PCC-IISFJD
V.4

COOPERATIVE SCIENTIFIC PROJECT

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1. INTRODUCTION

The Fundación Jiménez Díaz Health Research Institute (IIS-FJD) is an institution committed to the development of scientific activity and to medium- and long-term planning aimed at optimizing available resources and achieving its strategic objectives. Its core institution is the Fundación Jiménez Díaz University Hospital (HUFJD), with the Autonomous University of Madrid (UAM) serving as its main strategic partner. To strengthen its scientific structure, the Institute brings together several complementary and synergistic research groups affiliated with other partner institutions.

Accordingly, the current structure of the IIS-FJD includes resources and research groups from the following institutions:

- Fundación Jiménez Díaz University Hospital.
- Autonomous University of Madrid.
- Infanta Elena University Hospital.
- Rey Juan Carlos University Hospital.
- General de Villalba University Hospital.
- Centre for Energy, Environmental and Technological Research (CIEMAT), Public Agency (O.A.), State-Owned Entity (M.P.).

To coordinate all activities and functions carried out within the framework of the IIS-FJD, the Institute has a long-standing tradition of strategic planning, reflected in the development of successive Strategic Plans that have enabled the organization to achieve its objectives throughout each implementation period. The IIS-FJD currently operates under its 2024–2028 Strategic Plan, which is presently being implemented and further developed. This plan serves as the roadmap for strengthening the Institute's scientific excellence, enhancing translational research, fostering innovation, and maximizing the impact of its research activities on patients and society.

In parallel with strategic planning, which defines the institutional priorities and lines of action for the coming years, the Scientific Directorate coordinates the development of a Cooperative Scientific Project (in Spanish, PPC). This document sets out the priorities and future planning of the activities carried out by all research groups that form part of the scientific structure of the IIS-FJD. The CSP describes the challenges, activities and strategic objectives of the research groups, as well as the targets to be achieved during the implementation period of the Plan, in a manner aligned with the overall Strategic Plan of the institution.

Specifically, the present IIS-FJD Cooperative Scientific Project (CSP) is structured into the following sections:

- Introduction: presentation of the Institute's planning framework in the scientific domain.
- Justification and structure of the research areas: description of the process followed to establish the current scientific structure of the IIS-FJD.
- Description of the research areas: presentation of the challenges, objectives and planned activities of the research groups for the coming years.
- Strategic research objectives: relationship between the Cooperative Scientific Project (CSP) and the Institute's overall Strategic Plan, together with a description of the scientific objectives shared by both documents.

2. JUSTIFICATION AND STRUCTURE OF THE RESEARCH AREAS

The purpose of this section of the Cooperative Scientific Project (PPC) is to describe the steps that have been taken within the IIS-FJD to achieve its current scientific structure, as well as to present the research groups that make up each of the research areas currently established within the Institute.

2.1. Process for defining and justifying the research areas

The current configuration of the IIS-FJD research areas is based on the work carried out during the development of the 2009–2013 Strategic Plan and its subsequent revisions in 2013, 2018 and 2023.

The definition of the IIS-FJD strategic research areas during the preparation of the 2009–2013 Strategic Plan resulted from a prioritization process based on the scientific activity data of the various research groups. The initial evaluation process of the research groups, aimed at assessing their scientific quality and suitability for inclusion within the IIS-FJD, was based on the following criteria:

- Previous scientific track record of the research groups.
- Active funded R&D projects and clinical trials.
- Interaction among groups.
- Strategic objectives of each research groups.

Until October 2013, the IIS-FJD was structured into seven research areas: five thematic areas and two cross-cutting areas.

This structure, described in the 2009–2013 Strategic Plan, was reviewed during the preparation of the Institute's subsequent 2014–2018 Strategic Plan. The review process began in October 2012. As a first step, updated information was collected following a methodology similar to that used in the previous assessment. Subsequently, a series of structured meetings were held between October 2012 and June 2013, involving research group leaders and scientific opinion

leaders from the IIS-FJD, together with management staff and senior executives. The purpose of these meetings was to conduct an internal strategic assessment of the IIS-FJD's capabilities and environment, and to define the strategic priorities and action plans that would guide the Institute during the following five-year period.

The proposals, including the new structure, were reviewed by the Research Committee and presented throughout 2013 to the Executive Board, the UAM Monitoring Committee, and the External Scientific Advisory Board (ESAB). These governing and advisory bodies provided recommendations, which were subsequently incorporated.

As a final outcome, a new configuration of research areas was established and approved by the Institute's highest governing body. This configuration was based on criteria related to organizational structure, scientific productivity, scientific excellence, and the multidisciplinary nature of the research groups. As a result, the number of thematic areas was reduced to four, while the two cross-cutting areas were maintained.

Subsequently, during the development of the 2024–2028 Strategic Plan throughout 2023, the participants involved in the planning process contributed to a further review of the IIS-FJD scientific structure.

Since this most recent review, all research groups and area coordinators have expressed their agreement with the current scientific structure. Consequently, no further revisions have been considered necessary to modify the IIS-FJD research areas, except for the renaming of the area previously entitled "Genetics and Genomics", which has been redesignated as "Genomics and Epidemiology."

2.2. Current scientific structure of the IIS-FJD

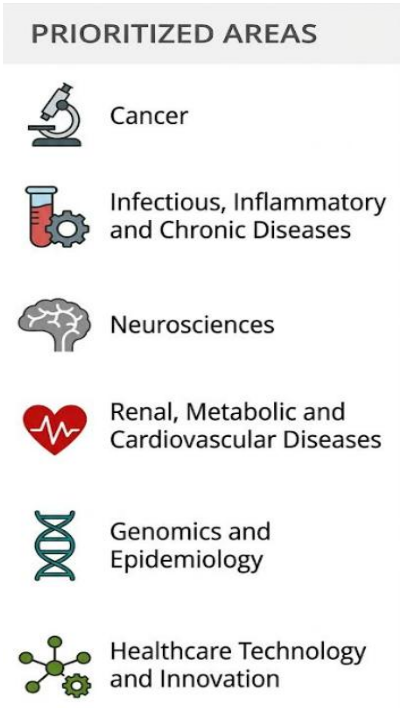
As noted above, in the 2009–2013 Strategic Plan, the structure of the IIS-FJD was organized around five thematic research areas and two cross-cutting research areas, which were prioritized on the basis of the analyses conducted during the development of the Strategic Plan.

Subsequently, based on criteria of scientific quality and strategic relevance, and as a result of changes in the composition of the research groups (including staff retirements and other developments), the Research Areas and the groups assigned to them were redefined in 2013.

In addition, in 2014, a FJD-CIEMAT Collaboration Agreement was signed, leading to the establishment of a Joint Advanced Therapies Unit headed by Dr Juan Bueren. Furthermore, an Endowed Chair was created with the research group led by Dr Marcela del Río in the field of Regenerative Medicine and Tissue Bioengineering. These proposals, which included the incorporation of new research groups, were presented to the Executive Board, the UAM Monitoring Committee, and the External Scientific Advisory Board, and were subsequently approved by the Institute's highest governing body in 2013 and 2014.

Over the following years, new research groups were progressively incorporated into the Institute, all of them aligned with the scientific areas already established. As a result, no further review or modification of the Institute's scientific structure has been required, except for the aforementioned change in the name of one research area.

Consequently, the IIS-FJD currently comprises a total of 19 research groups and 10 associated groups, organized into the following scientific areas:



CANCER AREA

- Pathological Anatomy Group.
- Medical Oncology Group.
- Haematology Group.
- Associated Groups:
    - General surgery, Thoracic surgery, Neurosurgery and Other surgical specialties Associated Group.
    - Radiation Oncology Associated Group.

INFECTIOUS, INFLAMMATORY AND CHRONIC DISEASES AREA

- Allergy and Immunology Group.
- Infectious Disease and Tropical Medicine Group.
- Microbiology Group.
- Pneumology Group.
- Rheumatology and Bone Metabolism Group.
- Associated Group:
    - Traumatology Group.

NEUROSCIENCES AREA

- Neurology Area.
- Psychiatry and Mental Health Group.
- Mitochondrial Calcium Signalling Group.

CARDIOVASCULAR, RENAL AND METABOLIC DISEASES (CRM) AREA

- Cardiology Group.
- Nephrology and Hypertension, Vascular Pathology and Diabetes Group.
- Lipid Pathology: Clinical and Experimental (adults and children) Group.

- Associated Groups:
    - Cardiac and Vascular Surgery Group.
    - Urology Group.

GENOMICS AND EPIDEMIOLOGY AREA

- Genetics and Genomics of Rare and Complex Diseases Group.
- Genetic Susceptibility to Rare and Complex Diseases Group.

HEALTHCARE TECHNOLOGY AND INNOVATION AREA

- Innovation in Ophthalmology Group.
- Medical Engineering Development and Innovation Group.
- New Therapies Research Group.
- Associated Groups:
    - Medical and Surgical Innovation Associated Group.
    - Preventive Medicine, Public Health and Primary Care Associated Group.
    - Advanced Therapies Group.
    - Regenerative Medicine and Tissue Bioengineering Associated Group.
    - Nursing Associated Group (UAM): Extracorporeal Circulation and Perfusion.

3. INTEGRATION OF THE GENDER DIMENSION INTO IIS-FJD RESEARCH

The Fundación Jiménez Díaz Health Research Institute (IIS-FJD) considers the promotion of gender equality and its integration into scientific activities carried out by its professionals to be among its strategic priorities.

To this end, the Institute has established an Equality Plan, which sets out the institution's objectives and planned actions in this area for the coming years. In line with this strategy, this section of the Cooperative Scientific Project (CSP) outlines a series of guidelines and recommendations for all IIS-FJD research groups aimed at incorporating the gender dimension into their scientific activities.

Nevertheless, the description of each IIS-FJD Research Area also includes the specific guidelines and considerations applicable to that particular area with regard to the integration of the gender dimension in research.

Guidelines for the Integration of the Gender Dimension into IIS-FJD Research

1. Before initiating any scientific activity, consideration should be given to whether the gender dimension should be incorporated into hypothesis generation and study design, ensuring that it is integrated from the outset of the research process.
2. Whenever possible, and where applicable, all research conducted by IIS-FJD professionals should consider the origin and nature of the samples used, in order to assess potential gender-related differences and perform differential analyses when discrepancies between sexes are identified.
3. In the analysis of the following types of studies, data obtained from both men and women should be taken into consideration to enable differential analyses aimed at identifying differences in outcomes that may provide added value to the conclusions reached:
    a. Genetic studies.
    b. Observational studies (including epidemiological studies).
    c. Clinical trials.

   d. Research projects involving the use of human samples, such as biomarker discovery, diagnostic methods, and related applications.

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4. CANCER RESEARCH AREA

The research groups within the Cancer Research Area carry out research activities across three complementary levels: basic research, translational (or applied) research, and clinical research. The ultimate goal of all cancer research groups is to contribute to improving disease prevention and diagnosis, while increasing cure rates and enhancing patients' quality of life. Basic research within the Cancer Area focuses on cancer biology, with the aim of identifying the molecular alterations involved in tumour development, progression, and resistance to conventional treatments that may be reversed and subsequently explored through applied research. This second stage, namely translational or preclinical research, is aimed at studying biomarkers, identifying new therapeutic targets, and evaluating novel drugs using laboratory models and molecular pathology, pharmacodynamic, and pharmacogenetic approaches.
Finally, clinical research brings together the efforts of both basic and clinical researchers, focusing on previously identified biomarkers and assessing the efficacy and safety of new treatments. The ultimate objective is to improve the diagnosis, prevention, and treatment of cancer in patients.

