repair, coordinated by Patricia Rico.*

The activity of the groups in the programme was also particularly recognized outside of CIBER. Xavier Trepats received an *ERC Advanced Grant* worth € 2.5M to establish the basis for a new generation of biological robots. The researcher María Vallet-Regí has continued with the execution of the VERDI project, also financed through an *ERC Advanced Grant*. Ángel Raya received an award in the Life Sciences category in the 2020 edition of the City of Barcelona Awards.

As regards the development of innovative drugs, such as advanced therapies, CIBER-BBN has continued its participation as a stakeholder of the AEMPS in the European project STARS-CSA: Strengthening Training of Academia in Regulatory Science and also participated in the virtual event 1st European Stakeholder Workshop of STARS. CIBER-BBN has also continued to be part of ASEBIO's Advanced Therapies Group.

In a year marked by the SARS-COV-2 pandemic, researchers from the programme became involved in the fight against COVID-19. Researchers from José Becerra's group identified a new drug that could mitigate the consequences of SARS-CoV-2 infection, while the laboratory of José Carlos Rodríguez Cabello's group was validated by the Instituto de Salud Carlos III for the development of COVID-19 diagnostic tests using PCR tests.

NANOMEDICINE PROGRAMME

Coordinator: **M. Pilar Marco Colás**

In addition to the Early stage projects and intramural collaborations, a great effort has been made in preparing competitive proposals for both European and national calls. During 2020, a project was awarded in the AES 2020-Health Research Projects call in the area of nanomedicine: "*Innovative strategies for therapy against tumor stem cells: activating dopamine receptors with protein nanoparticles*" coordinated by José Luis Corchero. In addition, the project of the Challenges-Collaboration 2019 call "*DROPLITE, New rapid test for the detection of female hormones in assisted reproduction clinics*" has begun, coordinated by the company DROPLITE S.L. and the Nanobiotechnology for Diagnostics (Nb4D) group, with J. Pablo Salvador as PI of the project.

During 2020, two projects were completed with excellent results:

- >> The European project (H2020) SMART4FABRY “*Smart multifunctional GLA-nanoformulation for Fabry Disease*”, coordinated by CIBER (PI: Dr. Nora Ventosa). The project has resulted in a product that has been awarded Orphan Drug designation by the EMA. This designation entails a whole series of advantages and facilities for the pharmaceutical development of the product until it is ready for clinical use.
- >> AES 2017 Project “*Design of protein nanomedicines for targeted treatments in pancreatic cancer*” coordinated by José Luis Corchero.

In addition, researchers from the CIBER-BBN Nanomedicine programme have continued with ongoing projects with national and international funding, including:

- >> The European project (ERANET-TRANSCAN-2) PROSCANEX “*Exploitation of extracellular vesicles for precision diagnostics of prostate*”, led by Jesús Martínez de la Fuente.
- >> The European project (ERANET-EURONANOMED-3) ABISens “*Monitoring of Acquired Brain Injury and recovery biomarkers by the combined label-free nanoSensing of multiple circulating molecules*” coordinated by Laura Lechuga.
- >> The RETOS- Knowledge Generation 2018 project “*Nanoplasmonic sensor platform for biomimetic analysis and without markings of cellular immunotherapy- SENSECELL*”, led by María Soler.
- >> Worth highlighting are the ERC *Advanced Grant* projects underway granted to PIs from the nanomedicine programme (Jesús Santamaría and Luis Liz-Marzán).

Laura Lechuga has been awarded the *Rei Jaume I* Prize in New Technologies for her long innovative career in the field of nanobiosensors and the *National Research Prize 2020*, granted by the Ministry of Science and Innovation. The programme researcher Luis M. Liz Marzán has been included for 7 consecutive years (2014-2020) in the Clarivate Analytics *Highly Cited Researchers* list, one of the most reputable classifications in the international scientific community.

TRAINING PROGRAMME

During 2020, the situation derived from the Covid pandemic has had a strong impact on the proper functioning of the training programme.

The planned calls for mobility actions, which finance stays of researchers in other CIBER-BBN research groups, or in other external groups (national or foreign), were suspended due to mobility restrictions that were in force for most of the year.

However, in the first months of the year, it was possible to carry out stays granted in the 2019 calls but planned for the beginning of 2020.

Regarding the research initiation grants in the form of internship contracts for young researchers, the fact that the hiring quota was made known after the summer and the unusual activity in the laboratories together with the face-to-face restrictions have prevented developing the programme as is usually done by incorporating new personnel into the groups.

PLATFORMS: NANBIOSIS

Coordinator: **Jaume Veciana Miró**

In 2020, the agreement was signed between the three nodes that constitute NANBIOSIS (CIBER, CCMIJU and BIONAND) and that regulates the goals and operation of the ICTS.

Due to the situation generated by the pandemic, some of the NANBIOSIS services have been temporarily suspended or postponed. However, NANBIOSIS has opened a procedure to prioritize projects related to the virus called "COVID-19 Rapid Access Call".

Of special note is the project "*Point-of-care tests for the rapid detection of SARS-COV-2 (POC4CoV)*", led by Pilar Marco, to develop virus diagnostic technologies, and in which four NANBIOSIS units collaborate (U2, U3, U29 and U1). This project provides compact and robust point of care (PoC) diagnostic technologies for the precise, rapid and simultaneous detection of different disease-related biomarkers of SARS-COV-2 infection.

There have been numerous collaborations carried out by NANBIOSIS in the fight against coronavirus, among which the following stand out:

- >> Laura Lechuga (U4) directs the European project CONVAT, to create a nanotechnological device with biosensors capable of quickly detecting the presence of the coronavirus.
- >> Miriam Royo (U3) participates in a project that seeks to develop molecules with neutralizing properties of SARS-CoV-2, for the treatment of hospitalized patients.
- >> Ramón Martínez Máñez (U26) leads the Diacovid Project for the development of a rapid point-of-care (POC) test, based on nanosystems with molecular gates to detect SARS-CoV-2

NANBIOSIS's participation in the European project SAFE-N-MEDTECH (H2020) has continued, the objective of which is to create an open access platform based on online tools for companies and reference laboratories for the development, testing, evaluation, scale-up and commercial exploitation of medical and diagnostic devices based on nanotechnology. During 2020 CIBER-BBN has coordinated the WP3: *Preclinical research in medical technologies and one of the pilot cases* (led by the company Stryker), and has worked on an in vivo trial in rabbits to study implant efficacy in accordance with GLP standards.

During this year some relevant projects for NANBIOSIS have been completed:

- >> The European project (H2020) coordinated by CIBER, SMART4FABRY, which highlights the work carried out by four of the NANBIOSIS units (U6, U1, U3 and U20). The project has been a successful case of cooperation between NANBIOSIS units, as well as a success in transferring results to the industry.
- >> Two of the equipment expansion projects co-financed by FEDER Funds for ICTS, in the CSIC (U2, U4, U6 and U8) and in the IBEC (U7), information available on the NANBIOSIS YouTube channel.
- >> PRONANBIOSIS II project financed at the national level by the Revitalization Actions "Networks of Excellence", for the coordinated management and promotion of NANBIOSIS ICTS.

In summary, despite the anomalous situation of 2020, the high participation of NANBIOSIS in research projects and results has been maintained (+1000 accesses, +100 national and 50 international projects, +100 publications in JCR journals with mention of NANBIOSIS and + 20 theses).



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

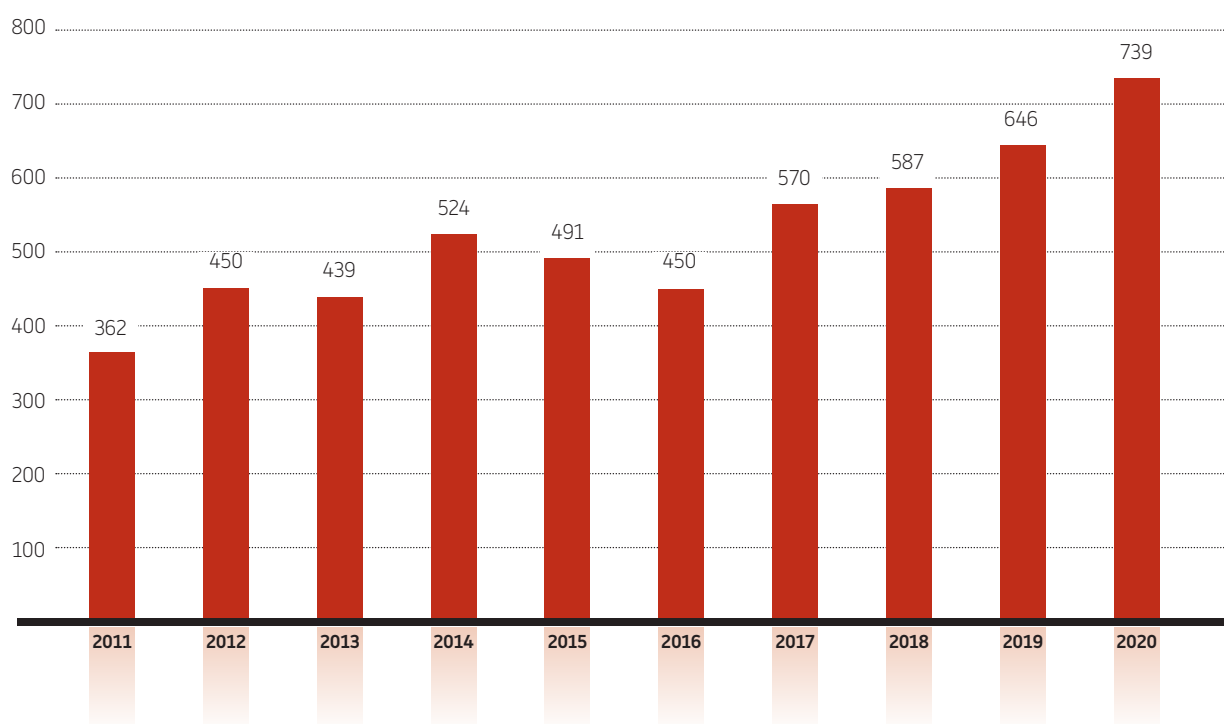
| | |
|-------|-----|
| TOTAL | 739 |
| Q1 | 558 |
| D1 | 211 |

Collaborations

| | |
|-----------|----|
| CIBER-BBN | 66 |
| CIBER* | 86 |

*Among various thematic areas




» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|---|
| 55,470 | Trepast X. When cellular forces became visible. Nature Reviews Molecular Cell Biology. 2020. |
| 41,845 | Chen X., Wang F., Fernandez E., Roelfsema P.R. Shape perception via a high-channel-count neuroprosthesis in monkey visual cortex. Science. 2020;370(6521):1191-1196. |
| 38,637 | Monteil V., Kwon H., Prado P., Hagelkruys A., Wimmer R.A., Stahl M. et al. Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2. Cell. 2020. |
| 27,398 | Lewandowski W., Vaupotic N., Pocięcha D., Gorecka E., Liz-Marzan L.M. Chirality of Liquid Crystals Formed from Achiral Molecules Revealed by Resonant X-Ray Scattering. Advanced Materials. 2020;32(41). |
| 27,398 | Zhao Y., Bertolazzi S., Maglione M.S., Rovira C., Mas-Torrent M., Samori P. Molecular Approach to Electrochemically Switchable Monolayer MoS ₂ Transistors. Advanced Materials. 2020;32(19). |
| 21,567 | Dhillon P., Park J., Hurtado del Pozo C., Li L., Doke T., Huang S. et al. The Nuclear Receptor ESRRA Protects from Kidney Disease by Coupling Metabolism and Differentiation. Cell Metabolism. 2020. |
| 20,042 | Lynch C.J., Bernad R., Martinez-Val A., Shahbazi M.N., Nobrega-Pereira S., Calvo I. et al. Global hyperactivation of enhancers stabilizes human and mouse naive pluripotency through inhibition of CDK8/19 Mediator kinases. Nature Cell Biology. 2020;22(10):1223-1238. |
| 17,127 | Lopes Alves I., Collij L.E., Altomare D., Frisoni G.B., Saint-Aubert L., Payoux P. et al. Quantitative amyloid PET in Alzheimer's disease: the AMYPAD prognostic and natural history study. Alzheimer's and Dementia. 2020. |
| 16,836 | Acosta S., Quintanilla-Sierra L., Mbundi L., Reboto V., Rodriguez-Cabello J.C. Elastin-Like Recombinamers: Deconstructing and Recapitulating the Functionality of Extracellular Matrix Proteins Using Recombinant Protein Polymers. Advanced Functional Materials. 2020;30(44). |
| 16,836 | Manzano M., Vallet-Regi M. Mesoporous Silica Nanoparticles for Drug Delivery. Advanced Functional Materials. 2020;30(2). |

» CIBER-BBN Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
|  Aguilar de Armas, M ^a Rosa | 16 | 13 | 5 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencia y Tecnología de Polímeros | Madrid |
|  Albericio Palomera, Fernando | 45 | 22 | 8 | Universidad de Barcelona - Facultad de Química | Barcelona |
|  Arús Caralto, Carles | 10 | 5 | - | Universidad Autónoma de Barcelona - Departamento de Bioquímica y de Biología Molecular | Barcelona |
|  Becerra Ratia, José | 14 | 10 | 2 | Universidad de Málaga - Facultad de Ciencias | Málaga |
|  Bellón Caneiro, Juan Manuel | 13 | 5 | 1 | Universidad de Alcalá - Facultad de Medicina | Madrid |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|---------------------|-----------|-----------|--|-----------------|
|  Calonge Cano, Margarita | 10 | 6 | 3 | Universidad de Valladolid - Instituto de Oftalmobiología Aplicada | Valladolid |
|  Corcoy Pla, Rosa | 17 | 12 | 5 | Instituto de Investigacion del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Engel López, Elisabeth | 6 | 5 | 1 | Fundación Instituto de Bioingeniería de Cataluña | Barcelona |
|  Eritja Casadellà, Ramon | 9 | 8 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña | Barcelona |
|  Fernández Jover, Eduardo | 9 | 7 | 1 | Universidad Miguel Hernández - Instituto de Bioingeniería | Alicante |
|  Gómez Ramírez, Rafael | 24 | 22 | 8 | Universidad de Alcalá - Facultad de Farmacia | Madrid |
|  Gómez Ribelles, José Luis | 26 | 18 | 2 | Universidad Politécnica de Valencia - Centro de Biomateriales e Ingeniería Tisular | Valencia |
|  González Martín, María Luisa | 5 | 3 | - | Universidad de Extremadura - Facultad de Ciencias | Badajoz |
|  Gorostiza Langa, Pau | 5 | 5 | 1 | Fundación Instituto de Bioingeniería de Cataluña | Barcelona |
|  Hernando Pérez, María Elena | 36 | 22 | 6 | Universidad Politécnica de Madrid - ETSI Telecomunicación | Madrid |
|  Hornero Sánchez, Roberto | 18 | 13 | 1 | Universidad de Valladolid - E.T.S. Ingenieros de Telecomunicaciones | Valladolid |
|  Jané Campos, Raimon | 13 | 8 | 3 | Fundación Instituto de Bioingeniería de Cataluña | Barcelona |
|  Laguna Lasasosa, Pablo | 26 | 22 | 3 | Universidad de Zaragoza - Instituto de Investigación en Ingeniería de Aragón | Zaragoza |
|  Lechuga Gómez, Laura María | 10 | 9 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Institut Català de Nanociència i Nanotecnologia | Barcelona |
|  Liz Marzán, Luis Manuel | 36 | 32 | 25 | CIC biomaGUNE | Guipúzcoa |
|  López Higuera, José Miguel | 16 | 12 | - | Universidad de Cantabria - Edificio I+D+I de ing. de Telecomunicación | Cantabria |
|  Mangues Bafalluy, Ramon | 19 | 15 | 10 | Instituto de Investigacion del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Marco Colás, María Pilar | 10 | 9 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña | Barcelona |
|  Martínez Barca, Miguel Ángel | 21 | 8 | 3 | Universidad de Zaragoza - Instituto de Investigación en Ingeniería de Aragón | Zaragoza |
|  Martínez de la Fuente, Jesús | 32 | 24 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencia de Materiales de Aragón | Zaragoza |
|  Martínez Mániz, Ramón | 29 | 24 | 12 | Universidad Politécnica de Valencia - Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico | Valencia |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|------------|
|  Pedraz Muñoz, José Luis | 28 | 27 | 12 | Universidad del País Vasco - Facultad de Farmacia | Álava |
| Peris Serra, José Luis | 8 | 7 | - | Asociación Instituto de Biomecánica de Valencia | Valencia |
|  Raya Chamorro, Ángel | 4 | 4 | 4 | Fundación IDIBELL | Barcelona |
|  Rodríguez Abreu, Carlos | 19 | 13 | 4 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña | Barcelona |
|  Rodríguez Cabello, José Carlos | 20 | 16 | 9 | Universidad de Valladolid - Bioforge | Valladolid |
|  Ruiz Romero, Cristina | 13 | 10 | 2 | Servicio Gallego de Salud - Complejo Hospitalario Universitario A Coruña | A Coruña |
|  Samitier Martí, Josep | 18 | 13 | 5 | Fundación Instituto de Bioingeniería de Cataluña | Barcelona |
|  Santamaría Ramiro, Jesús | 54 | 41 | 18 | Universidad de Zaragoza - Instituto Universitario de Investigación en Nanociencia de Aragón | Zaragoza |
|  Santos Lleó, Andrés | 9 | 7 | 1 | Universidad Politécnica de Madrid - ETSI Telecomunicación | Madrid |
| Schwartz Navarro, Simó | 11 | 11 | 6 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) - Hospital Vall d'Hebron | Barcelona |
|  Setoain Peregó, Xavier | 27 | 21 | 13 | Universidad de Barcelona - Hospital Clínic de Barcelona | Barcelona |
|  Trepas Guixer, Xavier | 6 | 6 | 5 | Fundación Instituto de Bioingeniería de Cataluña | Barcelona |
|  Vallet Regí, María | 28 | 23 | 9 | Universidad Complutense de Madrid - Facultad de Farmacia | Madrid |
|  Ventosa Rull, Nora | 25 | 24 | 9 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencias de Materiales de Barcelona | Barcelona |
|  Vilaboa Díaz, Nuria | 9 | 8 | 3 | Servicio Madrileño de Salud - Hospital La Paz | Madrid |
|  Villa Sanz, Rosa | 11 | 10 | 4 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Microelectrónica de Barcelona | Barcelona |
|  Villaverde Corrales, Antonio | 28 | 25 | 17 | Universidad Autónoma de Barcelona - Instituto de Biotecnología y Biomedicina | Barcelona |
| Farre Ventura, Ramón* | 18 | 9 | 2 | Universidad de Barcelona - Facultad de Medicina | Barcelona |
| Muñoz Fernández, María Ángeles* | 14 | 10 | 2 | Servicio Madrileño de Salud - Hospital Gregorio Marañón | Madrid |

*CIBER-BBN Associated Groups

PATENTS OWNED BY CIBER 2020

Applications

National

- Method for the diagnosis, prognosis and monitoring of Alzheimer's disease using techniques.
- Method for the Rapid Detection and Diagnosis of Staphylococcus Aureus.
- Method for the rapid detection of *Candida auris* and the diagnosis of infection caused by this pathogen.

European

- A Synthetic Hydrogel and Its Use for Immunotherapy and 3D-Printing.
- Electrochemical sensor systems for sensing analytical reactions and biological operations and methods.
- Acquisition Device to Limit Leakage Current in Electrophysiological Signal Recording Devices.
- Material platforms for simultaneous solid-phase presentation of boron and cell adhesion domains as antitumor strategy for carcinomas.
- A stretchable opto-mechanical material composed by a metallic and or dielectric nanostructure array embedded into a wrinkled elastomer.
- Cell-Penetrating Peptides.
- Layered Substrate and Uses Thereof.

PCT

- Therapeutic nanoconjugates and uses thereof.
- Method to produce enzymes.
- Protein nano- or microparticles as artificial inclusion bodies.
- Nanovesicles and its use for nucleic acid delivery.

National Phases

- Porous material for the detection of *Candida albicans*, the diagnostic method that uses it and preparation method thereof. (Europe, Australia, Canada, China, South Korea, Singapore, Hong Kong, Japan)
- Therapeutic Nanoconjugates and Uses Thereof. (Canada, Japan, Unites States., India, Europe, China)

Granted Patents

National

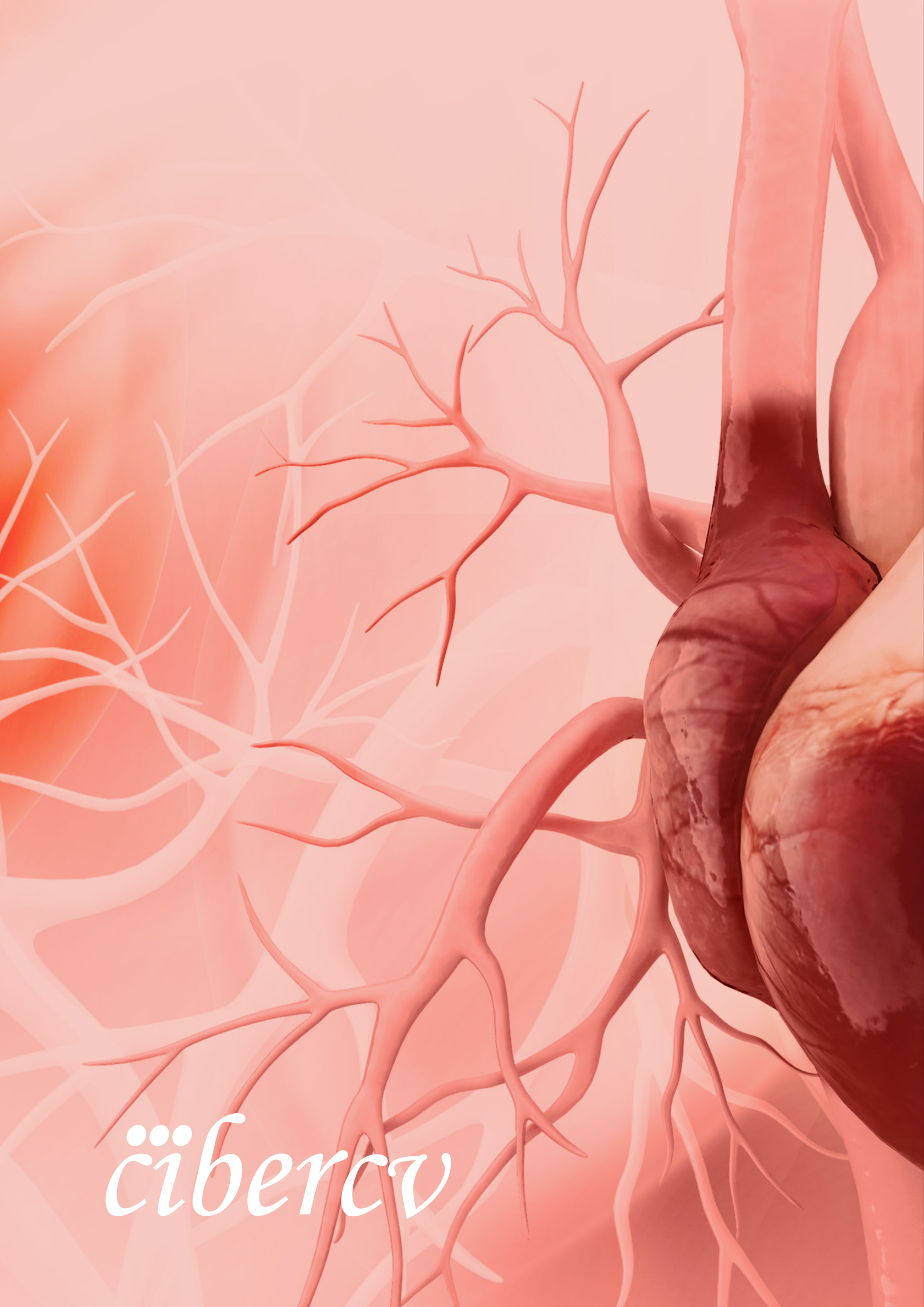
- Graphene transistor system for measuring electrophysiological signals.

International

- Methods and reagents for efficient and targeted delivery of therapeutic molecules to CXCR4 cells. (United States)

CLINICAL GUIDES AND CONSENSUS DOCUMENTS 2020

- Strengthening the integration of eye care into the health system: methodology for the development of the WHO package of eye care interventions.
- Use of abemaciclib, palbociclib and ribociclib in combination, for the treatment of locally advanced or metastatic breast cancer.
- Manual of Clinical Practice in Epilepsy. Diagnostic-therapeutic recommendations of the SEN 2019.
- PET-CT in lymphomas. Guide of the Spanish Group of Lymphomas and Bone Marrow Transplantation (GELTAMO).
- Clinical Approach to Flash Glucose Monitoring: An Expert Recommendation



čiberov



**CARDIOVASCULAR
DISEASES**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Francisco Fernández-Avilés

Despite the exceptional situation of 2020, this fourth year of CIBERCV's trajectory has been very positive.

Important advances have been made in cardiovascular research, particularly the various contributions to the COVID-19 pandemic and a clear strengthening of collaboration between research groups, both within the CV area and with the other thematic areas of the CIBER.

In this period, the CIBERCV has exceeded 750 top-level scientific publications, with more than 20% of them in the first decile and around 60% in the first quartile. In addition, several research projects have been selected in calls for national and international grants, thus obtaining financing that contributes significantly to promoting the sustainability and competitiveness of the area. In this regard, the bb-ECHO project stands out, requested through the CIBER and funded in the call for Independent Clinical Research. This project, coordinated by the CIBERCV, is a prospective, multicenter and open study to evaluate the efficacy of esmolol in the early identification of cardiovascular disorders induced by cirrhosis, diabetes mellitus and cardiotoxic treatments and should provide answers to questions of great clinical relevance for patients with this type of pathology. This study has the participation of 12 Spanish hospitals, among which are groups from the CIBERCV and from other thematic areas (CIBERDEM, CIBEREHD and CIBERONC), under the coordination of Dr. Bermejo, deputy director of CIBERCV and researcher at Hospital Gregorio Marañón from Madrid.

In the field of communication, the CIBERCV has made 642 appearances in the media, 18 press releases and has carried out 57 dissemination activities. Worth highlighting is the communication campaign of the CIBER #QueSigalaCiencia, whose winning video was presented by researchers from the CV area.

In addition, in 2020 the work of the CIBERCV with the Spanish Medicines Agency has continued to create a National Registry of Ventricular Assist Devices. This milestone is of great importance as it will provide very relevant data for the treatment of chronic heart failure to the National Health System.

In conclusion, despite the difficulties of 2020, the CIBERCV has continued to face the challenges with great motivation and a strong commitment to the CIBER consortium, which has resulted in a cooperative scientific activity of the highest level. This is in large part thanks to the efforts of all the people involved and the framework of stability offered by the CIBER. We consider this to be essential to promoting cooperative research of excellence in Spain, with the aim of helping to reduce the impact of cardiovascular diseases in our environment and generating prosperity as well as leading research, innovation and training in this discipline within the national and international framework.



PROGRAMMES

P1: MYOCARDIAL DAMAGE AND ITS CONSEQUENCES

Coordinators: **Francisco Fernández-Avilés** and **Juan Delgado Jiménez**

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

Within the research line of Myocardial Healing and Remodeling, the Project “Prevalence of cardiac sequelae after infection by SARS-CoV-2” (CAR-VID Study) has begun, led by Dr. Fernández-Avilés’ group, in which four research groups of the CIBERCV participate (Hospital Gregorio Marañón, Hospital de Salamanca, CNIC and CIMA) as well as groups of the thematic areas CIBERESP, CIBERES and the REDISSEC network. This project aims to obtain an initial approximation of the prevalence of residual myocardial damage months after infection by SARS-CoV-2 and has been funded by the Francisco Soria Melguizo Foundation. The CAR-VID study is an example of multidisciplinary collaborative research in which basic and clinical researchers participate with a clear translational focus in the area of cardiovascular diseases.

In the line of genetic myocardial damage, the multicenter study entitled “Clinical characteristics and natural history of cardiac glycogenosis due to genetic variants in PRKAG2” stands out, having as its objective to describe the phenotype and natural history of patients with variants in PRKAG2 in an extensive international multicenter cohort. This study has been coordinated by the group led by Dr. García Pavía and has the participation of 27 national and international centers, six of them collaborators of the CIBERCV. The study has been published as an original work in the Journal of the American College of Cardiology. In addition, it was awarded by the Spanish Society of Cardiology as the best abstract of the congresses of the American and European Societies of Cardiology 2020 and has been selected as the best communication of the section of Familial Heart Diseases and Cardiovascular Genetics at the congress of the Spanish Society of Cardiology 2020.

As regards the line of research dedicated to Heart Failure, the most relevant milestone has been the publication of the article “Dynamics of serum potassium during hospitalization for Acute Heart Failure” in the journal Clinical Research in Cardiology. This work was led by Dr. Delgado’s group with the participation of ten CIBERCV research groups in collaboration with the REDINSCOR II network. This study aimed to describe the prevalence

and dynamics of potassium during Acute Heart Failure and assess its prognosis, studying the data of 1,779 hospitalized patients. The results showed how hyperkalemia on admission is an independent factor associated with hospital mortality and persistent hypokalemia is related to mortality at one year follow-up, thus generating knowledge of great value for clinical practice.

P2: ARTERIAL PATHOLOGY, MYOCARDIAL ISCHEMIA AND STRUCTURAL HEART PATHOLOGY

Coordinators: **Borja Ibáñez Cabeza** and **Alberto San Román Calvar**

Within programme 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.

In the research line of Myocardial Ischemia and Reperfusion, the REBOOT (*Treatment with Beta-blockers after myocardial infarction without reduced ejection fraction*) clinical trial has been launched, which studies the effect of beta-blockers in patients with acute myocardial infarction without reduced ejection fraction and which has already recruited 50% of the participants (4,200 patients). This trial, coordinated by Dr. Ibáñez's group, is the world's largest trial in this field, where numerous CIBERCV groups participate with the aim of improving clinical practice after a heart attack. This project has been supported by the Spanish Society of Cardiology and will have the altruistic participation of at least 55 Spanish and 25 Italian hospitals.

Within the research line of Aortic Valve Diseases, the RESA III study on the Spanish Registry of Acute Aortic Syndrome (RESA) stands out. The aim of this study is to assess the results in the management of this disease through a comparative study that covers the period 2005-2020. In this work, led by Dr. Barrabés's group, 30 Spanish hospitals collaborate to analyze advances in the management and reduction of mortality from acute aortic syndrome in Spain, obtaining highly relevant results.

In the research line of Valvular and Congenital Heart Disease, the work "Ramipril in High-Risk Patients with COVID-19" has been carried out, coordinated by the group led by Dr. San Román and in which 14 Spanish hospitals collaborate (nine of them members of CIBER). This study, which has achieved great clinical significance, investigates the relationship of COVID-19 with cardiovascular disease and the interaction of the virus with inhibitors of the Renin-Angiotensin-Aldosterone system, to the point of debating the need to withdraw this medication in high risk patients. In this work, the cohort of patients from the RASTAVI clinical trial, randomized to control or to Ramipril post-TAVI (percutaneous aortic valve implantation), was used to shed light on this issue and offer solid evidence of the need to maintain such treatment, especially in high risk patients.

P3: CARDIOVASCULAR EPIDEMIOLOGY AND RISK FACTORS

Coordinator: **Jaume Marrugat de la Iglesia**

Programme 3 has continued to promote research on the mechanism that links cardiovascular risk factors with the serious diseases they entail, with the ultimate goal of preventing and reducing the high impact of cardiovascular diseases on society.

As regards the research line of Epidemiology, cohorts, cardiovascular risk factors and risk functions, the launch of the CARGENCORS study (CARDiovascular GENetic risk score for Risk Stratification of patients positive for

SARS-CoV-2 virus) has been of great relevance. This study investigates the role of the genetic factors of coronary disease in the severity of COVID-19 and hopes to improve the stratification of the risk of serious complications, based on genetic risk scores (GRS) of coronary disease to predict the risk of coronary complications, including severe, critical and fatal forms of the disease. This project is led by Dr. Marrugat's group and has had the participation of other groups from CIBERCV (Hospital del Mar and Institut d'Investigació Biomèdica de Girona) as well as a group from the REDIAP network.

In the research line of Population studies and the genetic/epigenetic basis of complex cardiovascular traits, the publication of the article "Characteristics of HDL cholesterol particles and risk of coronary heart disease: a Mendelian randomization study" in the scientific journal *Metabolism* stands out. This study uses Mendelian randomization to analyze whether genetic instruments related to HDL-cholesterol levels, ApoA-I, HDL particle size, and cholesterol levels in HDL particle subtypes are associated with coronary artery disease. The results obtained support a causal relationship between some characteristics of HDL particles (diameter, cholesterol and triglyceride content in large particles, cholesterol content in small particles) and the risk of coronary heart disease. Four groups from CIBERCV collaborated in this work (two from Hospital del Mar, one from Hospital de la Santa Creu i Sant Pau and one from the Institute of Health Research of Aragón) as well as other groups from CIBERESP and CIBEROBN, coordinated by the group led by Dr. Elosua.

P4: MOLECULAR AND IMAGING BIOMARKERS, AND PRECISION CV MEDICINE

Coordinator: **Javier Díez Martínez**

Programme 4 has generated important advances in the field of biomarkers in relation to cardiovascular diseases.

In the research line focussed on the evaluation of known biomarkers, the clinical trial "Utility of carbohydrate antigen 125 in the titration of diuretics in patients with acute heart failure in renal failure" has been published in *The American Journal of Medicine*, carried out in collaboration by several groups of CIBERCV, led by the Dr. Sanchis' group. This study evaluates the usefulness of plasma levels of carbohydrate antigen 125 in the titration of diuretics in patients with acute heart failure and renal failure. The study showed that diuretic therapy guided by this biomarker was associated with an improvement in renal function parameters at 72 hours, compared to the standard arm of treatment. Similarly, benefits were observed in surrogate parameters of short-term clinical efficacy with no relevant safety issues.

Within the research line dedicated to the identification of new biomarkers, the study "Complement C5 protein as a marker of subclinical atherosclerosis" has been launched, coordinated by Dr. Blanco Colio's group, in collaboration with other CIBERCV groups. This study analyzes the temporal and topological changes in protein expression in human aortas with early atherosclerosis. Proteomic analysis of aortic tissue identified accumulation of complement proteins and activation in the intima of early atherosclerotic plaques. This was reflected in increased plasma C5 levels in asymptomatic individuals from two cohorts. Interestingly, plasma C5 levels correlated with markers of disease severity and events. Therefore, the identification of C5 as a biomarker of atherosclerotic burden at the subclinical level is a new potential tool of great interest for the prediction of cardiovascular risk.

TRAINING PROGRAMME

Coordinator: **José Antonio Barrabés Riu**

The main objective of the CIBERCV Training and Mobility Programme is to train young people to become cardiovascular researchers of the future to improve society's cardiovascular health. Likewise, this programme encourages the organization of workshops and specific courses in order to share the valuable advances and knowledge acquired by the CIBERCV researchers.

In 2020, calls for training and mobility grants have been affected by the pandemic situation and the vast majority of training activities have been carried out in a distance learning format.

Worth highlighting is the organization of online courses on different topics in the field of cardiovascular research such as atrial fibrillation, cardiac amyloidosis, heart failure, atherosclerosis, arrhythmias, heart transplantation, cardiological applications of 3D printing, and other advances in basic science and clinical excellence.

Within the CIBERCV, this programme remains the main training initiative and in 2020 it has contributed to the strengthening of quality translational research, promoting collaboration between the groups of the CV area and other thematic areas of the CIBER.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

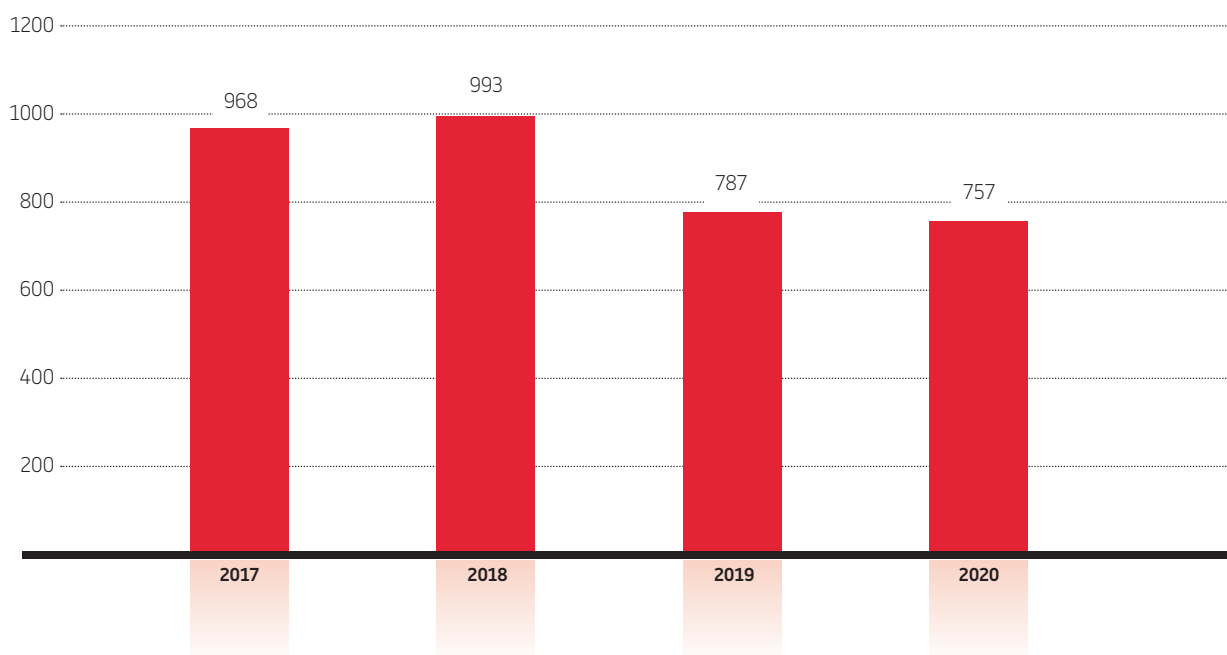
| | |
|---------|-----|
| TOTALES | 757 |
| Q1 | 441 |
| D1 | 157 |

Collaborations

| | |
|---------|-----|
| CIBERCV | 209 |
| CIBER* | 186 |

*Among various thematic areas

» Evolution of publications 2017-2020



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|--|
| 74,699 | Initial invasive or conservative strategy for stable coronary disease (Scopus ID: 85083171855; Pubmed ID: 32227755) |
| 74,699 | Early rhythm-control therapy in patients with atrial fibrillation (Scopus ID: 85090978522; Pubmed ID: 32865375) |
| 74,699 | Cardiac Myosin Activation with Omecamtiv Mecarbil in Systolic Heart Failure (Pubmed ID: 33185990) |
| 42,778 | The mutational constraint spectrum quantified from variation in 141,456 humans (Scopus ID: 85085542423; Pubmed ID: 32461654) |
| 42,778 | A structural variation reference for medical and population genetics (Scopus ID: 85085567000; Pubmed ID: 32461652) |
| 42,778 | Expanded encyclopaedias of DNA elements in the human and mouse genomes (Scopus ID: 85088796075; Pubmed ID: 32728249) |
| 42,778 | Evaluating drug targets through human loss-of-function genetic variation (Scopus ID: 85085564434; Pubmed ID: 32461653) |
| 42,778 | Na ⁺ controls hypoxic signalling by the mitochondrial respiratory chain (Scopus ID: 85088809211; Pubmed ID: 32728214) |
| 42,778 | Transcript expression-aware annotation improves rare variant interpretation (Scopus ID: 85085576216; Pubmed ID: 32461655) |
| 42,778 | Perspectives on ENCODE (Scopus ID: 85088796908; Pubmed ID: 32728248) |

» CIBERCV Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|-----------|
|  Andrés García, Vicente | 14 | 14 | 8 | Fundación Centro Nacional de Investigaciones Cardiovasculares | Madrid |
|  Badimon Maestro, Lina | 27 | 19 | 10 | Instituto de Investigación del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Barrabés Riu, Jose Antonio | 49 | 23 | 4 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) - Hospital Vall d'Hebron | Barcelona |
|  Bayés Genis, Antonio | 85 | 46 | 18 | Fundación Instituto de Investigación Germans Trias i Pujol - Hospital Germans Trias i Pujol | Barcelona |
|  Blanco Colio, Luis Miguel | 6 | 5 | 2 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Bosca Gomar, Lisardo | 9 | 7 | 5 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de investigaciones biomédicas Alberto Sols | Madrid |
|  Brugada Terradellas, Ramon | 19 | 14 | 8 | Fundación Instituto de Investigación Biomédica de Girona - Hospital Josep Trueta | Girona |
|  Chorro Gasco, Francisco Javier | 18 | 7 | 4 | Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) - Instituto de investigación sanitaria INCLIVA | Valencia |
|  Civeira Murillo, Fernando | 21 | 16 | 6 | Fundación Instituto de Investigación Sanitaria Aragón | Zaragoza |
|  Crespo Leiro, María Generosa | 36 | 21 | 11 | Servicio Gallego de Salud - Complejo Hospitalario Universitario A Coruña | A Coruña |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|--|-----------------|
|  Delgado Jiménez, Juan Francisco | 61 | 32 | 8 | Servicio Madrileño de Salud - Hospital Universitario 12 Octubre | Madrid |
|  Delpón Mosquera, Eva | 17 | 9 | 3 | Universidad Complutense de Madrid - Facultad de Medicina | Madrid |
|  Díez Martínez, Domingo Francisco Javier | 10 | 9 | 6 | Fundación para la Investigación Médica Aplicada | Navarra |
|  Elosua Llanos, Roberto | 13 | 5 | 0 | Consorti Mar Parc Salut de Barcelona | Barcelona |
|  Fernández-Avilés Díaz, Francisco | 69 | 33 | 8 | Servicio Madrileño de Salud - Hospital Gregorio Marañón | Madrid |
|  García Pavía, Pablo | 32 | 18 | 10 | Servicio Madrileño de Salud - Hospital Universitario Puerta de Hierro | Madrid |
|  González Juanatey, José Ramón | 69 | 42 | 10 | Servicio Gallego de Salud - Complejo Hospitalario Universitario Santiago | A Coruña |
|  Guerra Ramos, José María | 27 | 16 | 8 | Instituto de Investigación del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Ibáñez Cabeza, Borja | 51 | 26 | 14 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Málaga |
|  Jiménez Navarro, Manuel Francisco | 33 | 18 | 5 | Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Universitario Virgen de la Victoria | Madrid |
|  López-Sendon Hentschel, José Luis | 9 | 4 | 2 | Servicio Madrileño de Salud - Hospital La Paz | Madrid |
|  Marín Ortuño, Francisco | 53 | 37 | 8 | Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS) - Hospital Universitario Virgen de la Arrixaca | Murcia |
|  Marrugat de la Iglesia, Jaume | 13 | 10 | 5 | Consorti Mar Parc Salut de Barcelona | Barcelona |
|  Martínez Dolz, Luis | 33 | 21 | 5 | Fundación para la Investigación del Hospital la Fe - Hospital Universitario de La Fe | Valencia |
|  Martínez González, José | 12 | 9 | 8 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas de Barcelona | Barcelona |
|  Mayor Menéndez, Federico | 4 | 4 | 1 | Universidad Autónoma de Madrid - Centro de Biología Molecular Severo Ochoa | Madrid |
|  Mont Girbau, Josep Lluís | 50 | 19 | 7 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Ordóñez Fernández, Antonio | 6 | 3 | 1 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Hospital Virgen del Rocío | Sevilla |
|  Páramo Fernández, José Antonio | 11 | 5 | 2 | Universidad de Navarra - Clínica Universitaria de Navarra | Navarra |
|  Pérez-Villacastín Domínguez, Julián | 8 | 5 | 1 | Servicio Madrileño de Salud - Hospital Clínico San Carlos | Madrid |
|  Pompa Mínguez, José Luis de la | 6 | 5 | 2 | Fundación Centro Nacional de Investigaciones Cardiovasculares | Madrid |
|  Redondo Moya, Juan Miguel | 11 | 5 | 4 | Fundación Centro Nacional de Investigaciones Cardiovasculares | Madrid |
|  Salaices Sánchez, Mercedes | 9 | 8 | 1 | Universidad Autónoma de Madrid | Madrid |
|  San Román Calvar, José Alberto | 39 | 23 | 7 | Hospital Clínico Universitario de Valladolid | Valladolid |
|  Sánchez Fernández, Pedro Luis | 43 | 25 | 7 | Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León - Hospital Universitario de Salamanca | Salamanca |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|----------|
|  Sánchez Madrid, Francisco | 7 | 7 | 2 | Universidad Autónoma de Madrid | Madrid |
|  Sánchez Margallo, Francisco Miguel | 4 | 3 | 2 | Fundación Centro de Cirugía de Mínima Invasión Jesús Usón | Cáceres |
|  Sanchís Fores, Juan | 45 | 20 | 6 | Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) - Instituto de investigación sanitaria INCLIVA | Valencia |
|  Vázquez, Cobos Jesús María | 32 | 22 | 14 | Fundación Centro Nacional de Investigaciones Cardiovasculares | Madrid |
|  Zamorano Gómez, José Luis | 14 | 11 | 4 | Servicio Madrileño de Salud - Hospital Ramón y Cajal | Madrid |

CLINICAL GUIDES AND CONSENSUS DOCUMENTS 2020

- Classification, prevalence, and outcomes of anticancer therapy-induced cardiotoxicity: the CARDIOTOX registry
- Proportion of High-Risk/Very High-Risk Patients in Europe with Low-Density Lipoprotein Cholesterol at Target According to European Guidelines: A Systematic Review
- Lipid management in rheumatoid arthritis: a position paper of the Working Group on Cardiovascular Pharmacotherapy of the European Society of Cardiology
- Antithrombotic therapy and major adverse limb events in patients with chronic lower extremity arterial disease: systematic review and meta-analysis from the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy in Collaboration with the European Society of Cardiology Working Group on Aorta and Peripheral Vascular Diseases
- Real-world' observational studies in arrhythmia research: data sources, methodology, and interpretation. A position document from European Heart Rhythm Association (EHRA), endorsed by Heart Rhythm Society (HRS), Asia-Pacific HRS (APHRS), and Latin America HRS (LAHRS)
- Consensus document and recommendations on palliative care in heart failure of the Heart Failure and Geriatric Cardiology Working Groups of the Spanish Society of Cardiology
- Trends in the treatment of cardiogenic shock and prognostic impact of the type of treating centers
- Spanish Heart Transplant Registry. XXXI Official Report of the Heart Failure Association of the Spanish Society of Cardiology
- Coronavirus: the geriatric emergency of 2020. Joint document of the Geriatric Cardiology Section of the Spanish Society of Cardiology and the Spanish Society of Geriatrics and Gerontology
- Recommendations on antithrombotic treatment during the COVID-19 pandemic. Positioning of the Cardiovascular Thrombosis Working Group of the Spanish Society of Cardiology
- Expert Consensus on heart failure with reduced ejection fraction: beyond the guidelines.



