



Instituto
de Salud
Carlos III

ANNUAL REPORT 2017



Unión Europea

Fondo Europeo
de Desarrollo Regional
"Una manera de hacer Europa"



Unión Europea

Fondo Social Europeo
"El FSE invierte en tu futuro"



GOBIERNO
DE ESPAÑA

MINISTERIO
DE CIENCIA, INNOVACIÓN
Y UNIVERSIDADES



Instituto
de Salud
Carlos III

Edited by: Instituto de Salud Carlos III - Ministerio de Ciencia, Innovación y Universidades



Acknowledgements:

To all staff of ISCIII Areas and Units, for their active participation and effort in its development.

NIPO: 062170394

Copyright

Attribution non-commercial use

- Share alike by-nc-sa.

Commercial use of the original work or any derivate works are not permitted, the distribution of which should be done with the same license that governs the original work.



Design and layout:

Dayenu, Grupo de comunicación

General catalog of official publications:

<http://publicacionesoficiales.boe.es>

Publication included in the editorial program of the suppressed Ministry of Economy, Industry and Competitiveness and edited by the Ministry of Science, Innovation and Universities, in accordance with the ministerial restructuring established by Royal Decree 355/2018, of June 6.

Free version of this report on Internet (PDF and EPUB format):

<http://publicaciones.isciii.es>

ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

REGULATIONS, ETHICS

- 6.1 Advisory Committee for Human Tissue and Cell Donation and Use; the National Registry of Research Projects
- 6.2 National Register of Biobanks
- 6.3 Bioethics Committee
- 6.4 Research Ethics Committee (CEI)
- 6.5 Research Ethics and Animal Welfare Committee (CElyBA)

Internationalisation

- 5.1 International Programmes

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

TECHNICAL AND SCIENTIFIC ACTIVITIES

- 3.1 Centres and Units
- 3.2 Intramural Research

TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational Medicine





ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

1.1 GOVERNING BODIES

Carlos III Institute of Health, O.A., M.P. (hereinafter ISCIII) is a Public Research Entity (OPI) and an autonomous legal entity whose aim is to carry out and offer high-quality scientific and technical services to the National Health System and to society as a whole.

In accordance with Additional Provision Four of Royal Decree 531/2017, of 26 May, which implements the basic organisational structure of the Ministry of Economy, Industry, and Competitiveness, ISCIII reports to the Ministry of Health, Consumer Affairs, Social Welfare (MSCBS) for the health, planning, and medical assistance activities it carries out. It reports to the MSCBS in coordination with the Ministry of Economy, Industry, and Competitiveness through the Secretary of State for Research, Development, and Innovation for applied research activities that are able to be transferred to the National Health System (SNS).

ISCIII partners with SNS research centres in order to contribute to structuring its research. It also accredits the Health Research Institutes (IIS) and Cooperative Research Networks in order to focus research on the intended objectives, to promote excellence in research, and to facilitate its own resources for research.

1.2 CENTRES, UNITS, SCHOOLS, AND FOUNDATIONS

ISCIII Centres and Units, national and international benchmarks, carry out research activities in the fields of biomedicine, environmental health, and public health in general. In every relevant field of research, programmes are designed to approach diseases from a preventive, diagnostic, and therapeutic standpoint, with researchers and technologists from all scientific disciplines working together. Their priorities mainly include research on infectious, chronic, rare, neurodegenerative, tropical, and occupational diseases; telemedicine; environmental health; epidemiology; public health; and healthcare.

ISCIII also provides advanced scientific and technical services that are national benchmarks which fully incorporate new technologies in order to improve health and social welfare.

Their services are focused on reference laboratories, surveillance and alerts, scientific and technical training and health education, scientific information and documentation, consulting on the transfer of research results, and the evaluation of technology and procedures applicable to clinical practice.

Centres and Units

Health Technology Assessment Agency (AETS)
National Library of Health Sciences (BNCS)
National Epidemiology Centre (CNE)
National Microbiology Centre (CNM)
National Centre of Tropical Medicine (CNMT)
National Environmental Health Centre (CNSA)
Research Institute for Rare Diseases (IIER)
Research Centre on Congenital Abnormalities (CIAC)
Healthcare Research Unit (Investén-ISCIII)
Telemedicine and e-Health Research Unit
Functional Unit for Research on Chronic Diseases (UFIEC)
National Stem Cell Bank (BNLC)
Biological Alert Laboratory Network (RE-LAB)
UCM-ISCIII Joint Centre for Research on Human Evolution and Behaviour

Schools

Through the National School of Public Health (ENS) and the National School of Occupational Medicine (ENMT), ISCIII carries out training, continuing education, and specialisation in the fields of health and health administration and management for medical and non-medical staff, without prejudice to the competences of other public bodies as well as the development of methodological, social sciences, and economic disciplines related to health.

Foundations

The following foundations are affiliated with ISCIII: The National Cancer Research Centre (CNIO), the National Centre for Cardiovascular Research (CNIC), and the National Centre for Research on Neurodegenerative Diseases (CIEN), which carry out their activities in the fields of oncology, cardiovascular disease, and neurological research, respectively.

1.3 HUMAN RESOURCES

In 2017, the trend observed in recent years of reducing ISCIII's own staff continued. The total number of staff members is 913, of which 496 are civil servants, 177 are permanent staff, and 240 are temporary staff (224 of them are associated with projects).

1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

Changes in human resources (2012-2017)

1 ORGANISATION

Staff Changes Carlos III Institute of Health 2012/2017		2012			2013			2014			2015			2016			2017			% change 2012-2017		
		♀	♂	Total	♀	♂	Total	♀	♂	Total	♀	♂	Total	♀	♂	Total	♀	♂	Total	♀	♂	%
Civil Servants	A1/G1	166	123	289	167	124	291	165	124	289	164	117	281	153	110	263	153	103	256	-7.83	-16.26	-11.42
	A2/G2	76	24	100	71	23	94	71	21	92	68	20	88	65	16	81	62	15	77	-18.42	-37.50	-23.00
	C1/G3	97	26	123	93	25	118	91	23	114	91	21	112	78	18	96	76	20	96	-21.65	-23.08	-21.95
	C2/G4	76	23	99	71	20	91	63	19	82	55	17	72	56	15	71	51	13	64	-32.89	-43.48	-35.35
	E/G5	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3	0.00	0.00	0.00
	Total...	416	198	614	403	194	597	391	189	580	379	177	556	353	161	514	343	153	496	-17.55	-22.73	-19.22
Permanent Staff	A1/G1	12	1	13	10	1	11	10	1	11	9	0	9	10	1	11	12	1	13	0.00	0.00	0.00
	A2/G2	4	0	4	4	0	4	4	0	4	4	0	4	3	0	3	3	0	3	-25.00	0.00	-25.00
	C1/G3	65	26	91	64	25	89	62	25	87	59	24	83	53	20	73	48	21	69	-26.15	-19.23	-24.18
	C2/G4	33	13	46	33	13	46	28	11	39	27	7	34	23	8	31	23	9	32	-30.30	-30.77	-30.43
	E/G5	50	18	68	50	17	67	47	18	65	45	17	62	43	17	60	41	19	60	-18.00	5.56	-11.76
	Total...	164	58	222	161	56	217	151	55	206	144	48	192	132	46	178	127	50	177	-22.56	-13.79	-20.27
Temporary Staff	A1/G1	130	40	170	113	41	154	107	38	145	112	37	149	132	46	178	120	48	168	-7.69	20.00	-1.18
	A2/G2	13	2	15	8	4	12	6	3	9	4	3	7	3	3	6	2	1	3	-84.62	-50.00	-80.00
	C1/G3	77	7	84	59	7	66	58	6	64	51	5	56	62	11	73	57	7	64	-25.97	0.00	-23.81
	C2/G4	2	0	2	1	0	1	1	0	1	1	0	1	0	1	1	3	0	3	50.00	0.00	50.00
	E/G5	4	2	6	4	2	6	1	2	3	0	1	1	0	2	2	0	2	2	-100.00	0.00	-66.67
	Total...	226	51	277	185	54	239	173	49	222	168	46	214	197	63	260	182	58	240	-19.47	13.73	-13.36
	806	307	1113	749	304	1053	715	293	1008	691	271	962	682	270	952	652	261	913	-19.11	-14.98	-17.97	
Total...	1113			1053			1008			962			952			913			-17.97			
	2012			2013			2014			2015			2016			2017						

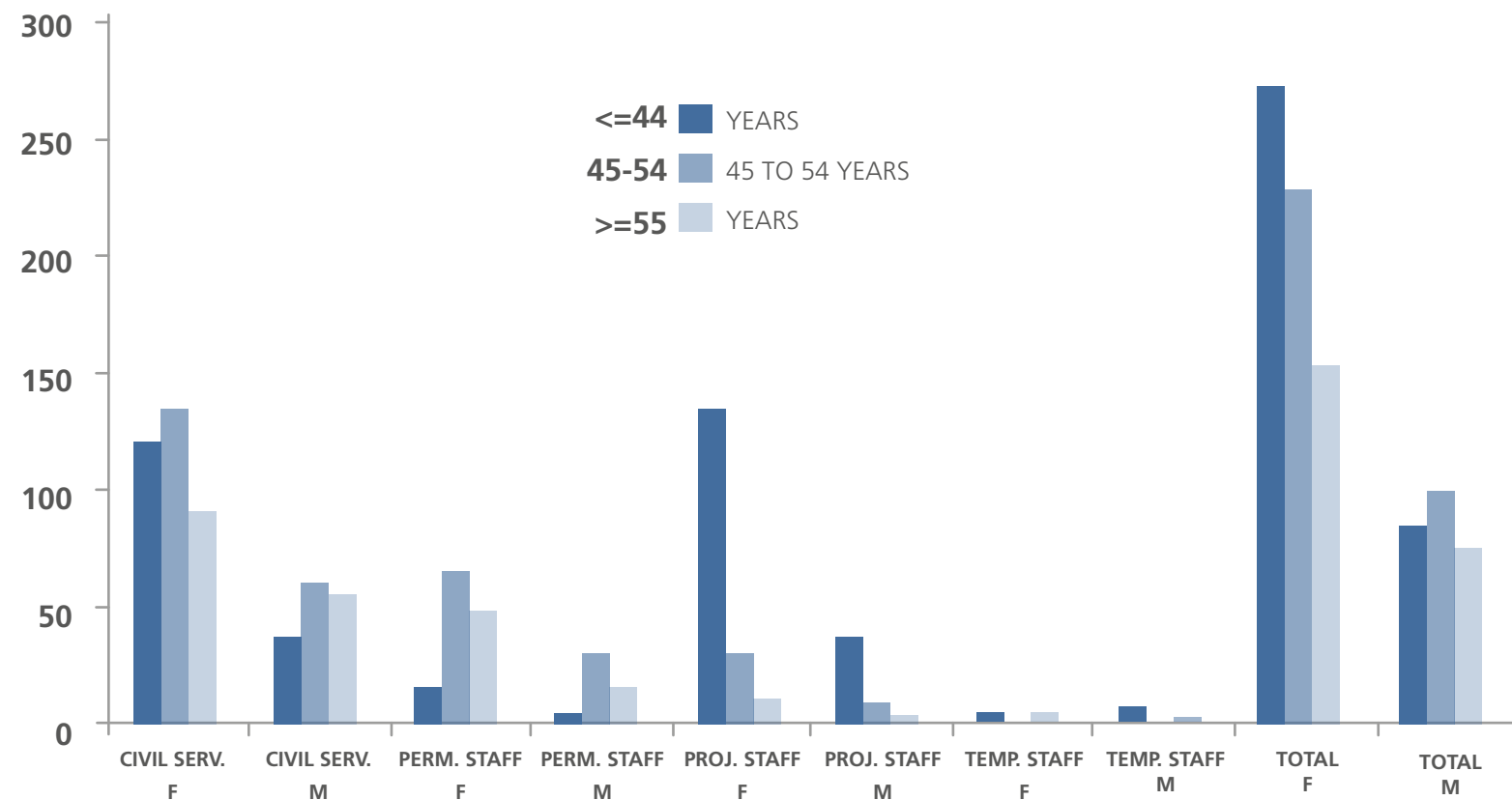
- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

Age/years	CIVIL SERVANTS		PERMANENT STAFF		PROJECT STAFF		TEMPORARY STAFF		TOTAL	
	F	M	F	M	F	M	F	M	F	M
<=44	120	37	15	4	134	37	4	6	273	84
45 - 54	134	61	65	30	29	9	0	0	228	100
>=55	90	54	47	16	12	3	4	2	153	75
	344	152	127	50	175	49	8	8	654	259
	496		177		224		16		913	

(F = female; M = male)



Temporary Staff

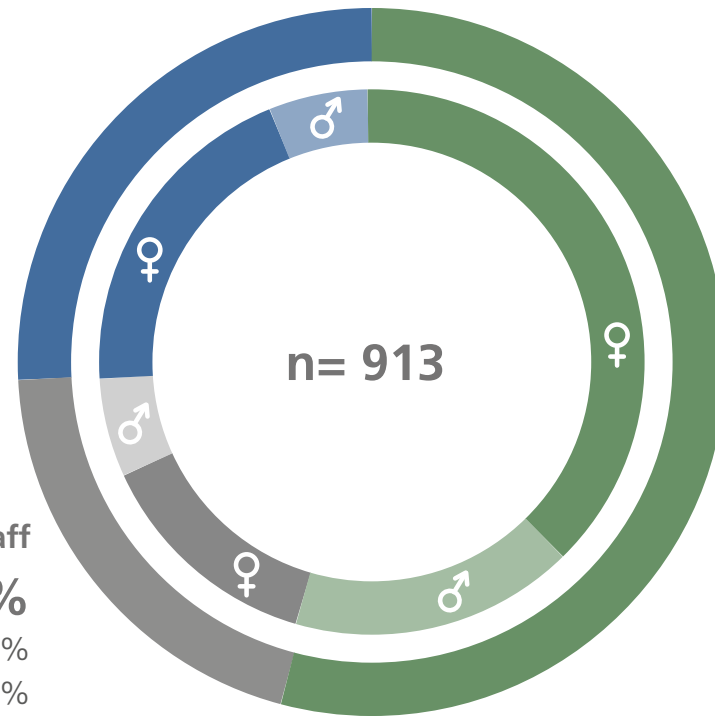
240 | 26%

♂ | 58; 6%
♀ | 182; 20%

Permanent Staff

177 | 20%

♂ | 50; 5%
♀ | 127; 14%



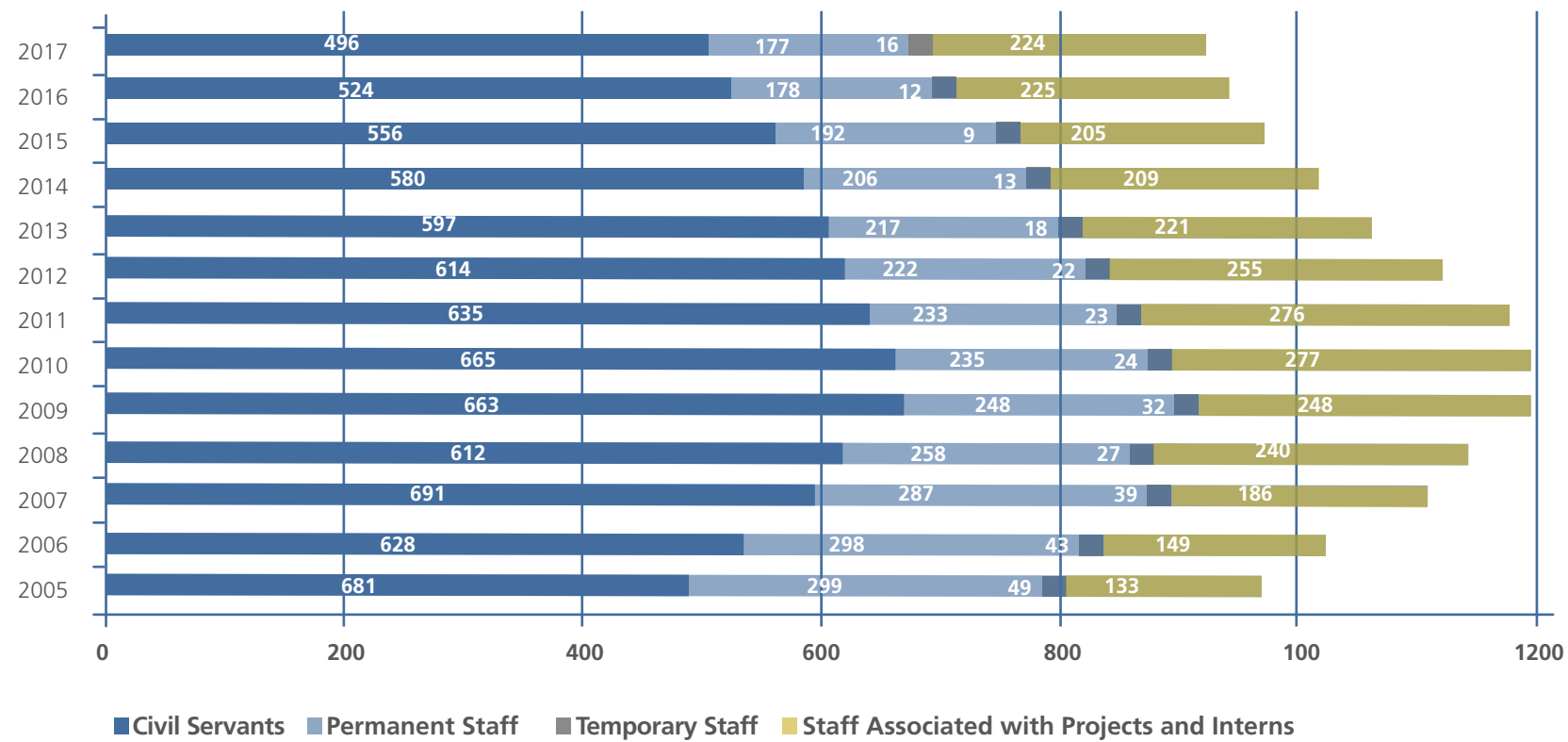
Civil Servants

496 | 54%

♂ | 153; 17%
♀ | 343; 38%

1 ORGANISATION

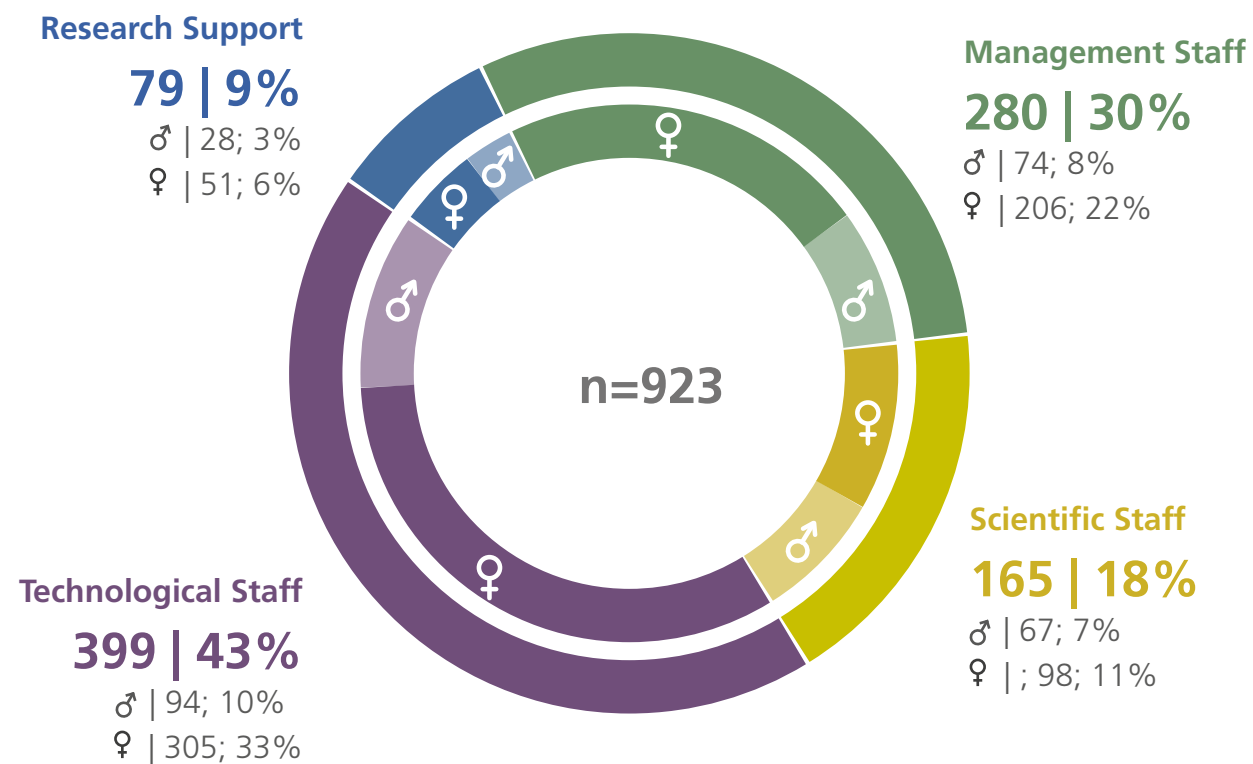
- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources



31-12-17 (Interns included)	Total	Gender	Distribution
Scientists	165	♀	98
		♂	67
Technologists	399	♀	305
		♂	94
Research Support Staff	79	♀	51
		♂	28
Management Staff	280	♀	206
		♂	74
	923		923

1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources



1.4 FINANCIAL RESOURCES

Budget approved for the 2017 fiscal year

The credit approved for ISCIII, O.A., M.P. for the 2017 fiscal year is **269,957.38** thousand Euros, **2,171.52** thousand Euros less (0.80%) than the 2016 fiscal year.

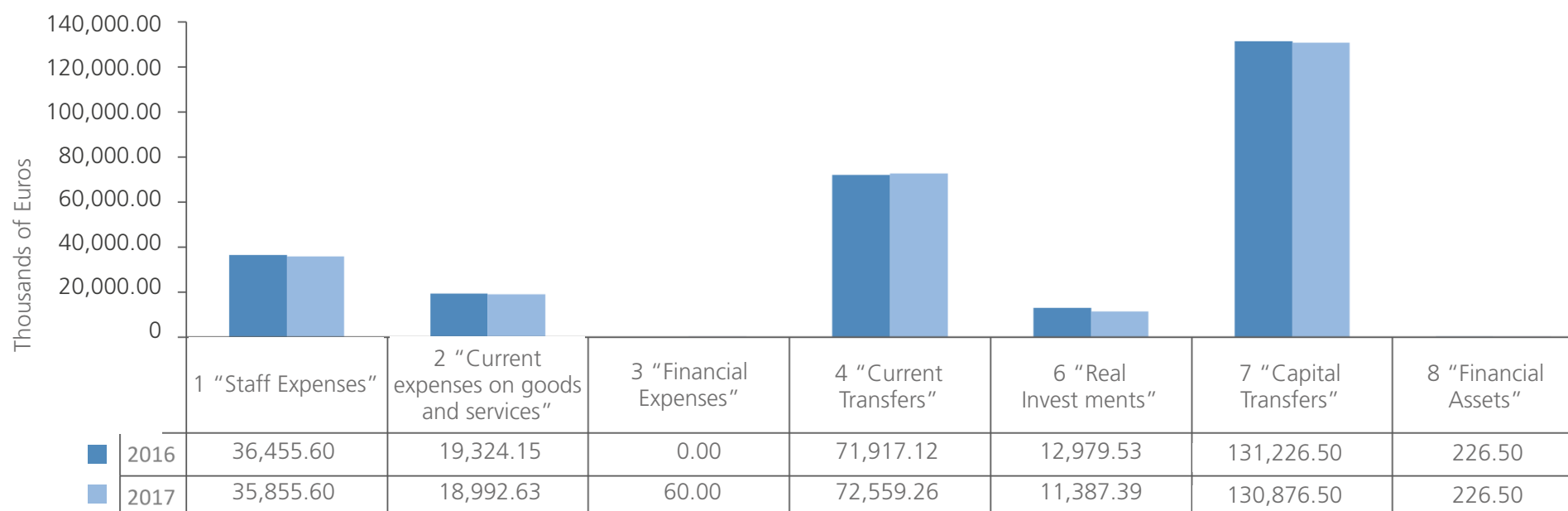
The distribution of funds is as follows:

EXPENSES

(In thousands of Euros)

Chapter	2016	2017	Difference	%
1. Staff Expenses	36,455.60	35,855.60	-600.00	-1.65
2. Current Expenses on Goods and Services	19,324.15	18,992.63	-331.52	-1.72
3. Financial Expenses	-	60.00	60.00	-
4. Current Transfers	71,917.12	72,559.26	642.14	0.89
6. Real Investments	12,979.53	11,387.39	-1,592.14	-12.27
7. Capital Transfers	131,226.50	130,876.50	-350.00	-0.27
8 "Financial Assets"	226.00	226.00	-	-
TOTAL	272,128.90	269,957.38	-2,171.52	-0.80

2017 Budget Expenses Comparative Statement



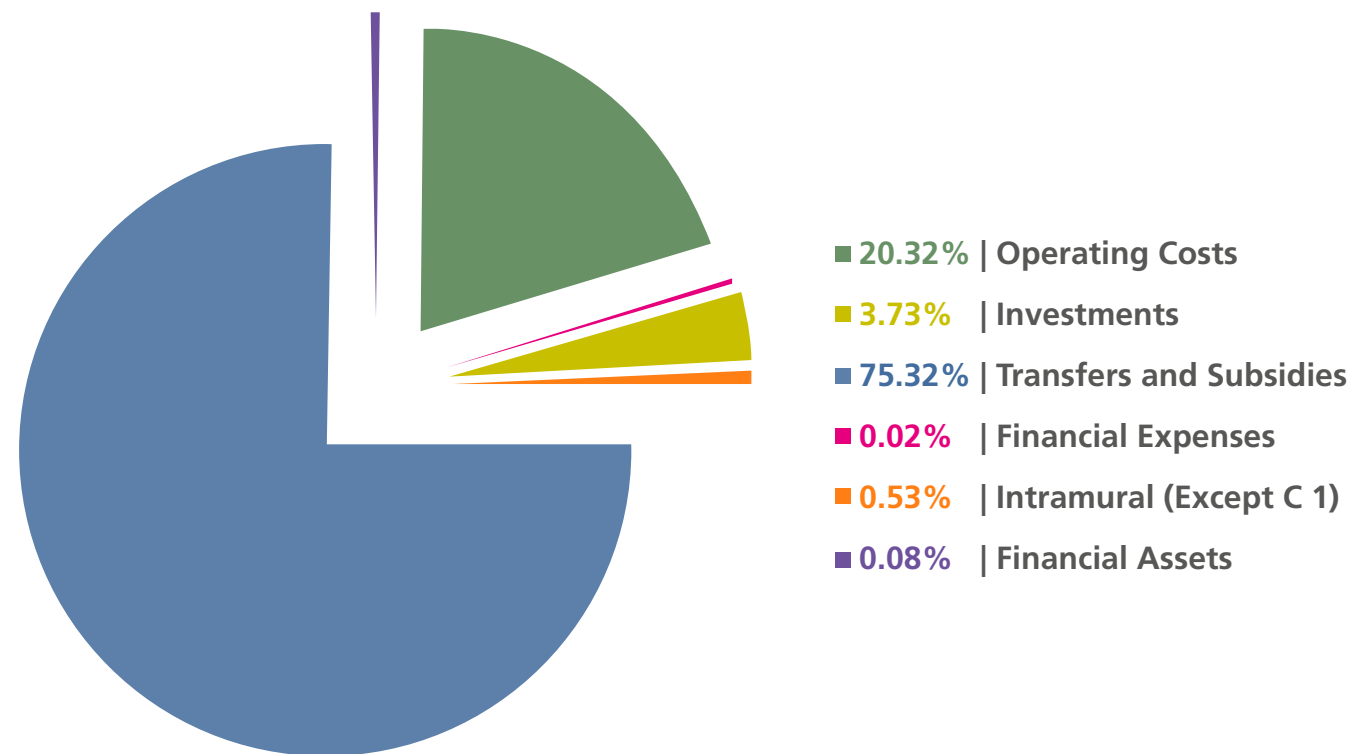
1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

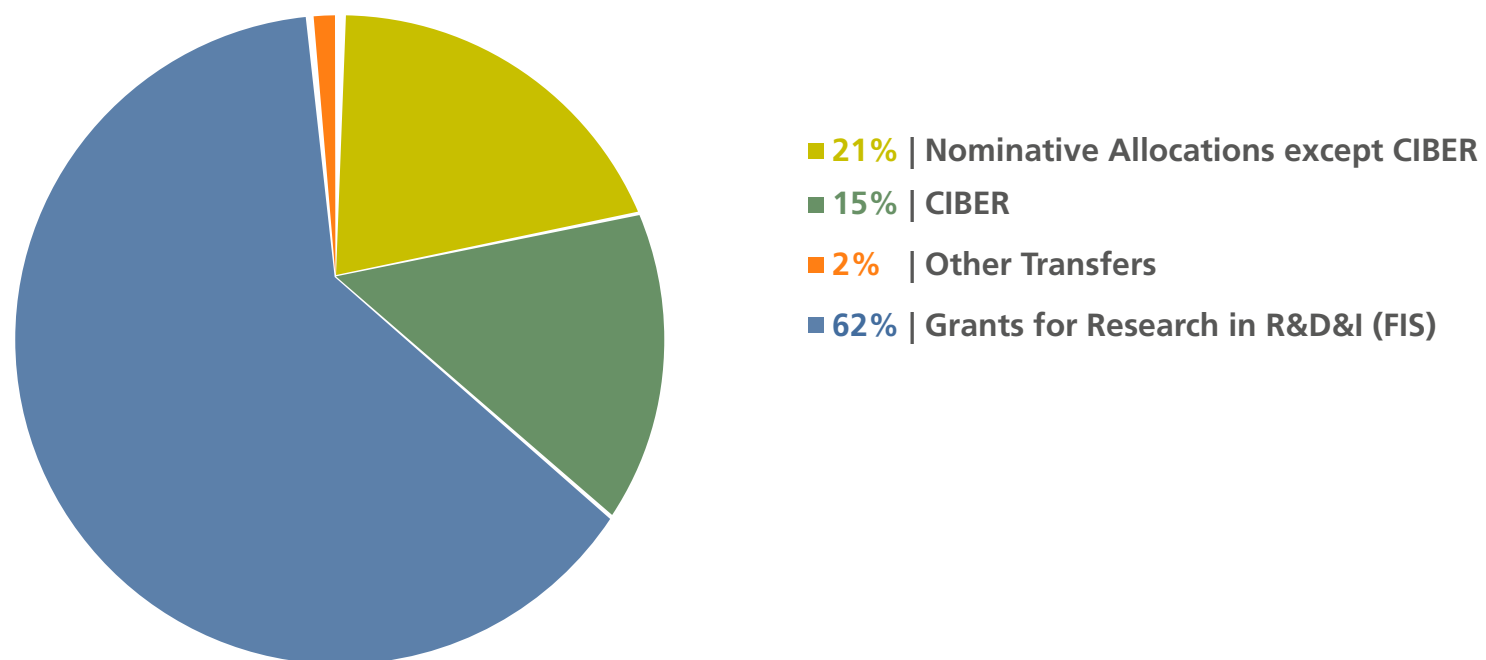
1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

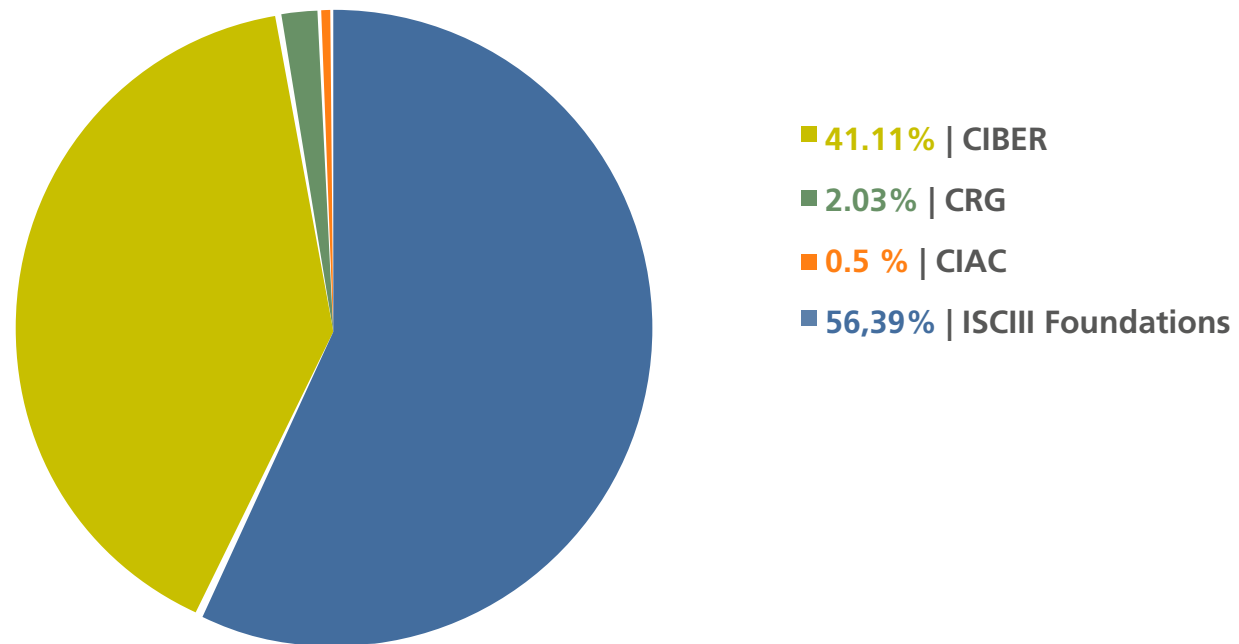
2017 Budget Distribution of Expenses



**2017 Budget
Distribution of Transfers and Subsidies**



**2017 Budget
EXPENSES**
Distribution of Nominative Allocations



1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

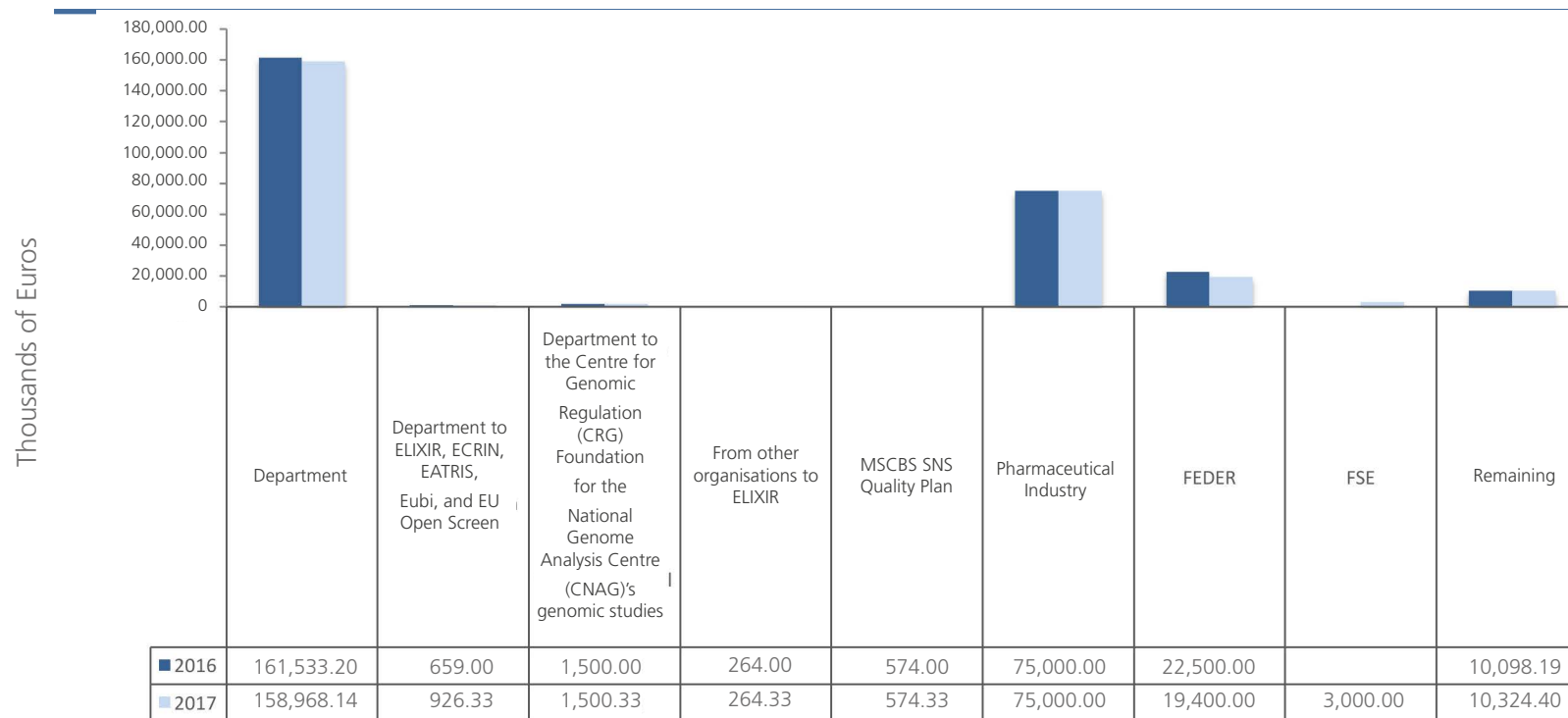


INCOME

SOURCE	2016	2017	Difference	%
MINECO	161,533.20	158,968.14	-2,565.06	-1.59
MINECO to ELIXIR, ECRIN, EATRIS, Eubi, and EU Open Screen	659.00	926.33	267.33	40.57
MINECO to the Centre for Genomic Regulation (CRG) Foundation for the National Genome Analysis Centre (CNAG)'s genomic studies	1,500.00	1,500.00	-	-
From other organisations to ELIXIR	264.00	264.00	-	-
MSCBS SNS Quality Plan	574.51	574.51	-	-
Pharmaceutical Industry	75,000.00	75,000.00	-	-
FEDER	22,500.00	19,400.00	-3,100.00	-13.78
FSE		3,000.00	3,000.00	
Remaining	10,098.19	10,324.40	226.21	2.24
TOTAL	272,128.90	269,957.38	-2,171.52	-0.80

In contrast to the 2016 General State Budgets, in the 2017 General State Budgets, there is not a specific transfer to MINECO for international fees, rather they are incorporated into an overall transfer. In this report, the transfer for international fees is maintained in order to facilitate comparison between both fiscal years.

