ANNUAL REPORT 20

Josep Carreras
LEUKAEMIA
Research Institute

ANNUAL REPORT / **2020**

President of the Board of Trustees

After three decades of work, we are facing a new challenge. We have to improve patients' quality of life but, above all, we must find a definitive cure for leukaemia. In 2010, therefore, the Josep Carreras Foundation, together with the Catalan Government (*Generalitat de Catalunya*), launched a historic and unprecedented project: the first European research centre devoted exclusively to leukaemia and other malignant blood diseases, and one of the few in the world.

The Josep Carreras Leukaemia Research Institute is a centre without precedent which, through the work and rigour of researchers from around the world, employs the most innovative technologies to gain the upper hand against this disease. That leukaemia will one day be a totally curable disease is now something that lies in the hands of clinical and basic researchers working for this purpose "

The Josep Carreras Leukaemia Research Institute is a monographic and multi-campus institute dedicated to promoting, developing, transferring, managing and disseminating research, scientific and technological knowledge, teaching and training in the field of leukaemia and other haematological malignancies.

Its mission consists in research into the epidemiological, preventive, clinical, translational and basic aspects of leukaemia and other haematological malignancies. Its vision is to become a research institute of national and international reference and its objectives are as follows:

- To understand the origin and development of leukaemia and other haematological malignancies
- To identify new therapeutic targets and apply increasingly more precise and less aggressive treatments
- Try to cure these diseases in 100% of cases.

The progress of the Institute is the result of a collective effort in which we all participate together, always keeping in mind that our best capital is human capital and that our main objective is the well-being of patients, increasing their quality and quantity of life.

Josep Carreras

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FOREWORD

Dr. Manel Esteller
Director
Josep Carreras Leukaemia Research Institute

We will always remember 2020 for the COVID-19 global health crisis, one of the biggest challenges we have faced in the recent times. In response to this crisis, the scientific community from all over the world joined its efforts to fight against the pandemic.

This year has been a good example of international collaboration in research, perhaps one of the greatest efforts ever made by the scientific community: joining forces worldwide from bioinformaticians, virologists, immunologists, geneticists, biochemists, cell biologists, pharmacologists… everybody lend a hand to understand the SARS-Cov-2 virus and the COVID-19.

The Josep Carreras Leukaemia Research Institute aims to promote biomedical research and the development of personalized medicine against Leukemia. This year, we went further to help in the area of coronavirus research, analyzing the relationship between Covid-19, leukemia, lymphoma and immunotherapy. This additional and coordinated effort has been possible thanks to the development and application of advanced genomic, proteomic and epigenomic analysis, used for different aspects of clinical and health sciences, such as biomarker discovery or drug target identification, among others.

At the Josep Carreras Leukaemia Research Institute, we are committed to this titanic effort and the increasing number of research groups (35 research groups in 2020) allows us to maintain a stable research structure and to have a qualified and well-trained generation, with access to reference laboratories and the appropriate technology, who will provide the answers to the future health challenges.

Sincerely,

ABOUT US / **WHO WE ARE**

The **Josep Carreras Leukaemia Research Institute** is a non-profit research institute based in Badalona (Barcelona), dedicated to biomedical research and personalized medicine in leukaemia and other malignant blood diseases. It conducts excellent research into the basic, epidemiological, preventive, clinical and translational aspects of leukaemia and other haematological malignancies.

The Josep Carreras Leukaemia Research Institute, directed by **Dr. Manel Esteller**, was launched in 2010 by the **Josep Carreras Foundation**, together with the **Catalan government**, and is the first European research centre devoted exclusively to leukemia and other malignant blood diseases.

Research efforts are imperative to provide patients with high-quality healthcare, and our specialists combine their extensive knowledge to focus on patients' needs. **Our aim is to understand the origins and development of leukaemia and other malignant haematological pathologies** with a view to their prevention, and **our efforts are directed towards identifying new therapeutic targets and developing effective treatments with fewer side effects** through cutting-edge research.

Given our efficient governance, the Josep Carreras Leukaemia Research Institute is a *Catalan Research Centre of Excellence* and forms part of the Catalan government's current research centre network. It is also accredited by the Spanish Ministry of Health as a *Health Research Centre of Excellence* and by the Spanish Association Against Cancer. The Institute also holds the *HR Excellence in Research Award* from the European Commission.

The ultimate goal of our interdisciplinary team is to ensure that leukaemia is a curable disease in all cases, and we won't stop until we have achieved this.

The Josep Carreras Institute is a **collaborative hub for basic and translational researchers** who work together on the fundamental biological and clinical aspects of leukaemia at our

state-of-the-art facilities, which provide an excellent work environment and serve as a magnet for outstanding researchers from all over the world.

It is home to 34 research groups and an increasing number of associated clinicians from five independent, coordinated scientific campuses: Hospital Clínic-UB Campus, Sant Pau Campus, Can Ruti Campus, Mar Campus and the Trueta Campus. Our laboratories on those clinical campuses allow us to collaborate closely with clinicians from the five associated hospitals: Hospital Clínic, Hospital de Sant Pau, Hospital Germans Trias i Pujol. Hospital del Mar and Dr. Josep Trueta Hospital.

ABOUT US / **MISSION, VISION AND VALUES**

MISSION

The Josep Carreras Leukaemia Research Institute's mission is to carry out research into the epidemiological, preventive, clinical, translational and basic aspects of leukaemia and other malignant blood diseases through innovation, with the ultimate aim of finding a cure.

VISION

The Josep Carreras Leukaemia Research Institute's vision is to be a world-renowned, multi-campus research centre of excellence that contributes towards improved outcomes and a cure for patients suffering from leukaemia and other malignant blood diseases through innovation, sustainability, social responsibility, talent and professional expertise.

VALUES

Altruism, in accordance with the Josep Carreras Foundation's principles

A close, patient-centred approach

Staff commitment

Corporate alignment of the three campuses and the Foundation

Participative scientific leadership

Continuing cooperation and the forging of alliances with stakeholders

Integration of research and healthcare

Continuous improvement and perseverance as a way of working

Conceptual, methodological and technological innovation

Management dynamics that respect the environment

Continuous evaluation and accountability

Efficacy and efficiency in the optimization of resources

Transparency and integration with the fabric of society

ABOUT US / **GOVERNING BODIES**

The highest governing body is the Board of Trustees, which is represented by the Josep Carreras Foundation, the Catalan government's Ministry of Business and Knowledge, the Catalan government's Ministry of Health, the Autonomous University of Barcelona (UAB), the University of Barcelona (UB), Badalona Town Council, the Directorate General for Health Research and Planning, the Catalan Institute of Oncology, the Northern Metropolitan Territorial Area Administration, the Catalan Foundation for Research and Innovation, Hospital Clínic / the August Pi i Sunyer Biomedical Research Institute (IDIBAPS), the UB Hospital Coordination Committee and the Research Centres of Catalonia Institution Foundation (iCERCA).

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University of Barcelona Hospital Coordination Committee

Domenec Espriu Climent – since 02.10.2020
University of Barcelona Hospital Coordination Committee

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Lluís Rovira Pato,
Director of the Research Centres of Catalonia Institution Foundation (iCERCA)

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Evarist Feliu Frasnedo, Coordinator of the ICO-Germans Trias i Pujol Campus since 15.07.2020, *ombudsman* of the Josep Carreras Leukaemia Research Institute

Members

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Joan Gómez Pallarès, Director General of Research of the Ministry of Business and Knowledge for the Generalitat, Government of Catalonia

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Francisco Ciruela i Alférez, Delegat of the Vice-chancellor of the University of Barcelona (UB) until 02.10.2020

Domenec Espriu Climent, vice-rector of research at the University of Barcelona since 02.10.20

Antoni Garcia i Prat, Managing Director, International Josep Carreras Foundation

Lluís Rovira i Pato (secretari), Director of the Institution CERCA of the Generalitat, Government of Catalonia

EXTERNAL SCIENTIFIC COMMITTEE

President

Prof. Lucio Luzzatto, Nigerian Haematology Association until early 2020

Prof. Francesco Lo Coco, Tor Vergata University of Rome since early 2020

Members

Prof. Robert Sackstein, Dana-Farber/Harvard Cancer Center in Boston

Prof. Francesco Lo Coco, Tor Vergata University of Rome

Prof. Alberto Orfao, Salamanca Centre for Cancer Research (CIC).

Prof. Brigitte Schlegelberger, University of Hanover

Prof. Maria Luisa Toribio Garcia, Centro de Biologia Molecular Severo Ochoa in Madrid, since 15.07.2020

Prof. Christoph Plass, German Cancer Research Center in Heidelberg, since 15.07.2020

Prof. Lucio Luzzatto, Nigerian Haematology Association

INTERNAL SCIENTIFIC COMMITTEE

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Lurdes Zamora Plana

José Tomás Navarro

Juan Manuel Sancho Cía

Sant Pau Campus

Javier Briones Mejide Campus Coordinator

Josep F. Nomdedeu Guinot

Joan Carles Souto Andrés

Ramon Mangues Bafalluy

Carol Moreno Anastasio

ABOUT US / **DIRECTOR**

Dr. Manel Esteller

Dr. Manel Esteller is Chairman of Genetics at the University of Barcelona's Faculty of Medicine and an ICREA Research Professor. Since May 2019, Dr. Esteller has been the Director of the Josep Carreras Leukaemia Research Institute. Dr. Esteller is considered to be among the top 0.1% of world scientists based on impact by Stanford University (METRICS). He is also a member of numerous international scientific societies and his work has been recognized by numerous awards, including the World Health Summit Award (2010), the Rey Jaime I Research Award (2013), the National Award in Oncology (2014), the Dr. Josep Trueta Medal from the Catalan government (2015), the National Research Award from the Catalan government (2015), the Gold Medal from the Parliament of Catalonia (2016), the International Award of Catalonia (2016), the Innovation in Healthcare Oncology Award (2018), the Narcís Monturiol Medal from the Catalan government (2020) and the Fernández-Cruz Award for excellence in biomedical research (2021).

Institut de Recerca
CONTRA LA LEUCÈMIA
Josep Carreras

ABOUT US / **DIRECTORS - SCIENTIFIC COORDINATORS**

Prof. Manel Esteller
Director

Prof. Evarist Feliu
President of the Delegate Committee

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Dr. Josep Maria Ribera
Clinical Research Vicedirector

Dra. Anna Bigas,
Basic Research Vicedirector

Dr. Albert Oriol
Applied Research Director

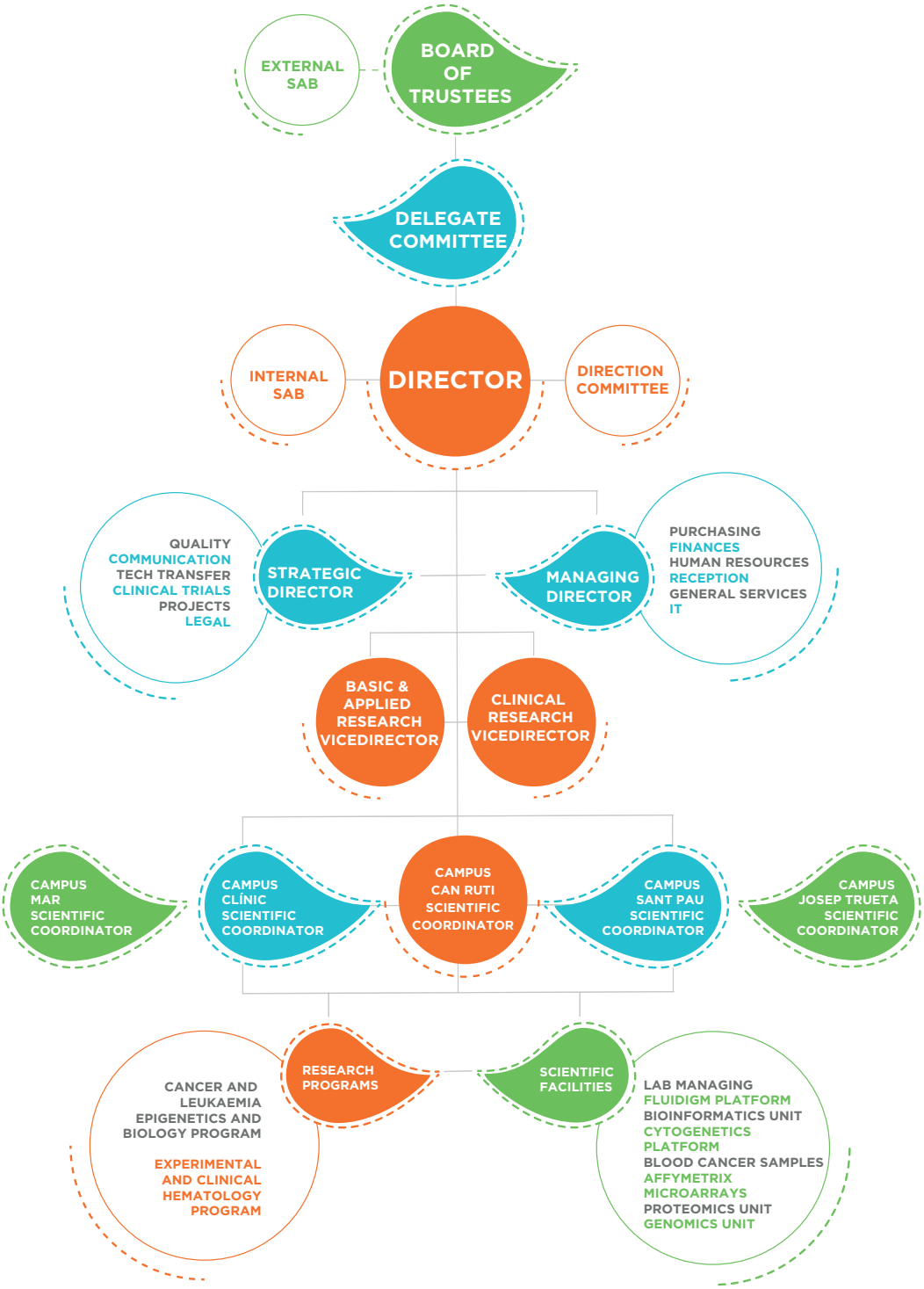
Dr. Francesc Solé Ristol, Can Ruti Campus Coordinator

Dr. Jordi Esteve Reiner
UB Clinic Campus Coordinator

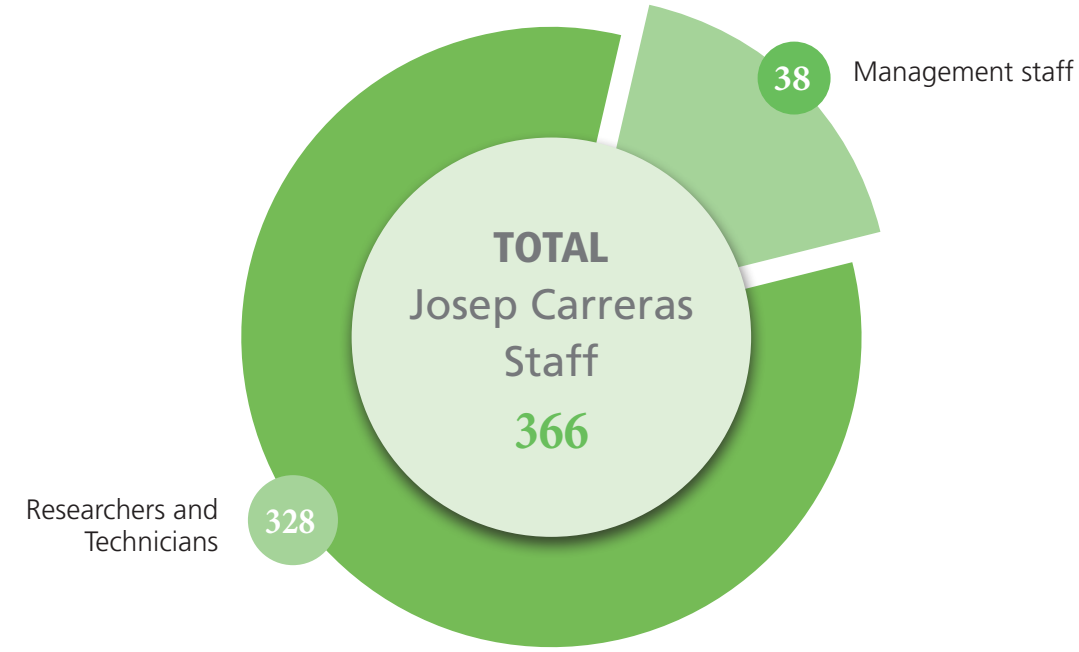
Dr. Javier Briones Mejide, Sant Pau Campus Coordinator

Dr. Rafael Marcos
Epidemiological Research Director

ABOUT US / **ORGANIZATIONAL CHART**



ABOUT US / **OUR STAFF**



Contracted
Josep Carreras Institute

2019	153
2020	195

Ascribed
Group Leaders

2019	18
2020	20

Ascribed
Clinical Staff

2019	99
2020	151

*Data updated in December 2022 due to improvements in institutional databases.

RESEARCH PROGRAMS

Our **35 research groups** study from fundamental science to the development of new treatments and diagnostics and are divided into two programs: the ***Cancer and Leukemia Epigenetics and Biology Program*** and the ***Experimental and Clinical Hematology Program.***

The groups of the **Cancer and Leukemia Epigenetics and Biology Program (PEBCL)** are:

15 groups

1. Cancer epigenetics
2. Cancer genetics
3. Chromatin biology
4. Chromatin, metabolism and cell fate
5. 3D chromatin organization
6. Epigenetics and immune disease
7. Lymphocyte development and disease
8. Regulatory genomics
9. Regulatory RNA and chromatin
10. Epigenetic control of haematopoiesis
11. Transcriptional dynamics in leukemia
12. Stem cells and cancer
13. Leukemia and immuno-oncology
14. Cancer heterogeneity and hierarchies
15. Cancer Immunogenomics

The groups of the **Experimental and Clinical Hematology Program (PHEC)** are:

20 groups

16. Acute lymphoblastic leukemia (ALL)
17. Barcelona endothelium team (BET)
18. Functional cytomics
19. Myeloid neoplasms
20. Immunohematology and glycobiology
21. Leukemia stem cell
22. Lymphoid neoplasms
23. Multiple myeloma
24. Myelodysplastic syndromes
25. Stem cell biology, developmental leukemia and immunotherapy
26. Stem cell transplantation and cellular immunotherapy
27. Epigenetic therapies
28. Lymphoma translational
29. Oncogenesis and antitumor drugs
30. Cellular immunotherapy and gene therapy
31. Hematological diseases, transplant and cell therapy
32. Descriptive and analytical epidemiology of cancer
33. Hematological diagnosis
34. Chronic lymphocytic leukemia
35. Hematology research

RESEARCH GROUPS

Cancer and Leukemia Epigenetics and Biology Program (PEBCL)

1

CANCER EPIGENETICS

Led by

Manel Esteller

Group members

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Research Associate

Blecua Carrillo Albornoz, Pedro
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Musulén Palet, Eva
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Esteve Puig, Rosaura
Postdoctoral Fellow

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Ferrer Aguilar, Gerardo
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PhD Student

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Popov, Anton
PhD Student

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Lab Technician

Aledón Andújar, Laila
Lab Technician

Overview

Malignant cells behave differently to the rest of the tissue; they present capacities reserved for stem cells, such as proliferation. Since all cells in an organism share the same genetic information, the difference between any cell type, including malignant cells, lies in the subset of information to which they have access. The term epigenetics refers to the many control layers that limit a cell's access to only those parts of the genome relevant to its organic function.

Our research

Our group aims to understand the fundamental epigenetic and epitranscriptomic mechanisms that act in living cells, such as DNA methylation and histone modification patterns and gene expression regulation through microRNAs. These mechanisms do not affect the cell's genetic information, only its availability, and its alteration may mark the beginning of abnormal behaviour. Malfunction of epigenetic control is one of the most poorly understood causes of human tumours and knowledge of this phenomenon is key to developing new strategies against tumour formation and cancer.

Our goals

To shed light on this emerging field, the Cancer Epigenetics group focuses on:

1. Defining the epigenome of cancer cells. The ability to identify the epigenetic differences, either on DNA or RNA, between a healthy cell and a transformed cell represents the starting point for our research. Knowledge of this area is fairly limited and our lab is currently carrying out intense research in this field.

2. Study of the epigenetic machinery and mechanisms. We are interested in understanding the role and function of DNA methyltransferases, the large group of proteins directly responsible for interacting with DNA and shaping the open or closed transcriptional state.

3. Use of epigenetic markers to predict response to antitumour therapies. Our group has a long-standing interest in translating the use of epigenetic knowledge gained from research into biomarkers to predict clinical outcomes.

4. Preclinical testing of epigenetic compounds. We are interested in the development and study of new epigenetic drugs that target DNA methylation and histone modification writers, readers and erasers, and that could exert an anti-cancer effect.

Our challenges

Cancer remains a horrible disease, and all new biomarkers and innovative approaches to treat the disorder are necessary and welcome additions. Our research has had an impact on the clinical outcome of several tumour types, from brain tumours to cancer of unknown primary, including subsets of leukaemia and lymphoma patients. Discovering the particular epigenetic and epitranscriptomic characteristics of each cancer type may help deliver personalized therapies to oncology patients.

Through our research, we hope to answer the following questions:

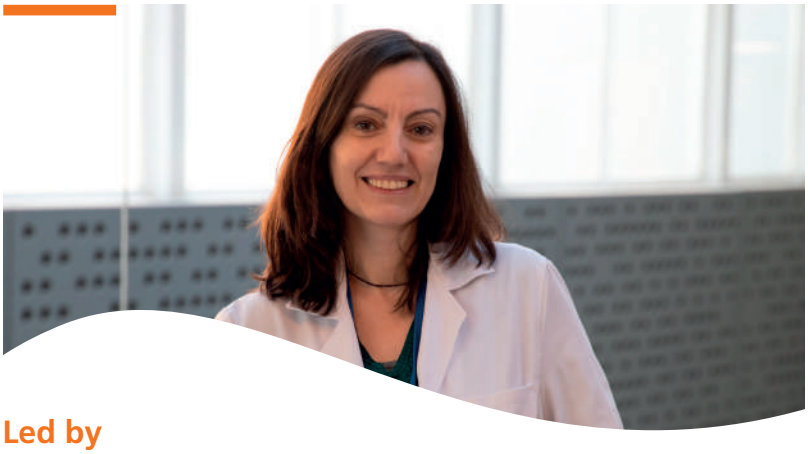
1. Will the epigenome map lead to a better understanding of cancer and guide global research to make this disease curable?

2. How can we transfer epigenetics research to prevent cancer and improve clinical management with a view to improving patients' quality of life?

3. Is there an ultimate epigenetic signalling pathway and context that can explain any cancer?

Keywords
Cancer epigenetics; DNA methylation; RNA epitranscriptomics; histone modification; epigenetic gene silencing.

2 CANCER GENETICS



Led by
Montse Sánchez-Céspedes

Group members

Sánchez-Céspedes, Montse
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Postdoctoral Fellow

Saigí Morguí, Maria
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PhD Student

Pros Simón, Eva
Lab Technician

Bartolessis Arias, Isabel
Lab Technician

Overview

Lung cancer causes over 1.3 million deaths annually and remains the deadliest type of cancer worldwide. Although efforts in recent years to fully characterize human cancer on a genetic and molecular level have provided important insights to increase our understanding of the gene alteration profile underlying the development of Lung Cancer, the impact of this knowledge in the survival of patients remains modest. Our group is devoted to the genetic, epigenetic and molecular study of the mechanisms that drive LC development. Ultimately, our purpose is to implement the clinical management of cancer patients and to design novel therapeutic strategies.

Our research

The complete genetic characterization of tumours is important to understand cancer development, promote the discovery of new drugs and improve the selection of patients that may benefit from a given cancer therapy. Our research uses the latest high-throughput sequencing technologies to create profiles and catalogues of the recurrently altered genes in cancer. We also have a keen interest in understanding the mechanisms by which the abnormal function of these genes contributes to cancer development.

Our goals

Our laboratory is currently engaged in a number of important projects:

1. Screening for factors that determine tumour immunoescape and the response to immunotherapy. We have become increasingly interested in the study of those biological factors, which allow tumours to escape control of the immune system and determine the response to immunotherapy.

2. Genomic and genetic profiling of lung tumours to identify novel targets for therapeutics and determinants for the primary and acquired response to tyrosine kinase inhibitors (TKIs). We use high-throughput genomic sequencing technologies, such as whole exome and RNA-sequencing, to gather information about the genetic background and gene expression profiles of lung tumours from both smokers and non-smokers.

