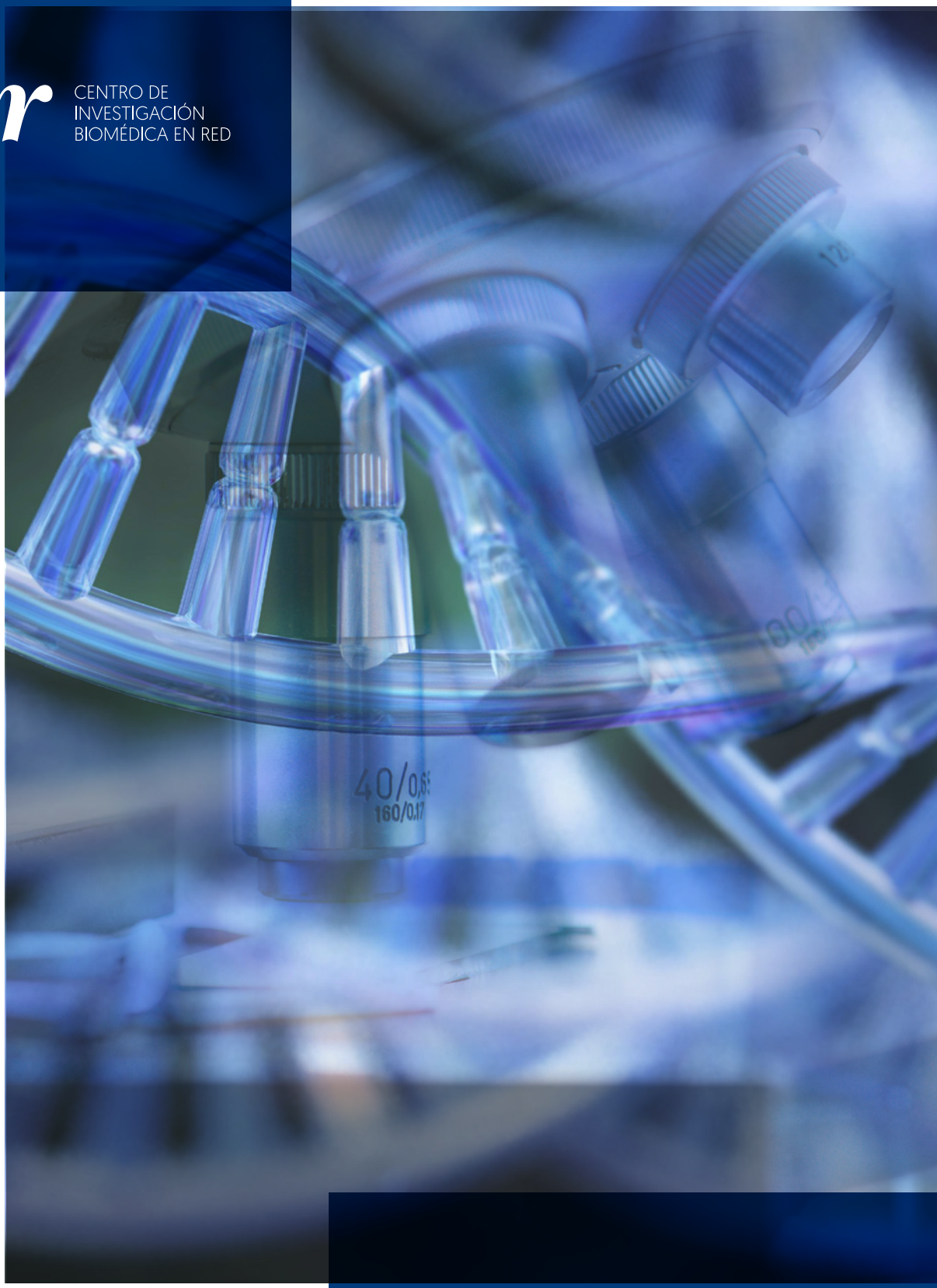
ciber

CENTRO DE
INVESTIGACIÓN
BIOMÉDICA EN RED



2023 ANNUAL REPORT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INDEX

BIOMEDICAL RESEARCH NETWORKING CENTER CONSORTIUM (CIBER)

THEMATIC AREAS OF RESEARCH

WELCOME FROM THE PRESIDENT OF CIBER'S GOVERNING BOARD

Marina Pollán Santamaría

It is a great pleasure for me to introduce this Report of the CIBER Consortium, where I have been involved as director of the Epidemiology and Public Health area (CIBERESP) and of which I will continue to be a part as a researcher. The CIBER Consortium, promoted by the Instituto de Salud Carlos III, has been growing since its inception and is now consolidated as a center of great stature, not only on account of its size but also because of its relevance within the system. Cristobal Belda deserves special mention because, as director of the Instituto de Salud Carlos III, he promoted the development of the consortium, as well as other structures and projects necessary for research in our country to continue to achieve great results.

This Report includes some of the most relevant activities that have taken place during 2023 within the thirteen thematic areas that make up the CIBER Consortium and the 509 research groups belonging to its 104 consortium member institutions.

I would of course like to thank the enormous work carried out by the CIBER research staff, always geared towards improving the health of the population through the prevention, diagnosis and treatment of the main diseases. They, a staff of more than 6,725 people between contracted and assigned personnel, are the ones who make all this possible.

During 2023, ten new groups of excellence in different areas were incorporated into the CIBER to conduct research in fields such as biomaterials, cardiovascular diseases, mental health, liver and digestive diseases, rare diseases, respiratory diseases, frailty and healthy ageing. Thus, the new groups came in to cover some of the needs identified in the research programs of the areas and contribute to the excellence and efficiency of the consortium. Four areas of the CIBER changed their scientific leadership, three of them led by women, furthering the promotion of female leadership and equality.

Among the highlights of the year 2023, to be noted here is the approval of the First Strategic Plan of the Consortium. This document provides an opportunity to boost cohesion and efficiency within the Consortium and will allow a better approach to the major challenges in health thanks to collaborative research and excellence. Some of the strategic actions that are outlined include the development of an HR policy, the creation of communication spaces between areas and Open Innovation programs, to name but a few.

Some of the actions implemented in the 2023 period will be of great importance for the Consortium in the coming years. One of these is the start of the ARISTOS program, a strategic project in Biomedicine and Health Sciences, led by the CIBER, which offers 27 positions for postdoctoral research personnel with highly competitive conditions. ARISTOS offers international, cross-sectoral and interdisciplinary research opportunities for postdoctoral staff who will be able to carry out their project within a CIBER group for a period of three years. The project is framed within the Horizon Europe program and the Marie Sklodowska-Curie actions and includes the participation and involvement of the 13 thematic areas of the CIBER.

At the same time, other national and international projects of great relevance were initiated. The MePRAM project or Immune4ALL, the latter with the participation of 4 CIBER areas, started in 2023 with highly innovative proposals for antimicrobial resistance or immunotherapy for solid tumors. Similarly, the EPROBES project kicked off in July. The European initiative, led by the CIBER, addresses the problem of obesity and its context using Artificial Intelligence.

To give some noteworthy figures, during the year 2023, the CIBER Consortium achieved over 4.5 million euros in funding through competitive funds and the awarding of 25 European projects. The scientific production of the CIBER has maintained its rates of previous periods with a total of 8,456 articles published in 2023 with over 64% being first quartile publications. In this period, 28 new inventions were also presented.

The CIBER Technology Development Platform and the Knowledge Transfer Office continued to work during 2023 on strengthening alliances and improving the processes of valorization, transfer and commercialization of technologies in the CIBER. In this regard, worth mentioning is the collaboration in the AseBio-TERAV-CIBER Forum on advanced therapies that took place in October at the Instituto de Salud Carlos III or the CIBER's participation in Transfiere and Biospain, forums where we work together with the industry in actions that allow us to reach patients more effectively.

With this patient-oriented approach, every year the "Investigar es Avanzar (Research is Progress)" conference is held, where space is shared with patient associations to strengthen ties and improve research, as well as the meeting of the Mental Health area. Other meetings of key importance are those aimed at young research personnel, among which we can highlight the conference for young people from the CIBER area of Cancer together with the CIBER of Obesity and Nutrition held in November at the University of Malaga and that of the respiratory diseases area held together with the infectious diseases area in the month of June in Madrid.

The Scientific Culture and Innovation Unit of the CIBER has also taken important steps during 2023 in maintaining the involvement of the research staff in dissemination and outreach tasks and strengthening ties with other institutions through the UCC+I. As a result of this institutional collaboration, activities have been carried out such as a round table at the Cancer Research Center of Salamanca coinciding with the 11th of February or the first edition of the Course on Communication and Dissemination of Science for CIBER personnel.

The great social interest of some of the research topics addressed by the CIBER makes it necessary to explain them in detail to the media, as was the case of the press conference on the report on the evolution of suicide in Spain, together with the Complutense University of Madrid. The data presented point to a growing trend in suicide mortality in Spain; one of the great health challenges to be addressed by all Spanish institutions, where efforts must be united to reverse the trend.

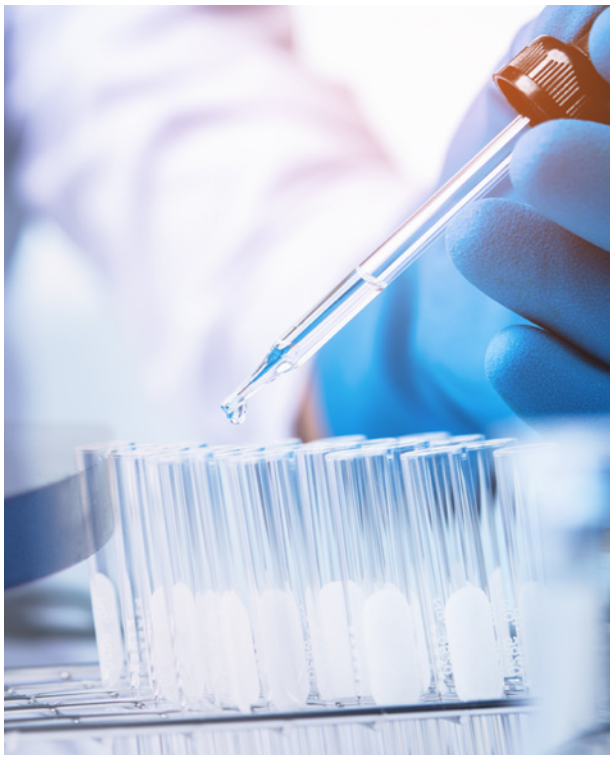
I cannot end these lines without highlighting the progress of the IMPaCT projects, and the work of the CIBER in the development of the Genomics and Impact Cohort axes. During the past year we have witnessed the unfolding of these projects, which are so important for Spanish science. The three IMPaCT axes were represented at a satellite event prior to the Conference on Personalized Medicine organized by the Spanish Presidency of the European Union in October at the Príncipe Felipe Research Center in Valencia.

INTERNAL ORGANIZATION

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

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

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



The CIBER currently has a staff of 810 people and 6,725 attached researchers, integrated within more than 500 research groups working in different locations, linked to more than 100 consortium institutions, belonging to different Administrations, Institutions and Autonomous Communities, from both the public and private sectors.

The governing, management and administrative bodies are as follows:

Governing Board and Permanent Commission

The **Governing Board**, chaired by the ISCIII Directorate, is made up of three ISCIII representatives and one institutional representative for each of the institutions in the consortium, appointed by their highest authority. It meets every six months.

The **Permanent Commission** is a delegated committee, formed by the ISCIII and 8 members of the Governing Board, and can be renewed annually. Both the functioning and the purposes of the governing, support and advisory bodies are established in the CIBER statutes.

Steering Committee and Advisory Committees

In each CIBER area there is a Steering Committee and an External Scientific Advisory Committee.

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

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

Scientific Directors

The Scientific Directors of the CIBER represent each of the thematic areas and chair the Steering Committees. During 2023, they were the following:

- **CIBER-BBN**
  Dr. Ramón Martínez Máñez
- **CIBERCV**
  Dr. Javier Bermejo Thomas
- **CIBERDEM**
  Dr. Eduard Montanya Mías
- **CIBEREHD**
  Dr. Rafael Bañares Cañizares
- **CIBERER**
  Dr. Pablo Lapunzina Badía
- **CIBERES**
  Dra. María Molina Molina
- **CIBERESP**
  Dra. Marina Pollán Santamaría
- **CIBERFES**
  Dr. Leocadio Rodríguez Mañas
- **CIBERINFEC**
  Dr. Jesús Oteo Iglesias
- **CIBERNED**
  Dr. Adolfo López de Munain
- **CIBEROBN**
  Dra. Mª del Puy Portillo Baquedano
- **CIBERONC**
  Dra. Anna Bigas Salvans
- **CIBERSAM**
  Dra. Ana González-Pinto Arrillaga

Code of Ethics

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

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

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

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

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

- Legal compliance
- Commitment to CIBER
- Professionalism
- Responsibility
- Complimentary gifts, courtesies and presents
- Conflict of interests
- Relations with suppliers
- Relations with other institutions
- Selection process
- Dissemination of information
- Confidential and restricted information
- Protection of personal data
- Performance of other activities
- Use of resources and means for the development of one's professional activity
- Care of facilities, equipment, spaces and rational use of resources
- Protection of assets

For more information, see the latest version of the CIBER Code of Ethics at:

https://www.ciberisciii.es/media/3101942/codigo-etico-ciber-v0.pdf

CIBER IN FIGURES

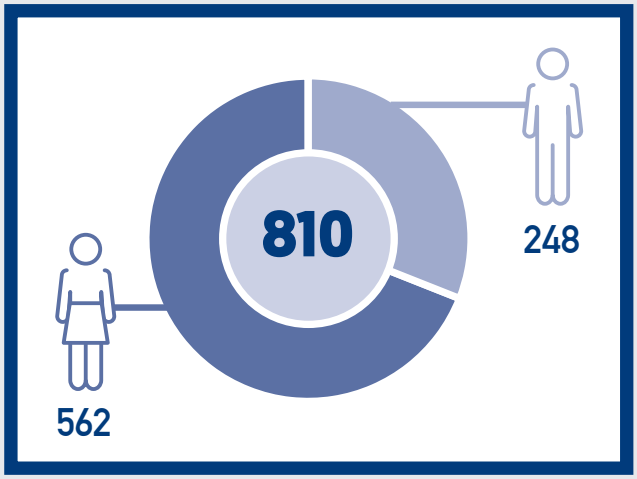
ECONOMIC DATA

TOTAL INCOME 2023

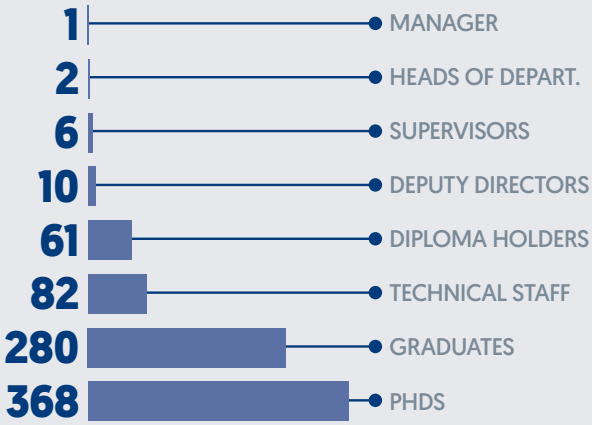
41.754.950,00 €

PERSONNEL

TOTAL BY GENDER



TOTAL BY CATEGORY

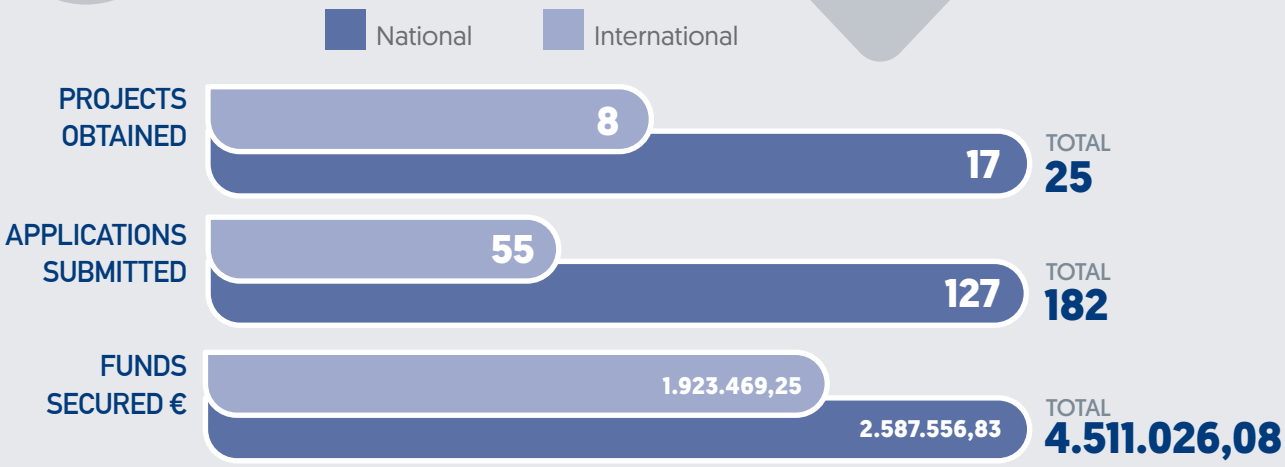


PRODUCTIVITY

TOTAL PUBLICATIONS 2023

8.456

PROJECTS



TRANSFER

COMUNICATION

PRESS RELEASES **147**
NEWS **809**
AGENDA EVENTS **452**
WEBSITE VISITS **331.110**
WEBSITE USERS **76.000**

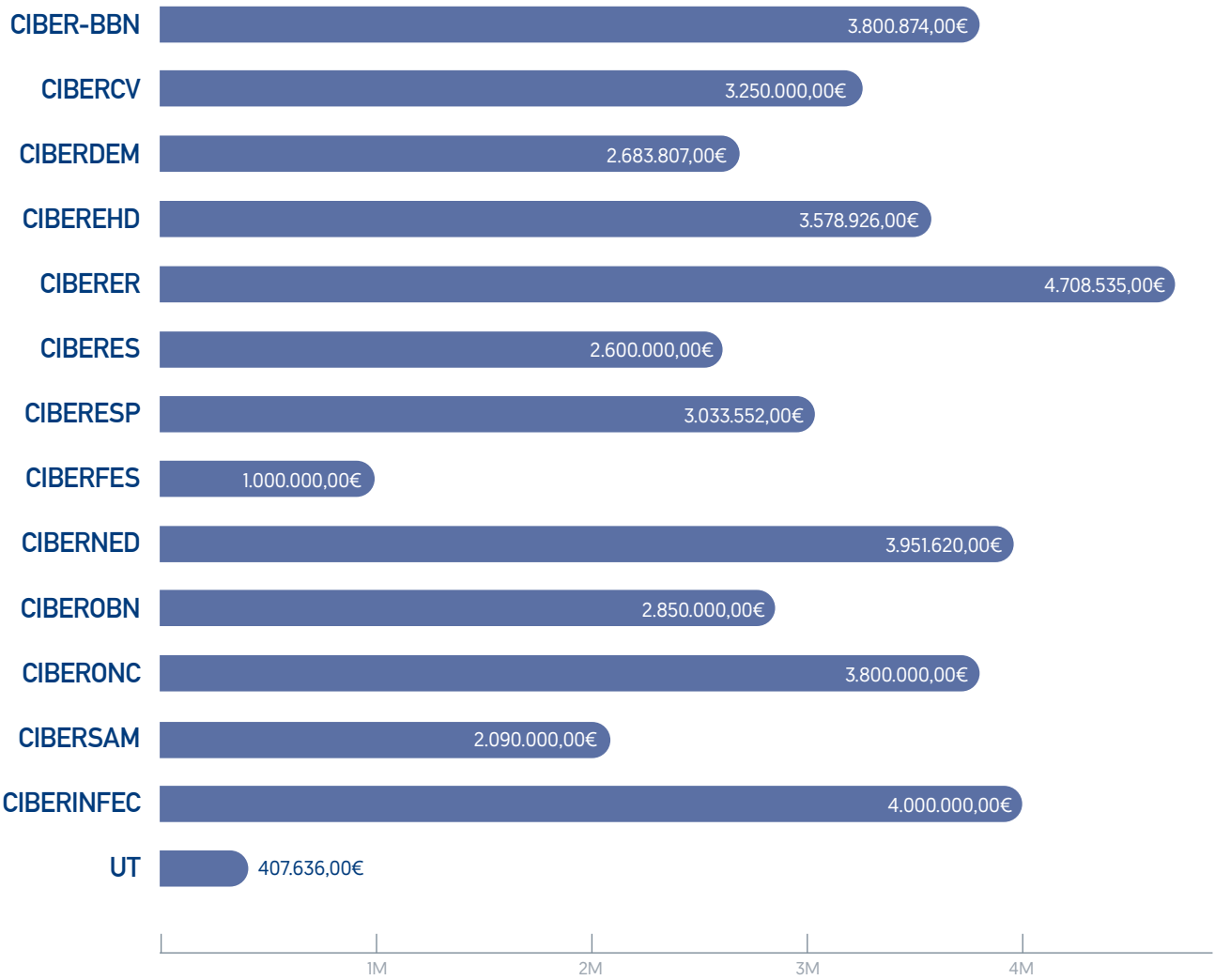
12.464 MEDIA IMPACTS
PRESS
INTERNET
RADIO & TV

928 YOUTUBE SUBSCRIBERS

69.858 FOLLOWEWRS IN **14** X ACCOUNTS

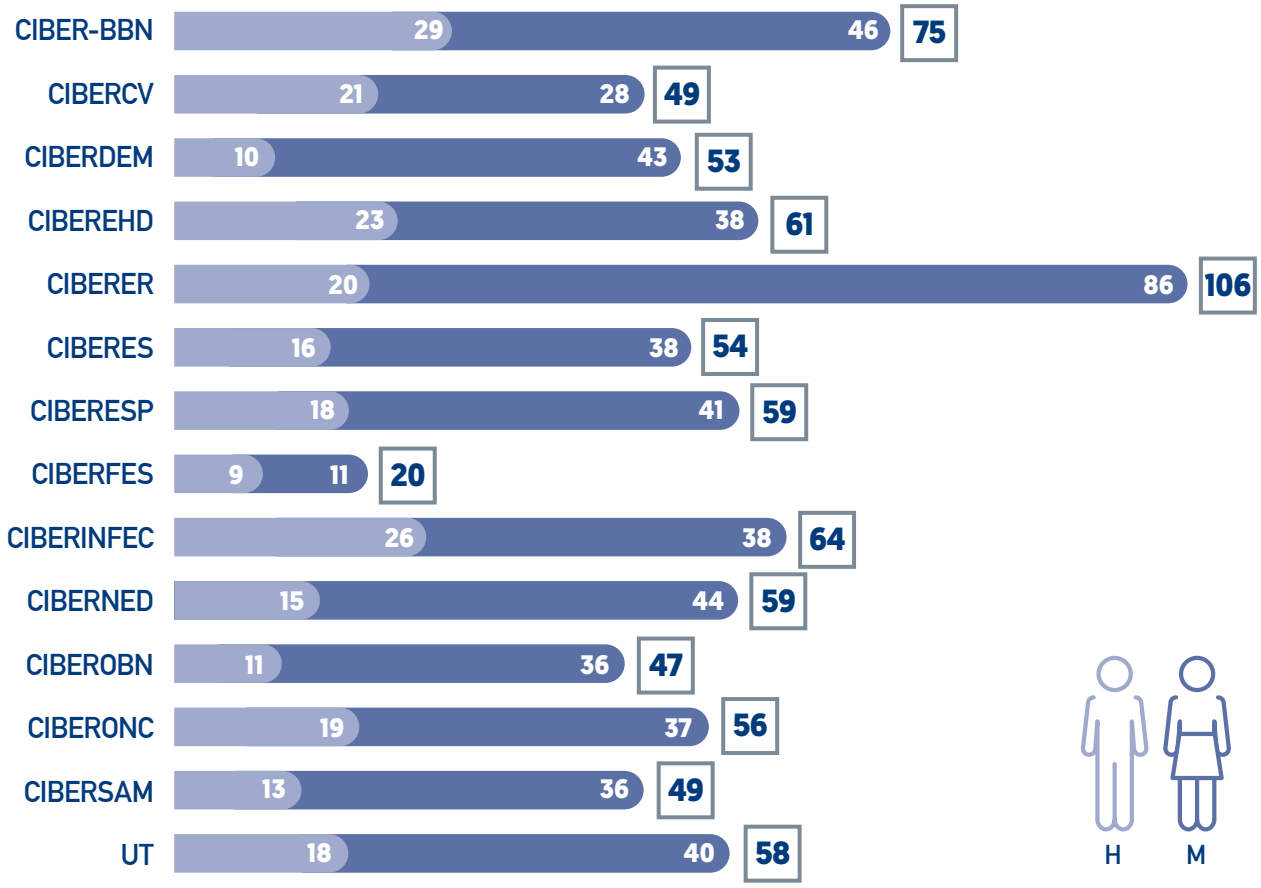
ECONOMIC DATA

Resources obtained by area in 2023

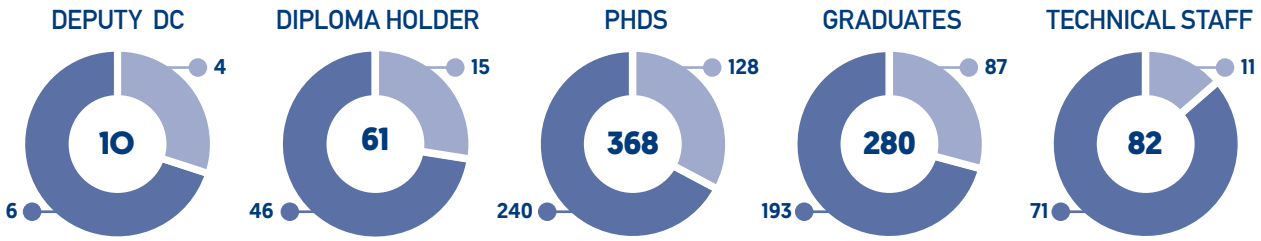


PERSONNEL

Contracted personnel by area and gender



ontracted personnel by category and gender



TRANSFER

Indicators

One of the main objectives of the CIBER is to transfer the knowledge generated by its research groups to society. In such a way that the research results are developed into protocols, services and products for the improvement of clinical practice and the quality of life of the population. To this end, the Knowledge Transfer area of the CIBER, formed by the Technological Development Platform and the Knowledge Transfer Office, serves as a link between our research personnel and other agents in the system (companies, private entities, associations, research agencies and others) to ensure effective cooperation with them so that the research results can be applied.

Throughout 2023 in the CIBER, 24 new priority patent applications were filed and there were four new software developments. In addition, 7 licensing contracts have been signed (3 from the CIBERER area, 2 from the CIBERNED area and 1 from the CIBERESP area) and 1 licensing option (CIBER-BBN area):

Technological Development Platform

During the year 2023, the CIBER Technological Development Platform was launched with the incorporation of 8 areas. During this year, 112 projects (intramural or external competitive projects managed by CIBER) have been analyzed (data as of December 2023) and meetings have been held with 117 CIBER research groups to learn about their lines of research. In addition, the platform's internal file management tool and the Knowledge Transfer Office have been developed for project monitoring and evaluation.

CIBER Innova Initiative

In 2023 a call for projects was launched to CIBER groups called CIBER Innova, which aimed to identify and assess therapeutic development and early-stage projects being carried out by CIBER groups. Once identified, these projects will form part of the CIBER project portfolio and, therefore, will be accompanied in the search for investment, funding, collaborations, etc., for their development and better valorization. Thus, by identifying them, classifying them and supporting them, a better transfer to the productive and clinical sectors will be promoted. Eighty-nine expressions of interest were received.

In addition, 60 of these were evaluated by the Kertor Foundation and were provided with a valuation report that will serve as a basis for the categorization and valuation of these projects.

Other outreach and collaboration actions with the system include:

- Attendance at scientific fairs in collaboration with the ISCIII and other entities in its field: the Transfiere Forum and BIOSPAIN 2023 were attended. More than 50 meetings were held at the latter fair with companies and investment funds, and further work was carried out with them after the event.
- Organization of the II ASEBIO-TERAV-CIBER Thematic Forum on Advanced Therapies (Madrid, ISCIII. October 31, 2023.
- Strategic cooperation with Farmaindustria. A meeting was held in spring 2023 with the association and its partners to present the CIBER's capabilities in public-private cooperation, followed by bilateral meetings with several companies to seek collaborations.
- In this regard, work has continued on supporting research personnel in applying for innovative projects and in participating in openn innovation programs, for exemple, 13 proposals were sudmitted to the FarmaBiotech program (Farmaindustria) and support was given to 5 Caixa Impulse projects presented from CIBER and other technology institutions with CIBER participation.
- In addition, work has continued on supporting the creation of spin-offs, commercialization, attendance at fairs, organization of events, dissemination and outreach, among other activities.

GENDER EQUALITY PLAN

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

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

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

Among the matters covered by gender equality plans are female under-representation, access to employment, professional classification, professional promotion and training, remuneration, work-life balance, working conditions and the prevention of sexual harassment and harassment based on gender.

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

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

In 2023, the CIBER's transversal training plan (2023-2025) included training in equal opportunities, as well as in the prevention of sexual or gender-based harassment. The aim of training in equality is to raise awareness of the problem of gender inequality and its direct consequences in the work and business environment, the ultimate objective being to avoid discrimination based on gender in the workplace. Training in the prevention of sexual or gender-based harassment is aimed at acquiring the appropriate training to adopt measures aimed at preventing sexual or gender-based harassment at work, guaranteeing a work environment free of discrimination and ensuring a healthy work environment.

For more information, please check the CIBER 2022-2026 Equality Plan at:

https://www.ciberisciii.es/media/3072366/plan-igualdad-ciber.pdf

COMMUNICATION

12 relevant CIBER news in 2023

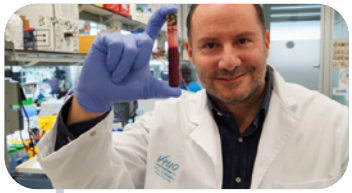
1 In January, the evolution of suicide in Spain in this millennium (from 2000-2021) was presented at a press conference.

2 On February 11th, the International Day of Women and Girls in Science, the Cancer Research Center (CIC) and CIBER joined forces to bring science closer to adolescent girls.

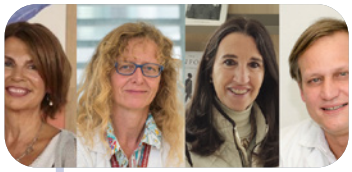
3 EThe Immune4All Project, which explores the feasibility of biomarkers for immunotherapy in solid tumors, began in March with the participation of 4 CIBER areas.

4 In mid-April, the pilot study of the IMPaCT Cohort was launched in 4 Autonomous Communities, which will analyze in 200,000 people why the Spanish population becomes ill and how to prevent this.

5 In May, CIBER researchers in collaboration with VHIR developed a new liquid biopsy tool that increases by 30% the sensitivity of tumor DNA detection in plasma.



6 In June, the Scientific Leadership of 4 areas of the CIBER Consortium was renewed with the appointments of: Ana González-Pinto (CIBERSAM), María Molina (CIBERES), María Puy Portillo (CIBEROBN) and Javier Bermejo (CIBERCV).



7 In July, the European eprObes Project for the prevention of childhood obesity, with a funding of 10M€, was presented.

8 A study published in August analyzed the spread of monkeypox according to geographic areas and different population groups.

9 EIn September three CIBER researchers received the National Research Award: Jesús Jiménez Barbero (CIBERES), José López Barneo (CIBERNED) and Rodrigo Fernández Jiménez (CIBERCV).

10 In October, the results of IMPaCT-GENóMICA were presented, a program that lays the groundwork for improving highly complex genetic diagnostics on an equitable basis throughout Spain.

11 In November, the second edition of the AseBio-TERAV-CIBER Forum connected academic research and the industrial capabilities of the Spanish biotechnology sector in advanced therapies.

12 In December, the incorporation of ten new groups of excellence to the Biomedical Research Networking Center (CIBER) was approved.

ACTIVIDADES DE LA UNIDAD DE CULTURA CIENTÍFICA 2023

Feb.11: "Demystifying myths about women scientists"

On the occasion of the International Day of Women and Girls in Science, a round table was organized collaboratively between the Scientific Culture Units of the Cancer Research Center (CIC) CSIC-University of Salamanca and CIBER. To kick off this round table - held in Salamanca at the CIC headquarters - challenging questions were posed to high school students about the participation of women in science. Marina García Macía (CIBERFES), David Martín Hernández (CIBERSAM) Isabel Rojas de Pablo (CIBERONC) and Pablo Ramos Hernández (University of Salamanca), shared their research and passions, seeking to demystify the erroneous perception that scientists are "weirdos". They addressed myths such as the idea that scientific careers are for men, that one needs an innate vocation to be a scientist, among others. Students actively participated by expressing their agreement or disagreement with these myths. The round table concluded with positive messages about the role of women in scientific research and the importance of collaboration between research centers.

>> More information

Madrid Science Week

#ImproCiencia. Science and theater came together again in the fifth edition of #ImproCiencia, the traditional CIBER science outreach event of the Madrid Science Week. Our researchers Elena González (CIBER), María Insenser (CIBERDEM), Jéssica González (CIBERES) and Javier Santos (CIBEREHD) presented a small sample of the research carried out at the center to high school students.

The setting for this annual event, which took place on November 14, was the Ernest Lluch auditorium of the Instituto de Salud Carlos III, on the Chamartín Campus.

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

>> Video summary

>> More information

First CIBER course on Communication and dissemination of science

On May 25th and 26th, the first course on the communication and dissemination of science aimed exclusively at CIBER contracted research staff took place in Zaragoza.

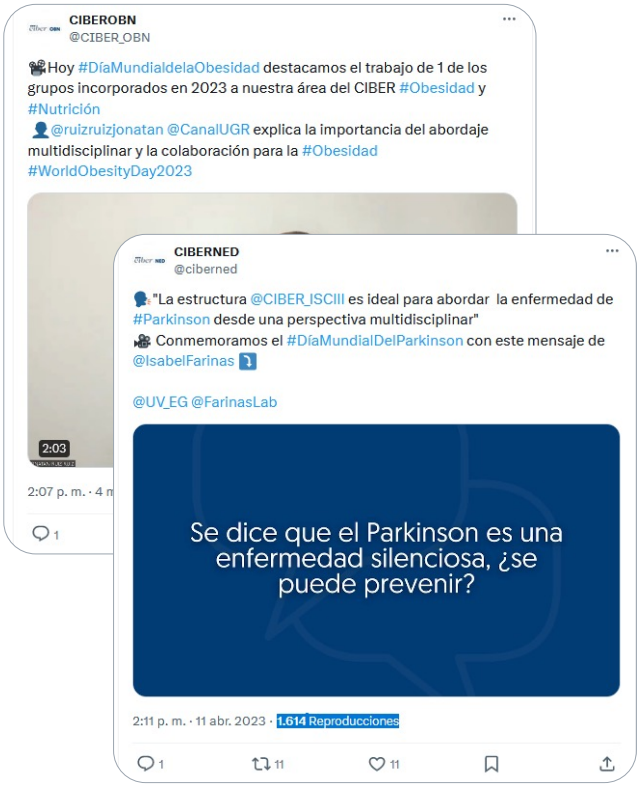
The course, organized by the Scientific Culture and Innovation Unit (UCC+i) of the CIBER, had the collaboration of IIS Aragón, the University of Zaragoza and several UCC+i of the same university, as well as that of the Complutense University of Madrid (UCM). The program included a theoretical and a practical part where CIBER speakers and UCC+i staff shared their presentations.

Nearly 50 researchers from the different areas of the CIBER were able to share during these days the keys to maintain an effective relationship with the media, the main tools for dissemination, as well as to learn first-hand about the experiences of other CIBER colleagues.

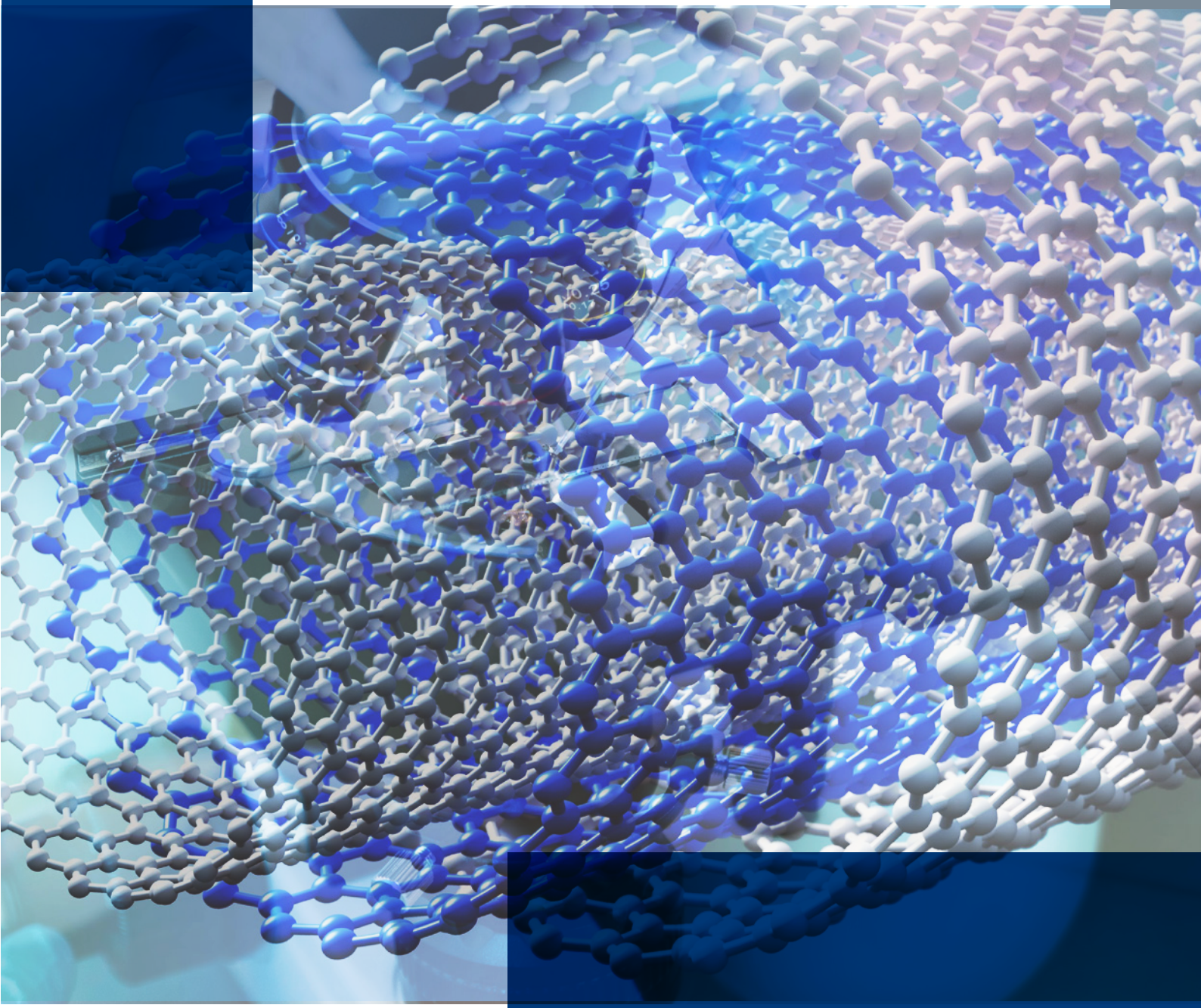
The course was held at the CIBA facilities and the University of Zaragoza.

Social media campaigns

Throughout the year, several campaigns were also carried out on social networks on the occasion of various World Days related to different pathologies. The campaigns involved the participation of CIBER research staff aimed at raising awareness of neurodegenerative diseases such as ALS, Parkinson's and Alzheimer's, as well as cancer and obesity. These Twitter campaigns, with more than 1,600 video views, were mainly aimed at raising public awareness of these diseases, promoting prevention and supporting patients and their families.



BIOENGINEERING, BIOMATERIALS & NANOMEDICINE



ciber | BBN

WELCOME FROM THE SCIENTIFIC DIRECTOR

Ramón Martínez Máñez

In line with the main mission of the CIBER consortium, which is cooperative research, CIBER-BBN has promoted seed calls with the thematic areas of CIBERESP, CIBERNED and CIBEREHD, as a result of which seven funded projects are currently underway. The annual compilation of the cooperative activities of the BBN groups showed that more than half of the collaborations are with groups from other thematic areas and that these inter-area interactions increase over time.

Early Stage Plus projects approved for funding at the end of 2022 started in 2023, all of them coordinated by postdoctoral staff hired in BBN groups and in intra- or interCIBER collaborations. This initiative had a second edition in 2023, in which three additional projects were launched.

In the valorization call, four new projects are being funded since 2023, which aim to increase the TRL of technologies that must have a minimum TRL of 3 to be eligible for funding.

In November 2023 we held the annual conference in Santander, in a very special edition organized jointly with CIBEREHD. We are pleased to say that the objective of stimulating scientific collaborations, mutual knowledge of the areas and the exploration of new lines of research was achieved. At the end of the year, the call for seed projects was closed with a very significant participation.

The Santander event also included a special session for young research staff organized by a youth committee created for this purpose, which was highly appreciated by the attendees. This session was an opportunity to promote greater interaction and collaboration between researchers of different levels of experience.

The scientific production in 2023 in terms of publications is similar to that of 2022 with an increase in the percentage of publications in Q1 (around 73%) and maintaining the indicator corresponding to D1 (28%).

At the international level, we highlight two important milestones. On the one hand, ARISTOS (Marie Skłodowska-Curie COFUND program), a strategic project led by CIBER and funded with €3.8 million by the European Commission, was launched in June 2023. The first call for proposals was open between July and September, and all applications received were sent for review by an external panel. ARISTOS offers 27 three-year postdoctoral contracts in all thematic areas. We also highlight the start of the NABIHEAL project (Horizon Europe), coordinated by CIBER. NABIHEAL aims to develop multifunctional bio materials based on nanotechnology to facilitate the healing of complex wounds.

Other current inter-area collaborations are the participation of CIBER-BBN groups in initiatives of other areas, such as the strategic projects of CIBERONC, or in large competitive projects coordinated by other thematic areas, such as some projects of the call for Personalized Precision Medicine (ISCIII) and which CIBER coordinates.

The ICTS NANBIOSIS implemented in 2023 a new open and competitive access system through two annual calls. Another activity undertaken was the design and execution of new integrated solutions for advanced biomedical challenges within the framework of the European SAFE-N-MEDTECH project, which successfully completed its work in 2023.

Finally, I would like to thank the CIBER-BBN community for their dedication and work in support of collaborative research at CIBER.

Warm regards to you all.

PROGRAMS & PLATFORMS

BIOENGINEERING AND MEDICAL IMAGING

Raimon Jané / COORDINATOR

During the year 2023, there were 48 active intramural collaborations in this research program, 15 of which were new proposals (11 of them in collaboration with other areas):

- NANOPTOGEN. Combining Niosome and Optogenetics Technologies to Photosensitize Neural tissue. Lawrence Humphreys (E. Fernández).
- CARDIO-ING. Bioengineering and artificial intelligence to improve diagnosis and prognosis of cardiovascular diseases in clinical practice. María Elena Hernando.
- KCarDiab. Multiscale characterization of the ventricular remodeling in diabetic cardiomyopathy for arrhythmic risk assessment and potential therapeutic effects of nutraceutical interventions with products of the Mediterranean diet. Aida Oliván (P. Laguna).
- Wearexper. Physical activity and physiological biomarkers from wearable devices for personalized exercise medicine. Raquel Bailón (P. Laguna).
- FIRESTONE. Fast Identification of caRbapEnemaSe-producing enTerObacteriaceae by RamaN spectroscopy. Adolfo Cobo García (J.M. López).
- ORIFICE. ORgan-on-Chip For photonic characterization of living cElls. Adolfo Cobo García (J.M. López).
- PET-CART. PET/CT in patients with lymphoma treated with CAR-T therapy. Xavier Setoain.
- simNM. New software for the generation of realistic brain PET and SPECT images. Aida Niñerola (X. Setoain).
- PSCI. Application of PET and SPECT images in cardiovascular infections. Andrés Perissinotti (X. Setoain).
- IMPRIND. Improving image processing and quantification for brain MRI and PET in neurodegenerative disorders. Roser Sala-Llonch (X. Setoain).
- ADICHIP. Browning and whitening adipose cells on-chip. Xavier Muñoz Berbel (R. Villa).
- CHEMFETONBIO. Chemical Functionalization Strategies of Graphene Solution Gated Field Effect Transistors with Oligonucleotides for Biosensing. Elisabet Prats (R. Villa).
- QBD. Towards a quantitative assessment of bipolar disorder. Jordi Aguiló (R. Villa).
- M&M. mHealth Methods in Mental Health Research: Designing an Objective Tool to Assess Mental Health in Epidemiologic and Clinical Studies. Jordi Aguiló (R. Villa).
- ARISE. Avoiding and reducing stress to improve transplant surgery and recovery. Jordi Aguiló (R. Villa).

The clinical areas addressed by these new proposals are ocular diseases (1), neurological diseases (6), cancer (1), cardiovascular diseases (4), metabolic diseases (1) and infectious diseases (2).

As for seed projects with other CIBER areas, the following projects have been initiated in 2023 calls.

CIBERNED-BBN Calls:

- GROKE. Advanced graphene-based neural interfaces for therapeutic intervention monitoring after brain stroke. Xavier Illa (R. Villa).

- MINN4PAK. Mapping Intranasal Nanoconjugates for Parkinson: MRI Analysis of CNS Targeting and Biodistribution. Ana Paula Candiota (C. Arús).

The following projects coordinated by CIBER-BBN staff have been approved from the calls for Early Stage Plus projects aimed at promoting collaborations in which CIBER-BBN contracted doctoral staff are coordinators:

- Quan-TAU-PET. Quantification tools for a novel tau PET marker in a rare neurological disease: 18F-PI-2620 in Progressive Supranuclear Palsy. Raúl Tudela (X. Setoain).
- Tattoo4Sleep. Comfortable tattoo skin electrodes for sleep disorders monitoring. Xavier Illa (R. Villa), Gonzalo César Gutiérrez (R. Hornero), Yolanda Castillo (R. Jané).
- DHOC. Diabetic heart on chip for multiscale characterization of the ventricular remodeling in diabetic cardiomyopathy. Aida Oliván (P. Laguna), Teodora Randelovic (M. Á. Martínez).

BIOMATERIALS & ADVANCED THERAPIES

M. Rosa Aguilar de Armas / COORDINATOR

The scientific activity of the program has been structured around 41 active intramural collaborations, with seven new proposals initiated in 2023:

- RADIOPROTECT. New therapeutic clinical solutions for the treatment of damaged radiated skin. M. Rosa Aguilar.
- NANOMEXOS. NANOsystems based on Mesoporous nanoparticles and EXOSomal membranes for the treatment of amyloidosis derived from Type 2 Diabetes Mellitus. Daniel Arcos.
- NANODelivery. Engineering on-demand protein coronas for improved NANOparticle drug Delivery to tumors. Montserrat Colilla (D. Arcos).
- PLAQUER. Novel PLA films including quercetin. M. Luisa González.
- NANOORGAN. New technologies in organoid development: Platform for modeling infectious diseases. Nanotechnology-based therapies. M. Ángeles Muñoz.
- 3D-COAT. Developing smart 3D-printed antibacterial mesh coatings for hernia repair. M. Gemma Pascual.
- BELLA. Biohybrid Elastin-like/Lactic Acid Hydrogels for Cardiac Tissue Engineering. Sergio Acosta (J.C. Rodríguez Cabello).

The clinical areas addressed by these new proposals have been infectious diseases (2), skin diseases (1), cardiovascular diseases (1), metabolic diseases (1), cancer (1) and bone diseases (1).

In 2023, the following Early Stage Plus collaborative projects coordinated by staff of this program were started::

- EAL- ALS. New therapeutic strategy based in boron compounds for muscle systemic treatment of amyotrophic lateral sclerosis (ALS). Patricia Rico (G. Gallego).
- WoundPLAst. Micro-structured patterned PLA films to promote wound healing. Margarita Hierro (M. Luisa González), Clara Escudero (N. Vilaboa).