2017 Budget: Income Comparative Statement



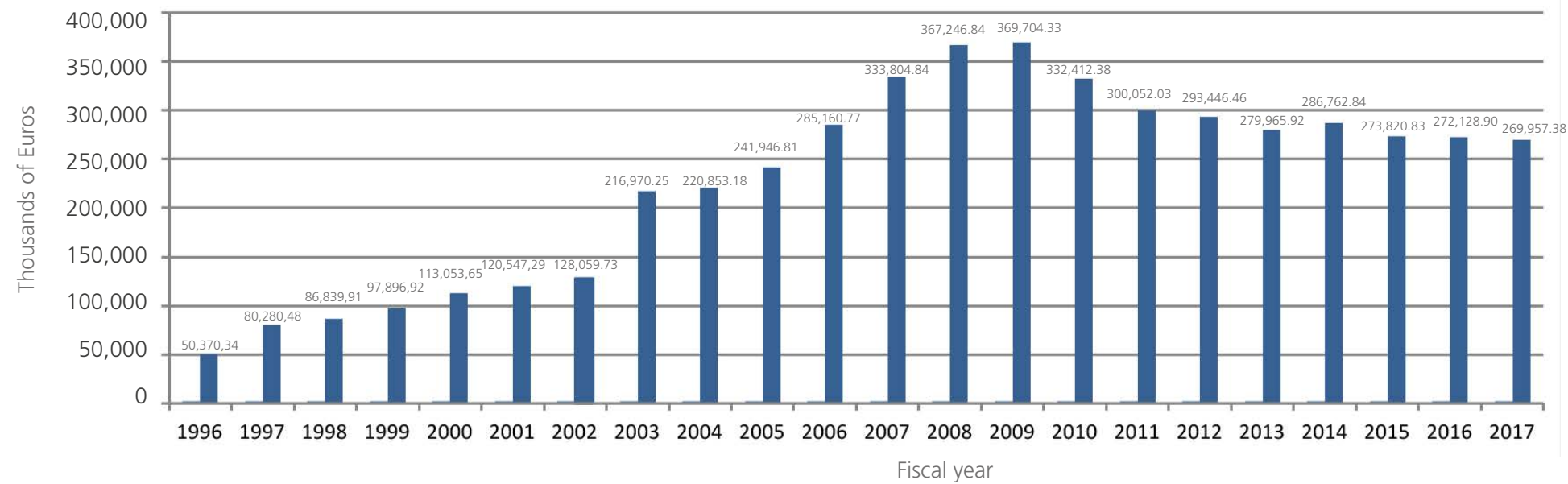
1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

A total of 58.90% of the credits proposed in the expenditure statement are financed with transfers from the department and 27.78% with income derived from the execution of the provisions of the Sixth Additional Provision of Law 29/2006, of 26 July, on guarantees and rational use of medicines and medical devices. In the 2016 fiscal year, these percentages were 59.36% and 27.56%, respectively.

The evolution of the approved budget during the 1996 - 2017 period as well as the evolution of income that has financed the budgets over the last years are also shown.

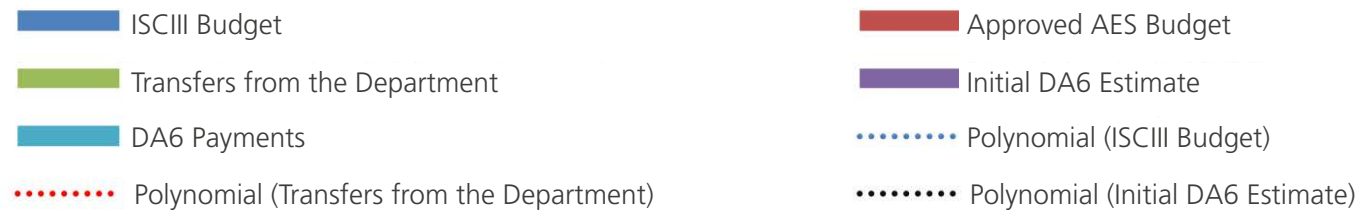
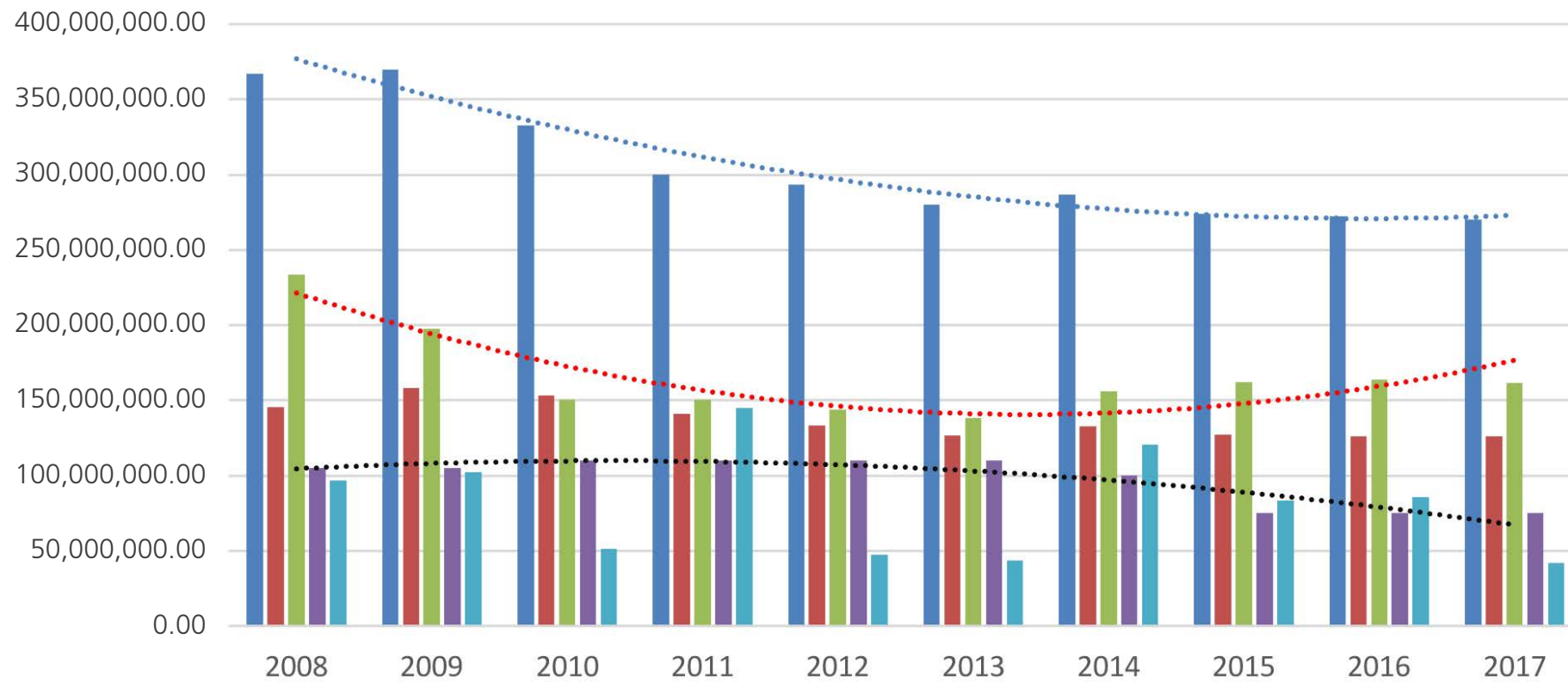
CARLOS III INSTITUTE OF HEALTH
Evolution of approved budget 1996 -2017



1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources

Evolution of ISCIII Budget and Main Sources of Funding 2008-2017



1 ORGANISATION

- 1.1 Governing Bodies
- 1.2 Centres, Units, Schools, and Foundations
- 1.3 Human Resources
- 1.4 Financial Resources



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT



2

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2.1 HEALTH RESEARCH AND DEVELOPMENT STRATEGY (AES 2013-2016)

In 2017, the Spanish National Plan for Scientific and Technical Research and Innovation for the 2013 - 2016 period (hereinafter the Spanish National R&D&I Plan) was extended until the publication of a new plan in December. The Spanish National Plan comprises four National Programmes, deployed in Sub-programmes, and two Strategic Actions, which are integrated into the 4th programme called 'The National Programme for Research Aimed at the Challenges of Society'.

The Health Research and Development Strategy 2013-2016 (hereinafter AES) is included in the Health, Demographic Change and Wellbeing Challenge, which is fully aligned with Horizon 2020. This is a specific, programmatic action whose goal is to contribute to strengthening citizens' health and well-being and to develop preventive, diagnostic, therapeutic, rehabilitative, and palliative measures for diseases. To do so, it seeks to reinforce and increase the international competitiveness of R&D&I of the National Health System (hereinafter SNS) and of related industries with the aim of positioning Spain at the forefront, where health serves as a fundamental axis of economic and social development.

In order to achieve these objectives, the AES proposes a set of instrumental, synergistic, and complementary actions that form the National Sub-programmes for Training and Incorporation, part of the National Programme for the Promotion of Talent and Its Employability and the National Sub-programmes for Institutional Reinforcement and the Generation of Knowledge. These, in turn, form part of the National Programme for Fostering Excellence in Scientific and Technical Research of the National R&D&I Plan. Each of the sub-programmes brings together one or more measures. Those conducted in 2017 as part of the AES framework were:

National Programme for Training Talent and Its Employability

National Sub-programme for Training:

- Pre-doctoral contracts for training in health research
- Grants for training in health research management (FGIN)
- 'Río Hortega' contracts

National Sub-programme for Incorporation:

- Contracts for health research management in the IIS
- 'Miguel Servet' type I and II contracts
- 'Sara Borrell' contracts
- 'Juan Rodés' contracts
- Contracts for the intensification of research activity in the SNS

National Sub-programme for Mobility:

- Mobility grants for research staff

National Programme for Fostering Excellence in Scientific and Technical Research

National Sub-programme for Knowledge Generation

- Health Research Projects
 - A. Health Research Projects
 - B. Technological development projects in health
- Additional actions in the joint international programming

National Sub-programme for Institutional Reinforcement

- Incorporation of new groups into the CIBER consortium
- Platforms to Support Research in Health Science and Technology

As a **novelty**, in the 2017 call, grants for the **Platforms to Support Research in Health Sciences and Technology** were included within the National Sub-programme for Institutional Reinforcement.

The Sub-Directorate General for Research Assessment and Promotion (hereinafter SGEFI) of ISCIII has been the relevant body for managing this procedure and ISCIII has been the managing body for the activities arising from the AES, which are carried out through a single competitive call.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

National Programme for the Promotion of Talent and its Employability

National Sub-programme for Training:

The **pre-doctoral contracts for training in health research** are aimed at the initial training phase of health science and technology researchers devoted to the writing of a doctoral thesis. There are two types:

PFIS contracts: pre-doctoral contracts for training in health research are meant for researchers whose group leaders were awarded a health research project from the AES in the 2016 call.

In the 2017 call, 54 contracts were funded, twice the number funded in 2016.

REGION	PFIS 2017							
	Applications Eligible			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	13	6	19	6	1	7	576,800	36.84
Aragón	1	0	1	1	0	1	82,400	100.00
Asturias	1	2	3	0	0	0	0	0.00
Baleares	0	1	1	0	0	0	0	0.00
Canarias	2	1	3	1	0	1	82,400	33.33
Cantabria	1	0	1	0	0	0	0	0.00
Castilla y León	6	0	6	2	0	2	164,800	33.33
Castilla-La Mancha	1	0	1	1	0	1	82,400	100.00
Cataluña	43	15	58	14	5	19	1,565,600	32.76
C.Valenciana	11	3	14	3	2	5	412,000	35.71
Extremadura	0	0	0	0	0	0	0	0.00
Galicia	10	0	10	2	0	2	164,800	20.00
Madrid	24	16	40	10	3	13	1,071,200	32.50
Murcia	1	1	2	1	0	1	82,400	50.00
Navarra	1	2	3	0	1	1	82,400	33.33
País Vasco	1	3	4	0	1	1	82,400	25.00
Rioja (La)	0	0	0	0	0	0	0	0.00
TOTAL	116	50	166	41	13	54	4,449,600	32.53

(M = Male, F = Female, T = Total)

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

i-PFIS contracts: IIS-Company doctorates in health sciences and technology. This is the fourth year that these contracts are offered. They are meant for public-private collaboration achieved by carrying out part of the training programmes in workplaces in private companies and accredited Health Research Institutes (IISa).

REGION	i-PFIS 2017							
	Eligible Applications			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	0	4	4	0	2	2	164,800	50.00
Aragón	2	1	3	0	0	0	0	0.00
Castilla y León	0	1	1	0	0	0	0	0.00
Cataluña	7	2	9	5	1	6	494,400	66.67
C.Valenciana	1	1	2	1	0	1	82,400	50.00
Galicia	2	0	2	1	0	1	82,400	50.00
Madrid	3	2	5	1	0	1	82,400	20.00
Murcia	2	0	2	0	0	0	0	0.00
TOTAL	17	11	28	8	3	11	906,400	39.29

For both modalities, these amounts correspond to the total duration of the grant. The financial allocation is €20,600 per year for a maximum of 4 years.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



The **'Río Hortega' contracts** are work contracts for professionals who have successfully completed Specialised Healthcare Training:

REGION	'Río Hortega' contracts 2017								Success Rate (%)
	Eligible Applications			Funded				Amount in €	
	F	M	T	F	M	T			
Andalucía	26	7	33	10	1	11	591,052	33.33	
Aragón	4	1	5	2	1	3	161,196	60.00	
Asturias	3	0	3	2	0	2	107,464	66.67	
Canarias	1	1	2	0	1	1	0	0.00	
Cantabria	1	0	1	0	0	0	53,732	50.00	
Castilla y León	5	2	7	0	1	1	0	0.00	
Castilla-La Mancha	4	1	5	0	1	1	53,732	14.29	
Cataluña	47	20	67	17	8	25	53,732	20.00	
C.Valenciana	8	8	16	1	3	4	1,343,300	37.31	
Extremadura	1	0	1	0	0	0	0	0.00	
Galicia	3	3	6	2	2	4	214,928	66.67	
Madrid	32	14	46	12	4	16	859,712	34.78	
Murcia	1	3	4	0	1	1	53,732	25.00	
Navarra	5	0	5	2	0	2	107,464	40.00	
País Vasco	4	0	4	0	0	0	214,928	25.00	
TOTAL	145	60	205	48	23	71	3,814,972	34.63	

The financial allocation is €26,866 per year for a duration of two years. In the 2017 call, 71 contracts were funded, significantly more than in previous calls: 48 in 2016 and 51 in 2015.

In terms of the **grants for Training in Health Research Management (FGIN)**, 20 eligible applications were received and 9 were granted, with a financial allocation of €21,000 and duration of 36 months.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

National Sub-programme for Incorporation:

This was the 4th year that contracts for **Health Research Management (GIS) in accredited Health Research Institutes (IISa)** were offered. They are aimed at managers so that they may carry out support activities for managing R&D&I in the IISa.

Those IISa who had an active Health Research Management Contract granted in the 2015 or 2016 AES were not allowed to participate in this call.

REGION	GIS 2017							
	Eligible Applications			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	1	1	2	1	1	2	161,196	100.00
Castilla y León	1	1	2	1	0	1	80,598	50.00
Cataluña	7	1	8	4	1	5	80,598	50.00
C.Valenciana	2	2	4	1	1	2	402,990	62.50
Galicia	1	0	1	1	0	1	80,598	100.00
Madrid	6	3	9	5	3	8	644,784	88.89
País Vasco	2	0	2	1	0	1	161,196	50.00
TOTAL	20	8	28	14	6	20	1,611,960	71.43

The financial allocation for these contracts is €26,866 per year during 3 years.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

The **'Miguel Servet' type I** contracts are meant for PhDs with an accredited research trajectory in centres within the scope of the SNS. They also include a 3-year research project.

The financial allocation for these contracts is €40,500 per year during 5 years. The amount for the project is also shown in the table.

REGION	'Miguel Servet' Type I 2017							
	Eligible Applications			Funded				Success Rate (%)
	M	H	T	M	H	T	Amount in €	
Andalucía	14	13	27	3	1	4	1,102,500	14.81
Aragón	1	1	2	0	0	0	0	0.00
Asturias	2	0	2	0	0	0	0	0.00
Baleares	1	2	3	0	2	2	590,900	66.67
Canarias	1	0	1	0	0	0	0	0.00
Cantabria	1	1	2	0	0	0	0	0.00
Castilla y León	4	2	6	0	0	0	0	0.00
Castilla-La Mancha	2	0	2	0	0	0	0	0.00
Cataluña	22	14	36	3	3	6	0	0.00
C.Valenciana	14	4	18	0	0	0	1,711,971	16.67
Extremadura	1	1	2	0	1	1	301,485	50.00
Galicia	5	4	9	1	1	2	605,000	22.22
Madrid	13	6	19	0	0	0	0	0.00
Murcia	2	3	5	0	0	0	0	0.00
Navarra	2	1	3	0	1	1	302,500	33.33
País Vasco	4	3	7	0	0	0	0	0.00
Rioja (La)	1	0	1	0	0	0	0	0.00
TOTAL	90	55	145	7	9	16	4,614,356	11.03



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

The **Miguel Servet type II** contracts are aimed at doctors in the final year of a Miguel Servet contract.

REGION	'Miguel Servet' Type II 2017							
	Eligible Applications			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	1	2	3	1	2	3	273,375	100
Baleares	1	1	2	1	1	2	182,250	100
Cantabria	0	1	1	0	1	1	91,125	100
Castilla y León	1	1	2	1	1	2	182,250	100
Cataluña	5	2	7	5	2	7	678,375	100
C.Valenciana	1	0	1	1	0	1	91,125	100
Galicia	1	3	4	1	3	4	384,750	100
Madrid	3	1	4	3	1	4	374,625	100
Navarra	0	1	1	0	1	1	101,250	100
País Vasco	1	0	1	1	0	1	91,125	100
TOTAL	14	12	26	14	12	26	2,450,250	100

The financial allocation for these contracts is either €40,500 or €45,000 in the first year. It is then co-funded at 75% and 50% in the following years. It has a duration of 3 years.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

The **'Sara Borrell' contracts** are meant for recently-qualified doctors in centres included in the SNS.

REGION	'Sara Borrell' contracts 2017							
	Eligible Applications			Funded				Success Rate (%)
	M	H	T	M	H	T	Amount in €	
Andalucía	26	9	35	3	2	5	402,990	14.29
Aragón	1	1	2	0	0	0	0	0.00
Baleares	2	1	3	0	0	0	0	0.00
Canarias	1	0	1	0	0	0	80,598	16.67
Cantabria	3	0	3	1	0	1	0	0.00
Castilla y León	1	3	4	0	0	0	80,598	33.33
Castilla-La Mancha	0	2	2	0	0	0	0	0.00
Cataluña	47	23	70	10	4	14	0	0.00
C.Valenciana	11	5	16	3	0	3	1,128,372	20.00
Extremadura	0	1	1	0	0	0	0	0.00
Galicia	5	1	6	0	0	0	0	0.00
Madrid	29	16	45	3	5	8	644,784	17.78
Murcia	2	0	2	0	0	0	0	0.00
Navarra	4	0	4	1	0	1	80,598	25.00
País Vasco	5	1	6	1	0	1	241,794	18.75
TOTAL	137	63	200	22	11	33	2,659,734	16.50

The financial allocation for these contracts is €26,866 per year during 3 years.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

The **'Juan Rodés' contracts** are for medical staff who have previously completed a 'Río Hortega' Contract. They are carried out in SNS healthcare facilities that are part of an IISa.

The healthcare-related part is to be carried out in an IIS hospital. The recipient of the contract must simultaneously carry out the research activity according to the proposal submitted.

REGION	'Juan Rodés' contracts 2017							
	Eligible Applications			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	3	1	4	3	1	4	720,000	100.00
Aragón	3	0	3	3	0	3	540,000	100.00
Castilla y León	1	0	1	0	0	0	0	0.00
Cataluña	8	0	8	7	0	7	1,260,000	87.50
C.Valenciana	2	0	2	2	0	2	360,000	100.00
Galicia	0	2	2	0	2	2	540,000	50.00
Madrid	6	0	6	3	0	3	360,000	100.00
TOTAL	23	3	26	18	3	21	3,780,000	80.77

The financial allocation for these contracts is €45,000 per year during 3 years.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

The objective of the **contracts for the intensification of research activity in the SNS** is to hire specialised physicians or professionals who hold a degree in nursing in SNS centres so that they may perform part of the medical care activities of professionals, who are simultaneously carrying out research activities. Around 50% of the workday dedicated to providing healthcare attention in 2017 has been freed up annually.

The financial allocation for these contracts is €30,000 per year for physicians and €15,000 for nursing staff.

REGION	Intensification 2017								Success Rate (%)
	Eligible Applications			Funded				Amount in €	
	F	M	T	F	M	T			
Andalucía	2	11	13	0	1	1	30,000	7.69	
Aragón	1	2	3	0	0	0	0	0.00	
Asturias	0	1	1	0	0	0	0	0.00	
Baleares	1	1	2	0	1	1	30,000	50.00	
Canarias	1	1	2	0	1	1	0	0.00	
Cantabria	0	1	1	0	0	0	30,000	50.00	
Castilla y León	1	4	5	0	2	2	0	0.00	
Castilla-La Mancha	0	1	1	0	0	0	60,000	40.00	
Cataluña	8	18	26	4	7	11	0	0.00	
C.Valenciana	3	6	9	0	0	0	315,000	42.31	
Galicia	2	4	6	1	0	1	30,000	16.67	
Madrid	10	18	28	0	2	2	60,000	7.14	
Murcia	1	2	3	0	0	0	0	0.00	
Navarra	0	3	3	0	1	1	30,000	33.33	
País Vasco	0	1	1	0	0	0	0	0.00	
TOTAL	30	74	104	5	15	20	585,000	19.23	

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

National Sub-programme for Mobility:

The objective of these grants is to fund placements in one of the following modalities:

Mobility of SNS healthcare professionals and researchers (M-BAE)

The objective of this grant is to fund SNS healthcare professionals' and researchers' placements at prestigious national or foreign institutions.

REGION	M-BAE 2017							
	Eligible Applications			Funded				Success Rate (%)
	F	M	T	F	M	T	Amount in €	
Andalucía	0	1	1	0	0	0	0	0.00
Aragón	0	1	1	0	1	1	7,475	100.00
Baleares	1	0	1	1	0	1	7,360	100.00
Castilla y León	1	1	2	0	1	1	17,710	100.00
Cataluña	12	11	23	8	9	17	7,360	50.00
C.Valenciana	1	1	2	1	1	2	441,880	73.91
Galicia	1	0	1	1	0	1	6,640	100.00
Madrid	6	7	13	1	5	6	116,150	46.15
País Vasco	0	1	1	0	1	1	49,335	100.00
TOTAL	22	23	45	12	18	30	653,910	66.67

The financial allocation for these contracts from €80 to €115 per day of the placement at the centre, according to whether it is a Spanish or foreign centre, and its duration varies between 2 and 12 months.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

Mobility of research staff contracted within the framework of the AES (M-AES)

This grant is aimed at those who have PFIS, i-PFIS, Río Hortega, Sara Borrell, Juan Rodés, and Miguel Servet Type I and II contracts. It is meant for placements abroad.

REGION	M-AES 2017							
	Eligible Applications			Funded				Success Rate (%)
	M	H	T	M	H	T	Amount in €	
Andalucía	1	1	2	1	0	1	11,765	50.00
Cataluña	5	6	11	5	6	11	5,785	100.00
C.Valenciana	8	2	10	7	2	9	117,910	100.00
Galicia	2	1	3	2	1	3	16,055	100.00
Madrid	4	2	6	4	2	6	37,505	100.00
Navarra	1	0	1	1	0	1	11,765	100.00
País Vasco	1	0	1	1	0	1	56,770	90.00
TOTAL	22	12	34	21	11	32	257,555	94.12

The financial allocation is €65 per day during the placement at the centre for a duration between 2 and 6 months in the case of PFIS, i-PFIS, Río Hortega, Juan Rodés, and Miguel Servet type I and II contract holders and up to 12 months for Sara Borrell contract holders.

In summary, under the National Programme for Training Talent and Its Employability of 2017, a total 343 grants were funded for a total amount of €26,350,737.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

NATIONAL PROGRAMME FOR FOSTERING EXCELLENCE IN SCIENTIFIC AND TECHNICAL RESEARCH

National Sub-programme for Knowledge Generation:

Within the Sub-programme for Knowledge Generation, grants are offered for Research Projects in Health (both for the Research Projects in Health and for the Technological Development Projects in Health modalities) and for Additional Activities in the International Programme.

RESEARCH PROJECTS IN HEALTH

The objective of this call is to fund projects in any of the following modalities:

- **Research Projects in Health.** Projects of proven quality whose principle objectives are to: a) transfer and apply scientific and technical knowledge in order to improve the prevention, diagnosis, and treatment of diseases as well as activities promoting public health and health services; b) foster synergy, drive talent and employability, and strengthen the governance structures that add scientific and technical skills to SNS healthcare facilities; c) promote the funding of emerging researchers' first research projects that are of proven quality.

A total of 1,797 applications were received and 659 were funded at a cost of €68,531,230.

The regions which requested the most projects were Catalonia (36%), Madrid (21%), and Andalusia (11%). This was also the case in terms of funding: 36.57%, 21.70%, and 10.32%.

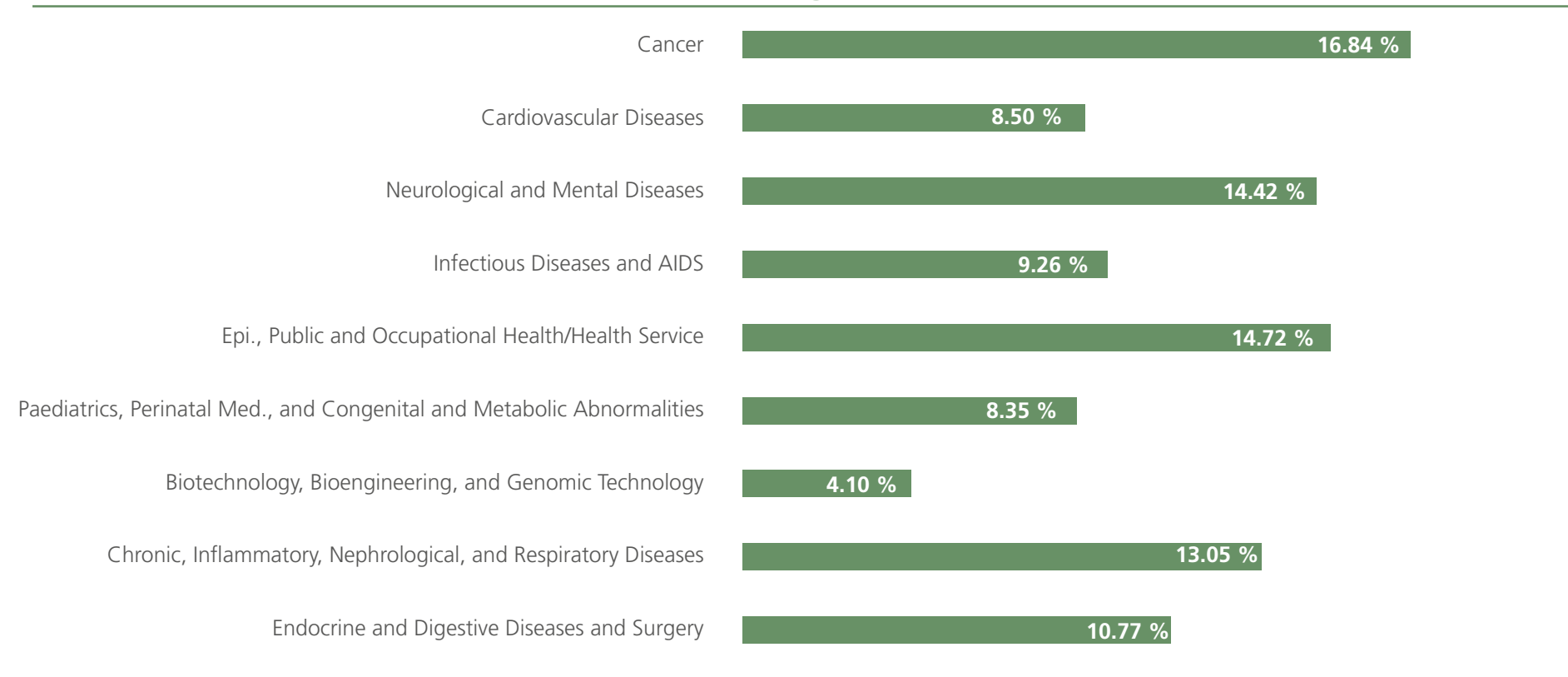


RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

Graph. Funding for Research Projects in Health by Thematic Area.

Concessions According to Thematic Area. % of the Total



- **Technological Development Projects in Health**, are grants for projects of an applied nature that have the objective of promoting innovation in SNS healthcare centres and the transfer of innovative solutions as well as the generation of benefits for the community. At the same time, they allow for alliances to be established between research bodies and companies in the pharmaceutical, biotechnology, and medical and healthcare technology sectors.

A total of 119 requests were received and 31 were funded for a total of €2,036,980. Grants were distributed in Andalusia, Cantabria, Castile and Leon, Catalonia, Valencia Community, Galicia, Madrid and Navarre.

COMPLEMENTARY ACTIONS TO INTERNATIONAL JOINT PROGRAMMING INITIATIVES

The objective of this action is to fund research projects in the international joint programming initiatives in health. These projects are carried out within the framework of the transnational consortia in which ISCIII has committed to support relevant collaborative projects, where Spanish research teams participate alongside teams from other countries.

The public international calls within the framework of the additional activities were:

- **AAL**: Active and Assisted Living Programme.
- **JPI-MYBL**: Joint Programming Initiative More Years, Better Lives: The Potential and Challenges of Demographic Change.
- **EU-LAC Health**: Defining a Roadmap for Cooperative Health Research between the EU and Latin America-Caribbean Countries: a Policy Oriented Approach.
- **EDCTP**: The European & Developing Countries Clinical Trials Partnership.
- **JPI AMR**: Joint Programming Initiative on Antimicrobial Resistance Research.
- **ERA-CVD**: European Research Area Network on Cardiovascular Diseases.
- **NEURON bio**: Network of European Funding for Neuroscience Research.
- **NEURON ELSA**: Network of European Funding for Neuroscience Research.
- **JPND**: Joint Programming on Neurodegenerative Disease Research.
- **E-RARE**: ERA-Net for Research Programmes on Rare Diseases.
- **TRANSCAN**: ERA-Net on Translational Cancer Research.

- **JPI HDHL**: Joint Programming Initiative A Healthy Diet for a Healthy Life.
- **ERACoSysMed**: Systems Medicine to address clinical needs.
- **EuroNanoMed**: European Network for translational collaborative RTD projects on Nanomedicine.
- **CYTED**: Ibero-American Programme for the Development of Science and Technology.

A total of 89 applications were received and 24 were funded for a total of €2,735,625.

Table. Number of Groups and Researchers Participating in European Programmes

Programme	Number Of Groups	Number Of Researchers
ERACoSysMed	1	7
ERA-CVD	1	4
E-RARE	4	29
EU-LAC Health	2	14
EuroNanoMed	5	23
JPI HDHL	1	10
JPND	2	3
NEURON	1	4
TRANSCAN	7	23
TOTAL	24	117



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

A summary of all data on the National Sub-programme for Knowledge Generation is detailed below.

Table. Amount granted and success rate by grant and by gender

Action	Eligible	Eligible Women	Eligible Men	Awarded	% Awarded	Awarded Women	Awarded Men	% Awarded Women	% Awarded Men	Amount (€)
DTS	119	40	79	31	26.05	11	20	35.48	64.52	2,036,980.00
PI	1,797	818	978	659	36.67	295	364	44.76	55.24	68,531,229.80
AC	89	23	66	24	26.97	6	18	25.00	75.00	2,735,624.87
TOTAL	2,005	881	1123	714	35.61	312	402	43.70	56.30	73,303,834.67

Table. Distribution of Grants Funded According to the Region

REGION	PI		DTS		AC		TOTAL	
	No. of grants	Amount (Euros)	No. of grants	Amount (Euros)	No. of grants	Amount (Euros)	No. of grants	Amount (Euros)
Andalusia	68	6,938,170	3	167,970	2	299,998	73	7,406,138
Aragon	15	1,628,237			1	98,010	16	1,726,247
Asturias	15	1,589,033					15	1,589,033
Balearic Islands	6	479,765					6	479,765
Basque Country	22	1,774,163			1	149,999	23	1,924,161
Canary Islands	7	503,058					7	503,058
Cantabria	7	603,790	1	33,550			8	637,340
Castile - La Mancha	1	7,865					1	7,865
Castile And Leon	13	1,499,493	1	79,200			14	1,578,693
Catalonia	241	25,547,737	8	607,090	8	827,659	257	26,982,486
Extremadura							0	0
Galicia	34	3,502,224	3	177,650			37	3,679,874
La Rioja							0	0
Madrid	143	15,955,302	10	651,310	10	1,156,963	163	17,763,575
Murcia	13	1,055,483					13	1,055,483
Navarre	30	3,051,103	1	33,550	2	202,996	33	3,287,649
Valencia Community	44	4,395,809	4	286,660			48	4,682,469
TOTAL	659	68,531,230	31	2,036,980	24	2,735,625	714	73,303,835

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

National Sub-programme for Institutional Reinforcement:

Within the National Sub-programme for Institutional Reinforcement, a call for grants was issued for the incorporation of new groups into the CIBER consortium and the Platforms to Support Research in Health Sciences and Technology.

INCORPORATION OF NEW GROUPS INTO THE CIBER CONSORTIUM

This action is intended to develop and strengthen the CIBER Consortia, reinforcing the areas of Respiratory Diseases, Diabetes and Associated Metabolic Disorders, and Hepatic and Digestive Diseases through the incorporation of new groups.

Table. Incorporation of Groups into CIBERs Distribution by Thematic Area and Gender

Thematic Area	Applications		Awarded				2017 Funding
	M	W	M	% Awarded Men	W	% Awarded Women	
Diabetes And Associated Metabolic Disorders	3	2	1	33.33	0	0.00	45,000.00
Hepatic And Digestive Diseases	4	8	0	0.00	3	37.50	135,000.00
Respiratory Diseases	11	1	2	18.18	0	0.00	90,000.00
TOTAL	18	11	3	16.67	3	27.27	270,000.00

Table. Incorporation of new groups into CIBER. Distribution by gender and Region

REGION	Applications		Awarded		2017 Funding
	Men	Women	Men	Women	
Andalusia	3		1		45,000.00
Asturias	2		1		45,000.00
Canary Islands		1			
Catalonia	8	4		3	135,000.00
Galicia	1	1	1		
Madrid	3				
Valencia Community	5	1			45,000.00
TOTAL	22	7	3	3	270,000.00

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

PLATFORMS TO SUPPORT RESEARCH IN HEALTH SCIENCES AND TECHNOLOGY

The 2017 AES call included grants for Platforms to Support Research. The thematic areas included in the call were the following:

- Biobanks.
- Innovation in medical and healthcare technology.
- Clinical research and clinical trials.
- Proteomics, genotyping, and cell lines.
- Bioinformatics.