4.1. Structure of the Area

The Cancer Research Area is currently coordinated by Dr Federico Rojo Todo and comprises the following research groups and group leaders

Pathological Anatomy Group

Leaders: Federico Rojo Todo and Mª Socorro Rodríguez Pinilla.

Objectives:

The group focuses on two main areas of research and innovation: breast cancer and T-cell lymphomas. In both fields, the primary objectives are: 1) to identify robust biomarkers capable of predicting resistance to current therapies and, 2) To develop new therapeutic strategies to overcome resistance to first-line treatments.

Medical Oncology Group

Leaders: Jesús García-Foncillas, Javier Zenón Martín Broto and Manuel Dómine Gómez.

The primary objective of the group is to bridge basic research and clinical research in order to identify and characterize novel potential therapeutic targets and signalling pathways, mainly in small-cell lung carcinoma, colorectal cancer, pancreatic cancer, sarcomas, and melanoma. These studies are conducted using patient tumour samples, from which corresponding immunodeficient animal models are also generated to facilitate the investigation of disease mechanisms and the evaluation of new therapeutic approaches

Haematology Group

Leader: Mª Pilar Llamas Sillero.

The group pursues several complementary objectives focused on improving the efficacy and persistence of CAR-T cell immunotherapy for haematological malignancies. Its current research lines include chronic myeloid leukaemia; thrombotic and haemorrhagic disorders; lymphomas and chronic lymphocytic leukaemia (CLL); frailty assessment in elderly patients with haematological malignancies; characterization of COVID-19 in onco-haematology patients; evaluation of cardiotoxicity in lymphoma patients receiving anthracycline-based therapies; value-based healthcare through the assessment of health outcomes using PROMs (Patient-Reported Outcome Measures) and PREMs (Patient-Reported Experience Measures) in patients with haematological malignancies; and the use of digital health tools to personalize the follow-up and monitoring of onco-haematology patients.

Associated Groups within the Cancer Research Area

- General Surgery, Thoracic Surgery, Neurosurgery and Other Surgical Specialties Group. Leaders: Ángel Celdrán Uriarte, José Julio Zapatero Gaviria, Ignacio Muguruza Trueba and Ricardo Díez Valle.

  The group's activities are aimed, among other objectives, at contributing to improved knowledge, diagnosis, treatment and prevention of thoracic neoplasms, as well as facilitating the translation of these advances into clinical practice.

- Radiation Oncology Group. Head: Ignacio Azinovic.

In recent years, advances in information technology have enabled significant technological developments aimed at increasing the precision of radiotherapy treatments. These include three-dimensional imaging, automatic segmentation of organs at risk, Image-Guided Radiation Therapy (IGRT), and Surface-Guided Radiation Therapy (SGRT), all of which contribute to improving the quality of radiotherapy delivery. These advances have made it possible to administer high doses per fraction while achieving better preservation of adjacent healthy tissues, resulting in greater benefits for patients. In addition, treatment times have been significantly reduced.

4.2. Scientific objectives and future challenges

OBJECTIVES OF THE CANCER RESEARCH AREA

1. To deepen the understanding of epigenetic, genetic, transcriptomic and proteomic alterations in solid and haematological tumours.
2. To advance research into the mechanisms of resistance to current therapies, focusing both on tumour cells themselves and on the study of the immune system and the tumour stroma. This includes investigating non-coding RNA sequences, tumour metabolism, and the role of exosomes in treatment response.
3. To further elucidate tumorigenic mechanisms at the single-cell level through the use of state-of-the-art technologies.
4. To explore the use of novel bispecific agents in routine clinical practice and clinical trials
5. To advance the study and therapeutic targeting of the tumour microenvironment, including the development of new drugs and clinical trials; to explore innovative technologies and approaches for a better understanding of the tumour microenvironment; and to assess strategies aimed at modulating the pro-tumorigenic microenvironment in order to maximize therapeutic benefit.
6. To investigate, using prospective samples, tumour-cell and immune-system biomarkers capable of identifying patients who are most likely to benefit from next-generation therapies.

FUTURE CHALLENGES OF THE CANCER RESEARCH AREA

1. Development of alternative research models (humanized mice, organoids, and 3D cultures) to recreate different human tumour models across a broad spectrum of tumorigenesis stages.

2. Routine implementation of high-throughput diagnostic technologies for the diagnosis and monitoring of patients with solid and haematological malignancies, including epigenomics, next-generation sequencing, transcriptomics, and proteomics.
3. Development of novel high-throughput and minimally invasive diagnostic tools in oncology, including epigenomics, next-generation sequencing, transcriptomics, proteomics, liquid biopsy, and imaging techniques, aimed at patient stratification and disease monitoring.
4. Advancement of novel therapeutic approaches, including new drugs, bispecific agents, radiopharmaceuticals, nanoparticles, and related technologies, together with the identification of efficacy and resistance biomarkers and, where appropriate, the development of imaging techniques for treatment monitoring.
5. Development and application of artificial intelligence tools for the identification of predictors of response to innovative therapies.
6. Promotion of value-based healthcare, including the assessment of health outcomes through PROMs (Patient-Reported Outcome Measures) and PREMs (Patient-Reported Experience Measures) in patients with haematological malignancies and solid tumours.
7. Expansion of digital health technologies to enable personalized follow-up and monitoring of patients with haematological malignancies and solid tumours.

4.3. Research lines and main collaborative projects

Given that the work of pathologists is primarily focused on diagnosis, all members of the Pathology Department collaborate with members of the other research groups according to their respective areas of expertise and participate in all ongoing project. Given that the work of pathologists is primarily focused on diagnosis, all members of the Pathology Department collaborate with members of the other research groups according to their respective areas of expertise and participate in all ongoing project. The Area also participates in and promotes a total of 470 clinical trials, including 330 early-phase trials (Phase I, I/II and II) and 140 late-phase trials (Phase II/III, III, III/IV, IV and other studies).
Efforts will be made to further strengthen collaboration among the various groups within the Cancer Research Area, with the aim of increasing the number of competitive research projects, fostering the generation of patents, and enhancing knowledge transfer to industry.

To this end, collaboration with cross-cutting and research support groups will be encouraged, the acquisition of new shared-use research platforms will be promoted, and the development of multidisciplinary doctoral theses will be fostered.

4.4. Forecast of the main innovations to be developed in the coming years

The proposal of the Cancer Research Area is aligned with the main objectives of the Health, Demographic Change and Wellbeing Challenge of the Spanish Strategy for Science, Technology and Innovation, and is aimed at improving the health and well-being of patients with both solid and haematological tumour. From different perspectives, and through a variety of strategies and objectives, all research groups within the Cancer Area seek to improve current therapies for patients with different types of solid and haematological malignancies. This will be achieved by optimizing treatment efficacy through a better understanding of disease mechanisms and by developing innovative diagnostic and therapeutic tools that contribute to the strengthening of the healthcare system, the advancement of innovation, and technological development.

Expected scientific and technological contributions

1. To identify new biomarkers of resistance to targeted cancer therapies, thereby improving patient selection for treatment and contributing to the development of novel diagnostic tools.
2. To integrate the biological processes of tumours into a comprehensive ecosystem-based view that includes the patient's immune response in the prediction of the clinical efficacy of targeted and non-targeted therapies against specific therapeutic targets, thus improving the understanding of disease mechanisms.
3. To generate data providing proof of concept for new therapeutic strategies aimed at preventing or reversing resistance to current cancer treatments, thereby creating opportunities for the clinical development of treatment approaches that improve the health and well-being of these patients.

Potential effects on population's health

Cancer is one of the leading causes of death in our setting and is associated with a substantial emotional, social and economic burden. Although significant progress has been made in recent

years in understanding the biology of certain tumour subtypes, there remain orphan entities with limited response to conventional treatments and poor prognosis. Furthermore, resistance to new therapies and treatment-related adverse effects have not been eliminated, and their underlying etiopathogenic mechanisms remain poorly understood. Consequently, there is still an important unmet need to improve the identification of patients with de novo resistance, in order to minimize the use of ineffective treatments associated with toxicity and high economic costs. In these patients, we will investigate alternative therapeutic approaches aimed at overcoming treatment resistance. We will explore combinations of therapies and propose new clinical trials. Finally, we are beginning to understand that cancer is a systemic disease and that an ecosystem-based view of the tumour may help us better understand tumour response and metabolic adaptation to therapies. This knowledge will contribute to advancing precision medicine for patients with both solid and haematological malignancies.

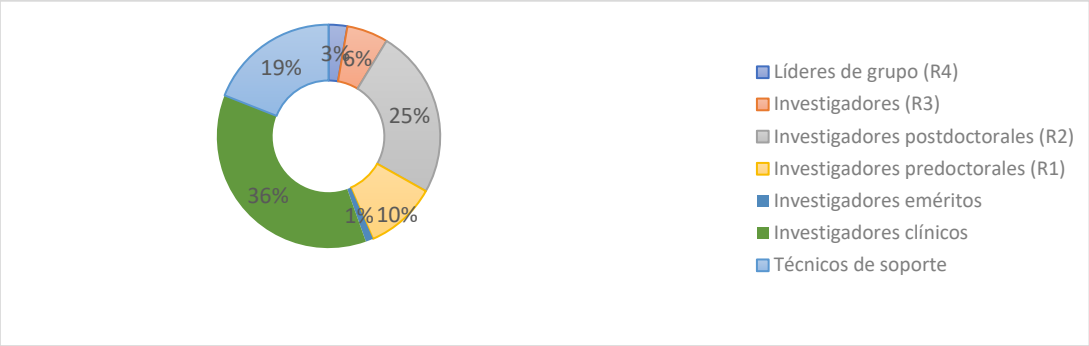
Technology transfer strategy

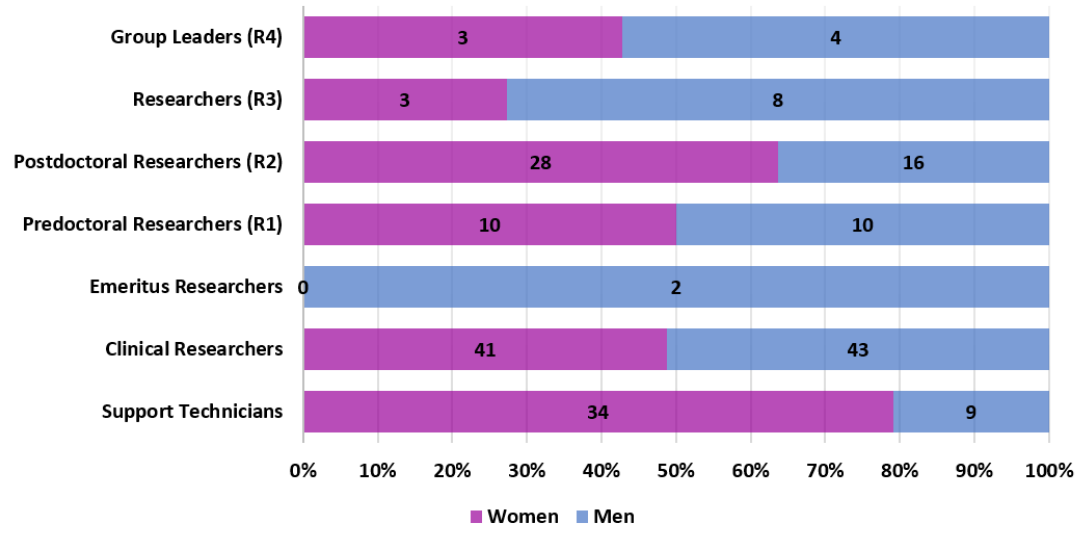
All significant advances generated within the Area will be discussed with the Technology Transfer Office of the Institute in order to support and protect results with patent potential. In recent years, four patents related to the discovery of mechanisms of resistance to cancer therapies have been filed. Two of these patents, concerning the S492R mutation and other EGFR mutations, are already being commercially exploited. In addition, the Area maintains several collaboration agreements with industry.

