

2025 Call for the IRB Barcelona International PhD Fellowship Programme (ref.01/25.1/IRB)

TERMS & CONDITIONS

Section II, article 6, letters c) and q) of the Articles of Association of the Fundació Institut de Recerca Biomèdica (IRB Barcelona) (hereafter referred to as IRB Barcelona or the Institute) establish that the Institute will promote activities that address collaboration and knowledge transfer and also launch fellowship calls and subsequent granting of these awards.

Accordingly, this document is to announce a fellowship call included in the IRB Barcelona International PhD Programme. The fellowships are assigned to students enrolled on a PhD programme who perform and defend their PhD theses under the supervision of group leaders at IRB Barcelona.

I. Objective

These Terms and Conditions serve to regulate the award of PhD fellowships for the academic year 2025–2026.

II. Fellowship Call

The following will be offered in this call:

- Up to 5 doctoral contracts associated with the Severo Ochoa Accreditation 2023, funded by the "Ministerio de Ciencia e Innovación (MICINN)" (herein referred to as Severo Ochoa doctoral contracts).
- Up to 3 FPI doctoral positions associated with the "Proyectos de Generación de Conocimiento 2024" Call (funded by the Agencia Estatal de Investigación AEI- MICINN).
- Up to 2 Adaptmet three-year fellowships funded by the DN- Marie Skłodowska-Curie Actions call of the European Commission. This project has received funding from the European Union's Horizon Europe programme under grant agreement 101169223.
- Up to 1 SPOILCONTROL fellowship funded by the DN- Marie Skłodowska-Curie Actions call of the European Commission, to work at BSC under the supervision of Dr. Toni Gabaldón. This project has received funding from the European Union's Horizon Europe programme.









The FPI positions will be regulated by the MICINN call, following the conditions of this government agency. Details of the evaluation criteria are provided in Annex 2.

All fellowship awardees will be contracted by IRB Barcelona. Fellowships will be renewable on a yearly basis and up to 4 years from the date of signature of the employment contract by the awardee, provided that he/she complies with all the requirements of point X of this call.

The awardee's supervisor will be the group leader at IRB Barcelona previously assigned and agreed with the awardee before the signature of the fellowship. This group leader will oversee that the duties assigned to the awardee are fulfilled and will notify IRB Barcelona's Academic Office and the Chair of Graduate Training of any incident, alterations in the fulfilment of the allocated duties, or other pertinent circumstances so that corrective measures can be applied and/or proceedings can be started to withdraw the fellowship.

III. Requirements and Selection Criteria

IRB Barcelona will recruit prospective doctoral candidates of any nationality, gender, culture, religion, sexual orientation or age to undertake a PhD in biomedicine.

- 1. The programme is aimed at students who have completed one of the following options by September 2025:
 - a) studies that lead to an official Spanish (or from another country of the European Higher Education Area) university degree in Biology, Chemistry, Biochemistry, Pharmacy, Physics, Medicine or related fields and that have 300 credits (ECTS), of which at least 60 must correspond to master level.
 - b) a degree in a non-Spanish university not adapted to the European Higher Education Area and that gives access to doctoral studies in Biology, Chemistry, Biochemistry, Pharmacy, Physics, Medicine or related fields in Spain.
- 2. Candidates are selected exclusively on merit, on the basis of their curricula. The academic grades and curriculum vitae of each applicant are evaluated, as well as recommendation letters and a motivation letter. No selection criteria for positive or negative discrimination are applied.

Applicants should indicate the Research Group(s) to which they wish to apply (up to 2). Details of the projects available are provided in Annex 1.









IV. Application Procedure

1. Applications can be made online at http://phd.irbbarcelona.org/. The application deadline is 15:00 CET on 10 January 2025.

The tentative calendar for this call is as follows:

Call opening: 15 November 2024

Deadline for candidacies: 10 January 2025, 15:00 CET Deadline for referees: 13 January 2025, 15:00 CET

Pre-selection Period End: 3 February 2025

Group Leader's Panel Presentations (online): 27 February 2025

Interviews at IRB Barcelona: 3-4-5 March 2025 Notification to candidates: 14 March 2025

Start date of fellowships: from September 2025

If the application deadline is extended, the updated information will be available on the IRB Barcelona's website.