3. Genetic alterations at epigenetic factors: biological understanding and opportunity for novel therapeutics. Over the past 15 years, our group has provided key information to understanding cancer biology. Currently, we are using high-throughput technologies to understand tumour development and to identify molecular vulnerabilities that can be used therapeutically.

Our challenges

Recent epidemiological data point to a worrying increase in the incidence of LC in those who have never smoked, particularly women. The reasons are not well understood, a fact that limits the design of prevention measures.

Through our research, we hope to answer the following questions:

1. What are the genetic and molecular abnormalities that trigger the development of cancer, particularly Lung Cancer?
2. How can we use genetic/molecular information to identify novel targets to implement Lung Cancer therapeutics?
3. What is the molecular basis for the lack of response to immunotherapy?
4. How can we predict and prevent acquired resistance to targeted therapeutics?

Keywords
Targeted therapeutics; immunotherapy; epigenetic regulation; SWI/SNF-complex; MYC/MAX-pathway.

3 CHROMATIN BIOLOGY

Led by
Álex Vaquero

Group members

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Marazuela Duque, Ana
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Overview

The members of the sirtuin family of NAD$^+$-dependent enzymes are key coordinators of this response, as they play an important role in the crosstalk between the environment and the genome, at both cellular and physiological level. In particular, they play a key role in the maintenance of genome stability, epigenetics, metabolic homeostasis, and cell differentiation and development. The relevance of sirtuin function is highlighted by their involvement in some of the most common human pathologies, including cancer (such as blood malignancies), diabetes and other endocrine-related diseases, neurodegenerative diseases and ageing.

Our research

The chromatin biology lab's primary purpose is understanding the mechanisms of the stress response and their impact on cancer and ageing. Specifically, the group focuses its efforts on defining the contribution of sirtuins to this response in the maintenance of genome stability, epigenetics and metabolic homeostasis.

To fulfil this main objective, the group's work encompasses a wide range of research areas, from basic aspects of sirtuin biology to their contribution in the development of human pathologies such as leukaemia and ageing.

Our goals

We aim at the identification of novel mechanisms and factors involved in the onset and development of blood malignances, and the creation of tools that could be helpful for its diagnosis and treatment. In this regard, the group's main objectives are:

1. To understand the enzymatic duality of sirtuins and their specific contribution to sirtuin function. In particular, we focus our efforts on the poorly understood topic of ADPRT activity.

2. To characterize sirtuin-dependent mechanisms of genomic stability, including constitutive heterochromatin integrity, DNA damage signalling and repair, and cell cycle checkpoint control.

3. To define the role of sirtuins in B-cell differentiation and characterize their functional implication in cancer, particularly in the context of haematopoietic pathologies such as leukaemia and lymphoma. Our main efforts are currently focused on two types of leukaemia, paediatric B-ALL and AML.

4. To understand the involvement of sirtuin function in the beneficial effects of nutrient restriction on ageing development.

5. To develop a new methodology to measure the activity of sirtuins *in vivo*.

Our challenges

Through our research, we seek to answer the following questions:

1. What is the physiological mechanism associated with the genotoxic and metabolic stress response?

2. What is the contribution of the sirtuin family of enzymes to the maintenance of genome stability after stress?

3. What is the implication of these mechanisms in the onset and development of blood cancers and ageing?

Keywords
Stress response; sirtuins; epigenetics; leukaemia; ageing.

4

CHROMATIN, METABOLISM AND CELL FATE

Led by

Marcus Buschbeck

Group members

Buschbeck, Marcus
Senior Group Leader

Malinverni, Roberto
Postdoctoral Fellow

Diesch, Jeannine
Postdoctoral Fellow

Corujo Garcia, David
Postdoctoral Fellow

Winkler, René
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Guberovic, Iva
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PhD Student

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PhD Student

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PhD Student

Meers, Oliver Patrick
PhD Student

Valero Lázaro, Vanesa
Lab Technician

Overview

We focus on understanding the molecular aspects of chromatin regulation and have a long-standing interest in the study of histone variants. We want to find ways to translate knowledge about chromatin regulation into therapeutic tools for the management of diseases such as blood cancers.

Our research

We seek to bridge the gap between basic molecular research and translational research by exploring chromatin regulation, in particular the molecular biology of histone variants. We aim to exploit this knowledge for the identification of novel intervention strategies for the treatment of blood cancers. We focus on the continuum of myeloid diseases, ranging from the premalignant expansion of altered clones to chronic myelodysplastic syndromes and acute myeloid leukaemia.

Our goals

Through our research, we aim to gain a better understanding of the epigenetic mechanisms that contribute to the development of blood cancers. By functionally mining the chromatin regulatory space, we further aim to provide new starting points by identifying novel drug targets. In this regard, our research focuses on two main lines:

1. To mine the chromatin regulatory space to identify novel drug targets that can either help improve current treatments or intercept disease at an early asymptomatic stage.
2. We study histones from the protein core of the nucleosome, particularly the variant macroH2A that led to two major discoveries: its major role in nuclear organization and its ability to bind metabolites through its mostly understood macrodomain, establishing a direct link between chromatin and metabolism.

Our challenges

Through our research, we hope to answer the following questions:

1. How do epigenetic mechanisms operate on the molecular level?
2. How do chromatin and, in particular, histone variants contribute to cell fate transitions?
3. How can we exploit this knowledge for the development of novel therapeutic strategies?

Keywords
Myelodysplastic syndrome; acute myeloid leukaemia; chromatin; nuclear organization; histone variants.

5
3D CHROMATIN ORGANIZATION

Led by
Biola M. Javierre

Group members

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Senior Group Leader

Fanlo Escudero, Lucia
Postdoctoral Fellow

Rovirosa Mulet, Llorenç
PhD Student

Tomás Daza, Laureano
PhD Student

Ramos Morales, Alberto
PhD Student

Nieto-Aliseda Sutton, Andrea
PhD Student

Urmeneta Floristán, Blanca
PhD Student

Cabrera Pasadas, Monica
PhD Student

Overview

Our group combines cutting-edge experimental and bioinformatics approaches to understand the specific 3D chromatin organization of normal and malignant haematopoiesis and its interaction with non-coding determinants and trans-regulatory elements. Our long-term goal is to keep making progress in the fight against cancer. We will not stop until a cure is found.

Our research

Since 2018, our work is focused on the study of the molecular mechanisms driving healthy and malignant haematopoiesis under a three-dimensional perspective. We are deeply interested in the unexplored noncoding DNA, which encompasses DNA that does not contain genes but that regulate the expression of remote genes, and the alterations of this. For that, we are developing new methods to study the spatial genome architecture and integrating this data with different methods in epigenetics, biochemistry and functional genomics to provide fundamental insight on normal and malignant haematopoiesis.

Our goals

Our lab's main research goals are as follows:

1. To define the cell type-specific 3D chromatin organization in human haematopoietic cells. we aim to investigate whether the dynamic changes in chromatin interactions between gene promoters and regulatory elements can shape transcription decisions controlling haematopoiesis.

2. To identify the altered DNA topology in blood cancer. Genome architecture plays a key role in genome expression regulation. Chromatin interactions are therefore crucial for cellular health, and errors in these interactions can give rise to the development of a broad range of diseases, including blood cancer.

3. To prioritize new candidate genes and pathways related to blood cancer. By studying the physical interactions between gene promoters and regulatory elements, we will be able to connect blood cancer determinants to putative target genes, thereby prioritizing new candidate genes and pathways and offering an insight into the genomic regulatory mechanisms underlying cancer.

Our challenges

As in other complex diseases, most of mutations and epimutations associated with blood cancers lie in non-coding regions, frequently at enhancers, and potentially exert their roles by altering the regulation of the target genes. However, these non-coding determinants remain unexplored because the vast majority of regulatory elements that control transcriptional activity of each gene in each cell type are unknown.

Through our research, we hope to answer the following questions:

1. Can the dynamic changes in chromatin interactions shape the transcription decisions controlling haematopoiesis?

2. How does the altered genome architecture drive malignant transformation?

3. What is the role of non-coding determinants in cancer predisposition and development?

Keywords
Genome architecture; spatial-temporal chromatin organization; haematopoiesis; blood cancer; cis non-coding determinants; enhancer-promoter interactions.

6
EPIGENETICS AND IMMUNE DISEASE

Led by
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Overview

We aim at understanding the mechanisms underlying the deposition and removal of epigenetic modifications in immune cells, the influence of genetic and environmental determinants, and the acquisition of epigenetic alterations in immune-mediated disease including primary immunodeficiencies, autoimmune and autoinflammatory diseases. We also investigate the impact of the epigenetic regulation of immune cells in the microtumour environment.

Our research

We started these lines of research more than 10 years ago, by studying the occurrence of DNA methylation alterations in the context of systemic lupus erythematosus (SLE), an archetypical systemic autoimmune disease. Later on, we performed new studies with MZ twins discordant for common variable immunodeficiency (CVID), the most prevalent symptomatic primary immunodeficiency.

More recently, our team also demonstrated the occurrence of DNA methylation alterations in monocytes in representative autoinflammatory syndromes. We have shown that alterations in the DNA methylome of peripheral blood monocytes reflect the disease activity in rheumatoid arthritis mediated by the elevated levels of inflammatory cytokines present in such state.

Our goals

Our main lines of research and specific goals are:

1. To understand the role of epigenetic control and its upstream determinants in relation with immune function. We aim at understanding how immune cell-cell crosstalk, cytokines and other factors, cell signalling pathways and transcription factors determine epigenetic control and impact immune cell function.

2. To identify epigenetic alterations in immune-mediated diseases and investigate their clinical relevance. Our studies focus on different diseases including primary immunodeficiencies, such as common variable immunodeficiency (CVID) and hyper IgM type 2 syndrome, and autoimmune diseases, such as rheumatoid arthritis, systemic sclerosis and systemic lupus erythematosus.

3. To investigate the effects of immunomodulators and epigenetic compounds in shaping the epigenome and responses of immune cells. We dissect the molecular consequences of different immunomodulators as well as inhibitors of epigenetic enzymes in immune cells.

Our challenges

The study of epigenetic dysregulation can help understand the determinants of immune dysregulation and can have an impact in the treatment of these diseases. Therefore, with our research we want to answer:

1. How do immune cells translate the surrounding information provided by the direct contact with other cells or the cytokines and other molecules into epigenetic profiles that determine their responses?

2. What is the relevance of the epigenetic alterations that are found in different immune mediated diseases in relation to the aberrant function of these cells?

3. How can we apply the knowledge on the epigenetic dysregulation in immune-mediated disease to the clinics?

Keywords
Epigenetics; DNA methylation; Immune-mediated disease; autoimmune disease; primary immunodeficiency.

7

LYMPHOCYTE DEVELOPMENT AND DISEASE

Led by
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Overview

B-cell lymphopoiesis is a complex developmental process that involves several cellular transitions, including cell commitment and early and late cellular differentiation. Proper transcriptional control at each cellular transition is essential for the correct development of B lymphocytes. How specific gene expression programmes are selected and maintained, thus resulting in the proper generation of B cells, remains a fundamental question in biology. Conversely, how the aberrant establishment of cell- and lineage-specific gene transcriptional programmes leads to the development of B-cell malignancies such as leukaemia and lymphoma also requires extensive research.

Our research

Our current research focuses on four main lines:

1. Understanding the entire role of HDAC7 in early and terminal B-cell development. HDAC7 is an epigenetic modulator that represses functional or lineage-inappropriate gene expression in B lymphocytes

2. Establishing HDAC7 as a novel biomarker and potential therapeutic target in pro-B acute lymphoblastic leukaemia (pro-B-ALL) and diffuse large B-cell lymphoma (DLBCL). We found that the deregulation of HDAC7 may be involved in the pathogenesis of acute lymphoblastic leukaemia.

3. Working towards precision medicine against DLBCL heterogeneity using organoid culture systems. We are investigating additional epigenetic regulators in normal and aberrant B-cell generation and implementing 3D organoid cultures from DLBCL sample patients.

4. Improving immunotherapy combinatorial therapy in DLBCL. R-CHOP is the gold standard treatment for DLBCL patients. R-CHOP therapy combines anti-CD20 antibody (immunotherapy) with cyclophosphamide, doxorubicin, vincristine and chemotherapy

Our goals

Acute lymphoblastic leukaemia (ALL) is the most common type of cancer in children under a year old. Even though the chances of survival in infants suffering from ALL have improved significantly in recent years, an exhaustive study of the mechanisms underlying this disease is still required to make further therapeutic advances. Therefore, our group focus on:

1. To understand how gene silencing is established during normal and aberrant B-cell differentiation.
2. To transfer our basic knowledge in the epigenetics and transcriptional control of B-cell development to the clinical setting for infant B-ALL and DLBCL patients.
    - 2.1. To identify small molecules aimed at HDAC7 targeted modulation for combinatorial and precision medicine in infant pro-B-ALL with MLL-AF4 rearrangement.
    - 2.2. To identify novel targets for the design of next-generation immunotherapies in DLBCL.
3. To implement a 3D organoid platform for DLBCL patient samples to perform compound library screenings aimed at unveiling new drugs for use in combinatorial therapy with current immunotherapy in a personalized manner.

Our challenges

Through our research, we aim to answer the following questions:

1. How do B lymphocytes decide their identity? How is gene silencing established?
2. Why does HDAC7 expression improve the prognosis of some haematological diseases?
3. Why is HDAC7 underexpressed in pro-B-ALLA and DLBCL?
4. How can we restore HDAC7 expression in pro-B-ALL and DLBCL to impair disease progression?
5. Can we implement 3D organoids from DLBCL patients aimed at drug screening towards a precision medicine strategy and immunotherapy improvement?

Keywords

B lymphocyte development; Epigenetics and transcriptional regulation; HDAC7;
B cell acute lymphoblastic leukaemia (B-ALL); Diffuse large B-cell lymphoma (DLBCL).

8 REGULATORY GENOMICS

Led by
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Group members

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Overview

Regulation of gene expression is the fine-tuning of the synthesis of the functional product of genes and is one of the most fundamental processes in life. It is the process that makes different cell types have different properties and differentiates unhealthy from healthy cells. Gene expression is regulated by internal signals (the activity of other genes, mutations, etc.) and by external signals (diet, temperature, pharmacological therapies, etc.).

Our research

Our research focuses on three main areas:

1. Firstly, we study the effect of the environment on gene expression changes that are transmitted from parents to their offspring. We want to understand how information about our exposure to different environments may be encoded in molecules - other than DNA - inside germ cells that are transmitted between generations.

2. Secondly, we work on non-coding RNAs and other non-coding elements that influence gene expression. We are interested in which non-coding elements affect gene expression and how.

3. Finally, we want to understand how epigenetic drugs affect gene expression and chromatin in different genomic contexts. Epigenetic drugs currently used in the clinic include those for the treatment of patients with acute myeloid leukaemia and myelodysplastic syndrome. A more in-depth understanding of the effects of these drugs and how they work may lead to improved or more personalized medicine in the future.

Our goals

Our aim is to contribute to a better understanding of gene regulation and the consequences of drug treatments and inter-individual genetic variation in gene expression. Although most of our research is based on data from animal model organisms or cell lines, we hope that, in the long term, the knowledge acquired will increase our understanding about humans. Extensive aberrant gene expression and genome deregulation are extremely common in cancer, especially haematological forms, and treatments targeting gene regulation pathways are being used for haematological malignancies. Last, but not least, we hope that the data we generate and the analysis methods we develop serve as useful tools for the wider research community.

Our challenges

We hope that our research sheds light on the following questions:

1. Which epigenetic mechanisms are involved in the transmission of acquired or variable traits between generations in humans and other animals?

2. Which non-coding DNA elements affect gene expression and therefore potentially phenotype?

3. How drugs (such as those used for the treatment of blood cancers) affect gene expression and the function of the non-coding parts of our genome?

Keywords
Bioinformatics; gene regulation; epigenetic inheritance; germline; genomics.

9 REGULATORY RNA AND CHROMATIN

Led by
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Overview

We study the emerging roles of noncoding RNAs as key regulators of gene expression in physiological cellular programmes and at the onset or during progression of human diseases, with a major focus on tumorigenesis and neurodevelopmental diseases. The research carried out by our group combines biochemical, cellular and global genomic approaches to dissect mechanisms of gene expression regulation with the participation of ncRNAs, with the ultimate aim of revealing molecules of therapeutic/biomarker interest for clinical translation.

Our research

The lab focuses on a variety of RNA and RNA-binding protein functions in the context of changing cellular conditions. Our interest concentrates on the noncoding transcriptome, with the main aim of separating the wheat from the chaff to reveal true biologically relevant molecules and to understand how they are connected to broader gene regulatory networks.

Cancer research has led the way in the study of noncoding RNAs, but the abundance and key roles of the noncoding transcriptome in the human brain are being increasingly recognized. Importantly, common dysregulated mechanisms in different pathological contexts and with the involvement of ncRNAs, are emerging.

Our goals

Our research aims to gain a better understanding of the biological relevance of ncRNAs for an informed use in therapeutic strategies. Recently, our group's research has taken advantage of state-of-the-art global transcriptomic approaches to identify ncRNA candidates that act as master regulators of oncofoetal genes, thereby revealing their validity as biomarkers in human cancer.

In addition to our work related to cancer, the group has been developing new experimental tools for research into Rett syndrome, a neurodevelopmental disorder usually caused by loss-of-function mutations in the epigenetic regulator MeCP2.

Our challenges

Through our research, we hope to answer the following questions:

1. What is the precise contribution of the non-coding transcriptome to tumour biology?
2. How can we use RNA tools to improve treatment or diagnosis of human disease?
3. How can we better model neurodevelopmental diseases such as Rett syndrome to understand key initial changes in gene expression programmes?

Keywords
Noncoding RNAs; cancer epigenetics; gene expression regulation; stem cells; Rett syndrome.

10

EPIGENETIC CONTROL OF HAEMATOPOIESIS

Led by

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Overview

DNA methylation-related genes are among the most frequently mutated in blood malignancies. Traditionally, studies aimed at understanding the effect of aberrant DNA methylation in cancer patients have focused on gene promoters. However, recent findings focus on enhancers as the most important regions in dynamic DNA methylation studies. We aim to understand how aberrant DNA methylation dynamics impact on the chromatin structure at enhancers during blood cancer onset and progression.

Our research

We study how aberrant DNA methylation at distal gene regulatory regions poisons the chromatin to trigger corrupted gene expression signatures in cells, thus eventually leading to the onset and progression of haematological neoplasms. This line of research has implications for a broad spectrum of patients suffering from blood diseases sharing an abnormal genome-wide DNA methylation landscape.

Our goals

We aim to unravel the different layers of intricated epigenetic information that specify which subsets of genes are expressed in every one of the cells of the haematopoietic system, thereby defining their cellular identity. We hope to apply this knowledge to better understand how and when deleterious transcriptional programmes leading to cellular transformation are activated, thus leading to the discovery of new treatments that will potentially end up in improving the quality of life of patients suffering from a wide range of blood diseases.

Our challenges

There is an urgent need for novel therapies for acute myeloid leukemia, since barely any drugs introduced in the last decades have increased the overall survival its patients. Hence, our research aims to shed light on the following questions:

1. What is the interplay between DNA (hydroxy) methylation and chromatin dynamics at distal gene regulatory regions during haematopoietic cell fate decisions?

2. What are the molecular mechanisms underlying the role of TET2 in the epigenetic control of the chromatin at distal gene regulatory regions during leukaemia onset and progression?

3. What is the role of mRNA methylation-mediated post-transcriptional control in myeloid cell differentiation?

Keywords
DNA methylation; TET enzymes; Chromatin; Haematological malignancies; Stem cells.

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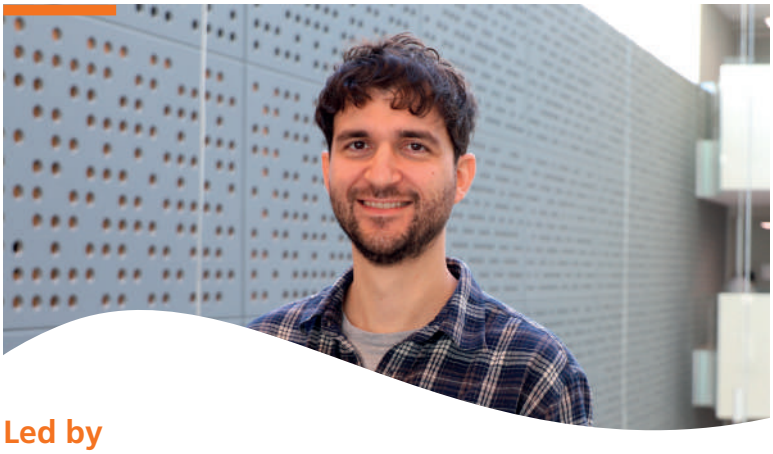
TRANSCRIPTIONAL DYNAMICS IN LEUKEMIA



Led by
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Overview

Haematopoietic differentiation is a tightly regulated process that maintains blood production throughout life. The transcriptional changes that haematopoietic cells undergo during differentiation are controlled at multiple levels and an accurate integration of all of them is essential to ensure the production of sufficient numbers of blood cells at all stages of differentiation. However, most of the acute myeloid leukaemia (AML) cases have mutations in transcriptional regulators and chromatin modifiers. These mutations alter transcriptional dynamics and can impair normal differentiation.

Our research

We study the mechanisms that regulate transcription during haematopoietic differentiation and investigate the leukaemogenic potential of mutations in transcriptional regulators and epigenetic modifiers. We are also looking into the role of mutations in proteins that drive the three-dimensional organization of the genome.

Our goals

Our main goals are:

1. To understand the role of mutations in hematopoietic transcription factors and chromatin regulators in acute myeloid leukaemia (AML). Using genetic models to mimic these mutations, we aim to dissect their impact on gene expression and thus understand how they promote a selective advantage.

2. To characterize the impact of inflammatory signalling on normal hematopoietic differentiation and during leukemic progression. We want to understand the impact of inflammation on the progression of myeloid malignancies and how are they linked to the most common mutations.

Our challenges

Acute myeloid leukaemia (AML) is the one of the most aggressive forms of leukaemia, and there is an urgent need to find new treatment options. While we now know **what** genes are recurrently mutated in AML, we still do not understand **why** these mutations are malignant. Through our research, we aim to answer the following questions:

1. What transcriptional mechanisms are deregulated in acute myeloid leukaemia?
2. How do inflammatory signals influence leukemic progression?
3. Can we use inflammatory modulation to attenuate the severity of myeloid malignancies?

Keywords
Haematopoiesis; chromatin; AML; MDS; cohesin; inflammation.

12

STEM CELLS AND CANCER

Led by
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Overview

Our research group investigates how to generate and maintain the stem cells in the hematopoietic system under physiological conditions but also how these processes are mimicked by the tumors for their perpetuation. We constantly improve our research by implementing novel technology to understand the process of normal and malignant hematopoietic development. Our research includes basic studies at the molecular level to understand cellular processes in the context of mouse models and human patients.

Our research

Our research comprises from basic biochemical research to the analysis of animal models that reproduce the pathologies of interest and allow us to study the functional relevance of new hypothesis. The ultimate goal is to confirm the importance of the findings and study possible therapeutic applications through the analysis of patient samples. In this sense we have devoted special efforts to understand the regulation of hematopoietic stem cells, as a tool to understand the mechanisms that regulate leukemia initiation and maintenance.

Our goals

We are currently working on several projects that deal with different functional aspects of normal hematopoietic stem cell regulation as well as leukemia initiating cells:

1. Generation of hematopoietic stem cells. Our current studies are focused on understanding the signals that the embryo uses to form these self-renewing cells that maintain the hematopoietic system throughout the life of the organism.

2. Understanding T Acute Lymphoblastic Leukemia (T-ALL) development and T-cell lymphoma. We study the signals that regulate the generation and maintenance of normal and leukemic cells, as well as leukemic stem cells (LSCS). With this aim we have developed in vitro and in vivo experimental models that complement the analysis of patient samples.

3. GATA2 deficiency syndrome. We are collaborating in an international consortium to understand the contribution of GATA2 mutations to pediatric Myelodysplastic syndrome and transformation to Acute Myeloid Leukemia (AML). We are developing humanized blood animal models of this syndrome.

4. Understanding cell transformation. We work closely with the Research Group for Molecular Mechanisms of Cancer and Stemness directed by Dr. Lluís Espinosa, and we take advantage of our discoveries in hematopoietic cells to understand epithelial tissues and vice versa.

Our challenges

Through our research, we aim to understand the following:

1. What signals are imposed in embryonic HSCs that affect the adult hematopoietic system?
2. What are the molecular mechanisms that impose resistance to treatment in T-ALL cells?
3. What are the basic mechanisms that control cell transformation?