4.5. Integration of the gender dimension

The IIS-FJD is firmly committed to respect and equality among all its members. In this regard, one of its objectives is to uphold and promote an equal opportunities policy across all its activities, regardless of gender, ethnicity, ideology, age, sexual orientation, or religion. The Institute seeks to ensure compliance with the principles of equal treatment for women and men at all levels and to guarantee fairness in the allocation of resources and opportunities. The IIS-FJD has endorsed the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers (C&C). The Institute comprises 1,134 professionals from a variety of backgrounds, of whom 60.40% are women. The IIS-FJD includes 540 researchers corresponding to R1, R2, R3 and R4 profiles according to the European EURAXESS classification, 9 emeritus

researchers, 389 non-PhD clinical researchers, 167 scientific and technical support staff working across the different research platforms, and 29 professionals belonging to the administration and management area. A representative figure is attached.





With regard to cancer studies, it should be taken into account that certain tumours are more prevalent in one sex than the other. In these cases, an intentional effort will be made to increase the representation of the underrepresented sex, so that such differences do not bias the overall statistical results. It should also be noted that some cancers are exclusive to a particular sex, such as prostate cancer, endometrial carcinoma, and cervical carcinoma, among others

4.6. Training needs

The research groups within the Cancer Research Area have identified the following training needs:

- Researcher Training Course. The continuous acquisition of scientific knowledge, attitudes, competencies and skills by all Area professionals, including researchers, physicians and technical staff, according to their roles and levels of responsibility, will be promoted in order to ensure the quality of the priority research lines and areas defined in the present programme.
- Theoretical, practical and methodological training aimed at enabling the appropriate use of biotechnological and bioinformatics resources, as well as the application of the techniques required for the development of research activities.
- Promotion of interaction between clinical and basic scientists through the creation of a "scientific cultural community" as the foundation for translational research.

5. INFECTIOUS, INFLAMMATORY AND CHRONIC DISEASES RESEARCH AREA

The main characteristic of this Area is the broad range of diseases it addresses and its multidisciplinary nature. In general, the research lines within this Area focus on the study of the mechanisms of cellular and tissue damage and repair associated with infectious, inflammatory and chronic diseases. Among other topics of interest, the Area addresses major public health challenges, including respiratory diseases, allergic and immune-mediated disorders, infectious diseases, and musculoskeletal disorders.

5.1. Structure of the area

The Infectious, Inflammatory and Chronic Diseases Research Area is currently coordinated by Dr Victoria del Pozo Abejón and Dr Raquel Largo Carazo and comprises the following research groups and group leaders.

Allergy and Immunology Group

Leaders: Gloria Álvarez Llamas, Blanca Cárdaba Olombrada, Javier Cuesta Herranz, Victoria del Pozo Abejón, Vanesa Esteban Vázquez y Joaquín Sastre Domínguez.

Infectious Diseases and Tropical Medicine Group

Leaders: José Miguel Benito Huete, Alfonso Cabello Úbeda, Miguel Górgolas Hernández-Mora and Norma Rallón Afanador.

Microbiology Group

Leaders: Jaime Esteban Moreno, Ricardo Fernández Roblas and Ignacio Gadea Gironés.

Pneumology Group

Leaders: Germán Peces-Barba Romero and María Jesús Rodríguez Nieto.

Rheumatology and Bone Metabolism Group

Leaders: Gabriel Herrero-Beaumont, Miguel Ángel González Gay and Raquel Largo Carazo.

Associated Group within the Infectious, Inflammatory and Chronic Diseases Research Area

- Traumatology Group. Leader: Emilio Calvo Crespo.

5.2. Scientific objectives and future challenges

The objectives and future challenges of the Infectious, Inflammatory and Chronic Diseases Research Area are:

- To establish prognostic, diagnostic and disease progression biomarkers, as well as therapeutic targets, in different diseases within the Area, including infectious, allergic and asthmatic diseases.
- To investigate the pathogenic mechanisms underlying musculoskeletal diseases, particularly osteoarthritis and rheumatoid arthritis, and assess their potential therapeutic implications.
- To analyse extracellular vesicles in biological fluids and evaluate their diagnostic and therapeutic potential in various inflammatory diseases, including asthma, allergy, anaphylaxis, HIV infection and hepatitis C virus (HCV) infection.
- To define endotypes and phenotypes in allergic and respiratory diseases, including anaphylaxis, which are essential for the development of new diagnostic, therapeutic and preventive strategies.
- Development of new proteomic and metabolomic analysis strategies based on mass spectrometry, including imaging and single-cell techniques, for the identification of diagnostic and prognostic biological markers in liquid biopsy.
- Development of research projects in biomaterials, biofilms, mycobacteria, COVID-19 and bacteriophages, with a particular focus on these fields.
- Development of spatially resolved multi-omics studies to enable the *in situ* investigation of the mechanisms operating in different pathological conditions.
- Clinical research on new therapies against infectious agents, particularly HIV, HBV, and sexually transmitted infections.
- Evaluation and development of new vaccines, as well as infection models.
- Investigation of the interactions between cancer and HIV infection and their impact on the immune response.

Assessment of the burden of comorbidities associated with HIV infection and related conditions.

- Investigation of chronic inflammation associated with HIV infection.
- Identification of immune correlates of functional cure in HIV infection, using patients known as Long-Term Elite Controllers (LTECs) as a potential model of functional cure.
- Identification of mechanisms of T-cell immune response evasion as a prerequisite for improving therapeutic strategies aimed at controlling the HIV viral reservoir.
- High HCV fitness or replicative capacity as a novel mechanism of resistance to direct-acting antivirals in non-responder patients.
- Lethal mutagenesis as a new broad-spectrum antiviral strategy against highly variable RNA viruses.
- Virus-host interactions and the sequelae of infection following HCV clearance: investigation of epigenetic changes and the search for cDNA.
- Study of the active resolution of inflammation in joint diseases.
- Sarcopenia in chronic inflammatory diseases: development of therapeutic approaches based on the modulation of purinergic mediators.
- Metabolic dysfunction-associated fatty liver disease and cardiovascular risk in rheumatoid arthritis: prevalence and pathogenic mechanisms.
- Investigation of cardiovascular risk in autoimmune diseases, particularly rheumatoid arthritis, systemic lupus erythematosus, and Sjögren's syndrome. Evaluation of surrogate markers of cardiovascular disease in these patients.
- Application of artificial intelligence to ultrasound-based diagnosis in autoimmune diseases.

5.3. Research lines and main collaborative projects

Description of the main collaborative projects among the groups within the area

At present, continuous collaborations are maintained between the **traumatology** group and the **rheumatology** group. This collaboration includes several patient-related observational studies (mainly retrospective studies), as well as participation in clinical trials (DURATIOM) and competitive research projects.

An ongoing collaboration is also maintained between the **rheumatology** group and the **pneumology** group in the field of respiratory infections, particularly mycobacterial infections. This research line currently has no dedicated funding, although retrospective observational studies are being conducted.

In addition, collaboration continues between the **rheumatology** group and the **Infectious Diseases and Tropical Medicine** group on several studies, mainly observational in nature, as well as through participation in shared clinical trials such as SHORTEN-II.

A further collaboration exists between the **pneumology** group and the Allergy and **immunology** group, resulting in the creation of the Multidisciplinary Asthma Unit (UMA), which has been accredited as a Centre of Excellence and High Complexity by the Spanish Society of Pulmonology and Thoracic Surgery (in Spanish known as SEPAR) and the Spanish Society of Allergy and Clinical Immunology (in Spanish known as SEAIC).

Description of the main collaborative projects between the groups and other research areas

- Research on anaphylaxis, including the use of animal experimental models, in collaboration with the group led by Nerea Méndez-Barbero and the Experimental Surgery Unit.
- Clinical research project in collaboration with the Nephrology Department of the Fundación Jiménez Díaz University Hospital (FJD): CAR-TCD19 therapy for refractory lupus nephritis (CART-NEL). Project reference: ICI24/00034. Principal Investigator: Alberto Ortiz Arduán.
- Spain CKD Cause (SpaCKDc) (PMP21/00109), in collaboration with the group led by Alberto Ortiz Arduán. Research project on Chronic Kidney Disease (CKD) and its progression, conducted jointly with the Nephrology Department of the Fundación Jiménez Díaz University Hospital (FJD).
- Collaboration with Dr José Fernández Ferro from the Neurology Department of the Rey Juan Carlos University Hospital (HURJC) and Dr Borja Ibáñez from the Spanish National Centre for Cardiovascular Research (CNIC) and the IIS-FJD, within the framework of studies on ischaemic stroke and metoprolol.
- Collaboration with Dr Almudena Milán and Dr Diana Villacres from the Internal Medicine-Geriatrics Department of Fundación Jiménez Díaz University Hospital (HUFJD) in the study of primary sarcopenia and its treatment.

- Collaboration with the Internal Medicine, Cardiology, and Gastroenterology Departments of the IIS-FJD in the study of cardiovascular risk and lipid metabolism disorders in patients with systemic autoimmune diseases.
- Collaboration with the Genomics Group in the investigation of various aspects related to COVID-19.

Description of the Main Collaborative Projects Between the Groups and Other Institutions

- Evaluation of mechanisms triggered by the food allergens Pru p 3 and Ara h 2, and development of targeted immunotherapy, in collaboration with the Centre for Plant Biotechnology and Genomics (CBGP-UPM).
- Identification and validation of metabolites in anaphylaxis, developed in collaboration with CEU San Pablo University.
- Integration of clinical anaphylaxis and molecular data through data science approaches, developed in collaboration with Alfonso X el Sabio University (UAX) and the Health Research Institute of Hospital Universitario de La Princesa (IIS-Princesa).
- Development of preclinical models for hepatic steatosis, the use of prebiotics and probiotics, osteoarthritis, and oncological diseases, in collaboration with ITF Research Pharma, S.L.U. and Lifesome Therapeutics S.L.
- New non-invasive tools for the assessment of donor kidneys to support decision-making and increase kidney donation rates (OPTIREN). This project is carried out in collaboration with Fundación Jiménez Díaz University Hospital, Puerta de Hierro University Hospital (Madrid), Marqués de Valdecilla University Hospital (Cantabria), Clinical University Hospital of Valladolid, and Germans Trias i Pujol University Hospital (Barcelona). It is supported by the ALCER Kidney Patients Association.
- Deciphering the Metabolism of Thoracic Aortic Aneurysm through Molecular Imaging: from Silent Development to the Identification of Diagnostic Biomarkers. In collaboration with the IIS-FJD Proteomics Laboratory, the Fundación Jiménez Díaz Cardiac Surgery Department, and the Maastricht Multimodal Molecular Imaging Institute - Division of Imaging Mass Spectrometry in the Netherlands.
- Collaboration between the Infectious Diseases Group and the GIBI Group of the Complutense University of Madrid, as well as with other national groups (GEIO, GEIM, RENIM, SECOT) and international groups (ESGIAI, ESGMYC, ESGB).