çiberdem



**DIABETES
AND ASSOCIATED
METABÓLIC
DISEASES**







WELCOME FROM THE SCIENTIFIC DIRECTOR

Eduard Montanya Mias

The year 2020 has been marked at all levels by the Covid-19 pandemic. After the hampering of the activities of the CIBERDEM groups, brought about by the stay-at-home orders from the months of March to May, with the great healthcare burden this meant for the clinical groups, and the limitation in mobility and in-person access to the research centers, the activity of the groups has evolved towards a gradual normalization, although in many cases not fully and with differences between territories and centers. The limitations imposed by the health situation have not, however, been an impediment to maintaining interaction and collaboration between the groups which have quickly adapted to non-face-to-face meetings. A good example of this has been the ability to reformulate and continue to hold the CIBERDEM Annual Meeting in virtual format.

In terms of scientific production, the impact of the pandemic has so far been quite low if measured in terms of the scientific publications of 2020. This may be due to the fact that a large majority of them are a reflection of the activity carried out prior to the start of the pandemic. Thus, it will not be until next year when we will be able to gauge the impact more accurately. In fact, in 2020 CIBERDEM has increased its scientific production both in quantity, with more than 360 publications, and in quality, with 74% of them in the first decile and quartile. The publications also show the maintenance of the high collaborative activity of the CIBERDEM groups both at the CIBER and international level, with 53% and 39% of collaborative publications, respectively. It is noteworthy that some of the publications already reflect the first results of the work of the CIBERDEM researchers in relation to COVID-19, in terms of the impact on and management of patients with diabetes. Our website shows the most relevant publications of each group in detail and the Annual Report details the main achievements of 2020 by research programs.

Among the actions of the year 2020, worth highlighting is the increase in the collaboration between the CIBER areas brought about by the development of joint projects, an aspect in which CIBERDEM has actively participated. Amongst others, we would like to make note of the participation of CIBERDEM in the calls IMPaCT (Precision Medicine Infrastructure associated with Science and Technology, AES 2020), Europe Management Networks / Europe Technology Centers (AEI 2020) or in the Independent Clinical Research call (AES 2020) with the granting of 4 collaborative projects with CIBERDEM participation. At the internal level of CIBERDEM, the actions to reinforce the collaborative activity between the groups and to promote and support young researchers should be highlighted. A good example of this is the fact that the mobility programme has been maintained

despite the limitations derived from the health situation. Similarly, three CIBERDEM intramural projects have been developed led by young researchers and in which a total of 7 groups from the area participate.

CIBERDEM has maintained its commitment to bringing the results of research closer to society, participating in outreach activities such as Diabetes Experience Day or World Diabetes Day and to consolidate its institutional ties with patient associations. Regarding its presence at the institutional level in scientific societies, CIBERDEM has been present at the Congresses of the Spanish Diabetes Society, the European Association for the Study of Diabetes and at the EURADIA meetings.

To learn more about the activity and achievements of CIBERDEM in 2020, I invite you to consult the Scientific Report and also to expand the information by visiting our website (www.ciberdem.org) as well as following us on Twitter (@ciberdem).

Kind regards



PROGRAMMES

PROGRAMME 1. EPIDEMIOLOGY, GENETICS AND EPIGENETICS OF DIABETES MELLITUS. CHRONIC COMPLICATIONS AND COMORBIDITIES

Coordinator: **Ángela Martínez Valverde**

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

Based on the exploitation of the results of the di@bet.es study, which established the incidence of type 2 diabetes in Spain (Rojo-Martínez et al., *Sci Rep.* 2020), the incidence and regression of metabolic syndrome have been described in our country, identifying the target populations to establish prevention strategies (Cuesta et al., *BMJ Open Diabetes Res Care* 2020, 8 (1): e001715). In addition, the “Diabetes Incidence Study in the Basque Country” has been completed, establishing an incidence of diabetes of 5.37 cases / 1000 people / year in the Basque Country, significantly lower than that obtained in the national study of 11.6 cases / 1000 people / year.

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

A multicenter study has been led in more than 500 adult subjects with type 1 diabetes mellitus (DM1) without cardiovascular disease, in comparison with the population without diabetes, in which the circulating lipoprotein profile has been determined by means of conventional and advanced analysis (nuclear magnetic resonance spectroscopy), revealing significant discrepancies with the conventional method as well as a more unfavorable lipoprotein profile in women with DM1. This is relevant data in the field of personalized medicine and prevention of cardiovascular disease in this group. (Amor et al., *Cardiovasc Diabetol.* 2020, 19 (1): 126).

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

The anti-inflammatory and antioxidant properties of peptidomimetics inhibitors of transcription factors have been described in experimental atherosclerosis (La Manna et al., *Antioxidants* 2020, 9: 754) and, in preclinical models, it has been proven that the treatment improves proteinuria and renal function, as well as micro- and

macrovascular damage associated with type 2 diabetes (Opazo-Rios et al., *Int J Mol Sci.* 2020; 21 (12): 4225; Opazo-Rios et al., *BMJ Open Diabetes Res Care.* 2020; 8 (1): e001242).

In collaboration with CIBERHED, it has been described in a murine model of nonalcoholic steatohepatitis (NASH) that the inhibition of the protein tyrosine phosphatase 1B (PTP1B) confers protection against structural and functional alterations of the intestinal barrier that occur during NASH. This effect is due in part to a greater sensitivity to GLPs in the pro-inflammatory context of this pathology (Rubio-Caballero et al., *Mol Metab.* 2020).

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

We are participating in the European ePREDICE study, the first clinical study to examine the effect of different interventions (lifestyle modifications and pharmacological treatment) on microvascular complications in subjects with prediabetes in Europe. A group leader is a member of the steering committee of the ePREDICE consortium and CIBERDEM participates as a patient recruitment center, biobank, central laboratory and in the determination of biomarkers.

In transgenic mice, the overexpression of the *Srebf2* gene has been described to have beneficial effects on metabolic parameters and confers protection against a high-fat high-sucrose diet (Andrés-Blasco I et al., *Nutrients* 2020; 12 (10) : 3130).

In collaboration with CIBEROBN, it has been shown that the phenolic compounds of virgin olive oil increase macrophage-specific reverse cholesterol transport (Cedó L et al. *Biomedicines* 2020; 8: 226). In collaboration with CIBERCV, a derivative of vitamin B3, nicotinamide, has been shown to prevent LDL oxidation, vascular inflammation, and arteriosclerosis when administered as a dietary supplement (Méndez-Lara KA et al. *Antioxidants* 2020 ; 9: 1162).

PROGRAMME 2. MOLECULAR AND CELLULAR DETERMINANTS OF THE FUNCTION, DAMAGE AND PROTECTION OF PANCREATIC ISLETS. REGENERATIVE MEDICINE AND ADVANCED THERAPIES.

Coordinator: **Franz Martín Bermudo**

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

Vitamin D receptor (Vdr) expression has been reported to decrease in pancreatic islets in murine models of type 1 and type 2 diabetes. Furthermore, sustained overexpression of Vdr in β -cells helps to preserve their mass and function, protecting against diabetes (Morró et al., *Diabetes* 2020).

Treatment with the anti-inflammatory molecule alpha1-antitrypsin reverses glucose intolerance and restores the insulin-secretory response to glucose in mice that overexpress hIAPP in pancreatic islets. Through co-cultures of macrophages and pancreatic islets, it has been reported that alpha1-antitrypsin also blocks the cytotoxic action of macrophages activated by hIAPP on β -cells (Rodríguez-Comas et al., *Mol Metab* 2020).

It has been established that molecules based on dendrimer systems can act as inhibiting agents of the formation of amyloid protein deposits in pancreatic islets, which could potentially act as anti-amyloid agents in type 2 diabetes (Lozano-Cruz et al., *Chemistry A European Journal* 2020).

The circulating blood protein Wisp1 has been determined to induce the proliferation of β -cells in murine and human pancreatic islets, suggesting that Wisp1 could be a therapeutic agent to induce the expansion of β -cells in people with diabetes (Fernandez-Ruiz et al., *Nat Commun* 2020).

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

The molecular mechanisms of pancreatic tumorigenesis have been studied combining genetic, epigenetic and biochemical studies, reporting that the transcription factor HNF1A, the main gene involved in monogenic diabetes, is also a tumor suppressor that regulates another gene mutated in pancreatic ductal adenocarcinomas (Kalisz et al, *EMBO J* 2020).

Within the framework of the international DECODE Diabetes consortium, which includes 4 CIBERDEM groups (<https://cordis.europa.eu/project/id/789055>), the sequencing of nearly 3000 samples with monogenic diabetes has been completed.

It has been described that, in trained mice muscle, the improvement of insulin sensitivity takes place through the release of exosomal microRNAs, which regulate gene expression in the liver, having an impact on the overall metabolic profile. These exosomal microRNAs could be used to treat lipid and hydrocarbon metabolic alterations (Castaño et al., *Proc Natl Acad Sci USA* 2020).

Upregulation of long noncoding RNA 13 in beta cells has been reported to activate the pro-inflammatory STAT1 pathway, increasing beta cell inflammation and contributing to the pathogenesis of type 1 diabetes. This finding provides new information regarding the molecular mechanisms underlying diseases associated with single nucleotide polymorphisms, opening the door to new therapeutic approaches based on long non-coding RNA (González-Moro et al., *Proc Natl Acad Sci USA* 2020).

3. Application of new technologies to the treatment of diabetes

A mathematical algorithm has been developed which detects aerobic exercise, making it possible to predict the onset of hypoglycemia associated with exercise (Ramkissoon et al., *IEEE J Biomed Health Inform* 2020).

PROGRAMME 3. CELLULAR AND MOLECULAR MECHANISMS INVOLVED IN THE DEVELOPMENT AND PROGRESSION OF TYPE 2 DIABETES AND IDENTIFICATION OF NEW THERAPEUTIC TARGETS.

Coordinator: **Antonio Zorzano Olarte**

1. Inflammation as a pathogenic process in diabetes mellitus: Role of adipose tissue and interaction with other tissues or organs.

The intake-induced response to succinate has been shown to be improved in type 2 diabetics after bariatric surgery (Astiarraga et al., *Diabetes Care* 2020). These results are relevant given the role that the succinate receptor SUCNR1 has in the regulation of the anti-inflammatory programming in the macrophage.

Mitofusin 2 (MFN2) protein has been established as an essential regulator of macrophage function, through changes in ROS production and cytokine release (Tur et al., *Cell Reports* 2020; Lloberas et al., *Autophagy* 2020).

The ingestion of glucose, in contrast to the ingestion of lipids and proteins, has been identified to produce a greater increase in the gene expression of inflammatory mediators in leukocytes. The expression of the anti-inflammatory cytokine IL10 was very high, suggesting a compensatory mechanism against postprandial inflammation that may be attenuated in obesity (Martínez-García et al., *Clin. Nutr.* 2020).

The release mechanisms of adrenic acid (Astudillo et al., *Biomolecules* 2020) and palmitoleic acid (Monge et al., *Biomolecules* 2020) in macrophages have been described, providing new concepts to understand the role of these molecules.

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

GLP-2 has been documented to exhibit metabolic actions in adipose tissue in both human and murine models (Ejarque et al., *Br.J. Pharmacol.* 2020).

The regulation of autophagy has been analyzed, its alterations being associated with the development of metabolic diseases such as DM2 (Sebastián y Zorzano, *Dev. Cell.* 2020). Connection mechanisms have been described between the two pathways of protein degradation, the ubiquitin-proteasome system and autophagy, which, if preserved during aging, could prevent associated metabolic diseases. (Sun-Wang et al., *Age- ing Res Rev.* 2020).

LRP1 protein (*low-density lipoprotein receptor-related protein 1*) has been described to regulate insulin sensitivity and could be considered a therapeutic target in the treatment of metabolic diseases (Benítez-Amaro et al., *Metabolism* 2020).

3. Identification of predictive biomarkers for the progression of diabetes.

Pregnancy and fertility rates in very obese women with PCOS after bariatric surgery have been reported to be high, with few maternal and neonatal complications (Benito et al., *J. Clin. Endocrinol. Metab.* 2020).

Girls with polycystic ovary syndrome (PCOS) have been reported to have reduced concentrations of circulating miR-451a, miR-652-3p, miR-106b-5p, and miR-206, and circulating miR-451a levels have been documented to be a biomarker to guide the diagnosis and treatment of polycystic ovary syndrome in adolescence (Diaz et al., *J. Clin. Endocrinol. Metab.* 2020).

An open-source R package, called rMSIproc, has been developed that implements a complete data processing workflow for Mass Spectrometry Imaging (MSI) experiments performed with TOF- or FT-based mass spectrometers that constitutes a powerful computational tool to develop the full potential of MSI (Ràfols et al., *Bioinformatics* 2020)..

4. Determinants of insulin resistance: molecular mechanisms involved.

Loss of function of the p85 α protein in brown adipose tissue has been reported to improve its thermogenic functionality, adiposity and body weight induced by a high-fat diet, as well as insulin resistance and hepatic steatosis. (Gómez-Hernández et al., *Mol. Metab.* 2020).

TRAINING PROGRAMME

Coordinator: **Ángel Nadal Navajas**

The three intramural projects awarded in the call for intramural projects for young researchers belonging to CIBERDEM have been developed. The aim of the call was to stimulate and increase the competitiveness of young CIBERDEM researchers and promote cohesion and collaboration between research groups in the area. The mobility grant programme has continued to finance stays in CIBER groups and international groups despite the mobility limitations due to the COVID-19 pandemic situation and 3 stays in CIBER groups were carried out as well as 1 international stay.

The XI CIBERDEM Annual Meeting was held for the first time in virtual format. The meeting was held on November 3-5 with the participation of more than 190 CIBERDEM researchers and featured key note lectures, oral presentations and communications, the latter in parallel sessions. Despite the limitations of the virtual format, an active participation of the researchers was achieved, who shared their advances in diabetes research.

For the third year running, CIBERDEM has organized the joint SED-CIBERDEM Symposium at the XXXI National Congress of the Spanish Diabetes Society (SED). The Symposium focused on research on the development of non-alcoholic fatty liver disease, the role of the succinate / SUCNR1 axis in obesity and type 2 diabetes, and alterations of the pancreatic alpha cell in diabetogenic conditions.

In the context of the various training activities that CIBERDEM organizes in collaboration with Merck Sharp & Dohme Spain, this year the CIBERDEM / MSD 2020 Annual Symposium was held in virtual format and its central themes were the recently published results from the study di@bet.es on the incidence and regression of metabolic syndrome and the exploitation of the population database SIDIAP of Catalonia on the cost of type 2 diabetes.

CIBERDEM has launched the third edition of the Expert Postgraduate Course of the University of Barcelona 2020-2021 “Chronic Complications of Diabetes Mellitus,” which awards 15 European ECTS credits.

The training activities organized by the CIBERDEM groups have been carried out since March in virtual format.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

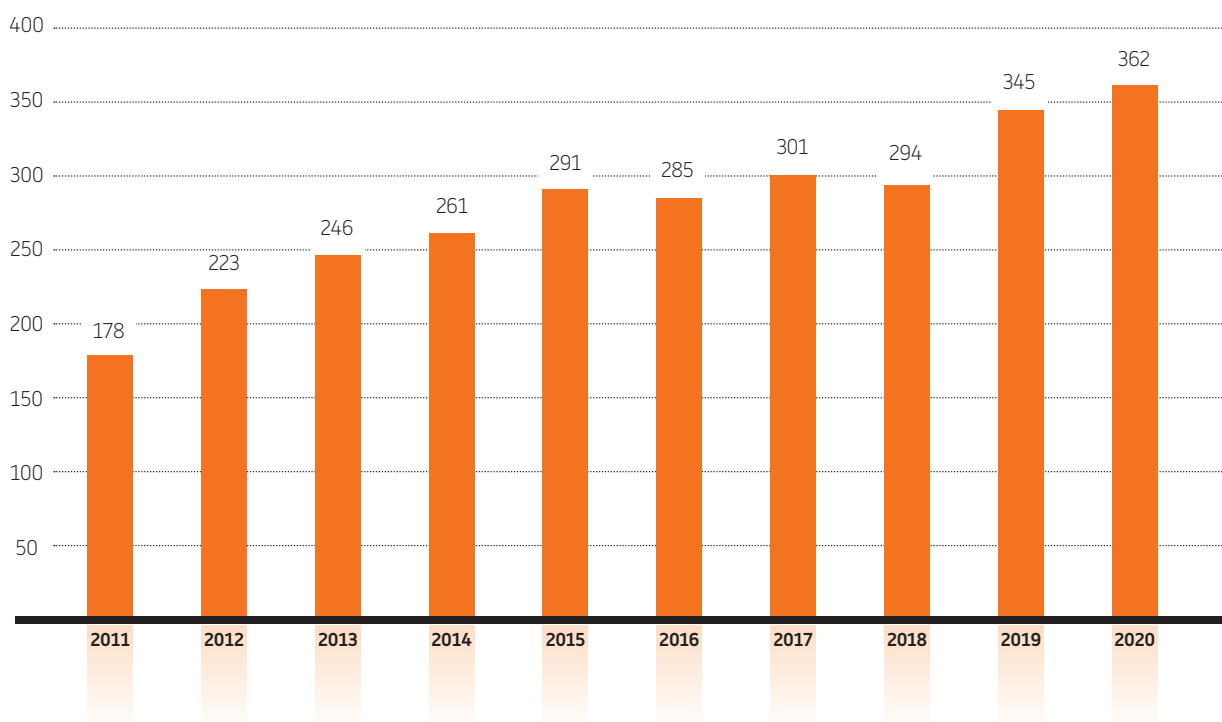
| | |
|---------|-----|
| TOTALES | 362 |
| Q1 | 269 |
| D1 | 100 |

Collaborations

| | |
|----------|-----|
| CIBERDEM | 55 |
| CIBER* | 163 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|---|
| 30,039 | Biessels GJ, Nobili F, Teunissen CE, Simó R, Scheltens P. Understanding multifactorial brain changes in type 2 diabetes: a biomarker perspective. <i>The Lancet Neurology</i> 2020; 19(8):699-710. |
| 29,497 | Fresquet V, Garcia-Barchino MJ, Larrayoz MJ, Celay J, Vicente C et al. Endogenous retroelement activation by epigenetic therapy reverses the Warburg effect and elicits mitochondrial-mediated cancer cell death. <i>Cancer discovery</i> 2020; 20-1065. |
| 25,34 | Bornstein SR, Rubino F, Khunti K, Mingrone G, Hopkins D, Birkenfeld AL et al. Practical recommendations for the management of diabetes in patients with COVID-19. <i>The Lancet Diabetes and Endocrinology</i> 2020; 8(6):546-550. |
| 25,34 | Vujosevic S, Aldington SJ, Silva P, Hernández C, Scanlon P, Peto T, Simó R. Screening for diabetic retinopathy: new perspectives and challenges. <i>The Lancet Diabetes and Endocrinology</i> 2020; 8(4):337-347. |
| 25,34 | Kohsaka S, Lam CSP, Kim DJ, Cavender MA, Norhammar A et al. Risk of cardiovascular events and death associated with initiation of SGLT2 inhibitors compared with DPP-4 inhibitors: an analysis from the CVD-REAL 2 multinational cohort study. <i>The Lancet Diabetes and Endocrinology</i> 2020; 8(7):606-615. |
| 25,34 | Rubino F, Cohen RV, Mingrone G, le Roux CW, Mechanick JI, Arterburn DE, Vidal J et al. Bariatric and metabolic surgery during and after the COVID-19 pandemic: DSS recommendations for management of surgical candidates and postoperative patients and prioritisation of access to surgery. <i>The Lancet Diabetes and Endocrinology</i> 2020; 8(7):640-648. |
| 22,673 | Borén J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease: pathophysiological, genetic, and therapeutic insights: a consensus statement from the European Atherosclerosis Society Consensus Panel. <i>European Heart Journal</i> 2020; 41(24):2313-2330. |
| 21,567 | Sadiku P, Willson JA, Ryan EM, Sammut D, Coelho P et al. Neutrophils Fuel Effective Immune Responses through Gluconeogenesis and Glycogenesis. <i>Cell Metabolism</i> 2020; Epub 2020 Dec 10. |
| 21,567 | Herkenne S, Ek O, Zamberlan M, Pellattiero A, Chergova M et al. Developmental and Tumor Angiogenesis Requires the Mitochondria-Shaping Protein Opa1. <i>Cell Metabolism</i> 2020; 31(5):987-1003.e8. |
| 16,019 | Astiarraga B, Martínez L, Ceperuelo-Mallafré V, Llauradó G, Terrón-Puig M. Impaired succinate response to a mixed meal in obesity and type 2 diabetes is normalized after metabolic surgery. <i>Diabetes Care</i> 2020; 43(10):2581-2587. |

» CIBERDEM Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|------------|
|  Carmen Álvarez Escolá | 6 | 6 | 1 | Universidad Complutense de Madrid - Facultad de Farmacia | Madrid |
|  Jesús Balsinde Rodríguez | 8 | 8 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Biología y Genética Molecular | Valladolid |
|  Manuel R. Benito de las Heras | 2 | 2 | 1 | Universidad Complutense de Madrid - Facultad de Farmacia | Madrid |
|  Francisco Blanco Vaca | 30 | 25 | 7 | Instituto de Investigación del Hospital de la Santa Creu i Sant Pau | Barcelona |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|--|-----------------|
|  Jorge Bondía Company | 5 | 3 | 1 | Universidad Politécnica de Valencia - Instituto Universitario de Automática e Informática Industrial | Valencia |
|  Fàtima Bosch Tubert | 5 | 5 | 3 | Universidad Autónoma de Barcelona - Centro de Biotecnología animal y Terapia Genética | Barcelona |
|  Deborah Burks | 6 | 4 | 0 | Fundación Centro de Investigación Príncipe Felipe | Valencia |
|  Alfonso L. Calle Pascual | 11 | 9 | 4 | Servicio Madrileño de Salud - Hospital Clínico San Carlos | Madrid |
|  Luis Castaño González | 21 | 15 | 1 | Asociación Instituto de Investigación Sanitaria de Biocruces - Hospital Universitario Cruces | Vizcaya |
|  Francesc X. Correig Blanchart | 23 | 20 | 13 | Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili | Tarragona |
|  Jesús Egido de los Ríos | 24 | 21 | 8 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Héctor F. Escobar Morreale | 10 | 5 | 1 | Servicio Madrileño de Salud - Hospital Ramón y Cajal | Madrid |
|  Jorge Ferrer Marrades | 2 | 2 | 2 | Fundación Centro de Regulación Genómica | Barcelona |
| Joan J. Guinovart Cirera | 8 | 4 | 1 | Fundación privada Instituto de Recerca Biomèdica (IRB-Barcelona) | Barcelona |
|  Lourdes Ibáñez Toda | 9 | 8 | 0 | Fundación para la Investigación y Docencia Sant Joan de Déu - Hospital Sant Joan de Déu | Barcelona |
|  Francisco Martín Bermudo | 9 | 5 | 2 | Universidad Pablo de Olavide - Centro Andaluz de Biología del Desarrollo | Sevilla |
|  Ángela María Martínez Valverde | 9 | 8 | 3 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas Alberto Sols | Madrid |
|  Luis Masana Marín | 23 | 18 | 10 | Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili | Tarragona |
|  Diego Mauricio Puente | 42 | 29 | 11 | Instituto de Investigación del Hospital de la Santa Creu i Sant Pau | Barcelona |
|  Eduard Montanya Mías | 10 | 6 | 4 | Fundación IDIBELL - Hospital Universitario de Bellvitge | Barcelona |
|  Ángel Nadal Navajas | 8 | 8 | 1 | Universidad Miguel Hernández - Instituto de Bioingeniería | Alicante |
|  Anna Maria Novials Sardà | 9 | 6 | 3 | Instituto de Investigaciones Biomédicas August Pi i Sunyer - Centro Esther Koplowitz | Barcelona |
|  José Tomás Real | 18 | 9 | 1 | Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) - Instituto de Investigación Sanitaria INCLIVA | Valencia |
|  Gemma Rojo Martínez | 19 | 12 | 4 | Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Regional Universitario Carlos Haya | Málaga |
|  Rafael Simó Canonge | 33 | 25 | 14 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) - Hospital Vall d'Hebron | Barcelona |
|  Mario Vallejo Fernández de la Reguera | 4 | 3 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas Alberto Sols | Madrid |
|  Manuel Vázquez Carrera | 5 | 4 | 3 | Universidad de Barcelona - Facultad de Farmacia | Barcelona |
|  Joan J. Vendrell Ortega | 13 | 10 | 7 | Fundación Instituto de Investigación Sanitaria Pere Virgili - Hospital Universitario Juan XXIII | Tarragona |
|  Josep Vidal Cortada | 41 | 32 | 8 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Antonio Zorzano Olarte | 12 | 12 | 4 | Fundación privada Instituto de Recerca Biomèdica (IRB-Barcelona) | Barcelona |

CLINICAL GUIDES AND CONSENSUS DOCUMENTS 2020

- *Low-density lipoproteins cause atherosclerotic cardiovascular disease; pathophysiological, genetic and therapeutic insights. A consensus statement from the European Atherosclerosis Society Consensus Panel.* Borén J, Chapman MJ, Krauss RM, Packard CJ, Bentzon JF et al. *Eur. Heart J* 2020; 41(24): 2313–2330.
- *Consensus document of an expert group from the Spanish Society of Arteriosclerosis (SEA) on the clinical use of nuclear magnetic resonance to assess lipoprotein metabolism (Liposcale®).* Pintó X, Masana L, Civeira F, Real J, Ibarretxe D, et al. *Clin Investig Arterioscler.* 2020; 32(5): 219-229.
- *Atherogenic Dyslipidaemia 2019. Consensus document of the Atherogenic Dyslipidaemia Group of the Spanish Arteriosclerosis Society.* Juan F. Ascaso JF, Millán J, Hernández-Mijares A, Blasco M, Brea A, Díaz A, Pedro-Botet J, Pintó X, SEA Atherogenic Dyslipidemia Working Group. *Clin Investig Arterioscler.* 2020; 32(3): 120-125.
- *Algoritmo de tratamiento de la insuficiencia cardíaca en el paciente con diabetes mellitus tipo 2 de la redGDPS.* Adán Gil FM, Barrot de la Puente J, Cebrián-Cuenca AM, Franch-Nadal J, Pardo Franco JL, Ruiz Quintero ML, Torres Baile JL. *Diabetes Práctica* 2020; 11(04):117-162
- *Actualización de 2020 del algoritmo de tratamiento de la hiperglucemia en la diabetes mellitus tipo 2 de la redGDPS.* Mata M, Artola Menéndez S, Díez Espino J, Ezkurra Loiola P, Franch Nadal J, García Soidán FJ. *Diabetes Práctica* 2020;11(02):41-76.
- *Actualización de 2020 del algoritmo de tratamiento de la hiperglucemia en la diabetes mellitus tipo 2 de la redGDPS.* Mata M, Artola Menéndez S, Díez Espino J, Ezkurra Loiola P, Franch Nadal J, García Soidán FJ. *Diabetes Práctica* 2020;11(02):41-76.

PATENTS OWNED BY CIBER

Patents applied for:

- *Method and System for Enhancing Monitoring Glucose.* Method and system for the identification of compounds in complex biological or environmental samples.

PCTs applied for:

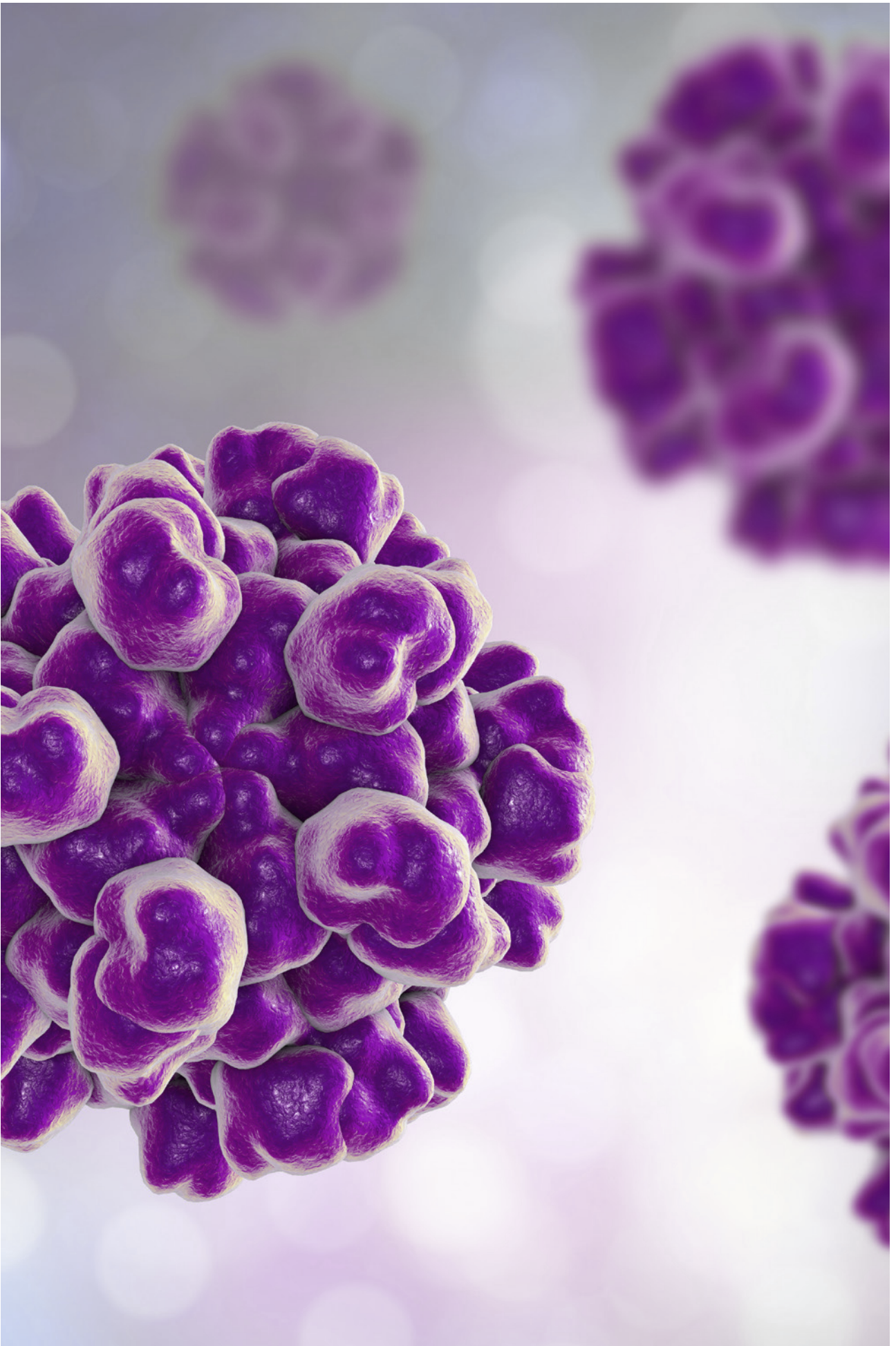
- *Succinate as a biomarker for selecting a bariatric surgical procedure and for predicting type 2 diabetes remission after bariatric surgery.*



čiberehd



**LIVER AND
DIGESTIVE
DISEASES**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Rafael Bañares Cañizares

During 2020, the liver and digestive diseases area (CIBEREHD) dedicated its research effort to diseases of the liver and the gastrointestinal tract. As a whole, these are diseases with a high prevalence, with a great impact on the quality of life of patients and which are sometimes associated with high mortality, making their social repercussion undeniable.

The research activity of the CIBEREHD is articulated in three main programmes: 1) Liver damage mechanisms/ evolution into advanced cirrhosis and transplant 2) Gastrointestinal pathophysiology: inflammatory disease and motility disorders and 3) Hepatic and digestive oncology. These three programmes have clinical and translational research groups, which allows a multidisciplinary and collaborative approach covering practically all the diseases in the area.

The CIBEREHD has been characterized from its beginnings, and also in this year 2020, for the high quantity and quality of its scientific production with nearly 700 annual publications and its strong international leadership. Furthermore, this activity is clearly reflected in the generation of clinical practice documents of great value to society.

The contribution of CIBEREHD to the success of hepatitis C treatment should not be forgotten, both in the leadership of its researchers in the different elimination plans and in the generation of highly valuable scientific information.

The CIBEREHD is not oblivious to the need of maintaining the degree of training of its researchers and of generational renewal. For this reason, during this year 2020, as has been done in previous years, successive support programmes have been consolidated for emerging researchers and novice researchers. Furthermore, this year the foundations have been laid for the start in 2021 of an ambitious predoctoral training programme (Jaume Bosch contract) clearly aimed at promoting the collaborative activity of translational groups. On the other hand, and within the same strategy of generating training activities with added value, in 2021 a series of transversal courses will be launched (bioinformatics, experimental models), also aimed at researchers in the initial phases of their research careers.

During this year 2020, the area has been sensitive to the need to contribute research support platforms to its groups and to other areas. In this regard, CIBEREHD has a highly qualified bioinformatics platform that will be remodeled in 2021 to increase its visibility and expand its offer to other areas of the CIBER.

Undoubtedly, the area will face significant challenges in the coming years. Not only must it adapt its research activity to the changes in the incidence of different diseases such as metabolic fatty liver disease, inflammatory bowel disease, hepatocarcinoma or colon cancer, but it must also address the need to increase its funding sources, incorporate the voice of patients into the design of the research strategy, as well as clearly communicate the results obtained to society. This is our commitment.



PROGRAMMES

P1. LIVER DAMAGE MECHANISMS / EVOLUTION INTO ADVANCED CIRRHOSIS AND TRANSPLANT

Coordinators: **Jordi Gracia Sancho, Javier Ampuero Herrojo y Manuel Luis Rodríguez Perálvarez**

During 2020, several multicenter projects and consensus documents on liver transplantation with international repercussions have been launched as a result of the close collaboration between the CIBEREHD and the Spanish Society for Liver Transplantation (SETH). Prominent among these are the consensus document on non-heart beating donation published in *Transplant International* (doi: 10.1111/tri.13619) and the guide on the expansion of liver transplantation criteria published in *Transplantation* (doi: 10.1097/TP.0000000000003281). Furthermore, with the arrival of the 2019 coronavirus pandemic (COVID-19), a multicenter collaborative project was launched including the 24 adult liver transplantation units in Spain in which the standardized incidence and mortality rates of COVID-19 have been studied for the first time in an immunosuppressed population. The article has been published in the prestigious *Journal of Hepatology* (doi: 10.1016/j.jhep.2020.07.040) and the conclusions obtained on the influence of immunosuppressive treatment on the severity of COVID-19 have been very useful to improve the care of these patients.

Regarding mechanisms of liver damage and evolution into liver cirrhosis and transplantation during 2020, two relevant consensus documents have been published led by researchers from CIBEREHD. First, a guide with recommendations for conducting clinical trials in patients with decompensated cirrhosis has been coordinated within the framework of the LIVERHOPE consortium, a project that is part of the European Horizon 2020 research and innovation framework program (*J Hepatol* doi: 10.1016/j.jhep.2020.08.009). Secondly, the first Clinical Practice Guide for Alcoholic Liver Disease in Spain has been prepared, in which 28 experts have participated and which examines aspects related to the epidemiology and natural history of the disease (*Gastroenterol Hepatol* doi: 10.1016/j.gastrohep.2019.09.006). In addition, several original high-impact studies have been published which have been possible thanks to the collaboration of various CIBEREHD centers. Among these, worth highlighting are the findings that people diagnosed with metabolic steatosis with advanced fibrosis have a higher risk of developing type 2 diabetes mellitus and arterial hypertension (*J Hepatol* doi: 10.1016/j.jhep.2020.02.028) and that some mechanisms have been identified by which non-selective beta-blockers could

alter survival in patients with refractory ascites (*J Hepatol* doi: 10.1016/j.jhep.2020.05.011).

Translational research activity has also led to the publication of various studies in high-impact journals, the result of collaboration between CIBEREHD groups. To be highlighted are two studies with a high potential to be applied in the treatment of chronic liver disease. A multidisciplinary study demonstrated the anti-fibrotic activity of a new therapeutic strategy focused on treating epigenetic disorders that occur during chronic liver disease (*Gut*: <http://dx.doi.org/10.1136/gutjnl-2019-320205>). Also in 2020, a study focused on the repositioning of drugs for the treatment of chronic liver disease and liver fibrosis was published, demonstrating the beneficial effects of the antiretroviral rilpivirine in pre-clinical models of cirrhosis (*Gut*: doi: 10.1136/gutjnl-2019-318372).

P2.GASTROINTESTINAL PATHOPHYSIOLOGY: INFLAMMATORY DISEASE AND MOTILITY DISORDERS

Coordinator: **Pere Clavé Civit**

The year 2020 has been the year of the beginning of the Covid-19 pandemic and the activities of the groups of this program have quite logically been affected. Even so, the overall scientific production of the groups has been maintained and some of them have even collaborated in various research projects related to the pandemic. During 2020, 2 strategic actions have been developed (Oropharyngeal Dysphagia and Celiac Disease) that include both clinical research and innovation projects on these pathologies addressed by specific groups, and for the first time the concept of “Research from the point of view of the patient” has been considered during the CIBEREHD Meeting.

The most important scientific milestones of the programme during 2020 are as follows:

a) Oesophageal-gastro-duodenal pathology. To be highlighted are the publication of the Consensus Protocol with different national societies (AEG, SEED, SEAP) on gastric cancer screening in low-prevalence populations and a national study on the clinical approach to premalignant gastric lesions. Advances in *Helicobacter Pylori* (HP) infection have focused on both diagnostic and therapeutic aspects: The evaluation of the psychometric characteristics of different tests and the molecular characterization of the different strains that can cause infection in the same individual or the molecular diagnosis of patients with low infection density; as well as trials with different therapeutic combinations and studies from the European HP Registry.

b). Inflammatory Bowel Disease. This is probably the area with the greatest interaction between the CIBEREHD research groups. Different factors have contributed to the increase in interaction, notably the success of the GETECCU Group's activity and the high efficiency offered by the exploitation of the Eneida Registry data. The milestones in this research line are multiple and include studies on the natural history of the disease, genetic determinants, extraintestinal complications, the role of interventional endoscopic and surgical treatment and multiple pharmacological treatment algorithms, all of them with the common denominator of being multicenter cooperative studies nationwide. Regarding basic studies in this area, those referring to the role of various cytokines in the inflammatory cascade associated with Ulcerative Colitis and Crohn's disease, various metabolites of microbial origin and the relationship between the expression of certain genes in the clinical evolution of the disease and therapeutic response stand out.

c) Neuro-gastroenterology and functional digestive disorders. The 2020 milestones of this line include European position papers on the practice of functional digestive examinations during the pandemic and the relationship between COVID-19 and the appearance of neurosensory alterations associated with oropharyngeal dysphagia.

Advances have been made in the study of postprandial neurophysiological and sensory responses of the gastrointestinal tract in response to ingestion using combinations of CNS study methods and the hedonic response of subjects. Various studies have made progress in the pharmacological treatment of swallowing

disorders and in the description of the biomechanical and neurophysiological effects of different oropharyngeal sensory stimulants.

P3. HEPATIC AND DIGESTIVE ONCOLOGY

Coordinator: **Maria Reig Monzón**

Hepato-biliary-pancreatic and digestive tract cancer is a frequent cause of death in the general population, a high burden of care in hospitals and health centers entailing a very high healthcare and pharmaceutical cost. For this reason, the CIBEREHD has a programme dedicated to this pathology. Its approach, however, goes beyond the programme itself and involves various CIBEREHD groups in transversal lines of work focused on partial aspects of the problem and where knowledge is contributed from other fields such as molecular biology, genetics, immunology, epidemiology or clinical intervention. Studies in liver cancer have maintained the analysis of the incidence of cancer after viral cure, verifying that the oncogenic risk remains unchanged in patients with cirrhosis. A survey on the impact of the pandemic on liver cancer has been carried out which has recently been published.

Researchers from CIBEREHD have led studies with various immunomodulatory molecules for the treatment of hepatocellular carcinoma. In the field of colorectal cancer, a quality publication rate has been maintained both in relation to population screening programs and in terms of family risk. This has been the result of clinical research associated with genetic analysis in collaboration with various CIBEREHD groups or from other fields. Finally, the research activity in cholangiocarcinoma continues to be solid with the identification of circulating metabolites that could serve as markers for the early diagnosis of the disease in patients with primary sclerosing cholangitis, a pre-cancerous entity, and for the distinction between histology of cholangiocarcinoma or hepatocellular carcinoma in small nodules of cirrhotic livers. In this sense, despite the pandemic, all the groups have had a large scientific production (clinical, basic and translational), with the program having 30 publications dedicated to colon cancer, 88 publications in the field of hepatocellular carcinoma and 25 on cholangiocarcinoma.

TRAINING PROGRAMME

Coordinator: **Sofía Pérez del Pulgar Gallart**

Due to the current situation of the pandemic, this year the CIBEREHD training / teaching programme has limited the holding of short stays or face-to-face meetings aimed at following up collaborative projects, but attendance at training courses and participation in scientific meetings, mostly in online format, has been promoted. In addition, CIBEREHD has endorsed different national and international training activities.

Within the training / teaching programme, a total of 22 training actions have been carried out in which mainly young researchers have participated: 13 national courses, 2 international courses, 4 national stays, 1 international stay and 2 collaborative meetings. Furthermore, the CIBEREHD has endorsed the organization of 2 courses developed at the national level and 2 international courses: “Digital 2020 BCLC Update in Liver Cancer” organized by the BCLC group of the Hospital Clinic of Barcelona, and the “Webinar: Precision Medicine and COVID-19” organized by Jesús Bañales and Manuel Romero. Simultaneously, the CIBEREHD has, once again, endorsed the undertaking of LiverSeminars (<https://liverseminars.eu/>), an initiative led by Jordi Gracia from IDIBAPS (Barcelona) and Rafael Bañares from IISGM (Madrid), and designed to promote collaborative translational research in hepatology, not only in Spain, but also internationally.

As can be seen, the highest indicator is that of national courses due to the pandemic situation.

As a novelty, during the XIV Scientific Conference this year, a Young Researchers Workshop was organized with the aim of:

- >> Making the opportunities offered by the CIBEREHD Training Program known to young researchers.
- >> Offering young researchers the opportunity to present the results of their work and / or research projects.

To this end, the researchers Isabel Gómez-Hurtado (IIS Isabial, General University Hospital of Alicante), Rocío Gallego (Institute of Biomedicine of Seville, Virgen del Rocío University Hospital) and Mar Coll (IDIBAPS, Hospital Clínic de Barcelona) shared their “success stories” as researchers who received Training Grants to carry out short-term training stays in national or foreign locations. Furthermore, among the more than 80 posters presented during the Annual Meeting, 3 prizes were awarded to the best posters. The winners were Álex Clavería-Cabello (CIMA, University of Navarra), David Porras (Institute of Biomedicine, University of León) and Alba Garrido Trigo (IDIBAPS, Hospital Clínic de Barcelona).

PLATFORMS

BIOINFORMATICS PLATFORM

Coordinator: **Juanjo Lozano Salvatella**

In a very difficult year due to the global SARS-COV2 pandemic, the Bioinformatics platform continues to actively collaborate in the operation of CIBEREHD. The fruit of this activity is reflected in 22 scientific publications.

The collaboration established with the Gastrointestinal and Pancreatic Oncology area has generated a very relevant publication that is related to the biological role of a microne in the progression of pancreatic tumor affecting patient survival.

- Vila-Navarro E, Fernandez-Castañer E, Rovira-Rigau M, Raimondi G, Vila- Casadesus M, Lozano JJ, Soubeyran P, Iovanna J, Castells A, Fillat C, Gironella M. *MiR-93 is related to poor prognosis in pancreatic cancer and promotes tumor progression by targeting microtubule dynamics*. *Oncogenesis*. 2020 May 4;9(5):43.

The platform's staff has been part of a team of researchers in the international arena-among them the CIBEREHD-and organizations from nine European countries, coordinated and led from Barcelona by the European Foundation for the Study of Chronic Liver Failure (EF Clif). The role of amino acid synthesis in inflammatory response in Acute on Chronic Liver Failure (ACLF) syndrome has been studied by means of metabolic interaction network analysis.

- Zaccherini G, Aguilar F, Caraceni P, Clària J, Lozano JJ, Fenaille F, Castelli F, Junot C, Curto A, Formentin C, Weiss E, Bernardi M, Jalan R, Angeli P, Moreau R, Arroyo V. *Assessing the role of amino acids in systemic inflammation and organ failure in patients with ACLF*. *J Hepatol*. 2020 Dec 1:S0168-8278(20)33821-6.

In the area of Inflammation in liver disease, a study has been published investigating the genes involved in decompensated cirrhosis and which are also related to the origin of bacterial infections.

- Pose E, Coll M, Martínez-Sánchez C, Zeng Z, Surewaard BGJ, Català C, Velasco M, Lozano J, Ariño S, Fuster D, Niñerola-Bazán A, Graupera I, Muñoz É, Lozano F, Sancho-Bru P, Kubes P, Ginès P. *PD-L1 is overexpressed in liver macrophages in chronic liver diseases and its blockade improves the antibacterial activity against infections*. *Hepatology*. 2020 Nov 20.

Other collaborations in which the platform is involved is in the discovery of new therapeutic targets in the regulation of angiogenesis processes.