2. For more information, applicants can consult IRB Barcelona's webpage or contact IRB Barcelona's Academic Office at <u>academicoffice@irbbarcelona.org</u>

V. Applications

Applicants should send a completed online application form, together with the following documents:

- 1. Curriculum vitae specifying education and experience, including career breaks, and supported by pertinent documents.
- 2. A motivation letter (maximum 2 pages) highlighting their research experience and academic achievements and explaining why they are interested in IRB Barcelona and in a particular research group.
- 3. A scanned copy of their certified Academic Record. These documents must show the grades attained in exam periods. If the certified academic records are not in Spanish or English, applicants should also attach a translation in one of the above-mentioned languages.
- 4. Any additional files considered relevant to the application
- 5. Two recommendation letters from university lecturers or scientists with whom they have studied or worked. Candidates are responsible for ensuring that referees submit these letters. Applications not supported by these letters will not be eligible. If the applicant has previously worked with a researcher at IRB Barcelona, any letter of reference from said person cannot be included as one of the two reference letters requested. However, it can be sent to provide additional support for the application.









Applicants will be asked to upload the following documents in English. Please note that all the documents provided should be in PDF format.

VI. Selection

An Evaluation Committee will appraise eligible. This committee will have representatives of group leaders at IRB Barcelona. The evaluation will be independent, impartial, objective, and free of conflicts of interest, and the selection will be open, efficient, transparent, fair, and merit-based. The PhD Advisory Committee and Academic Office will oversee the remote and interview stages of the selection process.

Applicants will receive continuous support from the Academic Office through the helpdesk (email, phone), which will notify them of the outcome of the preselection. Candidates with the highest scores will be invited for an online interview. Those who do not pass the threshold established will be excluded from further consideration. Applicants who do not pass this evaluation will be informed why and will be provided with the instructions to follow to start a redress procedure.

Offers of admission will be made to the successful candidates shortly after the interview period. Candidates positively evaluated but with an insufficient score to receive a fellowship will be put on a reserve list to cover possible renunciations and future positions.

Awardees will receive a formal invitation letter.

The following evaluation criteria will be used by the Evaluation Committee during the pre-selection phase:

Evaluation criteria	Score (points)	Sub criteria	Weight	Threshold
Academic record and CV	1–10	Academic and/or professional curriculum in relation to the stage of the candidate's career (graduate studies, grades, institution), including career breaks. Research experience (diverse fields /sectors, publications, participation in projects). International mobility (studies abroad, secondments, etc). Scientific-technological quality (courses, workshops). Fellowships/awards received, supervision, knowledge transfer, communication and other relevant merits.	50%	60%









Motivation Letter	1–10	Strength and relevance of the candidate's motivation towards the research conducted at IRB Barcelona. Interest in any specific IRB Barcelona research group.	20%	50%
Letters of reference	1–10	Reference letters supporting the candidacy will be assessed taking into account the relevance of the content and the person who signs the letter in relation to the candidate's target research groups.	30%	50%

The overall score of the pre-selection phase will be calculated by multiplying the score obtained for each criterion (1–10 points) by the weight assigned to each one (as seen in the table). Only applications that are above the thresholds established for all criteria will be considered. This procedure will lead to a score out of 10. A ranking will be obtained in a consensus meeting. In case of a draw in the total score between applications, candidates will be prioritized on the basis of the weight of each criterion. If two candidates have the same scores for all evaluation the criteria, both will be invited to interviews.

During the Candidate's Presentation Panels and Interview phases, additional criteria (see below) will be taken into consideration:

Evaluation criteria	Score (points)	Sub criteria	Weight	Threshold
Candidate's potential	1–10	Ability to present complex reasoning in English. Independent thinking, creativity, and organisation capacity. Leadership skills, team working capacity, and maturity.	40%	50%
Motivation	1–10	Strength and relevance of motivation for applying to IRB Barcelona. Motivation towards the research lines offered by the different nodes.	30%	50%
Academic background and theoretical fundamentals	1–10	Suitability of the candidate's academic background to undertake the research lines offering projects in the call.	30%	50%

The overall score in the interview phase will be calculated by multiplying the score obtained for each criterion (0-10 points) by the weight assigned to each one (as seen in the table in %). This procedure will lead to a total score out of 10. A ranked list of candidates will be drawn up. In the event of a draw in the total score, candidates will be prioritized on the basis of the weight of each criterion. When scores on all evaluation criteria are still the same, preference will be given to









candidates from under-represented groups (e.g. on the basis of gender, disability or refugee backgrounds).

On 9 December 2014, IRB Barcelona was awarded the "HR Excellence in Research" logo. This recognition reflects the commitment of the Institute to continuously improving its human resources policies in line with the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers. More information about our OTM-R (Open, Transparent, Merit-based Recruitment) policy can be found at the following <u>link</u>.

VII. Documentation

Each candidate selected during the interviews must present the following documents to complete the selection procedure.

1. Degree certificate or official notification of degree award. Non-Spanish nationals must present: 1) a certified copy and sworn translation of the degree certificate or equivalent obtained in a university abroad; and 2) a certified copy and sworn translation of the certificate showing the subjects studied.