Keywords
Embryonic hematopoiesis; T-ALL; CTCL; GATA2; Notch; NFkB; hematopoietic stem cell; leukemic stem cells.

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LEUKEMIA AND IMMUNO-ONCOLOGY

Led by

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Overview

Juvenile myelomonocytic leukemia (JMML) is a rare and aggressive type of pediatric blood cancer that affects mainly children under two years of age and occurs when bone marrow production of white cells becomes severely dysregulated. Hematopoietic stem cell transplantation (HSCT) is currently the only available treatment for patients, although just two out of three children affected by the disease survive.

Our research

Since 2020, our work has focused on the study of the molecular mechanisms driving JMML and the exploration of alternative therapeutic strategies specifically designed for these patients. To achieve this, we incorporate different methods into epigenetics, systems biology, functional genomics and biochemistry, to help address critical questions about the origin and progression of JMML and to identify new therapeutic targets for the treatment of this disease.

Our goals

The specific goals of our research program are as follows:

1. To create a centralized JMML sample repository and patient-derived xenograft (PDX) collection. In collaboration with clinical teams at different hospitals around the country and with the endorsement of the Spanish Society of Pediatric Hematology and Oncology (SEHOP), we are creating a national JMML patient sample repository and PDX collection, that will be instrumental for the development of our research program.

2. To develop a comprehensive molecular analysis of JMML patients to define accurate diagnostic and stratification criteria. We aim to explore the non-coding genome of JMML patients to identify new genetic alterations that can drive JMML or contribute to the pathogenesis of the disease by other means. This information will help improve our knowledge of JMML and develop more accurate criteria for the diagnosis and management of JMML patients.

3. To identify new potential therapeutic targets and develop specific therapies for the treatment of JMML. HSCT is currently the only effective therapy for the treatment of JMML. However, only two out of three children with this disease survive. Thus, new therapies specifically designed to treat JMML patients are needed. To achieve this, we are collaborating with other research groups and with biotechnology companies to identify specific JMML therapeutic targets and explore strategies for their clinical use for the treatment of JMML patients.

We are confident that our results will have an important impact on the diagnosis and treatment of JMML by increasing knowledge of the disease and expanding the therapeutic options open to these patients. Moreover, our close collaboration with clinical teams in the development of this project will guarantee that our most promising discoveries have a rapid and direct impact on JMML patients.

Our challenges

With our research, we aim to answer the following questions:

1. What is the relevance of non-coding somatic mutations in the generation and development of JMML?

2. Can non-coding mutations predict the prognosis of JMML patients?

3. What are the best therapeutic targets for the development of JMML-specific treatments?

Keywords
Leukemia; JMML; PTPN11; experimental therapeutics; CAR-T cells; rare diseases; pediatric diseases; sequencing; diagnosis; therapeutic targets; preclinical models; drug discovery.

14

CANCER HETEROGENEITY AND HIERARCHIES

Led by
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Overview

Our laboratory studies the key signals governing stem cell and cell fate specification during malignant progression and the mechanisms by which different signaling pathways control cell plasticity in cancer. Specifically, we use in vivo lineage tracing, live imaging, cytometry and expression profile analysis as experimental tools to achieve our goals. Our group combines murine transgenic models, patient-derived xenografts and 3D organoids to unravel cellular hierarchies within tumors, to gain a better understanding of cancer heterogeneity and drug resistance.

Our research

Cancer is a heterogeneous disease with a cellular hierarchical organization that is largely unexplored in many tumor subtypes. Moreover, in some cases hierarchical relationships among stem cells, progenitors and differentiated cells remain unsolved due to the high degree of cellular plasticity, which allows cells to switch between different cellular stages.

Our goals

We are a newly created group passionate about cellular hierarchies and tumor heterogeneity. Our main lines of research and specific goals are:

1. To illustrate cellular hierarchies within tumors. We use a well-established hierarchical model to study multipotency in tumors. Now, we are separately monitoring three mammary epithelial compartments to measure the presence of multipotency within breast tumors. Our hypothesis is that breast tumors are indeed sustained by different subpopulations, which self-maintain independently

2. To discover cytotoxic agents for specific cellular subpopulations. A therapy based on a combination of several drugs to target different cellular populations could eradicate primary tumors, thereby preventing relapse and metastasis. We want to screen for natural compounds that selectively kill specific subsets of cells that are responsible for tumor maintenance and/or intrinsically resistant to current therapies.

3. To target the tumor niche to prevent the spread of cancer. One of our main objectives is to generate in vivo tools that will allow us to study new therapeutic targets to prevent relapses in hematological cancer. To that end, our lab works on different strategies, which include murine and human models, to test a panel of drugs currently used as a standard of care for non-Hodgkin's lymphoma (NHL) and explore the role of senescence in tumors cells, as well as in their microenvironment.

Our ultimate mission is to understand the tumor heterogeneity between different patients with a view to improving their treatment of choice by searching for novel and personalized therapeutic strategies.

Our challenges

We hope to answer the following questions through our research:

1. How can cellular plasticity improve treatment for cancer patients?

2. Can we achieve truly personalized medicine by identifying single or combinatorial therapies to target different cellular populations at the same time?

3. Can we prevent metastasis and/or relapses by targeting the most frequently colonized tissues?

Keywords
Cellular hierarchies; heterogeneity; cell plasticity; senescence; tumour microenvironment.

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CANCER IMMUNOGENOMICS

Led by
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Overview

Our research lies at the interface of artificial intelligence, molecular biology and medical oncology, and we bring together experts from all three fields. We use computational approaches to study the interaction between genetic variants in cancer genomes and multiple aspects of cancer, ranging from the immune response against tumors to the susceptibility of cancer cells to different treatments.

Our research

Over the last two decades, there has been an explosion of three main types of big data in cancer research. We use three types of data:

1. Germline genotypes from cancer patients, this is, the base non-altered genome of individual people being diagnosed with cancer.

2. Somatic tumor genomes, being the particular genomes of individual tumors, with its unique set of alterations.

3. The amount and composition of cells in tumors coming from single-cell sequencing.

Until now, these three different aspects of tumor immunobiology have mostly been studied on an individual basis. However, it is now evident that the three factors are inextricably linked and should be studied as a whole.

Our goals

Our main goal is to understand how genetic variation influences the immune response against cancer cells and vice versa. Specifically, we are working on the following lines:

1. Understanding how inherited genetic variants change the immune response against cancer cells.

2. Understanding how inherited genetic variants interact with biological sex to influence cancer predisposition. We are using the MareNostrum supercomputer to analyze genetic data from hundreds of thousands of cancer patients from this biological sex perspective, to identify genetic variants that predispose to cancer differently depending on gender.

3. Integration of protein structure and genetic data to identify new cancer-associated mutations.

4. Creating a molecular and cellular map of the tumor microenvironment in bladder cancer.

Our challenges

Through our research, we hope to answer the following questions:

1. Is it possible to use a person's genetic data to predict whether he/she will develop cancer?

2. Which genes play a role in the development of cancer?

3. How do genetic variants change the immune response against cancer cells?

Keywords
Computational biology, cancer genomics, big data, GWAS, bladder cancer.

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ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

Led by
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Overview

Our research focuses on analysing the genomic and epigenomic landscape of patients with adult ALL (acute lymphoblastic leukaemia) to find out genetic alterations that predict patients' response to treatment and to identify new alternative (targeted) therapies to apply to those patients. In this way, we aim to design more personalized treatments to increase the probability of survival of ALL patients.

Our research

The group's current research is divided into two main areas, according to the two main subtypes distinguished in ALL:

1. Precursor B-cell acute lymphoblastic leukaemia (BCP-ALL):

BCP-ALL is the most prevalent ALL subtype and accounts for 75% of ALL cases. Although it is a highly heterogeneous disease at genetic level, different cytogenetic subtypes have been identified and, more importantly, their prognosis has been clearly established in many clinical trials. This has allowed clinicians to stratify patients according to their genetic profile to schedule intensive or less intensive treatments.

2. T-cell acute lymphoblastic leukaemia (T-ALL):

T-ALL is the least common ALL subtype (25% of adult ALL cases), and the most complex and heterogeneous at genetic level, with a dismal prognosis. to improve the survival rate of patients with T-ALL, we first need to obtain detailed and relevant molecular information to accurately define the risk and thus decide on the treatment.

Our goals

We are convinced that new treatments for ALL patients can be obtained only through basic research. Therefore, our goals are:

1. To identify the genetic alterations leading to treatment resistance and disease recurrence in adult ALL.

2. To accurately define the risk of ALL by genetic analysis at diagnosis and relapse in order to decide on the most appropriate treatment.

Our challenges

Although ALL is a rare form of cancer, it has a huge impact on patients, their relatives and the health system. To find new therapies and provide new knowledge, our research hopes to:

1. Decipher the genetic complexity of ALL at both diagnosis and relapse.

2. Identify critical genetic lesions in ALL cells that could be targetable with new drugs.

Keywords
Acute lymphoblastic leukaemia; adults; genomic analyses; minimal residual disease; treatment resistance.

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BARCELONA ENDOTHELIUM TEAM (BET)

Led by

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Overview

Blood vessel endothelium crosses each and every tissue and presents unique structural and functional properties in each vascular bed. This cellular heterogeneity is reflected by the structural and functional heterogeneity of the whole endothelium as a complex system. Due to its location, the endothelium is exposed to all kinds of physiological and pathological stimuli and constitutes the first barrier to many drug interventions.

This organ has the capacity to constantly adapt to environmental changes by modulating vasomotor tone, haemostatic balance and inflammatory reactions, among other responses. Endothelial activation could lead to an irreversible state known as endothelial dysfunction that, in a broad sense, leads to various non-adaptive alterations of the functional phenotype that constitute a net liability to the host.

Our research

Our group has extensive experience in the study of the endothelial dysfunction that develops in association with different vascular pathologies, such as the early complications associated with hematopoietic cell transplantation, obesity, chronic kidney disease, thrombotic microangiopathies and sepsis.

We also explore strategies for the protection of this endothelial dysfunction to improve patient health. In this regard, one of our main interests is to evaluate different compounds that potentially exhibit the capacity to protect the endothelium and to decipher their mechanisms of action.

Our goals

Our main lines of research are:

1. To characterize the endothelial activation and dysfunction associated with cardiometabolic diseases through *in vitro* models.

2. To elucidate the mechanisms that lead to endothelial dysfunction.

3. To investigate agents with potential protective effects on the endothelium to prevent complications.

4. To find soluble markers with prognostic and diagnostic value for vascular complications.

5. To study complement pathways and complement deficiencies in thrombotic microangiopathies.

6. To assess platelet physiology and alterations of haemostasis by using perfusion devices to explore adhesive and cohesive properties of platelets under flow conditions.

Our challenges

Hematopoietic cell transplantation (HCT) has been the major curative therapy for several hematological, metabolic and neoplastic disorders. However, the efficacy of this procedure is limited by life-threatening complications, the most important of which is graft versus host disease (GvHD), which has a high mortality rate. Through our research, we aim to answer the following questions:

1. What are the pathophysiologic mechanisms that characterize endothelial dysfunction?

2. How can we avoid the vascular complications associated with hematopoietic cell transplantation?

3. Which is the role of the complement system in vascular complications?

Keywords
Endothelium; Inflammation; Diagnostic and prognostic markers; Thrombotic microangiopathies (TMA); Drugs.

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FUNCTIONAL CYTOMICS

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Overview

The ability to bridge large-scale and single-cell approaches at a functional level is key to identifying biomarkers expressed in rare cells, and particularly in cancer stem cells (CSCs). Our interdisciplinary group investigates and develops key experimental approaches to understand the principles underlying the emergence and prevention of tumourigenesis and cancer therapy resistance, with the aim of translating biomedical science to integrated clinical practice and public health through certified transfer processes in cooperation with trusted allies and partners.

Our research

Our current research projects use innovative approaches to study the expression of primitive stem cell markers during the origin, progression and maintenance of cancer and the management of cancer; the quality and safety of haematopoietic blood progenitor and stem cell grafts; the role of myeloid-derived suppressor cells in immunotherapy and targeted therapy for clinical decision-making; new cytomic strategies for whole blood and marrow immunostaining; the use of natural compounds for cancer treatment; and the accurate detection and significance of minimal residual disease in acute leukaemia.

Our goals

Our goal is to provide patients with a wide range of scientific support strategies, through precision, oversight and accuracy, to achieve:

1. Clinical implementation of functional cytomic assays, and precision/personalized high-quality assays for individual patients by integrating functional cytomics.

2. Translation of functional screening to novel clinical strategies. Measurement of the impact of exogenous interventions such as drug exposure on tumour cell phenotype.

3. An understanding of drug resistance and prediction of effective drug combinations.

4. A reduction in costs by obtaining specialized instrumentation and personnel for the execution of cytomic screening in partnership with stakeholders and biotechnological partners.

5. Functional and immunophenotyping datasets aimed at understanding complex functional-to-phenotype correlations, thereby accelerating discovery of the biology of leukaemogenesis and the clinical implementation of novel therapies.

Our challenges

Since personalized medicine aims to provide the right therapy, in the right dose, thereby improving patient stratification and disease prediction, we expect to achieve:

1. Better diagnosis and earlier intervention. Cytomic analysis could determine precisely whether patients are susceptible to drug toxicities and make it possible to choose the optimal treatment strategy.

2. Individualized drug selection. Here we consider which molecular and functional models best predict how a patient will respond to a therapy to develop accurate and cost-effective tests.

3. Drug development challenges. A better understanding of the clinical observations made during individualized drug development and conventional therapy will help identify new disease subtypes and their associated molecular pathways, and design drugs that target them with more efficient trials.

Keywords
Cytometry; cancer stem cells; cytome; human cytome project.

19

MYELOID NEOPLASMS

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Overview

Genetic profiling for haematological malignancies involves chasing a moving target. Not so long ago, leukaemias were stratified based on karyotype abnormalities. In recent years, however, knowledge of molecular genetics in haematology has increased significantly, thus offering new clinical opportunities. It has now been shown that gene expression, mutations and other genetic and epigenetic abnormalities also have diagnostic, prognostic and therapeutic implications.

Our research

Since 2004, our group has been studying MN, with a particular focus on characterizing genetic and epigenetic lesions to find new diagnostic, prognostic and therapeutic markers that could help us better diagnose and treat patients with these diseases. First, we started with karyotype and single nucleotide polymorphism arrays (SNP-A) to help us detect alterations at chromosome level, and we are currently performing studies at gene level (mutational profile studies) and analysing the impact that telomere size could have on the development of the disease.

Our goals

The aim of our group is to apply our research to myeloid neoplasms (MN), specifically three distinct haematological diseases: chronic myelomonocytic leukaemia, myelodysplastic syndromes and myeloproliferative neoplasms (PV, ET, MFP and CML), with a view to finding better tools for diagnosis and prognosis stratification and achieving individualized targeted therapies (personalized medicine). Therefore, our research focuses mainly on the following areas:

1. Chronic myelomonocytic leukaemia (CMML). The aim of our research is to characterize the type, frequency and prognostic impact of mutations and cytogenetic alterations detected by SNP arrays in patients with low-risk CMML and, then, study its epigenetic changes (DNA methylation and miRNAs expression).

2. The classification and prognosis of the group of diseases termed myelodysplastic syndromes (MDS). This knowledge will also contribute to a better understanding of MDS biology and a better stratification of the prognosis of these patients, which would also help with the selection of the most appropriate treatment for each one.

3. Chronic myeloid leukaemia (CML). The aim of our research is to determine whether or not we can find any genetic marker at CML diagnosis that could explain a patient's toxicity to tyrosine kinase inhibitors, or identify which patients will achieve a molecular response. We are also seeking a technique with higher sensitivity than QRT-PCR.

4. *BCR-ABL1* negative classic myeloproliferative neoplasms (MPNs). We study several genomic changes in an attempt to associate them with cytological subtypes, laboratory parameters, clinical complications and probability of transformation to either MF or AML.

Our challenges

Our research is highly socially relevant because we promote capacity building, advancing knowledge, help in making informed decisions and improve the health in general terms, with economic benefits for the whole society. Through our research, we aim to answer the following questions:

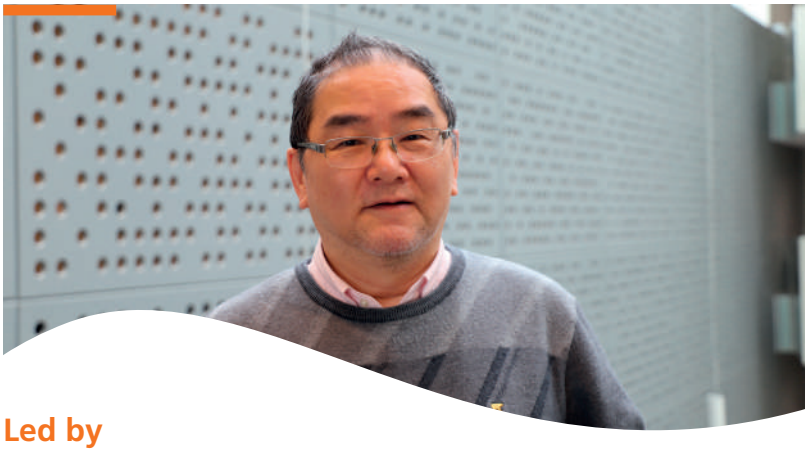
1. How can we improve diagnosis, prognosis stratification, treatment response and life expectancy in chronic myelomonocytic leukaemia?

2. How can we improve diagnosis, prognosis stratification, treatment response and life expectancy in myelodysplastic syndromes?

3. How can we improve diagnosis, prognosis stratification, treatment response and life expectancy in myeloproliferative neoplasms?

Keywords
Myeloproliferative neoplasms; chronic myeloid leukaemia; myelodysplastic syndromes; MPN/MDS; acute myeloid leukaemia.

20 IMMUNOHEMATOLOGY AND GLYCOBIOLOGY



Led by
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Overview

The ABO blood group system is one of the most important blood group systems in transfusion medicine. The ABO polymorphism consists of A and B glycan antigens on red blood cells (RBC) and antibodies against A and B antigens in the sera of individuals who do not express these antigens. In humans, A and B antigens are also present on epithelial and endothelial cells, depending on the ABO genotype/phenotype of the individual. Because of this, ABO matching is also crucial in cell, tissue and organ transplantation.

Our research

We study the molecular genetic mechanisms for the expression of genetically incompatible glycan antigens and have thus far revealed several potential mechanisms, including the appearance of FORS1 induced by the deletion of exon 3 or 4 of the AT mRNA. Because altered splicing is a hallmark of cancer, this mechanism may be responsible, at least partially, for FORS1 expression in group A and AB individuals.

We also investigate the potential mechanism by which incompatible A antigens appear in group O individuals through complementation by recombination of DNA or trans-splicing of RNA and also expression of FORS1 due to changes in specificity resulting from incorrect intra-Golgi localization of modified glycosyltransferases.

Our goals

Cancer growth indicates that the cancer cell-killing activities of natural immunity against genetically incompatible and/or cryptic glycans are ineffective and insufficient. However, they can be improved through active and/or passive immunization. Therefore, our goals are:

1. To investigate the use of genetically incompatible and/or cryptic glycan antigens as molecular targets for medical intervention.
2. To explore the possibility of using forced expression of genetically incompatible glycans to make cancer cells susceptible to natural immunity.

Our challenges

If successful, the active immunization we advocate for could revolutionize the cancer treatment landscape, thereby dramatically reducing the financial burdens on patients and society. Through our research, we aim to answer the following questions:

1. What is the molecular genetic/epigenetic basis of glycan alterations in cancer?
2. Can we use cancer-specific glycans as molecular targets for cancer detection and immunotherapy?
3. Does the minitransfusion/injection of mismatched red blood cells expressing genetically incompatible and/or cryptic glycans improve humoural and cellular immunity against cancer cells expressing cancer-specific glycans?

Keywords
Genetically incompatible glycan antigens; cryptic glycan antigens; cancer immunotherapy; disease susceptibility; ABO polymorphism.

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LEUKEMIA STEM CELL

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Overview

Many leukaemias originate in a population of leukaemic stem cells, which are responsible for initiating and maintaining the disease. Our group investigates the biology and sensitivity of stem cells that sustain tumours such as acute myeloid leukaemia (AML), myelodysplastic syndromes (MDS), chronic myelomonocytic leukaemia (CMML) and acute lymphoblastic leukaemia T (ALL-T).

Our research

Our work focuses on searching new therapeutic targets for blood disorders enabling us to identify new biomarkers that can be used for prognostic and/or diagnostic purposes, thereby gaining greater insight into the biology behind leukemic processes. New knowledge will help us develop new drugs that specifically attack the population of leukemic stem cells.

Due to the similarities between leukemic stem cells and healthy haematopoietic stem cells, our research group is striving to develop therapies that trigger the terminal differentiation of the population of leukemic stem cells, which eliminates their capacity to initiate and maintain the disease and enhances its chemosensitivity.

Our goals

Our main goal is to understand the biology of leukemic stem cells and identify pharmacological mechanisms that will enable us to modulate their functionality and eliminate them selectively. To achieve this, we adopt a dual approach: on the one hand, we study the underlying biological mechanisms responsible for these neoplasms and, on the other, we develop new therapeutic approaches with the potential for clinical application.

Our challenges

Due to the biological properties of leukemic stem cells, understanding how they work and identifying the differences between these and healthy haematopoietic stem cells is essential to design new more efficient and selective therapies that can be personalized for each patient. Therefore, our research aims to:

1. Understand how leukemic stem cells work.
2. Identify therapeutic targets and develop new drugs for leukemic stem cells.
3. Determine the prognostic and diagnostic value of these therapeutic targets as biomarkers for leukaemia.
4. Describe the differences between leukemic stem cells and healthy haemopoietic stem cells.

Keywords
Leukaemia; leukaemic stem cell; drug development; haematopoiesis; differentiation therapies.

22 LYMPHOID NEOPLASMS

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Overview

Our research is focused on the study of rare lymphomas, such as those that affect immunosuppressed patients, in terms of both clinical and genetic aspects. We have made important contributions to this field and our current objective is to reveal genetic and epigenetic characteristics of lymphoid neoplasms that occur mainly in immunosuppressed individuals. The purpose is to identify markers to improve the accuracy with which these patients are managed. Furthermore, we aim to implement liquid biopsy as a tool for diagnosis and follow-up of aggressive lymphomas.

Our research

Our group focuses mainly on the research of AIDS-related lymphomas (ARLs). The most frequent ARLs are diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL) and Hodgkin lymphoma (HL). Plasmablastic lymphoma (PBL) and primary effusion lymphoma (LEP) are less frequent, but typically present in immunosuppressed individuals. We also study other haematological disorders with an increased incidence in the HIV-positive population such as Castleman disease (CD).

Our main areas of research are:

1. Genetic studies on HIV-related lymphomas. Although HIV-infected patients are treated with the same regimens as HIV-negative individuals, their survival rate is lower due to the higher susceptibility to infections and secondary neoplasms.

2. Liquid biopsy in aggressive lymphomas. This technique could be useful to diagnose DLBCL earlier, and in a more comprehensive and accurate manner than with tissue biopsy alone.

3. Genetic studies on plasmablastic lymphoma. Plasmablastic lymphoma (PBL) is a rare B-cell lymphoid neoplasm that especially affects immunocompromised individuals and has a poor prognosis.

Our goals

We believe that genetic and epigenetic profiles will help clarify the mechanisms involved in lymphomagenesis and identify potential biomarkers, thus allowing cases to be classified more effectively. The possible diagnostic and/or prognostic impact of these markers could pave the way for the design of new targeted therapies, thus leading to new treatment approaches and improving the outcome of patients suffering from the lymphomas on which our research focuses, i.e. AIDS-related lymphomas, plasmablastic lymphoma and Castleman disease.

Our challenges

We expect that the results of our studies will lead to changes in the management of these rare lymphoid neoplasms and improve the poor prognosis of some lymphoid malignancies, such as plasmablastic lymphoma. Through our research, we hope to answer the following questions:

1. What genetic and epigenetic mechanisms are involved in the development of HIV-related lymphomas?

2. Which biomarkers can be used for an earlier diagnosis of lymphoid neoplasms in populations at high risk of developing these disorders, such as HIV-infected and transplanted patients?

3. How can we apply liquid biopsy in the diagnosis and follow-up of aggressive lymphomas?

Keywords
Non-Hodgkin's lymphoma; Hodgkin lymphoma; HIV; Epstein-Barr virus; diagnosis; prognosis; marker; treatment; targeted therapy; early detection.