Table. Platforms to Support Research in Health Science and Technology by Thematic Area and Gender

PLATFORM	Applications		Awarded		2017- 2019 Fund-ing
	Women	Men	Women	Men	
Bioinformatics	5	12	4	11	3,487,714.82
Clinical Research And Clinical Trials	11	21	11	21	7,678,165.00
Innovation In Medical And Healthcare Technology	10	24	7	23	4,704,536.10
Proteomics, Genotyping, And Cell Lines	7	17	6	17	5,016,532.82
Biobanks	17	25	14	24	6,422,938.50
Total	50	99	42	96	27,309,887.25



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

Table. Platforms to Support Research in Health Science and Technology by Region and Gender

AUTONOMOUS COM-MUNITY	Applications		Awarded		Funding 2017- 2019
	Women	Men	Women	Men	
Andalusia	5	8	4	8	2,982,470.02
Aragon	2	2	2	2	348,975.00
Asturias	1	0	1	0	150,150.00
Basque Country	1	0	1	0	1,356,300.00
Canary Islands	0	3	0	3	217,800.00
Cantabria	2	4	0	4	373,560.00
Castile And Leon	17	22	16	21	813,999.98
Catalonia	2	10	1	10	7,567,928.38
Extremadura	0	1	0	1	102,300.00
Galicia	1	7	1	7	1,687,838.90
Madrid	15	30	12	28	9,466,489.98
Murcia	0	2	0	2	137,775.00
Navarre	2	3	2	3	551,100.00
Valencia Community	2	7	2	7	1,553,199.98
Total	50	99	42	96	27,309,887.25

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2.2 BIOMEDICAL RESEARCH NETWORKING CENTRES (CIBER)

ciberMed isciiii

WWW.CIBERNED.ES

In 2017, CIBERNED held a very special edition of its annual Scientific Forum, the Alzheimer's Global Summit Lisbon 2017. It was jointly organised by CIBERNED, the CIEN Foundation, the Queen Sofia Foundation, and the Champalimaud Foundation. This event has become a meeting point for the greatest national and international experts in neurodegenerative diseases. National and international researchers who are world-renowned in their fields of research, such as Nobel Prize winner John O'Keefe, Richard Axe, Drs Hanna and António Damásio, Dr Kenneth S. Kosik, and Dr Maria Grazia Spillantini, participated as speakers at this summit.

ciber isciiii

WWW.CIBERISCIIII.ES

In 2017, three new scientific areas were incorporated into the CIBER: Oncology, Cardiovascular Diseases, and Frailty and Ageing.

In the **area of Mental Health (CIBERSam)**, the VOZ Project survey was carried out. It seeks to identify the needs of people with schizophrenia/psychosis and their caregivers, which is to meet their emotional needs. Spanish Mental Health Confederation, Madrid Association of Friends and Family Members of People with Schizophrenia (AMAFE), and CIBERSAM.

Researchers in the **area of Respiratory Diseases (CIBERes)** carried out the study: *"Lung function in early adulthood and health in later life: a transgenerational cohort analysis."* It demonstrated that following a simple technique at an early age would help implement preventative, follow-up, and therapeutic measures.



In the **area of Physiopathology of Obesity and Nutrition (CIBERobn)**, the “Mediterranean Diet, Metabolites, and Cardiovascular Diseases” project is of note. In this project, the Department of Nutrition of Harvard University and CIBERobn’s PREDIMED group participated (2017-2021). The aim of this study is to perform a high-resolution metabolomic analysis to identify predictive markers of cardiovascular pathology.

In addition, researchers from the **area of Diabetes and Associated Metabolic Diseases (CIBERdem)** participated in the TRIGR (Trial to Reduce IDDM in the Genetically at Risk) clinical trial on type 1 diabetes prevention in children who are genetically at risk of developing diabetes.

A multicentre study coordinated by researchers in the **area of Epidemiology and Public Health (CIBEResp)** evaluated the effect of the flu vaccine on prevention of hospitalisation of people over age 65 in Spain. The vaccine was 36% (22-47) effective in preventing hospitalisations. In patients without high-risk medical conditions, efficacy was 51% (15-71). The maximum efficacy of the vaccine was observed against subtype A (H1N1) pdm09 (49%, 32-62).

The **area of Rare Diseases (CIBERer)** has secured multimillion-Euro collaboration agreements for the development and authorisation of gene therapy for rare diseases in Spain. Rocket Pharmaceuticals Ltd., a gene therapy company, has signed exclusive worldwide codevelopment and licensing agreements for gene therapy vectors worth up to €8 million. Gene therapy is created for new treatments for rare diseases that affect blood cells through the CIEMAT, CIBERER, and IIS-FJD.

The SIOVAC study, by the **area of Cardiovascular Diseases (CIBERCv)**, which was carried out thanks to the multicentric collaboration between CIBERCv groups, provided findings that required an immediate change in clinical treatment guidelines for pulmonary hypertension.

In the **area of Frailty and Healthy Ageing (CIBERFes)**, the creation of the first clinical cohort on frailty in Europe should be highlighted. This project will be submitted in the Health Research and Development Strategy 2018. A total of 14 CIBERFes groups are going to collaborate on it.

The **area of Cancer (CIBERonc)** has strengthened its collaboration with the Spanish Association Against Cancer Scientific Foundation to co-fund (up to €150,000) a project coordinated by CIBERonc members through the AECC’s 2018 call for projects. It is focused on supporting high-quality cancer research projects that are orientated towards translational research.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

Highlighted publications

CIBERSAM: Hay SI, Abajobir AA, Abate KH, Abbafati C, Abbas KM, Abd-Allah F, et al. GBD 2016 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017 Sep 16;390(10100):1260-1344. doi: 10.1016/S0140-6736(17)32130-X. PMID: 28919118.

CIBERES: Minutti CM, Jackson-Jones LH, García-Fojeda B, Knipper JA, Sutherland TE, Logan N, et al. Local amplifiers of IL-4R α -mediated macrophage activation promote repair in lung and liver. *Science* 2017 Jun 9;356(6342):1076-1080. doi: 10.1126/science.aaj2067. PMID: 28495878.

CIBEROBN: Martínez-Sánchez, Seoane-Collazo, Contreras, Varela, Villarroya, Rial-Pensado, 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. doi: 10.1016/j.cmet.2017.06.014. PMID:28683288.

CIBERDEM: Ramírez S, Gómez-Valadés AG, Schneeberger M, Varela L, Haddad-Tóvolli R, Altirriba J et al. Mitochondrial Dynamics Mediated by Mitofusin 1 Is Required for POMC Neuron Glucose-Sensing and Insulin Release Control. *Cell Metab*. 2017; 25 (6):1390–1399.e6. doi:10.1016/j.cmet.2017.05.010. PMID:28591639.

CIBERESP: Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, et al. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ* 2017; 357:j1550. DOI: 10.1136/bmj.j1550. PMID: 28446428.

CIBERBBN: Gallego I., Manning B., Prades J.D., Mir M., Samitier J., Eritja R. DNA-Origami-Driven Lithography for Patterning on Gold Surfaces with Sub-10 nm Resolution. *Adv Mater*. 2017 Mar; 29(11). DOI: 10.1002/adma.201603233. PubMed ID: 28060403.

CIBERER: Roca-Ayats N, Balcells S, Garcia-Giralt N, Falcó-Mascaró M, Martínez-Gil N, Abril JF, et al. GGPS1 Mutation and Atypical Femoral Fractures

with Bisphosphonates. *N Engl J Med*. 2017 May 4;376(18):1794-1795. DOI: 10.1056/NEJMc1612804. PMID: 2846786.

CIBEREHD: Lens S, Alvarado-Tapias E, Mariño Z, Londoño MC, Llop E, Martínez J et al. Effects of All-Oral Anti-Viral Therapy on HVPG and Systemic Hemodynamics in Patients With Hepatitis C Virus-Associated Cirrhosis. *Gastroenterology*. 2017 Nov; 153(5):1273-1283.e1. doi: 10.1053/j.gastro.2017.07.016. PMID: 28734831. Estudio realizado dentro del plan hepatitis. Grupos: Dr. Forn y Dr. García Pagan

CIBERCV: 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. PMID: 28067899. DOI:10.1038/nm.4266.

CIBERFES: Gomez-Cabrera MC, Garcia-Valles R, Rodriguez-Mañas L, Garcia-Garcia FJ, Olaso-Gonzalez G, Salvador-Pascual A et al. A New Frailty Score for Experimental Animals Based on the Clinical Phenotype: Inactivity as a Model of Frailty. *J Gerontol A Biol Sci Med Sci*. 2017 Jul 1; 72(7):885-891. PMID: 28329258. DOI: 10.1093/gerona/glw337.

CIBERONC: Robles-Valero J, Lorenzo-Martín LF, Menacho-Márquez M, Fernández-Pisonero I, Abad A, Camós M et al. A Paradoxical Tumor-Suppressor Role for the Rac1 Exchange Factor Vav1 in T Cell Acute Lymphoblastic Leukemia. *Cancer cell*. 2017;32(5): 608-623.e9. PMID: 29136506. doi: 10.1016/j.ccell.2017.10.004.

CIBERNED: Perez-Villalba A, Sirerol-Piquer MS, Belenguer G, Soriano-Canton R, Muñoz-Manchado AB, Villadiego J, et al. Synaptic Regulator alpha-Synuclein in Dopaminergic Fibers Is Essentially Required for the Maintenance of Subependymal Neural Stem Cells. *The Journal of Neuroscience: the official journal of the Society for Neuroscience*. 2018;38(4):814-25. Epub 2017 Dec 7. doi: 10.1523/JNEUROSCI.2276-17.2017.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2.3 THEMATIC NETWORKS FOR COOPERATIVE RESEARCH IN HEALTH (RETICS)



ASTHMA, ADVERSE REACTIONS AND ALLERGIES NETWORK (ARADYAL) – RD16/0006

Website: <http://aradyal.org/>

The high level of internationalisation in this RETIC is notable; different groups coordinate and participate in European projects on the identification of genetic biomarkers involved in allergies and predictive biomarkers for sensitivity to allergens. Results applicable to diagnosis have been obtained: (i) discovery of mechanisms associated with severe phenotypes and comorbidities, (ii) identification of new clinically-relevant allergens, (iii) identification of carrier proteins and structural details on the binding site in drug reactions, (iv) and the development of dendrimer nanostructures, nanoparticles, and high-capacity

platforms. Advances have been made in treatment: (i) design and validation of dendrimer systems for immunotherapy, (ii) pharmacogenomic analysis and drug metabolism analysis, (iii) design of databases to collect the use and adverse effects of biological medications in allergy diseases in order to optimise the rational use of medications.



SPANISH MATERNAL AND CHILD HEALTH AND DEVELOPMENT RESEARCH NETWORK (SAMID) - RD16/0022

Website: www.redsamid.net

In 2017, a new group was added (n°13). It is under the direction of Dr E. Larqué and is dedicated to the experimental and clinical study of circadian rhythms. Group n°3 (Dr MC Pallás) patented a pasteurisation system (P201531186) for human milk for the milk bank. Collaboration between groups and the number of joint publications have increased along with funding from AES grants. Clinical protocols on foetal wellbeing, resuscitation, nutrition, and infections have been carried out. Experimental models for the study of malformations, toxicity, and lung maturity have been strengthened. The randomised multicentre study for the treatment of newborns with asphyxia will be presented in the clinical trials session at the Pediatric Academic Societies Meeting USA, Toronto 2018.



NETWORK FOR COLLABORATIVE RESEARCH ON TROPICAL DISEASES (RICET) – RD16/0027

Website: <http://www.ricet.es/>

Amongst the milestones reached by RICET, the following should be highlighted:

1. Sequencing of the entire *Leishmania infantum* genome.
2. Organising and Scientific Committee of the X National SEMTSI Congress
3. Report on Crimean-Congo haemorrhagic fever that confirms the identity of the CCHF virus in patients with those detected in ticks in 2010.
4. Case management manual and surveillance of leishmaniosis in the European region.
5. Efficient management of the T cell response, a critical factor in congenital transmission of *Trypanosoma cruzi*.
6. Consensus document on imported diseases and participation in the study carried out by the Ministry of Health, Social Services, and Equality for the detection of ticks with the Crimean-Congo haemorrhagic fever-causing virus in four Regions.



NETWORK FOR INFLAMMATION AND RHEUMATIC DISEASE RESEARCH (RIER) - RD16/0012

Website: <https://red-rier.org/>

In 2017, the RIER participated 46 projects, 9 of which are collaborative amongst the network's various groups and seven of which have international funding. Important components which stand out include experimental research that is aimed at transfer and the numerous multicentric collaborations in the area of genetics and in the development of biomarkers in chronic inflammatory diseases.

The most relevant results from RIER in 2017 include the generation of new knowledge that allows for a better understanding of the genetic and physiopathological bases of immune mediated inflammatory diseases. Advances have also been made in clinical translation, particularly in clinical stratification strategies for chronic arthritis in relation to its cardiovascular comorbidity and to therapeutic optimisation.

In 2017, results were disseminated through 162 articles in indexed journals, of which 60% belong to the first quartile and approximately a third are collaborative. In relation to transfer of results, three patents and one set of clinical practice guidelines stand out.



EYE DISEASES NETWORK: PREVENTION, EARLY DETECTION, AND TREATMENT OF PREVALENT, DEGENERATIVE, AND CHRONIC OCULAR PATHOLOGY (OFTARED) – RD16/0008

Website: <http://www.oftared.com>

The milestones achieved by OFTARED throughout 2017 include the following:

An homage to the previous General Coordinators and to the researcher Miguel F. Refojo, who recently passed away, at ISCIII headquarters. Among the attendees of the event were Ana Pastor, president of the Congress; José Manuel Romay, president of the Council of State; and Jesús Fernández Crespo, Director of the ISCIII. The retina sub-programme edited three guidelines: Diet in Retina Diseases, Clinical Practice Guidelines for Hereditary Retinal Dystrophies, and OCT Angiography. It also collaborated in multiple events for the Year of the Retina in Spain (Spanish Government, 2017). In addition, the Glaucoma sub-programme sponsored a practical guide entitled "Lifestyle and Glaucoma." The Ocular Surface sub-programme participated in the Dry Eye Workshop by the Tear Film and Ocular Surface Society. The Ocular Dioptrics sub-programme coordinated a multicentric study with autologous mesenchymal cells and edited two books with the participation of various groups from the Network. In addition, it grew the keratoconus database, which now includes 4,350 records, making it the largest in Europe. Furthermore, the high level of participation in the Interuniversity Master's Degree in Vision Science Research continues.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

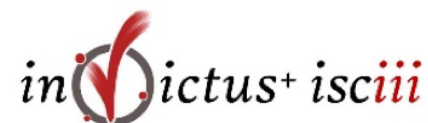
- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



SPANISH NETWORK FOR RESEARCH IN INFECTIOUS DISEASES (REIPI) - RD16/0016

Website: <http://www.reipi.org/>

In the area of microbial resistance, three new antimicrobial and antivirulence molecules and technology that allows for attenuated bacterial vaccines to be generated have been designed. Bioinformatic software has been developed for the characterisation of epidemic plasmids and for the design of useful diagnostic techniques for antifungal resistance. In the treatment of resistant microorganisms and complex infections, prognostic systems for certain infections have been developed and validated. Results have been obtained that change clinical practice in the treatment of certain microorganisms in patients with febrile neutropaenia and infectious endocarditis. The REIPI groups have participated in the development of various national and international clinical guidelines. In the area of infections in transplants, the utility of immunological monitoring of CMV infection, the importance of respiratory virus infections in lung transplants, and the significance of rectal colonisation by multiresistant enterobacteria have been established.



CEREBROVASCULAR DISEASES NETWORK (INVICTUS +) - RD16/0019

Website: <http://redinvictus.es/>

Results from INVICTUS+ studies have achieved: the development of software that allows for the diagnosis of a stroke as well as a prediction about its progress and temperature control of the patient; evidence that p53 and its negative regulator MDM2 regulate brain repair following cerebral ischaemia; the identification of a gene (PATJ) related to functional recovery following an ischaemic stroke; verification that BDNF levels are inversely correlated with ca-

pillary glucose levels in acute stroke patients; the development of a transgenic mouse that expresses the catalase antioxidant enzyme in the mitochondria, allowing for research into the impact of free radicals on the brain following an *in vivo* stroke; demonstration that the expansion of ICH is greater in patients anticoagulated with VKA and antiaggregants than that of patients who do not take antithrombotic agents; confirmation of the neuroprotective role of antioxidant administration in hyperglycaemic mice and female rats and its clinical efficacy in patients treated with a mechanical thrombectomy.



HEALTH SERVICES RESEARCH ON CHRONIC PATIENTS NETWORK (REDISSEC) - RD16/0001

Website: <https://www.redissec.com>

In 2017, REDISSEC led more than 140 projects on the “characterisation of chronicity and compared efficacy”, 59 of which are in collaboration with other groups in the network. Amongst the results of these projects, 651 articles with REDISSEC’s signature stand out, of which 128 were published in 2017. A call for mobility between groups was organised and the network participated in the 2nd edition of the University Expert Course in Health Services Research and Chronic Diseases (University of Alcalá). In addition to the V REDISSEC Conference, the I Multi-PAP International Conference was organised. We were present in different consortia and national and international projects. In addition to its webpage, REDISSEC sponsors other platforms: the ATLAS VPM website (<http://cort.as/-2vSS>), the RECH website (<http://cort.as/-2sVO>), the PYDeSalud website (www.pydesalud.com), the e-mpodera project (<http://cort.as/-2sVc>), a website for the prevention of skin carcinoma (<http://cort.as/-2sVj>), the CAMISS project (<http://cort.as/-2vSY>), the CARESS-CCR project (<http://cort.as/-2sVm>), and the multimorbidity and poly-medication project (<http://multipap.es/>).



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

SPANISH NETWORK OF MULTIPLE SCLEROSIS (REEM) - RD16/0015

Website: <http://www.reem.es/>

It participated in international “big data” studies with very relevant clinical results published in first quartile (Lancet Neurology, Ann Neurol, Neurology). It has researched biomarkers associated with the progress of multiple sclerosis (MS) and response to treatments. The identification of predictive biomarkers in isolated radiological syndromes is of note (Brain). It continued to study the influence of environmental factors (EBV, CMV and HERV-W, microbiota) in MS and its experimental model. It was determined that connectivity is affected in MS due to broad involvement of white matter and grey matter connective structures. Preclinical studies in animal models and a phase 1b clinical trial on the treatment of MS and optic neuromyelitis with dendritic cells have been performed. All of these works have given rise to 85 articles in high/medium impact international journals. Different scientific and educational activities have been organised. Of note are the II European Meeting on Optic Nerve Degeneration and a course on MS at the Menéndez Pelayo International University.

CELL THERAPY NETWORK (TERCEL) - RD16/0011

Website: <http://www.red-tercel.com/>

The cell therapy network has established itself as the most relevant collaborative research group in this scientific field in Spain and in Europe. It has a high capacity for scientific production in journals of impact, for achieving competitive research projects on the national and European level, and for clinical trials on cellular medications in collaboration with companies whose results are transferable to the SNS (Lancet 2016; 388:1281-90). Among its recent activities, its leading role in the TACTICS international group, which had European and American participation, is of note. This led to position papers on cellular therapy in cardiology (European Heart Journal. 2017;38: 2532–2546). The strengthening of a good clinical practice in cellular therapy platform for providing information and fighting fraud, carried out in collaboration with the AEMPS, should also be highlighted.

La nefrología en España

KIDNEY RESEARCH NETWORK (REDINREN) – RD16/0009

Website: <http://redinren.org/>

Milestones achieved: 1. Integration of the Biobank into the National Network (PROGRAMA4-ELSI), participating in projects aimed at improving the results of dialysis, providing support and facilitating knowledge on immuno-glomerulopathy, biomarkers of cardiorenal disease, and therapeutic targets in preclinical studies and clinical trials. 2. Integration of the NEFRONA study into the international CKD-PC Consortium. 3. Creation of a national registry of autosomal dominant polycystic kidney disease 4. End of follow-up on the PROGRESER cohort. 5. End of patient recruitment for the STARMEN clinical trial on membranous nephropathy. 6. Start of the PROERCAN01 (Effect of RAS Blockers on Chronic Kidney Disease Progression in Elderly Patients With Non Proteinuric Nephropathies) randomised clinical trial.

SPANISH AIDS RESEARCH NETWORK (RIS) – RD16/0025

Website: <http://www.retic-ris.net/>

In 2016, the AIDS Research Network (RIS) started a new five-year period. The RIS' evaluation was the best of all the RETICS. At the moment, it comprises 42 groups and 350 researchers. Among the milestones achieved, the following should be highlighted: 1) RIS' new webpage and social media presence. 2) The RIS cohorts that, in addition to the CoRis Cohort, have more than 12,000 patients. They have generated special patient cohorts with extreme phenotypes such as long-term nonprogressors (280 patients), elite controllers (800 patients), and special groups such as the vertical transmission population CoRISPe (344 patients). 3) The HIV Biobank currently has available more than 30,000 vials available belonging to 11,000 patients from different cohorts in the network. It has ISO 9001 2015 accreditation. 4) To date, the RIS has conducted more than 60 clinical trials and generated 10 vaccine prototypes, of which two have entered the clinical phase.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



ADDICTIVE DISORDERS NETWORK (RTA) - RD16/0017

Website: www.redrta.es

In 2017, the network carried out intensive research work on the medical consequences of alcohol use disorder and the psychiatric comorbidity associated with the consumption of psychostimulants. More than 150 original articles have been published, of which more than 40% correspond to collaborative publications within the network's groups. In terms of milestones, it should be highlighted the registry of a cohort of patients who seek treatment for alcohol use disorder. It has already reached around one thousand cases registered in ten centres across the nation (CohRTA study) and provides samples for genetic and biomarker studies. Further activities which should be highlighted include discoveries involving the role of neuroinflammation in addictive disorders, especially signals mediated by chemokines and natural immunity as well as the identification of biological mechanisms (including endocannabinoid and inflammatory mechanisms) that mediate inducement to vulnerability to alcohol and cocaine in adolescence and which have the precipitating factors of aggression/abuse, stress, and early exposure to drugs. Lastly, it should be highlighted the validation studies on brief alcohol abuse interventions.



PRIMARY CARE PREVENTION AND HEALTH PROMOTION RESEARCH NETWORK (REDIAPP) – RD16/0007

Website: www.rediapp.org

In 2017, redIAPP had 14 projects in its network, 104 projects in the different groups, and 221 publications (IF=654.613). Amongst its most notable successes is the development of *The EVIDENT Diet Quality Index*, which is associated with cardiovascular risk and its components and also with arterial stiffness. It has also been demonstrated that patients with a cardiovascular risk of 7.5 - 9.9% may benefit from treatment with statins, depending on whether they are at a greater risk of diabetes, costs, and patient preference. Furthermore, redIAPP has driven the creation of the *Iberian Network on Arterial Structure, Central Hemodynamics, and Neurocognition*. In terms of depression and anxiety prevention, it has demonstrated the efficacy and cost-effectiveness of the predictD intervention; developed the *predictplus-prevent* website, which is open to citizens; demonstrated the cost-effectiveness of the "Sonreír es Divertido" web programme; and showed the effectiveness of the Benzored intervention, which reduces benzodiazepine use by 45% and remains effective at the three-year mark.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations





2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2.4 PLATFORMS TO SUPPORT RESEARCH IN HEALTH SCIENCES AND TECHNOLOGY

The Platforms are stable structures for collaborative research conducted in networks in fields that are multidisciplinary. Their purpose is to provide high-level scientific, technical, and technological support to R&D&I centres and in particular to other stable collaborative structures (CIBER, RETICS, and IIS).



BIOBANKS PLATFORM - PT17/0015

Website: <http://www.redbiobancos.es>

The Biobanks Platform brings together 52 centres and over 600 agents across Spain. It is the main vehicle for facilitating access to quality human biological samples along with their associated information to the scientific community. It carries out its work in strict compliance with ethical and legal requirements that guarantee respect for donors' rights. In 2017, the platform managed 2,438 requests and 85,304 transfers of samples. These generated 281 indexed scientific publications which reference to Biobanks in the Platform.

The Biobanks Platform is in a process of continuous improvement of its management procedures for samples, data, and transfers. Furthermore, it promotes numerous educational activities, amongst which the University Master's Degree in Biobanks, organised by the Catholic University of Valencia, and the VIII National Biobanks Conference held in Cartagena are notable. Among other activities, it also organises monographic courses, mobility grants.



BIOMOLECULAR AND BIOINFORMATICS RESOURCES PLATFORM (PRB2) - PT17/0019

Website: <http://www.prb2.org>

The Biomolecular and Bioinformatics Resources Platform (PRB2) comprises Proteo-Red, CeGen, INB and BNADN, and BNLC.

Its objective is to provide cutting-edge technology to the scientific community and, as a priority, to the SNS. The high demand for this service is reflected the platform's mention in 148 publications.

The PRB2 carries out research projects that uphold its level of competitiveness. The result of this activity is its presence in the main international consortia in its sector and the publication of 422 articles in 2017.

The activities are disseminated through its webpage, congresses, conferences, and scientific meetings. In addition, it runs an extensive training programme.



Website: <http://www.itemas.org/>

The ITEMAS platform currently comprises 31 nodes of innovation as well as 38 hospitals and health centres and 105 non-healthcare centres as collaborators.

Of the 31 nodes of innovation, stand out:

- 14 centres have innovation management systems that are certified according to UNE 166002:2014 (5 have been certified in 2017).
- More than 1200 innovators submitted ideas to the innovation support units.
- Important innovative activities: 716 ideas gathered, 612 innovation projects in the development phase, 459 in transfer, and 421 that have reached the market.

- 188 patents being exploited and 83 software records that have generated approximately €10 million over the last five years.
- During 2017, 13 online training sessions on innovation management for a total of 19 teaching hours taught and an average attendance of 67 attendees/workshop.
- Actions to promote the Platform, such as its presence in a stand shared with BIOCAT at the Spring 2017 BioEurope Congress and the creation of a corporate video: "ITEMAS: Innovation for the Benefit of Patients" https://www.youtube.com/watch?v=c_Kg10r84tQ&feature=youtu.be



CLINICAL RESEARCH AND CLINICAL TRIALS UNITS PLATFORM (SCREN) – PT17/0017

Website: <https://www.scren.es/>

The SCReN (Spanish Clinical Research Network) platform is a clinical research support structure comprising 29 research units, or UICECs (Clinical Research and Trials Units), in hospitals and primary care centres throughout the SNS. SCReN's activity is focused on providing services to highly-complex independent clinical research projects, all of which are multicentric. To do so, it makes 120 professionals available to clinical researchers. These professionals are subsidised by the 2013-2016 Spanish National R&D&I plan through the AES, managed by ISCIII's Sub-Directorate General for Research Assessment and Promotion, and are cofunded with FEDER funds. They work on 102 research projects and carry out the following activities: overall management and regulatory support, pharmacovigilance tasks, data and methodological-biostatistical management, and monitoring. In addition, the harmonisation of procedures through the creation of the SCReN Quality Management System, the availability of advanced project management tools, and the creation of an "electronic Trial Master File" by SCReN should be noted. These aspects facilitate collaborative, decentralised, and multicentric work.



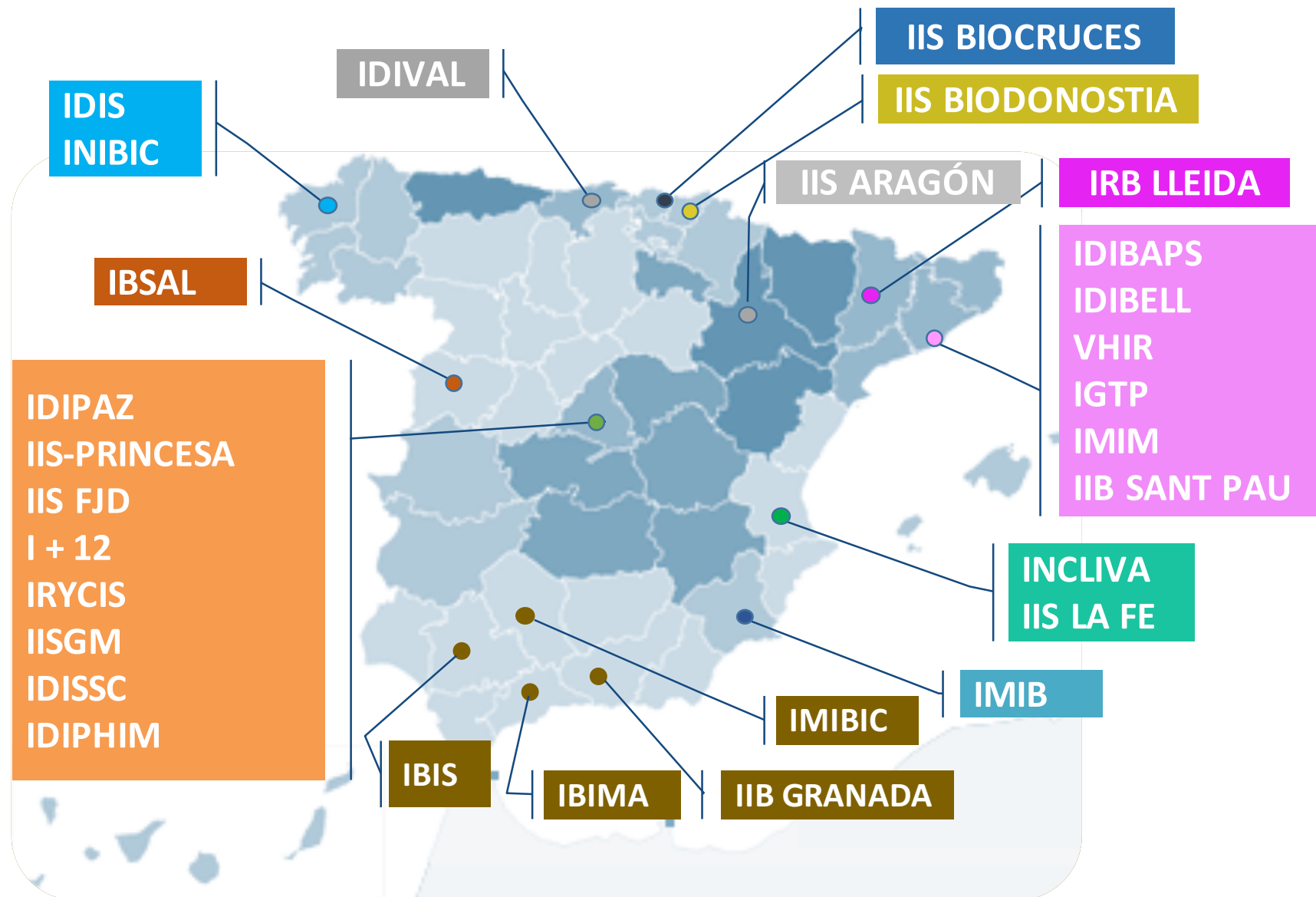
RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



2.5 HEALTH RESEARCH INSTITUTES (IIS)

In 2017, ISCIII concluded the inquiry into the renovation of accreditation for the five IISs that requested it. They are the following:

- Sant Pau Biomedical Research Institute (IIB SANT PAU)
- The Clinical Hospital of Valencia’s Healthcare Research Institute Foundation (INCLIVA)
- The 12 de Octubre Hospital Research Institute (i+12)
- The Maimónedes Biomedical Research Institute of Cordoba (IMIBIC)
- The Biodonostia Healthcare Research Institute (IIS BIODONOSTIA)

In 2017, the configuration and creation of the Evaluation Commission was completed pursuant to the terms established in R.D. 279/2016, of 24 June, on accreditation of biomedical or healthcare research institutes.

The ISCIII’s IIS monitoring group together with the Technical Commission, continued attending to requests for information on accreditation procedures, renovation of accreditation, requests for significant changes to already-accredited IISs or to new requesters, as well as requests for any other information required by the aforementioned institutions.

The ISCIII, along with the Technical Commission, continued preparing the accreditation evaluation guide as required by the aforementioned Royal Decree.



2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2.6 FOUNDATIONS

CARLOS III NATIONAL CENTRE FOR CARDIOVASCULAR RESEARCH FOUNDATION (CNIC)

<http://www.cnic.es>

Carlos III Spanish National Centre for Cardiovascular Research Foundation (F.S.P.), CNIC, is a national public foundation under the Ministry of Economy, Industry, and Competitiveness and was created through an ISCIII initiative. It receives significant private financial support through the Pro-CNIC Foundation. The CNIC's objective is to promote cardiovascular health through basic research, translational medicine, and training. It aims to contribute to advan-

ce in scientific knowledge in the cardiovascular field and the translation of knowledge to the prevention, diagnosis, and treatment of cardiovascular diseases.

The CNIC's scientific area (29 research groups) is organised into two departments: Basic Research and Clinical Research. They are entirely interconnected through six multidisciplinary programmes grouped into three research areas:

- Vascular Physiopathology
- Physiopathology of the Myocardium
- Cellular and Developmental Biology

The CNIC has Technical Units that provide fundamental scientific services to the CNIC's research laboratories and external users. The units also offer specialised training on using equipment and on employing various techniques. The

CNIC currently comprises the following units: Proteomics, Genomics, Cello-mics, Microscopy, Transgenesis, Comparative Medicine, Pluripotent Stem Cell Technology, Viral Vectors, Bioinformatics, and the Advanced Imaging Unit.

The CNIC renewed its accreditation as a “Severo Ochoa Centre of Excellence” for the 2016-2019 period.

Scientific Production

In 2017, the CNIC generated 272 publications, 245 of them in JCR-indexed journals, 77% in first quartile journals and 42% in first decile journals. A total of 54% of the publications were led by a CNIC researcher. In regards to collaboration, 28% of the publications were created in collaboration with other national institutions; 43% with both national and international institutions; 23% solely with international institutions; and lastly, 6% of the works are by CNIC authors alone. This year, 32% of the publications have been published in Golden Open Access.

Highlighted publications

Bartolome-Izquierdo N, de Yebenes VG, Alvarez-Prado AF, Mur SM, Lopez JA, Roa S, et al. miR-28 regulates the germinal center reaction and blocks tumor growth in preclinical models of non-Hodgkin lymphoma. *Blood*. 2017;129(17):2408-19. DOI: 10.1182/blood-2016-08-731166

Pontes-Quero S, Heredia L, Casquero-Garcia V, Fernandez-Chacon M, Luo W, Hermoso A, et al. Dual ifgMosaic: A Versatile Method for Multispectral and Combinatorial Mosaic Gene-Function Analysis. *Cell*. 2017;170(4):800-14 e18. DOI: 10.1016/j.cell.2017.07.031

Solanas G, Peixoto FO, Perdiguero E, Jardi M, Ruiz-Bonilla V, Datta D, et al. Aged Stem Cells Reprogram Their Daily Rhythmic Functions to Adapt to Stress. *Cell*. 2017;170(4):678-92 e20. DOI: 10.1016/j.cell.2017.07.035

Fernandez-Jimenez R, Galan-Arriola C, Sanchez-Gonzalez J, Aguero J, Lopez-Martin GJ, Gomez-Talavera S, et al. Effect of Ischemia Duration and Protective Interventions on the Temporal Dynamics of Tissue Composition After Myocardial Infarction. *Circ Res*. 2017;121(4):439-50. DOI: 10.1161/CIRCRES-AHA.117.310901

Fernandez-Jimenez R, Barreiro-Perez M, Martin-Garcia A, Sanchez-Gonzalez J, Aguero J, Galan-Arriola C, et al. Dynamic Edematous Response of the Human Heart to Myocardial Infarction: Implications for Assessing Myocardial Area at Risk and Salvage. *Circulation*. 2017;136(14):1288-300. DOI: 10.1161/CIRCULATIONAHA.116.025582

Gonzalez-Lopez E, Gagliardi C, Dominguez F, Quarta CC, de Haro-Del Mo-

ral FJ, Milandri A, et al. Clinical characteristics of wild-type transthyretin cardiac amyloidosis: disproving myths. *Eur Heart J*. 2017;38(24):1895-904. DOI: 10.1093/eurheartj/ehx043

Aguero J, Galan-Arriola C, Fernandez-Jimenez R, Sanchez-Gonzalez J, Ajmone N, Delgado V, et al. Atrial Infarction and Ischemic Mitral Regurgitation Contribute to Post-MI Remodeling of the Left Atrium. *J Am Coll Cardiol*. 2017;70(23):2878-89. DOI: 10.1016/j.jacc.2017.10.013

Fernandez-Alvira JM, Fuster V, Pocock S, Sanz J, Fernandez-Friera L, Laclaustra M, et al. Predicting Subclinical Atherosclerosis in Low-Risk Individuals: Ideal Cardiovascular Health Score and Fuster-BEWAT Score. *J Am Coll Cardiol*. 2017;70(20):2463-73. DOI: 10.1016/j.jacc.2017.09.032

Fernandez-Friera L, Fuster V, Lopez-Melgar B, Oliva B, Garcia-Ruiz JM, Mendiguren J, et al. Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors. *J Am Coll Cardiol*. 2017;70(24):2979-91. DOI: 10.1016/j.jacc.2017.10.024

Fuster V, Frazer J, Snair M, Vedanthan R, Dzau V, Committee on Global H, et al. The Future Role of the United States in Global Health: Emphasis on Cardiovascular Disease. *J Am Coll Cardiol*. 2017;70(25):3140-56. DOI: 10.1016/j.jacc.2017.11.009

Lopez-Melgar B, Fernandez-Friera L, Oliva B, Garcia-Ruiz JM, Penalvo JL, Gomez-Talavera S, et al. Subclinical Atherosclerosis Burden by 3D Ultrasound in Mid-Life: The PESA Study. *J Am Coll Cardiol*. 2017;70(3):301-13. DOI: 10.1016/j.jacc.2017.05.033

Mazzanti A, Maragna R, Vacanti G, Kostopoulou A, Marino M, Monteforte N, et al. Hydroquinidine Prevents Life-Threatening Arrhythmic Events in Patients With Short QT Syndrome. *J Am Coll Cardiol*. 2017;70(24):3010-5. DOI: 10.1016/j.jacc.2017.10.025

Takemoto Y, Ramirez RJ, Kaur K, Salvador-Montanes O, Ponce-Balbuena D, Ramos-Mondragon R, et al. Eplerenone Reduces Atrial Fibrillation Burden Without Preventing Atrial Electrical Remodeling. *J Am Coll Cardiol*. 2017;70(23):2893-905. DOI: 10.1016/j.jacc.2017.10.014

Uzhova I, Fuster V, Fernandez-Ortiz A, Ordovas JM, Sanz J, Fernandez-Friera L, et al. The Importance of Breakfast in Atherosclerosis Disease: Insights From the PESA Study. *J Am Coll Cardiol*. 2017;70(15):1833-42. DOI: 10.1016/j.jacc.2017.08.027

Gonzalez N, Quintana JA, Garcia-Silva S, Mazariegos M, Gonzalez de la Aleja A, Nicolas-Avila JA, et al. Phagocytosis imprints heterogeneity in tissue-resident macrophages. *J Exp Med*. 2017;214(5):1281-96. DOI: 10.1084/jem.20161375

Enamorado M, Iborra S, Priego E, Cueto FJ, Quintana JA, Martinez-Cano S, et al. Enhanced anti-tumour immunity requires the interplay between resi-



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

dent and circulating memory CD8+ T cells. *Nat Commun.* 2017;8:16073. DOI: 10.1038/ncomms16073

Garcia-Prieto J, Villena-Gutierrez R, Gomez M, Bernardo E, Pun-Garcia A, Garcia-Lunar I, et al. Neutrophil stunning by metoprolol reduces infarct size. *Nat Commun.* 2017;8:14780. DOI: 10.1038/ncomms14780

Matesanz N, Bernardo E, Acin-Perez R, Manieri E, Perez-Sieira S, Hernandez-Cosido L, et al. MKK6 controls T3-mediated browning of white adipose tissue. *Nat Commun.* 2017;8(1):856. DOI: 10.1038/s41467-017-00948-z

Perez-Garcia A, Marina-Zarate E, Alvarez-Prado AF, Ligos JM, Galjart N, Ramiro AR. CTCF orchestrates the germinal centre transcriptional program and prevents premature plasma cell differentiation. *Nat Commun.* 2017;8:16067. DOI: 10.1038/ncomms16067

Minguet S, Klasener K, Schaffer AM, Fiala GJ, Osteso-Ibanez T, Raute K, et al. Caveolin-1-dependent nanoscale organization of the BCR regulates B cell tolerance. *Nat Immunol.* 2017;18(10):1150-9. DOI: 10.1038/ni.3813

de Carcer G, Wachowicz P, Martinez-Martinez S, Oller J, Mendez-Barbero N, Escobar B, et al. Plk1 regulates contraction of postmitotic smooth muscle cells and is required for vascular homeostasis. *Nat Med.* 2017;23(8):964-74. DOI: 10.1038/nm.4364

Oller J, Mendez-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;23(2):200-12. DOI: 10.1038/nm.4266

R&D Activities: Fundraising

In 2017, CNIC had more than 230 active national grants awarded to the Centre's researchers through competitive calls. The funds of these grants totalled more than €31 million, including both grants that ended in 2017 as well as those which began this year. Of this total, €23.6 million came from public entities and €3.8 million from private entities. These financial data do not include the €4 million that the centre has available from its accreditation as a "Severo Ochoa Centre of Excellence" (2016 - 2019).

