2017

ANNUAL REPORT

ciber

Centro de Investigación Biomédica en Red

Index

THE CONSORCIO CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED

THEMATIC RESEARCH AREAS

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CONSORCIO CENTRO DE INVESTIGACIÓN BIOMÉDICA EN RED

Presentation by the CIBER's Managing Director

Manuel Sánchez Delgado

In 2017 we celebrated the CIBER's tenth anniversary and there could be no better way to do this than by having three new areas join us: Cardiovascular Diseases (CIBERCV), Cancer (CIBERONC) and Frailty and Healthy Ageing (CIBERFES). These areas comprise a total number of 110 excellence research groups, belonging to universities, hospitals or research institutes.

Over these ten years the CIBER has gradually grown to the point of becoming one of the largest centres of biomedical research at the present time. It now has a staff of 908 contracted personnel and around 6000 attached researchers, members of over 400 research groups, all physically at a distance from each other and associated with 104 institutions in the consortium. Thanks to its excellent development, the CIBER received the "Recognition of the Technology and Health Foundation 2017".

I would like to take advantage of this opportunity to congratulate the three new managers for their good work this first year and for the proper integration of the new groups in the consortium. I would also like to extend my congratulations to all the researchers forming part of the CIBER for the scientific results obtained in the 2017 period: a total number of 6237 publications, 3629 of which are in the first quartile and 1824 in the first decile.

As regards transfer, 17 new patent applications were submitted in this period, 1 utility model, 1 trade mark and 3 software registrations, and 6 licence contracts were signed.

The total income –stemming from the sums transferred by the Instituto de Salud Carlos III, subsidies for projects, provision of services and others– exceeded 42 million euros (42,055,713.51€). 88 of the 118 competitive projects under way in 2017 resulting from aid were Spanish, 25 European and 5 from the U.S.A..

Since internationalisation is one of our main objectives, specific action was taken intended to boost the participation of our groups in international projects, for both training - as 3 courses were given on relevant aspects in the presentation of international proposals- and from the international platform, which resulted in in a considerable increase in the number of consultations by researchers, over 100 specific enquiries, 52 requests for support for presentation, 10 requests for seeking partners and 10 requests for appraisals of research proposals, whose results will be seen in the coming years.

The dissemination of the results of CIBER research to society in 2017 resulted in sending 101 press releases to the media. 785 news items and 514 agenda events were published on our websites and 21 CIBER newsletters were sent to the over 5000 subscribers. It should be stressed that CIBER's presence on social networks such as Twitter continues to extend, today exceeding 24,000 followers.

The positive balance of all of this means that we can conclude 2017 with the satisfaction of work well done at the CIBER through everyone's efforts. Many thanks to all of you who form part of these excellent results!

Internal Organisation

The Consorcio Centro de Investigación Biomédica en Red, M.P. (CIBER), set up under the auspices of the Instituto de Salud Carlos III (ISCIII), fosters excellence research into Biomedicine and Health Sciences done in the National Health System and in the Science and Technology System.

After the three new areas (CIBERCV, CIBERFES and CIBERONC) joined this in 2017, the scientific programme of the CIBER is based on the following thematic research areas:

- Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)
- Cardiovascular Diseases (CIBERCV)
- Diabetes and 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 908 persons and around 6000 attached researchers, forming part of over 400 research groups, working in separate locations, associated with 104 institutions in the consortium and belonging to administrations and public and private sector institutions of Spain's different "Autonomous Communities" or regional administrative areas.

The 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 for each of the institutions in the consortium, appointed by the senior authority of these. It meets every six months.

The Permanent Commission is a delegated commission made up of the ISCIII and 8 members of the Governing Board, who can be renewed annually. Both its operation and the support and assessment functions of the governing bodies are established in the statutes of the CIBER.

Management Committee and Advisory Committees

There is a Management Committee and an External Advisory Scientific Committee in each area of the CIBER.

The Management Committee is made up of the Scientific Director of each Area, the programme coordinators and the Managing Director of the CIBER, as well as a representative of the Instituto de Salud Carlos III.

The External Advisory Scientific Committee is a body providing scientific assessment and support, made up of relevant personalities in the field of health sciences who are well-known for their professional or scientific careers compatible with the objectives of the centre. This body is in charge of carrying out the annual appraisal of the areas and their research groups.

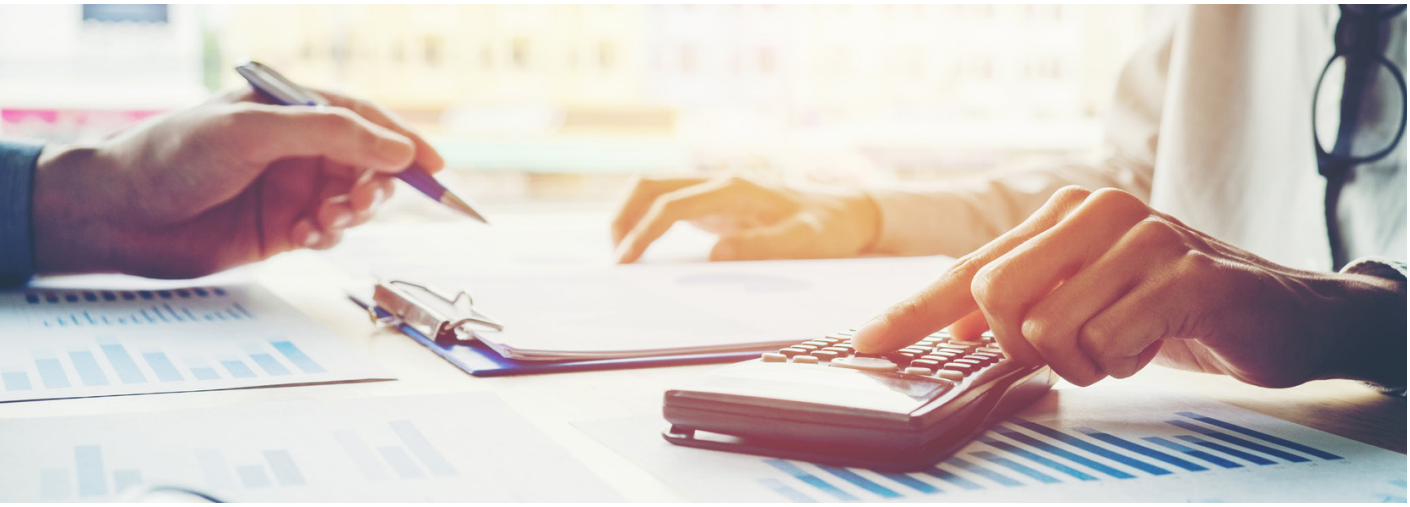
At the present time the statutes are being modified to incorporate representatives and patients' associations in the Management Committees of the CIBER areas.

Scientific Directors

The Scientific Directors of the CIBER represent each of the thematic areas and preside over the Management Committees. In 2017, they were the following persons:

- Scientific Director of the CIBER-BBN: Dr. Ramón Martínez Máñez
- Scientific Director of the CIBERCV: Dr. Francisco Fernández-Avilés
- Scientific Director of the CIBERDEM: Dr. Eduard Montanya Mias
- Scientific Director of the CIBEREHD: Dr. Jordi Bruix Tudó
- Scientific Director of the CIBERER: Dr. Pablo Lapunzina Badía
- Scientific Director of the CIBERES: Dr. Ferrán Barbé Illa
- Scientific Director of the CIBERESP: Dr. Miguel Delgado Rodríguez*
- Scientific Director of the CIBERFES: Dr. Leocadio Rodríguez Mañas
- Scientific Director of the CIBEROBN: Dr. Carlos Diéguez González
- Scientific Director of the CIBERONC: Dr. Joaquín Arribas López
- Scientific Director of the CIBERSAM: Dr. Eduard Vieta Pascual

* As from December 2017, the new Scientific Director of the CIBERESP has been **Dr. Marina Pollán Santamaría.**



Economic data

CIBER

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	TOTAL
	26.303.330,00	10.819.642,80	2.402.067,86	2.530.672,85	**42.055.713,51**

Total expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	78.471,87	593.362,19	497.803,08	**1.169.637,14**
Groups	1.278.820,30	4.807.175,07	17.475.103,75	**23.561.099,12**
Training	-	267.942,08	1.820.682,17	**2.088.624,25**
Programmes	84.477,84	860.907,63	358.002,64	**1.303.388,11**
Platforms	88.089,15	338.487,49	480.073,42	**906.650,06**
Transfer	25.407,42	152.998,44	218.830,70	**397.236,56**
Intramural projects	29.659,79	448.089,47	25.342,15	**503.091,41**
External projects	217.346,81	2.516.668,39	3.445.428,22	**6.179.443,42**
Technical Unit	44.696,81	1.074.964,14	1.328.139,46	**2.447.800,41**
TOTAL	1.846.969,99	11.060.594,90	25.649.405,59	**38.556.970,48**

CIBER-BBN

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	3.960.160,00	545.869,87	28.153,83	95.786,92	376.239,61	**5.006.210,23**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	66.108,34	63.241,93	**129.350,27**
Groups	137.160,60	350.225,20	1.094.239,93	**1.581.625,73**
Training-Capacity-building	-	28.706,35	1.572.391,95	**1.601.098,30**
Programmes	1.895,20	23.256,77	180.015,28	**205.167,25**
Platforms	71.479,34	87.090,41	58.086,03	**216.655,78**
Transfer	7.500,00	64.111,89	91.356,01	**162.967,90**
Intramural projects	-	16.377,18	-	**16.377,18**
External projects	60.788,61	307.322,19	724.857,02	**1.092.967,82**
TOTAL	278.823,75	943.198,33	3.784.188,15	**5.006.210,23**

CIBERCV

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	-	3.285.000,00	-	-	-	**3.285.000,00**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	71.470,04	51.135,06	57.788,40	**180.393,50**
Groups	82.009,00	259.882,53	766.524,57	**1.108.416,10**
Training	-	-	-	**0,00**
Programmes	-	4.968,75	-	**4.968,75**
Platforms	-	-	-	**0,00**
Transfer	-	-	-	**0,00**
Intramural projects	-	-	-	**0,00**
External projects	-	-	-	**0,00**
TOTAL	153.479,04	315.986,34	824.312,97	**1.293.778,35**

CIBERDEM

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	2.796.280,00	183.491,64	41.855,00	100,00	58.163,20	**3.079.889,84**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	821,59	116.134,27	49.229,95	**166.185,81**
Groups	40.531,94	157.190,33	2.168.575,47	**2.366.297,74**
Training	-	17.031,31	-	**17.031,31**
Platforms	-	94.666,07	-	**94.666,07**
Intramural projects	-	7.550,11	-	**7.550,11**
External projects	0,00	298.815,89	129.342,91	**428.158,80**
TOTAL	41.353,53	691.387,98	2.347.148,33	**3.079.889,84**

CIBEREHD

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	3.653.580,00	161.194,00	45.124,12	259.180,47	240.950,46	**4.360.029,05**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	63.421,70	25.282,24	**88.703,94**
Groups	59.743,61	280.541,81	2.689.770,48	**3.030.055,90**
Training	-	36.244,52	-	**36.244,52**
Platforms	2.991,00	18.839,22	89.886,83	**111.717,05**
Transfer	-	8.207,82	-	**8.207,82**
Intramural projects	11.281,58	153.348,38	-	**164.629,96**
External projects	36.109,99	313.231,19	571.128,68	**920.469,86**
TOTAL	110.126,18	873.834,64	3.376.068,23	**4.360.029,05**

CIBERER

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	4.905.860,00	455.806,67	816.664,42	105.278,23	-	**6.283.609,32**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	142.405,34	39.462,91	181.868,25
Groups	-	99.321,66	3.318.881,72	3.418.203,38
Training	-	14.235,26	96.895,03	111.130,29
Programmes	58.817,05	506.322,00	-	565.139,05
Platforms	1.917,10	27.425,94	225.067,47	254.410,51
Transfer-Traslación	2.253,14	62.189,05	33.789,61	98.231,80
Intramural projects	-	-	-	0,00
External projects	59.109,77	597.879,87	553.825,09	1.210.814,73
TOTAL	122.097,06	1.449.779,12	4.267.921,83	**5.839.798,01**

CIBERES

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	2.632.420,00	529.088,52	658.200,68	172.598,71	-	**3.992.307,91**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	28.960,94	56.098,78	85.059,72
Groups	351.860,91	474.185,27	1.624.298,81	2.450.344,99
Training	-	32.907,26	96.653,27	129.560,53
Programmes	-	5.554,59	4.015,20	9.569,79
Platforms	1.429,62	473,53	44.613,97	46.517,12
Transfer	2.677,28	13.411,08	93.685,08	109.773,44
Intramural projects	11.445,34	96.869,50	-	108.314,84
External projects	24.535,72	317.439,69	284.453,42	626.428,83
TOTAL	391.948,87	969.801,86	2.203.818,53	**3.565.569,26**

CIBERESP

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	2.916.660,00	170.959,31	-	8.500,00	478.758,13	**3.574.877,44**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	35.153,77	32.982,19	**68.135,96**
Groups	164.787,50	729.888,50	1.669.429,82	**2.564.105,82**
Training	-	46.936,13	-	**46.936,13**
Programmes	16.997,66	232.578,94	173.972,16	**423.548,76**
External projects	1.878,17	183.547,18	286.725,42	**472.150,77**
Intramural projects	-	-	-	0,00
TOTAL	183.663,33	1.228.104,52	2.163.109,59	**3.574.877,44**

CIBERFES

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	-	780.000,00	-	-	-	**780.000,00**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	9.559,95	20.133,04	**29.692,99**
Groups	34.397,84	33.880,67	173.130,35	**241.408,86**
TOTAL	34.397,84	43.440,62	193.263,39	**271.101,85**

CIBEROBN

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	2.887.230,00	532.622,30	32.132,23	29.000,00	-	**3.480.984,53**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	508,49	47.590,46	44.811,57	92.910,52
Groups	119.603,12	696.915,49	1.628.264,05	2.444.782,66
Training	-	25.707,79	-	25.707,79
Programmes	828,85	56.536,48	-	57.365,33
Platforms	277,09	50.826,54	62.419,12	113.522,75
Transfer	12.977,00	5.078,60	-	18.055,60
Intramural projects	4.798,09	107.924,62	-	112.722,71
External projects	20.511,03	153.450,04	309.046,34	483.007,41
TOTAL	159.503,67	1.144.030,02	2.044.541,08	**3.348.074,77**

CIBERONC

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	-	3.735.000,00	-	-	-	**3.735.000,00**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	5.671,75	22.958,81	43.390,61	72.021,17
Groups	205.125,51	1.163.610,83	903.898,96	2.272.635,30
Training	-	31.021,83	41.226,88	72.248,71
Programmes	2.440,72	20.579,34	-	23.020,06
Platforms	-	-	-	0,00
Transfer	-	-	-	0,00
Intramural projects	-	-	-	0,00
External projects	-	-	-	0,00
TOTAL	213.237,98	1.238.170,81	988.516,45	**2.439.925,24**

CIBERSAM

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	2.199.190,00	440.610,49	779.937,58	41.028,33	-	**3.460.766,40**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Scientific Management, Scientific Secretariat, Communication	-	9.933,55	65.381,46	**75.315,01**
Groups	83.600,27	561.532,78	1.438.089,59	**2.083.222,64**
Training	-	35.151,63	13.515,04	**48.666,67**
Programmes	3.498,36	11.110,76	-	**14.609,12**
Platforms	9.995,00	59.165,78	-	**69.160,78**
Intramural projects	2.134,78	66.019,68	25.342,15	**93.496,61**
External projects	14.413,52	344.982,34	586.049,34	**945.445,20**
TOTAL	113.641,93	1.087.896,52	2.128.377,58	**3.329.916,03**

UT

Total resources

INCOME 2017	ISCIII transfer	Subsidies for projects	Provision of services	Other income	Own funds applied	TOTAL
	351.950,00	-	-	1.819.200,19	276.650,22	**2.447.800,41**

Total Expenses

PROJECT	Inventoriable sum applied	Supplies and other expenses for work	Personnel applied	TOTAL expense
Economic resources	44.696,81	919.453,56	-	**964.150,37**
Human resources	-	-	1.328.139,46	**1.328.139,46**
Prevention of Occupational Hazards	-	123.995,25	-	**123.995,25**
Communication	-	31.515,33	-	**31.515,33**
TOTAL	44.696,81	1.074.964,14	1.328.139,46	**2.447.800,41**

Personnel

Distribution of contracted personnel by areas, category and sex

	MEN	WOMEN	Total
CIBER-BBN	36	69	105
Doctor	22	42	64
Graduates	13	18	31
Diploma holder		1	1
Technical staff	1	8	9
CIBERCV	15	59	74
Doctor	6	19	25
Graduates	9	30	39
Technical staff		10	10
CIBERDEM	15	58	73
Doctor	9	28	37
Graduates	3	18	21
Diploma holder		2	2
Technical staff	3	10	13
CIBEREHD	37	69	106
Doctor	16	21	37
Graduates	16	33	49
Diploma holder	1	5	6
Technical staff	4	10	14
CIBERER	27	98	125
Doctor	18	52	70
Diploma holder		1	1
Graduates	7	28	35
Technical staff	2	17	19
CIBERES	18	54	72
Doctor	4	20	24
Graduates	11	16	27
Diploma holder	1	7	8
Technical staff	2	11	13

	MEN	WOMEN	Total
CIBERESP	16	56	72
Doctor	5	11	16
Graduates	9	32	41
Diploma holder	1	10	11
Technical staff	1	3	4
CIBERFES	8	12	20
Doctor	5	5	10
Graduates	3	7	10
CIBEROBN	24	56	80
Doctor	8	11	19
Graduates	14	27	41
Diploma holder	1	8	9
Technical staff	1	10	11
CIBERONC	20	54	74
Doctor	13	24	37
Graduates	7	15	22
Technical staff		15	15
CIBERSAM	11	60	71
Doctor	4	17	21
Graduates	5	32	37
Diploma holder		3	3
Technical staff	2	8	10
CIBERUT	8	28	36
Doctor	1		1
Graduates	7	25	32
Technical staff		3	3
Grand Total	**235**	**673**	**908**

Significant activities

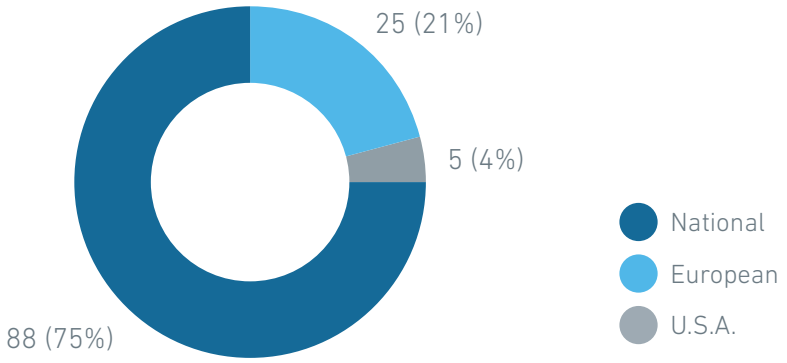
Projects

Number of projects under way in yearly period 2017, resulting from competitive aid:

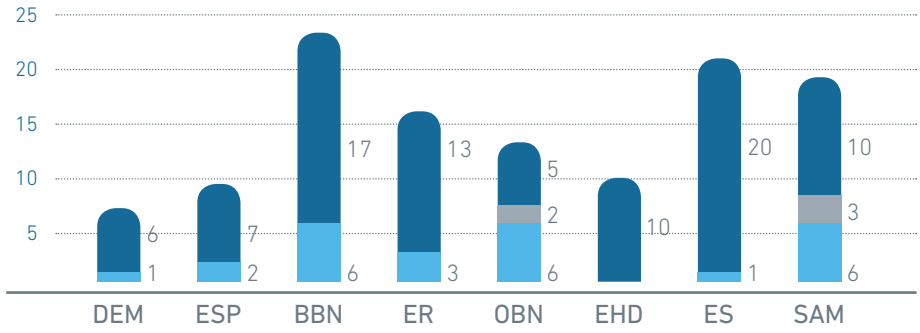
Body / Aid	Subsidies being applied 2017	BBN	DEM	EHD	ER	ES	ESP	OBN	SAM
European	25	6	1	-	3	1	2	6	6
U.S.A.	5	-	-	-	-	-	-	2	3
National	88	17	6	10	13	20	7	5	10
ISCIII - FIS	30	-	-	3	5	11	4	2	5
ISCIII - Other	21	3	2	3	1	5	3	3	1
MECD	2	2	-	-	-	-	-	-	-
MINECO	20	11	4	1	1	1	-	-	2
Private foundations	13	-	-	3	6	2	-	-	2
Other public aid	2	1	-	-	-	1	-	-	-

Throughout 2017, CIBER has obtained the following aid from competitive calls.

Competitive Projects under way according to source of funds



Competitive projects under way by thematic area

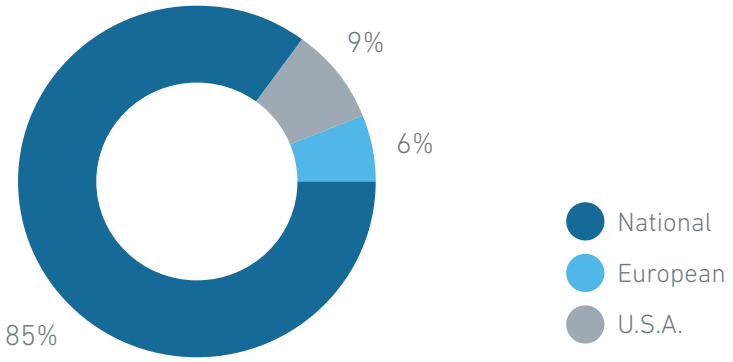


Date granted	Body	Name of project	TOTAL GRANTED
02/03/2017	FUNDACIÓN RAMÓN ARECES	1. Activación de la inmunidad innata en células deficientes en disferlina: nuevas dianas terapéuticas. 2. Inhibidores de fosfodiesterasas como tratamiento para la Ataxia de Friedreich 3. Identificando el sensor celular de nucleótidos y su interactoma	292.725,00 €
22/03/2017	CE	Proyecto IPMT - WIDESPREAD	64.725,00 €
29/03/2017	FUNDACIÓN LA CAIXA	*Valorisation and commercialisation of hiparco-score technology. Prediction of positive response to cpap therapy for resistant hypertension patients*	70.000,00 €
24/04/2017	INSTITUTO DE SALUD CARLOS III	10PAFIP neuroimagen: estudio longitudinal a largo plazo (10 años) de los cambios estructurales cerebrales en pacientes con psicosis del espectro de esquizofrenia	3.728,88 €
29/06/2017	Fundación BBVA	Identificación de nuevos predictores en la progresión de la Fibrosis Hepática	40.000,00 €
01/07/2017	CE	EAT2BENICE	340.077,45 €
31/07/2017	MECD	Ayuda José Castillejo	9.288,00 €
01/08/2017	CALIFORNIA WALNUT COMMISSION	*The relation of walnuts and ala to myocardial damage after myocardial infarction*	88.616,81 €
17/08/2017	NIH	*Mediterranean diet, metabolites, and cardiovascular disease 2R01HL118264-05*	153.319,30 €
15/09/2017	JEROME LEJEUNE FOUNDATION	*Identifying new mechanisms by which DYRK1A regulates the expansion of the cerebral cortex*	40.000,00 €
09/10/2017	THE COMPANY OF BIOLOGIST	*Assist with travel and accommodation for early career scientists for the conference entitled "Organ crosstalk in energy balance and metabolic disease"*	2.000,00 €
20/10/2017	FUNDACIÓ LA MARATÓ	*Marcadors en sang de la qualitat del greix de la dieta i incidència d'ictus isquèmic en una població mediterrània."*	160.750,00 €
20/11/2017	FUNDACIÓN INOCENTE INOCENTE	3 Proyectos Inocente	90.000,00 €
27/11/2017	MINECO	Ayuda para contratación de personal técnico de apoyo PTA.	39.000,00 €
04/12/2017	INSTITUTO DE SALUD CARLOS III	Plataforma Red Nacional de Biobancos - plat. Apoyo a la Investigación en Ciencias y Tecnologías de la Salud	597.300,00 €
05/12/2017	CONSELLERIA ILLES BALEARS	Ayuda para contratación de personal técnico de apoyo PTA.	60.000,00 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Estudio sobre la eficacia de la potenciación de reserva cognitiva en niños, adolescentes y adultos jóvenes de alto riesgo genético para esquizofrenia o trastorno bipolar	96.013,50 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Efectos de un programa integral de terapia cognitiva basada en mindfulness, psicoeducación y rehabilitación funcional en el trastorno bipolar	81.070,00 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Estudio de las subregiones del hipocampo en 1os episodios de psicosis. Análisis longitudinal a 10 años	79.860,00 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - PAFIP-Familias: estudio del funcionamiento neuropsicológico y variantes genéticas asociadas en familiares de pacientes con trastornos del espectro de la esquizofrenia.	73.810,00 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	Ayuda Miguel Servet II	91.125,00 €
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - ¿Podríamos prevenir la leucemia linfocítica crónica? Investigamos el papel de las infecciones en sus precursores, las linfocitosis b monoclonales (MLB)	100.430,00 €

Date granted	Body	Name of project	TOTAL GRANTED
05/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Identificación de QTLS moleculares y sus interacciones con factores ambientales (GXE) en poblacion infantil	21.780,00 €
08/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Evaluación de la capacidad pronóstica y del papel funcional de microrna candidatos en el adenocarcioma ductal pancreático	75.020,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Nanoterapia dirigida y radioterapia SBRT combinada para la eliminación selectiva de células madre tumorales en cáncer de páncreas	76.230,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Papel de la mioesteatosis en el desarrollo y la presistencia de la debilidad muscular	93.170,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Redefiniendo clínica y molecularmente las malFormaciónes vasculares complejas	99.220,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	*AC TRANSCAN 2 exploitation of extracellular vesicles for precision diagnostics of prostate cancer. PROSCANEXO*	98.010,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	*AC ERARE_ mutation-targeted gene and pharmacological therapies for dystrophic and junctional epidermolysis bullosa: MUTAEB*	130.680,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	*AC impact of mediterranean diet, inflammation and microbiome on plaque vulnerability and microvascular dysfunction after an acute coronary syndrome. A randomized, controlled, mechanistic clinical trial.*	148.830,00 €
11/12/2017	INSTITUTO DE SALUD CARLOS III	FIS - Desarrollo pulmonar anormal vs. envejecimiento acelerado en la epoc: una aproximación a paritr del análisis de redes multinivel	99.220,00 €
TOTAL COMPETITIVE AID FUNDS OBTAINED IN 2017			3.415.998,94 €

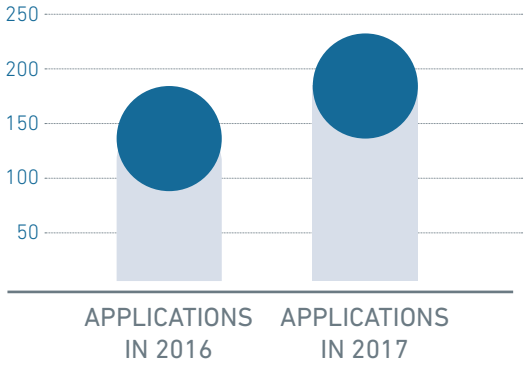
There are also 10 proposals for European projects which have already gone into their second stage.

Source of competitive funds obtained in 2017



There were 230 applications for competitive external financing projects in 2017, rising by 27% as compared with the previous year.

Applications for competitive aid submitted



Transfer

One of the main aims of the CIBER is the translation 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 population's quality of life. To this end, the Technology Transfer area of the CIBER acts as a nexus between our researchers and companies, private organisations, public research centres and other innovation agents to put into practice cooperation between them and make sure that the results of research can finally be applied.

Throughout 2017 17 new applications for patents were submitted at the CIBER, with 1 utility model, 1 trade mark and 3 software registrations. 6 licence contracts were also signed.

Thematic area	Priority patent applications	Other IPRs	Licences
CIBER-BBN	8	1	4*
CIBERDEM	1	0	0
CIBEREHD	3	0	1*
CIBERER	0	0	2*
CIBERES	1	0	0
CIBERESP	0	1	0
CIBEROBN	3	3	0
CIBERSAM	1	0	1
CIBERCV	0	0	0
CIBERONC	0	0	0
CIBERFES	0	0	0

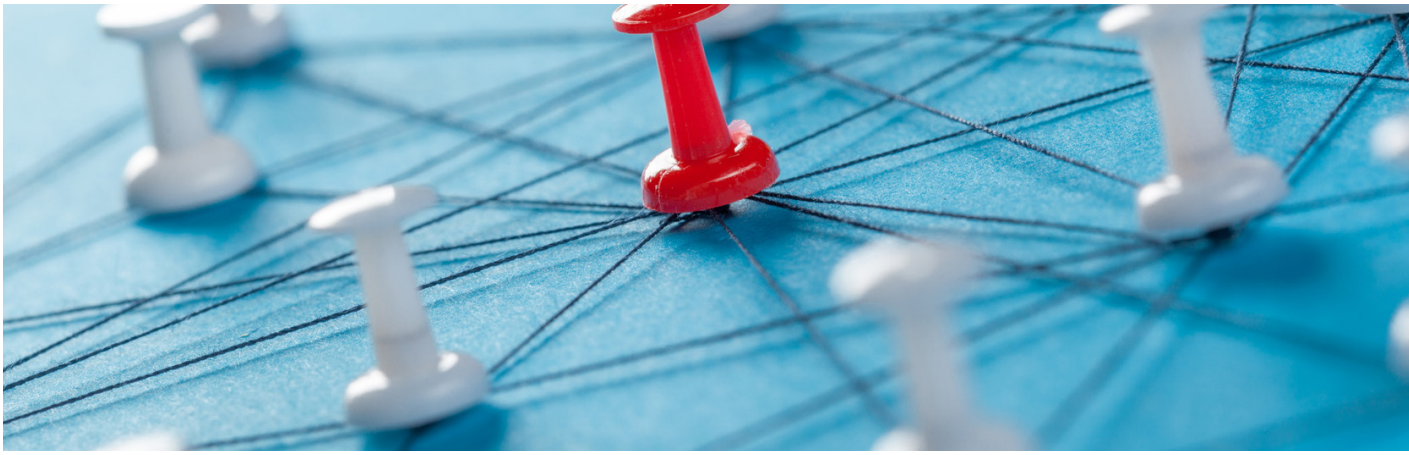
*One of the licences is a patent shared by CIBERER and CIBER-BBN, and another between CIBEREHD and CIBER-BBN. That is why the figures in the table come to over 6.

In 2017 we should also stress having obtained a new designation for Metformin as an orphan drug (OD) by both the European Medicines Agency (EMA) and by the U.S. institution (FDA), for treatment of Lafora disease. This represents the sixth OD sponsored by the CIBER (CIBERER Area).

As for the ongoing support for creation of technology-based companies emerging from CIBER Groups, in 2017 the company Epidisease, a CIBER *spin off* (arising in the CIBERER), has formalised the investment of the Fundación Botín by means of the Mind the Gap programme and a NEOTEC, among other sources of financing and investment.

As an example, other steps connected with the transfer of knowledge and public-private cooperation that have been taken are as follows:

- Dozens of CDAs and MTAs negotiated and signed.
- Marketing activities, as well as including the publication of technological offers and marketing and direct contact with companies, involve participation in forums, trade fairs and symposia. Amongst other forums, the CIBERES area has for example submitted proposals at the Farmaindustria Farma-Biotech Programme, in the *Johnson &Johnson Quick Fire Challenge* o *Healthio 2017*.
- A guide explaining to researchers how to develop orphan drugs for rare diseases, available at this link has been published by the CIBERER area along with the Spanish Agency for Medicines and Health Products (AEMPS).
- Several symposia have also been arranged by the CIBERER area:
  - *Rare Diseases Registries Workshop* at the Hospital Universitario La Paz de Madrid, financed by the Consumers, Health, Agriculture and Food Agency of the European Commission (CHAFEA), attended by over 130 healthcare professionals, patients' organisations, researchers, the pharmaceutical industry and public administrations to analyse the situation of those registries..
  - CIBERER and the Platform for *Malalties Minoritàries* oarranged symposia on the designation of OD in Barcelona and Madrid at which the process of OD was explained, with great success as regards attendance.
- In the CIBER-BBN area four projects for ISCIII Transfer were carried out in 2017 with the financial aid of four companies. Three of these projects concluded through reaching the end of the intended implementation period, accomplishing the objectives set at the start. A new call for transfer projects was made, with the start of six new projects being intended in early 2018.
- Over the last month in the year we started to design a call for valorisation projects, which has been published in 2018. The CIBER-BBN will finance the projects selected, after evaluating the applications submitted, in order for these projects to increase the TRL (Technology Readiness Levels, level of maturity of technology) of tis technologies in a step towards their exploitation and marketing.



Internationalisation

Last 11 May 2015 the CIBER's Platform for Support for Internationalisation was set up. This Internationalisation Platform emerged as a joint initiative of the areas of Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Rare Diseases (CIBERER) and Respiratory Diseases (CIBERES), of the Centro de Investigación Biomédica en Red (CIBER), in order to reinforce and coordinate the efforts intended to promote its researchers' participation in European Programmes and to create a common structure for fostering internationalisation and leadership in research and innovation in these three thematic areas.

During 2017 the internationalisation platform continued with its. training work, giving three training courses on relevant aspects in the presentation of international proposals, "Writing successful proposals in ERC calls", "*Cost and Synergy Grants*" and "Financing opportunities for young researchers", as well as a specific session in the field of rare diseases under the title of "Designation and development of orphan drugs. Symposium paper: financing opportunities for clinical research".

In order to improve its international impact, specific meetings have been held with NCPs and with the head of the H2020 programme in order to establish smoother relations. This greater level of Communication has led to CIBER being invited to the Forum for Strategic Definition of the WP2018-2020 and to taking an active part in defining the Work Programmes for 2017 and IMI calls as scientific experts. It has also decided to include specialised profiles in the main search pages for partners (Fit4Health, health competence, Cordis, IMI) and capacity profiles have been made for presentation at events. The recognition of CIBER researchers on an international scale was reflected by means of its participation in decision-making forums.

The platform has also placed special emphasis on establishing smooth relations with the different national representatives and national points of contact by means of specific meetings, acting as a point of contact on an institutional level. In this field we should stress the appointment of CIBER researchers as evaluators and international experts (Mara Parellada, ERANET-Neuron; Celso Arango, ER StG; Elisabet Vilella, COST; José Luis Ayuso, H2020).

The platform has given awareness-raising talks on the relevance of internationalisation for the area symposia sessions. The success of these events is vouched for by the considerable increase in the number of researchers' enquiries (100 specific consultations, 52 requests for support for presentation, 10 requests for seeking partners and 10 requests for evaluations of research proposals) which already see the platform as an effective tool for help and a point of reference for clearing up doubts connected with International Programmes.

In the field of support for submission of proposals, CIBER has put forward 66 new proposals and obtained financing in 11 international projects, obtaining over 1,186,000 Euros in external funding.

Other programmes for international and institutional relations:

CIBERCV

In 2017 CIBERCV got its work under way by arranging several activities due to have international repercussions:

The persons in charge promoted the organisation of a CIBERCV-MP meeting at the European Parliament for discussing different initiatives in order to present these to the CIBER and design the future of cardiovascular research Europe-wide. It has also made an effort to increase communication in progress for the coming calls for European projects.

CIBERCV also takes part as organiser in the Workshop-Cardiology-CIBERCV as part of the *Annual Congress of the European Society for Clinical Investigation* (Barcelona in May 2018). The active role of its researchers is accredited by over 90 communications at this international-scale congress, where talks have also been arranged with national and foreign guests. The aim is for the young researchers at the CIBERCV to get in touch with each other to encourage intra-Ciber collaboration work and work with young people from other countries in order to promote international mobility.

CIBERSAM

This year the CIBERSAM's international visibility focussed on its researchers' participation in decision-making bodies. In this respect we should mention that Juan Nacher was chosen as a member of the Neuroscience Panel at Hungarian Scientific Research Fund and that Carmen Moreno, Mara Parellada and Celso Arango were designated as members of the advisory committee for paediatric studies of the European Medicines Agency (EMA). Julio Bobes García and Paz García-Portilla González are experts from the EMA.

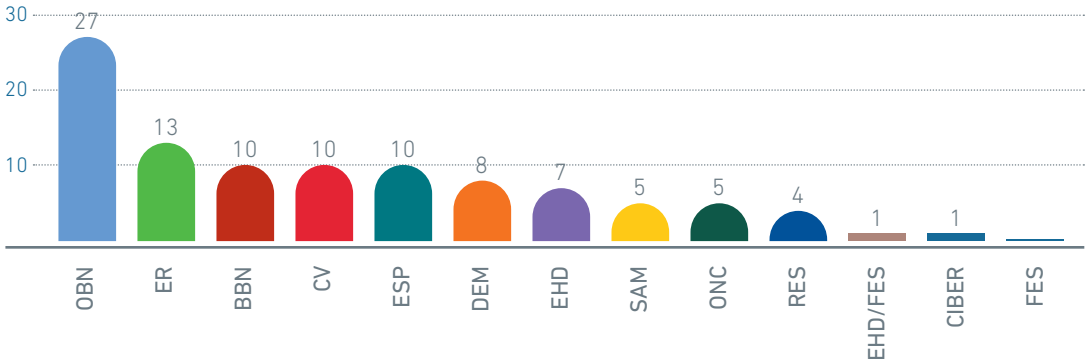
CIBERSAM researchers are also taking part as experts on different committees: Celso Arango is on the scientific committee of the ERANET-neuron, Josefina Castro was appointed as child and adolescent expert at the ECNP (*European College of Neuropsychopharmacology*) and José Manuel Menchón is a member of the Management Committee of the "*European Network for Problematic Usage of the Internet*".

It should also be highlighted that Celso Arango is the president of the *European College of Neuropsychopharmacology* (ECNP), Carmen Moreno is co-director of the Child and Adolescent Network of the ECNP (*European College of Neuropsychopharmacology*), Eduard Vieta is co-editor of the Schizophrenia Bulletin and of the *American Journal of Psychiatry* and Iria Grande is co-editor of *Frontiers in Psychiatry*. In the same way in the *European Psychiatric Association* Julio Bobes García is co-chair of the psychopharmacology section and Pilar A. Sáiz is the general secretary of the ECNP Suicide Network. We should lastly mention that José Luis Ayuso is a member of the International Advisory Board for the implementation of CIE 11 and Ana González-Pinto is an advisor of the European Horizon *2020 R link* study and member of the *International Society of Bipolar Disorders* (ISBD).

Communication

In 2017 101 press releases were issued on results of research, events, appointments or other content concerning the research groups.

CIBER Press releases 2017

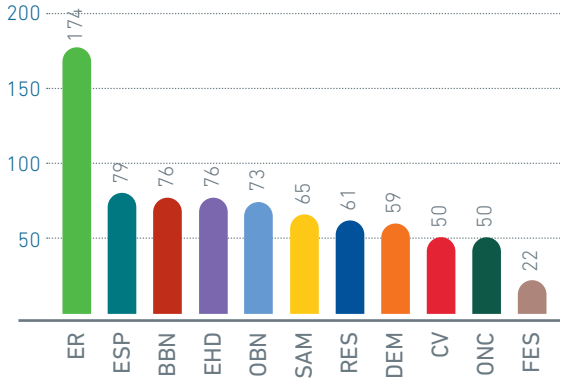


Web pages:

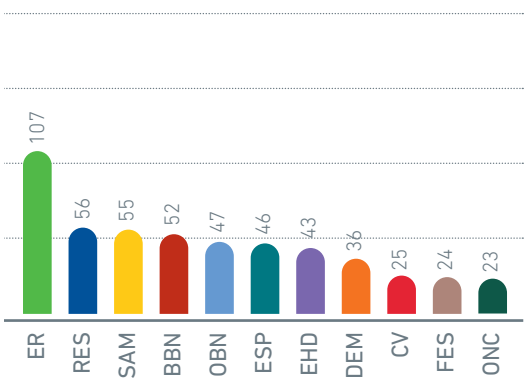
The web pages of the 3 new areas were started up in Spanish and 2 of these in English: www.ciberonc.es ; www.ciberonc.es/en ; www.cibercv.es ; www.cibercv.es/en ; and www.ciberfes.es

785 news items and 514 agenda events were published on the websites of the different areas.

Web news items 2017

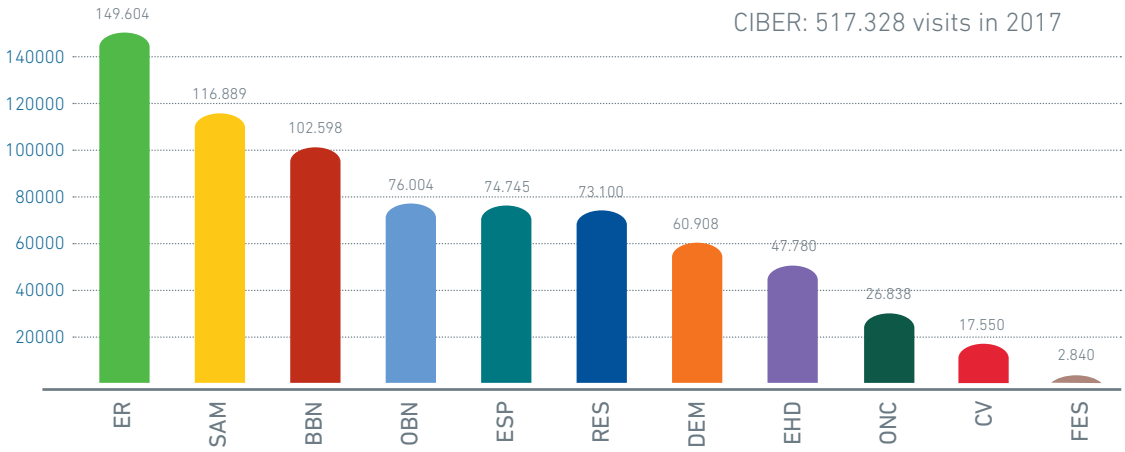


Events on the agenda 2017



CIBER website visits in 2017

CIBER: 517.328 visits in 2017

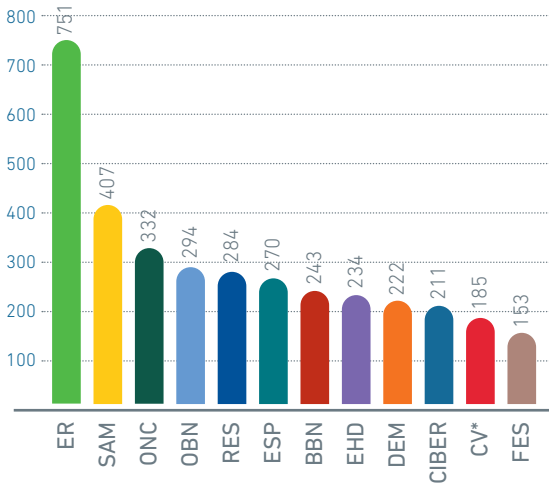


CIBER Newsletters

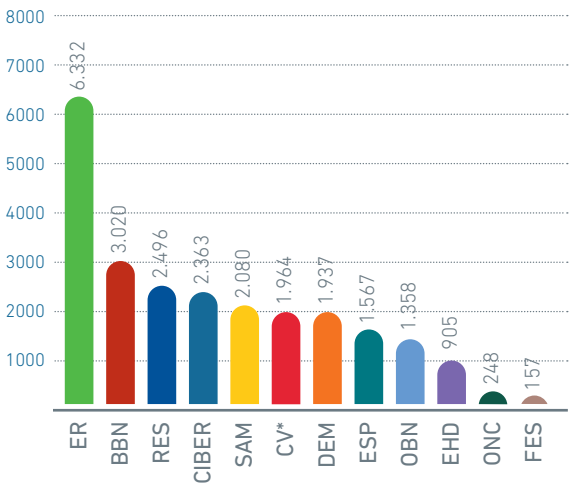
In 2017 five CIBER newsletters were sent to a total number of over 5000 subscribers http://www.ciberisciii.es/comunicacion/boletines and five newsletters were issued in the areas of BBN, DEM, EHD, ESP, RES and SAM. In July the monographic newsletters of the OBN, CV and ONC areas were issued. At the CIBERER ten scientific newsletters and six social newsletters were brought out.

Dissemination on Social Networks

Updates on twitter 01/01/17 – 31/12/17



Total number of followers 31/12/17



* Transfer of the Twitter account of the RIC (Start 21/03: 6483 tweets / 1721 followers)

CIBER Activity of the Madrid Science Week and corporate video

In order to commemorate these 10 years of CIBER research a corporate video of the CIBER was made. The video explains –in a sketching format – what the CIBER and its collaborative research are, as well as other relevant aspects of the Centre (the CIBER in figures). See video

In November the BiomediCINE event was held at the Cine Estudio del Círculo de Bellas Artes de Madrid as part of the programme for Madrid Science Week. The corporate video of the CIBER was presented at this event, along with the three new research areas (CIBERFES, CIBERONC and CIBERCV) the "¿Lo ves?" [See it?] project of the CIBERER.

2

THEMATIC RESEARCH AREAS

ciber-bbn

Bioengineering, Biomaterials
and Nanomedicine

Scientific Director's Presentation

Ramón Martínez Máñez

Over 2017 CIBER-BBN has kept up an excellent level of scientific work, with an increase in the number of scientific publications, recovering from the slight drop that had been seen in the last few years. We go on maintaining high quality standards, with roughly 70% of our production in first quartile journals and getting close to 30% in the first decile.

We have also seen an improvement in the indicators (press releases, number of appearances in the media, presence in the social networks, etc.) connected with communication and the visibility of our work for society.

The Management Committee has made an effort with the assistance of a consultancy company in the preparation of a strategic plan for coming period 2018-2021. This process has meant an in-depth reflection on the centre's model which has involved a review of procedures and research initiatives, such as the traditional intramural projects, that now take on a more flexible format. New valorisation projects have been conceived, with additional financing, to increase the TRL level of technologies and encourage their ISCIII Transfer. New parameters based on scientific quality and cooperation have also been set to annually evaluate the Groups and to accept changes of the principal investigator.

Although the strategic plan meant an important milestone in 2017, I would also like to stress the commitment taken on to propose a project focussing on nanomedicine as a key technology for solving the problems of ageing in European society for the call for new preparatory actions for new *FET Flagships*. CIBER-BBN has piloted the ambitious NANO4P (Nanomedicine for People) project, which aims to generate knowledge and develop technologies enabling increasing the average number of years with no illness.

In the scope of Technology transfer, four projects co-financed with businesspersons have been taken on, representing a success as regards attracting private investment to our research.

We have gone on drawing closer to clinical work and at the Sessions held in Santander there were two clinical forums of great interest for outreach to doctors and researchers.

Because of the limitations existing to contracting and giving priority to researchers' contracts, the always highly-valued launching grants for young researchers could not be arranged this time. We hope to be able to recover this initiative in the next few years.

As regards NANBIOSIS, the MINECO has been requested for revalidation of the ICTS, the annual evaluation period used as a basis for assigning economic incentives has been readjusted and the infrastructure has continued to be publicised at national and international forums.

As a result of the annual evaluation of the Research Groups for their work done in 2016 one group has been discontinued.

In cooperation with other thematic areas we have closed a call for projects along with CIBERER and CIBERES at which four projects were financed. 2017 was the first year for the three new thematic areas. This aspect means excellent cooperation opportunities for our CIBER. In fact, work has been done on a collaborative initiative with CIBERONC which we hope to extend to other areas in the future.

The following pages will provide further information which I hope will be of interest to you. There is no question that the work done by the CIBER-BBN in a year is hard to sum up in just a few pages, and I would like to take this opportunity to thank the whole BBN and CIBER community for the daily efforts made, at the same time as wishing to encourage them to go on working as we have up to now, with our sights set on continuing to progress along the path towards knowledge and excellence.

With best regards,

Scientific Programmes

Bioengineering and Medical Imaging

Coordinator: Jordi Aguiló Llobet

The 21 intramural projects in the programme went on in 2017.

In the call for inter-CIBER projects between CIBER-BBN, CIBERER and CIBERES, approval was obtained for the Ans-resp-weaning project which is developed by the Groups of Pablo Laguna (CIBER-BBN) and Lluís Blanch (CIBERES) with the aim of studying cardio-physiological parameters as predictors of successful suspension of mechanical ventilation in patients in a critical state.

As regards projects, the following ones were also continued, financed by external funds:

- *IMI2 RADAR-CNS: Remote Assessment of Disease and Relapse – Central Nervous System* coordinated by King´s College in London and Janssen Pharmaceutica NV, with the participation of Jordi Aguiló's group at the Universidad Autònoma de Barcelona and Pablo Laguna's group at the Universidad de Zaragoza, along with the group led by Josep María Haro (CIBERSAM).
- *GRAPHENE- CORE1:* a work package of the Graphene Flagship devoted to Biomedical Technologies coordinated by Prof. Kostas Kostarelos, from the University of Manchester, with the participation of Rosa Villa from the Centro Nacional de Microelectrónica.
- *Search for biomarkers for early detection of Alzheimer's disease in the cohort of the Vallecas Project*. Javier Pavía and Francisco del Pozo's Groups collaborate with Ramón Martinez Mañez's Group in this project with a 3-year duration, coordinated by the Fundación CIEN.

Apart from this, the Erasmus+ *E-MEDIVIP* project, an "e-learning platform in medical information technology to improve professional skills and practice in ITC" jointly led by Bilecik Seyh Edebali and Sakarya Universities from Turkey, in which researcher Margarita Juliá from Carles Arús's group at the Universidad Autònoma de Barcelona takes part, ended in November.