23 MULTIPLE MYELOMA

Led by
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Overview

Multiple myeloma is a cancer of plasma cells, a type of white blood cell that accumulates in the bone marrow and interferes with normal blood precursors and bone remodelling, thus causing anaemia, bone lesions, renal insufficiency and recurrent infections. Between four and five out of 100,000 people are diagnosed every year. Despite the fact that treatments and prognosis have greatly improved in recent years, multiple myeloma is not yet curable. It is a recurrent disease that can leave important sequelae after each relapse.

Our research

Our clinical research team participates in the main international collaborative phase I to phase III trials establishing the current standards of care, with a particular focus on the optimal combinations of agents with clinically relevant synergies.

Active trials are already focusing on the efficacy of next-generation combinations, including antibody-drug conjugates, T-cell engagers and CAR-T cells. We are interested in the identification of subjects unlikely to respond to optimized first-line strategies and, therefore, of ideal candidates for such trials with novel immunotherapeutic approaches.

Our goals

We believe that the drug combinations currently being evaluated can cure a proportion of patients with multiple myeloma. Furthermore, we believe that it should be possible to predict patients in whom such combinations are not curative so that we can promote early interventions with alternative agents, mainly based on immunotherapeutic approaches to prevent the clinical consequences of full-blown relapse and maintain a symptom-free response in patients.

On this regard, our main goals are:

1. To define standards of treatment that provide a long-lasting response in most individuals.
2. To identify patients who will probably be cured and will safely remain treatment-free.
3. To identify patients who are unlikely to be disease-free for long with current treatments and search for alternative treatment options that can be applied before recurring disease causes organic damage.

Our challenges

Full-blown multiple myeloma has devastating consequences that severely reduce patients' quality of life and autonomy and represent a huge burden for caregivers and families. Therefore, the diagnosis of multiple myeloma has a dramatic impact on individuals and society. Through our research, we hope to answer the following questions:

1. What patients are unlikely to obtain prolonged benefits from current standards?
2. Would they benefit from early intervention with alternative agents?
3. Can we identify patients who will potentially be cured or are unlikely to relapse and safely spare them the burden of continuous therapy?

Keywords
Multiple myeloma; synergistic combinations; immuno-drug conjugates; T-cell engagers; CAR-T cells.

24
MYELODYSPLASTIC SYNDROMES

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Overview

Myelodysplastic syndromes (MDS) are a heterogeneous group of haematological stem cell disorders that result in ineffective haematopoiesis, blood cytopenia, myelodysplasia and a significant risk of progression to acute myeloid leukaemia (AML). MDS is one of the most common haematological malignancies in the elderly and the severity of the disease depends on a variety of biological factors that translate into a spectrum of symptoms with a profound impact on the patient's quality of life and survival; a third of MDS patients will progress to AML and the remaining two thirds will suffer from a combination of chronic anaemia, recurrent infections and bleeding episodes.

Our research

Our research focuses on unravelling the heterogeneity of myelodysplastic syndromes (MDS), mainly using genomic techniques. We study MDS patients who harbor a specific cytogenetic alteration: the deletion of the long arm of chromosome 5. Our aim is to improve the genetic characterization of these patients by studying the impact of adjunct cytogenetic abnormalities on their prognostic stratification; how cytogenetics and mutations can influence the response to lenalidomide treatment; the molecular landscape of MDS through next-generation sequencing techniques; and, finally, intratumoural heterogeneity before and after lenalidomide treatment using single-cell techniques.

Our goals

Through our research, we intend to contribute to a better understanding of MDS from a genomic point of view, contributing to refine the current criteria to diagnose this disease and predict patient outcomes to select the best possible treatment. Hence, our research addresses the following lines:

1. Evaluating the feasibility of using peripheral blood samples to perform genetic analyses (SNP-A and NGS) in MDS.

2. Monitoring mutational burden in low-risk MDS patients through the use of sequential peripheral blood samples to minimize invasive techniques on these patients.

3. Genetic characterization of myelodysplastic syndromes / myeloproliferative neoplasms (MDS/MPN) to define the genetic changes that could contribute to the differential diagnosis and prognostic stratification of these patients.

4. Genetic characterization of therapy-related myeloid neoplasms.

5. Mechanisms of progression from clonal haematopoiesis to MDS.

Our challenges

Our research can translate into a more efficient use of public healthcare resources and improve the quality of life for patients. Therefore, we want to shed light on the following questions:

1. How might genomic techniques contribute to refining the current criteria for MDS diagnosis, prognostic stratification and treatment response?

2. Can peripheral blood samples be useful to monitor MDS patients through next-generation sequencing?

3. Could single-cell studies help us better understand intratumoral heterogeneity and clonal evolution from CHIP to MDS and TRMN (therapy-related myeloid neoplasms)?

Keywords
Myelodysplastic syndromes; chronic myelomonocytic leukaemia; intratumoural heterogeneity; myelodysplasia; cytopenias; CHIP; TRMN.

25

STEM CELL BIOLOGY, DEVELOPMENTAL LEUKEMIA AND IMMUNOTHERAPY

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Overview

Our group is interested in understanding the cellular origin, etiology and pathogenesis of childhood leukemia. We aim to ascertain the cell in which mutations occur and we strive to discover which cells are responsible for triggering relapses. Furthermore, we work to identify new therapeutic targets and develop more targeted, less toxic therapies. To achieve this, our laboratory uses various approaches, including genetic studies, epigenetic techniques and animal models, as well as adoptive cell immunotherapy tools.

Our research

Given that acute childhood leukemia (including the B, T and myeloid variants), and childhood cancer in general, are relatively uncommon illnesses, with around 500 cases in Spain each year, it does not represent a priority target for the pharmaceutical industry. As a result, there is a serious lack of active programs that aim to identify medicines to target childhood cancer. Our group has been investigating the origin of this diseases *in utero*, as well as its etiological causes and physiopathological mechanisms. In 2016, we began researching non-toxic, targeted adoptive cellular immunotherapies for these children with the aim of preventing the long-term effects of current chemotherapy.

Our goals

Our group is currently involved in various lines of research in pursuit of the following objectives:

1. To understand the aetiology and pathogenesis of leukaemia in breastfeeding infants. To do so, we use primary samples taken from patients and develop different animal and cellular models based on prenatal (embryonic, foetal) and postnatal (neonatal and adult) stem cells.

2. To gain a better understanding of the role of bone marrow (BM) stroma in chemoresistance in acute myeloid leukaemia (AML) and identify new therapeutic targets for AML, which is the most common form of leukaemia in adults and whose prevalence increases with age.

3. To improve adoptive cellular immunotherapies against ALL-B, ALL-T and AML. To achieve this, we are searching for new therapeutic targets and developing new CARs (chimeric antigen receptors) for the different types of acute leukaemia.

Our overall goal is to contribute towards curing 100% of childhood leukaemias or convert them into chronic conditions, without generating lifelong toxicities.

Our challenges

Childhood diseases have an enormous emotional impact on the patient's whole family and everybody around them. Moreover, we must not forget that children are the future of our society, so investing in their health will benefit the future of our society enormously. Through our research, we aim to:

1. Identify the cellular origin, cellular and molecular mechanisms, and the genetic and epigenetic composition of ALL-B in breastfeeding infants.

2. Contribute to the development of new therapeutic strategies in AML targeted towards reducing the resistance mediated through the BM microenvironment and that are particularly effective against LICs.

3. Develop adoptive cellular immunotherapies against ALL-B, ALL-T and AML using allogeneic T-cells without genome editing to eliminate TCR, CD3 and other molecules that play a role in immunological synapse.

Keywords
Paediatric leukaemia; stem cells; immunotherapy; MLL rearrangements; PDX models.

26
STEM CELL TRANSPLANTATION AND CELLULAR IMMUNOTHERAPY

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Overview

We conduct research into cell immunotherapy treatments for patients with advanced malignant blood disorders, who tend to have a very short life expectancy. To treat such patients, we develop CAR-T and CAR-NK therapies based on adding chimeric antigen receptors (CAR) to cells of the immune system, such as T-lymphocytes and NK cells, respectively. CARs help recognize and attack tumour cells exclusively, specifically and effectively, thereby preventing an autoimmune response and reducing secondary effects on healthy cells.

Our research

Former research from our group focused on the cytotoxicity mechanisms of CB-NK cells when they come into contact with MM tumor cells, in order to fight them. We discovered that they were able to regulate the cytotoxic or attack mechanisms depending on the characteristics of each tumor cell.

Later on, we started developing CART cells against BCMA to treat MM patients and achieved good results. We are currently improving cell immunotherapy treatments by combining CART with CB-NK cells. Moreover, we are studying how and why some tumor cells develop resistance to these therapies, with the aim of suppressing this resistance capacity.

Our goals

We are studying what happens at a molecular level between CART and CB-NK cells throughout the process of recognizing, contacting and attacking tumour cells in order to identify which proteins and defence strategies are used by CART, CB-NK and other cells in the immune system. Moreover, we are examining what happens within the environment of the cells when they meet tumour cells. This knowledge will help us develop better strategies to improve the efficacy of these therapies.

Through our research, we aim to achieve the best possible scenario: to cure patients and ensure that they do not relapse.

Our challenges

If we manage to enhance the efficacy of the CAR-T therapy and its permanence in patients to protect them from relapses, this breakthrough could be applied to patients with types of cancer other than MM. Therefore, through our research we hope to answer the following questions:

1. How are tumour cell resistance mechanisms against immune cells developed?

2. How can these tumour cell resistance mechanisms against immune cells be avoided?

3. How can the persistence and efficacy of CART cell treatment be increased?

Keywords
Multiple myeloma; B-cell malignancies; chimeric antigen receptors; T lymphocytes; NK cells; cord blood-derived NK cells; haematological malignancies; B-cell maturation antigen.

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EPIGENETIC THERAPIES

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Overview

Epigenetic therapies aim to modify the epigenome, the set of molecular processes that regulate gene expression without altering the DNA sequence and can change the course of a disease and its phenotype. There are now examples of epigenetic drugs for treating haematological malignancies approved by the United States Food and Drug Administration (FDA). However, the volume of promising preclinical evidence far exceeds the number of epigenetic research projects that have resulted in clinical applications to patients. Therefore, more translational studies that may lead to the development of more specific epigenetic drugs and more robust biomarkers are required.

Our research

Our research aims to ascertain the therapeutic benefit of targeting epigenetic alterations in cancer together with the epigenetic-based stratification of patients to predict therapy response. To achieve this, we develop research based on three specific aims:

1. Identification of the epigenetic alterations that act as drivers of tumour progression ("druggable epigenetic alterations").

2. Validation of epidrugs that can efficiently revert aberrant epigenomes in cancer.

3. Stratification of patients based on their epigenetic profile to predict response to immunotherapy.

Our goals

We aim to develop a translational research line (named "epigenetic therapies") that focuses on elucidating the epigenetic alterations that are druggable targets in a tumour, and the means to exploit them therapeutically within the framework of precision medicine.

Our challenges

Through our research, we aim to help answer the following questions:

1. Which epigenetic alternations represent targets for drugs to treat cancer?

2. How can we efficiently treat tumours caused by epigenetic alternations?

3. Who could benefit from therapeutic strategies based on epigenetics?

Keywords
Epigenetic drug; epigenetic editing; epidrug; haematological malignancies; targeted therapies.

28 LYMPHOMA TRANSLATIONAL

Led by
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Overview

Our research is centered on the development of innovative preclinical models of B-cell lymphoma that can be used to unravel the complex role of tumor-lymphoma crosstalk during the development of the disease and the acquisition of refractoriness in current regimens. To that end, we intend to reproduce the original composition and architecture of tumors in the laboratory to carry out a complete transcriptomic and proteomic analysis and develop new pharmacological entities in collaboration with academic experts and clinical-level pharmaceutical companies, all with a view to fostering the bench-to-bedside transfer of new and tailored therapeutic strategies.

Our research

We develop *in vitro* and animal models with the intention of more accurately recreating the context of onset and progression of the lymphoma in each patient. In this regard, we take account of fundamental parameters that until now have been largely unexplored in preclinical research, such as the architecture of the original tumor, the components of the immune system that accompany it and the defects in the regulation of the proteins – not only of the genes – that characterize it.

Our goals

Our main areas of research are:

1. Development of a patient-derived xenograft platform for the evaluation of new targeted therapies in aggressive B-cell lymphomas. To confirm the efficacy, safety and translationality of these studies, we propose that standard *in vitro* assays be associated with innovative *in vivo* models (PDX) to allow us, firstly, to work directly with primary tumor cells to validate the most effective therapies and the most relevant biological effects while taking into account the role of the tumor microenvironment; and, secondly, to guarantee that these therapies can be translated into clinical trials with molecular and genetic determination of the factors that condition the response to the best therapies tested in each patient.

2. Modulation of the lymphoid microenvironment by intrinsic protein homeostasis in aggressive B-cell lymphoma. We will characterize the ubiquitome of malignant B cells through proteomic profiling and correlate these intracellular complexes with the immunological pattern of each tumor model to validate the impact of tumor protein homeostasis on the development of B-cell lymphoma and the intratumoural infiltration of immune cells.

Our challenges

Through our research, we aim to understand the following:

1. To what extent intrinsic protein homeostasis can regulate the complex tumor-stroma crosstalk in different models of aggressive B-cell lymphoma.

2. How germinal center-derived lymphoma can be sensitized to immune checkpoint blockade therapy.

3. How multiomics analysis of paired treatment-naïve and therapy-refractory B-cell lymphoma can help in the design of efficient and personalized therapies.

Keywords
B-cell non-Hodgkin's lymphoma (NHL); tumor modelling; proteostasis; tumor microenvironment; immunotherapy.

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ONCOGENESIS AND ANTITUMOR DRUGS

Led by

Ramon Mangues

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Overview

Current treatments lack selectivity towards cancer cells, which induces insufficient anticancer activity and produces severe adverse effects that limit their dosage. We are developing self-assembling protein-based nanoparticles for the treatment of hematological and solid cancers that are highly selective in targeting receptors overexpressed in cancer stem cells. They display a wide therapeutic window by avoiding renal clearance while internalizing into and selectively eliminating cancer target cells and enhancing the uptake of the payload drug into cancer tissues, with negligible uptake or toxicity in normal tissues.

We have achieved high antitumor and antimetastatic effects using apoptotic, genotoxic or microtubule inhibitor drugs as payloads, and we are now testing novel payloads that use non-apoptotic cell death mechanisms.

Our research

We generate novel protein-based nanomedicines with a high therapeutic window that tackle unmet treatment needs in acute myeloid leukaemia (AML), diffuse large B-cell lymphoma (DLBCL) and colorectal cancer (CRC) using preclinical models and clinical translation, through:

1. The development of animal cancer models that are resistant to current therapy or disseminated for the study of the molecular mechanisms of cancer stem cell involvement in these processes, especially in cancer cells that overexpress the chemokine receptor CXCR4.

2. The development of drug nanoconjugates or protein-only nanoparticles for intravenous injection that use receptor-mediated targeted delivery of cytotoxic agents to cancer stem cells and incorporate novel drugs or polypeptide domains that exploit the higher capacity for apoptotic induction, or the triggering of cell death mechanisms as an alternative to apoptosis.

3. The development of artificial amyloid bodies for subcutaneous injection with capacity for the sustained release of therapeutic protein nanoparticles in the bloodstream that reach cancer tissues.

Our goals

Our aim is to develop nanomedicines that can effectively render cancers that have disseminated or relapsed sensitive to therapy by acquiring resistance to current therapy. In doing so, we expect to increase the cure and complete response rates, thereby leading to longer survival times.

An additional goal is to ensure that the repeated administration of these novel nanomedicines induces potent anticancer activity, while maintaining low or absent toxicity in normal tissues, associated with a lack of, or tolerable, side effects.

Finally, we also aim to develop a formulation of amyloid structured inclusion bodies whose capacity for the sustained release of therapeutic nanoparticles into the blood could be subcutaneously administered once a month. Their development will circumvent the need to administer the nanoparticles twice a week by intravenous injection, thus allowing patients to stay at home during treatment and avoid hospitalization.

Our challenges

Ninety percent of cancer patients die of metastases that do not respond to current treatments. Therefore, patients who develop metastases are considered incurable. Through our research, we aim to answer the following questions:

1. Is the selective elimination of cancer stem cells a relevant clinical target to improve therapy in different cancer types with acquired resistance and disseminated disease?

2. Will protein-based targeted nanoparticles that incorporate non-apoptotic and immunogenic cell death polypeptides increase cure, response and survival rates while reducing side effects once tested in patients?

3. What are the underlying mechanisms that dictate the highly selective accumulation of protein nanoparticles targeting the CXCR4 receptor we observe in cancer tissues?

Keywords
Biotechnology; nanomedicine; targeted drug delivery; oncotherapy; metastases.

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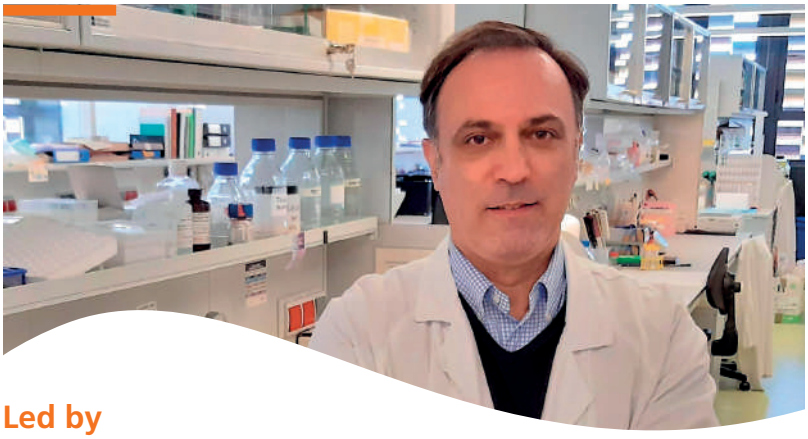
CELLULAR IMMUNOTHERAPY AND GENE THERAPY



Led by
Javier Briones

Group members

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Overview

The Cellular Immunotherapy and Gene Therapy Group is focused on the study of genetically modified T-cells expressing chimeric antigen-specific receptors (CARs) and their clinical application in patients with blood cancer.

Our research

Blood malignancies, like leukemia and lymphoma, are challenging diseases affecting one or more blood cell lineages. Traditional treatments include chemotherapy to deplete altered cells as much as possible, followed by bone marrow transplantation from a compatible donor, when appropriate.

The group currently focuses on studying T-cells genetically modified with chimeric antigen-specific receptors (CARs) and their clinical application in patients with blood cancer. Its current lines of research concentrate on the following aspects of cellular immunotherapy:

1. Functional antitumour research into subtypes of memory T-cells.

2. Study of the antitumour efficacy of memory stem T-cells genetically modified with CARs.

3. Development of new CARs targeted against haematological malignancies.

4. Development of clinical immunotherapy trials with CAR T-cells on patients with lymphoid neoplasms.

Our goals

Recently, a new and powerful immune cell type has been discovered called memory stem T cells. These are scarce but very special and, despite being roughly a 1% of the cells in our blood, they can find, attack and destroy cancer cells very efficiently. We have developed mechanisms to expand memory stem T cells in the lab and grow them in greater numbers, to make their action more potent and long-lasting.

Also, the genetic modification of patient-derived memory stem T cells to make them express CAR receptors, the so-called CAR-T therapy, is proving an enhanced anti leukemic potential in the clinical trials.

Keywords:
CAR-T; T-Cells; Lymphoid Neoplasms.

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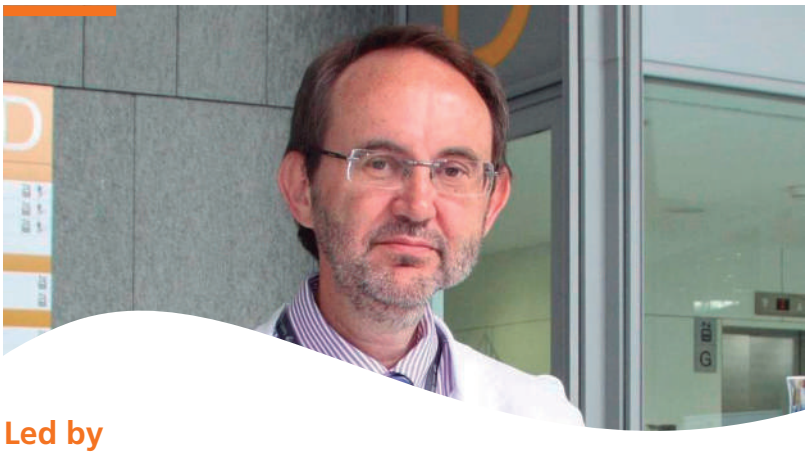
HEMATOLOGICAL DISEASES, TRANSPLANT AND CELL THERAPY



Led by
Jordi Sierra

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Lab Technician

Our research focuses on the molecular and cellular physiopathology of blood cancers, particularly on acute myeloid leukemia (LMA) and chronic lymphatic leukemia (CLL) where we seek to find new treatment options targeting molecular features. Also, we study the prognostic value of clinical and biological features in malignant hemopathies, like LMA and CLL.

We study the transplant of hematopoietic progenitors and its complications and develop new academic CAR-T cells enriched in T-memory stem cells to treat T and B Hodgkin lymphomas.

Our goals

The main goals of our research are:

1. Identify new prognostic parameters for risk and therapeutic stratifications.

2. Molecularly characterize acute myeloid leukemia and determine the prognostic value of known genes and other genes of uncertain significance.

3. Evaluate targeted therapy in cell lines and animal models (together with Dr. Mangues' group).

4. Reduce toxicity and increase the availability of allogeneic transplants.

5. Preclinical (mouse) and clinical studies on immunotherapy for lymphoproliferative diseases. Development of non-commercial CAR-T cell therapies.

Our challenges

It is paramount that we improve the prognosis of hematological patients by using new more precise therapies, and less toxic. Therefore, through our research, we aim to:

1. Improve the genotypic and immunophenotypic characterization of AML and CLL, to identify new prognostic factors and administer targeted therapy.

2. Improve the safety and effectiveness of hematopoietic transplantation and expand the number of patients who can benefit from it.

3. Develop new CAR-T products that enhance the currently commercially available ones.

Keywords
Hematopoietic transplantation; CAR-T cells; Immunotherapy; Acute Myeloid Leukemia; Chronic Lymphocytic Leukemia.

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DESCRIPTIVE AND ANALYTICAL EPIDEMIOLOGY OF CANCER

Led by
Rafael Marcos-Gragera

Group members

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Biostatistician

Overview

One of the main lines of research of the group is the epidemiology of hematological neoplasms, with the aim of determining the incidence, prevalence and survival of this type of cancer. The results obtained aim to provide useful and reliable information to design and/or improve the appropriate health resources and describe the population trends of this group of diseases.

Our research

Hematological neoplasms are a large group of diseases with a wide variability derived mainly from the type of cells that cause it. Also, the evolution and prognosis of each histological subtype of neoplasia is very diverse and it is necessary to deepen the knowledge of each of them. In this sense, population cancer records are a reference tool for establishing the incidence and survival of each type.

Our goals

Specifically, our research objectives aim at:

1. Establishing the prevalence, incidence and survival of myeloid, lymphoid and histiocytosis neoplasms globally and according to the respective subtypes.

2. To analyze the temporal trend of the incidence and survival of hematological neoplasms in the context of the evolving therapeutic background.

3. Determine epidemiological parameters based on sex and age.

4. Carry out etiological studies of hematological neoplasms according to each of the histological subtypes.

5. To study the genetic and environmental risk factors related to hematological neoplasms.

6. Describe the risk factors and epidemiology of multiple myeloma based on its precursor cells.

7. Analyze the associations between comorbidity and the survival of lymphoid and myeloid neoplasms.

8. Evaluate the population effectiveness of new therapies in a real population and the impact on survival.

9. Identify changes in the classification, definition and coding of hematological neoplasms and establish working protocols to have homogeneous tools that allow epidemiological comparisons at the international level.

Our challenges

Through our research, we aim to understand the following:

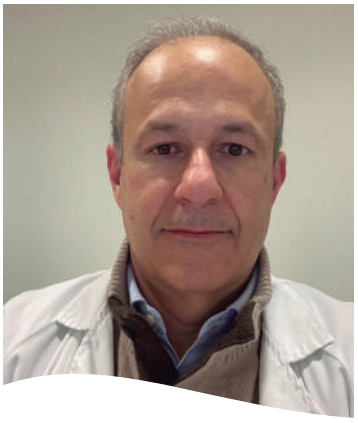
1. What is the incidence of hematological neoplasms in the territory?