NANOMEDICINE

M. Pilar Marco Colás / COORDINATOR

In 2023, 15 new proposals for intramural collaborations have been submitted, four of which are in collaboration with other CIBER areas. Thus, during this period there have been a total of 81 active collaborations in this Program. The new collaborations are:

- F7. Peptide-targeted polymeric micelles for an optimized cell internalization and anti-cancer treatment. Ibane Abasolo.
- hEaVy-METAL. High resolution tracking of Extracellular Vesicles functionalized with METALlic nanoparticles. Joaquín Seras (I. Abasolo).
- Nanobeacon. Tumor extracellular vesicles as nanobeacons for personalized diagnosis of triple negative breast cancer (TNBC) patients. Joaquín Seras (I. Abasolo).
- BBB-Glio. Treatment of aggressive Gliomas using Nanoparticulate systems for Blood-Brain-Barrier Crossing and Cancer Stem Cells Targeting. Fernanda da Silva Andrade (I. Abasolo).
- SH-PERMA. Development of a Smart Hydrogel for Periodontal Regenerative Medicine Applications. Fernanda da Silva Andrade (I. Abasolo).
- PATHERNO. Point-of-care optical device for antibiotic therapy tailoring and monitoring in nosocomial infections. Laura Lechuga.
- DEEPSCREENS. DEEP learning networks for Stratification of Cells by surfacE-Enhanced ramaN Scattering. Luis Liz-Marzán.
- AMATOX. CXCR4-targeted multivalent amanitin-nanoconjugates for precision medicines in colorectal cancer. Ugutz Unzueta (R. Mangues).
- FIBOLISM. Impact On Colorectal Tumor Metabolism When PDGFRβ Fibroblasts Are Depleted By Targeted Nanoparticles. Lorena Alba (R. Mangues).
- MitCer4AD. Mitochondria-Targeting Dendron-Ceria Nanoparticles in the Management of Alzheimer's Disease. Carlos Rodríguez Abreu.
- BBB_MedTech. Blood-brain barrier-on-a-chip (BBB-oC) for drug testing and physiopathological studies. Josep Samitier.
- CAP-NOSE. Determination of the nanoscale electrical properties of olfactory receptors (ORs) and their dependence on ligand binding: Towards the development of capacitance-operated odorant biosensors. Josep Samitier.
- TARGET-LIPO. Studying the intricacies of active targeting in nanoliposomal formulations. Mariana Köber (N. Ventosa).
- NANO4BRAIN. Multifunctional protein-only nanoparticles for nose-to-brain delivery. Esther Vázquez (A. Villaverde).
- NANOSARS. Structure and antigenicity of SARS-COV-2 antigens formulated as self-assembling nano- and micro-particles. Eloi Parladé Molist (A. Villaverde).

The clinical areas addressed by these new proposals have been rare diseases (1), infectious diseases (2), digestive diseases (1), metabolic diseases (2), neurological diseases (2), respiratory diseases (1) and cancer (6)

As for seed projects with other CIBER areas, the following projects have been initiated in 2023 calls.

CIBERESP-BBN Calls:

- MANEDH. Development of pioneering quantitative molecular diagnostic assays based on an innovative aptamer nanotechnological approach for high-throughput and point-of-care early diagnosis of HIV. M. Pilar Marco.
- NANO-FUN. Biomedical nanomotors for the treatment of fungal infections. Ramón Martínez Máñez.
- Triplex-POC-Flu/RSV. Triplex Hybridization-based Nanosystem for Point of Care Differential Diagnostic of Influenza and Respiratory Syncytial Virus. Ramon Eritja.

In 2023, the following Early Stage Plus collaborative projects began, coordinated by contracted staff from this program:

- DRUG2BRAIN. Microphysiological model of the blood–brain barrier (BBB)–brain parenchyma for the in vitro evaluation of permeability and efficacy of nanoformulations for brain delivery of small drugs and biomolecules. Monica Mir, Anna Lagunas (J. Samitier), José Luis Corchero (A. Villaverde).
- AβNANO. Amyloid-β burden and neuroinflammation dual-targeted nanomedicines for Alzheimer's disease. Santiago Grijalvo (C. Rodríguez Abreu).
- NbTx. Nanobodies as therapeutic agents against Pseudomonas aeruginosa infections. J. Pablo Salvador (P. Marco).
- NanoOncoTME. Mesoporous silica nanoparticles targeting tumor microenvironment as an innovative approach for breast cancer treatment. Alba García (R. Martínez Máñez).
- OCU-LIPID-FILMS-II. Films containing nanolipid complexes for the sustained release of timolol drug on the surface of the eye: project extension. Idoia Gallego (J.L. Pedraz), Lawrence Humphreys (E. Fernández).

NANBIOSIS ICTS PLATFORM

For the NANBIOSIS ICTS, 2023 has been the year of implementation of the new open access system through two annual calls. Of the 475 applications received throughout the year, 350 were received in the open access calls in February and June. Of these, 244 met the requirements of scientific quality and uniqueness and were therefore admitted as competitive and prioritized over the rest of the applications considered "on demand".

In addition, a system was created to promote NANBIOSIS' strategic services, "Cutting-Edge Biomedical Solutions" (CEBS), which offer users integrated solutions to advanced challenges, combining the expertise and capabilities of several units. This system for promoting "CEBS" offers users 5% discounts on the fees for the services involved in the development of these biomedical solutions. In 2023, two CEBS were designed and implemented, namely:

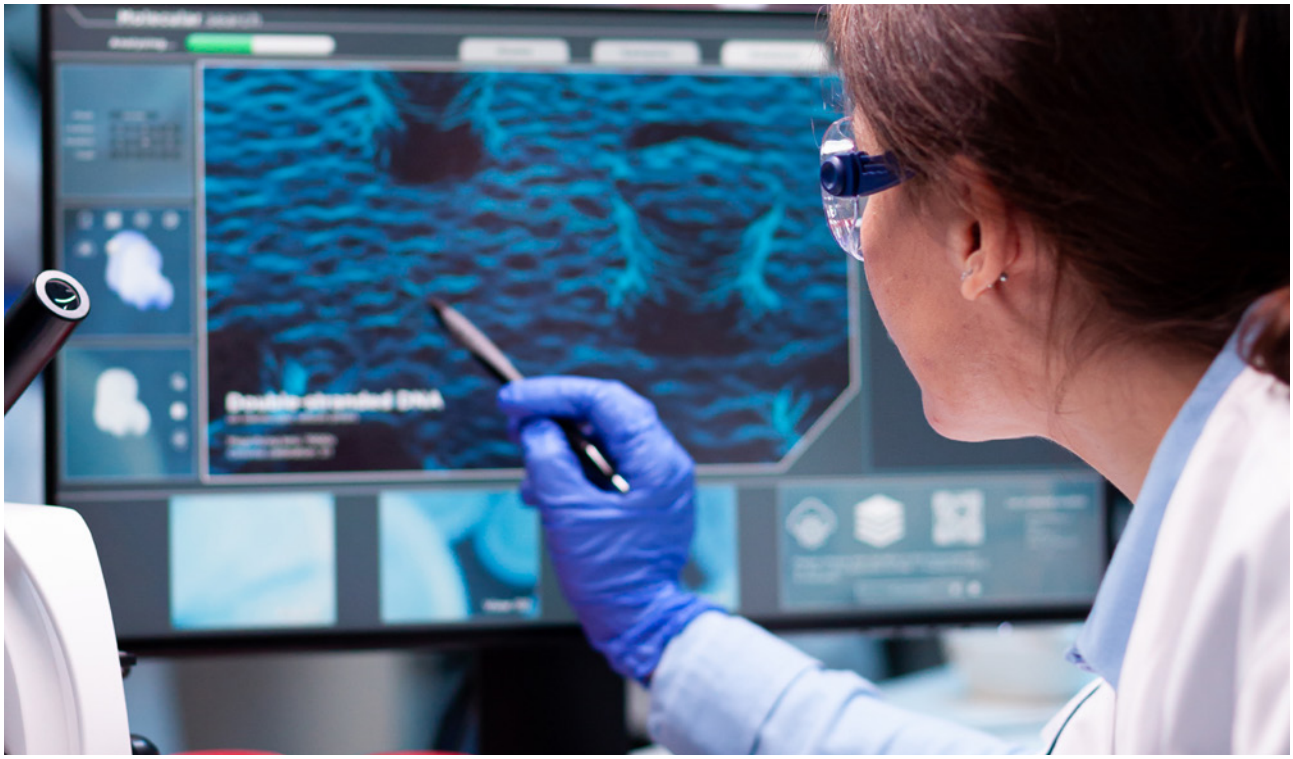
- Análisis de dispositivos biomédicos y propiedades antimicrobianas, con la participación de las unidades U16, U14, U19, U21, U22 y U24 en el marco del proyecto europeo SAFE-N-MEDTECH, y
- Producción y caracterización de nanopartículas antimicrobianas, con las unidades U6 y U16 en el marco del proyecto europeo NABIHEAL.

This has also been the year of ISO 9001- 2015 certification. The SAFE-N-MEDTECH project made it possible to support units interested in obtaining this accreditation. Specifically, certification has been obtained for the NANBIOSIS access request management system and coordination of the units, and units U2 (in development and production of monoclonal antibodies) and U28 (in nanoimaging services) have also been certified.

Following the execution plan of the SAFE-N-MEDTECH project, the non-profit entity OITBPathway has been created, in which NANBIOSIS has processed its participation through CIBER, undergoing a quality audit procedure by its coordinators. This platform will contribute to the internationalization of the ICTS.

In 2023, funding (70,000 euros) was obtained for the NANBIO-ACCESS project in the call for Networks of Excellence, a project that will last two years and whose main objectives are to strengthen the CEBS, implement a NANBIOSIS communication plan and improve the internationalization capabilities of the ICTS.

In terms of scientific results, in 2023 the participation of units U1 and U18 in the development of a new protein nanoparticle linked to an anticancer agent for the treatment of fibroblast-associated tumors should be highlighted. This particle shows promising results and low toxicity to non-tumor cells. Another important finding is the discovery, in collaboration with U6 and U20, of extracellular vesicles secreted by cancer cells that actively contribute to the formation of metastases in triple-negative breast cancer, the most aggressive breast cancer, and that could have relevance in diagnostic and prognostic applications.



TRAINING PROGRAM

Throughout 2023, the mobility initiatives that support researcher stays in different research groups, both within the CIBER consortium and in external groups, have been maintained.

In CIBER-BBN, mobility between research groups is considered a fundamental component to promote the training of research personnel in priority research areas, adapting to the needs of development and implementation of new techniques in the consortium.

The purpose of this initiative is to promote short stays in other research groups in order to facilitate the transfer of knowledge and technology, as well as to strengthen collaboration between the different CIBER groups. In addition, stays in external groups, both national and international, are considered, as long as they are aligned with the priority and strategic research lines of CIBER-BBN.

Also within the Training Program, a session for young researchers was organized within the framework of the annual meeting held in Santander together with CIBEREHD. Instead of holding a collaborative day as a stand-alone event, the decision was made to merge the meeting for young researchers and the annual meeting into a single event. This approach allowed us not only to optimize resources, but also to foster greater interaction and collaboration between researchers of different levels of experience.

The special session dedicated to young researchers, organized by a committee of young researchers constituted specifically for the meeting, addressed topics of general interest to all participants, with oral communications by young researchers from both areas, the invited talk “How to give visibility to your science beyond the research paper” by the company SIMBIONTE, and the poster session. Prizes were awarded to the best oral communications and posters.

Mobility Actions in 2023

Intra-Área Actions **1**

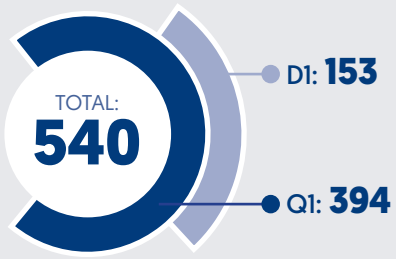
External Actions **13**

14

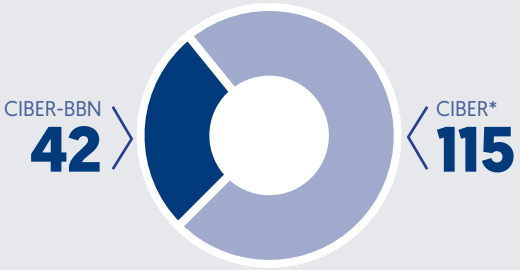
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
82,9	Tobias D.K., Merino J., Ahmad A., Aiken C., Benham J.L., Bodhini D. et al. Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine. Nature Medicine. 2023;29(10):2438-2457.
62,1	Scarabelli L., Sun M., Zhuo X., Yoo S., Millstone J.E., Jones M.R. et al. Plate-Like Colloidal Metal Nanoparticles. Chemical Reviews. 2023;123(7):3493-3542.
46,2	Nandhini K.P., Shaer D.A., Albericio F., de la Torre B.G.. The challenge of peptide nucleic acid synthesis. Chemical Society Reviews. 2023;52(8):2764-2789.
44,5	Mathiesen E.R., Alibegovic A.C., Corcoy R., Dunne F., Feig D.S., Hod M. et al. Insulin degludec versus insulin detemir, both in combination with insulin aspart, in the treatment of pregnant women with type 1 diabetes (EXPECT): an open label, multinational, randomised, controlled, non-inferiority trial. The Lancet Diabetes and Endocrinology. 2023;11(2):86-95.
41,2	Kechagia Z., Saez P., Gomez-Gonzalez M., Canales B., Viswanadha S., Zamarbide M. et al. The laminin–keratin link shields the nucleus from mechanical deformation and signalling. Nature Materials. 2023;22(11):1409-1420.
37,8	Duijvenboden S.V., Ramirez J., Orini M., Aung N., Petersen S.E., Doherty A. et al. Prognostic Significance of Different Ventricular Ectopic Burdens During Submaximal Exercise in Asymptomatic UK Biobank Subjects. Circulation. 2023;148(24):1932-1944.
29,9	Williams L.Z.J., Fitzgibbon S.P., Bozek J., Winkler A.M., Dimitrova R., Poppe T. et al. Structural and functional asymmetry of the neonatal cerebral cortex. Nature Human Behaviour. 2023;7(6):942-955.
29,4	Schamberger B., Ziege R., Anselme K., Ben Amar M., Bykowski M., Castro A.P.G. et al. Curvature in Biological Systems: Its Quantification, Emergence, and Implications across the Scales. Advanced Materials. 2023;:-.
29,4	Ni B., Mychinko M., Gomez-Grana S., Morales-Vidal J., Obelleiro-Liz M., Heyvaert W. et al. Chiral Seeded Growth of Gold Nanorods Into Fourfold Twisted Nanoparticles with Plasmonic Optical Activity. Advanced Materials. 2023;35(1):-.
29,4	Javadzadeh M., del Barrio J., Sanchez-Somolinos C.. Melt Electrowriting of Liquid Crystal Elastomer Scaffolds with Programmed Mechanical Response. Advanced Materials. 2023;35(14):-.

CIBER-BBN Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Abasolo Olaortua, Ibane	12	10	0	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Aguilar de Armas, María Rosa	7	6	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Arcos Navarrete, Daniel	21	19	0	Universidad Complutense de Madrid	MADRID
Arús Caralto, Carles	14	8	0	Universidad Autónoma de Barcelona	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Calonge Cano, Margarita	4	2	0	Universidad de Valladolid	VALLADOLID
Corcoy Pla, Rosa	15	8	5	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Engel López, Elisabeth	4	4	3	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Eritja Casadella, Ramón	10	8	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Fernández Jover, Eduardo	8	6	1	Universidad Miguel Hernández de Elche	ALICANTE
Franco Puntes, Víctor	9	8	2	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Gallego Ferrer, Gloria	17	14	5	Universidad Politécnica de Valencia	VALENCIA
Gómez Ramírez, Rafael	12	10	1	Universidad de Alcalá	MADRID
González Martín, María Luisa	4	3	2	Universidad de Extremadura	BADAJOZ
Gorostiza Langa, Pau	9	5	4	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Hernando Pérez, María Elena	23	11	2	Universidad Politécnica de Madrid	MADRID
Hornero Sánchez, Roberto	21	12	9	Universidad de Valladolid	VALLADOLID
Jané Campos, Raimon	11	6	1	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Laguna Lasaosa, Pablo	28	16	9	Universidad de Zaragoza	ZARAGOZA
Lechuga Gómez, Laura María	2	2	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Liz Marzán, Luis Manuel	27	20	14	Asociación Centro de Investigación Cooperativa en biomateriales, CIC biomaGUNE	GUIPÚZCOA
López Higuera, José Miguel	10	8	1	Universidad de Cantabria	CANTABRIA
Mangues Bafalluy, Ramón	12	11	3	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Marco Colas, María Pilar	3	3	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Martínez Barca, Miguel Ángel	23	16	8	Universidad de Zaragoza	ZARAGOZA
Martínez De La Fuente, Jesús	25	21	10	Agencia Estatal Consejo Superior de Investigaciones Científicas	ZARAGOZA
Martínez Mañez, Ramón	23	19	8	Universidad Politécnica de Valencia	VALENCIA
Muñoz Fernández, María Ángeles	9	7	5	Servicio Madrileño de Salud	MADRID
Pascual González, Mª Gemma	1	1	1	Universidad de Alcalá	MADRID
Pedraz Muñoz, José Luis	28	24	9	Universidad del País Vasco	ÁLAVA
Raya Chamorro, Ángel	6	6	4	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Rodríguez Abreu, Carlos	10	7	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Rodríguez Cabello, José Carlos	3	3	0	Universidad de Valladolid	VALLADOLID
Royo Expósito, Miriam	21	9	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Ruiz Romero, Cristina	6	5	3	Servicio Gallego de Salud	CORUÑA, A
Samitier Martí, Josep	14	13	2	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Santamaría Ramiro, Jesús	25	20	5	Universidad de Zaragoza	ZARAGOZA
Santos Lleó, Andrés	17	14	7	Universidad Politécnica de Madrid	MADRID
Setoain Peregó, Xavier	29	17	9	Universidad de Barcelona	BARCELONA
Trepat Guixer, Xavier	10	10	7	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Ventosa Rull, Leonor	10	8	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Vilaboa Díaz, Núria	4	4	0	Servicio Madrileño de Salud	MADRID
Villa Sanz, Rosa	19	16	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Villaverde Corrales, Antonio	18	16	4	Universidad Autónoma de Barcelona	BARCELONA

Clinical Guidelines

- MRI Study to detect glymphatic system impairment and characterize locus coeruleus integrity in the Alzheimer's disease continuum. Juan Domingo Gispert.
- Clinical Pathway for Intensified Recovery in Adult Surgery. Spanish Multimodal Rehabilitation Group.
- 2023 GEIS Guidelines for gastrointestinal stro- mal tumors. Spanish Sarcoma Research Group.

CARDIOVASCULAR DISEASES

ciber | cv

WELCOME FROM THE SCIENTIFIC DIRECTOR

Javier Bermejo Thomas

On behalf of the entire CIBERCV Steering Committee, I would like to highlight the milestones achieved during 2023 that consolidate and strengthen collaborative scientific activity in the Cardiovascular Area. In 2023, the cardiovascular area published more than 600 articles in top-level scientific journals. In the field of communication, the CiberCV has carried out more than 800 press appearances in both online and print media. Our Ciber is currently involved in several European projects, as well as in two multicenter projects of the Call for Independent Clinical Research Projects of the ISCIII (BbEcho and Maiden Studies) and Personalized and Precision Medicine (Ciber-SPANISH Study). This ability to attract external funding in national and international competitive public calls shows the potential of collaborative activity and highlights the achievements of the consortium when its efforts in the pursuit of excellence are aligned.

We have successfully completed the fifth evaluation of the External Scientific Advisory Committee, with a favorable report on our performance and very useful recommendations. Among these, the need to reinforce internationalization and excellence stands out, emphasizing the need to focus on some prioritized lines of research in order to try to achieve international projects with maximum competitiveness. In addition, it emphasized the need to continue promoting and rewarding multidisciplinarity, especially useful aspects in multidisciplinary research.

We face new risks for 2024, with the recommendations of our External Advisory Committee firmly in mind. We will rethink the structure of programs by replacing exhaustiveness with the identification of lines of research in which we anticipate maximum competitiveness in the medium term. We will focus on training initiatives and cross-cutting projects that involve multiple thematic areas and launch new bilateral calls with targeted thematic areas.

In conclusion, during 2023, the CIBERCV has continued to face its challenges with motivation and a strong commitment to the consortium, which has resulted in a cooperative scientific activity of the highest level. This is thanks to the efforts of the people involved and the framework of stability provided by the CIBER, which we consider fundamental for promoting cooperative research of excellence in Spain, with the aim of contributing to reducing the impact of cardiovascular diseases in our environment and generating prosperity, leading research, innovation, and training in this discipline within the national and international framework.

PROGRAMS & PLATFORMS

MYOCARDIAL DAMAGE AND ITS CONSEQUENCES

Francisco Fernández-Avilés Díaz y Juan Delgado Jiménez / COORDINATORS

This program highlights the launch of the Early-GENE project. A prospective, multi-center, randomized, placebo-controlled, double-blind, phase III clinical trial to evaluate the safety and efficacy of candesartan in preventing the development of DCM in asymptomatic carriers of DCM due to genetic mutation.

The primary endpoint is to assess whether early administration of candesartan (compared to placebo) prevents a significant decrease in the left ventricular ejection fraction (LVEF) ≥10%, or an increase in ventricular dilatation (left ventricular end-diastolic volume, LVEDV) ≥0% in genetic carriers of a DCM-causing variant without disease expression during a 3-year follow-up. Secondary endpoints include the proportion of participants progressing to a deterioration of LVEF or LVEDV of ≥10% compared with baseline at the end of follow-up measured by MRI, the proportion of individuals developing DCM (LVEF<50%), and the proportion of participants in each treatment group developing serious adverse events (SAEs), grade 3-4 adverse events (AEs), adverse reactions, or adverse events of special interest (AESIs). The estimated sample size of the study is 320 subjects, 160 per group..

ARTERIAL DISEASE, MYOCARDIAL ISCHEMIA & STRUCTURAL HEART DISEASE

Borja Ibáñez Fernández y Alberto San Román Calvar / COORDINATORS

Among the most relevant scientific milestones during 2023 within this program is the publication of the ESC Guidelines 2023 for the management of acute coronary syndromes (Eur Heart J. 2023;44:3720-3826), chaired by a CIBERCV group leader. It should be noted that the affiliation of the CIBERCV was stated on the cover of the ESC guidelines, increasing the visibility of the consortium and highlighting its leadership.

Also noteworthy within the program is the development of the REBOOT trial, which tests the benefits of beta-blockers in patients with normal ejection fraction and has already enrolled 8000 patients. This trial involves the participation of 15 CIBER- CV groups. The results of the study will be known in 2025. In the field of anthracycline cardiotoxicity, CIBERCV is participating in the RESILIENCE study, in which 5 CiberCV groups are also involved.

CARDIOVASCULAR EPIDEMIOLOGY & RISK FACTORS

Jaume Marrugat de la Iglesia / COORDINATOR

The highlight of this program is the CORDELIA project (Collaborative cOhorts Reassembled Data to study mEchanisms and Long-term Incidence of chronic diseAses), which has a cohort of 180,000 participants aged between 18 and 84 years, combining data from 33 component cohorts. These cohorts, selected mostly by random population sampling, represent all autonomous communities. The cohort includes frozen DNA samples from more than 100,000 participants and a mean follow-up of >11 years. It homogeneously integrates 84 variables related to risk factors and the incidence of cardiovascular disease.

A cohort profile document is currently being finalized and we hope to have completed the first and largest GWAS cohort with incident cardiovascular disease in southern Europe and the second in the world after the UK biobank.

The project is funded with close to 5 million euros and started in January 2023. One third of the DNA samples have already been genotyped and first results are expected by the end of 2025. This project includes the participation of 4 groups from CIBERCV, 4 from CIBERDEM, 1 from CIBERERER, 10 from CIBERESP, 1 from CIBERES and 1 from CIBEROBN, with 50 CIBER researchers involved, and represents the largest collaborative project of the CIBER at present.

MOLECULAR AND IMAGING BIOMARKERS, AND PRECISION CARDIOVASCULAR MEDICINE

Javier Díez Martínez / COORDINATOR

To be highlighted within this program is the start-up of the project: Integration of polygenic risk scores with multiparametric information in the patient-specific prediction of the onset, progression and therapeutic response to atrial fibrillation, aimed at the presence of clinical, imaging, biochemical and genetic markers that allow stratification of the risk of atrial fibrillation in patients with heart failure who have monitoring devices and the risk of progression from paroxysmal to persistent forms and in which the following groups in this research area are participating: University Clinical Hospital Santiago de Compostela (Santiago), University Hospital Salamanca (Salamanca), University Hospital Gregorio Marañón (Madrid), University Hospital 12 de Octubre (Madrid), University Hospital Virgen de la Victoria (Málaga), University Hospital San Carlos (Madrid), University Hospital Ramón y Cajal (Madrid), IBM Alberto Sols (Madrid), FIMA (Pamplona).

TRAINING AND MOBILITY PROGRAM

José Antonio Barrabés Riu / COORDINATOR

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

In 2023, 3 mobility grants have been awarded to CiberCV researchers for stays in Spanish and foreign research centers.

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

Within the CIBERCV this program remains the main training initiative and in 2023 has contributed to the strengthening of quality translational research, promoting collaboration between the groups in the CV area and other thematic areas of the CIBER.

INTERNATIONAL AND INSTITUTIONAL RELATIONS PROGRAM

Lina Badimón Maestro / COORDINATOR

The CIBERCV International Program works closely with all lines of research, promoting collaboration with the main research centers worldwide, as well as carrying out specific actions for the international promotion of CIBERCV research.

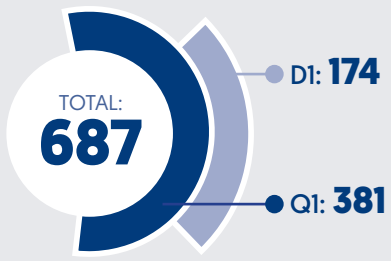
This program also offers support and advisory services to the CIBERCV research groups to compete with the best possibilities to apply for for international funding calls.

Also to be highlighted is the involvement of CIBERCV researchers in various international associations and working groups.

SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations

*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168,9	Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials
158,5	Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy
76,2	Seralutinib in adults with pulmonary arterial hypertension (TORREY): a randomised, double-blind, placebo-controlled phase 2 trial
39,3	Anticoagulation with edoxaban in patients with long atrial high-rate episodes ≥24 h
39,3	C-reactive protein modifies lipoprotein(a)-related risk for coronary heart disease: the BiomarCaRE project
39,3	Leadless pacemakers at 5-year follow-up: the Micra transcatheter pacing system post-approval registry
39,3	Clonal haematopoiesis and cardiac arrythmias: rhythm-altering mutations
39,3	Oral anticoagulation in device-detected atrial fibrillation: effects of age, sex, cardiovascular comorbidities, and kidney function on outcomes in the NOAH-AFNET 6 trial

CIBERCV Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Andrés García, Vicente	7	4	1	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	MADRID
Badimon Maestro, Lina	17	1	5	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Barrabes Riu, José Antonio	24	14	5	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Bayes Genis, Antonio	54	40	27	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Blanco Colio, Luis Miguel	3	1	0	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Bosca Gomar, Lisardo	8	5	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Briones Alonso, Ana María	3	3	1	Universidad Autónoma de Madrid	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Brugada Terradellas, Ramón	8	1	3	Fundación Instituto de Investigacion Biomédica de Girona, Dr. Josep Trueta	GIRONA
Civeira Murillo, Fernando	12	6	2	Fundación Instituto de Investigación Sanitaria Aragón	ZARAGOZA
Comin Colet, Josep	3	3	3	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Crespo Leiro, María Generosa	22	15	10	Servicio Gallego de Salud	CORUÑA, A
Delgado Jiménez, Juan Francisco	42	24	11	Servicio Madrileño de Salud	MADRID
Delpon Mosquera, María Eva	5	1	1	Universidad Complutense de Madrid	MADRID
Elosua Llanos, Roberto	7	4	3	Consorci Mar Parc Salut de Barcelona	BARCELONA
García Pavia, Pablo	27	17	12	Servicio Madrileño de Salud	MADRID
González Juanatey, José Ramón	44	16	6	Servicio Gallego de Salud	CORUÑA, A
Diez Martínez, Javier	14	8	12	Fundación para la Investigación Médica Aplicada	NAVARRA
Guerra Ramos, José María	26	12	6	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Ibáñez Cabeza, Borja	17	10	4	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Jiménez Navarro, Manuel Francisco	27	8	2	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	MÁLAGA
Marín Ortuño, Francisco	30	15	8	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	MURCIA
Marrugat de la Iglesia, Jaume	6	3	1	Consorci Mar Parc Salut de Barcelona	BARCELONA
Martínez Dolz, Luis	21	10	4	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	VALENCIA
Martínez González, José	6	5	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Mayor Menéndez, Federico	1	0	0	Universidad Autónoma de Madrid	MADRID
Mont Girbau, Josep Lluis	27	10	3	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Pérez-Villacastín Domínguez, Julián	8	5	2	Servicio Madrileño de Salud	MADRID
de la Pompa Minguez, José Luis	8	7	6	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	MADRID
Redondo Moya, Juan Miguel	8	1	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
San Román Calvar, José Alberto	31	12	4	Hospital Clínico Universitario de Valladolid	VALLADOLID
Sánchez Fernández, Pedro Luis	14	7	3	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	SALAMANCA
Sánchez Madrid, Francisco	16	8	4	Universidad Autónoma de Madrid	MADRID
Sánchez Margallo, Francisco Miguel	0	0	0	Fundación Centro de Cirugía de Mínima Invasión Jesús Usón	CÁCERES
Sanchís Fores, Juan	38	23	10	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA
Torres Sánchez, Miguel	0	0	0	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	MADRID
Vázquez Cobos, Jesús María	9	7	5	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	MADRID
Zamorano Gómez, José Luis	13	1	4	Servicio Madrileño de Salud	MADRID
Chorro Gasco, Francisco Javier	7	5	1	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA
Fernández-Avilés Díaz, Francisco	26	11	5	Servicio Madrileño de Salud	MADRID

DIABETES AND METABOLIC ASSOCIATED DISEASES

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Eduard Montanya Mías

In 2023 CIBERDEM has increased its scientific production with respect to the previous year, with an increase in quality, with 26% of publications in the first decile and 70% in the first quartile and an increase in the total and average impact factor per publication. Collaborative activity at both CIBER and international level has also increased, with 57% and 41% of collaborative publications, respectively. The most relevant publications of each group are detailed in this Report and on our web page.

As regards collaborative activity, worth mentioning is the participation in CIBER collaborative projects, such as the ARISTOS postdoctoral program in Biomedicine and Health Sciences, in which 27 postdoctoral researchers were accepted for a period of 3 years, one of them in CIBERDEM. In terms of internal collaborative activities of CIBERDEM, to be highlighted is the call for intramural projects 2023, aimed at promoting the presentation of collaborative projects in the CIBERDEM area in future competitive calls, which has been resolved with the award of two intramural projects, as well as mobility actions that have allowed stays in national and international CIBER groups. Both the Meeting of Young Researchers and the Annual Meeting have been two relevant activities, as a meeting point for the CIBERDEM research community, to strengthen the cohesion of the area. Collaboration with scientific societies such as the EASD Early Career Academy and the Spanish Diabetes Society has remained active, with the participation of a member of the EASD Early Career Academy committee as a speaker at the Young Researchers Meeting and the institutional presence of CIBERDEM at the XXXIV National Congress of the Spanish Diabetes Society.

In terms of translation and transfer, CIBERDEM members have prepared several clinical guidelines and consensus documents at both national and international level, in fields relevant to diabetes, and several patent applications have been filed in the field of biomarkers. CIBERDEM has participated in the CIBER INNOVA Call of the CIBER Technological Development Platform, for the elaboration of a portfolio of CIBER therapeutic projects, with the submission of several CIBERDEM projects, 2 of which have been prioritized for evaluation.

The Spanish Diabetes Federation (FEDE) has awarded CIBERDEM the "Recognition of Public Research in the Field of Diabetes" prize in recognition of our research activity in diabetes and for the translation of the results into clinical practice. The award, which was presented during the IX Edition of the FEDE - Mercedes Sánchez Benito Awards, within the framework of the VII National Congress of the Spanish Diabetes Federation (Madrid, October 7), reinforces CIBERDEM's firm commitment to bring the results of diabetes research closer to society and to people living with diabetes.

All information on the activity and achievements of CIBERDEM in the year 2023 can be found in this Scientific Report and further information can be found by visiting our website (www.ciberdem.org), as well as following us on social networks (@ciberdem).

Warm regards to all.

PROGRAMS & PLATFORMS

EPIDEMIOLOGY, GENETICS AND EPIGENETICS OF DIABETES MELLITUS. CHRONIC COMPLICATIONS & COMORBILITIES

Ángela María Martínez Valverde / COORDINATOR

EPIDEMIOLOGY OF DIABETES MELLITUS. CHRONIC COMPLICATIONS AND COMORBILITIES

Based on the di@bet.es study, a collaboration between 6 CIBERDEM groups and periodontists has revealed an association between periodontal disease and type 2 diabetes (Montero et al., J Clin Periodontol. 2023), and a collaborative CIBERDEM study has identified biomarkers of inflammation and muscle activity as predictors of type 2 diabetes beyond glucose (Ozcariz E. et al., Diabetes Res Clin Pract. 2023).

In collaboration with CIBEROBN, the first epidemiological study in Spain has been published on the characterization of the first cardiovascular event in more than 8,000 individuals with type 1 diabetes (Giménez-Pérez G. et al., Cardiovasc Diabetol 2023).

GENETICS, EPIGENETICS AND ENVIRONMENTAL FACTORS IN THE DEVELOPMENT OF DIABETES AND ITS COMPLICATIONS

In collaboration with CIBEROBN and CIBEREHD, the possible role of epigenetic biomarkers has been determined, which includes the expression of the miR-221-3p/222-3p cluster in human adipose tissue in the pathophysiology of obesity and type 2 diabetes (Gentile et al., Int J Mol Sci 2023).

A study has been led with CIBERER participation on the immunogenetic characteristics of type 1 diabetes (Urrutia et al., JCEM 2023).

MOLECULAR MECHANISMS ASSOCIATED WITH THE APPEARANCE AND PROGRESSION OF CHRONIC COMPLICATIONS OF DIABETES: THERAPEUTIC STRATEGIES

CIBERDEM has led a collaborative work with CIBERCV that describes an increase in the soluble receptor (s) LRP1/atrial natriuretic peptide (ANP) ratio in newly diagnosed patients with type 2 diabetes and that increased levels of sLRP1 and decreased levels of ANP normalize in patients with tight glycemic and metabolic control (García et al., Front Endocrinol 2023)

A real-life study of 26,000 individuals with type 2 diabetes has shown that persistent treatment with a GLP-1 agonist improved glycemic control, without finding positive effects on the prevention of cardiovascular events. Furthermore, 38% of the population studied showed therapeutic inertia (Palanca et al., Diabetes Ther 2023).

In collaboration with CIBERESP, a Cochrane systematic review has been published reporting on the effect of intensive glycemic control in the perioperative period in patients with diabetes (Bellon et al., Cochrane Database Syst Rev. 2023).

A collaborative CIBERDEM study used the SIDIAP real-world database demonstrating that rapid HbA1c reduction is not associated with progression of mild or moderate diabetic retinopathy (Simó et al., Diabetes Care 2023).

It has been described that the interrelationship between miR-155 and the SOCS1 protein is key in the progression of diabetes-associated chronic kidney disease. Inter-

ventions based on this axis improved renal dysfunction, inflammation and fibrosis in a preclinical model of type 1 diabetes (Prieto et al., Mol Ther Nucleic Acids 2023).

A study led by CIBERDEM with participation of CIBERCV and CIBERHED has shown that extracellular vesicles enriched in saturated fatty acids secreted by hepatocytes with lipid overload induce inflammation in the liver and insulin resistance in hepatocytes (García-Martínez et al., J Hep Rep 2023).

NUTRITIONAL AND LIFESTYLE ASPECTS IN THE DEVLOPMENT AMD PREVENTION OF DIABETES.

In a preclinical model of accelerated atherosclerosis, it has been found that the inclusion of walnuts in a diet rich in saturated fat reduces inflammation and favors a more stable atheroma plaque phenotype (Láza ro I. et al., Front Nutr 2023).

MOLECULAR AND CELLULAR DETERMINANTS OF PANCREATIC ISLET FUNCTION, DAMAGE AND PROTECTION. REGENERATIVE MEDICINE AND ADVANCED THERAPIES

Franz Martín Bermudo / COORDINATOR

PANCREATIC ISLET FUNCTION AND REGULATION: MOLECULAR AND CELLULAR BASIS AND THERAPEUTIC TARGETS

In dietary models of animals with type 2 diabetes, the presence of flavonoids and fiber in the diet improves the microbiota, intestinal health and increases the production of bioactive colonic metabolites, related to improved b-cell function and insulin resistance (García-Díez E. et al., Antioxidants 2023).

In animal models exposed to cold to induce thermogenesis, mRNA and microRNA transcriptomic analyses in different adipose tissues have identified key nodes in microRNA regulatory networks and transcription factors that control metabolism and immune response. (Rodo J. et al., Scientific Reports 2023).

The SUCNR1 signaling pathway, in adipocytes, participates in the regulation of body composition by maintaining adipose tissue mass and modulating the respiratory rate. This pathway acts as a metabolic sensor of nutrient-mediated leptin production and is involved in body weight homeostasis (Villanueva-Carmona T. et al., Cell Metabolism 2023). Alpha and gamma cytokines are key elements of the inflammatory response during insulitis, inducing a gene signature that correlates with the transcriptomic profile of b beta cells in people with type 1 diabetes. They thus contribute to the initiation and amplification of the autoimmune process, suggesting that treatments to protect b cells from autoimmune attack should target these two cytokines (Coomans de Brachene A. et al., Diabetologia 2023).

Metabolic reprogramming by inhibiting ATP-citrate lyase ameliorates metabolic alterations associated with unhealthy diets and within the context of aging (Sola-García A. et al., Commun Biol 2023).

Mcj (methylation-controlled J protein) silencing at the hepatic level prevents alcohol-induced hepatocyte damage by improving mitochondrial dysfunction, steatosis, inflammation and oxidative stress, restoring the NAD+/NADH ratio and SIRT1 function (Goikoetxea-Usandizaga N. et al., Hepatology 2023)

Endocrine disruptors affect survival, identity and glucagon secretion in α-pan creatic cells (Al-Abdulla R. et al., Int J Mol Sci, 2023; Dos Santos RS. et al., Int J Mol Sci 2023).

TYK2 inhibitor (deucravacitinib) protects β cells against the detrimental effects of proinflammatory cytokines, without affecting their function and survival (Dos Santos R.S. et al., Front Immunol 2023).

PREVENTIVE AND THERAPEUTIC STRATEGIES IN REGENERATIVE MEDICINE, CELL THERAPY AND GENE THERAPY

Proof of concept of the ability to produce insulin-producing cells from human fibroblasts by transcription factor-mediated direct reprogramming has been established. In addition, a protocol has been established that allows this reprogramming process (Fontcuberta-Pi Sunyer M. et al., Commun Biol 2023).

APPLICATION OF NEW TECHNOLOGIES TO THE TREATMENT OF DIABETES

The safety of a hybrid closed loop system with automatic suggestion of carbohydrate intake in adults with type 1 diabetes prone to hypoglycemia has been developed and evaluated. The system works well and improves patients' time in range in postprandial, exercise and post-exercise recovery situations (Mesa A. et al, Diabetes Res Clin Pract 2023).

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

Antonio Zorzano Olarte / COORDINATOR

INFLAMMATION AS A PATHOGENIC PROCESS IN DIABETES

Lipin-2 has been shown to act as a regulator of inflammation in a context of viral infection by reducing signaling through TLR3 and the generation of reactive oxygen species, as well as the release of mitochondrial DNA that will ultimately lead to the activation of the NLRP3 inflammasome (de Pablo et al. EMBO Rep 2023).

Altered expression of mitochondrial fusion and/or fission proteins has been described to promote the induction of inflammation through mechanisms that require mitochondrial DNA delocalization (Irazoki et al., Nat Commun 2023).

A novel inositol phospholipid containing omega-3 and omega-6 fatty acids has been reported to be produced during macrophage activation and could therefore be considered as a new metabolic marker of cellular activation (Monge, P et al., Bio- molecules 2023).

IDENTIFICATION OF MOLECULAR MECHANISMS AND NEW THERAPEUTIC TARGETS.

Alternative splicing forms of the human Mitofusin 2 gene product have been identified. These proteins localize uniquely to the endoplasmic reticulum, and enhance steatohepatitis in mice (Naón et al., Science 2023).

A new mechanism of adipocyte leptin production and its impact on the cellular biological clock has been identified (Villanueva-Carmona et al., Cell Metab 2023).

Succinate has been identified as a non-invasive biomarker during the development of metabolic liver disease (Marsal-Beltran et al., Metabolism 2023).

Increased levels of the stress cytokine GDF15 caused by metformin have been documented to allow full activation of AMPK in the liver (Aguilar-Recarte et al., Pharmacol Res 2023).

It has been determined that primary insulin resistance, through elimination of the insulin receptor in the liver,

is transferred to other peripheral tissues such as white adipose tissue. These effects were aggravated by using a fatty diet, and treatment with resveratrol reversed the previously mentioned effects (results submitted for publication).

Resveratrol has been reported to protect against amylin accumulation in pancreatic beta cells as well as its export and accumulation in hypothalamic neurons (results submitted for publication).

IDENTIFICATION OF BIOMARKERS OF RISK FOR DIABETES PROGRESSION.

It has been established that circulating progranulin (PGRN) levels are associated with markers of adiposity, inflammation and insulin sensitivity. PGRN could play a role in the metabolic adaptation of small-for-gestational-age infants during the first years of life, and contribute to the risk of obesity and type 2 diabetes in this population (Diaz et al., Pediatr Res 2023).

It has been described that in the first years of life the size of exosomes decreases, while their number increases; these changes are influenced by fetal growth. The size of exosomes may be an early marker of hepatic fat in childhood (Diaz et al., Front Endocrinol 2023).

A review of the clinical and biochemical characteristics of women with polycystic ovary syndrome (PCOS) and its persistence during and after menopause has been published, in which significant cardiometabolic associations are evident (Millán-de-Meer et al., Hum. Reprod Update 2023)).

TRAINING PROGRAM

Ángel Nadal Navajas / COORDINATOR

The main objective of the CIBERDEM Training Program is to foster the development and competitiveness of young research personnel and promote collaboration between CIBER research groups. The main actions carried out for this purpose are detailed below.

The three intramural projects for young people awarded in 2022 have been completed, with the participation of 6 CIBERDEM groups.

The Mobility Actions Program has registered an increase in applications with a total of 8 stays financed, 4 national (3 in CIBER groups) and 4 international groups.

The 14th Annual CIBERDEM Meeting was held on November 16 and 17 with more than 150 participants who presented the results of the research in diabetes developed by the CIBERDEM groups. The 4th Meeting of Young CIBERDEM Researchers was held on November 15 with the participation of more than 70 young researchers which served as a very relevant cohesive element.

As part of the collaboration between CIBERDEM and the Spanish Diabetes Society, CIBERDEM organized the SED-CIBERDEM Round Table, which took place during the XXXIV National Congress of the SED (April 20). The topics were focused on advances in the knowledge of the regulation of glucagon secretion by the insulin- degrading enzyme, new research with a potential impact on the treatment of diabetes and its complications, such as the anti-diabetic effects of GDF15 and the role of NAD+ precursors for the treatment of diabetic neuropathy.

CIBERDEM has participated, together with the other CIBER areas in the ARISTOS program (Postdoctoral Program in Biomedicine and Health Sciences, HORIZON-MS- CA-2021-COFUND-01) offering and co-funding a postdoctoral position in a CIBERDEM group (https://postdoc-aristos.com/).

Finally, it is important to note that it is impossible to detail in this report the numerous training activities organized at the individual level by the CIBERDEM groups.

COMMUNICATION AND DISSEMINATION TO SOCIETY

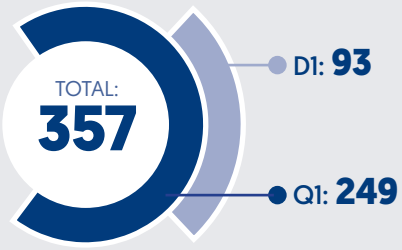
CIBERDEM maintains its commitment to bring research results closer to society, participating in dissemination actions, for example on the occasion of World Diabetes Day and collaborating with various initiatives of patient associations, the Spanish Diabetes Federation (FEDE), DiabetesCero, Canal Diabetes (audiovisual platform for patients with diabetes), etc. In 2023 CIBERDEM received the award "Recognition for Public Research in the field of Diabetes" in the IX Edition of the Spanish Diabetes Federation Awards– Mercedes Sánchez Benito.

CIBERDEM collaborates closely with the SED and the European Association for the Study of Diabetes (EASD). In this regard, CIBERDEM has been present at the XXXIV SED Congress (April 19-21), with a booth and the SED-CIBERDEM Table and with a CIBERDEM booth at the 50th EASD Annual Meeting (October 2-6).

SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations

*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
56,9	Naon D., Hernandez-Alvarez M.I., Shinjo S., Wieczor M., Ivanova S., Martins de Brito O. et al. Splice variants of mitofusin 2 shape the endoplasmic reticulum and tether it to mitochondria. Science. 2023 Jun 23;380(6651): eadh9351.
64,8	COVID-19 Host Genetics Initiative. A second update on mapping the human genetic architecture of COVID-19. Nature. 2023 Sep;621(7977): E7-E26.
46,9	Allesoe R.L., Lundgaard A.T., Hernandez Medina R., Aguayo-Orozco A., Johansen J., Nissen J.N. et al. Discovery of drug–omics associations in type 2 diabetes with generative deep-learning models. Nature Biotechnology. 2023;41(3):399-408.
44,5	Battelino T., Alexander C.M., Amiel S.A., Arreaza-Rubin G., Beck R.W., Bergenstal R.M. et al. Continuous glucose monitoring and metrics for clinical trials: an international consensus statement. The Lancet Diabetes and Endocrinology. 2023;11(1):42-57.
40,5	Haddad-Tovolli R., Claret M. Metabolic and feeding adjustments during pregnancy. Nature Reviews Endocrinology. 2023;19(10):564-580.
39,89	Romero-Gomez M., Zelber-Sagi S., Martin F., Bugianesi E., Soria B. Nutrition could prevent or promote non-alcoholic fatty liver disease: an opportunity for intervention. BMJ. 2023 Oct 9: 383: e075179.
39,3	Cuchel M, Raal FJ, Hegele RA, Al-Rasadi K, Arca M, Averna M et al. 2023 Update on European Atherosclerosis Society Consensus Statement on Homozygous Familial Hypercholesterolaemia: new treatments and clinical guidance. European Heart Journal. 2023;44(25):2277-2291.
39,3	Pennells L., Kaptoge S., Ostergaard H.B., Read S.H., Carinci F., Franch-Nadal J. et al. SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. European Heart Journal. 2023;44(28):2544-2556.
37,8	Walters R., Vasilaki E., Aman J., Chen C.-N., Wu Y., Liang O.D. et al. SOX17 Enhancer Variants Disrupt Transcription Factor Binding and Enhancer Inactivity Drives Pulmonary Hypertension. Circulation. 2023;147(21):1606-1621.
30,8	Beaumont R.N., Flatley C., Vaudel M., Wu X., Chen J., Moen G.-H. et al. Genome-wide association study of placental weight identifies distinct and shared genetic influences between placental and fetal growth. Nature Genetics. 2023;55(11):1807-1819.