The Photonics Engineering Group of the Universidad de Cantabria led by José Miguel López Higuera has joined the Instituto de Investigación Marqués de Valdecilla (IDIVAL) as a consolidated group. The same group has presented the feasibility of a highly innovative opto-electronic grid at the XIX Congreso de la *Sociedad Española de Oncología Radioterápica* (SEOR) held in Santander in June.

In the month of October Barcelona Liver Bioservices (BLB) was set up, as a spin-off of the IDIBAPS for development of preclinical studies in the field of liver diseases and hepatotoxicity. BLB, which was set up partly thanks to the CaixaImpulse programme, uses a liver on a chip system which imitates the microenvironment of the liver in a cell co-culture chamber with microfluidics and with researcher Rosa Villa from the CNM-CSIC participating in its design.

One of the principal researchers from the Bioengineering programme, Pablo Laguna, head of the CIBER-BBN group at the Universidad de Zaragoza (BSICoS), was appointed IEEE fellow at the *Institute of Electrical and Electronics Engineers* in the Engineering in Medicine and Biology Society -IEEE-EMBS-.

A work coordinated by Guadalupe Soria and with Raúl Tudela as first signatory, both of these researchers in Javier Pavía's Group at the Hospital Clínico in Barcelona, has won the Magna cum Laude award for the best paper granted by the European Society for Magnetic Resonance in Medicine and Biology at its annual Congress. These researchers have shown that there are differences in the functional networks of the brain between healthy rats and a specific rat model for Alzheimer's disease.

Programa de Biomateriales y Terapias avanzadas

Coordinator: Julio San Román del Barrio

In 2017 a national patent was extended to a PCT, and later on it was licensed to a company.

Financing was obtained for the inter-CIBER NanoCrisprAlbino Therapy project intended for developing a new advanced therapy intended for treating albinism. The NANOBIOCEL (CIBER-BBN) groups led by José Luis Pedraz and the group led by Lluís Montoliu (CIBERER) are collaborating in this project and it has been one of the four projects to have benefitted from aid as part of the internal CIBER call for carrying out multi-disciplinary projects between CIBER-BBN, CIBERER and CIBERES.

As regards European projects, researchers Luis Fernández and Iñaki Ochoa from the GEMMUZ Group are cooperating in the new European ORCHID project, which is intended to speed up the social and economic impact of the technology known as *Organ-on-Chip*. The BIOFORGE Group, led by José Carlos Rodríguez Cabello, develops new hydrogels for biomedical applications in the European BIOGEL consortium.

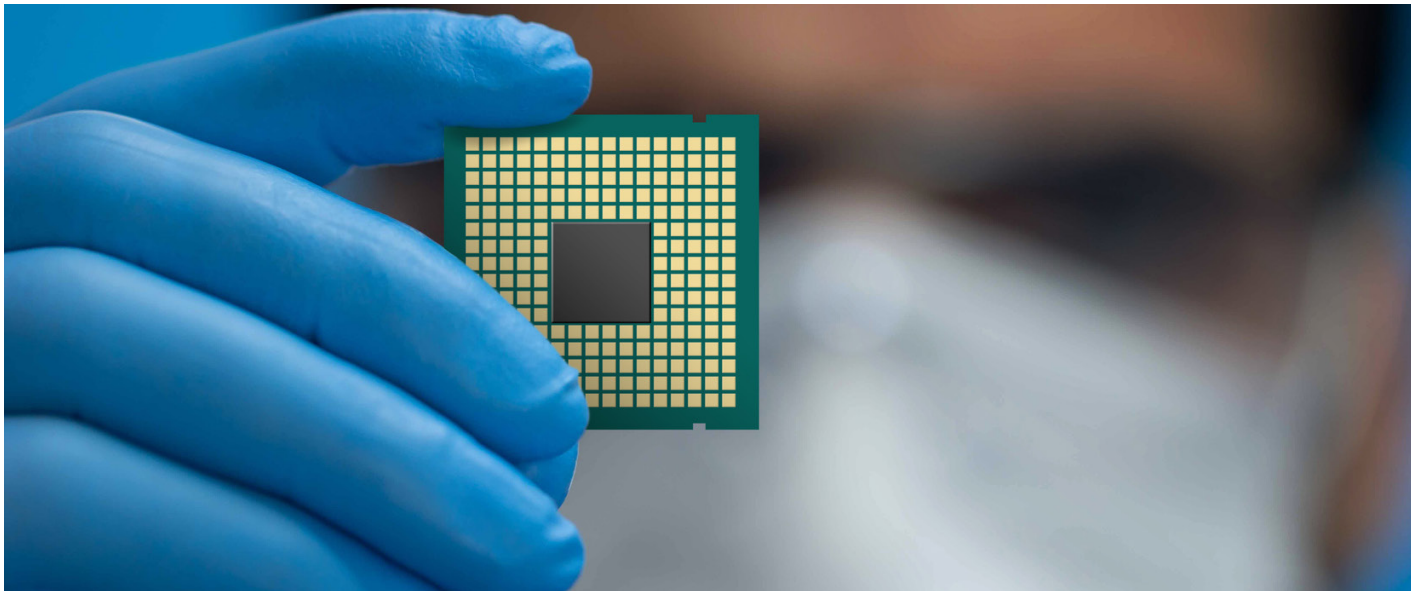
The Ocular Surface Group of the IOBA-UVA, led by Margarita Calonge, has opened the first multidisciplinary and referential unit for OculoFacial Pain (UniDOF) in Spain; it has been one of the three Spanish teams taking part in the HOLOCORE, clinical study, with which it seeks to prove the security and effectiveness of a cell therapy medication in patients with moderate to severe limbal stem cell-deficiencies due to corneal burns. Dr Calonge's team also cooperates in the projects entitled Integrated Training in Dry Eye Disease Drug Development (IT-DED3), and Drug Discovery and Delivery Network for Oncology and Eye Therapeutics (3D – NEONET), financed by means of the European Union Marie Sklodowska-Curie programme.

Juan Manuel Bellón and Gemma Pascual from the Universidad de Alcalá Group have taken part in a new study intended for use of the New Zealand white rabbit as an experimental animal for several models of repair of the abdominal wall. The report of this study was published in the prestigious Tissue Engineering journal.

As regards awards and distinctions, María Vallet Regí (CIBI-UCM) was awarded the 'Julio Peláez' prize for Pioneers in Physical, Chemical and Mathematical Sciences, granted by the Fundación Tatiana Pérez de Guzmán el Bueno. Dr Vallet was also presented as a new member of the American Institute for Medical and Biological Engineering (AIMBE), thus highlighting the extraordinary career of the Group led by her.

Ángel Raya, head of the CMR[B] Group, leads the new Clinical Translational Programme for Regenerative Medicine in Catalonia (P-CMR[C]) set up in cooperation with the IDIBELL and which is located at Duran i Reynals Hospital.

As regards transversal activities, the CIBER-BBN continues to be an Interested Party of the Advanced Therapies Committee (CAT) of the European Medicines Agency (EMA) and has continued relations with the Spanish Agency for Medicines and Healthcare products (AEMPS) in all aspects connected with the development of new advanced therapy products.



Nanomedicine Programme

Coordinator: M. Pilar Marco Colás

We should stress the efforts made by the CIBER-BBN to lead an initiative that has been submitted for the call for preparatory actions for future FET-FLAGSHIPS in the field of nanomedicine. The project is entitled "**Precision nanomedicine for People (Nano4P)**" (www.nano4p.eu). Researchers from different international organisations are involved in the proposal and there have been a large number of accession.

The researchers from the Nanomedicine programme of the CIBER-BBN have continued with the external financing projects obtained such as: the European SMART-4 FABRY project (*Smart mul- tifunctional GLA-nanoformulation for Fabry Disease*), coordinated by the CIBER (P.I.: Dr Nora Ventosa). On the national scale the TERARMET projects (Public-private RETOS project), PENTRI (Project Marató de TV3), Nano-ET-Leukemia (RETOS R+D+i projects) are still under way.

The funds obtained for undertaking certain projects in calls for public financing in both national and international spheres should be mentioned. The following research projects could be stressed:

- European "Integrated Precision Medicine Research Center of Excellence – IPMT CoE" project, in which CIBER-BBN along with the German Fraunhofer Institute for Biomedical Engineering (IBMT) take part as advisors of known prestige of the University of Cyprus (UCY)the institution coordinating the proposal.
- European "Exploitation of extracellular vesicles for precision diagnostics of prostate cancer – PROSCANEXO" project ERANET-TRANSCAN-2 (JTC2016). CIBER-BBN coordinates the project (P.I.: Jesús Martinez de la Fuente) along with different European partners.
- Jesús Santamaría has obtained an Advanced Grant from the European Research Council (ERC) with the CADENCE project "Catalytic Dual-Function Devices Against Cancer".

The following events and congresses concerning Nanomedicine have been attended and co-organised:

- *X Conferencia Anual de las Plataformas Tecnológicas de Investigación Biomédica*, 7-8 March 2017, Madrid.
- CLINAM European Foundation for Clinical Nanomedicine, Basel 7-10 May 2017.
- 2nd Summer School on Nanomedicine, Barcelona 28-29 September 2017, co-organised by CIBER-BBN.
- Annual meeting of the ETPN (European Technology Platform of Nanomedicine). Malaga, 17–19 October 2017, co-organised by CIBER-BBN.

One of the principal investigators of the Nanomedicine programme, Luis Manuel Liz Marzán, has again appeared in the list of the most cited scientists in the world published every year by Clarivate Analytics. He has also been designated as a new member of the European Academy of Science (EURASC), and has been given two awards, the 2017 Blaise Pascal Medal in Materials Science and the 2017 Advanced Materials Laureate. Pau Gorostiza, new P.I. of the Group, has received the "Fundaluce 2016" aid for research, for a project intended for restoring sight.

The CIBER-BBN has cooperated as a sponsor and has coordinated the Technical Office in Barcelona of the European Nanomedicine Society (ESNAM) whose president is Simó Schwartz, arranging the 2nd Summer school in Nanomedicine of the ESNAM held in Barcelona from 27-29 September.

Training Programme

Coordinator: Raimon Jané Campos

The Training Programme of the CIBER-BBN seeks to increase research skills of the staff forming part of the groups by improving the professional competence of the technical and research staff as a factor for change, by changing attitudes, knowledge and skills depending on the needs arising throughout development of their research work.

The main initiatives of the CIBER-BBN Training Programme are its grants for getting started in research and the mobility grant.

Unfortunately, in 2017 administrative limitations have meant that it has not been possible to arrange grants as aid for getting started in research, an endeavour which is very highly valued among the CIBER-BBN Groups as it allows young researchers still taking a master course to join the Groups.

Aid for mobility

The aim of this training programme is to act as an incentive for short stays at other research groups in order to facilitate the transfer of experience and technology and to foster cooperation between the different groups in the CIBER-BBN. These stays must be structured in priority and strategic work lines for our thematic area.

In 2017 there were two mobility calls, in April and September, and a total number of 18 subsidies for stays at groups external to the CIBER-BBN.

Three grants have been given as aid for mobility for research staff between CIBER-BBN groups, the call for these being permanent throughout the year.

No. of "Mobility" grants awarded

Year	No of intra-CIBER-BBN grants	No. of external grants	TOTAL NO. OF GRANTS AWARDED
2011	6	10	16
2012	6	9	15
2013	1	20	21
2014	2	17	19
2015	3	18	21
2016	4	13	17
2017	3	18	21

NANBIOSIS ICTS Platform

Coordinator: Jaume Veciana Miró

In 2017 the internal evaluation protocol of the units was updated to assign economic incentives, adapting the parameters stipulated by the MINECO for evaluating ICTS.

The NANBIOSIS was presented at international bodies, national companies, private research foundations and public research bodies, as well as at many national and international events. These included the Annual Conference of Platforms for Research into Biomedicine, where NANBIOSIS was presented in the main programme, ETPN2017, as well as through its participation in the MATERPLAT Platform, at which the NANBIOSIS Coordinator is co-leader of the Group for Innovation in Health and partnering events for seeking associates such as BioEurope (Berlin). NANBIOSIS was invited to present its activity at the annual session of the thematic areas of CIBERES, CIBEREHD, CIBERESP, CIBERSAM, CIBERDEM, or at the meeting of the Lung Cancer Group of the CIBERONC. There was also a second meeting of the Advisory Scientific Meeting of NANBIOSIS to discuss the strategic plan for infrastructure, which was held coinciding with the annual sessions of CIBER-BBN.

Similarly, the relation with EATRIS was promoted, establishing joint lines of action. In fact, the representatives of NANBIOSIS were invited to attend the *"Enhancing Predictivity in Medicines Development" Translational Medicine Conference forum* in Prague in September 2017, where they had a meeting with the EATRIS management.

The search for external financing from both public and private sources was a priority. The renovation of NANBIOSIS was requested as ITCS to the MINECO, currently in the evaluation stage. The collaborative schemes already started with companies were also followed up. Some examples are the projects entitled TERET, BIOTAPES and "Development of bioprinting and biotint systems for three-dimensional regeneration of cartilage and bone", all in the CHALLENGE-COLLABORATION programme, the European *BERENICE* project (FP7), the *DRIVE* project (H2020), or the *PRONANBIOSIS* project which allows, amongst others, the integration of NANBIOSIS and the improvement in its management. Several activities have been carried out such as the execution of the marketing plan, getting under way online promotion and activation of its presence on social networks. A new person also joined the programme to be able to carry out ICTS management tasks, such as for example the processing of almost 300 applications for access.

In an attempt to promote cooperation with companies, the design of an integrated service for Nanomedicine Cascade Characterisation, including the services required to characterise their physical-chemical attributes, their in vitro and in vivo biological properties (immunology, toxicology and efficiency), using appropriate animal models as knowledge basis to accelerate the ISCIII Transfer of research into nanomaterials and nanodevices to clinical practice. For the time being the units involved have been identified and meetings have been held with the parties responsible for determining the tests to be performed, the complementary services and the coordinators and interlocutors for each of the stages in the characterisation.

As well as maintaining cooperation with other infrastructures, the first actions with EATRIS have been designed for establishing long-term collaboration.

Scientific Production

PUBLICATIONS

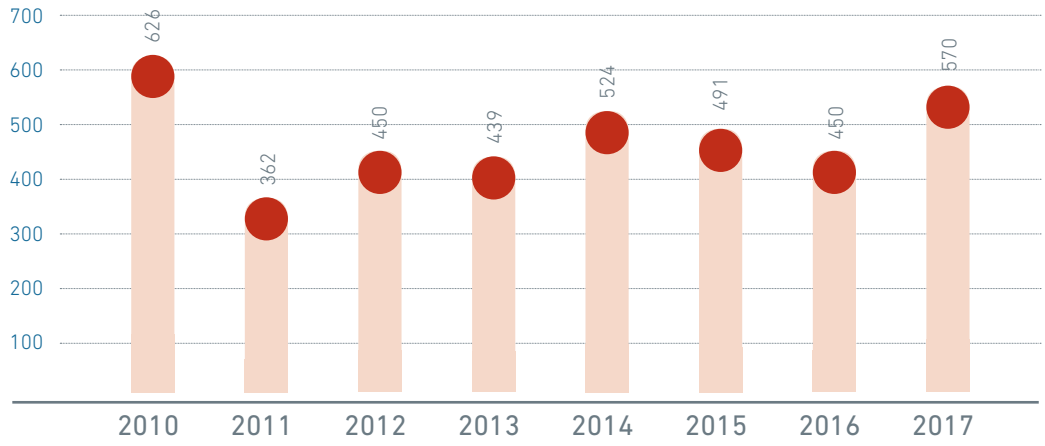
No. of publications in 2017

TOTAL	**570**
Q1	394
D1	167

Collaboration work

IntraCIBER	61
InterCIBER	69

Evolution of publications



Most relevant publications of the CIBER-BBN in 2017 by impact factor

Publication	Impact factor
Gil A., Albericio F., Alvarez M. Role of the Nozaki-Hiyama-Takai-Kishi Reaction in the Synthesis of Natural Products. Chemical Reviews. 2017;117(12):8420-8446.	47,9280
Feig D.S., Donovan L.E., Corcoy R., Murphy K.E., Amiel S.A., Hunt K.F. et al. Continuous glucose monitoring in pregnant women with type 1 diabetes (CONCEPTT): a multicentre international randomised controlled trial. The Lancet. 2017;390(10110):2347-2359.	47,8310
D'Avino G., Souto M., Masino M., Fischer J.K.H., Ratera I., Giovannetti G. et al. Conflicting evidence for ferroelectricity. Nature. 2017;547(7662):E9-E10.	40,1370
Oria R., Wiegand T., Escribano J., Elosegui-Artola A., Uriarte J.J., Moreno-Pulido C. et al. Force loading explains spatial sensing of ligands by cells. Nature. 2017;552(7684):219-224.	40,1370
Malinverno C., Corallino S., Giavazzi F., Bergert M., Li Q., Leoni M. et al. Endocytic reawakening of motility in jammed epithelia. Nature Materials. 2017;16(5):587-596.	39,7370

Publication	Impact factor
Rodríguez-Franco P, Brugués A, Marín-Llauradó A, Conte V, Solanas G, Batlle E. et al. Long-lived force patterns and deformation waves at repulsive epithelial boundaries.Nature materials. 2017;16(10).	39,7370
Reguera J., Langer J., Jimenez De Aberasturi D., Liz-Marzan L.M. Anisotropic metal nanoparticles for surface enhanced Raman scattering. Chemical Society Reviews. 2017;46(13):3866-3885.	38,6180
Yu R., Liz-Marzan L.M., Garcia De Abajo F.J. Universal analytical modeling of plasmonic nanoparticles. Chemical Society Reviews. 2017;46(22):6710-6724.	38,6180
Udayabhaskararao T., Altantzis T., Houben L., Coronado-Puchau M., Langer J., Popovitz-Biro R. et al. Tunable porous nanoallotropes prepared by post-assembly etching of binary nanoparticle superlattices. Science. 2017;358(6362):514-518.	37,2050
Gonzalez-Rubio G., Diaz-Nunez P., Rivera A., Prada A., Tardajos G., González-Izquierdo J. et al. Femtosecond laser reshaping yields gold nanorods with ultranarrow surface plasmon resonances. Science. 2017;358(6363):640-644.	37,2050

PATENTS OWNED BY CIBER

APPLIED FOR

Spanish

- Connection device for microfluidic circuits.
- Procedure for the exfoliation and transfer of graphene from a doped silicon carbide substrate to another substrate.

European

- Procedure for preparation of polymeric materials based on lactide, materials obtained by means of this procedure and their uses.

International

PCT

- Use of an adrenomedullin inhibitor for manufacturing a medication useful in the prevention and treatment of diseases reducing bone density.
- Compounds and their use as haptens for detection of S. aureus.
- Microfluidic chip, microfluidic device, procedure and associated usages.
- Microfluidic device and system for studying cell cultures.

European National/Regional Phase

- Intelligent bioimpedance sensor for biomedical applications.
- Bioreactor for cell co- culture.

U.S. National phase

- Bioreactor for cell-co-culture.

Validation in Germany, Spain, France, Italy and the United Kingdom

- A 1,4,5-trisubstituted 1,2,3-triazole mimetic of RGD or/and OGP10-14, procedure for obtaining this and its usages.

GRANTED

Spanish

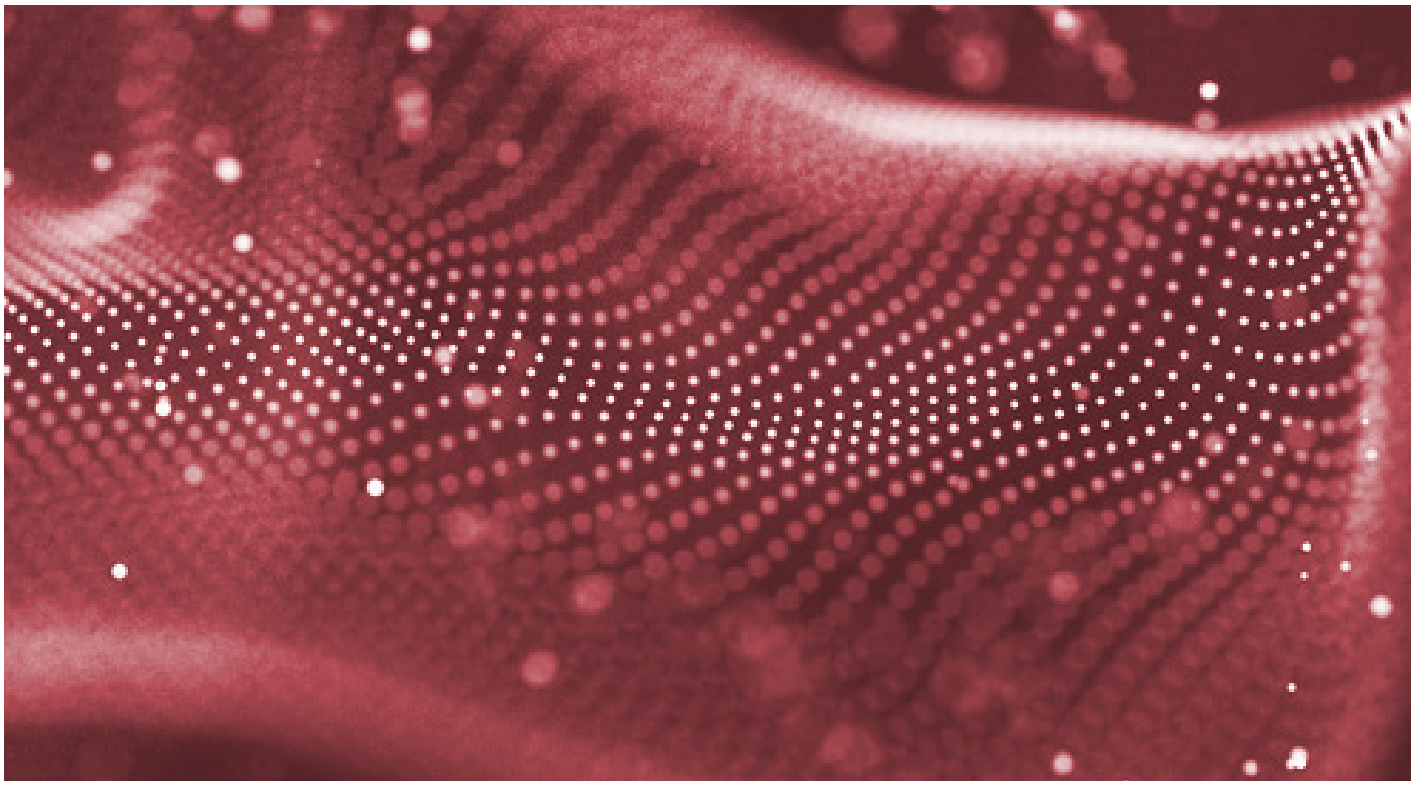
- Method for surface chemical activation of a solid silicon-based support by means of direct covalent anchorage of at least one biomolecule of nucleic acids.
- Bioactive glasses, scaffoldings of bioactive glasses and scaffoldings of bioactive glasses seeded with cells; preparation methods and their usages.

European

- A 1,4,5-trisubstituted 1,2,3-triazole mimetic of RGD or/and OGP10-14, procedure for obtaining this and its usages.

Clinical guides

- Consensus document on antiretroviral treatment in children and adolescents infected by human immunodeficiency virus.
- Clinical channel for bariatric surgery.
- Clinical channel for enhanced recovery in Gastro-oesophageal surgery.
- Manual for bariatric surgery for Primary Healthcare professionals.



CIBER-BBN Groups. Publications

Group leader	Total Publications	Q1	D1	Institution	Province
Aguiló Llobet, Jordi	7	4	3	Universidad Autónoma de Barcelona - Centro Nacional de Microelectrónica	Barcelona
Albericio Palomera, Fernando	34	21	10	Universidad de Barcelona - Facultad de Química	Barcelona
Arús Caraltó, Carles	6	4	1	Universidad Autónoma de Barcelona	Barcelona
Becerra Ratia, José	7	4	2	Universidad de Málaga - Facultad de Ciencias	Málaga
Bellón Caneiro, Juan Manuel	13	5	0	Universidad de Alcalá - Facultad de Medicina	Madrid
Calonge Cano, Margarita	16	7	0	Universidad de Valladolid - Instituto de Oftalmobiología Aplicada	Valladolid
Corcoy Pla, Rosa	8	2	1	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Engel López, Elisabeth	12	9	2	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Eritja Casadellà, Ramon	11	6	1	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña	Barcelona
Fernández Jover, Eduardo	12	9	2	Universidad Miguel Hernández - Instituto de Bioingeniería	Alicante
Gómez Ramírez, Rafael	19	15	3	Universidad de Alcalá - Facultad de Farmacia	Madrid
Gómez Ribelles, José Luis	18	8	3	Universidad Politécnica de Valencia - Centro de Biomateriales e Ingeniería Tisular	Valencia
González Martín, María Luisa	3	1	0	Universidad de Extremadura - Facultad de Ciencias	Badajoz
Gorostiza Langa, Pau	9	8	7	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Jané Campos, Raimon	20	9	1	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Laguna Lasaosa, Pablo	13	6	0	Universidad de Zaragoza	Zaragoza
Lechuga Gómez, Laura María	11	10	6	Agencia Estatal Consejo Superior de Investigaciones Científicas - Institut Català de Nanociència i Nanotecnología	Barcelona
Liz Marzán, Luis Manuel	31	29	19	CIC biomaGUNE	Guipúzcoa
López Higuera, José Miguel	5	3	0	Universidad de Cantabria - Edificio I+D+I de Ing. de Telecomunicación	Cantabria
Mangues Bafalluy, Ramon	17	13	7	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona

Group leader	Total Publications	Q1	D1	Institution	Province
Marco Colás, María Pilar	7	7	4	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña	Barcelona
Martínez Barca, Miguel Ángel	18	11	4	Universidad de Zaragoza	Zaragoza
Martínez de la Fuente, Jesús	9	9	5	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencia de Materiales de Aragón	Zaragoza
Martínez Máñez, Ramón	33	27	10	Universidad Politécnica de Valencia - Instituto Interuniversitario de Investigación de Reconocimiento Molecular y Desarrollo Tecnológico	Valencia
Pavía Segura, Javier	12	8	2	Universidad de Barcelona - Hospital Clínic de Barcelona	Barcelona
Pedraz Muñoz, José Luis	27	20	7	Universidad del País Vasco - Facultad de Farmacia	Álava
Peris Serra, José Luis	7	3	1	Asociación Instituto de Biomecánica de Valencia	Valencia
Pozo Guerrero, Francisco del[1]	16	12	3	Universidad Politécnica de Madrid - ETSI Telecomunicación	Madrid
Raya Chamorro, Ángel	10	4	3	Centro de Medicina Regenerativa de Barcelona	Barcelona
Ritort Farran, Félix	7	5	4	Universidad de Barcelona - Facultad de Física	Barcelona
Roa Romero, Laura María[2]	1	1	0	Universidad de Sevilla - Escuela Superior de Ingenieros	Sevilla
Rodríguez Abreu, Carlos	9	4	0	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña	Barcelona
Rodríguez Cabello, José Carlos	11	6	2	Universidad de Valladolid	Valladolid
Rubio Vidal, Núria	8	6	3	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Química Avanzada de Cataluña	Barcelona
Ruiz Romero, Cristina	14	9	2	Servicio Gallego de Salud - Complejo Hospitalario Universitario A Coruña	A Coruña
Samitier Martí, Josep	11	10	8	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
San Román del Barrio, Julio	18	11	4	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencia y Tecnología de Polímeros	Madrid
Santamaría Ramiro, Jesús	37	28	18	Universidad de Zaragoza - Instituto Universitario de Investigación en Nanociencia de Aragón	Zaragoza
Santos Lleó, Andrés	7	5	3	Universidad Politécnica de Madrid - ETSI Telecomunicación	Madrid

Group leader	Total Publications	Q1	D1	Institution	Province
Schwartz Navarro, Simó	7	6	1	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR) - Hospital Vall d´Hebron	Barcelona
Trepat Guixer, Xavier	10	10	9	Fundación Instituto de Bioingeniería de Cataluña	Barcelona
Vallet Regí, María	23	19	10	Universidad Complutense de Madrid - Facultad de Farmacia	Madrid
Veciana Miró, Jaume	24	20	10	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Ciencias de Materiales de Barcelona	Barcelona
Vilaboa Díaz, Nuria	9	5	3	Servicio Madrileño de Salud - Hospital La Paz	Madrid
Villaverde Corrales, Antonio	7	7	4	Universidad Autónoma de Barcelona - Instituto de Biotecnología y Biomedicina	Barcelona
Farré Ventura, Ramón*	26	17	6	Universidad de Barcelona - Facultad de Medicina	Barcelona
Muñoz Fernández, María Ángeles*	15	13	3	Servicio Madrileño de Salud - Hospital Gregorio Marañón	Madrid

1 Deceased in January 2018

2 Group deregistered in December 2017

* Associated CIBER-BBN Groups

ciberCV

Cardiovascular Diseases

Scientific Director's Presentation

Francisco Fernández-Avilés

Dear colleagues at the CIBER of Cardiovascular diseases (CIBERCV); I am writing to thank you for the great effort you have made in 2017. I feel that the balance of this first year of our thematic area is satisfactory, based on both the achievements attained and on my perception of the enthusiasm and commitment of the whole CIBERCV, which I have also clearly noticed inside and outside our organisation.

The transition from the Cardiovascular Research Network to the constitution and stabilisation of the CIBERCV ha not been a simple matter. Belonging to the CIBER Consortium gives us a budgetary stability that is impossible to attain by means of other financing tools of the Instituto de Salud Carlos III. This stable financing nevertheless goes along with an extremely high degree of responsibility. From both the standpoint of management and assessment, belonging to the most powerful biomedical research structure in this country implies an even greater degree of scrutiny by society and financing bodies. It is our duty to prove that the economic effort made by society to finance our cooperation is indeed a productive investment.

Thanks to the enormous dedication of all the Groups in 2017 we have developed the Master Plan 2017-2021 of the CIBERCV. This is our first scientific plan and one in which the objectives and work packages in each of the research programmes are explained. This master plan is a dynamic tool that we are going to look over again every year to make sure that this adapts to the needs and scientific capacities of our institution.

In 2017 we have also set up an objective and transparent pluri-annual assessment plan, which is agreed on with the different agents involved, from the research groups to the management of the Instituto de Salud Carlos III. The assessment process is by its own definition a complex aspect that must be seen as a tool for identification of the degree of accomplishment of the objectives of this institution. The thorough appraisal of this first year has thus enabled us to identify areas of excellence (e.g. over 800 articles JCR, 223 of which are in first decile journals with an accumulated impact factor of around 4000 points). It is similarly important to also have identified areas in which we need to improve (e.g. transfer of results to society and accomplishment of European projects). On this basis, in 2018 we can take greater advantage of our strong points and become more competitive.

Last but not least, in 2017 the conditions for the Training and Mobility Programme and of the International and Institutional Relations Programme have been drawn up. Both programmes are foundations for the CIBERCV's future and something which our institution has to work hard on to (1) identify and train the new generation of scientists and (2) to place this country's cardiovascular research and innovation among the most relevant and competitive in the world.

Scientific Programmes

Myocardial injury and its consequences

Coordinators: Francisco Fernandez-Avilés / Juan Cinca

Over this first year in our career, Programme 1, intended to understand and treat myocardial injury and its associated clinical consequences, has obtained some significant results from transfer in cooperation with the cardiovascular research network.

In the line of scar-forming and structural and electrophysiological remodelling, we should stress the article entitled *Long-Term Potassium Monitoring and Dynamics in Heart Failure and Risk of Mortality* published in Circulation in which three CIBERCV groups give evidence vouching for the relevance of potassium levels in the prediction of the risk of death in heart failure. Another major milestone for the CIBERCV was the worldwide coordination of the Global position paper on cardiovascular regenerative medicine published in European Heart Journal and in which the foundations are laid for translational research in cardiovascular regenerative medicine. In the area of basic research into mechanisms the study entitled "*Tbx20 controls the expression of the KCNH2 gene and of hERG channels*" is worthy of mention. This was published in the PNAS journal and coordinated by Dr Tamargo and examines the major role of Tbx20 in long QT syndromes.

In the line of genetically-caused myocardial injury we should highlight the work entitled "*Direct oral anticoagulants in patients with hypertrophic cardiomyopathy and atrial fibrillation*" published in Int J Cardiology and in which four Groups from the programme took part. In this it proved that direct-action anticoagulants are safe and just as effective as vitamin K-antagonists in patients with Hypertrophic cardiomyopathy (HCM). We must also mention the work entitled *Additional value of screening for minor genes and copy number variants in hypertrophic cardiomyopathy*, directed by Dr Brugada's group and published in *PLoS One*, in which four groups from the programme took part. Another important achievement in this direction was obtaining the multicentre project on Etiological diagnosis of advanced conduction disorders which will enable laying the genetic foundations of conduction disorders in young subjects requiring a pacemaker implant.

In the line of research into heart failure, thanks to the transfer performed with the Multicentre Register in Research in Heart Failure of Spain (i.e. REDISCOR I and II, and III starting now), one should emphasise three studies intended to improve clinical practice: (1) *Nutritional status is related to heart failure severity and hospital readmissions in acute heart failure*, (2) *Mid-range left ventricular ejection fraction: Clinical profile and cause of death in ambulatory patients with chronic heart failure* and (3) *Proposal of a novel clinical score to predict heart failure incidence in long-term survivors of acute coronary syndromes*, published in the International Journal of Cardiology in which the close cooperation between members in the line was vital. In this approach a major effort was also made in identifying *Clinical outcomes of temporary mechanical circulatory support as a direct bridge to heart transplantation: a nationwide Spanish* registry coordinated by Dr Crespo and published in Eur J Heart Failure.

Arterial pathology, myocardial ischaemia and structural pathology of the heart

Coordinators: David García-Dorado / Alberto San Román

Programme 2 of the CIBERCV on arterial disease, myocardial ischaemia- reperfusion and structural heart disease has published some cooperative articles with great impact in 2017. These include a major study which proved the capacity of different image markers in early cardiac magnetic resonance (Published in the *Journal of the American College of Cardiology – Cardiovascular Imaging*). The prognostic implications of haemo-erythrocyte proteins in these patients have also been described (published in Thrombosis Haemostasis). The SIOVAC randomised test analysed the effect of sildenafil on persistent pulmonary hypertension after valve surgery. The findings of this study, published in the *European Heart Journal*, are sure to change the recommendations of international guides on this subject.

Programme 2 also published cooperative articles which have produced substantial progress in the understanding of the mechanisms of this group of diseases, such as the in-depth characterisation of the proteomic footprint of myocardial ischaemic reperfusion published in Scientific Reports, the identification of the role of miRNA in the prevention of damage through reperfusion with urocortin, published in Scientific Reports, or the discovery of the role of nitric oxide in aneurysmatic aortic disease, in particular, its possible participation in the cell signalling responsible for the phenotype of Marfan syndrome, published in Nature Medicine. This study will be translated for patients in clinical tests which are being planned to start in 2018.

The transfer of knowledge generated in Programme 2 has progressed through patents and other initiatives. Patents have been submitted on biomechanical sensors applicable to the differential diagnosis between myocardial ischaemia and myocarditis (European Patent), an oral treatment to prevent adverse post-ischaemic remodelling by inhibiting the activation of calpain (European patent) or new risk biomarkers for cardiovascular diseases (International patent, already with a licence). The creation of a multicentre platform for preclinical research into lesions by reperfusion (CIBERCLAP) is one of the most important of other prominent aspects of transfer, as well as the introduction of genetically modified mouse models which are offered to all the participants of CIBERCV.

The power of cooperative research in Programme 2 is clearly proven by initiatives such as those of the acute coronary syndrome, low flow aortic stenosis, aortic regurgitation or transcatheter aortic valve implantation, some of which generate competitive funds, such as the registration of congenital heart disease or the registration of sudden death in congenital heart disease, both financed by the Instituto Nacional de Salud (Instituto de Salud Carlos III). In 2017, many patients were included in randomised clinical tests in patients with acute myocardial infarction and bicuspid aortic valve.

Some of the competitive subsidies obtained in Programme 2 were the European initiative H2020 COST on cardioprotection against reperfusion injury, EU-Cardioprotect, with the participation of several groups from this programme, as an example of the international outreach of the CIBERCV.

Cardiovascular epidemiology and risk factors

Coordinator: Jaume Marrugat

In 2017 the Epidemiology and Cardiovascular Risk Factors programme set forth its objectives for research and creation of transversal structures for the coming years. Furthermore, thanks to the earlier cooperation at the RIC, some major milestones have been attained in the different work areas:

Transfer Projects. A survey on population cohorts recruited all over the country was made. Twenty cohorts have agreed to take part, including roughly 85,000 participants. This proposal will enable constructing BigData to answer the crucial questions of cardiovascular epidemiology, which will go along with a clinical-epidemiological database and a repository of biological samples. Indicators of trends have also been obtained in the evolution of the body mass index and blood pressure worldwide (Lancet 2017;390:227-42. Lancet 2017:389:37-55), reinforcing the need for controlling these risk factors for cardiovascular illness (J Clin Lipidol 2017;11:1013-22).

Contribution to improving clinical practice. The ATHOS study has been completed, including roughly 8,500 patients with acute coronary syndrome (ACS) cared for at 31 hospitals. This contribution enables us to evaluate variability in handling patients with ACS at Spanish hospitals and provides an evaluation of performance in handling myocardial infarction, thanks to the EURHOBOP European benchmarking system coordinated by researchers from the Programme. Categorical information has also been published on the effectiveness of percutaneous coronary intervention in the elderly and patients with comorbidities in the acute phase (Int J Cardiol 2017; 249: 83-89) with major implications for clinical practice due to the infra-utilisation of this procedure in this age group. In primary prevention, an analysis has been made of the effectiveness of treatment with statins according to the level of cardiovascular risk and it was possible to estimate the number of patients required to be treated in order to prevent a cardiovascular event on the different risk levels (Clin Pharmacol Ther 2017).

Progress in knowledge on the mechanisms of pathology and potential new treatment strategies. In 2017 new genetic variants connected with hypertension were identified, indicating new mechanisms and therapeutic targets (Nat Genet 2017; 49: 403-415; Hypertension 2017,). Lipase lipoprotein was valued as a therapeutic target for controlling triglycerides and reducing the risk of coronary disease (JAMA 2017;317:937-46), validating the inhibition of the cholesterol ester transfer protein (CETP) as a therapeutic target for reducing the risk of heart disease, although the mechanism of this protection effect could be mediated by an increase in levels of HDL-cholesterol or a reduction in the levels of LDL-cholesterol (Circ Res 2017;121:81-8). DNA methylation markers associated with obesity were identified (Epigenetics 2017;12:909-16), with the functionality of particles of HDL-cholesterol (Arterioscler Thromb Vasc Biol. 2017 Mar;37(3):567-569) and with the risk of presenting heart diseases (Atherosclerosis 2017;263:323-33). It has also been proven that one of the potential mechanisms making the Mediterranean diet reduce the risk of cardiovascular illness is the improvement in the functionality of HDL cholesterol particles (Circulation 2017;135:633-43).

Molecular and imaging biomarkers, and precision CV medicine

Coordinator: Javier Díez

In the first few months since Programme 4 of the CIBERCV was got under way, we identified which projects already begun by the different groups could be useful for the objectives of the Programme and what synergies could be necessary to carry these out, from the methodological standpoint and that of obtaining and common use of resources.

Hence, in the case of Line 1 (Evaluation of known biomarkers) a significant thrust forward was given to the large-scale validation projects. In general terms these projects also need to be undertaken during 2018, since due to the number of patients and number of determinations required, these are medium-extended term projects.

As part of the projects in the field of heart failure, progress has been made as agreed with recruiting and analysis of samples. In the following yearly period (2018) we hope to have results of the large-scale validation of biomarkers in this field (interstitial myocardial fibrosis, CA125 in patients with cardio-renal syndrome, non-vasomotor effects of Sacubitril-Valsartan).

In a similar sense, in the field of the acute coronary syndrome, satisfactory progress is being made with the recruitment and measurement of biomarkers. In the following yearly period (2018) we hope to obtain results on a panel of miRNAs for differential diagnosis of ischaemic cardiomyopathy without coronary obstruction, the usefulness of ApoJ-Gly in early coronary ischaemia and troponin as risk biomarker in acute heart failure.

We should lastly add that Domingo Pascual, with the cooperation of the Management of Programme 4, got under way a platform for collecting information on samples and biomarkers available in the CIBERCV: The Platform for Personalised Network Cardiovascular Medicine (PMPcv. net), as part of Line 1.

In the case of Line 2 (Identification of new biomarkers) nosological entities on which to focus efforts have been identified. Hence, in the field of heart failure, projects have been identified in the fields of HFPEF, HFREF and cardio-oncology, as well as pre-clinical studies. The work for this year has already enabled identifying new potential biomarkers such as the IGBP2 or the intraventricular flow in the HFPRF, or the analysis of heart deformation by CMR in the HFREF.

In the field of ischaemic vascular disease, this includes projects on subclinical atherosclerosis, acute coronary syndrome and risk of coronary diseases, as well as other fields (aneurysm of the aorta, auricular fibrillation, early ageing). The work for this year has already enabled identifying new biomarkers associated with cardiovascular risk as parameters for the structure and composition of the plate or DNA methylation.

In the field of productivity, it should be stressed that in 2017 over 50 collaborative articles were indexed, with an average IF of 9.636 points (JCR), understandably not all of these being in the context of projects under way, since these have recently been started. The members of Programme 4 have furthermore produced two patents (F. Sánchez-Madrid and D. Pascual) and a spin-off (L. Badimón) and have obtained financing in national (V. Andrés, J. Cinca, M Rivera, J. Díez) and European projects (V. Andrés, J. Díez).

Training Programme

Coordinator: Borja Ibáñez

The CIBERCV Training Programme seeks to train young people to become future cardiovascular researchers in order to improve society's cardiovascular health.

To this end, the Training and Mobility Plan, coordinated by Dr Borja Ibáñez, has been designed in 2017. Some of the measures defined as priorities that could be stressed are:

- Annual "Jordi Soler-Soler" call for contracts for young researchers.
- Support for obtaining contracts for young researchers by means of the co-financing formula.
- Intra-CIBERCV mobility plan to foster short exchange visits between CIBERCV institutions (1-2 weeks).
- Extra-CIBERCV mobility plan to support CIBERCV researchers' stays at the world's main clinical and research centres for 3-4 months.
- Organisation and support for researchers' training by means of specific courses and workshops.

Different activities such as the ones listed below were already arranged through this training programme:

- **CIBER training sessions in model phenotyping** (27 November to 1 December 2017).
- **Practical "hands-on" course on Advanced Cardiac Imaging at the** Hospital Universitario de Salamanca (9-10 November 2017).
- **International Symposium on Cardiovascular Regeneration and Repair** (15-16 June 2017).

What is more, in the important area of scientific dissemination and forming a critical spirit for society, in 2017 Dr Bermejo took part in the Madrid Science Week 2017.

Scientific Production

PUBLICATIONS

No. of publications in 2017

TOTAL	**866**
Q1	531
D1	223

Collaboration work

IntraCIBER	168
InterCIBER	211

Most relevant publications of the CIBERCV in 2017 by impact factor

Publication	Impact Factor
Ridker PM, Revkin J, Amarenco P, Brunell R, Curto M, Civeira F, et al. Cardiovascular efficacy and safety of bococizumab in high-risk patients. N Engl J Med. 2017 Apr 20;376(16):1527-1539	72,4060
Cannon CP, Bhatt DL, Oldgren J, Lip GYH, Ellis SG, Kimura T, et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. N Engl J Med. 2017 Oct 19;377(16):1513-1524	72,4060
Abarca-Gómez L, Abdeen ZA, Hamid ZA, Abu-Rmeileh NM, Acosta-Cazares B, Acuin C, et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017 Dec 16;390(10113):2627-2642	47,8310
Khera AV, Won HH, Peloso GM, O'Dushlaine C, Liu D, Stitziel NO, et al. Association of rare and common variation in the lipoprotein lipase gene with coronary artery disease. JAMA. 2017 Mar 7;317(9):937-946	44,4050
Marouli E, Graff M, Medina-Gomez C, Lo KS, Wood AR, Kjaer TR, et al. Rare and low-frequency coding variants alter human adult height. Nature. 2017 Feb 9;542(7640):186-190.	40,1370
Fuster JJ, MacLauchlan S, Zuriaga MA, Polackal MN, Ostriker AC, Chakraborty R, et al. Clonal hematopoiesis associated with TET2 deficiency accelerates atherosclerosis development in mice. Science. 2017 Feb 24;355(6327):842-847.	37,2050
Oller J, Méndez-Barbero N, Ruiz EJ, Villahoz S, Renard M, Canelas LI, et al. Nitric oxide mediates aortic disease in mice deficient in the metalloprotease Adamts1 and in a mouse model of Marfan syndrome. Nat Med. 2017 Feb;23(2):200-212.	29,8860
Nus M, Sage AP, Lu Y, Masters L, Lam BYH, Newland S, et al. Marginal zone B cells control the response of follicular helper T cells to a high-cholesterol diet. Nat Med. 2017 May;23(5):601-610	29,8860
de Cárcer G, Wachowicz P, Martínez-Martínez S, Oller J, Méndez-Barbero N, Escobar B, et al. Plk1 regulates contraction of postmitotic smooth muscle cells and is required for vascular homeostasis. Nat Med. 2017 Aug;23(8):964-974	29,8860
Warren HR, Evangelou E, Cabrera CP, Gao H, Ren M, Mifsud B, et al. Genome-wide association analysis identifies novel blood pressure loci and offers biological insights into cardiovascular risk. Nat Genet. 2017 Mar;49(3):403-415	27,9590

Clinical Guides

- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017 Sep 21;38(36):2739-2791.
- Landmesser U, Chapman MJ, Stock JK, Amarenco P, Belch JJF, Borén J, et al. 2017 Update of ESC/EAS Task Force on practical clinical guidance for proprotein convertase subtilisin/kexin type 9 inhibition in patients with atherosclerotic cardiovascular disease or in familial hypercholesterolaemia. Eur Heart J. 2017 Oct 16.
- Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, Jeppsson A, et al. Case-based implementation of the 2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease. Eur Heart J. 2018 Jan 14;39(3):e1-e33.
- Ruiz CE, Hahn RT, Berrebi A, Borer JS, Cutlip DE, Fontana G, et al. Clinical Trial Principles and Endpoint Definitions for Paravalvular Leaks in Surgical Prosthesis: An Expert Statement. Eur Heart J. 2017 Apr 18.
- Caforio ALP, Adler Y, Agostini C, Allanore Y, Anastasakis A, Arad M, et al. Diagnosis and management of myocardial involvement in systemic immune-mediated diseases: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Disease. Eur Heart J. 2017 Sep 14;38(35):2649-2662.
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- *Guía de Práctica Clínica sobre Tratamiento de la Insuficiencia Cardiaca Crónica*. Ministerio de Sanidad, Servicios Sociales e Igualdad.