2. What is the survival of each of the histological subtypes of neoplasia?

3. How have changes in the coding of hematological neoplasms over time affected the epidemiological determinants of this group of diseases?

Keywords
Incidence; survival; mortality; lymphoid neoplasms; myeloid neoplasms; histiocytosis; hematological neoplasms.

33 HEMATOLOGICAL DIAGNOSIS



Led by
Josep Nomdedéu

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Medical Intern Resident

In our lab, we focus on both malignant and non-malignant hemopathologies to offer better diagnostics, understand its biological characteristics, and develop new treatments. We study acute leukemias multi-omics and platelet pathologies like thrombocytopenias, thrombocytopathies and thrombosis.

Malignant haemopathologies

1. Diagnostic activities: morphological, immunophenotyping, cytogenetic and molecular characterization of acute leukaemias).

2. Biological characteristics responding to therapy.

3. New treatments using cell line models aimed at molecular targets.

4. Genomic (microarrays) and proteomic platforms for diagnosis.

5. Murine models development.

Noncancerous haemopathologies

1. Diagnosis and characterization of thrombocytopenia, thrombocytopathies and other platelet pathologies.

2. In the framework of the GAIT-2 project (genetic analysis of idiopathic thrombophilia, phase 2), to seek new phenotypes that favor the development of thrombosis, specifically related to the structure and function of platelets and other blood cells.

Our challenges

Through our research, we aim to:

1. Consolidate the characterization of hematological tumors and complex, rare, and genetic noncancerous hematopathology's.

2. Include the results of mass-analysis genomic and proteomic platforms in diagnostic algorithms and establish prognostic factors for hematological disorders.

3. Develop functional cell culture and animal (murine) models.

4. Consolidate cooperation with the GAIT-2 project, especially regarding platelet and other blood cell participation in thrombosis generation.

Keywords
Malignant hemopathologies, thrombocytopathies, thrombosis.

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CHRONIC LYMPHOCYTIC LEUKEMIA

Led by
Carolina Moreno

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Maranjo Moga, Maria Esther
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Zamora Albiol, Nil
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Overview

Chronic lymphocytic leukemia (CLL), the most common adult B-cell malignancy in Western countries. It is characterized by the accumulation of monoclonal CD5+ B cells with a characteristic immunophenotype in peripheral blood, bone marrow, and lymphoid tissues. The clinical course of the disease is extremely heterogeneous and, as a result, the individual life-expectancy ranges from a few years to a virtually normal lifespan. Despite the important progress in its therapy, CLL is still considered an incurable disease.

Our research

Our group is constantly making hard efforts to gain further insights into the characteristics of the leukemic compartment and deepen on the impact of the tumour microenvironment. This knowledge can contribute to better understand the biologic events involved in the disease development and be used to develop new strategies for clinical management and therapy and eventually to improve the quality of life of patients with CLL.

Our group has been involved in several pivotal clinical trials that led to the approval of new drugs for CLL therapy. Also, we are involved in several projects focused on the characterization of residual leukemic cells, autoimmunity and mechanisms at work in BCR signaling.

Our goals

Our group is constantly making hard efforts to gain further insights into the characteristics of the leukemic compartment and deepen on the impact of the tumour microenvironment. This knowledge can contribute to better understand the biologic events involved in the disease development and be used to develop new strategies for clinical management and therapy and eventually to improve the quality of life of patients with CLL. Through our research, we aim to:

1. Make available better diagnosis, prognosis and therapeutical strategies in CLL.
2. Extend the knowledge of molecular and cellular events implicated in CLL development.
3. Prevent clinical relapses in CLL.
4. Design feasible approaches to monitor MRD in CLL.
5. Find a cure to CLL patients.

Our challenges

Inherent to the disease, CLL patients have a deregulated immune system, which predispose them to have disease complications, including recurrent infections and autoimmune phenomena. The understanding of how the immune cells of tumor microenvironment contribute to maintain the survival of leukemic cells is essential to design future therapeutic strategies aimed, not only at eradicating leukemic cells, but also at restoring the immune system.

In the last years our group has started some projects aimed at describing the immune status and functional characteristics of B and T cell populations during the evolution of the disease and after therapy with targeted therapies.

Keywords
Chronic Lymphocytic Leukemia, B-cell receptor signaling, minimal residual disease, liquid biopsy, tumor microenvironment.

35 HEMATOLOGY RESEARCH

Led by
David Gallardo

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Medical Intern Resident

Roqueta Ruiz, Carolina
Medical Intern Resident

Overview

The research group in hematology is devoted to clinical and translational trials in hematology, focused on diagnosis, prognosis and the development of new therapies to treat hematological malignancies such as leukemias and myelomas.

Our research

The group uses a variety of approaches such as genetic studies of the immune response, pharmacogenomics in response to treatment, analysis of polymorphisms as disease predictors and the study of cell populations using flow cytometry for the characterization of residual disease.

Our goals

Through our research, we aim to:

1. Investigate biological, clinical, and epidemiological aspects of hematological diseases

2. Carry out translational research projects focused on finding prognostic factors or treatment response predictors

3. Carry out clinical research, promoting participation in clinical trials for hematological diseases and participating in national and international cooperative groups.

Keywords

Hematology, myeloblastic leukemia, multiple myeloma, chronic lymphatic leukaemia, residual disease.

CORE FACILITIES

Proteomics Unit

Unit manager

Carolina de la Torre

Staff

Joan Josep Bech, Bernat Cucurull.

The Proteomics Unit of the Josep Carreras Leukaemia Research Institute, part of the Carlos III Health Institute (ISCIII) and the Proteomics Network ProteoRed, offers mass spectrometry services to the academic and to the private sector under request.

The unit's main activity is to promote the incorporation of proteomics as a key tool for the development of clinical and basic projects at our institution. Our main work consists of offering innovative, high-quality proteomic and peptidomic services that allow the best therapeutic and human health solutions to be selected.

How do we support you?

- By providing scientific and technological support to high-level research projects in the field of proteomics according to international standard procedures.
- By providing researchers with scientific advice, from the project's planning and experimental design stage to the execution phase, processing of samples and interpretation of results, and support during presentations and writing of results for publication.
- Through dissemination and training for researchers on the methodology and applications of the techniques offered.
- By contributing to the promotion of innovation in health technologies and the transfer of the knowledge generated to the public health service, and supporting genetic, epigenetic and pharmacogenetic diagnosis.

Our services

Proteomic analysis is a very powerful approach to addressing key challenges in clinical and health research. This approach can be used for different aspects of clinical and health sciences, such as biomarker discovery, drug target identification and food technology.

Biomarker discovery from a wide range of samples to improve precision medicine at different levels: a) early diagnostic, and b) prognosis to predict disease progression and guide treatment selection.

The Bioinformatics Unit

Unit manager

Manuel Castro

Staff

David Piñeyro, Abdessamad El Ayadi.

The Bioinformatics Unit at IJC provides both internal and external researchers with high-quality computational analysis services to cover all aspects of research projects related to clinical and biological data.

The Bioinformatics Unit offers a wide range of services, including experimental design for NGS or microarray experiments, statistical consulting, NGS and microarray data analysis and integration, scientific database management and software design and implementation. It also provides training on different bioinformatics topics and the use of HPC (high-performance computing) resources.

Services

- General services:
  - Bioinformatics data analysis, including consulting, experimental design advice, technology selection, final report generation and interpretation.
  - Support for project proposal writing, data provider selection and budget planning.
  - Custom bioinformatic analyses and tailored software development.
  - Clinical software development compliant with ISO-13485.
  - Large-volume data storage, management and submission to public repositories.
  - Bioinformatics analysis training.
- Bioinformatics analysis:
  - Epigenomics and epitranscriptomics: 5mC and 5hmC DNA methylation arrays (infinium methylation 450K and EPIC), whole-genome bisulfite sequencing (WGBS), reduced-representation bisulfite sequencing (RRBS), bsRNA-Seq, m6A and m1A RNA methylomes by NGS and array.
  - Genomics: whole-exome sequencing (WES), WGS, SNP and CNV arrays, ChIP-seq, Hi-C.
  - Transcriptomics: RNA-Seq, Ribo-seq, RIP-seq, iCLIP, CLIP-seq, single-cell transcriptomics.
  - Metagenomics: 16s rRNA.

CORE FACILITIES

Genomics Platform

Unit manager

Damiana Álvarez-Errico

Staff

Carles Arribas, Patricia Barrero.

The Genomics Unit aims to provide the IJC community and external researchers with scientific services. Several state-of-the-art technologies have been implemented in the unit to assess relevant genomic and epigenomic features and thus unravel basic molecular mechanisms of disease and contribute to the discovery of therapeutic targets and biomarkers.

The Unit is equipped with cutting-edge technology to offer solutions for both basic and translational epigenomic and genomic studies on many sample types (primary cells, cell lines, frozen and paraffin-embedded tissues). We have long-standing experience in array-based genome-wide DNA methylation analysis and pyrosequencing. We use next-generation sequencing (NGS) technology to investigate subsets of genes or specific genome regions with Illumina's MiSeqDx System.

The applications provided by the Genomics Unit at IJC are:

- Infinium MethylationEPIC™ BeadChip technology (Illumina)
- MiSeq™Dx NGS sequencer (Illumina)
- PyroMark™Q48 (Qiagen)

Single Cell Unit

Unit manager

Laura Palomo

The Single Cell Unit aims to provide scientific services to the Josep Carreras Institute community and is equipped with cutting-edge technology to apply single-cell technology to basic and translational genomic and transcriptomic studies. Single Cell approaches can reveal the cellular heterogeneity of tumors and help identify cells resistant to standard treatments or more prone to proliferate.

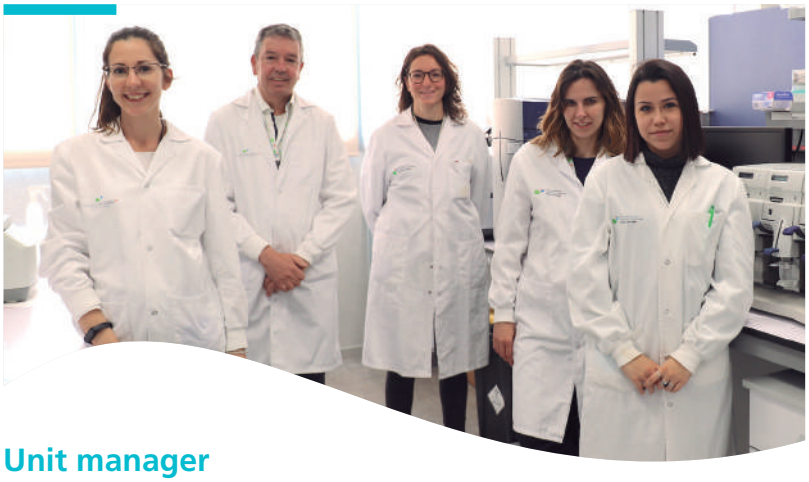
The Single Cell Unit is equipped with a Chromium™ Controller (10x Genomics), a Mission Bio Tapestri Platform and the C1 system (Fluidigm). These technologies provide a comprehensive, scalable solution for cell characterization, gene expression profiling and DNA sequencing of up to tens of thousands of cells.

Services

- Chromium™ Controller (10x Genomics):
  - Single-cell RNA-seq (gene expression)
  - Single-cell RNA-seq (gene expression) + Feature Barcoding
  - Single-cell immune profiling (gene expression + TCR/BCR)
  - Single-cell ATAC-seq
- Tapestri Platform (Mission Bio):
  - Single-cell targeted DNA-seq (mutation analysis)
  - Single-cell targeted DNA-seq (mutation analysis + CNV analysis)
  - Single-cell DNA-seq + cell-surface protein analysis
- C1 System (Fluidigm):
  - Single-cell mRNA sequencing
  - Single-cell targeted gene expression
  - Single-cell miRNA expression profiling

CORE FACILITIES

Microarrays Unit



Unit manager

Mar Mallo

Staff

Nuria de Haro, Jessica Tijero.

The Microarrays Unit (UM) is a service focused on DNA and RNA microarray solutions towards a personalized medicine and participates in the Cytogenetic European Quality Assessment (CEQA).

Services

Microarray studies can offer various solutions for cytogenetic applications:

- Detection of whole genome gains and losses at a high resolution.
- Analysis of whole genome absences of heterozygosity.
- SNPs genotyping and genome-wide association studies.
- RNA Analysis Solution
- Gene expression profile studies on either human or mouse are suitable for:
- Detection of genes and pathways involved in diseases, treatment responses and biological processes.
- Predictive models based on gene expression profiles.
- Pharmacogenomics and toxicogenomics studies.
- Alternative splicing detection.
- Classification of samples on gene signatures.
- Analysis of miRNA.
- Microarray analysis on compromised samples with degraded and/or low quantity samples.

Quality sample analysis

In addition, to the microarray procedure we also offer DNA and RNA quantification and quality control analysis.

High throughput qPCR

The Biomark HD system is a high throughput qPCR that runs IFCs in either real-time or end-point read modes, bringing PCR solutions to a range of applications. The 48x48 Dynamic Array combines up to 48 samples and 48 assays, generating 2304 different assays in one single run. The 96x96 Dynamic Array combines up to 96 samples and 96 assays, generating 9216 different assays. In addition, the FLEXsix IFC incorporates six 12x12 partitions that can be organized in any configuration, in up to six separate experimental runs.

Applications

- Genotyping.
- Targeted Gene expression.
- Digital PCR.

Equipment

- Affymetrix Research Platform: GCS3000 with autoloader.
- Agilent Bioanalyzer 2100.
- NanoDrop 2000 Spectrophotometer.

CORE FACILITIES

Cytogenetics Unit

Unit manager

Francesc Solé

Staff

Isabel Granada, M. Carmen Villena, Encarnació Santafé, Rebeca Jurado, Marisol Sandri.

The Cytogenetics Unit is responsible for analytical tests belonging to Special Hematology from samples of whole blood, serum, plasma, urine, body fluids, bone marrow, lymph nodes, spleen, and tumor masses. The available analysis include: Special Hemostasis, Erythropathology, Special Cytology, Immunophenotype, Cytogenetics and Molecular Biology.

The Cytogenetics Unit at Josep Carreras Leukaemia Research Institute includes the Laboratory of Cytogenetics of the Institut Català d'Oncologia (ICO).

Services

- Conventional cytogenetics culture and karyotype performance
- Fluorescence in situ hybridization (FISH) with commercial probes
- QF-PCR

Sample Handling Circuit Unit

Unit manager

Francesc Solé

Staff

Rocío Ruiz, Jessica Aranda, Aida Silverio.

The Sample Circuit-Biobank platform aims at managing the voluntary donation of samples from patients with haematological malignancies, as well as the subsequent processing, storage and supervision of the samples. The Sample Handling Circuit Unit receives the bulk of its samples from the Catalan Institute of Oncology at the Germans Trias i Pujol Hospital (ICO-HUGTP). Nonetheless, samples received from other hospitals are processed in an identical way.

All samples in the collection have an attached Informed Consent Form approved by the ICO-HUGTP Ethics Committee and signed by the patient in triplicate, one copy remains at the IJC. The patient maintains the right to revoke consent at any time and in this case the samples concerned will be destroyed.

Storage of Samples

For sample storage, plasma and serum samples are kept at -80ºC and the isolated cell populations for each sample are cryopreserved in liquid nitrogen tanks at -150ºC. The technical staff of the IJC have created a database of patients, donors and samples received and processed according to required specifications for the tracking of each sample in the collection.

The staff verify the quality, security and tracking of the data and samples throughout the process and starting at extraction. The IJC implements a knowledge management system to document, guarantee tracking and the confidentiality of the registers according to the current legislation.

MANAGEMENT UNITS

MANAGEMENT

Group members

Garrido Anglada, Ana
Strategic and Managing Director

Together with Dr Manel Esteller, Ana Garrido is part of the management team to contribute to the development of general policy, strategic planning, enabling, and translating scientific vision and strategic objectives into a clearly articulated operational strategy.

The main objectives of the Strategic and Managing Director are:

- Strategic and operational organization of the Institute.
- Management, in accordance with the marked guidelines of the governing bodies, human resources, hiring staff, incidents, separation and termination of employment contracts, HR organizational policies, as well as the management of scholarships and grants, encouraging policies of Corporate Social Responsibility and attracting and retaining talent.
- Detection of the needs derived from the activity of the Institute Research Groups and the rest of the units from the economic and management point of view.
- Implementation of an agile model focused on researchers that favours their performance and the best concentration in scientific activity.

RESEARCH GRANTS UNIT

Group members

El Bouhali El Mallem, Sanae
Project Manager

Gil Guiñon, Estel
Project Manager

Lagunas Vila, Laia
Project Manager

Morales Cuñado, Cristina
Project Manager

Padial Melián, Verónica
Project Manager

Its objective is the attraction of public and private competitive funding, both nationally and internationally, as well as the proactive management of research projects granted. We support researchers throughout the life cycle of projects, from the detection of opportunities, the preparation of proposals and the training of research consortiums, to the management of projects in all areas beyond the economic.

INNOVATION UNIT

Group members

Riera Guerra, Anna
Innovation Manager

Farrés Àlvarez, Clara
Innovation Project Manager

The aim is to promote and boost innovation to improve the quality of life of society from the transfer of knowledge and developed technologies.

MANAGEMENT UNITS

ECONOMIC MANAGEMENT UNIT

Group members

Boix Montemayor, Heura
Economic Development Manager

The Economic Development Manager manages and coordinates the financial control of the Institute. Its main functions are linked to the control and supervision of finances and, ultimately, it acts as a link between the Institute's management and accounting.

HUMAN RESOURCES UNIT

Group members

Jané Morales, Núria
HR Manager

Carmona Fernández, Carolina
HR Officer

Oliva Pardo, Lidia
HR Officer

Its mission is to plan, organize and execute all processes relative to the professional development of the staff and their commitment with the organization, within the framework of current regulations, including training opportunities and occupational risk prevention.

FINANCE UNIT

Group members

Calonge Cortés, María Cristina
Financial Manager

Finestres Martínez, Xavier
Finance Officer

Mure Fernández, Mireia
Finance Officer

Vilanova Cuadra, Yaiza
Finance Officer

Matos Silva, Awilda
Finance Support

Its mission is to keep track of the actual finance situation of the Institute, rigorously and transparently, to support data driven strategic decision making in the short, medium and long run.

PURCHASING UNIT

Group members

Jimenez Ferrer, Neus
Purchasing Manager

Capitan Fernández, Judit
Purchasing Officer

Reyes Iborra, Laia
Purchasing Officer

Vergés Colominas, Anna
Purchasing Officer

Ariza Cabello, Nieves
Public Tenders Specialist

Gerbolés López, Anna
Public Tenders Specialist

The unit's aim is to optimize purchasing at the institutional level according to the legal framework for public research bodies, to be more efficient, fast and agile, avoid unnecessary costs and save resources for research.

MANAGEMENT UNITS

IT UNIT

Group members

Jubany López, Marc
IT Manager

Contreras Peña, Francisco
IT Technician

Galligani, David
IT Technician

The unit's objective is to support the Institute's staff in the use and purchasing of IT components -hardware, software and systems- and keep the institutional IT systems online and secure while ensuring its efficiency.

DATA MANAGEMENT UNIT

Group member

Carrio Reig, Marta
Data Manager

Aimed at delivering and maintaining all necessary infrastructure to efficiently keep institutional data available at all levels: strategic, technical, administrative and for transparent accountability in front of local or international management bodies.

COMMUNICATION UNIT

Group members

Díaz López, Helena
Communication Manager

Troytiño Pérez, Isa Gavina
Communication Manager

Passionate about spreading the latest discoveries of our scientists and bring their research efforts closer to society, in any form. The unit strives to keep our partners closer and updated, and to foster the staff's sense of belonging.

LAB MANAGEMENT UNIT

Group members

Pérez Ladaga, Albert
Lab Manager

García Ferran, Alba
Lab Technician

Moreno Zambrana, Elisabet
Lab Technician

Saez González, Carlos
Lab Technician

The aim is to support researchers in their daily work in laboratories so that their research can be carried out with the best equipment, in the best state and with maximum safety.

MANAGEMENT UNITS

LEGAL SERVICES

Group member

Lafarga Traver, Josep Lluís
Legal Services Manager

Its mission is to support the Institute in all legal matters, particularly in establishing the collaboration framework with partner institutions, ongoing clinical trials and innovation aspects in biomedical research.

FACILITIES UNIT

Group members

Arqué Comas, Carles
Facilities Manager

Pérez García, María Isabel
Receptionist

The aim is to support as a facilitator, manager, and organizer for the prop-er functioning of all the sites of the Institute in terms of their resources and associated with the development of our activity.

SUPPORT UNIT

Group members

Amado Ballano, Erika
Management Assistant

Izquierdo Sánchez, Irma
Management Assistant

Marín Manzanera, Esperanza
Management Assistant

The Support Unit supports the governing bodies of the Institute in daily administrative tasks, agendas as well as in travel procedures.

COMMUNICATION

COMMUNICATION / **SELECTED PRESS RELEASES**

2020
February 11

Women in Science in the Josep Carreras Institute

The Josep Carreras Leukaemia Research Institute is one of the research centers in Catalonia with more equality in the recruitment of men and women with scientific, technological, and medical training and professions. Of the 189 active researchers, 109 are women. 50% of post-doctoral staff, associated researchers and laboratory technicians are women, as well as 64% of doctoral students. In terms of research management and leadership positions, of the Institute's 27 research groups, eight are led by women.

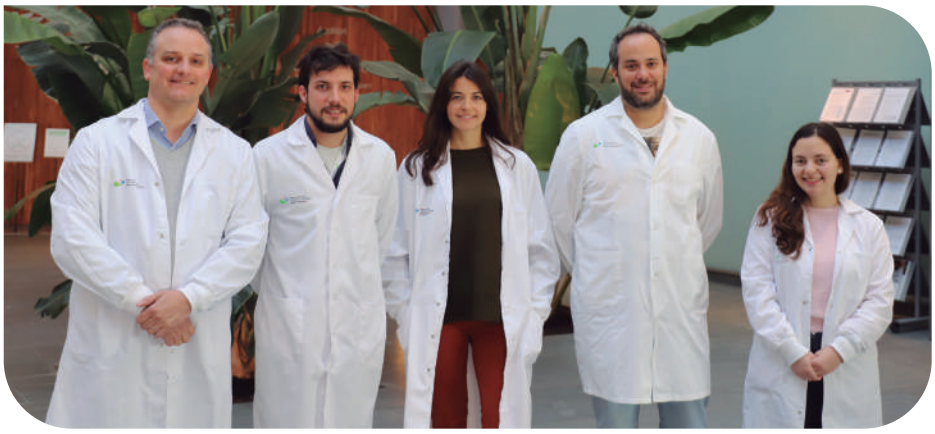
SELECTED PRESS RELEASES

2020 March 5

José María Ribera leads a study of the HARMONY project on Acute Lymphoblastic Leukemia

The principal investigator of the Institute Josep Carreras Acute Lymphoblastic Leukemia Research Group, José María Ribera, is leading a study of the HARMONY project to find out whether the deletion of a particular gene has prognostic significance in this disease in adults.

2020 March 11



Gael Roué starts a Gilead Grant Research Project on aggressive B-cell lymphoma

Gael Roué, leader of the translational lymphoma research group of the Josep Carreras Institute starts a project of a Gilead grant to study the Modulation of the lymphoid microenvironment by intrinsic protein homeostasis in aggressive B-cell lymphoma.

2020
April 30

Pablo Menéndez receives one of the European Research Council's Proof of Concept grants

The European Research Council has awarded Josep Carreras Institute's researcher Pablo Menéndez with one of the 55 Proof of Concept grants for researchers from centers throughout Europe.

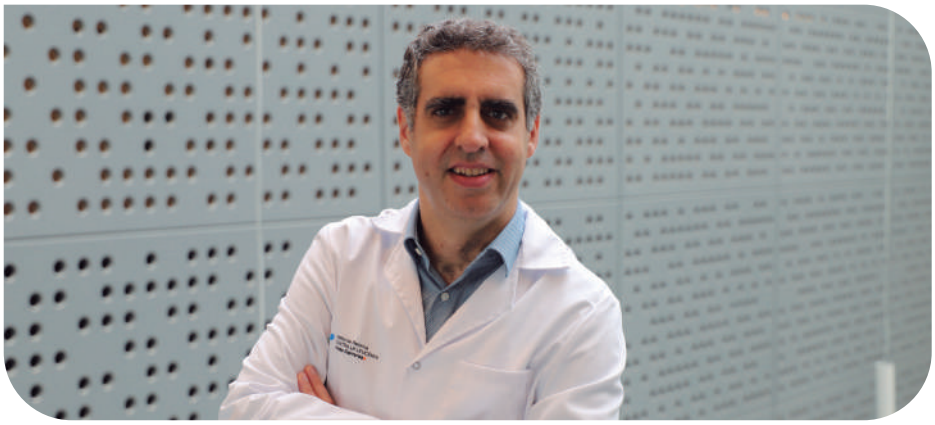
2020
May 18

The Proteomics Unit joins the COVID-19 Mass Spectrometry Coalition

The Josep Carreras Institute Proteomics Unit joins the International Mass Spectrometry Coalition, which is working to provide molecular-level information of SARS-CoV-2 to accelerate diagnostics and treatment of COVID19 pandemic.