CIBERDEM Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Balsinde Rodríguez, Jesús	8	7	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	VALLADOLID
Blanco Vaca, Francisco	35	24	9	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Bondia Company, Jorge	11	5	4	Universidad Politécnica de Valencia	VALENCIA
Bosch Tubert, Fátima	2	1	0	Universidad Autónoma de Barcelona	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Burks, Deborah	2	2	1	Fundación de la Comunidad Valenciana Centro de Investigación Príncipe Felipe	VALENCIA
Calle Pascual, Alfonso Luis	10	5	1	Servicio Madrileño de Salud	MADRID
Castaño González, Luis	21	14	7	Asociación Instituto de Investigación Sanitaria Biobizkaia	VIZCAYA
Correig Blanchart, Francesc Xavier	21	18	7	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA
Egido de los Ríos, Jesús	19	12	14	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Escobar Morreale, Héctor Francisco	12	5	4	Servicio Madrileño de Salud	MADRID
Ferrer Marrades, Jorge	6	6	4	Fundación Centro de Regulación Genómica	BARCELONA
Guillén Viejo, Carlos	1	1	0	Universidad Complutense de Madrid	MADRID
Ibáñez Toda, Lourdes	22	19	3	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Martín Arribas, María Ángeles	6	6	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Martín Bermudo, Francisco	14	13	2	Universidad Pablo de Olavide	SEVILLA
Martínez Valverde, Ángela María	18	14	8	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Mauricio Puente, Diego	43	26	11	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Montanya Mías, Eduard	14	9	4	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Nadal Navajas, Ángel	13	13	3	Universidad Miguel Hernández de Elche	ALICANTE
Novials Sardá, Anna María	6	3	0	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Real Collado, José Tomás	16	12	2	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA
Ribalta Vives, Josep	21	12	5	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Rojo Martínez, Gemma	18	14	2	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	MÁLAGA
Simó Canonge, Rafael	29	15	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Vallejo Fernández de la Reguera, Mario	1	1	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Vázquez Carrera, Manuel	6	5	4	Universidad de Barcelona	BARCELONA
Vendrell Ortega, Joan Josep	17	14	6	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA
Vidal Cortada, Josep	38	23	11	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Zorzano Olarte, Antonio	13	11	8	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	BARCELONA

Clinical Guidelines and Consensus Documents 2023

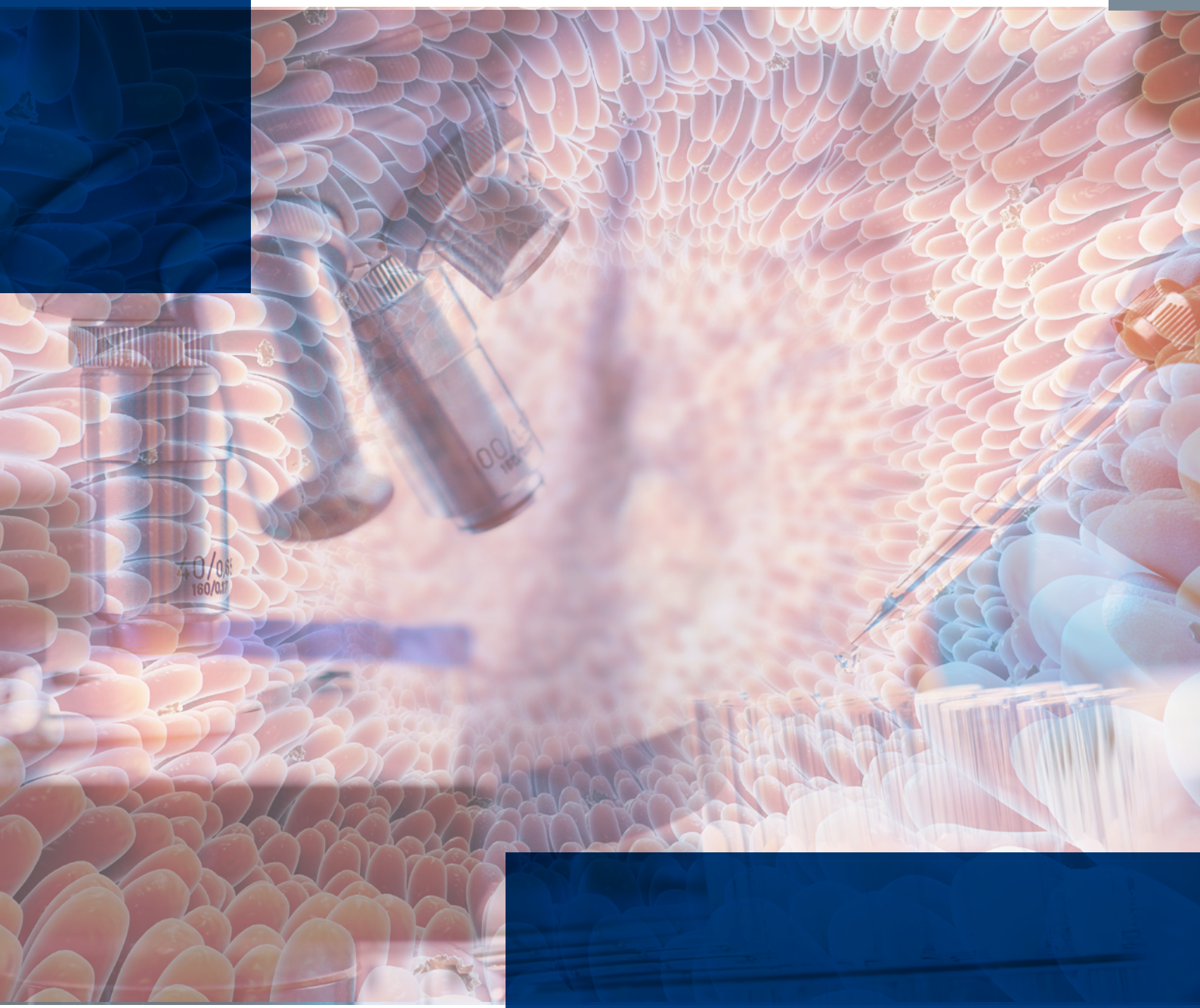
Three international and three national guidelines:

- 2023 Update on European Atherosclerosis Society Consensus Statement on Homozygous Familial Hypercholesterolaemia: new treatments and clinical guidance. European Heart Journal 2023; 44: 2277–2291. European Atherosclerosis Society.
- Continuous glucose monitoring and metrics for clinical trials: an international consensus statement. Lancet Diabetes Endocrinol 2023; 11: 42–57. Endorsed by: American Association of Clinical Endocrinologists, American Diabetes Association, Association of Diabetes Care and Education Specialists, DiabetesIndia, European Association for the Study of Diabetes, International Society for Pediatric and Adolescent Diabetes, Japanese Diabetes Society, Juvenile Diabetes Research Foundation.
- Consensus-based recommendations on physical activity and exercise in patients with diabetes at risk of foot ulcerations: a Delphi study. Braz J Phys Ther 2023; 27(2):100500. doi: 10.1016/j.bjpt.2023.100500. Associação Brasileira de Pesquisa e Pós-Graduação em Fisioterapia.
- Comprehensive approach to people with type 2 diabetes. Diabetes Knowledge Area of the Spanish Society of Endocrinology and Nutrition. Endocrinol Diabetes Nutr 2023; 70, Suppl. 1: 95-102. Sociedad Española de Endocrinología y Nutrición.
- Obesity and fertility. Position paper Endocrinol, Diabetes Nutr 2023; 70, Suppl. 1: 110-115. Spanish Society of Endocrinology and Nutrition, Spanish Society for the Study of Obesity, Spanish Fertility Society, Spanish Association of Urology, Spanish Society of Gynecology and Obstetrics, Spanish Society of Dietetics and Nutrition.
- Algorithm for the treatment of type 2 diabetes mellitus. RedGDPS 2023. Diabetes práctica 2023; 14(02):37-75. doi: 10.52102/diabet.pract.2023.2.art2. Network of Diabetes Study Groups in Primary Health Care.

Awards

CIBERDEM has received the award “Recognition of Public Research in the Field of Diabetes”, for its excellent research activity in diabetes and for the translation of the results into clinical practice, presented during the IX Edition of the Spanish Diabetes Federation Awards - Mercedes Sánchez Benito, within the framework of the VII National Congress of the Spanish Diabetes Federation (Madrid, October 7).

LIVER AND DIGESTIVE DISEASES



ciber | EHD

WELCOME FROM THE SCIENTIFIC DIRECTOR

Rafael Bañares Cañizares

During the year 2023, the area of liver and digestive diseases (CIBEREHD) has maintained its research development around liver and gastrointestinal tract diseases, globally characterized by their high prevalence, by their marked negative influence on the quality of life of patients and by their non-negligible mortality.

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

The high scientific quantity and quality of CIBEREHD has been maintained throughout this year. In fact, in 2023 the record number of publications in the area has been reached, over 800, with very high international leadership. In addition, the number of collaborative publications with other CIBER areas has continued to increase.

The CIBEREHD has maintained its commitment to the training of researchers in order to face generational replacement. During 2023 the CIBEREHD has continued its own pre-doctoral training program (Jaume Bosch contract) aimed at promoting collaborative activity in translational groups. Similarly, the third edition of the bioinformatics course has been carried out, which combines theoretical and practical classes with specialized faculty, and the training and teaching grants aimed at promoting national and international stays, as well as attendance at specialization courses, have also been maintained. In addition, we support young researchers, who do not yet have their own funding, by granting intramural projects specifically aimed at developing collaborative research that will enable them to apply for national calls for proposals in the near future.

Worth mentioning is that in 2023 we held the annual scientific conferences together with the area of Biotechnology, Biomaterials and Nanotechnology (CIBER-BBN), providing the optimal framework for establishing new collaborative synergies and thus structuring cross-cutting research projects.

During 2023 we have renewed the external scientific advisory board incorporating highly prestigious international researchers in the research fields of our area. After a first meeting with them, it became clear that the scientific health of the area is sound, although the need to vigorously promote the renewal of those group leaders close to retirement age was also expressed.

The area will undoubtedly face important challenges in the coming years: the adaptation of its scientific strategy to the current context of liver and digestive diseases, the need to increase its funding, the definitive incorporation of the patients' voice, as well as improving the communication of the results and advances obtained to society. Therefore, our commitment is to draw up a new multi-year scientific plan, which includes all the challenges and needs of the area, and which is fully aligned with the CIBER's strategic plan. This task, which will be developed during the next year, will be essential to meet the current challenges and bring to society the necessary return of our research activity.

PROGRAMS & PLATFORMS

MECHANISM OF LIVER DAMAGE, EVOLUTION AND PROGRESSION OF CIRRHOSIS AND LIVER TRANSPLANTATION

Rubén Francés Guarinos y Juan Manuel Pericàs Pulido / COORDINATORS

The year 2023 was once again a prolific one, and the resulting scientific production included multiple high-quality studies characterized by robust collaboration between CIBEREHD researchers, with researchers from other CIBER areas and with a host of international centers.

In the preclinical field, there have been numerous contributions, including several studies focused on portal hypertension (PHT) and cirrhosis. For example, a protein signature was identified through different omics tools capable of predicting the HVPG response in patients with HCV with sustained virological response (PMID: 37443448), endothelial biomarkers of PHT associated with the transcription factor CBX7 sensitive to pressure changes were characterized (PMID: 37151732), and metabolites such as ceramide and methionine could become key elements in prognostic tools (PMID: 36811400). It has also been possible to establish a precise systemic inflammatory profile in response to episodes of microbial antigen translocation (PMID: 36881247).

One study focused on alcoholic and metabolic liver disease, showed the increase of EpCAM+ CD133+ microvesicles in MASLD, suggesting its potential as a non-invasive biomarker (PMID: 37288714), and another study showed the role of StARD1 in the characteristic liver damage of alcoholic liver disease (PMID: 37473919).

Finally a study focused on the mechanisms of progression of liver damage and fibrosis has also characterized the relevance of the NRAS oncogene as a negative modulator through inhibition of necroptosis mechanisms (PMID: 37563155).

In terms of clinical studies, the development of a new noninvasive tool for the prediction of liver events in the general population is of note: the LiverRisk Score (PMID: 37572680). Another study validated the use of a noninvasive tool based on elastography to predict clinical events in patients with ACLD due to MASLD (PMID: 37573987). In PHT and hepatic vascular disease, one paper investigated the impact of anticoagulation on survival in patients with portal thrombosis (PMID: 36858157), another study investigated the incidence and prognostic factors for recurrence of non-cirrhotic portal thrombosis (PMID: 36058365) and a third focused on the evolution of portosystemic shunts after resolution of the triggering cause of liver disease (PMID: 38283756). A meta-analysis of individual data on cut-off points for liver fibrosis in MRI-elastography for NASH was published (PMID: 37121437), a field in which a relevant phase IIa clinical trial with efinopegdutide was led (PMID: 37355043). CIBEREHD researchers have also participated in other international clinical trials of high impact potential, as in the case of hepatitis B (PMID: 36697207).

In the field of alcohol-related liver disease and autoimmune hepatitis, we highlight the study showing the impact of the ALD phenotype on survival after an episode of variceal hemorrhage (PMID: 37183551) and the work that showed a lower efficacy of budesonide-based guidelines compared to prednisone/prednisolone (PMID: 36626622). In addition, CIBER researchers led an international consensus document on nomenclature, diagnosis and management of drug-induced hepatitis with autoimmune substrate (PMID: 37164270).

As regards liver transplantation we highlight the following: an important international work was led on alternative forms of revascularization of portal thrombosis in transplant recipients (PMID: 36690281), a study on the results of transplantation in portosinusoidal vascular disease (PMID: 36479977), a study demonstrating that time on the transplant waiting list has a notable influence on candidate frailty (PMID: 37767462), and a European consensus on the use of biomarkers in liver transplantation (PMID: 37711401).

GASTROINTESTINAL PATHOPHYSIOLOGY: INFLAMMATORY DISEASE AND MOTILITY DISORDERS

María Chaparro Sánchez / COORDINATOR

The CIBEREHD Gastrointestinal Pathophysiology program includes groups that develop their studies around four main lines of research: a) esophago-gastroduodenal acid peptic acid disease and Helicobacter Pylori (Hp); b) inflammatory bowel disease (IBD), celiac disease (CD) and eosinophilic esophagitis (EoE); c) functional digestive disorders and neuro-gastroenterology; and d) digestive cancer. The program's studies focus on the epidemiology, pathophysiology, diagnosis, prevention and treatment of these diseases through cooperative research, very often international and multidisciplinary, clinical and basic; and with a high level of clinical translation thanks to the great participation in consensus documents and national and international clinical practice guidelines and the registration of patents resulting from their research. In recent years, system biology and artificial intelligence analytical methods have been incorporated for frontier research. The results of this program are excellent and this is based fundamentally on the cooperative nature of the groups that comprise it, as well as their leadership capacity. This collaborative dynamic transcends the groups in the program and includes interaction with other CIBER thematic areas and with the CIBER's own platforms and those of the Instituto de Salud Carlos III, patient associations and society in general, with the aim of achieving cutting-edge health research. The most relevant milestones of the program in 2023 are:

ESOPHAGO- GASTRODUODENAL ACID PEPTIC DISEASES AND HELICOBACTER PYLORI (HP)

The European Registry on the management of Helicobacter Pylori infection (Hp-EuReg) has gone beyond the European setting and has materialized in a worldwide registry, led by CIBEREHD. There is a large body of evidence on the management of H. pylori infection derived from the registry that is of high impact. In addition, during 2023, two European projects (HORIZON-2022 and EU4H-2022), in which several CIBER groups also participate, both aimed at the prevention of gastric cancer, in which Hp-EuReg plays an essential role, have been initiated. A patent has been registered entitled Compounds for the treatment and/or prevention of an infection or disease caused by Helicobacter or Campylobacter, with CIBEREHD participation.

INFLAMMATORY BOWEL DISEASE (IBD), CELIAC DISEASE (CD) AND EOSINOPHILIC ESOPHAGITIS (EOE)

In the field of inflammatory bowel disease (IBD), the area has led projects on quality programs in the care of patients with IBD, highlighting the CIBER's vocation to serve society. Evidence has been generated on the epidemiology of IBD and studies on drugs in real clinical practice, which are essential to know the effectiveness and safety of drugs. An independent clinical trial has been completed to determine the feasibility of suspending anti-TNF drugs in patients with IBD in remission, which opens the way to efficiency in the use of these treatments. The study of the endoscopic approach to intestinal strictures (an orphan area) in Crohn's disease has continued with the leadership of independent clinical trials. The inclusion of pregnant patients with IBD in the DUMBO registry has been completed, covering the need to generate drug safety information in a population excluded from clinical trials.

As regards personalized medicine and systems biology, multiple advances have been made: we have completed the multiomics characterization of a cohort of newly diagnosed IBD patients and validated a panel of proteins of diagnostic value in clinical practice, which has led to the registration of a patent; we have completed the biomarker discovery phase to enable the selection of the most appropriate targeted therapy for IBD patients and we have initiated the validation phase; the first study using single-cell spatial transcriptomics in the intestine of patients with IBD has been published, which has made it possible to identify new populations of macrophages and neutrophils associated with the disease, among other milestones.

As for celiac disease (CD), our area leads epidemiological studies on this disease at national level following an exquisite methodology. Environmental factors that influence the development of the disease are being studied, suggesting that vaccination against rotavirus could have a protective effect on the development of celiac disease.

Finally, our program leads the international EoE CONNECT project, recognized as one of the main sources of information on eosinophilic esophagitis (EoE). We have identified a potential non-invasive marker of eosinophilic esophagitis derived from patient serum extracellular vesicles, a long-sought goal of great significance.

FUNCTIONAL DIGESTIVE DISORDERS AND NEURO-GASTROENTEROLOGY

We have described mechanisms underlying abdominal distension and potential therapeutic options in these patients, the role of colonic fecal impaction in the interpretation of gastrointestinal manometry results, the beneficial effects of guar gum and dextrin on the intestinal microbiota, the characteristic motor dysfunction in patients with mitochondrial neurogastrointestinal encephalopathy syndrome, the polygenic architecture of irritable bowel syndrome, as well as its genetic overlap with mental disorders, and for the first time in years, the real prevalence of disorders of the gut-brain interaction in Spain.

An artificial intelligence and machine learning algorithm has been developed to perform automatic mass screening for oropharyngeal dysphagia in all patients admitted to a hospital and to highlight this risk at the workstation of doctors, nurses and dieticians, which is a great benefit for frailty care.

DIGESTIVE CANCER

The application of the thermal liquid biopsy technique to the diagnosis of tumors has been developed as a rapid and non-invasive alternative. An analysis tool based on machine learning algorithms has been developed to generate a diagnostic model of the thermogram curves of serum samples that has been successfully applied to digestive pathologies (pancreatic cystic lesions, pancreatic cancer and colon cancer). A worm infection model (Galleria Melonella) has been developed to evaluate in vivo the active compounds against intestinal bacterial microbiota related to the development of colon cancer. In the same vein, we have demonstrated that the administration of isolated human intestinal mesenchymal stromal cells (iMSCs) protects against colorectal cancer associated with intestinal inflammation in an experimental murine model. This effect is associated with the modulation of the intestinal microbiota, so that the iMSC-microbiota interaction could be considered as a possible therapeutic target in clinical practice. Finally, a patent has been generated for a compound active against pancreatic cancer in preclinical trials (whose therapeutic target is NuPR1), which is a major milestone for such a lethal cancer.

HEPATIC AND DIGESTIVE ONCOLOGY

María Reig Monzón / COORDINATOR

Research in Liver and Digestive Oncology has maintained a high level of excellence, sharing its advances with the community through international guidelines for the management of cholangiocarcinoma (PMID: 37084797). We highlight that CIBEREHD investigators are at the forefront of an extensive international collaborative network, characterized by projects of a collaborative nature both within CIBEREHD itself and with other CIBER groups. A notable example is the IMMUNE4ALL precision medicine project (PMP22/00054).

In the translational field, we have focused our efforts on the study of NADPH oxidases in hepatocellular carcinoma (HCC), with special attention to the molecular mechanism regulated by NOX4 and its role in the epithelial-mesenchymal transition (PMID: 37463530). In addition, in the field of hepatoblastoma, a transcriptomic analysis of 180 epigenetic genes has highlighted the impact of epigenetics in this tumor, underlining how the pharmacological approach on epigenetic effectors reveals exploitable metabolic vulnerabilities to optimize the treatment of these patients (PMID: 37302584). Regarding cholangiocarcinoma, beyond published international guidelines (PMID: 37084797), we have identified prognostic biomarkers such as COMP/GNAI2/CFAI and ACTN1/MYCT1/PF4V through extracellular vesicles (PMID: 36868481).

In colon cancer, we have developed innovative diagnostic strategies, including a pioneering study on the role of serum methylation in serous lesions (PMID: 3812929). In addition, the ParCoFit study, a multicenter, open-label, parallel-group, randomized trial, revealed that screening by fecal immunochemical testing (FIT) failed to increase the participation of high-risk individuals in colon cancer screening.

In the field of immunotherapy (IO) and hepatocellular carcinoma, we have led not only in the proposal of new treatments (PMID: 38151184) but also the characterization of the profile of patients with liver dysfunction with immunotherapy-based regimens (PMID: 36632997) and the characterization of immune-mediated adverse effects (PMID: 37977714).

The most relevant projects of the groups involved in the area of liver and digestive cancer, which are collaborative and in which more than one CIBEREHD group participates, are detailed below.

1. AECC2023/2027: Medicina de precisión para el hepatoblastoma: identificación de nuevas terapias y biomarcadores predictivos utilizando un biorepositorio europeo único. IP: Carolina Armengol; José Juan García Marín.
2. PID2021-122551OB-I00: Deciphering the role of the NADPH oxidase NOX4 in hepatocellular carcinoma: relevance in tumor cells and stroma and cross-talk with the TGF-beta pathway. IP: Isabel Fabregat.
3. AECC 2021/2025: Randomized controlled trial of colonoscopy versus fecal immunochemical testing in colorectal cancer screening. The COLONPREV study. IP: Antoni Castells
4. PMP22/00054: Exploring the Feasibility of predictive and pharmacodynamics biomarkers of immunotherapy in solid tumors. IMMUNE4ALL, IP Enrique de Álava; IP HCC Maria Reig.
5. AECC 2024/2028: Rational to modulate the microbiome-induced endoplasmic reticulum stress as tool to avoid the immune evasion in Hepatocellular Carcinoma. RETO study. IP: Maria Reig.

TRAINING PROGRAM

Sofía Pérez del Pulgar Gallart / COORDINATOR

CIBEREHD 3RD BIOINFORMATICS COURSE

Coordinators: Ana Corraliza and Juanjo Lozano.

Date: November 15, 20 and 22 (theory-online); November 27 (in-person training); December 12 (online tutorial).

Methodology: 3 theoretical sessions (Introduction to R and Rstudio; Introduction to statistics in R; Transcriptomics; RNA sequencing - 6 hours) and 1 practical session in small groups (From transcriptomic data collection to final results: Resolving real cases. 4 hours). Number of participants: 48 people.

2023 COLLABORATIVE CIBEREHD AND CIBER-BBN MEETING

In this first scientific mereting held jointly with CIBER-BBN, we wanted to give a special role to young researchers by setting up an ad hoc scientific committee made up of 3 researchers from CIBEREHD (Rut Espinosa, Elisa Melón and Rocío Montero) and 3 researchers from CIBER-BBN (Alba García, Inmaculada García and Denise Marrero). With the support of the training programs of both areas, the young committee organized the following activities:

Young researchers workshop: "How to give visibility to your science beyond your research paper", María Guillot (Simbionte).

Poster session: Poster Tour and voting (via mobile App) for the best paper presented by a young researcher.

Award ceremony for the best oral communications and posters: Scientific monologue by Elisabet Prats, postdoctoral researcher at CIBER-BBN.

- Premio a la mejor comunicación oral: Pedro Rodrigues (Liver Diseases Group, IIS Biodonostia).
- Premio al mejor póster: Elisa Melón (Inflammatory bowel disease Group, IDIBAPS).

OTHER TRAINNG ACTIONS

Participation in courses/workshops/seminars:24 national and 6 international actions.

Organization of seminars/symposia: 23 actions endorsed by CIBEREHD, 3 of them developed internationally: "OGiP Seminars" organized by Sergi Castellví, "The BCLC 2023 update: evidence and value-based approach in real-world practice" organized by María Reig and "Liver Seminars" (https://liverse- minars.eu/), initiative led by Jordi Gracia and Rafael Bañares.

MOBILITY ACTIONS 2023

Marta Campos (IDIBAPS, Barcelona) made an international stay in the laboratory of Dr. Kate Kelley (UCLA, San Francisco, USA)).

Ana Martínez-Alcocer (IDIBAPS, Barcelona) spent 5 weeks at the Complutense University of Madrid under the supervision of Javier Cubero in the group led by Rafael Bañares.

Anabel Fernández (IDIBAPS, Barcelona) spent one week at CiMUS under the supervision of Rubén Nogueiras (Carlos Diéguez Group, CIBEROBN).

Meritxell Llorens (VHIR, Barcelona) spent one week in the laboratory of Dr. Esteban Domingo (CBMSO-CSIC, Madrid).

The following tables show the different training actions carried out::

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

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

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

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

● COURSE
● ENDORSE
● STAY

BIOINFORMATICS PLATFORM

The Bioinformatics platform continues to collaborate actively in the functioning of CIBEREHD and CIBER, with a fruitful year 2023, as reflected in the number of publications and funded projects as a result of its support.

The 3rd CIBEREHD Bioinformatics Course has been organized and coordinated together with Dr. Sofía Pérez del Pulgar. The satisfaction questionnaire shows that it was very favorably evaluated by the students with excellent acceptance ratings, an improvement on the previous year's evaluation.

A collaboration established with the group led by Dr. Juan Carlos García-Pagán has generated a very relevant publication with the discovery that clinical variables and the addition of the values of the metabolites ceramide (d18:1/22:0) and methionine are able to predict with a low margin of error the risk of developing decompensated liver cirrhosis.

- Nicoară-Farcău O, Lozano JJ, Alonso C, Sidorova J, Villanueva C, Albillos A, Genescà J, Llop E, Calleja JL, Aracil C, Bañares R, Morillas R, Poca M, Peñas B, Augustin S, Tantău M, Thompson M, Perez-Campuzano V, Baiges A, Turon F, Hernández-Gea V, Abraldes JG, Tapias EA, Torres F, Bosch J, García-Pagán JC; PreDesCI Study Investigators. Metabolomics as a tool to predict the risk of decompensation or liver-related death in patients with compensated cirrhosis. Hepatology. 2023 Jun 1;77(6):2052-2062. PMID: 36811400.

Successive high impact publications have resulted from the fruitful relationship established years ago with Dr. Jordi Gracia, and as part of a team of researchers at the international level such as:

- Ortega-Ribera M, Gibert-Ramos A, Abad-Jordà L, Magaz M, Téllez L, Paule L, Castillo E, Pastó R, de Souza Basso B, Olivas P, Orts L, Lozano JJ, Villa R, Bosch J, Albillos A, García-Pagán JC, Gracia-Sancho J. Increased sinusoidal pressure impairs liver endothelial mechanosensing, uncovering novel biomarkers of portal hypertension. JHEP Rep. 2023 Mar 8;5(6):100722. PMID: 37151732.

In the field of research related to immunotherapy as a therapeutic strategy to fight cancer, our group has participated in the discovery that the CD5L protein could be an important target for the treatment of many solid tumors.

- Sánchez-Moral L, Paul T, Martori C, Font-Díaz J, Sanjurjo L, Aran G, Téllez É, Blanco J, Carrillo J, Ito M, Tuttolomondo M, Ditzel HJ, Fumagalli C, Tapia G, Sidorova J, Masnou H, Fernández-Sanmartín MA, Lozano JJ, Vilaplana C, Rodriguez-Cortés A, Armengol C, Valledor AF, Kremer L, Sarrias MR. Macrophage CD5L is a target for cancer immunotherapy. EBioMedicine. 2023 May 91:104555. PMID: 37054630.

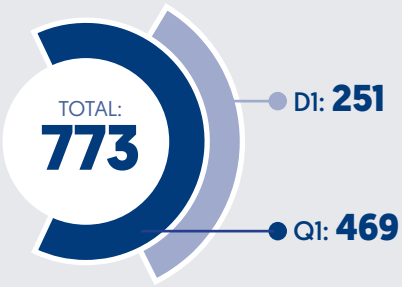
The platform continues to collaborate with important academic groups and other areas of the CIBER for the discovery of genetic signatures related to ischemic stroke.

- Arbaizar-Rovirosa M, Gallizioli M, Lozano JJ, Sidorova J, Pedragosa J, Figuerola S, Chaparro-Cabanillas N, Boya P, Graupera M, Claret M, Urra X, Planas AM. Transcriptomics and translatomics identify a robust inflammatory gene signature in brain endothelial cells after ischemic stroke. J Neuroinflammation. 2023 Sep 11;20(1):207. PMID: 37691115.

SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations

*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168,9	Sandborn W.J., Vermeire S., Peyrin-Biroulet L., Dubinsky M.C., Panes J., Yarur A. et al. Etrasimod as induction and maintenance therapy for ulcerative colitis (ELEVATE): two randomised, double-blind, placebo-controlled, phase 3 studies. Lancet. 2023 Apr 8;401(10383).
168,9	Serra-Burriel M., Juanola A., Serra-Burriel F., Thiele M., Graupera I., Pose E. et al. Development, validation, and prognostic evaluation of a risk score for long-term liver-related outcomes in the general population: a multicohort study. Lancet. 2023 Sep 16;402(10406):988-996.
158,5	Loftus E.V., Panes J., Lacerda A.P., Peyrin-Biroulet L., D'haens G., Panaccione R. et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med. 2023 May 25;388(21):1966-1980.
82,9	Larrayoz M., Garcia-Barchino M.J., Celay J., Etxebeste A., Jimenez M., Perez C. et al. Preclinical models for prediction of immunotherapy outcomes and immune evasion mechanisms in genetically heterogeneous multiple myeloma. Nat Med. 2023 Mar;29(3):632-645.
82,9	Gines P., Thiele M., Graupera I., Serra-Burriel M., de Knegt R.J., Lammert F. et al. Screening for fibrosis to diagnose liver diseases early: the LIVERSCREEN project. Nat Med. 2023 Apr;29(4):774-775.
65,1	Calvisi D.F., Boulter L., Vaquero J., Saborowski A., Fabris L., Rodrigues P.M. et al. Criteria for preclinical models of cholangiocarcinoma: scientific and medical relevance. Nat Rev Gastroenterol Hepatol. 2023 Jul;20(7):462-480.
65,1	Verstockt B., Salas A., Sands B.E., Abraham C., Leibovitzh H., Neurath M.F. et al. IL-12 and IL-23 pathway inhibition in inflammatory bowel disease. Nat Rev Gastroenterol Hepatol. 2023 Jul;20(7):433-446.
65,1	Huang D.Q., Singal A.G., Kanwal F., Lampertico P., Buti M., Sirlin C.B. et al. Hepatocellular carcinoma surveillance - utilization, barriers and the impact of changing aetiology. Nat Rev Gastroenterol Hepatol. 2023 Dec;20(12):797-809.
64,8	Pallett L.J., Swadling L., Diniz M., Maini A.A., Schwabenland M., Gasull A.D. et al. Tissue CD14+CD8+ T cells reprogrammed by myeloid cells and modulated by LPS. Nature. 2023 Feb;614(7947):334-342.
45,042	Feagan B.G., Sands B.E., Sandborn W.J., Germinaro M., Vetter M., Shao J. et al. Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial. Lancet Gastroenterol Hepatol. 2023 Apr;8(4):307-320.

CIBEREHD Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Albillos Martínez, Agustín	46	33	20	Universidad de Alcalá	MADRID
Andrade Bellido, Raúl	25	21	14	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	MÁLAGA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Armengol Niell, Carolina	18	13	10	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Bañares Cañizares, Rafael	49	35	21	Servicio Madrileño de Salud	MADRID
Berenguer Haym, Marina	40	23	10	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	VALENCIA
Bujanda Fernández de Pierola, Luis	50	31	20	Asociación Instituto de Investigación Sanitaria Biogipuzkoa	GUIPÚZCOA
Buti Ferret, María Asunción	23	14	9	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Calvet Calvo, Xavier	16	9	5	Fundación Instituto de Investigación e innovación Parc Taulí	BARCELONA
Cascante Serratosa, Marta	8	6	2	Universidad de Barcelona	BARCELONA
Castells Garangou, Antoni	79	50	28	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Clave Civit, Pere	13	6	0	Fundación Privada Salud del Consorcio Sanitario del Maresme	BARCELONA
Domenech Morral, Eugeni	16	7	1	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Esplugues Mota, Juan Vicente	4	4	2	Universidad de Valencia	VALENCIA
Esteban Mur, Juan Ignacio	12	6	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Esteve Comas, María	19	10	6	Fundación Mutua Terrassa	BARCELONA
Fabregat Romero, María Isabel	8	7	4	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Fernández-Checa Torres, José Carlos	20	15	11	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Fondevila Campo, Constantino	45	30	15	Servicio Madrileño de Salud	MADRID
Forns Bernhardt, Xavier	24	17	10	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Francés Guarinos, Rubén	22	14	7	Instituto de Investigación Sanitaria y Biomédica de Alicante	ALICANTE
García Marín, José Juan	17	12	8	Universidad de Salamanca	SALAMANCA
García Pagán, Juan Carlos	40	29	19	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Genesca Ferrer, Joan	39	28	17	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Gines Gibert, Pere	44	31	19	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
González Gallego, Javier	8	4	2	Universidad de León	LEÓN
Jover Atienza, Ramiro	9	4	1	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	VALENCIA
Lanas Arbeloa, Ángel	46	26	9	Fundación Instituto de Investigación Sanitaria Aragón	ZARAGOZA
Mata García, Manuel de la	15	12	5	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Mato de la Paz, José María	37	22	15	Asociación Centro de Investigación Cooperativa en Biociencias, CIC BIOGUNE	VIZCAYA
Pastor Anglada, Marçal	1	1	0	Universidad de Barcelona	BARCELONA
Pérez Gisbert, Javier	53	32	12	Servicio Madrileño de Salud	MADRID
Reig Monzon, María Elisa	15	11	8	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Romero Gómez, Manuel	45	30	20	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Salas Martínez, Azucena	31	18	10	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Sánchez de Medina López Huertas, Fermín	9	8	2	Universidad de Granada	GRANADA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Sangro Gómez-Acebo, Bruno Carlos	49	35	18	Universidad de Navarra	NAVARRA
Santos Vicente, Javier	32	9	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Soriano Pastor, Germán	23	18	14	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA

Linked Groups

GROUP LEADER	INSTITUTION - CENTER	PROVINCE
Caballería Rovira, Llorenç	Universidad Autónoma de Barcelona	BARCELONA
Calleja Panero, Jose Luis	Servicio Madrileño de Salud	MADRID
Casado Pinna, Marta	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Crespo García, Javier	Instituto de Investigación Marqués de Valdecilla	CANTABRIA
Cubiella Fernández, Joaquín	Servicio Gallego de Salud	CORUÑA, A
García Monzón, Carmelo	Servicio Madrileño de Salud	MADRID
Molina Infante, Javier	Fundación del Hospital Nacional de Parapléjicos	TOLEDO
Padillo Ruiz, Francisco Javier	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA

Clinical Guidelines and Consensus Documents 2023

- AEEH «Consensus about detection and referral of hidden prevalent liver diseases».
- Anesthesia and Critical Care for the Prediction and Prevention for Small-for-size Syndrome: Guidelines from the ILTS-iLDLT-LTSI Consensus Conference.
- Delphi Initiative for Early-Onset Colorectal Cancer (DIRECt) International Management Guidelines.
- Diagnosis and management of Barrett esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Guideline.
- EASL Clinical Practice Guidelines on acute-on-chronic liver failure.
- EASL-ILCA Clinical Practice Guidelines on the management of intrahepatic cholangiocarcinoma.
- ECCO Topical Review on Biological Treatment Cycles in Crohn's Disease.
- Enhanced recovery for liver transplantation: recommendations from the 2022 International Liver Transplantation Society consensus conference.
- European Society for Organ Transplantation Consensus Statement on Biomarkers in Liver Transplantation.
- Management of Established Small-for-size Syndrome in Post Living Donor Liver Transplantation: Medical, Radiological, and Surgical Interventions: Guidelines From the ILTS-iLDLT-LTSI Consensus Conference.
- Post Living Donor Liver Transplantation Small-for-size Syndrome: Definitions, Timelines, Biochemical, and Clinical Factors for Diagnosis: Guidelines From the ILTS-iLDLT-LTSI Consensus Conference.
- Preventing Small-for-size Syndrome in Living Donor Liver Transplantation: Guidelines from the ILTS-iLDLT-LTSI Consensus Conference.
- Recommendations for the integral diagnosis of chronic viral hepatitis in a single analytical extraction.

RARE DISEASES

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Pablo Lapunzina Badía

It is my honor to present in this Annual Report the scientific contributions of the groups that make up the area of Rare Diseases, which show the effort and involvement, as well as the arduous collaborative work that makes it possible for us to achieve our goals for the development of new therapies and the rapid diagnosis of rare diseases.

Our ultimate goal is the patients, who suffer from low-prevalence diseases, many of them unknown to a large part of society, but nevertheless, no less important.

Many of them have generally devastating symptoms and consequences that to this day still do not have effective treatments. Therefore, every result, from basic to clinical research, every advance in the field of rare diseases that is made, is fundamental for the lives of these patients.

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

We are generators of hope for patients and their families, so that their quality of life may be improved, so that the pain they suffer is more bearable, while we, from the predoctoral student to the most senior researcher, continue working to find a cure.

PROGRAMS & PLATFORMS

TRANSLATIONAL GENOMIC MEDICINE

Ángel Carracedo Álvarez / COORDINATOR

During 2023, the IMPaCT-GENóMICA program has continued to promote the establishment of a cooperative infrastructure for the performance of highly complex genetic studies, in order to accelerate the transfer of R&D&I and improve the efficiency in the use of resources of the National Health System. Of particular note:

- More than 2,000 patients have had access to the program for genomic analysis, and work is underway to obtain the diagnostics.
- Establishment of a network with more than 300 collaborators and more than 100 hospitals, together with a network of high-capacity genomic analysis centers.
- Training and dissemination activities, highlighting the second IMPaCT-GENOMICA Conference, held on October 9 in Madrid, to showcase these results and as a meeting point for professionals and patients.
- Creation of the IMPaCT-GENóMICA website.
- Somos FEDER Award received by Ángel Carracedo for his work and contribution as project coordinator.

Among the milestones of the Research Program (RP) we highlight the following:

- Ángel Carracedo's group has published a series of papers in different fields: autism, genome-wide association studies in non-small cell lung cancer or breast cancer, and variant analysis in COVID-19, among others.
- The study published in Int JMol Sci by Miguel Ángel Medina's group, in collaboration with CIBERCV, which identified the role of immunomodulator dimethyl itaconate as an inhibitor of angiogenesis.
- Salud Borrego's group has participated in several papers, most notably an article in Int J Mol Sci in which new candidate genes for familial thyroid cancer have been identified by WES; or Front Cell Dev Biol, in which macular dystrophies in patients are associated with a dominant splicing variant.
- Santiago Rodríguez de Córdoba's group has published several articles, most notably his article in Kidney Int on the relevance of thrombomodulin variants in atypical hemolytic uremic syndrome, as well as in Front Immunol on the role of a bacterial enzyme as an evasive factor of the immune system.
- Mario Fernández Fraga's group has published a study in Molecular Oncology in which they identify proteins whose role could be key in the progression of glioblastoma. Also noteworthy is the work published in Cardiovascular Diabetology, in collaboration with CIBEROBN, on the association of obesity or diabetes in pregnant mothers with a greater predisposition in their offspring.
- The group led by Joaquín Dopazo has developed the SPACNACS database, which makes it possible to advance in the knowledge of pathogenic variants and thus help in the diagnosis of rare diseases.
- We would like to highlight the work of ENoD in 2023: in addition to its activity as a transversal program in diagnostics, in intramural actions, participating in 2 of the 10 ACCI projects awarded in 2023; its contribution in the working groups with its key leadership in the Bioinformatics Working Group; and mainly for its close collaboration and support for the development of the IMPaCT-GENóMICA project.

Finally, we would like to highlight the participation of the groups of the Research Program in 9 proposals of the ACCI 2022 call, 6 of which obtained funding.

MITOCHONDRIAL AND INHERITED METABOLIC MEDICINE

Rafael Artuch Iriberri / COORDINATOR

The following are some examples of scientific advances in rare diseases:

Diagnostics:

- Importance of neonatal screening in treatable neurodevelopmental diseases such as BCKDK deficiency. Rafael Artuch's group. PMID 36729635.
- Identification of new biomarkers in inclusion body myositis (IBM) by multi-omics analysis and validation of new patient-derived 2D cellular models. Glória Garrabou's group. PMID 37627634 and 36860172.
- Importance of early identification of congenital myasthenic congenital syndromes for effective treatment. Miguel Ángel Martín's group. PMID 37176748.
- CRISPR/Cas9-based functional genomics strategy to decipher the pathogenicity of genetic variants in inherited metabolic disorders. Antonia Ribes's Group. PMID 37718653.
- Improved diagnosis and treatment for CAD protein deficiency. Alberto Marina's unit. PMID 37540500.
- New algorithm (ClínPrior) to improve diagnosis and discovery of new genes based on interactomes. Aurora Pujol's group. PMID 37679823.

Other milestones::

- Progress in the study of McArdle's disease, with the participation of patients through the EUROMAC registry. Ramon Martí's group. PMID 37488619.
- Advances in the understanding of the pathophysiology of Schaaf-Yang syndrome. Susanna Balcells Group. PMID 36243518.
- Description of ATAD3C functions in the mitochondrial membrane with implications in pediatric diseases. Eduardo Ruiz-Pesini group. PMID 38092275.
- Description of a new inborn error of metabolism caused by a defect in the synthesis of Coenzyme A. Group led by Bélen Pérez. PMID 36564894.
- Advances in the Study of MLC Patients. Manuel Palacin and Raúl Estévez's group. DOI:10.1016/j.dscb.2023.100079.
- New model for the study of neurotransmission defects based on iPSCs. Rafael Artuch's group. PMID 36740977.
- Description of the functions of two new deficiencies associated with RINT1 and DEGS1. Aurora Pujol's.

CIBERER ACCI intramural projects awarded in 2023 and coordinated by program members in 2023:

- Multi-omics and functional characterization of aging in phenylketonuria for the identification of new biomarkers and therapeutic options. F.J. Garcia.
- Multi-omics and functional integration in the diagnosis of mitochondrial energy metabolism diseases. F. Tort.
- Nanomedicine for drug delivery in inborn errors of metabolism: proof of concept in PMM2- CDG. B. Perez.

NEUROLOGICAL DISORDERS

Pía Gallano Petit / COORDINATOR

This Research Program (RP) is composed of 7 groups from different fields, ranging from clinical, genetic and pathophysiology in neurological pathologies, both of genetic and acquired origin.

At the scientific level, several publications stand out, such as the work published in the International Journal of Molecular Sciences, signed among others by Carlos Romá-Mateo and José Luis García-Giménez, Pascual Sanz and Mireia Moreno. It is the result of an intramural project and will contribute to improve the knowledge of Lafora disease thanks to the finding of differences in the production of microRNAs.

Also noteworthy is the work of Antioxidants (Basel) by Federico Pallardó's group on the role of microRNAs in rare autoimmune diseases.

In addition, collaborative studies have been published in journals such as Neuromuscular Disorders, Journal of Medical Genetics or Journal of Neurology, on neuromuscular diseases in which the units of Pía Gallano and Eduard Gallardo participate, together with clinicians from other units, on Duchenne and Becker muscular dystrophy, AChR deficiency syndrome or nemaline myopathy.

The article published in Amyloid in which Teresa Sevilla participates, describes a new Spanish endemic variant of hereditary transthyretin amyloidosis, both at GLu89Lys phenotypic level and clinical outcomes.

José Serratosa's group has continued to increase knowledge on epilepsies, through publications in Epilepsia and Epilepsia Open, delving into the course of adult familial myoclonic epilepsy and treatment.

Josep Dalmau stands out for his publication in Lancet Neurology of a retrospective cohort study presenting adverse neurological effects related to immune checkpoint inhibitors.

It has been a fruitful year for the Research Program groups, since once again this year, all of them have received funding in one of the current intramural calls for proposals. The 2020 projects were completed and work was done on the 2021 projects, in this case on new serological markers in patients with rare neuroimmu- nological disorders, led by Luis Querol with the participation of Josep Dalmau. Also, the project consisting of the first repository of methylation data from the Spanish reference population and improvement of the epigenetic study in patients with undiagnosed rare diseases (Epi-ENoD), with the participation of José Luis García-Giménez.

In the 2022 call, the groups led by Teresa Sevilla and Pía Gallano, participate as collaborators in 3 of the awarded projects. Also noteworthy is the participation of 4 groups from the program in 3 of the projects awarded through the Call for Working Groups, on Amyotrophic Lateral Sclerosis (ALS), organoids and gene editing and therapy.

As regards the ALS group, the participation of Ricard Rojas and Juan Francisco Vázquez stands out, together with other groups working on ALS, as well as the presence of patient associations. The main objectives are to strengthen the ALS Research Network and to set up the national ALS registry within GENRARE with the collaboration of the Luzon Foundation.

PEDIATRIC AND DEVELOPMENTAL MEDICINE

Cristina Fillat Fonts / COORDINATOR

The main activities and results linked to the objectives defined in the 2023 Action Plan are summarized below. Within the objectives of promoting the development of genomic diagnostic tools and deepening therapies for the diseases of interest to the Program, the following are highlighted:

- Advances in the development of artificial placentas and in neonatal and fetal brain measurements, from the group led by Eduard Gratacós.
- The identification of new variants causing hereditary muscular dystrophy associated with DTNA, the development of new diagnostic tools and the functional study of Gdap1 on mitochondrial function, from the group coordinated by Francesc Palau.
- Studies on the migration and invasion of Ewing sarcoma cells, from the group led by Javier Alonso.
- Developments in diagnostic tools and the identification of diseases associated with variants in the FGFR3 and PLXND1 genes, as well as preclinical studies of a new treatment for cardiovascular pathology in a model of Williams-Beuren syndrome, from the group coordinated by Luis Pérez Jurado.
- The studies on the use of genomic technologies in the study of autism spectrum disorders and the expansion of cases with clinical and genetic correlations in diseases such as hemophilia B, in patients with variants in SETD2, Snijders Blok-Campeau syndrome, among others, from the group led by Pablo Lapunzina.
- The identification of Ellis-van Crevelan syndrome as a skeletal ciliopathy related to DYNC2H1, by the group led by Víctor Ruiz Pérez.
- Advances in the understanding of the neuronal mechanisms regulated by Dyrk1A, from the group coordinated by Cristina Fillat.

Furthermore, there are numerous individual publications by the groups within this research line, which are described in more detail in the specific section for each group.

Also noteworthy are the 2 intramural projects awarded during 2023 coordinated by Ángela Nieto with the participation of the group led by Pablo Lapunzina and Lara Cantarero, respectively, and in which groups from other CIBERER Research Programs also participate.

SENSORINEURAL PATHOLOGY

Lluís Montoliu José / COORDINATOR

During 2023, the seven groups that make up the Sensorineural Pathology Research Program have obtained important scientific results, dissemination and collaboration with patient associations, both independently and in collaboration with other groups of the CIBERER. The year 2023 has been fruitful for this Research Program, since all the groups have received funding in one of the current intramural calls for proposals.

In 2023 the projects of the 2020 Intramural Cooperative Complementary Actions Call were closed and work was carried out on the development of the projects awarded in 2021, of which 3 are led by researchers of the program,: Almudena Fernández, Lluis Montoliu and Serena Mirra, and 5 have the participation of the Research Program groups: Gemma Marfany, Carmen Ayuso, José María Millán and Miguel Ángel Moreno.

In the 2022 call, funding has been granted to 2 projects led by groups of the Research Program: Gema García and José María Millán, and Carmen Ayuso's unit participates as a collaborator in another project.

In the call for Working Groups in 2023, 2 of the awarded groups are coordinated by Research Program groups: Almudena Fernández and Silvia Murillo. A total of 6 Research Program groups are participating in this call.

The projects awarded in the Call for New Experimental Models for Rare Diseases, in which Paola Bovolenta and Almudena Fernández are participating, have been completed.

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

Work has also been carried out on the final part of the project linked to the Biobanks and Biomodels Platform PT20 (2021-2023) of the ISCIII, in which Isabel Varela

and Lluís Montoliu participate, and on the presentation of the new CIBER unit granted PT23 (2024-2026).

CIBER was also designated as a new member of the World Hearing Forum (WHF) of the World Health Organization (WHO) for the period 2022-2025, at the initiative of Isabel Varela-Nieto.

Some events organized by Research Program groups include:

- XVIII International Conference on Translational Research and Precision Medicine: "Application of Personalized Medicine in prevention and public health", February 2, Fundación Jiménez Díaz, coordinated by Carmen Ayuso.
- Sign language: a tool to improve health care for patients with hearing loss, March 3, National Museum of Natural Sciences in the framework of World Hearing Day, coordinated by Isabel Varela-Nieto.
- Rare diseases: each one of them a minority but affecting millions of people, in-person course from 3 to 5 June, UIMP, coordinated by Lluís Montoliu and Almudena Fernández.
- UB-CIBERER Mini Symposium: Rare Neuromuscular Diseases, November 6, UB. Coordinated by Susanna Balcells, Gemma Marfany, Raquel Rabionet and Roser Corominas.
- 6th edition of the course 'Course on Bioinformatics Analysis of massive sequencing data applied to genetic diagnosis and translational research", online from November 20 - 29. Coordinated by Miguel Ángel Moreno and Matías Morín.

ENDOCRINE MEDICINE

Susan Webb / COORDINATOR

This Research Program is made up of only two full research groups and a third associated group, hence the importance of incorporating the additional strength of the 3 Linked Clinical Groups.

The groups associated to this Research Program during 2023 have published articles, among which we can highlight those of the group led by Antonio Moreno on myoclonic dystonia (published in Dev. Med. Child Neurol.), those carried out by the group led by Susan Webb on Cushing's disease (published in Eur. J. Endocrinol. and Front Endocrinol (Lausanne)) and acromegaly (published in Clin Endocrinol (Oxf) and J Clin Endocrinol Metab), and those carried out by the group led by Luis Castaño on Bartter syndrome (Sci Rep) and deficiency in sexual differentiation (PLoS One); the latter are works in collaboration with different pediatric centers such as the Renaltube group and in collaboration with the University of Bern (Switzerland).