- COVID-19 research conducted in collaboration with several national research groups, particularly those affiliated with the Spanish National Research Council (CSIC).
- Phage therapy, within the framework of the MePRAM personalized medicine project, in collaboration with research groups both within and outside CIBERINFEC working in this field.
- Study of functional cure of HIV infection in Spain, in collaboration with Dr Sarah Palmer from the Centre for Virus Research, The Westmead Institute for Medical Research and the Faculty of Medicine and Health, The University of Sydney School of Medicine, Sydney, Australia, and Dr Juan Carlos López Bernaldo de Quirós.
- Resistance to HIV infection in HIV-Exposed Seronegative (HESN) individuals, in collaboration with Dr Antonio Caruz, Immunogenetics Unit, Department of Experimental Biology, University of Jaén.
- Study of 3D-cultured muscle cells and the treatment of sarcopenia, in collaboration with Rey Juan Carlos University and Dr Sandra Cifuentes and Dr Joaquín Rams.
- Study of bone anabolic molecules, in collaboration with the Lead Discovery Center (Germany), led by Dr Thomas Kirmeier.
- Study of the resolution of inflammation in gout, in collaboration with Dr Enrique Calvo and the Rheumatology Group of the Infanta Leonor University Hospital, Madrid.
- Collaboration within the European Union COST Action network CA21110 - Building an Open European Network on Osteoarthritis Research (NetwOArk), a European network dedicated to osteoarthritis research.
- Application of artificial intelligence to the diagnosis of Sjögren's syndrome using ultrasound images of the parotid glands, in collaboration with the School of Engineering of the Complutense University of Madrid.

5.4. Forecast of the main innovations to be developed in the coming years

Patent applications for the diagnosis and identification of potential therapeutic targets in ascending thoracic aortic aneurysm.
Patent applications for predicting post-transplant renal function.
Development of new biomaterials, or modifications of existing biomaterials, for the treatment of infections and bone defects, which may lead to several patent applications.

Development of guidance documents on the diagnosis and management of osteoarticular infections, ranging from basic to highly applied aspects, within the framework of the Spanish delegation participating in the next Third International Consensus Meeting on Musculoskeletal Infections. The document produced during the previous consensus meeting, held in Philadelphia in 2018, has served as an international reference in this field.
Collaboration in the development of the new SEIMC Microbiological Protocol on Mycobacteria, and potentially in additional guidelines produced by this scientific society.
Evaluation of salivary biomarkers in patients with anaphylaxis.
Innovation in the treatment of anaphylaxis.
Implementation of biomarkers (non-coding RNAs) for the early diagnosis of allergic asthma in clinical practice. Efforts will be made to patent some of these findings.
Improvement of the control and eventual eradication of infectious diseases such as HIV and hepatitis. The main research lines include both basic and clinical studies, often conducted in combination, with a particular focus on HIV infection. This multidisciplinary approach offers significant opportunities for innovation in clinically relevant areas, including the development of improved treatments for HIV and the enhancement of diagnostic methods for infectious diseases. Furthermore, the recent incorporation of research on the interactions between cancer and HIV opens a promising avenue for innovation in this field.
Advancement of two expected patent applications related to the treatment of acute inflammatory diseases using pro-resolving lipid mediators, and to the modulation of the purinergic system for the treatment of muscle loss occurring in different clinical settings. Future work will focus on generating the preclinical evidence required for patent approval and on initiating clinical trials to support future licensing opportunities.
Further investigation of the molecular mechanisms responsible for hepatic lipid accumulation as a comorbidity in certain chronic systemic inflammatory diseases.
Development of artificial intelligence applications for the analysis of ultrasound images showing tissue alterations characteristic of autoimmune diseases, and evaluation of their potential use as diagnostic tools.

5.5. Training needs

- Training in the preparation and submission of European research projects.

- Experimental training courses in flow cytometry, cell culture, pathology (histology), animal experimentation, and imaging techniques.
- Training courses in data management and data science, reference management, scientific illustration and image design, statistics and bioinformatics, multi-omics technologies, and extracellular vesicle analysis.
- Development of multidisciplinary courses on biomaterial-associated infections (from basic research to clinical practice) for team members involved in this research area. In addition, seminars and courses on scientific publishing, bibliographic resources, doctoral thesis writing, and related topics are considered highly valuable.
- Statistical methods, multivariate statistics, and advanced SPSS data analysis.
- Clinical study design, according to both the purpose of the study and its temporal sequence.
- Bioinformatic analysis of omics data, including proteomics, RNA-seq, metabolomics, epigenomics, and related disciplines.
- Advanced courses in Scientific English (scientific writing and presentations), Advanced Excel, Adobe Illustrator, and GraphPad.

6. NEUROSCIENCES RESEARCH AREA

The research lines of the Neuroscience Research Area are focused on the genetic and clinical study of a variety of diseases and disorders affecting the Central Nervous System (CNS), including epilepsies (including rare diseases in which epilepsy is one of the manifestations), dementias, movement disorders, and suicidal behaviour. A research line dedicated to the development of gene therapy for Lafora disease, an ultra-rare form of progressive myoclonic epilepsy, has become firmly established within the Area. In addition, the Area includes research lines in psychiatric pharmacogenetics, suicide analysis and prevention, psychiatric care, and movement analysis in neurological and psychiatric disorder.

The more basic science-oriented researchers within these groups generate new knowledge through the study of animal models of disease (particularly Lafora disease epilepsy). This knowledge is subsequently translated to the clinical components of the groups, with the aim of identifying and developing new therapeutic strategies.

The Neuroscience Research Area works in close collaboration with the Genomics and Epidemiology Research Area, making use of shared platforms and technologies and developing joint research projects. In addition, the Neuroscience Area transfers diagnostic techniques developed through its research activities to the Genomics and Epidemiology Area for their use in routine clinical practice.

6.1. Structure of the area

The Neuroscience Research Area is currently coordinated by Dr Enrique Baca García and comprises the following research groups and group leaders.

Neurology Group

Leader: José M. Serratosa Fernández.

Psychiatry and Mental Health Group

Leader: Enrique Baca García.

Mitochondrial Calcium Signalling Group

6.2. Scientific objectives and future challenges

The future challenges of the Neurosciences area are:

- Development, validation, and implementation of systems for monitoring motor activity in neurological and psychiatric disorders, to assess the severity of the disease.
- Generation of diagnostic and therapeutic tools to improve the care and management of affected patients.
- Identification of genes involved in neurological and psychiatric disorders and their interactions with environmental factors to achieve more accurate and personalized genetic diagnosis and more effective treatment.
- Development and validation of therapeutic tools for Lafora disease epilepsy.
- Establishment of a gene therapy unit dedicated to research in animal models of neurological diseases.
- Establishment of reference units for the study of rare forms of dementia, movement disorders, and epilepsy.
- Accurate diagnosis of genetic dementias.
- Neuropharmacology and therapeutics for Parkinson's disease and movement disorders, including deep brain stimulation and the development and evaluation of novel pharmacological treatments.
- Neurogenetics of movement disorders, with a particular focus on dystonia, ataxia, and Parkinson's disease.
- Study of the factors which affect care delivery within public healthcare services for patients with mental disorders, particularly schizophrenia, affective disorders, and suicidal behaviour.
- Consolidation of the application of machine learning techniques for the analysis of genetic and healthcare databases in psychiatry.

- Investigation of the role of Ca^{2+} signals in brain metabolism, and generation of mice with tissue-specific disruption of aralar, allowing precise determination of its role and the potential treatment of epileptic seizures through a ketogenic diet.

6.3. Objectives and monitoring indicators

Objective	Indicator
Objective 1. To study the therapeutic effects of novel treatments in animal models of Lafora disease. To translate these findings into clinical practice through controlled clinical trials. To investigate the natural history of Lafora disease in order to compare the effects of different treatments in treated patients and in an untreated control population.	• Number of publications: Impact Factor (IF) and quartile ranking. • Participation in research projects: public/private and national/international. • Number of observational studies. • Number of clinical trials. • Participation in CIBER, research networks and consortia: national/international.
Objective 2. To establish registries of rare genetic epilepsies in order to assemble cohorts of patients carrying specific mutations who may be eligible for future clinical trials aimed at developing personalized treatments.	• Number of registries: national/international.
Objective 3. To characterize the phenotypes of genetic epilepsies in order to improve the clinical management and care of affected patients.	• Number of publications: Impact Factor (IF) and quartile ranking. • Number of guidelines, protocols and recommendations. • Participation in CIBER, research networks and consortia: national/international.

Objective	Indicator
Objective 4. To develop devices capable of detecting epileptic seizures and monitoring their frequency in patients' home environments.	• Number of devices under development. • Number of observational studies.
Objective 5. To investigate clinical-genetic correlations and biomarkers in familial dementias and in cognitively preserved nonagenarians.	• Number of publications: Impact Factor (IF) and quartile ranking. • Participation in research projects: public/private and national/international. • Number of clinical trials: national/international. • Number of observational studies. • Number of guidelines, protocols and recommendations. • Number of networks and consortia: national/international.
Objective 6. To identify subtypes of Parkinson's disease with distinct clinical courses and phenotypic characteristics. To investigate various aspects of Parkinson's disease, including the effects of safinamide, hypomimia, remission of parkinsonian tremor, and motor assessment using external monitoring devices.	• Number of publications: Impact Factor (IF) and quartile ranking. • Participation in research projects: public/private and national/international. • Number of clinical trials: national/international. • Number of observational studies. • Number of guidelines, protocols and recommendations.

Objective	Indicator
Objective 7. To study the factors affecting the delivery of care within public healthcare services for patients with mental disorders, particularly schizophrenia, affective disorders, substance use disorders, and suicidal behaviour.	• Number of publications: Impact Factor (IF) and quartile ranking. • Participation in research projects: public/private and national/international. • Participation in CIBER, research networks and consortia: national/international.
Objetivo 8. To investigate the role of Ca^{2+} signalling in brain metabolism and to elucidate the role of aralar and SCaMCs in human disease.	• Number of publications: Impact Factor (IF) and quartile ranking. • Participation in research projects: public/private and national/international. • Participation in CIBER, research networks and consortia: national/international.

6.4. Forecast of the main innovations to be developed in the coming years

In this Area, considerable efforts are being devoted to the validation and implementation of motor activity monitoring systems for neurological and psychiatric disorders, aimed at assessing disease severity. In addition, gene therapy based on an adeno-associated viral vector (AAV2/9) is currently being developed for the treatment of Lafora disease.

Neurology

Several projects currently underway within the Neurology Group have the potential to generate patentable results.