If the certified academic records are not in Spanish or English applicants should also attach a sworn translation in one of the above mentioned languages.

- 2. A sworn statement expressing intention to enrol on a university doctoral programme.
- 3. A sworn statement stating that he or she does not receive any other funding or fellowship grant.

(Non-compliance with points 2 and 3 will automatically lead to withdrawal of the fellowship and the awardee must return any amounts received to IRB Barcelona).

VIII. Communication of Fellowship Award

The Head of Human Resources and Academic Affairs department will officially inform successful candidates of the fellowship award.

IX. Rights of Awardees

- 1. Awardees will have the following general rights:
 - a) To be provided with the necessary assistance to perform their studies and research activities.









- b) To become a member of the research programme in which they will be undertaking PhD studies.
- c) To participate in bodies governing and representing the student community.
- d) To participate in complementary calls for funding to attend scientific congresses or to spend training periods in other centres upon approval of their supervisors and the director of IRB Barcelona.
- e) To have their intellectual and industrial property rights regulated in the employment contract with IRB Barcelona.
- 2. Awardees will have employment and Social Security rights derived from the employment contract with IRB Barcelona.
- 3. Awardees will be able to exercise intellectual property rights derived from their training activity in accordance with their contribution, as established in the Intellectual Property Law, Royal Decree 1/1996, 12 April. These rights will be independent, compatible, and accumulable with other rights that may arise from the research developed, without negatively affecting the rights of the joint effort when the awardees participate in or are associated with a joint research project.
- 4. Regarding possible industrial property rights of the awardees, these will be regulated by Law 24/2015, of July 24, 2015, on Patents, and Royal Decree 55/2002, of January 18, 2002, governing the exploitation and license of rights on discoveries made in public research organisations.

Said rights will not be linked to salary.

X. Responsibilities of Awardees

- 1. To fulfil the terms and conditions established in this call.
- 2. To enrol on a university doctoral programme.
- 3. To perform their research activity under the supervision of a group leader at IRB Barcelona for the duration of the fellowship. In addition, they must perform the activities foreseen in the research training and specialisation programmes of the Institute, as well as satisfactorily fulfil the objectives of the training programme.
- 4. To comply with the internal regulations of IRB Barcelona, particularly regarding working conditions and the prevention of occupational risks.
- 5. To prepare a report each year informing on the scientific progress of their theses. Moreover, they will present this report to their Thesis Advisory Committee, designated by the Institute.









- 6. To request approval from the group leader supervising their activity prior to the submission for publication or disclosure of any abstracts and/or publications based on research carried out at IRB Barcelona.
- 7. To undertake the duties that correspond to them as a result of being contracted by IRB Barcelona, as well as those associated with inclusion in the Social Security System.
- 8. To defend their theses and obtain the respective PhD degree by the end of the fourth year after the start of the fellowship. In exceptional cases, an extension of one year may be given for the defence of the thesis.

XI. Termination of Fellowships

The fellowship will be revoked if the awardee has withheld or falsified information. The fellowship will also be revoked if the awardee does not fulfil the responsibilities described in point X.

XII. Incompatibility

Awardees will be devoted exclusively to the research or technical training and specialisation activities defined in this call. The fellowships included in this call are not compatible with any other type of grant or fellowship from other public or private organisations.

XIII. Legal Regime

Awardees will be subjected to the legal regime applicable to PhD fellowships according to the law in force at the time of drawing up the contract.

XIV. Data Protection

In accordance with Regulation (EU) 2016/679 (General Data Protection Regulation), Organic Law 3/2018 of December 5, and other applicable regulations governing personal data protection, any personal data provided by applicants will be incorporated into the Academic file of IRB Barcelona, for which the Institute is the data controller. The purpose of keeping such data is to manage the relationship of the Institute with applicants. Applicants may exercise the rights of access, rectification deletion, opposition, transfer and expiry, as well as limitation in data processing of said information by contacting the Institute at the following e-mail address: dataprotection@irbbarcelona.org, or by writing to the following postal address: C/Baldiri Reixac, 10, 08028, Barcelona.









XV. Dissemination

Any information regarding this fellowship call will be placed on the announcement board on IRB Barcelona's website.

XVI. Clarification

The Director of IRB Barcelona or a designated representative will be responsible for clarifying queries regarding these terms and conditions.