In regards to international competitive projects, in 2017, the CNIC signed two contracts for the prestigious "European Research Council" grants: one ERC Advanced grant and one ERC Consolidator grant. The Centre had six active ERC grants in 2017. CNIC researchers participated in a total of seven projects funded by different ERA-NETS. The CNIC was especially successful in the ERA NET call for Cardiovascular Diseases (ERA-CVD): in the 2016 call, three projects were awarded to the CNIC (one of them with the CNIC as the coordinator). In 2017, the Centre also obtained funds for a project coordinated with

the E-RARE3 ERA-NET (rare diseases) that investigates new treatments for progeria. This year, the CNIC received funds from the United States for a research project by the Marfan Foundation as well as from France's Leducq Foundation, which funds international collaborative research on cardiovascular and neurovascular diseases. The CNIC is the first Spanish centre to coordinate a project from the Leducq Foundation. This project, funded as a whole for a total of €6 million U.S. dollars, will study how and why the capacity to develop new cardiac cells and repair the heart following an acute lesion is lost. The funds obtained through international calls in 2017 totalled €4.7 million.

R&D Activities: Technology Transfer

The CNIC is very active in the field of research results transfer. Its current technological offer comprises 16 patents. Seven patent requests were filed in 2017, taking into account extensions and new requests. Four of the currently-active patents have already been licensed to businesses for their development and commercialisation. Furthermore, the CNIC also generated results of interest to the private biotechnology/pharmaceuticals sector. In 2017, this resulted in the signing of two scientific collaboration agreements with different companies in order to carry out joint projects.

Training

The Centre's training activities are coordinated through a comprehensive training plan, called CNIC-JOVEN. It is designed to bring young people into biomedical research and create a talent pool of future researchers of excellence in the cardiovascular field. In 2017, the CNIC had 635 participants in different training programmes and workshops. The Participation is distributed as follows: the Acércate Programme for Bachelor students, eight; internships for professional training students, nine. Participation in internships for university students was as follows: (a) Cicerone Programme, 30; (b) Internship Programme, 82; (c) Master's Degree Scholarship Programme, 11; Pre-doctoral Programme, 89; and the Post-Doctoral Programme, 58. Participation in placements for medical professionals (programmes in collaboration with the Spanish Society of Cardiology) were as follows: Invesmir Programme, two; Res@CNIC Programme, 20, Cardio Joven Programme, one. It should be noted that four students completing internships at the CNIC received awards at the Archimedes University Competition from the MECED. In 2017, 20 doctoral thesis were defended. Lastly, training activities also included the Post-Graduate Programme, the BMM9 module of the Master's Degree in Molecular Biosciences from the Autonomous University of Madrid (8 participants), and a continuing education programme in which a cardiovascular pathophysiology course (91 attendees) and vascular biology course (226 attendees) were organised.



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

RESEARCH CENTRE FOR NEUROLOGICAL DISEASES FOUNDATION (CIEN)

<http://www.fundacioncien.es/>

The Research Centre for Neurological Diseases Foundation (CIEN) was created on 27 December 2002 through an agreement of the Council of Ministers. It is affiliated with the ISCIII. Its objectives include supporting, promoting, and coordinating research on neurological diseases, especially on neurodegenerative diseases. The CIEN Foundation collaborates with the Neurodegenerative Diseases area of the CIBER Consortium (CIBERNED). Since 2010, it has contributed to the development of a biobank of neurological samples (CIEN Tissue Bank), which forms part of the CIBERNED biobank platform. The cooperation between the CIEN FOUNDATION and CIBERNED has been recognised by the European Union through the inclusion of both entities in the International Network of Centres of Excellence in Neurodegeneration (CoEN) within the Joint Programme for Neurodegenerative Diseases. The CIEN Tissue Bank participates in the Spanish National Biobank Network Platform, sponsored by the ISCIII.

Highlighted Activities

- Approval was obtained for the Sat-CIEN-02 Clinical Trial from the Spanish Agency of Medicines and Medical Products and by the Central Ethics Committee.
- In 2017, the CIEN continued its participation as co-owner on the application for two active patents in national phases in different countries. Both are licensed to Raman Health Technologies.
- In May 2017, the fourth visit of the Vallecas Project concluded with 772 participants. By the end of 2017, a total of 658 volunteers had completed a fifth visit and a sixth round of visits was started, which 276 volunteers completed.
- Presentation of the “Vallecas Brain” canonical brain, a virtual model of a brain created based on the magnetic resonance images of more than 1,000 healthy brains of Vallecas Project volunteers who do not suffer from dementia and who are between 70 and 85 years old. The model serves as a control that individual magnetic resonance images can be compared to. In this manner, early identification of the typical anomalies observed in the onset of Alzheimer’s disease and other neurodegenerative diseases is possible.
- For the fifth consecutive year, the Vallecas Project Volunteer Day was held in recognition of these people’s collaboration on the research.
- Alzheimer León participated in the funding of the Vallecas Project,

thanks to the financial backing of dozens of sponsors who, in the latest edition of the Mano Amiga awards, joined forces to support research projects that seek to fight this disease.

- Throughout 2017, the Tissue Bank reached 800 case records and the number of brains donated from the Alzheimer’s Centre exceeded 130.
- ISCIII approved the new phase of development of the Spanish National Biobanks Network Platform (2018 - 2020), to which the TB-CIEN belongs.
- Alberto Rábano, Scientific Director of the TB-CIEN, was named Coordinator of the Spanish Neuropathology Group, which belongs to the Spanish Society of Neurology and the Spanish Society of Pathology.
- Various educational cooperation agreements were signed for the conduct of external internships (curricular and extracurricular) between various public universities and the CIEN Foundation. The Complutense University of Madrid and the Carlos III University have facilitated contact between students completing a Bachelor’s Degree in Psychology and the CIEN Foundation for both external internships and the Bachelor’s Degree/Master’s Degree final project.
- Call for the 2017 Queen Sofía Foundation-Mapfre Grant for the hiring of Ph.D. holders in engineering, neuroscience, physics, or bioinformatics for a research programme centred on the study of neurodegenerative disorders using an approach that combines mathematical modelling and computational simulation in order to characterise predictive algorithms.
- In 2017, the CIEN Foundation upheld its commitment to the Youth Employment Operational Programme of the Ministry of Education, Youth, and Sport of the Community of Madrid through the signing of a new agreement for the promotion of youth employment and implementation of the Youth Guarantee in R&D.
- In September, the CIEN Foundation, along with the Champalimaud Foundation, the Queen Sofía Foundation, and CIBERNED, held the Alzheimer’s Research & Care Global Summit Lisbon 2017 scientific summit. This edition of the already-consolidated International Congress on Research and Innovation in Neurodegenerative Diseases (CIEN) brought together prestigious scientists, such as Nobel Prize in Medicine winners Richard Axel (Columbia University) or John O’Keefe (University College London), at the Champalimaud Centre of the Unknown. The CIEN Foundation was represented by, amongst others, Dr Strange, who presented a predictive algorithm, based on five years of Vallecas Project research, for identifying conversion variables between a cognitively healthy state and mild cognitive impairment.
- Inauguration of the now-traditional “Memory Tree,” which in 2017 was again



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

set up in the Madrid City Hall and the Villa de Vallecas Market.

- In 2017, the number of mentions of the CIEN in the media was around 2,400, increasing by 48% with respect to 2016. For example, during the *Alzheimer's Global Summit Lisbon 2017* (Lisbon, September 18th –21st, 2017) alone, more than 350 mentions in the press (agencies and national and international media) were generated. Of these, 220 were in online media, plus the evident repercussions on social media, especially Twitter.
- In April 2017, an addendum was signed to the 2012 collaboration agreement between the Queen Sofía Foundation and the CIEN Foundation for the execution of the "FCIEN Tissue Bank (TB-CIEN)" project.
- In May 2017, the meeting of the National Group on Dementia was held. The purpose of the meeting was to work towards the development of the IV Axis of the National Alzheimer's Plan.
- In May 2017, Their Majesties the King and Queen of Spain, accompanied by Their Majesties the King and Queen of Spain Emeritus and other public figures, presided over the celebration of the 40th Anniversary of the Queen Sofía Foundation and the 10th Anniversary of the Queen Sofía Foundation Alzheimer's Centre at the CIEN Foundation's headquarters.

Scientific Production

In 2017, 31 original articles were published in specialised journals. Where 22 were published in first and second quartile journals with a mean impact factor of 7.564. This is an increase (11.36%) compared to 2016 and follows the upward trend observed in recent years. International collaborations continued, with 50% of the publications from studies carried out in collaboration with foreign institutions, 43.75% in collaboration with Spanish institutions, and the remaining 6.25% carried out solely by CIEN Foundation researchers.

Highlighted publications

Pérez-Canamas A, Benvegnù S, Rueda CB, Rábano A, Satrustegui J, Ledesma MD. Sphingomyelin-induced inhibition of the plasma membrane calcium ATPase causes neurodegeneration in type A Niemann-Pick disease. *Molecular psychiatry*. 2017 May. 22(5): 711-723. PMID: 27620840.

Rodriguez-Rodriguez P, Sandebring-Matton A, Merino-Serrais P, Parrado-Fernandez C, Rabano A, Winblad B, Avila J, Ferrer I, Cedazo-Minguez A. Tau hyperphosphorylation induces oligomeric insulin accumulation and insulin resistance in neurons. *Brain a journal of neurology*. 2017 Oct 13. PMID: 29053786.

Carro E, Bartolomé F, Bermejo-Pareja F, Villarejo-Galende A, Molina JA, Ortiz P, Calero M, Rábano A, Cantero JL, Orive G. Early diagnosis of mild cognitive impairment and Alzheimer's disease based on salivary lactoferrin. *Alzheimer's &*

dementia: diagnosis, assessment & disease monitoring. 2017 8:131-138. PMID: 28649597.

Medina M, Khachaturian Z, Rossor M, Ávila J, Cedazo-Mínguez A. "Toward common mechanisms for 'risk factors' in Alzheimer's syndrome. *Alzheimers Dement (NY)* 2017. 3(4):571-578. PMID: 29124116.

Bolós M, Llorens-Martín M, Perea JR, Jurado-Arjona J, Rábano A, Hernández F, Ávila J. Absence of CX3CR1 impairs the internalization of Tau by microglia. *Molecular neurodegeneration*. 2017 Aug 15. 12 (1): 59. PMID: 28810892.

López-Sánchez N, Fontan-Lozano A, Palle A, González-Álvarez V, Rábano A, Trejo JL, Frade JM. Neuronal tetraploidization in the cerebral cortex correlates with reduced cognition in mice and precedes and recapitulates Alzheimer's-associated neuropathology. *Neurobiology of aging*. 2017 Apr 18 56: 50-66. PMID: 28494436.

Ávila-Villanueva M, Fernández-Blázquez MA. Subjective Cognitive Decline as a preclinical marker for Alzheimer's Disease: The challenge of stability over time. *Frontiers in Aging Neuroscience*. 2017, Nov 21;9:377. PMID: 29201004.

Quinlan S, Kenny A, Medina M, Engel T, Jiménez-Mateos EM. MicroRNAs in neurodegenerative diseases. *Int. Rev. Cell Mol. Biol*. 2017. 334:309-343. PMID: 28838542.

Riancho J, Vazquez-Higuera JL, Pozueta A, Lage C, Kazimierczak M, Bravo M, Calero M, Gonzalezalez A, Rodriguez E, Lleo A, Sanchez-Juan P. MicroRNA Profile in Patients with Alzheimer's Disease: Analysis of miR-9-5p and miR-598 in Raw and Exosome Enriched Cerebrospinal Fluid Samples. *JAD*. 2017. 57 (2): 483-491. PMID: 28269782.

Ávila-Villanueva M, Medina M, Fernández-Blázquez MA (2017). The dimensional structure of subjective cognitive complaints. *Neuromethods* (in press).

SPANISH NATIONAL CANCER RESEARCH CENTRE FOUNDATION (CNIO)

<https://www.cnio.es/es>

In 2017, the CNIO's scientific activity was carried out by a total of 365 researchers and technicians organised into 22 Research Groups, four Clinical Research Units, and 19 Support Units across six Research Programmes (Molecular Oncology, Cancer Cell Biology, Structural Biology, Human Cancer Genetics, and Biotechnology) as well as two drug discovery sections in the Experimental Therapeutics Programme. The CNIO scientists' and technologists' activities are supported by various departments and areas responsible for different auxiliary tasks, including Scientific Management, the Technology Transfer Office, Communications, International Relations, Technical Management, and Administration. The 31st December 31



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

2017, the total number of CNIO staff was 406 employees.

Scientific Production

In 2017, the CNIO published a total of 217 articles. Of these, 26 were published in journals with impact factors of between 10 and 15 and 44 articles were published in journals with an impact factor greater than 15. In regards to publications with an impact factor greater than 15, 2017 has been the most productive year in the CNIO's history. Below are some of the most significant publications of 2017:

Highlighted publications

Brandt M, Grazioso TP, Fawal MA, Tummala KS, Torres-Ruiz R, Rodriguez-Peralles S, Perna C, Djouder N. mTORC1 inactivation promotes colitis-induced colorectal cancer. *Cell Metab.* 2017; Dec 21 [Epub ahead of print]. doi:10.1016/j.cmet.2017.11.006

Oldrini B, Hsieh WY, Erdjument-Bromage H, Codega P, Carro MS, Curiel-García A, Campos C, Pourmaleki M, Grommes C, Vivanco I, Rohle D, Bielski CM, Taylor BS, Hollmann TJ, Rosenblum M, Tempst P, Blenis J, Squatrito M, Mellinger IK. EGFR feedback-inhibition by Ran-binding protein 6 is disrupted in cancer. *Nat Commun.* 2017; 8(1):2035. doi: 10.1038/s41467-017-02185-w. PMID: 29229958

Bejarano L, Schuhmacher AJ, Méndez-Pertuz M, Megías M, Blanco-Aparicio C, Martínez S, Pastor J, Squatrito M, Blasco MA. Inhibition of TRF1 telomere protein impairs tumor initiation and progression in glioblastoma multiform mouse models and patient-derived xenografts. *Cancer Cell.* 2017; 32(5):590-607. doi: 10.1016/j.ccell.2017.10.006

Méndez-Pertuz M, Martínez P, Blanco-Aparicio C, Gómez-Casero E, García AB, Martínez -Torrecuadrada J, Palafox M, Cortés J, Serra V, Pastor J, Blasco MA. Modulation of telomere protection by the PI3K/AKT pathway. *Nat Commun.* 2017;8(1):1278. doi: 10.1038/s41467-017-01329-2. PMID: 29097657

Simón-Carrasco L, Graña O, Salmón M, Jacob HKC, Gutierrez A, Jiménez G, Drosten M, Barbacid M. Inactivation of Capicua in adult mice causes T cell lymphoblastic lymphoma. *Genes Dev.* 2017; 31(14):1456-1468. doi: 10.1101/gad.300244.117. PMID: 28827401

Olbrich T, Mayor-Ruiz C, Vega-Sendino M, Gomez C, Ortega S, Ruiz S, Fernandez-Capetillo O. A p53-dependent response limits the viability of mammalian haploid cells. *PNAS.* 2017;114(35): 9367-9372. doi: 10.1073/pnas.1705133114. PMID: 28808015

Carrillo-de-Santa-Pau E, Juan D, Pancaldi V, Were F, Martin-Subero I, Rico D,

Valencia A. Automatic identification of informative regions with epigenomic changes associated to hematopoiesis. *Nucleic Acids Res.* 2017; 45(16):9244-9256. doi: 10.1093/nar/gkx618

Nieto P, Ambrogio C, Esteban-Burgos L, Gómez-López G, Blasco MT, Yao Z, Marais R, Rosen N, Chiarle R, Pisano DG, Barbacid M and Santamaría D. A Braf kinase-inactive mutant induces lung adenocarcinoma. *Nature.* 2017; 548(7666):239-243. doi: 10.1038/nature23297. PMID: 28783725

Remacha L, Comino-Méndez I, Richter S, Contreras L, Currás-Freixes M, Pita G, Letón R, Galarreta A, Torres-Pérez R, Honrado E, Jiménez S, Maestre L, Moran S, Esteller M, Satrustegui J, Eisenhofer G, Robledo M, Cascón A. Targeted Exome Sequencing of Krebs Cycle Genes Reveals Candidate Cancer-Predisposing Mutations in Pheochromocytomas and Paragangliomas. *Clin Cancer Res.* 2017; 23(20):6315-6324. doi: 10.1158/1078-0432.CCR-16-225 PMID: 28720665

de Cárcer G, Wachowicz P, Martínez-Martínez S, Oller J, Méndez-Barbero N, Escobar B, González-Loyola A, Takaki T, El Bakkali A, Cámara JA, Jiménez-Borreguero LJ, Bustelo XR, Cañamero M, Mulero F, de Los Ángeles Sevilla M, Montero MJ, Redondo JM, Malumbres M. Plk1 regulates contraction of postmitotic smooth muscle cells and is required for vascular homeostasis. *Nat Med.* 2017;23(8):964-974. doi: 10.1038/nm.4364

Lozano-Torres B, Galiana I, Rovira M, Garrido E, Chaib S, Bernardos A, Muñoz-Espín D, Serrano M, Martínez-Mañez R, Sancenón F. An OFF-ON Two-Photon Fluorescent Probe for Tracking Cell Senescence in Vivo. *J Am Chem Soc.* 2017;139(26):8808-8811. doi: 10.1021/jacs.7b04985. PMID: 28625064

Sánchez-Valle J, Tejero H, Ibáñez K, Portero JL, Krallinger M, Al-Shahrour F, Tabarés-Seisdedos R, Baudot A, Valencia A. A molecular hypothesis to explain direct and inverse co-morbidities between Alzheimer's Disease, Glioblastoma and Lung cancer. *Sci Rep.* 2017;7(1):4474. doi: 10.1038/s41598-017-04400-6. PMID: 28667284

Olmeda D, Cerezo-Wallis D, Riveiro-Falkenbach E, Pennacchi PC, Contreras-Alcalde M, Ibarz N, Cifdaloz M, Catena X, Calvo TG, Cañón E, Alonso-Curbelo D, Suarez J, Osterloh L, Graña O, Mulero F, Megías D, Cañamero M, Martínez-Torrecuadrada JL, Mondal C, Di Martino J, Lora D, Martínez-Corral I, Bravo-Cordero JJ, Muñoz J, Puig S, Ortiz-Romero P, Rodríguez-Peralto JL, Ortega S, Soengas MS. Whole-body imaging of lymphovascular niches identifies pre-metastatic roles of midkine. *Nature.* 2017; 546(7760):676-680. doi: 10.1038/nature22977. PMID: 28658220

Krallinger M, Rabal O, Lourenço A, Oyarzabal J, Valencia A. Information Retrieval and Text Mining Technologies for Chemistry. *Chem Rev.* 2017;117(2):7673-7761. doi: 10.1021/acs.chemrev.6b00851. PMID: 28475312



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

Capella-Gutierrez S, Rabal O, Oyarzabal J, Valencia A, Krallinger M. LimTox: a web tool for applied text mining of adverse event and toxicity associations of compounds, drugs and genes. *Nucleic Acids Res.* 2017;45(W1):W484-W489. doi: 10.1093/nar/gkx462

Torres-Ruiz R, Martinez-Lage M, Martin MC, Garcia A, Bueno C, Castaño J, Ramirez JC, Menendez P, Cigudosa JC, Rodriguez-Perales S. Efficient Recreation of t(11;22) EWSR1-FLI1+ in Human Stem Cells Using CRISPR/Cas9. *Stem Cell Rep.* 2017;8(5):1408-1420. doi: 10.1016/j.stemcr.2017.04.014. PMID: 28494941

Muñoz S, Búa S, Rodríguez-Acebes S, Megías D, Ortega S, de Martino A, Méndez J. In Vivo DNA Re-replication Elicits Lethal Tissue Dysplasias. *Cell Rep.* 2017;19(5):928-938. doi: 10.1016/j.celrep.2017.04.032. PMID: 28467906

Tummala KS, Brandt M, Teijeiro A, Graña O, Schwabe RF, Perna C, Djouder N. Hepatocellular Carcinomas Originate Predominantly from Hepatocytes and Benign Lesions from Hepatic Progenitor Cells. *Cell Rep.* 2017;19(3):584-600. doi: 10.1016/j.celrep.2017.03.059. PMID: 28423321

Bakiri L, Hamacher R, Graña O, Guío-Carrión A, Campos-Olivas R, Martinez L, Dienes HP, Thomsen MK, Hasenfuss SC, Wagner EF. Liver carcinogenesis by FOS-dependent inflammation and cholesterol dysregulation. *J Exp Med.* 2017;214(5):1387-1409. doi: 10.1084/jem.20160935. PMID: 28356389

Peinado H, Zhang H, Matei IR, Costa-Silva B, Hoshino A, Rodrigues G, Psaila B, Kaplan RN, Bromberg JF, Kang Y, Bissell MJ, Cox TR, Giaccia AJ, Ertler JT, Hiratsuka S, Ghajar CM, Lyden D. Pre-metastatic niches: organ-specific homes for metastases. *Nat Rev Cancer.* 2017;17(5):302-317. doi: 10.1038/nrc.2017.6. PMID: 28303905

Marión RM, López de Silanes I, Mosteiro L, Gamache B, Abad M, Guerra C, Megías D, Serrano M, Blasco MA. Common Telomere Changes during In Vivo Reprogramming and Early Stages of Tumorigenesis. *Stem Cell Rep.* 2017;8(2):460-475. doi: 10.1016/j.stemcr.2017.01.001. PMID: 28162998

Competitive Funding

The CNIO funded a substantial part of its research through competitive projects from both national and international institutions as well as from private entities. In 2017, funding was obtained for 135 projects. Funding for 20 of them came from international consortia, three of which were led by the CNIO, and funding for 22 of them came from national consortia, seven of which were coordinated by the CNIO.

International Consortia: nine projects were funded by the European Commission, one by the Interreg Sudoe Programme, one by the Melanoma Research Alliance (MRA), four by the US NIH, one by the Paradifference Foundation, one by the US Department of Defense, one by Worldwide Cancer Research

(WCR, previously AICR), and two by the Elixir European Platform.

Individual International Projects: 12 by the European Commission (four grants from the ERC and eight Maria Skłodowska-Curie actions); six by Worldwide Cancer Research (WCR, previously AICR); two by the Prostate Cancer Foundation; one by the Howard Hughes Medical Institute (HHMI); two by the Melanoma Research Alliance (MRA); one by the US Department of Defense; one by the International Human Frontier Science Program Organization (HFSP); and one prize from the Beug Foundation.

Collaborative National Projects: ten by the ISCIII; three by the Spanish State Research Agency, MINECO; five by the Spanish Association Against Cancer (AECC); three by the La Marató TV3 Foundation; and one by the Madrimas Foundation.

Individual National Projects: 12 were funded by the ISCIII; 38 by MINECO; four by the Spanish Association Against Cancer (AECC); two by the BBVA Foundation; one by the AstraZeneca HealthCare Foundation; two by the FERO Foundation; one by the Atresmedia Corporation; one by the Olga Torres Foundation; one by the Leukaemia and Lymphoma Foundation; one by the Spanish Association of Gastroenterology; one by the Pfizer Foundation; and one by the Neurofibromatosis Project Foundation.

Training

The CNIO actively participates in the postgraduate programmes of various Spanish academic institutions, both in teaching as well as in offering the possibility of taking on students for training internships. In 2017, the CNIO signed new agreements with the University of Extremadura, the Complutense University of Madrid, and the International University of La Rioja. Agreements have also been signed with the Banco Santander Foundation, La Caixa Foundation, and with the Puerta de Hierro Secondary Education Institute and CESUR, in Madrid.

Twenty-one doctoral theses were defended in 2017. In 2017, La Caixa Foundation launched a new doctoral grant programme called inPhinit. The CNIO received two students with these grants. Of the 112 pre-doctoral students working at the CNIO in 2017, over 21% came from foreign universities.

The CNIO has a post-doctoral training programme subsidised by the Banco Santander Foundation in order to attract scientists who have spent part of their scientific career in England or the US. In 2017, a new collaboration agreement was signed in order to continue this programme. At the beginning of 2017, a scientist from the City University of New York (CUNY) was recruited. In addition, for the sixth consecutive year, the possibility of a business management and administration course was offered through the Instituto de Empresa to train scientists on innovation tasks.

Thanks to the CNIO Friends philanthropic platform, a second call of the CNIO Friends Post-Doctoral Contract Programme was launched in 2017; two scien-



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations

tists were hired for a period of two years. Furthermore, the person hired with the Play Therapy-CNIO Friends post-doctoral contract continued carrying out his/her paediatric cancer project for a second year. In 2017, CNIO Friends generated €300,000 income through the web platform, in addition to four bequests and inheritances.

In 2017, the CNIO had 44 post-doctoral students, of which more than a third come from prestigious foreign institutions.

There are three continuing education programmes for resident physicians. These are carried out by means of three-month placements in CNIO research groups. In 2017, the CNIO had 24 resident physicians from 18 different hospitals.

In 2017, two laboratory internship programmes were carried out. These programmes take place every year and are aimed at university students in their final or penultimate year. There were 99 students, three of whom were then taken on as pre-doctoral students.

In addition, 20 technicians completing professional training courses took part in the Workplace Training Programme through agreements with various secondary education institutions. Two of them were later hired as laboratory technicians.

The CNIO has a visiting scientist programme thanks to an agreement signed with the Jesús Sierra Foundation. In 2017, Raúl Rabadan of Colombia University in New York and Wolfgang Weninger, of the Royal Prince Hospital in Sydney, completed their placements at the CNIO thanks to this grant.

Thanks to the Women for Africa Foundation's "Science by Women" programme, the CNIO welcomed two female African researchers for a period of six months.

Events

The following events were organised in the CNIO in 2017:

Two CNIO Frontiers Meetings (CMF), funded in large part by La Caixa Foundation: CNIO -"La Caixa" Frontiers Meeting: Primary and Secondary Brain Tumors from 19th to 22nd February 2017; and the CNIO -"La Caixa" Frontiers Meeting: Molecular Chaperones in Cancer from 2nd to 4th May, 2017.

In addition to the CFMs, six other events were held: CNIO Meeting – Cell and Gene Therapy Catapult, 30th March 2017; II CNIO-IBIMA Symposium: Prostate cancer and other genitourinary tumours from 20 to 21 April 2017; the CIBERER Meeting, 21st November 2017; New insights in Cancer Discovery

from 26th to 27th September 2017; ONCO Emergence Forum from 14th to 15th December 2017; and the Metabocancer Kick off Meeting on 14th December 2017.

In the same way, training courses and workshops were held, such as the Innovative Medicines Initiative Workshop on Oncology on 12nd January 2017; the 2nd EuroMAbNet: Antibody Validation Workshop on 26th May 2017; Advanced cell sorting course from 3rd to 4th September 2017; How to successfully perform & analyse a multicolor Flow Experiment Workshop from 7th to 8th September 2017; and the Workshop Featuring Leica TCS SP8 DIVE AND Leica DMI8 S from 14th to 16th November 2017.

Within the CNIO Distinguished Seminars programme, 19 internationally-recognised speakers were invited. Five of these seminars were sponsored by the Banco Sabadell Foundation. Additionally, CNIO scientists also organised 45 ad-hoc seminars at the CNIO in 2017.

The Women in Science and Engineering Office (WISE Office) organised nine conferences within the WISE Seminars (<http://www.cnio.es/es/women-science/events.asp>). The DEAN office, through the student and post-doctoral associations, also organised a series of seminars.

The CNIO also carried out educational events for the general public, such as guided visits. In 2017, secondary students, primary students, and the general public from both the research sector and from any other field were received in the CNIO's facilities. A total of 490 people participated.

It also participates in activities such as the European Researchers' Night on 29th September, which 240 people ranging in age from eight to 99 years old attended, as well as Science Week, which 95 people attended.

Coinciding with International Cancer Day, in collaboration with the AXA Foundation and Vital Signs, the CNIO organised a workshop in which Nobel Prize winner Professor Harald zur Hausen gave a talk. Later, there was a colloquium which brought together Dr Blasco (CNIO), Dr Nieto (Alicante Institute of Neurosciences), and Dr Garrido (Ramón y Cajal Hospital).



RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



Highlighted Activities

2017 has been a year in which the CNIO renewed its image. It adopted a new logo which incorporates the word “cancer.” This new image — elegant, clear, and in keeping with our relationship with ISCIII — is another way to transmit the CNIO’s values and mission.

In 2017, a new start-up company, Senolytic Therapeutics, was founded. It is based on the results of the Manuel Serrano Group in the field of senescence. Based on the results of the Nabil Djouder group, a patent has been licensed to the Stemtek Therapeutics Company for the development of compounds to treat hepatocellular carcinoma and other tumours. In 2017, the CNIO requested five new patents.

Income generated from intellectual property rights was in excess of €550,000 in 2017. This income includes both, income from patents as well as income from the commercialisation of scientific tools such as monoclonal antibodies, for example. A total of 52 inventors, nearly 15% of CNIO researchers, contributed to this achievement.

In 2017, Manuel Serrano of the Molecular Oncology Programme and Alfonso Valencia of the Structural Biology and Biocomputation Programme moved their laboratories to other institutions.

The Structural Biology programme incorporated three new groups. Oscar Llorca, an international leader in the field of electronic cryo-microscopy, joined as the new Programme Director. In addition, the Iván Plaza Menacho group, from the Structural Biology Laboratory of the University of Basel, Switzerland, and the Rafael Fernández Leiro group, from the MRC Laboratory of Molecular Biology in Cambridge, UK, joined the CNIO.

In 2017, the CNIO External Scientific Assessment Committee evaluated two research programmes: the Clinical Research Programme and the Cancer Genetics Programme. Likewise, Nabil Djouder was promoted from Junior Group Chief to Senior Group Chief.

2

RESEARCH AND INNOVATION ACTIVITY MANAGEMENT

- 2.1 Health Research and Development Strategy (2013-2016)
- 2.2 Biomedical Research Networking Centres (CIBER)
- 2.3 Thematic Networks for Networks for Cooperative Research in Health (RETICS)
- 2.4 Platforms to Support Research in Health Sciences and Technology
- 2.5 Health Research Institutes (IIS)
- 2.6 Foundations



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

- 3.1 Centres and Units
- 3.2 Intramural Research

3.1 CENTRES AND UNITS

HEALTH TECHNOLOGY ASSESSMENT AGENCY

The **Health Technology Assessment Agency** (AETS) addresses the SNS' needs for scientific information and evidence related to determining the policy on healthcare benefits and improving its quality and efficiency. In order to do so, the AETS offers objective assessments of the health, social, ethical, organisational, and economic impacts of health techniques, procedures, and interventions to provide a scientific basis for the decisions made by authorities and other healthcare agents.

Since 2012 part of the AETS' technical services have belonged to the "Spanish Network of Agencies for Assessing National Health System Technologies and Performance." The AETS' participation in activities for European cooperation on Health Technology Assessment through Joint Action 3 EUnetHTA was particularly noteworthy in 2017.

Scientific and Technical Activities

The Spanish Network of Agencies for Assessing National Health System Technologies and Performance's Work Plan:

Health Technology Evaluation Reports

- Analysis of the efficacy and safety of peripheral neurostimulation on the sphenopalatine ganglion for the treatment of refractory chronic cluster headaches.
- Efficacy and safety of endovascular treatment with varicose vein adhesive in the lower limbs.
- Effectiveness and safety of oocyte cryopreservation in oncological patients.
- Hyperbaric Oxygen Therapy and Complex Regional Pain Syndrome (CRPS).
- Hyperbaric Oxygen Therapy for other uses: Fibromyalgia.
- Irisbond Eye-tracker (ALS)

Participation in methodological development lines

- Participation of patients in Health Technology Evaluation: methodological manual
- Methodological framework on the relationships between the Spanish Health Technology Assessment Agency network and SNS Services with industry.

- Development of tools for helping with the shared decision making that arises from clinical practice guidelines recommendations.

Monitoring Studies

- Left atrial appendage closure device (Ocluser) in patients with nonvalvular atrial fibrillation.
- Biodegradable oesophageal stents for benign pathologies.

New and Emerging Health Technology Detection System. SUMMARY-New Technologies

Thirteen new and emerging technologies were identified and evaluated in 2017.

New Research Projects 2017

- "CHRODIS-PLUS: Implementing good practices for chronic diseases" Project. A joint initiative of European Member States funded by the 3rd Health Programme. Duration: September 2017 - August 2020. The AETS is the leader Work Package 4 "Integration on National Policies".
- REDISSEC Thematic Network for Cooperative Research "Healthcare Services for Chronic Diseases Research Network." ISCIII Hub.

FID Health Programme

In 2017, the FID Health Programme continued. It seeks to identify, evaluate, and select innovative proposals from healthcare administrations within the Public Procurement for Innovation framework to be funded by multi-regional FEDER funds. The ISCIII, through the AETS, provides support for conducting the programme's call by carrying out the scientific evaluation of the proposals. In the second call (2017), the Regions (Autonomous Communities) submitted a total of 11 proposals, eight of which received a favourable evaluation.

Training and consultation activities

The AETS participates in post-graduate academic activities, hosts rotations of healthcare professionals, and collaborates in the organisation and teaching activities carried out by the National School of Public Health, the National School of Occupational Medicine and ISCIII training plan.

It also collaborates with the University of Alcalá de Henares as part of the Master's Degree in Cosmetic Medicine, with the Central University of Barcelona as part of the Post-Graduate Diploma in Therapies for Ageing, and with the Max Weber Institute-University of Castilla-La Mancha as part of the Master's



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

Degree in Economic Evaluation.

Likewise, the AETS is a member of the EUnetHTA Executive Board and represents ISCIII on the SNS's Commission on Benefits, Insurance, and Funding and on the Committee for Designation of Centres, Services, and Reference Units (CSUR), on the Advisory Committee for Orthoprosthesis Benefits, on the Advisory Committee for Benefits with Dietary Products, and on the AEMPS' Medicinal Products Committee.