- Figueiredo AM, Villacampa P, Diéguez-Hurtado R, José Lozano J, Kobialka P, Cortazar AR, Martinez-Romero A, Angulo-Urarte A, Franco CA, Claret M, Aransay AM, Adams RH, Carracedo A, Graupera M. *Phosphoinositide 3-Kinase-Regulated Pericyte Maturation Governs Vascular Remodeling*. *Circulation*. 2020 Aug 18;142(7):688-704.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

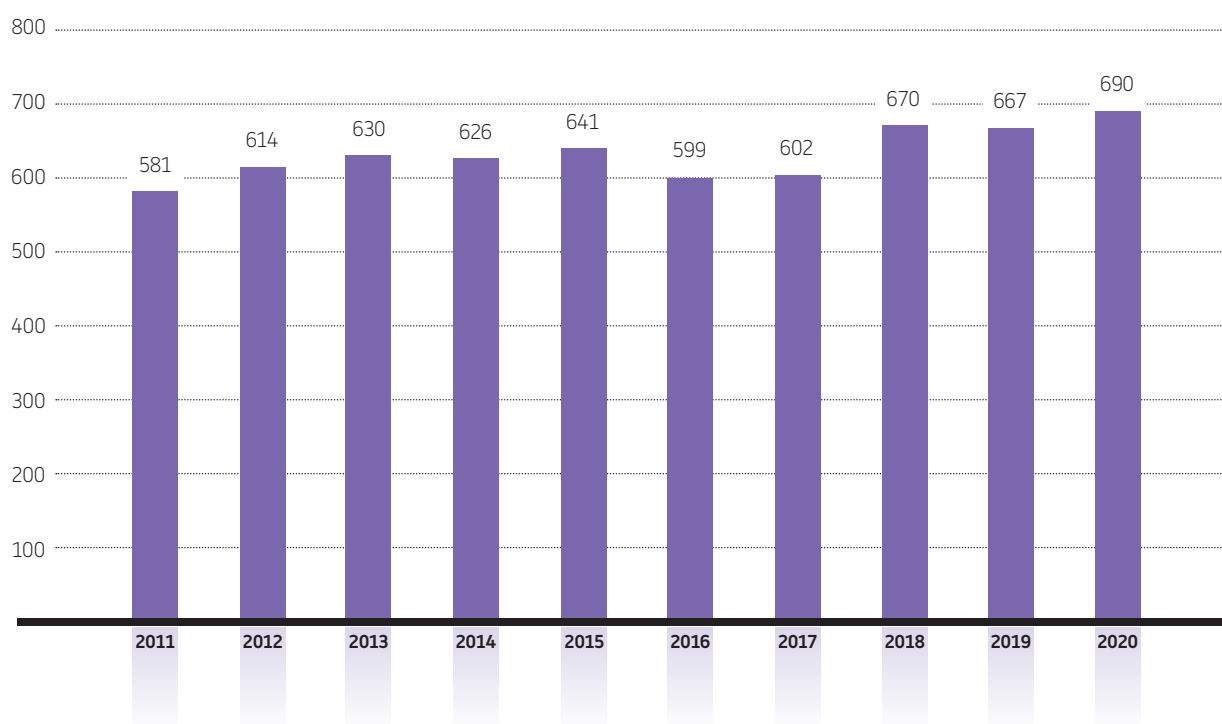
| | |
|---------|-----|
| TOTALES | 690 |
| Q1 | 396 |
| D1 | 204 |

Collaborations

| | |
|----------|-----|
| CIBEREHD | 200 |
| CIBER* | 146 |

*Entre varias áreas temáticas

» Evolution of publications




» 10 most relevant publications by impact factor

| IF | Publication |
|--------|--|
| 74,699 | Ellinghaus D., Degenhardt F., Bujanda L., Buti M., Albillos A., Invernizzi P. et al. <i>Genomewide association study of severe covid-19 with respiratory failure. New England Journal of Medicine.</i> 2020;383(16):1522-1534. |
| 41,845 | Bastard P., Rosen L.B., Zhang Q., Michailidis E., Hoffmann H.-H., Zhang Y. et al. <i>Autoantibodies against type I IFNs in patients with life-threatening COVID-19. Science.</i> 2020;370(6515). |
| 41,845 | Zhang Q., Liu Z., Moncada-Velez M., Chen J., Ogishi M., Bigio B. et al. <i>Inborn errors of type I IFN immunity in patients with life-threatening COVID-19. Science.</i> 2020;370(6515). |
| 40,689 | Tursi A., Scarpignato C., Strate L.L., Lanas A., Kruis W., Lahat A. et al. <i>Colonic diverticular disease. Nature Reviews Disease Primers.</i> 2020;6(1). |
| 30,223 | Simonetto D.A., Gines P., Kamath P.S. <i>Hepatorenal syndrome: pathophysiology, diagnosis, and management. BMJ (Clinical research ed.).</i> 2020;370:m2687. |
| 29,848 | Jung G., Hernandez-Illan E., Moreira L., Balaguer F., Goel A. <i>Epigenetics of colorectal cancer: biomarker and therapeutic potential. Nature Reviews Gastroenterology and Hepatology.</i> 2020. |
| 29,848 | Dotti I., Salas A. <i>A new model of intestinal epithelial regeneration: could patients benefit? Nature Reviews Gastroenterology and Hepatology.</i> 2020. |
| 29,848 | Salas A., Hernandez-Rocha C., Duijvestein M., Faubion W., McGovern D., Vermeire S. et al. <i>JAK-STAT pathway targeting for the treatment of inflammatory bowel disease. Nature Reviews Gastroenterology and Hepatology.</i> 2020. |
| 29,848 | Banales J.M., Marin J.J.G., Lamarca A., Rodrigues P.M., Khan S.A., Roberts L.R. et al. <i>Cholangiocarcinoma 2020: the next horizon in mechanisms and management. Nature Reviews Gastroenterology and Hepatology.</i> 2020. |
| 29,848 | Di Maira T., Berenguer M. <i>COVID-19 and liver transplantation. Nature Reviews Gastroenterology and Hepatology.</i> 2020. |
| 23,603 | Figueiredo AM, Villacampa P, Diéguez-Hurtado R, Lozano JJ, Kobialka P, Cortazar AR et al. <i>PI-3Kβ-Regulated Pericyte Maturation Governs Vascular Remodeling. Circulation.</i> 2020. |

» CIBEREHD Groups. Publications 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|---|-----------|
|  Albillos Martínez, Agustín | 26 | 18 | 12 | Universidad de Alcalá | Madrid |
|  Andrade, Raúl | 15 | 12 | 9 | Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) | Málaga |
|  Armengol Niell, Carolina | 12 | 9 | 3 | Fundación Instituto de Investigación Germans Trias i Pujol | Barcelona |
|  Azpiroz Vidaur, Fernando | 17 | 8 | 0 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Bañares Cañizares, Rafael | 23 | 16 | 12 | Servicio Madrileño de Salud | Madrid |
|  Berenguer Haym, Marina | 20 | 8 | 6 | Fundación para la Investigación del Hospital la Fe | Valencia |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|---|-----------------|
|  Bruix Tudó, Jordi | 16 | 11 | 6 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Bujanda Fernández de Pierola, Luis | 51 | 33 | 11 | Asociación Instituto Biodonostia | Guipúzcoa |
|  Buti Ferrer, María Asunción | 31 | 15 | 9 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Calvet Calvo, Xavier | 25 | 11 | 6 | Corporación Sanitaria Parc Taulí | Barcelona |
|  Cascante Serratos, Marta | 4 | 3 | 1 | Universidad de Barcelona | Barcelona |
|  Castell Ripoll, José Vicente | 7 | 5 | 2 | Fundación para la Investigación del Hospital la Fe | Valencia |
|  Castells Garangou, Antoni | 56 | 37 | 18 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Clave Civit, Pere | 14 | 9 | 2 | Fundación Privada Salud del Consorcio Sanitario del Maresme | Barcelona |
|  Domenech Morral, Eugeni | 21 | 3 | 1 | Fundación Instituto de Investigación Germans Trias i Pujol | Barcelona |
|  Esplugues Mota, Juan Vicente | 13 | 11 | 6 | Universidad de Valencia | Valencia |
|  Esteban Mur, Juan Ignacio | 19 | 8 | 4 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Esteve Comas, María | 22 | 5 | 3 | Fundación Mutua Terrassa | Barcelona |
|  Fabregat Romero, María Isabel | 9 | 5 | 3 | Fundación IDIBELL | Barcelona |
|  Fernández-Checa Torres, José Carlos | 20 | 18 | 8 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Barcelona |
|  Fondevila Campo, Constantino | 38 | 24 | 14 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Forns Bernhardt, Xavier | 27 | 15 | 9 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  García Marín, José Juan | 16 | 16 | 3 | Universidad de Salamanca | Salamanca |
|  García Pagán, Juan Carlos | 50 | 28 | 20 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  García-Samaniego Rey, Javier | 11 | 6 | 4 | Servicio Madrileño de Salud | Madrid |
|  Genesca Ferrer, Joan | 34 | 30 | 19 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Gines Gibert, Pere | 33 | 23 | 20 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Gómez Castilla, Jordi | 5 | 3 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Granada |
|  González Gallego, Javier | 9 | 5 | 2 | Universidad de León | León |
|  Guarner Aguilar, Carlos | 18 | 14 | 9 | Instituto de Investigación del Hospital de Santa Cruz y San Pablo | Barcelona |
|  Lanás Arbeloa, Ángel | 40 | 9 | 4 | Fundación Instituto de Investigación Sanitaria Aragón | Zaragoza |
|  Martín Sanz, Paloma | 5 | 5 | 3 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|--|-----------------|
|  Mata García, Manuel de la | 16 | 7 | 4 | Fundación para la Investigación Biomédica de Córdoba (FIBICO) | Córdoba |
|  Mato de la Paz, José María | 39 | 32 | 12 | CIC Biogune | Vizcaya |
|  Pares Darnaculleta, Albert | 18 | 12 | 4 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Pastor Anglada, Marçal | 2 | 2 | 1 | Universidad de Barcelona | Barcelona |
|  Pérez Gisbert, Javier | 55 | 16 | 7 | Servicio Madrileño de Salud | Madrid |
|  Romero Gómez, Manuel | 27 | 16 | 12 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Salas Martínez, Azucena | 21 | 9 | 8 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Sánchez de Medina López Huertas, Fermín | 12 | 7 | 2 | Universidad de Granada | Granada |
|  Sangro Gómez-Acebo, Bruno Carlos | 38 | 28 | 14 | Universidad de Navarra | Navarra |
|  Zapater Hernández, Pedro | 14 | 11 | 5 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Alicante |

Associated Clinical Groups

| Group Leader | Institution - Centre | Location |
|--|--|-----------------|
|  Beltrán Niclós, Ana Belén | Fundación para la Investigación del Hospital la Fe | Valencia |
|  Caballería Rovira, Llorenç | Universidad Autónoma de Barcelona | Barcelona |
|  Calleja Panero, Jose Luis | Universidad Autónoma de Barcelona | Barcelona |
|  Crespo García, Javier | Instituto de Investigación Marqués de Valdecilla | Cantabria |
|  Cubiella Fernández, Joaquin | Servicio Gallego de Salud | A Coruña |
|  García Monzón, Carmelo | Servicio Madrileño de Salud | Madrid |
|  Minguela Puras, Alfredo | Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS) | Murcia |
|  Molina Infante, Javier | Fundación para la Formación y la Investigación de los Profesionales de la Salud (FUNDESALUD) | Alicante |
|  Padillo Ruiz, Francisco Javier | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |

PATENTS OWNED BY CIBER

Patents applied for

- Método para el diagnóstico y/o pronóstico de esofagitis eosinofílica en saliva. (Method for the diagnosis and / or prognosis of eosinophilic esophagitis in saliva).
- *STARD1 inhibitors for the treatment of lysosomal disorders.*
- *Non-invasive method for the diagnosis or screening of colorectal cancer and/or precancerous stage thereof.* (PCT Patent).

Patents granted

- *Plasma micro-rnas for the detection of early colorectal cancer.* Patent in Canada.
- *Topical composition for the treatment of mucosal lesions and skin ulcers.* Patent in the United States.

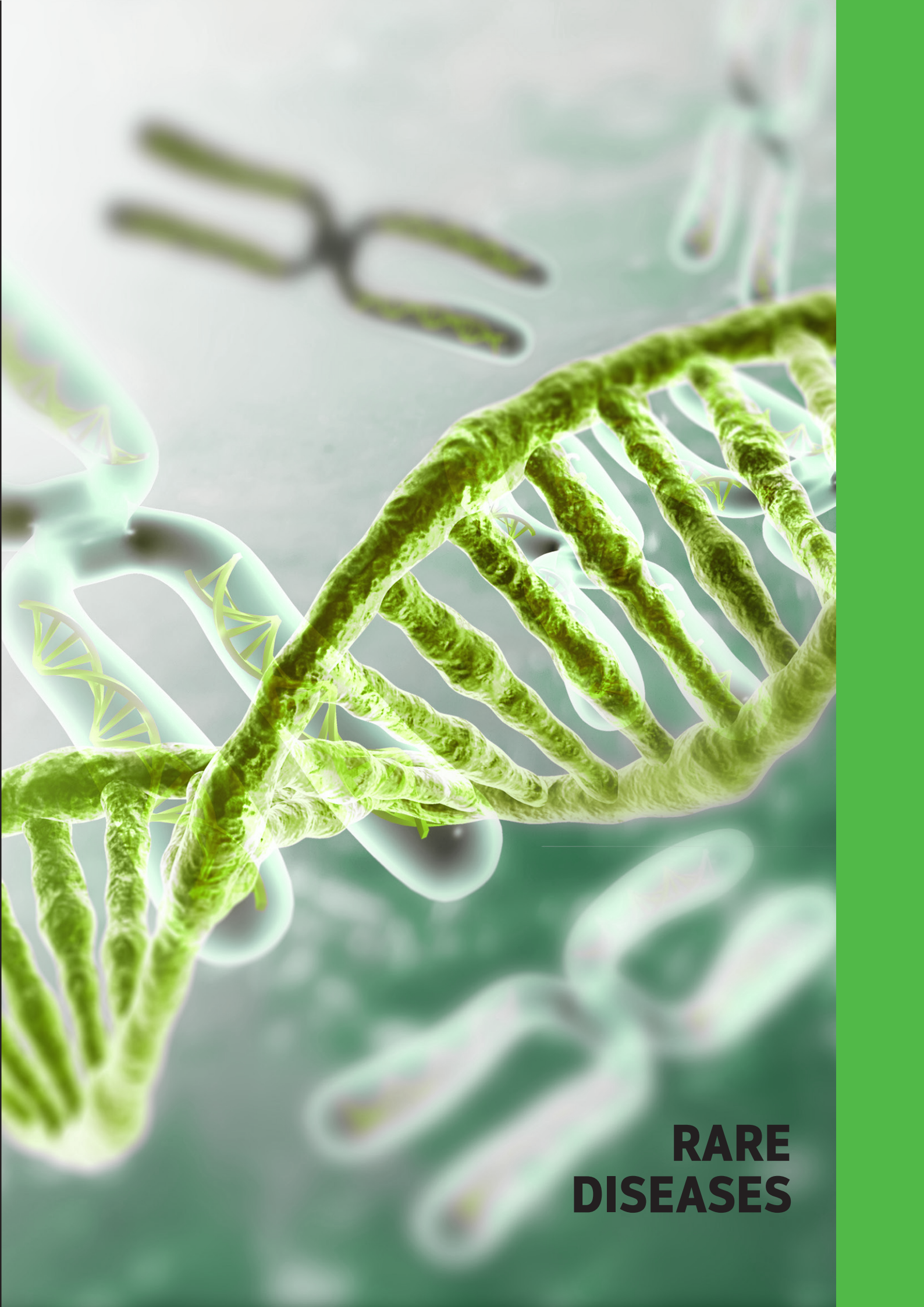
CLINICAL GUIDES

- *Assessment, Diagnosis, and Treatment of Dysphagia in Patients Infected With SARS-CoV-2: A Review of the Literature and International Guidelines.*
- *Recommendations by the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on the treatment of patients with inflammatory bowel disease associated with spondyloarthritis.*
- *Risk factors for vascular liver diseases: Vascular liver diseases: position papers from the francophone network for vascular liver diseases, the French Association for the Study of the Liver (AFLF), and ERN-rare liver.*
- *Pregnancy and vascular liver diseases: Vascular liver diseases: position papers from the francophone network for vascular liver diseases, the French Association for the Study of the Liver (AFLF), and ERN-rare liver.*
- *Porto-sinusoidal vascular disease. Vascular liver diseases: Position papers from the francophone network for vascular liver diseases, the French Association for the Study of the Liver (AFLF), and ERN-rare liver.*
- *Management of anticoagulation in adult patients with chronic parenchymal or vascular liver disease: Vascular liver diseases: Position papers from the francophone network for vascular liver diseases, the French Association for the Study of the Liver (AFLF), and ERN-rare liver.*
- *Congenital portosystemic shunts: Vascular liver diseases: Position papers from the francophone network for vascular liver diseases, the French Association for the Study of the Liver (AFLF), and ERN-rare liver.*
- *Consensus document of the Spanish Association for Study of the Liver on the treatment of hepatitis B virus infection (2020).*
- *COVID-19 and inflammatory bowel disease: questions arising from patient care and follow-up during the initial phase of the pandemic (February-April 2020).*
- *DOCUMENT DE POSICIONAMENT Epidemiologia, etiologia, diagnòstic i tractament de la pancreatitis crònica.*

- *Budd-Chiari syndrome.*
- *Hepatic adverse effects of immunotherapy and its impact on the management of patients with hepatocellular carcinoma.*
- *Drug induced liver injury and vascular liver disease.*
- *EASL recommendations on treatment of hepatitis C: Final update of the series.*
- *ECCO Guidelines on Therapeutics in Crohn's Disease: Surgical Treatment.*
- *Ultrasound by specialists in digestive pathology.*
- *European Society for Neurogastroenterology and Motility recommendations for conducting gastrointestinal motility and function testing in the recovery phase of the COVID-19 pandemic.*
- *Extrahepatic portal vein obstruction (EHPVO) in cirrhosis.*
- *Guía GETECCU 2020 para el tratamiento de la colitis ulcerosa. Elaborada con metodología GRADE.*
- *Ischemic cholangiopathy: An update.*
- *Portal cavernoma or chronic non cirrhotic extrahepatic portal vein obstruction.*
- *Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2020.*
- *Posttransplant Management of Recipients Undergoing Liver Transplantation for Hepatocellular Carcinoma. Working Group Report From the ILTS Transplant Oncology Consensus Conference.*
- *Recent (non-cirrhotic) extrahepatic portal vein obstruction.*
- *Recommendations of the Catalan Society of Digestology and the Catalan Society of Medical-Surgical Digestive Endoscopy for the re-establishment of endoscopy activity according to the evolution of the COVID-19 pandemic.*
- *Mesures de contenció en les unitats d'endoscòpia davant el COVID-19.*
- *Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on pouchitis in ulcerative colitis. Part 1: Epidemiology, diagnosis and prognosis.*
- *Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on topical therapy in ulcerative colitis.*
- *Recommendations of the Spanish Association of Neurogastroenterology and Motility (ASENEM) to restart the activity of gastrointestinal motility laboratories after the state of alarm called due to the COVID-19 pandemic.*
- *Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on screening and treatment of tuberculosis infection in patients with inflammatory bowel disease.*
- *Resumption of activity in gastroenterology departments. Recommendations by SEPD, AEEH, GETECCU and AEG.*
- *Sinusoidal obstruction syndrome.*
- *Social and medical support initiatives in vascular liver diseases in France, from child to adult.*
- *Spanish Guidelines for Diagnosis, Management, Treatment, and Prevention of DRESS Syndrome.*
- *Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases.*



çiberer



**RARE
DISEASES**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Pablo Lapunzina

Once again this year and despite the pandemic, the annual scientific report that includes the milestones of the CIBER for Rare Diseases shows the hard work and commitment of the groups that make it up, and I take this opportunity to thank everyone for their effort and dedication.

One need only observe the bibliometrics of the groups to appreciate their good results: since its inception, CIBERER publishes about 656 articles per year on average. This translates into a total of 698 publications in 2020, of which 57% are ranked in the top-tier.

Additionally, CIBERER continues to actively work towards the achievement of the IRDiRC objectives.

Proof of this are the 10 orphan drug designations of which it is a promoter. And specifically, during 2020, 2 additional designations were obtained for the treatment of Adrenoleukodystrophy and Epidermolysis Bullosa respectively, and work was carried out on the presentation of another 3 applications for designation.

As regards the progress made in the diagnosis of RD, I especially highlight the 2 ENoD and IMPaCT-GENÓMICA Programmes.

ENoD is CIBERER's Undiagnosed Rare Diseases programme. It is a cross-sectional, multidisciplinary and collaborative management model that currently collects clinical data from more than 400 undiagnosed patients with a diagnostic rate of 29%.

IMPACT-GENÓMICA is an ambitious infrastructure programme coordinated by CIBERER and funded by ISCIII. Its main objective is to provide the National Health System (NHS) with a collaborative structure for the implementation of Genomic Medicine in the NHS.

I take this opportunity to once again stress the urgency of recognizing the specialty of Clinical Genetics, an essential step so that the results of our research may lead to an improvement in care, diagnosis and the search for therapies for those affected.

Finally, CIBERER has a high international participation through various strategic programmes and projects in the field of Rare Diseases: Orphanet-Spain, for example, or the European Joint Program on Rare Diseases whose objective is to improve research, data usage and translation in RD. On the other hand, several CIBERER groups are active members of the European reference networks - ERN (European Reference Networks).

I want to close this introduction by thanking and highlighting the essential role of patient associations that work on the front line to give support and make the voice of those affected heard, both from our Patient Advisory Council and from our External Scientific Advisory Committee.



PROGRAMMES

TRANSLATIONAL GENOMIC MEDICINE PROGRAMME

Coordinator: **Ángel Carracedo**

The main objective of the programme is the implementation of the new genomic medicine and omics applications to the diagnostic practice of hospitals. During this year 2020, the group led by Dr. Mario Fernández Fraga, from the Center for Research in Nanomaterials and Nanotechnology (CINN) of Asturias, focused on epigenetics and systems biology, joined the programme.

To be highlighted among the main milestones of the programme in 2020 is the consolidation of the first database of genetic variability of the Spanish population. The platform, called Collaborative Spanish Variability Server (CSVS) collects a total of 2,027 genomes and exomes of unrelated Spanish individuals. The results of this work have been published in the prestigious journal *Nucleic Acids Research*. The work has been coordinated by researchers from the group led by Dr. Joaquín Dopazo.

As regards diagnosis, we highlight the international study published in *Nature Genetics* in which Dr. Ángel Carracedo's group has identified variants associated with the activity of 190 breast cancer predisposition genes. This work, in which researchers from Dr. Mercedes Robledo's group have also collaborated, reveals the enormous complexity of one of the most frequent tumors and lays the foundations for moving towards a more precise early diagnosis and personalized treatments. Fachal et al *Nat Genet* (2020).

In addition, Dr. Ángel Carracedo will coordinate the Genomic Medicine Programme from CIBERER, one of the 3 funded programmes in the Precision Medicine Infrastructure associated with Science and Technology (IMPACT) of the ISCIII. The programme is endowed with 7.25 million euros. The objective of the IMPACT Programme on Genomic Medicine is to create a collaborative structure for the implementation of genomic medicine in coordination with the National Health System (NHS).

MITOCHONDRIAL AND INHERITED METABOLIC MEDICINE PROGRAMME

Coordinator: **Rafael Artuch**

In this programme, research is carried out to improve knowledge of inherited metabolic diseases, especially in the areas of diagnosis and treatment of these diseases. In 2020, several relevant milestones have been reached, such as:

- >> The discovery of a new neurodevelopmental disease that causes serious intellectual and cardiac problems in pediatric patients. Groups led by Aurora Pujol and Rafael Artuch (Àngels Garcia Ca-zorla). PMID: 33015733.
- >> The clinical and functional characterization of two families with mitochondrial disorders associated with the genes 'NDUFA4' and 'NDUFA8'. Group led by Dr. Antònia Ribes. PMID: 33153867.
- >> The description of a new rare disease characterized by characteristic facial features, heart defects and developmental delay, called *TRAF7* syndrome, after the name of the gene that causes it. Group led by Dr. Susanna Balcells- PMID: 32376980.
- >> The proposal for the inclusion of the recently described *DNAJC12* gene in neonatal screening for hyperphenylalaninemia. Group led by Dr. Belén Pérez- PMID: 32333439.
- >> The standardization of a new test for a metabolic disease caused by mutations in the *CAD* gene. Group led by Dr. Alberto Marina- PMID: 32461667.
- >> The development of new brain cell models for the study of therapies in Sanfilippo type C syndrome. Groups led by Drs. Susanna Balcells and Antònia Ribes- PMID: 32121121.
- >> The proposal of a new therapeutic strategy in cellular models for phosphomannomutase 2 deficiency (PMM2-CDG). Group led by Dr. Belén Pérez - PMID: 32222543.
- >> The generation of a new *C. elegans* model that will allow progress in the study of the *X-ALD*- Group led by Dr. Aurora Pujol - PMID: 32017990.
- >> The European Medicines Agency (EMA) has designated dimethyl fumarate as an orphan drug for the treatment of adrenoleukodystrophy, a rare disease of neurometabolic origin that affects the nervous system and is frequently fatal. Group led by Dr. Aurora Pujol.

NEUROLOGICAL DISORDERS PROGRAMME

Coordinator: **Pía Gallano**

This year, Dr. Eduard Gallardo was appointed as the new CIBERER group leader at the Sant Pau Hospital in Barcelona, replacing Dr. Isabel Illa. Precisely in this unit, two publications stand out; the publication in *Neurology* of a study that identifies changes in brain structure related to cognitive and behavioral alterations in ALS, the result of a research coordinated by Drs. Ricard Rojas-García, and another by Jordi Díaz-Manera in *Brain* on the new genotype-phenotype correlations of those affected by sarcoglycanopathies, in which Dr. Lidia Gonzalez-Quereda (Dr. Pia Gallano's unit) has also participated.

In diagnostics, the publication in *Genes* of the design of a massive sequencing panel and study of a large cohort of patients undiagnosed with neuromuscular diseases stands out, which was born from a Cooperative and Complementary Intramural Action (ACCI) of the CIBERER, with Dr. Lidia González-Quereda as first author. It is coordinated by Dr. Pia Gallano and researchers from other CIBERER units have participated such as those led by

Dr. Eduard Gallardo and Dr. Jordi Díaz Manera, Andrés Nascimento (Dr. Rafael Artuch's unit), Glòria Garrabou (Dr. Jose María Grau's unit), as well as other external centers.

From the therapeutic point of view, to be highlighted is the publication in Expert Reviews in Molecular Medicine, whose authors are Drs. Pascual Sanz and José María Serratosa, of a review on neuroinflammation and progressive myoclonic epilepsies: from basic science to therapeutic opportunities.

Regarding the participation of Pdl (Research Programme) groups in the 2019 call for Cooperative and Complementary Intramural Actions (ACCI), 2 projects are coordinated by researchers from this programme: Drs. Jordi Díaz (also from Sant Pau) and Luis Querol (Dr. Eduard Gallardo's unit). This project that has the participation of Dr. Josep Dalmau's group.

The projects financed in the 2019 call of the Marató de TV3, in which the researchers of this Pdl participate, are the following:

- >> Therapeutic strategies for cystinuria (Dr. Federico Pallardó).
- >> Lafora's disease: role of the glia in the production of aberrant glycogen and neuroinflammation (Dr. Pascual Sanz).
- >> New therapies directed against subpopulations of fibroadipogenic cells involved in muscle degeneration (Dr. Xavier Suárez).
- >> Catalan Interhospital Network of genetic variants to improve genetic diagnosis in rare diseases (Drs. Pia Gallano, Adriana Lasa y Sara Bernal).

Also noteworthy is the project on the identification of biomarkers for the early diagnosis and prognosis of cardiomyopathy, scoliosis and diabetes in patients with Friedreich's ataxia, carried out by Drs. José Luis García and Marta Seco (Dr. Federico Pallardó's unit, which has also had the support of the Ataxia Federation of Spain (FEDAES)). Finally, the Mutua Madrileña Foundation project on epigenetic biomarkers for neonatal sepsis led by Dr. José Luis García.

This Pdl stands out for its great harmony with patient associations, such as the ASEM Federation and FEDAES, among others.

PEDIATRIC AND DEVELOPMENTAL MEDICINE PROGRAMME

Coordinator **Cristina Fillat**

Within the objective of promoting the development of genomic diagnostic tools for diseases of special interest to the Programme:

- >> Biallelic variants have been identified in the *PRKG2* gene in a new acromesomelic dysplasia, led by the group coordinated by Dr. Pablo Lapunzina;
- >> A new function of the mitochondrial protein *GDAP1* and its implications in Charcot-Marie-Tooth disease has been identified, led by the group coordinated by Dr. Francesc Palau;
- >> A new systematic classification of genetic mosaicism has been proposed that establishes a standardized language of communication and will help to improve knowledge about the molecular pathophysiology of mosaicism, in an international study coordinated by the group led by Dr. Pablo Lapunzina;
- >> Mutations in two genes has been shown to give rise to a syndrome with multiple congenital anomalies, in an international study coordinated by the group led by Dr. Víctor Luis Ruiz.

The groups coordinated by Drs. Luis Pérez Jurado and Manuel Posada have participated in the description of five new cases of a very rare neurodevelopmental syndrome caused by mutations in the *KAT6A* gene, which has allowed us to better understand it and expand its clinical phenotype, a work led by the group of Dr. Susanna Balcells from the Hereditary Mitochondrial and Metabolic Medicine Programme.

Beyond this, there are numerous individual publications of the groups within this line, described in more detail when talking about each group, together with the authorship of the books “Rare Diseases” and “Genetics for neurologists” by Drs. Francesc Palau and Pablo Lapunzina.

In addition, we have contributed to the training of professionals and the general population through the organization of various conferences sponsored by this Programme, as well as of patients in the context of the EURORDIS summer school (in Spanish) with training on the process of drug development.

We also highlight the recognition of FEDER (Spanish Federation of Rare Diseases) of the Pilot Plan for the Improvement of the Genetic Diagnosis of Rare Diseases in the Community of Madrid, Extremadura and the Balearic Islands, which defines care pathways that ensure access to the genetic diagnosis of patients and families suspected of suffering from a rare disease and in which the group coordinated by Dr. Pablo Lapunzina and the Linked Clinical Group coordinated by Dr. Jordi Rosell participate.

We also highlight the projects financed by the Marató de TV3 focused on rare diseases in which groups from this Programme participate, such as those coordinated by Drs. Luis Pérez Jurado, Pablo Lapunzina and Àngela Nieto and the project on lysine metabolism diseases financed by *the European Joint Programme on Rare Diseases* with the Spanish node led by Dr. Cristina Fillat and the participation of Drs. Antonia Ribes and Àngels Garcia-Cazorla from the Hereditary Mitochondrial and Metabolic Medicine Programme.

Finally, this year there has been a new addition to the programme, the group led by Dr. Angela Nieto from the Institute of Neurosciences of Alicante (CSIC) working on the deregulation of embryonic genes.

SENSORINEURAL PATHOLOGY PROGRAMME

Coordinator: **Lluís Montoliu**

To be highlighted at the scientific level is the generation of a new mouse model of hereditary retinal dystrophies caused by the *CERKL* gene published in *Invest Ophthalmol Vis* or the identification of new functions of the gene that causes Machado-Joseph disease in *Cells*, both led by the Dr. Gemma Marfany. A study by Dr. Lluís Montoliu's group was published in *Sci Reports* in which it has been determined that the limits of the gene responsible for OCA1 albinism are key to regulating expression. The *FASEB Journal* published a study led by Dr. Regina Rodrigo from Dr. José María Millán's group on neuroprotective effects and molecular mechanisms involved in the administration of Adalimumab, in the delay of retinal degeneration in mice with retinitis pigmentosa. Finally, a publication in *Frontiers in Genetics of the Animal Models Working Group*, coordinated by Dr. Silvia Murillo-Cuesta, which highlights the importance of animal models for research on rare diseases.

In the ACCI 2019 call, 2 projects have been financed coordinated by Dr. Serena Mirra (Dr. Gemma Marfany's group) and Dr. Rafael Vázquez (Dr. José María Millán's group).

The Mutua Madrileña Foundation financed a project by Dr. Gema García (Dr. José María Millán's unit) to search for biomarkers of response to treatment in patients with SMA and The Spanish National Organization for the Blind (ONCE) collaborated with two projects on rare ocular diseases led by Dr. Regina Rodrigo and Dr. Marta Cortón (Dr. Carmen Ayuso's group).

The Unit led by Dr. Isabel-Varela Nieto participates in a project- selected by the Fundación General CSIC within the Programme for a Long Lived Society Interreg VA- Spain-Portugal- on the identification of cholesterol nitrones, a family of antioxidant molecules for the treatment of hearing loss.

Events organized:

- >> International Symposium Ramón Areces Foundation “Understanding and reprogramming visual developmental disorders: from anophthalmia to cortical deficiencies”, January 30 and 31 at the Foundation’s headquarters, coordinated by Dr. Paola Bovolenta.
- >> III Practical Course on “Genomic Editing and Gene Therapy”, June 29 (online) coordinated by Drs. Almudena Fernández, Óscar Quintana and Matías Morín.
- >> IV Course “Bioinformatics analysis of massive sequencing data applied to genetic diagnosis and translational research”, September 28 - October 7 (online) coordinated by Drs. Miguel Ángel Moreno and Matías Morín.
- >> Meeting of the CIBERER Sensorineural Pathology Pdl, (online), in which the 7 research groups and the ACRÓMATES association participated.
- >> CIBERER Academia Seminars for patients on deafness (online) co-organized with FIAPAS, Drs. Miguel Ángel Moreno and Isabel Varela, on diagnosis, therapy and research on deafness on November 5, 12 and 19.

Acknowledgments: Dr. Isabel Varela-Nieto was appointed president of the SEEBM, Dr. Lluís Montoliu was appointed president of the Ethics Committee of the CSIC and was awarded the HS Raper medal for his research on pigmentation and albinism.

ENDOCRINE MEDICINE PROGRAMME

Coordinator: **Susan Webb**

To be highlighted are the publications during 2020 on Allan-Herndon-Dudley syndrome and pituitary pathology (Cushing syndrome and acromegaly). Allan-Herndon-Dudley syndrome, a defect in the thyroid hormone transporter MCT8, causes peripheral hyperthyroidism and hypothyroidism in the CNS as the thyroid hormones do not cross the blood-brain barrier (BBB) and cause serious neurological problems. In murine models, Dr. Ana Guadaño’s group administered T4 / T3 intranasally to prevent BBB, although it did not achieve its goal (Intranasal delivery of Thyroid hormones in MCT8 deficiency; *PLoS One*. 2020 Jul 20; 15 (7): e0236113). They are investigating other formulations for new therapeutic strategies of transport between the nose and the brain.

In an international collaboration of Dr. Luis Castaño’s group, they demonstrate through WES that genetic variants of the *DICER1* gene are associated with corticotropinomas and Cushing’s disease in 7 pediatric patients (Rare Germline *DICER1* Variants in Pediatric Patients With Cushing’s Disease: What Is Their Role?; *Front Endocrinol* (Lausanne). 2020 Jul 3; 11:43).

In “Molecular profiling for acromegaly treatment: a validation study; *Endocr Relat Cancer*. 2020 Jun; 27 (6): 375- 389”, four Linked Clinical Groups (those of Dr. Irene Halperin, Mónica Marazuela, Antonio Picó and Manuel Puig) collaborated with the group led by Dr. Susan Webb. In 100 patients with acromegaly, markers of response to treatment with somatostatin analogs were investigated, in an approach to personalized medicine. Although there was heterogeneity in the expression of genes associated with the response to somatostatin, E-cadherin was the best molecular predictor, concluding that its inclusion in therapeutic decisions should be evaluated when a patient is not cured after surgery.

Another international collaboration of this group in acromegaly is “Hypertension in acromegaly in Relationship to Biochemical Control and Mortality: Global ACROSTUDY Outcomes; *Front Endocrinol* (Lausanne). 2020 Nov 30;11:577173”. In 2,090 patients treated with Somavert, hypertension was observed in 1,344. Compared with the normotensive patients, hypertensive patients were older, and had more diabetes, hyperlipidaemia,

cardiovascular disease, and mortality. Both hypertension and hypopituitarism were independent predictors of mortality, concluding that prospective cardiovascular follow-up should be optimized to improve prognosis in acromegaly.

Research by Dr. Susan Webb's group on residual morbidity in Cushing's syndrome despite normalizing hypercortisolism after surgery and / or medical treatment, shows a persistent increase in intramuscular fat infiltration, worse performance in muscle function tests, more fatigue and worse quality of life (Thigh Muscle Fat Infiltration Is Associated With Impaired Physical Performance Despite Remission in Cushing's Syndrome; *J Clin Endocrinol Metab.* 2020 May 1;105(5):dgz329). This opens up the possibility of seeking strategies through exercise programs aimed at improving muscle performance, in collaboration with trainers from the INEF (National Institute of Physical Education), an entity with which a collaboration agreement has been signed. A similar work on residual myopathy in acromegaly was awarded as best communication in the area of Neuroendocrinology at the SEEN (Spanish Society of Endocrinology and Nutrition) congress in October 2020.

INHERITED CANCER , HAEMATOLOGICAL AND DERMATOLOGICAL DISEASES PROGRAMME

Coordinator: **Juan Antonio Bueren**

During 2020 the groups of this research programme have continued working towards the IRDIRC objectives. In addition, this year two new groups have been incorporated into the programme. The group led by Eduardo López Granados from the Research Institute of the La Paz University Hospital (IdiPAZ), focuses on the study of rare monogenic diseases of the immune system and the group led by Dr. Victoriano Mulero from the Faculty of Biology of the University of Murcia and the Biomedical Research Institute of Murcia (IMIB), a group that is dedicated to the generation and analysis of zebrafish models for the functional study and development of therapies for rare diseases.

This year, due to the limitations imposed by the pandemic, face-to-face events have been limited, including the annual meeting of the programme. Among the main milestones we highlight the following:

In diagnostics, we highlight the international study published in *Nature Genetics* in which Dr. Mercedes Robledo's group has participated, which has identified variants associated with the activity of 190 breast cancer predisposition genes. This work, in which researchers from Dr. Ángel Carracedo's group have also collaborated, reveals the enormous complexity of one of the most frequent tumors and lays the foundations for moving towards a more precise early diagnosis and personalized treatments. Fachal et al *Nat Genet* (2020).

As regards therapeutic developments, this year has once again been very productive. To be highlighted are the contributions made by Dr. Marcela del Río's group with the development of a tissue bioengineering product based on the use of patient cells corrected by means of genomic editing that has been designated as an orphan drug by the European Medicines Agency (EMA) for the treatment of recessive dystrophic epidermolysis bullosa.

In addition, the unit led by Dr. Juan Bueren has started the phase I trial of gene therapy for patients with erythrocyte pyruvate kinase at the H. Jiménez Díaz Foundation, as well as the phase II gene therapy trials of patients with Fanconi Anemia at the Niño Jesús Hospital and Stanford University, and LAD-I immunodeficiency at UCLA (USA).

TRAINING PROGRAMME

Coordinator: **Luis Pérez Jurado**

The normal development of the activities of this programme has been altered by the COVID-19 pandemic. Some courses were able to be reorganized in an online format, but others were canceled due to the impossibility of taking them to that format due to them being of a marked face-to-face nature.

>> Courses: Organization of courses and call for grants.

The CIBERER training programme directly organized a course and two others in collaboration with an association.

>> CIBERER Workshop on Single Cell Genomics.

>> EURORDIS SUMMER SCHOOL, 4th Edition. (Online format).

>> Conference on Designation, Development and Access of Orphan Medicines.

>> Courses: Call for attendance grants.

>> Bioinformatics analysis of massive sequencing data applied to genetic diagnosis and translational research. 13 grants were awarded.

>> Organization of a programme aimed at patients with rare diseases.

In 2020, the CIBERER Academia programme for patients was launched to contribute to the training of people affected by rare diseases and their families in relevant aspects of rare disease research. These seminars are aimed at all those people affected by some type of RD and their families, and at interested health professionals who work directly or indirectly with RD. Once the seminars are completed, they are made public on the CIBER YouTube channel. Specifically, three seminars grouped in a cycle on deafness have been held:

>> Deafness clinic.

>> Genetic diagnosis of deafness.

>> Research and future treatments for deafness.

Mobility grants

In 2020, mobility grants remained open to internal and external, national and international mobilities. The former were preferentially provided with external mobility granted only if they were of cross-cutting interest. Thus, various researchers were able to benefit from this programme to expand their training and advance the projects in which they were involved. The pandemic situation and restrictions on mobility particularly affected these grants. Despite the fact that two international mobility grants were granted, only one could be carried out as it had been programmed before the mobility restrictions. The following table shows the mobilities carried out in 2020.

| Beneficiary | Issuing Group | Receiving Group |
|---------------------------|--------------------------|---|
| José María Bermúdez Muñoz | IP: Isabel Varela Nieto | Molecular Carcinogenesis Group (Atenas) |
| Obdulia Sánchez Lijarcio | IP: Belén Pérez González | IP: Carmen Ayuso |

PLATFORMS

CIBERER BIOBANK

Coordinator: **Federico Pallardó Calatayud**

There are 871 biological samples of 72 different pathologies in the Biobank system which can be viewed in the new online catalogue search engine (<http://www.ciberer-biobank.es/Catalogo/>). During this year, the number of biological samples transferred has been a total of 23 samples from 6 transfer requests, half of which were from groups outside the CIBERER. This indicates an ever increasing visibility, due in part to the fact that we are integrated in different networks: the Eurobiobank with a single European catalogue, the Valencian Network of Biobanks and recently in the National Network of Biobanks and Biomodels Platform; and also, due to the updating of the Biobank website, in compliance with the 7 transparency recommendations of the National Biobank Network. In addition, new custody services have been established and two that started in previous years remain ongoing. One of our objectives continues to be the development and offering of new processing services for CIBERER researchers. Given the current pandemic, the detection of SARS-CoV-2 in cell cultures has been offered, in order to guarantee the safety of research personnel. This growing offer has meant that the number of services provided continues to increase annually, with a total of 50 services in 2020, which is practically three times those of the previous year. Part of the transfers and services have been made to external groups and biotechnology companies, which has allowed to generate revenue.

We continue to collaborate with Biobank networks. We are a member of the Valencian Network of Biobanks (since 2010), the Eurobiobank (since 2017) and we have been included in the National Network of Biobanks and Biomodels Platform in the call for ISCIII Platforms to support R & D & I in Biomedicine and Health Sciences. Collaboration agreements have been signed that have remained in force during this year with Biobanco IBSP-CV / FISABIO and Banco Nacional de ADN (DNA National Bank).

Regarding agreements with the industry, two collaboration agreements have been maintained with EpiDisease SL: the first within the framework of a “TEST ScoliPro®” project where the Biobank processes and stores the study samples and the second to determine telomerase activity of immortalized fibroblast lines in the CBK. In addition, another collaboration with EpiDisease SL has also started within the framework of a European project. Finally, a know-how license has been signed with the biotechnology company Seqplexing SL for the design of a kit for the detection of the SARS-CoV-2 virus in cell cultures.

We have participated in different media to disseminate our activity:

- >> VIII Biomedical Research Congress 2020, round table on rare diseases.
- >> World Day of Rare Diseases of the Autonomous Community of Valencia (CV) organized by the Alianza de Investigació Traslacional de Malalties Rares (Alliance for Translational Research of Rare Diseases) of the CV.
- >> XIII CIBERER Annual Meeting.

A total of 4 projects have been applied for during 2020 and 4 projects remain ongoing: I) ACCI-CIBE-RER Call, II) FEDER Funds 2018-2020 (Technological Innovation and Reinforcement of the Valencian Biobank Network), III) FIS and IV) National Plan project. These projects have made it possible to secure a financing of € 75,700.

BIOINFORMATICS PLATFORM FOR RARE DISEASES (BIER)

Coordinator: **Joaquín Dopazo**

Among the most relevant results of this year, worth highlighting is the dedication of the BIER platform to the EnoD program, in which, in addition to the conventional prioritization of potentially disease-causing variants, structural variants and expansion diseases and triplets are systematically searched for. Furthermore, a novel methodology has been developed for the detection of spinal muscular atrophy in NGS data (López-López et al., *Hum Mutat.* 2020 41: 2073-2077). As a result of receiving these data, the Spanish population genetic variability database, CSVS, has continued to grow and show its usefulness for filtering local polymorphic variants in numerous studies, as well as bringing different researchers into contact, thus making the samples it contains discoverable. The CSVS has recently been published (Peña-Chilet et al. *Nucleic Acids Res.* 2021; 49, D1: D1130-D1137) as an example of crowdsourcing. Finally, the ACCI “Mathematical models of disease mechanisms for drug reformulation in rare diseases”, led by Dr. María Peña, to automatically propose candidate drugs for repurposing continues to generate results. Several of these drugs have been validated (in Fanconi anemia) or are in the process of being validated with promising initial results (familial melanoma, retinitis pigmentosa).