CIBERCV Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Andrés García, Vicente	6	6	4	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Badimon Maestro, Lina	36	29	13	Inst. de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Bayés Genis, Antonio	49	30	14	Fundación Instituto de Investigación Germans Trias i Pujol - Hospital Germans Trias i Pujol	Barcelona
Blanco Colio, Luis Miguel	6	6	2	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Bosca Gomar, Lisardo	8	6	1	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones biomédicas Alberto Sols	Madrid
Brugada Terradellas, Ramon	25	13	3	Fund. Inst. de Investigación Biomédica de Girona - Hospital Josep Trueta	Girona
Chorro Gasco, Francisco Javier	18	8	2	Fund. para la Invest. del Hospital Clínico de la Com. Valenciana (Fund. INCLIVA) - Inst. de investigación sanitaria INCLIVA	Valencia
Cinca Cuscullola, Juan María	37	19	4	Instituto de Investigación del Hospital de la Sta. Cruz y San Pablo	Barcelona
Civeira Murillo, Fernando	21	14	4	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Crespo Leiro, María Generosa	36	21	13	Servicio Gallego de Salud - Complejo Hospitalario Universitario A Coruña	A Coruña
Delgado Jiménez, Juan Francisco	23	11	3	Servicio Madrileño de Salud - Hospital Universitario 12 Octubre	Madrid
Díez Martínez, Domingo Francisco Javier	19	15	6	Fundación para la Investigación Médica Aplicada	Navarra
Elosua Llanos, Roberto	21	14	8	Cons. Mar Parc Salut de Barcelona	Barcelona
Fernández-Avilés Díaz, Francisco	44	30	15	Servicio Madrileño de Salud - Hospital Gregorio Marañón	Madrid
García Pavía, Pablo	29	20	8	Servicio Madrileño de Salud - Hospital Univ. Puerta de Hierro	Madrid
García-Dorado García, Antonio David	77	42	15	Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) - Hospital Vall d´Hebron	Barcelona
González Juanatey, José Ramón	45	27	8	Servicio Gallego de Salud - Complejo Hospitalario Universitario Santiago	A Coruña
Ibáñez Cabeza, Borja	25	19	12	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
López-Sendon Hentschel, José Luis	1	1	1	Servicio Madrileño de Salud - Hospital La Paz	Madrid
Marín Ortuño, Francisco*	52	22	9	Fund. para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS) - Hospital Univ.Virgen de la Arrixaca	Murcia

Group Leader	Total Publications	Q1	D1	Institution	Province
Marrugat de la Iglesia, Jaume	45	27	14	Cons. Mar Parc Salut de Barcelona	Barcelona
Martínez González, José	9	7	5	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Invest. Biomédicas de Barcelona	Barcelona
Mayor Menéndez, Federico	3	2	1	Univ. Autónoma de Madrid - Centro de Biología Molecular Severo Ochoa	Madrid
Mont Girbau, Josep Lluis	80	52	15	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Ordóñez Fernández, Antonio	6	4	0	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Hospital Virgen del Rocío	Sevilla
Páramo Fernández, José Antonio	7	6	1	Universidad de Navarra - Clínica Universitaria de Navarra	Navarra
Pérez-Villacastín Domínguez, Julián	20	11	3	Servicio Madrileño de Salud - Hospital Clínico San Carlos	Madrid
Pompa Mínguez, José Luis de la	7	5	4	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Redondo Moya, Juan Miguel	24	15	7	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Rivera Otero, José Miguel	9	5	2	Fund. para la Investigación del Hospital la Fe - Hospital Universitario de La Fe	Valencia
Salaices Sánchez, Mercedes	12	6	2	Universidad Autónoma de Madrid	Madrid
San Román Calvar, José Alberto	34	13	8	Hospital Clínico Universitario de Valladolid	Valladolid
Sánchez Fernández, Pedro Luis	33	14	7	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León - Hospital Univ. de Salamanca	Salamanca
Sánchez Madrid, Francisco	13	8	2	Universidad Autónoma de Madrid	Madrid
Sánchez Margallo, Francisco Miguel	3	1	0	Fundación Centro de Cirugía de Mínima Invasión Jesús Usón	Cáceres
Sanchís Fores, Juan	31	14	7	Fund. para la Invest.del Hptal. Clínico de la Com. Valenciana (Fundación INCLIVA) - Inst. de investigación sanitaria INCLIVA	Valencia
Tamargo Menéndez, Juan	19	13	9	Universidad Complutense de Madrid - Facultad de Medicina	Madrid
Teresa Galván, Eduardo de	32	17	5	Fund. Púb. Andaluza para la Invest. de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Universitario Virgen de la Victoria	Málaga
Vázquez Cobos, Jesús María	18	16	6	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
Zamorano Gómez, José Luis	45	33	15	Servicio Madrileño de Salud - Hospital Ramón y Cajal	Madrid

* F. Marín replaces Mariano Valdés Chávarri


ciberdem
Diabetes and Associated
Metabolic Diseases

Scientific Director's Presentation

Eduard Montanya Mias

The presentation of the annual report is a good occasion to highlight everything that has been achieved during the year in the different fields of action of the CIBERDEM and also to reflect on the future. On the organisational level, CIBERDEM has set up a Strategic Plan this year for the 2017-20 period based on three major lines of action: consolidation and scientific leadership; obtaining resources and sustainability. One significant part of implementing the Strategic Plan this year has been the renovation of the External Scientific Advisory Committee, which will have a major role in the development of CIBERDEM actions. One initiative that we hope will be particularly fruitful is the institutional contact that the CIBERDEM has established with the *German Center for Diabetes Research*, which will be reinforced over 2018. We have also made an effort to foster relations with other thematic CIBER areas with the participation at our Annual Meeting of CIBERSAM and CIBER-BBN and holding a joint scientific session with CIBEROBN.

In the field of research work CIBERDEM has gone on raising its amount of scientific production, already having attained 300 publications a year, with an excellent quality level (average impact factor 5.7). The CIBERDEM Groups have kept up prominent cooperation work on the national and international scales, with 82% and 42% collaborative publications respectively. Our web page shows details of the most relevant publications of each group. Some of the specific achievements in 2017 that I would like to stress are the completion of the field work in the Di@bet.es study, which will enable establishing the incidence of diabetes in Spain and the associated risk factors, a vital aspect for establishing diabetes prevention policies, and to be able to evaluate their results later. In the field of knowledge transfer, CIBERDEM has taken part in the preparation of 7 guides and consensus documents, one of these international, and patentability studies have been carried out, with the presentation of an European Patent.

In the balance for 2017, we should also point out the initiatives in the Training Programme, in particular the CIBER and international programmes for mobility grants. In the field of Communication and Dissemination to Society, CIBERDEM has been admitted as a member of the Alliance for European Diabetes Research (EURADIA), from which CIBERDEM will help to define the future guidelines for research into diabetes in Europe. CIBERDEM has been present on an institutional level at the Congress of the Sociedad Española de Diabetes and that of the *European Association for the Study of Diabetes*, a presence which is going to be maintained in the future. CIBERDEM has shored up the commitment to make its research known to society by taking part in different measures such as the participation of CIBERDEM Groups in the DiabetesFEDE journal at the DiabetesCero congress and the Diabetes Experience Day.

Please consult the Report to find out details of the work done and achievements of the CIBERDEM in 2017.

With kind regards,

Scientific Programmes

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

Coordinator: **Ángela M. Martínez Valverde**

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

The field work has been completed in the di@bet.es study which will establish the incidence of diabetes in Spain and the associated risk factors.

As from the data collected in the di@bet.es study it has been established that the reference values of the TSH might not be appropriate for diagnosing hypothyroidism in individuals with morbid obesity (Valdés et al., Obesity 2017).

A new questionnaire has been developed for measuring the quality of life connected with the health of patients with diabetes type 1 (questionnaire ViDa1) providing information on their psychometric properties (Alvarado-Martel et al., *Front Psychol* 2017).

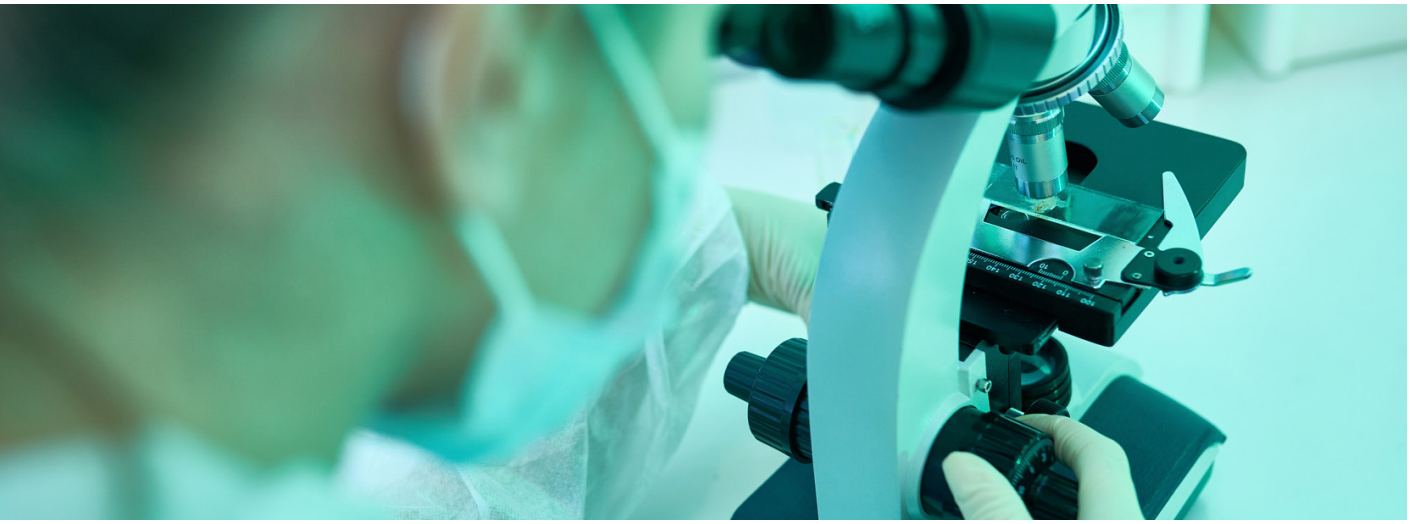
2. Genetics, epigenetics and environmental factors in the development of diabetes and its complications

A mutation which activates the STAT3 transcription factor in neonatal diabetes has been identified (Velayos et al., *Diabetes* 2017). The functional characterisation of mutations of the glucokinase gene causing hypoglycaemia and hyperinsulinism has been performed and a new mutation which has an activation effect has been identified, although its carrier suffers a slight form of late-onset hyperinsulinism (Martinez R et al., *Clin Endocrinol* 2017). New mutations have been characterised in STAP1 and LCAT genes in patients with inherited dyslipidaemia (Rial-Crestelo et al., *J Clin Lipidol* 2017).

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

In the context of participation in the European EUROCONDOR consortium (NCT01726075), it has been concluded that neurodegeneration is a key component in the pathogenesis of diabetic retinopathy in many patients with diabetes type 2 (Santos et al., *Diabetes* 2017) and it has been described that somatostatin protects the retinal pericytes from the inflammatory damage caused by the activation of the microglia (Mazzeo et al., *Exp Eye Res* 2017).

Preclinical studies have been performed on animal models. Treatment with sitagliptin in diabetic mice unleashed an antioxidant response in the kidney mediated by the drop-in levels of microRNAs miR-200 and miR-21, displayed in an improvement of proteinuria and renal fibrosis (Civantos et al., *Diabetes*, Metabolic Syndrome and Obesity: *Targets and Therapy* 2017). This same treatment administered topically to diabetic mice has been effective at preventing the neurodegeneration of the retina (Hernández et al., *Diabetología* 2017). In mice with non-alcoholic steatohepatitis the effectiveness of a dual agonist peptide of glucagon and GLP-1 receptors in the progression of this pathology has been displayed. This treatment also improved the regenerative capacity of the liver after partial hepatectomy (Valdecantos et al., *Hepatology* 2017). It has been shown that the administration of the GLP-1 analogue lixisenatide reduces atherosclerosis in insulin-resistant mice modulating the polarisation of macrophages (Vinué et al., *Diabetología* 2017).



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

Coordinator: **Franz Martín Bermudo**

1. Function and regulation of pancreatic islets: molecular and cellular bases and therapeutic targets

It has been shown that the rescue of natural TRF1 reduction with age by means of gene therapy improves the glucose intolerance associated with ageing (Dereveyanko et al., *Aging Cell* 2017).

In the Ngn3 gene an amplifying region has been identified which corrects its expression in pancreatic progenitor cells. "Cis" elements have been seen in this which are recruited for this function. (Van Arensbergen et al., *PloS One* 2017).

Islets deficient in GATA6 activity have an altered secretion of insulin, a lower content in the hormone, immature insulin granules, a disorganised endoplasmic reticulum and swollen mitochondria. In adult beta cells the loss of GATA6 affects the expression of genes which are vital for their functioning (Villamayor et al., Diabetes 2017).

In pro-opiomelanocortin (POMC) neurons, it has been described that the protein of mitochondrial membrane Mitofusin 1 is able to couple the detection of the circulating levels of nutrients with the metabolism of glucose. Its alteration also affects the homeostasis of glucose (Ramírez et al., Cell Metab 2017).

At low concentrations of glucose, the pancreatic islets increase the expression of miR-708. Their potential target is probably the Neuronatin protein (Nnat). The increase in the expression of miR- 708 alters glucose-stimulated insulin secretion (GSIS), which recovers after over-expressing Nnat. miR-708 inhibition recovers the damage in GSIS produced by the low concentrations of glucose. The over-expression of miR-708 suppresses the proliferation of beta cells and induces their apoptosis (Rodriguez-Comas et al., Diabetes 2017).

An ALX3 deficit increases the risk of congenital malformations associated with gestational diabetes (García-Sanz et al., Sci Rep 2017).

2. Mechanisms producing lesion and regeneration of pancreatic islets

The proliferation capacity of adult beta cells is very low. A system enabling selecting the beta cells which are proliferating has been developed, based on incorporating EdU and its later purification by means of flow cytometry (Carballar et al., Sci Rep 2017).

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

The conditional suppression of Jarid2 in pancreatic progenitors reduces the area of endocrine cells at the time of birth. This is due to a prenatal alteration, in the process of differentiation and proliferation of those cells. The role of Jarid2 occurs after endocrine differentiation. Jarid2 is necessary to complete the activation of the beta cell differentiation programme, which means that their manipulation can be used for improving protocols for obtaining beta cells from stem cells (Cervantes et al., *Sci Rep* 2017).

A platform has been created for cell culture based on self-assembling peptide nanofibres (RAD16-I), functionalised with extra-cellular matrix peptides for the redifferentiation and generation of insulin-producing cells which could be used in diabetes cell therapy (Aloy-Reverté, Tissue Engineering: Part A, 2017).

Lastly, an Investigational Medicinal Product has been developed, with the aim of using insulin-producing cells obtained from human embryonic stem cells in clinical trials.

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

Coordinator: **Antonio Zorzano Olarte**

1. Determinants of insulin resistance: molecular mechanisms involved

It has been proven that alterations in methylation and expression of genes involved in the regulation of energy homeostasis are related with foetal growth and neonatal corporal composition and could be among the first mechanisms modulating later susceptibility to diabetes (Díaz et al., *Diabetes* 2017).

Apart from this new mechanism by means of which PPARβ/δ and FGF21 regulate levels of VLDL receptors and influence the development of hepatic steatosis have been described (Zarei et al., *Mol Metab* 2017). It has also been shown that VLDL particles and apolipoprotein C-III induce reticulum stress and inflammation and attenuate insulin signalling through the TLR2–like receptor in mouse skeletal muscle cells (Botteri et al., *Diabetología* 2017).

It has also been proven that there is a need for intact MTORC1 signalling to regulate two processes required for elimination of damaged mitochondria, i.e. in what represents the start of general autophagy and targeting uncoupled mitochondria to the autophagic machinery through PINK1/Parkin proteins (Bartolomé et al., *Mol Cell Biol* 2017).

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

It has been proven that circulating concentrations of chronic low-grade inflammation markers in young healthy adults are not only influenced by obesity, but also by abdominal adiposity, fasting and glucose ingestion and in some cases by sex and sexual hormones (Escobar-Morreale et al., *Clin Nutr* 2017).

It has also been shown that lipin-2 protein controls excessive formation of IL-1β in macrophages by different mechanisms, including the activation of NLRP3 inflammasome, indicating that lipin-2 is a key matter in the negative regulation of the NLRP3 inflammasome (Lordén et al., *J Exp Med* 2017).

It has lastly been described that the stem cells derived from mesenteric adipose tissue (ASCs) of patients with Crohn's disease have a more proliferative, inflammatory, invasive and phagocytic phenotype than the equivalent cells of healthy donors, regardless of the clinical stage (Serena et al., *Stem Cell Rep* 2017).

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

It has been proven that mitochondrial dynamics mediated by Mitofusin 1 in hypothalamic POMC neurons constitute an intrinsic mechanism for detection of nutrients and reveal an unrecognised bond between this subassembly of neurons and insulin release (Ramírez et al., *Cell Metab* 2017).

It has also been proven that the effects of hepatic glycogen in the ingestion and homeostasis of glucose are mediated by the vagus nerve in mice (López-Soldado, et al., *Diabetología* 2017). The lack of glycogenin has also been shown to promote the accumulation of muscular glycogen, which impairs the muscular function (Testoni et al., *Cell Metab* 2017).

4. Identification of danger biomarkers for the progression of diabetes

A new metabolomic strategy for studies of stable isotope tracers based on RMN has been undertaken and validated (Vinaixa et al., *Angew Chem Int Ed Engl* 2017), increasing the identification of metabolites obtained from cell extracts.

Activators of protein Mitofusin 2 have also been identified by means of a strategy consisting of seeking transcriptional stimulators (Miret-Casals et al., *Cell Chem. Biol* 2017).

Training Programme

Coordinator: Ángel Nadal Navajas

As the main innovation in the Training Programme for 2017, CIBERDEM has included the call for grants for international mobility, five of these having been awarded. The national mobility programme has continued with the call for intraCIBERDEM and interCIBER aid, with two applications granted. Both programmes are to continue in 2018.

Our VIII CIBERDEM Annual Meeting was held on 17-19 May, with the participation of roughly 150 CIBERDEM researchers, and the presentation of 86 communications, counting oral papers and posters. Speakers from all the groups in the CIBERDEM and the two platforms took part in this. The meeting was also attended by the scientific directors of the CIBER-BBN and the CIBERSAM, who presented the organisation and lines of research in their areas, as well as the possibilities for cooperation and synergies between the Groups from the different centres. The NANBIOSIS (CIBER-BBN) platform was also presented.

As part of the training activities with the other thematic areas of the CIBER, we held the first joint CIBERDEM – CIBEROBN workshop on diabetes and obesity, with communications given by each CIBER thematic area and over 100 participants. We also took part, along with CIBERESP and CIBEROBN, at the Encounter for Excellence in Public Health Research held in September in Menorca.

In the setting of the training activities that CIBERDEM organises in cooperation with MSD, this year the Annual Symposium entitled "La Diabetes a Debate 2017: Diabetes in the Knowledge Frontier" was on the main theme of ageing and diabetes, focussing on the dual areas of basic research and its clinical applicability. The videoconferences were a great success, with a large number of viewings.

A postgraduate course for experts in chronic complications of diabetes was arranged with the Universidad de Barcelona.

CIBERDEM Groups have done a great deal of work arranging congresses, courses, symposia, seminars and scientific debates in Spain and abroad, contributing to the training of researchers. CIBERDEM has taken part in the organisation of the 1st FEBS3+ Joint Meeting of the *French-Portuguese-Spanish Biochemical and Molecular Biology Societies*, held in Barcelona on 23-26 October, and has arranged the satellite symposium CIBERDEM-MSD on Future Therapies in Diabetes.

Scientific Production

PUBLICATIONS

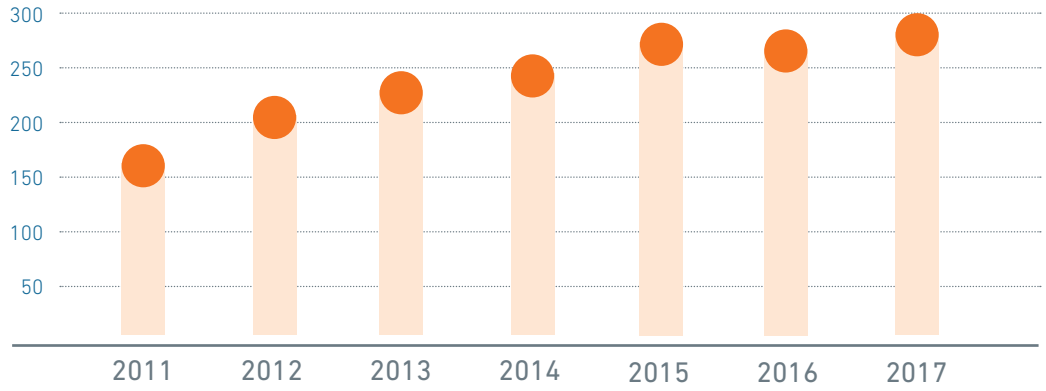
No. of publications in 2017

TOTAL	**301**
Q1	198
D1	82

Collaboration work

IntraCIBER	43
InterCIBER	110

Evolution of the publications



Most relevant publications of the CIBERDEM in 2017 by impact factor

Publication	Impact factor
GARG SK, HENRY RR, BANKS P, BUSE JB, DAVIES MJ, FULCHER GR ET AL. Effects of Sotagliflozin Added to Insulin in Patients with Type 1 Diabetes. The New England Journal of Medicine. 2017;377(24): 2337-2348.	72.41
MAILLO C, MARTÍN J, SEBASTIÁN D, HERNÁNDEZ-ÁLVAREZ M, GARCÍA-ROCHA M, REINA O ET AL. Circadian- and UPR-dependent control of CPEB4 mediates a translational response to counteract hepatic steatosis under ER stress. Nature Cell Biology. 2017 19(2): 94–105.	20.06
PADRÓ T, CUBEDO J, CAMINO S, BÉJAR MT, BEN-AICHA S, MENDIETA G ET AL. Detrimental Effect of Hypercholesterolemia on High-Density Lipoprotein Particle Remodeling in Pigs. Journal of the American College of Cardiology. 2017;70(2): 165-178.	19.90
STANDL E, SCHNELL O, MCGUIRE DK, CERIELLO A, RYDEN L. Integration of recent evidence into management of patients with atherosclerotic cardiovascular disease and type 2 diabetes. The Lancet Diabetes and Endocrinology. 2017;5(5):391-402.	19.74
TAN GS, CHEUNG N, SIMÓ R, CHEUNG GC, WONG TY. Diabetic macular oedema. The Lancet. Diabetes and Endocrinology. 2017;5(2):143-155.	19.74
VIDAL J, CORCELLES R, JIMÉNEZ A, FLORES L, LACY AM. Metabolic and Bariatric Surgery for Obesity. Gastroenterology. 2017;152(7):1780-1790.	18.39

Publication	Impact factor
NADAL A, QUESADA I, TUDURI E, NOGUEIRAS R, ALONSO-MAGDALENA P. Endocrine-disrupting chemicals and the regulation of energy balance. Nature Reviews Endocrinology. 2017;13(9):536-546.	18.32
RAMÍREZ S, GÓMEZ-VALADES AG, SCHNEEBERGER M, VARELA L, HADDAD-TOVOLLI R, ALTIRRIBA J ET AL. Mitochondrial Dynamics Mediated by Mitofusin 1 Is Required for POMC Neuron Glucose-Sensing and Insulin Release Control. Cell Metabolism. 2017;25(6):1390-1399.e6.	18.16
TESTONI G, DURAN J, GARCÍA-ROCHA M, VILAPLANA F, SERRANO AL, SEBASTIÁN D ET AL. Lack of Glycogenin Causes Glycogen Accumulation and Muscle Function Impairment. Cell Metabolism. 2017;26(1):256-266.e4.	18.16
LECUBE A, SIMÓ R, PALLAYOVA M, PUNJABI NM, LÓPEZ-CANO C, TURINO C ET AL. Pulmonary Function and Sleep Breathing: Two New Targets for Type 2 Diabetes Care. Endocrine Reviews. 2017;38(6): 550-573.	15.75

Patents held by CIBER

Spanish

- Improvement of autologous stem cell transplantation derived from adipose tissue in patients with Crohn's disease.

Clinical Guides and consensus documents

- Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology. Sanz M, Ceriello A, Buysschaert M, Chapple I et al. Diabetes Research and Clinical Practice 2017; doi:10.1016/j.diabres.2017.12.001.
- Update on Diagnosis and Treatment of Diabetic Retinopathy: A Consensus Guideline of the Working Group of Ocular Health (Spanish Society of Diabetes and Spanish Vitreous and Retina Society). Corcóstegui B, Durán S, González-Albarrán MO, Hernández C, Ruiz-Moreno JM et al. Journal of Ophthalmology 2017; doi.org/10.1155/2017/8234186.
- Evidence-based recommendations and expert consensus on enteral nutrition in the adult patient with diabetes mellitus or hyperglycemia. Sanz-Paris A, Álvarez Hernández J, Ballesteros-Pomar MD, Botella-Romero F, León-Sanz M et al. Nutrition. 2017;41:58-67.
- Guía de actualización en diabetes mellitus tipo 2. Alemán JJ, Álvarez F, Artola S, Ávila L, Barrot J et al. Fundación Red de Grupos de Estudio de Diabetes (redGDPS) 2017.
- Prevención, diagnóstico y tratamiento de la obesidad. Posicionamiento de la Sociedad Española para el Estudio de la Obesidad de 2016. Lecube A, Monereo S, Rubio MA, Martínez-de-Icaya P, Martí A et al. Endocrinología, Diabetes y Nutrición 2017;64(S1):15-22.
- Recomendaciones de vitamina D para la población general. Documento de consenso del Grupo de Trabajo de Osteoporosis y Metabolismo Mineral de la Sociedad Española de Endocrinología y Nutrición. Varsavsky M, Rozas Moreno P, Becerra Fernández A, Luque Fernández I, Quesada Gómez JM et al. Endocrinología, Diabetes y Nutrición 2017;64(S1):7-15.
- Genómica en Medicina. Una guía práctica. Pérez M, Tolosa A, Pedrola L, Calabria I, Monzo C et al. Medigene Press 2017.

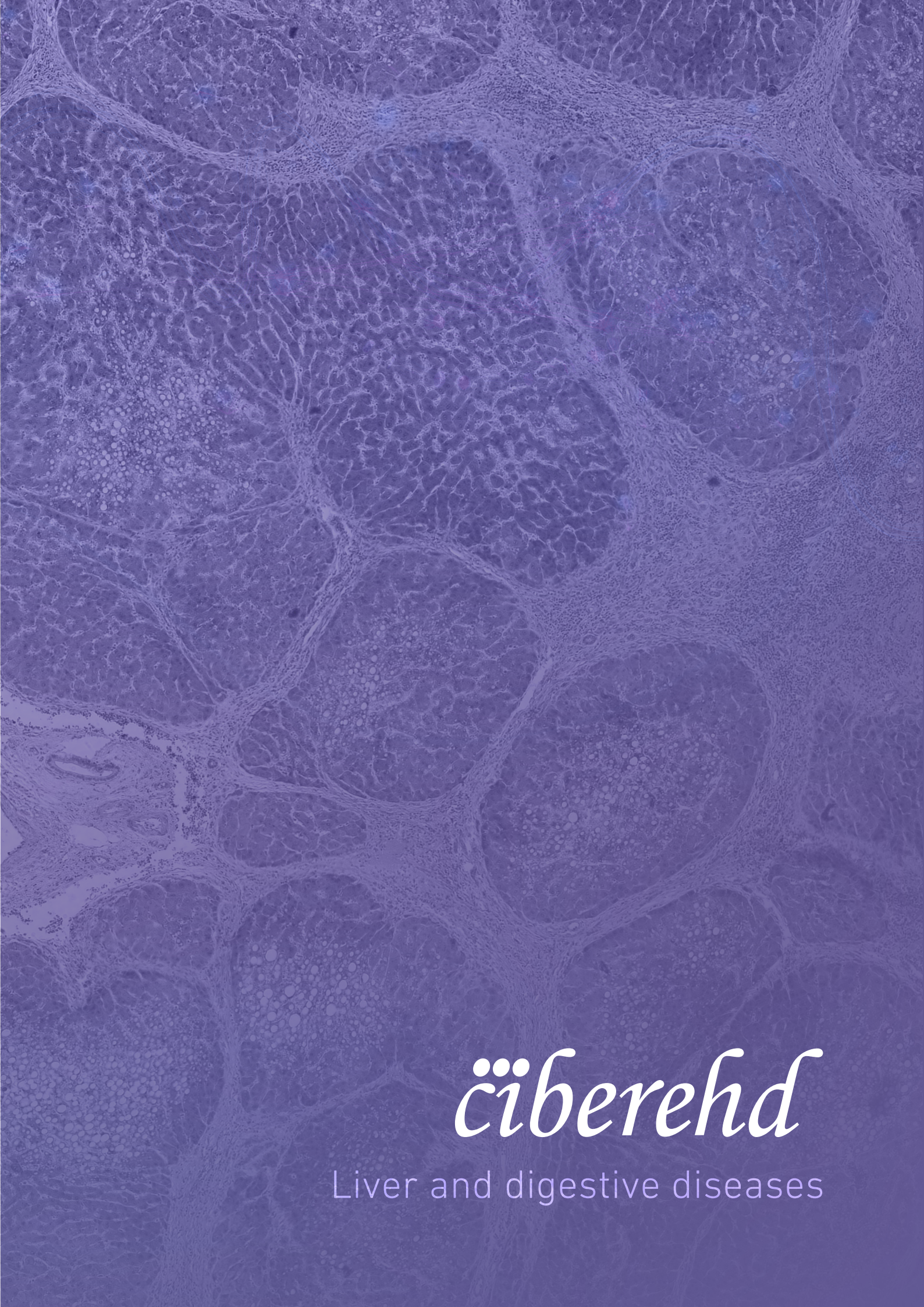
CIBERDEM Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Álvarez Escola, Carmen	5	4	3	Universidad Complutense de Madrid - Facultad de Farmacia	Madrid
Álvarez García, Elvira[1]	1	0	0	Universidad Complutense de Madrid - Facultad de Medicina	Madrid
Ascaso Gimilio, Juan Francisco	16	13	2	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA) - Instituto de Investigación Sanitaria INCLIVA	Valencia
Balsinde Rodríguez, Jesús	1	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Biología y Genética Molecular	Valladolid
Benito de las Heras, Manuel Román	2	1	0	Universidad Complutense de Madrid - Facultad de Farmacia	Madrid
Blanco Vaca, Francisco	14	10	5	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Bondía Company, Jorge[2]	-	-	-	Universidad Politécnica de Valencia - Instituto Universitario de Automática e Informática Industrial	Valencia
Bosch Tubert, Fátima	9	8	5	Universidad Autónoma de Barcelona - Centro de Biotecnología animal y Terapia Genética	Barcelona
Burks, Deborah	3	2	0	Fundación Centro de Investigación Príncipe Felipe	Valencia
Calle Pascual, Alfonso Luis	7	5	2	Servicio Madrileño de Salud - Hospital Clínico San Carlos	Madrid
Castaño González, Luis	10	7	1	Asociación Instituto de Investigación Sanitaria de Biocruces - Hospital Universitario Cruces	Vizcaya
Correig Blanchart, Francesc Xavier	14	12	6	Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili	Tarragona
Egido de los Ríos, Jesús	19	16	5	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Escobar Morreale, Héctor Francisco	8	7	5	Servicio Madrileño de Salud - Hospital Ramón y Cajal	Madrid
Ferrer Marrades, Jorge	3	2	1	Instituto de Investigaciones Biomédicas August Pi i Sunyer - Centro Esther Koplowitz	Barcelona
Guinovart Cirera, Joan Josep	2	2	1	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Ibáñez Toda, Lourdes	12	8	6	Fundación para la Investigación y Docencia Sant Joan de Deu - Hospital Sant Joan de Deu	Barcelona

Group Leader	Total Publications	Q1	D1	Institution	Province
Martín Bermudo, Francisco	7	4	3	Universidad Pablo de Olavide - Centro Andaluz de Biología del Desarrollo	Sevilla
Martínez Valverde, Ángela María	11	10	5	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Masana Marín, Luis	25	14	6	Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili	Tarragona
Mauricio Puente, Diego	30	16	6	Fundación Instituto de Investigación Germans Trias i Pujol - Hospital Germans Trias i Pujol	Barcelona
Montanya Mias, Eduard	10	6	2	Fundación IDIBELL - Hospital Universitario de Bellvitge	Barcelona
Nadal Navajas, Ángel	6	4	2	Universidad Miguel Hernández - Instituto de Bioingeniería	Alicante
Novials Sardá, Anna María	33	23	8	Instituto de Investigaciones Biomédicas August Pi i Sunyer - Centro Esther Koplowitz	Barcelona
Rojo Martínez, Gemma	15	9	2	Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Regional Universitario Carlos Haya	Málaga
Simó Canonge, Rafael	35	20	8	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR) - Hospital Vall d´Hebron	Barcelona
Vallejo Fernández de la Reguera, Mario	2	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Vázquez Carrera, Manuel	6	5	2	Universidad de Barcelona - Facultad de Farmacia	Barcelona
Vendrell Ortega, Joan Josep	15	13	4	Fundación Instituto de Investigación Sanitaria Pere Virgili - Hospital Universitario Juan XXIII	Tarragona
Vidal Cortada, Josep	14	10	5	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Zorzano Olarte, Antonio	17	15	9	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona

1 In 2017 Elvira Álvarez replaced Enrique Blázquez

2 The group joined in January 2018



ciberehd

Liver and digestive diseases

Scientific Director's Presentation

Jordi Bruix Tudó

In 2017 high-level scientific activity continued with a large number of publications in journals with great impact. In many cases the results obtained had a direct impact on patients' health care. This translation displays the consolidation of the CIBEREHD as a powerful research structure with results in the ongoing benefit of the public. All of this took place in spite of the budget difficulties and the limitations for taking on new staff.

The annual report sets forth the most relevant results in the different Programmes of the CIBEREHD and means anyone can see the gradual increase in cooperative studies with international impact in all the programmes both in Spain and abroad. One interesting factor is that international collaboration work is often led by researchers from the CIBEREHD, which results in recognition being attained.

Research has been relevant in basic aspects, but as has been stressed, this was particularly significant in translation to patients affected by liver and digestive diseases. Different clinical practice guides based on scientific evidence have been published, as well as consensus documents in which the criteria and methods to be used in both basic and clinical research are defined.

Lastly, the CIBEREHD is backed by shared platforms which have played a relevant role on both the training level and in boosting highly competitive research.

Scientific Management and the Management Committee as a whole continue to implement the four-year action plan, while a redesigning process has been started to tackle the evolutionary changes so vital in the scientific management of any area of knowledge. One relevant aspect in which work is being done is generational relief and gender balancing on all levels. The identification of young researchers with scientific career ambitions is being kept up in order to guarantee maintenance of research culture in Biomedicine. In this respect, in 2017 the call for incorporating new teams in vital complementary spheres was opened and in 2018 three groups led by researchers will be joining.

Scientific Programmes

Liver injury mechanisms / evolution into advanced cirrhosis and transplant

Coordinator: Rafael Bañares Cañizares

The work done by Programme 1 in 2017 has gone on with its development in the strategic orientation of the CIBEREHD. We should highlight the wide range of its research work covering practically all liver diseases, excluding liver cancer and viral hepatites.

As part of the priority strategic lines we should stress the fostering of international relations; as occurred in earlier years, collaboration work with groups from other countries has been encouraged in the setting of different consortiums and European projects, which displays the programme's internationalisation capacity. It is nevertheless a priority objective to increase the leadership of European projects in the coming years. In the same fund-raising line, the groups in the programme were able to maintain their own lines for project financing and for recruiting human resources in competitive calls, which enables the critical mass of the programme to be maintained.

From the standpoint of cooperation between groups in the programme we should emphasise the considerable increase in cooperative studies performed by basic scientists; in fact, this year a "map of interactions" has been drawn up for the purpose of determining possible firm alliances with a view to sustained development of network activities with great scientific value. Similarly, the common presence of collaborative studies between basic and clinical scientists has been maintained. Hence, some of the publications with greatest impact are precisely a result of these interactions. The different cooperative strategic actions financed by the CIBER itself also generated some major results in 2017 such as the development of a mouse model with humanised liver, whose application to the research lines of different groups in the programme has some great potential scope. Similarly, a network has been established for research into the role of extracellular vesicles in acute and chronic liver diseases involving the capacity to be set up as a future technological platform as well as the scientific cooperation itself.

As regards scientific results, production has been significant, with a large number of publications in the first decile in this speciality, as well as the generation of clinical practice guidelines, as a final expression of the capacity for translation of research work to the patient. The researchers from the programme have furthermore taken on a good deal of their work to the technology sector, with the development of patents, licencing of some of these and development of technology-based companies. With no detriment to the importance of all the scientific results of the programme, we should stress the large number of high-quality publications connected with the impact of treatment of hepatitis C in the natural history of cirrhosis and transplants. There has thus been a precise description of how the treatment of hepatitis C attenuates the degree of portal hypertension, reduces the need for liver transplants and limits the seriousness of reinfection in the graft. As well as their clear scientific impact, these results indicate the essential importance of cooperative research for translating the results of research work to society.

Gastrointestinal physiopathology: inflammatory bowel disease and motility disorders

Coordinador: Pere Clavé Civit

Clinical-Scientific relevance of the subjects in the programme

This programme includes digestive diseases of great prevalence and impact on the health and quality of the population's life, structured in three overall lines: a) Oesophageal–gastroduodenal pathology; b) Inflammatory bowel syndrome; and c) Neuro-gastroenterology, alterations of digestive motility and functional disorders. Knowledge of the physiopathology, diagnosis, epidemiology, prevention and treatment of these diseases is furthered by means of cooperative and multidisciplinary research among investigators with clinical, basic and epidemiological orientation. At the same time, a line of cooperation was created between basic researchers by means of a strategic IntraCIBEREHD action which involves most of the groups. During 2017 the merger of two research groups was consolidated, one group joined, and the group leaders were replaced.

a) Oesophageal-gastroduodenal pathology.
   The innovations in 2017 in this area focus on the development of new ultrafast tests of infection by *Helicobacter pylori* and on the publication of different guides and consensus on the strategies for eradicating infection and of different studies and phase IV clinical tests comparing the effectiveness and security of many different antibiotic combinations. The study of the adverse effects of non-steroidal anti-inflammatory drugs in peptic disease and its complications (mainly digestive haemorrhage) also occupies a relevant place in this line of research, as well as new studies on oesophageal-gastric cancer.

b) Inflammatory bowel disease.
   This is the most productive line in this area and the one to which most human and material resources are allocated. The research is directed at the primary causes of immune dysfunction and recognition of genetic and environmental determinants conditioning the phenotypic development of each IBD. The results for 2017 are very relevant as regards the treatment of perianal Crohn's disease with stem cells, the publication of many studies and clinical trials comparing the effectiveness and security of different immune-modulatory treatments in different phases of the disease (active/remission) and the appearance of studies which evaluate the complications of different types (nutritional, quality of life) and optimum clinical handling. This line also includes research projects connected with celiac disease, an area in which a new group is joining.

c) Neuro-gastroenterology, alterations of digestive motility and functional digestive disorders.
   2017 was a significant year for the study of disorders such as IBS, with a prevalence of 15% of the general population, or such as Oropharyngeal Dysphagia (OD), which affects 50% of the patients who have suffered from a stroke, neurodegenerative diseases and frail elderly persons. The 2017 studies focus on the mechanisms for CNS dysfunction associated with these pathologies, the role of the diet in their physiopathology and treatment, on the mechanisms for abdominal distension and handling of intestinal gas and on the role of intestinal permeability. On a training level one should stress the World Dysphagia Summit held in Barcelona with the cooperation of CIBEREHD.

Epidemiology, prevention and treatment of infection by the hepatitis virus

Coordinator: Xavier Forns Bernhardt

The evolution of the hepatitis programme is marked by the consolidation of new treatments against hepatitis C (DAA) and its boosting of cooperation between groups.

Its success in 2017 is vouched for by the number and quality of the articles resulting from multi-centre studies. Some of the ones deserving mention are: 1) Evaluation of the effectiveness and safety of antiviral treatment in 1200 patients with cirrhosis and advanced age (*Am J Gastroenterol*. 2017;112(9):1400-1409); 2) Prospective evaluation of the effectiveness and safety of sofosbuvir and simeprevir in patients infected by genotype 4 (*Aliment Pharmacol Ther.* 2017;45(3):468-475); 3) Evaluation of regimes based on sofosbuvir plus an NS5A inhibitor in patients infected with genotype 3 (*J Viral Hepat*. 2017;24(4):304-311); and 4) Analysis of the effectiveness of different therapeutic patterns in patients infected with genotype 4 (*Clin Gastroenterol Hepatol*. 2017;15(6):945-949). Different researchers from the programme have led international multi-centre tests which study new therapeutic patterns (*Lancet Gastroenterol Hepatol*. 2017;2(11):814-823).

In translational research we should stress the participation in an international consortium which has proven the relevance of the lambda-3 interferon in inflammatory processes and of hepatic fibrogenesis (Nature Genetics (*Nat Genet.* 2017;49(5):795-800) while a study of basic virology (*J Virol*. 2017;91(10) analyses the evolutionary advantage of the phenotypic diversity of HCV.

Some major contributions have also been made in hepatitis B. There was a prospective evaluation of the risk of reactivating infection in patients with past or active HBV, infection in the setting of treatment for hepatitis C (*Aliment Pharmacol Ther*. 2017;45(8):1156-1161). A second prospective international multi-centre study (*Hepatology*. 2017;66(5):1444-1453) accredits the long-term benefit of treatment with nucleotide analogues in patients with cirrhosis by HBV as regards the reduction of complications resulting from cirrhosis. In translational research work one should stress the development and characterisation of a mouse model for infection by HDV (*J Hepatol*.2017 ;67(4):669-679).

Certain studies resulting from the National Hepatitis C Plan should lastly be highlighted. Here two studies ought to be mentioned: first of all, a paper (Gastroenterology. 2017 Nov;153(5):1273-1283) analysing the impact of antiviral treatment in patients with cirrhosis by virus C and portal hypertension, and which shows a significant improvement of this in one-third of the patients treated and cured with DAA only six months after completion of the treatment. In a second study there was an evaluation of the impact of hepatitis C treatment in patients on the waiting list for a liver transplant; the work shows that in patients treated for the infection and cured there is a substantial improvement in the liver function, to such an extent that up to 25% of them manage to be taken off the waiting list (*J Hepatol*. 2017 Dec;67(6):1168-1176).

The involvement of the principal investigators from the programme in the preparation of Clinical Guides (Treatment of Hepatitis B, European Association for the Study of the Liver, *J Hepatol*. 2017;67(2):370-398; Handling Hepatitis C http://aeeh.es/wp-content/uploads/2017/06/consenso.pdf) also proves to be of great importance.

Hepatic and Digestive Oncology

Coordinator: Bruno Sangro Gómez-Acebo

Clinical-scientific relevance of the subjects in the programme

Cancer is one of the first causes of death of the general public. Both colorectal and hepatic cancer are among the three most commonly-found cancers, while gastric, oesophageal or pancreatic cancer have less prevalence, but mean a high healthcare burden.

As a whole, hepatic and gastrointestinal cancer is one of the most frequent causes of death in the adult population. It should thus be considered a health problem of the first degree, and furthering research plans connected with cancer must be seen as a priority.

Current situation of research into liver and gastrointestinal cancer

Knowledge of the reasons and mechanisms giving rise to the appearance of cancer and its progression to more aggressive forms of the disease is the basis for the reduction in mortality from cancer that we have been observing in the last five decades. This in-depth knowledge is being acquired through the co-ordinated activity of specialists focussing on partial aspects of the problem: molecular biology, genetics or immunology, epidemiology, and clinical intervention.

This last aspect proves vital for allowing biological knowledge to entail progress in healthcare and for what is known as Precision Medicine to become a reality. Over the last few years it has been detected that the failure to apply certain strategies of diagnosis, prevention or treatment of liver and digestive tract cancer may be due to the insufficient attention given to the representativeness of the human samples analysed in the preclinical studies and the limited information that can be obtained from cell or animal models.

Recent progress

Thanks to the cooperation of groups and researchers with different fields of knowledge there have been some interesting steps forward in this field. The stages defining the transition of preneoplastic lesions to cancer in situ and finally established cancer in oesophageal, colorectal and hepatic cancer have been characterised. The demarcation of the correlation between phenotypic pattern and molecular anomalies has been started.

Progress has been made in obtaining markers which enable perfecting the diagnosis of the two main varieties of liver cancer by non-invasive methods. Advances have also been made in learning the performance of markers of hereditary risk to develop digestive cancer enabling identifying individuals at risk for them to take part in follow-up plans enabling detecting the disease in earlier stages in which potentially curative treatment can be applied.

From the therapeutic standpoint, there has also been progress in the improvement of certain advanced endoscopic procedures for treatment of pancreatic and digestive tract cancer, as well as intra-arterial procedures for treatment of hepatic cancer. The groups in this programme have furthermore helped to define the therapeutic utility of new drugs in hepatic cancer and to generate hypotheses on new molecular targets for identification of drugs whose development is to be completed in the coming years.

Training Programme

Coordinator: Joan Caballería Rovira

The CIBEREHD promotes training of researchers (attached and contracted staff: postdoctoral, predoctoral, nurses and technical staff) for increasing the level of research and facilitating the interaction between groups. These tasks are coordinated through the Training Plan.

The CIBEREHD Training Plan is implemented in the following measures:

a) training stays at CIBEREHD centres.

b) short training stays in Spain or abroad (maximum 8 weeks and exceptionally up to 3 months).

c) intramural visiting teacher programmes.

d) holding training courses or activities considered to be of interest for the CIBEREHD.

e) promoting scientific activities arranged by members of the CIBEREHD (sponsoring and financing seminars, symposia, courses for postgraduates), cooperating with activities for training scientific associations and virtual training activities given on the web page.

In 2017, a total number of 33 grants were awarded. The beneficiaries of the aid were 12 attached and 21 contracted members. The activities financed were 3 short stays abroad (Canada, England and France), 1 national (Universidad de Valladolid), 3 stays at CIBEREHD Groups, 15 training courses and activities in Spain and 8 courses abroad.

Some of these activities that could be highlighted are training stays at CIBEREHD Centres: Isabel Gallego (Dr J. Gómez's group). at Dr J. I. Esteban's group (Barcelona), Isabel Nerea (group of Dr. R. Francés) at J.C. García Pagan's group (Barcelona) and Dr Quian Chen (Dr J. I. Esteban's group) in the group of Dr J. Gómez/E. Domingo (Madrid).

10 Courses directed by CIBEREHD researchers have been co-financed and/or endorsed. The Postgraduate Course of the Asociación Española para el Estudio del Hígado (AEEH) and of the Asociación Española de Gastroenterología (AEG) have also been sponsored, to be held at the same time as the annual congress of both associations.

In 2017 the "Liver Seminars" were launched, as an activity under the auspices of, and co-financed by, the CIBEREHD, coordinated by Dr R. Bañares and Dr J. Gracia. This involves a monthly lecture by a speaker of known repute which is given alternately at IDIBAPS (Barcelona) or the Hospital Gregorio Marañón (Madrid) and simultaneous broadcast to the other centre and open to researchers. On the same day meetings between the expert and interested researchers are scheduled.

Strategic Actions

In 2016 three Strategic Actions were granted:

1). FRG mice with humanized liver to study human liver diseases and drug-induced liver injury.
Principal Investigator: J.C. Fernández-Checa.

2). Use of human tissue in translational gastroenterology research.
Principal Investigator: P. Clavé.

3). *Estudio de la comunicación celular por exosomas en la enfermedad hepática.*
Groups participating: Juan Manuel Falcón-Pérez (Group J.M. Mato).

In 2017 there was a call for new investigators with the aim of facilitating starting an independent research career with application to competitive projects as P.I. The two grants provided in 2017 were for M.C. Londoño (X. Forns Group) and for Isabel Nerea Gómez-Hurtado (R. Francés Group).

Platforms

Bioinformatics. Liver Diseases

Coordinator: Juanjo Lozano Salvatella

The Bioinformatics platform is taking an active part in the operation of this CIBER, as is shown by the 11 publications issued as a result of its support during 2017. The most relevant publication is connected with the mechanism for action of immunosuppressants in the field of liver transplants, in which a project from the "Marató", led by our group, in the framework of an international collaboration scheme, was published:

- Whitehouse G, Gray E, Mastoridis S, Merritt E, Kodela E, Yang JHM, Danger R, Mairal M, Christakoudi S, Lozano JJ, Macdougall IC, Tree TIM, Sanchez-Fueyo A, Martinez-Llordella M. IL-2 therapy restores regulatory T-cell dysfunction induced by calcineurin inhibitors. Proc Natl Acad Sci U S A. 2017 Jul 3;114(27):7083-7088 2017.

Cooperation with CIBEREHD Groups continues to generate relevant publications.

Inflammation in the Liver Disease Area:

- Rius B, Duran-Güell M, Flores-Costa R, López-Vicario C, Lopategi A, Alcaraz-Quiles J, Casulleras M, Lozano JJ, Titos E, Clària J. *The specialized proresolving lipid mediator maresin 1 protects hepatocytes from lipotoxic and hypoxia-induced endoplasmic reticulum stress*. FASEB J. 2017 Dec;31(12):5384-5398.

Inflammatory Bowel Disease Area:

- Planell N, Masamunt MC, Leal RF, Rodríguez L, Esteller M, Lozano JJ, Ramírez A, Ayrizono MLS, Coy CSR, Alfaro I, Ordás I, Visvanathan S, Ricart E, Guardiola J, Panés J, Salas A. *J Crohns Colitis*. 2017 Oct 27;11(11):1335-1346.

It should be stressed that a project financing Meritxell Gironella from the Gastrointestinal and Pancreatic Oncology Group as Principal Investigator, forming the platform as investigating team, whose title is PI17/01003 "Evaluation of the prognostic capacity and of the functional role of microRNA candidates in pancreatic ductal adenocarcinoma" will be financed by the Instituto de Salud Carlos III in the next three years.

Finally, in respect of the bioinformatic tool (MIRComb), which has been developed in our group to study interactions between microRNA and their target genes, the investigator in charge Maria Vila Casadesús got the highest mark in her doctoral thesis: *Design of bioinformatic tools for integrative analysis of miRNA-mRNA interactome applied to digestive cancers*.

CIBERHEP. Chronic Hepatitis B

Coordinator: David Tabernero Caellas

The chronic hepatitis B platform CIBERHEP is a cooperation scheme between the CIBER and the Asociación Española para el Estudio del Higado (AEEH). At the present time this is the main database for patients being treated for chronic hepatitis B in Spain. In 2016 the database and its associated web page were updated, thus extending the data collected to carry out more exhaustive studies on the follow-up of patients in antiviral treatment with entecavir (ETV) and tenofovir (TDF), especially focussing on safety and side-effects of these, at the same time as simplifying the recording of this data.

In 2017, they proceeded to check patients already registered in the databases for updating this new data collected. Hence, up to now 1464 patients treated with analysable data have been entered in the database, monitored at 27 centres in 9 different regional administrative areas. 388 of these are being treated with ETV, 897 with TDF and 23 with both. The review and updating of this data has enabled us to carry out studies whose main conclusions were: 1) A high percentage of subjects with chronic hepatitis B would benefit from treatment with TAF in renal clinical practice; 2) Low rate of clinical and adverse renal events in subjects with chronic hepatitis B in treatment with TDF or ETV in clinical practice. These studies were recently sent as summaries to the national congress of the Sociedad Española de Patología Digestiva.