Barcelona, 15 November 2024

Maribel Labrid

Head of Human Resources and Academic Affairs







ANNEX 1. Research projects

IRB Barcelona research group	Group Leader	Research Node	Description of the research project
Quantitative Stem Cell Dynamics Lab	Dr. Alejo Rodríguez- Fraticelli	Preclinical Models of Cancer; Cell Pathophysiology	Exploring "Cell Learning" in Healthy and Malignant Stem Cells Can individual cells retain memories of their experiences? While typically associated with neurons, recent discoveries suggest that even immune and single-celled organisms can "learn" from their environments. The Fraticelli Lab at IRB Barcelona is inviting PhD candidates to join our team and explore cellular memory across diverse experimental and computational projects. Our lab is developing lineage tracing and reporter systems to record environmental interactions in real-time, capturing "memories" in single cells and blood stem cells, both healthy and malignant. PhD candidates have the opportunity to work on a variety of research paths: Experimental PhD candidates will take on the challenge of implementing in situ CRISPR screens and multi-color recorder systems to uncover the epigenetic underpinnings of cellular learning in hematopoiesis and leukemia. Computational PhD candidates will dive into rich single-cell analysis, including the interpretation of complex data generated from our unique perturbation and recorder systems to understand how and when cells learn from their environmental history Candidates will gain hands-on experience with a range of advanced methods, including stem cell culture, transfection, FACS, CRISPR gene editing, and single-cell sequencing. Computational candidates will additionally learn data analysis for cell barcoding, DNA methylation, and single-cell bioinformatics.







			Working with our team and collaborating across labs (at Oxford, CRG, ETH Zurich, MIT, and beyond), candidates can expect mentorship and opportunities to shape this research area, advancing our understanding of stem cell memory and its potential implications in health and disease.
Pediatric Cancer Epigenetics Lab	Dr. Alexandra Avgustinova	Preclinical Models of Cancer; Cell Pathophysiology	Childhood cancers are believed to be rooted in aberrant development, a notion supported by their (i) generally low mutational burden, (ii) high prevalence of single (often epigenetic) driver events and (iii) occurrence during confined developmental periods. Yet, the exact origins of developmental tumours remain one of the principal enigmas of pediatric oncology.
			A prime example are malignant rhabdoid tumours (MRTs): they are astoundingly genomically simple but extremely deadly childhood cancers that arise almost exclusively in the first two years of life, and are driven by biallelic inactivation of the SWI/SNF chromatin remodelling complex subunit SMARCB1 (>95% of cases).
			We still do not know what determines oncogenic competence upon SMARCB1-loss. The PhD student will investigate the defining features of the local and systemic niches that support MRT initiation and tumour growth, using cutting edge methods including transgenic mouse models, single-cell resolution wholemount imaging and computational modelling. Ultimately, we will seek to disrupt the MRT niche integrity in search of novel treatment strategies for MRTs.
Mitochondrial Biology and Tissue Regeneration Lab	Dr. Ana Victoria Lechuga- Vieco	Preclinical Models of Disease; Cell Pathophysiology	Mitochondrial Drivers in Tumor Immunology In cancer cells, mitochondrial DNA (mtDNA) plays a pivotal role in dictating their metabolic options and is critical in the definition of the tumor microenvironment. The significance of de novo mtDNA mutations in the tumorigenic process is well-documented. In turn, antigen presentation is crucial for developing immune tolerance and initiating immune responses









			against cancer. However, the impact of different mitochondrial haplogroups – specific variations in the mtDNA sequence that have been fixed during evolution– on intercellular signaling and response to immunotherapy remains to be explored. The crucial role of mtDNA-encoded genes in shaping cellular transcriptome and metabolome offers a powerful tool for investigating antigen presentation from cancer to CD8 T cells. During this project, we will employ innovative methodologies to create novel cancer cell models that retain identical nuclei whilst swapping mitochondrial genomes, along with preclinical in vivo and ex vivo models to study mitochondrial–derived antigens and the priming of T-cell responses. Exploring how the mitochondrial genome influences intercellular communication within tumors will offer new insights into tumor behavior and resilience.
Signalling and Cell Cycle Lab	Dr. Angel Nebreda	Preclinical Models of Cancer; Cell Pathophysiology	Exploring tumor vulnerabilities by targeting stress kinase signaling We are investigating molecular mechanisms of tumorigenesis, especially regarding how protein kinases in general, and the stress-activated p38 MAPK pathway in particular, regulate tumor development and the response to cancer therapies. Ongoing projects in the group address two main topics: (1) Cancer cell homeostasis and chemoresistance mechanisms, and (2) Cross talk between cancer cells and stromal cells. Our work combines biochemical approaches and experiments in cultured cells with studies using mouse models and chemical tools. We are performing a number of genetic and chemical screenings to find new actionable targets that can be used to boost current cancer therapies as well as to design new targeted therapies for particular tumor types. Candidates will contribute to the identification of therapeutic opportunities based on the modulation of protein kinases, either alone or in combination with other drugs.
Cell Signaling Lab	Dr. Francesc Posas & Dr.	Cell Pathophysiology	Decoding cellular adaptation: From yeast to humans