RESOURCE MAP FOR RARE DISEASES (MAPER)

In 2020, information continued to be collected for the MAPER database. The data on research projects and clinical trials accessible through the MAPER website are the following:

- >> 1165 biomedical research projects included and 797 clinical trials collected.
- >> 740 Principal Investigators with at least 1 project or trial included in the database.
- >> Presentation of results at the IX Conference “Investigar es Avanzar”. Rare Diseases Day. CosmoCaixa. February 28th. Madrid.
- >> Presentation of results in events during the celebration of World Rare Diseases Day. Centro Creer IM-SERSO. February 29. Burgos.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

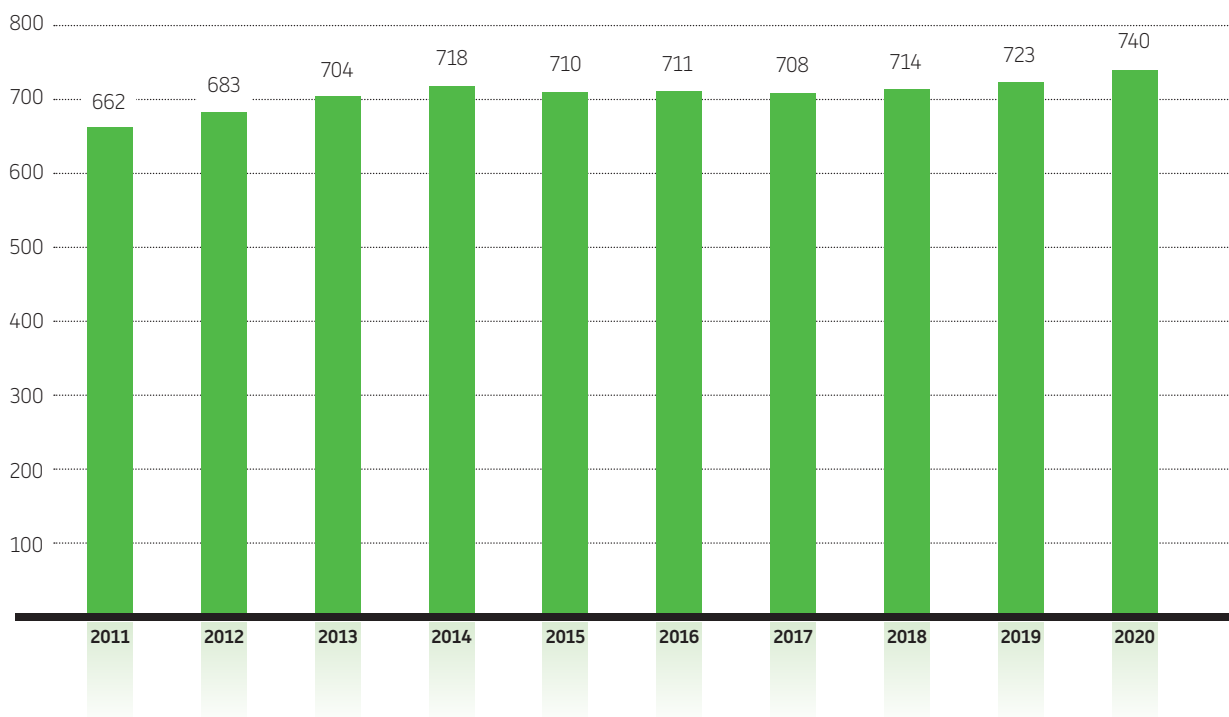
| | |
|--------|-----|
| TOTALS | 740 |
| Q1 | 459 |
| D1 | 196 |

Collaborations

| | |
|---------|-----|
| CIBERER | 114 |
| CIBER* | 148 |

*Among various thematic areas



» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|--|
| 42,779 | Hernansanz-Agustín P, Choya-Foces C, Carregal-Romero S, Ramos E, Oliva T, Villa-Piña T, et al. <i>Na⁺ controls hypoxic signalling by the mitochondrial respiratory chain</i> . <i>Nature</i> 2020. 10. 586(7828):287-291. PMID 32728214. doi 10.1038/s41586-020-2551-y. |
| 41,846 | Zhang Q, Bastard P, Liu Z, Le Pen J, Moncada-Velez M, Chen J, et al. <i>Inborn errors of type I IFN immunity in patients with life-threatening COVID-19</i> . <i>Science</i> 2020. 10. 370(6515). PMID 32728214. doi: 10.1126/science. abd4570. |
| 30,822 | González-Fernández Á, Bermúdez Silva FJ, López-Hoyos M, Cobaleda C, Montoliu L, Del Val M, Leech K. <i>Non-animal-derived monoclonal antibodies are not ready to substitute current hybridoma technology</i> . <i>Nat Methods</i> 2020. 11. 17(11):1069-1070. PMID 33020658. Di: 10.1038/s41592-020-00977-5. |
| 27,603 | Fachal L, Aschard H, Beesley J, Barnes DR, Allen J, Kar S, et al. <i>Fine-mapping of 150 breast cancer risk regions identifies 191 likely target genes</i> . <i>Nat Genet</i> 2020. 01. 52(1):56-73. PMID 31911677. Doi: 10.1038/s41588-019-0537-1. |
| 27,603 | Landi MT, Bishop DT, MacGregor S, Machiela MJ, Stratigos AJ, Ghiorzo Pet al. <i>Genome-wide association meta-analyses combining multiple risk phenotypes provide insights into the genetic architecture of cutaneous melanoma susceptibility</i> . <i>Nat Genet</i> . 2020. 05. 52(5):494-504. PMID: 32341527DOI: 10.1038/s41588-020-0611-8. |
| 20,589 | Martínez-López D, Roldan-Montero R, García-Marqués F, Nuñez E, Jorge I, Camafeita E, et.al <i>Complement C5 Protein as a Marker of Subclinical Atherosclerosis</i> . <i>J Am Coll Cardiol</i> 2020 04. 75(16):1926-1941. PMID: 3232710. DOI: 10.1016/j.jacc.2020.02.058. |
| 20,071 | Lim ET, Uddin M, De Rubeis S, Chan Y, Kamumbu AS, Zhang X, et al. <i>Rates, distribution and implications of postzygotic mosaic mutations in autism spectrum disorder</i> . <i>Nat Neurosci</i> . 2020 sep. 23(9):1176. PMID: 32665711. DOI: 10.1038/s41593-020-0681-z. |
| 19,819 | Montazeri Z, Li X, Nyiraneza C, Ma X, Timofeeva M, Svinti V, et al. <i>Systematic meta-analyses, field synopsis and global assessment of the evidence of genetic association studies in colorectal cancer</i> . <i>Gut</i> 2020 Aug. 69(8):1460-1471. PMID: 31818908. DOI: 10.1136/gut-jnl-2019-319313. |
| 18,274 | Millstein J, Budden T, Goode EL, Anglesio MS, Talhouk A, Intermaggio MP et al. <i>Prognostic gene expression signature for high-grade serous ovarian cancer</i> . <i>Ann Oncol</i> 2020 09. 31(9):1240-1250. PMID: 32473302. DOI: 10.1016/j.annonc.2020.05.019. |
| 18,274 | Michielin O, van Akkooi A, Lorigan P, Ascierto PA, Dummer R, Robert C, et al. <i>ESMO consensus conference recommendations on the management of locoregional melanoma: under the auspices of the ESMO Guidelines Committee</i> . <i>Ann Oncol</i> 2020 11. 31(11):1449-1461. PMID : 32763452. DOI : 10.1016/j.annonc.2020.07.005. |

» CIBERER Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|-----------|
|  Alonso García de la Rosa, Javier (*) | 15 | 5 | 3 | Instituto de Salud Carlos III | Madrid |
| Antiónolo Gil, Guillermo (**) | 7 | 5 | 0 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Artuch Iriberrí, Rafael | 38 | 20 | 10 | Fundación para la Investigación y Docencia Sant Joan de Déu | Barcelona |




| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
|  Ayuso García, Carmen | 15 | 8 | 1 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Balcells Comas, Susana (*) | 26 | 15 | 4 | Universidad de Barcelona | Barcelona |
|  Botella Cubells, Luisa María | 8 | 4 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Bovolenta, Paola | 1 | 1 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Bueren Roncero, Juan Antonio | 12 | 10 | 3 | Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas | Madrid |
|  Caballero Molina, María Teresa | 28 | 3 | 2 | Servicio Madrileño de Salud | Madrid |
|  Carracedo Álvarez, Ángel | 39 | 21 | 12 | Universidad Santiago de Compostela | Santiago |
|  Castaño González, Luis | 6 | 4 | 0 | Asociación Instituto de Investigación Sanitaria de Biocruces | Vizcaya |
|  Cuezva Marcos, José Manuel | 6 | 4 | 3 | Universidad Autónoma de Madrid | Madrid |
|  Dalmau Obrador, Josep | 1 | 1 | 0 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Del Río Nechaevsky, Marcela | 9 | 3 | 1 | Universidad Carlos III | Madrid |
|  Dopazo Blázquez, Joaquin | 7 | 6 | 3 | Fundación Pública Andaluza Progreso y Salud | Sevilla |
|  Estévez Povedano, Raúl | 4 | 3 | 1 | Universidad de Barcelona | Barcelona |
|  Fernández Fraga, Mario | 1 | 1 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Asturias |
|  Fillat Fonts, Cristina | 19 | 17 | 5 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Gallano Petit, María Pía | 14 | 7 | 3 | Instituto de Investigación del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Gallardo Vigo, Eduardo | 19 | 15 | 11 | Instituto de Investigación del Hospital de la Santa Cruz y San Pablo | Barcelona |
|  Garesse Alarcón, Rafael | 6 | 3 | 1 | Universidad Autónoma de Madrid | Madrid |
|  Gratacos Solsona, Eduard | 31 | 13 | 8 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Grau Junyent, Josep (*) | 11 | 8 | 1 | Hospital Clínico de Barcelona | Barcelona |
|  Guadaño Ferraz, Ana Cristina (**) | 3 | 1 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Lapunzina Badía, Pablo Daniel | 39 | 16 | 6 | Servicio Madrileño de Salud | Madrid |
|  López Granados, Eduardo | 3 | 1 | 0 | Servicio Madrileño de Salud | Madrid |
|  Marfany Nadal, Gemma | 11 | 6 | 2 | Universidad de Barcelona | Barcelona |
|  Marina Moreno, Alberto (*) | 12 | 7 | 5 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Valencia |
|  Martí Seves, Ramón | 10 | 7 | 7 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca | Barcelona |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|--|-----------------|
|  Martín Casanueva, Miguel Ángel | 23 | 10 | 2 | Servicio Madrileño de Salud | Madrid |
|  Medina Torres, Miguel Ángel | 11 | 11 | 2 | Universidad de Málaga | Madrid |
|  Millán Salvador, José María | 9 | 5 | 2 | Fundación para la Investigación del Hospital la Fe | Valencia |
|  Montoliu Jose, Lluís | 9 | 7 | 4 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Montoya Villarroya, Julio | 6 | 3 | 1 | Universidad de Zaragoza | Zaragoza |
|  Moreno Galdó, Antonio José | 7 | 5 | 1 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca | Barcelona |
|  Moreno Pelayo, Miguel Ángel | 5 | 2 | 0 | Servicio Madrileño de Salud | Madrid |
|  Mulero Méndez Vitoriano | 3 | 3 | 3 | Universidad de Murcia | Murcia |
|  Navas Lloret, Plácido | 11 | 7 | 4 | Universidad Pablo de Olavide | Sevilla |
|  Nieto Toledano, María Ángela | 2 | 2 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Alicante |
| Nunes, Virginia (**) | 1 | 1 | 1 | Fundación IDIBELL | Barcelona |
|  Palacín Prieto, Manuel | | | | Institut de Recerca Biomèdica de Barcelona | Barcelona |
|  Palau Martínez, Francesc | 8 | 5 | 1 | Fundación para la Investigación y Docencia Sant Joan de Déu | Barcelona |
|  Pallardó Calatayud, Federico | 18 | 10 | 3 | Universidad de Valencia | Valencia |
|  Pérez González, María Belén | 9 | 3 | 2 | Universidad Autónoma de Madrid | Madrid |
|  Pérez Jurado, Luis | 18 | 15 | 7 | Universidad Pompeu Fabra | Barcelona |
|  Perona Abellón, Rosario | 1 | 1 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Puig Sardá, Susana | 36 | 26 | 14 | Servicio de Bioquímica y Genética Molecular del Hospital Clínico Barcelona | Barcelona |
|  Pujol Onofre, Aurora | 19 | 14 | 7 | Fundación IDIBELL | Barcelona |
|  Ribes Rubió, Antònia | 13 | 6 | 1 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Robledo Batanero, Mercedes | 30 | 21 | 12 | Fundación Centro Nacional de Investigaciones Oncológicas | Madrid |
|  Rodríguez de Córdoba, Santiago | 2 | 2 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Ruiz Pérez, Víctor Luis | 6 | 6 | 4 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Salido Ruiz, Eduardo | 1 | 0 | 0 | Fundación Canaria de Investigación Sanitaria | Tenerife |
| Santos Hernández, Javier (**) | 3 | 1 | 1 | Universidad Autónoma de Madrid | Madrid |
|  Sanz Bigorra, Pascual | 8 | 4 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Valencia |
|  Serratos Fernández, José M ^a | 5 | 1 | 0 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|---|-----------|
|  Sevilla Mantecón, María Teresa | 15 | 9 | 4 | Instituto de Investigación Hospital Uip la Fe | Valencia |
|  Surrallés Calonge, Jordi | 6 | 5 | 2 | Universidad Autónoma de Barcelona | Barcelona |
|  Varela Nieto, Isabel | 9 | 4 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Vicente García, Vicente | 16 | 5 | 1 | Fundación para la Formación e Investigación Sanitarias de la Región de Murcia | Murcia |
|  Webb, Susan | 6 | 6 | 1 | Instituto de Investigacion del Hospital de la Santa Cruz y San Pablo | Barcelona |

(*) PI replaced ; (**) Group withdrawn

Linked Clinical Groups

| Paediatric and Developmental Medicine Research Programme | |
|--|--|
|  | Encarna Guillén. Hospital Virgen de la Arrixaca, Murcia |
|  | Feliciano J. Ramos. Hospital Lozano Blesa, Zaragoza |
|  | Jordi Rosell. Hospital Son Espases, Palma de Mallorca |
| | Isabel Tejada. Hospital Cruces, Bilbao (*) |
| Inherited Metabolic Medicine Research Programme | |
| | Luis Aldámiz-Echevarría Azuara. Hospital Cruces, Bilbao |
|  | M ^a Luz Couce. Hospital Clínico de Santiago de Compostela, A Coruña |
|  | Luis González Gutiérrez-Solana. Hospital Infantil Niño Jesús, Madrid |
|  | Eduardo López Laso. Hospital Reina Sofía, Córdoba |
| | Guillem Pintos. Hospital Germans Trías i Pujol, Barcelona |
|  | Mireia del Toro. Hospital Vall d'Hebrón, Barcelona |
| Endocrine Medicine Research Programme | |
| | Irene Halperin. Hospital Clínic, Barcelona |
|  | Antonio Picó. Hospital General de Alicante, Alicante |
| | Manuel Puig Domingo. Hospital Germans Trías i Pujol, Barcelona |
|  | Alfonso Soto. Hospital Virgen del Rocío, Sevilla |
| Inherited Cancer, Haematologic and Dermatological Diseases Research Programme | |
|  | Isabel Badell Hospital de la Santa Creu i Sant Pau, Barcelona |
|  | Cristina Beléndez. Hospital Gregorio Marañón, Madrid |
|  | Albert Català. Hospital San Joan de Déu, Barcelona |
|  | Julián Sevilla. Hospital Infantil Niño Jesús, Madrid |
| | Joan-Lluís Vives-Corrns. Hospital Clínic, Barcelona (*) |

(*) Group withdrawn in 2020

PATENTS OWNED BY CIBER 2020

Patents applied for

- European Patent EP20382027.9: *Gene editing for the treatment of epidermolysis bullosa*. Group led by Dr. Marcela del Río.
- European Patent EP20382568.2: *Pyruvate kinase deficiency (PKD) gene editing treatment method*. Group led by Dr. Juan Antonio Bueren.
- European Patent EP20382792.8: *mesenchymal stem cells co-expressing CXCR4 and IL-10 and uses thereof*. Group led by Juan Antonio Bueren.
- Spanish Patent P202031320. *Composición farmacéutica para el tratamiento de la enfermedad de Charcot-Marie-Tooth*. Groups led by Dr. José Manuel Cuezva and Dr. Francesc Palau.

Patents granted

- Patent granted in the United States: *Mass spectrometry-based methods for the detection of circulating histones H3 and H2b in plasma from sepsis or septic shock (ss) patients*. Group led by Dr. Federico Pallardó.

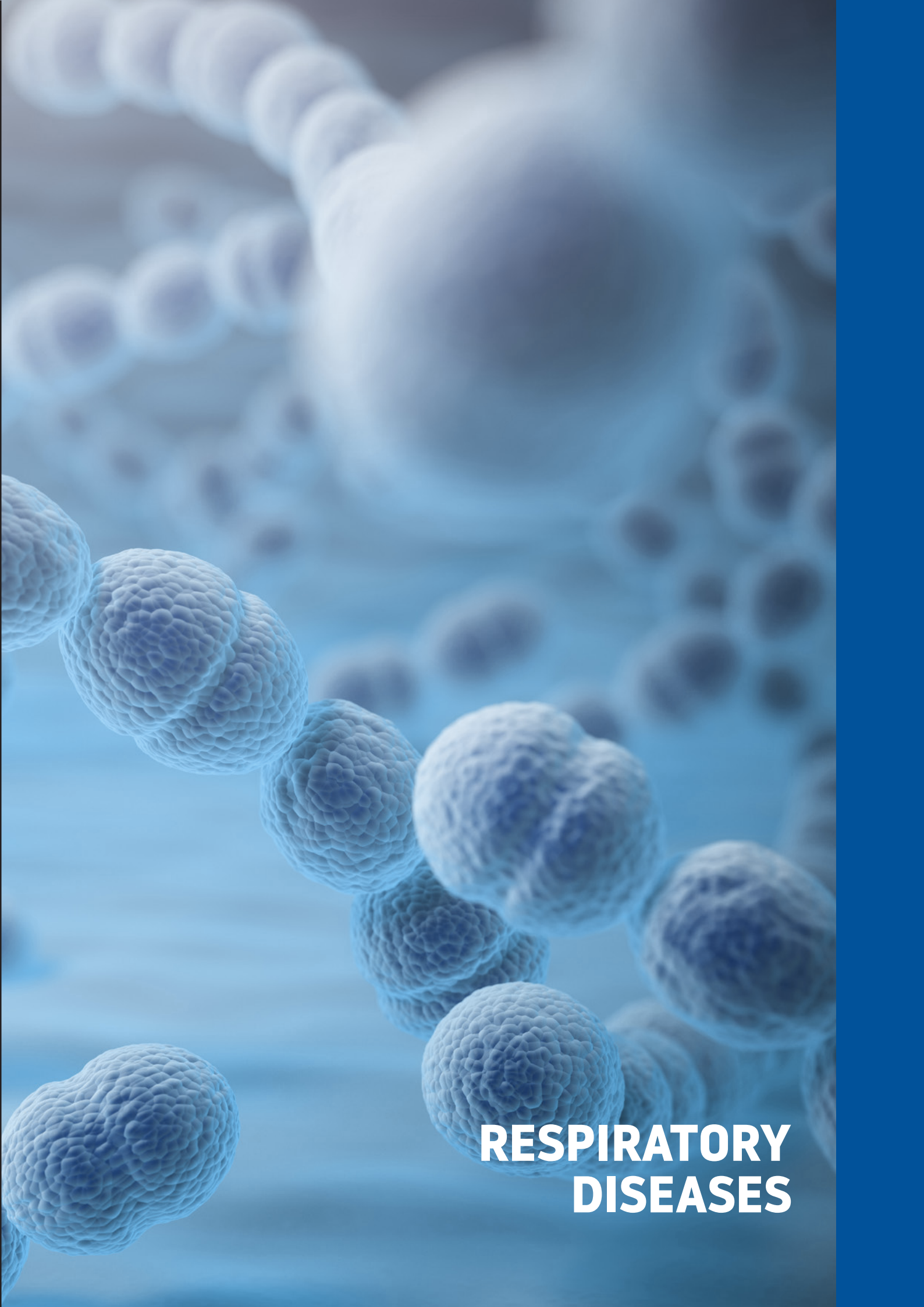
CLINICAL GUIDES

- *A Consensus on the Diagnosis and Treatment of Acromegaly Comorbidities: An Update.*
- *Spanish Guidelines for Diagnosis, Management, Treatment, and Prevention of DRESS Syndrome.*
- *Safety of drug use in patients with a primary mitochondrial disease: An international Delphi-based consensus.*
- *Early non-social behavioural indicators of autism spectrum disorder (ASD) in siblings at elevated likelihood for ASD: a systematic review.*
- *Genetics, diagnosis, management and future directions of research of pheochromocytoma and paraganglioma: a position statement and consensus of the Working Group on Endocrine Hypertension of the European Society of Hypertension.*
- *Review of Pharmacological Strategies with Repurposed Drugs for Hereditary Hemorrhagic Telangiectasia Related Bleeding.*
- *Social Camouflaging in Females with Autism Spectrum Disorder: A Systematic Review.*
- *HOMA-IR in acromegaly: a systematic review and meta-analysis.*
- *Practical guidelines to manage discordant situations of SMN2 copy number in patients with spinal muscular atrophy.*
- *Consensus guideline for the diagnosis and management of mannose phosphate isomerase-congenital disorder of glycosylation.*
- *Effects of Prebiotic and Probiotic Supplementation on Lactase Deficiency and Lactose Intolerance: A Systematic Review of Controlled Trials.*
- *Bone Status in Patients with Phenylketonuria: A Systematic Review.*

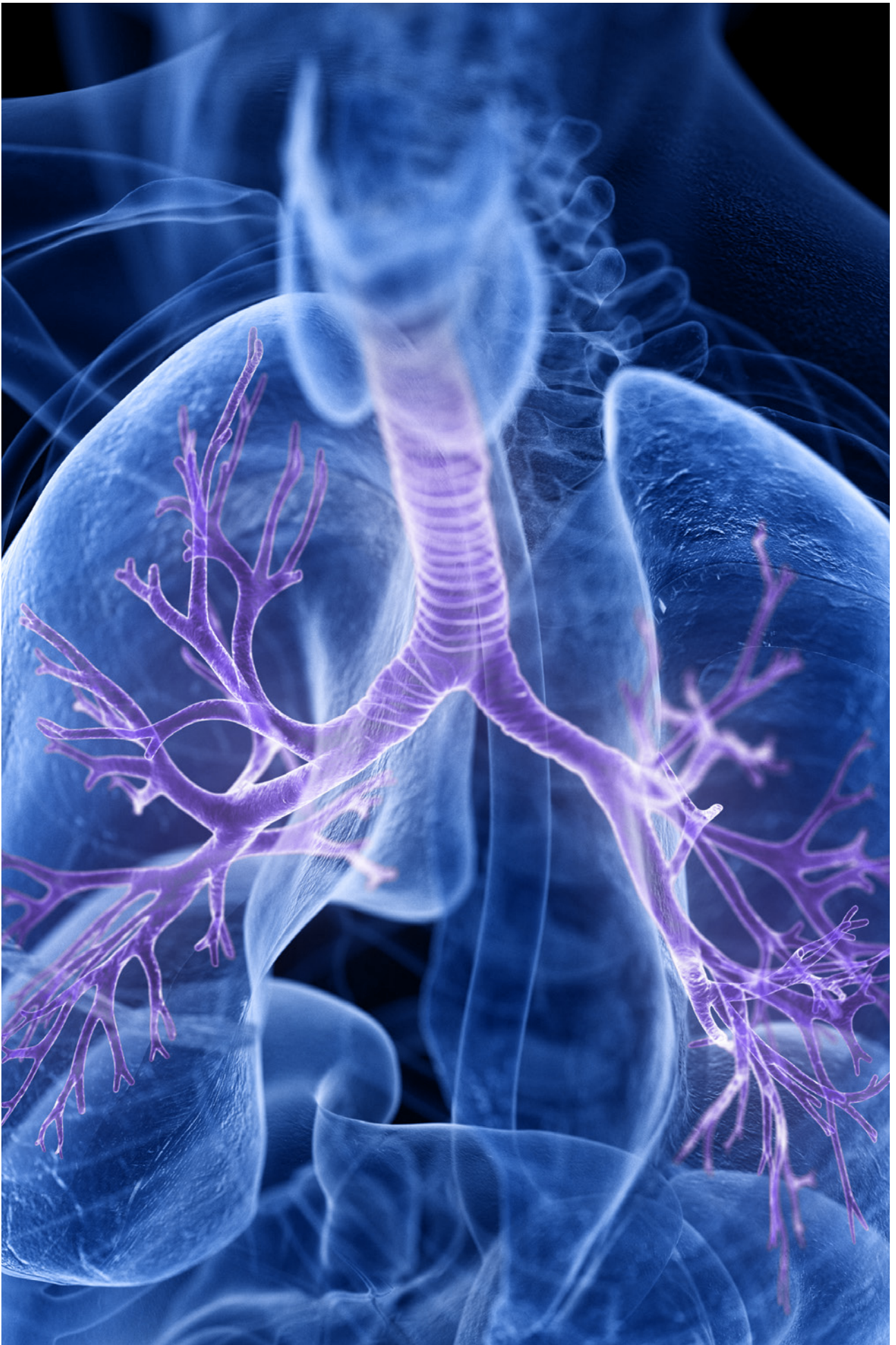
- *Consensus guideline for the diagnosis and treatment of tetrahydrobiopterin (BH4) deficiencies.*
- *Mutational Screening of BRCA1/2 Genes as a Predictive Factor for Therapeutic Response in Epithelial Ovarian Cancer: A Consensus Guide from the Spanish Society of Pathology (SEAP-IAP) and the Spanish Society of Human Genetics (AEGH).*
- *Ethical publication of research on genetics and genomics of biological material: guidelines and recommendations.*
- *Clinical practice guidelines for laboratory diagnosis of epidermolysis bullosa.*
- *Heparin therapy in placental insufficiency: Systematic review and meta-analysis.*
- *European interdisciplinary guideline on invasive squamous cell carcinoma of the skin: Part 1. epidemiology, diagnostics and prevention and Part 2. Treatment.*
- *ESMO consensus conference recommendations on the management of locoregional melanoma: under the auspices of the ESMO Guidelines Committee.*
- *Aging-Related Disorders and Mitochondrial Dysfunction: A Critical Review for Prospect Mitoprotective Strategies Based on Mitochondrial Nutrient Mixtures.*
- *Neurofibromatosis type 2 in Phelan-McDermid syndrome: Institutional experience and review of the literature.*
- *International Consensus on the Use of Genetics in the Management of Hereditary Angioedema.*
- *Executive Summary of the Consensus Document on the Diagnosis and Management of Patients with Primary Immunodeficiencies.*



čiberes



RESPIRATORY DISEASES





WELCOME FROM THE SCIENTIFIC DIRECTOR

Ferran Barbé Illa

Dear Friends:

Below, you will find the most significant data that summarizes a large part of the activity of CIBERES during the year 2020.

2020 will forever remain engraved in our memory. As I mentioned in my “Open Letter” of March 18, we have faced the greatest health challenge of our generation, so allow me, once again, to thank all of you for your commitment and your dedication to serving COVID-19 patients, either through direct care or your research work. This has proven essential for the management and control of the pandemic. The importance and need for collaborative science of which CIBER is an example has been evidenced in recent months.

CIBERES is actively participating in research on COVID-19. I would like to highlight two projects that started in 2020 and are a good example of our collaborative activity. On the one hand, the CIBERESUCICOVID project led by Antoni Torres, which works to determine risk factors and prognosis of COVID-19 infected patients admitted to Spanish ICUs since the pandemic began. The project is possible thanks to the help that CIBERES received from the COVID-19 Fund and that was granted by the ISCIII to support research projects that improve the clinical approach to COVID-19 and has the participation and scientific endorsement of SEMICYUC and SEPAR and more than 50 ICUs from all over Spain.

In addition, the DEXA-COVID-19 project led by Jesús Villar dedicated to the investigation of how to optimize the dose of dexamethasone in patients with acute respiratory failure (ARF) thanks to the help received from the call for Independent Clinical Research Projects (ICI). A network of 28 hospitals participates in the research and has the collaboration of two other CIBER areas.

These two major projects demonstrate the quality of the work of CIBERES researchers and entails, apart from a huge effort, an enormous responsibility given the societal expectations placed upon them.

In addition to these projects, CIBERES has maintained a very important activity despite the difficulties imposed by the pandemic. 2020 has been the year with the highest number of publications since our inception, also increasing inter- and intra CIBER collaborations.

Our young researchers meetings were organized with a record number of attendees and their communications have, once again, been published in an online supplement of the Archives of Bronconeumology.

I would like to especially thank the teaching committee, responsible for the organization, for the great effort put in to ensure the implementation of the event in such complex circumstances.

I want to end this letter by reiterating my gratitude to each and every one of you for your work and your example this year. I am especially proud to be able to represent a group of professionals who, like those of CIBERES, demonstrate their worth in such difficult circumstances.

My very best regards and my best wishes to you all.



PROGRAMMES

CHRONIC RESPIRATORY DISEASES

Coordinator: **Juan Fernando Masa Jiménez**

Asthma

The asthma patient follow-up database has been completed with 512 patients and the first analysis has been published (CTA in press IF: 5.1). A new database of asthmatic patients treated with biologics has been completed and a first article has been published on how COVID-19 has affected these patients (JACI in practice, IF: 7.2). The articles *Upper and Lower Airways Functional Examination in Asthma and Respiratory Allergic Diseases. Considerations in the SARS-CoV-2 Post-Pandemic Situation* have been published. (JIACI, IF 5.1). Part of the group has published 4 articles on occupational asthma and other groups have published 3 articles on biomarkers in asthma and 4 on specific topics related to asthma.

COPD

The project has made steady progress as planned in each WP. Active follow-up cohorts are ongoing. Some of the more complete cohorts have already made some publications. In the evaluation of biomarkers, the BIOMEPOC has continued its development with the blind analysis of clusters based on proteomic signatures and some determinations of various omics have been made. BIOEARLY COPD published the first analysis. The Son Espases cohort (70% of the total sample) is being monitored. The WP dedicated to the validation of lung function trajectories has met its intended objectives which have been published. The project to evaluate therapeutic response has begun field work with the participation of 12 centers nationwide.

Cancer

Three manuscripts related to SAIL and SAILS studies of nocturnal hypoxia and lung cancer have been published. A SEPAR grant was received to investigate soluble PDL1 levels in these cohorts and other markers of nocturnal hypoxia. A coordinated FIS was obtained to continue investigating nocturnal hypoxia biomarkers in lung cancer, SAHS and COPD with an animal model and a prospective cohort (ECCO Cohort). The TRAIL 1 project on radiomics and response to immunotherapy in LC is also underway, as well as projects related to metabolomics and LC, including a SEPAR scholarship (PROMOTER).

Regarding biomarkers, we highlight the REFINE project integrated within the SEPAR oncology PII (Integrated Research Programme), which consists of a record of the use of the EarlyCDT autoantibody test in the characterization of pulmonary nodules.

The line of lung cancer and COPD has published various original works in Q1 journals throughout 2020. The 5 publications of 2020 have been disseminated through CIBERES.

Sleep

Work has continued on the key objectives of the proposal, combining experimental and clinical research:

- >> Characterization of the phenotypes of sleep-disordered breathing through the use of Big Data and biomarkers.
- >> Implementation of telemedicine and simplified diagnostic systems, an innovative model for personalized care of patients with sleep apnea.
- >> Study of the impact of respiratory sleep disorders at the systemic level and on diseases related to aging such as cancer, alterations and the molecular mechanisms involved.
- >> Relationship between sleep disturbances and chronicity.

INFECTIOUS RESPIRATORY DISEASES

Coordinator: **Antoni Torres Martí**

Host-Pathogen Interaction

- >> Prevention against pneumococcal disease: evaluation of the impact of current vaccines; characterization of new vaccine antigens; determination of the protective effect of the MTBVAC vaccine.
- >> Diagnostics: metabolomic profile analysis in urine sample from patients with respiratory infection; generation of microarrays of exosomes isolated from serum of patients with pneumonia, for their recognition by lectins; Molecular recognition of carbohydrates by receptors in pathogens.
- >> Antibiotic resistance: determination of the role of integrative and conjugative elements in (i) multidrug resistance of *Haemophilus parainfluenzae*, (ii) resistance to macrolides in *Streptococcus pyogenes*; Determination of populations tolerant to antibiotics in *H. influenzae*.
- >> Antibacterial therapies: demonstration of the antimicrobial effect of nanoparticles, endolysins, peptides, lipopeptides, bicyclic amine esters, and blocking of essential metabolic genes.
- >> Virulence factors: demonstration of the role of *pknH* and *ackA* genes in the virulence of *Mycobacterium* and *H. influenzae*, respectively.

Scientific production: 27 scientific articles, defense of 6 doctoral theses, 1 patent applied for:

Tuberculosis

- >> 46 publications: metabolomic profile, immune response and effect of tobacco smoke, use of IGRAs, prognostic algorithms for TB risk, molecular detection of resistance, use of mucosa for diagnosis, epidemiological studies on transmission in prisons (Costa Rica) and Africa-Europe migration routes, recurrences in MDR-TB (Argentina) and genetic analysis, review of a 20-year study of MDR-TB (Spain), the MTBVAC vaccine confers trained immunity, and better protection than aerosol BCG.

- >> 5 clinical trials scheduled or in progress: *Nyaditum resae* (Georgia), its ability to improve the microbiota after treatment (South Africa), transcriptomic signature of tuberculous granuloma, safety and immunogenicity of MTBVAC in newborns, and in adults with and without latent infection.
- >> 4 new projects: effect of the hypothalamic-pituitary axis on susceptibility to TB according to sex, search for prognostic biomarkers, use of anti-inflammatory drugs to improve TB treatment (will include clinical trial), and development of new therapeutic regimens for TB.

Pneumonia:

- >> Identification of biomarkers of cardiovascular events in CAP, and immunological markers and endothelial damage associated with organ dysfunction during pneumonia and the effect of corticosteroids.
- >> Immunoglobulins, stem cells, and bacterial vectors may be new approaches to the treatment of CAP.
- >> Some essential oils inhibit environmental microorganisms that cause CAP.
- >> The pneumococcal 13-serotype vaccine (PNV13) in children has reduced the disease in children and adults. The ability of the immune system to evade, form biofilm or genetic recombination is associated with emerging non-VCN13 serotypes.
- >> Antibiotic resistance, virulence, antibiotic treatment and new biofilm approaches have been defined in patients with mechanical ventilation and with non-cystic fibrosis bronchiectasis.
- >> Validation of diagnostic techniques, participation in clinical trials and in the development of national and international guidelines for the management of COVID-19. Review and update of the management of pneumonia due to other pathogens.
- >> The lipopolysaccharide-induced acute lung injury model in rats is the one that best reproduces the acute respiratory distress syndrome.
- >> Organization of an international symposium and a national forum.

DIFFUSE RESPIRATORY DISEASES

Coordinator: **Francisco Pérez Vizcaino**

Pulmonary Hypertension

- >> The 4th Research Meeting on Pulmonary Hypertension (Ciberes) was held. Universidad Complutense (Madrid).
- >> Exercise is feasible, safe and effective in pulmonary arterial hypertension (PAH) (*Eur Heart J* 2020; ehaa696).
- >> Severe vitamin D deficiency is very prevalent and is a predictor of high risk and mortality in PAH (*J Clin Med*. 2020; 9:448).
- >> Vitamin D deficiency aggravates PH in rat model. *Am J Physiol Lung Cell Mol Physiol*. 2020 Oct. 1;319(4): L627-L640.
- >> Analysis of protein networks and decreased glycolysis in thromboembolic PH endothelium. *Sci Rep*. 2021; 11:5583; *Am J Respir Cell Mol Biol*. 2020 Nov;63(5):710-713.
- >> Role of Kv7 channels in PH. *Hypertension* 2020; 76:1134-1146.

- >> ACE2 and ADAM17 expression in PAH and implications in COVID-19. *J Heart Lung Transplant.* 2020; 39:1167-1169.
- >> Role of PSGL-1 in PH in scleroderma model. *Arthritis Rheumatol* 2020; 72: 477-487.
- >> Role of Na⁺ in hypoxic pulmonary vasoconstriction response. *Nature* 2020; 586 (7828): 287-291.
- >> Design of the β 3-adrenergic agonist treatment in chronic pulmonary hypertension secondary to heart failure trial. *JACC Basic Transl Sci.* 2020; 5 (4): 317-327.
- >> Impact of PH on exercise capacity in patients with chronic obstructive pulmonary disease. *Arch Bronconeumol.* 2020; 56 (8): 499-505.
- >> Treatment of portopulmonary hypertension. REHAP registry analysis. *Intern Med J.* 2020. doi: 10.1111/imj.14751.

Acute Lung Injury

- >> Serum miRNA metabolomic and gene expression profiles of peripheral blood transcriptomics, autoantibodies and exosomes identified as biomarkers for pathophysiological mechanisms in ARDS and Covid-19.
- >> Role of nuclear envelope in DNA damage and role of TRPV4 and purinergic receptors during cell stretching.
- >> Beneficial effects of instillation of type II alveolar cells, mesenchymal stem cells, heparin and antithrombin in preclinical models of acute lung damage.
- >> Initiation of a pro-senescent damage response in preclinical models of acute lung damage and in human samples.
- >> Development of in vitro models of ARDS based on extracellular matrix with hydrogels for cells 3D culture by means of bioprinting.
- >> 4D image of ARDS combining Computational Fluid dynamics to understand the mechanism of abnormal flow in ARDS in pigs.
- >> Role of mechanical power versus impulse pressure in ventilator-induced lung damage.
- >> Use of deep learning on the role of asynchrony and prognosis of patients on mechanical ventilation.
- >> Study of post-intensive care syndrome and related cognitive phenotypes.

Pulmonary Fibrosis

- >> Development of TERC^{-/+} CastEIJ mice (TERC heterozygous and telomere length similar to humans), an experimental model with short telomeres, ready to be used in future experimental studies.
- >> Study of the antifibrotic effects of GSE4 peptide administered with nanoparticles in a murine model of pulmonary fibrosis (*FASEB J.* 2021 Mar;35(3): e21422).
- >> MUC1 bioactivation is implicated in pulmonary fibrosis. *Thorax* 2020; 75:132-142.
- >> Genetic characterization studies of “telomeric” pulmonary fibrosis. (*Orphanet J Rare Dis.* 2019; 14:82).
- >> Study of gene expression profile and biomarkers in idiopathic pulmonary fibrosis. *Thorax* 2020;76:152-60; *Am J Respir Crit Care Med.* 2020; 201:564-574; *BMJ Open Respir Res.* 2021;8(1): e000827.

TRAINING PROGRAMME

Coordinator: **Laura Amado Rodríguez**

The healthcare emergency created by SARS-CoV-2 has inevitably conditioned the actions carried out by the Training Programme throughout 2020. The restrictions and quarantines necessary to control the pandemic have resulted in the complete elimination of face-to-face meetings, and all mobility programmes, both for attendance to courses and to carry out training stays.

The main training action of the Programme throughout 2020 has been the XIII Training Days, which for the first time in CIBERES history have been carried out in virtual format. The Conference was held on November 19 and 20, in a morning and afternoon session. This format has made it possible to significantly increase the number of attendees compared to previous years, maintaining a reasonable number of communications taking into account the impact of the pandemic on the scientific activity of the groups:

- >> Number of people registered: 174
- >> Number of communications received and evaluated: 48
- >> Number of selected oral communications: 20
- >> Number of posters: 24
- >> Number of awarded communications: 6

The conference programme, as well as the link to the online sessions and posters, is accessible through the link to the Conference website (<https://jornadasdocencia.ciberes.org/>). As in 2019, the meeting has resulted in the publication of all the abstracts of the communications received, plus two communications of the Mobility Grants for long stays carried out in 2019. These have been published in a Congress Supplement format, in the journal Archives of Bronchopneumology, first quartile. This publication is accessible through the link:

<https://www.archbronconeumol.org/es-vol-56-num-sc2-sumario-X0300289620X00C20>

The cancellation of numerous face-to-face events throughout 2020 has also caused a drastic reduction in the number of endorsements requested. In addition, the majority of endorsements granted have been for online events (1 canceled, 5 online, 4 face-to-face), compared to the 100% being in face-to-face format in the events endorsed by CIBERES in 2019.

Finally, the generalization of the virtual format observed throughout the year has led to the modification of the rules of the training grants in order to include registration to events and online courses among the actions financed. The aim has been to adapt to the changing needs of CIBERES researchers.

PULMONARY BIOBANK PLATFORM

Coordinator: **Cristina Villena Portela**

1. Publications:

Margalida Esteva Socias; Fernando Gómez Romano; José Antonio Carillo Ávila; Alicia Loreto Sánchez Navarro; Cristina Villena Portella. Impact of different stabilization methods on RT-qPCR results using human lung tissue samples. Scientific Reports. *Springer Nature*, 2020. ISSN 2045-2322.

Esteva-Socias M, et al. A. Detection of the EGFR G719S Mutation in Non-small Cell Lung Cancer Using Droplet Digital PCR. *Front Med*. 2020 Nov 13; 7:594900.

Teresa Escámez Martínez, M^a Antonia Fortuño Cebamanos, Máximo Francisco Fraga Rodríguez, Lluís Gallart Millán, Jacobo Martínez Santamaría, Alberto Rábano Gutiérrez del Arroyo, Montserrat Torà Barnadas, Vanesa Val Varela, Cristina Villena Portella. Guía de la Red Nacional De Biobancos para el manejo de muestras humanas en investigación biomédica recomendaciones ante la pandemia de covid-19. Red Nacional de biobancos – Plataforma Biobancos PT17 ISCIII. 12/04/2020.

Cristina Villena. Big Data: Consideraciones en el uso de muestras biológicas humanas. e-salud y cambio del modelo sanitario. Coordinadores: Javier Sánchez-Caro y Fernando Abellán. Colección Bioética y Derecho Sanitario. Fundación Merck.

2. Participation in scientific events:

Biobanking and personalized medicine in oncology - success stories. Europe Biobank Week 2020 - Biobanking for a healthier world. Mesa redonda. EBW 2020 Virtual Conference. 17/11/2020-20/11/2020. Organizador: ESBB y BBMRI-ERIC.

Round Table: "Investigaciones Recientes en FQ". VII Congreso de la Federación Española de Fibrosis Quística. Ponencia invitada. Valencia (Online). Fecha: 12,18-19/12/2020.

Organization of the Webinar "Biosafety measures in the management of COVID-19 in Biobanks". Spanish Association of BioSecurity (AEBioS) and the National Network of Biobanks. 8/4/2020.

"Management of biological samples. Traceability. " III Bioethics and Good Clinical Practice Course. IdISBa for researchers. October 23, 2020. GoToWebinar. IdISBa.

"What is a biobank and what is it for?" CEI-IB IV Training Days: New challenges in research in the context of the Covid-19 pandemic. 20 NOV 2020. Webex. CEI-IB, IdISBa and Dirección General de Acreditación, Docencia e Investigación en Salud CAIB.

3. Research Projects:

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

Coordination of the Biobank Platform (PT17). ISCIII platforms to support R & D & I in Biomedicine and Health Sciences of the Strategic Action in Health Plan 2017-2020. PT17 / 0015/0001. FIS (ISCIII). 2018- 2021. PI: Cristina Villena. Granted: 597.300 €.

Synergia Programme. Interaction between the Wnt and NFkB pathways in inflammatory processes and progression of lung cancer. Analysis of genomic profiles and liquid biopsy. SYN17 / 02. IdISBa. 01/01/2018 until: 31/12/2020. PI: Antonia Obrador, Jaume Sauleda. Collaborators: Cristina Villena, Margalida Esteva. Granted: 55.394 €.

4. Doctoral Theses:

Optimization of tissue samples for the development and validation of disease biomarkers: OPTIMARK project. University of the Balearic Islands. PhD student: Esteva, Margalida. Director: Cristina Villena; Antonia Obrador.