Also worth mentioning is the important collaboration between the groups belonging to this Research Program, as can be seen in the collaborative research on Cushing's syndrome and acromegaly. Thus, the article in J Clin Endocrinol Metab includes authors from the groups of Susan Webb (1st, last and coordinator of the group) and Luis Castaño (Dr. Gaztambide). Also, the article published in Eur J Endocrinol is a new publication of the European registry of Cushing's syndrome ERCUSYN which is led by Susan Webb's group, while Front Endocrinol (Lausanne) is a work carried out between Susan Webb's and Luis Castaño's groups. In addition, 2 papers have been published on acromegaly and REMAH (Spanish Molecular Registry of Pituitary Adenomas), one in collaboration with Mónica Marazuela. Finally, another REMAH collaborative work on molecular characterization of non-functioning pituitary tumors should also be highlighted because the first author is a CIBERER postdoctoral fellow (Joan Gil) from the group led by Susan Webb.

Also noteworthy is Susan Webb's participation in a consensus document published in Nature Medicine, chosen precisely because of her experience in rare diseases and Patient Reported Outcome Measures -PROMs.

HEREDITARY CANCER, HEMATOLOGIC AND DERMATOLOGICAL DISEASES

Juan Antonio Bueren / COORDINATOR

This Research Program is made up of 10 research groups and 5 Linked Clinical Groups that have worked during 2023 to achieve different scientific, translational and collaborative milestones:

- Advances in the knowledge of molecular bases of disease. We highlight, among others: the study of the regulatory effects of miRNAs on gene expression and tumorogenesis in gastric cancer, carried out by Rosario Perona's group; studies on the compensatory effect of a FANCA variant in patients with Fanconi anemia, carried out by Jordi Surrallés' group; the molecular and clinical characterization of a mutation in antithrombin deficiency by the group led by Javier Corral; the identification of genetic modulators in haploinsufficiencies by the group led by Eduardo López Granados; and the work of Maria Luisa Cayuela on the identification of aptamers that regulate myelopoiesis in congenital netropenia syndromes.
- Case reports and clinical guidelines: the genetic and familial study of a Von-Hippel-Lindau patient by Luisa Botella's group, and the development of clinical guidelines and establishment of consensus for the management of hereditary angioedema by Teresa Caballero's group are relevant.
- Development of diagnostic and prognostic tools: Javier Corral's group has highlighted the role of long read sequencing for the identification of structural variants in hematological disorders. We also highlight the study by Mercedes Robledo on the identification of differential markers in patients with pheochromocytoma at increased risk of metastasis.

Also noteworthy are the studies of immune response after COVID vaccination in patients with inflammation-mediated diseases, studies carried out by Eduardo López's group.

- Advances in the therapeutic field: Of note are the international clinical programs of Juan A. Bueren's group in gene therapy for Fanconi anemia, immunodeficiency due to leukocyte adhesion deficiency and pyruvate kinase deficiency, as well as the signing of the license agreement with Kiji Therapeutics for genetically modified mesenchymal stem cell technology for graft-versus-host disease. Also relevant is the agreement of Marcela del Rio's group with CURE-EB to finalize the regulatory preclinical phase prior to the clinical trial of patients with Epidermolysis Bullosa. Luisa Botella has identified tacrolimus as a potential treatment for hereditary hemorrhagic telangiectasia. In the collaborative field, the study in which several Research Program groups have participated together with the linked clinical group of Julián Sevilla, demonstrating the restoration by gene therapy of the transcriptional program of hematopoietic stem cells in Fanconi anemia, is relevant.
- Intellectual property protection: two patents have been applied for in 2023 from the Research Program: José Carlos Segovia, who proposes a non-genotoxic conditioning procedure for hematopoietic stem cell transplantation; the second, Víctor Mulero, who proposes the repositioning of drugs for the treatment of anemias.
- Finally, worth mentioning is the participation of the Research Program in 5 ACCIs awarded in 2022 and 5 working groups.

TRAINING PROGRAM

Luis Pérez Jurado / COORDINATOR

The CIBERER Training Program has developed its main actions in 2023 along two main lines:

- Courses: Organization and call for attendance grants.
- Mobility Grants.

ORGANIZATION OF COURSES AND SEMINARS

The CIBERER Training Program participated in the organization or co-organization of the following courses:

- EURORDIS SUMMER SCHOOL, 7th Edition. Developed in hybrid format.
- I Course on nanopore sequencing. In-person course.
- Course "GATK Workshop 2023: From reads to diagnostic and secondary findings". In person.

CALL FOR ATTENDANCE GRANTS

Grants were also awarded to attend the following courses:

- EURORDIS Summer School, 7th Edition. 1 grant.
- Course: "Training on strategies to foster solutions of undiagnosed rare disease cases". 2 grants.
- Course: "Brain organoids Summer School". 2 grants.
- Course: "Exploitation of R&D results and technologies for research personnel". 1 grant.
- Course: "UIMP Course: Rare diseases: each one rare, but affecting millions of people". 1 grant.
- Course: "GATK Workshop 2023: From reads to diagnostic and secondary findings". 9 grants.
- Course on Bioinformatics Analysis of massive sequencing data applied to genetic diagnostics and translational research, 6th Edition. 5 grants.
- I Course on nanopore sequencing. 6 grants.

ATTENDANCE TO TRAINING COURSES ORGANIZED BY CIBER

In addition, the training program provided support for 7 people to attend the course on Communication organized by the CIBER.

MOBILITY GRANTS

In 2023, mobility grants continued to be open to internal and external, national and international mobilities, with the former being provided preferentially. Thus, several researchers were able to benefit from this program to broaden their training and advance the projects in which they were involved.

The following table shows the mobilities granted in 2023:

Mobilities granted

BENEFICIARY	ISSUING GROUP	RECEIVING GROUP
Benítez Quesada, Yolanda	Lapunzina Badía, Pablo D.	Carracedo, Ángel
Cavero Moreno, Débora	Surrallés, Jordi	Bueren, Juan Antonio
Centeno Pla, Mónica	Balcells Comas, Susanna	Glial and Neuronal Biology, Lund University-Lund (Suecia)

BENEFICIARY	ISSUING GROUP	RECEIVING GROUP
Crespo González, Ariadna	Santos Ocaña, Carlos	Mulero Méndez, Víctor
Fernández Cancio, Mónica	Moreno Galdó, Antonio José	Dopazo Blázquez, Joaquín
Fernández Suárez, María Elena	Borrego López, Salud	Corral de la Calle, Javier
Fernández-Caballero Palomeque, Lidia	Ayuso, Carmen	Institute of Molecular and Clinical Ophthalmology Basel (IOB) - Rivolta, Carlo-Basilea (Suiza)
Garrido Rodríguez, Pedro	Corral de la Calle, Javier	BIOBIX Lab-Gante (Bélgica)
Herráiz Gil, Sara	del Río Nechaevsky, Marcela	Dopazo Blázquez, Joaquín
Lozano Gil, Juan Manuel	Mulero Méndez, Víctor	Bueren, Juan Antonio

BIOBANK PLATFORM

Federico Pallardó Calatayud / COORDINATOR

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

There are 1440 biological samples in the Biobank regime, from 89 different pathologies available for consultation in the online catalog (http://www.ciberer-biobank.es/Catalogo/).

Samples have been received from 221 new donors, many recruited in collaboration with various RD patient associations.

Transfer of samples: 297 biological samples transferred, 186 as biobank samples destined for 5 research projects with the remaining 111 samples in custody.

The provision of processing services to CIBERER/CIBER researchers has been continued and the offer has meant that the number of these services has continued to grow, with a total of 193 in 2023.

Custody Service. A new CIBERER custody service has been initiated and two services initiated in previous years have been completed, with a group external to CIBERER and a biotechnology company, resulting in a revenue of 850 €.

The CBK continues to collaborate with Biobank networks: in the Valencia Biobank Network, the CBK is responsible for managing applications for prospective RD collections in the Valencia Region; collaboration in the ISCIII National Biobank and Biomodels Network Platform and in the Eurobiobank, with the CBK catalog available on their respective websites.

We maintain different types of collaborations::

- Collaboration with institutions: Agreements with IBSP-CV/FISABIO and Banco Nacional de ADN and the sample deposit agreement with INCLIVA for the creation of a collection of fibroblasts from control donors.
- Collaboration with patient associations:
  - ENACH Association (Neurodegenerative disease due to cerebral accumulation of iron)
  - AFASW Alliance of Families Affected by Wolfram Syndrome
  - DDX3X España Association
  - FEDERAS, Spanish Federation of Nooman's Syndrome and other RASopathies
  - Tarlov cysts
  - ADECYL,

Another of our objectives is to participate in Research Projects, specifically: i) ISCIII Biobanks Platform (Strategic Action in Health PT20/00118) and ii) ACCI-CIBERER21 Call, TeraTRAF: Approach to therapy in pathologies due to pathogenic mutations in TRAF7 and an EJP RD project, Genomit.

GENOMIT: A multi-omics approach for the diagnosis and monitoring of mitochondrial diseases. We also collaborated in 2 ACCI projects as a CIBERER platform. These projects have allowed us to obtain additional funding for the CBK.

The CBK team has attended and participated in 13 different events where the activity of the biobank has been disseminated, most notably the following two initiatives:

- The podcast "The science of the singular" of Share4Rare and CIBERER,
- The "CuadeERnos" of the FEDER Foundation.

As a result of the management of the CBK, we have collaborated in the publication:

- Damián, A., Núñez-Moreno, G., Jubin, C., Tamayo A., Rodríguez de Alba, M., Villaverde, C., Fund, C., Delépine, M., Leduc, A., Deleuze, JF., Mínguez, P., Ayuso, C., Corton, M. Long-read genome sequencing identifies cryptic structural variants in congenital aniridia cases. Hum Genomics. 2023 Jun 2;17(1):45. doi: 10.1186/s40246-023-00490-8.

BIER PLATFORM

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

It is important to note that the high confidence variant detection rate (STRONG) is 23%, almost double that reported in the literature for reanalysis of undiagnosed cases. Although we do not receive feedback from all, in general the feedback we receive is confirmatory. Collaborations have also been extended to more groups, including Antonio Moreno of the VHIR, Victoriano Mulero of the Instituto Murcia de Investigación Biosanitaria, and Verónica Cantarín of the Hospital Infantil Universitario Niño Jesús.

Following the pattern of previous years, the ENoD data have increased and made more precise the data base of genetic variability of the Spanish population, CSVS(https://csvs.clinbioinfosspa.es/), which has continued to prove its usefulness for filtering local polyomorphic variants in numerous studies, as well as for putting different researchers in contact with each other, thus making the samples it contains discoverable. CSVS now also includes secondary findings and PRSs.

Aware of the importance of taking into account other types of mutations not clearly detectable by conventional exome prioritization, a bioinformatics tool, MIGNON (https://babelomics.github.io/MIGNON/), has been developed for the analysis of gene expression data.

Another tool developed is SPACNACS, a collaborative web server that allows us to know the population frequencies of CNVs in the Spanish population, opening up the possibility of discovering new CNV-type variants that may be causal or modifying in human diseases. Additional studies on the local impact of CNVs on some phenotypes and on pharmacogenomic variants have also been carried out. Like CSVS, it is freely available at: http://csvs.clinbioinfosspa.es/spacnacs/

Finally, the Personalized Medicine Module (PMM), a tool to support the clinical diagnosis of rare diseases, with which more than 6500 diagnoses have been performed in a pilot project at the Virgen del Rocío Hospital (https://www.clinbioinfosspa.es/content/pilot-project-clinical-use-genomics-data-precision-diagnosis-rare-diseases). A demonstrator is available at: http://www.clinbioinfosspa.es/tools/mmp.

In addition, BIER also plays an important training role by providing courses or specific training to CIBERER members or groups, such as internal training sessions for the IMPaCT project or other training activities of greater scope such as the GATK workshop.

MAPER PLATFORM

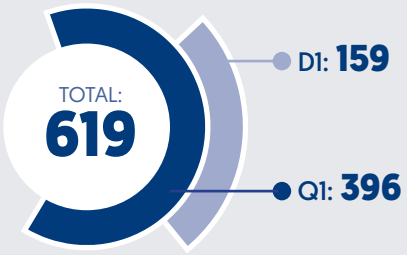
Data on research projects and clinical trials accessible through the MAPER website are as follows:

- 1258 biomedical research projects included and 797 clinical trials collected.
- 896 Principal Investigators with at least 1 project or trial included in the database.

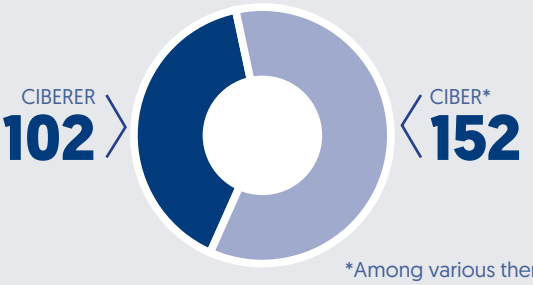
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
202.731	Borobia AM, Carcas AJ, Pérez-Olmeda M, Castaño L, Bertran MJ, García-Pérez J, et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. Lancet: 398 (10295): 121-130, PMID: 34181880.
176.082	Breast Cancer Association Consortium, Dorling L, et al. Breast cancer risk genes - Association analysis in more than 113,000 women. N Engl J Med: 384 (5): 428-439, PMID: 33471991.
168.9	Axel Schambach, Christian J Buchholz, Raul Torres-Ruiz, Klaus Cichutek, Michael Morgan, Ivana Trapani, Hildegard Büning. A new age of precision gene therapy. Lancet: 403(10426):568-582. PMID: 38006899.
158.5	Marwan G. Fakih, Lisa Salvatore, Taito Esaki, Dominik P. Modest, David P. Lopez-Bravo, Julien Taieb, Michalis V. Karamouzis, Erika Ruiz-Garcia, Tae-Won Kim, Yasutoshi Kuboki, Fausto Meriggi, David Cunningham, Kun-Huei Yeh, Emily Chan, Joseph Chao, Yaneth Saportas, Qui Tran, Chiara Cremolini, and Filippo Pietrantonio. Sotorasib plus Panitumumab in Refractory Colorectal Cancer with Mutated KRAS G12C. N Engl J Med: VOL. 389 NO. 23. PMID: 37870968.
157.375	Francesca Crovetto, Fàtima Crispi, Rosa Casas, Andrés Martín-Asuero, Roger Borràs, Eduard Vieta, Ramon Estruch, Eduard Gratacós, IMPACT BCN Trial Investigators. Effects of Mediterranean Diet or Mindfulness-Based Stress Reduction on Prevention of Small-for-Gestational Age Birth Weights in Newborns Born to At-Risk Pregnant Individuals: The IMPACT BCN Randomized Clinical Trial. JAMA-J Am Med Assoc: 326(21):2150-2160. PMID: 34874420.
120.7	Crovetto F., Crispi F., Gratacos E. Mediterranean Diet or Mindfulness-Based Stress Reduction and Prevention of Small-for-Gestational-Age Birth Weights in Newborns. JAMA-J Am Med Assoc: 327 (13): 1293-1294. PMID: 35380584.
82.9	Fox T., Bueren J., Candotti F., Fischer A., Aiuti A., Lankester A., Albert M. et al. Access to gene therapy for rare diseases when commercialization is not fit for purpose. Nat Med: 29(3):518-519. PMID: 36782029.
82.9	Barata C., Rotemberg V., Codella N.C.F., Tschandl P., Rinner C., Akay B.N., et al. A reinforcement learning model for AI-based decision support in skin cancer. Nat Med: 29 (8): 1941-1946. PMID: 37501017.
82.9	Byrne AB, et al. Genomic autopsy to identify underlying causes of pregnancy loss and perinatal death. Nat Med: 29(1):180-189. PMID: 36658419.
82.9	Studying severe long COVID to understand post-infectious disorders beyond COVID-19 Brodin P., Casari G., Townsend L., O'Farrelly C., Tancevski I., Loffler-Ragg J., Mogensen T.H., Casanova J.L., et al. Nat Med: 28 (5): 879-882. PMID: 35383311.

CIBERER Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alonso García de la Rosa, Francisco Javier	9	1	6	Instituto de Salud Carlos III	MADRID
Artuch Iriberri, Rafael	44	12	21	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Ayuso García, Carmen	29	3	16	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Borrego López, Salud	8	0	3	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Botella Cubells, Luisa María	2	0	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Bovolenta Nicolao, Paola	2	0	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Bueren, Juan Antonio	13	3	8	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	MADRID
Caballero Molina, María Teresa	14	3	6	Servicio Madrileño de Salud	MADRID
Carracedo, Ángel	17	7	13	Universidad de Santiago de Compostela	CORUÑA, A
Castaño González, Luis	10	3	8	Asociación Instituto de Investigación Sanitaria Biobizkaia	VIZCAYA
Corral de la Calle, Javier	28	10	17	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	MURCIA
Cormand Rifa, Bru	13	7	8	Universidad de Barcelona	BARCELONA
Dalmau Obrador, Josep	4	4	4	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Del Río Nechaevsky, Marcela	8	3	6	Universidad Carlos III de Madrid	MADRID
Dopazo Blázquez, Joaquin	7	1	4	Fundación Pública Andaluza Progreso y Salud	SEVILLA
Fernández Fraga, Mario	12	4	9	Agencia Estatal Consejo Superior de Investigaciones Científicas	ASTURIAS
Fillat i Fonts, Cristina	8	1	5	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Gallano Petit, María Pia	15	0	1	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Gallardo Vigo, Eduardo	23	9	14	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Garrabou Tornos, Gloria	40	12	31	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Gratacós Solsona, Eduard	27	4	14	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Lapunzina Badia, Pablo Daniel	38	7	20	Servicio Madrileño de Salud	MADRID
López Granados, Eduardo	7	1	4	Servicio Madrileño de Salud	MADRID
Marfany Nadal, Gemma	3	1	2	Universidad de Barcelona	BARCELONA
Marina Moreno, Alberto	12	5	8	Agencia Estatal Consejo Superior de Investigaciones Científicas	VALENCIA
Martí Seves, Ramón	10	1	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Martín Casanueva, Miguel Ángel	29	6	18	Servicio Madrileño de Salud	MADRID
Medina Torres, Miguel Ángel	11	6	8	Universidad de Málaga	MÁLAGA
Millán Salvador, José María	10	1	5	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	VALENCIA
Montoliu José, Lluis	4	1	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Moreno Galdó, Antonio José	15	1	4	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Moreno Pelayo, Miguel Ángel	4	0	2	Servicio Madrileño de Salud	MADRID
Mulero Méndez, Victoriano	9	6	7	Universidad de Murcia	MURCIA
Nieto Toledano, María Ángela	1	1	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	ALICANTE
Palacín Prieto, Manuel	3	2	2	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	BARCELONA
Pallardó Calatayud, Federico	8	3	4	Universidad de Valencia	VALENCIA
Palau Martínez, Francesc	11	2	2	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Pérez González, María Belén	9	2	4	Universidad Autónoma de Madrid	MADRID
Pérez Jurado, Luis	11	2	6	Universidad Pompeu Fabra	BARCELONA
Perona Abellón, Rosario	4	0	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Puig Sardá, Susana	36	14	23	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Robledo Batanero, Mercedes	25	8	16	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Oncológicas Carlos III	MADRID
Rodríguez de Córdoba, Santiago	7	3	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Ruiz Pesini, Eduardo	3	1	1	Universidad de Zaragoza	ZARAGOZA
Ruiz Pérez, Víctor Luis	3	0	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Salido Ruiz, Eduardo	1	0	0	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	GRAN CANARIA
Santos Ocaña, Carlos	6	2	5	Universidad Pablo de Olavide	SEVILLA
Sanz Bigorra, Pascual	4	0	2	Agencia Estatal Consejo Superior de Investigaciones Científicas	VALENCIA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Sevilla Mantecón, María Teresa	14	0	4	Fundación para la Investigación del Hospital Universitario y Politécnico la Fe de la Comunidad Valenciana	VALENCIA
Surrallés Calonge, Jordi	5	0	2	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Varela Nieto, Isabel	17	2	8	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Webb, Susan	10	0	5	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA

Clinical Guidelines and Consensus Documents 2023

- European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma—update 2023.
- Expert Review and Consensus on the Treat-to-Target Management of Hereditary Angioedema: From Scientific Evidence to Clinical Practice.
- Systematic review of drug therapy for chorea in NXK2-1-related disorders: Efficacy and safety evidence from case studies and series.
- A systematic review on machine learning approaches in the diagnosis and prognosis of rare genetic diseases.
- GWAS and meta-analysis identifies 49 genetic variants underlying critical COVID-19.
- Epimutation detection in the clinical context: guidelines and a use case from a new Bioconductor package.
- Immune-Related Disorders Associated with Ménière's Disease: A Systematic Review and Meta-analysis.
- Evaluating the implementation of community engagement guidelines (EVALUA GPS project): a study protocol.
- Recommendations for the future management of thrombocytopenia in patients with liver cirrhosis: A modified RAND/UCLA appropriateness method.
- Genetic counselling and testing in pulmonary arterial hypertension: a consensus statement on behalf of the International Consortium for Genetic Studies in PAH.
- Transitional Care for Young People with Movement Disorders: Consensus-Based Recommendations from the MDS Task Force on Pediatrics.
- Consensus recommendations on communication, language and speech in Phelan-McDermid syndrome.
- Management of phaeochromocytoma and paraganglioma in patients with germline SDHB pathogenic variants: an international expert Consensus statement.
- European Achondroplasia Forum guiding principles for the detection and management of foramen magnum stenosis.
- Expert Consensus on the Long-Term Effectiveness of Medical Nutrition Therapy and Its Impact on the Outcomes of Adults with Phenylketonuria.
- The p.C759F Variant in USH2A Is a Pathogenic Mutation: Systematic Literature Review and Meta-Analysis of 667 Genotypes.
- Consensus document of the Spanish Society of Paediatric Infectious Diseases and the Advisory Committee on Vaccines of the Spanish Association of Pediatrics for vaccination of immunosuppressed individuals.

RESPIRATORY DISEASES

ciber | ES

WELCOME FROM THE SCIENTIFIC DIRECTOR

María Molina Molina

Dear Researchers:

I am writing this brief note as Scientific Director of the Respiratory Diseases Networking Biomedical Research Centre (CIBERES) to present the annual report for the year 2023, describing the progress, achievements and challenges faced during this period.

The year 2023 has been a time of significant progress and consolidation for our research center. Among the most important milestones, I would like to highlight the following:

Advanced Scientific Research: during the past year, our researchers have carried out a number of innovative projects that have contributed significantly to the advancement of knowledge in the field of respiratory diseases. The quality of our publications in high impact journals has been maintained, covering a wide range of study areas, from molecular biology to clinical epidemiology.

National and International Collaborations: We have strengthened our collaborations with other research centers, both nationally and internationally, participating in joint projects and networks that have allowed us to broaden our scope and access additional resources and knowledge. We are also working on alliances with different companies, which will increase our capacity to develop new projects.

Education and Training: During the past year, we have continued to promote the training and professional development of young researchers in the field of respiratory diseases. Our training programs have contributed to the training of more than 200 researchers from various groups, thus contributing to the growth and renewal of the scientific community in this field.

Knowledge Transfer: We have carried out various knowledge transfer activities with the aim of valorizing the results of our research and contributing to the improvement of public health. The momentum of the CIBER Knowledge Transfer Platform has been fundamental to this task.

Despite our achievements, we are aware that there are still important challenges ahead. In particular, we face the need to continue promoting interdisciplinary collaboration, strengthening our collaborative networks and increasing the visibility and impact of our research nationally and internationally.

In summary, 2023 has been a year of consolidation and progress for CIBERES, in which we have achieved important results in our mission to contribute to the knowledge, prevention and treatment of respiratory diseases. I am confident that, with the commitment and dedication of all members of our scientific community, we will continue to reach new milestones and contribute to the well-being of society.

I am sincerely grateful for the support and collaboration of all those who have made these achievements possible, and I am sure that together we will continue to advance towards our common goals.

I would like to end with special thanks to German Peces Barba who has retired in 2023. His contribution to CIBERES has been pivotal, both from the leadership of his group and as scientific director of the Pulmonary Biobank Platform.

Best regards to all,

PROGRAMS & PLATFORMS

CHRONIC RESPIRATORY DISEASES

José Luís López Campos / COORDINATOR

During the first year of the new line of research in COPD, we launched the P4COPD strategic project. The online database (Red-Cap) was created, the protocol was finalized and the ethics committees of the participating centers reviewed/approved the protocol and the centers started recruitment. A position paper has been drafted in coordination with experts from around the world on how to apply lung function trajectories to clinics (The Lancet). In addition, we have registered, together with Lungs Europe and other organizations in Europe, an EUhealth project, HL4L (Healthy Lungs for Life), in which CIBER is leader of work package number 3, and which will be aligned with the COPD research line to establish the materials and pilot projects to perform lung function testing in several schools in Europe of different socioeconomic levels. Joint project publications on proteomic and microbiome studies are ongoing and are nearing the submission stage.

In the area of Sleep, during 2023 we have conducted translational and clinical research to enhance personalized medicine in respiratory sleep disorders, to study the mechanisms involved in the relationship between respiratory sleep disorders and other comorbidities, as well as to develop new innovative tools for the management of respiratory sleep disorders. Among the publications carried out in this period, the following stand out: Sánchez-de-la-Torre M, et al. Adherence to CPAP Treatment and the Risk of Recurrent Cardiovascular Events: A Meta-Analysis. JAMA. 2023; Zamarrón E et al. Continuous Positive Airway Pressure Effect on Albuminuria Progression in Patients with Obstructive Sleep Apnea and Diabetic Kidney Disease: A Randomized Clinical Trial. Am J Respir Crit Care Med. 2023; Caballero-Eraso C et al. Rearrangement of cell types in the rat carotid body neurogenic niche induced by chronic intermittent hypoxia. J Physiol.2023; Pinilla L. Hypoxic burden to guide CPAP treatment allocation in patients with obstructive sleep apnoea: a post hoc study of the ISAACC trial. Eur Respir J. 2023.

In the area of asthma, two work packages have been developed to meet the strategic objectives of the asthma research line. In work package 1, the cohorts of asthmatic patients have been maintained and data analysis has continued. A total of 13 publications have been produced with analyses of data obtained from the two databases of patients with asthma, nine of which have been published in first quartile journals. The work package is related to the analysis and validation of biomarkers in the diagnosis and classification of asthma. There has been a total of 8 publications, five of which have been published in first quartile journals. During 2023, the assessment of the last 3 years was completed, receiving a score of 11 out of 15, and the new project for the coming years was approved with a rating of 12 out of 15.

INFECTIOUS RESPIRATORY DISEASES

Carmen Ardanuy Tisaire / COORDINATOR

The three lines of research of the Infectious Respiratory Diseases Program of CIBERES have progressed adequately throughout 2023. The researchers of these lines have actively participated in the joint meeting of the CIBERES and CIBERINFEC areas, facilitating networking between researchers of this program and the thematic area of Infectious Respiratory Diseases, and reinforcing previous ties. Researchers from the three lines have held at least one face-to-face meeting per line, and other more specific virtual meetings. The researchers have attracted funding from public and private organizations. The knowledge generated has been reflected in publications, communications to congresses, patents and defense of doctoral theses.

In the Tuberculosis Line worth highlighting are the start of studies on the mechanism of action of heat-killed M. manresensis (hkMm), preclinical and clinical trials, on clinical trials with the RUTI vaccine, the continuity of genotyping of M. tuberculosis strains isolated in Catalonia, Almeria and Aragon, and studies on drugs analyzed in the Hollow Fiber system, and on combinations of reused and synergistic drugs for tuberculosis.

In the New Targets line of research, of note are the identification of epigenetic mechanisms associated with the sequelae after respiratory syncytial virus infection, the identification of receptors associated with severe COVID-19, as well as the role of monoamine oxidase B in the differential immune response of COVID-19 patients. In addition, the first glycan with a three-dimensional hairpin structure has been synthesized, and it has been demonstrated that the interaction of Siglec-15 with T cells depends on the presence of glycans in the CD11b integrin; differential patterns of glycosylation and recognition by lectins that identify Haemophilus haemolyticus and H. influenzae have been identified; a new mechanism of resistance (blaCTX-M-15) in H. parainfluenzae has been described; and new targets have been identified after transcriptomic analysis of H. influenzae during respiratory infection.

In the Pneumonia Research Line, the advances in SARS-Cov-2 pneumonia, the identification of new markers of bacterial coinfection or severity, the identification of a predictive test for mortality, the demonstration of the role of viral load in prognosis, the genomic analysis of the virus in relation to treatment in chronic infections and the differentiating transcriptomic analysis are noteworthy. In severe pneumonia, new predictive markers of VAP have been described, diagnostic tools for sepsis have been designed for use at the patient's bedside, and preventive tools have been validated in animal models. In chronic bacterial infections, biomarkers have been identified that predict response to treatment, drugs active against biofilm have been tested, and genetic adaptation to antibiotic treatment has been described. Also noteworthy is the translation of these results to clinical guidelines and position papers, and the dissemination in a conference of the Research Line.

DIFFUSE RESPIRATORY DISEASES

Francisco Pérez Vizcaíno / COORDINATOR

The CIBERESUCICOVID study is a multicenter project led by Ciberes that encompasses a cohort of more than 8000 patients with COVID-19 in 55 intensive care units (ICUs). Its main outcomes through 2023 include specific analyses on HIV patients, the long-term impact on survivors, risk factors associated with mortality, and the use of biomarkers such as procalcitonin and C-reactive protein to detect bacterial co-infections.In addition, biomarkers such as IL-6 and cfDNA have been investigated, as well as the determinants of pulmonary sequelae and the impact of intubation time during the different waves of the pandemic. Treatments such as remdesivir and different adjuvant therapies, including the use of corticosteroids in a personalized manner according to clinical phenotypes, have also been evaluated. Other topics addressed are hyperglycemia in critically ill patients and the relationship between microRNA profiles

and pulmonary function in survivors, as well as radiological features.

As regards respiratory distress syndrome (ARDS), significant advances have been made, such as the long-term investigation of animal models, the effects of dexamethasone and metoprolol, and various personalized ventilatory strategies. The role of extracellular vesicles and mesenchymal stem cells in the treatment of acute lung injury has also been explored. In relation to the pathophysiology, diagnosis and prognosis of ARDS, outcomes in patients older than 80 years of age, transcriptomic endotypes, and the pulmonary metabolome in patients with COVID-19 have been studied.

Advances in the treatment of pulmonary hypertension (PH) have included the identification of predictors of response to PDE5 inhibitors, the impact of exercise on circulating biomarkers, and the investigation of different therapeutic targets in experimental models. The modulation of ion channels and exercise capacity in post-COVID-19 patients has also been studied.

Regarding pulmonary fibrosis, clinical trials such as MADI-ET, which examines the role of diet in the adverse effects of pirfenidone, have been investigated. In addition, mitochondrial dysfunction in mesenchymal stem cells and its relationship to idiopathic pulmonary fibrosis have been studied. A multicenter study on personalized precision medicine is being carried out to improve the diagnosis and treatment of diffuse fibrosing interstitial lung diseases.

Finally, Ciberes organized the 7th Meeting on Pulmonary Hypertension Research.

COVID AND OTHER RESPIRATORY VIRUSES

Jessica González Gutiérrez / COORDINATOR

The program is organized around a project entitled: Advancing insights into predictive factors and pathogenic pathways of lung injury, abnormal post-acute pulmonary repair, and non-respiratory manifestations following severe COVID-19 respiratory infection: the RESILIENCE project.

The program is based on a multidisciplinary collaboration between several CIBER groups, as well as other inter-CIBER entities, which have devoted the last years to the study of severe COVID-19 (and other respiratory viruses) and its long-term effects. The objective is to unify the different cohorts to establish a national network dedicated to post-COVID follow-up, which will serve as a basis for collaborative projects both nationally and internationally.

In addition, the aim is to create a platform for future clinical trials in this area. This initiative seeks to deepen the understanding of the respiratory and extrapulmonary sequelae of COVID-19 and other respiratory viruses, from both a clinical and molecular perspective, in order to identify new biomarkers and potential therapeutic targets. In collaboration with the National Institute of Epidemiology, the post-COVID impact on the national health care system will be assessed, with the ultimate goal of developing a consensus document that will improve the identification and management of patients affected by COVID-19 sequelae. One of the most important goals of this program is, based on the lessons learned from COVID-19, to prepare the system to combat other future pandemics that are yet to come.

TRAINING PROGRAM

Laura Amado Rodríguez / COORDINATOR

In 2023, the CIBERES Training Conferences were held in parallel with the Scientific Conferences, and the CIBER of Infectious Diseases was invited to hold its Training Conferences jointly, on June 15 and 16 in Madrid, with an attractive joint program of interest to both CIBER areas. With over 200 registered participants, 30 oral communications (17 from CIBERINFEC and 13 from CIBERES), and more than 80 posters were presented.

The program is available at: https://jornadas.cientifis.com/c-ciber-es-infec/

During the Conference, a training workshop on "Technology Transfer, technological development and project valorization" was given by Juan Luque, responsible for the CIBER Technology Development Platform, and Luzma García, coordinator of the CIBER Technology Transfer area.

As in previous years, all the papers have been published in a special issue of the journal Archivos de Bronconeumología, available at the following link: https://www.archbronconeumol.org/en-vol-60-num-sc1-summary-X0300289623X0012X?local=true

Within the call for mobility, two grants were awarded in 2023 for intraCIBER stays and six grants for international stays.

Within the call for further training, seven grants were awarded for training courses of interest to CIBERES research staff and eight grants for attendance at at national and international conferences for the presentation of CIBER project results.

In addition, this year, twenty-seven researchers from the area presented their work at the American Thoracic Society Congress (ATS Congress) held in Washington DC (USA) from May 19 to 24 and at the European Respiratory Congress (ERS) held in Milan (Italy) from September 9 to 13, thanks to the "CIBERES Training Action: ATS/ERS 2023" and the "CIBERES Strategic Action: ERS 2023". Travel grants of between 1,500 and 2,000 euros were awarded to cover the registration, travel and accommodation expenses of young CIBERES researchers presenting their work derived from CIBERES programs and lines of research in oral communication or poster format. The action was highly valued by the participating researchers, and both the CIBERES Training Program and the Scientific Direction of the area consider that it is a very beneficial initiative for the young researchers in the area, not only at a scientific level, but at a personal level as well.

PULMONARY BIOBANK PLATFORM

Cristina Villena Portela / COORDINATOR

The CIBERES Pulmonary Biobank Platform (PBP) has recruited 150,194 samples from 7,248 donations and provided 7,381 samples in nearly 94 requests. It is worth highlighting its increased participation in the design phases of national multicenter projects, establishing common traceability and pre-analytical control systems for all samples from the same cohort. In 2023 it has provided support in the assessment, design and start-up in the recruitment, traceability, handling, shipping and conservation of biological samples, in national projects such as:

1. HYPNOSA: collaboration with the "Spanish Registry of patients with sleep apnea and daytime sleepiness, HYPNOSA project", promoted by the Spanish Sleep Network. 15,069 samples (urine, serum, plasma, buffy-coat and RNA-preserved blood) from 564 donations have already been collected.
2. IMPaCT: participation since 2021, coordinating the working group focused on determining the sample collection of the IMPACT Cohort. In 2023, work has been done on the sample collection circuits, defining the areas of work in Primary Care and on the training of the multidisciplinary technical staff.
3. METASleep: participation in the design of the multicenter project "Impact of Sleep Disordered Breathing Management in the Control of Systemic Hypertension: METAS- LEEP Project".

Leadership of the CIBER unit in the ISCIII Platform of Biomodels and Biobanks. The membership of the CIBER unit in this Platform has been renewed in the 2023 call for the period 2024-2026. This unit is formed by members of CIBERES, CIBERER, CIBERONC, CIBEREHD, CIBERDEM, CIBERSAM, CIBERBBN, the CIBER Technology Development Platform, the 2 CIBER biobanks, 1 biobank associated with CIBERSAM, and those responsible for the CIBER Databases. Led by the CIBERES PBP, its main objective is to identify and create a map of CIBER capacities, as well as to harmonize the CIBER Biobanks.

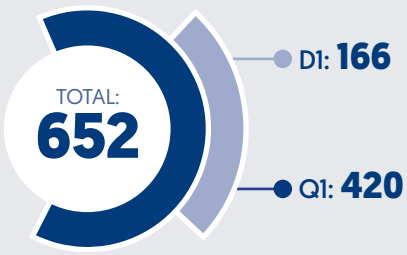
Implementation of a new technological platform for the management of inventories and sample requests of the PBP, and creation of a web portal for researchers to consult inventories in real time.

Dr. German Peces Barba has left the scientific direction of the PBP at the end of 2023 and has been replaced by Dr. Borja García-Cosio Piqueras.

SCIENTIFIC PRODUCTION

PUBLICATIONS

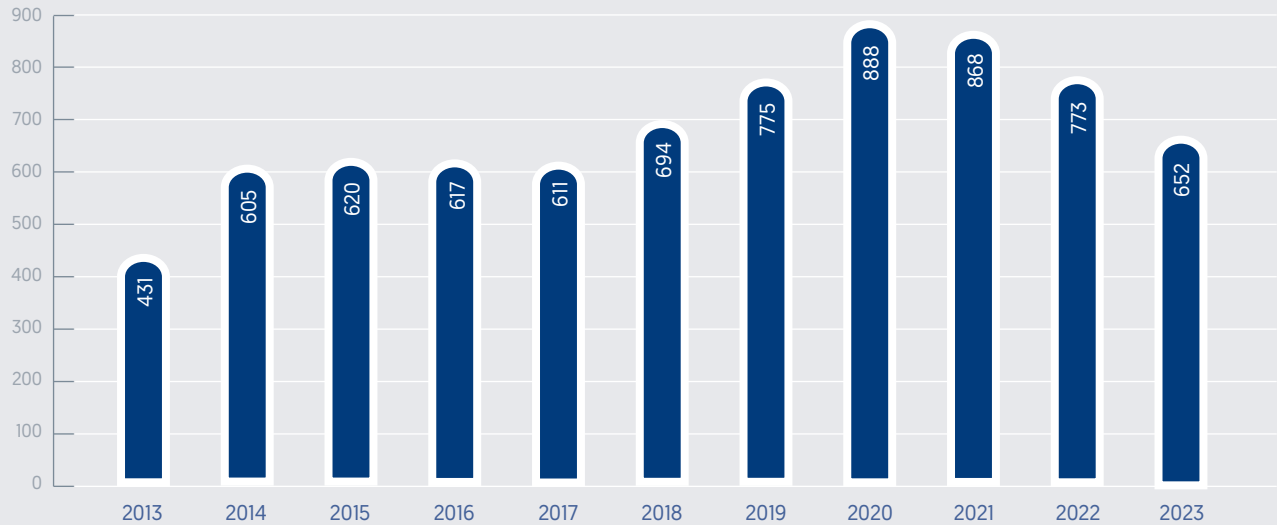
No. of publications in 2023



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
168,9	Guinea J.. Rezafungin and invasive candida infections: a new game changing antifungal?. The Lancet. 2023;401(10370):3-5.
158,5	Agusti A. Biologics for COPD - Finally Here. New England Journal of Medicine. 2023;389(3):274-275
76,2	Soriano J.B., Marin J.M., Celli B.R. Post-bronchodilator spirometry in chronic obstructive pulmonary disease. The Lancet Respiratory Medicine. 2023;11(1):13-14.
76,2	Jose Soler-Cataluna J., Miravitlles M., Fernandez-Villar A., Izquierdo J.L., Garcia-Rivero J.L., Cosio B.G. et al. Exacerbations in COPD: a personalised approach to care. The Lancet Respiratory Medicine. 2023;11(3):224-226
56,3	Dominguez J., Boeree M.J., Cambau E., Chesov D., Conradie F., Cox V. et al. Clinical implications of molecular drug resistance testing for Mycobacterium tuberculosis: a 2023 TBnet/RESIST-TB consensus statement. The Lancet Infectious Diseases. 2023;23(4):e122-e137.
46,9	Mazzolini R., Rodriguez-Arce I., Fernandez-Barat L., Pinero-Lambea C., Garrido V., Rebollada-Merino A. et al. Engineered live bacteria suppress Pseudomonas aeruginosa infection in mouse lung and dissolve endotracheal-tube biofilms. Nature Biotechnology. 2023;:-.
46,9	Quintana J.I., Atxabal U., Unione L., Arda A., Jimenez-Barbero J. Exploring multivalent carbohydrate-protein interactions by NMR. Chemical Society Reviews. 2023;52(5):1591-1613.
38,9	Gonzalez J., Benitez I.D., Motos A., Torres A., Barbe F., de Batlle J. et al. Driving pressure and adjunctive therapies in pulmonary sequelae of COVID-19 patients under invasive ventilation. Intensive Care Medicine. 2023;:-
38,9	Russell L., Pene F., Martin-Loeches I. Multidrug-resistant bacteria in the grey shades of immunosuppression. Intensive Care Medicine. 2023;49(2):216-218.
38,9	De Pascale G., Martin-Loeches I., Nseir S. Antifungal stewardship in critically ill patients. Intensive Care Medicine. 2023;49(6):681-684.

CIBERES Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Agustí García Navarro, Alvar	54	34	11	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Almendros López, Isaac	9	4	1	Universidad de Barcelona	BARCELONA
Ardanuy Tisaire, María Carmen	4	1	0	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Barberá Mir, Joan Albert	15	10	3	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Barbé Illa, Ferrán	38	23	11	Instituto de Investigacion Biomédica de Lleida. Fundación Dr. Pifarre	LLEIDA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Barreiro Portela, Esther	15	10	2	Consorci Mar Parc Salut de Barcelona	BARCELONA
Blanch Torra, Lluis	18	12	3	Fundación Instituto de Investigación e innovación Parc Taulí	BARCELONA
Cardona Iglesias, Pere Joan	13	8	6	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Corral Peñafiel, Jaime	4	3	1	Fundación para la Formación e Investigación de los Profesionales de la Salud de Extremadura (FundeSalud)	CÁCERES
Cortijo Gimeno, Julio	2	1	0	Universidad de Valencia	VALENCIA
Fernández Muñoz, Ángel Esteve	22	12	6	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
García Río, Francisco José	43	31	9	Servicio Madrileño de Salud	MADRID
Garmendia García, Juncal	11	7	5	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Jiménez Castro, David	19	13	4	Servicio Madrileño de Salud	MADRID
Lopez-Campos Bodineau, Jose Luis	45	24	4	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Lorente Balanza, José Ángel	10	5	3	Servicio Madrileño de Salud	MADRID
Martín Montañés, Carlos	8	4	1	Universidad de Zaragoza	ZARAGOZA
Martinón Torres, Federico	17	8	5	Servicio Gallego de Salud	CORUÑA, A
Molina Molina, María	10	9	4	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Mullol Miret, Joaquim	41	29	11	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Muñiz Albaiceta, Guillermo	12	5	3	Fundación para la Investigación e Innovacion Biosanitaria en el Principado de Asturias (FINBA)	ASTURIAS
Muñoz Gall, Xavier	44	26	6	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Muñoz García, Patricia	34	15	8	Servicio Madrileño de Salud	MADRID
Peces Barba Romero, Germán	17	10	4	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Pérez Vizcaíno, Francisco	10	10	6	Universidad Complutense de Madrid	MADRID
Pozo Abejón, María Victoria del	21	19	5	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Relló Condomines, Jordi	19	14	8	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Ruiz Cabello Osuna, Jesús	6	6	3	Asociación Centro de Investigación Cooperativa en biomateriales, CIC biomaGUNE	GUIPÚZCOA
Torres Martí, Antoni	59	41	18	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Villar Hernández, Jesús	27	21	15	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	PALMAS, LAS
Yuste Lobo, José Enrique	5	5	0	Instituto de Salud Carlos III	MADRID

Clinical Guidelines and Consensus Documents 2023

- Vaccination against Community-Acquired Pneumonia in Spanish Adults: Practical Recommendations by the NeumoExperts Prevention Group
- European Respiratory Society/American Thoracic Society Technical Standard on Standardisation of the Measurement of Lung Volumes - 2023 Update.
- Recommendations of the Spanish Antibiogram Committee (COESANT) for in vitro susceptibility testing of antimicrobial agents by disk diffusion.

EPIDEMIOLOGY & PUBLIC HEALTH

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Marina Pollán Santamaría

CIBERESP researchers have made it possible for 2023 to be a good year. Scientific productivity has remained very high, at levels similar to the years of the pandemic, when it skyrocketed. We have published 1310 articles, half of them in journals ranking in the first quartile impact factor and 27% in journals of the first decile. In addition, one out of every four articles has been carried out through collaboration between CIBERESP groups, and the same proportion with groups from other thematic areas of the CIBER. We continue to be the most collaborative CIBER thematic area, and also the most efficient as it is the one that generates more knowledge (number of articles) per unit of economic resources received from the ISCIII. Our research also has a high level of internationalization, as shown in the authorship of scientific articles and in the research projects carried out through European consortia and, to a lesser extent, with American, Asian and African centers.

We have transferred the knowledge we have generated to society through dozens of joint press releases between CIBERESP and the Scientific Culture Units and Press Offices of our Institutions, be they universities, health research institutes/health centers, other research centers and the health administration itself. Finally, as can be seen in the detail of the programs, there has been an enormous activity of transfer to decision-makers in health and other public policies. To this end, we develop clinical practice guidelines, as do other thematic areas, and we also advise on legislative projects, guide public health strategies, and evaluate public health plans, programs and interventions, among other actions.

Marina Pollán and Beatriz Pérez have led our contribution to the IMPACT initiative, which is to establish a cohort of 200,000 adults across Spain, and is progressing well. The pilot phase was completed and as of March 2024 there were 16 IMPaCT centers recruiting participants throughout Spain after the training of its members. We will have more than 25 centers before the summer, biological samples arrive every day and in good conditions to the biobank located at the ISCIII, and countless scientific, logistical and administrative challenges have been overcome thanks to the collaboration of many CIBER and primary care researchers, the staff of the administrations of the Autonomous Communities and the permanent support of the CIBER Technical Unit. The IMPaCT cohort is an example of how much can be done through collaboration.

Finally, we have continued our activities in training young researchers, funding intramural projects, and collaborating with other areas, such as the completion of large-scale projects on long-term COVID-19 or on the outbreak of mpox in Spain. All this bodes well for 2024, because it is not a question of facing the future, but of building it by all of us giving our very best, and that is what we, the researchers at CIBERESP, have been doing.

PROGRAMS & PLATFORMS

EPIDEMIOLOGY & CONTROL OF CHRONIC DISEASES

Mª José Sánchez Pérez / COORDINATOR

The Program has continued its scientific activity.

MCC-SPAIN

The MCC-Spain project, led by M. Kogevinas and M. Pollán, continues to be used as a study of prognostic factors in colorectal, breast or prostate cancer. Collaboration with large international consortia (PRACTICAL - prostate cancer, SToP - Gastric cancer, Interlymph, ICGC & CRuCIaL - LLC, BCAC & CONFLUENCE - breast cancer, CORECT & GECCO - colorectal cancer and MetalGWAS - metal consortium and GWAS just starting) has been maintained. In 2023, 18 papers were published, 8 of them with international consortia.

GEN-RISK

The Genrisk project, led by V. Moreno, relies heavily on MCC-Spain. In 2023, 2800 samples of colon, breast, prostate and control cancer cases have started to be analyzed for targeted metabolomics, and about 1000 for non-targeted. The annotation systems of the web-application Polymorphic genetic susceptibility in cancer (chronic diseases/traits) have been updated, and improvements have been incorporated for the interactive selection of markers. The computer and remote analytical platform has been upgraded to facilitate genetic and statistical analysis. An R software package (SNPannot) has been developed to perform annotations of genetic polymorphisms. A workshop was held on Polygenic Risk Scores (PRS) derived from genome-wide association studies (GWAS) in GenRisk-MCC Spain.

Collaborations have been established with new researchers from CIBERONC and CIBEREHD.

EPIDEMIOLOGICAL SURVEILLANCE OF CANCER (VICA)

The VICA subprogram, coordinated by M.J. Sánchez and P. Fernández, has continued to advance in the development of the Spanish Cancer Epidemiological Information System (SIEC), in collaboration with the Spanish Network of Cancer Registries (REDECAN) and the Spanish Association Against Cancer (AECC)

An analysis pipeline has been developed to evaluate the effect of sociodemographic indicators standardized for Spain and Portugal on municipal mortality by different types of cancer in the Iberian Peninsula, in collaboration with the Instituto Nacional de Saúde Doutor Ricardo Jorge (Lisbon, Portugal) for updating the Municipal Atlas of Cancer Mortality in Spain and Portugal (AMOCAPE) and to study the influence of socioeconomic factors on spatial patterns.

A revision of the geocoding protocols of the GEO-CIBER application was carried out, adapting the execution scripts to the new output variables of the geocoding systems it integrates.