	Eulàlia de Nadal		Cells are constantly challenged by fluctuations in their environment and they must rapidly rewire their internal circuitry, meeting new demands without losing their identity to maximize fitness. Failure to adapt can lead to decreased cellular function, impaired survival, and potentially cell death, ultimately compromising viability. Our lab seeks to unravel the molecular mechanisms behind these adaptive processes, focusing on signaling pathways and adaptive responses that shape cell fate decisions. Our multidisciplinary approach combines cutting-edge techniques in proteomics, genomics, transcriptomics, and single-cell analyses to decode the language of cellular adaptation. PhD candidates will have the opportunity to engage in innovative research opportunities: From discovering novel gene functions essential for stress adaptation through genetic screens (CRISPR-screens in yeast or mammals) to biochemical identification of novel targets controlled by stress-activated protein kinases and define their impact in cell physiology. Together, we aim to define novel mechanisms controlling cellular adaptation. We leverage cutting-edge single-cell RNA sequencing (scRNA-seq), to uncover the heterogeneity in the adaptive response. We then link these molecular profiles to phenotypic profiling to gain and gain insights into the diverse cellular strategies employed of adaptive strategies. Join our stimulating and collaborative scientific environment, where you'll work alongside a multidisciplinary team and engage with international collaborators. By understanding how cells mount adaptive responses, we aim to unlock new insights into health and disease.
Microtubule organization in cell proliferation and differentiation Lab	Dr. Jens Lüders	Cell Pathophysiology; Preclinical Models of Disease	Role of the microtubule network in building specialized cell types and Tissues









	Tuesdakiasa			The microtubule cytoskeleton provides cells with mechanical support, mediates intracellular transport, and segregates the chromosomes during cell division. These functions are crucial for cell proliferation and differentiation and thus the formation and maintenance of tissues. For example, malfunctioning of the microtubule cytoskeleton is linked to both impaired development and degeneration of the brain. This project aims to elucidate how the microtubule network is organized in induced pluripotent stem cells (iPSCs) and remodeled during differentiation to support the formation of specialized tissues such as neuroepithelium. As part of an international team, the student will address these questions using human iPSC culture, iPSC differentiation into different cell types, CRISPR-mediated genome editing, and advanced microscopic imaging techniques including super resolution microscopy.
Gene Lab	Translation	Dr. Lluis Ribas	Cell Pathophysiology	The impact of somatic mutations in transfer RNAs upon cancer development and aging We have discovered that somatic degeneration of human tRNA genes is a prevalent phenomenon that takes place in both healthy and cancer cells (1). Internal regions of tDNAs constitute hotspots of somatic mutagenesis whose intensity is directly linked to the transcriptional activity of each gene. The mutational load at tDNAs is not found at other genes transcribed by Pol III, and accumulates in tDNAs at rates up to 10-fold higher than in protein-coding genes. Somatic mutations at tDNAs happen in both healthy and cancer cells, accumulate with age, and are capable of generating mutant chimeric tRNAs that decrease the quality of the human proteome through specific and ubiquitous amino acid substitutions. We have begun to generate cell lines that express the mutant chimeric tRNAs that we most often detect in human tumors. We are seeking a motivated Ph.D. student to push this project forward. Experience in cell culture and an









			interest in studying cancer and aging from the perspective of fundamental cell biology are needed. (1) Murillo et al., submitted to Nature.
Development and Growth Control Lab	Dr. Marco Milán	Preclinical Models of Cancer; Cell Pathophysiology	Identification and elimination of aneuploid cells in development Aneuploidy, which is the major cause of miscarriages in humans, is pervasive in early human embryos but is robustly dampened during development to lead to healthy births. A mechanistic understanding of the identification and elimination of aneuploid cells remains poorly understood. We use Drosophila to characterize whether this process relies on cell interactions and to identify the underlying molecular mechanisms. This project will certainly have implications in understanding the major cause of miscarriages in humans.
Structural Characterization of Macromolecular Assemblies Lab	Dr. Maria Macias	Chemical and Structural Biology	Deciphering the Molecular Mechanisms of TGFβ Signaling in health and disease Our research group is dedicated to understanding the molecular mechanisms underlying cell signaling and gene expression. We focus on the TGFβ signaling pathway and the role of SMAD transcription factors in development and in disease. Our long-term goal is to identify vulnerable sites within the SMAD complexes with cofactor to develop novel therapies for cancer and rare diseases such as Myhre syndrome. We are seeking highly motivated PhD students with: A strong background in molecular and structural biology. Experience in protein biochemistry, cell biology, or structural biology techniques. As a PhD student, you will learn in our laboratory: Structural Biology: Employing techniques such as NMR, X-ray crystallography and cryo-EM to determine the high-resolution structures of the complexes. Molecular Biology and Biochemistry: Performing biochemical and cellular experiments to study protein-protein interactions and effects of the compounds in modulating TGFβ signaling pathways.