5. Extraordinary activities:

Collaboration with the IdISBa Biobank in the implementation, management and operation of the collection of Biobank COVID19 samples of the Balearic Islands in response to the pandemic. 34,696 samples were collected from 1,374 patients. 11 sample requests were received for COVID-19 projects.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

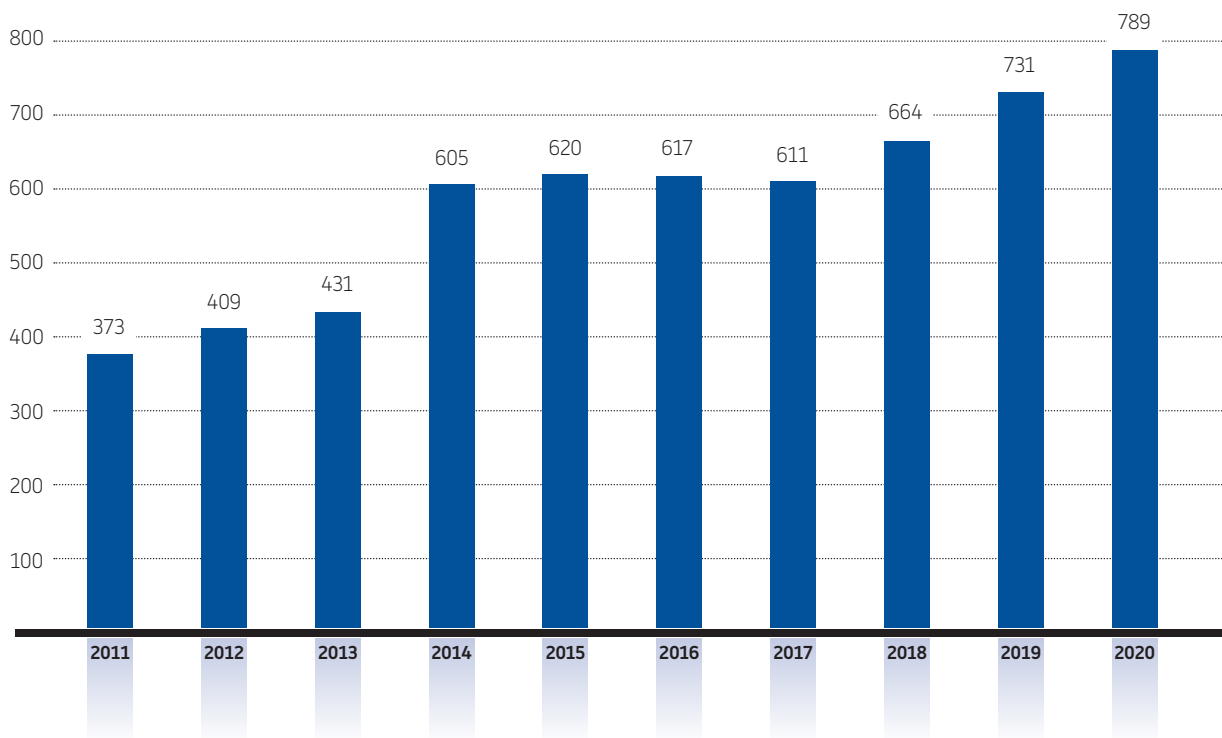
| | |
|---------|-----|
| TOTALES | 789 |
| Q1 | 391 |
| D1 | 156 |

Collaborations

| | |
|---------|-----|
| CIBERES | 196 |
| CIBER* | 159 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|----------|---|
| 25,0940 | Villar J., Ferrando C., Martinez D., Ambros A., Munoz T., Soler J.A. et al. <i>Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. The Lancet Respiratory Medicine.</i> 2020;8(3):267-276. |
| 25,0940 | Guillen-Guio B., Lorenzo-Salazar J.M., Ma S.-F., Hou P.-C., Hernandez-Beeftink T., Corrales A. et al. <i>Sepsis-associated acute respiratory distress syndrome in individuals of European ancestry: a genome-wide association study. The Lancet Respiratory Medicine.</i> 2020;8(3):258-266. |
| 25,0940 | Martinez-Garcia M.A., Campos-Rodriguez F., Gozal D. <i>Obstructive sleep apnoea in acute coronary syndrome. The Lancet Respiratory Medicine.</i> 2020;8(4):e15. |
| 17, 6790 | Torres A., Loeches I.-M., Sligl W., Lee N. <i>Severe flu management: a point of view. Intensive Care Medicine.</i> 2020. |
| 17, 6790 | Penuelas O., Muriel A., Abaira V., Frutos-Vivar F., Mancebo J., Raymondos K. et al. <i>Inter-country variability over time in the mortality of mechanically ventilated patients. Intensive Care Medicine.</i> 2020. |
| 17, 6790 | Garnacho-Montero J., Martin-Loeches I. <i>Clinical management of sepsis can be improved by artificial intelligence: no. Intensive Care Medicine.</i> 2020. |
| 17, 6790 | Huang D.T., Ramirez P. <i>Biomarkers in the ICU: less is more? Yes. Intensive Care Medicine.</i> 2020. |
| 17, 6790 | Martin-Loeches I., Pova P., Nseir S. <i>A way towards ventilator-associated lower respiratory tract infection research. Intensive Care Medicine.</i> 2020. |
| 17, 6790 | Trahtenberg U., Slutsky A.S., Villar J. <i>What have we learned ventilating COVID-19 patients? Intensive Care Medicine.</i> 2020;46(12):2458-2460. |
| 17, 4520 | Masa J.F., Mokhlesi B., Benitez I., Mogollon M.V., De Terreros F.J.G., Sanchez-Quiroga M.A. et al. <i>Echocardiographic changes with positive airway pressure therapy in obesity hypoventilation syndrome long-term pickwick randomized controlled clinical trial. American Journal of Respiratory and Critical Care Medicine.</i> 2020;201(5):586-597. |

» CIBERES Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
|  Agustí García Navarro, Álar | 46 | 34 | 12 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Álvarez Martínez, Carlos José | 5 | 5 | 3 | Servicio Madrileño de Salud | Madrid |
|  Ardanuy Tisaire, María Carmen | 11 | 4 | 3 | Fundación IDIBELL | Barcelona |
|  Barbé Illa, Ferrán | 72 | 38 | 15 | Instituto de Investigación Biomédica de Lleida. Fundación Dr. Pifarre | Lleida |
|  Barberá Mir, Joan Albert | 17 | 8 | 2 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Blanch Torra, Lluís | 51 | 26 | 6 | Corporación Sanitaria Parc Taulí | Barcelona |
|  Cardona Iglesias, Pere Joan | 22 | 15 | 4 | Fundación Instituto de Investigación Germans Trias i Pujol | Barcelona |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
| Farré Ventura, Ramon | 18 | 9 | 2 | Universidad de Barcelona | Barcelona |
|  Fernández Muñoz, Ángel Esteve | 29 | 9 | 6 | Fundación IDIBELL | Barcelona |
| García González, Pedro | 6 | 4 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  García Río, Francisco José | 47 | 34 | 12 | Servicio Madrileño de Salud | Madrid |
|  Garmendia García, Juncal | 5 | 3 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Gea Guiral, Joaquim (*) | 32 | 22 | 1 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Jiménez Castro, David | 15 | 9 | 2 | Servicio Madrileño de Salud | Madrid |
|  López-Campos Bodineau, José Luis | 61 | 41 | 19 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Lorente Balanza, José Ángel | 14 | 5 | 3 | Servicio Madrileño de Salud | Madrid |
|  Martín Montañés, Carlos | 9 | 7 | 3 | Universidad de Zaragoza | Zaragoza |
| Masa Jiménez, Juan Fernando (**) | 26 | 12 | 5 | Fundación Instituto de Investigación Germans Trias i Pujol | Cáceres |
|  Monsó Molas, Eduard | 18 | 5 | 1 | Corporación Sanitaria Parc Taulí | Barcelona |
| Morcillo Sánchez, Esteban (***) | 4 | 2 | 0 | Universidad de Valencia | Valencia |
|  Montserrat Canal, Josep María | 15 | 8 | 3 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Mulla Mir, Joaquín | 58 | 31 | 19 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Muñoz Albaiceta, Guillermo | 14 | 7 | 0 | Corporación Sanitaria Parc Taulí | Madrid |
|  Muñoz Gall, Xavier | 85 | 39 | 14 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Muñoz García, Patricia | 55 | 20 | 8 | Servicio Madrileño de Salud | Madrid |
|  Peces Barba Romero, Germán | 22 | 12 | 4 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Pérez Vizcaíno, Francisco | 10 | 8 | 5 | Universidad Complutense de Madrid | Madrid |
|  Pozo Abejón, María Victoria del | 20 | 11 | 7 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Rello Condomines, Jordi | 65 | 24 | 11 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Ruiz Cabello Osuna, Jesús | 16 | 12 | 7 | CIC biomaGUNE | Guipúzcoa |
|  Torres Martí, Antoni | 103 | 48 | 19 | Hospital Clínico y Provincial de Barcelona | Barcelona |
|  Villar Hernández, Jesús | 45 | 22 | 16 | Fundación Canaria Instituto de Investigación Sanitaria de Canarias | Canarias |

(*) Group PI replaced by Barreiro Portela, Esther

(**) Group PI replaced by Corral Peñafiel, Jaime

(***) Group PI replaced by Cortijo Gimeno, Julio

PATENTS OWNED BY CIBER 2020

Patents granted

- EP3234185 (Europa) Fecha : 08/04/2020 y 6810834 (Japon) Fecha : 21/07/2020. “*Method for predicting response to continuous positive air pressure treatment*” Inventores: Barbé Illa, Eduard Ferran; Sánchez de la Torre, Manuel; Gozal ,David; Khalyfa, Abdelnaby; Sánchez de la Torre, Alicia; Martínez García, Miguel Angel. Titulares: IRB Lleida 53,85%/ CIBER 38,46%/ Fundación Hospital la Fe 7,69%
- CA2876527 (Canada) Fecha: 21/04/2020 “*Micobacterias inactivadas para su uso por vía oral en la prevención de la tuberculosis*”. Inventors: Cardona Iglesias, Pere-Joan; Vilaplana Massaguer, Cristina; Marzo Escartín, Elena. Titulares: Institut germansTries i Pujol (IGTP) 66,7%/ CIBERES 33,3% Licenciada a Manremyc.

Priority Applications 2020

- EP20383140.9 Fecha: 22/12/2020 “*In vitro method for predicting mortality in COVID-19 patients*” Titulares: (IECSCYL-IBSAL)/Kelvin, Mr. David Joseph/Gerencia Regional de Salud de Castilla y León/(FIBHGM)/ Universidad de Valladolid/IDIBAPS/CIBER/UB/Hospital Clinic. Inventors: Bermejo Martín,. Jesús Francisco; Almansa Mora,. Raquel; Santos Tedim Sousa Pedrosa,. Ana Sofia; Bustamante Munguira,. Elena; Tamayo Lomas, Luis Mariano; Aldecoa Álvarez- Santullano, César; Dominguez-Gil Gonzalez, Marta; Eiros Bouza, Jose María; Kelvin,. David Joseph; Barbé Illa, Ferrán;Torres Martí, Antoni; Micheloud Giménez, Dariela Edhit; Gómez García, Jose Manuel; González Rivera, Milagros.

National Phase Applications 2020

- PCT/EP2019/053586. Fases nacionales Europa. Fecha: 11 /9/2020 “*Method and apparatus for the cardiovascular assessment of a subject in need thereof*” Fecha : 13/2/2019 Inventors: Santos Oviedo,. Arnoldo de Jesús; Ruiz-Cabello Osuna, Jesús María. Titulares: CIBER 90%; CIC Biomagune 10%.
- PCT/EP2019/064885. Fases nacionales Europa. Fecha: 31/12/2020 “*In vitro method for the diagnosis or detection of non-tuberculous mycobacteria*” Fecha: 6/6/2019 Inventores: Dominguez, Jose; Latorre, Irene; Torrelles Jordi. Titulares: IGTP 65% , OSU 30%, CIBER 5%.
- PCT/EP2019/066055 Fases nacionales USA. Fecha: 18/12/2020 “*Identification of metabolomic signatures in urine samples for tuberculosis diagnosis*” Fecha: 18/6/2019 Inventors: Dominguez, Jose; Prat Aymerich, Cristina; Izquierdo, José Luis. Titulares: IGTP 55% CIBER 45%.

Licenses 2020

- PCT/EP2015/080183 Licenciada a 17/09/20 a Onira Research S. L “*Method for predicting response to continuous positive air pressure treatment*”. Inventors: Barbé Illa, Eduard Ferran; Sánchez de la Torre, Manuel; Gozal, David; Khalyfa, Abdelnaby; Sánchez de la Torre, Alicia; Martínez García, Miguel Ángel. Titulares: IRB Lleida 53,85%/ CIBER 38,46%/ Fundación Hospital la Fe 7,69%.

CLINICAL GUIDES

- *ERS statement on chest imaging in acute respiratory failure.*
- *Framework to Support the Process of Decision-Making on Life-Sustaining Treatments in the ICU: Results of a Delphi Study.*
- *Nebulised heparin as a treatment for COVID-19: scientific rationale and a call for randomised evidence.*
- *International variation in the management of severe COVID-19 patients.*
- *Hospital-Acquired Pneumonia. Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) Guidelines*
- *Updated guidance on the management of COVID-19: From an american thoracic society/european respiratory society coordinated international task force.*
- *Update of the treatment of nosocomial pneumonia in the ICU.*
- *Management of Community-Acquired Pneumonia in Immunocompromised Adults: A Consensus Statement Regarding Initial Strategies.*
- *Summary of recommendations and key points of the consensus of Spanish scientific societies (SEPAR, SEMICYUC, SEMES; SECIP, SENEQ, 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.*
- *Evaluation of the quality of evidence supporting guideline recommendations for the nutritional management of critically ill adults.*
- *Guide of the National Network of Biobanks for the management of human samples in biomedical research. Recommendations for the COVID-19 pandemic.*



ciberesp



**EPIDEMIOLOGY
AND PUBLIC HEALTH**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Marina Pollán Santamaría

The pandemic has conditioned the activity of CIBERESP researchers. As with the professionals of the health-care system, Spanish epidemiologists have been involved in responding to this important public health problem. More than 50% of the CIBERESP groups work in administrations and institutions directly related to the management of the pandemic. In addition, many of the national experts who have reported or advised in different areas are part of our network.

Among the collaborative activities of COVID-19, in addition to the actions carried out by the subprogramme for influenza and respiratory viruses of PREVICET, we highlight the National Sero-epidemiological ENE-COVID Study and the MINDCOVID project to measure the impact on mental health. CIBERESP researchers have studied the first epidemic wave, achieved projects in different COVID calls with different objectives (modelling of the pandemic, seroprevalence in vulnerable populations, relationship between confinement and gender violence, molecular epidemiology, effect of confinement in adolescents and their mothers, detection of SARS-CoV-2 in the environment, among others) and have contributed to providing information on the effect of preventive measures, and the adequacy of healthcare procedures (MAPAC subprogramme).

Among the activities not related to COVID-19, the scientific production of the INMA cohort of MCC-Spain stands out, as well as the collaborative publications on other communicable diseases of the PREVICET programme, the collaboration with CIBEROBN in the PREDIMED studies; participation in the European Human Biomonitoring proposal, the Energy Poverty and Gender Violence lines, the WORKSS project, the virtual library of BibliINDICA healthcare activity indicators, the activity of the international BiblioPro platform and new strategic lines of “Resistance to antimicrobials”, “Real World Data” and “Efficiency and equity of the healthcare system”.

In 2020, we launched a call for intramural projects to encourage the collaboration of CIBERESP groups among each other and with other CIBER areas and to facilitate the leadership of young researchers, selecting the 5 best according to the evaluation carried out by our External Scientific Advisory Committee.

Due to the pandemic, the training programme, coordinated by Beatriz Pérez-Gómez, has not been able to carry out most of the planned activities, except for the funding of scholarships for young researchers to attend the meeting of the Spanish and Portuguese Epidemiology Society and the CIBERESP communications table at said meeting.

Finally, worth highlighting is the participation in the call for IMPaCT Personalized Medicine, in which CIBERESP leads the project to create a national cohort, with the participation of the rest of the CIBER areas, the National Health System and the National Institute of Statistics.

May this brief summary serve as recognition of all the work carried out by the CIBERESP researchers during such a difficult year.



PROGRAMMES

PROGRAMME 1: EPIDEMIOLOGY AND CONTROL OF CHRONIC DISEASES

Coordinator: **M^a José Sánchez Pérez**

The Programme has continued with the scientific activity of the three strategic subprogrammes.

MCC-Spain

The MCC-Spain project, led by Manolis Kogevinas and Marina Pollán, is being used as a study of prognostic factors in patients with colorectal, breast or prostate cancer. The follow-up of cases and controls to know their vital status has been completed and the first results of quality of life in breast cancer have been presented.

In 2020, 17 scientific articles have been published in indexed journals.

The control population of MCC-Spain will provide information on the effects of the pandemic in the CONTENT project financed by La Caixa (PI: Manolis Kogevinas).

Gen-risk

The Gen-risk project, led by Victor Moreno, funded by the AECC (Spanish Association Against Cancer), relies heavily on the MCC-Spain study. Its objective is to improve cancer prevention through personalized strategies, searching for biomarkers to identify which people have a higher risk of developing colorectal, breast, stomach, prostate cancer and chronic lymphocytic leukemia, in order to better guide the prevention of these tumors, reducing both morbidity and the social and economic impact they entail.

The pandemic has caused a delay in the genotyping of the samples. As an alternative, epidemiological and genetic data have been requested from the UK Biobank to validate the results obtained in the studies carried out in Spain and to develop instruments for Mendelian randomization analysis.

Epidemiological Surveillance of Cancer

The Epidemiological Surveillance of Cancer subprogramme, coordinated by M^a José Sánchez and Pablo Fernández, has developed a remote GEO-CIBER application for the geocoding of 10,000 cases of breast, colon-rectum and lung cancer, included in the Multilevel Population Study of Socioeconomic Inequalities in the Geographical Distribution of Incidence, Mortality and Survival of Cancer in Spain (ISCIII), which assesses the impact of socioeconomic inequalities on the incidence and survival of the 3 most common cancers in Spain.

In 2020, a strategic project financed by the AECC Scientific Foundation was obtained: *High Resolution Study of Social Inequalities in Cancer: a population-based multilevel study (HiReSIC)*, in collaboration with CIBERONC and the Spanish Network of Cancer Registries (REDECAN). A CIBERESP-AECC agreement has also been established to create a Cancer Epidemiological Information System in Spain, in collaboration with REDECAN. In addition, 2 collaborative scientific articles have been published on socioeconomic inequalities in colorectal cancer survival.

Seroepidemiological survey of the SARS-CoV-2 virus infection in Spain (ENE-COVID)

The Lancet has published the design, methodology and results of the ENE-COVID Study, coordinated by Marina Pollán, a population-based cohort study to investigate seropositivity for SARS-CoV-2 in the non-institutionalized Spanish population, confirming an immunity of 5% of the Spanish population after the first epidemic wave.

CIBERESP has led and published results of the ENE-COVID study in the *British Medical Journal*, estimating that the lethality of SARS-CoV-2 infection in non-institutionalized population in Spain is between 0.8% and 1.1%.

P2. COMMUNICABLE DISEASE PREVENTION, SURVEILLANCE AND CONTROL (PREVICET)

Coordinator: **Pere Godoy García**

The Programme has carried out the scientific activity of the strategic subprogrammes and lines of research:

Flu and respiratory viruses subprogramme

The project on the effectiveness of the flu and pneumococcal vaccination (PI: Àngela Domínguez, PI19/00354) has been started with researchers from PREVICET groups and other CIBERESP groups, and the rest of the studies on the effectiveness of the flu vaccine have been ongoing and have generated 6 articles on the flu.

Within the framework of the National Epidemiological Surveillance Network, PREVICET have participated in the special surveillance of COVID-19 with the description of the first epidemic wave of COVID-19 in Spain in *Eurosurveillance* (PI: Amparo Larrauri) and collaborated in the study JAN-COVID. Deserving special mention is the participation in the I-MOVE-COVID-19 (Horizon 2020) project to strengthen the surveillance of COVID-19.

Immunopreventable diseases subprogramme

An article on the whooping cough project has been published in the EID on the effectiveness of chemoprophylaxis with Azithromycin in household contacts of cases. Work has been done on projects on invasive pneumococcal disease (PI: 17/00337) and molecular epidemiological surveillance of *Streptococcus pneumoniae* and determination of its invasiveness. *Quo vadis, Quo invadis?* study (PI19/00104) with the defense of a doctoral thesis and publication of 6 articles. We continue working on the project on nasopharyngeal microbiota and rhinovirus infection (P17/00349) and on the "Study of vaccine failure in immunopreventable viral diseases", led by Carmen Muñoz-Almagro and Àngela Domínguez.

Viral hepatitis subprogramme

CIBERESP has collaborated with CIBEREHD in the publication on risk factors and seroprevalence of hepatitis B and C virus infection and work continues collaboratively on the project of traceability of hepatitis E virus infection through epidemiological study and the study of complete viral sequences.

Tuberculosis subprogramme

The project on risk factors for tuberculosis in contacts of pulmonary TB cases (PI18/01751, PI: Pere Godoy) has been collaboratively worked on and preliminary results have been presented at the International Tuberculosis Day 2020 in Barcelona as well as communications in the 1st online congress of the SEE (Spanish Society of Epidemiology). The protocol of the collaborative project on risk factors for infection in children of immigrant families visiting relatives in countries of origin has also been published.

Outbreaks subprogramme

Results have been presented in four articles of the collaborative project on Norovirus outbreaks (project PI16/02005).

Emerging and re-emerging diseases subprogramme

PREVICET researchers continue to work on the MARVEEE project to make risk maps of vector-borne diseases (2 articles) and the environmental factors of transmission of mosquito-borne pathogens in Europe have been reviewed (*Environmental Research*). We have also analyzed the distribution in Spain of *Culex pipiens*, and other pathogens, estimating the impact that climate change may have on their distribution (*Environmental Research*), led by Jordi Figuerola, Diana Gómez Barroso and Cristina Rius. Finally, work has continued on the project “Parallel evolution in Iberian viruses and bats: potential relationship with emerging viral diseases” (PI: Juan Emilio Echevarría).

PROGRAMME 3: BIOLOGICAL AND BEHAVIORAL DETERMINANTS IN THE CONTRACTION AND SPREAD OF COMMUNICABLE DISEASES IN VULNERABLE POPULATIONS

Coordinator: **Juan Carlos Galán Montemayor**

Coinciding with the change in the management of the programme and the COVID-19 pandemic, the activity, challenges and objectives for 2020 have been considerably altered. In the more general and cross-cutting objectives of the programme, a new subprogramme on antimicrobial resistance (including antibiotics, antivirals and antiparasitics) has been created, following the recommendations of the external advisory group.

The COVID-19 pandemic has hindered the development of the initiatives initially proposed in the subprogrammes, but others have been developed related to the transmission and acquisition of infectious agents and their dissemination in the general population. Four groups of this programme have led national research projects on this virus from different perspectives (molecular epidemiology, epidemic modeling, prognostic biomarkers and prolonged COVID). Three of these 4 projects are collaborative actions between members of the same programme, between programmes or interCIBER. Among these collaborative projects, worth highlighting is the project on the molecular epidemiology of SAR-CoV-2, the SeqCOVID project, stemming from the national network for the surveillance of variants of SARS-CoV-2, and promoted by the Ministry of Health itself and the Center for Coordination of Health Alerts and Emergencies. In addition, members of this programme have led the protocol-guide for the COVID diagnosis of the Spanish Society of Infectious Diseases and Clinical Microbiology.

Actions of the Infectious Diseases Transmissible through Organic Fluids subprogramme

The subprogramme presented a spontaneous table at the I Virtual Congress of the SEE in October 2020, moderated by one of the coordinators of the subprogramme. The table had the general title “Emergence and re-emergence of Sexually Transmitted Infections: challenges for Public Health”. In this table, 3 members of the subprogramme participated who presented collaborative works with other researchers of the subprogramme. There are 5 active projects on infectious diseases in sexually transmitted infections, the relationship to reproductive health and their relationship with cancer. One of them has the cooperation of the researchers of the subprogramme. Members of this subprogramme have published collaborative works on this topic not only with members of the programme itself, but also with members of programme 2. Collaborative projects have been initiated to quantify the impact of COVID in chronic infectious disease screening programmes.

Actions of the Antimicrobial Resistance subprogramme

This subprogramme has researchers with great international impact, such as researchers who lead or collaborate in European networks (surveillance network in gonococci or plasmid transmitted resistance). However, the fact that its beginning coincided with the COVID-19 pandemic has not facilitated interactions between groups. There are common projects among the groups that have served as the basis for the development of this subprogramme, such as the collaborative project on the evolution of antibiotic resistant bacteria, as well as publications among these researchers, based on mathematical modeling to predict the emergence of resistance. Collaborative projects have been started to estimate the impact of COVID on the selection of resistant bacteria in ICUs.

PROGRAMME 4: SOCIAL DETERMINANTS OF HEALTH

Coordinator: **M^a José Sánchez López**

Gender violence subprogramme

During 2020, the European project “Masculinities and violence against women among young people: identifying discourses and developing strategies for change using a mixed methods approach” was promoted. In addition, 4 projects obtained in national competitive calls are active. It should be noted that one of them (*Sexual Violence associated factors and perceptions among youth*), has been achieved in the CIBERESP call, this being a collaborative project in which 4 groups of the Programme participate. Moreover, in 2020, more than 10 collaborative articles have been published or are in the process of being published. An agreement has been reached with representatives of the Unidad de Investigación del Ministerio de Interior (Research Unit of the Ministry of the Interior) to carry out two studies based on the VIOGEN registry to analyze the impact of confinement on intimate partners violence against women. It should also be noted that researchers from the Programme have been called to form part of committees of international experts, such as the GREVIO group of the Council of Europe (<https://www.coe.int/en/web/istanbul-convention/grevio>) or the committee of experts in charge of the design of the new Sexual Health survey.

Energy Poverty and Health subprogramme

The Energy Poverty and Health subprogramme has made it possible to promote a new line of research, through collaboration between various groups in the programme, as well as with researchers from various institutions. In its last year, and despite the fact that most of the researchers in this subprogramme had to dedicate themselves to the pandemic, among the products derived from this subprogramme, the collaborative articles published in various scientific journals stand out, as well as the spontaneous table on energy poverty and

health held at the last SEE congress, with the presence of multiple communications derived from the subprogramme. It should also be noted that the work entitled “Geographical inequalities of energy poverty in the city of Barcelona” obtained the CIBERESP award for the best communication presented by young research staff. Finally, and as an innovative product, it should be noted that a pilot website has been designed that will allow to interactively view and consult different indicators on energy poverty and health.

Real World Data subprogramme

This subprogramme has published various collaborative articles in 2020, many of them analyzing data related to the pandemic, such as “Effects of long-term exposure to air pollutants on the spatial spread of COVID-19 in Catalonia, Spain” (*Environmental Research*), or “Association between the New COVID-19 cases and air pollution with meteorological elements in nine counties of New York State” in *IJERPH*. Among the collaborative projects obtained this year, to be highlighted are the international project “Seroprevalence and the socioeconomic and health impact of COVID-19 on general and vulnerable populations” obtained in the *Pfizer Global Medical Grants*, the *COVID-19 competitive Grant programme*, and the project “IMPSEROCOVID19, impact and seroprevalence of the COVID-19 disease”, obtained in the call of the SUPERA COVID-19 fund.

PROGRAMME 5: EPIDEMIOLOGY AND PREVENTION IN ENVIRONMENTAL AND OCCUPATIONAL HEALTH

Coordinator: **Marieta Fernández Cabrera**

Nutrition and Health

1. Collaboration with CIBEROBN in the PREDIMED-PLUS trial, evaluating the efficacy of a hypocaloric Mediterranean diet and exercise on cardiovascular risk (20 articles). 2. Role of diet in child neurodevelopment and obesity: demonstrating the benefit of fish intake on child attention capacity (*Int J Epidemiol*) and of the Mediterranean diet against obesity (*Int J Obesity*). 3. Influence of prenatal and postnatal nutritional formulas on metabolic programming and infant development (*Nutrients; Children*).

Environment and Health

Influence of the urban exposome (pollution, green spaces, noise and buildings) on obesity and blood pressure at an early age, showing the need to implement prevention programs aimed at the young and more vulnerable population (*JAMA New Open; Env Poll; Env Int; EHP*). Other findings:

- a) Relationship between pollution, organophosphate pesticides and electromagnetic fields and brain connectivity and morphology (*EHP; Environ Res; Env Int*).
- b) Markers of longevity and exposure to green spaces and pollution (*Environ Pollut; EHP; Int J Environ Res Public Health; Environ Int; IJERPH*).
- c) Climate change and mortality in 650 cities of the world (*BMJ. Environ Res*).
- d) DNA methylation as a marker of exposure to air pollution and smoking in pregnancy and early years, and its association with neurological development (*BMC Med. Psycho Med. Transl Psychiatry. Environ Int*).
- e) Identification of molecular biomarkers (DNA, sRNAs and proteins) in complex diseases: cancer, neurodegenerative diseases (Huntington).
- f) Participation with groups from other programmes in the “StoP Consortium: risk factors in stomach cancer”, and in the global initiative “NCD Risk Factor Collaboration”.

Biomonitoring of human exposure

In the European project HBM4EU (European Human Biomonitoring Initiative), heading WP14 (Effect biomarkers):

1. Implementation of effect biomarkers to clarify the causal pathways between exposure and adverse health effects (Environ Int). 2. Analysis of the impact of exposure to pollutant mixtures on human health: theoretical bases (Environ Int) and “proof of concept” (Reprod Toxicol).

Strategic subprogramme: INMA Project “CHILDHOOD AND THE ENVIRONMENT”

1- Improvement of child development and Disease Prevention:

- >> Evidence that the infant’s weight gain in the first years determines the risk of wheezing and lung development (Peralta *Eur Respir J*; Derakhshan *Lancet Diabetes Endocrinol*).
- >> Effects of pre- and postnatal exposure to metals/phenols/phthalates on child development (Llop *Eur J Epidemiol*; Lozano, Soler-Blasco, *Mustieles Environ Int.*; Zhang *JAMA New Open*).
- >> Social and family determinants of risk of child poverty and social exclusion (Gonzalez et al. 2020).
- >> Incidence of whooping cough in children before and after the introduction of vaccination in pregnancy (Arnedo-Pena 2020).

2- Research in INMA and COVID-19:

- >> GWAS COVID-19: providing population controls for COVID-19 cases (GSA array).
- >> Seroepidemiological study.
- >> Confinement due to COVID-19 and obesity in adolescents and their mothers.
- >> Predictive factors of perceived stress in adolescents and their mothers.
- >> Detection of SARS-CoV-2 in atmospheric aerosol, in outdoor and indoor environments, as a surveillance and alert tool for SARS-CoV-2 transmission.

PROGRAMME 6: HEALTH SERVICES EVALUATION

Coordinator: **Antonio Serrano Blanco**

The activity of P6 is divided into two strategic collaborative sub-programmes.

Estimation of the health and social burden of chronic diseases

We highlight the launch of the project “MINDCOVID-Mental health Impact and Needs associated with COVID-19: a comprehensive national evaluation in Spain” (www.mindcovid.org) with 10 CIBERESP groups, 6 CIBERSAM, 1 CIBERCV and 7 Networks groups. MINDCOVID is a longitudinal study in 3 populations: health workers (n~10,000), COVID-19 patients (n=2,500) and close contacts (n=3,500). The online platform of the WORKSS project -Evaluation of the impact of social benefits on the relationship between work careers and cause-specific mortality has also been activated in a cohort of Social Security affiliates in Spain 2004-2016 (<https://www.upf.edu/cisal/workss>), with information on 753,341 members (Group PIs: C. Borrell, V. Serra and FG Benavides). A new virtual library of healthcare quality indicators and methodological tools (BiblioINDICA) has been conceptualized (PI groups V. Serra and J. Alonso) and a Cost Action CA16216-OMEGA-NET has been initiated (<http://omeganetcohorts.eu>) by the group led by FG Benavides.

Health status measurement

We highlight the development of the BiblioPRO International website (www.biblioprointernational.org), (as an expansion to a repository for Europe and other countries (CIBERESP group PIs: I. Ferreira, J. Alonso, V. Serra and FG Benavides; CIBERSAM PI JM Haro; G509 CIBERNED; G13, G14 and G10 REDISSEC) and the project “Measuring mental well-being as an indicator for monitoring population health” (Group PIs: C. Borrell and J. Alonso).

A new subprogramme “Efficiency and equity of the healthcare system” has been started, where we start projects of economic evaluation and therapeutic adherence with the collaboration of researchers from P1, P6 and P7 of CIBERESP, and of the redIAPP. We participate in the EquityCancer-LA project (Improving equity in access to early cancer diagnosis: implementation research in different health systems in Latin America) of the H2020 initiative (CIBERESP PI A. Serrano and CIBERSAM PI JM Haro) and in Genrisk of P1 with the project “Genetic and metabolomics screening towards precision medicine in cancer prevention”.

Dr. Jordi Alonso has stood out in the list of the “highest cited researchers (Psychiatry / Psychology) 2020” (WOS ranking).

Dr. Maria Rubio Valera has obtained an *ERC-Starting Grant*: “IMA-cRCT Efficacy and efficiency of the intervention of initial adherence to drugs: randomized controlled trial and economic model”, financed by the EU with more than one million euros.

The groups have published more than 80 scientific articles (mostly in Q1 journals) useful for improving health care and facilitating clinical, organizational, research or service planning management. We highlight 4 publications in *The Lancet*.

We have developed several transfer products such as the ERN clinical practice guidelines and other clinical decision support tools and reports from the Spanish Network of Health Technology Assessment Agencies, the Diputació de Barcelona (Barcelona City Council) or the Department of Health of Catalonia.

Finally, we have initiated the fusion of P6 and P7. The resulting programme will have 8 groups.

PROGRAMME 7: CLINICAL EPIDEMIOLOGY

Coordinator: **José Ignacio Pijoan Zubizarreta**

The programme has a strategic subprogramme, MAPAC, and two additional lines of research.

MAPAC (Improvement of the Appropriateness of the Clinical and Healthcare Process)

This subprogramme is based on the hospital MAPAC commissions led by programme researchers. During the year 2020, it has continued its work to identify practices of low clinical value based on the scientific evidence available and has established recommendations for the appropriateness of practice in more than 30 healthcare practices. This year has been focused heavily on aspects related to COVID. Their evaluations and recommendations have informed clinical decisions at the hospital level: use of Remdesivir, Tocilizumab and corticosteroids in hospitalized patients, validity of rapid antigenic tests, usefulness of prognostic models of admitted patients, etc. through MAPAC interaction in the multidisciplinary COVID working groups of its centers. Work on information dissemination and training has been started through the translation and adaptation of the book “Treatments on trial” that is going to be disseminated this year and the holding of specialized dissemination workshops and seminars: “Evidence in times of COVID: where to find it” to make known the activities carried out at the international level regarding the updating and summarizing of the evidence generated on COVID-19. The results of a multicenter survey on the attitude of NHS professionals towards low-value practices have been published. Funding has been obtained from a cooperative project to promote shared

decision-making with patients in the area of prostate cancer screening, an area in which the programme is also currently developing a cooperative project to evaluate the validity of opportunistic screening with PSA.

The synthesis research line has published several articles on methodological development in relation to conducting systematic reviews of diagnostic tests, screening and prognostic studies. Moreover, it has designed, validated and published a “toolbox” for the generation of systematic reviews and has continued its publications of works on the effect of gender in synthesis research. In addition, it has developed methodological transfer through the workshop “What do we mean when we refer to prognosis” for the interpretation of studies for the evaluation of prognostic factors and their inclusion in systematic reviews of the scientific literature.

The methodological development research line has obtained intramural funding from CIBERESP in a project in which five groups from the programme are participating “Redesign of Bin-CE: a free tool to calculate the Sample Size Requirement for Randomized Clinical Trials using a Composite Endpoint. Bin-CEII Study”. The aim of the programme is to optimize the calculation of the sample size in clinical trials the results of which are presented in the form of composite variables. A web tool has been made available that allows an adaptation of said calculation, considering the degree of correlation between the component result variables.

Finally, within a cooperative project financed by the ISCIII, more than 3,000 healthcare professionals from the NHS have been trained and accredited in the use of good clinical practice for the prevention of neonatal sepsis associated with the use of central vascular lines.

TRAINING PROGRAMME

Coordinator: **Beatriz Pérez-Gómez**

The Training Programme has maintained in its programming for 2020 its two basic lines of action: mobility actions, aimed at facilitating contact and work with other national or international groups, and further training actions, aimed at improving and rewarding quality of scientific works or to promote their dissemination in Public Health forums.

Due to the pandemic, the calls for mobility grants, for both national and international stays, had to be suspended.

Within the further training grants, the Meeting for Excellence in Research in Public Health that CIBERESP organizes annually in the Summer School of Public Health in Lazareto of Maó in Menorca, extramural in nature, and a tool to promote collaboration with other CIBER areas and promoting quality research in Public Health, was also cancelled.

On the other hand, CIBERESP's collaboration with the Spanish Epidemiology Society (SEE) has been maintained with the funding of the Awards for the 10 best communications presented by young research staff at the SEE Annual Scientific Meeting, which is held together with the Congress of the Portuguese Association of Epidemiology, Ibero-American Congress of Epidemiology and Public Health SESPAS/SEE. This year, for the first time, it was held in virtual format. The award includes a diploma and covers the registration fee of the award-winner at the meeting of the following year. Also, within this first virtual congress of the SEE held in October 2020, the CIBERESP impromptu roundtable took place. The Award to the best communications was presented to the CIBERESP table, consisting on this occasion in the financing of the registration fee of the 7 best communications selected for presentation.

The Training Programme also encourages that training or scientific activities carried out by other entities establish special, more favorable conditions for CIBERESP members to participate.

PLATFORMS

BIBLIOPRO 2020

BiblioPRO is a virtual repository of Patient Reported Outcomes (PROs). Its mission is to promote the measurement of PROs through: exhaustive inclusion and standardized information on instruments in Spanish through systematic literature reviews; scientific evaluations; and specialised training.

The Scientific Committee includes 17 researchers from 14 different institutions (including CIBERESP, CIBERSAM, CIBERNED and REDISSEC).

Repository:

- >> Registered users: 2,682 new users (cumulative total: 22,128).
- >> Instruments: 294 new instruments identified (total: 2,236 instruments).
- >> Monthly website visits: 59,787 sessions (a decrease of 20,000 visits compared to 2019, especially during the COVID confinement, although the rebound percentage decreased by 18% indicating greater interest in web content).
- >> Sublicenses: 619 licenses requested and 452 granted (cumulative total: 3,471).
- >> Systematic revision: cleansing of 461 instruments and elimination of 85 completed (due to duplication, not meeting inclusion criteria or not having a Spanish version).

BiblioPro International:

- >> Publication of the new BiblioPRO International website (www.biblioprointernational.org) in September 2020.
- >> New distribution agreements for the following instruments:
 - European versions of the SF Health Surveys (QualityMetric): 59 languages.
 - Test of adherence to inhalers (Chiesi, SEPAR), 24 languages.

Pre-agreement with the University of Warwick: sublicense in Spanish of the *WEMWBS-Warwick-Edinburgh Mental Well Being Scale*.

EMPRO Platform:

- >> The new online platform for the EMPRO tool has been published (<https://empro.imim.es>).
- >> Its use only requires a request via email to organize the evaluation, upload of materials and give access to evaluators.
- >> International pilot test on instruments for oral health in older adults with 13 instruments.
- >> Cross-cultural adaptation for use in China (*EBM Centre of Tsinghua University School of Clinical Medicine*: BiblioPRO Scientific Committee supervision).

Competitive research projects:

- >> “Application of PRO instruments in Spain” (PI16 / 00130-ISCIH / FEDER), 2017-2021. PI Olatz Garin), Team: CIBERESP and BiblioPRO Scientific Committee.
- >> “CEAD-Contextualizing Evidence for Action in Diabetes in low-resource Settings” (H2020 European Re-

search Council 2018 Starting Grant (Grant number: 804761 — CEAD). PI: LA Parker. Participation: Diabetes Health Profile validation (DHP-18).

- >> “SISAQOL-Setting International Standard in Analyzing Patient-Reported Outcomes and Quality of Life endpoints. (IMI-Project: 945052) PI: Andrew Bottomley. Participation: Advisory Committee of the international consortium.

Training and dissemination:

- >> Completion of 4 courses on “Results Reported by Patients” (Gilead and Gaspar Casal Foundation).
- >> Presentation of the video “BiblioPRO and the Results Perceived by Patients” (CIBER Science Week).
- >> Participation in the translation into Spanish of the “Dictionary of Quality of Life and Health Outcome Measurement” prepared by the *International Society for Quality of Life Research*.
- >> Collaboration with the CIBERSAM instrument bank: possibility of connections between the two websites for common instruments and joint informative conferences.

Publications:

- >> Validation of the Spanish version of the questionnaire on Patient Empowerment in Long-Term Conditions. PLoS ONE 2020; 15(6): e0233338. <https://doi.org/10.1371/journal.pone.0233338>.
- >> Adaptation and validation of the PEDSQLTM Oral Health Scale for toddlers in Chilean population. BMC Oral Health 2020; 6;20(1):6. <https://doi.org/10.1186/s12903-019-0984-1>.
- >> Cross-cultural adaptation and validation of the Spanish version of the Orthognathic Quality of Life Questionnaire for patients with dentofacial deformities. J Craniomaxillofac Surg. 2020, 31:S1010-5182(20)30232-8. <https://doi.org/10.1016/j.jcms.2020.10.004>.
- >> BiblioINDICA Report. Barcelona: Agència de Qualitat i Avaluació Sanitàries de Catalunya. Health Department. Generalitat of Catalunya; 2020. CIBERESP-REDISSEC joint initiative.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

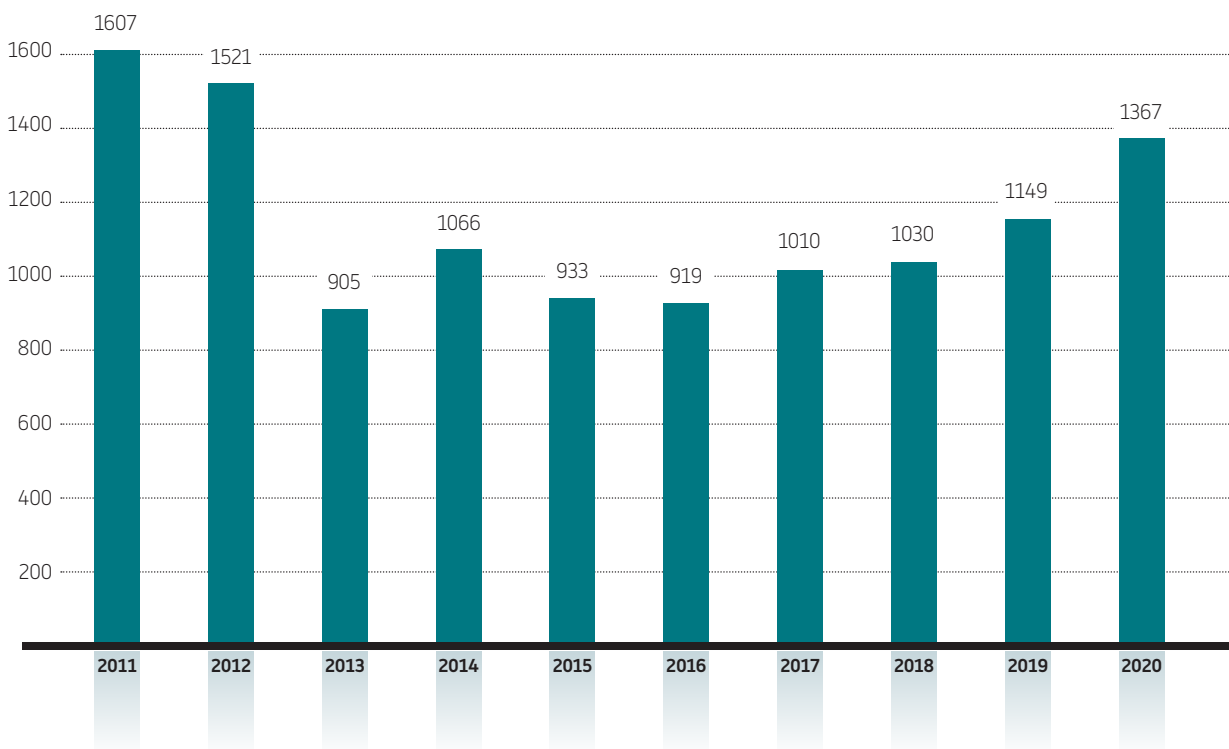
| | |
|--------|------|
| TOTALS | 1367 |
| Q1 | 764 |
| D1 | 347 |

Collaborations

| | |
|----------|-----|
| CIBERESP | 382 |
| CIBER* | 274 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|---|
| 60,392 | Pollan M., Perez-Gomez B., Pastor-Barriuso R., Oteo J., Hernan M.A., Perez-Olmeda M. et al. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. The Lancet. 2020. |
| 30,223 | Pastor-Barriuso R., Perez-Gomez B., Hernan M.A., Perez-Olmeda M., Yotti R., Oteo-Iglesias J. et al. Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: Nationwide seroepidemiological study. The BMJ. 2020;371. |
| 21,597 | Menendez C., Quinto L., Castillo P., Fernandes F., Carrilho C., Ismail M.R. et al. Quality of care and maternal mortality in a tertiary-level hospital in Mozambique: a retrospective study of clinicopathological discrepancies. The Lancet Global Health. 2020;8(7):e965-e972. |
| 12,339 | Peralta GP, Abellan A, Montazeri P, Basterrechea M, Esplugues A, González-Palacios S, et al. Early childhood growth is associated with lung function at 7 years: a prospective population-based study. The European respiratory journal. 2020;56(6). |
| 10,228 | Burte E., Leynaert B., Marcon A., Bousquet J., Benmerad M., Bono R. et al. Long-term air pollution exposure is associated with increased severity of rhinitis in 2 European cohorts. Journal of Allergy and Clinical Immunology. 2020;145(3):834-842.e6. |
| 8,834 | Peralta G.P., Marcon A., Carsin A.-E., Abramson M.J., Accordini S., Amaral A.F.S. et al. Body mass index and weight change are associated with adult lung function trajectories: The prospective ECRHS study. Thorax. 2020. |
| 8,382 | Vrijheid M., Fossati S., Maitre L., Marquez S., Roumeliotaki T., Agier L. et al. Early-life environmental exposures and childhood obesity: An exposome-wide approach. Environmental Health Perspectives. 2020;128(6):1-14. |
| 7,707 | García-Esquinas E, Ortolá R, Martínez-Gómez D, Damián J, Prina M, Rodríguez-Artalejo F et al. Causal effects of physical activity and sedentary behaviour on health deficits accumulation in older adults. International journal of epidemiology. 2020. |
| 7,577 | Garcia-Perez J., Fernandez de Larrea-Baz N., Lope V., Molina A.J., O'Callaghan-Gordo C., Alonso M.H. et al. Residential proximity to industrial pollution sources and colorectal cancer risk: A multicase-control study (MCC-Spain). Environment International. 2020;144. |
| 7,275 | Luque-Fernandez M.A., Goncalves K., Salamanca-Fernandez E., Redondo-Sanchez D., Lee S.F., Rodriguez-Barranco M. et al. Multimorbidity and short-term overall mortality among colorectal cancer patients in Spain: A population-based cohort study. European Journal of Cancer. 2020;129:4-14. |