Highlighted publications

L.M. Sánchez-Gómez, M. Polo-deSantos, J.I. Rodríguez-Melcón, J.C. Angulo, S. Luengo-Matos. Braquiterapia de alta tasa de dosis como monoterapia en cáncer de próstata: una revisión sistemática sobre eficacia y seguridad. *Actas Urol Esp.* 2017; 41(2):71-81. <http://dx.doi.org/10.1016/j.acuro.2016.06.001>. PMID: 27496770.

Luis García-Olmos, Francisco Rodríguez-Salvanés, Maurice Batlle-Pérez, Río Aguilar-Torres, Carlos Porro-Fernández, Alfredo García-Cabello, Montserrat Carmona, Sergio Ruiz-Alonso, Sofía Garrido-Elustondo, Ángel Alberquilla, Luis María Sánchez-Gómez et al. Development and validation of a risk stratification model for prediction of disability and hospitalisation in patients with heart failure: a study protocol. *BMJ Open* 2017;7:e014840. doi:10.1136/bm-

jopen-2016-01484. PMID: 28600367.

García-Pérez L, Linertová R, Álvarez-de-la-Rosa M, Bayón JC, Imaz-Iglesia I, Ferrer-Rodríguez J, Serrano-Aguilar P. Cost-effectiveness of cell-free DNA in maternal blood testing for prenatal detection of trisomy 21, 18 and 13: a systematic review. *Eur J Health Econ* (2017). <https://doi.org/10.1007/s10198-017-0946-y>.

Ortega Maján MT, Júdez Legaristi D, Hernández Torres A. Improvement in Pensioners Quality of Life after Treatment with Mineral-Rich Medicinal Waters. *J Geriatr Med Gerontol* 2017, 3:025. DOI: 10.23937/2469-5858/1510025. ISSN:2469-5858.

Communications to Congresses

In 2017, 16 presentations were made at national and international congresses.



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

NATIONAL LIBRARY OF HEALTH SCIENCES

The National Library of Health Sciences (BNCS) was created as a National Centre of ISCIII on 2 August 1996 (RD 1893/1996), taking on the role of directing and coordinating all the Institute's libraries. Likewise, the BNCS offers its services to the National Health System (SNS in its Spanish acronym), providing documentary support and acting as a point of reference on a wide range of issues related to scientific information on health for all national and regional healthcare administration units. It is organised as follows:

Chamartín Campus (headquarters): offers bibliographical support for the ISCIII's teaching, scientific, and research activities, principally in the area of Public Health, Healthcare Administration and Management, Epidemiology, Occupational Health, and Health Education as well as the teaching activities of the National School of Public Health (ENS) and the National School of Occupational Medicine (ENMT).

Majadahonda Campus: provides documentation support and attends to consultations on matters of bibliographical, reference, or scientific information. This library's paper collection specialised on the thematic areas that the researchers on this campus work on, have been transferred to the Chamartín campus library due to remodelling work.

Initiatives for Dissemination of Spanish Scientific Information

Since its creation in 2001, the Spanish Virtual Health Library has belonged to the International Network of Virtual Health Libraries. This network currently has the participation of 30 countries in Latin America, Africa, and Asia. It comprises over 100 national, thematic, and institutional virtual libraries and is coordinated by BIREME (Latin American and Caribbean Center on Health Sciences Information). This year, the centre celebrated its 50th anniversary (<http://50anos.bireme.org/>).

It is important to note that in 2017 the number of SciELO Spain visits doubled with respect to 2016. It now receives more than 16 million annual visits (an average of 1,388,339 per month). Likewise, it has worked on adopting the XML JATS standard as a new model of publication and has subscribed to the "Sant Joan d'Alacant Declaration in Defence of Open Access to Scientific Publications by the Group of Editors of Spanish Journals on Health Sciences (GERECS)."

1.1- Virtual Health Library - Spain (<http://bvsalud.isciii.es>)

IBECS

Spanish Health Sciences Bibliographic Index
<http://ibecs.isciii.es>

227 indexed journals
168,209 articles (an increase of more than 10,480 records with respect to 2016)
28,400 links to full-text articles included in SciELO Spain

SciELO

Scientific Electronic Library Online
Collection of Spanish health sciences journals. Open access to journals, articles, and statistics. <http://scielo.isciii.es>

60 publications
Over 34,000 full-text articles (html and pdf)
Over 16 million visits and over 20.5 million pages downloaded (in both cases, duplicating 2016 figures)
The SciELO page accounts for 93.18% of the ISCIII's web traffic
Integrated into the Web of Science (WoS) through the SciELO Citation Index
Available on Google Scholar
Available in open-access directories: Hispana/DOAJ/OAISTER/ROAR/OpenDOAR

LIS-España

Health Information Finder

Health sites subject to quality control
2,361 entries in Information for Professionals
1,920 entries in Information for Citizens
The content is integrated into the LIS-Regional portal

DeCS

Health Sciences Descriptors

Spanish (Spain) translation of the trilingual (ES/EN/PT) biomedical term thesaurus created by BIREME based on the National Library of Medicine's MeSH
Translation of 474 new descriptors
Translation of 106 modified descriptors
Review of the translation of 1,147 already-existing descriptors

1.2 National Health Sciences Catalogue (CNCS)

CNCS

National Health Sciences Catalogue

140,000 bibliographic records from 287 libraries
Information downloaded from 19,194 journals
67,927 paper collections and 382,377 digital collections integrated
View online: <http://www.cncs.online/vufind/>

1.3 BNCS Social Networks

Channels

An Institutional Repository Twitter account was created @REPISALUDisciii
BNCS Twitter account (@BNCSisciii), 565 followers
SciELO Spain Twitter account (@scielospain), 4.9 thousand followers
BVS Spain Twitter account (@bvs_spain), 2.3 thousand followers
IMIENS Twitter account (@IMIENS_UNED), 777 followers



TECHNICAL AND SCIENTIFIC ACTIVITIES

- 3.1 Centres and Units
- 3.2 Intramural Research

Library Services

The BNCS provides access to ISCIII researchers, National School of Public Health and National School of Occupational Medicine students, and any user accredited as an SNS researcher, teacher, or health professional. In 2017, 2,960 users were assisted. The library manages bibliographic resources that comprise 40,648 publications, of which 36,531 are monographs, 2,591 are periodicals, and the rest are audiovisual materials. Of all the periodicals, 272 are subscription journals from the most important scientific publishers in the field of health sciences. In 2017, 964 publications were catalogued and 224 books were lent out. As part of the collaboration agreement between ISCIII and the CNIC and CNIO foundations, over 900 titles (journals, monograph series, and electronic books) can be jointly accessed online. Similarly, full-text books and electronic journals were accessed more than 74,000 times.

A total of 94,110 direct bibliographic searches in databases subscribed to by the BNCS, such as Web of Science (88%) or SCOPUS (9.7%), were made.

In 2017, the inter-library lending and document request services managed 7,895 requests. Of these, 4,469 were from ISCIII researchers. A total of 95.06% of these documents were obtained, with an average time for obtaining them of less than 24 hours. There were 3,194 requests from other Spanish academic and health system libraries. The material was provided in 85% of cases, with an average time for providing them of less than four hours.

Publishing Programme

Twenty-two titles were published: 14 monographic works and two periodical publications in electronic format, two educational pamphlets: one by the National Epidemiology Centre (CNE) in Spanish and English in both print and electronic format and another printed pamphlet by the Scientific Culture Unit. In addition, four new volumes of the "More than Health" collection were published.

Free access to all of the ISCIII's electronic publications from 2009 on is available online at <http://publicaciones.isciii.es/>. The portal has an alert system for registered users that has 2,398 subscribers.

Collaborations

The BioMed Central (BMC) publishing house is one of the most widely-recognised platforms for open access biomedical journals. Since 2005, ISCIII researchers have published regularly in BioMed Central journals. The ISCIII's association with this platform, signed in July 2015, streamlines and facilitates the publishing process for individual articles and helps reduce publishing costs, in addition to showing the ISCIII's support for the open access move-

ment. In 2017, 28 articles by the institution's researchers have benefited from this agreement. The most requested journals were BMC Public Health (five articles), BMC Medicine, Parasites & Vectors, and the Journal of Translational Medicine (three articles each). In total, articles have been requested from 17 different journals of the group, 16 of which belong to the BMC publishing house and one to SpringerOpen.

The ISCIII, through the BNCS, is working on the launch of its institutional repository (REPISALUD), along with the CNIC and CNIO foundations.

The REPISALUD content is structured around five communities: Research, Institutional, Teaching, Scientific Events, and Publishing Programme. Within these, subcommunities have been created which group together the centres and departments that belong to each of the institutions that participate in the repository. In 2017, informative sessions have been held at ISCIII to prepare for the launch of the repository and document deposit by the institution's researchers.

Training

The BNCS taught modules on scientific documentation in different diploma, expert, and Master's degree courses at the National School of Public Health, the National School of Occupational Medicine, UNED, and Madrid Region, amongst others. In addition, workshops were taught on PubMed and on health sciences bibliographic database searches for internal ISCIII staff.

Publications and Congresses

Primo-Peña, Elena. Management licenses in Repisalud. XVI Seminar for Centres for Environmental and Protected Natural Spaces Documentation. Oleiros, La Coruña, 27-29 September 2017.

Bojo Canales, Cristina. Adoption of the XML JATS standard in SciELO Spain. III International Workshops for Health Sciences Journals. Miguel Hernández University of Elche, 24-25 November 2017.

Primo-Peña, Elena. Institutional and thematic repositories in health. III Workshop on Information and Health, Department of Documentation, Complutense University of Madrid, 15 December 2017.

Bojo Canales, Cristina. The SciELO (Scientific Electronic Library Online) network: perspective following 20 years of operation. Hosp Domic. 2017; 1(4):211-20. Available at: DOI: <http://doi.org/10.22585/hospdomic.v1i4.31>



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

MUSEUM OF PUBLIC HEALTH AND HYGIENE

The Museum of Public Health and Hygiene, under the BNCS, is included in the Directory of Museums and Collections of Spain, the largest and most thorough database in the country promoted by the Ministry of Education, Culture, and Sport. In addition, following implementation of the Domus Comprehensive System of Museographic Documentation and Management developed by the Ministry, it belongs to the Digital Network of Spanish Museum Collections. This network includes a collective online catalogue, CER.ES (<http://ceres.mcu.es>), which brings together information and images from the museums that belong to it. Currently, it has 1,376 bibliographic documents catalogued. They may be viewed online through the BNCS Catalogue. In 2017, an information sheet on the bubonic plague medical panels, a reproduction of the original print of 'Der Doctor Schnabel von Rom,' was re-edited in Spanish and English. In 2017, 12 guided visits were given, two of which took place as part of Science Week. The other visits were for students from the ENS and groups of professionals, students, and people interested in the history of public health in Spain.

NATIONAL EPIDEMIOLOGY CENTRE

The mission of the National Epidemiology Centre (CNE) is centred on analysis of the state of public health in Spain, disease surveillance (the CNE manages the National Network for Epidemiological Surveillance-RENAVE), the impact of health policies on the population, the training of epidemiologists and specialists in preventative medicine and public health, research in public health, and Spain's contribution to European epidemiological surveillance for the European Centre for Disease Control (ECDC).

Scientific and Technical Activities

Within the scope of its healthcare competencies and under the tutelage of the MSCBS, the CNE collaborates on all activities, plans, and actions to control, prevent, and/or eradicate diseases. The areas of activity are focused on:

- 1) Chronic Diseases and Health Policy Impacts:** aimed at providing relevant information and performing research in the epidemiology of cancer and its determinants from a public health perspective focused on controlling and preventing this set of diseases. **Applied Epidemiology:** epidemiology of neurodegenerative diseases. Monitoring the impact of health

2017 Scientific Activity

National Research Projects	Competitive Calls Projects	International Research Projects	National Publications	International Publications
36	44	24	22	155

policies, ageing, disability, and the methods for assessing them. Registry of diseases caused by prions. Mental health epidemiology. Online update of mortality, analysis and inequality, and social determinants. Epidemiology of deaths due to external causes and analysis of disability and accident rates. **Analysis of the state of health:** epidemiology of cardiovascular and metabolic diseases and of its risk factors. Monitoring the impact of health policies, ageing, disability and the methods for assessing them.

2) Communicable Diseases: management of RENAVE. Contribution to the surveillance of communicable diseases in the EU. Participation in case surveillance networks for the ECDC, the WHO, and the EFSA and contact person in the EU for diseases under epidemiological surveillance. Programme to end tuberculosis (WHO). Development of the daily mortality monitoring system (MOMO). Monitoring of food-borne and zoonotic vaccine-preventable diseases. Management of surveillance systems involved in monitoring of flu activity and respiratory viruses. Analysis of surveillance information for flu control and prevention. Creation and launch of the Surveillance System for Healthcare-Associated Infections. Participation in the Strategic Plan for Antimicrobial Resistance Control. Support to the MSCBS on environmental health and dietary health. Monitoring of epidemiological surveillance of new diagnoses of hepatitis C virus infection included in the SNS' Strategic Plan for Approaching Hepatitis C. Surveillance of HIV and risk behaviours. Consulting for the CCAES on surveillance and control of communicable diseases.

3) Risk Behaviours and Socially-Vulnerable Populations: surveillance of alcohol and psychoactive substance consumption and assessment of policies for its control, in collaboration with the Spanish National Drug Strategy and the EMCDDA; evaluation of policies on early diagnosis of HIV, rapid tests and self-tests, in collaboration with the Spanish National AIDS Plan; evaluation of policies on social conduct and inequalities.

Epidemiology and Public Health Research

The main lines of research according to thematic area were: **1) Environmental Epidemiology and Cancer:** advance knowledge about the causes of cancer, mainly the environmental factors (non-hereditary) and their interaction with genetic determinants with a view to prevention. **2) Applied Epidemiology:** ageing and predictors of mortality and disability. Dementia, Parkinson, and prion diseases. Morbidity and mortality due to external causes. **3) Analysing the state of health:** impact of Law 28/2005, on Healthcare Measures Against Smoking. Addiction, obesity, and cardiovascular risk factors. Role of heavy metals in chronic diseases. **4) HIV/AIDS/STIs:** natural infection history of HIV (CoRIS and GEMES cohorts). Epidemiology and progression of HIV infection in immigrants. Diagnostic delay in HIV infection. Reproductive health of HIV+ women. Human papillomavirus epidemiology. Methodology of longitudinal cohort studies on HIV+ subjects. **5) Risk Behaviours and Socially-Vulnerable Populations:** project translating the experience of Spain and European countries in relation to policies to reduce the harm from substance use to some Eastern European countries, in collaboration with CHAFEA. Evaluation of social inequalities and the impact of different socio-economic determinants on mortality. **6) Communicable Diseases:** research applied in the public health field to provide evidence on related aspects such as natural history, the impact of risk factors on the development of disease in the population, and evaluation of intervention measures implemented in the community for the prevention of communicable diseases. Assessment of the effectiveness of the flu vaccine in Spain and Europe. Estimation of the disease burden of the flu. Development of methodology for assessing the severity of flu epidemics and pandemics.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

Highlighted publications

del Amo J, et al. Inequalities by educational level in response to combination antiretroviral treatment and survival in HIV-positive men and women in Europe. Socio-economic Inequalities and HIV Working Group for Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in Euro-Coord. *AIDS* 2017 14;31(2):253-262.

Alvaro-Meca A, Berenguer J, Díaz A, Micheloud D, Aldamiz-Echevarria T, Fanciulli C, et al. Stroke in HIV-infected individuals with and without HCV coinfection in Spain in the combination antiretroviral therapy era. *PLoS One*. 2017;12(6): e0179493. <https://doi.org/10.1371/journal.pone.0179493> FI (2016): 2,806. Q1. Ranking: 15/64. Categoría: MULTIDISCIPLINARY SCIENCES

Boix R, Cano R, Gallego P, Vallejo F, Fernández-Cuenca F, Noguer I and Larrauri A. Hepatitis C hospitalizations in Spain, 2004-2013: a retrospective epidemiological study. *BMC Health Serv Res* 2017 Jul 5; 17(1):461. DOI 10.1186/s12913-017-2410-

Gherasim A, Martínez-Baz I, Castilla J, Pozo F, Larrauri A, the cycEVA working group (2017) Effect of previous and current vaccination against influenza A(H1N1)pdm09, A(H3N2), and B during the post-pandemic period 2010-2016 in Spain. *PLoS ONE* 12(6): e0179160. <https://doi.org/10.1371/journal.pone.0179160>.

Velasco E, Gomez-Barroso D, Varela C, Diaz O, Cano R. Non-imported malaria in non-endemic countries: a review of cases in Spain. *Malar J*. 2017 16:260. DOI 10.1186/s12936-017-1915-8.

López-Perea N, Masa-Calles J, Torres de Mier MV, Fernández-García A, Echevarría JE, De Ory F, Martínez de Aragón MV. Shift within age-groups of mumps incidence, hospitalizations and severe complications in a highly vaccinated population. Spain, 1998–2014. *Vaccine*. Volume 35, Issue 34, 3 August 2017, Pages 4339-4345.

Gullón P, Varela C, Martínez EV, Gómez-Barroso D. Association between meteorological factors and hepatitis A in Spain 2010–2014. *Environment International* 2017 102 230–235.

Lope V, et al. GEICAM, the Spanish Breast Cancer Group. Physical activity and breast cancer risk by pathological subtype. *Gynecol Oncol*. 2017 Mar;144(3):577-585. doi: 10.1016/j.ygyno.2016.12.014. Epub 2017 Jan 3. PMID: 28057355. FI: 4.959. D1.

García-Pérez J, Morales-Piga A, Gómez-Barroso D, Tamayo-Uria I, Pardo Romaguera E, López-Abente G, Ramis R. Risk of bone tumors in children and residential proximity to industrial and urban areas: New findings from a case-control study. *Sci Total Environ*. 2017 Feb 1;579: 1333-1342. doi: 10.1016/j.scitotenv.2016.11.131. PMID:27916304. FI: 4.9. D1.

Regidor E, Vallejo F, Granados JAT, Viciano-Fernandez FJ, de la Fuente L, Barrio G. Authors' reply- Mortality decrease according to socioeconomic groups. *Lancet* 2017; 389:1795.

Sordo L, Barrio G, Bravo MJ, Indave BI, Degenhardt L, Wiessing L, Ferri M, Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ*. 2017; j1550

Galán I, Simón L, Boldo E, Ortiz C, Fernández-Cuenca R, Linares C, Medrano MJ, Pastor-Barriuso R. Changes in hospitalizations for chronic respiratory diseases after two successive smoking bans in Spain. *PLoS One*. 2017 May 24;12(5):e0177979.

Simón L, Pastor-Barriuso R, Boldo E, Fernández-Cuenca R, Ortiz C, Linares C, Medrano MJ, Galán I. Smoke-Free Legislation in Spain and Prematurity. *Pediatrics*. 2017;139. pii: e20162068.

Martino D, Pringsheim TM, Cavanna AE, Colosimo C, Hartmann A, Leckman JF, Luo S, Munchau A, Goetz CG, Stebbins GT, Martinez-Martin P; Members of the MDS Committee on Rating Scales Development. Systematic review of severity scales and screening instruments for tics: Critique and recommendations. *Mov Disord*. 2017; 32: 467-473.

García López FJ, Ruiz-Tovar M, Almazán-Isla J, Alcalde-Cabero E, Calero M, de Pedro-Cuesta J. Risk of transmission of sporadic Creutzfeldt-Jakob disease by surgical procedures: systematic reviews and quality of evidence. *Euro Surveill* 2017;22(43).

Training

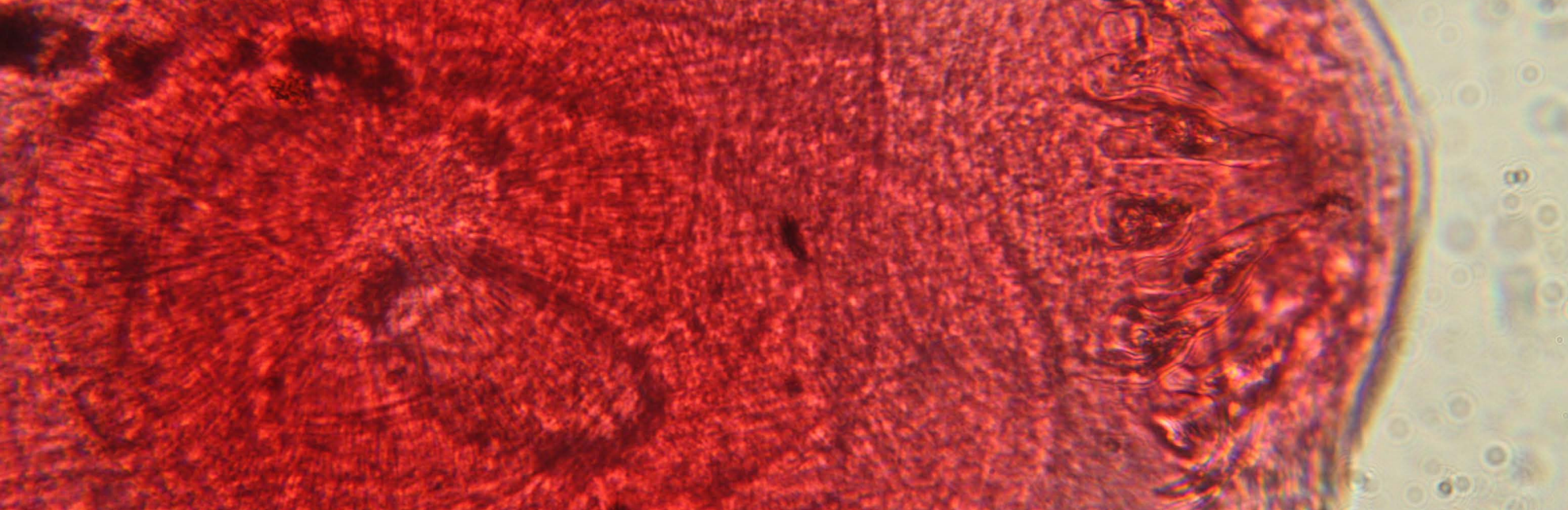
The CNE took part in 9 seminars, was involved in 23 teaching programmes, had 14 MIR rotations, hosted 14 training placements, directed 10 doctoral theses, and participated in 11 thesis committees. Theses read: 2.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

NATIONAL MICROBIOLOGY CENTRE

The National Microbiology Centre (CNM) has the specific mission of providing scientific and technical support to the General State Administration, the Regions, and the SNS for preventing, diagnosing, and treating infectious diseases.

The CNM started its activity in 2017 in a new building on the Majadahonda campus. The CNM has managed to group its different laboratories and units in this new location.

Highlighted Activities

The CNM alert system has been operating 24 hours per day, seven days a week for all of 2017. During this time, the Alert System intervened in all the health alerts activated by the Centre for Coordination of Alerts and Emergencies (CCAES) at the request of the Regions as well as on all occasions it was required to do so at the request of the Biological Alert Laboratory Network (RE-LAB). In this context, in 2017, work continued on analysis of the prevalence of Crimean-Congo Haemorrhagic fever in *Hyalomma* ticks in different regions. This work was started in 2016 following the report of the first indigenous case in Spain.

In the field of international outbreaks, in 2017, an analysis was performed based on the complete genome sequencing of serogroup W *Neisseria meningitidis* strains in the global context of the expansion of this serogroup on the international level.

Routine massive sequencing has been implemented in listeria, meningococcus, multidrug-resistant gonococcus, and carbapenemase-producing bacteria surveillance, following the time frames recommended by the ECDC.

Scientific and Technical Activities

The CNM operates 25 microbiology surveillance programmes for infections relevant to public health, which are revised and renewed annually. These programmes generate data that is very important to produce knowledge of the diseases surveilled, allowing for control and/or prevention measures to be developed by the health authorities.

The CNM received around 60,000 requests for diagnoses and/or reference through its sample management programme. It has performed over 100,000 tests in all of its activities for surveillance programmes, alerts, outbreaks, service portfolio, and contracts with institutions and businesses. In addition, more than 100,000 DNA sequences were carried out by the CNM's Genomics Unit.

Scientific Production

In 2017, the data generated from research projects being conducted as well as the diagnostics and surveillance programmes carried out by the various units of the CNM was used over 193 publications in national and international journals as well as in many presentations at scientific congresses and meetings. Some notable works published by the different Reference and Research Laboratories are the following:

Highlighted publications

Abad R, Medina V, Fariñas MDC, Martínez-Martínez L, Bambini S, Dari A, Medini D, Pizza M, Vázquez JA. "Potential impact of the 4CMenB vaccine on oropharyngeal carriage of *Neisseria meningitidis*". *J Infect.* 2017 Dec;75(6):511-520. doi: 10.1016/j.jinf.2017.09.021.

Cabrerizo M, García-Iñiguez JP, Munell F, Amado A, Madurga-Revilla P, Rodrigo C, Pérez S, Martínez-Sapiña A, Antón A, Suárez G, Rabella N, Del Campo V, Otero A, Masa-Calles J. First Cases of Severe Flaccid Paralysis Associated with Enterovirus D68 Infection in Spain, 2015-2016. *Pediatric Infect Dis J.* 2017.; 36: 1214-1216

Sánchez S, Llorente MT, Herrera-León L, Ramiro R, Nebreda S, Remacha MA, Herrera-León S. Mucus-Activatable Shiga Toxin Genotype stx2d in *Escherichia coli* O157:H7. *Emerg Infect Dis*. 2017 Aug;23(8):1431-1433. doi: 10.3201/eid2308.170570.

Martín-Vicente M, Medrano LM, Resino S, García-Sastre A, Martínez I (*). TRIM25 in the regulation of the antiviral innate immunity. *Front Immunol*. 2017; 8:1187. PMID: 29018447. DOI: 10.3389/fimmu.2017.01187.

Cortegano I, Rodríguez M, Martín I, Prado MC, Ruíz C, Hortigüela R, Alía M, Vilar M, Mira H, Cano E, Domínguez M, de Andrés B, Gaspar ML. Altered marginal zone and innate-like B cells in aged senescence-accelerated SAMP8 mice with defective IgG1 responses. *Cell Death Dis*. 2017; 8(8):e3000. doi: 10.1038/cddis.2017.351. PMID: 28817118.

Bernal-Martínez L, Gil H, Rivero-Menéndez O, Gago S, Cuenca-Estrella M, Mellado E, Alastruey-Izquierdo A. Development and validation of a High Resolution Melting Assay to detect azole resistance in *Aspergillus fumigatus*. *Antimicrob Agents Chemother*. 2017 Sep 11. pii: AAC.01083-17. doi: 10.1128/AAC.01083-17.

Martínez-Sernández V, Perteguer MJ, Mezo M, González-Warleta M, Gárate T, Valero MA, Ubeira FM. *Fasciola* spp: Mapping of the MF6 epitope and antigenic analysis of the MF6p/HDM family of heme-binding proteins. *PLoS One*. 2017 Nov 21;12(11):e0188520. doi: 10.1371/journal.pone.0188520. eCollection 2017.

Luque-Larena, Juan J.; Mougeot F, Arroyo B, Vidal MD, Rodríguez-Pastor R, Escudero R, Anda P, Lambin X. 2017. Irruptive mammal host populations shape tularemia epidemiology. *PLoS Pathog*. 16;13(11). ISSN 1553-7366.

Negredo A, de la Calle-Prieto F, Palencia-Herrejón E, et al. Autochthonous Crimean-Congo Hemorrhagic Fever in Spain. *N Engl J Med*. 2017 Jul 13;377(2):154-161. doi: 10.1056/NEJMoa1615162. PubMed PMID: 28700843

A.I. Vela, P. Villalon, J.A. Saez Nieto, G. Chacon, L. Dominguez, J.F. Fernandez-Garaiabal. Detection and characterization of *Streptococcus Pyogenes* from animal clinical specimens. *EMERG INFECT DIS* 2017; 23: 2011-2016.

Melero JA, Mas V, McLellan JS. Structural, antigenic and immunogenic features of respiratory syncytial virus glycoproteins relevant for vaccine development. *Vaccine*. 2017 Jan 11;35(3):461-468. doi: 10.1016/j.vaccine.2016.09.045.

Calonge E, Bermejo M, Diez-Fuertes F, Mangeot I, Gonzalez N, Coiras M, Jimenez Tormo L, García-Perez J, Dereuddre-Bosquet N, Le Grand R, Alcamí J. Different Expression of Interferon Stimulated Genes in Response to HIV-1 Infection in Dendritic Cells According to Their Maturation State. *J Virol*. 2017 Feb 1. pii: JVI.01379-16. doi: 10.1128/JVI.01379-16.

Participation in International Consortia

CNM professionals participate in a large number of international consortia, networks, and projects. For strategic reasons, participation in the 3rd Health Programme with the EMERGE Efficient Response to Highly Dangerous and Emerging Pathogens at EU Level project.

The CNM collaborates on the coordination of the ViroRed thematic network for the Ibero-American Programme of Science and Technology for Development (CYTED), which currently comprises laboratories from health institutes and universities in 14 Latin American countries, Portugal, and Spain.

In this field, ISCIII has the Leishmania Unit of the Parasitology Research and Reference Laboratory as a WHO Collaborating Laboratory as well as the Neisseria, Listeria, and Bordetella Unit of the Vaccine-Preventable Bacterial Disease Research and Reference Laboratory as an external Reference Laboratory for the SIREVA II Network of the Pan-American Health Organization (PAHO)/WHO.

Training

Numerous teaching and educational activities were carried out. In 2017, over 200 rotations of external personnel were received and national and international visitors took part in development and training activities.

The most significant activities in this regard are:

- Official Master's Degree in Microbiology for Public Health and Infectious Disease Research coordinated by the University of Alcalá de Henares, with over 60 professors from the CNM taking part.
- Master's Degree in Virology from the Complutense University of Madrid (UCM) in which, through a collaboration agreement between ISCIII and the UCM, 20 CNM researchers either gave lessons or coordinated courses.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

NATIONAL CENTRE OF TROPICAL MEDICINE

The National Centre of Tropical Medicine (CNMT) was created by an Order dated 27 December 2001 (published in the Official State Journal (B.O.E.) n°. 10 of 11 January 2002) with the objective of reinforcing care, research, and teaching on tropical diseases and establishing scientific and technical cooperation programmes with countries where these pathologies are present.

Highlighted Activities

Renewal of the Collaborative Tropical Disease Research Network. RD16CI-II/0003/0001. End: 2021

Beginning of studies to certify the elimination of onchocerciasis on Bioko island, Equatorial Guinea. The NTD Support Center, a Task Force for Global Health project, through the FCSAI and with funding from the Bill & Melinda Gates Foundation.

Start of an Action Plan for the Programme for Research and Cooperation on Neglected Tropical Diseases and other Tropical Diseases in Bahir Dar, Amhara State, Ethiopia.

Participation on the Organising and Scientific Committee of the X Congress of the Spanish Society of Tropical Medicine and International Health, held in October in Bilbao.

Scientific and Technical Activities

New Research Projects and Actions for International Cooperation on Development:

- Verification of the interruption of onchocerciasis transmission on Bioko island, Equatorial Guinea, funded by the NTD Task Force through the FCSAI Foundation. The CNMT participates as PI.
- Coordination of the Collaborative Tropical Disease Research Network (RICET): Programme for the Prevention and Control of High-Impact Imported, Emerging, or Re-emerging Tropical Diseases RD12/0018/0001

Highlighted publications

Pérez-Molina JA, López-Polín A, Treviño B, Molina I, Benito A, López-Vélez R; +Redivi Study Group. 6-year review of +Redivi: a prospective registry of imported infectious diseases in Spain. *J Travel Med.* 2017 Sep 1;24(5). doi: 10.1093/jtm/tax035. PubMed PMID: 28931128.

Ncogo P, Romay-Barja M, Benito A, Herrador Z. Prevalence of anemia and associated factors in children living in urban and rural settings from Bata District, Equatorial Guinea, 2013. *PLoS One.* 2017 May 3;12(5):e0176613. doi:10.1371/journal.pone.0176613. eCollection 2017. PubMed PMID: 28467452; PubMed Central PMCID: PMC5415132.

Gómez-Barroso D, B, Aparicio P, Benito A. Spatial clustering and risk factors of malaria infections in Bata district, Equatorial Guinea. *Malar J.* 2017 Apr 2;16(1):146. doi:10.1186/s12936-017-1794-z. PubMed PMID: 28403879; PubMed Central PMCID: PMC5389164.

Herrador Z, Muro A, Benito A. Mediterranean spotted fever in Spain, 1997-2014: Epidemiological situation based on hospitalization records. *PLoS One.* 2017 Mar 29;12(3):e0174745. doi: 10.1371/journal.pone.0174745. eCollection 2017. PubMed PMID: 28355307; PubMed Central PMCID: PMC5371374.

Berzosa P, Valladares B, Riloha M, Benito A. Profile of molecular mutations in *pfdhfr*, *pfdhps*, *pfmdr1*, and *pfcr1* genes of *Plasmodium falciparum* related to resistance to different anti-malarial drugs in the Bata District (Equatorial Guinea). *Malar J.* 2017 Jan 13;16(1):28. doi: 10.1186/s12936-016-1672-0. PubMed PMID: 28086777; PubMed Central PMCID: PMC5237300.

Alvarez P, Benito A, Ramos JT, Holguín Á. Evaluation of four commercial virological assays for early infant HIV-1 diagnosis using dried blood specimens. *Pediatr Res.* 2017 Jan;81(1-1):80-87. doi: 10.1038/pr.2016.183. Epub 2016 Sep 21. PubMed PMID: 27653084.

Navarro M, Löscher T, Albajar-Viñas P, Pritsch M. Cross-sectional, descriptive study of Chagas disease among citizens of Bolivian origin living in Munich, Germany. *BMJ Open.* 2017 Jan 16;7(1):e013960. doi: 10.1136/bmjopen-2016-013960.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



Training

Doctoral Theses:

- Lancha de la Cruz, María de los Reyes. Thesis Director: María Teresa Blasco Hernández/Juana Cristina Francisco del Rey. “Factors that Influence the Reproductive Healthcare of Women in El Salvador” Doctoral Thesis. University of Alcalá de Henares. Defended on 13 July 2017. “Outstanding, Cum Laude”.
- María Romay Barja. Knowledge, Attitudes, and Practices on Malaria in Equatorial Guinea. Directors: Agustín Benito Llanes and Patricia Marín García, Madrid. Presented at the Dept. of Medicine and Surgery, Psychology, Preventative Medicine, Public Health, Immunology, Medical Microbiology, Nursing, and Oral Medicine of the King Juan Carlos University, 2017.

NATIONAL ENVIRONMENTAL HEALTH CENTRE

The National Environmental Health Centre (CNSA) contributes to protecting the health of the Spanish population by evaluating its exposure to environmental pollution. The CNSA's laboratories operate under a quality management system and are accredited according to the UNE-EN ISO/IEC 17025 standard by the National Accreditation Entity (ENAC) for 156 tests.

Highlighted Activities

- Broadening of the competences of the National Reference Laboratory on Air Quality (LNRCA) according to Royal Decree 39/2017, of 27 January, modifying Royal Decree 102/2011, of 28 January, regarding improvements in air quality. (Directive 2015/1480/EC).
- Steering committee for the European Project HBM4EU: Development of the European Initiative on Human Biomonitorisation. H2020 Programme. Coordination of the Spanish Hub.
- CNSA Scientific Workshop “Monitoring the Environment and Measuring Exposure: We Take Care of your Health”, on the occasion of the celebrations of the ISCIII's 30th anniversary. Majadahonda, 2 March 2017.
- Meeting of the steering committee for the HBM4EU European Project, Majadahonda, 4-5 May 2017.
- I Scientific and Technical Workshop for the founding of the National Human Biomonitoring Hub. 1 June 2017.
- First national map of the active population's exposure levels to perfluorode contaminants.
- European Week of Human Biomonitoring – Berlin, 4-8 September 2017. Presidency, coordination, and organisation of sessions regarding the structure and establishment of the European Quality Guarantee Programme for human biomonitoring studies.
- Start of national BEA study: Biomonitoring in Adolescents, in coordination with the Ministry of Agriculture and Fisheries, Food, and Environment (MAPAMA)



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



Scientific and Technical Activities

More than 150,000 analyses and more than 170 toxicity bioassays were performed. Creation of 100 reports for the European Food Safety Authority (EFSA) as experts in active substance and phytosanitary product risk assessment.

As the **National Air Quality Reference Laboratory**, organization of three cross-comparison exercises with 18 “in situ” air quality networks from regions and local entities for sulphur dioxide and carbon monoxide. Creation of technical documentation and supervision of five air quality monitoring networks and one test laboratory, according to RD 39/2017.

As the **Associated Laboratory of the Spanish Meteorology Centre and custodian of the National Ozone Standard**, a calibration of 29 ozone transfer standards.

Participation on the Board of Directors of both the National Radiation Protection R&D Platform (PEPRI) and a COST EMF-MED Action group, a European network for cooperation on research and technology on the beneficial biological effects of electromagnetic fields.

Scientific and technical support and consulting for the Command Post during the 2017 CANTABRIA exercise. Military Emergencies Unit (UME) - Ministry of Defence.