			Bioinformatics: Predict potential protein-protein and protein-
T l . l' l	D D 1	Darlinian	compound binding sites with Al-powered tools.
Translational Control of Coll	Dr. Raúl Méndez	Preclinical Models of	A Mechanistic Approach to Chronic Stress Responses in Metabolic Liver Disease and Cancer
Control of Cell Cycle and Differentiation	Menaez	Models of Cancer; Cell Pathophysiology	This project investigates the cellular and molecular mechanisms through which dietary fat consumption impairs the liver's capacity to maintain effective stress response mechanisms. We have identified several signaling pathways that may be crucial to this process and are exploring methods to therapeutically modulate these pathways. Our hypothesis is that modulating these factors may restore the liver's capacity to respond to stress and reverse the epigenetic memory induced by parental dietary fat consumption, which predisposes the liver to damage and cancer. Ultimately, this research aims to identify new therapeutic targets for treating liver cancer in aging populations with high dietary fat intake.
			The project employs cutting-edge multi-omic analyses—including epigenomic, epitranscriptomic, translatomic, and metabolomic profiling—in genetically modified mouse models of liver disease, along with analyses of patient samples. This comprehensive approach will enable us to characterize the molecular landscape underlying metabolic liver disease and to identify potential intervention points for therapy.
Growth Control and Cancer Metastasis Lab	Dr. Roger Gomis	Preclinical Models of Cancer	Understanding metastasis drug resistance We propose to elucidate drug-tolerant persister BCa cells, which develop following treatment, can persist in the body in a latent state, and can metastasize. We believe that there is an extensive phenotypic heterogeneity and plasticity present in BCa cells/tissues prior to treatment, which influences chemotherapy resistance and promotes resistant cancer cell development. Research has been hindered by their heterogeneity and the technical difficulties presented by the extremely low number of cells necessary for disease progression and by the requirement of an extra-cellular







			environment for drug resistant plasticity. We now propose to gain previously unappreciated understanding at the genetic, epigenetic, biochemical, and cellular levels of the chromatin and transcriptional regulatory mechanisms that establish drug resistant latent state and subsequent metastasis progression, and then to exploit this information for therapy.
Stem Cells and Cancer Lab	Dr. Salvador Aznar	Preclinical Models of Cancer; Cell Pathophysiology	The candidates will be able to join any of three ongoing projects in the lab: Cancer-associated cachexia (CAC) is a syndrome involving severe muscle and fat wasting, chronic inflammation, and altered metabolism, affecting many patients with metastatic cancer. It is the cause of over 40% of deaths related to cancer. Despite its impact, CAC remains incurable and difficult to diagnose early. This project explores the role of Schwann cells in driving CAC, as they communicate with metabolic tissues, triggering changes that fuel tumor growth and exacerbate cachexia. Using an oral squamous cell carcinoma (SCC) and triple-negative breast cancer mouse models, the study investigates molecular changes in metastatic cells, immune and Schwann cells, as well as main metabolic organs, transcriptomic and metabolomic analyses to identify biomarkers and potential therapeutic targets for energy-wasting syndrome associated with cancer. While the brain circadian clock senses the overall daily systemic changes (such as light/dark, awake/asleep), each peripheral tissue must have its own clock that gates the brain-
			derived information to adjust it to their needs. We now appreciate that circadian communication between these peripheral organs is also critical to the overall health of a body, but this communication becomes desynchronized during aging, leading to accelerated aging phenotypes. We will now perform a novel, in-depth study of how a specific organ—the







liver—communicates in a circadian manner with other tissues, and how food intake affects the circadian health of the liver. We chose to initially start with the liver as it is a central organ for controlling the body's circadian rhythm, but once we have the circadian atlas from the liver in different circumstances (young vs aged, with or without chronic stressors), we will move on to studying other tissues as the "informing" tissue of inter-organ communication. Further, our daily choices in food have a drastic effect on our liver health (such as eating diets with a high content of palm oil). In this project, we will elucidate the molecular basis for disturbances in the circadian communications stemming from the liver, and importantly, how to reverse them therapeutically. Importantly, we will understand how chronic stressors (such as a high-fat diet) can lead to permanent decay of the circadian health of the liver, and how to revert that. We believe that the results from this project will translate in relatively short times to clinicallyrelevant therapies. Results from the initial stage of this project on the liver will expedite the analyses of other organs in the future, which will expand our repertoire of tools for developing therapies to synchronize the human circadian communication between organs. Overall, we aim to prevent circadian desynchronization during aging—and thus reduce, prevent, or even reverse accelerated biological aging in humans, with an expanded healthspan as well as lifespan.