» CIBERESP Groups. Publications 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|---|-----------|
|  Alemany Vilches, M ^a Eulalia | 37 | 23 | 8 | Instituto Catalán de Oncología | Barcelona |
|  Alonso Caballero, Jordi | 42 | 24 | 12 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Belza Egozcue, María José | 26 | 14 | 5 | Instituto de Salud Carlos III - Centro Nacional de Epidemiología | Madrid |
|  Bonfill Cosp, Xavier | 55 | 27 | 20 | Instituto de Investigación del Hospital de la Santa Creu i Sant Pau | Barcelona |
|  Borrell Thio, Carme | 54 | 17 | 10 | Agencia de Salud Pública de Barcelona | Barcelona |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
|  Bueno Cavanillas, Aurora | 58 | 38 | 6 | Universidad de Granada - Facultad de Medicina | Granada |
|  Calderón Sandubete, Enrique José | 10 | 3 | 0 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Hospital Virgen del Rocío | Sevilla |
|  Casabona Barbara, Jordi | 27 | 12 | 5 | Fundación Instituto de Investigación Germans Trias i Pujol - Centro de estudios epidemiológicos sobre las infecciones de transmisión sexual y sida de Cataluña | Barcelona |
|  Castilla Catalán, Jesús | 74 | 50 | 21 | Instituto de Salud Pública de Navarra | Navarra |
|  Chirlaque López, M ^a Dolores | 79 | 58 | 33 | Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS) - Dirección General de Salud Pública | Murcia |
|  Daponte Codina, Antonio | 18 | 6 | 4 | Escuela Andaluza de Salud Pública | Granada |
|  Delgado Rodríguez, Miguel | 70 | 45 | 5 | Universidad de Jaén - Facultad de Ciencias de la Salud | Jaén |
|  Domínguez García, Ángela | 34 | 12 | 7 | Universidad de Barcelona - Facultad de Medicina | Barcelona |
|  Echevarría Mayo, Juan Emilio | 22 | 9 | 8 | Instituto de Salud Carlos III - Centro Nacional de Microbiología | Madrid |
|  Emparanza Knörr, José Ignacio | 11 | 1 | 0 | Asociación Instituto Biodonostia - Hospital Donostia | Guipúzcoa |
|  Ferreira González, Ignacio | 20 | 9 | 2 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) - Hospital Vall d'Hebron | Barcelona |
|  Figueiras Guzmán, Adolfo | 60 | 37 | 7 | Universidad de Santiago de Compostela - Facultad de Medicina | A Coruña |
|  Figuerola Borrás, Jordi | 30 | 19 | 8 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Estación Biológica de Doñana | Sevilla |
|  Galán Montemayor, Juan Carlos | 22 | 5 | 1 | Servicio Madrileño de Salud - Hospital Ramón y Cajal | Madrid |
|  García Benavides, Fernando | 25 | 7 | 1 | Universidad Pompeu Fabra - Centro de Investigación en Salud Laboral | Barcelona |
|  Gómez de la Cámara, Agustín | 15 | 6 | 2 | Servicio Madrileño de Salud - Hospital Universitario 12 de Octubre | Madrid |
|  Ibarluzea Maurologoitia, Jesús | 75 | 60 | 28 | Asociación Instituto Biodonostia - Subdirección de Salud Pública de Guipuzkoa | Guipúzcoa |
|  Larrauri Cámara, Amparo | 24 | 12 | 11 | Instituto de Salud Carlos III - Centro Nacional de Epidemiología | Madrid |
|  López Espinosa, María José ¹ | 31 | 22 | 14 | Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO) | Valencia |
|  López Medina, María José | 36 | 16 | 4 | Agencia de Salud Pública de Barcelona | Barcelona |
|  Lumbreras Lacarra, Blanca | 28 | 13 | 3 | Universidad Miguel Hernández | Alicante |
|  Marcos Dauder, Ricard | 9 | 6 | 4 | Universidad Autónoma de Barcelona | Barcelona |
|  Martí Puig, Eulalia | 11 | 11 | 7 | Universidad de Barcelona | Barcelona |
|  Menéndez Santos, Clara | 31 | 18 | 13 | Hospital Clínic de Barcelona | Barcelona |
|  Morales Suárez-Varela, María Manuela | 17 | 6 | 2 | Universidad de Valencia - Facultad de Medicina | Valencia |
|  Moreno Aguado, Víctor | 73 | 59 | 22 | Instituto Catalán de Oncología | Barcelona |
|  Moya Simarro, Andrés | 38 | 25 | 12 | Universidad de Valencia - Facultad de Medicina | Valencia |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|-----------|
|  Muñoz Almagro, María Carmen | 88 | 40 | 27 | Fundación para la Investigación y Docencia Sant Joan de Déu - Hospital Sant Joan de Déu | Barcelona |
|  Olea Serrano, Nicolás | 33 | 29 | 12 | Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) - Hospital Clínico San Cecilio | Granada |
|  Pollán Santamaría, Marina | 58 | 38 | 14 | Instituto de Salud Carlos III - Centro Nacional de Epidemiología | Madrid |
|  Porta Serra, Miquel | 28 | 17 | 8 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Rius Gibert, Cristina | 31 | 14 | 3 | Agencia de Salud Pública de Barcelona | Barcelona |
|  Rodríguez Artalejo, Fernando | 63 | 39 | 15 | Universidad Autónoma de Madrid | Madrid |
|  Ruiz Pérez, Isabel | 21 | 10 | 5 | Escuela Andaluza de Salud Pública | Granada |
|  Sáez Zafra, Marc | 35 | 26 | 7 | Universidad de Girona | Girona |
|  Sánchez Pérez, Mará José | 67 | 47 | 22 | Escuela Andaluza de Salud Pública | Granada |
| Sanfeliu Pujol, Coral | 4 | 2 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas de Barcelona | Barcelona |
|  Schröder Helmut | 25 | 19 | 3 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Serra Sutton, Victoria | 11 | 6 | 3 | Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS) | Barcelona |
|  Serrano Blanco, Antonio | 15 | 10 | 2 | Fundación para la Investigación y Docencia Sant Joan de Déu - Parc Sanitari Sant Joan de Déu | Barcelona |
|  Sunyer Deu, Jordi | 124 | 89 | 63 | Fundación Privada Instituto de Salud Global Barcelona (ISGlobal) - Campus Mar | Barcelona |
|  Tardón García, Adonina | 68 | 58 | 19 | Universidad de Oviedo - Facultad de Medicina | Asturias |
|  Villanueva Belmonte, Cristina ² | 126 | 92 | 64 | Fundación Privada Instituto de Salud Global Barcelona (ISGlobal) - Campus Mar | Barcelona |
|  Vioque López, Jesús ³ | 37 | 29 | 6 | Universidad de Alcalá - Facultad de Medicina | Madrid |
|  Zamora Romero, Javier | 39 | 17 | 11 | Servicio Madrileño de Salud - Hospital Ramón y Cajal | Madrid |
| Amo Valero, Julia del* | - | - | - | Instituto de Salud Carlos III - Centro Nacional de Epidemiología | Madrid |

1 up until 30/10/2020 Carmen Íñiguez Hernández

2 up until 01/05/2020 Emmanouil Kogevinas

3 up until 01/10/2020 Francisco Bolumar Montrull

* CIBERESP Associated Group

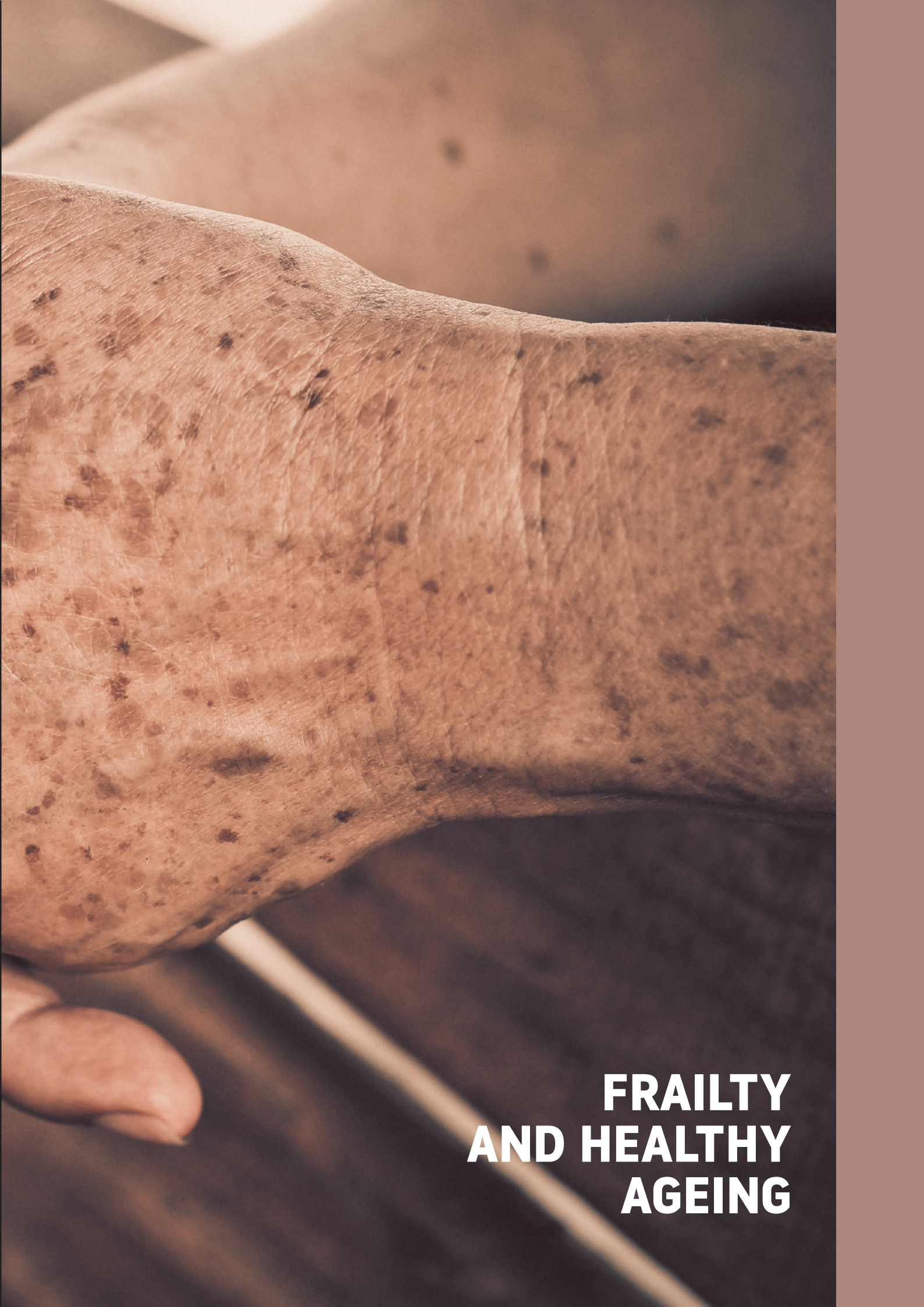
PATENTS OWNED BY CIBER 2020

Patents applied for

- “Gut microbiota composition and uses thereof”.



çiberfes



**FRAILTY
AND HEALTHY
AGEING**





WELCOME FROM THE SCIENTIFIC DIRECTOR

Leocadio Rodríguez-Mañas

In 2020, CIBERFES has seen the organic consolidation of its structure, as the composition of the External Scientific Committee was finally approved by the governing bodies, which had to be renewed due to the death of one of its members, Prof. Francisco del Pozo. The renewal of several of the group PIs has also begun- five out of twenty- along with the departure of the IDIAP Jordi Gol Group (University Institute for Primary Health Care Research Jordi Gol), which will be replaced, as per agreement the Institute's management, in the next AES call (2022).

During 2020, collaborations with other CIBER areas have been strengthened, particularly in the case of CIBERER and, to a lesser extent, with the other areas, while the existing ones were maintained and even intensified. Collaborations have been consolidated with leading groups (Johns Hopkins, University of Toulouse, INGER of Mexico, Aston University, Harvard University, University of Melbourne, Università Cattolica del Sacro Cuore-Roma, University of Milan, among others) and other cooperative networks, like the Canadian Frailty Network. Collaboration continues with the WHO ageing programme through the Clinical Consortium of Healthy Ageing-CCHA, in the generation of documents on the management of COVID in the elderly population and in the treatment of these patients when they are institutionalized.

We have continued to sign research contracts with the pharmaceutical industry, but also with the technology sector, through the consortia created within the projects financed by EIT-HEALTH. The industrial activities arising from CIBERFES Groups have been maintained and one of them is participating in the Innovative Public Procurement programme, with the possibility of bringing new products to the market that improve the management of people who are frail or at risk of becoming so.

In 2020, we have participated in and led European calls in several programmes, mainly H2020 and EIT-Health. Of note is the continuation of the H2020 DIABFRAIL-LATAM project, endowed with 4 million euros, coordinated by CIBERFES and in which 4 groups from our CIBER participate, and the start of the pilot study to validate the POSITIVE technological platform, in which two CIBERFES groups participate.

Our average Impact Factor, the percentage of first author and the percentage in the first decile has continued to increase. The main contributions have continued to focus on aspects of omics in frailty, basic mechanisms of ageing related to mitochondrial function and the processes associated with longevity and functional deterioration, the role of physical exercise and, in the clinical area, prognostic markers (including functional status) in hospitalized COVID patients and the utility of quantitative amyloid PET in the diagnosis of Alzheimer's disease.

se. We have also achieved findings in sarcopenia, osteoporosis, and nutrition, providing evidence that suggests the existence of different clinical frailty phenotypes (with / without sarcopenia; with / without disability).

Finally, regarding institutional relations with international research and health policy organizations, worth highlighting are the contacts established with those responsible for their coordination within WHO to collaborate and participate in the United Nations “Decade of Healthy Ageing” initiative led by the WHO.



PROGRAMMES

P1 - BASIC, CLINICAL AND ENVIRONMENTAL MECHANISMS ASSOCIATED WITH THE DEVELOPMENT OF FRAILITY. IMPACT ON HEALTHCARE SYSTEMS

Coordinator: **José Viña Ribes**

The member groups have approached the problem of frailty from various points of view and clinical trials, absolutely essential aspects.

Dr. Bolaños highlights an interesting study where he links glucose metabolism in the astrocyte with the effects of cannabinoids (Jimenez-Blasco D et al. Nature 2020).

Along the same lines, Dr. Arévalo has observed that phagocytosis of neuronal debris by microglia increases with ageing; phagocytosis can be a neuroprotective characteristic of the glia. (Yan-guas-Casás N et al. Aging Cell 2020)

Dr. Enríquez highlights the study for mitochondrial metabolism demonstrating that sodium controls hypoxic signaling in the mitochondrial respiratory chain (Hernansanz-Agustín P et al. Nature 2020) as well as the publication (Nicolás-Ávila JA et al. Cell 2020) which describes a macrophage network that is important for maintaining mitochondrial homeostasis in the heart.

Dr. Manuel Muñoz has studied the peripheral concentrations of decarboxylated osteocalcin and has shown that this can be a useful tool to identify the risk of cardiovascular disease (Sci Rep 2020).

Dr. Acuña has focused on the role of melatonin, very recently related to the treatment of viral diseases, activating a clinical trial to explore the efficacy and safety of melatonin in COVID-19 patients admitted to the ICU.

Dr. J.A. Madrid works with circadian rhythms and specifically with sleep (Bano-Otalora B et al. J Pineal Res. 2020) and disruption induced by changes in the light-dark cycle and the role of melatonin.

Dr. Matheu has identified the existence of a population of lymphocytes in neurogenic regions in both young and old individuals. In collaboration with other CIBERFES groups, they have validated frailty biomarkers which

they have identified and patented, financed with a grant for Technological Development in Health from the Instituto Carlos III.

Dr. Andrés-Lacueva has participated in the standardization of the nomenclature of polyphenol metabolism compounds and in the development of software to identify food intake data and associate it with metabolomics data.

Dr. Ara has related movement and frailty, using the Toledo cohort. He has obtained funding for the study of the impact of sedentary lifestyle, obesity, and physical activity on brain ageing.

In their high impact publications, the group led by Dr. Izquierdo, shows us the importance of exercise both in elderly people, as well as those hospitalized or after discharge (Izquierdo M et al. BMJ 2020) (Martínez-Velilla N et al. Eur Respir J 2020).

Dr. Viña studies physical exercise to delay frailty, renewing a project with FGCSIC. He has demonstrated the role of the BCLXL protein in the long-term health of centenarians (Borrás C et al. Int J Mol Sci. 2020). In collaboration with various CIBERFES groups, relevant support has been obtained from the Francisco Soria Foundation to study the role of mitochondria in ageing.

P2 - TACKLING FRAILITY. DETECTION, SCREENING, DIAGNOSIS AND TREATMENT. HEALTHCARE MODELS

Coordinator: **Francesc Xavier Nogues Solan**

The translational clinical research in frailty of the CIBERFES programme has been, despite the COVID pandemic, very active in various fields of the principal investigators.

The group led by Juan Antonio Madrid has stood out in their research on alterations in the circadian rhythm of hospitalized patients and in critical care units, and the impact of melatonin on biorhythms. In addition, its spin-off participates in the European project Clarify.

Pedro Abizanda's group has obtained a project of the H2020 programme on care in patients with dementia and an epidemiological study related to COVID-19 from the ISCIII in social health centers. The FRAILMERIT project was stopped due to COVID-19, but its publication activity has been very relevant on various topics related to ageing, such as anemia, frailty, nutritional status and COVID-19 itself. In addition, this group has obtained funding from the ISCIII for its project "Validation of the molecular pattern for the diagnosis and stratification of frailty"

The group led by Mikel Izquierdo has published various results on COPD patients and hospitalized patients. His doctoral students have stood out for their theses on physical exercise and functional and cognitive impairment in older patients with lung cancer, sarcopenia and physical impairment.

Ander Matheu's group has made progress in the validation of a molecular pattern associated with brittleness which they have identified and patented. To this end they have obtained the project "molecular pattern validation for the diagnosis and stratification of frailty" with other CIBERFES groups. In addition, they have characterized the expression of markers of inflammation and oxidative stress in samples from the Primary Care cohort.

The group led by Manuel Muñoz has investigated bone microarchitecture with new dual-energy X-ray absorptiometry techniques and other complex techniques in type 2 diabetes and parathyroid disease.

Cristina Andrés' group, with the MAPLE PCIN-2015-238 project, has laid the foundations of nutrient and

polyphenol intakes for the future development of dietary recommendations in the elderly population and their impact on intestinal permeability and plasma microbiota in elderly subjects.

Francisco José García García's group (ETES group) has been very involved in the fight against COVID-19. Despite this, it has managed to create and validate the FTS5 Scale (short form) useful in multiple settings (clinical, research, public health) and the development and standardization of "muscle power" as a predictor variable for adverse events in the elderly.

The group led by Feliciano Priego has focused on the development of methods for the directed analysis of lipid families in biological samples with potential application in clinical studies and the evaluation of a healthy value of extra virgin olive oil based on its phenolic profile.

Xavier Nogués' group in Barcelona has shown a higher incidence of cardiovascular events and higher mortality compared to tamoxifen in patients with breast cancer and treatment with aromatase inhibitors. On bone quality, he has published papers on microindentation in patients with monoclonal gammopathy of uncertain significance. In 2020, this group has been granted by the ISCIII for its project: "Estudio del eje intestino-corazón. Asociación entre la inflamación cardiovascular y los cambios del sistema inmune inducidos por el VIH".

The group led by Leocadio Rodríguez-Mañas has continued to work on the frailty phenotype, clinical instruments and diagnostic algorithms, sarcopenia and nutrition. New MID-FRAIL data were collected. The group continued the H2020 project DIABFRAIL-LATAM and initiated its project "Understanding the role of arterial stiffness, body composition and insulin resistance on the onset or worsening of frailty status, disability and mortality" funded by Abbott Laboratories.

TRAINING PROGRAMME

Coordinator: **Pedro Abizanda Soler**

During 2020 and due to COVID-19, the face-to-face training activities of CIBERFES were postponed. Both the spring meeting coinciding with the SEMEG Congress in Albacete in April 2020, and the autumn meeting, were postponed until the pandemic is resolved and the researchers regain their mobility.

Some new actions have been maintained as well as others which had already been carried out in previous years, such as:

- >> Call for mobility grants for CIBERFES researchers to finance or co-finance national or international stays, preferably within the area.
- >> Participation of various groups in the INJOY Summer School EIT-HEALTH, University of Barcelona.
- >> Collaboration in consensus documents, such as the one developed by the Ministry of Health entitled “Recommendations for addressing frailty in the health crisis situation generated by COVID-19” and which will soon be presented for approval in the Public Health Commission of the Interterritorial Council.
- >> Participation in the 10th edition of the International Conference on Frailty and Sarcopenia (ICFSR 2020), Toulouse.
- >> Participation with several presentations in the online meeting organized by the Spanish Society of Geriatric Medicine (SEMEG) “20 years of SEMEG”.
- >> Participation with several presentations in the “First virtual congress of the Spanish Geriatrics and Gerontology Society”.
- >> Edition of the two reference textbooks in Spanish for specialists in Geriatric Medicine and for medical students, with the participation of numerous CIBERFES groups:
 - Pedro Abizanda Soler, Carlos Cano Gutiérrez. *Medicina Geriátrica, una aproximación basada en problemas*, 2ª Ed. Elsevier España SL; Barcelona: 2020. ISBN: 978-84-9113-523-4.
 - Pedro Abizanda Soler, Leocadio Rodríguez Mañas. *Tratado de medicina geriátrica. Fundamentos de la atención sanitaria a los mayores*, 2ª Ed. Elsevier España SL; Barcelona: 2020. ISBN: 978-84-9113-298-1.

In addition to the CIBERFES collective activities, the different groups have carried out training activities linked in some way to the consortium, consisting of teaching in Master's degrees on ageing, doctoral programmes, classes in faculties, accredited training courses or national and international conferences. Participation in CIBER's I Call for #QueSigaLaCiencia videos with an informative video entitled: “Healthy ageing” and its inclusion on the CIBER website, in a section on scientific culture: “inspiring women”.

Some activities planned for 2020 have been postponed to 2021 or 2022, such as the completion of a Masters in Frailty and Healthy Ageing, and the scientific meeting in Albacete, coinciding with the SEMEG Congress.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

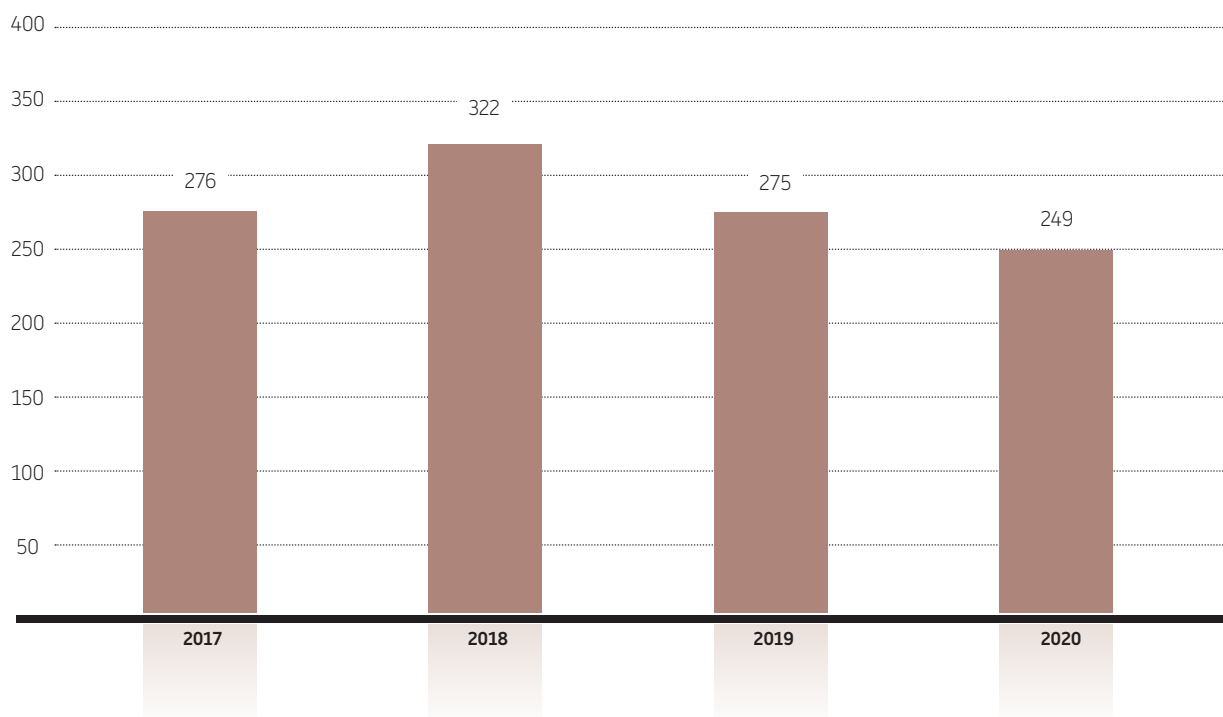
| | |
|--------|-----|
| TOTALS | 249 |
| Q1 | 153 |
| D1 | 51 |

Collaborations

| | |
|----------|----|
| CIBERFES | 17 |
| CIBER* | 66 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|--------|---|
| 60,392 | Use of renin-angiotensin-aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: a case-population study (Scopus ID: 85085205357; Pubmed ID: 32416785) |
| 42,778 | Glucose metabolism links astroglial mitochondria to cannabinoid effects (Scopus ID: 85087664497; Pubmed ID: 32641832) |
| 42,778 | Na ⁺ controls hypoxic signalling by the mitochondrial respiratory chain (Scopus ID: 85088809211; Pubmed ID: 32728214) |
| 30,223 | Exercise in people over 85. (Scopus ID: ; Pubmed ID: 32024635) |
| 17,127 | Quantitative amyloid PET in Alzheimer's disease: the AMYPAD prognostic and natural history study (Scopus ID: 85083288243; Pubmed ID: 32281303) |
| 14,251 | Plasma p-tau181 accurately predicts Alzheimer's disease pathology at least 8 years prior to post-mortem and improves the clinical characterisation of cognitive decline (Scopus ID: 85088662307; Pubmed ID: 32720099) |
| 13,946 | Association of Physical Education with Improvement of Health-Related Physical Fitness Outcomes and Fundamental Motor Skills among Youths: A Systematic Review and Meta-analysis (Scopus ID: 85083239028; Pubmed ID: 32250414) |
| 13,116 | Functional role of respiratory supercomplexes in mice: SCAF1 relevance and segmentation of the Qpool (Scopus ID: 85085896405; Pubmed ID: 32637615) |
| 13,116 | Nuclear WRAP53 promotes neuronal survival and functional recovery after stroke (Scopus ID: 85092683833; Pubmed ID: 33028529) |
| 12,587 | A small molecule G6PD inhibitor reveals immune dependence on pentose phosphate pathway (Scopus ID: 85084444552; Pubmed ID: 32393898) |

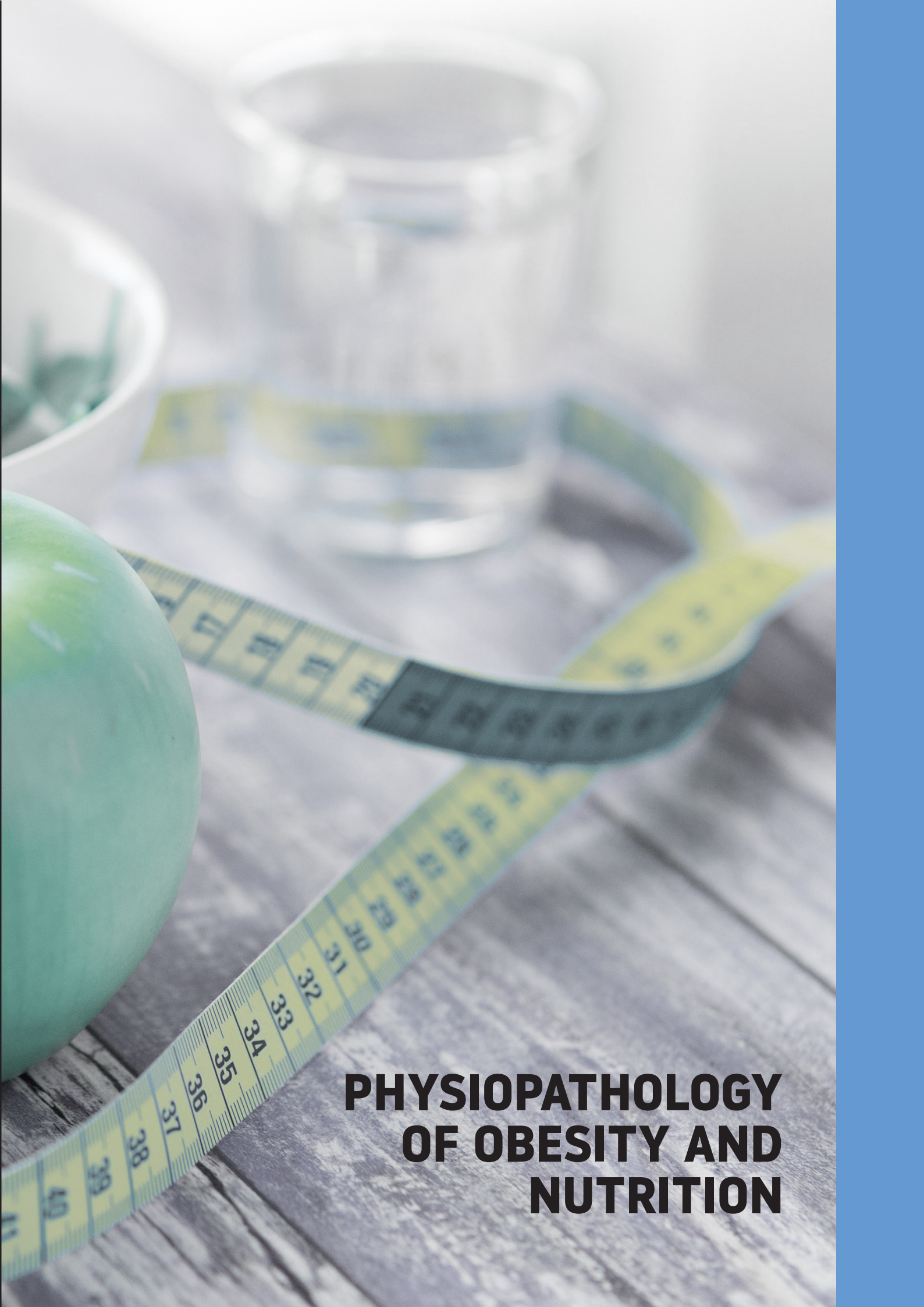
» CIBERFES Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|-------------|
|  Abizanda Soler, Pedro | 6 | 1 | 0 | Servicio de Salud de Castilla-La Mancha | ALBACETE |
|  Acuña Castroviejo, Darío | 5 | 1 | 1 | Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) | GRANADA |
|  Andrés Lacueva, María Cristina | 16 | 12 | 5 | Universidad de Barcelona | BARCELONA |
|  Ara Royo, Ignacio | 20 | 15 | 2 | Universidad de Castilla-La Mancha | CIUDAD REAL |
|  Bolaños Hernández, Juan Pedro | 5 | 3 | 3 | Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León | SALAMANCA |
|  Nogués Solan, Francesc Xavier | 11 | 7 | 1 | Consorci Mar Parc Salut de Barcelona | BARCELONA |
|  Enríquez Domínguez, José Antonio | 5 | 3 | 2 | Fundación Centro Nacional de Investigaciones Cardiovasculares | MADRID |
|  Arévalo Arévalo, María Angeles | 12 | 8 | 4 | Agencia Estatal Consejo Superior de Investigaciones Científicas | MADRID |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|---|-----------------|
|  Garcia García, Francisco José | 8 | 7 | 2 | Fundación del Hospital Nacional de Paraplégicos | TOLEDO |
|  Izquierdo Redin, Mikel | 30 | 26 | 11 | Universidad Pública de Navarra | NAVARRA |
|  Madrid Pérez, Juan Antonio | 3 | 1 | 0 | Universidad de Murcia | MURCIA |
|  Matheu Fernández, Ander | 11 | 10 | 2 | Asociación Instituto Biodonostia | GUIPUZCOA |
| Molinuevo Guix, José Luis | 15 | 9 | 7 | Fundación Barcelonabeta Brain Research Center | BARCELONA |
|  Moreno Casbas, Teresa | 15 | 4 | 2 | Instituto de Salud Carlos III | MADRID |
|  Muñoz Torres, Manuel | 9 | 5 | 0 | Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) | GRANADA |
|  Priego Capote, Feliciano | 11 | 7 | 1 | Fundación para la Investigación Biomédica de Córdoba (FIBICO) | CORDOBA |
|  Rodríguez Mañas, Leocadio | 18 | 11 | 4 | Servicio Madrileño de Salud | MADRID |
|  Serra Rexach, José Antonio | 17 | 11 | 4 | Servicio Madrileño de Salud | MADRID |
|  Viña Ribes, José | 22 | 16 | 4 | Fundación Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) | VALENCIA |



čiberobn



PHYSIOPATHOLOGY OF OBESITY AND NUTRITION





WELCOME FROM THE SCIENTIFIC DIRECTOR

Carlos Diéquez González

A year has passed since the last report in 2019. Obviously the 2020 annual report and my comments are related to the COVID19 pandemic and how this has affected us at all levels. During this period, as a society we have had to incorporate new habits related to primary prevention in order to fight the coronavirus and we have had to accept limitations in mobility and the performance of our working capacity. In our case, given the high number of healthcare personnel we have, this has forced us to take this on as an absolute priority beyond the responsibilities of research and management, which are those inherent to the CIBEROBN activity.

On a practical level, we were all forced to make immediate drastic changes in our usual way of working. In many cases we had to abruptly close facilities, which affected not only our research work, but also aspects related to the training of our researchers. Even our way of communicating has been affected, both with the rest of the people that make up the CIBEROBN, as well as with the subjects and patients of the different cohorts under follow-up. These changes were only possible thanks to the continued effort of all and the support from the ISCIII Direction and Management bodies and, in particular, from the CIBER structure. This has allowed us to reach a new normal within the exceptionality that is making it possible to achieve the planned objectives and face some new challenges, on which I will expand in more detail.

One of the main challenges was related to the monitoring of cohorts, which largely represent the core of the Nutrition Programme's work. To the obvious challenges related to mobility restriction and difficulties in obtaining samples, we needed to add the possible influence this could have on ongoing studies. Given the SARS-CoV-2 virus pandemic, a study was launched on the seroprevalence of infection in some cohorts. Given the longitudinal design of PREDIMED-Plus, the periodic evaluation of a multitude of parameters and knowing who has contracted the infection or not will allow us in the near future to know the following:

1) clinical characteristics and predictive markers of infection; 2) the effect of the pandemic on adiposity, depressive symptoms, cognition and quality of life; and 3) the impact on cognitive function. Additionally, and given the current pandemic situation, the Obesity Programme expanded its objectives to cover the need to gain knowledge regarding Obesity and related Eating Disorders, as well as the impact of COVID19, and detection of factors of biological-behavioral vulnerability associated with worsening of symptoms during and after confinement. Finally, to be highlighted are the changes in relation to the Training Programme. The mobility restrictions forced us to embrace the virtual format.

Although there are irreplaceable aspects, such as the exchange of personnel in laboratories, we have managed

to mitigate aspects related to seminars, conferences, etc. In fact, the experience in some of these aspects is robust enough to foresee that some of these changes will become part of our future strategy.

Based on all of the above, a reflection on the influence that the events of 2020 may entail in our future activity is perhaps still pending. From a very general point of view, there is no doubt that we have a much more informed and much more sensitive society regarding the need for a strong research system in biomedicine. More specifically, this should stimulate us to convey to that same society the relevance of our work in the field of obesity and nutrition. Society is undoubtedly very familiar with what a pandemic is, but it is not aware that there are “silent pandemics” such as obesity, which is responsible for a high percentage of mortality in the absence of a pandemic and which also markedly increases that induced by COVID19 infection. Achieving this is our challenge as researchers and as responsible members of our society.

In this context, our most sincere thanks to all those involved in healthcare work during this period.



PROGRAMMES

NUTRITION PROGRAMME

Coordinators: **Jordi Salas-Salvadó, Dolores Corella y Estefanía Toledo**

The Nutrition Programme is one of the two CIBEROBN programmes (Nutrition and Obesity) that includes epidemiological research on obesity and nutrition for which important milestones have been achieved related to the recruitment, monitoring 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 and controlled clinical trial with intensive 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. At the end of 2020, a mean follow-up of 5 years of the more than 6,800 participants successfully randomized, even in COVID-19 times, has been achieved. Other milestones are publications derived from the PREDIMED study, as well as the follow-up and several publications of the cohort "Follow-up of the University of Navarra" (SUN) (n = 23,000). Milestones have also been reached in the publications of the CORDIOPREV study, a randomized controlled trial with a Mediterranean diet intervention in secondary cardiovascular prevention, the WAHA study (WAlnuts and Healthy Aging), an international intervention trial with walnuts. Equally noteworthy milestones are the advances in recruitment, monitoring and publication of the results of recently initiated studies: MELIPOP (Multicenter randomized controlled trial with Mediterranean diet and physical activity in children focused on the prevention of childhood obesity.), PREDI-DEP (Prevention of recurrent depression with a Mediterranean diet. PREDI-DEP), PREDIMAR (Prevention with Mediterranean Diet of Recurrent Arrhythmias in patients with atrial fibrillation), MEDICAR (In collaboration with SEAT, study in 14,000 workers to evaluate the relationship between lifestyle and health), IMPACT ("Improving mothers for a better Prenatal Care" of the Hospital Clinic de Barcelona in collaboration with other centers), CORALS (cohort of children to assess risk factors for obesity), and the European studies H2020 STOP ("Science and Technology in Childhood Obesity Prevention", on policies to prevent and address childhood obesity, SWEET "Sweeteners and sweetness enhance rs: 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, 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”.

Several dozen publications have been made in journals of high international impact in 2020, among them the following stand out:

- Carbohydrate quality changes and concurrent changes in cardiovascular risk factors: A longitudinal analysis in the PREDIMED-Plus randomized trial. *Am J Clin Nutr* 2020.
- Glycolysis/gluconeogenesis- and tricarboxylic acid cycle-related metabolites, Mediterranean diet, and type 2 diabetes. *Am J Clin Nutr* 2020.
- Biomonitoring of 45 inorganic elements measured in plasma from Spanish subjects: A cross-sectional study in Andalusian population. *Sci Total Environ* 2020.
- Prediabetes diagnosis criteria, type 2 diabetes risk and dietary modulation: The CORDIOPREV study. *Clin Nutr* 2019.

OBESITY PROGRAMME

Coordinators: **Francisco Tinahones, Fernando Fernández-Aranda, M^a Pui Portillo y Empar Lurbe**

Despite the impact suffered by the pandemic situation due to COVID-19, in 2020 the consolidation of the Obesity Programme subprogrammes in response to the CIBEROBN Strategic Plan has continued. In addition, the ties of collaboration among the different groups have been strengthened as well as collaborations between the Obesity and Nutrition programme, and concerted efforts have been made regarding research on COVID-19, within the CIBER and through collaborations with international groups. In this regard, the actions carried out have resulted 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 an international level.

Relevant International Publications

At regards scientific production, the following publications deserve particular mention as an example of both intra- and inter-CIBER, as well as international collaborations:

- Peyrou M et al. *Nat Commun.* 2020 May 1;11(1):2132. PMID: 32358539; Arnoriaga-Rodríguez M, et al. *Cell Metab.* 2020 Oct 6;32(4):548-560.e7. PMID: 33027674; Arnoriaga-Rodríguez M, et al. *Microbiome.* 2020;8(1):59. PMID: 32354351; Mayneris-Perxachs J, et al. *Microbiome* 2020;8(1):136. PMID: 32951609; Fernández-Real JM, et al. *Gut.* 2020: gutjnl-2020-322662. PMID: 32994309. Heras V, et al., *Cell Metab.* 2020 Dec 1;32(6):951-966.e8. PMID: 33080217; Steward T et al., *Psychol Med.* 2020 Jul 23;1-9. PMID: 32698931; Bryois J et al., *Nat Genet.* 2020 May;52(5):482-493. PMID: 32341526. Paz-Graniel I et al. *Eur J Nutr.* 2020 Oct 30. PMID: 33125576; Izquierdo AG, et al., *FASEB J.* 2020 Feb;34(2):2312-2325. PMID: 31908001; Trepiana J et al., *Pharmaceuticals* 2020 Sep 30;13(10):285. PMID: 33008087; Falkner B, Lurbe E. *Hypertension.* 2020 May;75(5):1142-1150. Epub 2020 Mar 30. PMID: 32223379.

International Projects

As regards the obtaining of international resources, where members of the CIBEROBN obesity programme participate as PIs and / or coordinators, the following projects deserve special mention:

- 1) Network for blood pressure research in children and adolescents. HyperChildNET (CA 19115). COST Action (2020- 25). Coordinator E.Lurbe/ PI: F. Fernandez-Aranda;

- 2) Stratification of Obese Phenotypes to Optimize Future Obesity Therapy (SOPHIA). PIs: G Frühbeck/ JM Fernández-Real-(2020-25)-Horizon 2020 Ref 875534-2;
- 3) Paternal RNA-mediated epigenetic inheritance of metabolic disorders: impact of weight loss on the human sperm (HEROS) JPI-HDHL. European Union (2019-21)- Horizon 2020, Ref. AC18/00012, PI: JM Fernández-Real;
- 4) International Training Network (Marie Curie-H2020): Gut-brain-axis: Targets for improvement of cognition in the elderly (SMARTAGE) (2020-24)- Ref. 859890, PI JM Fernández-Real;
- 5) Personalized prediction of cognition through the human microbiota. (ThinkGut) Interreg-POCTEFA (Horizon 2020) (2019-2022), Ref EFA345/195)
- 6) Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviours (Eat2beNICE) Horizon 2020 (2017-22) (Ref 728018); PI: F. Fernández-Aranda and J. Salas-Salvado;
- 7) Prevention and Remediation of Insulin Multimorbidity in Europe. Horizon 2020 (2020-24) (Ref. PRIME 847879). The last two have been in collaboration with the nutrition programme.

Participation in international Guidelines

Similarly, to the intense scientific activity must be added the participation in the elaboration of Clinical Guidelines, as well as in Consensus and Positioning Documents related to obesity and clinical nutrition of National and European Obesity and Diabetes Societies.

- Stabouli S, Redon J, Lurbe E. Redefining hypertension in children and adolescents: A review of the evidence considered by the European Society of Hypertension and American Academy of Pediatrics guidelines. *J Hypertens*. 2020 Feb;38(2):196-200. PMID: 31584513.
- Borghi C, Tsioufis K, Agabiti-Rosei E, Burnier M, Cicero AFG, Clement D, Coca A, Desideri G, Grassi G, Lovic D, Lurbe E, Kahan T, Kreutz R, Jelakovic B, Polonia J, Redon J, Van De Borne P, Mancia G. Nutraceuticals and blood pressure control: a European Society of Hypertension position document. *J Hypertens*. 2020 May;38(5):799-812. PMID: 31977574.

Publication and coordination, in the *European Eating Disorders Review*, of consensus action guidelines in the confinement of patients, relatives and therapists (translated into 20 languages, the result of international collaboration) of open access (Fernández-Aranda et al., 2020 ; PMID: 32346977 / With more than 13,000 downloads) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7267370/bin/ERV-28-239-s001.pdf>

Dissemination

As regards internationalization, the CIBEROBN Obesity programme, and its component members, have maintained their usual activity in the organization of workshops and specific symposiums related to obesity and nutrition, this year in on-line format, within the European Society for Clinical Investigation (ESCI), European Congress on Obesity (ECO), European Society of Endocrinology (ESE) and it organized the World Congress of the Eating Disorders Research Society (XXVI Annual Eating Disorders Research Society Meeting) (F. Fernández-Aranda as President) (<https://edresearchsociety.org/2020/index.php>).

At the level of leadership and social / scientific dissemination, various initiatives have been carried out during the past year 2020. Two special issues, in international Q1 journals, have been led by members of the Obesity programme (JM Fernández-Real and F-Fernandez-Aranda) “Microbiota and endocrine disorders” Reviews in *Endocrine and Metabolic Disorders / Eating disorders during COVID-19 Pandemic-European Eating Disorders Review*, with CIBEROBN leading this issue [https://onlinelibrary.wiley.com/doi/toc/10.1002/\(ISSN\)1099-0968.eating-disorders-covid-19](https://onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1099-0968.eating-disorders-covid-19), with four collaborative contributions (PMID: 32974994/ PMID: 32954595/ PMID:

32852142/ PMID: 32815293). Creation, validation and coordination of a scale (CIES) that measures the impact of the confinement measures on eating disorders and obesity, the result of an international collaboration (translated into 19 languages). Fernández-Aranda et al 2020; PMID: 32954595 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7537123/bin/ERV-9999-na-s003.pdf>

As regards social dissemination and promotion of the scientific spirit among young people, during 2020 the annual Crazy about Nutrition course (sponsored by the La Pedrera Foundation) has continued to be organized at the Hospital de Bellvitge (Coordinator: F. Fernández-Aranda).

Participation/creation of specific networks

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 including relevant CIBEROBN groups. The cooperative research it develops addresses the identification of new factors controlling adipose tissue browning, the implication of alterations in adipose plasticity in ageing and the interaction with the immune system from a holistic approach aimed at advancing the understanding of adipose tissue and its health implications. Worth highlighting is the cooperative project developed to understand the biological ageing of adipose tissue through the differential analysis of the transcriptome of adipose tissue of healthy and elderly individuals, in both men and women. The data, already obtained and in the process of global analysis, allow a better understanding of the extent to which changes in obesity are associated with accelerated or distorted ageing of adipose tissue.

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.

Members of the “Value of Treatment” Workgroup of the European Brain Council / European Psychaitric Association.

TRAINING PROGRAMME

Coordinator: **Manuel Tena-Sempere**

As in previous years, the main focus of the CIBEROBN Training Programme has been on the youngest members of the teams. In its original planning, the programme's main objective was to promote the training of researchers (especially emerging researchers and those consolidating their careers) in obesity and nutrition, favoring their mobility as much as possible and helping to consolidate their professional careers as independent researchers in this thematic area. In its initial configuration, the programme also contemplated the development of collaborations with other CIBER thematic areas, aimed at reinforcing the continuous training of the members of our Area.

Unfortunately, the COVID-19 pandemic, and the measures associated with the state of alarm enacted in March 2020, have had a very significant impact on the development of the activities of the training programme in our CIBER area, which have been severely affected due to the pandemic- in force for most of 2020-and the associated mobility restrictions, both nationally and internationally.

In this regard, and in line with the development of the programme, the main training activities initially planned by the training programme were aimed at financing training stays for CIBEROBN members in other reference research groups, both national and international. Specifically, at the beginning of 2020, three training stays had already been approved, in addition to others that were under evaluation. All of these were interrupted by the outbreak of the pandemic and the associated health measures. Some of these stays are being re-evaluated for their implementation in 2021, subject to the evolution of the pandemic at the national and international level.

The CIBEROBN training programme had also promoted active participation and / or organization of scientific events throughout 2020, the development of which was equally impacted by the pandemic. For example, The Workshop "Fat sensing and the brain control of puberty", which was approved by the International University of Andalusia for its celebration in November 2020, after a highly competitive selection process supported by our CIBER, was postponed to 2021, with CIBEROBN maintaining its commitment with this event. In the same way, CIBEROBN supported similar initiatives, in the form of workshops or thematic meetings, promoted by some of its groups, such as the group led by Prof. Fernando Fernández-Aranda or Prof. Jordi Salas, who had planned the development of international scientific meetings, organized with the support of the CIBEROBN. The holding of these events was postponed or transformed into a virtual format (for example, the *Eating Disorder Research Society* meeting, finally held in October 2020), with the continued support of the CIBEROBN.