Furthermore, in 2017 the results of the validation of the PA- GE-B marking system in the Spanish population of patients with chronic hepatitis B in antiviral treatment and analysis of the effectiveness and renal safety of ETV and TDF in this cohort of patients were published in journal Digestive Diseases and Sciences [Riveiro-Barciela, M., Tabernero, D., Calleja, J. L. et al. Dig Dis Sci (2017). doi:10.1007/ s10620-017-4448-7].

e-CATCH. Diagnosis and advice for treatment of liver cancer

Coordinator: Jordi Bruix Tudó

The e-Catch platform aims to offer diagnostic and therapeutic orientation services in patients with liver cancer by means of electronic enquiries. The possibility of evaluating both reports and imaging techniques enables reviewing the information available by the doctors that they consult on a reliable basis and giving guidance based on scientific evidence. In 2016 a contract was established with the pharmaceutical company Bayer, which financed the telemedicine activity.

In 2017 over 50 consultations were made over the platform. Apart from the consultancy services, the platform has enabled transporting tomography or resonance images in order to validate the results of multi-centre studies and thus to guarantee the validity of the image readings by independent radiologists.

Hepa-C. Database of patients with Chronic Hepatitis C

Coordinador: Xavier Forns Bernhardt

During the year 2017 the Hepa-C multi-center registry of patients with hepatitis C treated in Spain has presented as a major milestone the publication of 9 original papers with an accumulated impact factor of 66,309, which are listed below:

1. Alonso S, Riveiro-Barciela M, Fernández I, Rincón D, Real Y, Llerena S, Gea F et al. "Effectiveness and safety of sofosbuvir-based regimens plus an NS5A inhibitor for patients with HCV genotype 3 infection and cirrhosis. Results of a multicenter real-life cohort." Journal of Viral Hepatitis 2017;24(4):304-311.
   Impact factor: 4,179.
2. Fernández-Carrillo J, Crespo G, De la Revilla J, Castells L, Buti M, Montero JL, Fábrega E et al. "Successful Continuation of HCV Treatment Following Liver Transplantation." Transplantation 2017;101(5):1009-1012.
   Impact factor: 3,69.
3. Perelló C, Carrión JA, Ruiz-Antorán B, Crespo J, Turnes J, Llaneras J, Lens S et al. Effectiveness and safety of ombitasvir, paritaprevir, ritonavir ± dasabuvir ±ribavirin: an early Access programme for Spanish patients with genotype 1/4 Chronic hepatitis C virus infection. J Viral Hepat. 2017 Mar;24(3):226-237.
   Impact factor: 4,179.
4. Fernández Carrillo C, Lens S, Llop E, Pascasio JM, Crespo J, Arenas J, Fernández I et al. "Treatment of Hepatitis C Virus Infection in Patients With Cirrhosis and Predictive Value of Model for End-Stage Liver Disease: Analysis of Data From the Hepa-C Registry." Hepatology 2017;65(6):1810-1822.
   Impact factor: 11,711.
5. Calleja JL, Crespo J, Rincón D, Ruiz-Antorán B, Fernandez I, Perelló C, Gea F et al. "Effectiveness, safety and clinical outcomes of direct-acting antiviral therapy in HCV genotype 1 infection: results from a Spanish real-world cohort." Journal of Hepatology 2017;66(6):1138-1148.
   Impact factor: 10,59.
6. Crespo J, Calleja JL, Fernández I, Sacristrán B, Ruiz-Antorán B, Ampuero J, Hernández-Conde M et al. "Real-World effectiveness and safety of oral combination antiviral therapy for hepatitis C virus genotype 4 infection." Clinical Gastroenterology and Hepatology 2017;15(6):945-949.
   Impact factor: 7,68.
7. Fernández I, Muñoz-Gómez R, Pascasio JM, Baliellas C, Polanco N, Esforzado N, Arias A et al. "Efficacy and tolerability of interferon-free antiviral therapy in kidney transplant recipients with chronic hepatitis C." Journal of Hepatology 2017;66(4):718-723.
   Impact factor: 10,59.
8. Mariño Z, Pascasio-Acevedo JM, Gallego A, Diago M, Baliellas C, Morillas R, Prieto M et al. "High efficacy of Sofosbuvir plus Simeprevir in a large cohort of Spanish cirrhotic patients infected with genotypes 1 and 4". Liver Int 2017;37(12):1823-1832.
   Impact factor: 4,12.

9. Lens S, Fernández I, Rodríguez-Tajes S, Hontangas V, Vergara M, Forné M, Calleja JL et al. "Interferon-free Therapy in elderly patients with advanced liver disease". Am J Gastroenterol 2017;112(9):1400-1409.
   Impact factor: 9,57.

Four new studies have also been got under way, two of which were presented during the congress of the American Association for the Study of Liver Diseases (AASLD) celebrated in October in Washington D.C.:

1. *Effectiveness, safety and clinical outcomes of paritaprevir/ombitasvir/r + dasabuvir 8 weeks: results from a Spanish real world cohort (Hepa-C), Hepatology 2017*;66 Sppl 1: A1555. By principal investigator José Antonio Carrión (Hospital. del Mar in Barcelona)
2. *Efectiveness and safety of elbasvir/grazoprevir treatment for HCV patients in real-life clinical practice: results from Spanish Hepa-C cohort. Hepatology 2017*;66 Sppl 1: A1105. By principal investigator José Luís Calleja (Hospital Puerta de Hierro in Majadahonda).

REHEVASC. Register of Vascular Diseases of the Liver.

Coordinator: Juan Carlos García –Pagán

The REHEVASC platform has been running since 20 September 2011. This is a Register of patients diagnosed with 4 vascular diseases of the liver in Spain of the type considered to be "Rare Diseases" with a prevalence under 5/10,000 inhabitants. It covers diseases with non-cirrhotic portal hypertension (NCPH):

- Non-cirrhotic non-tumoural portal thrombosis (PVT).
- Idiopathic portal hypertension (IPH).
- Budd-Chiari syndrome (BCS).
- Congenital hepatic fibrosis (CHF).

Its main aim is to provide a "uniform" diagnosis and treatment for these diseases as well as to improve this diagnosis and treatment of these diseases and be able to perform collaborative studies enabling furthering knowledge of them.

In 2017, the following proportions of new patients were diagnosed and registered:

PVT: 35 patients, obtaining a final register of 262 patients in 2017.

IPH: 15 patients, obtaining a final register of 106 patients in 2017.

BCS: 7 patients, obtaining a final register of 73 patients in 2017.

CHF: 1 patient, obtaining a final register of 10 patients in 2017.

Scientific Production

PUBLICATIONS

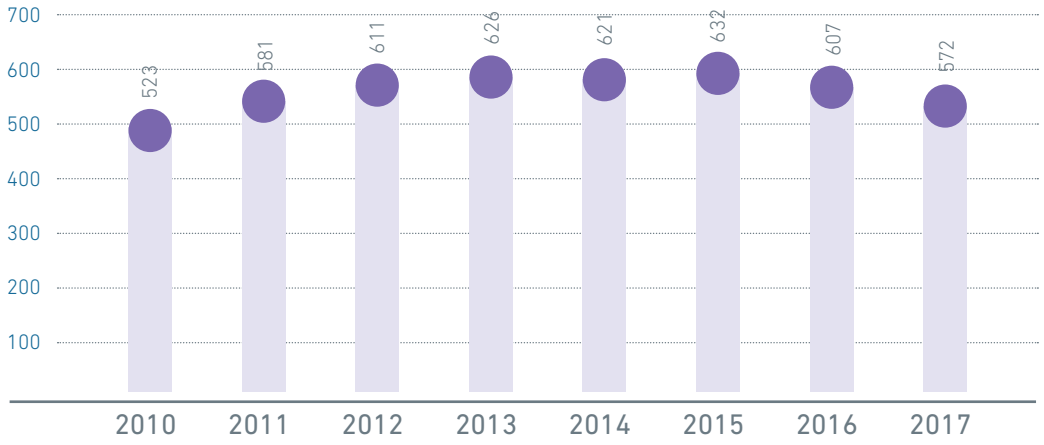
No. of publications in 2017

TOTAL	**611**
Q1	160
D1	325

Collaboration work

IntraCIBER	165
InterCIBER	97

Evolution of the publications



Most relevant publications of the CIBEREHD in 2017 by impact factor

Publication	Impact Factor
Sandborn W.J., Su C., Sands B.E., D'Haens G.R., Vermeire S., Schreiber S. et al. Tofacitinib as induction and maintenance therapy for ulcerative colitis. New England Journal of Medicine. 2017;376(18):1723-1736.	72,4060
Lanas A., Chan F.K.L. Peptic ulcer disease. The Lancet. 2017.	47,8310
El-Khoueiry A.B., Sangro B., Yau T., Crocenzi T.S., Kudo M., Hsu C. et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): An open-label, non-comparative, phase 1/2 dose escalation and expansion trial. The Lancet. 2017.	47,8310
Bruix J., Qin S., Merle P., Granito A., Huang Y.-H., Bodoky G. et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): A randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet. 2017.	47,8310

Feagan B.G., Sandborn W.J., D'Haens G., Panes J., Kaser A., Ferrante M. et al. Induction therapy with the selective interleukin-23 inhibitor risankizumab in patients with moderate-to-severe Crohn's disease: a randomised, double-blind, placebo-controlled phase 2 study. The Lancet. 2017;389(10080):1699-1709.	47,8310
Zabala-Letona A., Arruabarrena-Aristorena A., Martin-Martin N., Fernandez-Ruiz S., Sutherland J.D., Clasquin M. et al. MTORC1-dependent AMD1 regulation sustains polyamine metabolism in prostate cancer. Nature. 2017;547(7661):109-113.	40,1370
Forns X., Lee S.S., Valdes J., Lens S., Ghalib R., Aguilar H. et al. Glecaprevir plus pibrentasvir for chronic hepatitis C virus genotype 1, 2, 4, 5, or 6 infection in adults with compensated cirrhosis (EXPEDITION-1): A single-arm, open-label, multicentre phase 3 trial. The Lancet Infectious Diseases. 2017.	19,8640
Nicoletti P, Aithal GP, Bjornsson ES, Andrade RJ, Sawle A, Arrese M et al. Association of Liver Injury From Specific Drugs, or Groups of Drugs, With Polymorphisms in HLA and Other Genes in a Genome-Wide Association Study.Gastroenterology. 2017;152(5).	18,3920
Egoavil C, Juárez M, Guarinos C, Rodríguez-Soler M, Hernández-Illán E, Alenda C et al. Increased Risk of Colorectal Cancer in Patients With Multiple Serrated Polyps and Their First-Degree Relatives.Gastroenterology. 2017.	18,3920
Garcia-Pras E., Gallego J., Coch L., Mejias M., Fernandez-Miranda G., Pardal R. et al. Role and therapeutic potential of vascular stem/ progenitor cells in pathological neovascularisation during chronic portal hypertension. Gut. 2017.	16,6580

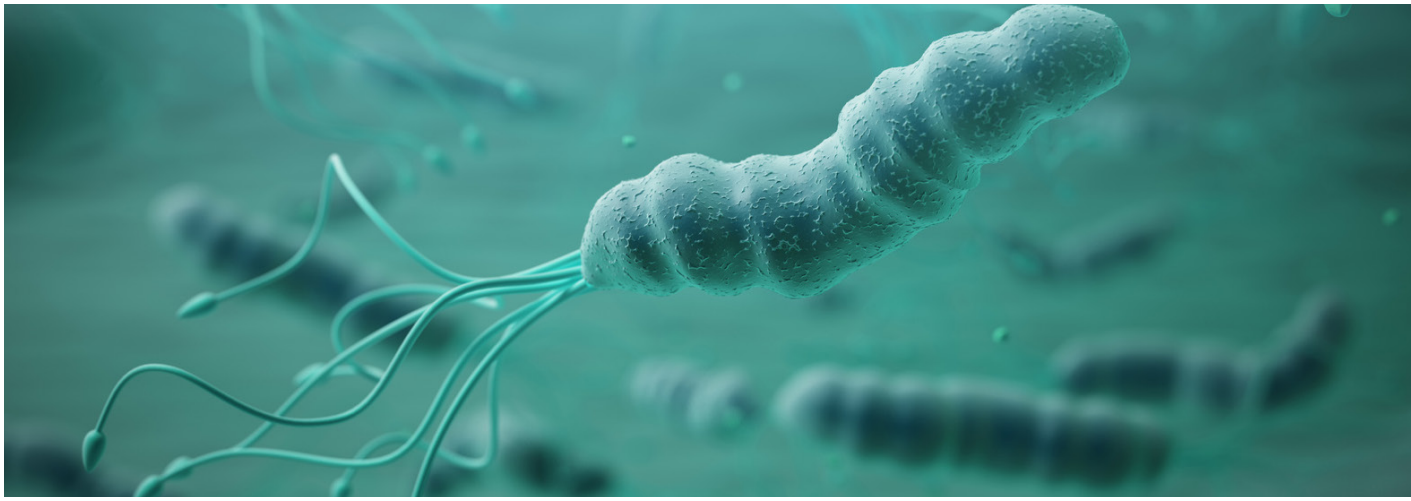
CIBEREHD PATENTS 2017

Applied for

- *Biomarkers for colorectal cancer* (EP 17382267.7).
- *Use of ciclopirox as a modulator of the heme group biosynthesis and in the treatment of porphyrias and other diseases* (EP17382371.7).
- *Computerized optical analysis methods of MR (magnetic resonance) images for quantifying or determining liver lesions* (JP2017-549070).
- *A 3-protein signature to assess prognosis and therapeutic regimen in liver cancer* (300257875).

Granted

- *Ceria nanoparticles for use in the treatment of hepatocellular carcinoma* (EP16163838.2).
- *In vitro method for identifying pancreatic cancer or intraductal papillary mucinous neoplasm of the pancreas*. (EP16382182.0).
- Plasma microRNAs for the detection of early colorectal cancer (US 15/181,578).
- *Bioadhesive platform to perform bioactive treatment* (16382365.1 1455).
- Método de obtención de datos útiles para predecir o pronosticar la transmisión vertical, la cronificación y/o el aclaramiento del virus de la hepatitis c (PCT/ES2016/070115).



Clinical Guides

- *Actualització en el Tractament de la Infecció per Helicobacter pylori.*
- *PRODiGGEST (Protocolos asistenciales para mejorar la gestión interdisciplinar de las enfermedades digestivas en el ámbito hospitalario): Manejo de la anemia y de la ferropenia en la hemorragia digestiva Avalado por la Asociación Española de Gastroenterología.*
- *Recommendations of the Spanish Working Group on Crohn's Disease and Ulcerative Colitis (GETECCU) on the monitoring, prevention and treatment of post-operative recurrence in Crohn's disease.*
- *Vascular diseases of the liver. Clinical Guidelines from the Catalan Society of Digestology and the Spanish Association for the Study of the Liver.*
- *European Society for Swallowing Disorders FEES Accreditation Program for Neurogenic and Geriatric Oropharyngeal Dysphagia.*
- *ELITA consensus statements on the use of DAAs in liver transplant candidates and recipients.*
- *International Liver Transplantation Society Consensus Statement on Hepatitis C Management in Liver Transplant Candidates.*
- *International Liver Transplantation Society Consensus Statement on Hepatitis C Management in Liver Transplant Recipients.*
- *Management of antithrombotic therapy after bleeding in patients with coronary artery disease and/or atrial fibrillation: expert consensus paper of the European Society of Cardiology Working Group on Thrombosis.*
- *3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management.*

CIBEREHD Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Martínez Albillos, Agustín	8	6	5	Universidad de Alcalá. Facultad de Medicina	Madrid
Andrade, Raúl	9	9	5	Fund. Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS). Hptal. Univ. Virgen de la Victoria	Málaga
Armengol Niell, Carolina	19	13	7	Fund. Instituto de Investigación Germans Trias i Pujol.	Barcelona
Azpiroz Vidaur, Fernando	25	17	6	Fund. Hptal. Univ. Vall d'Hebrón - Institut de Recerca (VHIR)	Barcelona
Bañares Cañizares, Rafael	22	15	5	Servicio Madrileño de Salud. Hospital Gregorio Marañón	Madrid
Berenguer Haym, Marina	24	16	4	Fund. para la Investigación del Hospital Universitario de La Fe	Valencia
Bruix Tudó, Jordi	22	13	7	Hospital Clínico y Provincial de Barcelona	Barcelona
Bujanda Fernández de Pierola, Luis	26	17	10	Asociación Instituto Biodonostia. Hospital Donostia	Guipúzcoa
Calvet Calvo, Xavier	22	14	4	Corporación Sanitaria Parc Taulí	Barcelona
Castell Ripoll, Vicente	6	3	1	Fundación para la Investigación del Hospital la Fe	Valencia
Castells Garangou, Antoni	37	21	9	Hospital Clínico y Provincial de Barcelona	Barcelona
Clave Civit, Pere	23	10	3	Fundación Privada Salud del Consorcio Sanitario del Maresme	Barcelona
Domenech Morral, Eugeni (1)	23	13	5	Fundación Instituto de Invest. Germans Trias i Pujol	Barcelona
Esplugues Mota, Juan Vicente	13	11	4	Universidad de Valencia. Facultad de Medicina de Valencia	Valencia
Esteban Mur, Juan Ignacio	25	13	6	Fund. Hptal. Univ. Vall d'Hebrón - Institut de Recerca (VHIR)	Barcelona
Esteban Mur, Rafael	36	26	13	Fundación Hospital Universitario Vall d'Hebrón - Institut de Recerca (VHIR)	Barcelona
Fernández-Checa, José Carlos	12	10	4	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instit. de Invest. Biomédicas de Barcelona	Barcelona
Forns Bernhardt, Xavier	35	24	10	Hospital Clínico y Provincial de Barcelona	Barcelona
Francés Guarinos, Rubén	12	9	3	Fund. para la Invest. Sanitaria y Biomédica de la Com. Valenciana (FISABIO). Hptal. Gen. Univ. de Alicante	Alicante
García-Buey, Luisa (2)	3	2	0	Servicio Madrileño de Salud. Hospital Universitario La Princesa	Madrid

Group Leader	Total Publications	Q1	D1	Institution	Province
García-Marín, José Juan	13	10	3	Universidad de Salamanca	Salamanca
García Pagán, Juan Carlos	24	19	9	Hospital Clínico y Provincial de Barcelona	Barcelona
García-Samaniego Rey, Javier	13	7	2	Servicio Madrileño de Salud. Hospital La Paz	Madrid
Genesca Ferrer, Joan	21	14	11	Fund. Hptal. Universitario Vall d'Hebrón - Institut de Recerca (VHIR)	Barcelona
Gines Gibert,Pere	29	23	9	Hospital Clínico y Provincial de Barcelona	Barcelona
Gómez Castilla, Jordi	5	3	0	Ag. Estatal Consejo Sup. de Invest. Científicas. Instituto de Parasitología Y Biomedicina López Neyra	Granada
González-Gallego, Javier	15	9	2	Universidad de León. Instituto Biomedicina de León	León
Guarner Aguilar, Carlos	13	9	4	Instituto de Invest. del Hospital de la Santa Cruz y San Pablo	Barcelona
Lanas Arbeola, Ángel	37	22	9	Instituto Aragonés de Ciencias de la Salud. Hospital Clínico Universitario Lozano Blesa	Zaragoza
Martín Sanz, Paloma	1	0	0	Ag. Estatal Consejo Sup. de Invest. Científicas. Inst. de Investigaciones Biomédicas Alberto Sols	Madrid
Mata García, Manuel de la	20	14	5	Fundación para la Investigación Biomédica de Córdoba (FIBICO). Hospital Universitario Reina Sofia	Córdoba
Mato de la Paz, José María	32	27	10	CIC BIOGUNE	Vizcaya
Navasa Anadón, Miguel	14	10	4	Hptal. Clínico y Provincial de Barcelona	Barcelona
Panés Díaz, Julián	33	17	10	Hospital Clínico y Provincial de Barcelona	Barcelona
Pares Darnaculleta, Albert	15	8	5	Hospital Clínico y Provincial de Barcelona	Barcelona
Parrilla Paricio, Pascual (3)	10	5	0	Fundación para la Formación e Investigación Sanitaria de la Región de Murcia (FFIS). Hospital Universitario Virgen de la Arrixaca	Murcia
Pastor Anglada, Marçal	3	3	0	Univ. de Barcelona Facultad de Biología. Universidad de Barcelona	Barcelona
Pérez-Gisbert, Javier	35	18	11	Servicio Madrileño de Salud. Hospital Universitario La Princesa	Madrid
Romero Gómez, Manuel	22	14	8	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío	Sevilla

Group Leader	Total Publications	Q1	D1	Institution	Province
Salmerón, Francisco Javier	8	5	1	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO. Hospital Clínico San Cecilio	Granada
Sánchez de Medina López Huertas, Fermín	14	11	5	Universidad de Granada. Facultad de Farmacia	Granada
Sangro Gómez-Acebo, Bruno	30	24	13	Clínica Universidad de Navarra	Navarra

(1) The P.I. replaces Cabré Gelada, Eduard
(2) Group deregistered in 2018
(3) Group deregistered in 2018

Linked Groups

Group Leader	Institution	Province
Beltrán Niclós, Ana Belén	Fund. para la Investigación del Hospital la Fe	Valencia
Caballería Rovira, Llorenç	Universidad Autónoma de Barcelona	Barcelona
Calleja Panero, José Luis	Universidad de Alcalá	Madrid
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
Padillo Ruiz, Francisco Javier	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	Sevilla


ciberer
Rare Diseases

Scientific Director's Presentation

Pablo Lapunzina Badia

Dear colleagues,

Our research has a clearly translational approach, in order to seek diagnoses and therapies for the greatest possible number of Rare Diseases (RD). By incorporating mass sequencing technologies in genetic analysis, we have identified the genes responsible for a large number of RD. This has meant that it has been possible to develop new applications and biological tests, that are being implemented on a large scale in prenatal and postnatal diagnosis of genetic diseases. To speed up this progress in genetic research it is vital to get under way the National Genomic Medicine Plan, which is currently being debated at the Senate, so as to be able to provide a transversal response to the diagnosis needs arising through RD.

In the therapeutic field, we are promoting six orphan drugs in Europe, four of which have also been designated as such in the United States. We are also already working on clinical trials in advanced stages to obtain treatments with avant-garde techniques with gene therapy.

I would lastly like to take this opportunity to stress the work done side by side with those affected. Our commitment to the FEDER (Federación Española de Enfermedades Raras) and to the other organisations of those affected is not only simply continuing, but something we are working on day by day to shore this up and increase it in the coming years.

In this respect we have included patients' associations in different bodies of the CIBERER, such as the External Advisory Scientific Committee and the Patients' Advisory Board. Together we are making progress and will continue to do so in order to accomplish these goals.

I would like to thank all the members of the CIBERER for the work done every day in the benefit of the persons affected by RD, as reflected below in this new edition of the CIBERER scientific report.

Scientific Programmes

Genetic Medicine

Coordinator: Ángel Carracedo Álvarez

In 2017, the Genetic Medicine Programme has continued to lead the implementation of new genomic medicine and other omic applications in diagnostic practice in hospitals. This same year there has been cooperation in such relevant studies as the ones performed by Ángel Carracedo's group, which has identified 65 new loci of risks in breast cancer and was published in the journal *Nature*, or the work published in *Genome Biol* in which Guillermo Antiñolo and Joaquín Dopazo's Groups are cooperating, on studies of the whole exome for identification of new genes involved in Hirschsprung's disease.

Three pieces of research of the CIBERER unit led by Santiago Rodríguez de Córdoba's group have identified new factors for genetic predisposition for the atypical haemolytic uremic syndrome (aHUS) and possible environmental factors unleashing this. All three articles have been published at almost the same time, two of these in Kidney International and the other in *Journal of the American Society of Nephrology*.

2017 stood out for being a highly prolific year in therapeutic research in this research programme. Some of the milestones attained, such as the designation of metformin as an orphan drug for treatment of Lafora disease vouch for this. The studies have been made by Pascual Sanz and José Serratosa's group. The designation of propranolol has also been attained as new orphan drug for treatment of Von Hippel-Lindau's disease. This designation has been achieved thanks to the preclinical research done by Luisa Botella's group with the cooperation of the Alianza Española de Familias de Von Hippel-Lindau.

Relevant articles for treatment of rare diseases have also been published, such as the work done by Erwin Knetch in cooperation with Aurora Pujol on the effect of tauroursodeoxycholic acid (TUDCA) in X-linked adrenoleukodystrophy published in *Acta Neuropathol* and the collaborative work done on the prevention of hereditary angioedema with the C1 inhibitor of Maite Caballero, which has been published in the *New England Journal of Medicine*.

We should lastly stress that two new group leaders have been appointed over the year: Luisa María Botella has been appointed CIBERER Group leader at the Centro de Investigaciones Biológicas (CSIC) replacing Carmelo Bernabéu, and Maite Caballero at the Hospital La Paz to replace Margarita López Trascasa.

Inherited Metabolic Medicine

Coordinator: Rafael Artuch Iriberri

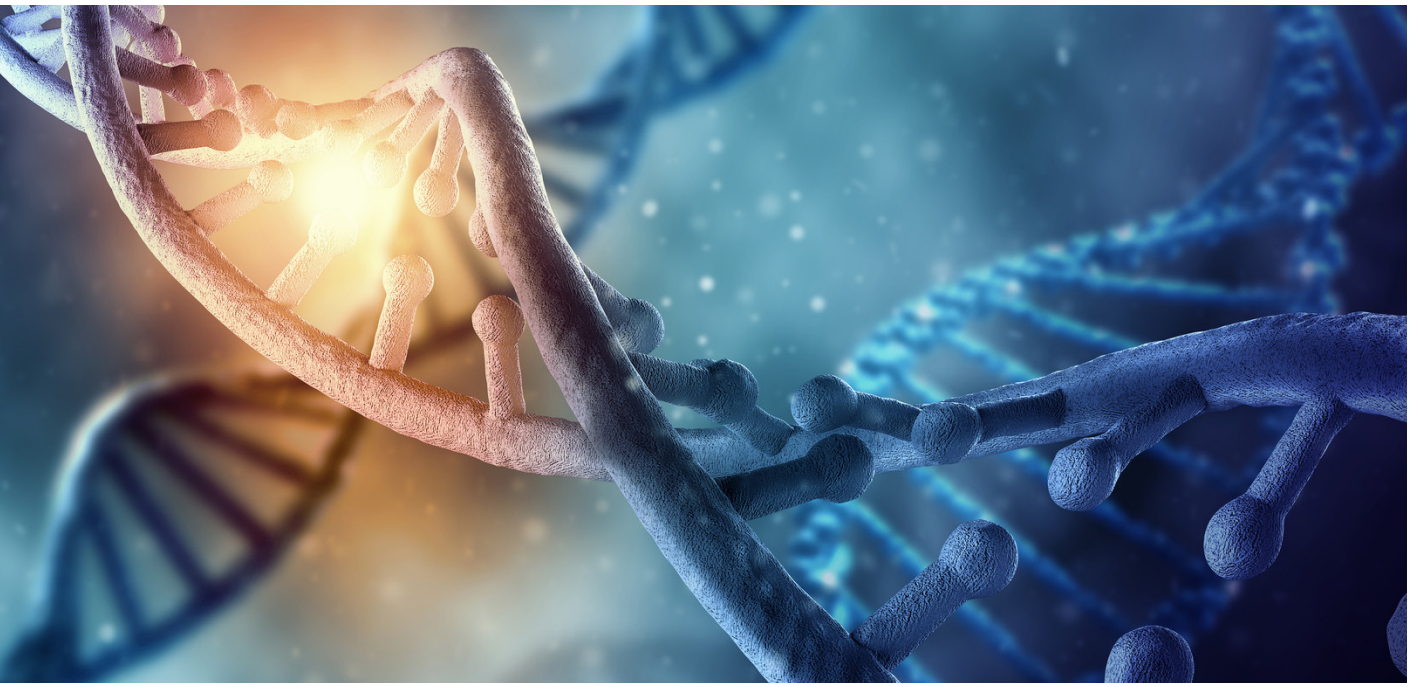
We should stress the organisation of internationally relevant symposia and congresses by the Inherited Metabolic Medicine area. For example, in 2017 a CIBERER-Fundación Ramón Areces symposium was held at which the main international specialists in amino acid transport defects covered aspects concerning the mechanisms of pathologies associated with these defects and the therapies developed. This was coordinated amongst others by the groups led by Virginia Nunes and Manuel Palacín. Another important international encounter was on primary hyperoxaluria, at which the progress made in translational research was presented. This was coordinated by the CIBERER group led by Eduardo Salido. Lastly, the Group for Minority Adult Diseases held a session at which it dealt with such matters as associations of patients with low prevalent diseases, the genetics of mitochondrial diseases (from childhood to adulthood), etc.

We should also give some examples of several findings made by this programme:

- Better understanding of the molecular mechanisms of rare diseases thanks to the identification of several microRNAs as minimally invasive biomarkers of propionic acidemia (groups coordinated by A. Ribes and M.B. Pérez González), or the research done by the groups coordinated by R. Estévez and V. Nunes helping to gain a better understanding of a physiopathological process in astrocytes involved in megalencephalic leukoencephalopathy (MLC), a rare type of leukodystrophy.
- Discovery of possible channels for treatment of rare diseases thanks to D-serin –a diet supplement – which improves the neuronal function of a patient with a mutation of the glutamate receptors associated with atypical Rett syndrome with severe encephalopathy (P.I. of the Group: R. Artuch).
- Discovery of a mutation predisposing to rare fracture of the femur in patients taking drugs for osteoporosis. This finding, of great clinical significance, has been published in the prestigious journal New *England Journal of Medicine* (P.I. of the Group: D. Grinberg).
- Identification of the gene causing Opitz C syndrome in the only person diagnosed in Catalonia with this ultra-rare disease (P.I. of the Group: D. Grinberg).
- Generation of murine models with the main characteristics of Niemann-Pick disease type C (P.I. of the Group: D. Grinberg).

Lastly, thanks to the donations of patient's associations, the Groups have got projects such as the following under way:

- Development of new treatments in CDG (P.I.: M. B. Pérez González – donation from the Asociación Española del Síndrome de CDG).
- Test on compassionate use for treatment of cerebral adrenoleukodystrophy (Group P.I.s: A. Pujol and R. Artuch - Donation through the Hotel Barcelona Princess).



Mitochondrial and Neuromuscular Medicine

Coordinator: Francesc Palau Martínez

On the scientific level we should stress the progress made as regards tackling diseases which have the physiopathological target of mitochondria and affect the individual's bioenergetic balance, through the study of the genome-mitochondria communication and of physiopathology and disease mechanisms in cell and IPSC models, of the promotion of translational research and of therapeutic research from the development of animal models to the preclinical stage and biomarkers, especially in neuromuscular pathologies.

Some of the more significant achievements in the therapeutic stage are the search for therapeutic strategies for mitochondrial diseases with nucleosides or approaches with gene therapy.

Major work continues to be done by the groups in the programme as regards registries: *Registro Español de Enfermedades Neuromusculares NMD-ES, Registro de Enfermedades Mitocondriales* (in cooperation with AEPMI-Asociación de Enfermos de Patologías Mitocondriales and the Fundación Ana Carolina Díaz Mahou) and the Registry of patients affected by McArdle's disease (EUROMAC).

The groups in the programme have also taken an active part in cooperation with patient's associations such as AEPMI and ASEM (*Federación Española de Enfermedades Neuromusculares*), amongst others.

Lastly, they arranged different meetings or events of interest, from which we could highlight the following:

- 5th Annual Scientific Meeting of the Research Programme, held on 12 December at the Hospital San Joan de Déu de Barcelona.
- International Symposium: Defects in aminoacid transport, coordinated by three CIBERER groups; the ones led by Jorguina Satrústegui, Virginia Nunes and Manuel Palacín, held on 20 and 21 November, at the headquarters of the Fundación Ramón Areces in Madrid.
- Participation of several investigators at the National Congress of Neuromuscular Diseases, arranged by the *Federación Española de Enfermedades Neuromusculares* (Federación ASEM) and the Asociación de Enfermos Musculares de Granada (ASEMGRA), held in that city on 24 and 25 November.
- Session on limb-girdle muscular dystrophy LGMD1F, associated with the transportin-3 gene (HIV carrier), organised by the *Asociación Conquistando Escalones de familias* LGMD1F, the Regional Health Ministry of the Generalitat Valenciana Authority, IIS La Fe, the Universitat de València and the CIBERER, held at the Hospital La Fe de Valencia on 22 September with the participation of the groups led by Juan J. Vilchez and Ramón Martí.

Paediatric and Developmental Medicine

Coordinator: Montserrat Milá Recasens

We will now sum up the main activities and results connected with the objectives defined in the Action Plan 2017:

- Fostering the development of genomic diagnosis tools for the diseases of interest for the programme:

  The main part of the transversal project for "Characterisation and contribution to genetic diagnosis of a cohort of patients with intellectual disabilities, autism and/or epilepsy" was carried out all through 2017. Three full research groups are taking part in this project (PIs: M. Milá, L. Pérez Jurado and P. Lapunzina) from this PdI, along with a group from the Genetic Medicine Research Programme (PI: J. Dopazo) and the four clinical groups connected with the Paediatric and Developmental Medicine Group (Group PIs: E. Guillén, F. Ramos, J. Rosell and M.I. Tejada). Clinical information on over 200 cases has been compiled, now being in the phase for reinterpreting the genetic information available and of generation of new information via exomes and genomes.

- Contributing to training of healthcare professionals and the general public.

  This PdI has arranged activities for this purpose such as the "40th Annual Meeting of the ECEMC and Refresher Course on Research into Congenital Defects" 19 to 21 October, the Informative Symposium on Giant Congenital Nevus: Beyond rarity, on 12 July, the Workshop in Bone Dysplasia from 4 May in La Paz, the CIBERER DNA Day 2017: Non-invasive Prenatal Diagnosis from 24 April, the II Scientific Session for Parents and Professionals 11q (Jacobsen Syndrome) from 8 July or the Symposium on Dysmorphology for Clinical Doctors on 25 October.

Apart from this there are many individual publications of the groups in this approach, described in further detail in the sections on each group.

Sensorineural Pathology

Coordinator: Lluis Montoliu José

In 2017 the 7 groups forming the programme have obtained some major scientific results, in dissemination and cooperation with patient's associations, both independently, and in cooperation with other CIBERER groups.

On the scientific level we should stress the development of new cell and animal models of RD, above all oriented towards leadership in the preclinical research into sensorineural RD, as well as the development of genomic diagnosis tools and the discovery of new genes.

On the cooperation level we should stress that practically all the groups in the programme have a project granted in the ACCI call for 2017.

Special mention should be given to the fact that 6 groups in the programme have in 2017 jointly taken part in an intramural project: "Phenotyping and analysis of new animal and cell models of sensorineural diseases generated by means of CRISPR-Cas9 technology", which consolidates the continuity of the intramural project previously granted and reinforces the strategic positioning and the collaboration work done between the groups.

In the training field, several courses have been arranged:

- **8th Sessions on Training in Phenotyping animal models,** arranged by Isabel Varela-Nieto, 27 November to 1 December at the Facultad de Veterinaria of Universidad Complutense de Madrid.
- **Practical course on gene edition with CRISPR in rare diseases,** arranged by Lluis Montoliu and José Carlos Segovia, 7 July, at the Centro Nacional de Biotecnología in Madrid.

The Groups in the programme also cooperated with patients' associations, stressing the signing of the agreement with the *Federación de Asociaciones de Retinosis Pigmentaria de España* (FARPE) and the Fundación Lucha contra la Ceguera (FUNDALUCE) to promote research into inherited retinal dystrophies (DHR).

The short documentary film "¿Lo ves?" (*See it?*), by Patty Bonet, which shows the daily life of a person with albinism and which was backed by the programme and the association for aiding persons with albinism (ALBA) won different awards and recognitions in 2017.

Carmen Ayuso was awarded the National Genetics Prize, in the category of research into applications of genetics; Paola Bovolenta has been selected for the Scientific Committee of the European Research Council (ERC); and Isabel Varela-Nieto was given the Award for Research into Hearing Deficiencies by the Confederación Española de Familias de Personas Sordas (FIAPAS), in the Healthcare Category.

Different meetings or events of interest were also arranged, the following being particularly worthy of mention:

- 7th Annual Scientific Meeting, 4 December at the Instituto de Investigaciones Biomédicas "Alberto Sols" in Madrid.
- International Symposium: Non-invasive prenatal diagnosis and reproductive genetic diagnosis, coordinated by the unit led by Carmen Ayuso, 8 and 9 June, at the Fundación Ramón Areces in Madrid.
- Informative session on Usher's syndrome, arranged by José María Millán and Carmen Ayuso, 21 September at the Hospital La Fe in Valencia.
- 2nd Session on the Human Genome, 28 November, organised by Miguel Angel Moreno-Pelayo, from the Hospital Ramón y Cajal in Madrid.

Endocrine Medicine

Coordinator: Susan Webb

As its main transversal activity in 2017 the Endocrine Medicine programme carried out the final stage in the project entitled: "Silent corticotroph adenomas: Do these constitute a subtype of non-functioning hypophysary adenoma with a more aggressive clinical conduct?" Financed by CIBERER and intended to be closed in 2018. This project reviewed the classification of this type of adenomas.

Apart from the major contribution of the Linked Clinical Groups one should take into account that this Research Programme is made up of only three full research groups and a fourth associated group.

Work has been done by the Endocrine Medicine Programme with CIBER's own funds in the dissemination of research and contact with the patient through different measures in 2017: such as the 5th National Encounter of Patients with Acromegaly from 18 November at the Hospital Universitario HM San Chinarro in Madrid.

As regards significant scientific progress, the culmination of the longitudinal study on growth of healthy and non-obese population in Barcelona carried out by the Group led by A. Carrascosa and which includes data on 742 girls and 710 boys and in which over 25,000 anthropometric evaluations have been made, valuing the weight and size from birth until reaching the adult size in each of these. The results of this study provide a tool which is enabling changing clinical practice by establishing different patterns of normality, thus freeing paediatricians from single and rigid references which led to unnecessary interventions and furthermore covered up possible problems which did not get a timely intervention, all depending on whether they were later or early-maturing. This data constitutes a world first and the WHO itself has got contacts under way to take these as a reference.

Inherited Cancer, Haematological and Dermatological Diseases

Coordinator: Juan Antonio Bueren Roncero

In 2017 the groups in this research programme went on working towards IRDIRC objectives. In this respect, several scientific events were promoted, such as the programme's own scientific meeting, which took place at the CNIO in November, the VIII International Congress of the Red Española de Investigación in Fanconi Anaemia and the ***Genome Instability Network of Barcelona (GINBAR) Meeting***.

With regard to therapeutic developments, we can stress the signing of several major co-development and world licensing agreements and the exclusive on vectors of gene therapy generated by Juan Bueren's group on new treatments against rare diseases affecting blood cells. One can also stress the work of Marcela de Río's group focussing on new therapeutic approaches for epidermolysis bullosa, specifically therapies based on targeted-RNA and gene edition of COL7A1 by CRISPR/Cas9 published in *Nucleic Acids Res* and *Mol Ther* respectively.

Another milestone to be stressed is the work done at Javier Benítez's group, where pathway STAT3 is identified as a potential therapeutic target for certain endocrine tumours. The article published in *Clin Cancer Res*.

As regards new discoveries with application in diagnosis, Jordi Surrallés's group has taken part in a work published in *J Clin Invest* which has identified a new gene (RFWD3) causing Fanconi anaemia, an inherited disease caused by mutations in some of the genes connected with DNA repair. This group has also identified a new genetic syndrome caused by mutations in both copies of the FANCM gene, these results being published in *Genet Med*.

A study performed by Vicente Vicente's group has identified new mutations in the main endogenous anticoagulant, antithrombin, which causes antithrombin deficiency in patients with thromboses. The results of this work were published in the *Journal of Biological Chemistry*.

Training Programme

Coordinator: Luis Pérez Jurado

The main action taken in the CIBERER Training Programme has been in these two overall forms:

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

The third usual approach, for Predoctoral grants, had to be limited to closing the ones opened in the 2016 call, since the 2017 call could not be made due to administrative limitations.

Courses: Organisation and calls for aid for attendance

The CIBERER Training Programme arranged a course directly with its own additional call for attendance grants and six additional calls for attendance at courses with teaching coordination by CIBERER researchers were offered.

- Practical course with gene edition (CRISPR) Arranged by CIBERER-ISCIII, CNB-CSIC and CIEMAT. A session applied to real cases of gene edition, training led by Lluis Montoliu's group. July 2017.

Calls for aid for attendance at courses and training activities arranged by CIBERER and external groups:

- Rare Diseases Registries Workshop, March 2017, Hospital Universitario La Paz, Madrid.
- VIII Jornadas de Training en fenotipado de modelos animales, Nov-December 2017 Facultad de Veterinaria-Hospital Clínico Veterinario UCM, Madrid.
- ESGCT Spring School 2017 Granada, April 2017.
- EURORDIS Summer School Castelldefels, Barcelona, June 2017.
- NGS and Clinical Genetics: preparing samples, analysis and interpretation of data, June 2017, INGEMM, Madrid.
- Bioinformatic analysis of mass sequencing data applied to the clinical setting, November 2017 INGEMM, Madrid.

Mobility grants

In 2017, mobility grants continued to be open for internal and external, national and international mobility schemes. The former was awarded on a preferential basis and the external mobility grants were only awarded if they involved transversal interest. This means that different researchers could benefit from this programme to extend their training and further the projects in which they were involved.

No. of mobility grants: 9 awarded, which represents a dropin comparison with the 12 granted in 2016. 7 of these were intramural, 1 national extramural and 1 last international extramural grant.

The following table shows the mobility grants awarded in 2017:

Name	Issuing Group	Beneficiary Group
Juliana Salazar Blanco	PI María Pía Gallano Petit	PI Joaquin Dopazo Bázquez
Adelaida Celaya	PI Isabel Varela Nieto	PI Eduardo Salido
Laura González Simarro	PI Virginia Nunes	PI Isabel Varela Nieto
Beatriz Morte Molina	PI Juan Bernal	PI Joaquin Dopazo Blázquez
Gema Garcia García	PI Jose Mª Millán Salvador	PI Miguel Ángel Dopazo Pelayo
Carla Rubio Villena	PI José Serratosa	U. de Salamanca
Azahara Civera	PI Francesc Palau Martínez	PI Jorgina Satrústegui Gil Delgado
Beatriz Morte Molina	PI Juan Bernal	PI Miguel Ángel Medina Torres
María José Bermúdez	PI Isabel Varela Nieto	U. de Montpellier

Platforms

To facilitate the research work done by the CIBER for Rare Diseases and the scientific community 3 support platforms were arranged: CIBERER Biobank, BIER, and MAPER. We will now stress their main achievements in this last yearly period. Special mention should be given to the work done through Orphanet, a vital tool in the field of RD which had its 20th anniversary in 2017. The Spanish team, coordinated by CIBERER since 2010, has continued with its work in translating and identifying healthcare and research resources available in this country, making a great effort in quality control this year and updating the data of expert or benchmark centres, incorporating ERN in its database, as well as the translation of emergency guides and disability datasheets.

CIBERER Biobank

Coordinator: Francesc Palau Martínez

Summary of the main activities and results linked with the objectives defined in the Action Plan 2017:

Objective 1: Providing the Biobank with biological samples

The total number of samples in the biobank at the end of 2017 is 675 in over 70 different pathologies (http://www.ciberer-biobank.es).

Objective 2: Fostering a Plan for Strategic Alliances and Dissemination

Collaboration work

- Member of the Red Valenciana de Biobancos (RVB) since 2010.
- Cooperation Agreement with the IBSP-FISABIO Biobank.
- Framework agreement with the Banco Nacional de ADN since 2008.
- Plataforma Red Nacional de Biobancos (PRNB) of the ISCIII since 2010, forming part of several work groups.
- Cooperation with the PRNB and the Universidad Católica de Valencia in the University Master Course in Biobanks.
- Member of the Eurobiobank since March 2017.

Measures for disseminating the work done by the Biobank

- 10th Annual Meeting of the CIBERER (poster); presentation of the biobank at FISABIO; Annual Meeting of RD-Connect/Eurobiobank; 8th Congress of the National Network of Biobanks (poster); and 3rd Congress for RD in the Valencian Community.

Publications

- S Martí, M León, C Orellana, J Prieto, X Ponsoda, C López-García, JJ Vílchez, T Sevilla, J Torres. Generation of a disease-specific IPS cell line derived from a patient with Charcot-Marie-Tooth type 2K lacking functional GDAP1 gene. Stem Cell Research, Volume 18, January 2017, 99 1-4.

- Consuegra I, Rodríguez-Aierbe C, Santiuste I, Bosch A, Martínez-Marín R, Fortuto M A, Díaz T, Martí S, and Muñoz-Fernández MA. Isolation methods of peripheral blood mononuclear cells in Spanish biobanks: an overview. Biopreservation and Biobanking 2017 Aug;15(4):305-309.
- M. Seco-Cervera et al. Circulating miR-323-3p is a biomarker for cardiomyopathy and an indicator of phenotypic variability in Friedreich's ataxia patients. Scientific Reports – Nature 2017 Jul 12;7(1):5237.
- R Urreizti et al. A De Novo Nonsense Mutation in MAGEL2 in a Patient Initially Diagnosed as Opitz-C: Similarities Between Schaaf-Yang and Opitz-C Syndromes. – Nature Scientific Reports vol 7, Art num.: 44138 (2017).
- C Fuster-García et al. USH2A Gene Editing Using the CRISPR System. Molecular Therapy - Nucleic Acids Vol 8, p529–541, 15 Sept 2017.

Objective 3: Generating an added value for CIBERER Groups.

Provision of Services

Portfolio of services for CIBERER researchers: safekeeping of samples, establishment of cell cultures and generation of lymphoblastic lines, techniques for quality control of samples (analyses of the integrity of DNA and genetic print).

Development of new services: culture of myoblasts, immortalisation of fibroblasts (at the request of several CIBERER groups) and generation of IPS cells.

In 2017 there were 42 services for processing and safekeeping samples, establishment of cell cultures, cell immortalisation and advice for CIBERER Groups.

Objective 4: Fostering and backing new lines of action in rare diseases

Collaboration work in projects:

- FP7 HEALTH 2012-INNOVATION: RD-Connect: An integrated platform connecting registries, biobanks and clinical bioinformatics for RD.
- New diagnostic approaches for inherited syndromes with bone marrow failure for treatment with innovative therapies (SHIMO) PI: Julián Sevilla. IPS: J. Bueren, J. Surallés, P. Lapunzina, S. Webb, I. Badell and J. Sevilla.

BIER. Bioinformatics for Rare Diseases.

Coordinator: Joaquin Dopazo Blázquez

In 2017 the BIER has coordinated one ACCI project (ACCI-2016-25, the continuation of 06-ACCI2015) in which it has developed an advanced version of a system for storage and management of genomic data (exomes, panels or whole genomes). The software was developed in cooperation with Genomics England Ltd and it has the fastest and most scalable processing engine for genomic data in the world. Eight centres took part in the project and hospitals from five autonomous communities: La Paz, Fundación Jiménez Díaz, Ramón y Cajal, Centro de Biología Molecular (Madrid), Virgen del Rocío (Seville), Hospital del Mar (Barcelona), HU La Fe (Valencia), Universidad de Santiago de Compostela (Galicia). At the present time it has several hundreds of clinical exomes, whole exomes and even whole genomes.

The software developed is being used for the analysis of the 1000 genomes of the NaGen project (http://www.navarrabiomed.es/es/nagen-proyecto-genoma-navarra), around 100 of which have been analysed, and for the analysis of the exomes of the EnoD project, 130 of which have been completed at the present time.

The BIER has been working on the Spanish population genetic variant server (CSVS: http://www.ciberer.es/bier/csvs) which contains data on allele frequencies of variants currently obtained from 1600 exomes. The CSVS is one of the most complete databases of genetic variation of local population currently existing. The CSVS is on the Beacons list (https://beacon-network.org/) of the GA4GH.

MAPER. Interactive map with Information on Rare Disease Projects

Coordinator: Pablo Lapunzina Badía

In 2017 information continued to be compiled for the MAPER database, which is the interactive map developed by the CIBERER with information on the biomedical research resources under way in Spain on rare diseases. This year progress has been made and new resources have been added. The data on the validated research projects accessible through the MAPER web in 2017 is as follows:

- 658 biomedical research projects and 539 clinical trials included.
- 81 financing agencies take part in the financing of research into RD.
- 515 principal researchers are included in the database.
- 190 research centres included.
- Presentation of results at the annual meeting of CIBERER in 2017 and at the Agencia Española del Medicamento (AEMPS) and FEDER cooperation symposium on 14 December 2017.