Fundraising

The following management assignments remained active:

ISCIII-National Meteorological Agency (AEMET), “Analysis of samples from the EMEP/VAG/CAMP network, dedicated to surveillance of background pollution and support for management of the network’s quality”, ISCIII-MAPAMA: “Research on the presence and surveillance of persistent organic pollution and other substances in humans”. and ISCIII-MAPAMA “Improvement of the quality of the data from the Spanish networks for air quality”, ISCIII-INIA: “Scientific testing and evaluation of the area of toxicology, metabolism, and risk evaluation of active substance workers”, ISCIII-MSCBS: “Evaluation of risk to human health of products with phytosanitary activity”, 400 collaboration agreements with different public and private entities for dosimetric control.

Signing of nine new collaboration agreements for air quality control.

European Projects: HBM4EU and ICARUS-H2020 (Air pollution) and BRIDGE-Health (EC 3rd Health Programme).

National Projects: TAVS-CM: “Advanced technology in health surveillance” of the DGU-CAM. AESI 2016, the creation of the “National Centre for the Coordination of Biosurveillance Studies on the Spanish Population”, and AESI 2016 “Evaluation of the Toxicological Role of PAHs associated with PM10 using zebra fish embryos”.

Alfonso X el Sabio University: “Use of Embryos for Toxicological Evaluation: Pedagogical Impact”, and “Development of a System of Measurement for the Dielectric Characterisation of Organisms in Toxicological Trials”. Obtaining of a contract for a research technician in ISCIII from the Youth Employment Operational Programme of the Community of Madrid (YEI-POEJ).

Participation in Standardisation and Institutional Representation Committees

Presidency of the AEN/CTN 77 “Environment” Technical Standardisation Committee, presidency and membership in the AEN/CTN 77/SC 02 “Air” Subcommittee, membership in the AEN/CTN 77/SC 01 “Water” Subcommittee, and membership in the AEN/CTN 215 “Electromagnetic Fields” committee, membership in the AEN/CTN 77/SC 05 “Waste” Subcommittee. Participation in WGs 21, 34, and 42 of CEN/TC 264 “Air Quality”.

Membership in the Quality and Treatment Commission of the Spanish Association of Water Supply and Sanitation (AEAS) and Work Group III: Water Quality of the Climate Change and Health Observatory.

Participation in the “Analysis Methods” work group on the implementation of RD 314/2016, on radioactive substances in water intended for human consumption.

Participation in WG2: Harmonization of Individual Monitoring in Europe and WG3: Environmental Radiation Monitoring. Participation in the European SHAMISEN Project.

Highlighted publications

Bartolomé, et al.: “Perfluorinated alkyl substances in Spanish adults: Geographical distribution and determinants of exposure”, *Sci. Total Environ.* 2017 doi: 10.1016/j.scitotenv.2017.06.031.

Schwedler, G., et al.: “Human biomonitoring pilot study DEMOCOPHES in Germany: Contribution to a harmonized European approach”, *Int. J. Hyg. Environ. Health*, 2017. doi: 10.1016/j.ijheh.2017.01.012.

Ramos, J.J., et al.: “Organochlorinated pesticides levels in a representative sample of the Spanish adult population: The Bioambient.es Project”, *Int. J. Hyg. Environ. Health*, 2017. doi: 10.2016/j.ijheh.2016.10.005.

Cullen, E., et al.: “Phthalate exposure in Ireland: Results of the DEMOCOPHES Human Biomonitoring study”. *Int. J. Environ. Res. Public Health*, 2017. doi:10.3390/ijerph14121456.

Ganzleben, C., et al.: “Human biomonitoring as a tool to support chemicals regulation in the European Union”. *Int. J. Hyg. Environ. Health*, 2017. <http://dx.doi.org/10.1016/j.ijheh>.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

European reports:

- Criteria for prioritization of biomarkers, matrices and analytical methods (2017).
- Prioritized list of biomarkers, matrices and analytical methods for the 1st HBM4EU round of substances (2017).
- Database of candidate laboratories for the analysis, development and support for the Quality Assurance program of 1st HBM4EU round of substances (2017).
- The Quality Assurance/Quality Control Scheme for the European HBM platform (2017-2021)

Training

Co-direction of the Environmental Health module in the Master's in Public Health degree at the ENS.

Teaching and advising in Military Emergency Unit practical schools, Ministry of Defence, 13-17 of November.

Organising and teaching of internal and external seminars, teaching in six courses (four Master's courses) organised by various Spanish universities and the ENS.

Tutoring of placements under the Ramón y Cajal programme for researchers of the University of Granada.

Co-Direction of end-of-degree projects (TFG), end-of-Master's projects (TFM), and tutoring of external internships in collaboration with the Complutense University of Madrid and the Rey Juan Carlos University. Mentoring of internships for Specialised Technicians in Environmental Health and Chemistry.

RESEARCH INSTITUTE FOR RARE DISEASES

The objective of the Research Institute for Rare Diseases (IIER) is to promote and carry out basic and clinical research, training and support for health models, and innovation in healthcare for rare diseases.

Scientific and Technical Activities

Biobank

The National Rare Disease Biobank (BioNER) continues its activity at the heart of the ISCIII's Biobank Platform and the European Eurobiobank and RD-CONNECT networks. In 2017, 285 new donors were recorded.

Genetic Diagnosis Services

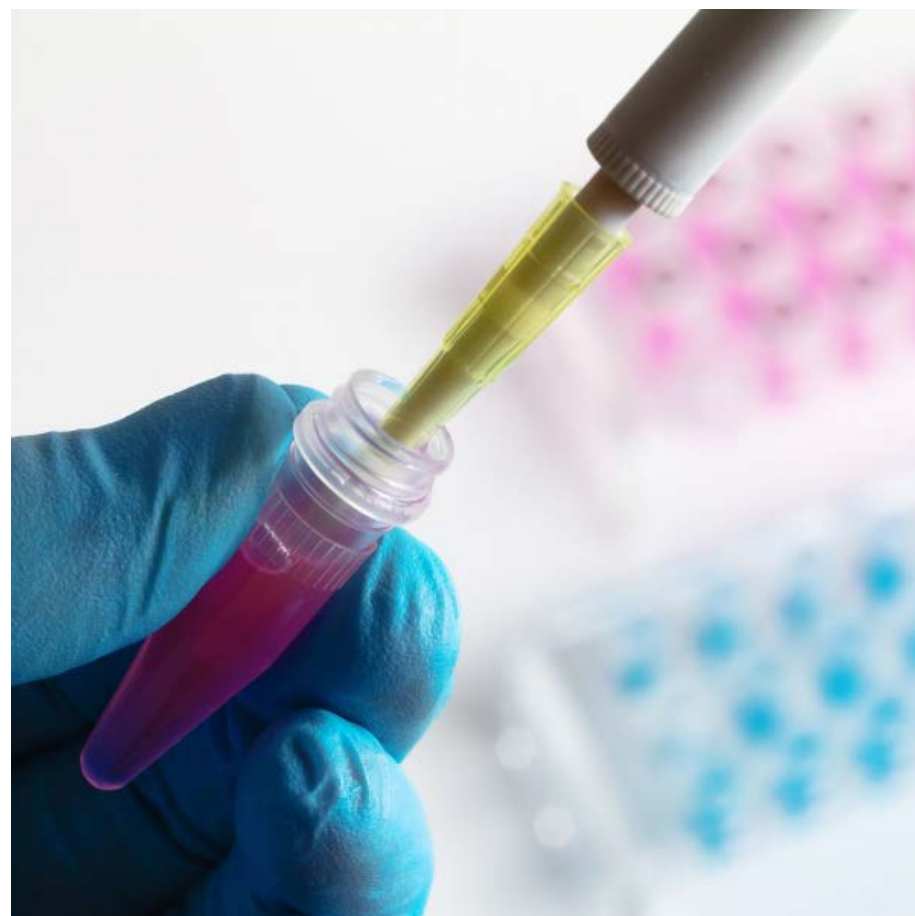
The genetic diagnosis unit is the only Spanish laboratory accredited by National Accreditation Entity (ENAC), according to the ISO15189 quality standard, for identifying genetic abnormalities in retinoblastoma. It diagnoses rare childhood tumours and alpha-1 antitrypsin deficiency. It is also responsible for genetic diagnoses for the rare undiagnosed disease programme and for BioNER. Over the course of this year, 3,425 tests were carried out on 386 cases. In addition, it has included another 30 cases of rare tumours, analysing 60 gene panels.

Patient and Organisation Consultation System

A certain increase has been noted in the number of consultations received in 2017. A total of 784 consultations were received, of which 138 were on issues related to rare diseases and the remaining 646 were related to toxic oil syndrome.

Lines of Research in Rare Diseases

The IIER conducts basic and translational research in the field of rare diseases, toxic oil syndrome, and autism spectrum disorder (ASD). The main lines of research are: 1) the role of abnormalities in the innate immune system in rare diseases; 2) the study of rare paediatric tumours: genetic abnormalities and cellular therapy; 3) gene and cellular therapy in congenital muscular dystrophy and rare tumours; 4) the involvement of microRNA in rare disease development and their role as biomarkers; 5) the application of new genetic analysis technology to diagnosing rare diseases; 6) the epidemiology of rare diseases;



7) risk factors and the prevention of congenital anomalies, work carried out in collaboration with the CIAC (see this centre's section in the annual report); 8) collaboration on CIBERer-ISCIII research activities and the ISCIII's Biobank platform; 9) in the field of translational research, participation in different projects on quality of life and economic impact of patients with lupus erythematosus as well as the development of clinical practice guidelines on Fabry disease; 10) development of three-dimensional cultures (organoids) in order to model rare diseases that affect the liver, and 11) identification of disease-modifying genes in rare pulmonary diseases.

Special Programmes

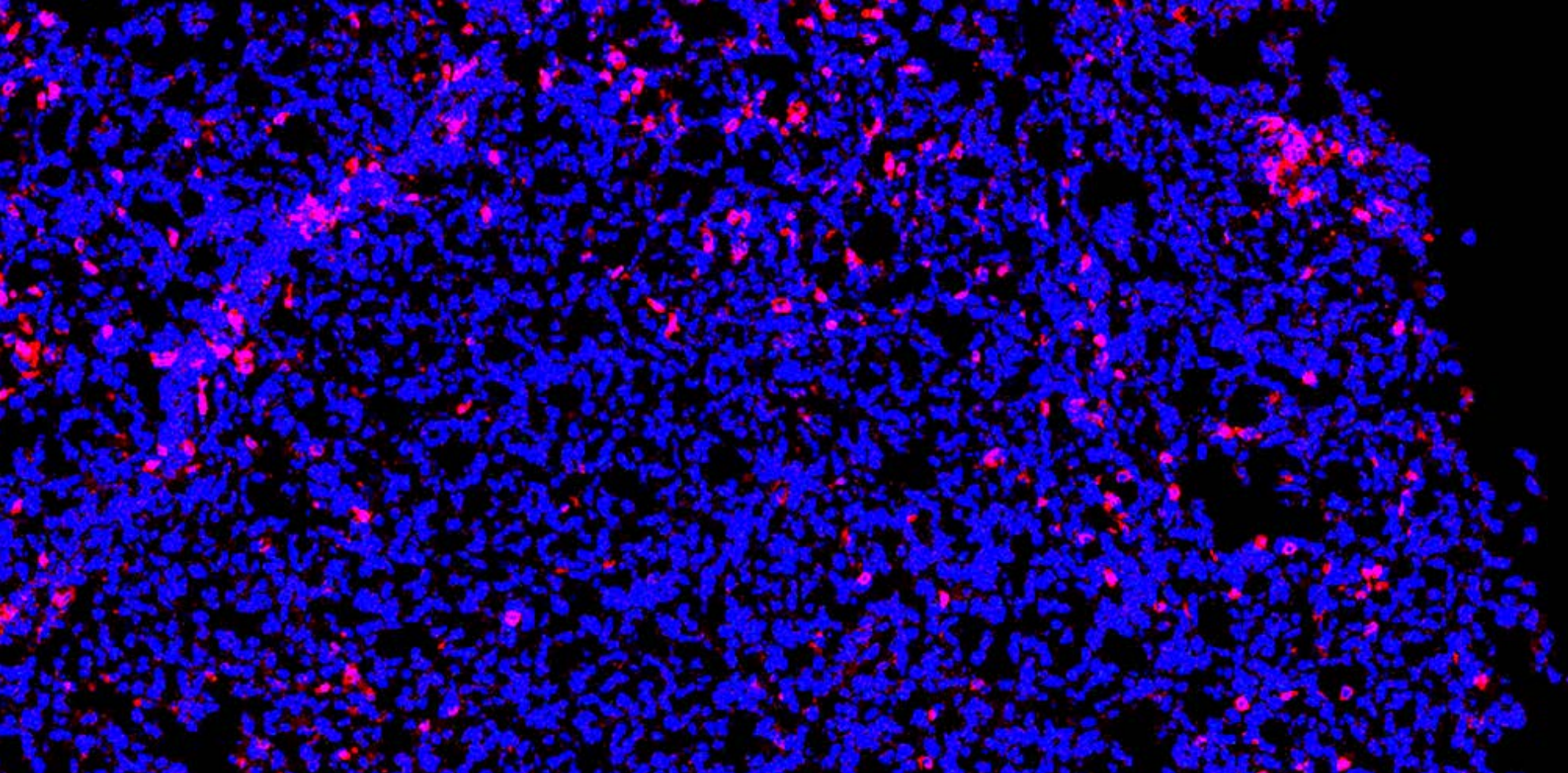
The IIER operates the following programmes: 1) monitoring the toxic oil syndrome cohort in a total of 14,696 cases, identifying 260 deaths in 2017; 2) collaboration on the development of a population-based screening programme for the early detection of autism spectrum disorders (ASDs) in Salamanca

3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

and Zamora provinces, in collaboration with the University of Salamanca, with over 20,000 children screened since its beginnings and contributions made to the validation process of the new MCHAT-R screening tool; 3) at the Cellular Biotechnology unit, once participation in a Phase 1 Clinical Trial (EudraCT: 2008-000364-16; clinicaltrial.gov number: NCT01844661) was complete, it proceeded with analysis of samples from the study; 4) direction and coordination of the European project on ASDs in the European Union.

The Rare Undiagnosed Disease Programme - SpainUDP

The IIER, which started this programme in 2011, collaborates with the Undiagnosed Diseases Network International. The network, created in 2015, is implementing communication systems for complex cases and opening lines of collaboration amongst groups. The IIER has a case registration system and a process for analysing them. It collaborates with the Puerta de Hierro University Hospital on those cases that require specific studies on the clinical phenotype. This programme contributes not only to providing diagnostic services but also to research. From the year of its creation to the end of 2017, Spain UDP admitted a total of 135 cases, of which 66 were incorporated in 2017, whereas 19 left the programme for various reasons. Throughout this year, 11 cases were diagnosed and the genomic study in another two cases ended without finding candidate genomic variations that could explain the patient's disease.

National Rare Diseases Registry

In 2017, work on the development of the National Rare Disease Registry (ReeR) continued, participating in the meetings of the MSCBS working groups aimed at creating standardisation and data validation processes. Furthermore, the Spanish Rare Diseases Registries Research Network (SpainRDR) continues its work on patient registration. In 2017, 498 patient registration requests were received. Of these, 284 were processed and 189 cases were awaiting codification of their disease. In addition, developments in four new patient registries were finalised.

Consultation and Dissemination Activities

The IIER, through its Director, belongs to the Advisory Committee for the Rare Disease Registry Platform of the European Commission's Joint Research Centre in Ispra, Italy. It is also the president of the International Conference on Rare Diseases and Orphan Drugs. On her part, Dr Eva Bermejo, IIER scientist, is the current Chair of the Executive Board of the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR).

Highlighted publications

Cidre-Aranaz F. et al. EWS-FLI1-mediated suppression of the RAS-antagonist Sprouty 1 (SPRY1) confers aggressiveness to Ewing sarcoma. *Oncogene* 2017;36(6):766-776. IF: 7.519, PMID: 27375017

Katschnig A.M. et al. EWS-FLI1 perturbs MRTFB/YAP-1/TEAD target gene regulation inhibiting cytoskeletal auto-regulatory feedback in Ewing sarcoma. *Oncogene* IF: 7.519, PMID: 28671673

Berdasco M. et al. DNA Methylomes Reveal Biological Networks Involved in Human Eye Development, Functions and Associated Disorders. *Sci Rep.* 2017;7(1):11762. IF: 4.259, PMID: 28924151

Mutz C.N. et al., Banerji V., Kovar H. EWS-FLI1 confers exquisite sensitivity to NAMPT inhibition in Ewing sarcoma cells. *Oncotarget* 2017;8(15):24679-24693. IF: 5.168, PMID: 28160567

Schwentner R. et al. The role of miR-17-92 in the miRegulatory landscape of Ewing sarcoma *Oncotarget* 2017;8(7):10980-10993. IF: 5.168. PMID: 28030800

Huertas-Martinez J., et al. DNA methylation profiling identifies PTRF/Cavin-1 as a novel tumor suppressor in Ewing sarcoma when co-expressed with Caveolin-1. *Cancer Letter* 2017; 386:196-207 IF: 6.375. PMID 27894957

Ruiz-Pinto S. et al. Exome array analysis identifies ETFB as a novel susceptibility gene for anthracycline-induced cardiotoxicity in cancer patients. *Breast Cancer Res Treat.* 2017; IF: 3.626, PMID: 28913729

He T. et al. High-throughput RNAi screen in Ewing sarcoma cells identifies Leucine rich repeats and WD repeat Domain containing 1 (LRWD1) as a regulator of EWS-FLI1 driven cell viability. *Gene* 2017; 596:137-146. IF: 2.415. PMID 27760381

Pérez de Castro I. et al. Editorial: Aurora Kinases: Classical Mitotic Roles, Non-Canonical Functions and Translational Views. *Front. Oncol.* 2017; 7:48. IF: 4,66 PMID: 28382277

Matamala N. et al. Characterization of novel missense variants of SERPINA1 gene causing alpha-1 antitrypsin deficiency. *Am J Respir Cell Mol Biol.* 2017; Dec 12. IF: 4.10. PMID: 29232161

Matamala N. et al. Identification of Novel Short C-Terminal Transcripts of Human SERPINA1 Gene. *PLoS One.* 2017; Jan 20;12(1):e0170533. IF: 3.057. PMID: 28107454

Lara B. et al. Spanish Registry of Patients With Alpha-1 Antitrypsin Deficiency: Database Evaluation and Population Analysis. *Arch Bronconeumol.* 2017;Jan;53(1):13-18. IF: 2,979. PMID: 27323654

Sernadela P. et al. Linked Registries: Connecting Rare Diseases Patient Registries through a Semantic Web Layer. *Biomed Res Int.* 2017;8327980. Epub 2017 Oct 29. IF 2,476 PMID:29214177

Sánchez-Díaz. et al. Monitoring Huntington's Disease Mortality across a 30-Year Period: Geographic and Temporal Patterns 2017; *Neuroepidemiology*, 47 (3-4), pp. 155-163. IF 2,886 PMID: 27883994

Rincón E. et al. Mesenchymal stem cell carriers enhance antitumor efficacy of oncolytic denoviruses in an immunocompetent mouse model. *Oncotarget.* 2017;Jul 11;8(28):45415-45431. IF: 6,35 PMID: 28525366

Macia A. et al. Engineered LINE-1 retrotransposition in nondividing human neurons. *Genome Res.* 2017;Mar; 27(3):335-348 IF: 11,35 PMID: 27965292

Moreno R. et al Human Menstrual Blood-Derived Mesenchymal Stem Cells as Potential Cell Carriers for Oncolytic Adenovirus. *Stem Cells Int.* 2017;2017:3615729. IF: 3,54 PMID: 28781596

Almazán-Moga A. et al. Hedgehog Pathway Inhibition Hampers Sphere and Holoclone Formation in Rhabdomyosarcoma. *Stem Cells Int.* 2017;7507380. IF: 3,54 PMID: 28243259

Training

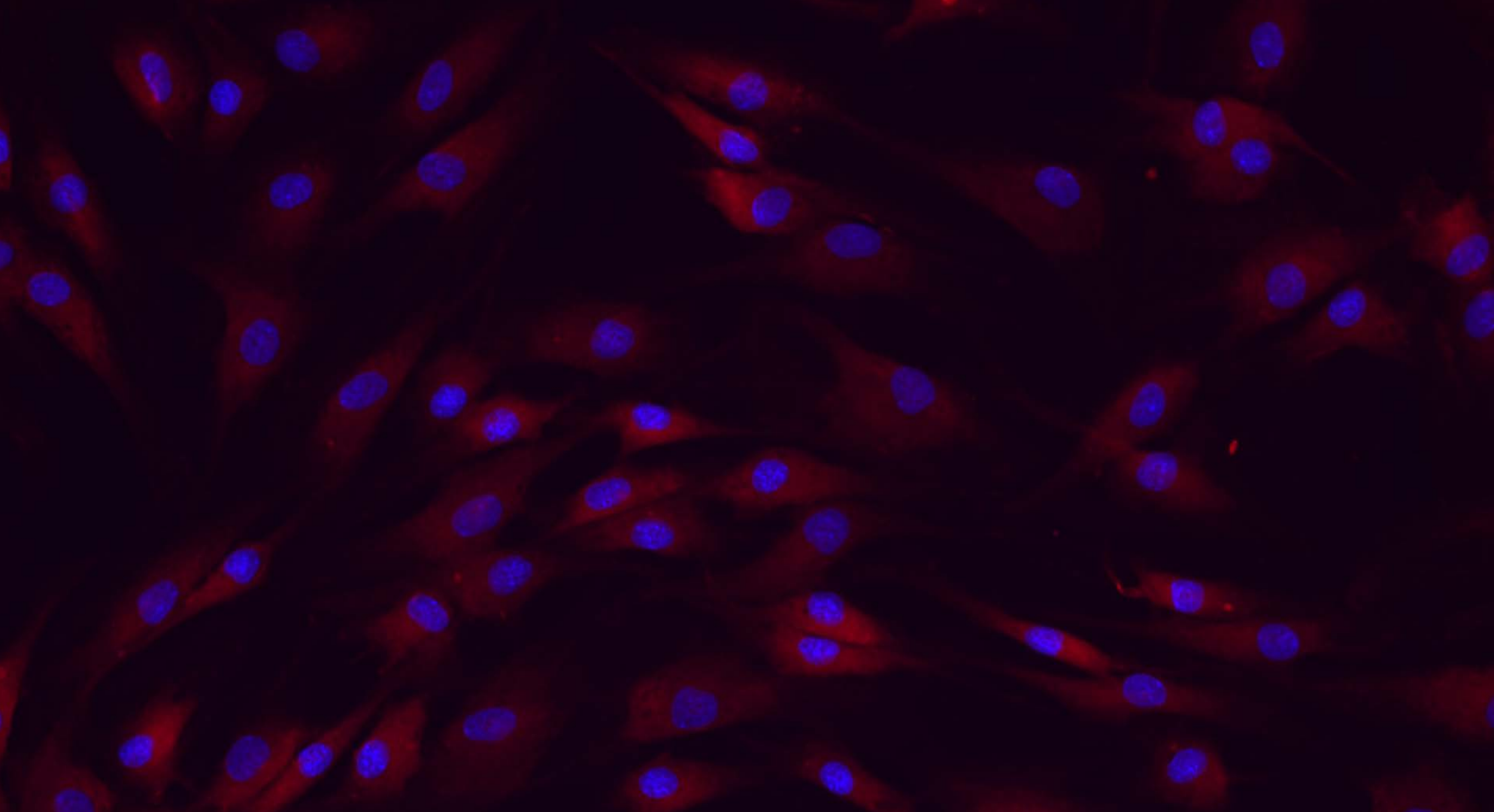
The IIER contributes to post-graduate training for professionals in the field of rare diseases and autism in collaboration with universities and interest groups.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

- 3.1 Centres and Units
- 3.2 Intramural Research

RESEARCH CENTRE ON CONGENITAL ANOMALIES

ISCIII's Research Centre on Congenital Abnormalities (CIAC) carries out its activity on the Spanish Collaborative Study of Congenital Deformations (ECEMC) (scientific group of the ASEREMAC-Spanish Association for the Registry and Study of Congenital Deformations), within the framework of the agreement established with the ISCIII, under the technical coordination of the IIER and the supervision of the Sub-Directorate General of Applied Services, Training, and Research (SGSAFI).

The ECEMC is a clinical-epidemiological research programme on congenital defects. It has a multidisciplinary and translational approach and is structured as a thematic network for cooperative research. It has a clinical network that includes more than 400 physicians (mainly paediatricians) throughout Spain. It is structured into three sections: Epidemiology and Clinical Genetics, High-Resolution and Molecular Cytogenetics, and Clinical Teratology. It carries out its activity in three lines of research: (a) epidemiological surveillance of congenital defects in the ECEMC and analysis of associated variables and factors; (b) clinical study on children with congenital defects in the ECEMC; and (c) epidemiological analysis of teratogens.

The ECEMC has two information services on teratogens: one for medical professionals (SITTE - Telephone Information Service on Teratogens) and another for the general public (SITE - Telephone Information Service for Pregnant Women).

Regarding its participation in research networks, the group has been part of the Rare Disease Biomedical Research Networking Centre (CIBERER) since its foundation in 2006. It is also part of following international networks:

- IICBDSR (International Clearinghouse for Birth Defects Surveillance and Research www.icbdsr.org),
- EUROCAT (European Surveillance of Congenital Anomalies www.eurocat-network.eu), and
- ENTIS (European Network of Teratology Information Services www.entis-org.eu).

Highlighted Activities

- Maintains the “Clinical Network of the ECEMC (Spanish Collaborative Study of Congenital Deformations),” comprising more than 400 physicians all over.

- Dysmorphological and clinical evaluation of 818 newborn babies and fetuses with congenital defects (CD) in Spain.
- Cytogenetic study (high resolution and molecular): 205 studies (ECEMC scope).
- Handles SITTE consultations on risks in prenatal development: 833 queries from physicians and 2,534 consultations from the general public.
- Epidemiological surveillance of CDs in Spain (ECEMC scope); European surveillance in the EUROCAT scope (www.eurocat-network.eu), and global epidemiological surveillance of CDs in the ICBDSR scope (www.icbdsr.org).
- Has participated (co-authorship of a chapter) in the book: “Rare Diseases Epidemiology: Update and Overview”. Second edition. Posada M, Taruscio D, Groft SC. *Advances in Experimental Medicine and Biology* 1031. Ed. Springer. Madrid, 2016. pp. 16-27 (ISBN 978-3-319-67144-4).
- Participates in the following projects:
 - “Collaborative Project on the Frequency of Hypospadias” international project.
 - “Collaborative Projects on the Mortality/Survival of Selected Non-Cardiac Defects” (17 subprojects),
 - “Global Epidemiology of Gastroschisis” international project of the ICBDSR.
- Chairs the ICBDSR Executive Committee.
- Participates in the activities of the Joint Research Centre-EUROCAT.
- Participates in the National Human Biomonitoring Hub of ISCIII’s CNSA.
- Participates in the “Spanish Agency of Medicines and Medical Devices (AEMPS) Experts Network”.
- Participates in international and national scientific, technical, and advisory committees.
- Participated in the organisation of the third World Birth Defects Day (WBDD) (3 March 2017) and coordinated in 2017 the fourth WBDD to be held in 2018.
- Participated in the organisation of the “44th Annual Meeting of the International Clearinghouse for Birth Defects Surveillance and Research, and Scientific Session on Zika”, in Austin (Texas, USA), 13-15 November 2017.
- Organised of the “40th Annual Meeting of the ECEMC” and the “CD Research Update Course”. Zumárraga (Guipúzcoa), 19-21 October

2017 [2.2 Community of Madrid-SNS CFCPS Credits. File 07-AFOC-03052.8/2017].

- Participated in five international and seven national congresses and scientific meetings.

Training

- Teaching in the “Master’s Degree in Pharmacoepidemiology and Pharmacovigilance”. School of Medicine. University of Alcalá de Henares.
- Participation as lecturers for continuing education activities on seven occasions.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

HEALTHCARE RESEARCH UNIT - INVESTÉN-ISCIII

The Healthcare Research Unit (Investén-ISCIII) has worked for years on promoting research in nursing care and other disciplines related to this field. Its resources are public and available for all National Health System (SNS) professionals interested in care research. The unit's goal is to develop a national strategy to promote and coordinate multidisciplinary and translational research in health care, strengthening its integration into everyday clinical practice, with the goal of ensuring that health care is of the best quality and based on valid and trustworthy research results. The unit is organised into five areas: 1) Strategic Planning, 2) Training, 3) Consultancy, 4) Transfer and Use of Results, and 5) Research and Innovation in Care. Furthermore, it has collaboration from an advisory body, the Consulting Commission, whose duties include advising the unit on all issues that promote and facilitate research in care.

Highlighted Activities

- The number of students in the University Doctoral Programme in Comprehensive Care and Health Services, which is run in collaboration with the University of Jaén, University of Lleida, University of Vic and Carlos III Institute of Health, continues growing.

- Two cohorts of Centres Committed to Excellence have been completed. There is now a total of 18 centres and 81 Spanish healthcare institutions. In December 2017, the third call for candidate centres closed. A total of eight new centres representing 12 Regions are in the programme.

Scientific and Technical Activities

- Organisation of the XXI International Nursing Research Conference.
- Workshop for patients in the SueñOn® project.
- Dysphagia Care Technical Workshop.
- Course on the implementation of best practices guidelines, two courses on systematic reviews, and an accreditation course for leaders in systematic reviews by the Joanna Briggs Institute.
- Collaboration agreements with 16 Regions and two international institutions.
- Organisation of an online course: "Research methodology applied to healthcare" and launch of two massive open online courses (MOOCs) with more than 2,300 students registered.

2017 Projects

- European Project: Chronic diseases and promoting healthy ageing across the life cycle (CHRODIS-PLUS).
- European Project: CARE 4 DEM- DEMENTIA CAREGIVERS SUPPORT (2017-1-IT02-k214-036545)
- European Collaboration: European Innovation Partnership on Active and Healthy Ageing. A2 and A3 action groups.
- National Collaboration: participation in the REDISSEC thematic network (RD12/0001/0016) and start of our participation in the CIBERfes-ISCIII.
- Without external funding: SueñOn® Project.

Highlighted publications

Albornos-Muñoz L, Melián-Correa E, Acosta-Arrocha A, Gallo-Blanco C, Béjar-Bacas F, Alonso-Poncelas E, Serra-Estrada M, González-María E, Moreno-Casbas MT. Falls assessment and interventions among older patients in two medical and one surgical hospital wards in Spain: a best practice implementation project. *JBIS Database System Rev Implement Rep*. 2018 Jan;16(1):247-257. doi: 10.11124/JBISRIR-2017-003349

Bousquet, Philippe Jean & Bewick, Michael & Cano, A & Eklund, P & Fico, Giuseppe & Goswami, Nandu & Guldmond, Nick & Henderson, D & J. Hinke, M & Liotta, Giuseppe & Mair, Alpana & Molloy, David & Monaco, Alessandro & Monsonís Payá, Irene & Nizi ska, Adrianna & Papadopoulou, Homer & Pavlickova, A & Pecorelli, Sergio & Prados-Torres, Alexandra & de Oliveira-Alves, B. (2017). Building bridges for innovation in ageing: Synergies between Action Groups of the EIP on AHA. *The journal of nutrition, health & aging*. 21. 92-104. 10.1007/s12603-016-0850-7

Serrano-Gemes G, Rich-Ruiz M. *Enferm Intensiva*. 2017 Apr - Jun;28(2):48-56. doi: 10.1016/j.enfi.2016.10.007

Vidal-Thomàs MC, Yañez-Amoros B, Torrens I, Torres-Solera E, Esteva M. Knowledge and attitudes of primary care nurses about the management of patients with insomnia. *Enferm Clin*. 2017 May - Jun;27(3):186-192. doi: 10.1016/j.enfcli.2016.11.006

Romero-Franco, Natalia & Montañó, Juan & Fernández-Domínguez, Juan & Jimenez-Reyes, Pedro. (2017). Validity and reliability of a digital inclinometer to assess knee position sense in an open kinetic chain. *Journal of sport rehabilitation*. 10.1123/jsr.2017-0221

Oliva Pascual-Vaca Á, Punzano-Rodríguez R, Escribá-Astaburuaga P, Fernández-Domínguez JC, Ricard F, Franco-Sierra MA, Rodríguez-Blanco C. Short-Term Changes in Algometry, Inclinometry, Stabilometry, and Urinary

pH Analysis After a Thoracolumbar Junction Manipulation in Patients with Kidney Stones. *J Altern Complement Med*. 2017 Aug;23(8):639-647. doi: 10.1089/acm.2017.0041

Fernández-Domínguez JC, de Pedro-Gómez JE, Morales-Asencio JM, Bena-sar-Veny M, Sastre-Fullana P, Sesé-Abad A. Health Sciences-Evidence Based Practice questionnaire (HS-EBP) for measuring transprofessional evidence-based practice: Creation, development and psychometric validation. *PLoSOne*. 2017 May 9;12(5):e0177172. doi: 10.1371/journal.pone.0177172

Cidoncha-Moreno MÁ, Ruíz de Alegría-Fernandez de Retana B. Barriers to the implementation of research perceived by nurses from Osakidetza. *Enferm Clin*. 2017 Sep - Oct;27(5):286-293. doi: 10.1016/j.enfcli.2017.03.015



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

TELEMEDICINE AND E-HEALTH RESEARCH UNIT

The Telemedicine and e-Health Research Unit promotes and carries out R&D&I activities and training in the field of ICT applied to health. Its lines of activity are: a) development of PITES: Open Platform for Innovation in Telemedicine and e-Health, with specific actions in the fields of active and assisted living (AAL) and mobile health (mHealth); b) standardisation and interoperability of information systems and the electronic health record (EHR); c) creation of repositories for the secondary use of information and knowledge extraction; d) ICT training (empowerment) in patients and professionals; e) reliability analysis of complex monitoring environments and in the safe use of medical devices in contexts of active and assisted living (AAL); f) analysis of guarantees, protection, safety, and electromagnetic compatibility (EMC) in telemedicine applications; and g) evaluation of mobile telehealth e-services.

Scientific and Technical Activities

2017 Projects

- ERASMUS+ 2017-1-IT02-KA204-036545, CARE4DEM – Dementia Carers Support. (PI-ISCIII: Mayte Moreno Casbas and Adolfo Muñoz Carrero)
- CHRODIS PLUS - JA 2017-2020. Joint Action addressing chronic diseases and promoting healthy ageing across the life cycle. Coordinator: Antonio Sarría Santamera (ISCIII, ES).
- DGVI-1127-15. Friendly care for seniors. La Palma del Condado (Huelva) Town Hall and IMSERSO. (PI: Victoria Ramos González)

Highlighted publications

S. de Miguel-Bilbao, J. Blas, V. Ramos "Responses to Comments on Assessment of Polarization Dependence of Body Shadow Effect on Dosimetry Measurements in the 2.4 GHz Band" *Bioelectromagnetics*. 2017 DOI: 10.1002/bem.22079

Sánchez-de-Madariaga R, Muñoz A, Lozano-Rubí R, Serrano-Balazote P, Castro AL, Moreno O et al. Examining database persistence of ISO/EN 13606 standardized Electronic Health Record extracts: relational vs. noSQL approaches. *BMC Med Inform Decis Mak.* (2017) 17:123. DOI 10.1186/s12911-017-0515-4

García-Olmos L, Rodríguez-Salvanés F, Batlle-Pérez M, Aguilar-Torres R, Porro-Fernández C, García-Cabello A, et al. Development and validation of a risk stratification model for prediction of disability and hospitalization in patients



with heart failure: a study protocol. *BMJ Open*. 2017; 7(6): e014840. DOI 10.1136/bmjopen-2016-014840

Adolfo Muñoz, Mario Pascual. Coordinadores: PITES-ISA: New services based on telemedicine and e-health aimed at interoperability, patient safety and decision support. Instituto de Salud Carlos III – Ministerio de Economía, Industria y Competitividad. N.I.P.O. 062170368

3

TECHNICAL AND SCIENTIFIC ACTIVITIES

- 3.1 Centres and Units
- 3.2 Intramural Research

Patents

- Title: App for supervision and virtual care of patients during personalised walking sessions in home-based phase II cardiac rehabilitation programmes. Patent No. (pending); pre-deposit in the Research Results Transfer Office (OTRI). Title-Holding Entity: ISCIII and the Ramón y Cajal University Hospital Biomedical Research Foundation. Inventors: Mario Pascual Carrasco, Santiago Pérez de la Cámara, Carmen de Pablo Zarzosa, Elisa Velasco Valdazo, J.M. Maroto Montero
- Title: App for supervision and virtual guidance of patients during personalised relaxation sessions in home-based phase II cardiac rehabilitation programmes. Same as above.
- Title: Structured and custom made multimedia educational programme for phase II cardiac rehabilitation. Patent No. (pending). Title-Holding Entity: ISCIII and the Ramón y Cajal University Hospital Biomedical Research Foundation. Inventors: Mario Pascual Carrasco, Santiago Pérez de la Cámara, Carmen de Pablo Zarzosa, Elisa Velasco Valdazo, J.M. Maroto Montero
- Title: Three-dimensional geolocalised representation of data on non-ionising radiation exposure. Patent No. M-001874/2017. Title-Holding Entity: ISCIII: Authors: Victoria Ramos González and Silvia de Miguel Bilbao

Training

Doctoral Theses: “Smart Technology and its Electromagnetic Environment for the Safe Administration of Medication in the Internet of Things.” Doctoral Thesis. Authors: María Dolores Marcos García. Director: Dr José Luís Bardasano Rubio. Co-director: Dr María Victoria Ramos González. University of Alcalá de Henares, School of Medicine, Department of Medicine and Medical Specialties. Doctorate Programme in Health Sciences (RD 1397/2007) - D325. Mark: Outstanding. Defended on 5 April 2017.