The content of the web https://vica-ciberesp.isciii.es/ has been updated with new functionalities.

A workshop on survival estimation and modeling and a workshop on the use of the GEO-CIBER application have been held.

Two collaborative scientific articles have been published in Q1 indexed journals and one article is currently under review. Five communications have been presented at national and international scientific conferences.

EUROPEAN PROSPECTIVE INVESTIGATION INTO CANCER AND NUTRITION (EPIC)

In the EPIC-Spain cohort, funding has been obtained for a new intramural CIBERESP project and a State Research Agency consolidation project on allostatic load, environmental factors and colon-rectal cancer in the EPIC-Spain cohort, in collaboration with other thematic areas: CIBERONC and CIBEROBN.

Thirty-six scientific articles have been published in D1 and Q1 indexed journals.

PREVENTION, SURVEILLANCE & CONTROL OF COMMUNICABLE DISEASES (PREVICET)

Pere Godoy García / COORDINATOR

FLU AND RESPIRATORY VIRUSES SUBPROGRAM

The groups of Ángela Domínguez, Cristina Rius and Carmen Muñoz-Almagro have worked on projects on the effectiveness of flu and pneumococcal vaccination (PI19/00354) (PMID:38005962), the transmission of SARS-CoV-2 among household contacts (PI21/01883) (PMID:37045853) and the intramural project (ESP22PI01) (PMID:37995118)

The groups led by Juan E. Echevarría, A. Larrauri and C. Muñoz-Almagro have participated in the European VEBIS study on effectiveness of COVID-19 and flu vaccines (VEBIS. ECDC OJ/2021/DPR/12924) in the framework of SiVIRA. Doctoral Thesis "Evaluation of the effectiveness and impact of vaccination programs based on the surveillance of influenza and COVID-19 in Spain". Acute respiratory infection in children after 2 years of pandemic (AESI-2021 PI21CIII/00019). The European project, RELECOV 2.0 (EU4H-2022- DGA-MS-IBA-01-02) has been awarded and papers on viral respiratory diseases have been published in collaboration with CIBERINFEC (PMID:38133281, 37239920, 36878013, 37242314, 37856529, 38062945).

IMMUNOPREVENTABLE DISEASES SUBPROGRAM

The groups led by Juan E. Echevarría and Amparo Larrauri have studied the causes of vaccine failure in measles, mumps and varicella (PI19CIII00041) and have evaluated the use of new molecular tools for integrated surveillance of both measles (PMID:37283922, 37103785) and mumps (PMID:37396375, 38140661).

The groups led by Ángela Domínguez and Carmen Muñoz-Almagro have studied the effect of the second year of the COVID-19 pandemic on invasive pneumococcal disease (IPD) (PMID:37896951) as well as the consolidation of WGS techniques for the molecular characterization of pneumococcus (PMID:38092657).

The effect of commensal bacteria of the nasopharyngeal microbiota on the development of IPD (PI19/00104) and evolution of multidrug resistant clones has been studied.

VIRAL HEPATITIS SUBPROGRAM

PhD Thesis: "Phylogenetic and Genomic Analysis of Hepatitis E Virus (HEV) causing disease from 2009 to 2019". The TrazHE project on HEV has been completed. The impact of universal vaccination against hepatitis B in adolescents in Spain, the cost of hepatitis A outbreaks and the intramural project on cases of childhood hepatitis of unknown origin have been studied.

OUTBREAKS SUBPROGRAM

The groups led by Ángela Domínguez and Cristina Rius have published articles on outbreaks of gastroenteritis of viral etiology in closed and semi-closed institutions (PMID:38073577, 37730810, 36717621) as a result of project PI16/02005.

TUBERCULOSIS SUBPROGRAM

Tuberculosis risk factors in contacts of pulmonary tuberculosis cases have been analyzed (PI18/01751), publications have been made on the LTBI cascade of care (PMCID:PMC10745640) and the prescription of LTBI treatment (PMID:38140204).

EMERGING AND RE-EMERGING DISEASES SUBPROGRAM

The groups led by Ángela Domínguez, Cristina Rius and Carmen Muñoz-Almagro are working on the MONKPOX-ESP22 project. (PMID:37971716).

Jordi Figuerola's group and other CIBER groups have characterized epidemiological aspects of West Nile virus (PMID:36851481, 37363246, 37469597), dengue (PMID:37945465) and transmitting mosquitoes (PMID:37414178). They have initiated the PID2022-142608NB-I00 project on zoonotic viruses and have participated in the preparation of different Surveillance Plans and Programs of the Ministry of Health and the Andalusian Regional Government on mosquito vectors and rabies in Spain.

DETERMINANTES BIOLÓGICOS Y CONDUCTUALES EN POBLACIONES VULNERABLES (DAPET)

Juan Carlos Galán Montemayor / COORDINATOR

This program focuses on 2 main lines of action: Antimicrobial resistance (including antibiotic and antiviral resistance) and infections transmitted by organic fluids focusing primarily on sexually transmitted infections.

The **antibiotic resistance subprogram** has consolidated its strategy of leading the approach to resistance from a public health perspective, with the holding of the second conference on visualization of antimicrobial resistance (Valencia, November 2023). The strategy is to involve in this action research leaders from other CIBER areas (CIBERINFEC, CIBERES, CIBERHED) or scientific institutions (Artificial Intelligence of UPV, INIBIC) or governmental institutions (PRAN). This is probably the greatest achievement of visualization of the activity and collaborations with other areas with interests in the field of antimicrobial resistance.

There are intramural projects funded by CIBERESP, such as "Population-based genomic epidemiology study tailored for surveillance and control of tuberculosis" coordinated by subprogram researchers Elisa Martró and Iñaki Comas. In this area of work, Dr. Comas' group has published in collaboration with Public Health and WHO a paper in Lancet Microbe (doi: 10.1016/S2666-5247(23)00252-5), a catalog of antibiotic resistance in tuberculosis in Spain and Mozambique in vulnerable population (Clin Inf Dis.2023, doi: 10.1093/ cid/ciad684) in collaboration with CIBERINFEC researchers. In other organisms, Dr. San Millán has published in PNAS (doi: 10.1073/pnas.2314135120) on resistance plasmid dispersal in enterobacteria in hospital settings. Dr. Baquero has published a paper on social and cultural factors influencing antibiotic consumption and thus antibiotic resistance (doi: 10.1016/j.tim.2022.12.010.)

The **subprogram of sexually transmitted infections** and through organic fluids has consolidated its participation in the SEE congress through a spontaneous table that in 2023 focused on mpox with the participation of several groups of this subprogram as well as research staff from other programs or representatives of official institutions. The program coordinators (Dr. Casabona and Dr. Galán), also members of the STI Steering Committee in SEIMC, participate in an official agreement with the Ministry of Health on STI awareness and visualization (https://www.boe.es/boe/dias/2023/04/15/pdfs/BOE-A-2023-9286.pdf). Many papers derived from the interCIBER action on mpox were published in 2023 published in *Nat. Commun* (doi: 10.1038/s41467-023-40490-9) by Dr. Casabona on asymptomatic mpox patients or in Int J Infect Dis (doi: 10.1016/j.ijid.2023.10.017) by Dr. Galán on the demonstration of mpox reinfection by genomic sequencing. Dr. Alemany has worked on HPV prevalence in men (doi: 10.1016/ S2214-109X (23)00305-4) in *Lancet Global Health*. Dr. Gonzalez-Candelas has published in *Lancet Microbe* (doi: 10.1016/S2666-5247(23)00219-7) genomic analysis of *Treponema pallidum*.

In summary, the program is progressing in the consolidation of collaborative actions and visibility of the 2 subprograms through training, interaction with other CIBERs and leading activities in the 2 fields of action. The high impact index of the publications demonstrates the quality of the groups that comprise the program, many of them in collaboration with other research personnel from different CIBER areas.

SOCIAL DETERMINANTS OF HEALTH

Mª José López Medina / COORDINATOR

In 2023, collaborative work has been carried out in the two subprograms in which all the groups of the Program participate: the subprogram on Social Inequalities in the Health of Young People in Spain, and the subprogram on Health Inequalities and COVID-19, both in the merging of different databases, as well as in the joint analysis and collaborative publications.

In terms of projects, it should be noted that during 2023 funding has been obtained for projects in various competitive calls on emerging and particularly relevant topics such as housing, childhood and health (Carme Borrell Group), equitable relations (Carme Borrell Group) or healthy aging (Antonio Daponte Group). In addition, projects related to health problems in trans and/or non-binary people living in Spain have been started (Mª José Belza Group), projects related to methodological support to literature reviews in collaboration with Cochrane (Marina Lacasaña's Group) and other projects such as PERISCOPE "Pan-European Response to the Impacts of COVID-19 and future Pandemics and Epidemics" have been completed (Mª José López's Group).

Some of the outstanding publications in the different groups include the following: Impact of the COVID-19 pandemic on the socioeconomic inequalities in mortality in Spanish provinces, Journal of Epidemiology and Global Health (Marc Saez Group); Socioeconomic inequalities in COVID-19 incidence during the first six waves in Barcelona, International Journal of Epidemiology (Carme Borrell Group); Efficacy of an adjuvant non-face-to-face multimodal lifestyle modification program for patients with treatment-resistant major depression: A randomized controlled trial, Psychiatry Research (Marina Lacasaña Group); Measurement of airborne nicotine, as a marker of secondhand smoke exposure, in homes with residents who smoke in 9 European countries, Environmental Research (Mª José López Group) and Free Access to Direct-Acting Antivirals in Spain: More Favorable Impact on Hepatitis C Mortality Among Highly Educated People, Clinical Infectious Diseases (Mª José Belza's Group). In addition, the article Persistent Gender Gap in Out-of-Hospital Cardiac Arrest in Spain during the period 2013-2018 (Antonio Daponte Group), has received the award for the article with the greatest projection in the year 2022 by the Spanish Council of Cardiopulmonary Resuscitation.

As for other dissemination outputs, during this year a Shiny web application of the "Atlas of the Social Determinants of Health in Spain" has been developed, which improves access to indicators of social determinants of health for which information is available for the different Spanish Autonomous Communities. This atlas has been led by Antonio Daponte's group and Marc Sáez's group, with the participation of the 6 groups of the Program. Other informative products worth mentioning are the documentary "Getting older with HIV" (Mª José Belza Group), the "Protocol for a comprehensive approach to victims of chemical submission and/or aggression by sharp objects", for professionals in the Andalusian health system (Marina Lacaña Group), or the dissemination in more than 20 press, radio and television media of a study on exposure to environmental tobacco smoke in cars (Mª José López Group).

EPIDEMIOLOGY AND PREVENTION IN ENVIRONMENTAL AND OCCUPATIONAL HEALTH

Marieta Fernández Cabrera / COORDINATOR

We have continued with the strategic objectives, focused on the description of exposure to environmental factors and their effects on health, leading (or participating in) numerous international and national research projects [P4COPD, GOLIAT, TOLIFE, IHEN, TWINAIR, AURORA 2021, RI-URBANS, EIRENE PPP, Equal-Life, ATHLETE, HYPAXE, Clean cities 2, MOBILISE-D, ONES, EU-CAN-Connect, Air-NB, Clean cities, EXPO-ENFANTS, Lily, EXPEC-TEEN, in metabolomics, transcriptomics, neonatal microbiota and exposome, HYPIEN, HBM4EU, PARC, PREDIMED PLUS, Stomach cancer Pooling-(StoP)] and maintained international collaborations with the Harvard School of Public Health, the HEEDS/USA consortium, and Central America (Panama-SENACYT).

Support has been given to the creation of the Interministerial Commission for Human Biomonitoring (CIBMH) for the implementation of a state program. CIBERESP research personnel are participating in technical groups to study exposure to certain chemical substances in the general population and specific groups.

Collaborative work with CIBERESP groups and other CIBER areas [CIBERES, CIBEROBN, CIBERSAM, CIBERDEM, CIBEREHD] has been strengthened and of note is the success in leadership-participation in CIBERESP intramurals (ENDOPOL, SMART, EPIDATA, etc.).

The main lines of research in environmental health have been: 1) Environmental pollutants and development; 2) Neurodevelopment and associated factors; 3) Thyroid function and iodine; 4) Precocious puberty and hormonal alterations, 5) Lifestyles and child health; 6) Urban health and development; 7) Perinatal health and development; 8) Genomics, health and development; 9) Determinants of use of health services; 10) Rare diseases; 11) Climate and morbimortality; 12) Communicable diseases; 13) Women's reproductive health (endometriosis) and intervention in specific stages; 14) Mediterranean diet, physical activity and behavioral support for primary prevention of chronic non-communicable diseases, 15) Diet, lifestyle and genetic determinants in gastric cancer; 16) Factors associated with the transmission of the Mediterranean diet from mothers to children. In occupational health: 1) Occupational health surveillance in the prevention of infection related cancer; and 2) Exposure to anesthetic gases in health professionals. Cross-cutting activities have continued, such as the validation-implementation of biomarkers of effect and the application of advanced statistical analysis in epidemiological studies.

Transfer products include: 1) Scientific and technical session on the environmental conditions of the formerly degraded areas in Parc de l'Alba and the potential impact on health, 2) Safe and healthy school environments, 3) 'Public Consultations: Update of the scientific opinion on polybrominated diphenyl ethers (PBDEs) in food', 4) Guide for professionals and general population on plastics, microplastics and nanoplastics, and their effects on human health; 5) Paradoxes of food plastics-Alimentta-Think tank for food transition.

INMA SUBPROGRAM

Collaborations continue to be priority actions. There are 24 active projects [involving CIBERESPx16, CIBEROBNx2,CIBERDEM,CIBERES,CIBERSAMx2,CIBERFES],RedSAMID, Red-Grimalt, REDISSEC], intramural, international consortia (EGG/EAGLE, PACE, NCD-RisC, HBM4EU, PARC, Consortium thyroid & pregnancy, CADSET), and 23 collaborative proposals approved, 14 external.

Strategic achievements include research on "adolescence" and sexual development, sleep disorders, stress, mental health, physical activity-sedentarism, obesity, cardiometabolic health, inflammatory markers, internal-external exposures (exposome), mycobiome, metabolomics. Follow-up has begun in INMA-Menorca (25 years), INMA-Sabadell (18 years), and is preparing INMA-Granada (23 years), INMA-Gipuzkoa (18 years) and INMA-Asturias (18 years).

INMA is committed to generational renewal and the promotion of young researchers to continue with the scientific excellence achieved to date (2023: 33 collaborative articles: Q1 (87.9%), D1 (36.4%).

RESEARCH IN HEALTH SERVICES AND CLINICAL PRACTICE

Antoni Serrano Blanco / COORDINATOR

We work with CIBERESP, CIBERES, CIBERSAM, CIBER-BBN, CIBERCV, CIBERNED, RICAPPS and other organizations. We have held two workshops on strategic communication of results with the participation of all P6 groups.

EFFICIENCY AND EQUITY OF THE HEALTH SYSTEM SUBPROGRAM

In 2023, we continued to disseminate the results of the CIBERPOSTCOVID project led by Victoria Serra and Antoni Serrano. We have continued the collection of follow-up data from the cohorts of the MIND-COVID study (https://mindcovid.org), led by Jordi Alonso. We started the QCOA project with the systematic review of PROMS/PREMS in elderly people applicable to home care. From the B-long project (PI: Ignacio Aznar; Lucy Parker), we presented the results through a social theater play. ECONOS (econos.org) already includes >75,000 data. We have redesigned Bin-CE (PI: Josep Ramón Marsal, Blanca Lumbreras), a tool to calculate sample size for randomized clinical trials.

HEALTH AND SOCIAL BURDEN OF DISEASE

We have started the study "Impact of low emission zone regulations in the city of Barcelona on the incidence of cardiac arrhythmias" (PI: Begoña Benito; Ignacio Ferreria) so far including 400 patients with cardiac devices. We continue with the projects WEMWEBS (PI: Gemma Vilagut); Mental-GPS (PI: Jorge Arias); Persistent COVID in healthcare personnel (PI: Mireia Utzet), and the "Impact of COVID-19 on acute cardiovascular disease care" (PI: Aida Ribera).

We continue to work on the cohorts (1) WORKss, with people affiliated with the Continuous Working Lives Sample, and which in 2024 will be linked to mortality data (https://www.cisal.upf.edu/workss/esp); (2) COSAMar (PI: Consol Serra) a cohort of healthcare workers from the Hospital del Mar with 4,800 professionals; and (3) MATER (PI: Consol Serra), a retrospective cohort on pregnancy and social benefits of female healthcare workers.

CLINICAL ADEQUACY AND SHARED DECISION MAKING

In 2023, we initiated the following: (1) recruitment for a randomized clinical trial to assess the impact of the implementation of PROMs and PREMs in routine clinical practice; (2) the European Salvovar trial (salvovar. eu) to improve the decision-making process in the treatment of people with ovarian cancer with poor prognosis; (3) the PRIMS project (PI: Dimelza Osorio), to develop a tool for patient reporting of near-miss incidents in hospital care; and (4) the RECEP-HAD study (PI: Aida Ribera), to evaluate outcomes and person-centered experiences and the economic impact of comprehensive geriatric home hospitalization.

The project "Comparative investigation of effectiveness for shared decision making in the treatment of localized prostate cancer with new and traditional modalities" (PI: Blanca Lumbreras) has shown that, ten years after diagnosis, overall survival is high and does not differ between treatments. The IMA clinical trial (PI: Maria Rubio-Valera) has recruited >3,000 users.

We have developed the MAPAC_DX APP to optimize the request for CT scans; Meta-DiSc 2.0 to perform meta-analysis of diagnostic test accuracy; and InTeQ to self-report the frequency of performing the correct inhalation technique using any type of inhaler.

TRAINING PROGRAM

Mònica Guxens Junyent / COORDINATOR

In 2023, the Training Program has continued to maintain the two basic lines of action of its program: mobility actions, aimed at facilitating contact and work with other national or international groups; and improvement actions, aimed at enhancing the quality of scientific work and its dissemination in Public Health forums.

In 2023, mobility actions have been promoted by means of a document agreed upon by all the CIBER training programs. At the national level, 3 short stays between CIBERESP groups have been financed. International mobility has also been promoted with the financing of 7 stays, through short stays of between one month and three months in international research centers of excellence. These actions have made it possible to promote the professional development of our own research personnel and, in one case, to obtain an international doctorate mention.

As part of the further training actions, the Meeting for Excellence in Public Health Research was held in Tarragona. This action aims to promote quality research in Public Health. This year's edition was attended by 6 young CIBERESP researchers, 2 senior CIBERESP panelists and the coordinator of the CIBERESP Training Program.

Once again this year, CIBERESP has continued its collaboration with the Spanish Society of Epidemiology by financing the Awards for the 10 best communications presented by young researchers at the Annual Meeting of the Spanish Society of Epidemiology, which was held in conjunction with the Congress of the Portuguese Association of Epidemiology. The award includes a diploma and covers the cost of registration for the following year's meeting. Also, within the SEE meeting, the CIBERESP spontaneous round table took place, which through the Award for the best papers presented to the CIBERESP round table, finances the registration of the 7 best papers selected for presentation.

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

BIBLIOPRO PLATFORM

BiblioPRO (https://www.bibliopro.org/) is a virtual repository of Patient Reported Outcomes (PROs).

Its mission is to promote the measurement of PROs through the comprehensive inclusion of instrument information in Spanish through systematic reviews, scientific evaluations and training.

The BiblioPRO Scientific Committee includes 18 researchers from 15 institutions (CIBERESP, CIBERSAM, CIBERNED and RICAPPS)

The BiblioPRO platform contains 2,731 PROs and its technical data sheet (characteristics, development, EMPRO evaluation and ICHOM and COMET recommendations).

REPOSITORY (2023)

- New registered users: 2,523, (31,000 accumulated, 9% increase).
- Website visits: 73.008, (6% less).
- New instruments: 329, totaling 2.731 (12% increase).
- Sublicences: 428 sublicences processed.
- New BiblioPRO-International web site: improved functionalities for users and data management.

BIBLIOPRO INTERNATIONAL
(www.bibliopro international.org)

There are 191 instrument versions available (46% increase)

COMPETITIVE RESEARCH PROJECTS

ISCIII PI21/00026.Implementation of PROMs and PREMs in routine clinical care: evaluation of their requirements and impact 2022-2024. PI: Olatz Garin. Grupos: Alonso, Jordi; Ferreira, Ignacio.

ISCIII PI22/00845. Evaluation of person-centered outcomes and experiences of comprehensive geriatric hospital at home care: need for a set of multipurpose tools (RECEP-HAD) 2022-2024. PI: Aida Ribera. Groups: Alonso, Jordi; Ferreira, Ignacio.

TRAINING AND RESEARCH SUPPORT ACTIVITIES

- Lecture: "PREMS and PROMS Experience and results of the patient in healthcare". Catalan Society of Health Care Quality.
- Lecture: "PROMs and PREMs: advances and use in the evaluation of surgical practice.
- 15th Scientific Meeting on Evaluation of digital technologies in diagnostics and surgery.
- Webinar: "Quality of life and value based care in oncohematology patients". https://www.youtube.com/watch?v=IVkN64iLOdk
- Webinar: "Machine learning asociado a telemedicina y predicción de PROMs". https://www.youtube.com/watch?v=QvOiK3x0p2k
- Lecture: "Training day on Advances in Oncology aimed at volunteers. Cancer: where are we and where are we going? AECC-Catalonia Against Cancer.

CONSULTING ACTIVITIES

- Selection of PROs for the IMP/00021 IMPaCT project (Infrastructure for Precision Medicine associated with Science and Technology) Coordinator: ISCIII.
- Sublicensing management for Naveta: Telepharmacy platform with PROMs/PREMs. Coordinator: FARUPEIB
- Visualization of prescription and interpretation of PROs in the Electronic Health Record in Catalonia (HES). Coordinator: Department of Health (Catalonian Government).
- Participation in the Advisory board of the H2O Project (IMI Grant Agreement 945345). Coordinator: University of Vienna.

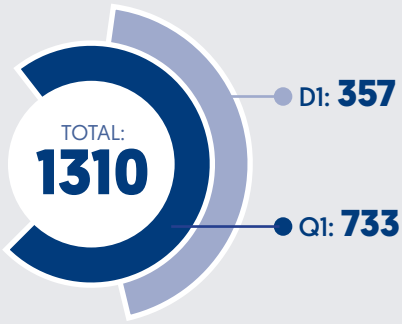
PUBLICATIONS 2023

- Miret C et al. Reference values of EORTC QLQ-C30, EORTC QLQ-BR23, and EQ-5D-5L for women with non-metastatic breast cancer at diagnosis and 2 years after. Qual Life Res. 2023;32(4):989-1003. Groups: García, Susana and Alonso, Jordi.
- Arias de la Torre J et al. Reliability and cross-country equivalence of the 8-item version of the Patient Health Questionnaire (PHQ-8) for the assessment of depression: results from 27 countries in Europe. Lancet Reg Health Eur. 2023;31:100659. Groups: Serra-Sutton, Victoria and Alonso, Jordi.
- Pardo Y et al. Patient-centered care in Coronary Heart Disease: what do you want to measure? A systematic review of reviews on patient-reported outcome measures. Qual Life Res. 2023;32(5):1405-1425. Groups: Alonso, Jordi and Ferreira, Ignacio.

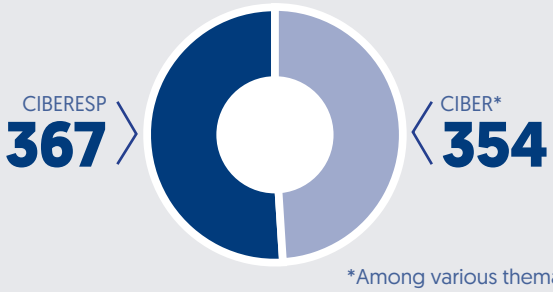
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor*

IF	PUBLICATION
168,9	Iungman T., Cirach M., Marando F., Pereira Barboza E., Khomenko S., Masselot P. et al. Cooling cities through urban green infrastructure: a health impact assessment of European cities. The Lancet. 2023;401(10376):577-589.
158,5	Castilla J, García Cenoz M, Abad R, Sánchez-Cambronero L, Lorusso N, Izquierdo C et al. Effectiveness of a Meningococcal Group B Vaccine (4CMenB) in Children.The New England journal of medicine. 2023;388(5).
76,2	Nieuwenhuijsen M., de Nazelle A., Garcia-Aymerich J., Khreis H., Hoffmann B. Shaping urban environments to improve respiratory health: recommendations for research, planning, and policy. The Lancet Respiratory Medicine. 2023.
50,0	Arias-de la Torre J., Vilagut G., Ronaldson A., Bakolis I., Dregan A., Martin V. et al. Prevalence and variability of depressive symptoms in Europe: update using representative data from the second and third waves of the European Health Interview Survey (EHIS-2 and EHIS-3). The Lancet Public Health. 2023;8(11):e889-e898.
34,3	Martínez-Martínez F.J., Massinga A.J., De Jesus A., Ernesto R.M., Cano-Jimenez P., Chiner-Oms A. et al. Tracking SARS-CoV-2 introductions in Mozambique using pandemic-scale phylogenies: a retrospective observational study. The Lancet Global Health. 2023;11(6):e933-e941.
17,69	Ranzani O., Alari A., Olmos S., Mila C., Rico A., Ballester J. et al. Long-term exposure to air pollution and severe COVID-19 in Catalonia: a population-based cohort study. Nature Communications. 2023;14(1).
17,03	Pinar-Marti A., Gignac F., Fernandez-Barres S., Romaguera D., Sala-Vila A., Lazaro I. et al. Effect of walnut consumption on neuropsychological development in healthy adolescents: a multi-school randomised controlled trial. eClinicalMedicine. 2023;59.
13,8	Donat-Vargas C., Schillemans T., Kiviranta H., Rantakokko P., de Faire U., Arrebola J.P. et al. Blood Levels of Organochlorine Contaminants Mixtures and Cardiovascular Disease. JAMA network open. 2023;6(9):e2333347.
13,6	Arias de la Torre J., Ronaldson A., Alonso J., Dregan A., Mudway I., Valderas J.M. et al. The relationship between air pollution and multimorbidity: Can two birds be killed with the same stone? European Journal of Epidemiology. 2023;38(4):349-353.
11,8	Mustieles V., Balogh R.K., Axelstad M., Montazeri P., Marquez S., Vrijheid M. et al. Benzophenone-3: Comprehensive review of the toxicological and human evidence with meta-analysis of human biomonitoring studies. Environment International. 2023;173.

*Con autoría CIBERESP y colaborativas

CIBERESP Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alemany Vilches, María Eulalia	21	15	5	Instituto Catalán de Oncología	BARCELONA
Alonso Caballero, Jordi	38	20	11	Consorci Mar Parc Salut de Barcelona	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Belza Egozcue, María José	28	13	7	Instituto de Salud Carlos III	MADRID
Bonfill Cosp, Xavier	60	25	11	Fundación Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Borrell Thio, Carme	45	12	3	Agencia de Salud Pública de Barcelona	BARCELONA
Bueno Cavanillas, Aurora	56	33	13	Universidad de Granada	GRANADA
Calderón Sandubete, Enrique José	14	11	8	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Casabona Barbara, Jordi	37	10	7	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Castilla Catalán, Jesús	64	35	16	Instituto de Salud Pública de Navarra	NAVARRA
Chirlaque López, María Dolores	66	43	18	Fundación para la Formación e Investigación Sanitarias de la Región de Murcia (FFIS)	MURCIA
Daponte Codina, Antonio	6	3	2	Escuela Andaluza de Salud Pública	GRANADA
Delgado Rodríguez, Miguel	46	25	12	Universidad de Jaén	JAÉN
Diez Domingo, Javier	6	3	3	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	VALENCIA
Domínguez García, Ángela	33	8	4	Universidad de Barcelona	BARCELONA
Echevarría Mayo, Juan Emilio	32	13	7	Instituto de Salud Carlos III	MADRID
Ferreira González, Ignacio	19	9	2	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Figueiras Guzmán, Adolfo	69	36	17	Universidad de Santiago de Compostela	CORUÑA, A
Figuerola Borras, Jordi	32	24	12	Agencia Estatal Consejo Superior de Investigaciones Científicas	SEVILLA
Galán Montemayor, Juan Carlos	29	14	7	Servicio Madrileño de Salud	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Ibarluzea Maurolagoitia, Jesús	70	52	26	Asociación Instituto de Investigación Sanitaria Biogipuzkoa	GUIPÚZCOA
Lacasaña Navarro, Marina	39	25	14	Escuela Andaluza de Salud Pública	GRANADA
Larrauri Cámara, Amparo	25	15	9	Instituto de Salud Carlos III	MADRID
López Espinosa, María José	49	35	23	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	VALENCIA
López Medina, María José	24	13	6	Agencia de Salud Pública de Barcelona	BARCELONA
Luciano Devis, Juan Vicente	26	12	3	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Lumbreras Lacarra, Blanca	23	14	2	Universidad Miguel Hernández de Elche	ALICANTE
Martí Puig, Eulalia	11	9	7	Universidad de Barcelona	BARCELONA
Menéndez Santos, Clara	16	8	7	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Morales Suárez-Varela, María Manuela	26	5	0	Universidad de Valencia	VALENCIA
Moreno Aguado, Víctor	48	31	10	Instituto Catalán de Oncología	BARCELONA
Muñoz Almagro, María Carmen	54	28	12	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Moya Simarro, Andrés	46	27	14	Universidad de Valencia	VALENCIA
Olea Serrano, Nicolás	51	42	24	Fundación Pública Andaluza para la Investigación Biosanitaria de Andalucía Oriental – Alejandro Otero	GRANADA
Pollán Santamaría, Marina	39	24	12	Instituto de Salud Carlos III	MADRID
Porta Serra, Miquel	17	13	7	Consorci Mar Parc Salut de Barcelona	BARCELONA
Rius Gibert, Cristina	31	10	9	Agencia de Salud Pública de Barcelona	BARCELONA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Rodríguez Artalejo, Fernando	61	45	13	Universidad Autónoma de Madrid	MADRID
Sáez Zafra, Marc	26	13	6	Universidad de Gerona	GIRONA
Sánchez Pérez, María José	54	34	12	Escuela Andaluza de Salud Pública	GRANADA
Schröder, Helmut	29	20	8	Consorci Mar Parc Salut de Barcelona	BARCELONA
Serra Pujadas, Consol	25	12	6	Universidad Pompeu Fabra	BARCELONA
Serra Sutton, Victoria	13	7	4	Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS)	BARCELONA
Serrano Blanco, Antonio	12	6	4	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Sunyer Deu, Jordi	121	89	56	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	BARCELONA
Tardón García, Adonina	68	42	26	Universidad de Oviedo	ASTURIAS
Villanueva Belmonte, Cristina	134	102	65	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	BARCELONA
Vioque López, Jesús	46	34	16	Universidad Miguel Hernández de Elche	ALICANTE
Zamora Romero, Javier	52	24	7	Servicio Madrileño de Salud	MADRID

Clinical Guidelines and Consensus Documents 2023

- Guidelines for the indication, use and authorization for the dispensing of prescription drugs by nurses in: oral anticoagulation.
- Executive summary. Diagnosis, treatment and prophylaxis of influenza virus infection. Consensus statement of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), the Spanish Society of Pediatric Infectious Diseases (SEIP), the Spanish Association of Vaccinology (AEV), the Spanish Society of Family and Community Medicine (SEMFYC) and the Spanish Society of Preventive Medicine, Public Health and Health Management (SEMPSPGS).
- Recommendations for the rational use of medication in the pharmacological treatment of respiratory diseases: Chronic Obstructive Pulmonary Disease.
- Protocol for early detection of cervical cancer in Catalonia.
- MLuq Protocol: A Proposal for the Immobilization of the White Weapon, Preservation of DNA Traces, and Its Chain of Custody.
- Document on interpretation and clinical utility of antiretroviral resistance studies.

- Recommendations on Pre-Exposure Prophylaxis for the Prevention of HIV Infection in Spain.
- Plastics, microplastics and nanoplastics and their effects on human health. Guide for professionals.
- Clinical guidelines for influenza vaccination.
- Clinical guidelines for vaccination against SARS-CoV-2.
- Clinical guidelines on vaccines: antigens and trade names.
- Clinical guidelines on Vaccination schedule by Autonomous Communities and Cities.
- Clinical guidelines on Vaccination against herpes zoster.
- Clinical guidelines on immunization against respiratory syncytial virus.
- Clinical guidelines on pneumococcal vaccines.
- Vascular closure devices in living-donor nephrectomy: a much-needed systematic review and meta-analysis focusing on safety.
- Basal procalcitonin, C-reactive protein, interleukin-6, and presepsin for prediction of mortality in critically ill septic patients: a systematic review and meta-analysis.
- Contribution of Low CD4 Cell Counts and High Human Immunodeficiency Virus (HIV) Viral Load to the Efficacy of Preferred First-Line Antiretroviral Regimens for Treating HIV Infection: A Systematic Review and Meta-Analysis.
- Acupuncture for the prevention of chemotherapy-induced nausea and vomiting in cancer patients: A systematic review and meta-analisis.

FRAILTY AND HEALTHY AGING

ciber | FES

WELCOME FROM THE SCIENTIFIC DIRECTOR

Leocadio Rodríguez Mañas

During 2023, CIBERFES reached a series of relevant achievements in all its lines of action based on a collaborative approach. Among the findings with potential clinical impact, of note are the publication of the first trial demonstrating the effectiveness of an intervention on hospitalized frail patients with reduced mortality and functional deterioration three months after discharge, another trial confirming the benefits of an exercise program on functional deterioration during hospitalization, the definition of treatments of choice in the prevention of fragility fractures, the development of models for the early detection of preclinical cognitive impairment, the identification of circular RNA in frail subjects and in centenarians, the role of the bone-vascular axis and the usefulness of new ultrasound signals after analysis with Artificial Intelligence for the diagnosis of frailty with prognostic value of response to exercise programs. In animal models, new findings were made on the functioning of oxidative phosphorylation generating oxidative stress in skeletal muscle and brain, opening avenues of intervention for sarcopenia or cognitive alterations, the role of estradiol in brain development by gender, the role of caloric restriction in regenerative capacity and that of a compound present in coffee and some foods to prevent frailty.

Several projects have been completed, the most important being: a middle-aged cohort in which new frailty phenotypes have been described, another on mitochondrial damage in the genesis and progression of frailty with the development of biomarkers for clinical use, and a third focused on the evaluation of a physical exercise program in elderly patients after valve replacement. Projects have been initiated, including the MIRATAR-INMAGE Project, with the participation of 2 FES groups and 2 BBN groups. The MYSELF-AGE proposal has been submitted to the ERC Synergy Grants program, with the participation of 4 FES groups and one NIA-NIH group.

Collaborations have been consolidated or established de novo with the WHO (Clinical Consortium on Healthy Aging), the Pan American Health Organization-PAHO (DIABFRAIL-LATAM Project), the University of Leuven, McGill University and Northwestern University.

On an individual level, of note is the Lifetime achievements Award of the International Conference on Frailty and Sarcopenia Research (ICFRS) to Dr. Leocadio Rodríguez Mañas, the ESTRATEGIA NAOS Award of the Ministry of Social Rights, Consumer Affairs and Agenda in the field of healthcare to the VIVIFRAIL program, led by Prof. Mikel Izquierdo, and the Award for the best published article of the SES year 2023: to the group led by Prof. M.A. Rol.

As regards dissemination, we highlight the reinforcement of CIBERFES visibility activities through the agreement with Canal Senior. Also noteworthy is the organization of the International Symposium "1st Severo Ochoa conference on: Astrocyte-neuron metabolic coupling in organismal (patho)physiology", held in Salamanca (29-30 June 2023) and headed by Prof. J.P. Bolaños.

In terms of training activities, the Guillén Llera training seminars have been consolidated and an agreement has been reached to hold six international virtual seminars in 2024 with leading figures in the field of basic, clinical and epidemiological research on aging.

PROGRAMS & PLATFORMS

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

José Viña Ribes / COORDINATOR

Dr. Andres Lacueva's group, working in the field of personalized nutrition, observed that a higher intake of dietary fiber especially benefits older people who have the E4 haplotype. The interaction of diet with Alzheimer's disease is of interest in this program. These findings and those of Dr. Viña's group, coincide in the interest in observing that the administration of genistein, a phytoestrogen present in soy, delays the onset of dementia in prodromal Alzheimer's patients.

Dr. Bolaños' group, interested in the interaction between astrocytes and neurons, has observed that the oxidation of fatty acids organizes the mitochondrial supercomplexes, and that free radicals are involved in this process; his work has been published in Nature metabolism. In the same area of interest, Dr. Arevalo's results show that neuroestradiol is of enormous importance in the formation of the male and female brain in specific effect throughout the configuration of adult neural networks.

In relation to energy metabolism and its systemic functions, Dr. Enriquez's group has studied that there is a relationship between the homeostasis of proteins and the stability of mitochondrial complex 1, which will allow us to search for new drugs that regulate mitochondrial respiration at the level of this complex. Dr. Viña's group has observed that mice treated with harmol show a delay in the onset of frailty, glycemia is improved and physical exercise and muscle strength are enhanced. These energetic effects are paradoxically mediated by peripheral modulation of monoamine oxidase b and the GABA receptor. Published in Nature communications.

The importance of mitochondrial implications in frailty was pointed out by Dr. Izquierdo's group, which showed the effects of multicomponent exercise on muscle capacity in elderly patients. The importance of this exercise has received the Estrategia NAOS Award in the field of healthcare, for the project "Promotion of physical exercise for the prevention of frailty and falls in the elderly 'VIVIFRAIL'

Program 1 is also interested in bone, with research led by the groups of Dr. Nogués and Dr. Muñoz. Dr. Nogués has published a meta-analysis in the British Medical Journal, showing that all osteoporosis treatments prevent second fragility fractures, but that mass-forming drugs have better results. Dr. Muñoz presented results showing the role of sclerostin in the development of arteriosclerosis in patients underlining the importance of the bone-vascular axis.

Dr. Matheu studied RNA synthesis showing that centenarians from the Basque Country have specific characteristics in terms of circular RNA synthesis associated with frailty.

Dr. Rol, a recognized leader in sleep research, has received the Spanish Sleep Society Award for the best published work of the year 2023 for her work on chronodisruption in cancer patients.

TACKLING FRAILTY. DETECTION, SCREENING, DIAGNOSIS AND TREATMENT. HEALTHCARE MODELS

Xavier Nogués Solan / COORDINATOR

All the members of our program have continued to carry out significant healthcare and research work during the year 2023 aimed at caring for frail patients and improving their quality of life.

I would like to highlight several of the program's achievements. The MIRATAR Project for digital transformation aimed at implementing technological improvements in the care of the elderly patient, in which the groups led by Dr. P. Abizanda and Dr. L. Rodríguez Mañas participate. This project shows us the path that medicine will take in a few years with the application of artificial intelligence in the service of health. The technology is already a reality but we do not really know what its limits will be. I would also highlight the awarding of the NAOS Strategy Prize by the Spanish Ministry of Social Rights to the project for the promotion of physical exercise in the field of the frail patient. We know that sarcopenia is related to frailty and the importance of regular physical exercise seems overwhelmingly logical. Promoting exercise as a prescription, as if it were a drug to be prescribed, will be one of the achievements for sure in the not-too-distant future.

Another important achievement has been the development of a predictive model for early detection of cognitive impairment, very relevant for the early initiation of treatments against dementia. At the health care level, but with great scientific relevance, we should highlight the benefits of reminiscence therapy in reducing anxiety and depression in hospitalized elderly patients. Admission to a hospital is not pleasant, so all the benefits that we can apply at that time to reduce the detrimental effect on the elderly patient is of great importance for their quality of life.

In terms of translational research, I would like to highlight the achievements in the study of healthy nutritional metabolomics associated with the risk of frailty and its progression. A balanced diet is likely to contribute to the healthy aging that we all want, and therefore it will be very important to know what is healthiest for the elderly through the different types of metabolites. In populations with specific diseases such as people affected by the Human Immunodeficiency Virus, we have described biomarkers related to premature aging. With regard to centenarians, another relevant achievement has been the identification for the first time of circular RNAs differentially expressed in fragile individuals.

As regards media impact, our program has presented the report on "Aging and well-being: an X-ray of the elderly" at the Science and Technology Office of the Spanish Congress of Deputies, which could be considered as the White Paper on Healthy Aging.

The clinicians and researchers in our program will therefore continue to work, each in his or her own field, whether clinical, basic or translational, so that the elderly, who in the end will be each and every one of us, will have a better life, a better quality of life and a dignified, optimal and adequate health care for each person.

TRAINING PROGRAM

Pedro Abizanda Soler / COORDINATOR

GRANTS FOR RESEARCH, COURSES, CONFERENCES, ETC.

The main training activity of the year 2023 was the celebration of the "Fourth Guillén Llera Seminar", coinciding with the IKAGURE Strategy 10th Anniversary, which was held at the Biodonostia Institute in San Sebastian on November 19 and 20 under the coordination of Dr. Ander Matheu's group.

The meeting was structured in 4 main plenary sessions. The first one entitled "Multidisciplinary approach to frailty - clinical impact" included interventions from the clinical groups of CIBERFES (Leocadio Rodríguez-Mañas, Francesc Xabier Nogues, Pedro Abizanda, José Antonio Serra Rexach and Teresa Moreno), the second one entitled "Multidisciplinary approach to frailty - biological impact" included the participation of the groups of Francisco José García-García, Feliciano Prego, Ángeles Rol de Lama, José Viña, José Antonio Enríquez, Manuel Muñoz and Ander Matheu. The third session, entitled "Cellular Aging", was attended by the groups of Ander Matheu, Germaine Escames, Juan Pedro Bolaños, María Ángeles Arévalo, and Ignacio Ara. Dr. Pere Clavé from CIBEREHD gave a keynote lecture on "dysphagia as a geriatric syndrome" and proposed collaboration between the two areas of CIBER for studies on dysphagia. The last plenary session under the title "Healthy Aging" included presentations by Adolfo López de Munain (Biodonostia and CIBERNED), and the groups of María Cristina Andrés Lacueva, Francesc Xabier Nogues, Francisco José García-García, Ángeles Rol de Lama, Oriol Grau, José Antonio Serra Rexach and José Viña; the last plenary session under the title "Healthy Aging" included presentations by Adolfo López de Munain (Biodonostia and CIBERNED), and the groups of María Cristina Andrés Lacueva, Francesc Xabier Nogues, Francisco José García-García, Ángeles Rol de Lama, Oriol Grau, José Antonio Serra Rexach and José Viña. During the meeting, the foundations were laid for collaboration with CIBEREHD and NED.

As regards specific training activities of the groups, we participated in the " CIBER 2023 Course on Scientific Communication and Dissemination" (groups led by Marian Rol and Mayte Moreno); the group led by Dr. Juan Pedro Bolaños organized the "1st Severo Ochoa Conference on 'Astrocyte-neuron metabolic coupling in organismal pathophysiology' held in Salamanca on June 29-30; Manuel Muñoz's group was moderator in the 'Annual Review of Top Worldwide Congresses and Scientific Literature' held in Madrid, February 17-18 and participated in the Scientific Committee of the 'Annual Review of Congresses on Osteoporosis' held in Madrid on March 10-11; Mayte Moreno's group organized the "International Care Research Meeting, the Congress of Qualitative Research in Health and the International Conference of Doctoral Students in Valladolid with more than 530 attendees which included 9 pre-congress workshops.

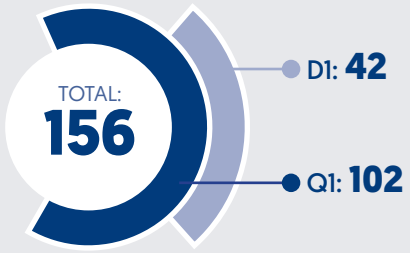
Some groups have carried out Intra-area training stays and all groups have carried out training activities in their work centers, participated in undergraduate and postgraduate teaching, tutored doctoral theses, graduate and master's dissertations, taught national and international courses, made presentations at national and international conferences and participated in Master's degrees related to CIBERFES objectives.

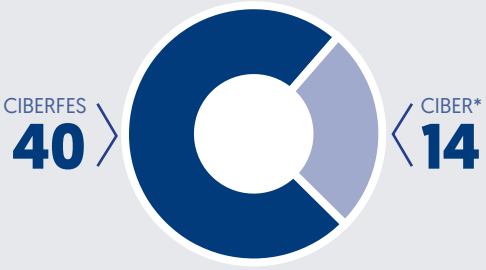
The next CIBERFES face-to-face meeting will be held in La Granja de San Ildefonso on March 11-13, 2024.

SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023





*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
64,8	Paredes A, Justo-Méndez R, Jiménez-Blasco D, Núñez V, Calero I, Villalba-Orero M, et al. γ-Linolenic acid in maternal milk drives cardiac metabolic maturation. Nature. 2023 Jun;618(7964):365–73.
64,8	Paredes A, Justo-Méndez R, Jiménez-Blasco D, Núñez V, Calero I, Villalba-Orero M, et al. Author Correction: γ-Linolenic acid in maternal milk drives cardiac metabolic maturation. Nature. 2023 Jul;619(7968):E24.
49,6	Valenzuela PL, Carrera-Bastos P, Castillo-García A, Lieberman DE, Santos-Lozano A, Lucia A. Obesity and the risk of cardiometabolic diseases. Nat Rev Cardiol. 2023 Jul;20(7):475-494. doi: 10.1038/s41569-023-00847-5. Epub 2023 Mar 16. PMID: 36927772.
39,89	Händel MN, Cardoso I, von Bülow C, Rohde JF, Ussing A, Nielsen SM, et al. Fracture risk reduction and safety by osteoporosis treatment compared with placebo or active comparator in postmenopausal women: systematic review, network meta-analysis, and meta-regression analysis of randomised clinical trials. BMJ. 2023 May 2;381:e068033.
39,3	Valenzuela PL, Ruilope LM, Santos-Lozano A, Wilhelm M, Kränkel N, Fiuza-Luces C, Lucia A. Exercise benefits in cardiovascular diseases: from mechanisms to clinical implementation. Eur Heart J. 2023 Jun 1;44(21):1874-1889. doi: 10.1093/eurheartj/ehad170. PMID: 37005351.
34,3	Ramírez-Vélez R, Silva DR. The challenge of promoting physical activity in low-income and middle-income countries. Lancet Glob Health. 2023 Aug;11(8):e1158–9.
32,4	Wculek SK, Heras-Murillo I, Mastrangelo A, Mañanes D, Galán M, Miguel V, et al. Oxidative phosphorylation selectively orchestrates tissue macrophage homeostasis. Immunity. 2023 Mar 14;56(3):516-530.e9.
29,0	Altomare D, Barkhof F, Caprioglio C, Collij LE, Scheltens P, Lopes Alves I, et al. B; Amyloid Imaging to Prevent Alzheimer's Disease (AMYPAD) Consortium. Clinical Effect of Early vs Late Amyloid Positron Emission Tomography in Memory Clinic Patients: The AMYPAD-DPMS Randomized Clinical Trial. JAMA Neurol. 2023 Jun 1;80(6):548-557. doi: 10.1001/jamaneurol.2023.0997. PMID: 37155177; PMCID: PMC10167601.
26,1	García-Hermoso A, López-Gil JF, Izquierdo M, Ramírez-Vélez R, Ezzatvar Y. Exercise and Insulin Resistance Markers in Children and Adolescents With Excess Weight: A Systematic Review and Network Meta-Analysis. JAMA Pediatr. 2023 Dec 1;177(12):1276–84.
24,0	Stens NA, Bakker EA, Mañas A, Buffart LM, Ortega FB, Lee DC, et al. Relationship of Daily Step Counts to All-Cause Mortality and Cardiovascular Events. J Am Coll Cardiol. 2023 Oct 10;82(15):1483–94.