Scientific Production

PUBLICATIONS

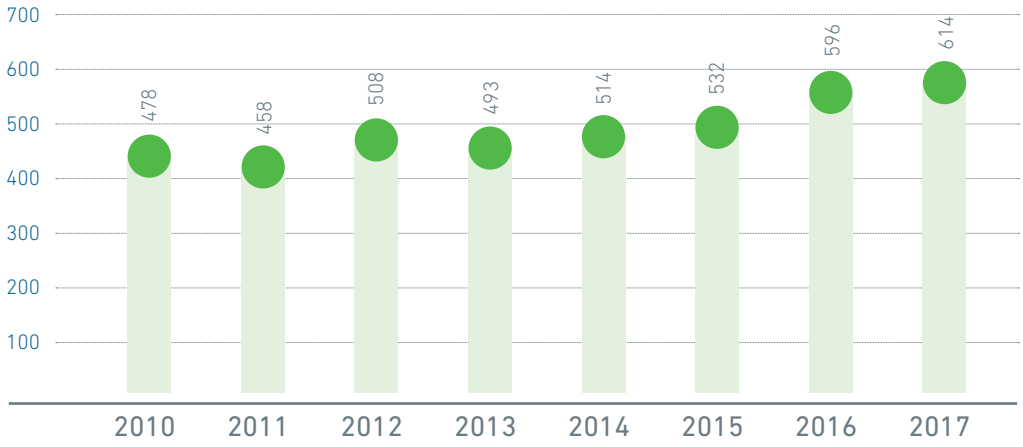
No. of publications in 2017

TOTAL → **614**

Q1 → 372

D1 → 147

Evolution of the publications



Most relevant publications of the CIBERER in 2017 by impact factor

Publication	Impact Factor
GGPS1 Mutation and Atypical Femoral Fractures with Bisphosphonates. N Engl J Med 05. 376(18):1794-1795	72,406
Prevention of Hereditary Angioedema Attacks with a Subcutaneous C1 Inhibitor. N Engl J Med. 03. 376(12):1131-1140	72,406
Ataluren in patients with nonsense mutation Duchenne muscular dystrophy (ACT DMD): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Sep. 390(10101):1489-1498	47,831
Association analysis identifies 65 new breast cancer risk loci. Nature International 11. 551(7678):92-94	40,137
Mutations in the histone methyltransferase gene KMT2B cause complex early-onset dystonia. Nat Genet Feb. 49(2):223-237	27,959
Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. May. 49(5):680-691	27,959

Publication	Impact Factor
Genomic analyses identify hundreds of variants associated with age at menarche and support a role for puberty timing in cancer risk. Genet Jun. 49(6):834-841	27,959
Identification of ten variants associated with risk of estrogen-receptor-negative breast cancer. JNat Genet Dec. 49(12):1767-1778	27,959
Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. Nat Genet. May. 49(5):680-691	27,959
Autoantibodies in chronic inflammatory neuropathies: diagnostic and therapeutic implications. Nat Rev Neurol. Sep. 13(9):533-547	20,257

Clinical Guides:

- Guidelines for diagnosis and management of the cobalamin-related remethylation disorders cblC, cblD, cblE, cblF, cblG, cblJ and MTHFR deficiency.
- Consensus guideline for the diagnosis and treatment of aromatic l-amino acid decarboxylase (AADC) deficiency.
- Proposed recommendations for diagnosing and managing individuals with glutaric aciduria type I: second revision.
- *Protocolos de diagnóstico y tratamiento de los Errores Congénitos del Metabolismo.*
- *Diagnóstico genético de la epidermólisis bullosa: recomendaciones de un grupo español de expertos.*
- *Guía de Práctica Clínica para las Distrofias Hereditarias de Retina. Grupo de trabajo de la Guía de Práctica Clínica para las Distrofias Hereditarias de Retina Ministerio de Sanidad, Servicios Sociales e Igualdad. Servicio de Evaluación del Servicio Canario de la Salud; 2017. Guías de Práctica Clínica en el SNS.*
- *Guía de actuación en las Anomalías de la Diferenciación Sexual (ADS) / Desarrollo Sexual Diferente (DSD).*
- The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update.
- Expert Opinion in Orphan drugs: current and emerging pharmacotherapies for hereditary hemorrhagic telangiectasia.
- *Diagnóstico y bases moleculares de MEN-1.*

CIBERER Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Antiñolo, Guillermo	10	5	2	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío	Sevilla
Artuch Iriberri, Rafael	30	9	7	Fundación para la Investigación y Docencia Sant Joan de Déu	Barcelona
Ayuso, Carmen	14	7	3	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Benítez, Javier	40	15	0	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid

Group Leader	Total Publications	Q1	D1	Institution	Province
Bermejo Sánchez, María Eva	10	3	2	Instituto de Salud Carlos III. Centro de Investigación de Anomalías Congénitas	Madrid
Bernal, Juan	6	4	2	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Botella Cubells, Luisa María	9	3	0	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro de Investigaciones Biológicas	Madrid
Bovolenta, Paola	6	2	2	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro de Biología Molecular Severo Ochoa	Madrid
Bueren, Juan Antonio	17	7	3	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	Madrid
Caballero Molina, María Teresa	12	2	2	Serv. Madrileño de Salud. Hptal. La Paz	Madrid
Cardellach López, Francesc	14	5	3	Hospital Clínico y Provincial de Barcelona	Barcelona
Carracedo, Ángel	26	5	11	Universidad de Santiago de Compostela. Facultad de Medicina	A Coruña
Carrascosa, Antonio	7	2	1	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	Barcelona
Castaño González, Luis	7	3	1	Asociación Instituto de Investigación Sanitaria de Biocruces. Hospital Universitario Cruces	Vizcaya
Cuezva, José Manuel	7	6	0	Universidad Autónoma de Madrid. Centro de Biología Molecular Severo Ochoa	Madrid
Dalmau Obrador, Josep	5	2	3	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Del Río Nechaevsky, Marcela	9	4	5	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	Madrid
Dopazo Blázquez, Joaquín	9	3	5	Fundación Pública Andaluza Progreso y Salud. Hospital Virgen del Rocío	Sevilla
Estévez Povedano, Raúl	3	1	1	Univ. de Barcelona. Facultad de Medicina	Barcelona
Fillat, Cristina	6	1	3	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Gallano Petit, María Pía	5	2	14	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Garesse, Rafael	4	2	1	Universidad Autónoma de Madrid	Madrid
Giraldo Castellano, Pilar (1)	10	4	1	Instituto Aragonés de Ciencias de la Salud. Hospital Miguel Servet	Zaragoza
González Manchón, Consuelo (2)	3	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro de Investigaciones Biológicas	Madrid
Gratacós, Eduard	52	8	17	Hospital Clínico y Provincial de Barcelona. Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Grinberg, Daniel	16	10	3	Univ. de Barcelona. Facultad de Biología	Barcelona
Illa Sendra, Isabel	13	5	1	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona
Knecht, Erwin	3	0	2	Fundación Centro de Investigación Príncipe Felipe	Valencia
Lapunzina Badía, Pablo Daniel	35	6	4	Serv. Madrileño de Salud. Hptal. La Paz	Madrid
Marfany Nadal, Gemma	1	0	0	Univ. de Barcelona. Facultad de Biología.	Barcelona

Group Leader	Total Publications	Q1	D1	Institution	Province
Martí Seves, Ramón	10	8	0	Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR)	Barcelona
Martín Casanueva, Miguel Ángel	30	13	5	Servicio Madrileño de Salud. Hospital Universitario 12 de Octubre	Madrid
Medina Torres, Miguel Ángel	12	7	4	Universidad de Málaga. Facultad de Ciencias	Málaga
Milà, Montserrat	38	16	12	Hospital Clínico y Provincial de Barcelona	Barcelona
Millán Salvador, José María	2	1	1	Fund. para la Invest. del Hospital la Fe	Valencia
Montoliu José, Lluis	7	4	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro Nacional de Biotecnología	Madrid
Montoya Villarroya, Julio	8	5	1	Univ. de Zaragoza. Facultad de Veterinaria	Zaragoza
Moreno Pelayo, Miguel Ángel	2	1	1	Servicio Madrileño de Salud. Hospital Ramón y Cajal	Madrid
Navas, Plácido	11	2	3	Universidad Pablo de Olavide. Centro Andaluz de Biología del Desarrollo	Sevilla
Nunes, Virginia	3	2	0	Fund. IDIBELL. Hospital Durán y Reynals	Barcelona
Palacín, Manuel	3	1	1	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Palau Martínez, Francesc	5	4	0	Fundación para la Investigación y Docencia Sant Joan de Deu. Hospital Sant Joan de Déu	Barcelona
Pallardo Calatayud, Federico	12	8	0	Universidad de Valencia. Facultad de Medicina de Valencia	Valencia
Pérez González, María Belén	16	7	4	Universidad Autónoma de Madrid. Centro de Biología Molecular Severo Ochoa	Madrid
Pérez Jurado, Luis	6	2	3	Universidad Pompeu Fabra. Facultad de ciencias experimentales y de la salud	Barcelona
Perona Abellón, Rosario	6	3	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Posada de la Paz, Manuel	13	1	1	Instituto de Salud Carlos III. Instituto de Investigación en Enfermedades Raras	Madrid
Pujol Onofre, Aurora	7	0	6	Fund. IDIBELL. Hospital Duran y Reynals	Barcelona
Ribes, Antonia	7	3	2	Hospital Clínico y Provincial de Barcelona. Instituto de Bioquímica Clínica	Barcelona
Rodríguez de Córdoba, Santiago	9	3	3	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro de Investigaciones Biológicas	Madrid
Rubio Zamora, Vicente	9	4	2	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Biomedicina de Valencia	Valencia
Ruiz Pérez, Victor Luis	6	2	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Salido, Eduardo	6	4	2	Fund.Canaria de Investigación Sanitaria (FUNCANIS). Hospital Univ. de Canarias	Santa Cruz de Tenerife
Sanz, Pascual	4	1	2	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Biomedicina de Valencia	Valencia
Satrústegui Gil Delgado, Jorgina	6	2	2	Universidad Autónoma de Madrid. Centro de Biología Molecular Severo Ochoa	Madrid
Serratosa, José	7	3	3	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid

Group Leader	Total Publications	Q1	D1	Institution	Province
Surrallés, Jordi	5	0	4	Universidad Autónoma de Barcelona. Facultad de Biociencias	Barcelona
Varela Nieto, Isabel	14	6	2	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Vicente García, Vicente	19	7	5	Fund. para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS). Hospital José María Morales Meseguer	Murcia
Vilchez Padilla, Juan Jesús	13	6	3	Fund. para la Invest. del Hospital la Fe	Valencia
Webb, Susan	15	5	1	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	Barcelona

(1) y (2) Withdrawn groups in 2017

Linked Groups

Group Leader	Institution	Province
Aldámiz-Echevarría, Luis	Hospital de Cruces	Bilbao
Badell, Isabel	Hospital de la Santa Creu i Sant Pau	Barcelona
Beléndez, Cristina	Hospital Gregorio Marañón	Madrid
Català, Albert	Hospital Sant Joan de Déu	Barcelona
Couce, Mª Luz	Hospital Clínico de Santiago de Compostela	A Coruña
Del Toro, Mireia	Hospital Vall d'Hebrón	Barcelona
González Gutiérrez-Solana, Luis	Hospital Infantil Niño Jesús	Madrid
Guillén, Encarna	Hospital Virgen de la Arrixaca	Murcia
Halperin, Irene	Hospital Clínic	Barcelona
López Laso, Eduardo	Hospital Reina Sofía	Córdoba
Picó, Antonio	Hospital General de Alicante	Alicante
Pintos, Guillem	Hospital Germans Trías i Pujol	Barcelona
Puig Domingo, Manuel	Hospital Germans Trías i Pujol	Barcelona
Ramos, Feliciano	Hospital Lozano Blesa	Zaragoza
Rosell, Jordi	Hospital Son Espases	Palma de Mallorca
Sevilla,Julián	Hospital Infantil Niño Jesús	Madrid
Soto, Alfonso	Hospital Virgen del Rocío	Sevilla
Tejada, María Isabel	Hospital de Cruces	Bilbao
Vives-Corrons, Joan Lluis	Hospital Clínic	Barcelona


ciberes
Respiratory Diseases

Scientific Director's Presentation

Ferrán Barbé Illa

Dear Colleagues,

Please allow me to start this letter by giving the two new groups which have joined us through the 2017 AES call a warm welcome to the CIBERES. These are the groups led by Dr. José Luis López Campos (Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla) and Dr. Guillermo Muñiz Albaiceta (Fundación para la Investigación e Innovación Biosanitaria en el Principado de Asturias). The Seville group investigates COPD, lung circulation, cystic fibrosis and bronchiecstases and sleep and ventilation, while the group from Oviedo works basically on the study of different mechanisms responsible for respiratory failures in the critical patient. I am quite sure that being joined by both these groups will increase the opportunities for cooperation between groups and the quality of work and scientific production of CIBERES.

I would like to go on by congratulating you since, in spite of the difficulties which biomedical research in Spain is going through, CIBERES has increased its percentage of publications in the first quartile and first decile in 2017, as well as the number of publications written in cooperation with international groups. Some other good examples of our work are the fact that last year we were the CIBER area presenting most projects to European calls and we continue to apply for new patents. All this vouches for your good work and willingness to continue with your endeavours in spite of the difficulties involved.

We have also improved as regards communication of our work to society; news has been generated and has been disseminated either on our website, which has a rising number of visits, and over social networks. This is nevertheless an aspect in which there is still room for improvement and I would like to encourage you to announce your work, taking advantage of the excellent amplifier that CIBERES represents for this purpose.

Our aim at the management committee is always to improve the management of CIBERES resources by endowing this with better structures and possible tools in keeping with the framework that has been set for us by the administration. I should thus declare my satisfaction with the success of such initiatives as the Teaching Sessions performed along with CIBERFES which have materialised in a call for interCIBER collaborative projects for which many good proposals have been put forward.

I would like to end my letter by thanking you another year for your hard work and commitment and congratulating all the CIBERES researchers for the excellent results achieved in 2017.

Scientific Programmes

Chronic Respiratory Diseases

Coordinator: **Juan Fernando Masa Jiménez**

Asthma line:

As part of the project entitled 'Study of the underlying mechanisms of the genesis and evolution of asthma', the group has included roughly 300 patients in the cohort, creating a biorepository which stores biological samples to use in this and future projects.

The group has obtained funding from the Instituto de Salud Carlos III (FIS PI17/01950), SANOFI and CIBERES, with an intramural project for identifying miRNAs as possible biomarkers and new therapeutic targets in asthma and COPD.

One patent (P201730947) has been applied, which will enable developing differential biomarkers in asthma.

COPD line:

The profiles for differentiated gene expression in patients with fragile COPD and eosinophilia have been determined.

The methodology for studying the respiratory microbiome has been defined (*IJCOPD-2017, FMicrobiol-2017; ATM- 2017; ERJ-2017; BMCMicrobiol-2017; Arch-Bronconeumol-2017*).

A relationship between respiratory microbiome and COPD phenotypes was established.

Adaptive traits of micro-organisms with regard to the evolution of COPD have been defined.

The bases for antibiotic resistance of NTHi have been defined (*Cell InfectMicrobiol.* 2017).

Multilevel description of markers associated with exacerbation (ERJ-2017).

Picking up *in vivo* images of specific pulmonary neutrophilic inflammation with nanotracer Ga68 (*SciRep*-2017).

The influence of pulmonary function in early ages was revealed with prognosis (*LancetRM*-2017). Description of the relationship between the endotype and response to treatment (*Lancet*-2017).

OSA line:

A population study covering 70,469 patients treated for sleep apnoea (OSA) with CPAP shows that the treatment is associated with a reduction of mortality in men.

The most complete national collection of patients with suspected OSA is available, including over 700 subjects.

A specific score may be useful for predicting OSA patient's response to CPAP treatment in terms of blood pressure control.

Handling OSA with home respiratory polygraphy is similarly effective to polysomnography, at a lower cost.

Treatment for OSA in primary care can be given for roughly half of the patients with suspected OSA.

In patients with the obesity-hypoventilation syndrome, treatment in the medium term with VNI or CPAP is more effective than modification of their lifestyle.

For the first time we have described that intermittent hypoxia (IH) increases the incidence of tumours in different organs and spontaneous tumorigenesis, particularly in the lung.

The SAVE study has shown that treatment with CPAP in patients with OSA is not effective for secondary cardiovascular prevention.

Cancer line:

We go on working with three lung cancer cohorts (IASLC, CIBERES and Early-COPD) of patients in stages Ip/IIp.

An intramural grant has been awarded for the study of the findings from these cohorts based on systems biology.

The recruitment of patients with lung cancer in advanced stages for the study of epigenetics in ganglion samples.

The screening cohort has over 700 individuals and the recruitment of patients in the SAIL and SAILS studies has been completed.

Infectious Respiratory Diseases

Coordinator: Antoni Torres Martí

The MTBVAC vaccine is safe and immunogenic in murine and neonatal human models and gives more protection than BCG. There are derivatives which express antigens of other infections. New vaccines based on other lines of tuberculosis are made.

There are genetic, genomic and epidemiological databases of strains causing outbreaks, which enable identifying prevalent strains among originating populations in countries with a high immigration rate and designing molecular tests which detect transmission and identify clonal strains.

The immunological and transcriptional response is studied with lesions and blood of active or latent tuberculosis patients. The storage of samples, diagnosis of tuberculosis by means of nanoparticles and tests to detect resistances have been improved. There are metabolites in the urine which are connected with tuberculosis.

Families of new anti-tuberculosis compounds and their targets have been characterised. Nanoparticles with bedaquiline or rifampicin are active against the bacillus. *Nyaditum resae* is studied in a comorbidity model in experimental animal models. There are clinical tests with ibuprofen. Tobacco smoke reduces the presence of tuberculosis macrophages and the activity of rifampicin.

Our researchers have demonstrated that 60 % of the serotypes causing CAP by pneumococcus in Spain are contained in conjugated vaccine VCN 13v. Roughly 20% of the exacerbations of bronchiectasis treated in hospital are caused by multi-resistant bacteria.

In 2017 Pneumocoper has contributed to publishing new international guides of clinical practice in respiratory infections.

Seven experimental randomised studies have been completed on the prevention and treatment of serious pulmonary infections and are currently being sent to journals with a high scientific impact factor. A randomised clinical test in over 400 patients has been published (Intensive Care Med 2017) on

the effects of the lateral-Trendelenburg position in the prevention of ventilator-associated pneumonia.

The following review on the microbiome has also been published:

- Faner R, Sibila O, Agustí A, Bernasconi E, Chalmers JD, Huffnagle GB, Manichanh C, Molyneaux PL, Paredes R,Pérez Brocal V, Ponomarenko J, Sethi S, Dorca J, Monsó E. *The microbiome in respiratory medicine: current challenges and future perspectives*. Eur Respir J. 2017 Apr 12;49(4).

It should also be stressed that the 22nd International Symposium on Infections in the Critically Ill Patient (Oporto 2017) was arranged.

Diffuse Respiratory Diseases

Coordinator: Francisco Pérez Vizcaíno

Main achievements in 2017:

- 1st Meeting for Research into Pulmonary Hypertension in Spain, which involved over 80 researchers from both CIBERES and other organisations.
- Getting under way the Spanish Registry on Pulmonary Hypertension associated with Respiratory Disease (REHAR).
- Demonstration of the different effect of targeted therapy of pulmonary hypertension on circulating biomarkers (endothelial progenitor cells and endothelial microparticles).
- Publication of the *Guía de Diagnóstico y Tratamiento de la Hipertensión Pulmonar*, backed by the Sociedad Española de Neumología y Cirugía Torácica (SEPAR), with the participation of several CIBERES members.
- Study of the role of miR-1 on pulmonary endothelial dysfunction and the activity and expression of channels of voltage-dependant potassium.
- Establishment of an international consortium for the analysis of physiopathological mechanisms involved in pulmonary hypertension associated with co-infection with schistosoma and HIV:
- Determination of the status of vitamin D, its prognosis value in patients with arterial pulmonary hypertension.
- Worsening of pulmonary hypertension through a vitamin D deficit in the rat.
- First results with advanced imaging techniques (PET and MRI) in pulmonary hypertension.
- Generation of TERT and TERC constructions with mutations of patients with idiopathic pulmonary fibrosis and transfection to cell lines.
- Determination of the effect of GSE4 expression on telomerase activity by in vitro TRAP test in cells expressing GSE4 or treatment with GSE4 nanoparticles.
- Determination of the effect of PLGA/PEI nanoparticles charged with GSE4 in a model of pulmonary fibrosis with bleomycin and monitoring by means of SPECT: inhibition of fibrosis markers, deposition of collagen and recovery of telomerase activity.
- Insulation and characterisation of mesenchymal stem cells of patients with idiopathic pulmonary fibrosis and in donors.

- Approval and starting to include patients in the MA39293-DIET (MADIET) clinical trial to study the effect of diet on the adverse gastrointestinal effects of pirfenidone in idiopathic pulmonary fibrosis. EudraCT number: 2016-003827-45. Sponsor: CIBERES.
- Identification of acid sphingomyelinase, interleukin -6 and urate crystals as mediators of the pulmonary vascular dysfunction associated with acute pulmonary damage.
- Completion of the first phase of the genomic study of ARDS with 7.8 million genetic variants in 672 patients with sepsis.
- Start of recruitment of patients for the Gen-Sep study (Genetics and Biomarkers in Sepsis-induced ARDS) to identify biomarkers as candidates for diagnosis and prognosis of ARDS in patients with pulmonary and extrapulmonary origin sepsis.
- Identification of biomarkers based on microRNAs mir155-3p, miRNA-27a-5p and miRNA-146a-5p and their modulation by FasL and IL-1β.
- Completion of in vitro and in vivo studies of anticoagulant treatment with heparin, anti- thrombin or antithrombin along with heparin in experimental ARDS.
- Final phase of the clinical trial entitled "Effectiveness of dexametasone in treatment of Moderately severe persistent Respiratory Distress".
- Completion of the observational study entitled "International Practice Variation in Weaning Critically Ill Adults from Invasive Mechanical Ventilation".
- Analysis of cell therapy with native type II pneumocytes and which overexpress anti-inflammatory genes in a model of acute pulmonary injury.

Training Programme

Coordinator: **Cristina Prat Aymerich**

In 2017, the expectations of the CIBERES Teaching Programme were kept up in its four strategic actions:

1. Grants for starting research

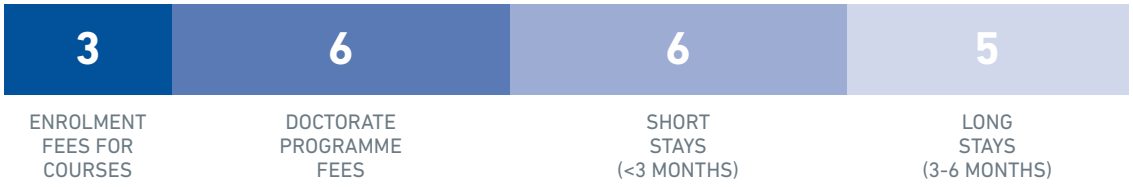
With the aim of contracting young researchers for one year in a research project of the CIBERES groups, the official Training Programme for research staff (FPI) keeps its co-financing ratio at 66% from the teaching training programme itself and 33% from the beneficiary group in question.

In 2017 three calls were launched with a total number of eleven grants being awarded.

2. Improvement and mobility programme. Training Grants.

In 2017, the results of this programme display an upward trend in the award of grants for long-term stays (3-6 months) after the increase in its economic endowment. Twenty mobility grants were awarded, split into four categories: three applications for payment of enrolment fees, six applications for payment of Doctorate Programme fees, six applications for stays in another city (<3 months) and 5 applications for stays in a different city (3-6 months) focussing on two areas – Canada and the United Kingdom.

CIBERES MOBILITY /IMPROVEMENT GRANTS 2017
Number of applications



3. Grants for recruiting external funding

This programme, which encourages internationalisation at CIBERES, awarded one grant in 2017 for co-financing the services of a consultant in preparing a European project.

4. CIBERES-CIBERFES Training Days 2017

In 2017 the tenth CIBERES Training Sessions were held along with CIBERFES in Madrid, on 19 and 20 October, at the Ernest LLuch room in the Escuela Nacional de Sanidad in Madrid.

This year the Teaching Committee awarded a special "Constancio González" prize to the best oral paper and three prizes for the best oral papers and posters which were selected from 16 oral papers and 46 posters presented. The active participation of CIBERFES researchers in these events should be highlighted. The work done by the eight researchers who were given a grant for starting research in 2016 was also presented, revealing the need for these grants, in view of the fact that 75% of the candidates obtained a pre-doctoral contract before completing the contract term.

As a result of the cooperation emerging between CIBERES-CIBERFES areas at the training sessions there was a proposal to launch a call for collaborative CIBERES-CIBERFES intramural projects in early 2018, in order to present collaborative projects which may be proposed for coming European or international calls (2019-2020).

Pulmonary Biobank Platform

Coordinator: Cristina Villena Portella

The biobank's own work to improve its service:

Congresses

- Villena C, et. al, on behalf of R&D working group of Spanish Biobank Platform. P*reliminary results from OPTIMARK project about potential quality biomarkers*. Global Biobanking Week, Estocolomo, 2017.
- Esteva-Socias, M et. al. *Detection of the EGFR G719S mutation in non-small cell lung cancer by non-invasive blood-based analyses using droplet digital PCR*. 1st ASEICA Educational Symposium, Madrid, 2017.
- Rábano A, Artiga MJ, Bahamonde O, Belar O, Bermudo R, Castro E, De la Puente R, Escámez T, Fraga M, Jauregui L, Novoa Io, Peiró-Chova L, Piñero E, Rejón JD, Ruiz-Miró M, Vieiro P, Zazo S, Villar V y Villena C. *La variabilidad del RIN: resultados preliminares del proyecto OPTIMARK*. Congreso Nacional de Biobancos, Cartagena, 2017.
- Pons DG, et. al *On behalf of PBP. Establecimiento de un circuito de recogida de muestras de pulmón de donantes de órganos entre la Plataforma Biobanco Pulmonar CIBERES y la Coordinación de Trasplantes del HUSE. Congreso Nacional de Biobancos, Cartagena, 2017.*
- Campaner MA, et. al. *Cómo organizar a posteriori una gran cohorte iniciada en 2010 y no morir en el intento: estudio clínico ISAAC. Congreso Nacional de Biobancos*, Cartagena, 18- 20 octubre 2017.
- Esteva-Socias M, *on behalf of PBP. New research challenges: biological samples of human origin*. X Jornadas de formación CIBERES-CIBERFES, Madrid, 2017.
- Esteva-Socias M, *amb el suport de la PBP i la Red Nacional de Biobancos. Nous reptes en investigació: les pròpies mostres d'origen humà. IV Jornada IdISBa, Mallorca, 2017.*

Research Projects

- Optimisation of tissue samples for developing and validating disease biomarkers: project OPTIMARK. PI16/00528. Multi-centre project. PI: C. Villena. FIS-ISCIII. 2017-2019.
- National Biobanks Network Platform – ISCIII. PT17/0015/0001. Unidad Coordinadora de la Plataforma Biobancos AES 2017. PI: C. Villena. FIS-ISCIII. 2018-2020.
- Interaction between the Wnt and NF-kB channels in inflammatory processes and progression of lung cancer. Analysis of genomic profiles and liquid biopsy. SYN17/02. PI: Antonia Obrador Hevia and Jaume Sauleda Roig. Contributors: C. Villena and M. Esteva. IdISBa. 2018-2019.

Doctoral theses under way

Margalida Esteva as part of the OPTIMARK (FIS) project.

Quality

In 2017 the Quality Management System was adapted to the new ISO 9001:2015 standard, passing the annual internal audits for its certification. The collection of unhealthy samples has also increased, reaching 95,621 samples from over 2000 patients subjected to pulmonary explants, organ donors and conventional surgery, and around 28,479 from 912 patients of other specific pathologies.

Member:

1. *European, Middle Eastern & African Society for Biopreservation & Biobanking*.
2. *International Society for Biological and Environmental Repositories*.
3. National Biobanks Network Platform (PRNBB)-ISCIII AES 2013-2016.

Training activities

Participation in three university master courses, one university course and the CIBERES 2017 Training Sessions.

Scientific activity resulting from the biobank

http://biobancopulmonar.CIBERES.org/es/projects

Scientific Production

PUBLICATIONS

No. of publications in 2017

TOTAL → **597**

Q1 → 312

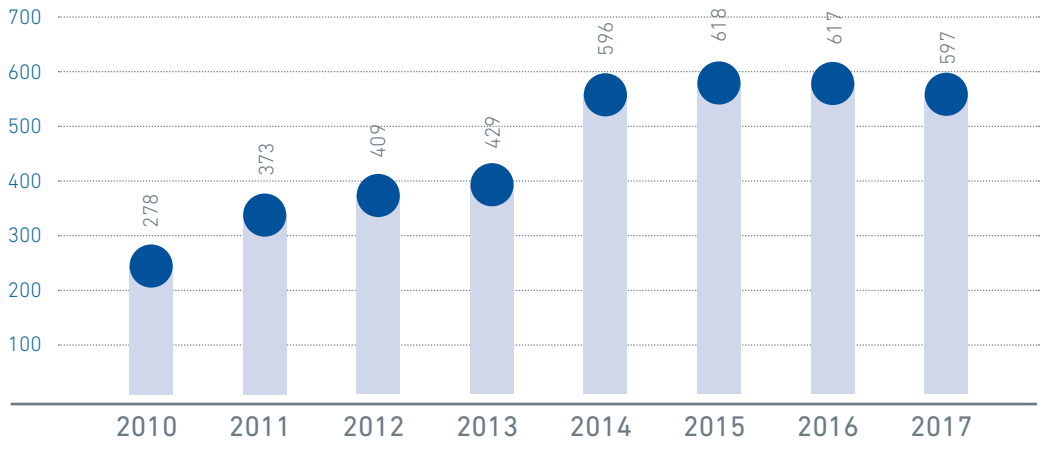
D1 → 145

Collaboration work

IntraCIBER → 169

InterCIBER → 107

Evolution of the publications



Most relevant publications of the CIBERES in 2017 by impact factor

Publication	Impact Factor
Wilcox M.H., Gerding D.N., Poxton I.R., Kelly C., Nathan R., Birch T. et al. Bezlotoxumab for Prevention of Recurrent Clostridium difficile Infection. New England Journal of Medicine. 2017;376(4):305-317.	72,406
Agusti A., Celli B., Faner R. What does endotyping mean for treatment in chronic obstructive pulmonary disease? The Lancet. 2017;390(10098):980-987.	47,831
Oria R., Wiegand T., Escribano J., EloseguiArtola A., Uriarte J.J., Moreno-Pulido C. et al. Force loading explains spatial sensing of ligands by cells. Nature. 2017;552(7684):219-224.	40,137
Minutti CM, Jackson-Jones LH, García-Fojeda B, Knipper JA, Sutherland TE, Logan N. et al. Local amplifiers of IL-4Rα-mediated macrophage activation promote repair in lung and liver. Science (New York, N.Y.). 2017.	37,205
Elosegui-Artola A., Andreu I., Beedle A.E.M., Lezamiz A., Uroz M., Kosmalska A.J. et al. Force Triggers YAP Nuclear Entry by Regulating Transport across Nuclear Pores. Cell. 2017;171(6):1397-1410.e14.	30,410

Brindle KM, Izquierdo-García JL, Lewis DY, Mair RJ, Wright AJ. Brain Tumor Imaging. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2017;35(21).	24,008
Drager LF, McEvoy RD, Barbe F, Lorenzi-Filho G, Redline S, INCOSACT Initiative (International Collaboration of Sleep Apnea Cardiovascular Trialists).. Sleep Apnea and Cardiovascular Disease: Lessons From Recent Trials and Need for Team Science. Circulation. 2017;136(19).	19,309
Cullinan P., Munoz X., Suojalehto H., Agius R., Jindal S., Sigsgaard T. et al. Occupational lung diseases: From old and novel exposures to effective preventive strategies. The Lancet Respiratory Medicine. 2017.	19,287
Rello J. Theranostics in severe influenza. The Lancet Respiratory Medicine. 2017.	19,287
Agusti A., Dekhuijzen P.R. Maximal bronchodilation: a therapeutic target in COPD? The Lancet Respiratory Medicine. 2017;5(7):540-542.	19,287

CIBERES Patents 2017

New applications

- "In vitro method for identifying scales of severity in patients with bronchial asthma". (P201730739).
- "Method for predicting response to continuous positive air pressure treatment" (EP 15817217.1 Europe, CA2970703 Canada, JP2017-533495 Japan, AU 2015367460 Australia, 15/535,731 USA).

Granted

- "Inactivated mycobacteria for their use in oral administration for preventing tuberculosis" Date granted: 28/2/2017 inventors: Cardona Iglesias, Pere-Joan; Vilaplana Massaguer, Cristina; Marzo Escartín, Elena Cotitularidad: Institut Germans Tries i Pujol (IGTP) 66.7%/ CIBERES 33.3% (US9579371).

Clinical Guides

- Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary.
- *Manual SEPAR de Procedimientos. Gasometría Arterial.*
- An Official American Thoracic Society Workshop Report: Noninvasive Identification of Inspiratory Flow Limitation in Sleep Studies.
- Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline.
- International Guidelines for the Management of Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia.
- Guidelines for the Management of HAP/VAP of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESCIM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latino-americana del Tórax (ALAT).
- *Normativa sobre el tratamiento farmacológico de la fibrosis pulmonaridiopática.*

CIBERES Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Agustí García Navarro, Álvar	43	26	18	Hospital Clínico y Provincial de Barcelona	Barcelona
Álvarez Martínez, Carlos José	10	7	2	Servicio Madrileño de Salud. Hospital Universitario 12 de Octubre	Madrid
Ardanuy Tisaire, María Carmen	18	8	1	Fundación IDIBELL. Hospital Univ. de Bellvitge	Barcelona
Barbé Illa, Ferrán	38	19	12	Instituto de Investigación Biomédica de Lleida. Fundación Dr. Pifarre	Lleida
Barberá Mir, Joan Albert	26	17	10	Hospital Clínico y Provincial de Barcelona	Barcelona
Blanch Torra, Lluis	45	24	19	Corp. Sanitaria Parc Taulí	Barcelona
Bouza Santiago, Emilio	50	29	13	Servicio Madrileño de Salud. Hospital Gregorio Marañón	Madrid
Cardona Iglesias, Pere Joan	15	10	1	Fund. Instituto de Investigación Germans Trias i Pujol. Hospital Germans Trias I Pujol	Barcelona
Casals Carro, Cristina	2	2	1	Universidad Complutense de Madrid. Facultad de Biología	Madrid
Del Pozo Abejón, María Victoria	15	5	0	Instituto de Investigación Sanitaria Fund. Jiménez Díaz	Madrid
Farre Ventura, Ramón	26	17	6	Universidad de Barcelona. Facultad de Medicina	Barcelona
García López, Ernesto	8	8	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro de Invest. Biológicas	Madrid
García Río, Francisco José	23	10	7	Servicio Madrileño de Salud. Hospital La Paz	Madrid
Gea Guiral, Joaquim	26	12	6	Consorci Mar Parc Salut de Barcelona. Hospital del Mar	Barcelona
González Mangado, Nicolás	21	14	5	Instituto de Investigación Sanitaria Fund. Jiménez Díaz	Madrid
Lorente Balanza, José Ángel	19	13	7	Servicio Madrileño de Salud. Hospital Universitario de Getafe	Madrid
Marimón Ortiz de Zarate, José María	19	9	6	Asociación Instituto Biodonostia. Hospital Donostia	Guipúzcoa
Martín Montañés, Carlos	9	2	0	Universidad de Zaragoza	Zaragoza
Masa Jiménez, Juan Fernando	17	10	4	Fundación para la Formación y la Investigación de los Profesionales de la Salud (FUNDESALUD). Hospital San Pedro de Alcántara	Cáceres
Menéndez Fernández, Margarita	4	4	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Inst. de Química Física Rocasolano	Madrid

Group Leader	Total Publications	Q1	D1	Institution	Province
Monsó Molas, Eduard	19	11	4	Corporación Sanitaria Parc Taulí	Barcelona
Montserrat Canal, Josep María	20	7	4	Hospital Clínico y Provincial de Barcelona	Barcelona
Morcillo Sánchez, Esteban Jesús	1	0	0	Universidad de Valencia. Facultad de Medicina	Valencia
Mullol Miret, Joaquín	35	22	14	Hospital Clínico y Provincial de Barcelona. Inst. de Investigaciones Biomédicas August Pi I Sunyer	Barcelona
Muñoz Gall, Xavier	76	34	15	Fund. Hospital Universitario Vall d´Hebrón - Institut de Recerca (VHIR). Hospital Valle Hebrón	Barcelona
Nieto Martín, Amelia	8	7	3	Agencia Estatal Consejo Superior de Investigaciones Científicas. Centro Nacional de Biotecnología	Madrid
Obeso Cáceres, Ana	3	3	2	Universidad de Valladolid. Facultad de Medicina	Valladolid
Pérez Vizcaíno, Francisco	7	3	1	Universidad Complutense de Madrid. Facultad de Farmacia	Madrid
Regueiro Comesaño, Verónica (1)	3	3	0	Fundación de Investigación Sanitaria de las Islas Baleares Ramón Llull (FISIB). Hospital Universitario Son Espases	Mallorca
Relló Condomines, Jordi	35	15	11	Fundación Hospital Universitario Vall d´Hebrón - Institut de Recerca (VHIR). Hospital Valle Hebrón	Barcelona
Ruiz Cabello Osuna, Jesús	13	9	2	Universidad Complutense de Madrid. Facultad de Farmacia	Madrid
Torres Martí, Antoni	49	28	11	Hospital Clínico y Provincial de Barcelona	Barcelona
Villar Hernández, Jesús	24	13	6	Fund. Canaria de Investigación Sanitaria (FUNCANIS). Hospital Univ. de Gran Canaria Dr. Negrín	Las Palmas

(1) Group deregistered in 2018

Linked Group

López-Campos Bodineau, Jose Luis, Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío (Sevilla).

ciberesp

Epidemiology and Public Health

Scientific Director's Presentation

Marina Pollán Santamaría

In 2017, CIBERESP redesigned its Strategic Plan considering the analysis of strengths, weaknesses, opportunities and threats to take a strategic position as a benchmark in the field of public health both in Spain and abroad. In December there was a change in Scientific Management, and I agreed to take on this position in order to consolidate the good work done by CIBERESP under the management of Miguel Delgado. The study of inequalities in health, the impact of healthcare policies, research into risk factors favouring the appearance of the main diseases in this country, the importance of surveillance systems as useful tools for providing us with new knowledge, investigation into primary and secondary prevention and the assessment of healthcare practices are key factors for CIBERESP. The over 1000 scientific articles published in 2017 display a high degree of cooperation.

CIBERESP has seven research programmes and one for training. In programme 1 the MCC study, with over 10000 participants, has confirmed the reduction of risk associated with compliance with international recommendations on diet and exercise for the main tumours, has proven the beneficial effect of the Mediterranean diet in less-commonly studied tumours (prostate and gastric cancer) and a possible relationship between trihalomethanes and breast cancer.

Programme 2 has obtained several European projects and contributed publications on the effectiveness of the influenza vaccine, the risk of introducing different viruses from imported cases, the analysis of the virulence of zoonotic pathogens and new protocols for fast diagnosis of influenza.

Programme 3 has presented its conclusions on "Immigration and health in the context of the crisis in Spain" and the platform for Longitudinal studies in Immigrating Families has published its initial results.

Programme 4 provides information on the social determinants of health and several projects were got under way in 2017. From its roughly one hundred publications we could highlight a systematic review on the risk of mortality after the treatments for substitution of opioids, published in the BMJ.

Programme 5 includes the project entitled Childhood and Environment (INMA) which monitors the development of over 2000 boys and girls, showing the effect that contamination has on the development of the brain and attention deficits after birth. Groups from the programme contribute to the recruitment and monitoring of PREDIMED.

Programme 6 in the cohort of Employment Lives analyses the association between employment career and mortality. We should also stress the results on violence in childhood and suicide and the relationship between co-payment and adherence. BiblioPRO continues to be a reference in PRO instruments.

Programme 7 has published results of the EMPARO cohort of patients with vesical cancer and a geospatial analysis of diet and cardiovascular mortality. The programme held sessions on Systematic Reviews, with new methodological prospects.

Lastly, the Training Programme enabled national and international mobility of many researchers, consolidating cooperation with CIBEROBN and CIBERDEM for Excellence Encounters in Public Health.

Scientific Programmes

Epidemiology and control of chronic diseases

Coordinator: Mª José Sánchez Pérez*

Over this year, Programme 1 continued with its scientific work in the strategic sub-programme (MCC-Spain). It also got under way a new GENRISK sub-programme on the use of genetic susceptibility markers for designing personalised screening strategies of chronic diseases.

Lastly, we continued with the work done by the other sub-programmes, including EPIC (focussing not only on cancer, but on other chronic diseases such as diabetes, cardiovascular complaints, dementias, inflammatory bowel diseases ...), ENRICA, mammographic density and breast cancer, DARIOS, FRESCO, POIBC, morbidity-mortality through traffic injuries in elderly drivers and the platform for cancer registries in the population.

MCC-Spain

The MCC study has published 15 articles, most in first quartile and first decile journals. Some of the results of the study disseminated this year are the publication of a colorectal cancer risk model including risk factors and genetic variants, the protective effect of the Mediterranean diet against prostate cancer and gastric cancer, the reduction of risk associated with greater adherence to international recommendations on diet and physical exercise for breast, prostate and colorectal tumours, the relationship between trihalomethanes and breast and colorectal cancers, the relationship between serological markers of *Helicobacter pylori* and gastric and colorectal cancer and the role of working night shifts in colon and rectal cancer. The last meeting (10th encounter) was held from 17th to 18th October in Alcalá de Henares. The aim of the event, which was attended by 40 researchers from 14 CIBERESP groups, was to update the projects under way, including the monitoring study of these cases in order to research into the prognostic role of many of the exposures analysed, as well as the consideration of future lines. This was also attended by two guests: Dr Richard Martin, professor of Clinical Epidemiology of Bristol University, who gave the lecture entitled "*Using genomic data to inform prostate cancer prevention and treatment strategies*" and Dr Ángel Lanas, Scientific Director of the Instituto de Investigación Sanitaria de Aragón, who presented the lecture "Aspirin and colon cancer: from investigation to prevention".

GENRISK

A collaborative Intranet was designed, registered with the domain genrisk.org. A face-to-face meeting of the interested groups was held on 4 July 2017 in Barcelona, attended by 27 persons from 19 groups with interest in the action. Priority objectives and persons in charge of furthering these objectives were defined. In Granada on 24-25 November there was also an introductory course on statistical analysis of studies in genetic epidemiology, attended by 15 persons from 10 groups.

* Until December the Coordinator was Marina Pollán Santamaría

Communicable disease prevention, surveillance and control

Coordinator: Pere Godoy García*

Details of some of the most relevant projects in the CIBERESP's PREVICET programme are given below:

- January 2017 saw the start of the project entitled "Factors associated with outbreaks of acute gastroenteritis by norovirus" (FIS-PI16/02005) in which the groups of Á. Domínguez and C. Rius (PI Angela Domínguez) took part.
- The project known as "Effectiveness of vaccine against pertussis in pregnant women: case and control study in Catalonia and Navarre" (FIS-PI15/01348) was also continued, with the participation of the groups led by Á. Domínguez, J. Castilla, C. Rius and M.C. Muñoz's group (PI Pere Godoy) and which will also be active during 2018.
- In 2017 the results of "Effectiveness of anti-flu vaccine and anti-pneumococcal polysaccharide 23-valent in ≥65 years" (FIS-PI12/02079) were published. The groups of Á. Domínguez, E. Calderón, J. Castilla, C. Rius, M. Morales took part in this. Five articles were published.
- European projects "Setting up a sentinel system to assess the burden of whooping cough in EU/ EEA" and "Assessing the impact of conjugate vaccines on pneumococcal disease in Europe" financed by the ECDC.
- The group led by Amparo Larrauri, along with other groups, is taking part in two European projects on the effectiveness of the anti-flu vaccine, one in primary care (Call for tender of the ECDC) and another in hospitalised patients (Horizon 2020 EU 634446). Six Q1 articles were published.
- 2017 was the last year for the FIS project (FIS PI13/02123). Two articles were published on the impact and effectiveness of the vaccine and the research into effectiveness contributed to the GIVE 2016 reports (The Global Influenza Vaccine Effectiveness Collaboration).
- "Risk of complications in pregnant women admitted to hospital with serious flu infections": project: article being reviewed.
- "Research into Enterovirus infections causing severe neurological and systemic pathologies in the child population": article on the implication of EV-D68.
- Project entitled "Epidemiological and virological analyses of the viral agents included in the triple viral vaccine, new challenges" (AESI2015: PI15CIII/00023): Group J. E. Echevarría (PI Fernando de Ory and Aurora Fernández) and A. Larrauri's group; two international articles on parotitis and the value of IgG titration for diagnosis of infection in vaccinated persons.
- VIROBAT3 (SAF2013-47194-P) Project: J. E. Echevarría's group (PI Juan E. Echevarría) and J. Figuerola's group, on rabies and other viruses associated with bats. Two articles, one on the phylogeography of European bat virus type 1 and another describing the presence of Bartonella in Spanish bats. The VIROBAT 4 project has been granted enabling working in this approach to go on. Also J.E. Echevarría's group and J. Figuerola's group have published an article on diagnosis of infection by Zika virus in the Spanish Olympic team of Rio de Janeiro".

* Until December the Coordinator was Joan Caylà Buqueras

- The groups led by Jordi Figuerola and Cristina Rius have analysed the risk of introducing Zika, Dengue and Chikungunia viruses in Barcelona from imported cases. There has also been an analysis of the virulence of four different lines of the West Nile virus using mice as animal model and of the importance for communicating different zoonotic pathogens because of the feeding preferences of different species of mosquitos and culicoids.
- Carmen Muñoz's group in cooperation with the one led by Ángela Domínguez have developed a fast-diagnosis protocol based on a point of care molecular technique for the microbiological confirmation of influenza cases in under one hour (validity comparable to that of traditional molecular tests). The Spidnet Project is also worthy of mention: effectiveness of the 13-valent vaccine (Lancet Respiratory Medicine), and innovation in rapid non-invasive diagnosis of S. pneumoniae using the quantification of DNA in nasopharyngeal aspiration (*Plos One*). The article on the recent outbreak of enterovirus A71 is noteworthy.

Biological and Behavioural Determinants in the Contraction and Spread of Communicable Diseases in Vulnerable Populations

Coordinator: Jordi Casabona Barbarà

- Closing meeting of the MEISI Project. "Changes in health and healthcare of the immigrant population and vulnerable populations in a crisis context" PI: J. Casabona (P13/01962) (participation of J. Casabona and C. Rius's groups).
- Presentation of a diptych "Synthesis of results of the MEISI project. Immigration and health in the context of economic crisis in Spain" (available on the programme's web page).
- Implementation of the project entitled "Work, immigration and health in a cohort of immigrant population in Spain" (PI14/01146) PI: E Ronda (participation of L. de la Fuente, J. Casabona, F. G. Benavides groups).
- Implementation of SWEETIE Project "Study of prevalence of the virus of human papilloma and other sexually transmitted diseases and study of their determinants in male and female sex workers" PI: S. Sanjosé (participation of A. Moya, J. Casabona, F. Baquero and M.E. Alemany's Groups).
- Implementation of the project entitled "Study of diet habits and health in general of the Chinese population resident in Santa Coloma de Gramenet" PI: L Ferrer (participation of J. Casabona and F. G. Benavides's groups).
- Implementation of the HepCdetect II project entitled "Development and viability of strategies alternative to screening for detecting active infection by the hepatitis C virus in risk and difficult access groups PI: E. Martró (PI 15/00284) (J. Casabona's group)
- Implementation of the project entitled "New outreach approaches for the early diagnosis of active HCV infection and the description of the HCV transmission dynamics among PWID in Catalonia" PI: E. Martró. (GLD16-00135) (J. Casabona's group)
- Implementation of the project entitled "Molecular biology of HIV to characterise the source of these infections and their determinants in uses of drugs by parenteral administration and men who have sex with men" PI: E. Martró (participation of A. Moya and J. Casabona's groups).

- Implementation of the Project entitled "Evaluation of the feasibility of a transcontinental study on mother-child microbial transmission in a local population of Latin-American countries" (participation of A. Moya and E. Calderón's groups).
- Design of a strategy for communication and dissemination of the DAPET programme.
- Articles published in the framework of PELFI. Platform of Longitudinal Studies on Immigrating Families:
  - Hernado C, et al. Facilitators and barriers of participation in a longitudinal research on migrant families in Badalona (Spain): A qualitative approach. *Health Soc Care Community* 2017.
  - Hernando C, et al. Facilitators of participation and implementation of the PELFI subcohort of immigrant families. *Gac Sanit* 2017.
  - Cayuela A, et al. PELFI project: recruitment and socio-demographic characteristics of immigrant and local families of the subcohorts of Alicante and Barcelona *Rev Esp Salud Pública* 2017.

Other articles:

- Saludes et al. Community-based screening of hepatitis C with a one-step RNA detection algorithm from dried-blood spots: Analysis of key populations in Barcelona, *Spain J Viral Hepat* 2017.
- Reyes-Ureña et al. Differences between migrants and Spanish-born population through the HIV care cascade, Catalonia: an analysis using multiple data sources. *Epidemiol Infect* 2017.

Papers presented at congresses:

- *XXXV Reunión de la Sociedad Española de Epidemiología*.
- Hepatitis-C Communty Summit 2017.
- *II Congreso Nacional del Grupo de Estudio de las Hepatitis 2017*.
- 6th International Symposium on Hepatitis Care in Substance Users 2017.

Social determinants of health

Coordinator: Mª José López Medina*

With regard to international projects, researchers in programme 4 have taken part in different European projects, either as investigator, leader of Workpackage or PI. These projects are:

- "*Science and technology in childhood obesity policy*" (STOP);
- "*European Human Biomonitoring Iniciative*" (HBM4EU);
- "*Tackling secondhand smoke in Europe: assessment of SHS exposure according to policies, attributable disease and economic burden, and impact of interventions for reducing the exposure*";
- "*Lights, camera and action against dating violence*";
- "*Participatory Urban Living for Sustainable Environments*" (PULSE);
- "*Pan-European Urban Climate Service*" (PUCS);
- and "*Gender Specific mechanisms in coronary artery disease (CAD) in Europe*".