Some of these projects focus on the identification of novel biomarkers that may be used for the differential diagnosis of neurodegenerative diseases, such as Alzheimer's disease, as well as

biomarkers for epilepsy. Particularly noteworthy are the projects aimed at developing advanced therapies for diseases such as Huntington's disease and Lafora disease. A patent application has already been filed for the AAV2/9-CAG-hEPM2A vector, which is currently in the preclinical development phase. In addition, preparations are underway for the patent application of the AAV2/9-CAG-hEPM2B vector, thereby providing advanced therapeutic approaches targeting both genetic forms of Lafora disease.

In the future, these projects may lead to the development of new therapies for epilepsy, Parkinson's disease, and Huntington's disease, as well as novel diagnostic methods for genetic dementias.

Psychiatry and Mental Health Group

The Psychiatry and Mental Health Group is currently conducting several research projects that may lead to patentable results in the future.

Particular interest is focused on the monitoring of psychiatric disorders, especially affective disorders, schizophrenia, and substance use disorders. Among the consequences of mental illness, suicidal behaviour represents one of the group's main research lines.

The group also conducts research into the genetic and environmental factors involved in the development, progression, and treatment of mental disorders. These studies are expected to contribute to the identification of novel biomarkers, the development of innovative monitoring tools, and the implementation of more personalized diagnostic and therapeutic approaches in mental health.

In addition, the group is working on the application of machine learning techniques to the analysis of genetic and healthcare databases in Psychiatry, an approach that may have significant applications in the future.

Mitochondrial Calcium Signalling Group

A pesar de que este grupo se centra en la investigación básica, tiene algunos proyectos que pueden generar resultados prometedores.

One of the group's research lines focuses on identifying the pathophysiological mechanisms underlying diseases caused by mutations in proteins involved in calcium homeostasis in neurons, including calcium-dependent mitochondrial transporters. In addition, the group seeks to develop therapeutic approaches for these disorders. The group is currently conducting a project aimed at developing a gene therapy for citrin deficiency and is also carrying out drug screening and preclinical studies for Charcot-Marie-Tooth neuropathy.

6.5. Training needs

The research groups within the Neuroscience Research Area have identified the following training needs:

- Neuroimaging training course.
- Biostatistics training course.
- Tissue Bank training course.
- Applied Bioinformatics training course.
- Training course on the preclinical development of advanced therapies and gene therapy.

7. CARDIOVASCULAR, RENAL AND METABOLIC DISEASES (CRM) RESEARCH AREA

This strategic area is composed of three research groups and two associated groups, with strong links and collaboration among them. In fact, part of the experimental work carried out in Cardiology projects takes place in the Nephrology, Vascular Pathology, Hypertension and Diabetes laboratory. The latter is a large group comprising 16 Principal Investigators, who actively collaborate with one another as well as with other groups within both the IIS-FJD and the Fundación Jiménez Díaz University Hospital (HUFJD). This structure provides an ideal environment for the development of early-career researchers, who are mentored within this large collaborative group. The Area comprises a total of 95 researchers and maintains strong links with the Autonomous University of Madrid (UAM). In addition, the Cardiology Area has a particularly close relationship with Carlos III National Centre for Cardiovascular Research (CNIC), carrying out both experimental and clinical research projects jointly under a formal collaboration agreement.

The common objective of this research area is to deepen the understanding of the mechanisms of injury and repair in renal and urological, cardiovascular, metabolic diseases and diabetes, including those occurring from childhood onwards, with a view to identifying new molecules with diagnostic potential or therapeutic targets for patent development and their eventual clinical translation. Within this common objective, each group and subgroup focuses on specific cellular and molecular aspects (fibrosis, inflammation, apoptosis, transcription factors, intracellular signalling, cytokines, the renin-angiotensin system, etc.), specific diseases (atherothrombosis, myocardial ischaemia/reperfusion injury, idiopathic dilated cardiomyopathy, diabetic cardiomyopathy or nephropathy, glomerular disease, acute kidney injury, nephrotoxicity, renal fibrosis, etc.), or specific techniques (transcriptomics, proteomics, cardiac magnetic resonance imaging, molecular imaging, etc.), sharing methodologies and knowledge in order to accelerate discovery. In addition, there is significant activity in the clinical field, including both observational studies and clinical trials, sponsored either by industry or initiated by researchers from this and other centres.

There are numerous national and international collaborations, as well as collaborations within the institution itself, including the Pathological Anatomy Group, Haematology Group, Medical Oncology Group, Clinical Biochemistry Group, Infectious Diseases Group, Immunology Group, Microbiology Group, Rheumatology and Bone Metabolism Group, Orthopaedic Surgery and

Traumatology Group, Mineral and Bone Metabolism Group, Digestive Surgery Group, and Intensive Care Medicine Group.

7.1. Structure of the area

The Renal, Metabolic and Cardiovascular Diseases Research Area is currently coordinated by Dr Alberto Ortiz Arduán, Dr Carmen Gómez-Guerrero, and Dr Carmen Garcés Segura, and comprises the following research groups and group leaders.

Cardiology Group

Leaders: José Tuñón Fernández and Borja Ibáñez Cabeza.

Nephrology and Hypertension, Vascular Pathology and Diabetes Group.

Leaders: Luis Miguel Blanco Colio, Jesús Egido de los Ríos, Beatriz Fernández Fernández, Carmen Gómez-Guerrero, Emilio González-Parra, Óscar Lorenzo González, José Luis Martín Ventura, Alberto Ortiz Arduán, Adrián Mario Ramos Cortassa, Marta Ruiz Ortega, María Dolores Sánchez Niño, Ana Belén Sanz Bartolomé and Clotilde Vázquez Martínez.

Lipid Pathology: Clinical and Experimental (adults and children)

Leaders: Leandro Soriano Guillén and Carmen Garcés Segura.

Associated Groups within the Renal, Metabolic and Cardiovascular Diseases Research Area

- Cardiac and Vascular Surgery Associated Group. Leaders: Gonzalo Aldámiz-Echevarría Castillo and César Aparicio.
- Urology Group. Leader: Carmen González Enguita.

7.2. Scientific objectives and future challenges

Objectives and monitoring indicators

Objective	Indicator
Objective 1. The common objective of the research area is to deepen the understanding of the mechanisms of injury and repair in renal and urological, cardiovascular, metabolic diseases and diabetes, including those occurring from childhood onwards.	• Number of publications: maintain or increase the number of publications. • Number of research projects and clinical trials: maintain or increase the number of research projects and clinical trials. • Total number of researchers: maintain or increase the overall number of researchers. • Transferability of results: number of patents and innovation projects submitted. • Dissemination of results: quantify the number of press releases produced.
Objective 2. To study the cellular and molecular mechanisms involved in the pathogenesis of specific diseases.	
Objective 3. To apply different techniques for the identification of novel molecules with diagnostic or therapeutic potential, as well as other types of biomarkers.	
Objective 4. To discover and develop, at the preclinical and/or clinical level, new risk-monitoring and therapeutic approaches for clinical application in the prevention and/or treatment of these diseases.	

Future challenges

The future challenges of the Renal, Metabolic and Cardiovascular Diseases Research Area are:

- To address the pathogenesis and treatment of the cardiovascular-kidney-metabolic syndrome in a holistic manner, with the aim of improving population health, and specifically:
    - To improve the prognosis of kidney diseases through the development of new diagnostic and risk stratification tools and novel therapeutic strategies.
    - To improve the prognosis of metabolic diseases through the development of new diagnostic and risk stratification tools and novel therapeutic strategies.

- To improve the prognosis of cardiovascular diseases through the development of new diagnostic and risk stratification tools and novel therapeutic strategies.
- To implement new therapeutic strategies and Health Outcomes Assessment approaches in Urology.
- To implement a precision medicine programme for the treatment of obese adolescents.

7.3. Current collaborations

The groups that make up the Renal, Metabolic and Cardiovascular Diseases Research Area maintain an extensive network of collaborations with other research groups, institutions, and research infrastructures. The following sections describe the synergies established by the research groups within the Area.

Cardiology Group

The group participates in several projects at both the national and international levels. The major clinical trials led by the group are primarily scientifically driven, although the group also participates in trials related to the pharmaceutical industry.

The group leads major European consortia funded by the European Commission through the Horizon 2020 (H2020) programme. Particularly noteworthy are the European projects ERC-CoG "MATRIX" and the health-related H2020 project "RESILIENCE. The latter is coordinated by the group, in collaboration with other hospital departments (Haematology), and involves institutions from six European countries, as well as the European Society of Cardiology, Philips, and a patient association. The group also has a prominent role in another H2020 Health Programme project, RITA-MI2.

The group leads the largest clinical trial in the world evaluating the benefit of beta-blockers in patients with myocardial infarction and preserved cardiac function (REBOOT trial), involving more than 8,000 patients in Spain and Italy. In the field of basic research, the group also participates in European projects such as "BioClotAD", coordinated by Dr Marta Cortés Canteli under the Joint Programming on Neurodegenerative Disease Research (JPND), a joint initiative

of the European Union and the Carlos III Health Institute (ISCIII) within the framework of international joint programming projects. This consortium uses state-of-the-art molecular imaging technologies to develop a radiotracer capable of non-invasively identifying the procoagulant state associated with Alzheimer's disease. Borja Ibáñez serves as editor of several scientific journals, including the high-impact journal Journal of the American College of Cardiology (JACC), and leads a research group within the CIBER Cardiovascular Diseases Network (CIBERCV).

Nephrology and Hypertension, Vascular Pathology and Diabetes

The group maintains multiple national and international collaborations within the framework of projects funded by the National Plan, the European Union, and working groups within national and international scientific societies. In this context, the IIS-FJD coordinates the ISCIII Kidney Research Network (formerly RETIC REDINREN, currently RICORS2040), whose objective is to prevent the projected increase in kidney disease-related mortality in Spain by 2040.

Lipid Pathology: Clinical and Experimental (adults and children)

1. Puberty Group of the Spanish Society of Paediatric Endocrinology.

2. Nutrition Group of the Spanish Atherosclerosis Society.

3. Spanish Society of Adolescent Medicine.

4. Prof. Ana Claudia Latronico, **University of São Paulo, Brazil. Pioneer group in research on the molecular basis of precocious puberty.

5. Prof. Alejandro Lomniczi, Division of Neuroscience, Oregon National Primate Research Center/OHSU, USA. This group is a world leader in epigenetic studies of nutrition and puberty in experimental animal models.

Cardiac and Vascular Surgery Associated Group

The development of the group's activities requires close collaboration among cardiac surgeons, cardiologists, biomedical engineers and other healthcare professionals in order to improve the effectiveness and safety of surgical interventions in the cardiovascular field.

Ongoing projects:

- Collaborators in the NOMA Study: Multicentre, randomized, placebo-controlled, parallel-group, dose-finding clinical trial to evaluate the safety and efficacy of the intramuscular administration of allogeneic adipose tissue-derived mesenchymal cells in diabetic patients with critical limb ischaemia who are not candidates for revascularisation. Principal Investigator: Dr García Olmo. Collaborators: C. Aparicio and A. González.
- Collaborators in the PLIANT II Registry on iliac branch device outcomes. Collaborators: César Aparicio Martínez, Alejandro González García and Ana Arribas Díaz.
- Best Utility Model Award, Young Inventor Category 2023, granted by the Spanish Patent and Trademark Office (OEPM) to Ciro Baeza Bermejillo for utility model U202032664: Fenestrated endoprosthesis for arterial repair equipped with a fenestration positioning guide.