Master’s Degree Final Projects:

- Implementation of a Wearables-based System for the Neurophysiological Study of Movement Disorders. Author: David Reifs Jiménez. Tutor: Victoria Ramos González. Master’s Degree Final Project in the UOC University Master’s Degree in Telemedicine. June 2017. Mark: Outstanding.

- Teleophthalmology: Early Diagnosis of Glaucoma. Author: Pau Ten Figàs. Tutor: Victoria Ramos González. Master’s Degree Final Project in the UOC University Master’s Degree in Telemedicine. June 2017. Mark: Outstanding.
- Specifications of a reference model for a standardised Autonomous Community Rare Disease Registry based on EN-ISO 13606. Authors: Fernando Baez Rodríguez, Victoria Díaz Guirado, María Ángeles López Orive. III Master’s Degree in Systems Management and Information and Communications Technology in Health. October 2017. Mark: Outstanding.
- III Master’s Degree in Systems Management and Information and Communications Technology in Health. National School of Public Health - ISCIII. (2016-2017). Various courses. Professors: Santiago Pérez de la Cámara, Mario Pascual Carrasco, Adolfo Muñoz Carrero, Montserrat Carmona Rodríguez.
- Master’s Degree in Telemedicine and Bioengineering. Higher Technical School of Telecommunications Engineers of Madrid. Subject: Standardisation of electronic medical records. Professor: Adolfo Muñoz Carrero. November 2017, Madrid.
- XI E-Health and Telemedicine Meeting. The Digital Transformation of Health. Menendez Pelayo International University. June 2017, Santander. Direction (Adolfo Muñoz Carrero) and secretariat of the course (Mario Pascual Carrasco).
- Training on organisational support for complex interventions. Education and training for patients and professionals. HADAP Project; HAZLO Project. Professors: Montserrat Carmona Rodríguez, María José De Tena Dávila.
- Health Sciences Studies. Master’s Degree in Telemedicine 2016-2017. UOC. Open University of Catalonia. Subject: AAL Environment: Preferred Environment for Teleassistance. Professor: Victoria Ramos González.
- Higher course on occupational medicine 2017-2018. National School of Occupational Medicine, ISCIII.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

FUNCTIONAL UNIT FOR RESEARCH INTO CHRONIC DISEASES

The mission of the Functional Unit for Research into Chronic Diseases (UFIEC) is to carry out basic and translational research, reference diagnostics, and training on chronic diseases, thus becoming a resource for scientific and technical support for the most prevalent diseases in the context of the National Health System. The UFIEC's objective is to become a national and international reference centre for biomedical research on chronic diseases and a resource for scientific and technical support for the SNS, in accordance with guidelines of the WHO; the European Commission; and the MSCBS. Currently, the UFIEC comprises units involved in research and benchmark molecular diagnosis (human prionopathies). It also provides transversal services such as the Histology Unit and various platforms that provide technical support to the ISCIII.

Scientific and Technical Activities

The UFIEC's activities are aimed at neurodegenerative diseases (Alzheimer's, Parkinson's, amyotrophic lateral sclerosis, multiple sclerosis, prionopathies, etc.); cancer (colon, ovarian, breast, thyroid, lung, and nervous system); and inflammatory, metabolic, and mitochondrial pathologies. It addresses aspects of regenerative medicine (stem cells, iPSCs), pharmacological targets (signalling, structural models), cellular senescence, and animal models. In addition to activities directly related to research on chronic diseases, at the UFIEC, other

scientific and technical activities are carried out, among which the following stand out:

- Benchmark molecular diagnosis of human prionopathies (included within the ECDC's surveillance programme).
- Transversal technical support services such as the Histology Unit, the optical imaging platform for *in vivo* monitoring of animal models (IVIS), the Luminex platform, and the structural protein analysis equipment.

Fundraisings

The UFIEC's research activity has been funded through competitive funds: seven projects by the National Plan and four by the Health Research and Development Strategy (AES), as well as scientific and technical support agreements with companies (Servier, Pfizer, Seprox Biotech, IDP Pharma, Catalysis) and through collaboration with different institutions and consortia (NEUROSTEM-CM Consortium, the TB-CIEN Tissue Bank and the CIEN Foundation, the H120 (i+12) Research Institute, IdiPaz, the MinE International Consortium for the Study of Amyotrophic Lateral Sclerosis, the Spanish Association Against Cancer, the Spanish Research Group on Neuro-oncology, the FECMA Federation, the UAM, the UCM, and the Francisco de Vitoria University). UFIEC groups participate in the following RETIC collaborative networks: Cellular Therapy (TerCel); Asthma, Adverse Reactions, and Allergies (ARADYAL); in the

cancer thematic area of the CIBER-ISCIII public consortium (CIBERonc-ISCIII) and the CiberNED-ISCIII consortium; as well as in various international agreements: University of the Republic of Uruguay; IIBCE- Ministry of Education and Culture of Uruguay; and the INOV-Contacto AICEP Portugal Programme.

Participation in International Committees.

The UFIEC, through Dr Pilar Sánchez, is represented in the Scientific Committee of the IARC (International Agency for Research on Cancer), which belongs to the WHO, for international coordination of cancer research. Furthermore, Dr Miguel Calero is a national expert on the surveillance and diagnosis of human prion diseases for the ECDC. Dr Antonio de la Vieja participates in the EU-NETVAL (European Union Network of Laboratories for the Validation of Alternative Methods) as expert in the validation and implementation of methods aimed at the detection of endocrine disrupters.

Scientific Production

A total of 20 works were published in international journals and 40 communications were given:

Highlighted publications:

Carro E, Bartolomé F, Bermejo-Pareja F, Villarejo-Galende A, Molina JA, Ortiz P, et al. Early diagnosis of mild cognitive impairment and Alzheimer's disease based on salivary lactoferrin. *Alzheimers Dement (Amst)*. 2017 May 26; 8:131-138. doi: 10.1016/j.dadm.2017.04.002. PMID: 28649597.

Sepúlveda-Sánchez JM, Vaz MA, Balañá C, Gil-Gil M, Reynés G, Gallego O, et al. Phase II trial of dacomitinib, a pan-HER (human epidermal growth factor receptor) tyrosine kinase inhibitor, in recurrent GB patients with EGFR amplification. *Neuro Oncol*. 2017; 19(11):1522-1531. doi: 10.1093/neuonc/nox105. PMID: 28575464.

Ayuso JM, Monge R, Martínez-González A, Virumbrales-Muñoz M, Llamazares GA, Berganzo J, et al. Glioblastoma on a microfluidic chip: Generating pseudopalisades and enhancing aggressiveness through blood vessel obstruction events. *Neuro Oncol*. 2017; 19(4):503-513. doi: 10.1093/neuonc/now230. PMID: 28062831.

Talamillo A, Grande L, Ruiz-Ontañón, P, Velasquez C, Mollinedo P, Torices S, et al. ODZ1 allows glioblastoma to sustain invasiveness through a Myc-dependent transcriptional upregulation of RhoA. *Oncogene* 2017; 6(12): 1733-1744. doi: 10.1038/onc.2016.341. PMID: 27641332.

López FJG, Ruiz-Tovar M, Almazán-Isla J, Alcalde-Cabero E, Calero M, de Pedro-Cuesta J. Risk of transmission of sporadic Creutzfeldt-Jakob disease by surgical procedures: systematic reviews and quality of evidence. *Euro Surveill*.

2017 Oct;22(43). doi: 10.2807/1560-7917.ES.2017.22.43.16-00806. PMID: 29090678.

Mendes M, Peláez-García A, López-Lucendo M, Bartolomé RA, Calviño E, Barderas R, et al. Mapping the Spatial Proteome of Metastatic Cells in Colorectal Cancer. *Proteomics*. 2017 Oct;17(19). doi: 10.1002/pmic.201700094. PMID: 28861940.

Garranzo-Asensio M, Guzman-Aranguez A, Povés C, Fernández-Aceñero MJ, Torrente-Rodríguez RM, Ruiz-Valdepeñas Montiel V, et al. Toward Liquid Biopsy: Determination of the Humoral Immune Response in Cancer Patients Using HaloTag Fusion Protein-Modified Electrochemical Bioplatfoms. *Anal Chem*. 20;88(24):12339-12345. doi: 10.1021/acs.analchem.6b03526. PMID: 28193070

Cortegano I, Rodríguez M, Martín I, Prado MC, Ruíz C, Hortigüela R, et al. Altered marginal zone and innate-like B cells in aged senescence-accelerated SAMP8 mice with defective IgG1 responses. *Cell Death Dis*. 2017 Aug 17;8(8):e3000. doi: 10.1038/cddis.2017.351. PMID: 28817118

Ballester S, Ballester A. Editorial: IL-2/IL-2R axis modulation by mesenchymal stromal cells: interaction with immunosuppressive drugs? *J. Leuk. Biol* 2017; 101(3):617-619. doi: 10.1186/s13287-016-0304-5

Magro-Lopez E, Guijarro T, Martínez I, Martín-Vicente M, Liste I, Zambrano A. A two-dimensional human minilung system (model) for respiratory syncytial virus infections. *Viruses*. 2017 Dec 10:9 (12). doi: 10.3390/v9120379. PMID: 29232863

Gutiérrez-Salmerón M, Chocarro-Calvo A, Carcía-Martinez JM, De la Vieja A*, García-Jimenez C*. 2017. Epidemiological bases and molecular mechanisms linking obesity, diabetes, and cancer. *Endocrinol Diabetes Nutr*. 2017 Feb;64(2):109-117. DOI: 10.1016/j.endinu.2016.10.005. PMID: 28440775

Villanueva AA, Falcón P, Espinoza N, R LS, Milla LA, Hernandez-SanMiguel E, et al. The Netrin-4/ Neogenin-1 axis promotes neuroblastoma cell survival and migration. *Oncotarget* 2017; 8(6):9767-9782. doi: 10.18632/oncotarget.14213. PMID: 28038459

Rodríguez-Salas N, Dominguez G, Barderas R, Mendiola M, García-Albéniz X, Maurel J, et al. Clinical relevance of colorectal cancer molecular subtypes. *Crit Rev Oncol Hematol*. 2017;109:9-19. doi: 10.1016/j.critrevonc.2016.11.007. PMID: 28010901

Arrizabalaga O, Moreno-Cugnón L, Auzmendi-Iriarte J, Aldaz P, de Cáceres II, Garros-Regulez L, et al. High expression of MKP1/DUSP1 counteracts glioma stem cell activity and mediates HDAC inhibitor response. *Oncogenesis*. 2017; 6(12):401. doi: 10.1038/s41389-017-0003-9. PMID: 29284798

Peltomaa R, Benito-Peña E, Barderas R, Sauer U, González Andrade M, Mo-



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

reno-Bondi MC. Microarray-Based Immunoassay with Synthetic Mimotopes for the Detection of Fumonisin B1. *Anal Chem.* 2017;89(11):6216-6223. doi: 10.1021/acs.analchem.7b01178. PMID: 28475831

Riancho J, Vázquez-Higuera JL, Pozueta A, Lage C, Kazimierczak M, Bravo M, et al. MicroRNA Profile in Patients with Alzheimer's Disease: Analysis of miR-9-5p and miR-598 in Raw and Exosome Enriched Cerebrospinal Fluid Samples. *J Alzheimers Dis.* 2017; 57(2):483-491. doi: 10.3233/JAD-161179. PMID: 28269782

López-Rodríguez JC, Benedé S, Barderas R, Villalba M, Batanero E. Airway Epithelium Plays a Leading Role in the Complex Framework Underlying Respiratory Allergy. *J Investig Allergol Clin Immunol.* 2017;27(6):346-355. doi: 10.18176/jiaci.0201. PMID: 29199961

Torrente-Rodríguez RM, Ruiz-Valdepeñas Montiel V, Campuzano S, Pedrero M, Farchado M, Vargas E, et al. Electrochemical sensor for rapid determination of fibroblast growth factor receptor 4 in raw cancer cell lysates. *PLoS One.* 2017;12(4):e0175056. doi: 10.1371/journal.pone.0175056. PMID: 28376106

Mas S, Oeo-Santos C, Cuesta-Herranz J, Díaz-Perales A, Colás C, Fernández J, et al. A relevant IgE-reactive 28kDa protein identified from *Salsola kali* pollen extract by proteomics is a natural degradation product of an integral 47kDa polygalacturonase. *Biochim Biophys Acta Proteins and Proteomics.* 2017;1865(8):1067-1076. doi: 10.1016/j.bbapap.2017.05.007. PMID: 28502749

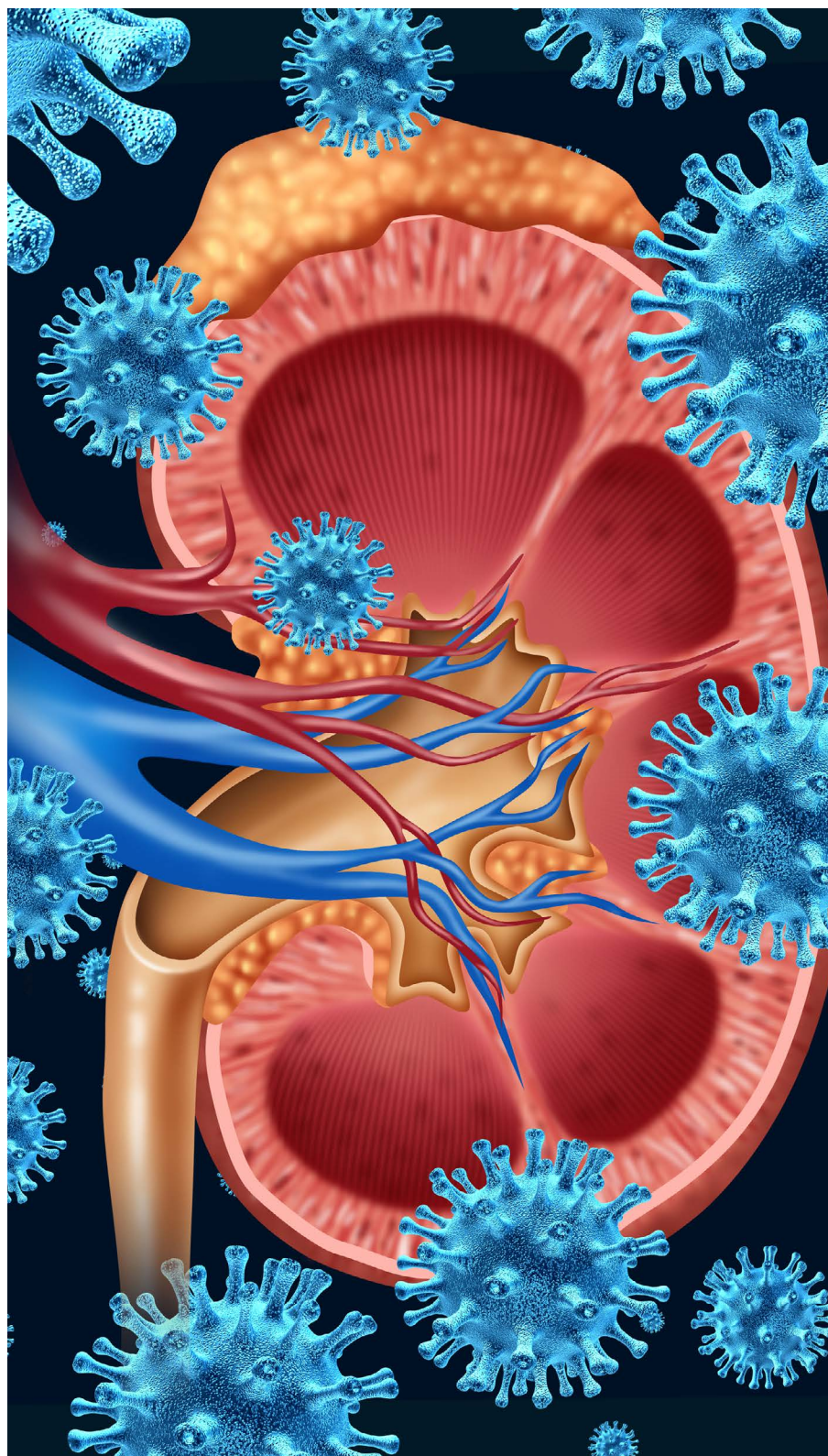
Rodríguez N, Peláez A, Barderas R, Domínguez G. Clinical implications of the deregulated TP73 isoforms expression in cancer. *Clin Transl Oncol.* 2017 Dec 11. doi: 10.1007/s12094-017-1802-3. PMID: 29230693

Patents

Methods for apolipoprotein detection, European request EP 16 794 966.8-1111 published on 3 May 2017.

Training

UFIEC groups play an important role in providing teaching and training on research. In 2017, they contributed to training with one finalised doctoral thesis and 15 more doctoral theses in process, six Master's Degree final projects, 11 Bachelor's Degree final projects, and five internships for Higher Professional Training (FPII) students, in addition to participating in classes and seminars.



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

CENTRAL SCIENTIFIC AND TECHNICAL UNITS AREA

The Central Scientific and Technical Units (UCCTs) Area of the Sub-Directorate General for Applied Services, Training, And Research (SGSAFI) includes the Veterinary, Bioinformatics, Electronic and Confocal Microscopy, Flow Cytometry and Genomics Units. Its main function is to provide high-quality scientific services to researchers from ISCIII's centres who request it.

Highlighted Activities

The Veterinary, Electronic and Confocal Microscopy, and Flow Cytometry Units achieved AENOR certification of their Quality Management System according to ISO Standard: 9001-2015. The Genomics Unit maintained its accreditation within the CNM quality system. Furthermore, the Bioinformatics Unit has strengthened its affiliation with the ISCIII's Bioinformatics Platform, forming part of the TransBioNet network.

Scientific and Technical Activities

The units' activities are focused on training, scientific and technical assistance, and providing services to ISCIII centres users. Likewise, they participate in their own research projects or collaborate with researchers at the institute.

Regarding the services provided by the various units:

- The Genomics Unit carried out more than 80,000 Sanger-type individual sequencings and generated around three terabytes of sequences by means of massive sequencing.
- A large part of this data has been processed by the Bioinformatics Unit, resulting in the analysis of around 1,500 bacterial genomes, 250 human exomes, and 250 transcriptomes.
- The Electronic Microscopy Unit has performed 21 diagnostic assays for the National Health System and 278 analyses requested by researchers.
- The Veterinary Unit has processed 263 requests for animal model experiments and carried out 16 botulism trials.
- The Flow Cytometry Unit has provided services to 87 users throughout ISCIII.

Scientific Production

15 works in international scientific journals have been published including both, scientific activity within own projects and collaborations with ISCIII's researchers.

Highlighted publications

Alvarado M, Martín-Galiano AJ, Ferrándiz MJ, Zaballos Á, de la Campa AG. Upregulation of the Pat AB Transporter Confers Fluoroquinolone Resistance to *Streptococcus pseudopneumoniae*. *Front Microbiol.* 2017 Oct 26;8:2074. doi: 10.3389/fmicb.2017.02074

Cortegano I, Rodriguez M, Martín I, Prado MC, Ruiz C, Hortigüela R, Alía M, Vilar MI, Mira H, Cano E, Domínguez M, de Andrés B, Gaspar ML. Altered marginal zone and innate-like B cells in aged senescence-accelerated SAMP8 mice with defective IgG1 responses. *Cell Death and Dis.* 2017 Aug 17;8(8):e3000. doi:10.1038/cddis.2017.351

Carrasco G, Monzón S, Jiménez P, Cuesta I, Bartolomé-Alvarez J, Valdezate S. First Draft Genome Sequence of a Clinical Strain of *Nocardia cerradoensis*. *Genome Announc.* 2017 Sep 28;5(39). pii: e00551-17. doi: 10.1128/genomeA.00551-17

Olmedillas E, Cano O, Martínez I, Luque D, Terrón MC, McLellan JS, Melero JA, Más V. 2017. Chimeric Pneumoviridae fusion proteins as immunogens to induce cross-neutralizing antibody responses. *EMBO Mol Med.* 12(9):e1005859

Training

Active participation in ISCIII's internal training programme, teaching in five courses for the following Units:

- Genomics (qPCR, preparation of libraries for massive sequencing)
- Bioinformatics (data analysis for massive sequencing)
- Electronic and Confocal Microscopy (image acquisition by confocal microscopy)
- Cytometry (Introduction to Flow Cytometry)
- The Veterinary Unit coordinated two category b courses and one category c course for management of animals for experimentation.

The Bioinformatics Unit directed two Master's Degree Final Projects.

NATIONAL STEM CELL BANK

The Management, Presidency, and Secretariat of the Technical Commission for the National Stem Cell Bank is under the Sub-Directorate General for Research on Cellular Therapy and Regenerative Medicine. It acts as a biobank network with hubs in Granada, Barcelona, and Valencia. It makes available to the scientific community all stem cell lines produced in our country.

On 27 February 2017, the representative of the INBIOMED Foundation officially communicated the entity's resignation as a National Stem Cell Bank (BNLC) hub. By means of a Resolution from ISCIII's Director, dated 9 March, this resignation was accepted and the destination of the induced pluripotent lines deposited was established.

A total of 35 induced pluripotent stem cells (iPS) were deposited in the BNLC in 2017. These lines have been developed in the following research centres: two in the Severo Ochoa Molecular Biology Centre (CBM); two in the Medical Research Centre of Navarre (CIMA); four in the Regenerative Medicine Centre of Barcelona (CMRB); one jointly between the GENYO centres, the Marqués de Valdecilla University Hospital, and IDIVAL; one in the Bioengineering Institute of Catalonia (IBIC); one at the August Pi i Sunyer Biomedical Research Institute (IDIBAPS); six at CSIC's Cajal Institute; two at the Josep Carreras Research Institute Against Leukaemia; two at the Alberto Sols Biomedical Research Institute; eight at the Pompeu Fabra University; one at the Vall d'Hebron Research Institute (VHIR); and five at the VHIR along with the CMRB.

Lines Requested

In 2017, the transfer of eight stem cell lines were requested and approved (three embryonic, five iPS) for three projects being carried out by three researchers:

- Embryonic lines: the VAL-3, VAL-4, and VAL-5 lines were requested for one research project.
- iPS lines: the N44SV.5, SP02#1, SP08#1, KiPS3F-7, and XF-iPSF44-3F-2 lines were requested for two research projects.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

OFFICE FOR THE TRANSFER OF RESEARCH RESULTS

In accordance with its statute, ISCIII's Office for the Transfer of Research Results (OTRI) is responsible for managing and coordinating the transfer of research results. The main activities carried out during 2017 are the following:

Patent Management

In 2017, OTRI has a portfolio of 66 patents, including requested and granted patents, and 18 patent families. From this total, 11 are Spanish and 55 are foreign or in the process of internationalisation. The new patent requests that are in process are:

Use of CD69 function modulators for the mobilisation and proliferation of hematopoietic precursors.

Combination product comprising a modified mesenchymal stem cell and an antigenic substance.

Intellectual Property Registries

In 2017, the registration of three works as intellectual property was requested. All of them correspond to software developments for mobile applications.

Licenses of Materials and Know-How

Various national and international agreements were developed in order to transfer and license the use of materials.

Dissemination of the Technological Offer: Attending Fairs and Congresses

In 2017, the OTRI actively participated in TRANSFIERE2017: European Forum for Science, Technology, and Innovation, held in Málaga. At ISCIII's events OTRI participated with a stand where the Institute's technical and scientific offer was disseminated.

Additionally, it continued disseminating its technological offer via email and through online portals such as the EEN (Enterprise Europe Network) or ISCIII's own website.

Other Activities: Consulting and Advising

Consulting and advising activities were carried out in relation to queries made by ISCIII researchers on patentability issues of research results and processing of various types of documents, such as ISCIII internal procedures. It is worth noting the use of Technological Reports on Patents from the OEPM, which has helped orienting research by finding relevant scientific information in patent documents.

SCIENTIFIC CULTURE AND INNOVATION UNIT

In 2017, ISCIII's Scientific Culture Unit (UCCIII+i) carried out a project funded by the Spanish Foundation for Science and Technology (FECYT) entitled ISCIII's Outreach for all (ISCIII within the reach of all) for the third consecutive year. This allowed for a series of activities for scientific education in the framework of the fairs and events that take place in our field, such as Science Week and European Researchers' Night.

The most notable activities carried out in 2017 were:

- Co-organisation of visits to ISCIII's Museum of Public Health and Hygiene along with a scientific photography exhibit entitled "The Invisible".
- 2nd workshop/educational course "Disseminate your Science" to provide researchers with tools for disseminating their knowledge.
- The scientific education programme in secondary education and Baccalaureate school centres "Science Goes to School".
- The workshop "Greenlight for Girls", an event held in ISCIII's headquarters and organised by the CISCO technology company in collaboration with ISCIII. Its objective is to inspire girls and stimulate their interest in the fields of Science, Technology, Engineering, and Mathematics (STEM fields) through practical workshops. Around 200 girls between 11 and 15 years of age participated in this activity.
- Likewise, contacts were established with the Fine Arts Department of the Complutense University of Madrid aimed at establishing collaborations to promote the interest of future artists in the world of research and science.

As part of European Researchers' Night: Radio workshop: "Tonight, CoRIS makes you the television star."

As part of Science Week:

- Presentation of a collection of books entitled "More than Health" in La Casa del Libro bookshop in Madrid. This year, the following titles were presented: Why do we Vaccinate?; HIV: Research Against the Great Epidemic of the XX Century; Extreme Temperatures and Health: How Heat Waves and Cold Snaps Affect Us; and Comprehensive Health.
- Colloquium: "Fighting Against HIV: Come Get to Know the CoRIS Cohort and HIV Biobank", and the "Chagas Disease in Madrid: a Phantom Threat" conference.
- Open House at ISCIII's Majadahonda Campus.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

BIOLOGICAL ALERT LABORATORY NETWORK

The Biological Alert Laboratory Network (RE-LAB) was created through Ministerial Order PRE/305/2009, of 10 February, modified by Order PRE/2565/2015, of 26 November, as a scientific and technical infrastructure for operational support for crisis management within the National Security System to respond to threats posed by dangerous biological agents.

Scientific and Technical Activities

The RE-LAB Management Unit coordinated the network reference laboratories' response to alerts of postal deliveries containing possible virulent biological agents that have occurred in various public institutions and private entities in the country throughout the year.

In 2017, the Valencian Institute of Agrarian Research's Plant Protection and Biotechnology Centre, of the Valencian Regional Government, was incorporated into RE-LAB. It is the national reference laboratory for wood bacteria and viruses of the Ministry of Agriculture, Fisheries, Food, and Environment.

The Management Unit participated in the creation of the Spanish declaration on measures for promoting trust in the prohibition of Biological and Toxin Weapons Convention (BTWC), coordinating the information provided by laboratories in the network.

Participation in work groups and institutional representation:

- The National Work Group for the execution of the European Union Chemical, Biological, Radiological and Nuclear (CBRN) Action Plan, coordinated by the Spanish Presidency's Department of National Security.
- Interministerial Group for the Prohibition of Biological Weapons (GRUPABI), coordinated by the Sub-Directorate General of Non-Proliferation and Disarmament of the Ministry of Foreign Affairs, European Union and Cooperation (MAEC).
- Participation in the Interministerial Contact Group for Resolution 1540 of the United Nations Security Council, coordinated by the MAEC.
- Designation of RE-LAB members as European Union experts to favour nation-wide implementation of the BTWC.
- Participation in the "Workshop in Support of the Biological Weapons Convention Extended Assistance Programmes" organised by the United Nations Office for Disarmament Affairs and by the Permanent Delegation of the European Union to the United Nations.

Training

Participation in the IV Course on Catastrophe Management of the Military Emergencies Unit.

XIV Course for Civil Guard CBRN Specialists (Level 3).

Course for First Responders to Emergencies with Biological Risks, City of Madrid Fire Department.

International Seminar on Biosafety and Biosecurity, Ministry of Foreign Affairs and Cooperation.



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

JOINT CENTRE FOR RESEARCH ON HUMAN EVOLUTION AND BEHAVIOUR (ISCIII-UCM)

This centre carries out activities in three areas of work: human evolution, ancient DNA, and cognitive neuroscience. In addition to research related to the Atapuerca archaeological site, the team collaborates in other archaeological sites including Pinilla del Valle (Madrid), Valle del Tejadilla (Segovia), Aroeira (Portugal), El Gegant (Barcelona), and Olduvai (Tanzania).



Publications

Human Evolution

As part of research line on human evolution, work continues on the study on different skeletal elements from the Sima de Atapuerca (Burgos) site in order to better understand the evolution of human anatomy. Publications have been numerous, but amongst them, we would like to highlight the following:

Arlegi, M., Gómez-Olivencia, A., Albessard, L., Martínez, I., Balzeau, A., Arsuaga, J. L., & Been, E. The role of allometry and posture in the evolution of the hominin subaxial cervical spine. *J Hum Evol.* 2017; 104: 80-99. doi: 10.1016/j.jhevol.2017.01.002

Arsuaga, J. L., Gómez-Olivencia, A., Sala, N., Martínez-Pillado, V., Pablos, A., Bonmatí, A.,... & Cuenca-Bescós, G. Evidence of paleoecological changes and Mousterian occupations at the Galería de las Estatuas site, Sierra de Atapuerca, northern Iberian plateau, Spain. *Quat Res.* 2017; 88(2): 345-367. doi.org/10.1017/qua.2017.46

Bartsiokas, A., Arsuaga, J. L., Aubert, M., & Grün, R. U-series dating and classification of the Apidima 2 hominin from Mani Peninsula, Southern Greece. *J Hum Evol.* 2017; 109: 22-29. doi: 10.1016/j.jhevol.2017.04.008

Bermúdez de Castro, J. M., Martínón-Torres, M., Arsuaga, J. L., & Carbonell, E. Twentieth anniversary of *Homo antecessor* (1997-2017): a review. *Evol Anthropol.* 2017; 26(4): 157-171. doi: 10.1002/evan.21540

Daura, J., Sanz, M., Arsuaga, J. L., Hoffmann, D. L., Quam, R. M., Ortega, M. C., & Souto, P. New Middle Pleistocene hominin cranium from Gruta da Aroeira (Portugal). *Proc Natl Acad Sci U S A.* 2017; 114(13): 3397-3402. doi: 10.1073/pnas.1619040114

Pablos, A., Pantoja-Pérez, A., Martínez, I., Lorenzo, C., & Arsuaga, J. L. Metric and morphological analysis of the foot in the Middle Pleistocene sample of Sima de los Huesos (Sierra de Atapuerca, Burgos, Spain). *Quat Int.* 2017; 433: 103-113. doi.org/10.1016/j.quaint.2015.08.044

Poza-Rey, E. M., Lozano, M., & Arsuaga, J. L. Brain asymmetries and handedness in the specimens from the Sima de los Huesos site (Atapuerca, Spain). *Quat Int.* 2017; 433: 32-44. doi.org/10.1016/j.quaint.2015.10.004

Quam, R. M., Martínez, I., Rosa, M., & Arsuaga, J. L. (2017). Evolution of Hearing and Language in Fossil Hominins. In *Primate Hearing and Communication* (pp. 201-231). Springer, Cham.

Ruiz, J., & Arsuaga, J. L. (2017). On the calculation of occlusal bite pressures for fossil hominins. *J Hum Evol.* 2017; 102: 67-71. doi: 10.1016/j.jhevol.2016.09.007



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

Studies on diet as well as the behaviour and social implications of hunting amongst the Atapuerca hominids have been carried out.

Lozano, M., de Castro, J. B., Arsuaga, J. L., & Carbonell, E. Diachronic analysis of cultural dental wear at the Atapuerca sites (Spain). *Quat Int.* 2017; 433: 243-250. doi.org/10.1016/j.quaint.2015.08.028

Lozano, M., Estalrich, A., Bondioli, L., Fiore, I., Bermúdez de Castro, J. M., Arsuaga, J. L.,... & Frayer, D. W. Right-handed fossil humans. *Evol Anthropol.* 2017; 26(6): 313-324. doi: 10.1002/evan.21554

Pérez-Pérez, A., Lozano, M., Romero, A., Martínez, L. M., Galbany, J., Pinilla, B., & Arsuaga, J. L. The diet of the first Europeans from Atapuerca. *Scientific Reports.* 2017; 7: 43319. doi:10.1038/srep43319

Rodríguez-Hidalgo, A., Saladie, P., Olle, A., Arsuaga, J. L., de Castro, J. M. B., & Carbonell, E. Human predatory behavior and the social implications of communal hunting based on evidence from the TD10. 2 bison bone bed at Gran Dolina (Atapuerca, Spain). *J Hum Evol.* 2017; 105: 89-122. doi: 10.1016/j.jhevol.2017.01.007

The origin of the accumulation of skeletons at the site is hugely significant in social and cognitive evolution because it could be the evidence of the first funerary behaviour in history.

Aranburu, A., Arsuaga, J. L., & Sala, N. The stratigraphy of the Sima de los Huecos (Atapuerca, Spain) and implications for the origin of the fossil hominin accumulation. *Quat Int.* 2017; 433: 5-21. doi.org/10.1016/j.quaint.2015.02.044

The study of the human population in the Holocene continues.

Galindo-Pellicena, M. Á., Pérez-Romero, A., Francés-Negro, M., Álvarez-Fernández, A., Iriarte, E., Arsuaga, J. L., & Carretero, J. M. The equids from the Bronze Age levels of the El Portalón site (Atapuerca, Burgos, Spain). *Quat Int.* 2017; 433: 124-141. doi.org/10.1016/j.quaint.2015.11.120

Pérez-Romero, A., Iriarte, E., Galindo-Pellicena, M. Á., García-González, R., Rodríguez, L., Castilla, M.,... & Alday, A. An unusual Pre-bell beaker copper age cave burial context from El Portalón de Cueva Mayor site (Sierra de Atapuerca, Burgos). *Quat Int.* 2017; 433: 142-155. doi.org/10.1016/j.quaint.2015.06.063

Ancient DNA

The study of human population dynamics in the Holocene has continued. For this study, a sampling and sequencing of human remains with the chronology of the Holocene has been carried out.

Rodríguez-Varela, R., Günther, T., Krzewinska, M., Storå, J., Gillingwater, T. H., MacCallum, M., & Götherström, A. (2017). Genomic Analyses of Pre-European Conquest Human Remains from the Canary Islands Reveal Close Affinity to Modern North Africans. *Current Biology.* 2017; 27(21): 3396-3402. doi: 10.1016/j.cub.2017.09.059

Lastly, work continued on the research line on wildlife, both in palaeontology and in genetics. Collaboration with the Universities of Stockholm and Uppsala (Sweden) on both animal and human ancient DNA continued.

Lira Garrido, J., Corchón Rodríguez, M.S. & Arsuaga, J.L. El ADN mitocondrial de los caballos solutrenses de Las Caldas (San Juan de Priorio, Asturias): una aproximación al estudio de las líneas maternas pleistocenas ibéricas. En: *Los niveles solutrenses de La cueva de Las Caldas (Asturias) (Corchón Rodríguez, M.S., ed), Universidad de Salamanca.* 2017. p. 337-351. ISBN: 978-84-9012-792-6.

Cognitive Neuroscience

Open lines of work include study of the neurophysiologic foundations of cognitive processes such as language, emotion, and social cognition.

Casado, P.; Martín-Loeches, M.; León, I.; Hernández-Gutiérrez, D.; Espuny, J.; Muñoz, F.; Jiménez-Ortega, L.; Fondevila, S.; de Vega, M. When syntax meets action: Brain potential evidence of overlapping between language and motor sequencing, in press.

Jiménez-Ortega, L, Espuny, J, Herreros de Tejada, P,Vargas-Rivero, C,Martín-Loeches, M. Subliminal Emotional Words Impact Syntactic Processing: Evidence from Performance and Event-Related Brain Potentials. *Front Hum Neurosci.* 2017; 11(192). DOI10.3389/fnhum.2017.00192

Patiño, F.Y.; Luque, M.; Terradillos-Bernal, M.; Martín-Loeches, M. Biomechanics of microliths manufacture: A preliminary approach to Neanderthal's motor constrains in the frame of embodied cognition. *J Anthropol Sci.* 2017; 95: 1-16. doi: 10.4436/JASS.95005

Martín-Loeches, M.; Ouyang, G.; Rausch, P.; Stürmer, B.; Palazova, M., Schacht, A. & Sommer, W. Test-retest reliability of the N400 component in a sentence-reading paradigm. *Lang Cogn Neurosci.* 2017; 32(10): 1261-1272. DOI:10.1080/23273798.2017.1330

Martín-Loeches, M. Art without Symbolic Mind. *Embodied Cognition and the*



TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

Origins of Visual Artistic Behavior. In: Thomas Wynn and Frederick Coolidge (Eds.) Cognitive Models in Palaeolithic Archaeology. Oxford University Press, New York. 2017 pp.113.