CIBERFES Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Abizanda Soler, Pedro	2	0	0	Servicio de Salud de Castilla La Mancha	ALBACETE
Andrés Lacueva, María Cristina	9	7	2	Universidad de Barcelona	BARCELONA
Ara Royo, Ignacio	12	7	0	Universidad de Castilla la Mancha	TOLEDO
Arévalo Arévalo, María Ángeles	3	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Bolaños Hernández, Juan Pedro	5	4	3	Fundación Instituto de Estudios de Ciencias de la salud de Castilla y León	SALAMANCA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Enríquez Domínguez, José Antonio	5	4	4	Fundación del Sector Público Estatal Centro Nacional de Investigaciones Cardiovasculares Carlos III	MADRID
Escames Rosa, Germaine	5	3	0	Fundación Pública Andaluza para la Investigación Biosanitaria de Andalucía Oriental – Alejandro Otero (FIBAO)	GRANADA
García García, Francisco José	6	5	0	Fundación del Hospital Nacional de Parapléjicos	TOLEDO
Grau Rivera, Oriol	9	7	6	Fundación Barcelonabeta Brain Research Center	BARCELONA
Izquierdo Redin, Miguel	35	22	9	Universidad Pública de Navarra	NAVARRA
Matheu Fernández, Ander	4	4	3	Asociación Instituto de Investigación Sanitaria Biogipuzkoa	GUIPÚZCOA
Moreno Casbas, Teresa	5	2	1	Instituto de Salud Carlos III	MADRID
Muñoz Torres, Manuel	7	5	0	Fundación Pública Andaluza para la Investigación Biosanitaria de Andalucía Oriental – Alejandro Otero (FIBAO)	GRANADA
Nogues Solan, Francesc Xavier	5	2	1	Consorci Mar Parc Salut de Barcelona	BARCELONA
Priego Capote, Feliciano	10	6	4	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Rodríguez Mañas, Leocadio	11	9	3	Servicio Madrileño de Salud	MADRID
Rol de Lama, María de los Ángeles	1	1	0	Universidad de Murcia	MURCIA
Serra Rexach, José Antonio	8	4	1	Servicio Madrileño de Salud	MADRID
Viña Ribes, José	18	13	4	Fundación para la Investigación del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA

INFECTIOUS DISEASES

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Jesús Oteo Iglesias

Dear colleagues,

It is a pleasure for me to address all of you in this letter in which I succinctly summarize the highlights of CIBERINFEC in 2023. It has been a very special year, the second year in the history of our research area, but the first in which we have begun to acquire a CIBER routine after the difficulties and peculiarities inherent to any start-up.

The first thing I would like to highlight is CIBERINFEC's commitment to the strategic pillars of the CIBER philosophy, promoting transversality and multidisciplinarity, the development of alliances and positioning at both scientific and social levels.

In this regard, during 2023, collaborative activities have been carried out with other CIBER areas at different levels, such as the celebration of the Young Researchers Conference with CIBERES, the participation of the scientific directions of CIBER-BBN and CIBEREHD in the Scientific Conference of the area held in November in Zaragoza, or the approval of a joint call for intramural seed projects with CIBER-BBN for 2024; not to mention the collaboration with CIBERESP and CIBERES in the strategic actions implemented in response to the health alerts for the monkeypox virus and the increase in invasive Streptococcus pyogenes infections in children, respectively.

Since its inception, CIBERINFEC has been committed to strengthening cooperative research with the launch, already in its first year, of a call for intramural projects in which funding was approved for seven projects that have been active during 2023. This action has been continued in 2023 with a second call that has been resolved with the favorable evaluation of eight projects led by young researchers, involving at least four research groups per project.

Within the strategic scope of developing alliances and positioning, I would like to highlight that CIBERINFEC has promoted the signing of a "Joint Action Protocol" between CIBER and the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC); a commitment to collaboration that will surely enhance national research capacity and, above all, that of transfer to the national health system.

In its commitment to the incorporation of new technologies in the research and surveillance of infectious diseases, CIBERINFEC has been actively working on the development of a bioinformatics platform; a project that is already well advanced and will start operating in 2024. In addition, the CoRIS cohort of HIV-infected patients from the AIDS Research Network has been incorporated as a CIBER platform. Another of the aspects on which CIBERINFEC has worked in 2023 is the promotion of a collaborative structure that facilitates both the agile execution of clinical trials in response to future health alerts, and national participation and leadership in large adaptive clinical trials in the field of infectious diseases. In this regard, the Steering Committee of the area approved the creation of a working group to lead its development and implementation from CIBER.

The training of young CIBERINFEC researchers has been another priority during 2023, with the approval of 14 grants for stays or attendance to courses, in addition to the promotion of their participation in intramural projects and the holding of the aforementioned Young Researchers Conference. Worth mentioning in this section is the holding of a workshop on "Surveillance and Control of Invasive Vectors", which was held in Tenerife in November 2023. CIBERINFEC also granted its scientific sponsorship to eight training and dissemination activities related to infectious diseases during 2023.

The scientific production of CIBERINFEC in 2023 has been relevant, even more so if placed in the context of the short distance covered so far by this thematic area, reaching a total of 570 publications of which 29% were published in D1 journals, 66% in Q1 journals. There were 145 intra-ciber collaborative publications and 218 inter-ciber publications. In addition, during 2023, five competitive projects with external CIBER funding were started or awarded.

Of note is the launch of the MePRAM project, on the application of precision and personalized medicine against antibiotic resistance, which brings together 29

CIBER groups, with the collaboration of CIBERES and CIBERESP groups, and which is creating a collaborative network of actors involved in this topic at the national level.

2023 has been an intense year for CIBERINFEC and I would like to sincerely thank you all for your efforts and commitment to strengthen the pillars on which our future activity will be developed. In this sense, the four scientific programs and the training program, with their coordinators at the head, have worked on the development of the different work plans and priority research lines of CIBERINFEC.

We have only just begun, there is still much to do and much to improve in order to optimize the operation of the area, but the achievements we are making along the way are no small feat. And all this is only possible thanks to the invaluable collaboration of the entire CIBERINFEC community. I encourage you to continue together to promote cooperative research of excellence in the field of infectious diseases in order to contribute to reducing their impact on society.

Warmest regards.

PROGRAMS & PLATFORMS

GLOBAL HEALTH, EMERGING AND RE-EMERGING INFECTIONS

Agustín Benito Llanes y Cristina Calvo Rey / COORDINATORS

This program includes the participation of 31 of the 46 CIBERINFEC groups. It is structured around 6 strategic research lines and 16 work packages:

SURVEILLANCE, PREVENTION AND CONTROL OF TROPICAL INFECTIONS BOTH IN OUR COUNTRY AND AT ORIGIN USING THE PLATFORMS OF CIBERINFEC GROUPS IN THIRD COUNTRIES.

During 2023, of particular note is the activity of REDIVI (Network of Hospital Units for the care of immigrants and travelers), which collects information on the impact of imported infectious pathology in our country as a result of migration and international travel, and the National Registry of Leishmaniasis (ReNLeish), which reports to the World Health Organization (WHO). More than 30,000 cases have been included, of which 54.9% are immigrants, 28.3% travelers and 16.8% VFR. Many strategies have been implemented in low resource countries (LMIC), such as the reinforcement of diagnostic capacity in laboratories with projects financed by AECID and the PROBITAS foundation, which have contributed to strengthening the healthcare system in Paraguay.

Screening programs for immigrants have been applied, such as the CRIBMI tool, a clinical decision support system for multi-disease screening in Primary Care. And there has been an in-depth study of numerous neglected diseases such as human fascioliasis and preventive chemotherapy strategies, snakebites or schistosomiasis in highly endemic areas, as well as the development of new integrated control strategies for onchocerciasis, lymphatic filariasis and loiasis.

The surveillance of arboviruses and invasive vectors with the detection of Aedes aegypti on the island of Tenerife and the island of Gran Canaria is very important because of its implications for the transmission of imported diseases.

SURVEILLANCE, PREVENTION AND CONTROL OF EMERGING AND RE-EMERGING NON-TROPICAL INFECTIONS.

In this area, the following stand out: the evaluation of the impact of the COVID-19 pandemic on the incidence of infections caused by multiresistant microorganisms, as well as the description of an extensive prospective series of necropsies of patients who died of COVID-19, in which it was observed that in 15.7% of the cases bacterial and fungal superinfections contributed to the death. Also worth mentioning is the participation as national coordinators in the evaluation by means of a randomized trial of the possible protective effect of the BCG vaccine in healthcare workers for severe SARS-CoV-2 disease (published in NEJM), or the participation in the review carried out by the ECDC on personal protective equipment in the transmission of SARS-CoV-2. In addition, the first prospective and population-based evidence of an association between individual concentrations of some contaminants and SARS-CoV-2 infection has been provided, the performance of the PanCOVID test in the hospital setting has been studied, as well as the immune response to vaccines in pregnant women and their children. Immunity in severe diseases or long-term sequelae has been analyzed. Finally, new vaccine

candidates have been analyzed.

In the field of bacterial infections, we have worked on the clinical and molecular characterization of the increase in invasive infections by S. pyogenes in children, as well as on the identification of biomarkers.

Other emerging infections studied have been the outbreaks of West Nile virus infection in Andalusia; the implication of the Toscana virus as a cause of idiopathic meningitis in Southern Spain; or the study of the environmental origin of emerging pathogens of the Candida orthopsilosis species and the possible role of climatic change in the origin of hybrids with infective capacity.

RESEARCH ON VECTOR/RESERVOIR/ PATHOGEN/END HOST/ENVIRONMENT INTERACTIONS AIMED AT UNDERSTANDING THE NATURAL CYCLE OF ZOONOTIC AGENTS AND THEIR RELATIONSHIP WITH ENVIRONMENTAL CHANGES WITHIN THE "ONE HEALTH" CONCEPT.

Based on ecological niche models, a basis has been established to evaluate the geographical risk of transmission of vector-borne diseases (VBDs), useful for studying the impact of tropical diseases in Spain and worldwide.

RESEARCH ON IMMUNITY AND PATHOGENESIS OF TROPICAL, EMERGING AND RE-EMERGING INFECTIOUS DISEASES.

PROMOTION AND RESEARCH IN THE DEVELOPMENT OF NEW DIAGNOSTIC METHODS AND THEIR APPLICABILITY IN THE CONTEXT OF GLOBAL HEALTH.

A national cohort has been created for the study of biomarkers of Chagas disease. The metabolomic and lipidomic profile of a cohort of individuals chronically infected with Trypanosoma cruzi has been studied. Chagas disease has been extensively studied by several groups in terms of diagnosis, biomarkers and potential therapeutic targets.

Work has been carried out on the optimization of molecular diagnosis of hepatitis E virus infection, as well as on the diagnosis of tegumentary leishmaniasis and the characterization of the species that cause it (with technology transfer to Bolivia (Universidad Mayor de San Simón (UMSS), Cochabamba).

The diagnosis of monkeypox virus with the characterization of mutations that confer resistance to anti-viral drugs and the diagnostic quality control program in the National Health System has also played an important role. Also worth mentioning is the description of a RT-LAMP method for the Crimean-Congo hemorragic fever virus and the analysis of the cases that have occurred in Spain.

RESEARCH ON THE DEVELOPMENT OF NEW TARGETS AND PREVENTION AND THERAPEUTIC STRATEGIES FOR TROPICAL, EMERGING AND RE-EMERGING INFECTIOUS DISEASES, BOTH ZOONOTIC AND WITH HUMAN RESERVOIR, INCLUDING GENE THERAPY.

Intensive efforts are being to develop tuberculosis vaccines in LMIC, presenting the rationale for measuring in clinical trials not only the direct but also the indirect effects of such candidates, including the reduction of its transmission, and in establishing various options for incorporating their evaluation in Phase 3 trial designs. COVID vaccines in special groups or the study of the appropriate recall dose interval have also been under study.

Malaria treatment with evidence of therapeutic efficacy and study of resistance with work carried out in both the Guinean and Angolan populations.

The description and characterization of a new compound with anti-prion activity with dual mechanism of action has been carried out, as well as the development of a new method for the generation of infectious recombinant prions in vitro as a model of sporadic transmissible spongiform encephalopathies.

We will continue to focus on the study of the impact of tropical infections in Spain and worldwide, through our platforms abroad (Africa and Latin America) as well as the early detection of emerging viral or bacterial infections. We are also involved in the study of biomarkers of infectious diseases, as well as the development of therapeutic targets for neglected tropical diseases or vaccines through our groups.

ANTIMICROBIAL RESISTANCE

Jesús Rodríguez Baño y Rafael Cantón Moreno / COORDINATORS

Twenty-one groups participate in CIBERINFEC Program 2, Antimicrobial Resistance.

The program, with seven lines of work, has developed projects and obtained different scientific achievements, which are summarized below: Participation in resistance surveillance programs, with the application of whole genome sequencing techniques, state-of-the-art platforms and bioinformatics analysis with the description of the dispersion of high-risk clones associated with refugees from armed conflicts and migrants.

National contact point with ECDC of the European networks EARS-Net y EUR-Gen-Net.

Release of the first RedLabra report with the participation of the level 2 reference laboratories, the level 3 reference laboratory (Centro Nacional de Microbiología, Instituto de Salud Carlos III) and CIBERINFEC groups.

The development of multicenter programs to monitor carbapenemase-producing microorganisms, including those affecting the pediatric population, their clinical implications and strategies to improve survival.

Promotion of personalized and precision medicine projects (MePRAM project) to combat antimicrobial resistance with the development of innovative therapies (microbiota transfer and phage therapy, among others) and pathogen-focused randomized clinical trials.

The study of microbiota in different pathologies and ecological strategies for its modulation.

Attracting funding for projects to address resistance with Artificial Intelligence tools focused on the vulnerable patient.

The development of programs to improve the use of antimicrobials in units with high antimicrobial use, long-stay centers, community infections. Antimicrobial prescribing performance programs from the patient's perspective.

Promoting internationalization with leadership and participation in proposals and development of projects funded by European agencies and international societies:

- Joint programing initiative on Antimicrobial resistance (JPI-AMR): 1) TEAPOTS "Tools for the Epidemiology of AMR Plasmids, One-Health Transmission and Surveillance"., 2) ISARPAE "Improving surveillance of antibiotic-resistant Pseudomonas aeruginosa in Europe",3) BASISCS. Bridging Antimicrobial resistance Surveillance systems In Community Settings across Europe y 4) INFORM-AFR. "International Fungal Network for One-Health Resistance Surveillance: Antifungal Resistanc".
- Horizon: 1) ECRAID "European Clinical Research Alliance on Infectious Diseases), 2) REVERSE. "pREVention and management tools for rEducing antibiotic Resistance in high prevalence, 3) ORCHESTRA. "Connec- ting European Cohorts to Increase Common and Effective Response to SARSCoV-2 Pandemic", 4) PRIMAVERA. "Predicting the Impact of Monoclonal Antibodies & Vaccines on Antimicrobial Resistance", 5) IN-ARMOR. "Therapeutic Epigenetic Enhancement of the Innate Immunity to Effectively Combat Antimicrobial Resistance") 6) EU-JAMRAI 2. "Joint Action Antimicrobial Resistance and Healthcare-Associated Infections 2", 7) European Society of Clinical Microbiology and Infectious Diseases (ESCMID) y 8) STARS. "Towards the implementation of STandardised Antifungal Resistance Surveillance: A multicentre point prevalence study in ICUs".

EDevelopment of vaccines against multidrug-resistant microorganisms, including M. tuberculosis.

Coordination and participation in clinical trials of new antimicrobials and strategies for the use of known antimicrobials against multidrug-resistant bacteria (coordinated trials: SIMPLIFY, ASTARTÉ, INTENSE, SHORTEN-2).

Leadership of clinical trials of diagnostic tests to improve the diagnosis of multidrug-resistant microorganisms.

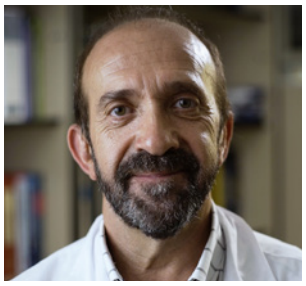
Development of new therapeutic molecules against infections by parasitic protozoa (trypanosomatids and free-living amoebae: Acanthamoeba and Naegleria fowleri).

Development of vehicles and new immunotherapies (nano-bodies and CAR cells) in the treatment of opportunistic pathogens resistant to antimicrobial treatments.

The development of artificial intelligence algorithms to interpret results in diagnostic systems.

Use of alternative laboratory models (organoids, Galleria, C. elegans, hollow-fiber) for the study of infections by multidrug-resistant microorganisms.

Advances in the development of sensors for the detection of multiresistant microorganisms.



HIV/AIDS AND SEXUALLY TRANSMIITEED INFECTIONS

Santiago Moreno Guillén y José Mª Miró Meda / COORDINATORS

ORGANIZATIONAL ASPECTS OF THE PROGRAM

The program committee has held five meetings during the year 2023. During these meetings progress has been made in the elaboration and approval of the strategic lines of Program 3, as well as the groups that will participate in each of them, in addition to the election of the coordinators of each of the Work Packages (WP) of this program. For the latter point, priority has been given to the participation of young researchers, gender balance (60% women) and a maximum of one representative per research group, to achieve the greatest possible representativeness. In addition, CoRIS/CoRISpe has been consolidated as a CIBERINFEC structure.

LINES OF RESEARCH OF EACH WORK PACKAGE (WP)

A) Structures – CoRIS/CoRISpe; maintenance and development of structures to integrate clinical and epidemiological data.

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

B) Epidemiology and Public Health. Characteristics of the HIV epidemic, improvement of management and Treatment, and quality of life. This line is structured into the following work packages:

- WP1. Epidemiological Studies
- WP2. Public Health Interventions
- WP3. Quality of Life
- WP4. Evolution of infection according to different treatments
- WP5. Special groups: pediatrics, adolescents, trans patients, patients with high degree of frailty, patients with social exclusion

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

- WP1. Epidemiological
- WP2. Clinical. Associated diseases and co-morbidities
- WP3. Biomarkers
- WP4. Pathogenic mechanisms
- WP5. Senolytic treatments

D) Co-infections and new infections. This line includes aspects such as the COVID observatory and immunosuppressed patients and HIV-hepatitis virus co-infection. In addition, this program has actively participated in the cross-cutting strategic action on Monkeypox coordinating WP1.

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

- WP1. Description and analysis of the CD and LTNP cohorts.
- WP2. Clinical evolution. Studies on loss of control.
- WP3. Virological mechanisms of persistence of infection.
- WP4. Immunological studies.

F) PrEP and sexually transmitted infections (STI):. PrEP implementation and consequences. This strategic line is structured into the following work packages:

- WP1. Creation and analysis of PREP cohorts.
- WP2. Epidemiology. Impact on new cases and evolution of the epidemic.
- WP3. Virological studies in PrEP escape/failure.
- WP4. Clinical trials. Therapeutic vaccines, immunomodulatory treatments.

G) Preventive vaccines. This line is structured iton the following work packages.

- WP1. Experimental models.
- WP2. New prototypes.
- WP3. Immunological and virological techniques for vaccine evaluation.
- WP4. Clinical trials.

The most outstanding contributions are the follwoing: a) Delayed diagnosis of HIV infection in pregnant women leads to a worse prognosis of the disease in their children, b) Initiation of antiretroviral treatment partially reverses the alterations in DNA methylation induced by HIV infection, c) Third case worldwide of HIV cure after stem cell transplant and d) New data on the mutation that protects against HIV but increases the risk of developing a rare muscular atrophy.

INFECTIONS IN NON-HIV IMMUNOSUPPRESSED PATIENTS AND HEALTHCARE ASSOCIATED INFECTIONS

José Mª Aguado García y Jordi Carratalà Fernández / COORDINATORS

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

The main scientific achievements of this Program in 2023 include:

The development of different biomarkers that allow the diagnosis of latent infection by Leishmania spp. of special interest in the immunosuppressed patient.

The study of the role of Torque tenovirus as a marker of immunosuppression in children and adults.

The role of different biomaterials and nanosystems in osteoarticular infection and in studies aimed at counteracting the action of biofilm and the antimicrobial effect of these materials.

The performance of trials aimed at improving the management of infection in transplant patients by monitoring the cellular response. As well as the study of infection by multiresistant bacteria in solid organ transplant recipients.

The development of studies on gliatoxin production in different fungi that open the door to new diagnostic and therapeutic targets for invasive fungal infection in immunocompromised patients.

The definition of a series of specific immune signatures to differentiate COVID19 from other infections that allow predicting the severity of the disease and the risk of death.

Knowledge of the role of certain substances, such as hypochlorite, and physical measures, such as hyperthermia, on biofilm development and response to infection in animal models.

Advancement of knowledge in the treatment of invasive aspergillosis in solid organ transplant patients, as well as in different aspects of the genetic risk (SNP polymorphisms) of various viral infections (CMV, BK virus, Torque tenovirus) and development of biomarkers to define the risk of infection and rejection in transplant recipient patients.

A multicenter study on the consequences of infection by nontuberculous mycobacteria in solid organ transplant patients.

The study of the development of azole resistance in Candida (especially related to Candida parapsilosis) and Aspergillus and the analysis of genetic aspects that mediate the risk of developing invasive infection by Aspergillus in immunocompromised population.

Contributions in the field of epidemiology and genetics of bacterial resistance. As well as the improvement in the knowledge of infection by Aspergillus spp. in patients with solid organ transplants.

The study of the behavior of infective endocarditis in different situations (patients with mulitvalvular involvement, elderly patients, children, etc.)

Evaluation of the role of oxidative stress and lipid peroxidation in sepsis and the usefulness of different biomarkers. In addition, the role of genetic variants in the risk of sepsis was evaluated.

A randomized multicenter study (SAFO trial) demonstrated that combined treatment with cloxacillin and fosfomycin does not improve therapeutic success compared to cloxacillin monotherapy in methicillin-sensitive Staphylococcus aureus bacteremia.

In an international multicenter study, we demonstrated that the combination of ceftazidime/avibactam in comparison with the best available therapy improves the clinical outcome of solid organ transplant patients with carbapenemase-producing Klebsiella pneumoniae bacteremia.

In a national multicenter study, we demonstrated that monotherapy with a cephalosporin is not inferior to combined treatment with beta-lactam and aminoglucoside in endocarditis due to viridans and galloliticus group streptococci, avoiding nephrotoxicity. This finding should be considered in future guidelines for the management of infective endocarditis and change standard practice.

Generation of evidence, through a multi-center study, that isavuconazole is a safe and effective alternative for the treatment of invasive fungal infection in solid organ transplant recipients.

Participation in an international randomized clinical trial (STOP-FLU trial) demonstrated that influenza vaccine with MF59 adjuvant resulted in a superior immunogenic response to standard vaccine in the solid organ transplant population.

STRATEGIC ACTIONS AND INTRAMURAL PROJECTS

Antonio Oliver / COORDINATOR

STRATEGIC ACTIONS

During 2023, the two strategic actions that CIBERINFEC promoted in 2022 in response to health alerts have been completed.

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

Given the significant increase in the notification of MPXV cases in Spain, and in other European countries, in the spring of 2022 CIBERINFEC considered the need to provide knowledge on aspects related to the response of the infected patient, the evolution and adaptation of the virus in its new environment and the methods for its control. From this need arose the first strategic action in response to health alerts promoted by CIBERINFEC in its still short history and, in collaboration with CIBERESP, has resulted in eight international scientific publications and 13 communications to congresses.

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

In autumn-winter 2022, the United Kingdom reported an unusual increase in infections by this microorganism, with a predominance of the usual non-invasive infections of the upper airway but also affecting invasive infections in children under 10 years of age.

By promoting this strategic action, CIBERINFEC has managed to characterize the population of S. pyogenes causing invasive infection in children, with a predominance of emm1 and emm12 type strains, and with the irruption of the so-called M1UK clone in Spain. It has also made it possible to study the risk factors associated with invasive infections by this microorganism, as well as to analyze the host immune response. All this has resulted in an international publication and two communications to congresses.

INTRAMURAL PROJECTS

In 2023, in addition to continuing the execution of the seven intramural projects approved in the 2022 call, another call has been launched with the main objectives of promoting translational cooperative research in at least four CIBER research groups, as well as promoting the leadership of young researchers.

The projects funded in the 2023 call were:

1) **Predictive algorithm for initiating early and safe antibiotic treatment withdrawal in abdominal sepsis based on clinical and transcriptomic markers.**

   This study aims to apply transcriptomics to programs to optimize the use of antimicrobials (PROA), with the objective of developing a predictive model for safe withdrawal of antibiotic treatment in sepsis after abdominal surgery, based on the clinical-molecular information generated.

2) **Pilot project for the development of a molecular surveillance network for antifungal resistance with integration of microbiological and clinical data. Fun-ResNet Project.**

   The main objective is to develop a pilot project to lay the foundations for a national antifungal resistance surveillance program. This involves the creation of shared databases covering clinical, microbiological and genomic data, allowing the study of the evolution of resistance and risk factors in patients with fungal infections. This proposal seeks to address the challenge of antifungal resistance in the context of One Health and focuses on investigating the presence of resistant fungi in both hospital and outdoor settings, as well as those isolated in invasive infections.

3) **Invasive Streptococcus pyogenes infections in children and adults: Evolution and microbiological, clinical, genetic and immune response risk factors.**

   The aim of this study is to study the evolution of the epidemic of Streptococcus pyogenes infections in children and adults, as well as to analyze the risk factors for its development, including the epidemiology of the circulating strains, study of virulence and immune evasion, clinical characterization, genetic determinants, and the immune response involved.

4) **Unlocking the diagnostic potential of the microbiome: A stool-based multi-omic approach for tuberculosis detection in children and people with HIV.**

   The aim of this project is to harness the interactions between the microbiome and the immune system that influence susceptibility to tuberculosis to discover new diagnostic markers. Specifically, it identifies microbiome-associated stool biomarkers to improve the accuracy of TB diagnosis, validates these markers in a multi-omic context, and explores new microbiota-related pathways affecting TB susceptibility.

5) **MAEMVI: Malaria and emerging arboviruses in migrants and travelers.**

   MAEMVI addresses the diagnosis of mosquito-borne infectious agents (Plasmodium parasites and arboviruses such as West Nile, Chikungunya, Dengue, Zika, Usutu, yellow fever, Mayaro or Sindbis viruses) in migrants and travelers from endemic areas. It aims to analyze the efficacy of diagnostic tests and the presence of resistance to first-line drugs, as well as to determine the transmission capacity of Spanish mosquito populations for imported arboviruses.

6) **National registry of extensively treated individuals with limited therapeutic options. RETO study.**

   The general objective of this project is to create a national cohort of extensively pretreated subjects with limited treatment options to better understand this complex clinical scenario, as well as to improve the treatment of these subjects at the national level.

7) **Biomarkers in bronchoalveolar lavage for the diagnosis and prediction of invasive pulmonary aspergillosis.**

   The main objective is to analyze the usefulness of quantification of fungal and host biomarkers in bronchoalveolar lavage for the diagnosis of invasive pulmonary asper-

gillosis, compared to the conventional approach based on molecular techniques and conventional microbiological techniques.

8) **Microbiological and clinical impact of the acquisition of resistance to new antibiotics in Enterobacteriaceae hyperproducing AmpC beta-lactamase.**

AmpC is a beta-lactamase that generates antibiotic resistance but may or may not be expressed. This study aims to demonstrate the usefulness of new antibiotics introduced in the clinic (with good activity against multidrug-resistant Enterobacteriaceae) against these bacteria with hyper-produced AmpC, as well as to analyze whether suboptimal concentrations can facilitate these bacteria to become resistant to these antibiotics and to elucidate the underlying mechanisms.

TRAINING PROGRAM

Mª del Carmen Fariñas Álvarez / COORDINATOR

During the course of the year 2023, the main focus of the CIBERINFEC Training program was to continue to maintain its primary objective of promoting training in the field of infectious diseases, with special attention to providing opportunities for young researchers as future scientific leaders in this field.

Nine mobility grants and 5 course registrations were financed. Eight sponsorships were granted for scientific activities, proposed by one or more researchers from CIBERINFEC groups and financed by public or private entities, with the aim of promoting the dissemination of scientific progress in infectious diseases and microbiology.

On June 15 and 16, the Conference for Young Researchers in collaboration with CIBERES was held in Madrid. This forum for the exchange of ideas and projects for the advancement of research collaboration was attended by more than 150 participants and numerous projects and research papers were presented. Highlights:

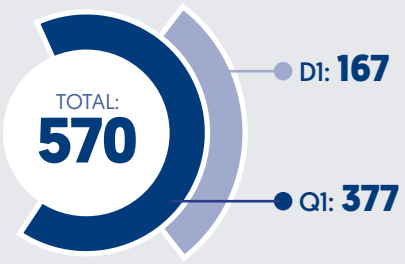
- Results of the strategic action on Invasive S. pyogenes infections in children.
- Training workshop on "Technology transfer, technological development and project valorization".
- Oral communications by young researchers from both CIBERINFEC and CIBERES.

On November 27, 28 and 29, a Workshop on Surveillance and Control of Invasive Vectors was held at the University Institute of Tropical Diseases and Public Health of the Canary Islands of the University of La Laguna in Tenerife.

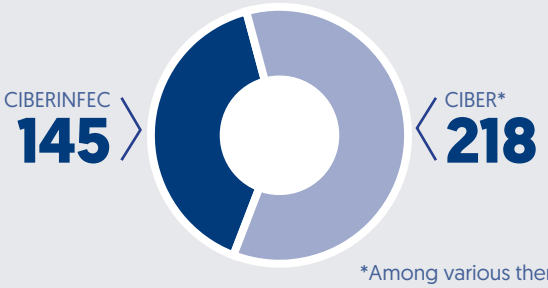
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168,9	Mitjà O, Alemany A, Marks M, et al. Mpox in people with advanced HIV infection: a global case series. Lancet. 2023;401(10380):939-949. doi:10.1016/S0140-6736(23)00273-8
158,5	Pittet LF, Messina NL, Orsini F, et al. Randomized Trial of BCG Vaccine to Protect against COVID-19 in Health Care Workers. N Engl J Med. 2023;388(17):1582-1596. doi:10.1056/NEJMoa2212616
158,5	Grinspoon SK, Fitch KV, Zanni MV, et al. Pitavastatin to Prevent Cardiovascular Disease in HIV Infection. N Engl J Med. 2023;389(8):687-699. doi:10.1056/NEJMoa2304146
86,2	Bermejo-Martin JF, García-Mateo N, Motos A, et al. Effect of viral storm in patients admitted to intensive care units with severe COVID-19 in Spain: a multicentre, prospective, cohort study. Lancet Microbe. 2023;4(6):e431-e441. doi:10.1016/S2666-5247(23)00041-11
86,2	Daneshnia F, de Almeida Júnior JN, Ilkit M, et al. Worldwide emergence of fluconazole-resistant Candida parapsilosis: current framework and future research roadmap. Lancet Microbe. 2023;4(6):e470-e480. doi:10.1016/S2666-5247(23)00067-8
86,2	Nelson KN, Churchyard G, Cobelens F, et al. Measuring indirect transmission-reducing effects in tuberculosis vaccine efficacy trials: why and how?. Lancet Microbe. 2023;4(8):e651-e656. doi:10.1016/S2666-5247(23)00112-X
82,9	Jensen BO, Knops E, Cords L, et al. In-depth virological and immunological characterization of HIV-1 cure after CCR5Δ32/Δ32 allogeneic hematopoietic stem cell transplantation. Nat Med. 2023;29(3):583-587. doi:10.1038/s41591-023-02213-x
82,9	Serrano-Villar S, Tincati C, Raju SC, et al. Microbiome-derived cobalamin and succinyl-CoA as biomarkers for improved screening of anal cancer. Nat Med. 2023;29(7):1738-1749. doi:10.1038/s41591-023-02407-3
82,9	Grillo S, Pujol M, Miró JM, et al. Cloxacillin plus fosfomycin versus cloxacillin alone for methicillin-susceptible Staphylococcus aureus bacteremia: a randomized trial. Nat Med. 2023;29(10):2518-2525. doi:10.1038/s41591-023-02569-0
76,2	Rangaka MX, Frick M, Churchyard G, et al. Clinical trials of tuberculosis vaccines in the era of increased access to preventive antibiotic treatment. Lancet Respir Med. 2023;11(4):380-390. doi:10.1016/S2213-2600(23)00084-X

CIBERINFEC Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Aguado García, José María	29	20	13	Servicio Madrileño de Salud	MADRID
Alcami Pertejo, José	9	9	4	Instituto de Salud Carlos III	MADRID
Arribas López, José Ramón	32	24	19	Servicio Madrileño de Salud	MADRID
Bargues Castelló, María Dolores	12	7	5	Universidad de Valencia	VALENCIA
Benito Llanes, Agustín	15	7	4	Instituto de Salud Carlos III	MADRID
Bou Arévalo, Germán	12	10	3	Servicio Gallego de Salud	CORUÑA, A

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Calvo Rey, Cristina	30	19	7	Servicio Madrileño de Salud	MADRID
Cantón Moreno, Rafael	45	26	9	Servicio Madrileño de Salud	MADRID
Carratalà Fernández, Jordi	34	19	8	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Castilla Castrillón, Joaquín	3	1	0	Asociación Centro de Investigación Cooperativa en Biociencias, CIC BIOGUNE	VIZCAYA
Cisneros Herreros, José Miguel	31	23	12	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
de los Santos Gil, Ignacio	5	4	3	Servicio Madrileño de Salud	MADRID
Dobaño Lázaro, Carlota	21	14	12	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	BARCELONA
Esteban Moreno, Jaime	28	15	2	Fundación Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Estrada Pérez, Vicente	1	1	1	Servicio Madrileño de Salud	MADRID
Fariñas Álvarez, María del Carmen	31	17	5	Instituto de Investigación Marques de Valdecilla	CANTABRIA
Gabaldón Estevan, Juan Antonio	9	8	2	Fundación privada Instituto de Recerca Biomédica (IRB-Barcelona)	BARCELONA
García García, Federico	20	16	9	Fundación Pública Andaluza para la Investigación Biosanitaria de Andalucía Oriental – Alejandro Otero (FIBAO)	GRANADA
Gascón Brustenga, Joaquim	11	9	6	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	BARCELONA
Gómez Rodríguez, Carmen Elena	6	5	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
González López, Juan José	26	15	8	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Gutiérrez Rodero, Félix	8	5	3	Fundación para la Investigación Sanitaria y Biomédica de la Comunidad Valenciana (FISABIO)	ALICANTE
Horcajada Gallego, Juan Pablo	25	19	4	Consorci Mar Parc Salut de Barcelona	BARCELONA
Jarrín Vera, Inmaculada	13	10	8	Instituto de Salud Carlos III	MADRID
Llor Vila, Carles	4	1	0	IDIAP Jordi Gol	BARCELONA
Lorenzo Morales, Jacob	24	19	3	Universidad de La Laguna	SANTA CRUZ DE TENERIFE

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Macías Sánchez, Juan	7	5	2	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Martínez Picado, Javier	22	17	7	Fundación Instituto de Investigacion Germans Trias i Pujol	BARCELONA
Mellado Terrado, Emilia	9	7	3	Instituto de Salud Carlos III	MADRID
Miro Meda, José María	47	32	18	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Molina Romero, Israela	25	20	10	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Moreno Guillén, Santiago	17	10	6	Servicio Madrileño de Salud	MADRID
Moreno Nuncio, Francisco Javier	5	1	1	Instituto de Salud Carlos III	MADRID
Navarro Gómez, María Luisa	19	8	1	Servicio Madrileño de Salud	MADRID
Oliver Palomo, Antonio	24	14	5	Fundación Instituto de Investigación Sanitaria Illes Baleares (IdISBa)	ILLES BALEARS
Oteo Iglesias, Jesús	13	8	4	Instituto de Salud Carlos III	MADRID
Pardo Jimeno, Julián	10	6	3	Fundación Instituto de Investigación Sanitaria Aragón	ZARAGOZA
Peraire Forner, José Joaquín	10	8	4	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA
Pérez Molina, José Antonio	8	7	7	Servicio Madrileño de Salud	MADRID
Resino García, Salvador	32	23	17	Instituto de Salud Carlos III	MADRID
Rivero Román, Antonio	21	13	4	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Rodríguez Baño, Jesús	34	23	13	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Sánchez-Seco Fariñas, María Paz	10	8	5	Instituto de Salud Carlos III	MADRID
Tamayo Gómez, Eduardo	11	10	5	Hospital Clínico Universitario de Valladolid	VALLADOLID
Torre Cisneros, Julián Carlos	14	9	5	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Vila Estape, Jordi	31	21	7	Fundación Privada Instituto de Salud Global Barcelona (ISGlobal)	BARCELONA

Clinical Guidelines and Consensus Documents 2023

- Clustering of autochthonous dengue cases in Ibiza.
- Antimicrobial stewardship in hospitals: Expert recommendation guidance document for activities in specific populations, syndromes and other aspects (PROA-2) from SEIMC, SEFH, SEMPSPGS, SEMICYUC and SEIP.
- Neglected Tropical Diseases Bulletin Chapter 3: Rabies.
- Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance.
- Consensus document for the management of schistosomiasis in Primary Care.
- Document on Management of liver disease in people living with HIV.
- ECDC Surveillance Report: Increase in Escherichia coli isolates carrying blaNDM-5 in the European Union/European Economic Area, 2012–2022.
- European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults.
- Executive summary of the consensus document of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) on the diagnosis and antimicrobial treatment of infections due to carbapenem-resistant Gram-negative bacteria.
- Executive summary. Diagnosis, treatment and prophylaxis of influenza virus infection. Consensus statement of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), the Spanish Society of Paediatric Infectious Diseases (SEIP), the Spanish Association of Vaccinology (AEV), the Spanish Society of Family and Community Medicine (SEMFYC) and the Spanish Society of Preventive Medicine, Public Health and Health Management (SEMPSPGS).
- Lassa fever in Nigeria, January-April 2023.
- Guidelines for clinical management of vectorborne diseases. National plan for prevention, surveillance and control of vector-borne diseases. Ministry of Health.
- Guide of recommendations for the prevention of Malaria in international travelers 2023.
- Identification of the Aedes aegypti mosquito in Gran Canaria.
- Identification of Aedes aegypti mosquito in Santa Cruz de Tenerife.
- Osteoarticular infections: septic arthritis, osteomyelitis and spondylodisciti.
- Management of liver disease in people living with HIV.
- National plan for prevention, surveillance and control of vector-borne diseases.
- Recommendations of the Spanish Antibiogram Committee (COESANT) for the preparation of Cumulative Antibiotic Sensitivity Reports.
- Recommendations on pre-exposure prophylaxis for the prevention of HIV infection in Spain.
- Recommendations for the integral diagnosis of chronic viral hepatitis in a single analytical extraction.
- Bacterial resistance in pediatrics.
- Revisiting the personal protective equipment components of transmission-based precautions for the prevention of COVID-19 and other respiratory virus infections in healthcare.
- Risk of the appearance of new autochthonous cases of Aedes-transmitted diseases in Spain.
- Spanish Antibiogram Committee (COESANT) recommendations for cumulative antibiogram reports.
- Spanish Association of Paediatrics Update on the diagnosis and treatment of tuberculosis.
- Pediatric tuberculosis and congenital tuberculosis.
- Update of European Society of Clinical Microbiology and Infectious Diseases coronavirus disease 2019 guidelines: diagnostic testing for severe acute respiratory syndrome coronavirus 2.
- Update of the consensus document on the aetiology, diagnosis and treatment of acute otitis media and sinusitis.

NEURODEGENERATIVE DISEASES

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Adolfo López de Munain Arregui

Dear Colleagues,

After three hard years of pandemic, we can say that 2023 has been a year of transition back to normality. From an economic management point of view and within the budget freeze we have had for years, we have concluded the year with an acceptable rate of implementation, which we hope will serve to justify a request for an increase in the CIBERNED budget in future years.

From a scientific point of view, our Annual Forum with the CIEN Foundation and the Queen Sofia Foundation was successfully held in Malaga. We have taken good note of the logistical problems and for the next forum we will all be staying in the same hotel, which will greatly facilitate networking. Otherwise, the balance of the year shows a certain flattening in the curve of scientific production, possibly as a delayed effect of the previous years which were far from normal.

At the end of 2023, the CIBER Strategic Plan was published. This plan sets the general framework to which the strategic plans of the areas must be adapted in the form of a 2024-2027 strategic plan, the bases of which we will seek to elaborate in aa extraordinary and expanded Steering Committee meeting, to be held in Miraflores de la Sierra, next March. I encourage you to send your suggestions and concerns regarding the future of CIBERNED in the coming years to the Area Coordinators.

We welcome José Luis Labandeira to the Steering Committee, who replaced Rafael Fernández-Chacón after the latter took over the direction of IBIS in Seville. Thanks to both of them for their collaboration and congratulations to Rafa for his new responsibilities, which we have no doubt he will execute with the same level of success and expertise to which we are accustomed.

At this moment we are closing the programming of the CIBERNED meeting that this year will be held coinciding with the World Parkinson's Disease Day in Bilbao, on April 10-12. I encourage you to complete the registrations as soon as possible both for those who attend as part of each group's quota as well as for those members who wish to attend with other funds.

In May 2024 a meeting of young CIBERNED researchers will be held in Vigo where discussions will be held on the future of which they will undoubtedly be the protagonists.

In 2024 the first CIBER congress will be held in Valencia at the end of November 2024, which will be a magnificent opportunity to learn in detail about the activity of other areas with which we will be able to interact in the form of joint projects.

After the relative failure of the first call of the ARISTOS program in 2023, a new opportunity opens up for the groups to recruit talent through this initiative, co-financed by CIBER, which can attract researchers who can ensure and strengthen the scientific excellence and continuity of the groups.

We say goodbye in 2023 to several researchers in the area such as Ana Pérez-Castillo to whom we thank for her dedication over so many years and to whom we wish a happy retirement. The doors of CIBERNED and its meetings will always remain open to Ana and those who have worked closely with her. I would like to end by congratulating all the CIBERNED researchers who received awards and distinctions from different organizations during the past year and who contribute to making the work of the center more visible. I hope that 2024 will be full of new successes, good luck to all of you and see you in Bilbao!

PROGRAMS & PLATFORMS

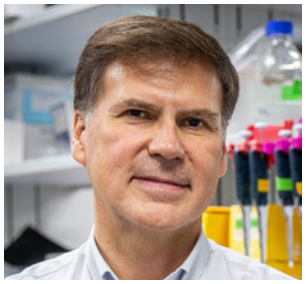
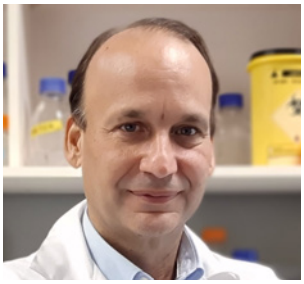
ALZHEIMER'S DISEASE AND OTHER DEGENERATIVE DEMENTIAS

Eva Carro Díaz y Alberto Lleó Bisa / COORDINATORS

In 2023, the important scientific work carried out by this program has continued, highlighting advances in the field of fluid and imaging biomarkers, genetic studies, as well as the search for new therapeutic targets. Precisely these aspects have been discussed at the International Congress on Neurodegenerative Diseases, which took place at the Auditorium in Malaga to coincide with World Alzheimer's Day, chaired by Queen Sofia and organized together with the Queen Sofia Foundation, CIBERNED and CIEN Foundation. During the celebration of this congress worth mentioning was the Keynote Lecture given by Prof. Jean-Charles Lambert based on a better understanding of the genetic architecture of Alzheimer's disease and the lecture by Prof. Nick Ashton on fluid biomarkers. In fact, several papers, in collaboration with international groups, on biomarkers for the diagnosis of dementia have been published in the last year in prestigious journals such as Nature Communications, Neurology or Alzheimer's and Dementia, which gives an idea of the special relevance of this line of research.

Also noteworthy is the incorporation of Dr. Tomás Sobrino's research group of the Galician Health Service to the Alzheimer's and other dementias program, contributing to enhance the lines of research that structure the program.

PARKINSON'S DISEASE AND OTHER NEURODEGENERATIVE MOVEMENT DISORDERS

José Luis Labandeira García, José Javier Lucas Lozano y Pablo Mir Rivera / COORDINATORS

The most relevant results and milestones of the program during 2023 have resulted in high impact publications and patents, and in the participation and promotion of clinical trials. Among the numerous publications we can only briefly comment on a few of them. Several studies have explored the hypothesis of excessive neuromelanin accumulation as a factor in the progression of Parkinson's disease (PD). Using rodents (Gonzalez-Sepulveda et al.) and non-human primates (Chocarro et al.), it was shown that neuromelanin accumulation can induce α-synuclein aggregation, suggesting future neuromelanin modulation therapies. Also in the field of new therapeutic strategies, Blesa et al. explored the use of low intensity focused ultrasound (LIFU) to induce focal openings of the blood-brain barrier to allow access to new therapies such as viral vectors for gene therapies. To better understand the relationships between peripheral disease and PD, Muñoz-Delgado et al. studied the immune response to peripheral inflammation and its relationship to PD in cohorts of patients. Focusing on the metabolic syndrome, associated with chronic peripheral inflammation, Pedrosa et al. identified in animal models and PD patients the generation of autoantibodies against angiotensin receptors as a possible link between peripheral inflammation and PD. Other groups in the program studied mitochondrial mechanisms involved in neurodegeneration (Jiménez-Gómez et al.), neuronal differentiation and neurogenesis (Domingo-Muelas et al.). In the field of Huntington's disease (HD), important contributions were made in the clarification of mechanisms involved in its pathophysiology, such as the reduction of the transcription factor Foxp2 in the thalamus (Rodríguez-Urgellés et al.). Other studies have identified biomarkers in HD such as laminin B1, which could pave the way for early neuroprotective therapies (Garcia-Forn et al.).

- Gonzalez-Sepulveda M, Compte J, Cuadros T, Nicolau A, Guillard-Sirieix C, Peñuelas N, Lorente-Picon M, Parent A, Romero-Giménez J, Cladera-Sastre JM, Laguna A, Vila M. Brain. PMID: 36717986.
- Chocarro J, Rico AJ, Ariznabarreta G, Roda E, Honrubia A, Collantes M, Peñuelas I, Vázquez A, Rodríguez-Pérez AI, Labandeira-García JL, Vila M, Lanciego JL. Brain. PMID: 37769648.
- Blesa J, Pineda-Pardo JA, Inoue KI, Gasca-Salas C, Balzano T, Del Rey NL, Reinares-Sebastián A, Esteban-García N, Rodríguez-Rojas R, Márquez R, Ciorraga M, Del Álamo M, García-Cañamaque L, Ruiz de Aguiar S, Rachmilevitch I, Trigo-Damas I, Takada M, Obeso JA. Sci Adv. PMID: 37075119.
- Muñoz-Delgado L, Labrador-Espinosa MÁ, Macías-García D, Jesús S, Benítez Zamora B, Fernández-Rodríguez P, Adarmes-Gómez AD, Reina Castillo MI, Castro-Labrador S, Silva-Rodríguez J, Carrillo F, García Solís D, Grothe MJ, Mir P. Mov Disord. PMID: 36912400.
- Pedrosa MA, Labandeira CM, Valenzuela R, Quijano A, Sanchez-Andrade M, Suarez-Quintanilla JA, Lanciego JL, Labandeira-Garcia JL, Rodriguez-Perez AI. Brain Behav Immun. PMID: 36535607.
- Jiménez-Gómez B, Ortega-Sáenz P, Gao L, González-Rodríguez P, García-Flores P, Chandel N, López-Barneo J. Nat Commun. PMID: 36859533.
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rez-Villalba A, Álvarez-Varela A, Barriga FM, Gil-Sanz C, Ortega F, Batlle E, Fariñas I. Nat Commun. PMID: 36690670.

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ALS AND OTHER NEUROMUSCULAR DISORDERS

Rafael Fernández-Chacón y Carmen Paradas López / COORDINATORS

Dr. Navarro's group has shown that gene therapy to over-express klotho and new drugs with bimodal action on Kv and TSPO improve progression in preclinical models of ALS. They have studied the role of various cytokines in the inflammatory response to spinal cord injury and have developed new decellularized grafts to repair severe nerve injury.

Dr. Paradas' group has focused on the characterization of the myogenic process and motoneuron-myofiber interaction in ALS. They have developed computerized muscle image analysis as a biomarker in ALS and have participated in several ALS clinical trials. Of note is the description of a new muscular dystrophy due to mutations in MAMDC2.

Dr. López de Munain's group has participated and promoted clinical trials in ALS and in facioscapulohumeral dystrophy type 1 and 2. They have described a new phenotype of muscular dystrophy associated with the SNUP gene. They are analyzing the potential of ahulkenoids in diseases associated with mutations in RYR1 and RYR in Myotonic Dystrophy type 1, and the findings have been partially transferred to MIRAMOON Pharma.

Dr. Osta's group has studied mitochondrial aconitase (Aco2) in patients proving that Aco2 activity can be used as a biomarker to improve disease prognosis. In collaboration with Dr. Naranjo's group, they have demonstrated that modulation of the ATF6-DREAM interaction with repaglinide induces neuroprotection in the animal model of ALS, SOD1G93A.

Dr. Fernández-Chacón's group studies the mechanisms of Kufs disease (CLN4) or adult autosomal dominant neuronal ceroid lipofuscinosis. The absence of the CSPalpha/DNAJC5 protein does not induce lipofuscinosis, but mutations in the DNAJC5 gene confer an abnormal function of the protein which, by cell autonomous mechanisms, causes neuronal pathology and triggers the phagocytic activity of mycroglia.

Dr. Martinez's group has shown that CK1 and TTBK1 inhibitors are able to restore TDP-43 homeostasis in lymphoblasts from Alzheimer's patients and to prevent cell-to-cell transmission of the disease. Functional characterization of lymphoblasts from patients with familial ALS (TBK1 mutation). They are developing new drugs and have shown that SGK1 inhibitors are neuroprotective agents.

Dr. Acevedo's group has generated and characterized new humanized models of TDP-43 and knock-in mice that model different aspects of human disease, identifying new functions for TDP-43, such as its role in the development of the nervous system or in the maintenance of interneurons in the cerebral cortex. They continue to identify mutations in ALS patients in this region.