SELECTED PRESS RELEASES

2020
July 22



Dr. Manel Esteller has been awarded the Narcís Monturiol Medal for scientific and technological merit from the Government of Catalonia

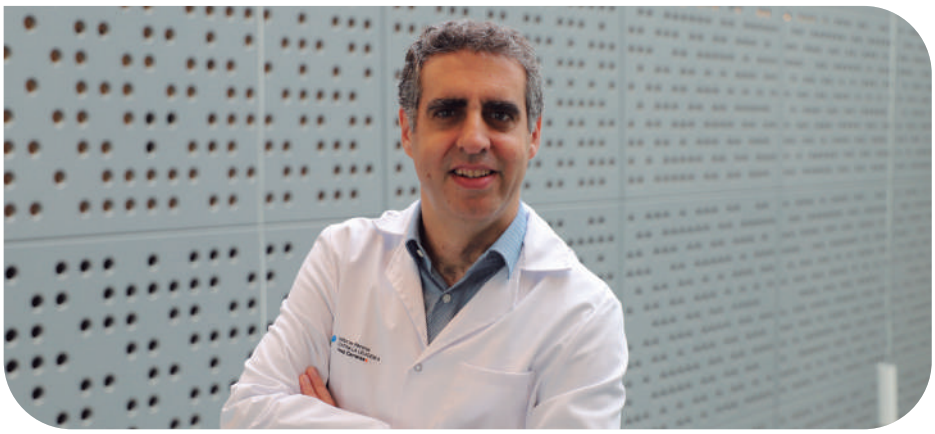
The researcher Manel Esteller, director of the Josep Carreras Leukaemia Research Institute, and leader in Cancer Epigenetics, has been awarded the Narcís Monturiol Medal for scientific and technological merit from the Government of Catalonia.

2020
September 29

New project on Diffuse Large B Cell Lymphoma, co-led by Biola M. Javierre and funded by the Deutsche José Carreras Leukämie Stiftung

The project, funded by the Deutsche José Carreras Leukämie Stiftung and co-led by Dr. Biola M. Javierre, Leader of the 3D Chromatin Organization Group, and Prof. Björn Chapuy, from the University of Gottingen (Germany), focuses on the study of the molecular bases of diffuse large B-cell lymphoma (DLBCL).

2020
November 18



Manel Esteller is referred as Highly Cited Researcher According to 2020 Web of Science Group List

Josep Carreras Leukaemia Research Institute director Manel Esteller has been named Highly Cited Researcher, according to the Highly Cited Researchers 2020 list from the Web of Science Group, released today.

2020
November 25

Dr. Marcus Buschbeck leads the European Network INTERCEPT-MDS focusing on the shared training and research in Myeloid Diseases

Dr. Marcus Buschbeck, group leader of the Josep Carreras Leukaemia Research Institute, coordinates the Innovative Training Network (ITN) INTERCEPT-MDS, a Marie Skłodowska Curie Action, funded by the European Commission under H2020 framework programme.

2020
December 31

Researchers from the Josep Carreras Institute received one of the five grants awarded worldwide by the Facebook founder's Foundation to study COVID-19

The epigenetics and immune diseases group, led by Dr Esteban Ballestar, obtained one of the five worldwide grants awarded by the Chan Zuckerberg Initiative.

COMMUNICATION / **SCIENTIFIC DISSEMINATION**

Health is a high-priority public issue, and the dissemination of basic health knowledge is essential to achieve optimal levels of development and human welfare across society as a whole. Knowledge transfer and dissemination of results from biomedical research are some of the key factors in tackling this challenge.

For this reason, it is vitally important to disseminate our work and strengthen our bonds with society and the public. We endeavour to integrate social corporate responsibility into our management model, a desire closely linked to the organizational values of the Josep Carreras Foundation.

In 2020, IJC actively participated in scientific dissemination, citizen participation and the engagement of high-school students to increase their understanding of what medical research involves. Examples include the Science Week at Badalona Town Council and Magic Badalona Running.

European Researcher's Night

Magic Badalona Running 2020

FACTS & FIGURES / **INNOVATION**

FACTS & FIGURES / **INNOVATION**

The Josep Carreras Institute is committed to knowledge transfer and assessing and searching for market opportunities in the broadest terms. As well as focusing on its own interests, it seeks to contribute to society and our country's progress. In 2020, the results of our research in terms of innovation were as follows:

3 new patents in 2020 (total accumulated 8):

- EP20382175.6 - CD22 targeting-moiety for the treatment of b-cell acute lymphoblastic leukemia (B-ALL) (priority date: 11/03/2020).
- EP20382293.7 - Selective resorbable functionalized nanoparticles, a process for obtaining thereof and their use in preventing and/or treating a disease and/or a disorder (priority date: 14/04/2020).
- EP20383021.1 - Compositions for use in the treatment of leukaemia (priority date: 23/11/2020).

3 new licensed technologies in 2020 (total accumulated 4)

1 new spin-off – OneChain Immunotherapeutics (2 active spin-off together with Leukos Biotech)

- CEO: Jorge Alemany
- Co-Founder and CSO: Prof. Pablo Menéndez
- Webpage: https://www.onechaintx.com/en/

OneChain Immunotherapeutics is an spin-off company from the Josep Carreras Leukaemia Research Institute (IJC) and the Catalan Institution for Research and Advanced Studies (ICREA), founded in June 2020 and based on the research led by Dr. Pablo Menéndez, with the aim of developing immunotherapies against haematological neoplasms using CAR-T therapies and, thus, being an instrument to bring innovative therapeutic solutions closer to patients.

The core technologies licensed to OneChain Immunotherapeutics consist in CD1A and CD22 CAR-T therapies, respectively, as preclinical candidates to further advance to the clinic. The spin-off was initially funded through a round of seed capital of €3,050,000 provided by Invivo Ventures, the Ministry of Industry, through CDTI-Innvierte, and the Josep Carreras Foundation

FACTS & FIGURES / **TEACHING AND TRAINING**

The Josep Carreras Institute offers a high-quality teaching programme for scientists and technicians interested in achieving a solid, up-to-date grounding in the field of leukaemia and malignant blood diseases. It organizes complementary training activities at all levels, from scientific conferences, seminars and technology sessions to specialized courses.

33 Scientific seminars

3 Training courses

In addition, the Josep Carreras Institute offers a Doctoral Degree in Haematology and a Master's Degree in Malignant Blood Diseases and participates in the teaching activities of degrees in medicine and biomedicine:

12 Theses read

48 Current doctoral theses

As an affiliate of the University of Barcelona and the Autonomous University of Barcelona, the Josep Carreras Institute provides training for new generations of scientists, and our researchers disseminate scientific knowledge and discoveries in several biomedical and related degrees and master's courses.

FACTS & FIGURES / COURSES AND SEMINARS

January 2020

Bivalent roles of Rho GEFs in cancer
Speaker: Dr Xose R. Bustelo, Instituto de Biologia Molecular y Celular del Cancer- IBMCC (Salamanca).

The causation of childhood B cell precursor ALL
Speaker: Isidro Sánchez-García. Instituto de Biologia Molecular y Celular del Cancer -IBMCC.

Engineering of bacteria to treat human diseases
Speaker: Luis Serrano. Centre for Genomic Regulation -CRG.

Targeting telomeres in càncer
Speaker: Maria a. Blasco. Spanish National Cancer Research Centre – CNIO.

Manipulating cell plasticity: gain and loss of cell identity
Speaker: Manuel Serrano. IRB Barcelona.

Tumor suppressor actions of the Thyroid Hormone Receptor
Speaker: Ana Aranda. Instituto de Investigaciones Biomedicas "Alberto Sols"

Gene Therapy approach in Bone Marrow Failure Syndromes
Speaker: Juan Antonio Bueren. CIEMAT.

Signaling and metabolic alterations at the core of prostate cancer aggressiveness
Speaker: Dr. Arkaitz Carracedo, ERC Consolidator Grant Ikerbasque Research Professor and Principal Investigator in Cancer Cell Signaling And Metabolism Lab in Bizkaia Science and Technology Park, Spain.

Aberrant activation of developmental programs in adult disease
Speaker: Ángela Nieto. Instituto de Neurociéncias de Alicante.

Tumor genomes shed light into somatic mutational processes and cancer vulnerabilities
Speaker: Núria López Vigas. Institute for Research In Biomedicine Barcelona, Spain,

Leukemia microenvironment at single cell resolution
Speaker: Iannis Aifantis. NYU Langone Health.

Histone variants & their chaperones: A flexible network adapting to changes
Speaker: Geneviève Almounzi. Centre de Recherche Institute Curie.

Normal and Neoplastic Stem Cells
Speaker: Irving L. Weissman. Stanford Institute for Stem Cell Biology and Regenerative Medicine.

FACTS & FIGURES / COURSES AND SEMINARS

Chromosomal instability and genome plasticity in cancer evolution, immune evasion and metastasis

Speaker: Charles Swanton. Francis Crick Institute.

Reactivation of tumor suppression function for cancer prevention and therapy

Speaker: Pier Paolo Pandolfi. Beth Israel Deaconess Medical Center.

Treating cancer with the immune System

Speaker: Antoni Ribas. UCLA Jonsson Comprehensive Cancer Center.

DAMPs and MAMPs regulate the delicate balance of tolerance in intestinal epithelial cells

Speaker: Laurence Zitvogen. Gustave Roussy Cancer Center.

Genetics and Therapy of Clonal Hematopoiesis and Myeloid Malignancies

Speaker: Ross Levine. Memorial sloan Kettering Cancer Center.

Unlock the potential of genomics with Novogene Europe - Leading Edge Next-Generation Sequencing and Bioinformatics Services

Speaker: Freddy Monteiro, Ph.D., Regional Account Manager at Novogene Europe

Understanding how females make a good egg

Speaker: Dr. Karen Schindler, Associate Professor in the Department of Genetics at Rutgers University, New Jersey.

Role of chromatin regulatory genes in breast cancer anthracycline resistance

Speaker: Dr. Jose. A Seoane, Instructor in Christina Curtis group at Sandford University.

February 2020

How can maths fight cancer?

Speaker: Prof. Víctor M. Pérez-García, Mathematical Oncology Laboratoru (MOLAB), University of Castilla-La Mancha, Spain.

Epigenetic Vulnerabilities of Human Glioma

Speaker: Dr. Alea A. Mills, Professor at Cold Spring Harbor Laboratoru, Long Island.

Dissecting mechanisms that govern cellular plasticity

Speaker: Dr. Bruno di Stefano, Ph. D fellow in the lab of Dr. Konrad Hochedlinger at Harvard University.

Health, Demographic Change and Wellness H2020 Social Challenge 1

March 2020

Exploring the 3D genomic ecosystems where genes and enhancers evolve

Speaker: Daniel Rico, PhD. NU Research Fellow. Head of Computational Epigenomics Laboratory, Newcastle University Biosciences Institute

May 2020

Evolution of regulatory landscapes

Speaker: Dr. José Luis Gómez-Skarmeta, Centro Andaluz de Biología del Desarrollo, Spain.

Signaling and metabolic alterations at the core of prostate cancer aggressiveness

Speaker: Dr. Arkaitz Carracedo, ERC Consolidator Grant Ikerbasque Research Professor and Principal Investigator in Cancer Cell Signaling And Metabolism Lab in Bizkaia Science and Technology Park, Spain.

September 2020

Studying chromatin as nexus between basic and applied research

Speaker: Markus Buschbeck. Cromatin, Metabolism and Cell Fate Group Leader in Bizkaia Science and Technology Park

October 2020

Cell-of-Origin, pathobiology and therapeutics of MLL-rearranged infant B-cell ALL

Speaker: Pablo Menéndez. Stem Cell Biology, Developmental Leukemia and Immunotherapy Group Leader.

MDS, clonal evolution disease. Ongoing projects

Speaker: Francesc Solé. Myelodysplastic Syndromes Group Leader.

Studying chromatin as nexus between basic and applied research

Speaker: Markus Buschbeck. Cromatin, Metabolism and Cell Fate Group Leader

November 2020

New therapeutic approaches for acute leukemias

Speaker: Ruth Risueño. Leukemia Stem Cell Group Leader.

Immune checkpoint blockade therapy in aggressive B-cell lymphoma

Speaker: Gael Roué. Lymphoma Translational Group Leader.

December 2020

Targeted drug delivery in cancer therapy

Speaker: Ramon Mangues. Oncogenesis and Antitumor Drugs Group Leader.

CAR T cells immunotherapy with memory subsets for hematological malignancies.

Speaker: Javier Briones. Cellular Immunotherpy and Gene Therapy Group Leader.

FACTS & FIGURES / **FINANCIAL DATA**

The Institute's pioneering mixed-funding model is partially financed by the Josep Carreras Foundation. It also receives core funding from the Catalan government and is reliant on competitive funding for its research activities.

In 2020, there was a 70,69% increase in income from public funds and the provision of services. With respect to spending, this increased by 72,47% compared to the previous year.

A total of 35,40% of IJC's outlay corresponds to staffing, with a 49,50% increase compared to the previous year.

The profit for the 2020 financial year was €539.136,00 but when the depreciation of investments is taken into account the result was a loss of €929.592,00.

FACTS & FIGURES /
FINANCIAL DATA

	2019	2020
INCOMES	**8.282.177**	**11.716.754**
Contributions from the generalitat	1.785.632	3.644.424
Other transfers (fijc)	1.530.075	870.000
Services	808.533	1.037.549
Project implementation	3.828.160	5.109.269
Overheads	329.777	1.055.512
OPERATIONAL EXPENSES	**7.794.444**	**10.755.270**
Staffing costs	1.884.503	3.806.854
Information technologies services	100.229	155.850
Communication	4.717	9.211
Building maintenance	666.237	720.273
Laboratories maintenance	170.127	114.049
Research support	179.387	277.880
Project implementation	3.828.160	5.109.269
Scientific-technical services (platforms)	323.246	197.975
Biobank	14.246	15.308
Management support services	175.680	225.595
Other	312.076	81.482
Vat prorata	65.032	26.812
Expenditure on investments pending activation	50.414	
Heritage	14.643	
Reimbursement of subsidies and other management losses	5.747	14.711
RESULT OF THE ACTIVITY	**487.734**	**961.484**
Extraordinary result	0	7.494
Operating income	487.734	968.978
Financial performance	-17.733	-39.386
Result before amortization	470.001	929.592
Amortization	-966.372	-1.468.728
RESULT	**-496.371**	**-539.136**

FACTS & FIGURES / **AWARDS**

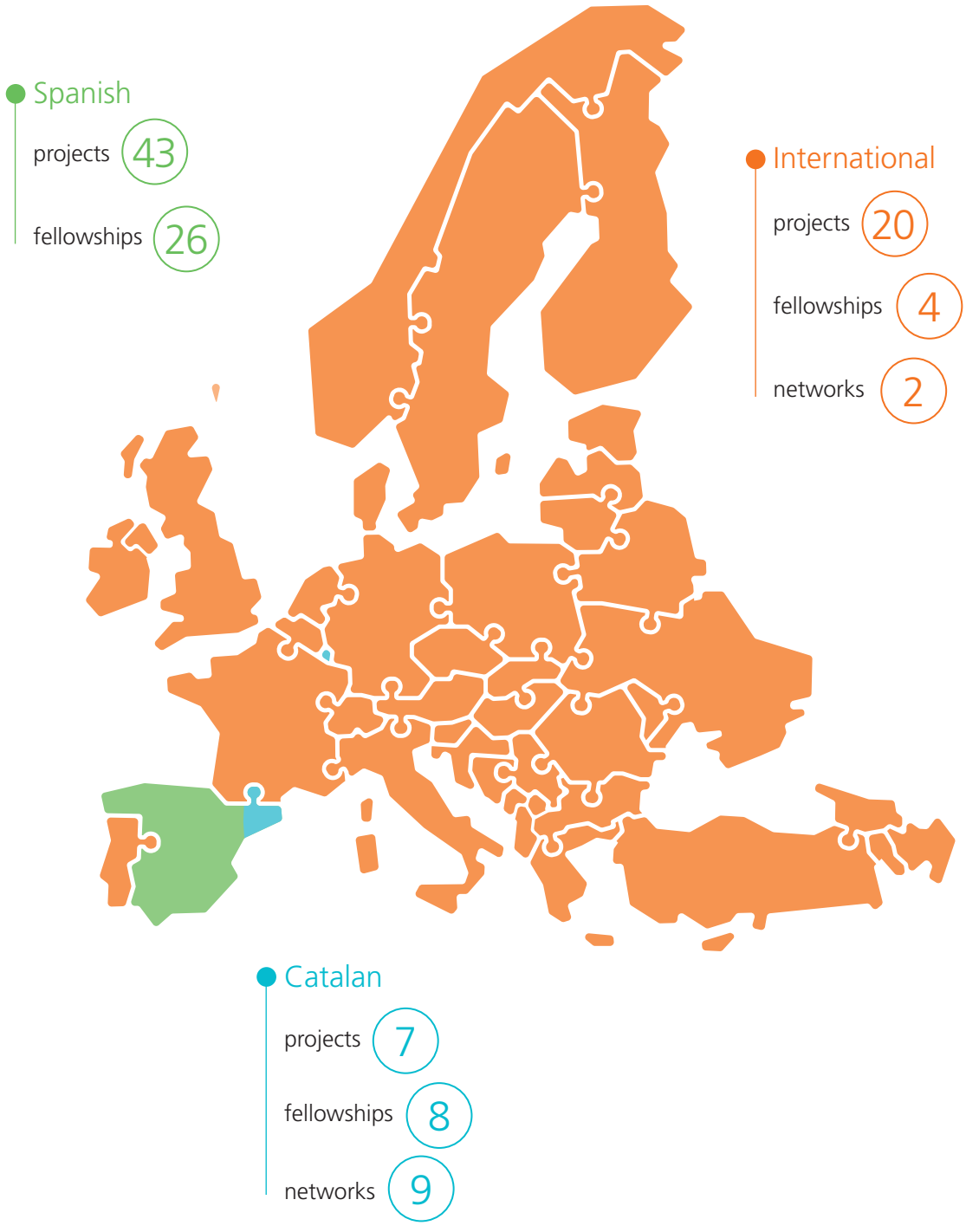
Given our efficient governance, the Josep Carreras Leukaemia Research Institute is a Catalan Research Centre of Excellence and forms part of the Catalan government's current research centre network. It is also accredited by the Spanish Ministry of Health as a Health Research Centre of Excellence and by the Spanish Association Against Cancer. The Institute also holds the HR Excellence in Research Award from the European Commission.

The Spanish Ministry of Health reconfirmed the status of the campus as a Centre for Health Research Excellence in its last evaluation in 2019. In addition, IJC has subscribed the European Charter and Code of Conduct for the Recruitment of Researchers and has obtained the HRS4R award.

Our researchers are highly competitive in a wide range of competitive grants launched at different levels (International, Spanish and Catalan):

Total Competitive Grants

Total	Projects	Fellowships	Nets
119	70	38	11



FACTS & FIGURES / **COMPETITIVE GRANTS AWARDED AND ACTIVE PROJECTS**

1. Cancer Epigenetics

2019 Generalitat de Catalunya, Fons Europeus desenvolupament 2019

PI: ESTELLER BADOSA, MANEL

Reference: IU16-016723

Title: Construcció, habilitació i adquisició d'equipaments d'edificacions singulars de recerca centrades en la cura de les leucèmies i d'altres hemopaties malignes

Period: 01/01/2018 - 31/03/2023

2016 Fundació La Marató de TV3, Marató 2016: Ictus i lesions medul·lars i cerebrals traumàtiques

PI: ESTELLER BADOSA, MANEL

Reference: 201711.31

Title: EPIGENESIS Project: EPIgenetic and GENEtic study combined with integromics and functional analysis to find genes associated with neurological deterioration after Ischemic stroke

Period: 01/06/2019 - 31/12/2021

2017 Fundación Científica de la Asociación Española Contra el Cáncer, Accelerator Award 2017

PI: ESTELLER BADOSA, MANEL

Reference: A26825

Title: ACRCelerate: Colorectal Cancer Stratified Medicine Network

Period: 02/08/2019 - 31/10/2023

2018 Fundación Científica de la Asociación Española Contra el Cáncer, Accelerator Award 2018

PI: ESTELLER BADOSA, MANEL

Reference: A29372

Title: PREDICT-Meso: PRE-malignant Drivers Combined with Target-Drug validation in Mesothelioma

Period: 01/04/2020 - 30/03/2025

2018 Ministerio de Ciencia, Innovación y Universidades, Acciones de dinamización «Redes Investigación»

PI: ESTELLER BADOSA, MANEL

Reference: RED2018-102471-T

Title: Metalofármacos Multifuncionales para Diagnosis y Terapia

Period: 01/01/2020 - 31/12/2021

2018 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: ESTELLER BADOSA, MANEL

Reference: RTI2018-094049-B-I00

Title: Epigenetic and Genetic Disruption of RNA Modifications in Cancer (EPIRNA)

Period: 01/01/2019 - 31/12/2021

2019 European Commission, MSCA-RISE-2019 Marie Skłodowska-Curie Actions - Research and Innovation Staff Exchange

PI: ESTELLER BADOSA, MANEL

Reference: 872391

Title: DevelOpmeNt of Cancer RNA TherapEutics (CONCRETE)

Period: 01/05/2020 - 30/04/2024

2019 Fundación Privada Olga Torres, Beques de recerca postdoctorals

PI: JOSHI, RICKY

Reference: N/A

Title: Studying the Clinical Impact of the Epitranscriptome for Colorectal Cancer Initiation, Progression and Treatment

Period: 01/01/2020 - 31/12/2021

2019 Ministerio de Ciencia, Innovación y Universidades, Retos Colaboración

PI: ESTELLER BADOSA, MANEL

Reference: RTC2019-006951-1

Title: Aproximación inmunoterapéutica al tratamiento del linforma de no-Hodgkin mediante el desarrollo preclínico y primeros ensayos clínicos de un inhibidor selectivo de HDAC6

Period: 01/01/2020 - 31/12/2022

2017 Fundación Científica de la Asociación Española Contra el Cáncer, Investigador AECC

PI: DAVALOS VEGA, VERONICA

Reference: INVES208DAVA

Title: EPINMUNE: Identificación de biomarcadores epigenéticos de predicción de respuesta a inmunoterapia

Period: 01/06/2019 - 30/11/2021.

2018 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts per a la incorporació de personal investigador postdoctoral al sistema català de ciència i tecnologia

PI: FERRER AGUILAR, GERARDO

Reference: 2018 BP 00250

Title: Senescence as a key factor in leukemogenesis and bone marrow homeostasis in aging

Period: 03/12/2019 - 02/12/2022

2018 Ministerio de Educación, Cultura y Deporte, Ayudas para la formación de profesorado universitario (FPU)

PI: BUENO COSTA, ALBERTO

Reference: FPU2017-02423

Period: 01/07/2019 - 31/07/2022

2019 Instituto de Salud Carlos III, Contratos Sara Borrell

PI: JANIN, MAXIME HENRI

Reference: CD19/00272

Title: Desarrollo de la isobutyl-deoxynyboquinone en Glioma Pontino Intrinseco Difuso: una oportunidad terapéutica en oncología pediátrica.