A large number of projects are furthermore under way nationwide, either Projects of the Fondo de Investigación Sanitaria (FIS), Instituto de Salud Carlos III or projects obtained in other competitive calls:

- "Care patterns and factors associated with ageing of the population in the survival of acute lymphatic leukaemia";
- "Association between energy poverty and health";
- "Exposure to environmental tobacco smoke in those under 12 years of age: estimation of the prevalence and measurement of markers in homes and vehicles";
- "Influence of social determinants, lifestyles, emotional welfare and use of non-conventional therapies in the evolution of breast cancer in a cohort of diagnosed women in Barcelona";
- "Evaluation of a project for integral prevention of child obesity in the pre-school stage in Barcelona (POIBA-2nd phase)";
- "Evaluation of the Treball als Barris" action;
- "Socio-economic and environmental inequalities in the geographical distribution of mortality in Andalusia (MEDEA3)";
- "Technological innovation of healthcare "e-salud" and auto-management for pluri-pathological patients" (EFRAILE);
- "Interventions for promoting active and healthy ageing in work centres";
- "Design and evaluation of the effectiveness of a selective prevention intervention on alcohol and cannabis consumption in vulnerable young people in the community sphere";
- "Partner violence in the couple among young people in Spain: epidemiological, impact on health, accessibility and use of socio-healthcare services against gender violence";
- and "Fast hepatitis C test in men who have sex with men: knowledge, prevalence and implications for screening in negative HIVs."

* Until December the Coordinator was Antonio Daponte Codina

It should be stressed that in 2017 different theses directed by investigators from the diverse Groups in programme 4 were defended. There were numerous scientific publications (over 150 articles), including such noteworthy items such as the letter in the Lancet and an original in BMJ. Results have also been disseminated by other channels, such as publication of books, chapters or videos summing up the main conclusions of some projects.

Epidemiology and prevention in environmental and employment health

Coordinator: Adonina Tardón García

In the Childhood and Environment Project (INMA cohort) in 2017, we carried out visits to the boys and girls of 11-12 years of age. In all, we visited roughly 2000 children who were given different physical examinations and we compiled information on different exposures and lifestyles, in cohorts of Asturias, Guipuzcoa, Granada, Minorca, Sabadell and Valencia.

We also published findings with regard to air contamination and development of the brain, such as prenatal exposure and worse attention function in childhood and identification of iron as a neuro-toxic element of air contamination. These findings were complementary to the association observed between exposure to green areas and an improvement of the attention function in childhood.

Exposure to new contaminants such as perfluorinated substances during pregnancy were associated with a greater risk of metabolic syndrome and intolerance to glucose in childhood, but not with a greater risk of obesity. We have communicated the low prevalence of appropriate levels of vitamin D in pregnant women and boys and girls in this country and finally we informed that 20% of the children with obesity at 4 years of age already also display cardiovascular atherogenic indices with the future repercussions that this could represent.

We have carried out mechanistic studies helping to understand the pathogenic role of endocrinal disruptors and their interaction with the genome and their effects on children's health.

We carried out the recruitment and monitoring of over 1000 individuals in the PREDIMED+DM project to determine the effect of an intensive loss of weight based on a pattern of traditional hypocaloric Mediterranean diet, physical activity and behavioural therapy against advice on this diet in the context of usual healthcare, on the incidence of primary cardiovascular events and DM2 at 6 months, one and two years of age.

In lung cancer and in the framework of the CAPUA study and the ILCCO consortium, we have made known that the individual's socio-economic level is a risk factor independent from smoking for developing lung cancer, we have communicated the existence of two new SNPs which seem to possibly be candidates for screening lung cancer and we have proven that gene-smoking interactions play a major role in the aetiology of this disease, as well as intervening in the part of its unknown inheritability.

Evaluation of healthcare services

Coordinator: Jordi Alonso Caballero

Continuous Cohort of Employment Records (MCVL): Financed for a further three-year period 2018-2020 (FIS PI17/00220), this has included the data for 2014, 2015 and 2016. The agreement signed by the INE, the Social Security and the UPF will enable learning the causes of death of the over 90,000 deceased from the members included in the MCVL scheme. The analysis of the association between employment careers and mortality will enable quantifying the impact of the labour market and health.

BiblioPRO: 3200 new users were registered (13,019 accumulated users) 360 new PRO (Patient-Reported Outcomes) questionnaires were identified, reaching the point of having over 1600 instruments available. The III Jornada Científica BiblioPRO was held (Madrid, 23 February 2017) with over 100 persons enrolled for it. Members of the scientific committee gave the course on "Development and Use of EMPRO for the standardised assessment of PRO measures". The FIS research project on "Application of PRO instruments in Spain" was got under way.

Victoria Serra (AQuAS). Has taken part in projects for assessment of complex interventions on the chronicity, integrated/coordinated care or tele-care (Act on Scale, Act on Dementia, mRESIST). She has continued with the line of work and teaching in the framework of the International School of Impact Assessment. We should highlight the publication in the Stroke journal with data from the online information system for ischaemic strokes in Catalonia, which combines clinical epidemiology and assessment of effectiveness in clinical practice.

Jordi Alonso (IMIM). In the most extensive meta-analysis performed until now on adolescents and young adults, the group quantified the importance of violence in childhood (abuse, harassment, partner and community) as a risk factor in suicidal conduct as well as the greater risk in the LGBT population. Researchers from this group take part as coordinators in Spain of the international study financed by Movember Foundation, "TrueNTH Global Registry – Prostate Cancer Outcomes" in which 12 countries take part and which is now in its second year of recruitment and follow-up.

Fernando G. Benavides (CISAL-IMIM/UPF). Based on the Surveys of Employment and Health Conditions (ECTS) of Colombia, Argentina, Chile, Panama, Nicaragua, El Salvador, Honduras, Guatemala, Costa Rica and Uruguay, the prevalence of exposure to ergonomic (repetitive movement) hygiene (noise) and psychosocial risks (demand) was calculated for the first time. This enables a better grasp of occupational health and could act as a basis for supervision of work and health in the region.

Antonio Serrano (PSSJD). Investigators in the group estimated the costs of non-initiation of medications and the impact of co-payment on this conduct. The evidence on the effectiveness of anti-depressants as compared with active monitoring in primary care was reviewed. The episodes of agitation, their interventions and their costs at a mental health hospital were also typified. Finally, the group organised the 11th Course on Economic Evaluation and Socio-healthcare policy at the Loyola Andalucía University, in cooperation with *King's College of London* and the *London School of Economics and Political Science*.

Clinical Epidemiology

Coordinator: José Ignacio Pijoán Zubizarreta

In 2017 two collaborative studies were published in the Clinical Epidemiology Programme:

- The first used geospatial analysis techniques to describe the differences in nutritional habits between different Spanish regions and associated these with differences in the prevalence of cardiovascular disease:
  Gómez de la Cámara A, De Andrés Esteban E, Urrútia Cuchí G, Calderón Sandubete E, Rubio Herrera MÁ, Menéndez Orenga M, Lora Pablos D. Variability of nutrients intake, lipid profile and cardiovascular mortality among geographical areas in Spain: The DRECE study. *Geospat Health*. 2017 nov 7;12(2):524. doi: 10.4081/gh.2017.524. PubMed PMID: 29239557.
- The second of these presented additional data on the EMPARO clinical cohort on patients with vesical cancer from seven hospitals, describing the clinical situation on diagnosis, the time intervals between the first symptoms and diagnosis and between diagnosis and treatment. It has also explored the effect of different healthcare circuits on some of these intervals. The results reflect the great organisational variability between centres and healthcare areas in the treatment of this pathology:
  Bonfill X, Martínez-Zapata MJ, Vernooij RWM, Sánchez MJ, Morales Suárez-Varela M, De la Cruz J, Emparanza JI, Ferrer M, Pijoan JI, Palou J, Schmidt S, Madrid E, Abraira V, Zamora J on behalf of the EMPARO-CU study group Clinical interval and diagnostic characteristics in a cohort of bladder cancer patients in Spain: a multicenter observational study. *BMC Research Notes*. 201710:708 https://doi.org/10.1186/s13104-017-3024-8

As a result of the cooperation between the Centro Cochrane Iberoamericano and our own programme, the "Jornadas sobre las Revisiones Sistemáticas para la práctica clínica y la investigación" were held, with the participation of researchers from almost all the groups in the programme. In these sessions there was a significant reflection on the current situation of systematic reviews, as a design of research and a tool for transfer of scientific knowledge to practice. Progress was also made in methodological, logistic, usage etc. considerations of new categories of SR such as review with indirect comparisons, qualitative reviews or on specific therapeutic categories such as mental health or physiotherapy.

We can lastly stress that as part of the MAPAC (Improvement of Adaptation of Healthcare and Clinical Practice) sub-programme, a major step forward has been made for establishing a network of synergies between the different MAPAC Committees which are being set up at a large number of National Health (SNS) centres. This is being done through a project in the programme entitled "Study for evaluation of the degree of agreement on the recommendations published in the Diana Salud portal", which gave information on the knowledge of healthcare professionals in management jobs in around twenty hospitals and areas of primary care of the existence of sources of information and recommendation of the suitability of practices and on their degree of agreement with a set of specific recommendations for their healthcare and organisational area of responsibility. At present the first cooperative publication on the results of the study is being published. A large number of the MAPAC type initiatives are surely going to be fostered on a local or cooperative scale, in a strategy for translation of knowledge.

Training Program

Coordinator: Beatriz Pérez-Gómez

This year the Training Programme has maintained its two basic lines of action: mobility and improvement.

In 2017 the categories of mobility grants, created to encourage cooperation of CIBERESP researchers with each other and with other groups, have been maintained. These grants are intramural, meaning that they are intended exclusively for personnel contracted or attached to CIBERESP. On the national level, three calls have been held, offering a total number of 16 grants for short stays at CIBERESP groups and four grants for short stays at other Spanish research groups not in the CIBERESP. International mobility has also been furthered. On one hand the three grants for 3-month stays that CIBERESP traditionally calls to enable its doctorate students to get the international mention have been maintained; there was also a call for three grants for international stays to promote the professional development of its own staff contracted by CIBERESP, including post-doctoral researchers, holders of university level qualifications and medium-level technical staff. Since the grants do not cover the whole cost of the stay, and there was sufficient budget, this year there was also a special call for supplementary assistance for this CIBERESP staff abroad.

Grants for improvement are extramural, meaning that they are open to researchers from outside the CIBERESP, and seek to promote quality research into Public Health. They are also a good tool for furthering cooperation with other CIBER areas. In 2017 the existing agreement with CIBEROBN was extended to the CIBERDEM to cooperate in the *Meeting for Excellence in Public Health Research* which is traditionally arranged by CIBERESP. This "Encounter for Excellence in Public Health" is intended to give young scientists being trained in Epidemiology and Public Health the chance to directly debate and swap ideas on their doctoral thesis projects with scientists accredited in Public Health in an informal setting. Through this agreement, 9 of the total number of 13 grants were financed by CIBERESP, while the area of Obesity and Physiopathology of Nutrition (CIBEROBN) and that of Diabetes and Metabolic Diseases (CIBERDEM) have financed two attendance grants specifically intended for doctorands in their own fields. Once again, cooperation was highly positive, meaning that the agreement will be maintained in 2018.

Apart from this, CIBERESP also continues financing the Prize for the 10 best papers presented by young research staff at the SEE Scientific Annual Meeting, which is held jointly with the Congress of the Portuguese Epidemiology Association, or at the *Ibero-American Congress of Epidemiology and Public Health*. In its present format, this award includes a diploma and covers the cost of registering the prize winner at the meeting for the following year. The training programme also continues to promote training and scientific activities being done to establish special more favourable conditions for CIBERESP members.

Platforms

BIBLIOPRO 2017

BiblioPRO can list the following achievements in 2017:

Repository:

- **Registered users:** 3200 new users. Average in the 2013-2016 period: 2100/year (13,019 accumulated users).
- **Monthly visits:** 10,000 visits/month (doubling the figure for 2016).
- **Sub-licences:** 561 applications handled (average 400/year for 2013-2016).
- **New instruments:** 360 new PROs included (a total number of 1677 of instruments).
- **Systematic review:**
  - PUBLICATIONS 2015: review of 2418 titles, 1515 abstracts and 911 articles completed. The extraction of data was completed.
  - PUBLICATIONS 2016: review of 2400 titles, 942 abstracts and 738 articles completed. The extraction of data was started.
- **New content:** 270 technical datasheets were verified and completed based on cooperation with the authors and bibliographic review.
- **New agreements on distribution:** the commercial distribution of Computer Vision Syndrome Questionnaire (CVS-Q) was arranged and the free distribution of Diabetes Self-Care Activities Questionnaire (DSCAQ).

3rd Scientific Symposium :

- This 3rd Scientific Symposium was held on 23 February 2017, with the participation of over 100 researchers: clinical practice (30%), investigation (21%), academics (20%), companies (17%), healthcare administration (9%).

  Accredited by CCFCPS (0.6 credits). Partial sponsorship of MSD and CHIESI. Guest speakers: Sir Nick Black, (U. London), Javier Rejas (Pzifer) and Chris Gibbons (U. Cambridge). 57 papers were submitted: Oral papers at plenary sessions (10), Oral papers at parallel sessions (27) and poster (20).

Research:

- Competitive research projects::
  - One FIS was obtained on: "Application of PRO instruments in Spain: systematic review and evidence-based recommendations ". PI O. Garin and team with researchers from the CIBERESP and the Scientific Committee (PI16/00130-ISCIII-FEDER). 2017-2019.
  - The coordinated FIS on: "Evaluation of the metric advantages of the new EQ-5D-5L and reference norms" was completed. PI12/00772. M. Ferrer PI and Coordinator. FIS coordinated with 4 subprojects led by CIBERESP groups (2014-2017).
- EMPRO evaluation: on the metric properties of PROs in children's oral health. In publication.
- Collaboration in the BIBLIOINDICA project for developing a library of healthcare indictors. A joint initiative of CIBERESP and REDISSEC.

Training:

- New edition of the semi-classroom course (15 -22 February 2017) "Development and Use of EMPRO: a tool for standardised evaluation of PRO measures". Teachers from the scientific committee of BiblioPRO. Accredited by the CCFCPS (0.9 credits)

Publications 2017:

- Alonso J, Ferrer M. La medida de resultados en salud desde la perspectiva del paciente. En: Juan del Llano. Monografías de política y gestión. Resultados reportados por los pacientes (PROs). *Fundación AstraZeneca*, 2017.
- Zaror C, et al. Impact of traumatic dental injuries on quality of life in preschoolers and school-children: A systematic review and meta-analysis. *Community Dent Oral* 2017 (in press).
- Martí-Pastor M, et al.Head-to-head comparison between the EQ-5D-5L and the EQ-5D-3L in general population health surveys. *Population Health Metrics* (under review).
- Hernández G, et al. Validity of the EQ-5D new 5-level version and reference norms for the Spanish population. *Quality of Life Research* (under review).
- Hernández G, et al. Validity of the five-level new version of the EuroQol (EQ-5D-5L) in asthma patients. *Journal of Medical Internet Research* (under review).

ciberesp

Health Inequality Observatory

The Health Inequality Observatory (Spanish - ODS) is a scientific portal specialising in Health Inequalities with open and free access, forming part of programme (P4) "Social determinants of health" of the CIBERESP, and with a budget from the programme until 2017.

This digital platform was set up in 2008 as a result of a strategic objective of the CIBERESP. Right from its beginnings it was conceived as a virtual space for fostering and furthering interaction and exchange of information among researchers in the health world and between the latter and civil society. Its official page is www.ods-ciberesp.org/.

In 2015, a report[1] was drawn up in which the scope of the observatory and its users' satisfaction were evaluated for the first time. The results suggested that although the platform significantly increased its social and scientific repercussions, it also had a good deal of room for improvement in terms of usability, design and operation.

To this end a new project was got under way in 2017 with the aim of reviewing the aims of the ODS and bringing in improvement measures to enhance its functionality and sustainability, which have been covered in a prototype of the new ODS platform.

Redesigned objectives

1. To be a platform for scientific dissemination of the CIBERESP for spreading part of the production of all the groups of all the CIBERESP programmes connected with health determinants and social inequalities in health.
2. To generate areas for scientific dissemination on health determinants and social inequalities in health, with useful and differentiated information both for professionals and the general public.
3. To enhance the current design, tools and functionalities of the ODS.

Current status

The prototype of the new ODS was started up in December 2017 and consists of several spaces for complying with the redesigned objectives of the ODS:

- The scientific area for furthering interaction among researchers.
- The prominent publications area with informative format.
- The area of benchmark professionals.

We will now show the first preliminary data with regard to the scope and usage of the new ODS web portal in its first few weeks of life. The period analysed comprises from the start of its launch (12/12/2017) until last 4/01/2018. Google Analytics tool was used for this purpose.

The new ODS website has received a total number of 148 visits and 637 pages have been viewed, with 4 pages viewed per session. Around 51.4% of the visits come from direct searches and the rest are from Google searches or organic traffic (20.3%), from other reference web portals such as CIBERESP (15.5%) and searches on social networks (12.2%). By geographical area, most of the visits to the ODS come from Spain (53.38%) and almost one third from Latin American countries.

1. Sánchez E, López MJ, García-Continente X, Artazcoz L, Borrell C. Evaluation report of the Observatory on Health Inequalities. Barcelona: CIBERESP; 2015.

Scientific Production

PUBLICATIONS

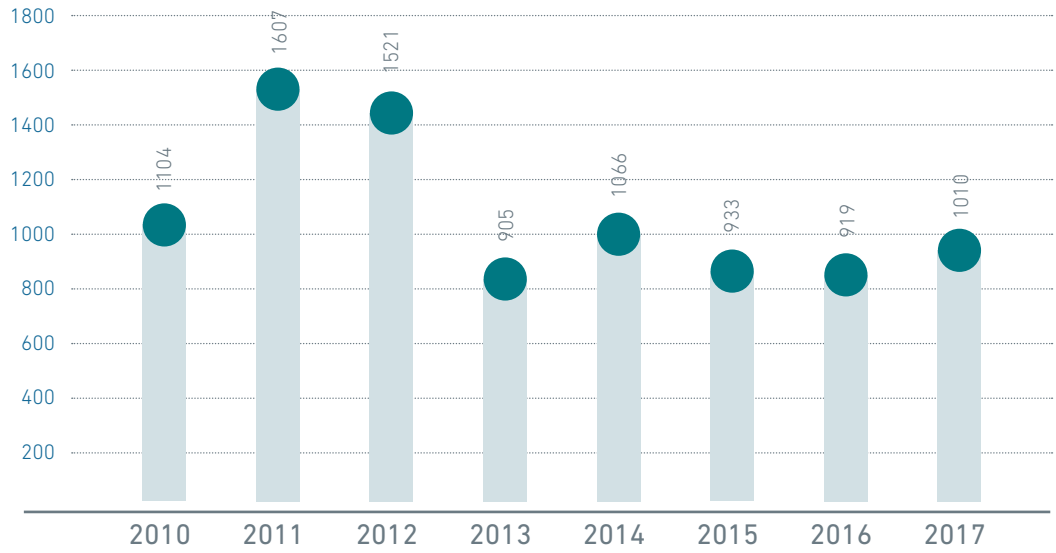
No. of publications in 2017

TOTAL	**1010**
Q1	619
D1	307

Collaboration work

IntraCIBER	323
InterCIBER	153

Evolution of the publications



Most relevant publications of the CIBERESP in 2017 by impact factor

Publication	Impact Factor
NCD Risk Factor Collaboration (NCD-RisC), Marrugat de la Iglesia Jaume, Vioque López Jesús, Ibarluzea Maurolagoitia Jesús, Porta Serra Miquel, Domínguez García Ángela et al. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. *Lancet* (London, England). 2017.	47,8310
Devereaux P.J., Biccard B.M., Sigamani A., Xavier D., Chan M.T.V., Srinathan S.K. et al. Association of postoperative high-sensitivity troponin levels with myocardial injury and 30-day mortality among patients undergoing noncardiac surgery. *JAMA - Journal of the American Medical Association*. 2017;317(16):1642-1651.	44,4050
Gatta G., Capocaccia R., Botta L., Mallone S., De Angelis R., Ardanaz E. et al. Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet—a population-based study. *The Lancet Oncology*. 2017;18(8):1022-1039.	33,9000

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Publication	Impact Factor
Lotta L.A., Gulati P., Day F.R., Payne F., Ongen H., Van De Bunt M. et al. Integrative genomic analysis implicates limited peripheral adipose storage capacity in the pathogenesis of human insulin resistance. *Nature Genetics*. 2017;49(1):17-26.	27,9590
Phelan C.M., Kuchenbaecker K.B., Tyrer J.P., Kar S.P., Lawrenson K., Winham S.J. et al. Identification of 12 new susceptibility loci for different histotypes of epithelial ovarian cancer. *Nature Genetics*. 2017;49(5):680-691.	27,9590
McKay J.D., Hung R.J., Han Y., Zong X., Carreras-Torres R., Christiani D.C. et al. Large-scale association analysis identifies new lung cancer susceptibility loci and heterogeneity in genetic susceptibility across histological subtypes. *Nature Genetics*. 2017;49(7):1126-1132.	27,9590
Degenhardt L., Glantz M., Evans-Lacko S., Sadikova E., Sampson N., Thornicroft G. et al. Estimating treatment coverage for people with substance use disorders: an analysis of data from the World Mental Health Surveys. *World Psychiatry*. 2017;16(3):299-307.	26,5610
Byrne K.S., Castano J.M., Chirlaque M.D., Lilja H., Agudo A., Ardanaz E. et al. Vasectomy and prostate cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Journal of Clinical Oncology*. 2017;35(12):1297-1303.	24,0080
Sordo L., Barrio G., Bravo M.J., Indave B.I., Degenhardt L., Wiessing L. et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ (Clinical research ed.)*. 2017;357:j1550.	20,7850
Moral S., Cuellar H., Avegliano G., Ballesteros E., Salcedo M.T., Ferreira-Gonzalez I. et al. Clinical Implications of Focal Intimal Disruption in Patients with Type B Intramural Hematoma. *Journal of the American College of Cardiology*. 2017;69(1):28-39.	19,8960

CIBERESP Groups. Publications

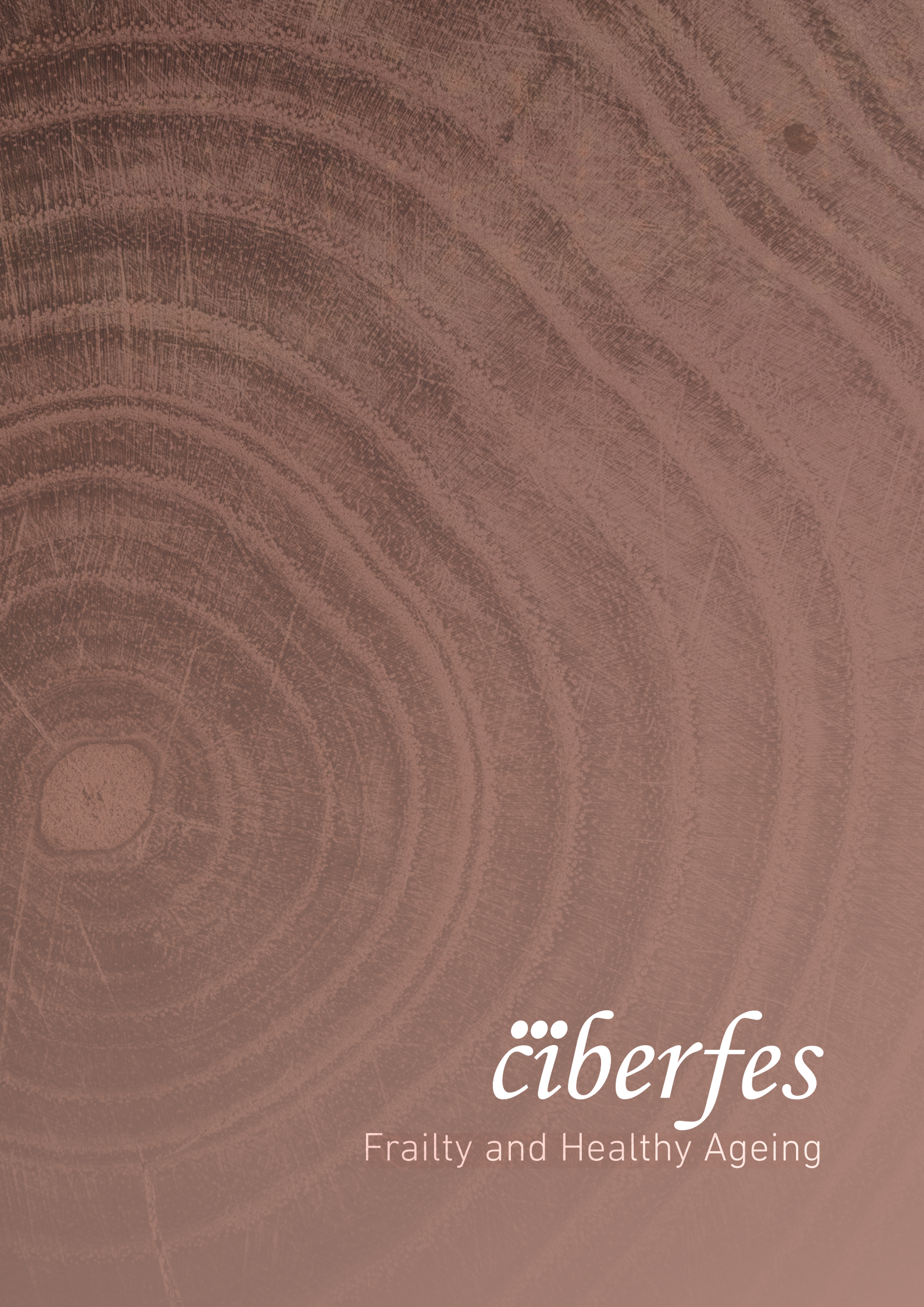
Group Leader	Total Publications	Q1	D1	Institution	Province
Alemany Vilches, Mª Eulalia[1]	23	13	4	Instituto Catalán de Oncología	Barcelona
Alonso Caballero, Jordi	29	24	18	Consorci Mar Parc Salut de Barcelona	Barcelona
Baquero Mochales, Fernando	30	20	12	Servicio Madrileño de Salud - Hospital Ramón y Cajal	Madrid
Bolumar Montrull, Francisco	28	24	8	Universidad de Alcalá - Facultad de Medicina	Madrid
Bonfill Cosp, Xavier	64	37	25	Instituto de Investigación del Hospital de la Santa Creu i Sant Pau	Barcelona
Borrell Thió, Carme	55	20	7	Agencia de Salud Pública de Barcelona	Barcelona
Bueno Cavanillas, Aurora	22	13	4	Universidad de Granada	Granada
Calderón Sandubete, Enrique José	14	5	3	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Hospital Virgen del Rocío	Sevilla
Casabona Barbara, Jordi	26	12	4	Fund. 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	104	71	30	Instituto de Salud Pública de Navarra	Navarra

Group Leader	Total Publications	Q1	D1	Institution	Province
Chirlaque López, María Dolores[2]	113	81	38	Fund. para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS) - Dirección General de Salud Pública	Murcia
Daponte Codina, Antonio	10	3	1	Escuela Andaluza de Salud Pública	Granada
Delgado Rodríguez, Miguel	30	21	5	Universidad de Jaén - Facultad de Ciencias de la Salud	Jaén
Domínguez García, Ángela	16	10	4	Universidad de Barcelona - Facultad de Medicina	Barcelona
Echevarría Mayo, Juan Emilio	4	2	2	Instituto de Salud Carlos III - Centro Nacional de Epidemiología	Madrid
Emparanza Knörr, José Ignacio	6	3	2	Asociación Instituto Biodonostia - Hospital Donostia	Guipúzcoa
Ferreira González, Ignacio	7	5	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR) - Hospital Vall d´Hebron	Barcelona
Figueiras Guzmán, Adolfo[3]	27	14	5	Universidad de Santiago de Compostela - Facultad de Medicina	A Coruña
Figuerola Borras, Jordi	10	6	2	Agencia Estatal Consejo Superior de Investigaciones Científicas - Estación Biológica de Doñana	Sevilla
Fuente Hoz, Luis de la	35	17	6	Instituto de Salud Carlos III - Centro Nacional de Epidemiología	Madrid
García Benavides, Fernando	12	5	1	Universidad Pompeu Fabra	Barcelona
Gómez de la Cámara, Agustín	15	10	4	Servicio Madrileño de Salud - Hospital Universitario 12 de Octubre	Madrid
Ibarluzea Maurolagoitia, Jesús	90	80	42	Asoc. Inst. Biodonostia - Subdirección de Salud Pública de Guipuzkoa	Guipúzcoa
Íñiguez Hernández, Carmen[4]	43	32	22	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	Valencia
Kogevinas, Emmanouil	136	114	65	Fund. Privada Instituto de Salud Global Barcelona (ISGlobal) - Campus Mar	Barcelona
Larrauri Cámara, Amparo	31	18	10	Instituto de Salud Carlos III - Centro Nacional de Epidemiología	Madrid
López Medina, María José	22	10	4	Agencia de Salud Pública de Barcelona	Barcelona
Lumbreras Lacarra, Blanca[5]	12	9	6	Universidad Miguel Hernández	Alicante
Marcos Dauder, Ricard	14	7	4	Universidad Autónoma de Barcelona	Barcelona
Martí Puig, Eulalia[6]	4	3	1	Universidad de Barcelona	Barcelona
Menéndez Santos, Clara	16	13	4	Hospital Clínic de Barcelona	Barcelona

Group Leader	Total Publications	Q1	D1	Institution	Province
Morales Suárez-Varela, María Manuela	18	4	1	Univ. de Valencia - Facultad de Medicina	Valencia
Moreno Aguado, Víctor	20	16	5	Instituto Catalán de Oncología	Barcelona
Moya Simarro, Andrés	25	12	4	Univ. de Valencia - Facultad de Medicina	Valencia
Muñoz Almagro, María Carmen	16	13	6	Fundación para la Investigación y Docencia Sant Joan de Deu - Hospital Sant Joan de Deu	Barcelona
Olea Serrano, Nicolás	22	17	11	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) - Hospital Clínico San Cecilio	Granada
Pollán Santamaría, Marina	41	33	11	Instituto de Salud Carlos III - Centro Nacional de Epidemiología	Madrid
Porta Serra, Miquel	12	6	2	Consorci Mar Parc Salut de Barcelona	Barcelona
Rius Gibert, Cristina[7]	12	5	1	Agencia de Salud Pública de Barcelona	Barcelona
Rodríguez Artalejo, Fernando	42	29	11	Universidad Autónoma de Madrid	Madrid
Rodríguez Farre, Eduard	3	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas - Instituto de Invest. Biomédicas de Barcelona	Barcelona
Ruiz Pérez, Isabel	19	10	4	Escuela Andaluza de Salud Pública	Granada
Sáez Zafra, Marc	10	3	0	Universidad de Girona	Girona
Sánchez Pérez, María José	77	50	20	Escuela Andaluza de Salud Pública	Granada
Schröder, Helmut	23	15	4	Consorci Mar Parc Salut de Barcelona	Barcelona
Serra Sutton, Victoria[8]	9	4	3	Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS)	Barcelona
Serrano Blanco, Antonio	12	7	0	Fundación para la Investigación y Docencia Sant Joan de Deu - Parc Sanitari Sant Joan de Deu	Barcelona
Sunyer Deu, Jordi	118	100	66	Fund. Privada Instituto de Salud Global Barcelona (ISGlobal) - Campus Mar	Barcelona
Tardón García, Adonina	57	39	17	Univ. de Oviedo - Facultad de Medicina	Asturias
Zamora Romero, Javier	25	16	12	Servicio Madrileño de Salud - Hospital Ramón y Cajal	Madrid
Amo Valero, Julia del*	-	-	-	Instituto de Salud Carlos III - Centro Nacional de Epidemiología	Madrid

* Grupo asociado CIBERESP

1 M.E. Alemany replaces Silvia Sanjosé.
2 M.D. Chirlaque replaces Carmen Navarro.
3 A. Figueiras replaces Juan Jesús Gestal.
4 C. Íñiguez replaces Ferrán Ballester.
5 B. Lumbreras replaces Idelfonso Hernández.
6 E. Martí replaces Xavier Estivill.
7 C. Rius replaces Joan A. Caylà.
8 V. Serra replaces Sonia Abillera.


ciberfes
Frailty and Healthy Ageing

Scientific Director's Presentation

Leocadio Rodríguez Mañas

At the CIBER into Frailty and Healthy Ageing (CIBERFES) the basic aim of our work is to search for replies and solutions enabling improving the quality of life of the elderly. Understanding that ageing is a process that starts long before old-age, and as put forward by the WHO, means a gradual loss of intrinsic capacity in which lifestyles, environmental agents and chronic diseases all have an influence. For this reason, our main endeavours will focus on preventing disability rather than prolonging longevity, doing so by the study of the earliest stages of disability from the study of frailty.

Frailty is a syndrome characterised by the existence of alterations in several physiological systems leading to difficulty in maintaining homeostasis, causing special vulnerability to low-power stressing agents. The frailty situation precedes, and is the main risk factor of, the development of disability and for this reason has become the main objective to prevent the development of disability, not easily reversible, unlike what occurs with frailty, which can indeed be reversed.

CIBERFES also handles longevity, but from a standpoint of healthy ageing. Knowledge of its modulating factors (physiological mechanisms, harmful agents, favourable and unfavourable interventions, etc.) represent the other side of the coin of frailty.

The CIBERFES is a network cooperative structure with 20 research groups located in 18 research centres in 8 of Spain's Autonomous Communities. These Groups are structured in 2 scientific programmes; one focussing on the channels and mechanisms causing frailty and/or generating a healthy ageing process and a second one centred on the preventive or corrective measures for developing frailty. The CIBERFES groups have gathered around these two programmes depending on their common lines of work, which enables us to combine efforts, optimise resources and take the greatest advantage of the knowledge generated.

Throughout 2017 we have consolidated our structure and our organisation, and we have started to undertake the tasks required to comply with our objectives. We should thus stress taking part in a joint call with CIBERES for intramural research projects, financed by CIBERES (our budget endowment does not enable us to provide funds); we have also cooperated in the meetings of CIBERES, and CIBERDEM; we have obtained funding by co-organising a training programme as part of the EIT-Health; research contracts with industry (Abbott) have been signed for exploiting data from the Estudio Toledo database; a cooperative project has been presented with the intention of establishing a clinical cohort among the CIBERFES groups oriented at learning the impact of frailty in clinical media, its modulators and the potential interventions, and we will be taking part as CIBERFES in the next H2020 call, coordinating a proposal. Along with these main achievements, which start to develop the strategic lines, several administrative and technical meetings have been held and the next scientific meeting has been planned, to take place in early April in Barcelona. Lastly, we continue to work on establishing institutional relations with research and international healthcare policy bodies.

Scientific Programmes

Basic, clinical and environmental mechanisms associated with the development of frailty. Impact on Healthcare Systems

Coordinator: **José Viña Ribes**

In 2017 many groups from Programme 1 are seeking biomarkers, especially for the risk of frailty and risk of transition from frailty to dependency.

Study of the mechanisms for developing frailty to propose interventions

We should highlight the fact that studies that were already being carried out have taken shape at the Laboratory of Dr Bolaños, in Salamanca, where a new knock-in mouse has been generated expressing the pro-glycolitic enzyme PFKFB3 in the neurons of the central nervous system (CAMKII-Cre/PFKFB3). The behavioural characterisation of the adult CAMKII-Cre/PFKFB3-KI mouse displays motor and cognitive dysfunction, as well as being overweight and diabetic. Dr Ander Matheu's laboratory has published reviews in Aging Cell identifying molecular channels and physiopathological processes of relevance in frailty and healthy ageing.

The group led by Dr Jose A. Enríquez has published an article in Nature, Cell and Science Translational Medicines this year, in which it describes the significant modulation of the ageing process and frailty in the stocks of mice with regard to the variants of mitochondrial DNA.

Study of the mechanisms by means of which interventions may delay the appearance of frailty

Dr Viña's laboratory in Valencia has verified the effect of exercise on the delay of frailty in a model of inactive mice, publishing the protocol "A New Frailty Score for Experimental Animals based on the Clinical Phenotype: Inactivity as a Model of Frailty". A major clinical trial has been completed, publishing and getting under way the personalised and specific programme of multi-component exercises for dealing with frailty. In this same line Dr Mikel Izquierdo is working on the possibility of implementing exercise for the elderly admitted to hospital in acute units and improvement of the detection of frailty from inertia signals.

Coordinated with other CIBER groups, Dr Manuel Muñoz's group has published in Sci Rep. 2017, "SNPs in bone-related miRNAs are associated with the osteoporotic phenotype", as well as Clinical Practice Guidelines and consensus documents "Consensus document on osteoporosis in males". Endocrinol Diabetes Nutr 2018, Spanish consensus on treat to target for osteoporosis. Osteoporos Int. 2018, Recommended vitamin D levels in the general population. Endocrinol Diabetes Nutr. 2017, Recommendations on the effect of antidiabetic drugs in bone.

Dr Cristina Andrés-Lacueva and her team have created software (MySQL) enabling inserting nutritional information from food questionnaires to estimate the nutrients and bioactive compounds by means of food composition tables complementary to those of USDA and Phenol Explorer.

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

Coordinator: Adolfo Díez Pérez

In 2017 CIBERFES Programme 2 underwent a transformation process from the RETICEF structure with additions and replacement of clinical groups. For all these reasons the achievements in 2017 involve initiatives and projects stemming from RETICEF, as well as reformulating a cooperative strategy for interaction between clinical groups and with basic groups.

The Toledo Study of Healthy Aging-TSHA has developed new tools for measuring frailty, has worked on interventions based on physical exercise and has extended its analysis of biological samples of the cohort in genetics and other omics. All of this was done in collaboration work with other groups from the CIBERFES and external groups. Another of the cohort studies in Albacete developed a precision tool for measuring the walking test in the frail population. The group of the Universidad Pública de Navarra has developed its studies on the effect of physical activity in joint projects with other CIBEFES groups. A cohort study has been structured in Donostia in parallel with the basic work that they had been doing. Two endocrinology groups, in Granada and Córdoba, have developed research into general and bone frailty. Progress has also been made in basic healthcare problems in frail patients such as dysphagia, pain or falls and improving circadian health in cooperation between the nursing groups from the ISCIII, and groups from Murcia and Granada. The studies on impact and intervention on nutrition and metabolomics on frailty of the Barcelona nutrition group are another of the endeavours under way.

In the bone frailty area as one of the components of the syndrome, big data studies have been completed to detect developments and clinical profiles associated with frailty led by one of the incorporated groups for primary healthcare in Barcelona. Genomic studies of association with fractures have also been carried out, as well as the discovery of a new genetic variant associated with serious complications of bone treatments. In all these studies the Barcelona groups have taken part in cooperation with several CIBERFES groups and in cooperation with groups from other CIBERs.

As could be expected from clinical groups, different CIBERFES components have taken an active part in drawing up national and international clinical guidelines on the frailty syndrome and other specific aspects of this. Clinical tests on pharmacological intervention have also been carried out.

All these elements are reflected in the large number of publications of impact created by the CIBERFES groups, a significant percentage of which are cooperative publications. This is doubtlessly the crucial evaluative element of the research generated by the Programme.

One of the main aspects of 2017 was the planning of a multicentre prospective clinical cohort to analyse frailty records and factors affecting its development, as well as creating a national biobank. The data is based on a frailty scale developed at CIBERFES. The clinical groups are therefore structured, and the foundations laid for their interaction with basic groups.

Training Programme

Coordinator: Pedro Abizanda Soler

At the CIBERFES, the training programme has the basic aim of promoting its researchers' training and consolidating their professional careers. For this reason, we got under way the programme by means of an open call system of grants to CIBERFES researchers to finance or co-finance national or international stays, preferably within the same area.

Priority in these grants is given to applications for stays at CIBERFES groups which are carrying out a project with the applicant's original CIBERFES Group. The applications for extramural mobility grants must include justification of transversal interest for other CIBERFES groups and their research programmes.

Other activities apart from this have been carried out, such as taking part in the *X Jornadas de Formación de CIBERES* on 19 and 20 October 2017, this being the first occasion when a joint session has been held at these sessions.

The encounter enabled publicising the research lines, the research work and the resources available of the groups and allowed inter-relations between its younger researchers from the two thematic areas. Different subjects were dealt with by means of over 15 oral papers and around 50 posters, such as the exhaustion of stem cells as promoters of frailty; the relationship between sarcopenia and frailty in the Toledo Study for Healthy Ageing; the validation of nutritional biomarkers for a better understanding of frailty phenotypes or the association between diabetes mellitus type 2, hip fractures and mortality after hip fractures.

As regards the relationship between healthy ageing and sport a proposal for a mixed protocol in cardiopulmonary exercise tests for the elderly with COPD was presented; a controlled randomised test of an intervention on exercise to enhance functional capacity in the very elderly in hospital, the effects of the multi-component programme on exercises for functional capacity and cognition in weak hospitalised patients, as well as the effectiveness of the Otago Exercise programme given as group training as compared with personalised training in adults from 65 to 80 years of age.

Furthermore in 2017 the draft for starting the Continuing Training in Geriatrics and Gerontology Programme was prepared, directed by professors Jose Viña and Leocadio Rodríguez Mañas and sponsored by the CIBERFES. This will consist of 11 training sessions to be given at the *Real Academia de Medicina de la Comunidad Valenciana (RAMCV)*, with the aim of giving the first programme coordinated by the RAMCV and CIBERFES, on Continuing Training in Geriatrics and Gerontology, a training and teaching activity seeking to inter-relate basic research with practical healthcare applications. This ongoing training is intended preferably for medical professionals in family and community medicine, but also for doctors from other specialities and in general for healthcare professionals devoting their careers to care for the elderly.

It is intended to provide tools and knowledge on basic Biogerontology and Clinical Geriatrics to be able to make an evaluation of the elderly patient, thus promoting healthy ageing and setting back the onset of frailty and its transition to dependence.

The students have to come into greater contact with the basics and methods of geriatric care, the concept of frailty and ageing, as well as tackling functional valuation criteria of special interest in the development of their profession. They must understand the need to develop healthcare models for quality of life.

One important aim of the course will be to initiate those attending in the basic concepts and stages of ageing so that they can critically appraise and properly construe a frailty situation as a stage preceding dependence. They will also learn the biological bases of ageing and the social conditioning factors of dependency in the elderly.

The two general lines of work will be:

- Basic and environmental mechanisms associated with the development of frailty.
- Tackling frailty from the standpoint of geriatric practice. Detection, screening, diagnosis and treatment. Healthcare models.

Scientific Production

PUBLICATIONS

No. of publications in 2017

TOTAL → **213**

Q1 → 120

D1 → 52

Collaboration work

IntraCIBER → 30

InterCIBER → 61

Most relevant publications of the CIBERFES in 2017 by impact factor

Publication	Impact Factor
Roca-Ayats N., Balcells S., Garcia-Giralt N., Falco-Mascaro M., Martinez-Gil N., Abril J.F. et al. GGPS1 mutation and atypical femoral fractures with bisphosphonates. New England Journal of Medicine. 2017;376(18):1794-1795.	72,406
Bayliss L.E., Culliford D., Monk A.P., Glyn-Jones S., Prieto-Alhambra D., Judge A. et al. The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study. The Lancet. 2017;389(10077):1424-1430.	47,831
Perales M., Artal R., Lucia A. Exercise during pregnancy. JAMA - Journal of the American Medical Association. 2017;317(11):1113-1114.	44,405
Guaras A.M., Enriquez J.A. Building a Beautiful Beast: Mammalian Respiratory Complex I. Cell Metabolism. 2017;25(1):4-5.	18,164
Duparc T., Plovier H., Marrachelli V.G., Van Hul M., Essaghir A., Stahlman M. et al. Hepatocyte MyD88 affects bile acids, gut microbiota and metabolome contributing to regulate glucose and lipid metabolism. Gut. 2017;66(4):620-632.	16,658
Cordtz RL, Hawley S, Prieto-Alhambra D, Højgaard P, Zobbe K, Overgaard S et al. Incidence of hip and knee replacement in patients with rheumatoid arthritis following the introduction of biological DMARDs: an interrupted time-series analysis using nationwide Danish healthcare registers. Annals of the rheumatic diseases. 2017.	12,811
Merino-Azpitarte M., Lozano E., Perugorria M.J., Esparza-Baquer A., Erice O., Santos-Laso A. et al. SOX17 regulates cholangiocyte differentiation and acts as a tumor suppressor in cholangiocarcinoma. Journal of Hepatology. 2017.	12,486
Matesanz N., Bernardo E., Acin-Pérez R., Manieri E., Perez-Sieira S., Hernandez-Cosido L. et al. MKK6 controls T3-mediated browning of white adipose tissue. Nature Communications. 2017;8(1).	12,124
Rahim I., Djerdjouri B., Sayed R.K., Fernandez-Ortiz M., Fernandez-Gil B., Hidalgo-Gutiérrez A. et al. Melatonin administration to wild-type mice and nontreated NLRP3 mutant mice share similar inhibition of the inflammatory response during sepsis. Journal of Pineal Research. 2017;63(1).	10,391

Publication	Impact Factor
Mendivil-Perez M., Soto-Mercado V., Guerra-Librero A., Fernández-Gil B.I., Florido J., Shen Y.-Q. et al. Melatonin enhances neural stem cell differentiation and engraftment by increasing mitochondrial function. Journal of Pineal Research. 2017;63(2).	10,391
Pera M., Larrea D., Guardia-Laguarta C., Montesinos J., Velasco K.R., Agrawal R.R. et al. Increased localization of APP-C99 in mitochondria-associated ER membranes causes mitochondrial dysfunction in Alzheimer disease. EMBO Journal. 2017;36(22):3356-3371.	9,792

Clinical Guides

National

- *Consensus document on osteoporosis in males. GARCIA MARTIN, ANTONIA / ROZAS MORENO, PEDRO JESUS / MUÑOZ TORRES, MANUEL*
- *Recommendations on the effect of antidiabetic drugs in bone. MUÑOZ TORRES, MANUEL / REYES GARCIA, REBECA / ROZAS MORENO, PEDRO JESUS*
- *Recommended vitamin D levels in the general population. GARCIA MARTIN, ANTONIA / MUÑOZ TORRES, MANUEL / REYES GARCIA, REBECA / ROZAS MORENO, PEDRO JESUS*

CIBERFES Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Abizanda Soler, Pedro	4	2	0	Servicio de Salud de Castilla La Mancha - Complejo Hospital General de Albacete	Albacete
Acuña Castroviejo, Darío	12	7	2	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) - Hospital Clínico San Cecilio	Granada
Andrés Lacueva, María Cristina	10	6	1	Univ. de Barcelona - Facultad de Farmacia	Barcelona
Ara Royo, Ignacio	11	4	2	Universidad de Castilla la Mancha - Facultad de Ciencias del Deporte	Toledo
Bolaños Hernández, Juan Pedro	5	3	3	Fund. Inst. de Estudios de Ciencias de la salud de Castilla y León - Instituto de Biología Funcional y Genómica	Salamanca
Díez Pérez, Adolfo	25	10	1	Consorci Mar Parc Salut de Barcelona - Hospital del Mar	Barcelona
Enríquez Domínguez, José Antonio	6	6	4	Fundación Centro Nacional de Investigaciones Cardiovasculares	Madrid
García Segura, Luis Miguel	14	9	5	Ag. Estatal Consejo Superior de Invest. Científicas - Instituto Cajal	Madrid
García García, Francisco José	12	7	5	Fundación del Hospital Nacional de Parapléjicos	Toledo
Izquierdo Redín, Miguel	26	12	7	Universidad Pública de Navarra	Navarra

Group Leader	Total Publications	Q1	D1	Institution	Province
Madrid Pérez, Juan Antonio	7	5	1	Universidad de Murcia	Murcia
Matheu Fernández, Ander	9	7	4	Asociación Instituto Biodonostia - Hospital Donostia	Guipúzcoa
Molinuevo Guix, Jose Luis	2	2	2	Fundación Barcelonabeta Brain Research Center	Barcelona
Moreno Casbas, Teresa	7	1	0	Instituto de Salud Carlos III - Unidad de Investigación en Cuidados de Salud	Madrid
Muñoz Torres, Manuel	5	2	1	Fundación para la Investigación Biosanitaria en Andalucía Oriental (FIBAO) - Hospital Clínico San Cecilio	Granada
Prieto Alhambra, Daniel	24	13	3	IDIAP Jordi Gol	Barcelona
Quesada Gómez, José Manuel	18	14	5	Fundación para la Investigación Biomédica de Córdoba (FIBICO) - Hospital Universitario Reina Sofía	Córdoba
Rodríguez Mañas, Leocadio	26	16	12	Servicio Madrileño de Salud - Hospital Universitario de Getafe	Madrid
Serra Rexach, José Antonio	5	2	1	Servicio Madrileño de Salud - Hospital Gregorio Marañón	Madrid
Viña Ribes, José	20	12	5	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (INCLIVA)	Valencia

ciberobn

Physiopathology of Obesity and Nutrition

Scientific Director's Presentation

Carlos Diéguez González

It is a pleasure for me to present the Annual Report on the work done by the CIBEROBN, representing the scientific work done in the field of Obesity and Nutrition of the CIBER public consortium. 2017 was in strategic terms a special year in which the new strategic plan to be in force until 2020 was got under way. The greatest difference from the previous one was that the scientific activity focussed on two programmes, "Nutrition" and "Obesity", with the aim of achieving even greater integration among the different groups forming the CIBEROBN. To bolster this integration new instruments have been created, such as the Intramural Projects, with the following main features:

A) Each of these has researchers belonging to at least four different groups.

B) In order to foster generational takeover, half of the PIs must be investigators and not Group Leaders.

C) The subject matter tackled must be based on an innovative project and not a continuation of pre-existing collaboration work.