Dr. Infante's group is studying the role of fibroblasts and circulating microvesicles in preclinical models of ALS. They have identified FOXO1 as a transcription factor in skeletal muscle dysfunction in ALS. They are studying cohorts of LRRK2 mutation carriers to identify biomarkers of premotor stages of Parkinson's disease, SCA3 patients (ESMI consortium) and Friedreich's ataxia patients for the development of a gene therapy trial.

NEUROINFLAMMATION AND NEURODEGENERATION

Manuel Comabella López / COORDINATOR

As a result of the incorporation of new groups in January, the Steering Committee decided, during the second half of the year, to establish a new research program focused on neuroinflammation in neurodegenerative pathologies, incorporating three new groups with extensive experience in multiple sclerosis.

Multiple sclerosis and other demyelinating diseases are the paradigm of autoimmune diseases, where neuroinflammation is the fundamental pathological feature. The relationship between neuroinflammation and neurodegeneration goes far beyond this group of diseases and permeates almost all neurodegenerative diseases, so that this phenomenon is present in almost all of them and constitutes a target of growing interest for the design of neuroprotective or neuro-restorative therapeutic approaches and the object of study of this transversal program of CIBERNED.

The main lines of research in this new program are the following:

- Clinical, genetic, immunological and molecular characterization of patients with inflammatory-based CNS diseases.
- Development of animal models of neuroinflammation and analysis of their relationships with neurodegeneration and brain proteinopathies.
- Study of the relationship between immunosenescence and the development of central or peripheral neurodegeneration.
- Study of environmental factors (climate, diet, lifestyle, toxic exposure, microbiota, etc.) potentially related to neuroinflammation and the development of neurodegeneration.
- Development of new therapeutic strategies to combat neuroinflammation, neurodegeneration and immunosenescence.

TRAINING PROGRAM

Teresa Iglesias Vacas / COORDINATOR

Among the most important activities of the CIBERNED Training Program throughout the year 2023 are the annual Scientific Forum, the virtual Scientific Sessions "CIBERNED Webinar Series", and the Training and Mobility Grants Plan.

The 17th Scientific Forum was held in Malaga from September 19 to 22. On September 21, World Alzheimer's Day, the official inauguration of the event took place, presided over by H.M. Queen Sofia, and included a keynote lecture by Dr. Jean-Charles Lambert, Director of Research at Inserm and the National Institute for Research in Health and Medicine in France, a world-renowned specialist in this disease.

The organization has been coordinated together with the CIEN Foundation, under the "International Congress on Neurodegenerative Diseases". The program, of high quality, has included lectures by renowned national and international research personnel, as well as from our area and some other research areas, and the participation of associations and the valuable testimony of a patient. During the event, the Young Researcher and Young Clinical Researcher Awards were presented to Dr. Estrella Fernández de Sevilla and Dr. María Carmona Iragui, respectively, who presented their excellent publications for which they have been awarded this prize in a dedicated session. A special "Flash Talks" session was also held by the young re-

search staff of a selection of the best posters from the different programs.

Throughout 2023, a total of seventeen Webinars were broadcast openly every two weeks, and certificates of attendance were awarded to predoctoral students as a valid scientific activity in their different Doctoral Programs. Research group leaders (6), predoctoral and postdoctoral researchers (11) from the different programs have participated as speakers. Most of the lectures have the express consent of the speaker and are available openly on the YouTube channel through the CIBER web page.

On June 22, 2023, an online roundtable seminar was held on "Scientific Controversies surrounding Lecanemab", following the FDA approval of this drug for the treatment of Alzheimer's disease. This session, with more than one hundred attendees, moderated by our Deputy Scientific Director, Miguel Medina, was attended by Alberto Lleó and Mercé Boada, who lead their groups at CIBERNED, and Pablo Martínez Lage from the CITA-Alzheimer Foundation. Clinical trials and future expectations in clinical practice were discussed.

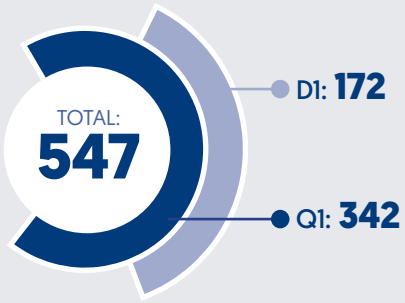
The commemorative scientific event "Celebrating the Year of Cajal", held on March 9, 2023 in Bilbao, has also received support, which was streamed and recorded, and has achieved numerous views on social networks.

The Training and Mobility Grants plan has financed the attendance to some international courses and seven stays, most of them in foreign centers of excellence, which have been enormously useful for the projects being developed by the recipients.

SCIENTIFIC PRODUCTION

PUBLICATIONS

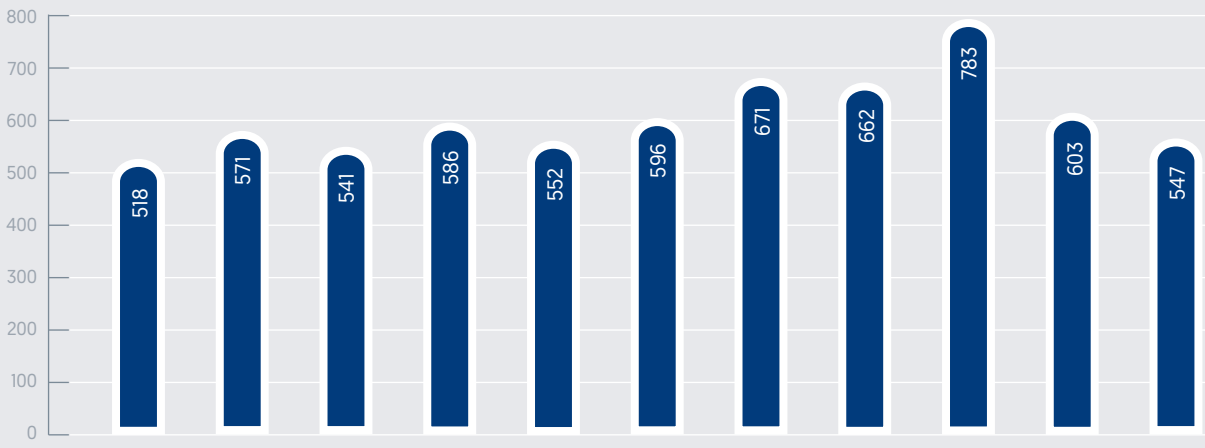
No. of publications in 2023



Collaborations

*Among various thematic areas

Evolution of publications



10 most relevant publications by impact factor

IF	PUBLICATION
64,8	A cross-species proteomic map reveals neoteny of human synapse development. Nature 2023: 622 (7981), 112-119
64,8	Senescence atlas reveals an aged-like inflamed niche that blunts muscle regeneration. Nature 2023: 613 (7942), 169-178
64,8	Protracted neuronal recruitment in the temporal lobes of young children. Nature Epub 2023 Dec 20
34,7	(New neurons) singing in the avian brain. Nat Rev Neurosci 2023: 24 (6), 333
30,8	Molecular basis for maternal inheritance of human mitochondrial DNA. Nat Gene 2023: 55 (19), 1632-1639
20,8	Fatty acids fuelling astroglia and beyond. Nat Metab 2023: 5 (8), 1253-1254
16,6	Control of a hippocampal recurrent excitatory circuit by cannabinoid receptor-interacting protein Gap43. Nat Commun 2023: 14 (1), 2303
16,6	Author Correction: Common variants in Alzheimer's disease and risk stratification by polygenic risk scores (Nature Communications, (2021), 12, 1, (3417), 10.1038/s41467-021-22491-8). Nat Commun 2023: 14 (1), 716
16,6	Transgenic NADH dehydrogenase restores oxygen regulation of breathing in mitochondrial complex I-deficient mice. Nat Commun 2023: 14 (1), 1172
16,6	Post-transcriptional control of a stemness signature by RNA-binding protein MEX3A regulates murine adult neurogenesis. Nat Commun 2023: 14 (1), 373

CIBERNED Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Acevedo Arozena, Abraham	1	1	0	Fundación Canaria Instituto de Investigación Sanitaria de Canarias	SANTA CRUZ DE TENERIFE
Alberch Vie, Jordi	15	11	5	Universidad de Barcelona	BARCELONA
Boada Rovira, Mercè	34	22	18	Fundació ACE, Institut Català de Neurociències Aplicades	BARCELONA
Bullido Gómez-Heras, Mª Jesús	4	3	2	Universidad Autónoma de Madrid	MADRID
Calero Lara, Miguel	32	11	4	Instituto de Salud Carlos III	MADRID
Camins Espuny, Antonio	23	17	6	Universidad de Barcelona	BARCELONA
Cantero Lorente, José Luis	6	5	1	Universidad Pablo de Olavide	SEVILLA
Carro Díaz, Eva	42	14	2	Instituto de Salud Carlos III	MADRID
Ceña Callejo, Valentín	4	3	0	Universidad de Castilla la Mancha	ALBACETE

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Comella Carnice, Joan Xavier	4	4	0	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Cuadrado Pastor, Antonio	15	13	6	Universidad Autónoma de Madrid	MADRID
De Felipe Oroquieta, Javier	3	1	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Del Río Fernández, J. Antonio	15	11	1	Fundación Instituto de Bioingeniería de Cataluña	BARCELONA
Fariñas Gómez, Isabel	2	2	0	Universidad de Valencia	VALENCIA
Fernández Chacón, Rafael	1	0	0	Universidad de Sevilla	SEVILLA
Fernández Ruiz, Javier	7	5	3	Universidad Complutense de Madrid	MADRID
Franco Fernández, Rafael	31	22	4	Universidad de Barcelona	BARCELONA
Fuentes Rodríguez, José Manuel	12	4	2	Fundación para la Formacion y la Investigación de los Profesionales de la Salud (FUNDESALUD)	CACERES
García Verdugo, José Manuel	10	6	4	Universidad de Valencia	VALENCIA
Gutiérrez Pérez, Antonia	14	12	2	Universidad de Málaga	MÁLAGA
Guzmán Pastor, Manuel	3	3	1	Universidad Complutense de Madrid	MADRID
Iglesias Vacas, Teresa	2	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Infante Ceberio, Jon	43	28	16	Instituto de Investigación Marques de Valdecilla	CANTABRIA
Kulisevsky Bojarski, Jaime	35	10	8	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Labandeira García, José Luis	11	7	4	Universidad de Santiago de Compostela	CORUÑA, A
Lanciego Pérez, José Luis	5	2	2	Fundación para la Investigación Médica Aplicada	NAVARRA
Lleó Bisa, Alberto	52	35	27	Instituto de Investigación del Hospital de la Santa Cruz y San Pablo	BARCELONA
Llorens Martí, María	17	8	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
López Barneo, José	9	5	3	Universidad de Sevilla	SEVILLA
López de Munain Arregui, Adolfo	39	23	8	Asociación Instituto Biodonostia	GUIPÚZCOA
Lucas Lozano, José Javier	1	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Martí Domenech, Mª Jose	56	28	22	Hospital Clínico y Provincial de Barcelona	BARCELONA
Martínez Gil, Ana	15	10	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Matute Almau, Carlos	16	13	4	Universidad del País Vasco	VIZCAYA
Mir Rivera, Pablo	25	14	9	Universidad de Sevilla	SEVILLA
Moratalla Villalba, Rosario	2	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Naranjo Orovio, José Ramón	6	5	3	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Navarro Acebes, Xavier	29	13	4	Universidad Autónoma de Barcelona	BARCELONA
Obeso Inchausti, José Ángel	23	15	11	Fundación HM Hospitales Madrid	MADRID
Osta Pinzolas, Rosario	6	5	2	Fundación Instituto de Investigación Sanitaria Aragón	ZARAGOZA
Paradas López, Carmen	7	7	3	Universidad de Sevilla	SEVILLA
Pérez Tur, Jordi	7	6	4	Agencia Estatal Consejo Superior de Investigaciones Científicas	VALENCIA
Rodríguez Álvarez, José	6	4	1	Universidad Autónoma de Barcelona	BARCELONA
Rodríguez Díaz, Manuel	1	1	0	Universidad de La Laguna	SANTA CRUZ DE TENERIFE
Sáez Valero, Javier	4	3	1	Universidad Miguel Hernández	ALICANTE
Soriano García, Eduardo	7	2	0	Universidad de Barcelona	BARCELONA
Torres Alemán, Ignacio	5	4	1	Achucarro Basque Center for Neuroscience	VIZCAYA
Trullàs Oliva, Ramón	17	11	6	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Vicario Abejón, Carlos	3	2	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID
Vila Bover, Miquel	11	6	3	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Vitorica Ferrández, Fco. Javier	4	4	1	Universidad de Sevilla	SEVILLA
Wandosell Jurado, Francisco	3	1	0	Agencia Estatal Consejo Superior de Investigaciones Científicas	MADRID

Clinical Guidelines and Consensus Documents 2023

- Post-covid. Multidisciplinary approach to the disease. Chap 8. Post-covid neurology.
- Lessons learned from a sporadic FUSopathy in a young man: a case report.
- New digital guide to parkinson's disease for nursing professionals.
- Emergencies in movement disorders.
- Dopamine agonist therapy in Parkinson's disease: Spanish expert consensus on its use in different clinical situations.
- Confusion of Evidence-Based Reviews and Guidelines.
- Recommendations for the approach of genetic studies in movement disorders, ataxias and paraparesis. Chapter 8: Genetic studies in ataxias.
- National guidelines for the management of ALS.

PHYSIOPATHOLOGY OF OBESITY AND NUTRITION

ciber | OBN

WELCOME FROM THE SCIENTIFIC DIRECTOR

María Puy Portillo Baquedano

In 2023 two new groups have joined CIBEROBN, the group led by Dr. Jonatan Ruiz, from the University of Granada, which develops its activity in the field of physical activity, and the group led by Dr. José María Ordovás, from IMDEA Alimentación, which works in the field of big data and artificial intelligence applied to obesity and nutrition. The aim of incorporating these two new groups was to cover two research areas that are considered to be indispensable and strategic in our CIBER area.

We have attracted significant resources through international and national projects led by CIBERobn researchers. Special mention should be made of the European EprObes project, which not only has the participation of CIBERobn researchers, but is coordinated from this area. This project, which is endowed with 10 million euros, will study how to prevent obesity throughout life, through the early identification of biomarkers, risk factors, prognostic factors and intervention at early stages. Artificial intelligence methodologies will be used for this purpose.

It should be noted that one of the major projects in this area, PREDIMED Plus, which completed its intervention phase at the end of 2022, has carried out its last year of follow-up of the cohort without intervention in 2023. This project has resulted in numerous publications, including the publication in JAMA Network Open on the effect of interventions on body composition.

The scientific production data are very positive, not only because of the number of articles published, but also in terms of their quality. Thus, we have publications in first decile journals, with high impact indexes, which are leading journals in the field, such as The Lancet (IF 168.9), Nature (IF 64.8), The Lancet Diabetes & Endocrinology (IF 44.5), Lancet Gastroenterology & Hepatology (IF 35.7).

In addition, at CIBERobn we have participated in the elaboration of numerous national and international guidelines, including the International Clinical Guidelines of the European Society of Hypertension. The members of this area have been very active in the participation and creation of Research networks.

It should also be noted that some CIBERobn researchers have received prestigious awards, such as the Gregorio Marañón Award and the International Hippocrates Award.

Furthermore, in 2023 we have continued to intensify collaborations with other CIBER areas, through the creation of calls for inter-area research projects, participation in the annual scientific conferences of other areas, the preparation of joint webinars and participation in joint events organized by CIBER. In addition, numerous collaborations have been established between our research groups and those of other areas, some of which have been reflected in the obtaining of funding in national and international calls for projects.

All of the above reflects the interest in working cooperatively in order to carry out ambitious research with a high scientific and social impact.

PROGRAMS & PLATFORMS

NUTRITION

Jordi Salas-Salvadó / COORDINATOR

The Nutrition program is one of the two CIBEROBN programs (Obesity and Nutrition) that includes epidemiological research in nutrition and in which important milestones have been achieved related to recruitment, follow-up and/or publication of results, as well as national and international collaborations. We highlight the advances in the follow-up and publications in the PREDIMED Plus study, a randomized controlled field trial with intensive intervention with an energy-restricted Mediterranean diet, increased physical activity and behavioral support compared to a control group to assess its effects on weight loss and reduction of cardiovascular events. At the end of 2022, the intervention of the more than 6800 randomized participants was completed and the trial is currently in the last year of follow-up of the non-intervention cohort. In PREDIMED Plus, the publication in JAMA Network Open on the effect of interventions on body composition stands out, as well as a series of high-impact publications on COVID-19 in the framework of a project of the Fundación Soria Melguizo. Also worthy of mention are the follow-up and publications of the "University of Navarra Follow-up" cohort (n=23,000), the CORDIOPREV study -a randomized controlled trial with intervention with a Mediterranean diet in secondary cardiovascular prevention-, and the multicenter cohort of children CORALS (n=1300; current median follow-up 3 years) with the aim of evaluating risk factors for obesity at 10 years. Milestones also include the advances in recruitment, follow-up and publication of results of studies initiated, many of them in collaboration with different CIBER groups or outside CIBER: PREDI-DEP (Prevention of Recurrent Depression with Mediterranean Diet), PREDIMAR (PREVENTION with Mediterranean Diet of Recurrent Arrhythmias in patients with atrial fibrillation, n=720), LifeBreast (Lifestyles and breast cancer) and the European H2020 studies "Sweeteners and sweetness enhancers: Impact on health, obesity, safety and sustainability", and PRIME "Prevention and Remediation of Insulin Multimorbidity in Europe", among others. In addition, other projects have continued, such as the EU-Project (H2020) entitled: Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing behaviors, JPI HDHL Identification and validation of integrative biomarkers of physical activity level and health in children and adolescents, JPI DEAL Metabolite markers of dietary intake, the SOPHIA Project: Stratification of Obese Phenotypes to Optimize Future Obesity Therapy, and the NIH projects within the PREDIMED study: "Mediterranean diet, metabolomics and cardiovascular disease" and "Lifestyle Interventions, metabolites, microbiome, and diabetes risk". There are also 3 projects on personalized medicine under development and, in addition, different European projects have started in 2023, among which the following are worth mentioning: (a) Combatting diet related non-communicable disease through enhanced surveillance (H2020; SEP-210824425; 2023-2025); (b) Empowering healthy lifestyle behavior through personalized intervention portfolios to prevent and control obesity during vulnerable stages of life (H2020; 101080645-2; 2023-2028); (c) a European Research Council Project to evaluate the effects of alcohol consumption according to a Mediterranean drinking pattern (UNATI trial); (d) Gut-brain-axis: Targets for improvement of cognition in the elderly - SMARTAGE (H2020-MSCA-ITN. 2020-2025; and e) the multi-collaborative CIBERobn Project Zero_HiddenHunger_EU: Tackling micronutrient malnutrition & hidden hunger to improve health in the EU (H2020-CL6- 2023-FARM2FORK-01; 2024-2027), as well as the project Peanut consumption on cognitive performance, weight management, and inflammation in young adolescents (The Peanut Institute 2023-2024).

At the same time, several national projects have been obtained from the National Research Agency and theInstituto de Salud Carlos III, some of them in collaboration between CIBEROBN researchers and researchers from

other CIBER areas, such as CIBERSAM and CIBEREHD.

The Gregorio Marañon Award and the International Hippocrates Award have also been granted to two CIBEROBN researchers, as well as other awards to women researchers.

In 2023, dozens of publications have been published in high impact international journals, among them:

- An Energy-Reduced Mediterranean Diet, Physical Activity, and Body Composition: An Interim Subgroup Analysis of the PREDIMED-Plus Randomized Clinical Trial. JAMA Netw Open. 2023; 6(10):e2337994. PMID:37851444.
- Carbohydrate quality, fecal microbiota and cardiometabolic health in older adults: a cohort study. Gut Microbes. 2023;15(2):2246185. PMID: 37610130.
- Metabolic syndrome criteria and severity and carbon dioxide (CO2) emissions in an adult population. Global Health. 2023;19(1):50. doi: 10.1186/s12992-023-00948-3. PMID: 37443076.
- Gut microbiota in nonalcoholic fatty liver disease: a PREDIMED-Plus trial sub analysis. Gut Microbes. 2023 Jan-Dec;15(1):2223339.
- Potential therapeutic implications of histidine catabolism by the gut microbiota in NAFLD patients with morbid obesity. Cell Reports Medicine 2023;4(12):101341. PMID: 38118419.

OBESITY

Fernando Fernández-Aranda / COORDINATOR

During the year 2023, the different subprograms of the Obesity Program have continued to strengthen the collaboration ties between the different groups, as well as collaborations with groups of the Nutrition Program. Actions in this sense have crystallized in leading publications both in the field of basic research, with preclinical models, and in clinical and translational work, as well as in obtaining European research resources and leadership at the international level.

Relevant International Publications: special mention should be made of the following as examples of intra- and inter-CIBER and international collaborations (26): 1st-Decile: *Sports Med.* (PMID: 37584843/IF: 9,8); *Br J Sports Med.* (PMID: 36623866/IF: 18,6); *J Am Coll Cardiol.* (PMID: 37676198/IF: 24.4); *JAMA Netw Open* (PMID: 37976057)/ IF: 13.8); *Lancet Gastroenterol Hepatol.* (PMID: 37028436/ IF: 35.7); *Nature* (PMID: 36991188/IF: 64.8); *Cell Metab.* (PMID: 37527658/IF: 29); *Nat Med.* (PMID: 37946056/IF: 82.9) ; *Lancet* (PMID: 36774932/IF: 168,9); *Nat. Commun.* (PMID: 37607954/IF: 16,6); *Sci. Adv.* (PMID: 37566655/ IF: 13,6); *BMJ* (PMID: 37813420/IF: 107.7); *Mol Psychiatry.* (PMC10914605/IF: 11); *J Intern Med.* (PMID: 36585892/ IF: 11.1); *Lancet Diabetes Endocrinol.* (PMID: 37385287/ IF: 44,5); *Lancet Diabetes Endocrinol.* (PMID: 36620967/ IF: 44,5); *Cell Metab.* (PMID: 37541251/IF: 29); *Gut.* (PMID: 35580962/IF:24,5); *BMC Med.* (PMID: 37833678/ IF:9,3); *Gut Microbes* (PMID: 37610130)/ 12,5 IF); *Gut Microbes* (PMID: 37345236/IF:12,5); *Diabetes Care*, (PMID: 36884283/IF: 16,2); *Hepatology* (PMID: 36717026/IF: 25,7); *J Am Coll Cardiol.* (PMID: 36631212/IF: 24.4).

International Projects (14) In terms of obtaining international resources, in which members of the CIBEROBN obesity program participate as PIs and/or coordinators, the following projects deserve special mention: (PRIME - H2020-Ref.847879); (Eat2beNICE - H2020-Ref. 728018). (INTEGRActiv - JPI HDHL-Ref. en ISCII: AC21_2/00033) (SOPHIA - H2020-Ref.: 875534-2); (SMARTAGE Marie Curie-H2020-Ref. 859890); (ThinkGut_Interreg-POCTE-FA-H2020_Ref.: EFA345/195); (eprObes-HorizonEurope-Ref.101080219-2); FitBack4Literacy Eramus+: Sport, Youth and EU 101089829).

National Projects (63) In terms of obtaining national resources, in which members of the CIBEROBN obesity program participate as PIs and/or coordinators, we highlight projects financed by the ISCIII-Ministry of Health; Ministry of Science, Innovation and Universities; SEIMC-GESIDA Foundation; "LA CAIXA" Foundation; National Sports Council; Andalusian Institute of Sport, Andalusian Government; Government of Navarra; Galician Government; IMDEA Foundation; AGAUR- Knowledge Industry Grants; European Funds Department, University and Culture- Balearic Islands Government.

Participation in National/International Guidelines (10), in addition to the intense scientific activity we have been involved in the preparation of the International Clinical Guidelines of the European Society of Hypertension.

Participation/creation of specific Networks (18) Several members of the subprograms participate in international associations, which allows for synergies with other groups with a high potential for research, design of cutting-edge projects in the area and dissemination in the scientific community. Highlights: Eating Disorders Research Society (EDRS); International Neuropsychological Society; European Endocrinology Society; European Association for the study of Obesity (EASO). Dissemination. We have maintained our usual activity in the organization of specific workshops and symposiums related to obesity and nutrition, within the European Society for Clinical Investigation (ESCI), European Congress on Obesity (ECO) and European Society of Endocrinology (ESE), SEEDO and SEEN.

TRAINING PROGRAM

Laura Herrero Rodríguez / COORDINATOR

During the year 2023 the CIBEROBN Training Program has continued with its main commitment to activities aimed at the youngest members of the groups. The lines of action have focused on the following areas:

MOBILITY

Four training stays of CIBEROBN members in international research groups (Italy, Portugal and Mexico) have been financed.

ANNUAL CIBEROBN SYMPOSIUM

The annual meeting of our CIBER area, entitled "Obesity and Nutrition in the 21st Century" is considered a priority element in the Training Program. Researchers Montserrat Fitó, Catalina Picó and Laura Herrero, together with Manolo Tena-Sempere as Training Program Coordinator and Leticia Álvarez as Deputy Scientific Director, were in charge of preparing the program and organizing the annual CIBEROBN Symposium on 24-25 May 2023 in Santiago de Compostela. We highlight the scientific quality of the speakers both from CIBEROBN and other CIBER areas and external speakers, the interaction between participants, the development of working meetings of the groups and of the Nutrition and Obesity programs.

ATTENDANCE AND ORGANIZATION OF COURSES AND CONGRESSES

Funding has been provided for training courses, such as the course on Animal Experimentation, for young CIBEROBN personnel. In addition, the participation of various young speakers and members of the CIBEROBN in the annual congress of the Spanish Society for the Study of Obesity (SEEDO) from 22 to 25 November in Seville was promoted and financed. Members of the CIBEROBN also participated as moderators of sessions at the congress. In fact, the pre-SEEDO course, which preceded the formal start of the congress on the afternoon of November 22, was organized jointly by SEEDO and the training area of CIBEROBN. Given the success of this initiative, which began in 2022 and which has led to synergies between SEEDO and CIBEROBN, there are plans to extend these joint activities in successive years.

SCIENTIFIC ENDORSEMENT

The Training Program has granted scientific endorsement to various activities related to Obesity and Nutrition, such as scientific guidelines and teaching at the Master's level. In all cases, the visibility of CIBEROBN has been promoted through the dissemination and publication of the activity on the CIBER website and social networks and in all the promotional material and program of activities.

DOCTORAL THESES

During the year 2023 a total of 63 doctoral theses have been completed by students from CIBEROBN groups, 29 of which have been international.

In conclusion, the CIBEROBN Training Program has sought to expand the range of activities offered to young staff of the groups as a key tool in their continuous training processes.

FATBANK PLATFORM

The milestones achieved in the FATBANK Platform during 2023 have been the following:

Introduction of 61 new cases, reaching 2,408 accumulated cases. Although some nodes still have cases pending registration in the management software.

Introduction of 1,632 samples (serum, plasma, buffy coat, stool and adipose tissue), reaching 71,019 cumulative samples available to the scientific community. Although some nodes still have samples pending registration in the management software.

Transfer of 628 samples of visceral tissue and subcutaneous tissue for different research projects.

Published articles where samples from the platform were used and where they are mentioned:

- Amin, A., Badenes, M., Tüshaus, J., de Carvalho, É., Burbridge, E., Faísca, P., ... & Adrain, C. (2023). Semaphorin 4B is an ADAM17-cleaved adipokine that inhibits adipocyte differentiation and thermogenesis. Molecular Metabolism, 73, 101731.
- Lluch, A., Latorre, J., Serena-Maione, A., Espadas, I., Caballano-Infantes, E., Moreno-Navarrete, J. M., ... & Ortega, F. J. (2023). Impaired Plakophilin-2 in obesity breaks cell cycle dynamics to breed adipocyte senescence. Nature Communications, 14(1), 5106.
- Oliveras-Cañellas, N., Castells-Nobau, A., de la Vega-Correa, L., Latorre-Luque, J., Motger-Albertí, A., Arnoriaga-Rodriguez, M., ... & Fernández-Real, J. M. (2023). Adipose tissue coregulates cognitive function. Science advances, 9(32), eadg4017.
- Marsal-Beltran, A., Rodríguez-Castellano, A., Astiarraga, B., Calvo, E., Rada, P., Madeira, A., ... & Fernández-Veledo, S. (2023). Protective effects of the succinate/SUCNR1 axis on damaged hepatocytes in NAFLD. Metabolism, 145, 155630.
- Oliveras-Cañellas, N., Moreno-Navarrete, J. M., Lorenzo, P. M., Garrido-Sánchez, L., Becerril, S., Rangel, O., ... & Fernández-Real, J. M. (2023). Downregulated adipose tissue expression of browning genes with increased environmental temperatures. The Journal of Clinical Endocrinology & Metabolism, dgad469.

The transfer of adipose tissue samples for the Potential relevance of mitochondria in adipose tissue physiology (ADIPOMT) project, funded by the CIBER (CIBEROBN), has begun in collaboration with all the nodes of the platform.

The coordinating node (Girona) has initiated an exhaustive review of the data entered in the management software by all the nodes (case data, consents, donation data, clinical data and samples).

The activity carried out in the Epigenomics platform during the year 2023, has focused on collaborative work with other CIBER and non-CIBER groups that have resulted in various publications, participation in research projects and scientific dissemination activity both in courses and national and international congresses through lectures given by invitation and interviews in the media.

Thus, during this year, the methylation pattern of a total of 1642 determinations was analyzed by methylation microarray, Next Generation Sequencing (NGS) or pyrosequencing.

The milestones achieved in the Metagenomics Platform during 2023 have been:

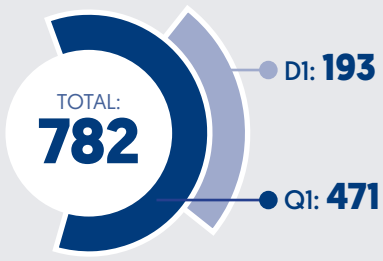
Analysis of 908 samples on the platform and management of a further 280 samples.

- Management, DNA extraction and analysis of 280 samples for the intraciber-obn project “Deciphering the impli cation of the gut microbiome in the effects of an ad li bitum Mediterranean diet compared with energy-reduced Mediterranean diet plus physical activity promotion using shotgun metagenomics sequencing”.

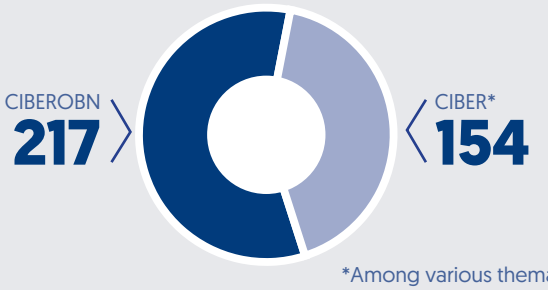
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168.9	Perdomo CM, Cohen RV, Sumithran P, Clement K, Fruhbeck G. Contemporary medical, device, and surgical therapies for obesity in adults.
82.9	Bugge A, Buntinx F, Cabrera de Leon A, Caixeta RB, Can G, et al. Global variation in diabetes diagnosis and prevalence based on fasting glucose and hemoglobin A1c.
64,8	Clarke J, Clays E, Cohen E, Compan-Gabucio L, Concin H, et al. Diminishing benefits of urban living for children and adolescents' growth and development.
64,8	Pairo-Castineira E, Rawlik K, Bretherick AD, Qi T, Wu Y, et al. GWAS and meta-analysis identifies 49 genetic variants underlying critical COVID-19.
44,5	Canton APM, Tinano FR, Guasti L, Montenegro LR, Ryan F, et al. Rare variants in the MECP2 gene in girls with central precocious puberty: a translational cohort study.
44,5	Argente J, Dunkel L, Kaiser UB, Latronico AC, Lomniczi A, et al. Molecular basis of normal and pathological puberty: from basic mechanisms to clinical implications.
40,5	Valenti L, Corradini E, Adams LA, Aigner E, Alqahtani S, et al. Consensus Statement on the definition and classification of metabolic hyperferritinaemia.
39,89	Gearhardt AN, Bueno NB, DiFeliceantonio AG, Roberto CA, Jiménez-Murcia S, et al. Social, clinical, and policy implications of ultra-processed food addiction.
37,8	Canfrán-Duque A, Rotllan N, Zhang X, Andrés-Blasco I, Thompson BM, et al. Macrophage-Derived 25-Hydroxycholesterol Promotes Vascular Inflammation, Atherogenesis, and Lesion Remodeling.
37,8	Gaba P, O'Donoghue ML, Park JG, Wiviott SD, Atar D, et al. Association between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIER-OLE.

CIBEROBN Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Argente Oliver, Jesús	26	13	5	Servicio Madrileño de Salud	MADRID
Baños Rivera, Rosa María	28	13	4	Universidad de Valencia	VALENCIA
Corella Piquer, Dolores	42	29	16	Universidad de Valencia	VALENCIA
Diéguez González, Carlos	23	17	14	Universidad de Santiago de Compostela	CORUÑA, A
Estruch Riba, Ramón	53	32	17	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Fernández Aranda, Fernando	58	37	14	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Fernández-Real Lemos, Jose Manuel	25	17	13	Fundación Instituto de Investigacion Biomédica de Girona, Dr. Josep Trueta	GIRONA

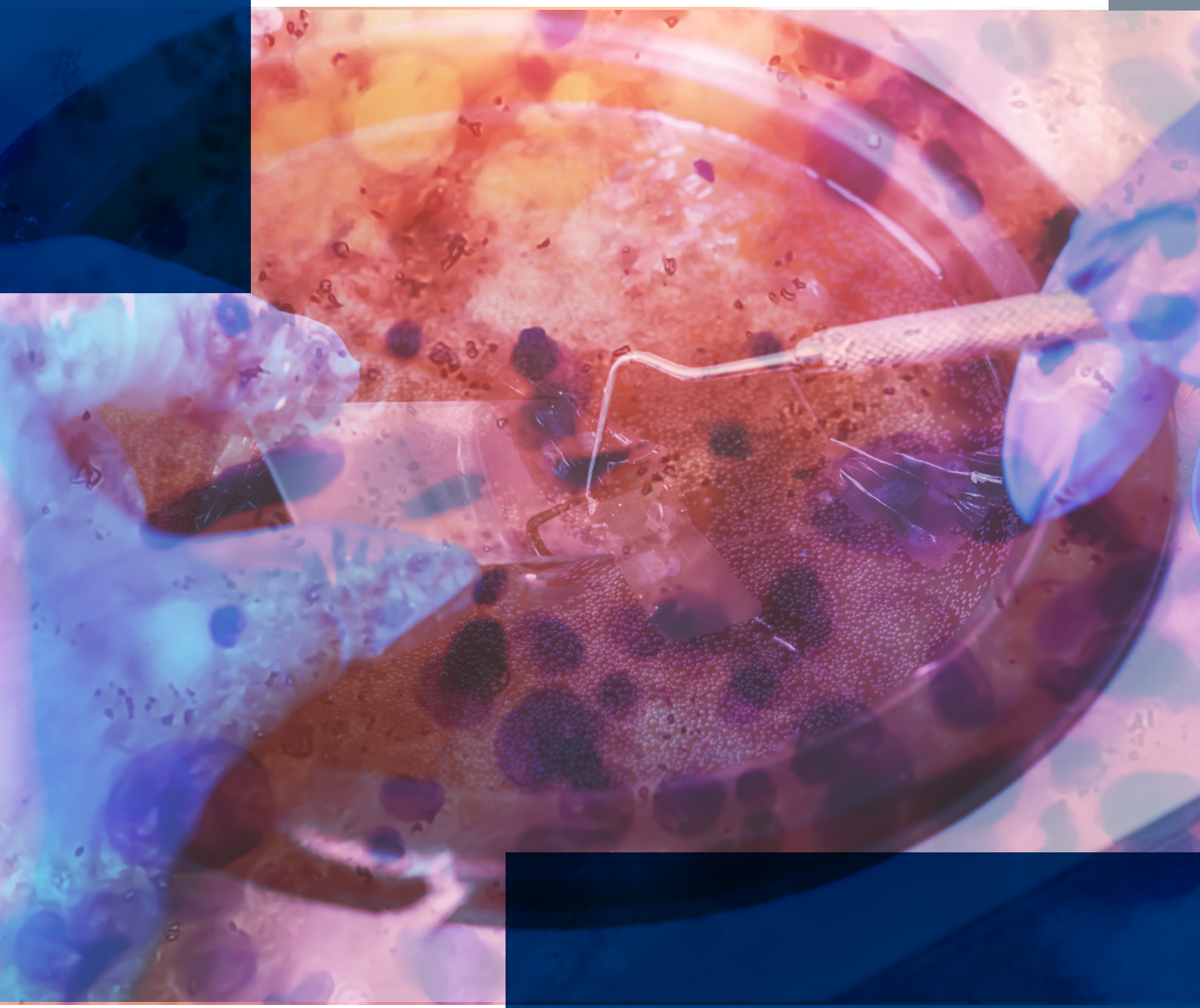
GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Fitó Colomer, Montserrat	62	46	19	Consorci Mar Parc Salut de Barcelona	BARCELONA
Frühbeck Martínez, Gema	33	21	8	Universidad de Navarra	NAVARRA
Gil Campos, María Mercedes	25	16	3	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Herrero Rodríguez, Laura	18	14	5	Universidad de Barcelona	BARCELONA
Lamuela-Raventos, Rosa María	37	28	17	Universidad de Barcelona	BARCELONA
López Miranda, José	36	21	11	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA
Lurbe Ferrer, Empar	19	7	2	Consorcio Hospital General Universitario Valencia	VALENCIA
Martínez González, Miguel Angel	92	52	19	Universidad de Navarra	NAVARRA
Moreno Aliaga, María Jesus	46	35	11	Universidad de Navarra	NAVARRA
Moreno Aznar, Luis Alberto	43	16	6	Fundación Instituto de Investigación Sanitaria Aragón	ZARAGOZA
Ordovás Muñoz, José María	36	28	12	Fundación Imdea Alimentación	MADRID
Ortega Martínez de Victoria, Emilio	57	32	15	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Osada García, Jesús de la	14	10	1	Universidad de Zaragoza	ZARAGOZA
Pico Segura, Catalina	13	9	2	Universidad de las Islas Baleares	ILLES BALEARS
Pintó Sala, Xavier	28	17	7	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Portillo Baquedano, María del Puy	11	8	3	Universidad del País Vasco	ÁLAVA
Romaguera Bosch, María Adoración	50	32	13	Fundación Instituto de Investigación Sanitaria Illes Baleares (IdISBa)	ILLES BALEARS
Ruiz Ruiz, Jonatan	51	28	9	Universidad de Granada	GRANADA
Salas Salvadó, Jordi	85	57	24	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA
Santos Lozano, José Manuel	22	14	7	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Seoane Camino, Luisa María	22	10	5	Servicio Gallego de Salud	CORUÑA, A
Serra Majem, Lluis	52	28	9	Universidad de las Palmas de Gran Canaria	LAS PALMAS
Tena Sempere, Manuel	32	24	12	Universidad de Córdoba	CÓRDOBA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Tinahones Madueño, Francisco	68	49	21	Fundación Pública Andaluza para la Investigacion de Málaga en Biomedicina y Salud (FIMABIS)	MÁLAGA
Tur Mari, Josep Antoni	81	53	20	Universidad de las Islas Baleares	ILLES BALEARS
Villarroya Gombau, Francesc	15	13	4	Universidad de Barcelona	BARCELONA

Clinical Guidelines and Consensus Documents 2023

- Multi-omics analysis in precision health: a practical guide for its performance and application.
- Guideline for the measurement of olfactory perception and analysis of its association with pathologies.
- A Comprehensive Guide to the Computation, Interpretation, and Applications of the Novel Biomarkers of Biological Aging for Precision Medicine.
- Nutritional genomics and biological sex.
- Advances in autophagy and computation applied to omics: A guide for their integration in precision health.
- Guidelines for action in primary health care.
- Perspectives on the application of CONSORT guidelines to randomized controlled trials in nutrition.
- Approach to obesity in the elderly population: a consensus report from the Diabetes, Obesity and Nutrition Working Group of SEMI (Spanish Society of Internal Medicine).
- Phase angle in applications of bioimpedance in health and disease.
- Expert Consensus on Morphofunctional Assessment in Disease-Related Malnutrition. Grade Review and Delphi Study.
- Nutritional ultrasound®: Conceptualisation, technical considerations and standardisation.
- Approach to obesity in the elderly population: a consensus report from the Diabetes, Obesity and Nutrition Working Group of SEMI (Spanish Society of Internal Medicine).
- Functional foods and nutraceuticals in the treatment of hypercholesterolemia: Statement of the Spanish Society of Arteriosclerosis 2023.
- Nutritional recommendations in the prevention and treatment of atherogenic dyslipidemia.
- Nutrition in residential centers for the elderly
- "Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD). Evidence-based European recommendations for the dietary management of diabetes. Diabetologia. 2023 Jun;66(6):965-985. doi: 10.1007/s00125-023-05894-8. PMID: 37069434."
- "2023 ESH Guidelines for the management of arterial hypertension".
- Humanization of socio-health care for people living with obesity.
- "EVIDENCE-BASED CLINICAL GUIDELINES ON BEHAVIORAL ADDICTIONS".
- Is apoB the best marker of residual risk?
- "Recommendations for the measurement of sexual steroids in clinical practice. A position statement of SEQCML/SEEN/SEEP".
- Pediatric Endocrinology Manual.
- Obesity and fertility. Position Statement.
- "Comprehensive approach to people with type 2 diabetes. Diabetes Knowledge Area of the Spanish Society of Endocrinology and Nutrition".
- Obesity and fertility. Position statement.
- "World Federation of Societies of Biological Psychiatry (WFSBP) guidelines update 2023 on the pharmacological treatment of eating disorders".

CANCER



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WELCOME FROM THE SCIENTIFIC DIRECTOR

Anna Bigas Salvans

Dear colleagues and friends,

I am pleased to present the CIBERONC annual report for the year 2023.

During 2023 the cancer area of CIBERONC has maintained its research activity around the pathology-focused programs designed since our inception. However, 2023 has been the year in which CIBERONC has implemented a new structure for our research programs, aimed at providing a more coherent organizational chart to favor interactions between the many groups that form part of the network and to exploit the multidisciplinary nature of our work. Thus, the four pathology-focused (vertical) programs have remained unchanged (except for breast cancer, which has been expanded to include gynecologic cancers) and have defined their main objective, following the suggestions of our External Scientific Advisory Committee (ESAC). As cross-cutting programs, one of a fundamental nature (Molecular Mechanisms of Cancer) and another of a more applied nature (Diagnosis and Precision Therapies) have been maintained.

In terms of scientific policy, at CIBERONC we have continued to work to establish new collaborations and strengthen our alliances with other research centers and CIBER areas, which has resulted in obtaining several outstanding projects in 2023, among which are: the project 4. EU project, which has coordinated the definition of the scientific priorities of the Cancer Mission by European experts; the JANE project, which aims to study cancer research networks and prepare the launch of 7 Networks of Expertise in cancer at the European level, or the Immune4ALL project, funded from the call for Personalized Medicine of the ISCIII, which aims to implement the use of predictive biomarkers in the immunotherapy of solid tumors.

Most importantly, 2023 was also the year in which the SPADA platform - the national registry of hereditary cancer variants - saw the light of day. Promoted by the Digestive Tract Tumors program and supported by the Scientific Directorate, it aims to be the national reference platform for the storage of these variants and the analysis of the information derived from them.

Finally, as every year, CIBERONC maintains its commitment to the training of young researchers. Thus, in 2023, 49 training activities, 19 national and international stays and 3 research initiation contracts have been sponsored for the youngest members of our network. Lastly, the Young Researchers meeting was held in Malaga in collaboration with the CIBEROBN area and was attended by 81 participants from both areas.

PROGRAMS & PLATFORMS

DIGESTIVE TRACT TUMORS

Gabriel Capellà Munar / COORDINATOR

The program has redefined its overall objective in 2023, focusing on the clinical stratification of malignant tumors of the digestive tract according to the (epi)genomic characteristics of the neoplastic cell and the tumor microenvironment.

As highlights of the scientific activity of the program, we mention the following:

Creation of the SPADA database: this is a Registry of Hereditary Cancer Variants, coordinated by C. Lázaro and G. Capellá. SPADA hosts HCV files and related minimal clinical information from diagnostic laboratories, as well as specific initiatives such as PANGENFAM. With 16 active centers and 12 in the process of joining, the database is hosted within CIBER and has collected variants from more than 4,200 individuals, totaling more than 1.15 million variants and 14,776 classifications. Eighty-four clinically relevant classifications with interpretive discrepancies have been identified, of which consensus has been reached on 80. SPADA is regularly used for variant classification.

ALIPANC. Five members of the Gastrointestinal Tumors Program interested in pancreatic cancer are core members of ALIPANC, the Alliance for Pancreatic Cancer Research, an initiative that brings together up to 40 groups interested in clinical and translational pancreatic cancer research. Under the leadership of N Malats, FX Real and T Macarulla, the Long-Term Survivors (LTS) study of pancreatic cancer has been launched. Up to 16 Spanish reference centers are contributing to this retrospective multicenter case-control study. LTS (survivors more than 5 years) and STS (Short-Term Survivors) (3-18 months OS) are matched by stage and age. Paraffin-embedded clinical biopsy specimens are used. So far, 244 STS cases and 107 matched controls have been enrolled.

MET-CRC-BIORESOURCE. Under the leadership of A. Cervantes, the program has explored the utility of transcriptomic signature classification of metastatic colorectal cancer by collecting and analyzing 134 matched samples of CRC primary tumor and liver metastases. Although the original project was halted due to the poor quality of the kerosene samples, the potential of the bioresource collected has been recognized. Thus, the work of the program will now focus on identifying organ-specific signatures of liver metastases with prognostic and predictive value, to discover new therapeutic targets and to study phenotypic plasticity. We anticipate that a comprehensive characterization of the molecular evolution and clinical trajectories of the disease will provide new biological insights into the metastatic process, revealing actionable targets for the prevention and treatment of liver metastases. A decision has been made to complement the available retrospective cohort with the recruitment of a new prospective cohort in 2024.

BREAST AND GYNECOLOGICAL CANCERS

Joaquín Arribas López / COORDINATOR

Following the restructuring of CIBERONC in 2022, the program which previously focused exclusively on breast cancer has expanded its scope in 2023 to encompass both breast cancer and gynecological cancers.

Highlights of the program's scientific activity in 2023 include:

Integration of New Research Groups: With the recent reorganization, our program has welcomed new research groups from the Precision Diagnostics and Therapeutics program, including those led by Rafael Lopez, MD, PhD, Xavier Matias Guiu, MD, PhD, Santiago Ramon y Cajal, MD, PhD, and Maria Jesus Vicent, PhD. From the area of Molecular Mechanisms of Cancer, we have added the group led by Piero Crespo, PhD. This expanded collaboration has already yielded significant results, such as the proposal funded by Drs. Albanell and Vicent to develop nanoparticles for RNA-based drug delivery and the partnership between Drs. Crespo and Arribas in the evaluation of scaffold protein levels in patient samples.

Central Laboratory for HER2 Analysis: The group led by Dr. Palacios acts as a central laboratory to evaluate HER2 through Immunohistochemistry (IHC) and Fluorescent In Situ Hybridization (FISH) techniques. This pivotal role supports the pCR-Guided Strategy without Chemotherapy with Subcutaneous Pertuzumab-Trastuzumab and T-DM1 in HER2-Positive Early Breast Cancer (PHERGain-2) project.

Collaboration with CIBER-BBN: Several of the groups in the program are interacting extensively with other areas of CIBER, especially in Nanotechnology. These interactions underline our commitment to interdisciplinary research, taking advantage of cutting-edge technologies and knowledge.

Three groups of the program, led by Emilio Alba, Gema Moreno and Joaquín Arribas, participate in the Immune-4all project (Exploring the Feasibility of Predictive and Pharmacodynamic Biomarkers of Immunotherapy in Solid Tumors), recently awarded in 2022 with more than 4,000,000 €, to find biomarkers of response/resistance to immune therapies.

The group led by Gemma Moreno participates in the project "New therapeutic strategies of immunotherapy for the treatment of ovarian cancer PMP- TA22/00076".

RESPIRATORY TRACT TUMORS

Luis Montuenga Badía / COORDINATOR

The program has redefined its overall objective in 2023, identifying sensitivity and resistance to new therapies as the most relevant common objective for the six groups that make up the program.

Highlights of the program's scientific activity in 2023 include:

Leader and collaborators in the INGENIO project (Integration of genomics, digital imaging and clinical information towards the optimization of precision oncology). National consortium, 17 research groups, budget granted: €3,196,600. PI: Luis Paz-Ares

CIBERONC-CIBERCV collaborative project awarded: "Inflammation and Cardiovascular Damage in Lung Cancer: Studying the Role of Immuno-modulatory Therapies in Reducing Cardiotoxicity and Vascular Injury." "InCaRe. Co-PIs Karmele Valencia and María Pilar Martín.