Epidemiological observations indicate that parental overnutrition of diets rich in fat is among the strongest predictors of fatty liver and liver cancer in their progeny. This suggests that the increasing incidence of non-alcoholic liver disease and liver cancer in recent decades might be partly related to the exposure of high levels of fat during gestation. However, the mechanisms underlying this effect are completely unknown. We recently published that palmitate not only contributes to metastasis, but also exerts a long-term epigenetic effect on metastatic cells. This detrimental









			"metastatic fat memory" is caused by epigenetic modifications in genes that make tumors much more sensitive to reexposure to fat. We now hypothesize that a similar epigenetic mechanism takes place due to the exposure to high-fat diets during gestation which ultimately increases the susceptibility to fatty liver disease and liver cancer later in life. We now aim to understand: i) How exposure to fatty acids during gestation affects the liver epigenome, transcriptome and metabolome of offspring. ii) How this predisposes the offspring to an increased risk of developing liver disease and liver cancer later in life. iii) Whether we can use this information for diagnostic and therapeutic purposes. We will use in vivo and in vitro functional assays in mouse models and 3D organoids of adolescent and adult patients with fatty liver diseases, combined with state-of-the-art molecular and therapeutic techniques, to characterize the liver at the transcriptomic, epigenetic, and metabolomic levels. Our project aims to increase our understanding of the fetal programming mechanisms of the liver, and how it is influenced by parental dietary habits. We propose to address a sensitive but critical issue: determining the potential risks that excessive consumption of diets rich in palmitic acid may have on the development of liver disease, and importantly, finding new
Innate Immune	Dr. Stefanie	Cell	therapeutic targets for its treatment. Studying environment-dependent functions of innate immune cells and their therapeutic potential Myeloid cells, such as macrophages, dendritic cells (DCs) and neutrophils, reside in various organs to respond to insults and are key to control immunity and inflammation. Different tissues comprise highly distinct milieus that impose context-dependent biochemical challenges on their resident cells, which is further aggravated during conditions such as cancer, obesity-related pathologies and aging. Yet, it is
Biology Lab	Woulek	Pathophysiology;	









			poorly known how innate immune cells survive in their different homing organs and maintain their functionality in disease settings. We investigate how macrophages, DCs and neutrophils adjust to distinct environments in health and non-infectious diseases. This is important, because dysfunctional myeloid cells cause uncontrolled inflammation or immune-paralysis with detrimental effects for patients. Given their power to orchestrate immune responses, it is now vital to reveal the precise (metabolic) adaptions of macrophages, DCs and neutrophils to changing milieus. This project will uncover and characterize the relevance of context-dependent (metabolic) adjustments for the pro- or anti-inflammatory functions of macrophages, DCs or neutrophils to healthy or diseases tissues, and dissect the underlying molecular mechanisms. The details of the project will be designed based on the interests of the successful candidate within the research lines of the group. Independent innovative approaches and adapted cutting-edge techniques will be used for analysis of mouse models, primary tissue culture and human samples; including multicolour flow cytometry, (single-cell) RNA sequencing, multiplex microscopy and spatial analyses, metabolomics, epigenetic analyses and various metabolic assays. The discovery of tissue-dependent adaptions by innate immune cells that impact their functions will transform translational research to integrate the environmental context and reveal novel "innate immunotherapies" to combat cancer and metabolic disorders.
Comparative	Dr. Toni	Computational	Project 1: Emergence of virulence and drug resistance in Candida pathogens What makes a pathogen a pathogen? How do they adapt to our immune system and the drugs we use to fight infection? What makes a microbe cross the line from a commensal to a pathogenic lifestyle? The Gabaldón Lab at IRB Barcelona is seeking PhD candidates to join our team and explore host-
Genomics Lab	Gabaldón	Biology	









microbe interactions through diverse experimental and computational projects.

Our group uses comparative omics and in-vitro experimental approaches to understand how microbes interact with the human host and how they adapt to our immune system and to anti-infective drugs.

Experimental PhD candidates will use in-vitro evolution, large-scale phenotyping, and CRISPR-Cas engineering to detect and study the functions of genes relevant for virulence and drug resistance.

Computational PhD candidates will develop and use bioinformatics tools to understand how relevant virulence traits or drug resistance evolve within populations and across species.

Candidates will gain hands-on experience with a range of advanced methods, including microbial culture, infection models, large-scale phenotyping, CRISPR gene editing, and bulk and single-cell RNA and DNA sequencing. Computational candidates will learn complex data analysis for genome and transcriptome sequencing (including single-cell), as well as machine learning and data science algorithms.