From a strategic standpoint, it was furthermore considered that the financing provided by the CIBER for these projects was to act as a "launching pad" to obtain preliminary results enabling these researchers to obtain external funding in a more or less immediate future. It should be stressed that the three projects selected for financing after an international evaluation involve certain features making them very appealing for different reasons: one of the projects involves getting under way a pilot project to enable transferring the experience obtained in adults in the field of PREDIMED to the prevention/treatment of obesity in early ages; another is part of the frontier research into human obesity to attempt to characterise the molecular taxonomy of the obese adipocyte in single-cell studies; the third examines the influence of the Mediterranean diet on cardiovascular risk with regard to thrombotic phenomena. It should be stressed that as well as being a clinical project, this has a molecular nutrition approach which implies a mechanistic-type tactic. These measures, which foster the integration of different CIBEROBN groups, have been accompanied by getting under way two new platforms (metagenomics and epigenetics) which have, along with the "Fatbank", generated new bonds and projects.

This report represents the work done by a total number of 33 groups from the CIBEROBN in 2017. I should like to stress the following points as regards its content:

- **Obtaining funding.** As well as continuing to be highly active in different national calls, special emphasis has been placed on obtaining funds from international sources. We ought to highlight the fact that a new NIH project has been obtained in cooperation with Harvard University on metabolomics in the PREDIMED, focussing on studying subjects with cardiovascular events. Financing was also obtained for a Horizon 2020 Project coordinated by the CIBEROBN (EU-Project H2020-SFS-2016-2): Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviours. Eat2beNICE.
- **Publications.** An outstanding level of scientific production has been achieved. Although the total number of publications has remained relatively stable (>500), it is notewor-

thy that there has been a significant 25% increase in the number of articles in D1, which is correlated with an increase in the total FI. This shows that the CIBEROBN is becoming consolidated as one of the European organisations with greatest scientific production in the field of obesity and nutrition. Although this data is outstanding in its own right, one aspect that should not go unnoticed is the fact that this is furthermore associated with a considerable increase of almost 20% in the number of publications written in cooperation by several groups in the CIBEROBN, as well as a similar increase in interCIBER cooperation work.

- **Transfer.** The CIBEROBN has been a reference through having generated the studies responsible for having the Mediterranean Diet included as an instrument for preventing disease in the Diet Guides of different countries, including the USA. This aspect has continued to be consolidated with the participation of researchers from the CIBEROBN in different international guides/ consensus documents. We have also gone on reinforcing transfer work in the form of contracts with different national and international bodies/companies.
- **Dissemination.** We are aware of the importance of communicating the findings made by our researchers, especially the ones whose direct repercussion is a positive influence on healthy habits of the general public and obese patients in particular. The efforts made in this sector are endorsed because the CIBEROBN is the body with greatest media impact of all the ones in the CIBER structure. We should also highlight our participation in the Campaign entitled "Prevención de la Obesidad, Aligera tú vida" [Obesity Prevention, lighten your life] which is promoted by the SEEDO and coordinated by two researchers (F. Casanueva and F. Tinahones) from the CIBEROBN.

In short, 2017 has been highly satisfactory with regard to the accomplishment of the goals set in the Strategic Plan. We are quite sure that in the coming years we will attain even greater successes which will work out in an improvement of our patients' healthcare and in general in the public's quality of life.

Scientific Programmes

Nutrition Programme

Coordinator: Jordi Salas Salvadó

As well as keeping the traditional groups, the Nutrition Programme was extended with new groups which joined this from June 2017 through the new organisation of the CIBEROBN (Nutrition and Obesity) programmes established in the Strategic Plan. This programme mainly includes epidemiological research into obesity and nutrition through different types of epidemiological studies, transversal studies, cases and controls, cohorts and clinical trials. Several of these studies are being carried out with different aims and sample sizes, as well as with different degrees of national and international cooperation and public or private funding. Some interesting results are being obtained in all of these, leading to a large number of publications, collaboration work, invitations to conferences and congresses, doctoral theses, national and international awards, participations in meta-analyses and applications for new projects. Although all the studies are important we should specifically stress the progress made in the PREDIMED and PREDIMED PLUS studies, as these are the ones with the largest sample size, using a nutritional intervention design and carried out on a multi-centre basis in which most of the groups in the nutrition programme take part. Due to their design and results, we would also like to stress the SUN cohort, the CORDIOPREV study, the WAHA study and the recently begun MELIPOP study.

PREDIMED STUDY:

- In 2017 several papers (over 15) have continued to be published in the PREDIMED study with different epidemiological designs and focussing on different outcomes (Diabetes: *Am J Clin Nutr 2017*, 105:723-735; Insuficiencia Cardiaca: *Eur J Heart Fail. 2017*; Mortalidad: *Am J Clin Nutr 2017*; 105, 1297-1304). ESome particularly significant papers are those which involve an in-depth study of the mechanisms by means of which the protective effects of the Mediterranean diet work, mainly the one published in Circulation (2017; 135: 633-643) entitled "Mediterranean Diet Improves High-Density Lipoprotein Function in High-Cardiovascular-Risk Individuals: A Randomized Controlled Trial".
- Several relevant papers have also been published on metabolomics in the PREDIMED study (most of them in cooperation with Harvard University) thus contributing to explaining new mechanisms by means of which diet could modulate cardiovascular disease and its phenotypes. The following papers should be highlighted: "Analysis of the relationship between lipidomic profiles and the incidence of cardiovascular events" (Am J Clin Nutr. 2017;106:973-983); "the relationship between metabolites of the choline channel and cardiovascular events" (Am Heart Assoc. 2017); "the relationship between plasmatic concentrations of ceramides and cardiovascular disease" (Circulation, 2017; 135:2028-2040); "Relationship between concentrations of tryptophan and cardiovascular disease" (J Nutr 2017); and "Investigation of metabolomic biomarkers in the urine and their relationship with the consumption of pulses in the Mediterranean Diet" (J Proteome Res. 2017), amongst others..
- The International Symposium on "Omics" in Nutrition was arranged at Harvard University and the "Boston Nutrition Obesity Research Center" Consortium which groups together several research centres from Boston, at the Harvard School of Public Health on 30 May 2017, followed by the meeting of the NIH project on metabolomics for the PREDIMED study.

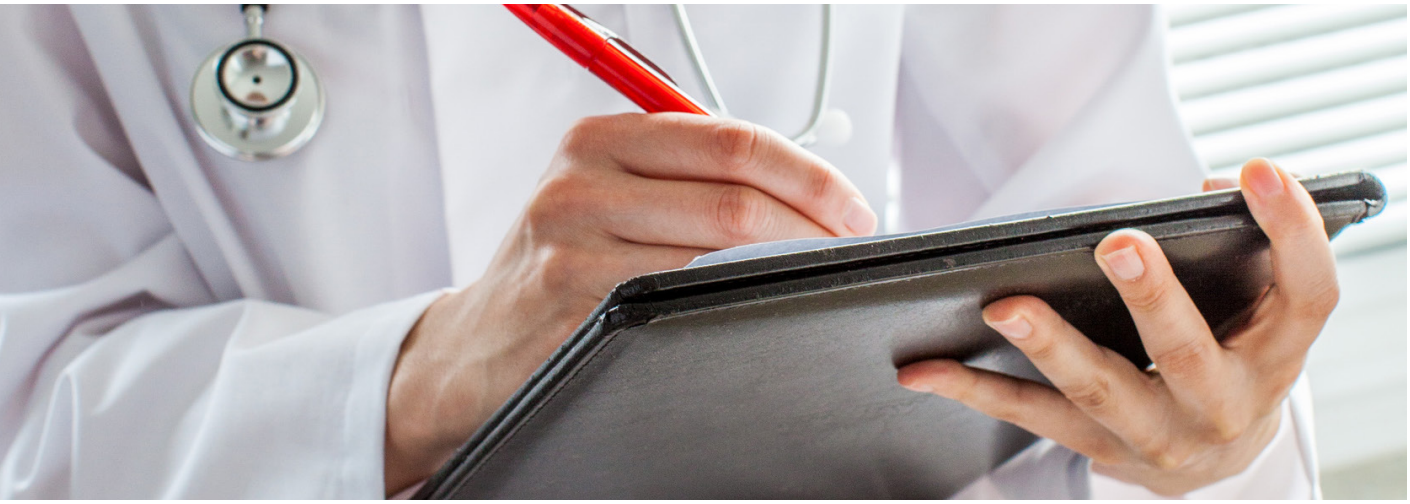
- Connected with the Mediterranean Diet, a review paper entitled: "Fruits, vegetables, and legumes: sound prevention tools" was published in the Lancet. 2017;390:2017-2018.
- The questionnaire with 14 points for adherence to the Mediterranean Diet validated and used in the PREDIMED study has been translated and validated in other countries.
- Through the IFMED (International Foundation of Mediterranean Diet) we took part in different relevant international meetings and forums on the healthy aspects of the Mediterranean diet, as well as on the influence of the Mediterranean Diet on sustainability.
- A symposium was arranged as part of the IUNS congress to talk over the most important milestones of the PREDIMED study.
- The renewal of a new NHI project for metabolomics at the PREDIMED has been obtained, focussing on other cardiovascular events as well as the primary ones, also in cooperation with the University of Harvard.
- The project financed by Marato-TV3 has been got under way on the scores for polygenic risk of diabetes modulated by obesity in the PREDIMED study.
- We took part in the international meta-analysis on the effects of consuming dairy products on hypertension by means of Mendelian randomisation published in the BMJ (2017;356:j1000).

PREDIMED Plus:

- The over 6800 randomised participants were followed up and weight loss results after 6 months, a year and two years were observed, as well as a favourable evolution of the cardiovascular risk markers in the intensive intervention group. PREDIMED PLUS results were disseminated at several national and international scientific meetings, stressing the Symposium by invitation held at NIH, Washington, in September 2017 and the congress of the IUNS in Buenos Aires.
- A session for training staff involved in the study was held in Madrid.
- Work has been done in preparing results for the initial papers of PREDIMED PLUS (pilot study, validation of diet scales, description of the cohort etc.), as well as on the preparation of other documents and important material in the study.
- The cooperation in PREDIMED PLUS continued at the International Consortium for GWAs of clinical trials on weight loss promoted by the NIH in the United States.
- A European sub-project was begun by several groups in the programme on the PREDIMED PLUS study (EU-Project (H2020-SFS-2016-2), entitled "Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviours. Eat2beNICE".
- The publications policy was updated and the policy for data sharing and Managing was drawn up.

SUN COHORT (Universidad de Navarra): There have now been 18 years' successful follow-up (>90% retention) of the SUN cohort, which has already grown to 22,800 participants, with an average follow-up over 10 years and more than180 papers published.

WAHA STUDY (Hospital Clínico de Barcelona): The follow-up of the WAHA (WAlnuts and Healthy Aging) study continued at the Hospital Clínic de Barcelona and Loma Linda University, issuing several publications and international collaboration work.



CORDIOPREV (Universidad de Córdoba): Follow-up of the patients recruited in this secondary prevention study with Mediterranean diet has continued, publishing several articles (microbiota and diet: Mol Nutr Food Res. 2017,61(12); and c-HDL and diabetes: Sci Rep. 2017;7:12499) and performing international collaboration work including the continuation of a European project on metabolomics along with PREDIMED and other partners.

PROJECT MELIPOP (multi-centre): Financing for the intramural projects has been obtained in 2017 to get the MELIPOP study under way. This is a randomised and controlled test with Mediterranean Diet and physical activity in children, concentrating on preventing child obesity.

OTHER STUDIES, PUBLICATIONS AND COLLABORATION WORK:

- Publication of a review on Obesity in the journal Nat Rev Dis Primers. 2017 15;3:17034.
- Participation of groups from the Programme in Projects PREVIEW (2014-2018); STOP and SWEET (2018); and PROMETEO 17/2017 on integration of omics.
- Governmental designation of a person from the programme as representative in Spain at the international WHO-UNICEF-OIEA forum on omics in obesity and malnutrition (Vienna, 2017)

GUIDES: Several national and international Guides have been published, some of the more noteworthy ones being: "Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation (Nutr Rev, 2017)"; "Proposed guidelines to evaluate scientific validity and evidence for genotype-based dietary advice (Genes Nutr. 2017)"; and "Utilizing nutritional genomics to tailor diets for the prevention of cardiovascular disease: a guide for upcoming studies and implementations (Expert Rev Mol Diagn. 2017)".

Obesity Programme

Coordinator: Gema Frühbek

Although the restructuring of the CIBEROBN Programmes did not represent any significant change for the Nutrition Programme, because all its work is structured around PREDIMED and PREDIMED+, for the Obesity Programme it meant a radical change and a challenge intended to prevent fragmentation in the search for common scientific objectives and to obtain a larger critical mass in companies with greater influence and significance.

The changes taken on in this respect have materialised in ground-breaking publications in both the sphere of basic research with preclinical models and in clinical works.

Some of the achievements are the findings leading to revealing the signalling channels involved in the modulation of peripheral metabolism by means of the thyroid hormones obtained by 41 CIBEROBN and international co-authors [Martínez-Sánchez N, et al. Hypothalamic AMPK-ER Stress-JNK1 Axis Mediates the Central Actions of Thyroid Hormones on Energy Balance. Cell Metab 2017 Jul 5;26(1):212-229.e12], the identification of the role of hepatic p63 in the regulation of steatosis through IKKβ/ER achieved by 27 CIBEROBN, CIBEREHD and international co-authors [Porteiro B, et al. Hepatic p63 regulates steatosis via IKKβ/ER stress. Nat Commun 2017 May 8;8:15111], as well as the essential participation of FGF15/19 as regulator of the expression of Pparγ2 in metabolic adaptation of the liver to the ingested fat achieved by a team made up of 22 CIBEROBN and CIBEREHD co-authors [Alvarez-Sola G, et al. Fibroblast growth factor 15/19 (FGF15/19) protects from diet-induced hepatic steatosis: development of an FGF19-based chimeric molecule to promote fatty liver regeneration. Gut 2017 Oct;66(10):1818-1828]. Likewise, in studies of patients we should stress the participation of CIBEROBN groups in major international consortiums with epidemiological, genetic and therapeutic aims. We should thus highlight the description of the changes in worldwide trends in the different weight categories over the last 40 years [NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet 2017 Dec 16;390(10113):2627-2642], the identification of mutations [Tommiska J et al. Two missense mutations in KCNQ1 cause pituitary hormone deficiency and maternally inherited gingival fibromatosis. Nat Commun 2017 Nov 3;8(1):1289] and the observation of which part of the antidiabetic effects of metformin is due to changes in the intestinal microbiota [Wu H et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nat Med 2017 Jul;23(7):850-858].

With regard to **clinical trials**, the active participation of CIBEROBN groups in the most relevant international multi-centre studies reveals the proven quality of both the healthcare and research work done by our CIBER. This is vouched for by the analyses of the possible cardiovascular impact of two known antidiabetics: canaglifozin [Neal B, et al. CANVAS Program Collaborative Group. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med 2017 Aug 17;377(7):644-65], and exenatide [Holman RR, et al EXSCEL Study Group. Effects of Once-Weekly Exenatide on Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2017 Sep 28;377(13):1228-1239]. Apart from all this hard-scientific work we should mention the participation in the drafting of Clinical Guides, as well as in positioning documents connected with obesity and clinical nutrition of national and European Obesity Societies.

Special mention is due for the work done in the **Neurocognition sub-programme**, in which the groups' participation is proving excellent in both inter-group collaboration work, and in external collaboration work done with other CIBERs (CIBERSAM, CIBERDEM and CIBERESP) and international groups. Dialogue between the groups is constant, thus facilitating synergies. The Neurocognition programme has for example allowed the recruitment of a good sample of participants in extreme weight situations (SEP). The

final sample of the transversal sub-programme consists of 508 women: 117 anorexia nervosa (AN), 20 low-weight controls, 119 normal weight controls, 16 overweight controls, 16 with bulimia nervosa (BN), 22 obese with binge eating disorder (BID), 75 obese without EBD and 123 morbid obese). On the longitudinal level there are 172 women evaluated after follow-up (6/12 post-treatment months): 43 AN, 55 controls and 74 obese after bariatric surgery. The collection of samples was completed in November 2017 and in the next few months the analysis of adipokines and gastrointestinal hormones in these is planned. The Neurocognition sub-programme has had a very good scientific production with a total number of 38 publications, most of these in Q1. We should similarly stress the application and recruitment of funding for research by means of the European project EU H2020 (H2020-SFS-2016-2) granted: Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviours/ Eat2beNICE (Ref 728018) PI F. Fernández-Aranda, in cooperation with other CIBEROBN groups, as well as the award of an autonomous project in the PERIS call [Pla Estratègic de Recerca i Innovació en Salut de l'Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR)] collaborating with other CIBEROBN groups, as well as other competitive calls such as the FIS. Guest lectures of foreign professors were also sponsored as part of this programme (Prof. Ashley Gearhardt).

There has been an increase in **visibility, general dissemination and diffusion** of the subjects studied by CIBEROBN in the media (press, radio, TV and internet), as well as a greater internationalisation by means of presentations at symposia and international congresses (EDRS 2017; ICED 2017; ECED 2017; ECO 2017; ECE 2017). The talent of researchers from the Obesity Programme has furthermore been acknowledged in reputed international awards of both young talent and senior investigators.

At the **VIII CIBEROBN Symposium** held in Madrid in June 2017, specifically devoted to Child and Teenage Obesity, the opportunity was used to bolster relations with the paediatrician currently President Elect of the European Association for the Study of Obesity (EASO), Prof. Nathalie Farpourt-Lambert, who in May 2018 became president of the EASO for a three-year period. Support was given to the SEEDO for the presentation of the Spanish candidacy to be the venue for the European Congress on Obesity (ECO) in 2021. Preference was given at the Symposium to the youngest researchers when giving the presentations, as well as to groups who had not had a chance to put forward their progress in preliminary activities. While the Symposium was held there was also an annual meeting of the Programme in order to consolidate the projects under way and set forth the new lines to be followed.

The data presented vouches for the great versatility of the groups forming the Obesity Programme with the capacity to undertake research on the highest level of neuroendocrinology, neurocognition, adipobiology, comorbidities and therapeutic optimisation. With all its extensive activities and successful outcomes, the Obesity Programme has made a dynamic contribution to all aspects of strengthening and developing the strategic approaches of CIBEROBN, which are leadership and scientific development, internationalisation, transfer, talent, communication and visibility.

Training Programme

Coordinator: Manuel Tena Sempere

The CIBEROBN Training Programme can be defined as a key tool for fostering continuous training, which is considered to be a key element on which the research work done by the groups in our centre can be sustained. As in previous years, the basic point of the programme has been to focus on the younger members of our teams, with the aims of promoting training for researchers (especially for emerging and consolidating investigators) in obesity and nutrition, encouraging their mobility and helping to consolidate their professional careers as independent researchers in this thematic area. In this same line training activities have been undertaken with other CIBER thematic areas, in the field of biomedical research into obesity and nutrition, intended to shore up our CIBER's commitment to the continuous training of its members.

In line with the development of the programme, the main training measures have been structured through financing training stays of CIBEROBN members at other national and international reference research groups. To this end the programme has since its beginnings had an open dynamic system for applications which, after its evaluation by the scientific and managing team, enables granting economic aid for going on training stays at CIBEROBN groups (other than the ones located in the city where the applying group is located), at other CIBER groups and at national and international groups not forming part of the CIBER structure. In the experience we have built up, these stays are extremely fruitful for the development of our programmes, since young researchers are trained in specific techniques which they later immediately apply to studies of their CIBEROBN group.

More specifically, during 2017, a total number of 7 applications for training stays of CIBEROBN researchers were financed, which mostly lasted for around 3 months (the maximum time that the programme allows for financing). The total amount of funds allocated to financing mobility is 18,528 €. This represents a figure basically similar to the one spent on stays held in 2016, stressing as a similarly positive aspect the high percentage of internationalisation, bearing in mind that ALL except for one of the stays applied for were at renowned foreign centres in both Europe and the United States. This strengthens not only the capacity for acquiring new knowledge and ground-breaking techniques in the field but also fosters the establishment of scientific relations and development of collaboration work on the top international level.

Apart from the mobility work mentioned above, the programme has continued with the dynamics already established in 2016, addressing the organisation and support for complementary training activities. In this setting we should give particular emphasis to the support for the second consecutive year for the *Encuentro de Doctorado de Excelencia*, in Mahón, promoted by the CIBERESP, and especially to the first joint research session between the CIBERDEM and CIBEROBN areas, which was held at the Salón de Actos Ernest Lluch, of the Instituto de Salud Carlos III on 20 November 2017. This session was intended to pool groups and lines of work from both CIBER areas by offering a number of presentations and talks given by prominent members in these areas. The programme, which was jointly drawn up by the heads of the Training Programmes of CIBERDEM and CIBEROBN, enabled those attending to get an updated view of lines of work and avant-garde technologies in the development of both CIBER areas. The sessions were attended by over 80 persons, as well as 15 speakers, and were jointly presented by the scientific directors of CIBERDEM and CIBEROBN. The training programme of our own CIBER funded the attendance of around 50 or its members, including researchers from the different groups and several speakers.

This set of activities has enabled complementing the training aspects of the programme, extending its scope to almost all the groups in the CIBEROBN. The strategy of the scientific management for next year is to go further into this approach, and new joint scientific sessions are already starting to be prepared with other thematic areas of the CIBER (CIBERHED and CIBERES) in 2018. This also involves active participation, which includes the scientific programme's preparing the next congress of the ESCI (European Society for Clinical Investigation), to be held in Barcelona in May 2018.

Lastly, as a training element of the greatest importance, we should stress in this section that in 2017 a total number of 80 Doctoral theses were completed (27 of these international), which represents the consolidation of a rising tendency in this important training activity, with a figure doubling the number of theses defended in 2011.

The global financing executed in this programme in 2017 came to 25,748 €. In perspective, the CIBEROBN training and mobility programme may be considered to be consolidated, and its flexibility means that it has become a valuable tool not only in researchers' professional development (especially that of the younger ones) but also in reinforcing international connections and collaboration work of the groups forming part of our CIBER.

FATBANK Platform

Platform Coordinator: José Manuel Fernández-Real

Node	Donors 2017	Accum. donors (incl. 2017)	SAMPLES 2017						
			Serum	Plasma	Buffy Coat	Visceral Ad. Tissue	Parietal Ad. Tissue	Thyroidal Ad. Tissue	Stools
Girona	54	518	878	1756	440	32	36	0	158
Pamplona	56	333	166	352	79	100	47	0	0
Santiago	25	178	395	800	100	50	25	0	0
Córdoba	18	108	163	220	79	0	10	0	3
Málaga	24	193	96	96	24	24	24	0	18
Total	**177**	**1330**	**1698**	**3224**	**722**	**206**	**142**		**179**

In 2017 the Girona biobank proceeded to contract one person exclusively working on the FatBank by means of the young people's guarantee plan, A number of milestones described below were set and accomplished.

- Updating of SOPs: ISO standards meant that there was considered to be a need to rewrite all the SOPs used in the processes for obtaining serum, plasma, buffy coat, stools and adipose tissue. We started again with all of these and after writing and checking them they were sent to the nodes.
- Certain errors not correctible by users were detected in the reviews of the data available from the computer application. These errors did not affect the traceability of samples but indicated wrong years in the donation. The computer programme was updated in order to correct the donors' coding.
- In years prior to 2017 the donation of stool samples of the FatBank was incorporated as a routine matter in the Girona node. We asked about the availability of other nodes to introduce this type of sample and the Cordoba node and the Malaga node joined this system.
- In spite of having reached the number of donors agreed to proceed to scientific exploitation of the samples and the associated data, the insertion of this data in the computer application had been left pending. To solve this problem a check was made in all the nodes to see what information is still to be introduced and to provide help by the coordinator node in any matters necessary.

Scientific Production

PUBLICATIONS

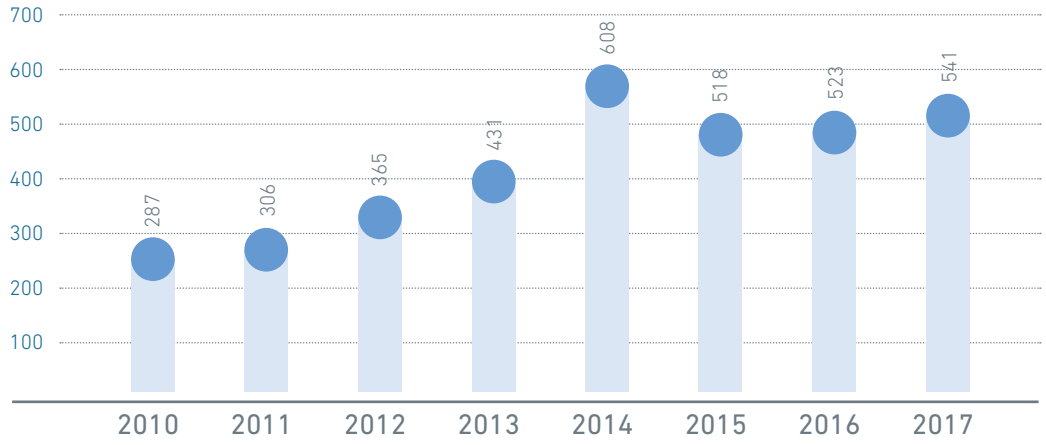
No. of publications in 2017

TOTAL	**541**
Q1	321
D1	129

Collaboration work

IntraCIBER	146
InterCIBER	161

Evolution of the publications



Most relevant publications of the CIBEROBN in 2017 by impact factor

Publication	Impact Factor
Toledo E, Martínez-González MA. Fruits, vegetables, and legumes: sound prevention tools. Lancet. 2017 Nov 4;390(10107):2017-2018	47,831
Wu H, Esteve E, Tremaroli V, Khan MT, Caesar R, Mannerås-Holm L, Ståhlman M, Olsson LM, Serino M, Planas-Fèlix M, Xifra G, Mercader JM, Torrents D, Burcelin R, Ricart W, Perkins R, Fernàndez-Real JM, Bäckhed F. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. Nat Med. 2017 Jul;23(7):850-858	29,886
Hernáez Á, Castañer O, Elosua R, Pintó X, Estruch R, Salas-Salvadó J, Corella D, Arós F, Serra-Majem L, Fiol M, Ortega-Calvo M, Ros E, Martínez-González MÁ, de la Torre R, López-Sabater MC, Fitó M. Mediterranean Diet Improves High-Density Lipoprotein Function in High-Cardiovascular-Risk Individuals. Circulation. 2017 Feb 14;135(7):633-643.	19,309
Perakakis N, Triantafyllou GA, Fernández-Real JM, Huh JY, Park KH, Seufert J, Mantzoros CS,.Physiology and role of irisin in glucose homeostasis. Nat Rev Endocrinol. 2017 Jun;13(6):324-337.	18,318

Publication	Impact Factor
Cui H, López M, Rahmouni K. The cellular and molecular bases of leptin and ghrelin resistance in obesity. Nat Rev Endocrinol. 2017 Jun;13(6):338-351.	18,318
Ramírez S, Gómez-Valadés AG, Schneeberger M, Varela L, Haddad-Tóvolli R, Altirriba J, Noguera E, Drougard A, Flores-Martínez Á, Imbernón M, Chivite I, Pozo M, Vidal-Itriago A, Garcia A, Cervantes S, Gasa R, Nogueiras R, Gama-Pérez P, Garcia-Roves PM, Cano DA, Knauf C, Servitja J, Horvath TL, Gomis R, Zorzano A, Claret M. Mitochondrial Dynamics Mediated by Mitofusin 1 Is Required for POMC Neuron Glucose-Sensing and Insulin Release Control Cell Metab. 2017 Jun 6;25(6):1390-1399.e6.	18,164
Martínez-Sánchez N, Seoane-Collazo P, Contreras C, Varela L, Villarroya J, Rial-Pensado E, Buqué X, Aurrekoetxea I, Delgado TC, Vázquez-Martínez R, González-García I, Roa J, Whittle AJ, Gomez-Santos B, Velagapudi V, Tung YCL, Morgan DA, Voshol PJ, Martínez de Morentin PB, López-González T, Liñares-Pose L, Gonzalez F, Chatterjee K, Sobrino T, Medina-Gómez G, Davis RJ, Casals N, Orešič M, Coll AP, Vidal-Puig A, Mittag J, Tena-Sempere M, Malagón MM, Diéguez C, Martínez-Chantar ML, Aspichueta P, Rahmouni K, Nogueiras R, Sabio G, Villarroya F, López M. Hypothalamic AMPK-ER Stress-JNK1 Axis Mediates the Central Actions of Thyroid Hormones on Energy Balance. Cell Metab. 2017 Jul 5;26(1):212-229.e12.	18,164
Martínez-González MA, Estruch R, Corella D, Ros E, Fitó M, Schwingshackl L, Salas-Salvadó J. Effects on health outcomes of a mediterranean diet with no restriction on fat intake. Ann Intern Med. 2017 Mar 7;166(5):378.	17,135
Porteiro B, Fondevila MF, Delgado TC, Iglesias C, Imbernon M, Iruzubieta P, Crespo J, Zabala-Letona A, Fernø J, González-Terán B, Matesanz N, Hernández-Cosido L, Marcos M, Tovar S, Vidal A, Sánchez-Ceinos J, Malagon MM, Pombo C, Zalvide J, Carracedo A, Buque X, Dieguez C, Sabio G, López M, Aspichueta P, Martínez-Chantar ML, Nogueiras R. Hepatic p63 regulates steatosis via IKKβ/ER stress. Nat Commun. 2017 May 8;8:15111.	12,124
Du W, Zhang L, Brett-Morris A, Aguila B, Kerner J, Hoppel CL, Puchowicz M, Serra D, Herrero L, Rini BI, Campbell S, Welford SM. HIF drives lipid deposition and cancer in ccRCC via repression of fatty acid metabolism. Nat Commun. 2017 Nov 24;8(1):1769.	12,124

Patents held by CIBER

National patents applied for

- Precision medicine intended for the diagnosis, prognosis and prediction of colorectal cancer (FIMABIS-16010) P201731237.
- Method for detecting and quantifying methylations in DNA (FIMABIS-17013). P201731370.

International patents applied for

- Method for Determining Susceptibility to Obesity. EP17382036.6.

Clinical Guides

National

- Prevention, diagnosis, and treatment of obesity. 2016 position statement of the Spanish Society for the Study of Obesity.
- Agència de Salut Pública de Catalunya. "Recomanacions per millorar la qualitat de les programa- cions de menús a l'escola" Barcelona: Published by the Agència de Salut Pública de Catalunya, 2017.
- La alimentación saludable en la etapa escolar.
- Valoración nutricional y evaluación de riesgos sobre el consumo de panga.

- Guía de Alimentación Cardiosaludable en Atención Primaria.
- Guía de salud ocular en el entorno universitario: Importancia de la Nutrición, la Actividad Física y de otros factores del estilo de vida.
- Guía Estrategia de Diabetes Comunidad Valenciana 2017-2021.
- Guía de Alimentación Cardiosaludable en Atención Primaria.
- Dyslipidemia management in patients with high cardiovascular risk in Spain. ALMA study.
- Consensus document on the management of the atherogenic dyslipidaemia of the Spanish Society of Arteriosclerosis.
- Consensus on the Statin of Choice in Patients with Impaired Glucose Metabolism: Results of the DIANA Study.
- Estrategia "Osasunbidea: caminando por la salud".
- Guidelines for consumption of dark chocolate. Pleasure and cognitive health?
- Vía Clínica de Cirugía Bariátrica.
- Guía práctica para la alimentación de personas mayores.
- Guía práctica para el manejo de las dislipemias.
- Prevention, diagnosis, and treatment of obesity. 2016 position statement of the Spanish Society for the Study of Obesity.
- Programa de consumo de frutas y verduras en las escuelas.
- Previniendo la obesidad en España mediante un impuesto a las bebidas azucaradas.
- Juego y comorbilidad: protocolo de intervención en pacientes con comorbilidad.
- Quality criteria in bariatric surgery: Consensus review and recommendations of the Spanish Association of Surgeons and the Spanish Society of Bariatric Surgery.

International

- Lifestyle recommendations for the prevention and management of metabolic syndrome: an international panel recommendation.
- Trending Cardiovascular Nutrition Controversies.
- IAEA - WHO – UNICEF - Analysis of Biological Pathways to Better Understand the Double Burden of Malnutrition and to Inform Action Planning.
- Essential Study Quality Descriptors for Data from Nutritional Epidemiologic Research.
- Utilizing nutritional genomics to tailor diets for the prevention of cardiovascular disease: a guide for upcoming studies and implementations.
- Atherogenic Dyslipidemia in Latin America: Prevalence, causes and treatment: Expert's position paper made by The Latin American Academy for the Study of Lipids (ALALIP) Endorsed by the Inter-American Society of Cardiology (IASC), the South American Society of Cardiology (SSC), the Pan-American College of Endothelium (PACE), and the International Atherosclerosis Society (IAS).
- A Practical Approach to the Management of Micronutrients and Other Nutrients of Concern in Food Exchange Lists for Meal Planning.
- Proposed guidelines to evaluate scientific validity and evidence for genotype-based dietary advice.
- Guide for Current Nutrigenetic, Nutrigenomic, and Nutriepigenetic Approaches for Precision Nutrition Involving the Prevention and Management of Chronic Diseases Associated with Obesity.
- Metabolic Surgery in the Treatment Algorithm for Type 2 Diabetes: A Joint Statement by International Diabetes Organizations.
- Obesity and Type 2 Diabetes: Two Diseases with a Need for Combined Treatment Strategies - EASO Can Lead the Way.

- Metabolic syndrome and cardiovascular disease after hematopoietic cell transplantation: screening and preventive practice recommendations from the CIBMTR and EBMT.
- The polypill in cardiovascular prevention: evidence, limitations and perspective - position paper of the European Society of Hypertension.
- Noninvasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients: a consensus article from the European Association of Cardiovascular Imaging, the European Society of Cardiology Council on Hypertension and the European Society of Hypertension.
- Non-invasive cardiovascular imaging for evaluating subclinical target organ damage in hypertensive patients.
- Variations in the Prevalence of Obesity Among European Countries, and a Consideration of Possible Causes.
- A Proposal of the European Association for the Study of Obesity to Improve the ICD-11 Diagnostic Criteria for Obesity Based on the Three Dimensions Etiology, Degree of Adiposity and Health Risk.

CIBEROBN Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Argente Oliver, Jesús	19	13	5	Servicio Madrileño de Salud - Hospital Infantil Universitario Niño Jesús	Madrid
Arós Borau, Fernando	23	15	7	Fundación Vasca de Innovación e Investigación Sanitarias - Hospital Universitario Araba. Sede Txagorritxu	Álava
Baños Rivera, Rosa María[1]	17	8	1	Universidad de Valencia - Facultad de Psicología	Valencia
Casanueva Freijo, Felipe	14	9	1	Servicio Gallego de Salud - Complejo Hospitalario Universitario Santiago	A Coruña
Corella Piquer, Dolores	41	29	11	Univ. de Valencia - Facultad de Medicina	Valencia
Diéguez González, Carlos	30	23	11	Universidad de Santiago de Compostela - CIMUS	A Coruña
Estruch Riba, Ramón	43	30	13	Hospital Clínic de Barcelona	Barcelona
Fernández Aranda, Fernando	33	23	4	Fundación IDIBELL - Hospital Universitario de Bellvitge	Barcelona
Fernández-Real Lemos, Jose Manuel	20	18	5	Fund. Inst. de Investigación Biomédica de Girona - Hospital Josep Trueta	Girona
Fiol Sala, Miguel	31	22	10	Fundación Instituto de Investigación Sanitaria Illes Balears (IdISBa) - Hospital Universitario Son Espases	I. Balears
Fitó Colomer, Montserrat	59	35	17	Consorci Mar Parc Salut de Barcelona	Barcelona
Frühbeck Martínez, Gema	30	19	9	Universidad de Navarra - Clinica Universitaria de Navarra	Navarra
Gil Campos, María Mercedes	21	7	2	Fund. para la Investigación Biomédica de Córdoba (FIBICO) - Hospital Universitario Reina Sofía	Córdoba

Group Leader	Total Publications	Q1	D1	Institution	Province
Lamuela-Raventos, Rosa María	30	18	9	Universidad de Barcelona - Facultad de Farmacia	Barcelona
Lapetra-Peralta, Jose	22	14	7	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla - Distrito Sanitario Atención Primaria de Sevilla	Sevilla
Lasunción Ripa, Miguel Angel	9	7	3	Servicio Madrileño de Salud - Hospital Ramón y Cajal	Madrid
López Miranda, José	22	17	8	Fundación para la Investigación Biomédica de Córdoba (FIBICO) - Hospital Universitario Reina Sofía	Córdoba
Lurbe Ferrer, Empar	12	9	3	Cons. Hptal Gral. Universitario Valencia - Fundación de Investigación del Hospital General Universitario de Valencia	Valencia
Martínez González, Miguel Ángel	47	28	16	Universidad de Navarra	Navarra
Martínez Hernández, Jose Alfredo	42	26	11	Universidad de Navarra	Navarra
Moreno Aznar, Luis Alberto	39	15	8	Fundación Instituto de Investigación Sanitaria Aragón	Zaragoza
Ortega Martínez de Victoria, Emilio[2]	36	26	13	Hospital Clínic de Barcelona	Barcelona
Osada García, Jesús de la	11	6	1	Universidad de Zaragoza	Zaragoza
Palou Oliver, Andreu	17	16	8	Universidad de las Islas Baleares - Facultad de Ciencias de Mallorca	I. Balears
Pintó Sala, Xavier	20	10	5	Fundación IDIBELL - Hospital Universitario de Bellvitge	Barcelona
Portillo Baqueda, María del Puy	19	10	1	Universidad del País Vasco - Facultad de Farmacia	Álava
Remesar Betlloch, Xavier	17	14	7	Universidad de Barcelona - Facultad de Biología	Barcelona
Salas Salvadó, Jordi	42	26	12	Fundación Instituto de Investigación Sanitaria Pere Virgili - Universidad Rovira i Virgili	Tarragona
Serra Majem, Lluis	49	24	14	Univ. de las Palmas de Gran Canaria	I. Balears
Tena Sempere, Manuel	27	23	10	Univ. de Córdoba - Facultad de Medicina	Córdoba
Tinahones Madueño, Francisco	48	35	10	Fundación Pública Andaluza para la Investigación de Málaga en Biomedicina y Salud (FIMABIS) - Hospital Regional Universitario Carlos Haya	Málaga
Tur Mari, Josep Antoni	73	22	5	Universidad de las Islas Baleares - Facultad de Ciencias de Mallorca	I. Balears
Villarroya Gombau, Francesc	10	9	5	Universidad de Barcelona - Facultad de Biología	Barcelona

1 R. Baños replaces Cristina Botella

2 E. Ortega replaces Emilio Ros


ciberonc
Cancer

Scientific Director's Presentation

Joaquín Arribas López

I would like to express the Scientific Management's satisfaction with the results obtained over this first year's work to all the members of CIBERONC. As stated in our Strategic Plan, the main aim for this period was to get the area launched properly. This was understood to mean the establishment of a good internal organisational structure, a synergic interaction routine between the research groups and an appropriate introduction of the members to the workings of the tools and processes of the CIBER in order to make sure that effective use is made of funding.

Hence, during this first year there have been over ten meetings, plus one meeting of each of the Research Programmes, in which the members updated their progress with regard to the collaborative scientific project that they are carrying out. One outcome of this successful integration work has been the over 350 articles published in 2017 with CIBERONC affiliation, the great majority of these in journals with a high impact factor including Nature, New England Journal of Medicine and the Lancet.

The launch of the area has also been promoted, giving this nationwide visibility and social exposure by presenting this at a large number of scientific encounters, as well as by arranging events in cooperation with other organisations, such as the Asociación Española de Investigación sobre Cáncer (ASEICA) or the II Reunión General, which was held at the Real Academia Nacional de Medicina. Further achievements and contributions for supporting scientific development were also made in this respect, such as the call co-funded with the AECC, or the endeavour for co-funding seed projects with CIBER-BBN.

Another prominent success was the Training and Mobility Programme, which has provided assistance for over 70 CIBERONC members by means of 7 calls for 4 different actions: training, mobility, getting started in research and promotion of young researchers.

On the administrative scale CIBERONC has also comfortably complied with the goals it had set, managing to consume up to 75% of the budget, which places it on a par with the more longstanding areas as regards the yield from its funding. Furthermore, in spite of the restrictions resulting from the delay in the General State Budgets law, up to 80 contracts of its own research staff have managed to be signed.

None of this would have been possible without the early constitution of our Management Committee, made up of the Coordinators and Co-coordinators of each Research Programme, who share a pre-clinical and clinical research profile on an equitable basis.

Another of the key milestones in 2017 was setting up the External Advisory Scientific Committee, which gave clear feedback on our performance during the first year and some useful recommendations for reinforcing the weaknesses detected. One of the plans for this second year, in which measures will be focussed on the increase of scientific production of CIBERONC, is the creation of the Work Modules. These are intended to promote collaborative scientific work targeting personalised medicine and the priorities of the European Commission.

Scientific Programmes

Gastrointestinal Tumours Programme

Coordinator: Gabriel Capellá Munar / Co-Coordinator: Josep Tabernero Caturla

The Programme of Digestive System Tumours has have had a good start, with the following scientific accomplishments:

In the field of study of susceptibility to developing cancer, we should stress the growth of the Familial Pancreatic Cancer Registry, which now has 80 families and over 200 individuals included in the register and undertakes Europe-wide projects intended to identify the contribution of genetic susceptibility to pancreatic cancer. Members from other programmes and other areas such as CIBEREHD and CIBERESP took part in this work.

In the field of personalised models, we should stress the increase in the number of PDX of different types of tumours available (over 200), placing special emphasis on PDX of paired samples for diagnosis and after progression, on the perpetuation of tumours with mutations in the BRAF gene. Progress has also been made in establishing a relevant collection of organoids. On one hand, there is a biobank of organoids derived from mice with the aim of studying the potential of immunotherapy and on the other hand a collection of organoids has been created from patients in whom genomic edition is applied for study. This technology has been made available to the scientific community through training workshops led by members of the CIBERONC.

As regards the development of liquid biopsy, work has been done on a coordinated basis in the compared analysis of the different methodological platforms available. We should stress the study of agreement between biopsy and circulating DNA with results laying the foundations for routine study of liquid biopsy.

At the same time collaboration work has been established, as reflected by the applications of seven of the members of the programme who have taken part jointly. These projects focus on colorectal and pancreatic cancer, and include aspects going from the study of aetiology to therapeutic aspects centring on immunotherapy.

Breast Cancer Programme

Coordinator: Atanasio Pandiella Atanasio / Co-Coordinator: Joan Albanell Mestres

Two of the significant achievements seen in the Breast Cancer Programme in 2017 had a translational and clinical basis. One of these refers to the approval of a new medication for use in clinical treatment of HER2-positive breast cancer. The drug, known as neratinib, is an agent which blocks tyrosine kinase activity of HER2, which is important in the oncogenic properties of this protein. One of the groups in the programme, led by Dr Miguel Martín, has been the leader in clinical development of this product. The clinical data on which the approval of neratinib was based was published in high-impact journals, such as Lancet Oncology. Another achievement worthy of mention is the participation of several groups from the programme in an attempt to find out the mechanisms of resistance to a drug used in breast cancer: T-DM1. Researchers from the groups led by Pandiella, Albanell and Arribas identified two resistance mechanisms. Both studies have been published in reputed journals in the field, such as Cancer Research and Clinical Cancer Research.

Respiratory Tract Tumour Programme

Coordinator: Luis Montuenga Badía / Co-Coordinator: Luis Paz Ares Rodríguez

Although this has been their first year's work, the groups have interacted together very well, and results are already being obtained in several of the collaborative objectives. It is true that some of us had already been cooperating in the RTICC, but other new members have also joined us.

In these few months our Programme has already published a large number of articles signed by the CIBERONC, some in very high-impact journals such as Cancer Discovery or New England Journal of Medicine, several of them as a result of intraCIBER collaborative work. With other CIBERONC groups co-operation is proving to be a very natural and smoothly-running process, especially with the Programme for Molecular Mechanisms. There is also very frequent contact with the Coordinator of the Lung Cancer Programme at CIBERES.

The Programme arranged four encounters in 2017 (two face-to-face and two by teleconference). Except for the first of these, all of them dealt with scientific aspects and the review of the collaborative project. Two members of the programme have taken part in activities in the Training and Mobility Programme.

As regards scientific objectives, an in-silico analysis enabled generating a list of relevant genes in Respiratory Tract Tumours and 48 samples were sequenced for a specific genetic panel. Progress has been made in the preclinical evaluation of new therapeutic strategies, such as the combination of FGFR inhibitors, YES1 inhibitors, new combinations of inhibitors for the NOTCH pathway and the effect of FAK inhibition on tumoural invasion. A retargeting analysis on 35 drugs has also been completed for their use in Squamous Cell Cancer.

A cohort of patients treated with immunotherapy has started to be set up in cooperation with CIBERES in which four organisations in the consortium will be involved. Luis Montuenga's group has published a Cancer Discovery on the synergic effect of the combined inhibition of members of the C5a/C5aR1 y PD-1 complement. The researchers in the Programme have also taken part in several studies for the identification of new biomarkers by means of liquid biopsy.

The three publications with greatest impact factor (IF) of the members of the programme with CIBERONC affiliation are: Antonia SJ et al. N Engl J Med (IF: 72.406) LPA (group 42). 2. Peters S et al. J Clin Oncol (IF: 24.008) LPA (group 42). 3. Ajona D et al. Cancer Discov (IF: 20.011) LM (group 35).

The following publications classified by IF are inter- or intra-CIBER collaborative publications: 1. Gettinger S et al. Cancer Discov (IF: 20.011) LM (group 35) and IM (group 34). 2. Siena S et al. Ann Oncol (IF: 11.855) LPA (group 42) and JMT (group 52). 3. Martin-Broto J et al. Ann Oncol (IF: 11.855) AC (group 13) and ACM (group 15).

Haematological Tumours Programme

Coordinator: Dolors Colomer Pujol / Co-Coordinator: Marcos González Diaz

The aims of the programme focus on gaining in-depth knowledge of the biology of these tumours, understanding the mechanisms for progression and resistance to treatment and of the identification of biomarkers enabling predicting the response to treatment and at the same time monitoring its effectiveness. The final objective is to contribute to better care and treatment of haematological patients.

In 2017, our programme made the following scientific progress:

The characterisation of the mutational profile of different entities by means of mass sequencing studies (Franco et al, Oncotarget, 2017; Karube et al, Leukemia 2017; Mando et al, Br J Haematol, 2017; Martinez-Trillos et al, Leuk Lymphoma 2017; Ramos et al, Am J Hameatol, 2017; Schmidt et al, Blood, 2017). Molecular markers enabling better classification of tumours have been described (Magnano et al, Ann Oncol 2017; Martinez-Leperche et al, Br J Haematol, 2017; Miyaoka et al Mod pathol. 2017); Navarro et al, Haematologia, 2017). An analysis was also made of the clinical impact of subclonal mutations in chronic lymphatic leukaemia (LLC) (Nadeu et al, leukemia 2017). SOX11 has been shown to regulate interaction with the microenvironment in the Mantle cell lymphoma (Balsas et al, Blood, 2017), and the specificity of HLA is seen to be associated with prognosis in the LLC (Garcia-Alvarez et al, *Plos One*, 2017); and furthermore the mesenchymal cells of myeloproliferative neoplasms have been characterised (Diaz de la Guardia et al Stem Cell Reports, 2017; Ramos et al, *Plos One* 2017).

There has been a description of the importance of monitoring residual disease by flow cytometry (Arana et al, Leukemia 2017) and the possibility of detecting alterations in the number of copies by means of quantitative PCR (Chillon et al, Ann Hematol, 2017) in MM. The Programme has also taken part in the standardisation of new diagnostic techniques (Hermitte et al, Leukemia 2017; Novakova et al, J Immunol. methods, 2017).

The anti-tumoural activity of an antibody against the constant region of the T cell beta receptor has also been described T (Maciocia et al, Nat Med, 2017). The activity of new targeted therapies has also been described: dual epigenetic modifiers (G9a and DNMTs) (San Jose et al, Nat Commun, 8:459, 2017), BTK L-inhibitors, (Vidal Crespo et al, Haematologica,2017) and BET inhibitors (Diaz et al, Haematologica, 2017). By means of in silico analysis it was described that APRT may be a target in cancer (Pey et al, Sci. Reports 2017).

And finally the results of different clinical trials on MM have also been described (Dimopoulos et al, Br J Haematol, 2017 and Blood Cancer J, 2017; La Huerta et al, 2017; San Miguel et al, Br J Haematol, 2017; Ovet-Loiseau et al, Blood 2017), as well as acute prolymphocytic leukaemia (Martinez-Cuadron et al, Leukemia, 2017), acute lymphoid leukaemia (Kantarjian et al, NEJM, 2017; Ribera et al Leuk Kymphoma 2017) and follicular lymphoma (Magnano et al, Ann Hematol, 2017; Alonso-Alvarez et al, Br J Haematol, 2017). A clinical trial has been started with an anti-CD19+ CART- 4-1BB-CD3z (ARI-0001) for resistant and refractory patients of leukaemias and lymphomas CD19+ completely generated in a CIBERONC group.