In this same regard, the pandemic also impacted the development of the Doctoral Excellence Meeting, in Mahón, promoted by the CIBERESP, for which the CIBEROBN had planned to maintain its participation (abruptly interrupted by the pandemic), and most notably, the organization of the annual meeting of our CIBER area, called "OBESITY AND NUTRITION IN THE 21ST CENTURY". Given that this annual meeting is considered a priority element in the training programme and in the cohesion programme of the CIBEROBN, many of the efforts of the training programme were aimed at ensuring its celebration, albeit in virtual format. In fact, the scientific programme, initially planned for a face-to-face meeting to be held on October 28-29 in Madrid, had to be adapted to a virtual format, which took place using the ISCIII telematic tools, on October 26-29, 2020, in the afternoon. Despite the remote format, the programme managed to gather a wide panel of top-level national and international speakers, including three plenary speakers and 12 regular speakers, linked to CIBEROBN and other institutions. More importantly, the number of registered and regular attendees to the sessions of this scientific meeting exceeded that of previous years, in face-to-face format.

The recognition of the need to adapt to the new situation marked by the pandemic and the success of the online model of the scientific meeting, have allowed the promotion of other complementary activities that, without causing excessive exhaustion due to the multiple online meetings, allowed to expand the training offer of

the CIBEROBN, extending its scope to practically all the CIBEROBN groups, linked to both obesity and nutrition programmes. As examples of initiatives started or executed during 2020 year, online scientific meetings were promoted in conjunction with other societies, such as SEEDO, coinciding with the celebration of Obesity Week (September 2020), and initiatives have been actively disseminated closely related to CIBEROBN topics, which included the seminar cycles of the Department of Preventive Medicine and Public Health of the University of Navarra (online format), and the *Annual Obesity Meeting 2020* (virtual), which was held in December 2020 with the participation of different speakers from our CIBER.

Along the same lines, during 2020 the planning of a joint cycle of virtual conferences of the CIBEROBN was initiated, in collaboration with the CiMUS and IMIBIC Institutes, which will be held on a monthly basis in 2021, and for which we anticipate the involvement of other institutions related to our CIBER area. We trust that the development of these and other initiatives of virtual training activities will allow not only to alleviate the limitations of the mobility activities of the training programme in the upcoming years (which we trust will be able to recover as soon as the health situation allows), but also become consolidated as complementary to the training actions promoted by our CIBEROBN.

Finally, and as a training element of utmost importance, we take this opportunity to highlight that in 2020 a total of 52 Doctoral Theses have been completed (23 of them international), marking the consolidation of a growing trend in this important training activity.

SCIENTIFIC PLATFORMS

Coordinator: **José Manuel Fernández-Real**

BIOBANCOS-FATBANK 2020

The FatBank's activity during 2020 was affected by the SARS-CoV-2 pandemic forcing the reorganization of the surgeries from which adipose tissue biopsies were obtained, and the temporary interruption of its activity, which has resulted in a decrease in the number of samples collected.

The main milestone achieved during 2020 was in relation to the request for samples for the OutBrat project, the first joint operation project of the FatBank, for which it was necessary for samples coming from the other nodes to be received at the Coordinator node in Girona. A summary of this and the subsequent delivery of samples to the researcher is detailed below:

Málaga node:

- >> 195 subcutaneous or parietal adipose tissue samples received
- >> 192 samples of subcutaneous or parietal adipose tissue delivered

Pamplona node:

- >> 185 subcutaneous or parietal adipose tissue samples received
- >> 184 subcutaneous or parietal adipose tissue samples delivered

Santiago node: 217 subcutaneous or parietal adipose tissue samples received

Córdoba node: 150 subcutaneous or parietal adipose tissue samples received

This request began in 2019 with the delivery of the samples corresponding to the Girona node (326 samples of subcutaneous or parietal adipose tissue).



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

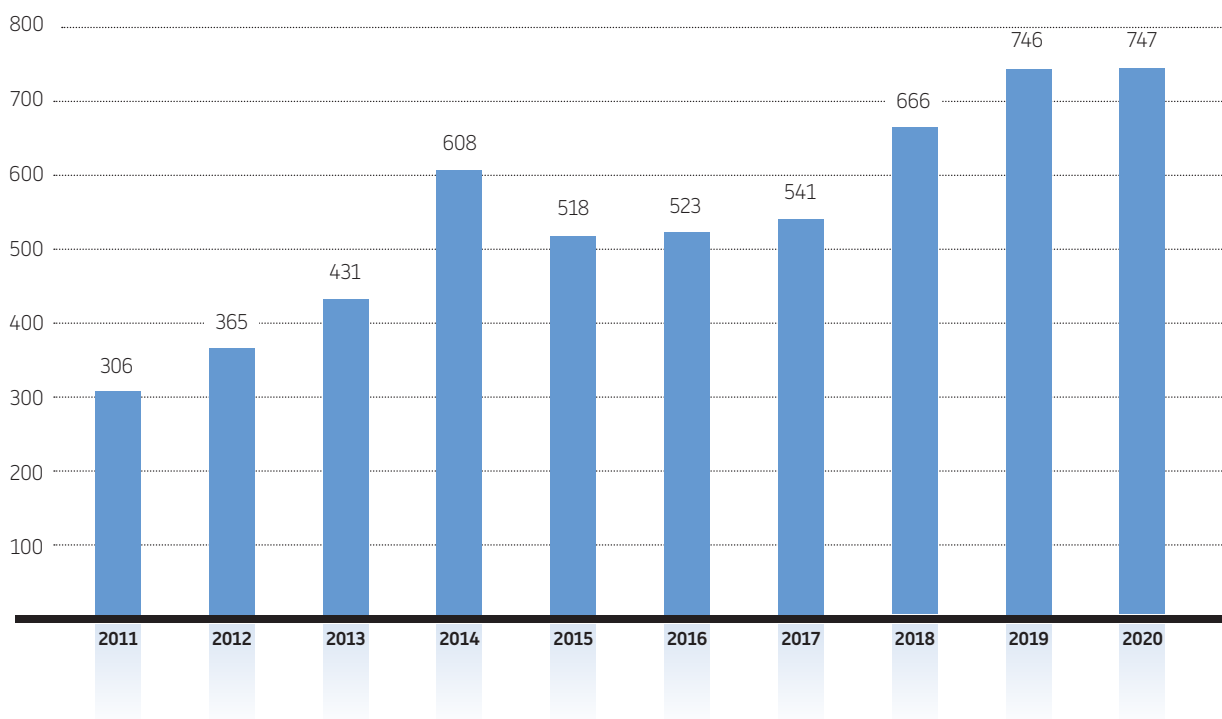
| | |
|--------|-----|
| TOTALS | 747 |
| Q1 | 454 |
| D1 | 114 |

Collaborations

| | |
|----------|-----|
| CIBEROBN | 145 |
| CIBER* | 213 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publicación |
|--------|---|
| 20,589 | Remnant Cholesterol, Not LDL Cholesterol, Is Associated With Incident Cardiovascular Disease (Pubmed Id: 33272365) |
| 20,86 | ADAR1-Dependent RNA Editing Promotes MET and iPSC Reprogramming by Alleviating ER Stress (Pubmed Id: 32396862) |
| 21,567 | Targeting Hepatic Glutaminase 1 Ameliorates Non-alcoholic Steatohepatitis by Restoring Very-Low-Density Lipoprotein Triglyceride Assembly (Pubmed Id: 32084378) |
| 21,567 | Obesity Impairs Short-Term and Working Memory through Gut Microbial Metabolism of Aromatic Amino Acids (Pubmed Id: 33027674) |
| 21,567 | Central Ceramide Signaling Mediates Obesity-Induced Precocious Puberty (Pubmed Id: 33080217) |
| 27,603 | Genetic identification of cell types underlying brain complex traits yields insights into the etiology of Parkinson's disease (Pubmed Id: 32341526) |
| 28,8 | Contribution of macronutrients to obesity: implications for precision nutrition (Pubmed Id: 32235875) |
| 38,637 | Metabolic Fingerprinting Links Oncogenic PIK3CA with Enhanced Arachidonic Acid-Derived Eicosanoids (Pubmed Id: 32559461) |
| 42,778 | Repositioning of the global epicentre of non-optimal cholesterol (Pubmed Id: 32494083) |
| 18,274 | A systematic review and meta-analysis of the 2007 WCRF/AICR score in relation to cancer-related health outcomes (Pubmed Id: 32067678) |

» CIBEROBN Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|---------------|
|  Argente Oliver, Jesús | 27 | 9 | 1 | Servicio Madrileño de Salud - Hospital Infantil Universitario Niño Jesús | Madrid |
|  Baños Rivera, Rosa María | 42 | 21 | 4 | Universidad de Valencia - Facultad de Psicología | Valencia |
|  Seoane Camino, Luisa María | 24 | 16 | 2 | Servicio Gallego de Salud - Complejo Hospitalario Universitario Santiago | A Coruña |
|  Corella Piquer, Dolores | 51 | 36 | 11 | Universidad de Valencia - Facultad de Medicina | Valencia |
|  Diéguez González, Carlos | 25 | 20 | 9 | Universidad de Santiago de Compostela - CIMUS | A Coruña |
|  Estruch Riba, Ramón | 53 | 38 | 8 | Hospital Clínic de Barcelona | Barcelona |
|  Fernández Aranda, Fernando | 32 | 23 | 8 | Fundación IDIBELL - Hospital Universitario de Bellvitge | Barcelona |
|  Fernández-Real Lemos, Jose Manuel | 19 | 16 | 7 | Fundación Instituto de Investigación Biomédica de Girona - Hospital Josep Trueta | Girona |
|  Romaguera Bosch, M Adoración | 48 | 34 | 11 | Fundación Instituto de Investigación Sanitaria Illes Balears (IdISBa) - Hospital Universitario Son Espases | Illes Balears |
|  Fitó Colomer, Montserrat | 66 | 46 | 11 | Consorci Mar Parc Salut de Barcelona | Barcelona |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|---|---------------|
|  Frühbeck Martínez, Gema | 32 | 16 | 2 | Universidad de Navarra - Clínica Universitaria de Navarra | Navarra |
|  Gil Campos, María Mercedes | 39 | 25 | 0 | Fundación para la Investigación Biomédica de Córdoba (FIBICO) - Hospital Universitario Reina Sofía | Córdoba |
|  Lamuela-Raventos, Rosa María | 28 | 22 | 8 | Universidad de Barcelona - Facultad de Farmacia | Barcelona |
|  Lasunción Ripa, Miguel Angel | 32 | 22 | 4 | Servicio Madrileño de Salud - Hospital Ramón y Cajal | Madrid |
|  López Miranda, José | 46 | 35 | 7 | Fundación para la Investigación Biomédica de Córdoba (FIBICO) - Hospital Universitario Reina Sofía | Córdoba |
|  Lurbe Ferrer, Empar | 16 | 5 | 2 | Consorcio Hospital General Universitario Valencia - Fundación de Investigación del Hospital General Universitario de Valencia | Valencia |
|  Martínez González, Miguel Ángel | 76 | 45 | 12 | Universidad de Navarra | Navarra |
|  Martínez Hernández, Jose Alfredo | 58 | 32 | 5 | Universidad de Navarra | Navarra |
|  Moreno Aznar, Luis Alberto | 54 | 28 | 4 | Fundación Instituto de Investigación Sanitaria Aragón | Zaragoza |
|  Ortega Martínez de Victoria, Emilio | 61 | 44 | 12 | Hospital Clínic de Barcelona | Barcelona |
|  Osada García, Jesús de la | 18 | 7 | 1 | Universidad de Zaragoza | Zaragoza |
|  Palou Oliver, Andreu | 13 | 12 | 1 | Universidad de las Islas Baleares - Facultad de Ciencias de Mallorca | Illes Balears |
|  Pintó Sala, Xavier | 39 | 25 | 4 | Fundación IDIBELL - Hospital Universitario de Bellvitge | Barcelona |
|  Portillo Baquedá, María del Puy | 12 | 9 | 2 | Universidad del País Vasco - Facultad de Farmacia | Álava |
|  Remesar Betllloch, Xavier | 18 | 12 | 6 | Universidad de Barcelona - Facultad de Biología | Barcelona |
|  Salas Salvadó, Jordi | 70 | 45 | 11 | Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili | Tarragona |
|  Santos Lozano, José M | 27 | 21 | 5 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Distrito Sanitario Atención Primaria de Sevilla | Sevilla |
|  Serra Majem, Lluís | 50 | 35 | 11 | Universidad de las Palmas de Gran Canaria | Illes Balears |
|  Tena Sempere, Manuel | 30 | 22 | 6 | Universidad de Córdoba - Facultad de Medicina | Córdoba |
|  Tinahones Madueño, Francisco | 77 | 48 | 10 | Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Regional Universitario Carlos Haya | Málaga |
|  Tur Mari, Josep Antoni | 92 | 65 | 16 | Universidad de las Islas Baleares - Facultad de Ciencias de Mallorca | Illes Balears |
|  Villarroya Gombau, Francesc | 18 | 12 | 3 | Universidad de Barcelona - Facultad de Biología | Barcelona |

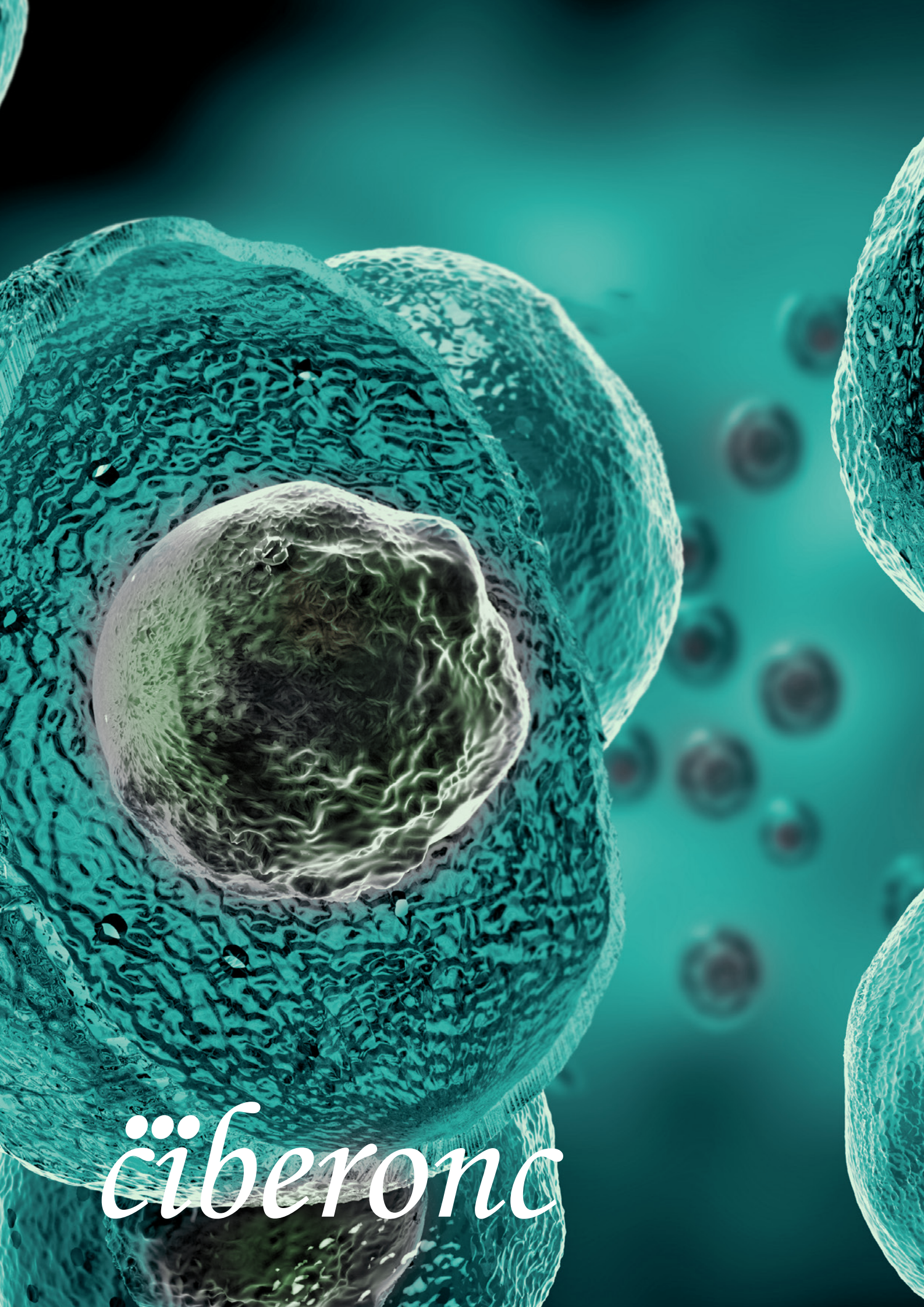
PATENTS OWNED BY CIBER 2020

Patents applied for

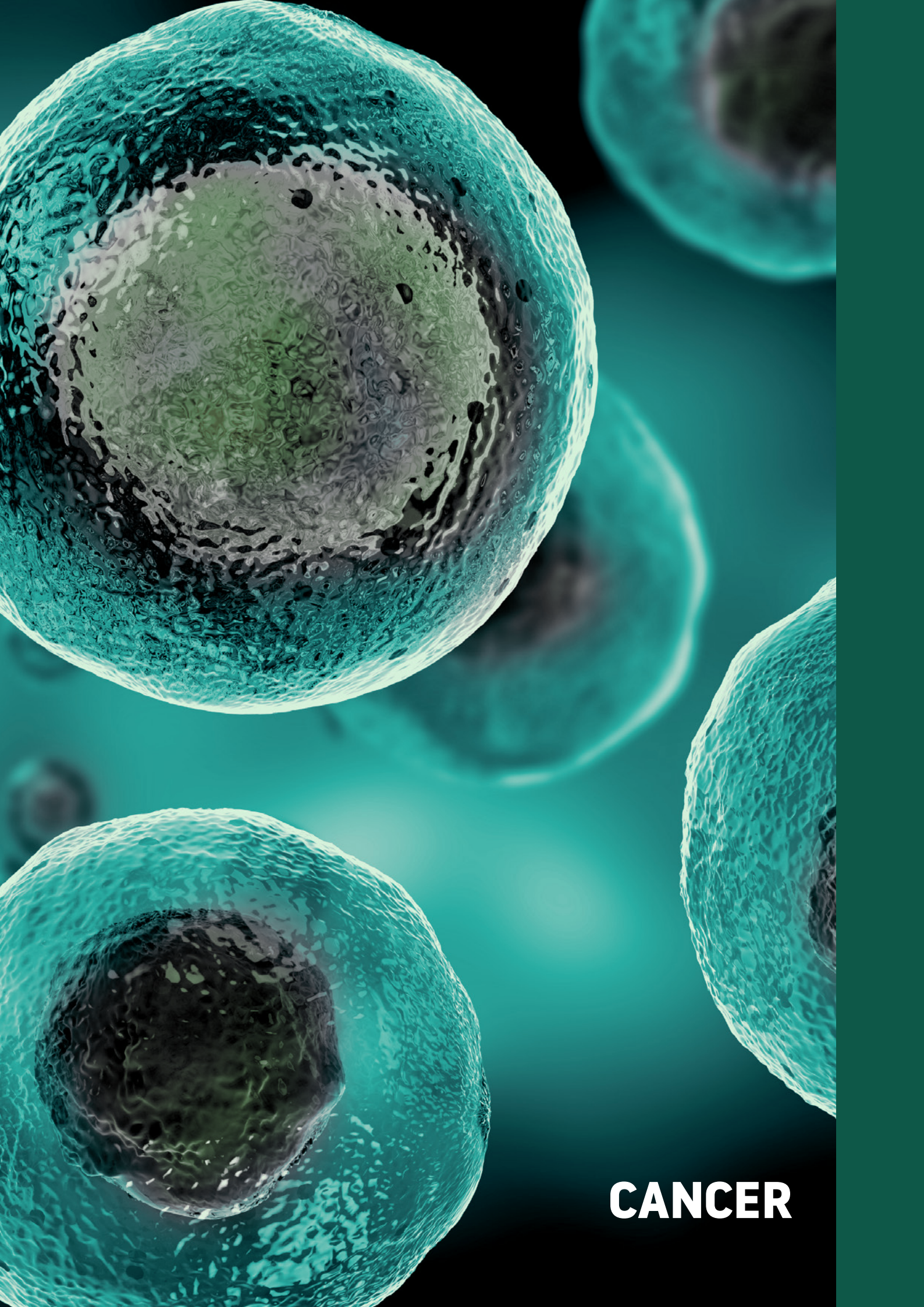
- *Gut microbiota composition and uses thereof*
- *Compositions and methods for treating metabolic disorders*

CLINICAL GUIDES

- Exposomics in the integration of omics markers with a gender perspective: Guide for its implementation.
- Sustainability and gender perspective in obesity research, prevention and treatment: A practical guide for its implementation.
- Tápers saludables y sostenibles: Guía práctica para su elaboración y evaluación.
- A guide to performing and improving polygenic risk score analyses in biomedical research and clinical practice.
- COVID-19: A cascade of Emotions. Healthy practical guide for emotional well-being in the university environment.
- Recommendations to improve lipid control. Consensus document of the Spanish Society of Cardiology.
- Triglycerides, HDL cholesterol and atherogenic dyslipidemia in the European guide for the management of dyslipidemias 2019.
- Atherogenic dyslipidemia 2019. Consensus document of the Atherogenic Dyslipidemia Group of the Spanish Society of Arteriosclerosis.
- Quantifying atherogenic lipoproteins for lipid-lowering strategies: Consensus-based recommendations from EAS and EFLM.
- Consensus document of a group of experts from the Spanish Society of Arteriosclerosis (SEA) on the clinical use of nuclear magnetic resonance in the study of lipoprotein metabolism (Liposcale).
- Nutraceuticals and blood pressure control: a European Society of Hypertension position document.
- Hydration Manual from the Community Pharmacy 2020.
- Medical treatment of type 2 diabetes mellitus: Recommendations of the Diabetes, Obesity and Nutrition Group of the Spanish Society of Internal Medicine.
- "ULTRAPROCESSED FOODS. Critical review, limitations of the concept and possible use in public health".
- HEALTHY FOOD FOR SCHOOL-AGE CHILDREN Guide for families and schools. 2020 Edition.
- Obesity and COVID-19: A Perspective from the European Association for the Study of Obesity on Immunological Perturbations, Therapeutic Challenges, and Opportunities in Obesity.
- Obesity and COVID-19: The Two Sides of the Coin.
- European Association for the Study of Obesity Position Statement on the Global COVID-19 Pandemic.
- OBEDIS Core Variables Project: European Expert Guidelines on a Minimal Core Set of Variables to Include in Randomized, Controlled Clinical Trials of Obesity Interventions.
- Guide to healthy eating for school-age children.
- Do we know what we're buying? Practical guide to understanding labeling.
- European Society of Endocrinology Clinical Practice Guideline: Endocrine work-up in obesity.



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CANCER





WELCOME FROM THE SCIENTIFIC DIRECTOR

Anna Bigas Salvans

It is a source of great pride for me –for the first time since I accepted the Scientific Directorate of CIBERONC– to compile and present to you the report of the activities that have been developed throughout 2020 in the area of cancer.

Undoubtedly, 2020 has been a year marked by the pandemic. The serious global health crisis has had very important repercussions in all areas, including, as could not be otherwise, that of research.

At CIBERONC, the year began with our annual meeting, which brought together more than 130 researchers from our scientific programmes at the National School of Health, and which turned out to be the one (and only) face-to-face meeting of the year. The meeting was also the setting for the annual awards for Best Young Leading Researcher and Best Researcher, awarded in this edition to Pablo Menéndez Buján and Laura Valle Velasco, respectively.

Throughout 2020, CIBERONC has focused on fostering interaction between groups from different disciplines and areas and promoting interaction between basic and clinical groups. As a result of this interaction, CIBERONC has a significant representation in the recently granted national platform for genomic medicine (IMPACT).

This panel has been created as an additional body for structural and scientific advice in our area and has endorsed the internal call for strategic projects for 2021, aimed at aligning groups in the area in view of the next Horizon Europe Mission on Cancer.

Despite the major effect that the pandemic has had on research work, it should be noted that CIBERONC has maintained its high level of activity, with more than 700 publications and an average impact factor over 8.2. Also relevant is the increasing participation of our researchers in dissemination activities, increasing the visibility of our cancer research.

Finally, CIBERONC has continued to foster the training of our youngest researchers, allocating a large part of the training programme budget to research initiation contracts for young graduates and graduates. Moreover, the annual meeting of Young Researchers has been held despite the pandemic which has been carried out online this year, breaking all registration and participation records by our researchers.

In short, 2020 has not been an easy year. I would like to take this opportunity to thank all the members of CIBERONC for your tireless and excellent work, and in particular those who have had to combine healthcare work with research activity. If oncology research has continued to advance despite the circumstances, it is the researchers who have made this possible.

Therefore, thanks to all of you who are a part of and make CIBERONC what it is every single day.



PROGRAMMES

DIGESTIVE TRACT TUMOURS PROGRAMME

Coordinator: **Gabriel Capellà Munar** • Co-coordinator: **Josep Tabernero Caturla**

PREMEDGI (*Research Program on PRecision MEdicine in GI Oncology*) articulates the activity of the CIBERONC Gastrointestinal Tumor Programme since last year with a focus on colorectal and pancreatic tumors. In 2020 the most relevant results of the Gastrointestinal Tumours Programme have been the following: As regards objective 1, the registry of variants of uncertain significance of repair genes contributed by 12 centers has reclassified more than 30 variants and the registry of ATM gene variants has completed a new classification for these variants (Feliubadaló L, et al. . Clin Chem. 2021) in collaboration with researchers from 6 CIBER groups, which represents its consolidation. Regarding objective 2 on the independent research project on predictive factors to response in neoadjuvant treatment of PDAC (clinically led by the groups of Jaime Feliu and Alfredo Carrato), the inclusion of patients will begin once healthcare care activity has normalized after the impact of COVID-19. The third objective of our programme aims to deepen the molecular classification of metastatic colorectal cancer led by Andrés Cervantes' group with the collaboration of 4 groups from the programme. A total of 153 cases of paired samples of primary tumor and metastasis have been identified, of which 43 are synchronous and the rest metachronous, the analysis of which is already underway.

Our program leads the liquid biopsy Work Module platform that promotes comparability of results between centers and has participated very actively in the experimental models module, continuing with the expansion of the PDX collection (*Patient Derived Xenografts*) for colon and pancreatic cancer and modified organoids and in the Cancer Bioinformatics and omics module.

As regards publications, we highlight that the group of Dr. Núria Malats has led the most collaborative publication of CIBERONC of this year's programme (Molina-Montes et al, *Gut*. 70 (2): 319-329, 2020) where in collaboration with professionals from CIBEREHD and CIBERESP, progress has been made in the relationship between diabetes and obesity and the risk of developing pancreatic cancer. Finally we highlight that Dr. Capellà, Dr. Tabernero and Dr. Campo (Haematological Tumours Programme) lead the Cancer WP of the IMPaCT-Genomics project whose main objective is to provide the National Health System (NHS) with a collaborative structure for the implementation of Genomic Medicine.

BREAST CANCER PROGRAMME

Coordinator: **Joaquín Arribas López** • Co-coordinator: **Federico Rojo Todo**

The Breast Cancer Programme has been marked in 2020 by the withdrawal of two great researchers from our field: Dr. Amparo Cano and Dr. Ana Lluch. Both have made very significant contributions to cancer research during their brilliant and extensive professional careers, both within and outside of CIBERONC. Their groups are now led by Dr. Gema Moreno and Dr. Emilio Alba, who have demonstrated the excellence necessary to give continuity to the work they carry out. At the same time, Dr. Gema Moreno has replaced Dr. Amparo Cano as coordinator of the Training Programme.

There has also been a change in the Coordination of the Programme, now being led by Dr. Joaquín Arribas, who will continue to have the support of Dr. Federico Rojo as Co-Coordinator.

Despite the difficulties of 2020, the CIBERONC Breast Cancer Research Programme has managed to maintain a good scientific production. The members of the Programme have published more than 40 new scientific articles, 25% of them in first decile journals, and up to 40% of them in collaboration with other CIBERONC groups. Among the articles led by the Programme, works such as the one published in the journal *EMBO Molecular Medicine* by Dr. Atanasio Pandiella's group, entitled *HER3 targeting with an antibody-drug conjugate bypasses resistance to anti-HER2 therapies*, stands out. Very high impact factor reviews have also been published, such as the one titled *Enhancing global access to cancer medicines*. This work, led by Dr. Javier Cortés, and in which Dr. Joaquín Arribas and Dr. Josep Tabernero have also participated, was published in *A Cancer Journal for Clinicians* (IF 508.702). Among the most relevant collaborations are publications in journals such as *The Lancet Oncology*, *European Urology*, *Cells*, *Nature Review*, *Sci Tran Med*, *Ann Oncol*, etc.

Among the collaborative actions of the Programme, the consolidation of the Collaborative Project with GEICAM stands out, in which the groups of Dr. Gema Moreno, Dr. José Palacios and Dr. Emilio Alba collaborate, and which aims to study the prognostic and/or predictive role of GSDMB and various biomarkers of cell plasticity and stemness in the development of metastases and resistance to treatment in HER2 + and triple negative breast cancer.

The Programme has also been active in participating in CIBERONC events, such as the III Meeting of Young Researchers, where the award for the best postdoctoral presentation was awarded to Dr. Enrique J. Arenas.

RESPIRATORY TRACT TUMOURS PROGRAMME

Coordinator: **Luis Montuenga Badía** • Co-coordinator: **Luis Paz-Ares Rodríguez**

During 2020, the programme has continued with numerous intra-programme collaborations and with other CIBER groups in the three fundamental objectives that we have set. Here are some examples of publications and other relevant collaborative activities: An article was published on the FGFR1-FGFR4 axis led by Dr. Paz-Ares' group, in collaboration with the groups of Drs. Amancio Carnero and Luis Montuenga. These groups are also very actively collaborating in the functional characterization of YES-1 in small cell lung carcinoma, especially from the point of view of its influence on the tumour microenvironment. Dr. Juan Pablo Rodrigo-Tapia's group has published collaborative articles on the NOTCH pathway with Dr. Gema Moreno-Bueno, on the involvement of RHO-GEF VAV2 in head and neck carcinogenesis in collaboration with Drs. Xosé Bustelo and Jesús Paramio, and a work on the immune landscape, also in head and neck tumors, in collaboration with members of the group led by Dr. Montuenga.

Dr. Camps's group and Dr. Montuenga's group have actively collaborated in epigenetic validation studies of genes with prognostic value in lung cancer, analysis of susceptibility or resistance genes in lung cancer patients with "extreme phenotypes". This last work is led by Dr. Pérez Gracia, from Dr. Ignacio Melero's group. Dr. Camps's group has published a review on liquid biopsy in lung cancer in collaboration with Dr. Paz-Ares. Regarding research projects, Dr. Silvestre Vicent obtained a project from the AECC in collaboration with Dr. Irene Ferrer. Dr. Marco Pérez, (Dr. Amancio Carnero's group) has obtained funding for four projects from various entities, all of them in collaboration with Dr. Enrique de Álava's group. Dr. Jon Zugazagoitia (Luis Paz-Ares' group) and Dr. Karmele Valencia (Luis Montuenga's group) were awarded two fellowships by the International Association for the Study of Lung Cancer (IASLC). In the programme, 5 doctoral theses have been defended and there has been an active participation in the CIBERONC Work Modules. Dr. Montuenga gave one of the presentations at the closing plenary session of the 2020 World Lung Cancer Congress and Dr. Luis Paz-Ares was elected the new President of the Spanish Association for Cancer Research (ASEICA). Dr. Paz-Ares and Dr. Montuenga participated as experts in the Panel organized by the *European Association of Personalized Medicine*, of which two position papers have been published. Dr. Montuenga participates in the IASLC *Molecular Staging Committee*, which has also published a recommendation article for the 9th edition of TNM staging in lung cancer. Dr. Paz-Ares and other members of his group participated in the update document of the consensus guidelines for the analysis of predictive biomarkers for non-small cell lung cancer of the Spanish Society of Pathology (SEAP) and the Spanish Society of Medical Oncology (SEOM).

HAEMATOLOGICAL TUMOURS PROGRAMME

Coordinator: **Dolors Colomer Pujol** • Co-coordinator: **Ramón García Sanz**

Most of the results obtained this year have been in collaboration between CIBERONC groups and national and international cooperative work groups. Worth mentioning this year are the publications related to the impact of COVID on hematological neoplasms.

In the pathological and molecular characterization of hematological neoplasms, worth highlighting are the epigenetic studies in multiple myeloma (MM) that have identified aberrant chromatin activation (*Genome Res.* 2020; 30: 1217-27) and the characterization of granulocytic-myeloid-derived suppressor cells (G-MDSCs) (*Blood* 2020; 136: 199-209). B-cell leukemia transdifferentiation to macrophage has been reported to involve reconfiguration of DNA methylation (*Leukemia* 2020; 34: 1158-62). In acute myeloblastic leukemia (AML), the response to treatment of patients older than 60 years of age has been analyzed (*Leukemia* 2020 Nov 19) and in Philadelphia-negative acute lymphoblastic leukemia (ALL-HR-11 trial) after treatment with chemotherapy or transplantation (*Blood* 2020 Nov 4).

To be highlighted among the development of new tools is the computer algorithm for the analysis of immunoglobulin rearrangements (IgCaller) (*Nat Commun.* 2020; 11: 3390), evaluating its applicability in clinical practice. The implementation of a NGS panel for the networking for diagnosis of AML has also been published (*Haematologica* 2020 Nov 12) and NGS techniques have been compared with new generation cytometry techniques (NGF) in residual disease in MM. (*Blood Cancer J.* 2020; 10: 108). Recommendations on how to perform single cell sequencing studies have been published (*Genome Biol.* 2020; 21 (1): 112), projects under development in the group.

In the section on preclinical models, epigenetic therapy has been described to eliminate tumour cells and prepare mitochondria to induce apoptosis mediated by BH3 mimetics (*Cancer Disco-v.* 2020; CD-20-1065). Preclinical trials with new immunotherapies have been described (*Oncogene* 2020;39:1185-97; *Haematologica* 2020;105:1032-1041). The CLL and AML PDX collection has been expanded and work is underway on 3D models in lymphoma, MM, and AML.

Regarding clinical trials, worth mentioning is the development of the chimeric antigen receptor (CAR) T-cell therapy clinical trial (CAR-T-ARI-001) led by CIBERONC researchers. The results were presented at the end of 2020 and the AEMPS has authorized CAR-T ARI-0001 for patients with LAL. We highlight the results in phase I and II (an inhibitor of histone deacetylases in AML (*J Clin Oncol.* 2020; 38: 4260-73); a conjugated antibody SLAMF7 / CS1 (*Clin Cancer Res.* 2020; 26: 2308-17) and an anti-CD38, isatuximab (*Leukemia.* 2020; 34: 3298-3309) in MM) and the leadership in the phase III trial ALCYONE (*Lancet.* 2020; 395 (10218): 132-141) in MM.

LOW PREVALENCE TUMOURS PROGRAMME

Coordinator: **Enrique de Álava Casado** • Co-coordinator: **Ignacio Melero Bermejo**

The challenge for our programme for 2020 was to carry out two cooperative research projects on two low-prevalence tumours, selected from a broad and heterogeneous group of entities such as those targeted by the Programme.

>> The first half of 2020 was dedicated to generating data within the cooperative project of the programme on uveal melanoma, a neoplasm in which up until now it had not been possible to carry out a translational project at the national level. For this project, the programme had obtained additional funding through an award granted by the GETHI (Spanish Group of Orphan and Infrequent Tumors) in 2017. Specifically, the program covered these two milestones:

- Evaluation and quantification of Endoglin (EDG) / MMP14 expression levels and HIPPO TAZ / YAP pathway effectors in 4 independent cohorts of paired uveal melanoma samples.
- Generation of EDG, MMP14, TAZ and YAP elimination models by genomic editing using CRISPR-Cas9 technology, which were used to evaluate the functionality of these molecules in *in vitro* and *in vivo* models of uveal melanoma.

These programme results are included in the application of the 2020 call for AECC strategic research projects, which is currently under evaluation. The generation of additional results from this first cooperative project of the Programme continues at the present time.

>> Throughout 2020, we carried out a second cooperative project aimed at the immunological landscape of uterine tumours. Each group provided tools, samples and clinical data on this tumour, in which no cooperative translational research had been carried out in Spain so far. The project was launched in September 2018, after the approval of the CIBERONC Scientific Advisory Board. Milestones through the end of December 2020 include:

- A pilot multi-parametric and multicenter study was carried out to characterize a small series of endometrial carcinomas by studying the stroma and tensegrity (Gomori path), the immunophenotypic characterization of stromal cells (Vectra-Polaris), and the genomic characterization of the tumour and stromal cells. This has allowed the molecular and architectural characterization of the invasive front of uterine malignant neoplasms: in particular, we have assessed whether these findings provide information of additional prognostic value to established prognostic factors.

The activity of this second cooperative project will continue until the end of 2021.

During 2020, the execution of two cooperative projects has continued in which the Programme has become involved to secure funding for the activity in uterine tumors : Project Marató-TV3 endometrial carcinoma (2019: € 396k); Project of excellence of the Junta de Andalucía on endometrial stromal sarcoma (2019: € 400k).

TUMOUR PROGRESSION MECHANISMS PROGRAMME

Coordinator: **Xosé R. García Bustelo** • Co-coordinator: **Jesús M. Paramio González**

In the area of discovery and characterization of protumorigenic molecules, Dr. Xosé Bustelo's group has identified the role of the VAV2 molecule in maintaining a state of regenerative proliferation in both head and neck and skin cancers. Diagnostic signatures have been derived from this work that allow better stratification of papillomavirus-negative head and neck patients (*Nat Commun* 11: 4788). Using a new pharmacomimetic mouse model generated by homologous recombination, the same group was able to demonstrate that inactivation of the catalytic activity of VAV2 could indeed be a suitable way to treat the aforementioned tumor types. These mice also made it possible to demonstrate that there were therapeutic windows in which positive therapeutic effects could be obtained without generating collateral problems in healthy organs (*Oncogene* 39: 5098; *Nat Commun* 11: 5808). Part of these works were carried out in collaboration with groups from CIBERONC (Dr. Jesús M. Paramio and Juan P. Rodrigo Tapia) and CIBEROBN (Dr. Carlos Diéguez). Dr. Arkaitz Carracedo's group has discovered new roles for the Lkb1 kinase in prostate cancer, demonstrating that the complete suppression of its activity is essential for the pathogenesis and, above all, for the metastatic capacity of this tumor (*J Exp Med* 217: e20191787). This work was carried out in collaboration with other members of the CIBERONC (Dr. Jesús M. Paramio). Finally, Dr. Pablo Menéndez (Anna Bigas' group) has characterized the genetic alterations that contribute to the development of hyperdiploid acute lymphocytic B-cell leukemia (B-ALL), the most common subtype among pediatric B-ALL. These have been associated with impaired condensin complex and Aurora B kinase (*Blood* 136: 313). This work has been carried out in collaboration with groups from CIBERONC (Dr. Juan P. Rodrigo Tapia) and CIBERER (Dra. Mireia Camós).

In the area of development of new experimental techniques, the Programme has developed a new method that will make it possible to analyze each of the stages of ribosome biosynthesis in human tumour cells, something which up until now had been difficult to achieve outside studies in yeast (group led by Dr. Xosé R. Bustelo, *Nat Commun* 11: 156).

In the area of development of new diagnostic and therapeutic tools, Dr. Pablo Menéndez has developed a new CAR-T system for the elimination of B-ALL cells (*J Immunother Cancer* 8: e000896). He has also established that one of the dangers associated with immunotherapy against the CD123 surface antigen used for the elimination of acute myeloid leukemia is the elimination of normal hematopoiesis in patients (*J Immunother Cancer* 8: e000845). Finally, the development by Dr. Joan Seoane's group of a new biopsy method based on the analysis of ctDNA present in the cerebrospinal fluid for the detection and diagnosis of patients with medulloblastoma is worth noting (*Nat Commun* 11: 5376). This work has been carried out in collaboration with other CIBERONC groups (Drs. Santiago Ramón y Cajal and Carlos López-Otín).

TRAINING PROGRAMME

Coordinator: **Gema Moreno Bueno** • Co-coordinator: **Núria Malats Riera**

The CIBERONC training programme has granted, throughout 2020, a total of 28 training grants in its different training, mobility, initiation to research in oncology and promotion of young researchers sub-programmes.

Thus, the training sub-programme has granted 15 grants for training courses: 11 of them for attendance to courses, 2 for organizing courses and 2 for sponsoring scientific events.

Of the 8 mobility grants granted, only 2 could be completed (1 national / 1 international) due to the health crisis situation. Due to the implementation of the State of Alarm because of the COVID-19 Pandemic, most of the requested grants were canceled as was the second call for this type of grants.

In 2020, a large part of the programme's budget was invested in the call for 10 initiation contracts for young researchers, contracts for initiation to research in oncology for the incorporation of young degree holders or graduates to groups in our network.

Finally, one of the activities of the programme with the greatest impact on the training of doctoral students and young doctors was the III CIBERONC Young Researchers Meeting. The meeting, which also had financial support from the programme, was held this year for the first time online due to the health situation and had the participation of 238 researchers who contributed 102 poster presentations, with 12 works selected for oral presentations.