Moreover, the group collaborates with professionals from other medical institutions and academic centres to share knowledge and resources, thereby contributing to overall progress in the field of cardiac and vascular surgery: César Aparicio Martínez: Associate Professor of Surgery, Faculty of Medicine, Complutense University of Madrid; Tomás Bolívar Gómez: Associate Professor of Surgery, Faculty of Medicine, Rey Juan Carlos University; Gala Fernández Martín Forero: Associate Professor of Surgery, Faculty of Medicine, Alfonso X el Sabio University; Ciro Baeza Bermejillo: Professor of Anatomy, FJD School of Nursing (UAM); Alejandro González García: Teaching Collaborator in Surgery, Faculty of Medicine, Complutense University of Madrid; Ana Begoña Arribas Díaz: Teaching Collaborator in Surgery, Faculty of Medicine, Complutense University of Madrid; Ciro Baeza Bermejillo: Teaching Collaborator in Surgery, Faculty of Medicine, Complutense University of Madrid.

Urology Associated Group

The group seeks to identify active projects, develop new research lines, and expand its collaboration network in order to improve knowledge of genitourinary disorders and enhance patient care.

The group currently collaborates with independent researchers, research groups, universities, and scientific societies, such as:

- The Advanced Therapies Group of the IIS-FJD in the development of innovative therapies for urological conditions such as urinary incontinence and erectile dysfunction, with two research projects in the field of regenerative medicine.
- The Spanish Urological Association (AEU). Through the AEU Multicentre Studies Research Platform, the group acts as sponsor of the national registry entitled "Adjustable Sling Treatment for Male Post-Surgical Stress Urinary Incontinence in Spain" and also participates as a collaborating investigator in several uro-oncology research projects.
- The Foundation for Research in Urology (FIU), through a clinical study focused on the treatment of high-risk non-muscle-invasive bladder tumours with BCG Moreau RJ immunotherapy as prophylaxis against recurrence and disease progression.
- The European Uro-Oncology Group (EUOG), through participation in a non-commercial Phase II clinical trial on the management of upper urinary tract urothelial carcinoma.
- UNICANCER, Health Cooperative Group (Groupement de Coopération Sanitaire-GCS in the clinical trial ALBAN: An open label, randomized, phase III trial, evaluating efficacy of Atezolizumab in addition to one year BCG (Bacillus CaLmette- Guerin) bladder instillation in BCG-naïve patients with high-risk non-muscle invasive Bladder cANcer".
- The VHL Alliance (Spanish Alliance of Families with von Hippel-Lindau Disease). The group collaborates through the donation of primary renal tumour cell cultures for the identification of biomarkers in patients with von Hippel-Lindau disease.
- The Latin American Renal Cancer Group (LARCG). The group collaborates in an international registry of renal tumours.
- The Department of Pharmacology and Therapeutics, Faculty of Medicine, Autonomous University of Madrid (UAM). Since 2008, the group has participated in several research projects (4) related to surgically donated adrenal glands, two of which have been funded by the Ministry of Economy and Competitiveness during the last ten years.

The Department of Urology also collaborates with the Oncology and Nephrology Departments of the HUFJD through the donation of samples for the following studies and research projects:

- Study: Multi Omics Data Cancer Diagnostics Therapies (TITANIA Study).
- Study: FJD-ENBIBA: EUROPEAN NEPHRECTOMY BIO-BANK.

7.4. Forecast of the main innovations to be developed in the coming years

Cardiology

Several projects currently underway may generate promising results. Among them is a European H2020 project that will be carried out over the next four years. The project is focused on the strategic area of cardiotoxicity associated with cancer treatments and is based on the development of new mitochondria-targeted therapies. Should the results prove successful, they may be subject to future patent applications.

In the coming years, joint developments will also be undertaken with companies and with other research centres such as the CNIC. The outcomes of these research activities may likewise become the subject of intellectual property protection in the future.

Nephrology and Hypertension, Vascular Pathology and Diabetes

Based on previous experience in obtaining patents related to novel biomarkers and therapeutic approaches in kidney disease, diabetes, and their cardiovascular complications, it can be anticipated that the coming years will continue to yield advances in the fields of biomarkers and new treatments with the potential to change clinical practice. Some of these patents are currently in the national validation phase in various countries, have entered into licensing agreements with companies, or are under negotiation. In order not to compromise future patent applications, other more advanced results with patent potential cannot be disclosed at this time. Furthermore, work is underway on the use of big data for the prevention and early diagnosis of diseases within the Area, which may have an immediate impact on routine clinical practice, particularly with regard to the gender perspective.

Building on two of the group's patented technologies, two collaborative projects are being developed in partnership with the Carlos III National Centre for Cardiovascular Research (CNIC) under the titles “Biomarkers of Subclinical Atherosclerosis” and “Treatment of Subclinical

Atherosclerosis". The results of these projects may have commercial exploitation potential in the coming years.

Lipid Pathology: Clinical and Experimental (adults and children)

The research group is currently conducting several projects that may lead to new inventions and promising results with potential for industrial protection and commercial exploitation. Among these projects, particular emphasis is placed on the study of genetic determinants of obesity and insulin resistance in the paediatric population, an international project based on genetic testing and phenotypic characterization of paediatric and adult individuals with severe obesity, and a study aimed at analysing the exposome of obese children and adolescents.

Associated Group

Urology

The Urology Group has several research lines that may lead to patentable results. Some of these lines include:

- Uro-oncology, in which projects related to testicular cancer are being developed in collaboration with other institutions such as the Spanish National Cancer Research Centre (CNIO). The group also has other active projects related to bladder cancer and prostate cancer.
- Functional Urology: characterization of the urinary and vaginal microbiome. Other research lines focus on overactive bladder syndrome, urinary incontinence, and recurrent urinary tract infections.

In the coming years, the group intends to develop research lines focused on the study of biomarkers and imaging techniques aimed at optimizing the diagnosis and treatment of oncological diseases, as well as promoting prospective studies to evaluate new surgical techniques across different areas.

Therefore, the results obtained from the projects currently underway, as well as those arising from new research lines, may be subject to industrial property protection and may have an impact on the market.

7.5. Integration of the gender dimension

The Area follows the IIS-FJD guidelines on promoting gender equality in scientific activities, both in the composition of research groups and in the conduct of research studies. A large proportion of the Area's research projects and clinical trials incorporate the gender dimension into their objectives and methodological design, as well as the differential analysis of data whenever gender-related differences are identified.

7.6. Training needs

The research groups within the Renal, Metabolic and Cardiovascular Diseases Research Area have identified the following training needs:

- Training in the use of Turnitin.
- Annual or biannual induction course for new researchers, similar to the programme provided for medical residents (in Spanish known as MIR), covering the structure and functioning of the IIS-FJD, as well as the use and interpretation of shared equipment, including quantitative analysis platforms, flow cytometers, and other common research facilities.

8. GENOMICS AND EPIDEMIOLOGY RESEARCH AREA

The GENOMICS and EPIDEMIOLOGY Research Area conducts its scientific activities in the pathophysiological, cellular, and molecular characterization of rare and common genetic diseases, as well as in the epidemiological analysis of these conditions and of infectious diseases. The Area is involved in the design, development, and validation of diagnostic tools, techniques, and algorithms, as well as new therapeutic and preventive strategies with clear clinical applicability. Its objectives include both its own research goals and a series of cross-cutting objectives, aimed at providing methodological support and specialized expertise to the other research groups and research areas within the Institute

8.1. Structure of the area

The Genomics and Epidemiology Research Area is currently coordinated by Dr Carmen Ayuso García and comprises the following research groups and group leaders.

Genetics and Genomics of Rare and Complex Diseases Group

Leaders: Carmen Ayuso García and Marta Cortón Pérez.

Genetic Susceptibility to Rare and Complex Diseases Group

Leader: Javier Santos Hernández.

8.2. Scientific objectives and future challenges

Specific objectives

1. To advance knowledge of the molecular basis of rare and complex diseases.
2. To develop algorithms for the analysis and interpretation of omics data through the application of Bioinformatics and Systems Biology.
3. Translation of biotechnology into postnatal diagnosis and prevention of genetic diseases through prenatal and reproductive diagnosis in different fields, including

ophthalmology, paediatrics, neurology, hereditary cancer, cardiology, nephrology, and others.

4. Development of therapeutic approaches based on pharmacogenetics (PGx), cell and gene therapies, and molecular targets.
5. Development of new experimental and innovative approaches, including single-cell studies and mosaicism analysis; long-read whole-genome sequencing (WGS) and optical genome mapping; validation of diagnostic kits for repeat expansion disorders; and new developments in NIPT and PGT-M/PGT-A.
6. To continue the automation of healthcare-associated infection surveillance, including through the use of artificial intelligence and other advanced technologies.
7. To develop tools that enable the dynamic measurement of healthcare coverage rates.

Cross-cutting objectives

1. Identification of genetic determinants and gene-environment interactions (GxE) in rare and common diseases (neurological, psychiatric, oncological, and cardiovascular) for the implementation of so-called genomic or personalized medicine.
2. Promotion of training and dissemination of the principles of Good Research Practice.
3. Analysis and implementation of organizational, ethical, and regulatory aspects in Genomics, Big Data, and Artificial Intelligence.

The research lines of the Genetics and Genomics of Rare and Complex Diseases Group are focused on the genetic, clinical, and epidemiological study of a wide range of hereditary and chromosomal disorders, with a strong translational component From a strategic perspective, the validation and implementation of new high-throughput sequencing technologies constitute a priority objective due to their direct applicability in clinical diagnosis, as well as their potential as experimental tools supporting the molecular characterization of multiple physiological and pathological processes. These technologies enable genetic diagnosis and genetic counselling for malformations and monogenic and genomic diseases throughout all stages of life, including preconceptional, embryonic, and fetal stages (particularly through prenatal testing using non-invasive techniques), as well as postnatal stages, including predictive genetic testing.

A crucial aspect is the analysis, harmonization, and implementation of new technologies (NGS and Artificial Intelligence) within an appropriate ethical and regulatory framework, enabling

both the primary and secondary use of omics information and health data for the generation of new knowledge (research) and the improvement of healthcare processes and patient care.

The Genetic Susceptibility to Rare and Complex Diseases Group focuses on the characterization of the genetic and epigenetic alterations underlying the origin and development of T-cell lymphoblastic neoplasms (T-LBL and T-ALL). The group analyses both the coding genome and the non-coding genome, with the aim of improving the diagnosis and prognosis of these diseases and proposing new targeted therapies based on the potentially pathogenic alterations identified through genomic analyses, within the framework of personalized precision medicine.

In 2024, a change to the IIS-FJD Structure of Areas and Research Groups was approved. Consequently, from 2025 onwards, the Genetics and Genomics Area will be renamed the Genomics and Epidemiology Area and will incorporate the Preventive Medicine, Public Health and Primary Care Group, which will be transferred from the Healthcare Technology and Innovation Area.
This change has been approved by both the Research Committee and the External Scientific Advisory Board of the IIS-FJD and, therefore, this new denomination has been incorporated into the present Cooperative Scientific Project document.