Period: 15/03/2020 - 14/03/2023

FACTS & FIGURES /
AWARDED AND ACTIVE PROJECTS

2019 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: MARTINEZ VERBO, LAURA

Reference: PRE2019-089958

Title: Disrupción epigenética y genética de las modificaciones del RNA en cáncer

Period: 01/08/2020 - 31/07/2024

2020 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts a Doctorats Industrials

PI: POPOV, ANTON

Reference: 2020 DI 20

Title: Novel algorithms for disruptive 3D microscopy data processing, visualization and analysis, using massive GPU parallelization and Artificial Intelligence (AI) applied to cancer epigenetics

Period: 01/11/2020 - 31/10/2023

2016 Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red (CIBER)

PI: ESTELLER BADOSA, MANEL

Reference: CB16/12/00312

Title: Centro de Investigación Biomédica en Red de Cáncer (CIBERONC)

Period: 01/10/2019 - 31/12/2021

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: ESTELLER BADOSA, MANEL

Reference: 2017 SGR 1080

Title: Acreditación como «Grupo Consolidado Reconocido» al Grupo de Epigenética del Cáncer

Period: 01/01/2017 - 30/09/2021

2. Cancer Genetics

2014 Fundación Científica de la Asociación Española Contra el Cáncer, Grupos Coordinados Estables 2014

PI: SANCHEZ CESPEDES, MONTSE

Reference: GCB14142170MONT

Title: Uso de estrategias moleculares de última generación para la identificación de nuevas dianas terapéuticas y marcadores pronósticos en tipos de carcinoma pulmonar pobremente caracterizados

Period: 01/08/2019 - 31/10/2020

2017 Ministerio de Ciencia, Innovación y Universidades, Programa Estatal de I+D+i Orientada a los Retos de la Sociedad

PI: SANCHEZ CESPEDES, MONTSERRAT AMADA

Reference: SAF2017-82186-R

Title: Functional disection of the MYC/MAX and SWI/SNF pathways regulation to bost the design of novel epigenetic cancer therapeutics

Period: 01/06/2019 - 30/09/2021

2018 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formación de doctores (FPI)

PI: VILARRUBÍ PORTA, ANDREA

Reference: PRE2018-084624

Period: 01/05/2020 - 30/06/2023

2019 Fundación Científica de la Asociación Española Contra el Cáncer, Investigador AECC

PI: ROMERO FERRARO, OCTAVIO ALFREDO

Reference: INVES19045ROME

Title: The CESAR Therapeutic strategy (Cancer's Epigenetic Short-circuit Adapted Response)

Period: 01/12/2019 - 30/11/2021

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: SANCHEZ CESPEDES, MONTSERRAT AMADA

Reference: 2017 SGR 721

Title: Grup de Gens i Càncer, Grup de Recerca Consolidat

Period: 01/01/2017 - 30/09/2021

3. Chromatin Biology

2017 Ministerio de Ciencia, Innovación y Universidades, Programa Estatal de I+D+i Orientada a los Retos de la Sociedad

PI: VAQUERO GARCIA, ALEJANDRO

Reference: SAF2017-88975-R

Title: Protección de la estabilidad del genoma por sirtuinas en condiciones de estrés y sus implicaciones en cáncer y envejecimiento

Period: 01/06/2019 - 30/06/2021

2017 Worldwide Cancer Research, April 2017 grant round

PI: VAQUERO GARCIA, ALEJANDRO

Reference: 18-0404

Title: Dissecting the specific contribution of Sirtuin ADP-ribosyltransferase and deacetylase activities in tumorigenesis

Period: 01/08/2019 - 31/10/2021

2020 Fundación Científica de la Asociación Española Contra el Cáncer, Proyectos Estratégicos AECC 2020

PI: VAQUERO GARCIA, ALEJANDRO

Reference: PROYE20042VAQU

Title: Deciphering the role of SIRT7 in B-cell development and Leukaemia formation

Period: 01/12/2020 - 30/11/2023

2016 Agència de Gestió d'Ajuts Universitaris i de Recerca, ajuts per a la incorporació de personal investigador postdoctoral al sistema català de ciència i tecnologia dins del programa Beatriu de Pinós (BP 2016)

PI: VAZQUEZ PRAT, BERTA NIEVES

Reference: 2016 BP 00250

Title: Mechanisms of Epigenetic Antagonism between SIRT2 and MOF and its implications in tumorigenesis

Period: 01/11/2019 - 30/11/2020

2018 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: CATELLÓ GARCÍA, JOSE MANUEL

Reference: PRE2018-084435

Period: 01/05/2020 - 31/08/2023

2019 European Commission, H2020 - MSCA - IF-2019 Marie Skłodowska-Curie Actions - Individual Fellowship

PI: VAZQUEZ PRAT, BERTA NIEVES

Reference: 895979

Title: Mechanisms of Sirtuin-dependent regulation of immunity and leukemogenesis (SirT-IMLEU)

Period: 01/12/2020 - 30/11/2022

2020 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts per a la contractació de personal investigador novell per a l'any 2020. FI-DGR 2020

PI: GÁMEZ GARCÍA-CERVIGÓN, ANDRÉS

Reference: 2020 FI_B 00293

Title: "Sirtuin-dependent protection of genome stability under stress and its implications in cancer and aging"

Period: 01/04/2020 - 31/03/2021

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: VAQUERO GARCIA, ALEJANDRO

Reference: 2017 SGR 148

Title: Grupo de Biología de la Cromatina, Grup de Recerca Consolidat

Period: 01/01/2017 - 30/09/2021

4. Chromatin, Metabolism and Cell Fate

2017 Instituto de Salud Carlos III, Contratos Sara Borrell

PI: DIESCH, JEANNINE

Reference: CD17/00084

Title: Characterisation of pro-invasive transcriptional programs regulated by the Fra-1 transcription factor

Period: 01/01/2018 - 31/12/2020

2015 European Commission, H2020-MSCA-ITN-2015 Marie Skłodowska-Curie Actions – Innovative Training Networks

PI: BUSCHBECK, MARCUS

Reference: 675610

Title: Chromatin-metabolism interactions as targets for healthy living (ChroMe)

Period: 01/03/2016 - 29/02/2020

2016 Instituto de Salud Carlos III, Proyectos integrados de excelencia

PI: BUSCHBECK, MARCUS

Reference: PIE16/00011

Title: Biomarkers and combinatorial drug targets for a personalized therapy for three major cancers.

Period: 01/01/2017 - 30/06/2021

2018 Josep Carreras Deutsche Leukämie Stiftung, Ayudas a proyectos de investigación

PI: BUSCHBECK, MARCUS

Reference: DJCLS 14R/18

Title: Understanding and targeting epigenetic alterations in the hematopoietic stem cell niche for MDS therapy

Period: 01/05/2019 - 30/04/2022

2018 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: BUSCHBECK, MARCUS

Reference: RTI2018-094005-B-I00

Title: Regulation of 3D chromatin architecture by histone variants and their metabolite binding capacity.

Period: 01/01/2019 - 31/12/2021

2016 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: LE PANNÉRER, MARGUERITE-MARIEGrup: Chromatin, Metabolism and Cell Fate

Reference: BES-2016-077251

Title: MacroH2A histone variants link genome architecture to metabolism

Period: 18/04/2017 - 17/04/2021

2017 Ministerio de Economia y Competitividad, Ayudas para Personal Técnico de Apoyo 2017

PI: CASQUERO GALINDO, RAQUELÇ

Reference: PTA2017-13669-I

Period: 30/06/2019 - 30/06/2022

2019 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: MEERS, OLIVER

Reference: PRE2019-088529

Title: Regulacion de la arquitectura tridimensional de la cromatina por parte de las variantes de histona macroh2a y su capacidad de unir metabolitos

Period: 01/10/2020 - 30/09/2024

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: BUSCHBECK, MARCUS

Reference: 2017 SGR 00305

Title: Modalitat GRPRE (Pre-Consolidats). Chromatin, Metabolism and Cell Fate.

Period: 01/01/2017 - 30/09/2021

2018, European Cooperation in Science and Technology (COST) Actions

PI: HURTADO BAGÈS, SARAH

Reference: CA18127

Title: International Nucleome Consortium (INC)

Period: 13/05/2019 - 12/05/2023

5.
3D chromatin Organization

2018 Fundació "La Caixa", "La Caixa" postdoctoral Fellowships Junior Leader - Incoming

PI: JAVIERRE MARTINEZ, BIOLA M

Reference: LCF/BQ/PI19/11690001

Title: Dynamic 3D Chromatin Organization in Human Hematopoiesis: revealing the contributions of non-coding genetic variants and mutations in blood malignancies with the aim of identifying novel disease-associated genes.

Period: 30/09/2019 -29/09/2022

2018 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: JAVIERRE MARTINEZ, BIOLA M

Reference: RTI2018-094788-A-I00

Title: Dynamic 3D Chromatin Organization in Human Haematopoiesis: description of novel genes associated with haematological disorders.

Period: 01/01/2019 -31/12/2021

2019 Deutsche José Carreras Leukämie Stiftung, Forshungsprojekte (R 19) 2019

PI: JAVIERRE MARTINEZ, BIOLA M

Reference: DJCLS 08R/2019

Title: Deciphering the Oncogenic Role of the PRC1 Complexes Through Integration of Functional and Spatial Genomics in Diffuse Large B-cell Lymphoma

Period: 01/09/2020 - 28/02/2023

2019 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts per a la contractació de personal investigador novell per a l'any 2019. FI-DGR 2019

PI: ROVIROSA MULET, LLORENÇ

Reference: 2019 FI_B 00017

Title: Desxifrant noves dianes moleculars per a teràpies contra la leucèmia Limfoblàstica aguda infantil

Period: 01/04/2019 - 31/03/2022

2019 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: TOMÁS DAZA, LAUREANO

Reference: PRE2019-088005

Title: Organizacion Dinamica 3d de la Cromatina en la Hematopoyesis Humana: descripcion de nuevos Genes Asociados a Enfermedades Hematologicas

Period: 01/08/2020 - 31/07/2024

6.
Epigenetics and immune disease

2017 Instituto de Salud Carlos III, Contratos predoctorales de formación en investigación en salud. Modalidad Contratos i-PFIS: doctorados IIS-empresa en ciencias y tecnologías de la salud

PI: BALLESTAR TARIN, ESTEBAN

Reference: IFI17/00034

Period: 15/01/2018 - /01/2022

2017 Ministerio de Ciencia, Innovación y Universidades, Programa Estatal de I+D+i Orientada a los Retos de la Sociedad

PI: BALLESTAR TARIN, ESTEBAN

Reference: SAF2017-88086-R

Title: Myeloid cells and Epigenetic Plasticity: Mechanisms and Implications in Autoimmune and other Inflammatory Processes

Period: 01/06/2019 - 30/09/2021

2018 Instituto de Salud Carlos III, Acciones complementarias de programacion conjunta internacional

PI: BALLESTAR TARIN, ESTEBAN

Reference: AC18/00057

Title: Integrative Multi-Omics Analysis of Primary Antibody Deficiency (PAD) Patients for Stratification According to Cellular Pathways

Period: 01/01/2019 - 31/12/2021

2015 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: LORENTE-SOROLLA MARTINEZ-ACITORES, CLARA

Reference: BES-2015-074528

Title: Mecanismos de Regulación Epigenética en Procesos de Diferenciación Mieloide Relevantes a Enfermedad Autoinmune

Period: 07/10/2019 - 20/02/2020

2018 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: FERRETÉ BONASTRE, ANNAGrup: Epigenetics and immune disease

Reference: PRE2018-083544

Period: 01/05/2020 - 30/06/2023

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: BALLESTAR TARIN, ESTEBAN

Reference: 2017 SGR 00720

Title: Grup de Cromatina i Malaltia Grup de Recerca Consolidat

Period: 01/01/2017 - 30/09/2021

7. Lymphocyte development and disease

2017 Ministerio de Ciencia, Innovación y Universidades, Programa Estatal de I+D+i Orientada a los Retos de la Sociedad

PI: PARRA BOLA, MARIA ISABEL

Reference: SAF2017-87990-R

Title: Transcriptional repressive mechanisms in early and terminal B cell differentiation

Period: 01/06/2019 - 30/09/2021

2019 Ministerio de Ciencia e Innovación, Acciones de dinamización «Europa Investigación»

PI: PARRA BOLA, MARIA ISABEL

Reference: EUR2019-103835

Title: B cell differentiation; unraveling gene silencing mechanisms

Period: 01/09/2019 - 30/05/2020

2017 Ministerio de Ciencia, Innovación y Universidades, Juan de la Cierva-formación

PI: DE BARRIOS BARRI, ORIOL

Reference: FJCI-2017-32430

Period: 11/11/2019 - 30/11/2020

2018 Ministerio de Ciencia, Innovación y Universidades, Ayudas para contratos predoctorales para la formacion de doctores (FPI)

PI: AMELER MARQUINA, AINARA

Reference: PRE2018-083183

Period: 01/05/2020 - 30/06/2023

2020 Fundación Científica de la Asociación Española Contra el Cáncer, Postdoctorales AECC 2020

PI: DE BARRIOS BARRI, ORIOL

Title: Targeted modulation of the transcriptional repressor HDAC7; towards precision medicine in MLL-AF4-rearranged infant PRO-B-ALL

Period: 01/12/2020 - 30/11/2022

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: PARRA BOLA, MARIA ISABEL

Reference: 2017 SGR 00149

Title: Grup de Diferenciació Cel·lular, Grup de Recerca Pre-Consolidat

Period: 01/01/2017 - 30/09/2021

8. Regulatory Genomics

2019 Ministerio de Ciencia, Innovación y Universidades, Generación del Conocimiento

PI: VAVOURI, TANIA SOULTANA

Reference: PID2019-111676GB-I00

Title: Evolution of new PIWI-interacting RNAs in a mammal (ASliceOfPi)

Period: 01/06/2020 - 31/05/2023

9. Regulatory RNA and chromatin

2017 Instituto de Salud Carlos III, Contratos predoctorales de formación en investigación en salud. Modalidad Contratos i-PFIS: doctorados IIS-empresa en ciencias y tecnologías de la salud

PI: GUIL DOMÈNECH, SÒNIA

Reference: IFI17/00006

Period: 01/01/2018 - 31/12/2021

2019 Fondo para la Investigación en Síndrome de Rett, 1ª Convocatoria de ayudas a la investigación en Síndrome de Rett de FINRETT

PI: GUIL DOMENECH, SONIA

Title: Transcriptómica unicelular para el análisis de subtipos neuronales diferenciados en un modelo celular humano de síndrome de Rett

Period: 01/11/2019 - 31/10/2020

2019 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: GUIL DOMENECH, SONIA

Reference: PID2019-111658RB-I00

Title: Pseudogenes as long noncoding oncofetal RNAs: functional characterization and implications for anticancer therapy.

Period: 01/06/2020 - 31/05/2023

2020 Sarcoma Foundation of America, 2020 Funding Opportunity Announcement

PI: GUIL DOMENECH, SONIA

Reference: AJT-PRJ2000408

Title: The role of pseudogenes as regulators of the IGF2BP2/IGF1R/RAS axis in rhabdomyosarcoma: functional characterization in myogenesis and implications for anticancer therapy

Period: 01/07/2020 - 31/12/2021

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: GUIL DOMENECH, SONIA

Reference: 2017 SGR 00722

Title: RNA regulador i cromatina, Grup de Recerca Consolidat

Period: 01/01/2017 - 30/09/2021

10. Epigenetic Control of Haematopoiesis

2019 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: SARDINA ORTEGA, JOSE LUIS

Reference: PID2019-111243RA-I00

Title: Unveiling TET2 impact on chromatin structure at the leukemic onset

Period: 01/06/2020 - 31/05/2023

2019 Worldwide Cancer Research, April 2019 grant round

PI: SARDINA ORTEGA, JOSE LUIS

Reference: 20-0269

Title: Uncovering the regulation of chromatin structure by TET2 during leukemic cell fate decisions

Period: 01/03/2020 - 28/02/2023

2019 Instituto de Salud Carlos III, Contratos Miguel Servet - Tipo 1

PI: SARDINA ORTEGA, JOSE LUIS

Reference: CP19/00176

Title: Role of TET2 in chromatin structure regulation during the onset and development of mieloid malignancies

Period: 01/01/2020 - 31/12/2024

11.
Transcriptional Dynamics in Leukemia

2019 Fundació "La Caixa", Junior Leader 2020

PI: CUARTERO BETRIU, SERGI

Reference: LCF/BQ/PI20/11760002

Title: The role of inflammation in myeloid malignancies

Period: 01/09/2020 - 31/08/2023

2019 Jerome Lejeune Foundation, Cycle 2019b- Down syndrome research

PI: CUARTERO BETRIU, SERGI

Reference: #1902

Title: Myeloid leukemia in Down syndrome: exploring the interplay between transcriptional regulation and immune signalling

Period: 01/04/2020 - 06/01/2023

2020 Leukemia Research Foundation, Hollis Brownstein Research Grants Program

PI: CUARTERO BETRIU, SERGI

Title: Identifying novel transcriptional vulnerabilities in MDS with cohesin mutations

Period: 01/09/2020 - 31/12/2021

15.
Cancer Immunogenomics

PI: PORTA, EDUARD

Reference: LABAE20038PORT

Title: A cellular and molecular map of bladder cancer to guide neoadjuvant treatment

Period: 01/12/2020 - 30/11/2023

16.
Acute Lymphoblastic Leukemia

2015 European Commission, H2020 JTI-IMI2 2015-06, Innovative Medicines Inniative (IMI)

PI: RIBERA SANTASUSANA, JOSEP MARIA

Reference: 116026

Title: Healthcare Alliance for Resourceful Medicines Offensive against Neoplasms in hematology (HARMONY)

Period: 01/01/2017 - 31/12/2021

2016 Fundación Científica de la Asociación Española Contra el Cáncer, Grupos Coordinados Estables de Investigación

PI: RIBERA SANTASUSANA, JOSEP MARIA

Reference: GC16173697BIGA

Title: Exploring Mechanisms of Resistance in Adult and Pediatric T-Acute Lymphoblastic Leukemia

Period: 01/11/2016 - 31/10/2021

2019 European Commission, IMI2-2019-19-01, Innovative Medicines Inniative (IMI)

PI: RIBERA SANTASUSANA, JOSEP MARIA

Reference: 945406

Title: Healthcare Alliance for Resourceful Medicines Offensive Against Neoplasms in Hematology – Plus (HARMONY PLUS)

Period: 01/10/2020 - 30/09/2023

2019 Instituto de Salud Carlos III, Proyectos de investigación en Salud

PI: GENESCA FERRER, EULALIA

Reference: PI19/01828

Title: Use of Next Generation Sequencing (NGS) as a unique genomic technique to apply to improve

diagnosis, prognosis and treatment of adult T-cell Acute Lymphoblastic Leukemia patients

Period: 01/01/2020 - 31/12/2022

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts per a la contractació de personal investigador novell per a l'any 2018. FI-DGR 2018

PI: GENESCA FERRER, EULALIA

Reference: 2018 FI_B 00970, 2019 FI_B100224, 2020 FI_B2 00210

Title: Estudio de la resistencia al tratamiento en la leucemia linfoblástica aguda de subtipo T (LAL-T) del adulto. Búsqueda de nuevas alternativas terapéuticas

Period: 01/06/2018 - 30/10/2021

17.
Barcelona Endothelium Team

2019 Deutsche José Carreras Leukämie Stiftung, Forshungsprojekte (R 19) 2019

PI: CARRERAS PONS, ENRIC

Reference: DJCLS 03R/2019

Title: Enhancement of endothelial regeneration and endothelial function during GVHD

Period: 01/01/2020 - 30/04/2022

19.
Genetics and Epigenetics in Myeloid Neoplasms

2016 Instituto de Salud Carlos III, Proyectos de investigación en Salud

PI: ZAMORA PLANA, LURDES

Reference: PI16/01200

Title: Biological predictive factors for achieving deep molecular response and relapse after tyrosine kinase inhibitor discontinuation in patients with Chronic Myeloid Leukemia

Period: 01/01/2017 - 30/09/2021

2019 Fundación Española de Hematología y Hemoterapia, Becas de Investigación de la FEHH (Convocatoria 2019-2020)

PI: ESTRADA BARRERAS, NATALIA

Reference:

Title: Biological predictive factors for achieving deep molecular response and relapse after tyrosine kinase inhibitor discontinuation in patients with Chronic Myeloid Leukemia

Period: 01/01/2020 - 31/12/2020

21.
Leukaemia Stem Cell Group

2016 Ministerio de Economia y Competitividad, Retos Colaboración

PI: MUÑOZ RISUEÑO, RUTH

Reference: RTC-2016-5205-1

Title: Nuevo tratamiento para la leucemia mieloide aguda y los síndromes mielodisplásicos

Period: 01/01/2016 - 30/06/2020

2017 Josep Carreras Deutsche Leukämie Stiftung, Ayudas a proyectos de investigación

PI: MUÑOZ RISUEÑO, RUTH

Reference: DJCLS08/R2017

Title: CARs for Treatment of Pediatric T-Cell Acute Lymphoblastic Leukemia

Period: 08/08/2017 - 31/10/2021

2019 Agència de Gestió d'Ajuts Universitaris i de Recerca, Ajuts destinats a l'obtenció de prototipus i a la valorització i transferència dels resultats d'investigació generada per equips de recerca de Catalunya (PRODUCTE)

PI: MUÑOZ RISUEÑO, RUTH

Reference: 2019PROD00031

Title: Teràpies basades en CADs com a nou mecanisme autofàgic per a leucèmia

Period: 23/07/2020 - 22/01/2022

2019 Fundació La Marató de TV3, Marató 2019: Càncer

PI: MUÑOZ RISUEÑO, RUTH

Reference: 201930

Title: Lysosomal impairment-based therapeutic approach for leukemia

Period: 30/07/2020 - 29/07/2023

2019 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: MUÑOZ RISUEÑO, RUTH

Reference: PID2019-111348RB-I00

Title: Chemosensitizers as a new therapeutic approach for acute myeloid leukemia (ChemoLeuko)

Period: 01/06/2020 - 31/05/2023

22.
Lymphoid Neoplasms

2019 Gilead Sciences, SL, 7ª Convocatoria de Becas Gilead a la investigación Biomédica en VIH, Enfermedades hepáticas y Hemato-oncología

PI: NAVARRO FERRANDO, TOMAS

Reference: GLD19_00121

Title: Disclosing the transcriptome of HIV-DLBCL for targeted therapy

Period: 01/01/2020 - 31/12/2021

2019 Instituto de Salud Carlos III, Proyectos de investigación en Salud

PI: NAVARRO FERRANDO, JOSE TOMAS

Reference: PI19/01588

Title: Comprehensive epigenomic analysis of plasmablastic lymphoma: Identifying epigenetic features to improve diagnosis and patient outcomes

Period: 01/01/2021 - 31/12/2022

24.
Myelodysplastic Syndromes

2016 Fundación Ramon Areces, Ayudas a la investigación

PI: SOLE RISTOL, FRANCESC

Title: Hacia la mejora del diagnóstico y tratamiento en anemias diseritropoyéticas congénitas.

Period: 08/03/2017 - 07/03/2020

2017 Instituto de Salud Carlos III, Proyectos de investigación en Salud

PI: SOLE RISTOL, FRANCESC

Reference: PI17/00575

Title: Aplicación de la secuenciación masiva (NGS) en el diagnóstico y pronóstico de síndromes mielodisplasicos/neoplasias mieloproliferativas.

Period: 01/01/2018 - 30/06/2022

2018 Fundación Científica de la Asociación Española Contra el Cáncer, Ayudas a proyectos de investigación en cáncer TRANSCAN (Translational Research on Rare Cancers)

PI: SOLE RISTOL, FRANCESC

Reference: TRNSC18003SOLE

Title: An integrated European platform to conduct translational studies in myelodysplastic syndromes based on the EuroBloodNet infrastructure

Period: 01/12/2018 - 30/11/2021

2018 Instituto de Salud Carlos III, Acciones complementarias de programacion conjunta internacional

PI: SOLE RISTOL, FRANCESC

Reference: AC18/00002

Title: An integrated European platform to conduct translational studies in myelodysplastic syndromes based on the EuroBloodNet infrastructure

Period: 01/01/2019 - 31/12/2021

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: SOLE RISTOL, FRANCESC

Reference: 2017 SGR 00288

Title: Modalitat GRC (Reconegut i Consolidat).