Development of organoids with matrices provided by

CIBER-BBN groups (in the framework of the intramural collaborative project between both areas - CIBERONC PDO 2.0 project).

Application for two TRANSCAN-3 projects: both in close collaboration between several groups of the program and with objectives ranging from the study of epigenetic resistance in lung cancer to the identification of biomarkers in liquid biopsy that predict resistance to immunotherapy in lung cancer patients.

Establishment of a framework agreement and start of a collaborative project with the association of patients and relatives affected by lung cancer (AEACaP).

HEMATOLOGICAL TUMORS

Ramón García Sanz / COORDINATOR

The program has redefined its overall objective in 2023, focusing on the clinical stratification of hematological malignancies according to the (epi) genomic characteristics of the neoplastic cell and the tumor microenvironment.

As highlights of the scientific activity of the program, the following are detailed:

Pathological/immunophenotypic/molecular characterization: development of new strategies to refine the diagnosis of lymphoid neoplasms and new preclinical models in different hematological diseases (36566271, 36928817, 37031299, 37304935, 38017105).

As a collaborative example, we highlight the characterization of the prognostic impact of genetic mutations according to the mutational status of IGHV in chronic lymphocytic leukemia (36566271, Leukemia, IF 11,4, D1). This work evidences the role of specific gene mutations according to IGHV mutational status, with some genetic alterations being prognostic only in patients with mutated IGHV (NOTCH1 and NFKBIE), non-mutated patients (TP53, BIRC3 and EGR2), or both (SF3B1 and XPO1). These findings underscore the need for detailed approaches to identify high-risk patients within distinct subgroups.

Development of diagnostic tools applicable to clinical practice with a primary focus on measurable residual disease (MRD): design of new tools, genetic characterization and identification of prognostic markers in different hematological malignancies (36566271, 37560801, 36325893, 37746159, 36494342, 36930848). Among the tools developed, an open-access algorithm has been developed for the identification of patients with MGUS-like characteristics with different clinical evolution (36930848, J Clin Oncol, IF 45,3, D1). This work, which includes a training population of >2500 monoclonal gammopathies and a validation cohort of >4500 patients, defines a phenotypic classification that could form part of the diagnostic process for multiple myeloma and light chain amyloidosis.

Promotion of clinical trials and controlled clinical trials based on MRD. Outcomes and management of new therapeutic strategies in relapsed/refractory multiple myeloma, including CAR T cells, within clinical trials (33626253, 36095849, 36179026, 37272512, 37269857, 37414060, 37486974, 36751513,36930848, 37102598, 38031761, 38048552). Among these, a national multicenter clinical trial (37414060, NCT04309981 and EudraCT, 2019-001472-11) focused on an academic CAR T cell in which 3 groups from the program are participating. The results of this pilot study indicate that this CAR T cell construct can provide deep and sustained responses with low toxicity.

MOLECULAR MECHANISMS OF CANCER

Xosé R. García Bustelo / COORDINATOR

The program has redefined its general objectives in 2023, focusing as a priority on the identification and validation of new genetic and non-genetic mechanisms that promote the development and evolution of tumors. This objective is associated with the validation of these mechanisms and, finally, with the development of new diagnostic and therapeutic tools derived from them. Part of our work is also to give methodological and scientific support to the other scientific programs of CIBERONC and other CIBER areas that need it. In this context, our program is also involved in the coordination of the CIBERONC Bioinformatics and Omics work module.

During 2023, we would like to highlight the following scientific advances made that serve to exemplify the activities indicated in the previous paragraph. At the intra-program level, we highlight collaborations that have allowed the development of a new artificial intelligence tool that allows the analysis of tumor genomic data quickly, effectively and without high computational time requirements (PMID 37260508); the characterization of new oncogenes (PMID 36476833); the identification of new layers of regulation and action of the MAPK-ERK pathway (PMID 36791195, PMID: 37463244) or the discovery of an an early signaling pathway involved in therapeutic resistance in colorectal tumors (PMID 37737566).

As collaboration between CIBERONC scientific programs, we highlight the discovery of a new therapeutic resistance system based on the uptake of chemotherapeutic agents by tumor stromal cells (PMID 36765091).

Finally, at the inter-area CIBER level, we would like to mention two studies carried out this year: (a) identification of the epigenomic profile associated with individuals affected by "GATA2 deficiency", a disease that is associated with the development of multiple systemic disorders and has a high risk of developing myelodysplastic syndromes and acute myeloid leukemia (PMID 36815365) and (b) development of a new technology that allows the detection of metabolites secreted by different types of cells, including tumor cells. The application of this technique allowed us, for example, to identify 5'-methylthiadenosine as a metabolite secreted by prostate cancer cells that mediates changes in the tumor stroma (PMID 38109528).

PRECISION DIAGNOSTICS AND THERAPEUTICS

Enrique de Álava / COORDINATOR

The Precision Diagnostics and Therapeutics Program, following the recommendations of the ESAC, has initiated a comprehensive action plan to implement precision medicine. This plan is characterized by a dual focus on discovering and clinically validating immune biomarkers and developing preclinical experimental models to unravel the complexities of immunotherapies.

Highlights of the program's scientific activity during 2023 include:

Publications aimed at evaluating diagnostic and therapeutic biomarkers in gynecologic cancer.

- Evaluation of Somatic Mutations in Urine Samples as a Noninvasive Method for the Detection and Molecular Classification of Endometrial Cancer. Clin Cancer Res. PMID: 37439797.
- Highly Sensitive Microsatellite Instability and Immunohistochemistry Assessment in Endometrial Aspirates as a Tool for Cancer Risk

Individualization in Lynch Syndrome. Mod Pathol. PMID: 36918055.

- Evaluation of somatic mutations in cervicovaginal samples as a noninvasive method for the detection and molecular classification of endometrial cancer. EBioMedicine. PMID: 37480623
- Noninvasive detection of microsatellite instability in patients with endometrial cancer. Int J Cancer. PMID: 36650670.

Publications related to osteosarcoma:

- ALPL-1 is a target for chimeric antigen receptor therapy in osteosarcoma. Nat Commun. PMID: 37291203. A group from the program, in collaboration with another from the Molecular Mechanisms Program, is working on the search for surface antigens that can be used in CAR-T models of solid tumors, particularly sarcoma. This collaboration between the two groups and an outstanding foreign group has made it possible to validate one of these antigens in osteosarcoma.

TRAINING PROGRAM

Gema Moreno Bueno / COORDINATOR

The main milestones of the Training and Mobility program in 2023 have been the following:

Training Program: action focused on providing young CIBERONC researchers with the opportunity to have continuous training through highly specialized courses. In addition, this activity also contributes to the scientific activity of the CIBERONC consortium by sponsoring national and international training courses as well as specialized symposia.

During 2023, the program funded a total of 46 actions to attend national and international training courses and another three to organize or sponsor national and international training courses.

Programa de movilidad: The mobility call finances stays between different CIBERONC groups (activity called intramural); in laboratories outside the CIBER (called extramural) and finally stays within CIBER groups (called interdisciplinary) aimed at improving training in different fields of specialization.

This activity is carried out, after prior evaluation of the needs and objectives of the requested proposal, through scientific stays of young CIBERONC researchers in different laboratories. Its objective is to improve the training of young researchers in specific methodologies and to strengthen national and international collaborations between scientific groups.

In 2023, the program granted a total of 19 actions: 3 intramural actions and 16 extramural actions (national or international).

Oncology Research Initiation Contracts: This action aims to introduce postgraduate students to translational oncology research by hiring them for a contract period of up to 6 months before starting an official PhD program in a selected CIBERONC group. To apply for one of these contracts, the interested group must propose a scientific project to be carried out by the selected candidate during the duration of the contract. In 2023, the program financed 3 contracts.

Promotion of Young Researchers: Meeting of Young CIBERONC Researchers.

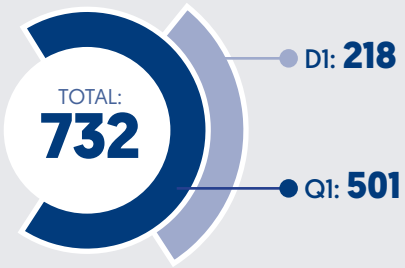
This action is considered an important training and scientific activity for young CIBERONC researchers. This meeting, organized as a scientific meeting, is entirely organized by PhD students and junior postdoctoral fellows (who make up the scientific organizing committee) and offers an excellent opportunity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

In 2023 the meeting was held on November 6 and 7, 2023 in the Aula Magna of the Faculty of Medicine (University of Malaga), organized in collaboration with CIBEROBN (obesity) and had 81 participants. A total of 53 abstracts were received and the scientific program included talks focused on: i. New therapeutic strategies in cancer treatment; ii. Immune escape mechanisms in cancer development; iii. Inflammation and obesity; iv. New technologies in biomedical research; and v. Reduction of clinical toxicities in combination therapies.

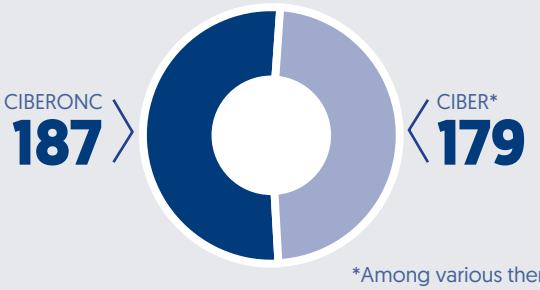
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168,9	de Langen A.J., Johnson M.L., Mazieres J., Dingemans A.-M.C., Mountzios G., Pless M. et al. Sotorasib versus docetaxel for previously treated non-small-cell lung cancer with KRASG12C mutation: a randomised, open-label, phase 3 trial. The Lancet. 2023;401(10378):733-746.
158,5	San-Miguel J., Dhakal B., Yong K., Spencer A., Anguille S., Mateos M.-V. et al. Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma. New England Journal of Medicine. 2023;389(4):335-347.
158,5	Ahn M.-J., Cho B.C., Felip E., Korantzis I., Ohashi K., Majem M. et al. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. New England Journal of Medicine. 2023;389(22):2063-2075.
82,9	Larrayoz M., Garcia-Barchino M.J., Celay J., Etxebeste A., Jimenez M., Perez C. et al. Preclinical models for prediction of immunotherapy outcomes and immune evasion mechanisms in genetically heterogeneous multiple myeloma. Nature Medicine. 2023;29(3):632-645.
76,2	Aix S.P., Ciuleanu T.E., Navarro A., Cousin S., Bonanno L., Smit E.F. et al. Combination lurbinectedin and doxorubicin versus physician's choice of chemotherapy in patients with relapsed small-cell lung cancer (ATLANTIS): a multicentre, randomised, open-label, phase 3 trial. The Lancet Respiratory Medicine. 2023;11(1):74-86.
65,1	Calvisi D.F., Boulter L., Vaquero J., Saborowski A., Fabris L., Rodrigues P.M. et al. Criteria for preclinical models of cholangiocarcinoma: scientific and medical relevance. Nature Reviews Gastroenterology and Hepatology. 2023;20(7):462-480.
64,5	Arora M., Moser J., Hoffman T.E., Watts L.P., Min M., Musteanu M. et al. Rapid adaptation to CDK2 inhibition exposes intrinsic cell-cycle plasticity. Cell. 2023;186(12):2628-2643.e21.
56,9	Pham V.N., Bruemmer K.J., Toh J.D.W., Ge E.J., Tenney L., Ward C.C. et al. Formaldehyde regulates S-adenosylmethionine biosynthesis and one-carbon metabolism. Science. 2023;382(6670).
51,1	Cortellini A., Tabernero J., Mukherjee U., Salazar R., Sureda A., Maluquer C. et al. SARS-CoV-2 omicron (B.1.1.529)-related COVID-19 sequelae in vaccinated and unvaccinated patients with cancer: results from the OnCovid registry. The Lancet Oncology. 2023;24(4):335-346.
50,5	Villacampa G., Tung N.M., Pernas S., Pare L., Bueno-Muino C., Echavarria I. et al. Association of HER2DX with pathological complete response and survival outcomes in HER2-positive breast cancer. Annals of Oncology. 2023;34(9):783-795.

CIBERONC Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Alba Conejo, Emilio	19	15	6	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	MÁLAGA
Albanell Mestres, Joan	28	17	10	Consorci Mar Parc Salut de Barcelona	BARCELONA
Aranda Aguilar, Enrique	16	14	7	Fundación para la Investigación Biomédica de Córdoba (FIBICO)	CÓRDOBA

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Arribas López, Joaquín	10	8	5	Consorci Mar Parc Salut de Barcelona	BARCELONA
Barbacid Montalbán, Mariano	6	3	2	Fundación Centro Nacional de Investigaciones Oncológicas	MADRID
Batlle Gómez, Eduard	4	4	3	Fundación Privada Instituto de Recerca Biomédica (IRB-Barcelona)	BARCELONA
Bigas Salvans, Anna	16	15	9	Consorci Mar Parc Salut de Barcelona	BARCELONA
Campo Guerri, Elías	22	16	9	Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Camps Herrero, Carlos	14	8	3	Consorcio Hospital General Universitario Valencia	VALENCIA
Capellà Munar, Gabriel	46	31	16	Fundació IDIBELL	BARCELONA
Carnero Moya, Amancio	7	6	3	Fundación Pública Andaluza para la Gestion de la Investigacion en Salud de Sevilla	SEVILLA
Carracedo Perez, Arkaitz	11	11	8	CIC BIOGUNE	VIZCAYA
Carrato Mena, Alfredo	14	12	5	Servicio Madrileño de Salud	MADRID
Cervantes Ruiperez, Andrés	18	14	5	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA
Colomer Pujol, Dolors	23	20	8	Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Crespo Baraja, Pedro	2	2	1	Agencia Estatal Consejo Superior de Investigaciones Cientificas	CANTABRIA
de Alava Casado, Enrique	6	5	1	Fundación Pública Andaluza para la Gestion de la Investigacion en Salud de Sevilla	SEVILLA
Esteller Badosa, Manel	19	16	9	Fundación Instituto de Investigación contra la Leucemia Josep Carreras	BARCELONA
Feliú Batlle, Jaime	33	21	6	Servicio Madrileño de Salud	MADRID
Garcia Bustelo, Xose Ramon	5	3	2	Fundación de Investigación del Cáncer de la Universidad de Salamanca	SALAMANCA
Garcia Sanz, Ramón	82	54	26	Fundación Instituto de Estudios de Ciencias de la Salud de Castilla y León	SALAMANCA
López Bigas, Núria	6	5	3	Instituto de Recerca Biomédica (IRB-Barcelona)	BARCELONA
López López, Rafael	31	23	5	Servicio Gallego de Salud	CORUÑA, A

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Malats Riera, Nuria	8	5	4	Fundación Centro Nacional de Investigaciones Oncológicas	MADRID
Martín Jiménez, Miguel	15	10	6	Servicio Madrileño de Salud	MADRID
Matías-Guiu Guia, Francisco Javier	26	16	9	Instituto de Investigacion Biomédica de Lleida. Fundación Dr. Pifarre	LLEIDA
Melero Bermejo, Ignacio	26	20	9	Universidad de Navarra	NAVARRA
Montuenga Badía, Luis	26	24	11	Fundación para la Investigación Médica Aplicada	NAVARRA
Moreno Biuena, Gema	12	6	2	Universidad Autónoma de Madrid	MADRID
Muñoz Terol, Alberto	11	9	2	Agencia Estatal Consejo Superior de Investigaciones Cientificas	MADRID
Noguera Salvà, Rosa	5	3	1	Fundación para la Investigacion del Hospital Clínico de la Comunidad Valenciana (Fundación INCLIVA)	VALENCIA
Orfao, José Alberto	27	20	10	Fundación de Investigación del Cáncer de la Universidad de Salamanca	SALAMANCA
Palacios Calvo, José	10	8	2	Servicio Madrileño de Salud	MADRID
Pandiella Alonso, Atanasio	12	11	2	Fundación de Investigación del Cáncer de la Universidad de Salamanca	SALAMANCA
Paramio González, Jesús María	19	16	6	Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT)	MADRID
Paz-Arés Rodríguez, Luis	37	32	17	Servicio Madrileño de Salud	MADRID
Piris, Miguel Ángel	15	12	8	Instituto de Investigación Sanitaria Fundación Jiménez Díaz	MADRID
Prosper Cardoso, Felipe	34	28	14	Fundación para la Investigación Médica Aplicada	NAVARRA
Ramón y Cajal Agüeras, Santiago	10	9	2	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Real Arribas, Francisco Xavier	8	5	3	Fundación Centro Nacional de Investigaciones Oncológicas	MADRID
Rodrígo Tapia, Juan Pablo	32	24	10	Fundación para el Fomento en Asturias de la Investigación Cientifica Aplicada y la Tecnología	ASTURIAS
San Miguel, Jesús Fernado	47	35	22	Universidad de Navarra	NAVARRA
Santos de Dios, Eugenio	5	4	2	Fundación de Investigación del Cáncer de la Universidad de Salamanca	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Santiesteban, María del Pilar	2	2	1	Agencia Estatal Consejo Superior de Investigaciones Cientificas	MADRID
Sanz Santillana, Guillermo	34	25	6	Fundación para la Investigación del Hospital la Fe	VALENCIA
Seoane Suárez, Joan	4	4	2	Fundación Privada Instituto de Investigación Oncológica Valle de Hébron-VHIO	BARCELONA
Suárez Puente, Xose Antón	7	4	2	Universidad de Oviedo	ASTURIAS
Tabernero Caturla, Josep Maria	21	17	13	Fundación Privada Instituto de Investigación Oncológica Valle de Hébron-VHIO	BARCELONA
Vicent Docón, María Jesús	3	2	2	Centro de Investigación Príncipe Felipe (CIPF)	VALENCIA

MENTAL HEALTH

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WELCOME FROM THE SCIENTIFIC DIRECTOR

Ana González-Pinto Arrillaga

In the year 2023, the World Health Organization (WHO) declared the end of the global health emergency due to COVID-19. Despite this end of cycle, the world is not the same as it was before the pandemic. Mental health is now in the focus of society's attention, and some pathologies such as depression and suicide have increased. In this context, CIBERSAM is committed to society, acting as a reference in the scientific dissemination of mental health. The social interest in knowing the pathologies and their solutions, and in finding answers to alleviate their discomfort is at the center of our interest in dissemination. Suicide prevention as an aspect of communication in various forums has been brought to the forefront. CIBERSAM has led the preparation of the report on the evolution of suicide in Spain in the child and adolescent population between 2000 and 2021. It has also focused attention and interest on the adolescent population with the "MensSana" project. This project is funded by the FECYT, and complements and gives continuity to "MenteScopia". Its objective is to address the prevention, diagnosis and treatment of mental illnesses using entertaining and accessible material on the functioning of the brain, the risk factors associated with mental illnesses and the impact they have on the daily lives of those who suffer from them. The material is designed to be of interest also to the most vulnerable population.

In terms of scientific production, there has been a commitment to excellent scientific production, with a notable increase in first decile publications and scientific cooperation. This collaboration crosses all borders since all the programs participate in international consortiums. Among the most important findings in which CIBERSAM has participated are the convincing evidence of the association between depressive pathology and cardiovascular mortality, as well as the association between schizophrenia and death due to cardiac pathology in patients with previous cardiovascular disease. This shows the importance of mental illnesses, their treatment and prevention, for the improvement of the overall health of the population. In addition to this, we have transversally contributed knowledge to the genetic basis of mental illnesses, transcriptomics, and inflammation linked to these pathologies.

CIBERSAM promotes scientific collaboration and is committed to generational change and equal opportunities for women and men. This year there has been a change in the Scientific Management. One third of all principal investigators and researchers at CIBERSAM are women, and there is a gender balance in program leadership. Worthy of note is the reading of doctoral theses and the incorporation of a significant number of young male and female researchers into CIBERSAM, which is not only desirable but absolutely necessary. Finally, our social perspective means that we place the patient at the center, which is why we collaborate and learn from patient associations, and a representative of these associations is a member of the External Scientific Advisory Committee.

PROGRAMS & PLATFORMS

DEPRESSION

Diego Palao Vidal / COORDINATOR

Depression is one of the leading causes of disability and health and social expenditure in the world. Suicide is the first cause of global external death and the third cause of years lost due to premature death in Europe.

Both health problems are research objectives of the Program and other CIBERSAM groups. During 2023, 318 collaborative articles were published on depression and almost 100 related to suicide in epidemiology, neurobiology and prevention. The 5 groups of the Program have published articles in top quality journals such as Nature Neuroscience, Lancet Psychiatry, Lancet Reg-Health-Europe, Lancet Pub-Health, Am J Psych, Psych o Psychol Med.

The effects of the COVID-19 pandemic on mental health, especially the increase in suicidal behaviors in young people, have been investigated, showing the persistence of some associated factors and the need for prevention. Research personnel of the program are working on the implementation of suicide prevention plans that, following WHO recommendations, are being developed at the autonomous community level, including survivors.

Participation continues in international working groups and consortia on resistant depression, electroconvulsive therapy (GenECT) and neuroimaging (GEMRIC, ENIGMA). Collaboration with the International Suicide Genetics Consortium (ISGC) produced a meta-analysis validating the identification of 12 loci associated with genetic risk of suicide attempts. Of note are the neuroimaging studies on volumetric differences in resistant depression treated with ECT versus TMS or the impact of ultra-processed foods on depression.

In addition, the groups continue to investigate the development and evaluation of diagnostic and prognostic biomarkers in neuroimaging, neurocognition, neurophysiology, immunometabolism and genetics. Thus, a work with CIBERER and CIBER-BBN has generated pluripotent stem cells (iPSCs) from patients with genetic deficiency of the enzyme Tyrosine-Hydroxylase for the study of L-Dopa-resistant neuropediatric parkinsonism.

To be highlighted is the increasing use of digital applications in the study of depression and suicide prevention through continuous monitoring that allows digital phenotyping and predictive analysis. Collaboration with the recommendations of the European Psychiatric Association promotes digital transformation to improve the accessibility and quality of services.

Particularly relevant are the studies of therapeutic interventions in depression (cognitive remediation, deep brain stimulation), their application in work environments or in professional groups. A study of the impact of patient suicide on Spanish psychiatrists helps to promote postvention in “second victims”.

The SURVIVE consortium (10 CIBERSAM groups) continues the extended cohort project to investigate suicidal behavior in Spain and the efficacy of secondary prevention strategies. The analysis of the SURVIVE-1 results is being developed and dissemination of these results has begun.

The research staff of the program actively participate in the dissemination of results in public media and social networks, contributing to the fight against stigma and improving the access of patients with depression and suicidal risk to diagnosis and effective treatments.

SCHIZOPHRENIA

Edith Pomarol-Clotet / COORDINATOR

The CIBERSAM Schizophrenia Program is the program that brings together the most research groups (14 groups) and the most fruitful in terms of publications and funded competitive projects.

In 2023, more than 250 scientific articles on schizophrenia with high impact (Q1 and Q2) have been published, of which 36% correspond to first decile articles, and 135 involve international collaboration.

These publications include different findings, such as predictive factors for the transition to psychosis in patients with the so-called high-risk mental illness, both cognitive and structural cortical changes. Functional neuroimaging studies, including a study that found reduced activation in the cerebral cortex associated with negative symptoms in schizophrenia. Other publications have examined the role of drugs, specifically stimulants, in the incidence of first psychotic episodes and the effect of cannabis and the polygenic risk score in relation to symptom progression.

In addition, the program groups have developed 35 new clinical trials, elaborated 19 clinical guidelines and are studying the registration of 2 new patents.

Ongoing collaborative projects include the examination of prognostic factors in the evolution and transition to psychosis in subjects with high-risk mental states, studies of the relationship between environment and genes in schizophrenia, and basic science studies such as the effects of cannabis using neurospheres, neurons and glia. There are also projects aimed at treatment optimization using multi-omics data and systems biology, and an important therapeutic study will investigate, after the first study of its kind, the use of deep brain stimulation in treatment-resistant patients.

Furthermore, we would like to highlight the media dissemination with the Joan Oró project that brings knowledge of neuroscience closer to young people and the award-winning MenteScopia project that promotes awareness, prevention and treatment of mental health.

Finally, it should be noted that in 2023 some members of the program have received several awards: the Margarita Salas Award in the category of scientific career and the Vila Saborit Award for the best publication of the year from the Catalan Society of Psychiatry and Mental Health and best researcher award from the Spanish Society of Psychiatry and Mental Health, for the article on fingerprints as a predictor of schizophrenia.

In summary, the CIBERSAM Schizophrenia Program has continued to demonstrate its excellence in research during 2023, through its active participation in scientific events, follow-up meetings, collaborative projects and discussion forums. These achievements reinforce its position as a benchmark in the study and treatment of schizophrenia at national and international level.

BIPOLAR DISORDER

Vicent Balanzá-Martínez / COORDINATOR

The CIBERSAM Bipolar Disorder Program, made up of six research groups and a linked clinical group, conducts basic-clinical research on bipolar disorders.

During 2023, the results of the research activity have been published in high impact journals, highlighting those indexed in the first decile, such as Lancet, World Psychiatry, Lancet Psychiatry, Lancet Public Health, PLoS Medicine, EClinicalMedicine, JAMA Network Open, Ageing Research Reviews, Psychiatry Research, Molecular Psychiatry, among others. Most of the articles are collaborative with groups from the program, other

CIBERSAM groups and international consortia, such as ENIGMA and GBD. Of note is the publication of 52 systematic reviews and meta-analyses.

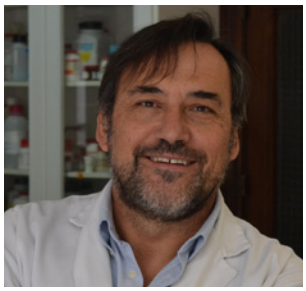
The program groups continue to research numerous aspects of bipolar disorders, such as the adaptation of the functional rehabilitation program for older adults, the identification of digital biomarkers of response to treatment using wearables, difficulties in emotional regulation, retinal thickness as a biomarker of cognitive performance, the relationship between intestinal dysbiosis and peripheral inflammation, the study of the reward system in mania, as well as the relationship between methylation, childhood trauma and suicidal behavior in bipolar disorder.

We have participated in the development of clinical guidelines and international consensus recommendations, such as those related to the functionality of older adults with bipolar disorder, the basic quality indicators for the clinical management of mood and psychotic disorders, the management of depression in adults with epilepsy, and the WHO guidelines on mental health at work. Fourteen competitive human resources contracts have also been secured, including the Marie Curie-Horizon Program, ISCIII and La Caixa.

Numerous state and international projects (Horizon, European Commission, ERASMUS+) have been initiated in 2023, including those on the validation of mitochondrial biomarkers for differential diagnosis with schizophrenia in early episodes, the use of transcriptomic data in blood and brain for the identification of biomarkers in bipolar disorder, as well as multimorbidity in people with CNS disorders. Among the international projects of the program's thematic area, those aimed at developing personalized treatment strategies in severe mental disorder, as well as the accurate differential diagnosis between bipolar and unipolar disorder by means of the clinical validation of the EDIT-B test, stand out.

Follow-up meetings of the program have generated new collaborative projects, including two personalized medicine projects on the use of genetics for psychiatric diagnosis and on differential diagnosis in schizophrenia, bipolar disorder and autism using fingerprinting, genomics and deep learning algorithms.

In 2023, members of the program have received, among others, the Andalusian Mental Health Federation Award (research study modality) and the European College of Neuropsychopharmacology (ECNP) Excellence Award.



THERAPEUTIC INNOVATION

Juan Carlos Leza / COORDINATOR

The groups that make up the program continue to maintain an extensive research activity in terms of publications, highlighting original preclinical and clinical research and in many cases mixed. Most of them are collaborative between groups of the program, of the CIBER consortium, and quite a number of them with international groups. They have also participated as authors in systematic reviews or as editors of special issues by invitation.

The activity of the Program's research staff has also been reflected in their participation in several clinical guidelines and clinical trials with new drugs and other treatment strategies, including virtual reality and neurocognitive stimulation techniques. In addition to numerous competitive projects, contracts have been signed with companies on topics related to innovation.

Members of the Program have coordinated or been invited to numerous science outreach events, events with patient associations, etc. In addition, many groups maintain very active social media accounts in the dissemination of scientific news in mental health research. Some examples of scientific achievements of the program groups are:

- Prevention of behavioral and neurochemical alterations with NAC supplementation during gestation.
- Mechanisms by which the nootropic ISRIB enhances the antidepressant effects of ketamine.
- Differential expression of miRNAs in human brain in pathways related to depression and suicide.
- Identification of PACAP peptide as capable of preventing the spread of alphasynucleinopathy.
- Identification of specific neuronal pathways involved in anxious and/or depressive symptomatology in chronic pain.

- Description of the neurobiological mechanisms of the acute effects of psilocybin.
- Creation, separation and differential culture of neurospheres and gliospheres from human olfactory epithelium.
- Development and validation of a model of mental disorders from olfactory neuroepithelium cells of patients as a tool for the evaluation and/or prediction of drug response.
- Identification of a genetic variation of the PACAP receptor and its relevance in the extinction of conditioned fear in women with a history of traumatic stress.
- Tool to assess whether MRI is able to detect patients at high risk of relapse after the first psychotic break with AI methods.
- Deep brain stimulation as an effective and safe alternative to treat complex and resistant forms of schizophrenia and bipolar disorder.
- Alterations in mitochondrial respiratory capacity as a biomarker of disease and clinical response in bipolar disorder.
- Monitoring of electrodermal activity in the early detection of symptoms and possible use in the evaluation of early response to treatment in mania and bipolar depression.
- Design and evaluation of a digital health platform for secondary prevention of suicidal behavior.
- Differences in gut microbiota in patients with anxiety, trauma and depression.
- Different endophenotypes in patients with eating disorders and personality disorders in inflammatory and oxidative pathways. Relationship with impulsivity and trauma.
- Relationship between cognitive alteration and coronary microvascular dysfunction.
- Fine segmentation techniques of the hippocampus and amygdala in MRI in schizophrenia and auditory hallucinations.
- Characterization of a population of immature excitatory neurons in adult human neocortex.

MENTAL DISORDERS OF THE CHILD AND ADOLESCENT

Inmacualada Baeza Pertegaz / COORDINATOR

The Child and Adolescent Psychiatry program aims to study mental disorders with onset in childhood and adolescence and is made up of six CIBER groups and a linked group (Celso Arango, Inmaculada Baeza as coordinator, Manuel Desco, Lourdes Fañanás, Rafael Tabarés-Seisdedos, José Antonio Ramos and Miguel Ángel González) who combine efforts and work collaboratively.

Among the most notable results of the program during the year 2023 is a total of one hundred publications, more than half of them collaborative among the CIBER groups and mostly in journals indexed in the first quartile according to the Journal Citation Report, including the Lancet Psychiatry, Acta Psychiatrica Scandinavica, Schizophrenia Bulletin or the Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP). The number of publications has increased in Q1 and D1 with respect to previous years. In addition, it should be noted that two articles published in JAACAP by collaborative groups of the program have been chosen among the 8 most influential articles published in 2023 in terms of their translationality.

Among the projects, both national and international, that have given rise to some of these publications, the study of genetic and epigenetic markers of vulnerability for mental disorder in children and adolescents exposed to child abuse, the AIMS-2-TRIALS clinical trial aimed at validating biological markers and developing new treatments for autism or the Running in the FAMILY study that aims to understand the mechanisms of intergenerational transmission of mental illnesses stand out. All of these are carried out collaboratively by groups from the child and adolescent psychiatry program as well as other national and international groups.

The child and adolescent psychiatry program has a clear translational value, moving from research to clinical practice with projects such as “BOOTSTRAP”, which not only evaluates the Internet use patterns of young people, but also assesses their impact on mental health,

and identifies risk behaviors with the aim of developing the necessary policy interventions. Another clear example of translation to clinical practice is the development of guidelines derived from the research conducted. Thus, in 2023, the members of the program have collaborated in the elaboration of several guidelines and consensus documents, among which we highlight: the guide for the care of perinatal bereavement, whose objective is to create an action protocol to facilitate and unify the assistance to women experiencing perinatal bereavement processes; the consensus for the care of autism in Europe; or the consensus on the care of people with Phelan-McDermid syndrome.

As for other merits, the members of the child and adolescent psychiatry program have been awarded several awards, including: the award for the best communication at the 23rd Congress of Hospitals, recognition for excellence in psychology and health 2023, and the award for the best communication at the Congress of the Spanish Association of Child and Adolescent Psychiatry (AEPNYA).

PSYCHOSOMATIC, ANXIETY AND IMPULSE CONTROL DISORDERS

Josep Antoni Ramos / COORDINATOR

The Psychosomatic, Anxiety and Impulse Control Disorders Program has published the results of its research in the main scientific journals of the specialty. Of note is the publication of 120 articles in the first decile and the considerable increase of articles in the first quartile, as a result of intraCIBERSAM and international collaborations. Research has been published on transcriptomic risk scores in attention deficit/hyperactivity disorder (ADHD); on genetic variants associated with irritable bowel syndrome and mental disorders; on the association between mental disorders and mortality; and on the development of a digital intervention for occupational stress and mental health. Studies have been published on coronary microvascular dysfunction and its association with cognitive function; on neuroinflammation in preclinical models of periodontal disease and depression; research on neural markers of response to cognitive-behavioral therapy (CBT) in children with obsessive-compulsive disorder; on neural predictors of CBT outcome in anxiety disorders; the effect expectancies of cocaine in patients with cocaine use disorder and ADHD have been studied; the development of a new animal model for mental disorders; psychological trauma and mental disorders; pharmacological management of borderline personality disorder; text mining methods to characterize suicidal thoughts and behaviors have been developed; and a study on severe suicide attempts has been carried out.

Active dissemination of the results in the media and participation in social projects to improve knowledge of mental disorders have been another aspect of the program.

A patent has been obtained for a new humanized model for mental disorders and the program leads and participates in innovation networks such as the TECSAM network (Innovation Network for New Technologies in Mental Health) and CRETSAM (Center for Research and Transfer in Mental Health).

In competitive research calls, projects have been obtained to improve the understanding and treatment of ADHD; the prevention of suicide; the reduction of the psychosocial impact of Covid-19 on workers in homes for the elderly or the disabled; to improve public health policies specific to adolescents from disadvantaged backgrounds; to conduct a clinical trial to investigate oral inflammation in patients with major depressive disorder; international projects to improve mental health in Europe; to study the efficacy of EMDR with transcranial direct current stimulation (tDCS) in the treatment of fibromyalgia, as well as to investigate biomarkers of compulsive disorders.

The level of participation in international platforms and consortia, such as COSMIC, ENIGMA, EMPOWER, DISCOvERIE, IMI EU-PEARL, the Psychiatric Genomics Consortium, RESPOND and TIMESPAM, is also noteworthy.

The development of research talent in the program has been endorsed by doctoral theses with quality mentions, and articles published by young researchers. Finally, we would like to highlight the award obtained in clinical innovation and the replacement of the coordinator of the program in November.

PROGRAMA DE FORMACIÓN

Esther Berrocoso Domínguez / COORDINATOR

During 2023, the Transversal Training Program has sponsored a total of 13 training actions, including training stays for research personnel and numerous initiatives aimed at enrolling in courses, congresses and research seminars, both face-to-face and online. Among these activities, in which CIBERSAM has collaborated or endorsed, the following stand out:

- The X Edition of the CIBERSAM Laboratory of Ideas, which was held in Reus, Tarragona, on April 20 and 21, under the theme "Challenges in Child and Adolescent Mental Health".
- The XX CIBERSAM Intensive Course on Introduction to Neuroscience Research, held in Barcelona on September 8, focused on schizophrenia and psychotic disorders.
- The CIBERSAM Instrument Bank Workshop, held in Barcelona on September 18, 2023. In addition, CIBERSAM participated in or endorsed other courses, such as:
- The 15th Edition of the Theoretical-Practical Course in Electroconvulsive Therapy in L'Hospitalet de Llobregat, March 22-24, 2023.
- The XXIV Symposium on Bipolar and Depressive Disorders in Barcelona, March 10, 2023.
- The 29th International Symposium on Controversies in Psychiatry in Barcelona, on April 20 and 21, 2023.
- The 11th Course on Statistics for Health Sciences in Barcelona, on May 5, 12 and 19, 2023.
- The 1st Course on Science Communication and Dissemination for CIBER contracted personnel in Zaragoza, held on May 25 and 26, 2023.
- The XI CIBERSAM Forum on Research in Psychiatry in Barcelona, on June 8 and 9, 2023.
- The MensSana Conference on the challenge of adolescence, bullying and suicide prevention in Granada, on September 12, 2023.
- The MensSana Conference "Bright Future: Prioritizing Mental Health in Youth" in Grenada, on September 13, 2023.
- The course on Neuroimaging: analysis and interpretation of results, from September 14, 2023 to April 11, 2024.
- The XII Course on Resistant Pathologies on October 26 and 27, 2023.
- The XXVI National Congress of Psychiatry in Salamanca, from November 23 to 25, 2023.
- The IX Meeting between Mental Health Researchers, Patients and Families, on December 12, 2023, at the Official College of Physicians of Madrid.

Another fundamental aspect of the Training axis is the Inter-University Master's Degree in Initiation to Research in Mental Health (https://www.mastersaludmental.unican.es/), which had 57 registrations in the 2023 edition. Of these, 39 students were enrolled in Type A Stay and 42 in Type B, with a total of 30 Master's Thesis presented. During this academic year, new CIBERSAM research groups were incorporated into the offer of Stays in Research Units.

PLATFORMS

OFFICIAL CIBERSAM PLATFORMS:

- **Instruments library**
- **DNA collections and biological samples**

EXTERNAL PLATFORM:

- **Collection of brains**

PLATFORMS IN REGULATION PHASE:

- **GRIDSAM**
- **Neuroimaging**

CIBERSAM's own platforms and the linked external platform have continued their trajectory as support instruments for projects and activities. The respective indicators, both in terms of their own activity and productivity, confirm a sustained trajectory over time.

The GRIDSAM platform has not developed any activity while awaiting its definitive homologation.

	INSTRUMENTS LIBRARY	DNA COLLECTIONS AND SAMPLES	NEUROIMAGING
EXISTING INSTRUMENTS	344		
ADDED INSTRUMENTS	2 new		
CONSULTATIONS OR REQUESTS FOR USE	14		9
FINANCED PUBLICATIONS	101		
TRAINING ACTIVITIES	1		
STORED IMAGES			34660
CONTRIBUTING GROUPS	3	10	5
USER GROUPS		1	2
PATIENTS INCLUDED		19352	
NEW PATIENTS		710	

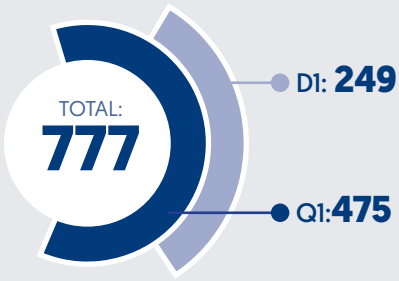
The activity of the external platform is reflected in the following indicators:

	BRAIN COLLECTION
NUMBER OF EXISTING SAMPLES (DIFFERENT SUBJECTS)	1.533
NUMBER OF NEW SAMPLES ADDED (DIFFERENT SUBJECTS)	106
NUMBER OF GROUPS USING SAMPLES	11
NUMBER OF CONSULTATIONS MADE	16
TRAINING ACTIVITIES	1

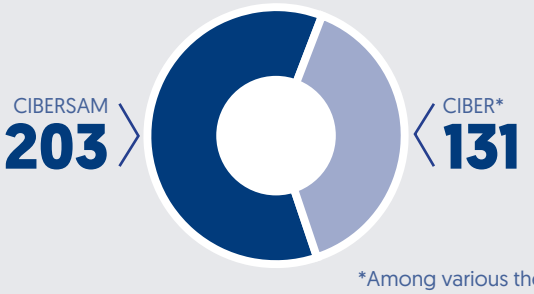
SCIENTIFIC PRODUCTION

PUBLICATIONS

No. of publications in 2023



Collaborations



*Among various thematic areas

Evolution of publications

10 most relevant publications by impact factor

IF	PUBLICATION
168,9	GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023 Jul 15;402(10397):203-234. doi: 10.1016/S0140-6736(23)01301-6. Epub 2023 Jun 22. Erratum in: Lancet. 2023 Sep 30;402(10408):1132. PMID: 37356446; PMCID: PMC10364581.
168,9	GBD 2019 Child and Adolescent Communicable Disease Collaborators. The unfinished agenda of communicable diseases among children and adolescents before the COVID-19 pandemic, 1990-2019: a systematic analysis of the Global Burden of Disease Study 2019. Lancet. 2023 Jul 22;402(10398):313-335. doi: 10.1016/S0140-6736(23)00860-7. Epub 2023 Jun 29. PMID: 37393924; PMCID: PMC10375221.
73,3	Vieta E. Tough times never last too long: the future of psychopharmacology. World Psychiatry. 2023 Feb;22(1):84-85. doi: 10.1002/wps.21066. PMID: 36640387; PMCID: PMC9840492.
73,3	Cortese S, Solmi M, Michelini G, Bellato A, Blanner C, Canozzi A, et al. Candidate diagnostic biomarkers for neurodevelopmental disorders in children and adolescents: a systematic review. World Psychiatry. 2023 Feb;22(1):129-149. doi: 10.1002/wps.21037. PMID: 36640395; PMCID: PMC9840506.
73,3	Dragioti E, Radua J, Solmi M, Gosling CJ, Oliver D, Lascialfari F, et al. Impact of mental disorders on clinical outcomes of physical diseases: an umbrella review assessing population attributable fraction and generalized impact fraction. World Psychiatry. 2023 Feb;22(1):86-104. doi: 10.1002/wps.21068. PMID: 36640414; PMCID: PMC9840513.
73,3	McIntyre RS, Alsuwaidan M, Baune BT, Berk M, Demyttenaere K, Goldberg JF, et al. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. World Psychiatry. 2023 Oct;22(3):394-412. doi: 10.1002/wps.21120. PMID: 37713549; PMCID: PMC10503923.
73,3	Fusar-Poli P, Estradé A, Stanghellini G, Esposito CM, Rosfort R, Mancini M, et al. The lived experience of depression: a bottom-up review co-written by experts by experience and academics. World Psychiatry. 2023 Oct;22(3):352-365. doi: 10.1002/wps.21111. PMID: 37713566; PMCID: PMC10503922.
73,3	Uher R, Pavlova B, Radua J, Provenzani U, Najafi S, Fortea L, et al. Transdiagnostic risk of mental disorders in offspring of affected parents: a meta-analysis of family high-risk and registry studies. World Psychiatry. 2023 Oct;22(3):433-448. doi: 10.1002/wps.21147. PMID: 37713573; PMCID: PMC10503921.
73,3	Wasserman D, Arango C, Fiorillo A, Levin S, Peters A, Rao P, et al. Improving mental health through fostering healthy lifestyles in young people: one of the targets in the WPA Action Plan 2023-2026. World Psychiatry. 2023 Oct;22(3):488-489. doi: 10.1002/wps.21146. PMID: 37713574; PMCID: PMC10503912.
64,8	Pairo-Castineira E, Rawlik K, Bretherick AD, Qi T, Wu Y, Nassiri I, et al. GWAS and meta-analysis identifies 49 genetic variants underlying critical COVID-19. Nature. 2023 May;617(7962):764-768. doi: 10.1038/s41586-023-06034-3. Epub 2023 May 17. Erratum in: Nature. 2023 Jul;619(7971):E61. PMID: 37198478; PMCID: PMC10208981.

CIBERSAM Groups, Publications in 2023

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Arango López, Celso	87	64	43	Servicio Madrileño de Salud	MADRID
Ayuso Mateos, José Luis	42	25	11	Universidad Autónoma de Madrid	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Baeza Pertegaz, María Inmaculada	82	61	34	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Berrocoso Domínguez, Esther	13	8	4	Universidad de Cádiz	CÁDIZ
Bortolozzi Biasoni, Analia	7	5	1	Agencia Estatal Consejo Superior de Investigaciones Científicas	BARCELONA
Crespo Facorro, Benedicto	40	26	17	Fundación Pública Andaluza para la Gestión de la Investigación en Salud de Sevilla	SEVILLA
Desco Menéndez, Manuel	19	11	5	Servicio Madrileño de Salud	MADRID
Fañanas Saura, Lourdes	46	26	14	Universidad de Barcelona	BARCELONA
González Pinto Arrillaga, Ana	61	32	17	Asociación Instituto de Investigación Sanitaria BIOARABA	ÁLAVA
González Torres, Miguel Ángel	16	11	9	Asociación Instituto de Investigación Sanitaria Biobizkaia	VIZCAYA
Haro Abad, Josep Maria	172	107	61	Fundación Privada para la Investigación y Docencia San Juan de Dios	BARCELONA
Ibáñez Cuadrado, Ángela	52	28	17	Servicio Madrileño de Salud	MADRID
Leza Cerro, Juan Carlos	46	27	14	Universidad Complutense de Madrid	MADRID
Meana Martínez, José Javier	33	21	9	Universidad del País Vasco	VIZCAYA
Menchón Magriña, José Manuel	29	23	12	Fundación Instituto de Investigación Biomédica de Bellvitge (IDIBELL)	BARCELONA
Nacher Rosello, Juan Salvador	33	18	11	Universidad de Valencia	VALENCIA
Olivares Diez, José Manuel	13	8	1	Servicio Gallego de Salud	PONTEVEDRA
Palao Vidal, Diego José	47	28	13	Fundación Instituto de Investigación e innovación Parc Taulí	BARCELONA
Pérez Sola, Víctor	74	45	29	Consorci Mar Parc Salut de Barcelona	BARCELONA
Pomarol Clotet, Edith	31	26	16	Fundación para la Investigacion y Docencia Maria Angustias Gimenez (FIDMAG)	BARCELONA
Ramos Quiroga, José Antonio	49	30	18	Fundación Hospital Universitario Vall d´Hebron - Institut de Recerca (VHIR)	BARCELONA
Rodríguez-Jiménez, Roberto	31	21	13	Servicio Madrileño de Salud	MADRID

GROUP LEADER	TOTAL	Q1	D1	INSTITUTION - CENTER	PROVINCE
Sáiz Martínez, Pilar Alejandra	39	25	16	Universidad de Oviedo	ASTURIAS
Tabarés Seisdedos, Rafael	28	17	12	Universidad de Valencia	VALENCIA
Vieta Pascual, Eduard	116	87	45	Fundación de Investigación Clínic Barcelona-Instituto de Investigaciones Biomédicas August Pi i Sunyer	BARCELONA
Vilella Cuadrada, Elisabet	27	16	7	Fundación Instituto de Investigacion Sanitaria Pere Virgili	TARRAGONA

Clinical Guidelines and Consensus Documents 2023

- Deep brain stimulation: approach to obsessive-compulsive disorder.
- Autism care pathway in Europe.
- Basic Quality Indicators for Clinical Care of Patients with Major Depression, Schizophrenia, and Bipolar Disorder.
- Common practical questions - and answers - at the British Association for Psychopharmacology child and adolescent psychopharmacology course.
- Consensus on pre-discharge clinical decision making in patients with schizophrenia.
- Consensus by the collective of psychiatrists for the clozapine update.
- Consensus recommendations on organization of care for individuals with Phelan-Mc-Dermid syndrome.
- Consensus recommendations on sleeping problems in Phelan-McDermid syndrome.
- Current knowledge, challenges and innovations in developmental pharmacology: A combined conect4children Expert Group and European Society for Developmental, Perinatal and Paediatric Pharmacology White Paper.
- Delphi panel to obtain clinical consensus about using long-acting injectable antipsychotics to treat first-episode and early-phase schizophrenia: treatment goals and approaches to functional recovery.
- Essential data dimensions for prospective international data collection in older age bipolar disorder (OABD): Recommendations from the GAGE-BD group.
- Assessment and clinical management of self-fharm in adolescence: evidence-based protocol.
- Functioning in older adults with bipolar disorder: A report on recommendations by the International Society of bipolar disorder (ISBD) older adults with bipolar disorder (OABD) task force.
- Clinical intervention guidelines for survivors of sexual violence.
- Guidelines to First Psychotic Episodes.
- Guidelines for victims of gender violence within the context of couples.
- Impact of the COVID-19 pandemic on the mental health of the general population and health care workers.
- Intensive and Preventive Approach to Suicidal Behavior Program (PAIPS)
- Proposed Recommendations for the Management of Depression in Adults with Epilepsy: An Expert Consensus.
- Electroconvulsive therapy (tec) protocol at the Muñoz de Cariñanos Hospital.
- Risks and benefits of clozapine and lithium co-prescribing: A systematic review and expert recommendations.
- Y ahora, ¿cómo te ayudo? (And how do I help you now?)
- Y tú, ¿sabes cómo preguntarme? (Do you know how to ask me?)

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