Future challenges

- Integration of basic (functional genomics and proteomics) and translational aspects: development, validation and harmonization of diagnostic techniques, as well as the discovery of new therapeutic targets.
- Molecular basis and Epidemiology of Rare and Complex Diseases: identification of new mechanisms, genes/loci and variants involved in genomic-based human diseases. Hidden genetic bases of disease, including cancer, cardiovascular disease, and neurodegeneration; Inherited Retinal Dystrophies, Intellectual Disability and Neurodevelopmental Disorders, and Ocular Malformations.
- Research into therapies applicable to genetic diseases: pharmacogenomics (PGx), pharmacological therapies, and novel therapeutic approaches, including gene therapy and gene editing (CRISPR/Cas9).

- Translation to clinical practice: development of diagnostic algorithms and clinical protocols/guidelines for rare and complex diseases:
    - New experimental approaches: single-cell and mosaicism studies; NIPT and PGT.
    - Development and validation of bioinformatics tools and algorithms for the reanalysis of undiagnosed cases, the evaluation of emerging technologies, and their translation into clinical practice.
        - Validation of NGS procedures (quality assurance, report format, panel and algorithm definition, and WES implementation).
        - Assessment of the scientific and societal impact of our research activities.
- Harmonization of regulatory and ethical aspects related to the use of genomics and health data within the Institute, as well as at national and international levels.
- Promotion of activities related to research ethics, the principles of scientific integrity, and good research practices.
- Development of epidemiological studies related to Healthcare-Associated Infections (HAIs) and hospital-relevant microorganisms (multidrug-resistant microorganisms and public health alerts), as well as communicable diseases.
- Evaluation of vaccination coverage among immunocompromised patients receiving care at our hospital.
- Assessment of impact in terms of disease burden and quality of life.

8.3. Research lines and main collaborative projects

INTERNATIONAL CONSORTIA AND PROJECTS:

Beyond 1 Million Genomes (ELSI), ERDC, Aniridia-Net Cost Action, Optic Atrophy-OPA8, GoOD.2) CIMBA (Consortium of Investigators of Modifiers of BRCA1/2), MERGE (Male Breast Cancer Genetics Consortium). International projects: NEXOME (Rivolta Lausanne University). WGS Easigenomics. Others: UCL, Oxford-University, INSERM, Semmelweis University, Hungary, EMQN (European Molecular Quality Network).

NATIONAL CONSORTIA:

IMPaCT-Genómica (WP1; Ético-legal, WP3; Data sharing, WP4; Cancer, IMPaCT-Data, IMPaCT Vuscan, TransBioNet, GEICAM (Spanish Breast Cancer Research Group), CLASSIFI_ER, GRUPOS DE TRABAJO-CIBERER: Bioinformatics (P. Mínguez), MODALT-EERR (MCortón), RNA Therapies (C. Ayuso), RNA-Seq (C. Ayuso), Secondary Genomic Findings (C. Ayuso), Epi-ENOD; Epigenomics (B. Almoguera), SpadaHC (Spanish variant database for hereditary cancer).

COLLABORATIONS WITH OTHER IIS-FJD GROUPS:

Nephrology and Hypertension, Vascular Pathology and Diabetes; Medical and Surgical Innovation; Advanced Therapies; Preventive Medicine, Public Health and Primary Care; Epidemiology and Biostatistics Unit; Pathology; Rheumatology and Bone Metabolism; Innovation in Ophthalmology; Medical Oncology; New Therapies Research; Haematology; Infectious Diseases and Tropical Medicine; Information Systems; Allergy and Immunology; Microbiology; Mitochondrial Calcium Signalling; Neurology; Lipid Disorders: Clinical and Experimental Research (Adults and Children).

8.4. Forecast of the main innovations to be developed in the coming years

Research lines with the potential to generate promising results over the next five years include:

1. Implementation of third-generation genomic analysis tools (Nanopore).
2. Incorporation of Systems Biology and Bioinformatics into the molecular characterization of undiagnosed rare diseases.
3. Integration of genomic data into electronic health records for clinical application, availability, and potential reuse to address future patient needs.
4. Incorporation of Big Data approaches, combining genomics with patients' clinical and demographic information, within the framework of genomic precision medicine.
5. Application of genomic, bioinformatics, and Artificial Intelligence techniques to common diseases.
6. Incorporation of emerging therapies into the management of monogenic diseases (EERR).

The Preventive Medicine, Public Health and Primary Care Group, which will be incorporated in future years, has several research lines. However, the line with the greatest potential for

generating patentable results is that focused on the epidemiology of infectious diseases, including vaccine-preventable diseases and vaccinology, as well as the epidemiology of HIV/AIDS. This research line is supported by several ongoing projects from which significant results are expected to be obtained in the coming years.

8.5. Integration of the gender dimension

The Genomics and Epidemiology Area is composed of a team of professionals committed to respect and equality among its members and seeks to promote the professional development of all its staff without discrimination on the grounds of gender or age.

8.6. Training needs

The research groups within the Genomics and Epidemiology Research Area have identified the following training needs:

- General training:
    - International Conference on Translational Research and Precision Medicine.
    - Annual CIBERER Meeting and Annual Meeting of the CIBERER Neurosensory Disorders Programme.
    - Training courses organized by CIBERER.
    - IIS-FJD Biomedical Seminars.
    - Training activities on Scientific Integrity: currently, an annual workshop is held. As a future need, it would be advisable to establish a structured training pathway for early-career researchers.
    - Good Clinical Practice (GCP) Course (biennial).
- Specific training:
    - Master's Degree in Genetics of Rare Diseases (Faculty of Medicine, Autonomous University of Madrid, Madrid).
    - Master's Degree in Bioinformatics Applied to Personalized Medicine and Health (National School of Public Health, Carlos III Health Institute, Madrid).
    - Genetics Department sessions and seminars (held weekly).

- 1–2 workshops/seminars with patients.
- A course on the analysis and interpretation of omics experiments is planned (IIS-FJD Bioinformatics Unit, every two years).

9. HEALTHCARE TECHNOLOGY AND INNOVATION RESEARCH AREA

This cross-cutting strategic area was created primarily around the application of new healthcare technologies for diagnosis and innovative treatments.

The specific objectives of this Area are directed, on the one hand, towards the development and implementation of new technologies related to the optimization of intraocular implants and the study of hereditary and degenerative eye disorders, as well as the diagnosis and treatment of dysphagia, the development of cochlear implants, and prognostic tools for chronic hepatitis. On the other hand, the Area focuses on understanding the mechanisms involved in the development of acute lung injury and kidney injury associated with sepsis, with the aim of designing new therapeutic strategies and identifying and characterizing biomarkers.

The cross-cutting nature of this Area has facilitated collaboration with other specialties and research groups, particularly Nephrology, through joint work on the development of new therapies for renal proteinosis; Haematology, through studies on the immunogenicity induced by vaccines in haematological malignancies; and Pulmonology, which is part of CIBERES and collaborates with the Intensive Care Medicine Group on research into mechanical ventilation. Likewise, the Ophthalmology Group maintains close links with the Genetics Group in the study of the hereditary aspects of ocular disorders

9.1. Structure of the area

This cross-cutting strategic area is composed of three established research groups and four associated groups and was created primarily around the application of new healthcare technologies for diagnosis and the implementation of innovative treatments.
The Area is composed of the following groups, which share a common goal: to translate research into clinical practice:

- Innovation in Ophthalmology, headed by Dr Ignacio Jiménez-Alfaro Morote.
- New Therapies Research: headed by Dr Damián García Olmo, Dr Carlos Cenjor Español, and Dr Mariano García Arranz.
- Development and Innovation in Medical Engineering, headed by Dr Eduardo Large Negro.

Associated Groups:

- Medical and Surgical Innovation, headed by Dr Dolores Martínez Pérez, Dr Luis Enrique Muñoz Alameda, Dr César Pérez Calvo, Dr Juan Carlos Porrés Cubero, and Dr Margarita Varela Morales.
- UAM Nursing: Extracorporeal Circulation and Perfusion, headed by Dr María Eva García Perea.
- Advanced Therapies (CIEMAT), headed by Dr Juan Bueren Roncero.
- Regenerative Medicine and Tissue Bioengineering (CIEMAT-UC3M), headed by Dr Marcela del Río.

9.2. Scientific objectives and future challenges

Scientific objectives

The scientific objectives of the different groups within the Area are focused on the search for new treatments derived from experimental studies. Among these objectives, the following are highlighted:

Innovation in Ophthalmology Group:

Develop Big Data systems in ocular diseases. Develop a cell therapy trial in inflammatory ocular pathology. Search for biomarkers for uveitis. Investigate the use and improvement of intraocular lenses and intracorneal ring implants in ocular diseases. Establish phenotype-genotype correlations in inherited retinal and choroidal diseases.

Medical Engineering Development and Innovation Group:

Develop Big Data systems in ocular diseases. Develop a cell therapy clinical trial for inflammatory eye diseases. Identify biomarkers for uveitis. Investigate the use and improvement of intraocular lenses and intracorneal ring implants in ocular diseases. Establish genotype-phenotype correlations in inherited retinal and choroidal diseases.

New Therapies Research Group:

Preclinical study in a porcine model of the ADSC secretome for perianal fistulizing disease in the context of Crohn's disease. Clinical trial for the treatment of complex perianal fistulizing disease using exosomes derived from mesenchymal stem cells. Study of mSEPT9 in rectal cancer, including its validation as a prognostic marker and as an objective monitoring tool within the Watch and Wait programme. Preclinical porcine trial for the treatment of intraluminal tumours using collagenase lavage. Clinical safety trial of treatment with peritoneal collagenase prior to

HIPEC in patients with pseudomyxoma. Randomized study on the need for nasal packing in septal and turbinate surgery and its impact on quality of life. Randomized study aimed at the rational use of antibiotics in septal and turbinate surgery.

Medical and Surgical Innovation Group:

Potential association of Molar-Incisor Hypomineralization with other congenital dental anomalies. Clinical study of the effect of O_2 saturation alterations in patients admitted to the Intensive Care Unit (ICU). Monitoring of the treatment of post-surgical neuropathic pain. Analysis of tumour progression and its relationship with regional anaesthesia.

Advanced Therapies Group:

Development of innovative therapies for diseases with a poor prognosis. Development of new treatments through gene therapy for hereditary diseases. Preclinical gene therapy studies based on a therapeutic strategy involving genome editing. In the field of regenerative medicine based on stem cell therapies, development of a clinical trial using genetically modified mesenchymal cells for the treatment of graft-versus-host disease.

Regenerative Medicine and Tissue Bioengineering Associated Group:

Development of tissue engineering models for the treatment of epithelial lesions and biotechnological applications. In vivo correction of skin disorders through gene editing using adenoviral vectors. Clinical trial with MSCs for the treatment of chronic wounds (EudraCT 2019-004637-16). Aptamer-based pharmacological therapy for epidermolysis bullosa and chronic ulcers. Manufacture of Advanced Therapy Medicinal Products (bioengineered epithelia) according to the A-in-D production system.

Nursing Associated Group (UAM):

Extracorporeal Circulation and Perfusion: comprehensive training of students and preparation for the competent professional practice of advanced clinical practice and research in extracorporeal circulation and perfusion, across all areas of application, thereby improving, through this advanced practice knowledge, the quality of care and patient safety provided to individuals requiring these techniques.

Future challenges

- Develop Big Data systems in ocular diseases to improve diagnosis and generate new therapies.
- Develop a cell therapy clinical trial for inflammatory eye diseases.