Project 2 (BSC): Diversity and prevalence of pathogenic microorganisms in fermented food products

This PhD position will be performed within the Marie Skłodowska-Curie-funded Doctoral Network "SPOILCONTROL," which aims to understand microbial communities within newly developed fermented beverages with low or no ethanol content. These organisms can be a source of spoilage in the product, as well as potentially risky pathogens. Alcoholic fermentation prevents growth/survival due to high ethanol content. However, limited data is available regarding no/low ethanol fermented beverages, such as dealcoholized wines, spirits, cocktails, beers (a recent and growing trend), as well as kombucha or water/fruit kefir. On the other hand, the source of many emerging fungal Candida









			pathogens that are not typical commensals of the human microbiota is unknown, but they have been found on the surface of market fruits or in low-alcohol beverages. For this project, we are seeking a computational candidate who will develop a pipeline for identifying microbial pathogens from sequencing data and will use genomics and metagenomics of diverse food products (provided by our consortium partners) to detect and study the diversity of pathogens. Further in-depth studies will be performed on selected (Candida) pathogens, which will be isolated and studied in the lab (by experimental collaborators) to characterize their virulence-related phenotypes and compare them to clinical isolates of the same or related species.
Laboratory of Molecular Biophysics Lab	Dr. Xavier Salvatella	Chemical and Structural Biology	Transcriptional condensates as drug targets for oncology We have recently shown how the activation domain of the androgen receptor can be targeted by drug-like small molecules for treating castration-resistant prostate cancer (Nat Struct Mol Biol 2023). The student joining our laboratory will investigate the mechanism by which these small molecules inhibit the function of their target.
Structural Bioinformatics and Network Biology Lab	Dr. Patrick Aloy	Computational Biology	Blending Biology, Chemistry and AI to Enable Personalized Systems Pharmacology Biological data is accumulating at an unprecedented rate, escalating the role of data-driven methods in computational drug discovery. The urge to couple biological data to cutting-edge machine learning has spurred developments in data integration and knowledge representation, especially in the form of heterogeneous, multiplex and semantically-rich biological networks. Today, thanks to the propitious rise in knowledge embedding techniques, these large and complex biological networks can be converted to a vector format that suits the majority of machine learning implementations. In this computational framework, complex connections between entities can be unveiled by means of simple arithmetic operations. Indeed, we demonstrate and experimentally







validate that these descriptors can be used to reverse and mimic biological signatures of disease models and genetic perturbations in vitro and in vivo. However, only a tiny fraction of the possible chemical space has been so far explored, meaning that most compounds able to modulate biological activities (i.e. drugs) are yet to be discovered. Accordingly, the main objective of my

laboratory is to couple bioactivity signatures and inverse design algorithms to generate new chemical entities with a desired functionality. In particular, we aim at generating new chemical entities (NCEs) to modulate the activity of a specific set of targets, selected from a combination of perturbagen profiles, to revert the pathological state induced by Alzheimer's disease (AD) and other complex disorders. All in all, the incorporation of machine learning methods to the drug discovery process is triggering the development of thousands of novel compounds, finally enabling personalized pharmacology.

References

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- Pauls et al. Identification and drug-induced reversion of molecular signatures of Alzheimer's disease onset and progression in AppNL-G-F, AppNL-F, and 3xTg-AD mouse models. 2021. Genome Med. 13:168.
- Bertoni et al. Bioactivity descriptors for uncharacterized chemical compounds. 2021. Nat Commun. 12: 3932.
- Duran-Frigola et al. Extending the small molecule similarity principle to all levels of biology with the Chemical Checker. 2020. Nat Biotechnol. 38: 1087–1096.









Molecular Modelling and Bioinformatics Dr. Modesto of oligon	The MMB group is an international leader in the simulation of nucleic acids from small oligos to the eukaryotic chromatin. We plan now to use our expertise in modelling techniques and our capability for experimental testing to design therapeutic oligonucleotides using AI techniques and the concept of polypharmacology to target several pathological gens using NA-based drugs.
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ANNEX 2. Evaluation criteria

1. Academic and/or scientific-technical trajectory of the candidate (up to 50 points).

Sub-criterion 1.a): Scientific-technical contributions (up to 45 points). The candidate's academic record and other curricular merits will be assessed, as well as their suitability for the tasks to be performed based on their training and professional experience.

Sub-criterion 1.b): Mobility and internationalisation (up to 5 points). The relevance and impact on the candidate's research trajectory of stays at national and international centres and/or in the industrial sector will be assessed, taking into account the prestige of the host institution and the activities carried out during the stay.

2. Suitability of the candidate for the research activities to be conducted (up to 50 points).

The candidate's suitability for the program, project, or research activities to be carried out will be assessed based on their prior education and experience. This assessment will take into account the added value that the completion of the project will bring to their research career, as well as the value contributed to the hosting institution and team.