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

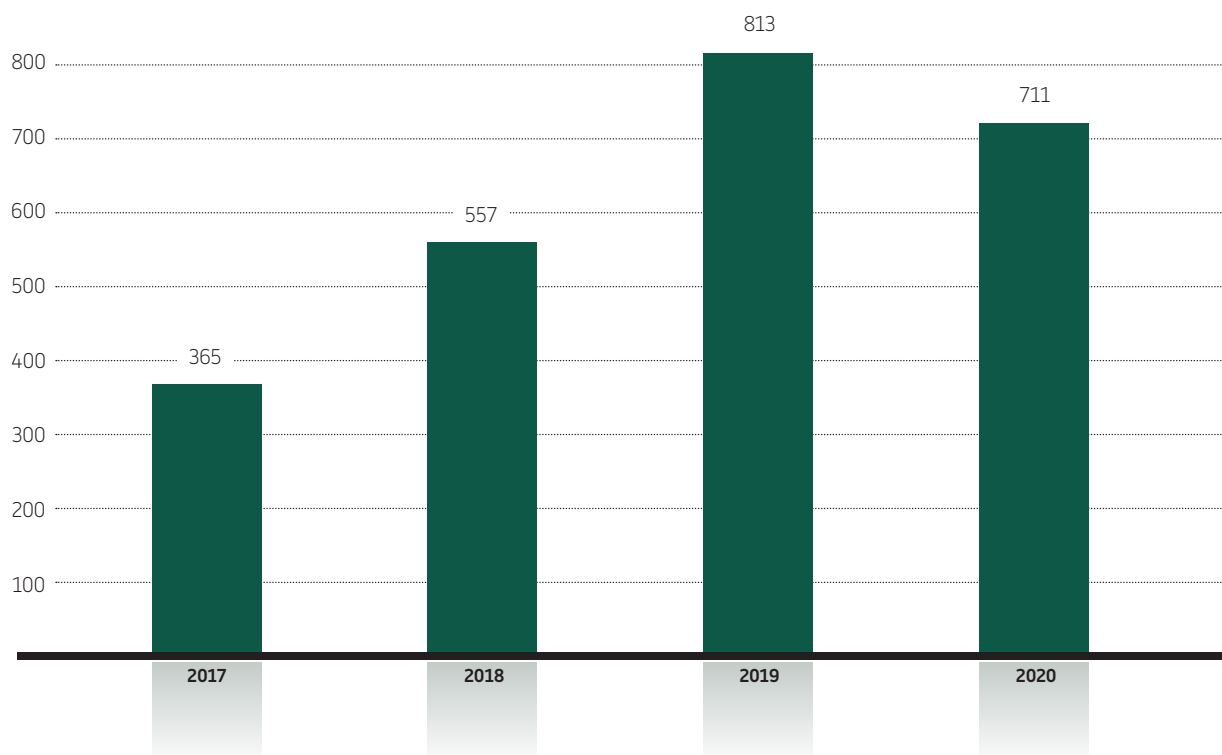
| | |
|--------|-----|
| TOTALS | 711 |
| Q1 | 456 |
| D1 | 238 |

Collaborations

| | |
|----------|-----|
| CIBERONC | 129 |
| CIBER* | 123 |

*Among various thematic areas

» Evolution of publications



» 10 most relevant publications by impact factor

| IF | Publication |
|------------|--|
| FI 508.702 | <i>Enhancing global access to cancer medicines. CA Cancer J Clin</i> 2020 Mar;70(2):105-124. doi: 10.3322/caac.21597. |
| FI 91.245 | <i>Oral Azacitidine Maintenance Therapy for Acute Myeloid Leukemia in First Remission. N Engl J Med</i> 2020; 383:2526-2537. DOI: 10.1056/NEJMoa2004444. |
| FI 94.444 | <i>Guidelines and definitions for research on epithelial-mesenchymal transition. Nature Reviews Molecular Cell Biology</i> volume 21, pages341-352(2020). |
| FI 54.908 | <i>Benchmarking single-cell RNA-sequencing protocols for cell atlas projects. Nature Biotechnology</i> volume 38, pages747-755(2020). |
| FI 53.44 | <i>BL-8040, a CXCR4 antagonist, in combination with pembrolizumab and chemotherapy for pancreatic cancer: the COMBAT trial. Nat Med.</i> 2020 Jun;26(6):878-885. doi: 10.1038/s41591-020-0880-x. Epub 2020 May 25. |
| FI 53.44 | <i>Implications of TP53 allelic state for genome stability, clinical presentation and outcomes in myelodysplastic syndromes. Nature Medicine</i> volume 26, pages1549-1556(2020). |
| FI 41.316 | <i>Adjuvant denosumab in early breast cancer (D-CARE): an international, multicentre, randomised, controlled, phase 3 trial. Lancet Oncol.</i> Volume 21, ISSUE 1, P60-72, January 01, 2020 |
| FI 33,752 | <i>Adjuvant nivolumab versus ipilimumab in resected stage IIIB-C and stage IV melanoma (CheckMate 238): 4-year results from a multicentre, double-blind, randomised, controlled, phase 3 trial. Lancet Oncol.</i> 2020 Nov;21(11):1465-1477. doi: 10.1016/S1470-2045(20)30494-0. Epub 2020 Sep 19. |
| FI 33,752 | <i>Pazopanib for treatment of typical solitary fibrous tumours: a multicentre, single-arm, phase 2 trial Clinical Trial. Lancet Oncol</i> 2020 Mar;21(3):456-466. doi: 10.1016/S1470-2045(19)30826-5. Epub 2020. |
| FI 33,752 | <i>Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. Lancet Oncol.</i> 2020 May;21(5):645-654. doi: 10.1016/S1470-2045(20)30068-1. Epub 2020 Mar 27. |

» CIBERONC Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|--|-----------|
|  Alba Conejo, Emilio | 15 | 10 | 4 | Universidad de Málaga | Málaga |
|  Álava Casado, Enrique de | 18 | 7 | 3 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Albanell Mestres, Joan | 19 | 10 | 5 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Aranda Aguilar, Enrique | 11 | 5 | 1 | Fundación para la Investigación Biomédica de Córdoba (FIBICO) | Córdoba |
|  Arribas López, Joaquín | 5 | 4 | 3 | Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO | Barcelona |
|  Batlle Gómez, Eduard | 4 | 3 | 3 | Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona) | Barcelona |

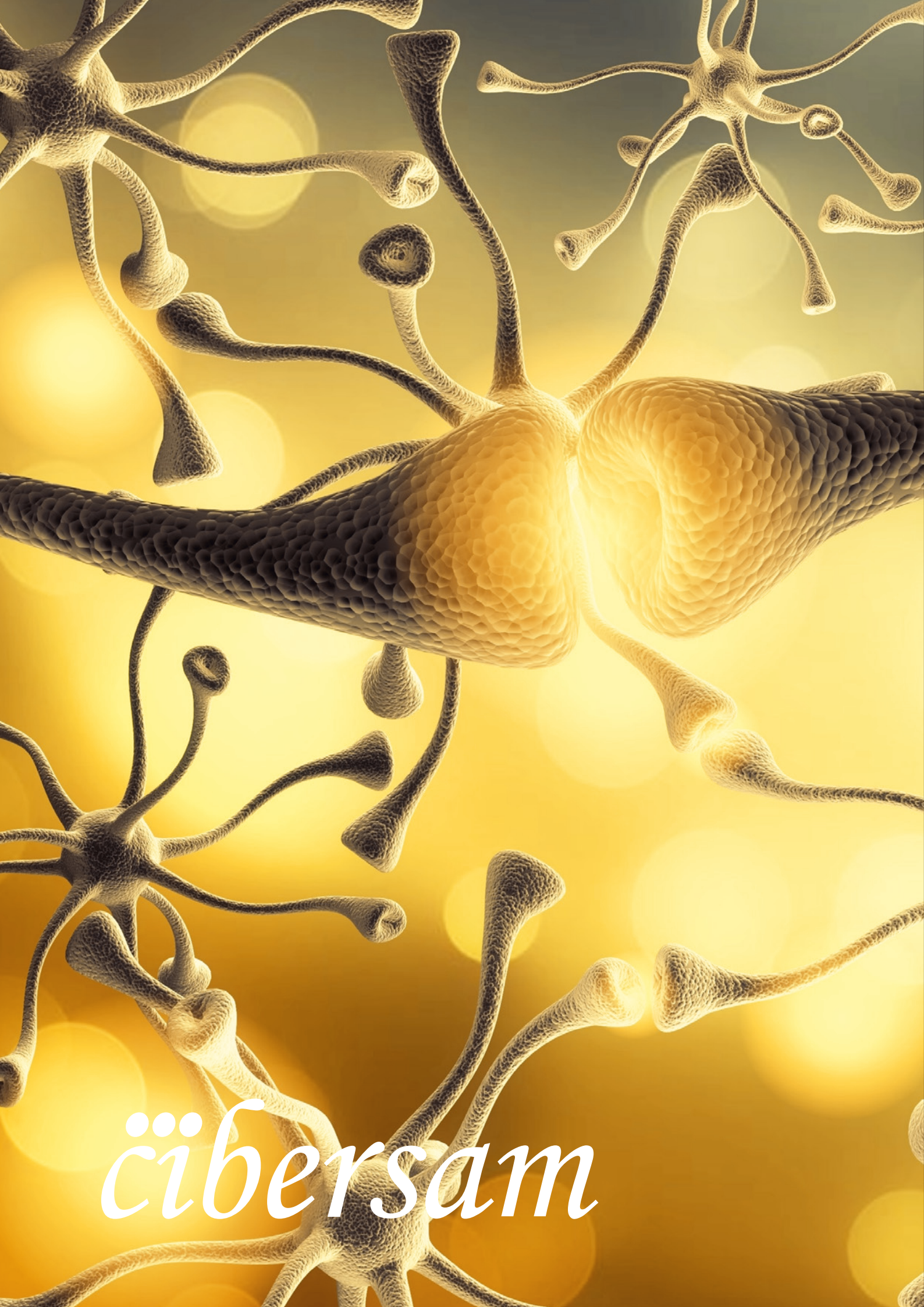
| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|--|--------------|----|----|---|-----------|
|  Bigas Salvans, Anna | 17 | 15 | 12 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Campo Guerri, Elías | 32 | 25 | 17 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Camps Herrero, Carlos | 16 | 7 | 0 | Consorcio Hospital General Universitario Valencia | Valencia |
|  Capellà Munar, Gabriel | 23 | 17 | 6 | Fundación IDIBELL | Barcelona |
|  Carnero Moya, Amancio | 7 | 7 | 3 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Carracedo Pérez, Arkaitz | 8 | 8 | 6 | CIC BIOGUNE | Vizcaya |
|  Carrato Mena, Alfredo | 19 | 10 | 4 | Servicio Madrileño de Salud | Madrid |
|  Cervantes Ruy Pérez, Andrés | 20 | 14 | 9 | Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) | Valencia |
|  Colomer Pujol, Dolors | 23 | 19 | 10 | Instituto de Investigaciones Biomédicas August Pi i Sunyer | Barcelona |
|  Crespo Baraja, Pedro | 1 | 0 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Cantabria |
|  Esteller Badosa, Manel | 29 | 25 | 15 | Fundación Instituto de Investigación contra la Leucemia Josep Carreras | Barcelona |
|  Feliú Batlle, Jaime | 11 | 5 | 3 | Servicio Madrileño de Salud | Madrid |
|  García Bustelo, Xosé Ramón | 7 | 6 | 4 | Fundación de Investigación del Cáncer de la Universidad de Salamanca | Salamanca |
|  García Sanz, Ramón | 35 | 25 | 7 | Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León | Salamanca |
|  López Lopez Rafael | 26 | 16 | 5 | Servicio Gallego de Salud | A Coruña |
|  López Otín, Carlos | 11 | 9 | 9 | Universidad de Oviedo | Asturias |
|  Malats Riera, Nuria | 16 | 13 | 5 | Fundación Centro Nacional de Investigaciones Oncológicas | Madrid |
|  Martín Jiménez, Miguel | 16 | 11 | 8 | Servicio Madrileño de Salud | Madrid |
|  Matias Guiu-Guià, Francisco Javier | 26 | 20 | 13 | Instituto de Investigación Biomédica de Lleida. Fundación Dr. Pifarre | Lleida |
|  Melero Bermejo, Ignacio | 22 | 16 | 13 | Universidad de Navarra | Navarra |
|  Montuenga Badía, Luis | 25 | 22 | 10 | Fundación para la Investigación Médica Aplicada | Navarra |
|  Moreno Bueno, Gema | 4 | 3 | 1 | Universidad Autónoma de Madrid | Madrid |
|  Muñoz Terol, Alberto | 3 | 3 | 2 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Noguera Salvà, Rosa | 7 | 6 | 1 | Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) | Valencia |
|  Oliver Pozo, Francisco Javier | 4 | 2 | 0 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Granada |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--|-----------|
|  Orfao de Matos Correia e Vale, José Alberto | 19 | 14 | 3 | Fundación de Investigación del Cáncer de la Universidad de Salamanca | Salamanca |
|  Palacios Calvo, José | 8 | 6 | 4 | Servicio Madrileño de Salud | Madrid |
|  Pandiella Alonso, Atanasio | 18 | 12 | 2 | Fundación de Investigación del Cáncer de la Universidad de Salamanca | Salamanca |
|  Paramio González, Jesús María | 13 | 9 | 4 | Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT) | Madrid |
|  Paz- Ares Rodríguez, Luis | 36 | 23 | 11 | Servicio Madrileño de Salud | Madrid |
|  Pérez Simón, José Antonio | 11 | 6 | 1 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Piris Pinilla, Miguel Ángel | 15 | 10 | 6 | Instituto de Investigación Sanitaria Fundación Jiménez Díaz | Madrid |
|  Prósper Cardoso, Felipe | 17 | 11 | 8 | Fundación para la Investigación Médica Aplicada | Navarra |
|  Ramón y Cajal Agüeras, Santiago | 16 | 9 | 6 | Fundación Hospital Universitario Vall d'Hebrón - Institut de Recerca (VHIR) | Barcelona |
|  Real Arribas, Francisco Xavier | 11 | 11 | 8 | Fundación Centro Nacional de Investigaciones Oncológicas | Madrid |
|  Rodrigo Tapia, Juan Pablo | 17 | 16 | 6 | Fundación para la Investigación e Innovación Biosanitaria en el Principado de Asturias (FINBA) | Asturias |
|  San Miguel Izquierdo, Jesús Fernando | 48 | 39 | 28 | Universidad de Navarra | Navarra |
|  Santisteban Sanz, María del Pilar | 6 | 5 | 3 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Madrid |
|  Santos de Dios, Eugenio | 1 | 1 | 1 | Fundación de Investigación del Cáncer de la Universidad de Salamanca | Salamanca |
|  Sanz Santillana, Guillermo | 49 | 31 | 19 | Fundación para la Investigación del Hospital la Fe | Valencia |
|  Seoane Suárez, Joan | 4 | 3 | 2 | Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO | Barcelona |
|  Taberero Caturla, José María | 12 | 11 | 11 | Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO | Barcelona |

PATENTS OWNED BY CIBER 2020

Patents applied for

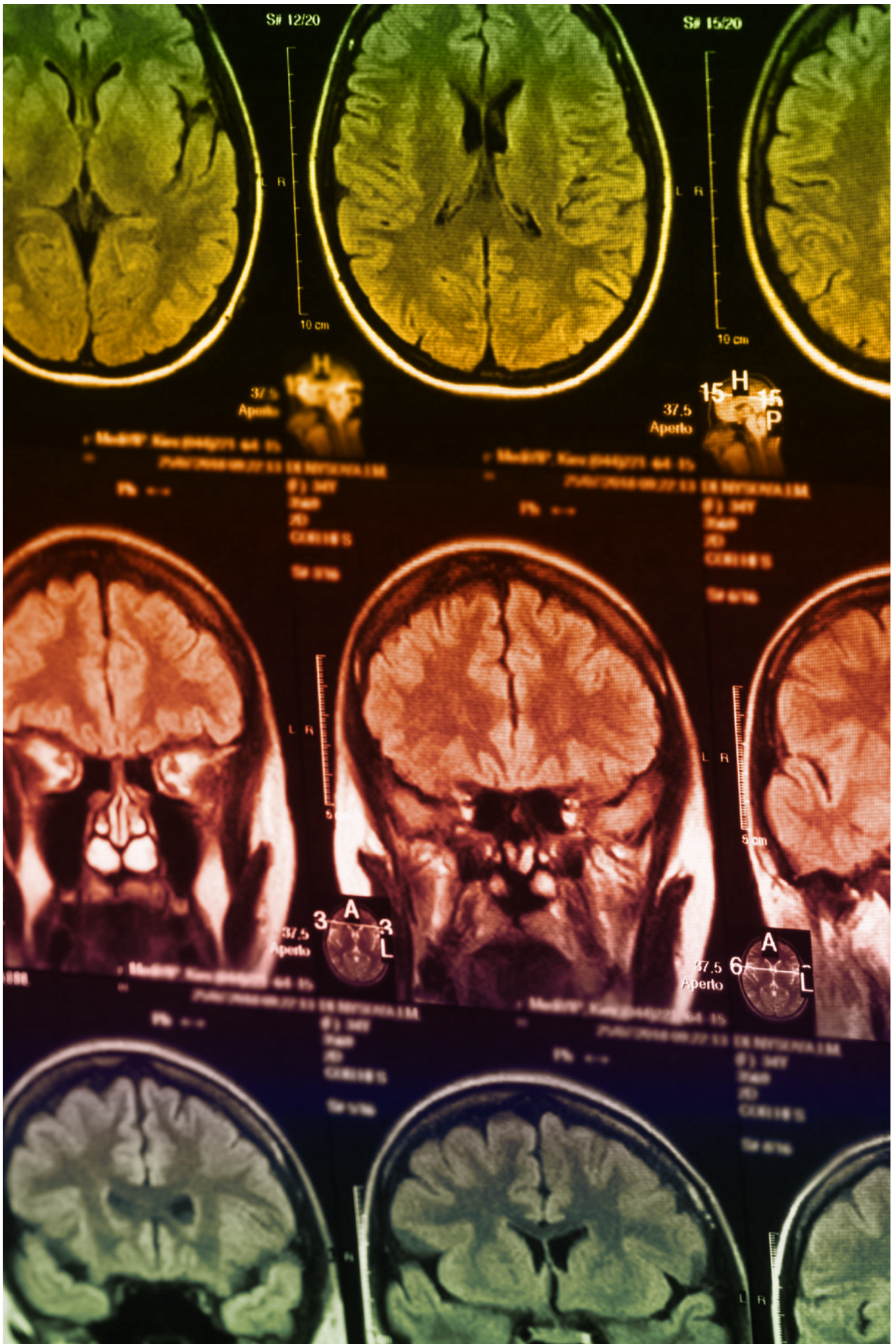
- *Biomarkers and method to predict or forecast response to treatment with BRAF and MEK inhibitors (BRAFi + MEKi) and for patient follow-up. PI CIBERONC Group: Emilio Alba Conejo.*



čibersam



MENTAL HEALTH





WELCOME FROM THE SCIENTIFIC DIRECTOR

Eduard Vieta Pascual

Without a doubt, 2020 has been a year we will never forget, especially due to the Covid-19 pandemic which has affected the entire planet, but also due to its direct and indirect effects on mental health, which are already becoming increasingly evident. Vaccines have contributed to showcase the value of biomedical research and advances in neuroscience will also help combat the psychological and psychiatric havoc that the virus has wreaked and the drastic measures that governments have taken to combat it. The CIBER mental health area, CIBERSAM, in an extremely complex context, has once again surpassed itself and has established a new record number of high-value scientific publications: no less than 852 articles, 23% of these in the top 10 % of high impact journals (such as New England Journal of Medicine, Drug Discovery, The Lancet, Nature or JAMA Psychiatry, among others), representing substantial advances in knowledge to combat mental illness. It is worth noting that 132 publications are collaborative between CIBER areas. In addition to the publications, CIBERSAM has published 15 clinical guides and the depression and suicide prevention white paper, has registered 3 patents and has collaborated in large international consortia on genetics and neuroimaging, with a prominent role. The interuniversity Master's degree for initiation to research in mental health, coordinated by CIBERSAM, has received 69 registrations. But this year 2020 I want to highlight above all the extraordinary response capacity of the CIBERSAM scientists, many of them clinicians who have not hesitated to put themselves in the front line to care for Covid-19 patients. Not only have they lent themselves to support care, but together with those who do not have clinical obligations, they have put themselves at the service of all through research activity. This has led to the publication of the remarkable number of 72 scientific articles on Covid-19 and mental health, and to obtaining competitive funds to further research this topic through 5 large projects. In addition, CIBERSAM has published 3 clinical guidelines on Covid-19 and mental health focused on children and adolescents, the protocol for conducting electroconvulsive therapy in safe conditions, and the problems of excessive internet use during the pandemic.

If last year I ended my presentation declaring myself proud of the investigating researchers of CIBERSAM, what can I say this year? It is not just an immense honor and privilege to be the Scientific Director of such an extraordinary group of health scientists - it is proof that the best is brought out in people when misfortune befalls humanity so massively, with a death toll in the millions and millions of people more whose mental health may suffer in the present and near future. CIBERSAM is a beacon in the dark that illuminates a more positive future, through collaborative, innovative and transformative translational research.



PROGRAMMES

DEPRESSION AND SUICIDE PREVENTION

Coordinator: **Diego Palao Vidal**

Every year more than 3,500 people die by suicide in Spain, in most cases associated with depression, the most prevalent mental illness. The fact that it especially affects young people makes suicide the third leading cause of years of potential life lost in our country. These data and the fact that it is a preventable cause of death, also associated with other mental illnesses, have made it a focus of research for other groups, in addition to those included in the Programme. During 2020, a substantial number of articles (n = 322) on depression and suicide have been published in collaboration with other CIBER groups and international research groups in epidemiology, neurobiology and prevention. Specifically, the Programme groups have published more than 100 articles, 23% in the first decile. Competitive financing has been obtained for 19 national and 13 international projects. The SURVIVE cohort study has been started, led by 8 CIBER-SAM groups, in which different preventive interventions will be studied and which will also allow, for the first time ever, the creation of a platform for monitoring suicidal behavior in Spain.

Epidemiological studies on depression and suicide include the first results of the effects of COVID-19 in the general population, in post-intensive care patients, the mentally ill, and in health professionals. Results of studies on the association of various sociodemographic factors, lifestyles, age and cognitive deficits in depression have also been published.

The results of the participation of various groups of the Programme in international consortia such as Gen-ECT-ic, GEMRIC and ENIGMA have continued to be disseminated, which have deepened the identification of the brain areas involved in the mechanism of action of electroconvulsive therapy, as well as the associated genetic, environmental, demographic, cognitive and psychosocial factors. Several groups are investigating the development and evaluation of possible diagnostic and prognostic biomarkers such as neuroimaging tests, neurocognitive, neurophysiological, inflammatory and genetic evaluations.

One of the most active research lines focuses on the study of the molecular bases and the therapeutic evaluation of drugs with new mechanisms of action such as the glutamatergic pathway, as well as the development of new therapeutic targets applying experimental stress models and a computational methodology.

During 2020, the Programme has obtained 12 competitive contracts and 13 doctoral theses have been presented, in addition to registering a patent (WO2020144327), the first one to publish a biomarker for major depression based on the ratio of proLRP1 / LRP1 proteins, and the LRP1-48 isoform sequenced by the group itself.

Also noteworthy is the progressive involvement of the groups in scientific outreach activities - this year mainly through webinars and online events - and the coordination of the “White Paper on Depression and Suicide” in Spain, a strategic instrument promoted by the main scientific societies.

SCHIZOPHRENIA

Coordinator: **Benedicto Crespo-Facorro**

Among the most notable results of the programme during 2020 are the more than 100 publications in the first decile according to the JCR ranking in the fields of psychiatry, neuroimaging, genetics, multidisciplinary sciences, neurology and neurosciences, a high percentage (80%) of these in collaboration with other CIBER groups. These figures reflect a growth in research publications in high impact journals, as well as greater collaboration between research member groups of CIBER.

Throughout 2020, within the programme finance has been secured for the following projects: the EU (PRISM) project, two ERANETNeuron projects, two participations in COST-H2020, a project funded by the NIH, and a project funded by The New York Academy of Science. Nationally, a total of 14 projects with PIs from CIBERSAM have obtained competitive funding in public calls. Here, too, there has been an increase in fundraising in international calls, reinforcing national fundraising through AES calls.

As regards human resources contracts, we highlight the incorporation of researchers through 2 Rio Hortega contracts, 6 Sara Borrell contracts, an ICREA, an ISCIII intensification, a PFIS, a FPU, 4 AGAUR, and a SAS specialist postdoctoral contract.

2 patents have been published:

- >> WO2020144327, Inventors: Carlos Spuch, Tania Rivera, Jose Manuel Olivares, Miguel Ángel Correa, Moses Pérez, Verónica Salgueiriño, Ana Sousa, María Blanco. Title: “In vitro method for the diagnosis or prognosis of neurodegenerative disorders”. This patent is the first to publish a plasma biomarker for major depression based on the ratio of proLRP1 / LRP1 proteins and the LRP1-48 isoform sequenced by our group using LC-ESI-MS / MS.
- >> Extension of patent EP 2 948 563 B entitled “Method for predicting extrapyramidal symptoms (EPS) induced by antipsychotic-based treatment”, in the name of the University of Barcelona, Hospital Clínic de Barcelona, IDIBAPS and CIBERSAM. Licensee: AB-BIOTICS. Researchers: Patricia Gassó, Sergi Mas, Amalia Lafuente, Miguel Bernardo.

Fifteen doctoral theses have been defended within the CIBERSAM groups.

Regarding other merits, the members of the programme and their work have been recognized with various awards at meetings, congresses, national and international symposia and by family associations.

Among the milestones of this programme we highlight the continuity of the First-Episode Psychosis Cohort (PEP) with a 15-year follow-up.

BIPOLAR DISORDER

Coordinator: **Ana González-Pinto**

170 articles stand out, 101 published in first quartile journals and 69 in first decile journals. Among these: Nature Genetics, JAMA Psychiatry, American Journal of Psychiatry, British Journal of Psychiatry, The Lancet Psychiatry, Cell and Psychological Medicine.

New national and international projects have been obtained (2 ISCIII, 1 from the Fundació Clínic per a la Recerca Biomèdica, 1 from the Ministère des Relations Internationales et de la Francophonie):

- >> Suicide Prevention and Intervention (SURVIVE): cohort study and nested controlled clinical trials of secondary prevention programmes for suicide attempts (in collaboration with the groups led by Ayuso, Bobes, González-Pinto, Leza, Pérez, Vieta, Crespo and Palao).
- >> Prediction of depressive relapse in bipolar disorder by continuous actigraphic monitoring: a 12-month prospective study (Vieta).
- >> Early intervention to improve cognitive reserve in subjects at risk and early stages of psychosis (in collaboration with the groups led by Bernardo and Vieta).
- >> Ministry of International Relations and La Francophonie- “Quebec-Catalonia cooperation in neuroimaging: a predictive approach to psychosis” (Pomarol).

Competitive contracts:

- >> Rio Hortega contract for Estela Salagre. Group led by Eduard Vieta.
- >> Miguel Servet II contract for Carla Torrent and for Joaquim Radua. Group led by Eduard Vieta.
- >> Basque Government Predoctoral Programme; UPV for Jessica Fernández. Group led by Ana González-Pinto.
- >> Contract: Juan de la Cierva- Elvira Lara. Group led by José Luis Ayuso.
- >> 3 CIBERSAM contracts. Groups led by Ana González-Pinto and Edith Pomarol.
- >> 1 Instituto de Salud Carlos III - PFIS. Group led by Edith Pomarol.
- >> 2 Sara Borrell contracts. Group led by Edith Pomarol.

Awards and distinctions:

- >> Eduard Vieta and Joaquim Radua ranked among the most influential scientists in the world (Clarivate Analytics 2020).
- >> Renewal of the UAM as a WHO Collaborating Center. Group led by José Luis Ayuso.
- >> 1st Prize of the Health Research Institute BIOARABA Research and Innovation Conference 2020 to Diet, oxidative stress and mental illness. Dra. Saínza García. Group led by Ana González-Pinto.
- >> Prize of the Institute for Health Research BIOARABA Jornadas de Investigación e Innovación 2020: “Absence of association between the level of lethality and the recidivism of suicide attempts in a Spanish province” to Ana González-Pinto.
- >> 1st prize in TOP10 Psychiatry: Ocular coherence tomography as a diagnostic parameter of functional impairment in bipolar disorder. Saínza García. Group led by Ana González-Pinto.
- >> Extraordinary doctorate award to Norma Verdolini for her doctoral thesis “Self- and hetero-aggression” Clinical implications in Bipolar Disorder and Mixed States”, directed by Eduard Vieta and Isabella Pacchiarotti.

Among the scientific achievements, 4 of the 6 doctoral theses defended stand out:

- >> Bipolar disorder and pregnancy: evaluation of obstetric and neonatal results. Eva Solé. University of Barcelona. Director: Eduard Vieta.
- >> Benzodiazepine overdose and falls in the elderly. Maria Jose Diaz. Director: Ana González-Pinto.
- >> Neuropsychological and functional MRI study in bipolar depression. Paloma Fernandez. Director: Edith Pomarol.
- >> Darío Moreno. New evidence on the determinants and course of subjective well-being in the general population: a focus on the aging population. Director: Jose Luis Ayuso.

THERAPEUTIC INNOVATION

Coordinator: **Juan Carlos Leza Cerro**

Among the most notable results are the more than 60 articles in publications in first decile journals, especially those published in the New England Journal of Medicine, Nature Communications, Alzheimer's and Dementia, Angewandte Chemie - Int Ed, Genome Biology, Biological Psychiatry, Molecular Psychiatry, Psychotherapy and Psychosomatics, JAMA Psychiatry, The Lancet, The Lancet Psychiatry, Brain, Science, Nature, Cell and Basic Research in Cardiology. The majority of these have been collaborative between groups of the Programme and within CIBERSAM, many of them with other CIBER scientific consortiums, Networks or ISCIII, and a substantial number with international collaborations. Nine clinical guidelines have also been published, five of them international.

As regards the securing of funds, numerous projects have been obtained from public state bodies (5 from the MCINN, 9 from the ISCIII, one from the National Plan on Drugs, several regional –Madrid, Catalonia, Valencia–), international (UE ERANET Neuron), the UE Commission (SYSCAN and H2020-MSCA-ITN-2020) as well as foundations.

Two contracts with companies: CSIC-miCure Therapeutics Ltd and the UCA-INiBICA with Laboratorios Esteve (WeLab).

Software Patent “CIBERSAMXnat: Neuroimaging data storage platform in Cloud environment” (M. Desco). Sol. M-007734/2020. 12/16/2020. Holders: CIBER, FIBHGM.

As regards Human Resources, several researchers from the groups that make up the programme have obtained competitive research contracts: Miguel Servet II, Juan de la Cierva, Río Hortega, Sara Borrell, SAS research specialist or JAE-Intro scholarships of the CSIC.

Participation in dissemination events such as the International Day of Women and Girls in Science, Science Week 2020, informative publications, articles in the press and interviews on radio and TV.

Of course, members of the Programme have coordinated, participated in or been invited to numerous national or international scientific forums, the vast majority in online format.

The most important scientific achievements include:

- >> Design and pre-clinical trial of a new molecule of oligonucleotides to reduce synthesis and avoid the accumulation of alpha-synuclein allowing delaying the development of Parkinson's disease.
- >> Demonstration that perineuronal networks, a specialized region of the extracellular matrix, regulate the connectivity and activity of interneurons in the prefrontal cortex.
- >> Implication of metalloproteinases in the neurobiology of depression and in the effect of fast-acting antidepressant drugs.
- >> Article published in The New England Journal of Medicine where the main advances in bipolar disorder are detailed.

- >> Identification of neuroimmune activation mechanisms in animal models and in samples from patients with depression and schizophrenia related to innate immunity receptors.
- >> Effective demonstration of the administration of omega-3 acids during adolescence in the prevention of PPI deficits and modulation of the anti-inflammatory / antioxidant pathways.
- >> Demonstration through proteomics in the olfactory neuroepithelium of cannabis users that cannabis can alter key processes in the developing brain, similar to those reported in mental disorders such as schizophrenia and bipolar disorder.
- >> Demonstration of the participation of dopaminergic transmission in Autism Spectrum Disorder in a pre-clinical model.

MENTAL DISORDERS OF THE CHILD AND ADOLESCENT

Coordinator: **Carmen Moreno Ruiz**

This Programme, made up of 6 clinical and basic CIBERSAM groups, develops research in mental disorders that have their onset in childhood and adolescence and has several European projects and collaborative projects with other linked CIBERSAM groups. Projects developed include the study of brain adaptations for motherhood during pregnancy and postpartum, phenomenology and neuroimmune pathways in repetitive and restrictive behaviors, phenomenological and genetic characterization of autism spectrum disorders, comorbidity and study of methylation patterns in ADHD and the study of the characterization of individuals at risk of psychosis as well as several intervention studies in this population.

This year's publications have been mainly in journals indexed in the first quartile according to the JCR ranking such as Nature Medicine, Nature Communications, Molecular Psychiatry, Neuropsychopharmacology, Lancet, Lancet Psychiatry, Biological Psychiatry, JAMA Psychiatry, JAMA Pediatrics, American Journal of Psychiatry, Molecular Psychiatry, and JAACAP among others.

Among the published results, to be highlighted is a meta-analysis of interventions for the prevention of bullying in schools, which shows their impact on reducing bullying and improving mental health. The long-term prognosis and comorbidity profile of adolescent-onset anorexia nervosa have been described. The Spanish version of the «Premonitory Urge for Tics Scale» has been validated in children and adolescents. The response to placebo in autism has been evaluated in 86 randomized trials, finding that it is around 20% and is predicted by factors related to design and participants.

Neuroimaging studies derived from participation in international consortia have found subtle but robust structural differences in different age groups in ADHD, ASD and OCD, highlighting differences in intracranial and hippocampal volume in children and adolescents with ADHD, and a similar pattern of brain alterations in early-onset and adult psychosis, although with low intracranial volume in children. Other studies have found that the appearance of psychosis in offspring with family risk is related to progressive cortical thinning and the presence of brain changes in both mothers and fathers that facilitate the response of parents to children's signals.

Genetic studies have found that family aggregation in impaired attention and working memory can constitute a factor of family vulnerability, and that psychiatric comorbidity in Asperger syndrome is different from other types of autism and is related to polygenic overlap and the shared contribution of common genetic variants to ADHD in children and adults.

Also noteworthy are an umbrella meta-analysis review on risk factors and protection of mental disorder in children and a meta-analysis on advances in the detection, prognosis and intervention of psychosis in adolescents.

PSYCHOSOMATIC, ANXIETY AND IMPULSE CONTROL DISORDERS

Coordinator: **Virginia Soria Tomás**

The Programme is made up of seven groups that carry out epidemiological, basic and / or clinical investigations covering a wide group of mental disorders with a great impact on the physical and psychological well-being of people. The main lines of research are aging and cognition, anxiety, obsessive-compulsive disorders (OCD) and impulsive spectrum disorders, neuroinflammation and pain.

The year 2020 has been marked by the Covid-19 health emergency and evaluations, interventions and recommendations have been developed aimed at assessing and mitigating its impact on the mental health of patients with psychiatric disorders, healthcare professionals (MINDCOVID) and the general population.

As regards participation in international epidemiological studies, to be highlighted are the identification of factors associated with the global burden of disease and declining fertility rates, as well as the response of different health systems; the development of the ATHLOS instrument for the evaluation of healthy aging; the association of perceived stress with depression and strategies to reduce treatment dropout rates.

In regard to cognitive disorders, results from the COSMIC project indicate that grand multiparous women have a higher risk of dementia, that depression in preclinical phases of dementia is attributable to brain changes and that a higher level of education reduces the risk of cognitive deterioration. Anxiety has also been associated with the risk of vascular dementia.

Diagnostic biomarkers, advances in clinical management, and research domain criteria (RDoC) in OCD have been critically reviewed. A specific genetic basis of OCD symptom dimensions has been identified. The largest structural neuroimaging study (ENIGMA) suggests alterations in brain development and maturation in OCD, while other results describe changes in cortico-striatum-thalamus-cortical functional connectivity as a marker of vulnerability. In generalized anxiety disorder, alterations in the cortico-limbic emotional regulation system have been described.

In eating disorders, the usefulness of interventions based on virtual reality has been demonstrated and dysfunctions in inflammatory signaling pathways and neurostructural and neurofunctional alterations have been identified. In borderline personality disorder, a decrease in plasma levels and expression of oxytocin receptors has been observed. Also noteworthy is the demonstration using proteomics in the olfactory neuroepithelium of cannabis users that cannabis can alter key processes in the developing brain.

Advances have been made in the genetic and epigenetic bases of attention deficit hyperactivity disorder (ADHD), confirming the shared contribution of genetic variants in children and adults. Results from the ENIGMA consortium identify structural brain differences in ADHD, ASD (Autism Spectrum Disorders) and OCD. In addition, the participation of dopaminergic transmission in ASD has been demonstrated through a preclinical model: Caspase3 coding gene depletion.

Other projects on animal models have demonstrated the modification of brain circuits of the opioid system in peripheral neuropathy. Also noteworthy is the identification of perivascular macrophages as regulators of stress-induced neuroinflammation in rats, as well as their role in the entry of bacterial lipopolysaccharides in neuroinflammation in experimental models of neuropsychiatric pathologies.

TRAINING PROGRAMME

Coordinator: **Juan Antonio Micó**

During 2020, the Training Programme has financed a total of 46 actions, including registrations to attend research courses and seminars for a total amount of € 12,332. The main activities that were sponsored were related to on-line participation in various events with the presence of CIBERSAM.

Among these: XX Symposium on bipolar and depressive disorders, 27th International Symposium on Updates and Controversies in Psychiatry, IX CIBERSAM International Forum for Research in Psychiatry, VIII Intensive Conference on Resistant Pathology, VI Meeting between Researchers in Mental Health, Patients and Families. In addition, there was broad participation in the sessions entrusted to the different CIBERSAM programmes at the XXII National Congress of Psychiatry.

The 2020 Ideas Laboratory could not be held face-to-face this year due to the Covid-19 pandemic. Taking into account that this is an event to facilitate the exchange of ideas and projects, as well as to stimulate joint research between CIBERSAM groups and other CIBER groups, the Steering Committee, in agreement with the organizers, decided to postpone the event until the appropriate conditions were met.

This year 2020, the Interuniversity Master in Initiation to Research in Mental Health, registered 69 enrollments. The number of students enrolled in type A stays was 37 and 40 in type B stays. Furthermore, a total of 33 Master's Dissertations were presented.

PLATFORMS

Coordinator: **Javier Meana Martínez**

CIBERSAM official platforms:

- >> Instruments library
- >> DNA and biological collections.
- >> Neuroimaging

Despite the fact that 2020 has been an atypical year for the development of scientific activity, the CIBERSAM platforms have continued their consolidation as support instruments to projects and activities. The respective indicators, both of its activity and productivity (publications, etc.) bear witness to a sustained trajectory over time.

The activity of the three official CIBERSAM platforms expressed in indicators is reflected in the following table:

| | Instruments Library | DNA and Sample Collections | Neuroimaging |
|-----------------------------------|---------------------|----------------------------|--------------|
| Existing Instruments | 326 | | |
| Added Instruments | 5 | | |
| Enquiries or applications for use | 30 | | 25 |
| Funded Publications | 98 | | |
| Training Activities | 1 | | |
| Stored Images | | | 23.979 |
| Contributing Groups | 4 | 15 | 3 |
| User Groups | | 2 groups (1 consortium) | 1 |
| Patients included | | 17.247 | |

The scientific productivity generated as a result of the use and exploitation of the CIBERSAM platforms in 2020 and a comparison with the data of 2018 and 2019 is reflected in the following table:

| Use of CIBERSAM Platforms by intraCIBER or external groups | 2018 | 2019 | 2020 |
|---|------|------|------|
| Total number of Publications | 24 | 37 | 23 |
| DNA and biological collections | 3 | 10 | 10 |
| Neuroimaging | 4 | 7 | 10 |
| Instruments Library | 2 | 8 | 6 |
| Total number of clinical trials | 0 | 1 | 1 |
| Instruments Library | 0 | 1 | 1 |
| Total number of Clinical Guides | 0 | 1 | 0 |
| Instruments Library | 0 | 1 | 0 |



SCIENTIFIC PRODUCTION

» Publications

No. of publications in 2020

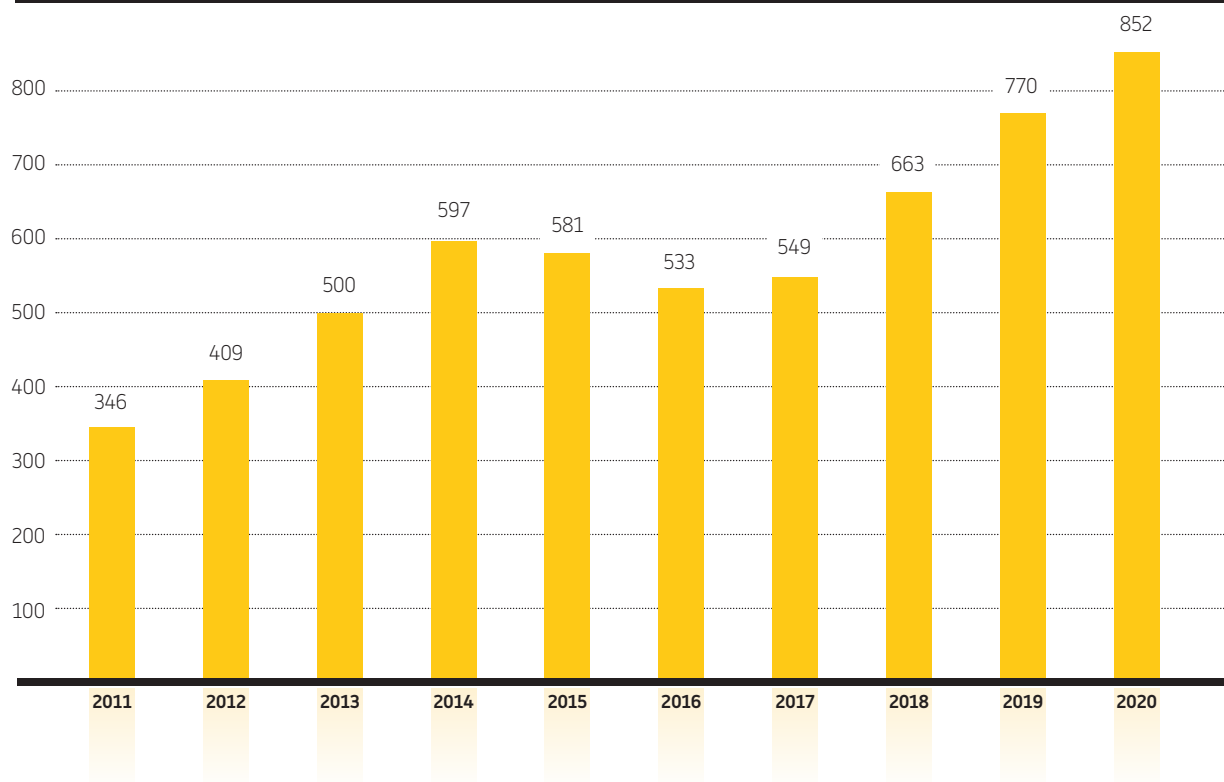
| | |
|--------|-----|
| TOTALS | 852 |
| Q1 | 516 |
| D1 | 197 |

Collaborations

| | |
|----------|-----|
| CIBERSAM | 234 |
| CIBER* | 132 |

*Among various thematic areas

» Evolution of publications




» 10 most relevant publications by impact factor




| IF | Publication |
|--------|---|
| 74,699 | Carvalho A.F., Firth J., Vieta E.. <i>Bipolar Disorder. The New England journal of medicine.</i> 2020;383(1):58-66. |
| 64,797 | Mantua V, Arango C, Balabanov P, Butlen-Ducuing F. <i>Digital health technologies in clinical trials for central nervous system drugs: an EU regulatory perspective.</i> Nature reviews. <i>Drug discovery.</i> 2020. |
| 60,392 | Reiner R.C., Wiens K.E., Deshpande A., Baumann M.M., Lindstedt P.A., Blacker B.F. et al. <i>Mapping geographical inequalities in childhood diarrhoeal morbidity and mortality in low-income and middle-income countries, 2000-17: Analysis for the Global Burden of Disease Study 2017.</i> The Lancet. 2020;395(10239):1779-1801. |
| 60,392 | GBD 2019 Universal Health Coverage Collaborators. <i>Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019.</i> Lancet. 2020 Oct 17;396(10258): 1250-1284. |
| 60,392 | Micah A.E., Su Y., Bachmeier S.D., Chapin A., Cogswell I.E., Crosby S.W. et al. <i>Health sector spending and spending on HIV/AIDS, tuberculosis, and malaria, and development assistance for health: progress towards Sustainable Development Goal 3.</i> The Lancet. 2020;396(10252):693-724. |
| 60,392 | Abbasfati C., Machado D.B., Cislighi B., Salman O.M., Karanikolos M., McKee M. et al. <i>Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950–2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019.</i> The Lancet. 2020;396(10258):1160-1203. |
| 60,392 | Abbasfati C., Machado D.B., Cislighi B., Salman O.M., Karanikolos M., McKee M. et al. <i>Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019.</i> The Lancet. 2020;396(10258):1223-1249. |
| 60,392 | Abbasfati C., Machado D.B., Cislighi B., Salman O.M., Karanikolos M., McKee M. et al. <i>Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019.</i> The Lancet. 2020;396(10258):1204-1222. |
| 60,392 | Abbasfati C., Machado D.B., Cislighi B., Salman O.M., Karanikolos M., McKee M. et al. <i>Five insights from the Global Burden of Disease Study 2019.</i> The Lancet. 2020;396(10258):1135-1159. |
| 60,392 | McIntyre R.S., Berk M., Brietzke E., Goldstein B.I., Lopez-Jaramillo C., Kessing L.V. et al. <i>Bipolar disorders.</i> The Lancet. 2020;396(10265):1841-1856. |

» CIBERSAM Groups. Publications in 2020

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|--------------|----|----|--------------------------------|-----------|
|  Arango López, Celso | 87 | 65 | 41 | Servicio Madrileño de Salud | Madrid |
|  Ayuso Mateos, José Luis | 38 | 26 | 5 | Universidad Autónoma de Madrid | Madrid |
|  Bernardo Arroyo, Miguel (*) | 74 | 52 | 28 | Hospital Clínic de Barcelona | Barcelona |
| Bobes García, Julio (*) | 55 | 30 | 12 | Universidad de Oviedo | Asturias |

| Group Leader | Publications | Q1 | D1 | Institution - Centre | Location |
|---|---------------------|-----------|-----------|--|-----------------|
|  Bortolozzi Biasoni, Analía | 6 | 6 | 1 | Agencia Estatal Consejo Superior de Investigaciones Científicas | Barcelona |
|  Crespo Facorro, Benedicto | 47 | 26 | 10 | Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla | Sevilla |
|  Desco Menéndez, Manuel | 18 | 11 | 4 | Servicio Madrileño de Salud | Madrid |
|  Fañanás Saura, Lourdes | 37 | 22 | 9 | Universidad de Barcelona | Barcelona |
|  González-Pinto Arrillaga, Ana | 46 | 20 | 8 | Asociación Instituto de Investigación Sanitaria BIOARABA | Álava |
|  Haro Abad, Josep Maria | 184 | 124 | 59 | Fundación para la Investigación y Docencia Sant Joan de Déu | Barcelona |
|  Ibáñez Cuadrado, Ángela | 47 | 23 | 9 | Servicio Madrileño de Salud | Madrid |
|  Leza Cerro, Juan Carlos | 56 | 29 | 15 | Universidad Complutense de Madrid | Madrid |
|  Meana Martínez, José Javier | 31 | 20 | 7 | Universidad del País Vasco | Vizcaya |
|  Menchón Magriñá, José Manuel | 63 | 47 | 15 | Fundación IDIBELL | Barcelona |
|  Micó Segura, Juan Antonio (*) | 7 | 5 | 2 | Universidad de Cádiz | Cádiz |
|  Nacher Rosello, Juan Salvador | 53 | 31 | 18 | Universidad de Valencia | Valencia |
|  Palao Vidal, Diego José | 36 | 22 | 4 | Corporación Sanitaria Parc Taulí | Barcelona |
|  Pazos Carro, Ángel Armando | 4 | 4 | 1 | Universidad de Cantabria | Cantabria |
|  Pérez Sola, Víctor | 68 | 39 | 16 | Consorci Mar Parc Salut de Barcelona | Barcelona |
|  Pomarol-Clotet, Edith | 34 | 22 | 12 | Fundación para la Investigación y Docencia María Angustias Giménez (FIDMAG) | Barcelona |
|  Ramos Quiroga, José Antonio | 37 | 17 | 6 | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Barcelona |
|  Tabarés Seisdedos, Rafael | 49 | 32 | 25 | Universidad de Valencia | Valencia |
|  Vieta Pascual, Eduard | 138 | 90 | 43 | Hospital Clínic de Barcelona | Barcelona |

Linked Clinical Groups

| Group Leader | Institution - Centre | Location |
|--|---|-----------------|
|  Olivares Díez, José Manuel | Servicio Gallego de Salud | Pontevedra |
|  Rodríguez Jiménez, Roberto | Servicio Madrileño de Salud | Madrid |
|  Vilella Cuadrada, Elisabet | Fundación Instituto de Investigación Sanitaria Pere Virgili | Tarragona |

(*) PI replaced

CLINICAL GUIDES

- *Depression in the Elderly. Consensus Statement of the Spanish Psychogeriatric Association.*
- *How mental health care should change as a consequence of the COVID-19 pandemic.*
- *Mental Health in Children and Adolescents in the era of COVID-19: Evidence and Recommendations from Professional Associations of Psychiatry and Clinical Psychology.*
- *The identification, assessment and management of difficult-to-treat depression: An international consensus statement.*
- *Strengthening mental health systems in low- and middle-income countries: recommendations from the Emerald programme.*
- *A transdiagnostic perspective of constructs underlying obsessive-compulsive and related disorders: An international Delphi consensus study.*
- *Electroconvulsive therapy protocol adaptation during the COVID-19 pandemic.*
- *Clinical practice guide. Pharmacological and psychological treatment of adult patients with severe mental disorder and substance use disorder.*
- *Depression and suicide 2020. Strategic document for the promotion of Mental Health.*
- *Clinical advances in obsessive-compulsive disorder: a position statement by the International College of Obsessive-Compulsive Spectrum Disorders.*
- *Expert consensus on information sheet proposals for patients under treatment with lithium.*
- *International Consortium on the Genetics of Electroconvulsive Therapy and Severe Depressive Disorders (Gen-ECT-ic).*
- *Preventing problematic internet use during the COVID-19 pandemic: Consensus guidance.*
- *Spanish consensus: Good clinical practices for the containment of people with mental disorders in a state of agitation.*
- *The CINP Guidelines on the Definition and Evidence-Based Interventions for Treatment-Resistant Bipolar Disorder.*

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