Collaborations with other teams: University of La Laguna, Rey Juan Carlos University, Humboldt University of Berlin's Psychobiology Department, Georg-August-Universität Göttingen, and the University of Colorado at Colorado Springs, USA.

Disseminating Knowledge

To meet the objective of making all types of scientific content known to the public, which is a priority for this team, three temporary exhibitions were designed and coordinated in the Museum of Human Evolution in Burgos:

Vermeer's Friend. The Eye and the Lens, in which the only authenticated microscope constructed by Anton van Leeuwenhoek was displayed. Leeuwenhoek is known in history for having developed a type of highly-powerful microscope. Thanks to him, in the XVII century, a world unknown until that moment opened up: protozoa, red blood cells, spermatozoa, and even bacteria. April.

Mountains, an enthralling subject that was approached from different perspectives: science (geology, botany, climatology, entomology, or topography), art (with works from the Prado Museum), mountain climbing, and from the spiritual perspective. For as long as we can remember, mountains have been considered an ideal place to cohabit with the gods. July.

What remains. Alberto Bañuelos presented his sculptures, which remind us of all the civilisations we know, and at the same time to none of them, since there is hardly a common denominator amongst all of them. December.



3

TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

3.2 INTRAMURAL RESEARCH

Intramural research refers to research carried out at ISCIII's own centres and associated joint units through competitive research projects, management delegation agreements, and collaboration agreements. Sources of funding for these competitive projects are varied in nature. They include the Spanish National R&D&I Plan programmes; Strategic Action in Health (AES) programmes within the Spanish National Plan; ISCIII's Intramural Research Programme; and other regional, national, and international public and/or private calls.

The information presented in this section brings together the results of scientific production from the ISCIII's schools and centres through various studies and indicators: analysis of scientific publications, research projects, and the hiring of research and research support staff. This information has been collected and analysed through Research Coordination Area (ACI).

RESEARCH COORDINATION AREA

The Research Coordination Area's (ACI) objective is to manage and coordinate activity related to research carried out at ISCIII within the framework of national and international calls.

It forms part of the Sub-Directorate General for Applied Services, Training, and Research (SGSFI). It carries out tasks such as: disseminating calls from public and private funding agencies for grants to fund projects and human resources; advising researchers on the preparation and submission of proposals; managing of national and international projects, agreements, contracts, and assignments; monitoring and justification of the grants; and financial monitoring and statistical analysis of the state of intramural research.

Projects Granted in 2017 Calls Funding

Projects	Programme	Number of Projects	Total Funding (€)
External Funding	International*	10	2,495,609.61
	National R&D&I Plan	8	1,256,406.40
	Others	2	21,516.47
ISCIII Funding	AESI Projects	23	1,963,180.00
	Other intramural	3	197,670.00
TOTAL		46	5,934,382.48

* six projects and four sub-projects (EU, ECDC, etc.)

Projects Granted by Thematic Area 2017

Thematic Area	Number of Projects
Cellular and Developmental Biology	2
Infectious diseases: Bacteriology	2
Infectious diseases: Mycology	1
Infectious diseases: Parasitology	3
Infectious diseases: Virology	1
Neurological diseases	1
Rare diseases	5
Immunology	1
Cancer research	2
Nursing research	1
Public health research	5
HIV/AIDS research	6
Others (FIS, ENS, OPE, OTRI, Biobanks, Bioethics)	15
Environmental toxicology	1
TOTAL	46

Human Resources Calls 2017 Number of contracts awarded per Centre

Centre	National R&D&I Plan (*)	Others	Total
CNM	2	7	9
CNE		1	1
CNSA	1	1	2
SGSAFI	2		2
UFIEC		2	2
TOTAL	5	11	16

(*) Calls pending resolution were excluded.

Publications and Theses in 2017

Centre	Publications	Theses
AETS	6	-
CNE	111	2
CNM	182	13
CNMT	10	2
CNSA	4	-
ENS	39	6
ENMT	1	-
IIER	21	3
INVESTEN	2	-
TELEMEDICINE	3	1
UFIEC	10	1
TOTAL	389	28

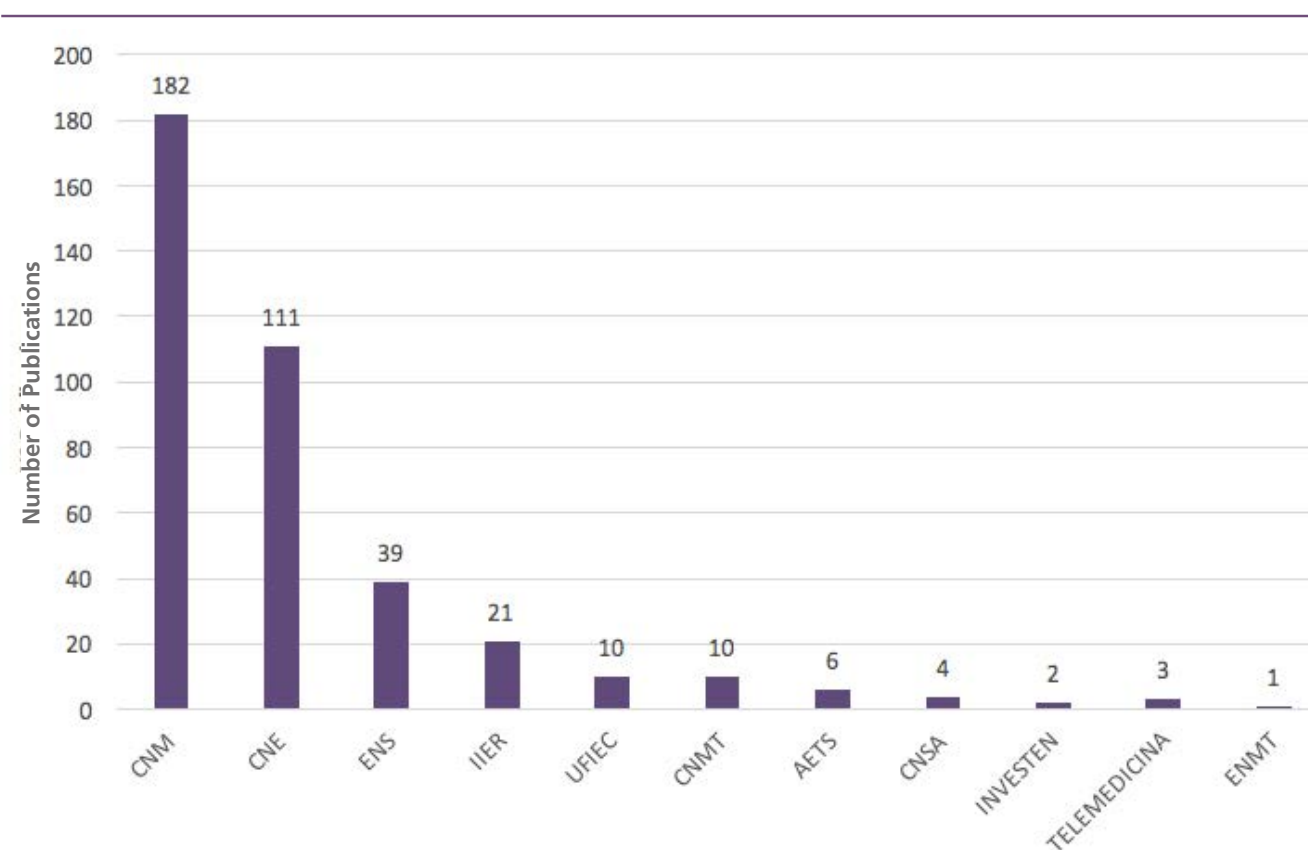


TECHNICAL AND SCIENTIFIC ACTIVITIES

3.1 Centres and Units

3.2 Intramural Research

2017 PUBLICATIONS





4

TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational
Medicine



4 TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational Medicine

4.1 NATIONAL SCHOOL OF PUBLIC HEALTH

The National School of Public Health (ENS), was founded in 1924. It offers specialised postgraduate training and continuing education in the areas of public health, health management and administration, international health, and related fields. It carries out research, technical studies, consulting, and other services in these areas for various public administrations and scientific, healthcare, and development aid entities.

Highlighted Activities

1. In 2017, the new Master's degree in public health was launched. It is offered by the National School of Public Health Joint Research Institute (ENS-IMIENS)

in the framework of the collaboration between the ENS and the National Distance Education University (UNED). It has a duration of two years. This Master's Degree, whose content and quality is similar to a face-to-face Master's degree in public health, is an opportunity for specialised professionals who work in public health but cannot dedicate one year to full-time study.

2. Amongst the IMIENS' activities, the launch of the Research Consolidation Plan at IMIENS stands out. It includes the following calls for research grants:

- Call for grants for carrying out joint research projects
- IMIENS call for grants for placements in other research centres
- IMIENS call for grants for the organisation of joint conferences
- Call for the dissemination of the IMIENS' activities

SUMMARY OF DATA ON THE ENS' ACTIVITY IN 2017

ENS Regulated Education 2017

ENS Regulated Education	2017	2016	2015
Master's Degrees	4	4	4
Diplomas	3	3	2
Short Courses	21	29	30
Teaching hours taught	3,852	3,525	3,236
ECTS ¹ Equivalent	321	282	260
Students	466	393	532

(1) ECTS: European Credit Transfer System

2017 TRAINING OFFER	Academic load (teaching hours)
Master's Degree in Public Health	1,500 (750)
University Master's Degree in Healthcare Administration	1,500 (750)
Master's Degree in Systems Management and Information and Communications Technology in Health	1,500 (750)
Master's Degree in Bioinformatics Applied to Personalised Medicine and Health	600 (360)
Specialisation in Health and Bioethics Law Diploma (online), VI edition	120
Specialisation in Health and Bioethics Law Diploma (online), VII edition	120
Specialisation in Public Health for Development Aid Diploma (online)	180
In-person continuing education courses/workshops	822

Students in training	2017	2016	2015
Total number of MIR in training programmes (R1, R2, R3, R4)	8	8	7
Number of students in Master's Degree and Diploma Programmes	225	192	281
Number of students in continuing education	241	201	251
Total students	466	393	532

4 TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational Medicine



4 TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational Medicine

Scientific Production

40 national and 57 international publications.

Highlighted publications

Goetghebeur MM, Wagner M, Samaha D, O'Neil W, Badgley D, Castro-Jaramillo H, Abrishami P, Sarria-Santamera A, Cleemput I, Tringali M.

Exploring values of health technology assessment agencies using reflective multicriteria and rare disease case. *Int J Technol Assess Health Care*. 2017 Jan;33(4):504-520. doi: 10.1017/S0266462317000915.

Ortiz C, Linares C, Carmona R, Díaz J. Evaluation of short-term mortality attributable to particulate matter pollution in Spain. *Environmental Pollution*. 2017; 224:541-551.

Repullo JR. Impacto económico del turismo sanitario. Retos para la sostenibilidad del sistema nacional de salud. [Capítulo 10]. En: Cantero-Martínez J. La liberalización de la asistencia sanitaria transfronteriza en Europa. Retos y desafíos para el Sistema Nacional de Salud. Aranzadi – Thomson. 2017: pp. 329-53.

Sordo L., Barrio G., Bravo M. J., Indave B. I., Degenhardt L., Wiessing L., Ferri M., Pastor-Barriuso R. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. *BMJ* 2017; 357: j1550.

Ramiro-González MD, Sanz-Barbero B, Royo-Bordonada MÁ. Childhood excess weight in Spain from 2006 to 2012. Determinants and parental misperception. *Rev Esp Cardiol*. 2017; 70:656-63.

4.2 NATIONAL SCHOOL OF OCCUPATIONAL MEDICINE

The National School of Occupational Medicine (ENMT-ISCIII) is a specialised centre for training, advice, and research and innovation on occupational medicine. It is the national reference centre for International Occupational Safety and Health Knowledge Network of the International Labour Organisation (ILO). It is also the reference centre counting with 11 teaching units at the first stage of the the Higher Course in Occupational Medicine.

In 2017, the ENMT signed four new collaboration agreements in the areas of training, research, and scientific associations. These collaborations are with the following stakeholders: Spanish Federation of Specialists in Occupational Care, collaborative agreements among University of Alcalá, ISCIII, National Social Security Institute, Institute for the Elderly and Social Services, and General Foundation of the University of Alcalá, with the aim of teaching of the Master's and Specialist's Degree in Medical Evaluations for Inability to Work and Dependency.

Teaching

Training indicators in the 2017 school year

11 courses/workshops in 2017	Format	CEC/ECTS credits	Hours
V Scientific Workshops on Occupational Health Review Studies	E.N.M.T. In-person	1 CEC	5
Introduction to Dermatoscopy for Occupational Health Physicians	E.N.M.T. In-person	0.9 CEC	7
Introduction to Hypoacusia for Occupational Health Physicians I and II	E.N.M.T. In-person	1 CEC/unit	6 units
Higher course on occupational medicine CUSMET 2017	E.N.M.T. Blended learning	–	800
Practical application of health surveillance protocols course	E.N.M.T. Online	4.5 CEC	45
The Prescription of Physical Exercise by Healthcare Professionals I and II	E.N.M.T. Online	6.3 CEC/unit	50 units
Master's Degree in Medical Evaluations for the Inability to Work and Dependency. (ISCIII-UAH-INSS-IMSERSO)	E.N.M.T. On-Line	60 ECTS	350

Research and Dissemination

Research projects underway in 2017

Project name	Funding entity	Participating entities
Elements of modelling in the analysis of stimulus-response tasks of interest to occupational health	ISCIII	ISCIII-U. INNSBRUCK (HOCHZIRL HOSP.)
CHRODIS-PLUS; tasks	ISCIII- EUROPEAN COMMISSION	ISCIII
Functional state in working-age people and non-traumatic spinal cord injury	ISCIII-U. Brisbane-Ciberned	ISCIII-U. Brisbane-Ciberned
Fatigue, falls and useful standards	ISCIII-UCV- CLINIC HOSP. –U. Navarra	ISCIII-UCV-UVEG-CLINIC HOSP. - U. Navarra

4 TRAINING ACTIVITIES

- 4.1 National School of Public Health
- 4.2 National School of Occupational Medicine

Highlighted publications

Caron A, Ayala A, Damián J, Rodríguez-Blazquez C, Almazán J, Castellote JM, Comin M, Forjaz MJ, de Pedro J; DISCAP-ARAGON research group. Physical activity, body functions and disability among middle-aged and older Spanish adults. *BMC Geriatr.* 2017 Jul 18;17(1):150. F. I (JCR): 2.61

Castellote JM, Kofler M, Mayr A, Saltuari L. Evidence for Startle Effects due to Externally Induced Lower Limb Movements: Implications in Neurorehabilitation. *Biomed Res Int.* 2017; 017:8471546. F. I (JCR): 2.476

Disability, support and long-term social care of an elderly Spanish population, 2008-2009: an epidemiologic analysis. *Int J Equity Health.* 2017 Jan 9;16(1):4. F. I (JCR): 1.589

Scientific dissemination:

Publishing of the Occupational Medicine and Safety Journal. Four issues annually.

	2010	2011	2012	2013	2014	2015	2016	2017
Original articles	16	24	23	17	17	15	12	11
Case Studies	-	-	-	-	10	8	5	4
Review articles	4	2	4	8	16	11	8	4
Others	10	10	11	7	15	7	9	6
Total articles	30	36	35	32	58	41	34	25
Supplements	-	1	-	1	2	-	1	-

4 TRAINING ACTIVITIES

4.1 National School of Public Health

4.2 National School of Occupational Medicine



INTERNATIONALISATION

5.1 International Programmes

5.1 INTERNATIONAL PROGRAMMES

ISCIII, in its role as a funding agency and through the AES (Strategic action for Health), participates in several international instruments and programmes for funding collaborative health research projects. It entails that part of the AES funding, is addressed to these transnational programmes, which are launched to meet challenges that countries working alone would find very hard to achieve. It includes:

- Coordination of joint calls between European countries and regions (ERA-Nets and ERA-Nets cofund).
- Public-public partnerships European Union — Member State multiyear programmes, launched pursuant to article 185 of the Treaty on the Functioning of the European Union (TFEU).
- Joint Programming Initiatives (JPIs) in which funding comes only from member states.
- European Joint Programmes (EJP), a new instrument in which programming and execution of research is combined.

Additionally, beyond the European framework, ISCIII participates in the following international research consortia:

- IRDiRC: International Rare Diseases Research Consortium.
- GloPID-R: Global Research Collaboration for Infectious Disease Preparedness, aimed at providing an effective response to new or re-emerging infectious disease with pandemic potential.
- IC PerMed: International Consortium for Personalized Medicine, officially launched in November 2016.
- Personalized Medicine Coalition.
- CGC: International Cancer Genome Consortium.

International Scientific Infrastructure

ISCIII has the legal mandate to represent Spain and cover the Spanish contribution to IARC (the WHO's International Agency for Research on Cancer) and to four European research infrastructures:

- ELIXIR: European Life Science Infrastructure for Biological Information.
- EATRIS-ERIC: Decentralised Infrastructure for Translational Medicine to support the development of new prevention, diagnostic, and therapeutic strategies for biomedical research and development.

- ECRIN-ERIC: Decentralised European clinical trials platform. The Spanish scientific hub is the Spanish Clinical Research Network (SCReN), which brings together facilities for clinical trials that are at the SNS hospitals and, that are funded by the ISCIII for networking and multi-site activities.
- EU-Openscreen-ERIC: Decentralised infrastructure for chemical, biology and molecule screening for therapeutic activity.

Similarly, the Institute collaborates within another infrastructure that is currently being prepared. It is included in the ESFRI roadmap:

- Euro-Biolmaging: decentralised infrastructure for the digitisation of medical imaging and biological microscopy.

Complementary Actions to the Joint Programming Initiatives

Through the Joint Programming Initiatives, ISCIII participates in transnational research consortia - ERA and international – with the objective of supporting significant projects involving Spanish research groups working with teams from other countries through the coordination and mobilisation of resources in strategic areas of European interest. Data on participation and funding are indicated in section 2.1 of this annual report.

A) H2020 – societal challenge 1 - Scope: Personalised Medicine

1. ERAPerMed. ERA-NET Cofund on Personalised Medicine. Coordinated by ISCIII and funded by the European Commission on Biomedicine, the ERA-Net has a budget of €32 million and the participation of 32 partners from 22 countries. In Spain, the CDTI, the Regional Government of Navarre, and the Catalonia Regional Government Health Department also participate as funders. Its duration is for five years and it started on 1 December 2017. On 8 February 2018, it launched its first call for projects (cofunded by the EU) which included two areas. Area 1: “Validation, pre-clinical, and clinical biomedical research – Translating basic to clinical research and beyond” (Module 1A: Pre-clinical research; Module 1B: Clinical research). Area 2: “Data analysis, management and protection – Integrating big data and ICT solutions” (Module 2A: Data and ICT – Enabling technology; Module 2B: Data and ICT – Towards application in health care).
2. ERACoSysMed: ERA-Net Cofund for Systems Medicine Research Programmes. Call (not cofunded): European Research Projects on Systems Medicine. Budget of €7.2 million, 12 funding agencies, five projects funded, one coordinated by a Spanish group funded by the ISCIII.



3. NEURON-3: The Network of European Funding for Neuroscience Research (ERA-Net cofund). Call (not cofunded): “Synaptic dysfunctions external to the central nervous system”. Budget of €15 million, 20 funding agencies from 17 countries, 12 projects funded, one coordinated by a Spanish group funded by the ISCIII. The other Spanish funder is AEI-MINECO.
4. ERA-CVD: European Research Area Network on Cardiovascular Diseases (ERA-Net cofund). Call (not cofunded): “Mechanisms of early atherosclerosis and/or plaque instability in coronary artery disease”. Budget of €7.3 million, 17 funding agencies from 16 countries, 10 projects funded, one coordinated by a Spanish group funded by the ISCIII.
5. Transcan-2: ERA-Net cofund for Translational Cancer Research. Call (not cofunded): “Minimal and non-invasive methods for early detection and/or progression of cancer”. Budget of €16.3 million, 23 funding agencies, 14 projects funded, five of them with Spanish participation funded by the ISCIII: seven research groups, three of them as coordinator. In Spain, they are also funders the AECC Foundation and FICYT (Asturias).
6. E-RARE-3: ERA-Net cofund for Research Programmes on Rare Diseases. Call (not cofunded): Innovative projects in rare disease research. Budget of €15 million, 21 funding agencies from 17 countries, 15 projects funded, of which three have the participation of four Spanish research groups, two of them as coordinators. The Spanish funding agency is the ISCIII:
7. EJP RD: European Joint Programme cofund for Rare Diseases. In preparation. Cofunding from the EU totals €55 million for five years (2019-2023) with an overall intensity of up to 70%. It is expected to have four pillars and five multidisciplinary work packets. It will launch four annual calls (the first two cofunded by the EU).
8. JPND: The Joint Programming on Neurodegenerative Disease Research
 - 8.1. JPstaiND: CSA in support of the sustainability and globalisation of the Joint Programming Initiative on Neurodegenerative Diseases. ISCIII is a coleader of work packet 2 (long-term sustainability) and contributor to work packet 3 (capacity extension), exploring the strengthening of the relationship with CELAC (Community of Latin American and Caribbean States) countries, and work packet 4 (alignment and outreach).
 - 8.2. JPco-fuND: ERA-NET cofund for establishing synergies between the Joint Programming on Neurodegenerative Diseases Research and Horizon 2020. Call (not cofunded): “Pathway analysis across neurodegenerative diseases”. Budget of €23 million, 22 funding agencies from 21 countries, 23 projects funded, of which two have the participation of Spanish re-

search groups, one of them as coordinator.

9. JPI MYBL Joint Programming Initiative: More Years Better Lives. Ageing and demographic change.
 - 9.1. J-AGE-II: CSA for implementation and alignment activities of the Joint Programming Initiative (JPI) ‘More Years – Better Lives – the Challenges and Opportunities of Demographic Change’.
 - 9.2. Call (not cofunded): “Ageing and place in a digitising world”. Budget of €6.2 million, 14 funding agencies from ten countries. For Spain, the funders are AEI-MINECO and ISCIII. ISCIII led work packet 2 (implementation), managing the secretariat of the call and also contributing to work packet 3 (alignment and monitoring of research programmes and policy) in relation to strengthening the relationship with CELAC (Community of Latin American and Caribbean States) countries.

Initiative based on Article 185 of the Treaty on the Functioning of the European Union

10. AAL-2: Active and Assisted Living Programme (2014-2020). To fund applied research for improving the lives of the elderly and to strengthen the European industrial fabric through demand for new products, systems, and/or services based on digitalisation and information and communications technology (ICT). It funds projects (Challenge-led cofunded call for proposals: “AAL packages/Integrated solutions” - budget: €16 million), the annual AAL forum, and other support measures such as the market observatory and the AAL2business, and the framework for interaction with investors. Seventeen EU countries, Norway, Switzerland, Israel, and Canada participate. Spain is represented by the MINETAD and the ISCIII, whose representative holds the Presidency (half of the second term).

FP7 – Health – Scope: Biregional EU - Latin America and Caribbean countries

11. EU-LAC Health: CSA “Defining a Roadmap for Cooperative Health Research between the EU and Latin America-Caribbean Countries: a Policy-Oriented Approach”.
 - 11.1. It is coordinated by ISCIII and funded by the FP7. It has also provided scientific and technical support to the health working group of the Senior Officers’ Meeting (SOM) of the Joint Initiative for Research and Innovation (JIRI) between the EU and CELAC (Community of Latin American and Caribbean States).
 - 11.2. Joint Transnational Call on Health Research and Innovation



INTERNATIONALISATION

5.1 International Programmes

(Topic: infectious diseases; Topic: neurodegeneration). Budget of €6.6 million, 21 funding agencies from 19 European and Latin American and Caribbean countries, 13 biregional projects funded, of which four include Spanish participation by the ISCIII. Two of these four are paid for by the AES, one is intramural, and the fourth biregional project is paid for in kind without an additional budget. It is a continuation of the biregional calls of the ERA-Net LAC.

B) H2020 – Societal Challenge 1 – Scope: Infectious Diseases

12.JPI AMR: Joint Programming Initiative on Antimicrobial Resistance Research. ISCIII is the institution affiliated with the President.

12.1. EXEDRA: CSA Towards Globalisation of the Joint Programming Initiative on Antimicrobial Resistance. ISCIII is the leader of work packet 2 (strategy, governance, and long-term sustainability) and a contributor to work packet 3 (globalisation and capacity extension), exploring strengthening the relationship with CELAC countries, as well as work packet 5 (research alignment in relation to the AMR Virtual Research Institute's project). AEI-MINECO also participates for Spain.

12.2. JPI-EC-AMR: ERA-Net Cofund for establishing synergies between the Joint Programming Initiative on Antimicrobial Resistance Research and Horizon 2020. Call (not cofunded): Comparison of prevention, control, and intervention strategies to prevent development, transmission, and infection caused by AMR through multidisciplinary studies including One Health approach. Budget of €27.3 million, 16 funding agencies from 15 countries.

Initiative based on Article 185 of the Treaty on the Functioning of the European Union

13. EDCTP-2: The European & Developing Countries Clinical Trials Partnership. Joint Research Programme 2014-2020 to fund clinical trials on forgotten diseases between the 15 participating EU countries and Switzerland and those of Sub-Saharan Africa, and to develop capacities for dealing with these ailments in this region of the world. The EU's cofunding for the septennium is €680 million. Spain is represented by ISCIII with a current initial commitment of €200,000 annually.

C) H2020 – Societal Challenge 2 - Scope: Bioeconomics

14.JPI HDHL: Joint Programming Initiative: A Healthy Diet for Healthy Life.

14.1. HDHL CSA 2.0: The second CSA for the JPI Healthy Diet for a Healthy Life. ISCIII is a contributor to work packet 2 (alignment of research activities and programmes on national, European and international level), exploring strengthening the relationship with CELAC countries, as well as work packet 5 (strategy and sustainability of the JPI HDHL).

14.2. ERA HDHL: ERA-NET cofund Biomarkers for Nutrition and Health implementing the JPI HDHL objectives. Call (not cofunded), in preparation: epigenome and Nutrition. It will be launched in the first quarter of 2018. The funders from Spain will be AEI-MINECO and the ISCIII.

14.3. HDHL INTIMIC: ERA-Net cofund INTesTInal MICrobiomics, diet and health, implementing JPI HDHL objectives. Call (not cofunded): Biomarkers in Nutrition and Health. Budget of €8.65 million, 12 funding agencies from nine countries, 15 projects funded, one of them with Spanish coordination funded by the ISCIII. In Spain, the AEI-MINECO also participated as a funder.

D) H2020 – Challenge: Industrial Leadership. Scope: Transnational I Key Enabling Technologies (KET)

15. EuroNanoMed III: ERA-Net cofund on NanoMedicine. Call (cofunded): European Innovative Research & Technological Development Projects in Nanomedicine. Budget of €14 million, 22 funding agencies, 16 projects funded, among them five with the participation of Spanish groups funded by the ISCIII. In Spain, the CDTI and AEI-MINECO also participated as funders.

Horizon 2020: Actions for Promotion and Results:

H2020 is the main international programme which funds research and innovation projects in different thematic areas in the European context. It has nearly €80 billion in community funding for the 2014-2020 period.

At the ISCIII's European Project Office, 2017 has been a year of intense work on raising awareness, promoting, and disseminating the Horizon 2020 (H2020) programme and the opportunities that are available in the area of health sciences. Activity during this period has focused on promotion, training, and support in the preparation of proposals. More than 20 training courses and workshops were organised and more than 40 other training actions were cooperated with. In addition, workshops promoting H2020 were held throughout the whole country to promote the next calls for the remaining years

5 INTERNATIONALISATION

5.1 International Programmes

(2018-2020). Calls for Societal Challenge 1 will be published yearly for nearly €1 billion. In order to contribute to this dissemination, consulting, and training activities, 12 informational newsletters were published and the website was updated continually. It is available at <http://eu-isciii.es>.

Within the Societal Challenge 1, the Spanish participation in 2017 has continued on the good path that was started in 2015 and 2016, both in terms of successful participation as well as in leadership. In total, since the launch of H2020 (2014-2017 period), Spain has coordinated 98 projects of the total of 690 actions funded in total, coming in second at EU level in terms of coordinated projects (14.20%). Translating this leadership into grants obtained, it should be highlighted that overall, with figures from the end of grants, Spain obtained accumulated funding for H2020 societal challenge one of more than €200 million for those four years 2014-17. This means a financial return of 9.56% over EU 28 funding. This means that Spain is getting back more funds than it provides as funding, so it is not any longer a net contributor to health research in this programme. This milestone places Spain in fifth position in the area of health, behind only the United Kingdom (21.14%), Germany (14.34%), the Netherlands (12.63%), and France (9.88%). On top of this return financial rate, the pull effect of ISCIII environment along with the National Health System should be noted, with nearly €94 million in direct returns, which represents 47% of successful participations and 42.5% of these financial returns (EU 28).

Additionally, it should be highlighted that in 2017, 17 proposals were submitted to the different international programmes (H2020, COST, DG SANTÉ). Four of them were funded, a success rate of nearly 25%, a higher figure than the habitual rate of around 10%.

The 2014 - 2020 EU Health Programme of the Directorate-General for Health and Food Safety of the EC (DG SANTÉ)

The EU's Health Programme has the objective of driving activities aimed at promoting health and preventing disease; being more prepared to protect citizens from health emergencies; coordinating responses on the European scale; supporting public health training; contributing to innovative, efficient, and sustainable healthcare; and lastly, improving access to specialised medicine in the case of specific diseases and strengthening healthcare and patient safety. The 28 EU member states as well as Iceland, Norway, Serbia, and Moldova participate in this programme.

In the 2017 work programme, the approved budget was €60.4 million. It was distributed for: grants (€38.85 million), prizes (€60,000), tenders (€14.5 mi-

llion), and other actions (€7.2 million).

Topics funded in 2017 were:

- “Supporting member states in mainstreaming health promotion and disease prevention in health and educational settings”: €250,000.
- European Reference Networks (ERNs): €4.6 million.

5 INTERNATIONALISATION

5.1 International Programmes

5 INTERNATIONALISATION

5.1 International Programmes

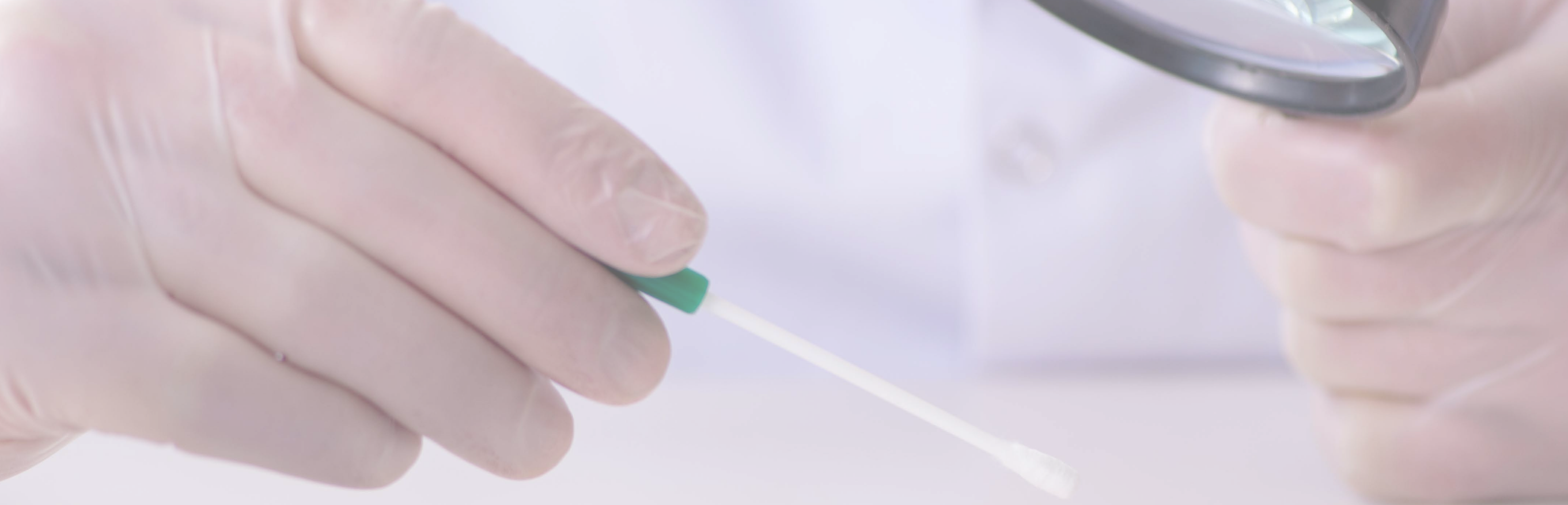
In addition, Joint Actions (JAs) were launched with a budget of €19.7 million, summarised in the following table.

The dissemination activities of the EU's Health Programme in Spain, which

JOINT ACTIONS (JAs)	NOMINATIONS	Partners, SPAIN	EU, COFUNDING
JA-01-2017: Inequalities in health	28	EASP, Andalusia	€2.5 million
JA-02-2017: Innovative consortia to fight against cancer	27	Catalan Institute of Oncology	€4.5 million
JA-03-2017: Vaccines	24	Miguel Servet Foundation - NA-VARRABIOMED	€3 million
JA-04-2017: Preparation and action at border entry points (air, sea, and land)	21	SG Foreign Health, MSCBS	€3 million
JA-05-2017: Electronic health (e-health)	30	SG Healthcare Information and Innovation, MSCBS	€2.7 million
JA-06-2017: Healthcare information	30	ISCIII	€4 million

have been promoted by the Contact Point located in the ISCIII, included the following:

- SEISIDA (Spanish Interdisciplinary AIDS Society): Seville, 21-22 March 2017.
- Rare Diseases Registries Workshop: Madrid, 21-22 March 2017.
- World Tuberculosis Day: Barcelona, 23 March 2017.
- Public Health Conference. Preparedness, Alert, and Response: Lessons Learned in Europe from the Last Cross-Border Health Infectious Threats: ISCIII, Madrid, 15 June 2017.
- Spanish Society of Epidemiology: Barcelona. 6-8 September 2017.



6

REGULATIONS, ETHICS

- 6.1 Advisory Committee for Human Tissue and Cell Donation and Use; the National Registry of Research Projects
- 6.2 National Register of Biobanks
- 6.3 Bioethics Committee
- 6.4 Research Ethics Committee (CEI)
- 6.5 Research Ethics and Animal Welfare Committee (CElyBA)

6.1 ADVISORY COMMITTEE FOR HUMAN TISSUE AND CELL DONATION AND USE; THE NATIONAL REGISTRY OF RESEARCH PROJECTS

The 14/2007 Law, dated on 3 July, on Biomedical Research, creates the Advisory Committee for Human Tissue and Cell Donation and Use, as a collegiate body, affiliated to ISCIII. It is a permanent and consultative body that is designed to advise and orient regarding research and experimentation with human embryo biological samples and tissues, and to contribute to update and disseminate scientific and technical knowledge on this matter.

In 2017, this body held four meetings within 41 research projects received information.

6.2 NATIONAL REGISTER OF BIOBANKS

The National Register of Biobanks was created by the same Biomedical Research Law, and implemented through the 1716/2011 Royal Decree, dated on 18 November, establishes the basic requirements for authorising and operating biobanks for biomedical research purposes and for handling biological samples of human origin. It regulates the operation and organisation of the National Registry of Biobanks for biomedical research.

As of 31 December, 95 biobanks and 1,555 collections were included in the registry. Within 2017, three new biobanks and 138 new collections were registered and integrated.

6.3 THE SPANISH BIOETHICS COMMITTEE

The Spanish Bioethics Committee (CBE), was created by the 14/2007 Law. It is an independent collegiate body for consultation on matters related to the ethical and social implications of Biomedicine and Health Sciences.

During 2017, the following reports were approved: "Public Funding of Pre-Exposure Prophylaxis Medication (PrEP) in HIV Prevention"; "Report from the

Spanish Bioethics Committee on Ethical and Legal Aspects of Surrogate Maternity"; and the report requested by the MSCBS on "Adaptation of Spanish Legislation to the UN's Convention on Disability".

6.4 RESEARCH ETHICS COMMITTEE

Projects reported on

During 2017, 96 research projects on human beings were reviewed. These projects came from ISCIII's centres and from the Foundations affiliated to the Institute.

Training and Dissemination Activities

Organisation and execution of the internal training course "Ethics of Research in Human Beings: Good Clinical Practices", at the ENS from 22 to 26 May and the IV Bioethics Congress: "New Challenges: European Data Protection Regulations, Big Data, and the Evaluation of Healthcare Technologies", on 17 and 18 November in ISCIII's Ernest Lluch conference hall.I.

6.5 RESEARCH ETHICS AND ANIMAL WELFARE COMMITTEE

During 2017, 22 research projects with animal procedures were reviewed. These projects came from ISCIII's centres and from the Foundations affiliated with the Institute as well as other centres outside the ISCIII.

6 REGULATIONS, ETHICS

- 6.1 Advisory Committee for Human Tissue and Cell Donation and Use; the National Registry of Research Projects
- 6.2 National Register of Biobanks
- 6.3 Bioethics Committee
- 6.4 Research Ethics Committee (CEI)
- 6.5 Research Ethics and Animal Welfare Committee (CElyBA)



Instituto
de Salud
Carlos III

ANNUAL REPORT **2017**