Low prevalence Tumour Programme

Coordinator: Enrique de Álava Casado / Co-Coordinator: Ignacio Melero Bermejo

Our Programme's challenge for 2017 was to organise a cooperative research project on low prevalence tumours, a very wide and varied group of entities. For this reason, most of the work this first year was concentrated on evaluating biomarkers in which at least two groups in the Programme had an interest, experience and properly characterised samples for studying. We finally selected Endoglin and ALCAM as relevant biomarkers for our programme in 2017. In actual fact, the action helping to integrate the scientific work of the groups in our programme most was a highly novel proposal for furthering the study of

the relevance of Endoglin (CD105) in uveal melanoma, a rare orphan tumour on which we had not initially intended to work. Each group provided tools, samples and clinical data on this tumour, on which no cooperative translational research had been done so far in Spain. We decided to take part along with the most relevant clinical groups in this country (outside the CIBERONC) in several calls for competitive financing. We thus managed to win the annual prize of the GETHI Group (Group Español de Tumores Huérfanos e Infrecuentes) for 2017, which also represented the first external funding administered by the CIBERONC as beneficiary organisation. We have also taken part in other calls with uveal melanoma projects, such as that of the Fundación Merck, whose resolution is still to be issued. In December we prepared another proposal along with Dutch and German groups for the Transcan-2 international call, which in 2017 was engaged precisely in the study of rarer neoplasms. We hope to obtain the Transcan because this would represent great backing for the internationalisation of our programme and CIBERONC.

Programme of Mechanisms of Tumour Progression

Coordinator: Xosé García Bustelo / Co-Coordinator: Anna Bigas Salvans

In line with the experimental plan set in the scientific project of our programme, in 2017 we developed new bioinformatic tools for in silico extraction of "omic" data enabling us to identify oncogenes, tumour-suppressant genes, genes modifying oncogenic signals, metabolomic programmes and genetic signatures which give rise to or take part in the progress of different types of tumour. This work, along with the parallel development of new experimental tools which enabled its validation and later study (animal models, cell models in 3D, organoids and xenografts of patients' cells) has enabled us to discover new channels involved in these processes. Part of this progress is the identification of a new suppressor gene involved in the development of triple-negative breast cancer (Suárez-Cabrera et al. Cancer Res 2017; PMID: 28108518; Dr J.M. Paramio's group), a new metabolic programme involved in prostate cancer (Zabala-Letona et al. Nature 2017; PMID: 28658205; Dr A. Carracedo's group), a new suppressor channel of tumours involved in the development of acute TLX- positive lymphocytic leukaemia (Robles-Valero et al. Cancer Cell 2017; PMID: 29136506; Dr X.R. Bustelo's group) and of a new biomarker enabling stratifying early breast cancer patients in accordance with a response to adjuvant therapies (Coleman et al. Lancet Oncol 2017; PMID: 29037984; Dr A. Carracedo's group). All this work, in line with CIBERONC philosophy, entailed highly multidisciplinary approaches enabling dissecting the processes being studied into basic, translational and clinical levels. Lastly, we have got new screenings under way in order to develop pharmacological inhibitors against some of the targets discovered over this year. We hope that during the year other research under way will shed new light on the mechanisms involved in the origin and progression of tumours allowing the development of new diagnostic and pharmacological tools to diagnose and treat oncological patients better.

Apart from the aforementioned scientific findings we should stress that three of the groups belonging to this programme have projects financed by the European Research Council. These include the groups led by Doctors J. Seoane (ERC Consolidator), A. Carracero (ERC Starting) and C. López-Otín (ERC Advanced). Members of the programme have collaborated with leadership work in scientific associations such as the European Association for Cancer Research (Dr. J. Seoane), the Asociación Española de Investigación sobre el Cáncer (Dr X.R. Bustelo, J.M. Paramio and A. Carracedo), the Asociación Española contra el Cáncer (Dr E. Santos and Dr J. Seoane) and the International Society of Experimental Hematology (Dr A. Bigas).

Training Programme

Coordinator: Amparo Cano García / Co-Coordinator: Anna Bigas Salvans

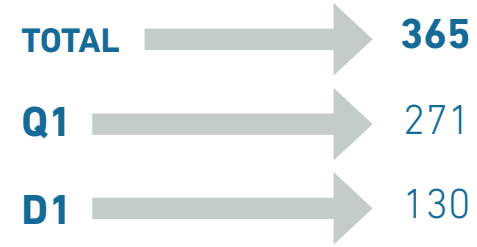
The most relevant activities in the Training Programme have been intended for the following sub-programmes:

1. Getting started in research. We should stress the launching grant programme (co-financed by the programme and the research groups); 6 months for pre-doctoral contracts in order to cover the period from completing the master to obtaining a pre-doctoral contract from other institutions. 14 grants were awarded out of a total number of 31 applied for.
2. Mobility. Financing short stays at national groups (11 stays financed, 9 of these at intra-CIBER groups) and 6 international ones, out of a total number of 25 applications.
3. Training intended for financing organisation and attendance at training courses. The organisation of three courses by researchers from the CIBERONC was financed (Genomics of Cancer, Organoids and Diagnosis of Leukaemias and Lymphomas) and attendance at courses outside CIBERONC for a total number of 11 researchers (post-doctoral, pre-doctoral and technical staff).
4. Promotion of young researchers. The attendance at the I Simposio Educacional ASEICA-CIBERONC of ten young researchers was promoted and financed, with a presentation of posters. One of them was awarded the second prize at the Symposium. In the setting of the Symposium, the Coordinator of the Training Programme, Amparo Cano, participated as a co-organiser of the round table entitled "ASEICA & CIBERONC Career Prospects for Cancer Researchers in Training" which had a large audience and was a great success with young researchers.

Scientific Production

PUBLICATIONS

No. of publications in 2017



Most relevant publications of the CIBERONC in 2017 by

Publication	Impact Factor
Rami-Porta R., Asamura H., Travis W.D., Rusch V.W. Lung cancer — major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer Journal for Clinicians. 2017;67(2):138-155.	187,04
Kantarjian H., Stein A., Gokbuget N., Fielding A.K., Schuh A.C., Ribera J.-M. et al. Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia. New England Journal of Medicine. 2017;376(9):836-847.	72,406
Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer.The New England journal of medicine. 2017.	72,406
El-Khoueiry A.B., Sangro B., Yau T., Crocenzi T.S., Kudo M., Hsu C. et al. Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): An open-label, non-comparative, phase 1/2 dose escalation and expansion trial. The Lancet. 2017.	47,831
Powles T., Duran I., van der Heijden M.S., Loriot Y., Vogelzang N.J., De Giorgi U. et al. Atezolizumab versus chemotherapy in patients with platinum-treated locally advanced or metastatic urothelial carcinoma (IMvigor211): A multicentre, open-label, phase 3 randomised controlled trial. The Lancet. 2017.	47,831
Petrylak DP, de Wit R, Chi KN, Drakaki A, Sternberg CN, Nishiyama H et al. Ramucirumab plus docetaxel versus placebo plus docetaxel in patients with locally advanced or metastatic urothelial carcinoma after platinum-based therapy (RANGE): a randomised, double-blind, phase 3 trial.Lancet (London, England). 2017.	47,831
Reig M., Bruix J. Lenvatinib: can a non-inferiority trial change clinical practice? The Lancet. 2018;391(10126):1123-1124.	47,831
Zabala-Letona A., Arruabarrena-Aristorena A., Martin-Martin N., Fernandez-Ruiz S., Sutherland J.D., Clasquin M. et al. MTORC1-dependent AMD1 regulation sustains polyamine metabolism in prostate cancer. Nature. 2017;547(7661):109-113.	40,137
Michailidou K., Lindstrom S., Dennis J., Beesley J., Hui S., Kar S. et al. Association analysis identifies 65 new breast cancer risk loci. Nature. 2017;551(7678):92-94.	40,137
Cobo I., Martinelli P., Flandez M., Bakiri L., Zhang M., Carrillo-De-Santa-Pau E. et al. Transcriptional regulation by NR5A2 links differentiation and inflammation in the pancreas. Nature. 2018;554(7693):533-537.	40,137

CIBERONC Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Álava Casado, Enrique de	5	2	2	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío	Sevilla
Albanell Mestres, Joan	10	9	7	Consorci Mar Parc Salut de Barcelona. Hospital del Mar	Barcelona
Aranda Aguilar, Enrique	9	6	2	Fundación para la Investigación Biomédica de Córdoba (Fibico). Hospital Universitario Reina Sofía de Córdoba	Córdoba
Arribas López, Joaquín	5	5	4	Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO	Barcelona
Batlle Gómez, Eduard	3	3	3	Fundación Privada Instituto de Recerca Biomédica (IRB-Barcelona)	Barcelona
Bigas Salvans, Anna	17	14	7	Consorci Mar Parc Salut de Barcelona. Hospital del Mar	Barcelona
Bosch José, Francesc Xavier	3	3	3	Fundación Idibell Hospital. Universitario de Bellvitge	Barcelona
Campo Guerri, Elías	18	13	12	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Camps Herrero, Carlos	9	7	2	Consorcio Hospital Gral. Universitario Valencia. Fund. de Investigación del Hospital Gral. Universitario de Valencia	Valencia
Cano García, Amparo	5	4	1	Universidad Autónoma de Madrid	Madrid
Capellà Munar, Gabriel	9	8	4	Fund. Idibell. Hospital Duran y Reynals	Barcelona
Carnero Moya, Amancio	3	3	2	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío	Sevilla
Carracedo Pérez, Arkaitz	11	9	7	CIC Biogune	Vizcaya
Carrato Mena, Alfredo	13	9	3	Servicio Madrileño de Salud. Hospital Ramon y Cajal	Madrid
Cervantes Ruipérez, Andrés	10	8	5	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación Incliva)	Valencia
Colomer Pujol, Dolors	15	12	7	Instituto de Investigaciones Biomédicas August Pi i Sunyer	Barcelona
Crespo Baraja, Piero	1	0	0	Ag. Est. Consejo Sup. de Investigaciones Científicas. Instituto de Biomedicina y Biotecnología de Cantabria	Cantabria
Santos de Dios, Eugenio	2	1	1	Fundación de Investigación del Cáncer de la Universidad de Salamanca. Centro de Investigación del Cáncer	Salamanca

Group Leader	Total Publications	Q1	D1	Institution	Province
Santisteban Sanz, María del Pilar	1	0	0	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Díaz-Rubio García, Eduardo	13	11	5	Servicio Madrileño de Salud. Hospital Clínico San Carlos	Madrid
Esteller Badosa, Manel	2	1	1	Fund. Idibell. Hospital Durán Reynals	Barcelona
Jaime Feliu Batlle	12	9	2	Serv.Madrileño de Salud. Hospital La Paz	Madrid
García Bustelo, Xose Ramon	7	6	4	Fundación de Investigación del Cáncer de la Universidad de Salamanca	Salamanca
González Díaz, Marcos	22	16	5	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	Salamanca
Lluch Hernández, Ana	3	3	3	Fundación Para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación Incliva)	Valencia
López López, Rafael	15	12	4	Servicio Gallego de Salud. Complejo Hospitalario Universitario Santiago	A Coruña
López Otín, Carlos	7	5	4	Universidad de Oviedo. Facultad de Medicina	Asturias
Malats Riera, Nuria	6	4	3	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid
Martín Jiménez, Miguel	7	4	3	Servicio Madrileño de Salud. Hospital Gregorio Marañón	Madrid
Matías-Guiu Guía, Francisco Javier	15	7	3	Instituto de Investigación Biomédica de Lleida. Fundación Dr. Pifarre	Lleida
Melero Bermejo, Ignacio	20	16	14	Universidad de Navarra. Clínica Universitaria de Navarra	Navarra
Montuenga Badía, Luis	9	7	3	Fundación para la Investigación Médica Aplicada	Navarra
Muñoz Terol, Alberto	1	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Investigaciones Biomédicas Alberto Sols	Madrid
Noguera Salva, Rosa	2	1	0	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación Incliva)	Valencia
Oliver Pozo, Francisco Javier	2	2	1	Agencia Estatal Consejo Superior de Investigaciones Científicas. Instituto de Parasitologia y Biomedicina López Neyra	Granada
Orfao de Matos Correia e Vale, Jose Alberto	3	2	2	Fundación de Investigación del Cáncer de la Universidad de Salamanca. Centro de Investigación del Cáncer	Salamanca
Palacios Calvo, José	6	3	0	Servicio Madrileño de Salud. Hospital Ramón y Cajal	Madrid
Pandiella Alonso, Atanasio	12	11	3	Fundación de Investigación del Cáncer de la Universidad de Salamanca. Centro de Investigación del Cáncer	Salamanca

Group Leader	Total Publications	Q1	D1	Institution	Province
Paramio González, Jesús María	16	13	4	Centro de Investigaciones Energéticas, Medioambientales Y Tecnológicas (CIEMAT)	Madrid
Paz-Arés Rodríguez, Luis	16	13	4	Servicio Madrileño de Salud. Hospital Universitario 12 de Octubre	Madrid
Pérez Simón, Jose Antonio	2	2	0	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla. Hospital Virgen del Rocío	Sevilla
Piris Pinilla, Miguel Ángel	5	3	1	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	Madrid
Prosper Cardoso, Felipe	6	5	3	Fundación para la Investigación Médica Aplicada	Navarra
Ramon y Cajal Agüeras, Santiago	8	6	3	Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO	Barcelona
Real Arribas, Francisco Xavier	5	5	3	Fundación Centro Nacional de Investigaciones Oncológicas	Madrid
Rodrigo Tapia, Juan Pablo	17	14	4	Fundación para el Fomento en Asturias de la Investigación Cientifica Aplicada y la Tecnología. Hospital Universitario Central de Asturias	Asturias
San Miguel Izquierdo, Jesús Fernando	13	11	7	Universidad de Navarra	Navarra
Sanz Alonso, Miguel Ángel	13	7	4	Fundación para la Investigación del Hospital La Fe. Hospital Universitario de la Fe	Valencia
Seoane Suárez, Joan	1	1	1	Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO	Barcelona
Tabernero Caturla, José María	9	8	6	Fundación Privada Instituto de Investigación Oncológica Valle de Hebrón-VHIO	Barcelona


ciber sam
Mental Health

Scientific Director's Presentation

Eduard Vieta Pascual

Yet another year the scientific report covering the achievements of the Mental Health CIBER in 2017 shows that the money invested in research has some extremely high benefits for society. One only need to look at the bibliometric indicators of the generation of knowledge promoted by CIBERSAM, with 549 top level publications (21% of which are in the first decile of the speciality), the clinical and preclinical innovation, with a rising figure of patents in response to the suggestions received in time by the outside evaluators, who pointed out this aspect as one of the few weak points in our areas, the large number of international awards, which have made 2017 one of the best years in scientific productivity since the start of CIBERSAM. If the result of the quantitative analysis is formidable, what can we say about the qualitative analysis! CIBERSAM has made a decisive contribution to getting to know more about the structural changes arising in the brain during pregnancy, which is a period of high emotional voltage, has taken part in the macroproject on the global burden of mental diseases (with 9 publications on the subject in The Lancet in 2017), has published a collaborative clinical trial on the pharmacogenetics of depression, has disseminated the findings of the greatest study on genetic association carried out on schizophrenia until now, and has published major progress in the neurobiology of bipolar disorder, depression, personality disorders, attention deficit disorder with hyperactivity and autism. With a growing focus on suicide and prevention of mortality associated with mental diseases, CIBERSAM has been true to its high degree of internationalisation, and a large number of European projects have been obtained, also with a highly significant number of projects financed by the United States (Brain and Behavior Research Foundation).

In 2017 CIBERSAM started to apply the 2017-2019 strategic plan, which includes a greater focus on the needs and participation of patients. This line includes the large–scale survey in the VOZ Project, focussing on identifying the needs of patients with schizophrenia/psychoses and their carers. The survey was promoted by the Confederación Salud Mental España, the Asociación Madrileña de Amigos y Familiares de Personas con Esquizofrenia (AMAFE) and CIBERSAM, with the cooperation of private industry. The CIBERSAM Training Programme has the exclusive Interuniversity Master on research into Mental Health, which has again beaten the record for applications for enrolment this year. Our platforms: The Library of Instruments on Mental Health and Disability, the Collection of DNA and the Neuroimaging platform, along with the external platform of the Brain Bank, have continued to collect samples to be used in collaborative intra- and inter-CIBER projects. On an international scale, CIBERSAM has become a privileged partner in taking part in large consortiums for research into genetics and neuroimaging. We trust we will keep up this rising pace of productivity, meritocracy and social return so characteristic of CIBERSAM over the coming years!

Scientific Programmes

Depression

Coordinator: Víctor Pérez Sola

Joining the CIBERSAM has enabled our groups to start lines of research which examine the prevalence of depression and its comorbidity with addictive disorders or inflammatory diseases. Epidemiological studies have shown the importance of early detection and effective treatment to prevent chronicity, as well as the importance of social and family factors in the evolution of depression, especially in the most fragile groups (the elderly and adolescents). Such factors as cognitive reserve or the remission of symptoms have been confirmed as essential prognostic factors in the medium and long term.

Suicide is one of the priority lines in the programme. To highlight this priority the groups involved have included suicide prevention in the name of the programme, which will now be known as "Depression and Suicide Prevention". CIBERSAM researchers took a highly active part in consensuses and European projects focussing on the evaluation of interventions in suicide prevention and several articles appraising such factors as bullying at school or pain in the risk population have been published.

In the line focussing on effectiveness, resistance and new therapeutic drugs in depression, findings have been published in the area of pharmacogenetics in populations such as adolescents and the largest clinical test published until now evaluating the effectiveness of pharmacogenetics in depression treatment, confirming its effectiveness in usual clinical practice. Greater knowledge has also been obtained of the mechanisms involved in anti-depression techniques such as Electroconvulsive Therapy and Deep Brain Stimulation. One should also stress the research into the evaluation of the effectiveness/efficiency of psychotherapeutic techniques proposing the implementation of specific techniques such as personalised medicine, e-health or virtual programmes for the diagnosis and/or treatment of depression in usual clinical practice. Different collaborative projects have also been started for creating and validating a functional rehabilitation programme for major depression as a new therapeutic strategy for the treatment of cognitive symptoms.

As regards the neurochemical bases for depression, several studies have focussed on the characterisation of the ventral cingulate cortex as a key cortical area in the physiopathology and treatment of depression, displaying the involvement of glial glutamate transporters via siRNAs in animal models of depression. Research has also been directed at the involvement of two subtypes of serotonergic receptors (5-HT1A and 5-HT2C) and of the alfa-2 adrenergic receptors in the mechanisms of action of ISRS, as well as in the use of these drugs for treating pain. The research connected with the implication of the 5-HT4 receptor and of B-catenin in the pathogeny of depression and the mechanisms of action of fluoxetine has also continued, as well as obtaining preliminary results on the anti-depressive potential of cannabidiol in animal models of depression.

Schizophrenia

Coordinator: Benedicto Crespo-Facorro

Some of the most significant results of the programme in 2017 are a number of 54 publications in journals indexed in the first decile according to the JCR in the area of Psychiatry: World Psychiatry, JAMA Psychiatry, Molecular Psychiatry, Biological Psychiatry, Schizophrenia Bulletin, Psychological Medicine, British Journal of Psychiatry; in the neuroimage area; Neuroimage; in the genetics area: Nature Genetics; Multidisciplinary Sciences area: Nature Communications, PLoS Me; in the neurology area: Nature Review Neurology; in the pharmacology & pharmacy area: Neuropharmacology; and in the Neurosciences area: Nature Neuroscience, Molecular Neurobiology, Neuropsychopharmacology.

Connected with this programme over 2017 three projects were obtained from the Brain and Behavior Research Foundation, one IMI2 RIA project, one H2020-MSCA-ITN-2016 project and a COST-H2020 participation. On the national scale, a total number of thirteen projects have been awarded competitive financing in public calls of the AES 2017. There are over twenty projects stemming from autonomous communities and private institutions. One should also stress the two Rio Hortega contracts obtained.

Two patents have been published: "Transgenic animal model of mood disorders". D. Arteta, M. Ferrer, L. Simón, A. Martinez, M. Uribarri, J.J. Meana and L.F. Callado. International Publication Number WO2013139676; "Method to predict the safety of the treatment with a nicotinic cholinergic receptor agonist". C. Cortijo, J.J. Meana, J. Ballesteros and A. García-Orad. International Publication Number WO 2013/156657. And another patent was submitted: APPLICATION. Registered industrial property title: METHOD FOR PREDICTING THE THERAPEUTIC RESPONSE TO ANTIPSYCHOTIC DRUGS. Inventors/authors/obtainers: Jesus Sainz Maza; Benedicto Crespo Facorro. Application number: P201730464.

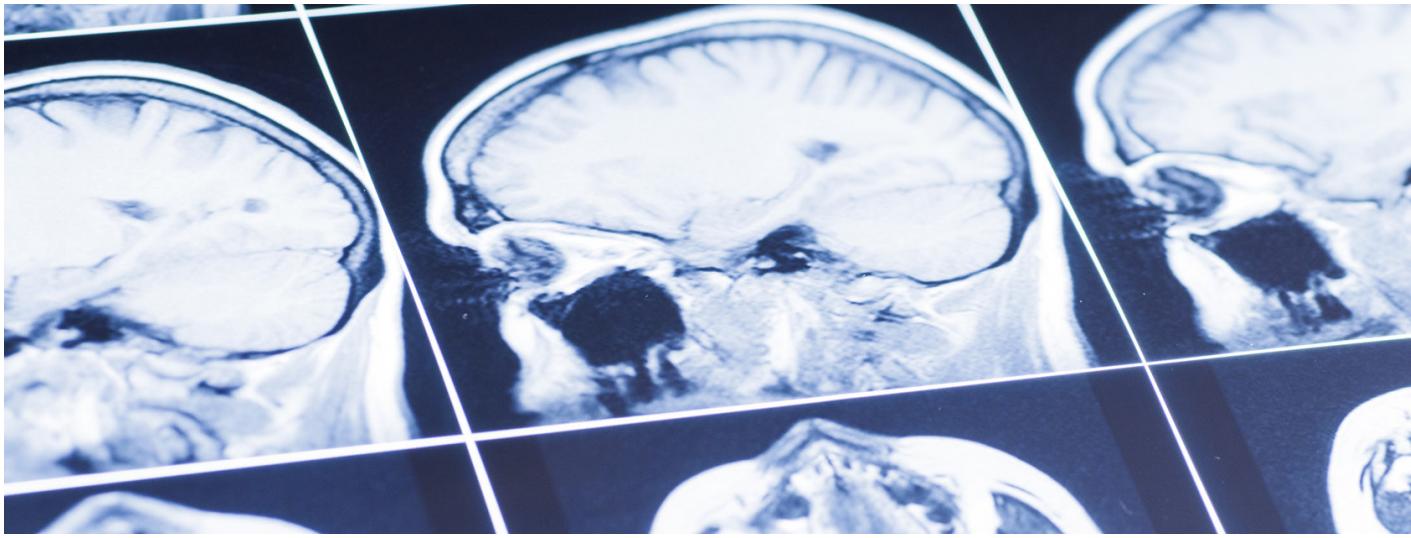
As regards other merits, the members of the programme and their work have been recognised with different awards at national and international meetings, congresses and symposia. The national and international recognition obtained by different groups for the quality of their work and the management done by them is also noteworthy.

Two awards for Professional careers: Jerónimo Saiz Ruiz. *Sociedad Española de Psiquiatría Congreso Nacional de Psiquiatría*, Barcelona, November 2017; and the Award for Professional Excellence 2017 to Dr Miquel Bernardo in the category of Medical Education by Barcelona Medical Association, November 2017.

Two awards for quality of doctoral theses: 1.- XXIII SEPB AWARD FOR THE BEST DOCTORAL THESIS, ACADEMIC YEAR 2015-2016. *Congreso Nacional de Psiquiatría*, Barcelona 2017. Alicia Valiente, for the work entitled Clinical and biological characterisation of Schizophrenia with a prevalence of negative symptoms; 2. Extraordinary doctorate award for doctoral thesis: Family factors and psychiatric disorders among Puerto Rican children and youth in two different sociocultural contexts. Doctorand: Olga Santesteban.

Most significant scientific achievements in 2017:

- Scientific management of the Instituto de Investigación Marqués de Valdecilla (IDIVAL), Dr Benedicto Crespo Facorro.
- Completion of the European Horizon2020 m-Resist project with the final approval of the European Commission. Dr Josep M. Haro.
- Creation of a network with the main hospitals in the Comunidad de Madrid for the evaluation of all the first psychotic episodes to be carried out uniformly and to be followed up longitudinally with standardised evaluations on those patients (project AGES-C). Dr. Celso Arango.



Bipolar Disorder

Coordinator: Ana González-Pinto

Some of the most relevant results of the groups forming the programme are the 21 articles in the first decile. The findings of these studies were published in journals of the greatest renown such as Lancet, Lancet Neurology, JAMA Pediatrics, World Psychiatry, Acta Psychiatrica Scandinavica, Neuroscience & Biobehavioral Reviews, Molecular Psychiatry, Journal of the American Academy of Child and Adolescent Psychiatry, Frontiers in Neuroendocrinology, Schizophrenia Bulletin and Psychotherapy and Psychosomatics.

The programme has a high index of internationalisation and scientific productivity, stressing the cooperative work done between CIBERSAM groups and other areas of the CIBER, as well as national and international collaboration.

Apart from these 12 projects with competitive financing were awarded in 2017 (MINECO-ISCIII, UE, Generalitat de Catalunya, Brain & Behaviour Research Foundation).

The awards and distinctions received by members of the programme were as follows:

- The 2017 Simon Bolivard Award on behalf of the APA-APAF. San Diego-California. USA (Eduard Vieta).
- 2017 Research award in the area of biological psychiatry. World Federation of Societies of Biological Psychiatry (Eduard Vieta).
- Eduard Vieta among the list of the most influential scientists in the world published by Clarivate Analytics. 2017 Highly Cited Researchers.
- "Vila Saborit" Award for the best publication of 2016 by the Catalan Society of Psychiatry and Mint Health: Amann et al. Brain structural changes in schizoaffective disorder compared to schizophrenia and bipolar disorder. Acta Psychiatr Scand 2016; 133: 23-33.
- Extraordinary Doctorate award: "*Biomarcadores diferenciales de la esquizofrenia*" (Leticia García). Directors: Julio Bobes y Mª Paz García-Portilla.
- XXIII SEPB Award for the best doctoral thesis "Long-term prognosis of the Bipolar Disorder with mixed episodes" (Iñaki Zorrilla). Director: Ana González-Pinto.

- VIII OSIARABA Research Sessions award for the best collaborative article OSI Ara- ba-UPV. De La Rosa et al. Determining if Borderline Personality Disorder and Bipolar Disorder are Alternative Expressions of the Same Disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry. 2017;78(8): e994-e999.
- Eduard Vieta named best researcher of the year for 2017 by the World Federation of Biological Psychiatry Associations.

Some of the more noteworthy scientific achievements accomplished by the different groups in the programme are:

- Doctoral thesis entitled "Potential neurocognitive endophenotypes for the bipolar disorder: Motor speed, Manual, Visual Memory, Processing speed" (Patricia Correa). Directors: Vicente Balanza and Gabriel Selva.
- Completion of the field study of the CIE-11 (OMS). Validity and clinical utility of the diagnostic criteria of the CIE-11 for Bipolar disorders.
- Preparation of the report on completion of the European project "Participation To Healthy Workplaces and inclusive Strategies in the Work Sector", (https://www.path-ways.eu/wp-content/uploads/pathways_report_assess.pdf) (Jose Luis Ayuso).
- Activation of the web site www.bipogent.cat intended to give information and recruit patients and controls (Eduard Vieta, Peter McKenna, Elisabet Vilella).
- Participation of FIDMAG researchers in the ENIGMA international consortium.
- Mónica Martínez-Cengotitabengoa admitted as member of the ECNP Bipolar Network.
- Ana González-Pinto appointed president of the SEPB.
- App developed for improving the wellbeing of the bipolar disorder (Ana González-Pinto).

Therapeutic innovation

Coordinator: Francesc Artigas Pérez

Some of the most relevant results of the groups in the programme in 2017 are the publication of 39 articles in D1 journals, most of these collaborative work (intra-CIBER, national and international). We should stress publications in leading journals such as The Lancet (FI:47.831), Nature Genetics (FI:27.959), World Psychiatry (FI:26.561), Nature Neuroscience (FI:17.839), Nature Communications (FI:12.124) and Molecular Psychiatry (FI:13.204). In the field of innovation, three patents have been applied for (P20173034, PCT/ES2017/070623 and P201730464), and a further three have been published (US15/549,653 Method for obtaining a pharmaceutical composition of polymeric nanoparticles...., WO2013139676 Transgenic animal model of mood disorders and WO2013/156657 Method to predict the safety of the treatment with a nicotinic cholinergic receptor agonist).

As regards funding, the previous year's amount has been exceeded, obtaining 40 grants/competitive projects from national public bodies (MINECO/FEDER: SAF2017-88126-R, SAF2017-86620-R, SAF2017-85888-R, SAF2016-75500-R, SAF2016-76046-R, PT17/0005/0001, DTS17/00122, CP16/00096, PIE16/00055 and ECT-2017-0371; MSSSI: 2017/085; FIS/ISCIII: PI16/00287, PI17/01766, PI17/00064, PI16/02037, PI16/00187, PI17/01066, PI17/00941, PI17/01056, PI17/00221 and PI17/00402), autonomous community bodies (Generalitat de Catalunya: 2017SGR717, PERIS-SLT006/17/00357 y COMRDI15-1-0017-07; Andalusia Authority: PI/0009/2017 and PI/0080/2017; Basque Government:

KK- 2017/00023, 2017222002 and 2016111021; UPV/EHU: US17/19; Community of Madrid: B2017/BMD-3867; IDIVAL: INNVAL16/03, CM16/00034, Next-Val2017 and Prim-Val2017), national foundations/hospitals (Fundación CNIC; Hospital Clínic: Conv-FU-17/2017) and European Union (HORIZON2020: 754907 and CA15211). Among the awards and distinctions received during 2017, stand out:

- CCB/07/09/0004: Simon Bolivar Award (APA) and Research Award (WFSBP) (Eduard Vieta). Dr Vieta appears on the list of most influential scientists in the world, published by Clarivate Analytics (2017 Highly Cited Researchers).
- CB07/09/2001: Scientific Management of IDIVAL (Benedicto Crespo Facorro).
- CB/07/09/0008: Award for the best oral paper (Inés Ibarra Lecue), 18 Annual Meeting of the *Sociedad Española de Investigación sobre Cannabinoides*.
- CB/07/09/0026: First prize for photography (José Luis Muñoz Madrigal), *VII Competition for scientific dissemination*, UCM.
- CB/07/09/0031: Prize for the best poster (Yolanda Sierra Palomares), *XIV Congreso Nacional de la SECAL* and Prize for Scientific Communication (Susana Carmona), *XII Premio madri+d*.
- CB/07/09/0034: Santiago Reig prize for young CIBERSAM researchers (Albert Ferrés Coy) and Prize for the best posters (Mireia Tarrés Gatius), CIBERSAM Ideas Laboratory.

The following are some of the prominent scientific achievements:

- Characterisation of the infralimbic prefrontal cortex as key area in the physiopathology and treatment of depression (Gasull-Camós et al., Transl Psychiatry 2017).
- Obtaining a nanoparticle from a cannabinoid derivative with therapeutic potential (Berrocoso et al., Nanomedicine 2017).
- Apoliproprotein ApoA1 combined with LPS has been identified as a key mechanism for the entry of inflammatory signals to the brain (Vargas-Caraveo et al., Sci Rep 2017).
- A model of dual impact of schizophrenia reveals alterations to neurochemistry and structure of inhibitory networks of prefrontal cortex and amygdala (Castillo-Gómez et al., eNeuro 2017).
- Synaptic and cognitive side-effects of antipsychotics are mediated by the transcription of Hdac2 via NF-κB (Ibi et al., Nat Neurosci 2017).
- Pregnancy causes structural changes in the brain of gestating mothers, with reductions of grey matter in zones involved in social cognition. (Hoekzema et al., NatNeurosci 2017).

Mental disorders of the child and adolescent

Coordinator: Josefina Castro Fornieles

The programme for mental disorders of the child and adolescent set up in 2010 is made up of six CIBERSAM groups (Celso Arango, Miguel Bernardo, Miguel Casas, Manuel Desco, Lourdes Fañanás, Rafael Tabarés-Seisdedos) and is intended to study mental disorders of early childhood and adolescence.

Some of the most significant results of the programme in 2017 are a number of 64 publications mainly in journals indexed in the first quartile according to the JCR including for example the Lancet Psychiatry, Acta Psychiatrica Scandinavica, Schizophrenia Bulletin or Journal of the American Academy of Child and Adolescent Psychiatry. 55 of these publications are in first quartile journals and 31 in the first decile.

There are also several European projects connected with the programme of mental disorders of the child and adolescent, including PSYSCAN, MATRICS, AGGRESSOTYPE, PreDICT-TB or APUS- eCig. Furthermore,

in 2017 three researchers have obtained financing from the Brain and Behavior Research Foundation by means of the NARSAD awards. On a national scale, competitive backing has been obtained from both public and private funds for a total number of 38 projects which have been active throughout 2017 on the psychotic disorders of the early childhood and adolescence, bipolar disorder, the risk of psychosis, the obsessive-compulsive disorder, the autism spectrum disorder, child abuse, attention deficit disorder or early-onset depression.

As regards other merits, the members of the programme for mental disorders of the child and adolescent have been awarded different prizes, including: the EPA Research Prize 2018 (in the category of Child and Adolescent Psychiatry); madri+d award for the best Scientific Paper; the third prize for the best poster in the "VI Catalan Congress of Mental Health"; and the prize for the best poster type communication in the "*XIV Congreso Nacional de la Sociedad Española para las Ciencias del Animal de Laboratorio (SECAL)*".

Some of the more noteworthy scientific achievements accomplished in 2017 are:

- The clinical, neuropsychological, neuroimage and genetic characterisation of children and adolescents with a high genetic risk of schizophrenia or bipolar disorder.
- The determination of how genetic factors may increase the vulnerability to the effects of adverse environmental conditions occurring in later stages of cell ageing developing in the first psychotic episodes.
- The demonstration of the effectiveness of cognitive-behavioural therapy in first psychotic episodes.
- The characterisation of different phenotypes in the Autist Spectrum Disorder.
- The determination of structural cerebral anomalies in the Attention Deficit Disorder.
- The description of the moderating role of certain genetic variants in the association of different types of trauma in diverse psychiatric pathologies.
- The study of the evolution of the psychiatric clinic and cognitive deficits in patients with anti-NMDA-R encephalitis.

Psychosomatic, Anxiety and Impulse Control Disorders

Coordinator: José Manuel Menchón Magriña

The programme focusses on epidemiological, clinical and basic research into a wide range of mental disorders and conditions which have great impact on people's mental health and psychological well-being. It is made up of eight groups, which are both clinical and basic and whose main lines of research are ageing, inflammation in relation with stress and anxiety disorders, longitudinal epidemiological studies and risk factors in the obsessive-compulsive spectrum, neurobiological and psychosocial aspects of pain.

One relevant aspect is the line of studies on the role of cannabinoids in pain with an improvement effect in animal models and their potential analgesic use. With regard to this potential effect and line of research, CIBERSAM has taken part along with the Universidad de Cádiz in the licensing of the patent to GB Sciences, an American company, for a formulation for release of cannabinoids for neuropathic pain. In another line connected with neuroinflammatory mechanisms, the role of cytokines, particularly chemotactic cytokines, as mediators in anti-inflammatory actions of noradrenalin has been described. The mechanisms for infiltration of liposaccharides in the central nervous system through lipoprotein carriers have also been identified.

From the epidemiological standpoint we have taken part in international epidemiological studies examining the burden of illness by age groups, gender and country. In this context we study such complications as suicide, functionality, psychological wellbeing and social determinants depending on the level of countries' economic development. Studies have also been carried out on the implementation of DSM-5 and the prevalence of specific mental disorders in accordance with this new classification.

In the ageing field the reliability and validity of the 'IDEAL Schedule' was determined, as an instrument developed to establish the staging of care needs in patients with dementia. We have also participated in an excellent review of the change of prevalence and incidence of dementia over time. Apart from this, in the field of the assessment, the utility of ecological assessment has been studied through the electronic tool known as 'Memind', proving its usefulness for this type of assessments. In the compulsivity line we have taken part in studies of international consortiums such as ENIGMA (Enhancing NeuroImaging Genetics through Meta-Analysis) in the OCD. As for behaviour and personality, we have specifically studied risk factors of personality, temperamental traits and cognitive factors in suicidal conducts. In this line of personality disorders, it is interesting to study the changes of psychopharmacological prescription in the borderline personality disorder of the last 15 years in which the widespread use of drugs for this disorder (88% of the patients) is confirmed and the tendency towards a lower use of benzodiazepines and anti-depressants, with greater use of atypical anti-psychotics.

Training Programme

Coordinator: Juan Antonio Micó Segura

The CIBERSAM has since its beginnings carried out a Training and Mobility Programme intended to be a benchmark in the learning and start of a research career in mental health in this country. This programme was updated in 2017 with the drafting of a Specific Standard for Regulating the Training and Mobility Programme.

The backbone of this Programme is the Official Master in Initiation to Research, which started in academic year 2013-2014.

Along with the Master participation and attendance at courses connected with different areas of research into mental health is promoted in both clinical and basic approaches by contributing to financing these.

Some of the more noteworthy of these courses are the ones arranged with the CIBERSAM's own accrediting support such as: The Ideas Laboratory, the Course on Neurosciences and the Course on the Instrument Platform. These courses are open to the participation of researchers from other CIBERs as well as those interested in general.

The programme also promotes and finances training stays at any other of the CIBERSAM groups, as well as at research groups of other CIBER or research centres of national or international prestige.

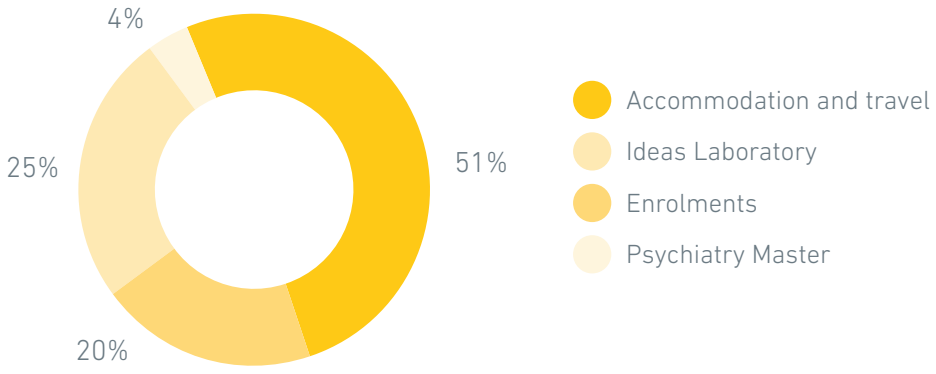
The Master on Initiation to Research in Mental Health is an inter-university course in which the Complutense de Madrid, Barcelona and Autónoma de Barcelona, Cádiz and Cantabria universities take part, being coordinated by the last of these. Eleven CIBERSAM groups officially take part in the teaching work and the others take part as contributors. The Master Programme (with 60 credits) is given on-line, combining this with practical-type research stays at the different groups in the CIBERSAM, in both clinical and basic approaches. These stays may be in a short or long cycle, depending on the category. The subjects tackle all the basic aspects required to get started in research into mental health, as well as learning about the neurobiological bases and different diagnostic, clinical and therapeutic approaches.

There are 37 pupils enrolled in the programme currently under way, including both Spanish and foreign students.

As regards the financing offered by the Programme, all the groups provide a set amount which is placed in a common pool and administered by the head of the programme depending on the training activities which are applied for.

Apart from the Master Course, the Training Programme has financed a total number of 25 enrolments for research courses and seminars and 50 mobility grants, coming to a total sum of 32,468 Euros.

Training expenses in 2017



Platforms

Coordinator: Javier Meana Martínez

Over 2017, the three CIBERSAM platforms along with the external platform –Brain Collections – have fulfilled the operative objectives set in the Strategic Plan. In parallel they have developed: I) strategies for technological improvement in the case of the Neuroimaging and DNA platforms; II) the proper agreements with the institutions backing the Neuroimaging Platform have been renewed and/or updated. The quality area of CIBERSAM has furthermore got under way a process of reviewing and adapting the procedures of the platforms to comparable criteria in accordance with standardised quality processes.

Objectives and achievements in 2017

	LIBRARY OF INSTRUMENTS		DNA COLLECTION		NEUROIMAGE	
	Objective	Achieved	Objective	Achieved	Objective	Achieved
Existing instruments	325	325				
Added instruments	5 new 25 updated	5 new 25 updated				
Consultations or applications for use made	13	13			18	19
Publications financed	60	73				
Training activities	1	1				
Images stored					14369	15623
Applications for use						
Groups contributed			6	3	13	13
User groups			13	2 consortia	7	7
Questionnaires collected						
Patients included			+1000	+503		
Applications for coordinated studies				2		

Number of publications which have used CIBERSAM Platforms	**26**
Platforms used in the publications:	
DNA collections	8
Neuroimaging platform	7
Library of instruments	6
Brain collections	5
Number of clinical trials which have used CIBERSAM Platforms	**2**
Platforms used in clinical trials:	
DNA collections	2
Number of patents which have used CIBERSAM Platforms	**1**
Platforms used in patents:	
Brain collections	1

Scientific Production

PUBLICATIONS

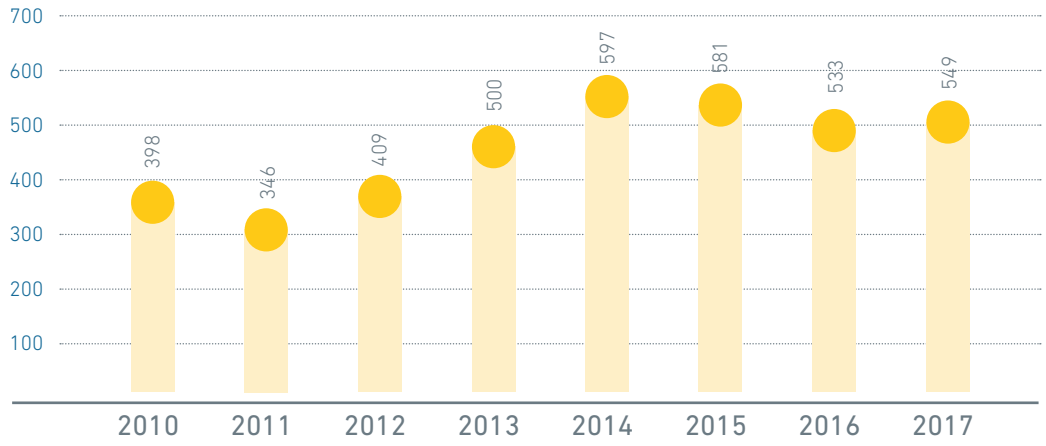
No. of publications in 2017

TOTAL	**549**
Q1	331
D1	117

Collaboration work

IntraCIBER	133
InterCIBER	86

Evolution of the publications



Most relevant publications of the CIBERSAM in 2017 by impact factor

Publication	Impact Factor
Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. Health effects of overweight and obesity in 195 countries over 25 years. New Engl J Med 2017;377(1):13-27.	72,4060
Reitsma MB, Fullman N, Ng M, Salama JS, Abajobir A, Abate KH, et al. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990–2015: a systematic analysis from the Global Burden of Disease Study 2015. Lancet 2017;389(10082):1885-1906	47,8310
GBD 2015 Healthcare Access and Quality Collaborators, Fullman N, Sorensen RJD, Bollyky T, McKee M, Nolte E, et al. Healthcare Access and Quality Index based on mortality from causes amenable to personal health care in 195 countries and territories, 1990–2015: a novel analysis from the Global Burden of Disease Study 2015. Lancet 2017;390(10091):231-266.	47,8310
Dieleman J, Campbell M, Chapin A, Eldrenkamp E, Fan VY, Haakenstad A, et al. Evolution and patterns of global health financing 1995-2014: Development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. Lancet 2017;389(10083):1981-2004	47,8310

Publication	Impact Factor
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Wang H, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, et al. Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970-2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390(10100):1084-1150.	47,8310
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Patent

Applied for

- "Method for predicting the therapeutic response to antipsychotic drugs". Benedicto Crespo. (P201730464)

Clinical Guides

- Care Protocol for Patients with Psychomotor Agitation.
- Effectiveness, efficiency and efficacy in the multidimensional treatment of schizophrenia: Rethinking project.
- *Guía de intervención mhGAP para los trastornos mentales, neurológicos y por consumo de sustancias en el nivel de atención de salud no especializada. Versión* 2.0. ISBN: 978-92-75- 31957-4 (Spanish version).
- *Guía de tratamiento del trastorno obsesivo-compulsivo en niños y adolescentes.*
- *La Guía SEPG sobre el uso de antipsicóticos en el paciente de edad avanzada. Psicogeriatría, 7.*
- Methodological recommendations for cognition trials in bipolar disorder by the International Society for Bipolar Disorders Targeting Cognition Task Force.
- Multidisciplinary consensus on the therapeutic recommendations for iatrogenic hyperprolactinemia secondary to antipsychotics.
- Protocol for the management of psychiatric patients with psychomotor agitation.
- Research Recommendations for Improving Measurement of Treatment Effectiveness in Depression.

- Seeing the doctor without fear: www.doctortea.org for the desensitization for medical visits in Autism Spectrum Disorders.
- The International College of Neuropsychopharmacology (CINP) Treatment Guidelines for Bipolar Disorder in Adults (CINP-BD-2017), Part 1: Background and Methods of the Development of Guidelines.
- The International College of Neuro-Psychopharmacology (CINP) Treatment Guidelines for Bipolar Disorder in Adults (CINP-BD-2017), Part 2: Review, Grading of the Evidence, and a Precise Algorithm.
- The International College of Neuro-Psychopharmacology (CINP) treatment guidelines for Bipolar disorder in adults (CINP-BD-2017), part 3: The clinical guidelines.
- Vía Clínica de cirugía bariátrica.
- Abordaje Integrador del Trastorno Límite de la personalidad.
- Evidence-based national suicide prevention task force in Europe: A consensus position paper.
- Prevalencia de trastornos mentales en Galicia.
- When the healthcare does not follow the evidence: The case of the lack of early intervention programs for psychosis in Spain.

CIBERSAM Groups. Publications

Group Leader	Total Publications	Q1	D1	Institution	Province
Arango López, Celso	36	26	16	Servicio Madrileño de Salud. Hospital Gregorio Marañón	Madrid
Artigas Pérez, Francesc	10	8	4	Ag. Est. Consejo Sup. de Investigaciones Científicas. Instituto de Investigaciones Biomédicas de Barcelona	Barcelona
Ayuso Mateos, José Luis	17	12	1	Servicio Madrileño de Salud. Hospital Universitario La Princesa	Madrid
Bernardo Arroyo, Miguel	36	23	8	Hospital Clínico y Provincial de Barcelona	Barcelona
Bobes García, Julio	28	13	4	Univ. de Oviedo. Facultad de Medicina	Asturias
Casas Brugué, Miguel	32	12	2	Fundación Hospital Universitario Vall d'Hebron – Institut de Recerca (VHIR). Hospital Vall d'Hebron	Barcelona
Crespo Facorro, Benedicto	26	17	7	Instituto de Investigación Marqués de Valdecilla. Hospital Universitario Marqués de Valdecilla	Cantabria
Desco Menéndez, Manuel	14	12	5	Servicio Madrileño de Salud. Hospital Gregorio Marañón	Madrid
Fañanas Saura, Lourdes	23	18	6	Universidad de Barcelona. Facultad de Biología. Universidad de Barcelona	Barcelona
González-Pinto Arrillaga, Ana	38	18	7	Fundación Vasca de Innovación e Investigación Sanitarias. Hospital Universitario de Álava – Sede Santiago	Álava

Group Leader	Total Publications	Q1	D1	Institution	Province
Haro Abad, Josep Maria	115	85	36	Fundación para la Investigación y Docencia Sant Joan de Déu. Parc Sanitari Sant Joan de Déu	Barcelona
Leza Cerro,Juan Carlos	7	6	3	Universidad Complutense de Madrid. Facultad de Medicina	Madrid
Mckenna, Peter J.	23	11	2	Fundación para la Investigación y Docencia María Angustias Giménez (FIDMAG). Hospital Hermanas Hospitalarias Benito Menni	Barcelona
Meana Martínez, José Javier	21	13	6	Universidad del País Vasco. Facultad de Medicina y Odontología	Vizcaya
Menchón Magriña, José Manuel	40	28	6	Fundación IDIBELL. Hospital Universitario de Bellvitge	Barcelona
Micó Segura, Juan Antonio	7	5	0	Universidad de Cádiz. Facultad de Medicina	Cádiz
Palomo Álvarez, Tomás	29	19	6	Universidad Complutense de Madrid. Facultad de Medicina	Madrid
Pazos Carro, Ángel Armando	5	3	1	Universidad de Cantabria. Facultad de Medicina	Cantabria
Pérez Sola, Víctor	59	31	13	Consorci Mar Parc Salut Barcelona	Barcelona
Sáiz Ruiz, Jerónimo	20	12	2	Servicio Madrileño de Salud. Hospital Ramón y Cajal	Madrid
Sanjuán Arias, Julio	18	8	0	Universidad de Valencia. Facultad de Medicina de Valencia	Valencia
Tabarés-Seisdedos, Rafael	42	35	16	Universidad de Valencia. Facultad de Medicina de Valencia	Valencia
Vieta Pascual, Eduard	83	54	12	Hospital Clínico y Provincial de Barcelona	Barcelona
Vilella Cuadrada, Elisabet	7	2	0	Fund. Instituto de Investigación Sanitaria Pere Virgili. Universidad Rovira y Virgili	Tarragona

Linked Groups

Group Leader	Institution	Province
Olivares Díez, José Manuel	Inst. de Investigación Sanitaria Galicia Sur	Pontevedra
Palao Vidal, Diego José	Corporación Sanitaria Parc Taulí	Barcelona
Rodríguez Jiménez, Roberto	Hospital Universitario 12 de Octubre	Madrid

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