- Develop a clinical trial for the treatment of perianal fistulizing disease using exosomes derived from MSCs.
- Develop a wound-healing model and its treatment using the ADSC secretome. Proposal of a clinical trial.
- Study/characterization of the ADSC secretome. Development of a porcine model of perianal fistula and subsequent submission of a clinical trial proposal.
- Validation of mSEPT9 in pancreatic tumours.
- Clinical trial with ADSCs for the treatment of urinary incontinence.
- Clinical trial with collagenase as an adjuvant to HIPEC.
- Completion of follow-up in the Phase I/II gene therapy clinical trials for Fanconi Anaemia A and LAD-I (Leukocyte Adhesion Deficiency Type I).
- Phase II gene therapy clinical trial for erythrocyte pyruvate kinase deficiency.
- Development of preclinical gene therapy studies for new hereditary diseases.

9.3. Research lines and main collaborative projects

The main collaborative projects between groups within the area are:
In vitro studies aimed at generating new therapies for inflammatory eye diseases.

- Clinical trial for the treatment of pemphigoid using cell therapy.
- Validation of the secretome and exosomes derived from adipose tissue-derived mesenchymal stem cells for the treatment of perianal fistulizing disease.
- Prognostic and therapeutic value of Septin 9 gene methylation in rectal and pancreatic diseases.
- Effect of collagenase as an adjuvant treatment in patients with pseudomyxoma, as well as its use in the treatment of peritoneal adhesions.

The main collaborations with groups from other areas are:

- Clinical trial using cell therapy for female urinary incontinence.
- Use of the Biow system to improve sleep in post-surgical patients.
- CAR-T cell therapy for patients with haematopoietic tumours.
- Phase I/II gene therapy clinical trials in Fanconi Anaemia A and LAD-I.
- Clinical trial using “artificial skin” in patients with complex wounds.

The main collaborations with other institutions are:

- Preclinical and clinical studies conducted in collaboration with groups belonging to the RICOR Advanced Therapies Network of the Carlos III Health Institute (ISCIII). Among the preclinical studies, notable examples include porcine models of peritoneal sepsis using fucosylated cells generated by the University of Murcia, and a subcutaneous wound model using mesenchymal cells generated at CIEMAT. Among the clinical trials, notable studies include the NOMA (NO More Amputations) trial, ARTROCELL (for the treatment of osteoarthritis), and the CELOPHIN trial for the treatment of pemphigoid, in addition to several compassionate-use programmes, all of them based on cells produced through the RICORS platform.
- Preclinical and clinical studies in collaboration with different ISCIII CIBER networks (CIBERER and CIBERES).
- Collaboration with the Spanish Wound Society in the development of new treatments. A clinical trial for the treatment of hard-to-heal wounds is currently being conducted by two groups from our Area together with the cell production facility of HUNJ.
- TAKEDA: study of the effect of cell therapy in the microenvironment of perianal fistulas. Our groups participate in a European consortium funded by Takeda to analyse the enzymes, proteins, bacteria, etc. present in the fistula microenvironment in order to determine the cause of cell therapy failure in some patients.
- EVOMED: development of an enzymatic treatment system as an adjuvant to HIPEC in peritoneal carcinomatosis. Clinical trial. A patent has been generated and licensed to EVOMED, and we are currently holding meetings with the Spanish Agency of Medicines and Medical Devices (AEMPS) for the approval of the first clinical trial.
- H2020 project for the optimisation and development of a clinical trial for faecal incontinence using cell therapy (CT). All stability studies have been completed with the final product associated with cells and nanoparticles. The clinical trial for faecal incontinence will begin in 2025.
- ISCIII RICORS Project. National Network for Advanced Therapies (TERAV). Participation in 4 publicly funded clinical trials.
- PEACHES for the generation of secretome derived from mesenchymal cells under GMP conditions and its future clinical use. Murine and porcine preclinical models have been generated and developed to support the clinical trial application before the Spanish Agency of Medicines and Medical Devices (AEMPS).

- JUSTA S.A. for the analysis of porcine and equine secretome. A dossier has been generated for its use in cosmetics, analysing secretome derived from MSCs at different cell passages and under different preservation systems.
- Histocell for the production of mesenchymal cells for the urinary incontinence clinical trial. Public funding has been obtained for our Institute to act as sponsor of a clinical trial for female urinary incontinence.

9.4. Forecast of the main innovations to be developed in the coming years

Among the patents and products expected to be developed and brought into clinical use during this period, the following may be highlighted

- Patents developed: Chemical Scalpel (US 2022/0047687, EU 23 193 298.9); licensed to Combat Medical. New treatment for adhesions (EU 20713699.5). New application of the secretome derived from modified cells (pending acceptance by the EU); co-filed with Peaches Biotech.
- Clinical trials: Treatment of perianal fistulas using secretome and/or exosomes derived from MSCs. Treatment of anal incontinence using myocytes associated with nanoparticles. Treatment of pseudomyxoma using HIPEC with adjuvant intraperitoneal collagenase pretreatment. Treatment of urinary incontinence using mesenchymal cells. Treatment of pemphigoid using MSCs.
- Clinical applications: Development and use of CAR-T cells for the treatment of haematopoietic tumours. Treatment of patients with pyruvate kinase deficiency or Fanconi anaemia through gene therapy.
- Development of training courses through the OPEREMOS programme.

9.5. Integration of the gender dimension

The Healthcare Technology and Innovation Area is composed of a team of professionals committed to respect and equality among its members and aims to promote the professional development of all its staff without discrimination on the grounds of gender or age. Likewise, the conditions targeted by the proposed preclinical and clinical studies are not gender specific.

Finally, it should be noted that both sexes are represented across all groups within the Area, with more than 55% of studies being led by women, and with women accounting for more than 55% of the personnel involved in the development and execution of the research activities

9.6. Training needs

The research groups within the Healthcare Technology and Innovation area have identified the following needs:

- Access to software to identify the most suitable journal for publication, as well as specific training courses on the software used by our Institute to calculate the percentage of text plagiarism.
- Development of a regulatory support system to facilitate the translation of newly developed treatments into clinical practice through clinical trials.
- Recruitment of a data manager to support the documentation and monitoring of the clinical trials that will be proposed.
- Optimization of a patient sample collection system to prevent sample loss and reduce the time required from research team members. It is necessary to establish a Standard Operating Procedure (SOP) and ensure that all personnel involved receive the appropriate training.

10. STRATEGIC RESEARCH OBJECTIVES

The IIS-FJD has a long-standing track record in defining medium- and long-term strategies, reflected in the development of Strategic Plans and Cooperative Scientific Projects. These documents establish the Institute's strategic objectives and indicators, including those specifically related to research.

Throughout 2023, work was carried out on the preparation of the new IIS-FJD Strategic Plan for the 2024–2028 period, which includes the following strategic objectives:

1. SCIENTIFIC ACTIVITY. Promote SCIENTIFIC EXCELLENCE through the generation of synergies and integration among the Institute's research groups, providing the necessary space, infrastructure, and resources.
2. TRANSLATION AND INNOVATION. Foster innovation and its TRANSFER TO THE PRODUCTIVE SECTOR, and orient research towards improving clinical practice.
3. PARTNERSHIPS AND INTERNATIONALISATION. Consolidate the INTERNATIONAL positioning of the Institute's groups, as well as EXTERNAL AND INTERNAL COLLABORATIONS, supported by a network of contacts and partners that drive their scientific development.
4. SUSTAINABILITY. Strengthen relationships with PUBLIC FUNDING AGENCIES and the PRIVATE SECTOR, consolidating stable lines of collaboration that enable funding in the medium and long term.
5. TRANSPARENCY AND QUALITY. Improve management procedures within the Institute in order to facilitate its activities, enhance outcomes, and maintain and strengthen its position in OPEN SCIENCE and in the POLICY of scientific integrity.
6. KNOWLEDGE. Consolidate the scientific culture within the organisation by improving the training and COMMUNICATION of professionals, promoting dissemination to SOCIETAL STAKEHOLDERS, and fostering engagement with citizens.

To fulfil these objectives, the IIS-FJD has defined and is currently implementing different action plans, encompassing all the activities to be undertaken by the institution within the framework of this Strategic Plan. In the vast majority of these action plans, a number of research objectives have been defined, which are measured and reviewed on an annual basis.

The indicators most directly related to scientific activity within the IIS-FJD are presented below (excluding economic activity indicators and those of an institutional or management nature).

ACTION PLAN	INDICATOR	OBJECTIVE
1.1. Scientific Plan	% of publications in which an IIS author is the lead author.	20%
	Publications arising from publicly funded projects published in Open Access during the evaluation period.	50%
	Number of Principal Investigators (PIs) with active collaborative, national, or international projects.	60
	Normalized citation rate during the evaluation period.	1
1.2. Human resources policy development plan	Number of Principal Investigators (PIs) with an R2 profile (Juan Rodés, etc.) or an R3 profile (Miguel Servet, Ramón y Cajal, etc.) according to the European EURAXESS classification.	30%
1.3. Consolidation plan for high-potential research communities	Number of IIS researchers conducting health care research.	25
	Number of associated Principal Investigators (PIs).	
1.4. Integration plan for external research groups	Percentage of publications co-authored by researchers from at least two institutions or entities that form part of the IIS	5%
	Percentage of publications co-authored by researchers from different IIS research groups.	5%
2.1. Clinical research promotion plan	% increase in non-commercial clinical studies.	15%
	% increase in commercial clinical studies.	10
2.2. Research results translation enhancement plan	Research results generated within the IIS that have been translated into clinical practice, at least in the healthcare centres that form part of the IIS (during the last 5 years).	5
	Number of industrial property registrations/know-how licences, or number of intellectual property licences, or number of newly licensed medical products or devices during the last 5 years.	2

ACTION PLAN	INDICATOR	OBJECTIVE
2.3. Clinical translation plan for academic research groups	Volume of publications involving collaboration by clinical researchers.	50%
	Volume of competitive public research projects involving collaboration by clinical researchers.	60
3.1. Internationalisation promotion plan	Number of projects funded through competitive European public funding calls during the last 5 years	1 out of 10 IP.
	% of publications with internal collaboration.	20%
3.2. Collaboration plan with other institutions and networks	Number of groups participating in legally recognized cooperative research networks or consortia.	12
3.3. Primary care integration promotion plan	Percentage of IIS researchers who are Primary Care personnel.	5% (or 30)
4.1. Public funding acquisition promotion plan	Projects awarded through competitive national public funding calls during the last year.	= previous year
	Success rate of projects submitted to competitive national public funding calls during the last year.	20%
4.2. Private funding acquisition promotion plan	% of funding, both competitive and non-competitive, derived from public funds.	50%
5.4. Data management, omics and open science plan	% of publications (original articles and reviews) published in Open Access journals, relative to the annual total.	50%
	% of projects with competitive national and/or international public funding in which at least one submission has been made to open-access data repositories.	50%
6.1. Scientific training plan	Number of researchers in training, classified as R1 according to the EURAXESS framework.	20
6.3. Corporate image consolidation plan	Percentage of publications produced during the last year by IIS researchers that include the IIS affiliation.	95%
6.4. Social stakeholder participation plan in IIS-FJD activities.	% of projects in which key non-scientific stakeholders have participated in the design and development of the project during the last 2 years.	10%

The remaining IIS-FJD indicators and objectives are set out in the Institute's Strategic Plan for the 2024–2028 period.