Period: 01/01/2017 - 30/09/2021

25.
Stem cell biology, developmental leukemia and immunotherapy

2014 European Commission, European Research Council, Consolidator Grants

PI: MENENDEZ BUJAN, PABLO

Reference: 646903

Title: Genomic, cellular and developmental reconstruction of infant MLL-AF4+ Acute Lymphoblastic Leukemia

Period: 01/01/2016 - 30/06/2021

2017 European Commission, European Research Council, Proof of Concept Grants 2018

PI: MENENDEZ BUJAN, PABLO

Reference: 811220

Title: Therapeutic immunotherapy targeting NG2 and CD22 antigens for MLL-rearranged and MLL-germline B-cell Acute Lymphoblastic Leukemia (IT4B-ALL)

Period: 01/01/2019 - 30/06/2020

2017 Instituto de Salud Carlos III, Proyectos de investigación en Salud

PI: BUENO UROZ, CLARA

Reference: PI17/01028

Title: Adoptive Cellular Immunotherapy with CD5-based single and dual CARs for Treatment of Pediatric T-Cell ALL and Fungal Infections After Allogeneic HSC Transplantation in Children

Period: 01/01/2018 - 31/12/2020

2017 Ministerio de Economía y Competitividad, Retos - Colaboración

PI: MENENDEZ BUJAN, PABLO

Reference: RTC-2017-6367-1

Title: Obtención de hematíes in vitro a partir de ipscs de donantes con fenotipos eritrocitarios seleccionados y optimizados mediante edición genómica, como alternativa a los paneles de hematíes actuales (ID-VITRORED)

Period: 01/09/2018 - 31/12/2021

2018 European Commission, H2020-SC1-BHC-2018-2020

PI: MENENDEZ BUJAN, PABLO

Reference: 825749

Title: Childhood Leukaemia: Overcoming distance between South America and Europe Regions (CLOSER)

Period: 01/01/2019 - 31/12/2023

2018 European Food Safety Authority, NP/EFSA/PRAS/2018/04

PI: MENENDEZ BUJAN, PABLO

Reference: NP/EFSA/PRAS/2018/04-CT1

Title: Explore the potential genotoxic effect of two pesticides (Permetrine and Clorpyriphos) in human stem cells at different ontogeny stages, and investigate their potential of inducing leukaemia in animal models of infant leukaemia.

Period: 01/02/2019 - 31/03/2020

2018 Fundació "La Caixa", Health Research 2018

PI: MENENDEZ BUJAN, PABLO

Reference: HR18-00069

Title: Next-generation CAR-DOT cells for allogeneic adoptive cancer immunotherapy (Allo_CAR_DOT)

Period: 01/09/2019 - 01/09/2022

2019 Deutsche José Carreras Leukämie Stiftung, Forshungsprojekte (R 19) 2019

PI: MENENDEZ BUJAN, PABLO

Reference: 19R2019

Title: Healthy Versus Non-Healthy Aging: Identifying Metabolic and Epigenetic Vulnerabilities of Single Leukemic Stem Cells in Acute Myeloid Leukemia Patients

Period: 01/06/2020 - 31/05/2022

2019 Fundación Científica de la Asociación Española Contra el Cáncer, Ideas Semilla AECC 2019

PI: MENENDEZ BUJAN, PABLO

Reference: IDEAS19005MENE

Title: Redirecting car t-cells to the bone marrow: improved car t-cell persistence and anti-leukemia effects while alleviating related toxicity

Period: 01/10/2019 - 30/09/2021

2019 Fundación Uno Entre Cien Mil, VI Beca Unoentrecienmil. Fundación para la investigación en el área de la leucemia aguda infantil del 2019

PI: MENENDEZ BUJAN, PABLO

Reference: 1entre100mil

Title: Towards a clinical translation of the CD1a-directed CAR for relapse/refractory cortical T-cell Acute Lymphoblastic Leukemia and Langerhans Cell Histioscytosis: feasibility, efficacy and safety

Period: 01/06/2019 - 31/05/2021

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2019 Ministerio de Ciencia, Innovación y Universidades, Retos Investigación

PI: MENENDEZ BUJAN, PABLO

Reference: PID2019-108160RB-I00

Title: IM3, a promising novel immunotherapeutic target for de novo and relapsed B-cell acute lymphoblastic leukemia

Period: 01/06/2020 - 31/05/2023

2017 European Commission, H2020-MSCA-IF-2017 Marie Skłodowska-Curie Actions - Individual Fellowship

PI: VELASCO HERNANDEZ, TALIA

Reference: 792923

Title: Acute Myeloid Leukemia Leukemic Initiating Cells: Contribution of hypoxia/HIF pathway to chemoresistance and relapse (HifLICs)

Period: 01/01/2019 - 31/12/2020

2017 European Commission, H2020-MSCA-IF-2017 Marie Skłodowska-Curie Actions - Individual Fellowship

PI: ZANETTI, SAMANTA ROMINA

Reference: 795833

Title: Innovative Therapeutic Strategies for Mixed Lineage Leukemia-rearranged B-cell Acute Lymphoblastic Leukemia (InTheMLLrBALL)

Period: 01/04/2018 - 31/03/2020

2017 Ministerio de Economia y Competitividad, Ayudas Juan de la Cierva - Incorporación 2017

PI: VINYOLES VERGES, MERITXELL

Reference: IJCI-2017-33172

Period: 01/02/2019 - 16/01/2022

2018 Lady Tata Memorial Trust, Lady Tata Inernational Awards

PI: LOPEZ MILLAN, MARIA BELEN

Title: Adoptive Cellular Immunotherapy using CARCD7 NK-cells and CARCD1a T-cells for Treatment of Pediatric T-Cell Acute Lymphoblastic Leukemia.

Period: 01/09/2019 - 31/08/2020

2019 Instituto de Salud Carlos III, Contratos Sara Borrell

PI: SÁNCHEZ MARTÍNEZ, DIEGO

Reference: CD19/00013

Period: 01/01/2020 - 31/12/2022

2019 Ministerio de Universidades, Ayudas para la formación de profesorado universitario (FPU)

PI: TIRADO CABRERA, NÉSTOR

Title: Explorando células efectoras alogénicas para inmunoterapia en leucemia aguda

Period: 01/11/2020 - 31/03/2024

2020 Fundación Científica de la Asociación Española Contra el Cáncer, Investigador AECC 2020

PI: LOPEZ MILLAN, MARIA BELEN

Reference: INVES20011LÓPE

Title: Estrategias terapéuticas innovadoras para pacientes con Leucemia Linfoblástica Aguda B infantil con reordenamiento MLL: NG2 y CD22 como dianas terapéuticas

Title: Innovative Therapeutic Strategies for Infant Mixed Lineage Leukemiarearranged B-cell Acute Lymphoblastic Leukemia: NG2 and CD22 as therapeutic targets

Period: 01/09/2020 - 31/08/2022

2017 Agència de Gestió d'Ajuts Universitaris i de Recerca, Grups de Recerca de Catalunya (SGR)

PI: MENENDEZ BUJAN, PABLO

Reference: 2017 SGR 00221

Title: Modalitat GRC (Consolidat). Concedit a IJC

Period: 01/01/2017 - 30/09/2021

2017 European Cooperation in Science and Technology (COST), Cost Actions

PI: MENENDEZ BUJAN, PABLO

Reference: CA16223

Title: Lukaemia GENe Discovery by data sharing, mining and collaboration (LEGEN)

Period: 26/10/2017 - 25/10/2021

28. Lymphoma Translational Group

2018 Instituto de Salud Carlos III, Proyectos de Investigación en Salud (AES 2018). Modalidad proyectos en salud

PI: ROUÉ, GAËL

Reference: PI18/01383

Title: Development of a patient-derived xenografts platform for the evaluation of new targeted therapies in aggressive B-cell lymphomas

Period: 01/02/2020 - 31/12/2021

2019 Gilead Sciences, SL, 7ª Convocatoria de Becas Gilead a la investigación Biomédica en VIH, Enfermedades hepáticas y Hemato-oncología

PI: ROUÉ, GAËL

Reference: GLD19_00058

Title: Modulation of lymphoid microenvironment by intrinsic protein homeostasis in aggressive B-cell lymphoma

Period: 01/01/2020 - 31/12/2021

2019 INTERREG POCTEFA, 3ª convocatoria de proyectos POCTEFA 2014-2020

PI: ROUÉ, GAËL – Coordinador del consorci

Reference: EFA360/19

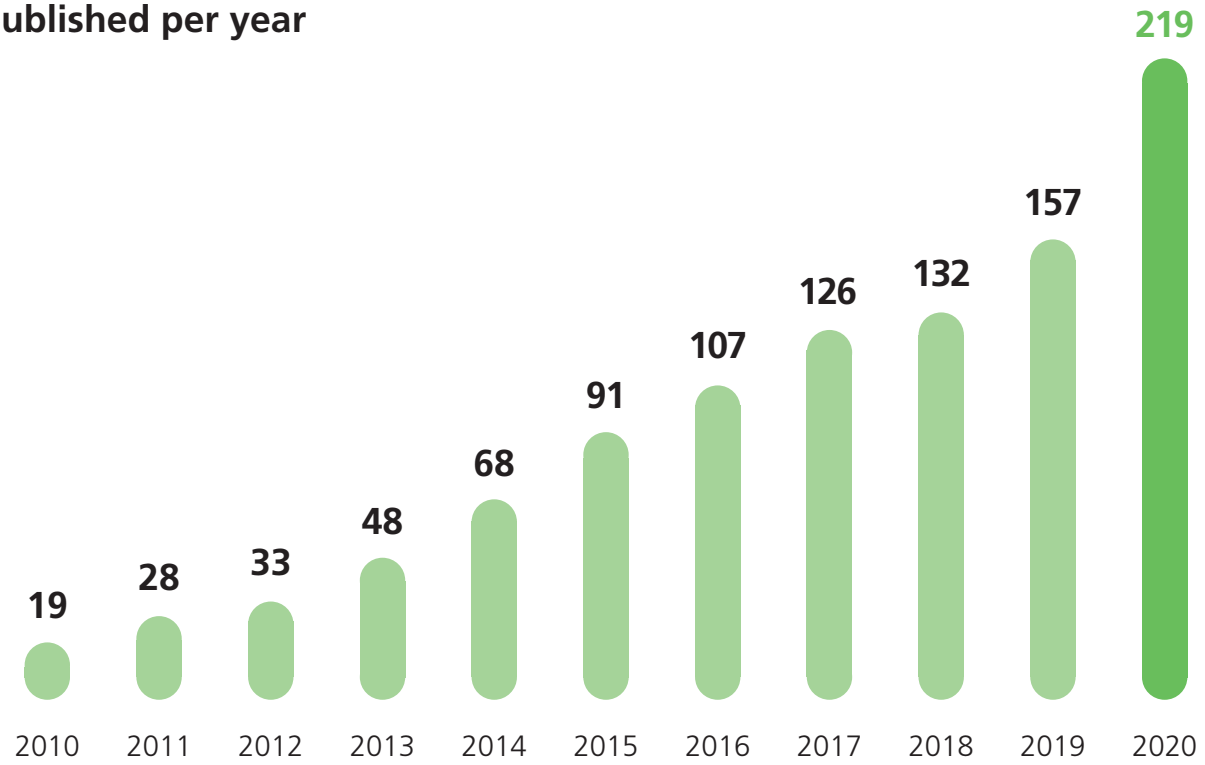
Title: Red cooperativa franco-española para el análisis de proteinopatías y el desarrollo de terapias individualizadas en cánceres hematológicos (PROTEOblood)

Period: 01/06/2019 - 31/05/2022

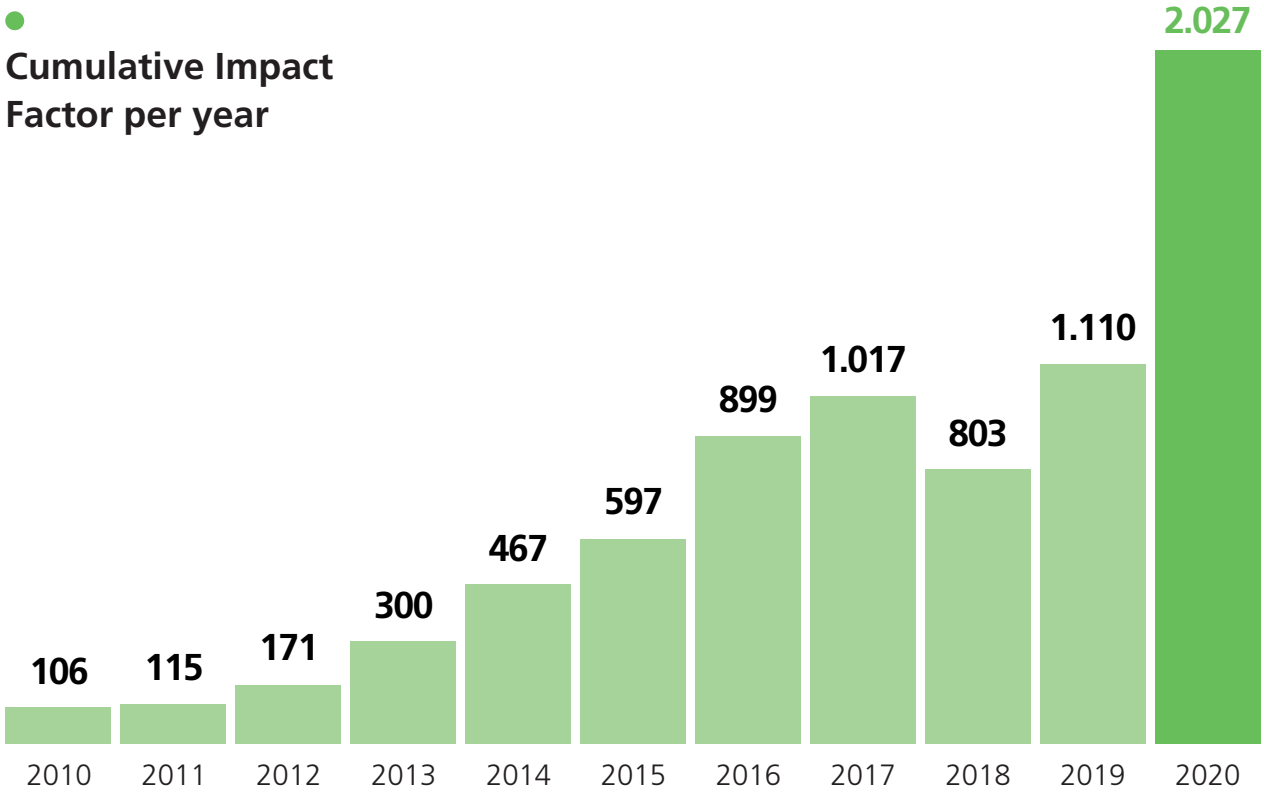
PUBLICATIONS / **INDICATORS**

219	131	80	68
Papers	Papers Q1	Papers D1	Papers with IF > 10

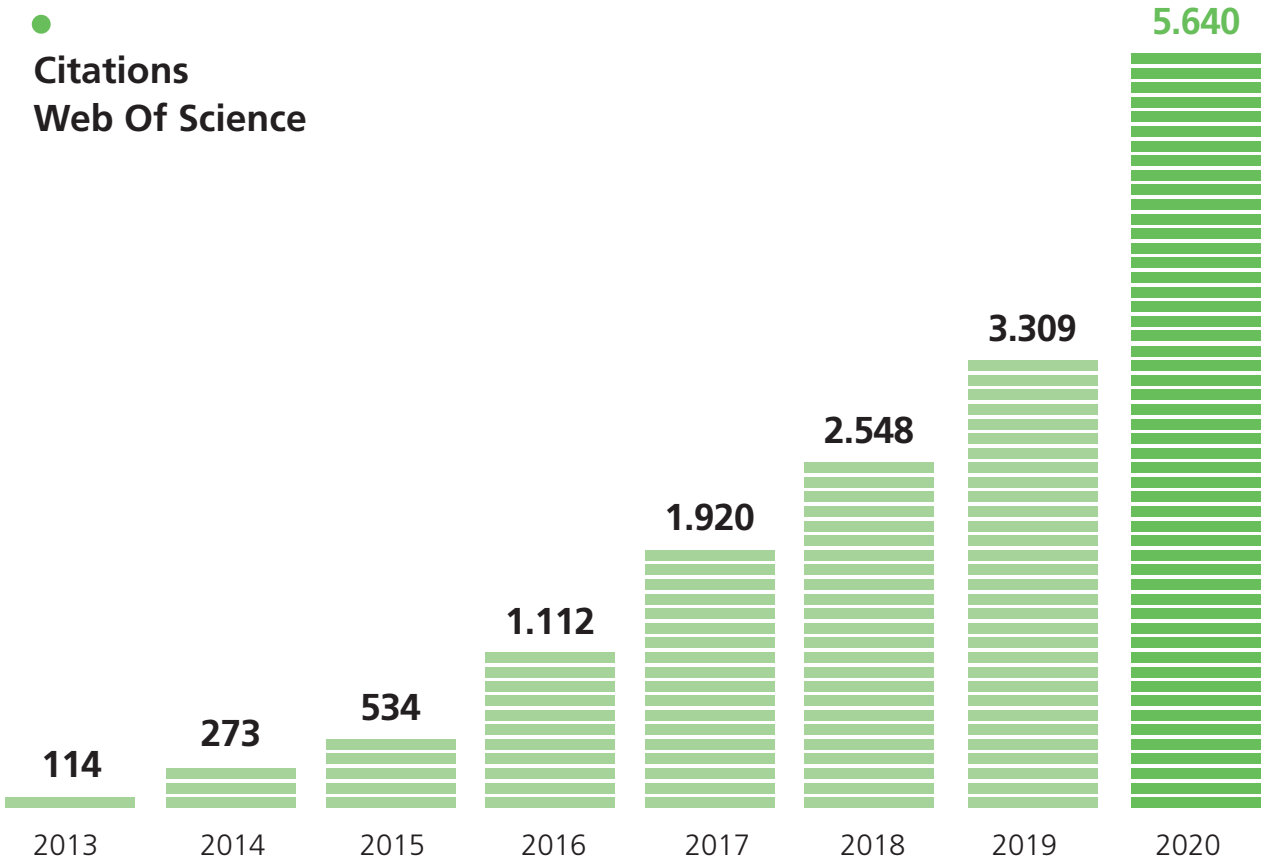
Number of indexed articles published per year



Cumulative Impact Factor per year



Citations Web Of Science



PUBLICATIONS / 2020 PUBLICATIONS

PEBCL/
CANCER AND LEUKEMIA EPIGENETICS AND BIOLOGY PROGRAM

1.
Cancer epigenetics

Capdevila J; Arqués O; Hernández Mora JR; Matito J; Caratù G; Mancuso FM; Landolfi S; Barriuso J; Jimenez-Fonseca P; Lopez Lopez C; Garcia-Carbonero R; Hernando J; Matos I; Paolo N; Hernández-Losa J; **Esteller M**; Martínez-Cardús A; Tabernero J; Vivancos A; Palmer HG. Epigenetic EGFR Gene Repression Confers Sensitivity to Therapeutic BRAFV600E Blockade in Colon Neuroendocrine Carcinomas. Clin Cancer Res 2020 Feb 15;26(4):902-909. doi: 10.1158/1078-0432.CCR-19-1266. Epub 2019 Oct 31. Impact Factor: 12,53 - Q1. PMID: 31672771

Fernández-Sanlés A; Sayols-Baixeras S; Castro DE Moura M; **Esteller M**; Subirana I; Torres-Cuevas S; Pérez-Fernández S; Aslibekyan S; Marrugat J; Elosua R. Physical Activity and Genome-wide DNA Methylation: The REgistre GIroni del COR Study MED SCI SPORT EXER 2020 Mar;52(3):589-597. doi: 10.1249/MSS.0000000000002174. Impact Factor: 5,41 - Q1. PMID: 31652233

Bueno-Costa A; **Piñeyro D**; Soler M; **Javierre BM**; Raurell-Vila H; Subirana-Granés M; Pasquali L; Martinez-Climent JA; **Esteller M**. B-cell leukemia transdifferentiation to macrophage involves reconfiguration of DNA methylation for long-range regulation Leukemia 2020 Apr;34(4):1158-1162. doi: 10.1038/s41375-019-0643-1. Epub 2019 Nov 12. Impact Factor: 11,53 - Q1 PMID: 31719676

Ikemori R; Gabasa M; Duch P; Vizoso M; Bragado P; Arshakyan M; Luis IC; Marín A; Morán S; Castro M; Fuster G; Gea-Sorli S; Jauset T; Soucek L; Montuenga LM; **Esteller M;** Monsó E; Peinado VI; Gascon P; Fillat C; Hilberg F; Reguart N; Alcaraz J. Epigenetic SMAD3 Repression in Tumor-Associated Fibroblasts Impairs Fibrosis and Response to the Antifibrotic Drug Nintedanib in Lung Squamous Cell Carcinoma. Cancer Res 2020 Jan 15;80(2):276-290. doi: 10.1158/0008-5472.CAN-19-0637. Epub 2019 Nov 6. Impact Factor: 12,70 - Q1. PMID: 31694906

Esteve-Puig R; Bueno-Costa A; Esteller M. Writers, readers and erasers of RNA modifications in cancer. Cancer Lett 2020 Apr 1;474:127-137. doi: 10.1016/j.canlet.2020.01.021. Epub 2020 Jan 25. Impact Factor: 8,68 - Q1. PMID: 31991154

Parra M; Baptista MJ; Genescà E; Llinàs-Arias P; Esteller M. Genetics and epigenetics of leukemia and lymphoma: from knowledge to applications, meeting report of the Josep Carreras Leukaemia Research Institute. HEMATOL ONCOL 2020 Oct;38(4):432-438. doi: 10.1002/hon.2725. Epub 2020 Mar 3. Impact Factor: 5,27 - Q2. PMID: 32073154

Martín-Fernández JM; Fleischer A; Vallejo-Diez S; Palomino E; Sánchez-Gilabert A; Ruiz R; Bejarano Y; **Llinàs P;** Gayá A; Bachiller D. New Bicistronic TALENs Greatly Improve Genome

Editing. Curr Protoc Stem Cell Biol 2020 Mar;52(1):e104. doi: 10.1002/cpsc.104. PMID: 32023363

Hanniford D; Ulloa-Morales A; Karz A; Berzoti-Coelho MG; Moubarak RS; Sánchez-Sendra B; Kloetgen A; **Davalos V**; Imig J; Wu P; Vasudevaraja V; Argibay D; Lilja K; Tabaglio T; Monteagudo C; Guccione E; Tsirigos A; Osman I; Aifantis I; Hernando E. Epigenetic Silencing of CDR1as Drives IGF2BP3-Mediated Melanoma Invasion and Metastasis Cancer Cell 2020 Jan 13;37(1):55-70.e15. doi: 10.1016/j.ccell.2019.12.007. Impact Factor: 31,74 - Q1 PMID: 31935372

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Janin M; Coll-SanMartin L; Esteller M. Disruption of the RNA modifications that target the ribosome translation machinery in human cancer Mol Cancer 2020 Apr 2;19(1):70. doi: 10.1186/s12943-020-01192-8. Impact Factor: 27,40 - Q1 PMID: 32241281

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Antiviral host factors, Interferon Stimulated Genes (ISGs) and T-cell responses associated with natural HIV control. PLOS PATHOG 2020 Aug 6;16(8):e1008678. doi: 10.1371/journal.ppat.1008678. eCollection 2020 Aug. Impact Factor: 6,82 - Q1. PMID: 32760119

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Rosselló-Tortella M; Llinàs-Arias P; Sakaguchi Y; Miyauchi K; **Davalos V**; Setien F; Calleja-Cervantes ME; **Piñeyro D**; Martínez-Gómez J; **Guil S**; **Joshi R**; Villanueva A; Suzuki T; **Esteller M**. Epigenetic loss of the transfer RNA-modifying enzyme TYW2 induces ribosome frameshifts in colon cancer. P NATL ACAD SCI USA 2020 Aug 25;117(34):20785-20793. doi: 10.1073/pnas.2003358117. Epub 2020 Aug 10. Impact Factor: 11,21 - Q1 PMID: 32778592

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3.
Chromatin biology laboratory

Li T; Garcia-Gomez A; Morante-Palacios O; Ciudad L; Özkaramehmet S; Van Dijck E; Rodríguez-Ubreva J; **Vaquero A; Ballestar E.** SIRT1/2 orchestrate acquisition of DNA methylation and loss of histone H3 activating marks to prevent premature activation of inflammatory genes in macrophages. NUCLEIC ACIDS RES 2020 Jan 24;48(2):665-681. doi: 10.1093/nar/gkz1127. Impact Factor: 16,97 - Q1 PMID: 31799621

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Simonet, NG; Thackray, JK; Vazquez, BN; Ianni, A; Espinosa-Alcantud, M; Morales-Sanfrutos, J; Hurtado-Bages, S; Sabido, E; **Buschbeck, M**; Tischfield, J; **De La Torre, C; Esteller, M**; Braun, T; Olivella, M; Serrano, L; **Vaquero, A**. SirT7 auto-ADP-ribosylation regulates glucose starvation response through mH2A1. SCI ADV 2020 Jul 24;6(30):eaaz2590. doi: 10.1126/sciadv.aaz2590. eCollection 2020 Jul. Impact Factor: 14,14 - Q1. PMID: 32832656

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4.
Chromatin, metabolism and cell fate

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HOSPITAL DE LA SANTA CREU I SANT PAU

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IMPPC Institut de Medicina Predictiva i Personalitzada del Càncer

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