Financiado por:

Proceso de selección para la contratación de Personal Investigador en el marco del Plan Complementario de Biotecnología aplicada a la Salud (C17.I1)

Plan de Recuperación, Transformación y Resiliencia – Financiado por la Unión Europea – NextGenerationEU

El Plan de Recuperación, Transformación y Resiliencia del Gobierno traza la hoja de ruta para la modernización de la economía española, la recuperación del crecimiento económico y la creación de empleo, para la reconstrucción económica sólida, inclusiva y resiliente tras la crisis de la COVID, y para responder a los retos de la próxima década.

La necesidad de reforzar y mejorar la gobernanza de la política de investigación e innovación ha sido puesta de manifiesto en diversas recomendaciones en el marco del semestre europeo. Con este objetivo, el **componente 17 incluye la inversión I1 "Planes Complementarios con las Comunidades Autónomas"**. Estos planes tendrán financiación conjunta y permitirán alinear la ejecución de fondos regionales, estatales y europeos.

Los Planes Complementarios con las Comunidades Autónomas (CCAA) se han implementado a través de la firma de ocho convenios que establecen un protocolo general de actuación para la colaboración entre la AGE, a través del Ministerio de Ciencia e Innovación y la Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC), en su caso, y las administraciones de las CCAA, en la ejecución de programas conjuntos de I+D+I en ocho áreas, siendo una de ellas **Biotecnología aplicada a la Salud**.

El Plan Complementario de Biotecnología aplicada a la Salud pretende impulsar el desarrollo de herramientas para diagnóstico, pronóstico y terapias avanzadas o dirigidas en medicina personalizada a través de la ciencia y la innovación a través de seis líneas de actuación prioritarias.

Este Plan Complementario, cogobernado y cofinanciado entre el Gobierno y siete Comunidades Autónomas (Castilla-La Mancha, Cataluña, Extremadura, Galicia, País Vasco, Aragón y Andalucía), y coordinado por el Instituto de Bioingeniería de Cataluña (IBEC), cuenta con un presupuesto total de 37,27 millones de euros, de los cuales 19,38 millones proceden del Ministerio de Ciencia e Innovación (MCIN) y el resto de las Comunidades Autónomas.

Para conseguir los objetivos del Plan Complementario en Cataluña, se han priorizado 16 "Proyectos Colaborativos" (ver Anexo A), según el procedimiento descrito en el "Llamado a Expresiones de Interés" (https://planescomplementariossalud.es/llamamientos/)

Con el fin de contratar a personal para la ejecución de dichos "Proyectos Colaborativos", se abre el siguiente Proceso de Selección:

Primero. – Objetivo

El presente **Proceso de Selección** tiene por objeto la **selección de personal investigador** para los "Proyectos Colaborativos" priorizados en el marco del Plan Complementario de Biotecnología en Cataluña (**Anexo A**). El **perfil y tareas del personal** a contratar para cada Proyecto Colaborativo se incluyen en el **Anexo B.**

Segundo. – Presupuesto destinado

El IBEC destinará un total de **1.323.000 €** para la contratación de **20 personas durante 18 meses**.

El IBEC ha realizado una evaluación de riesgos contra el fraude durante la preparación de este documento a través de su Grupo de Trabajo Antifraude. Para ello, se ha llevado a cabo una identificación y evaluación de los indicadores de riesgo y se han definido y establecido los protocolos y mecanismos necesarios en materia de prevención y detección de fraude.

Tercero. – Requisitos de las candidaturas

Estar en posesión de alguno de los siguientes títulos a fecha de cierre de la convocatoria: **dependiendo de la posición** a cubrir en cada proyecto colaborativo se requerirá **título de doctorado, título de máster o título universitario oficial** de un país del Espacio Europeo de Educación Superior, con un mínimo de 240 ECTS. A fecha de cierre de la convocatoria, las candidaturas han de poder acreditar dicha titulación.

Cuarto. – Proceso de solicitud

Las personas interesadas deberán presentar su candidatura a través del aplicativo online específico de IBEC (https://careers.ibecbarcelona.eu) entre el **22 de noviembre y el 22 de diciembre de 2022**. Para ello, deberán registrase y crear una cuenta en dicho aplicativo.

Las aplicaciones deberán incluir la siguiente documentación:

1) Datos del CV (a rellenar en el aplicativo)
2) "Proyecto Colaborativo" al que se postula (de los incluidos en el Anexo A). Se podrá incluir hasta un máximo de 3 opciones, indicando el orden de prioridad de estas.
3) Carta de motivación (a rellenar en el aplicativo)
4) Certificado o notificación oficial de otorgamiento de cada título académico donde conste la fecha de obtención del título. Si los documentos subidos a la plataforma online fueron emitidos en un idioma diferente al inglés, se debe adjuntar una traducción al inglés.

   Cuando así se requiera, los candidatos elegidos deberán acreditar, mediante documentos originales o fotocopias compulsadas de los mismos, los expedientes adjuntos a las solicitudes. Asimismo, el IBEC podrá solicitarles los certificados originales de cualquier información mencionada en su currículum vitae.

Solo se considerarán elegibles las solicitudes enviadas a través de la plataforma de solicitud en línea. Únicamente las solicitudes completas presentadas en la fecha límite serán evaluadas. Todos los datos personales requeridos por IBEC serán tratados de acuerdo con Reglamento General de

Protección de Datos de la UE (GDPR) y la Ley Orgánica 3/2018, de 5 de diciembre, de Protección de Datos Personales y garantía de los derechos digitales y demás normativa conexa aplicable.

Quinto. – Selección

IBEC está comprometido con los principios de la Carta Europea para Investigadores y el Código de Conducta para la Contratación de Investigadores (the Charter & Code). En 2015, el IBEC obtuvo la acreditación a la Excelencia en Recursos Humanos en Investigación en reconocimiento a nuestro compromiso continuo, la cual se ha renovado en 2022.

Nuestra Política de Reclutamiento y Selección se basa en la Estrategia OTM (Contratación Abierta, Transparente y Basada en el Mérito) http://www.ibecbarcelona.eu/jobs/ y acepta solicitudes sin distinción por ningún motivo. Se anima a postularse, especialmente, a mujeres y a personas con discapacidad. Nuestro compromiso con los principios OTM-R también se encuentra en nuestro plan de Género y Diversidad.

1. Verificación de los criterios de elegibilidad.
   a) Se comprobará la elegibilidad en base a la información proporcionada y a los criterios indicados en el punto Tercero.
   b) Este proceso será llevado a cabo por personal cualificado de IBEC.
   c) Solo las solicitudes que cumplan con todos los criterios de elegibilidad se incluirán en la fase de evaluación.

2. Evaluación:

   La evaluación de las candidaturas se realizará en dos fases. Fase I) evaluación del CV y Fase II) entrevista personal. El **peso** de cada uno de los **criterios** para la evaluación es de **60% para el CV y 40% para la entrevista**. Cada criterio se puntuará de 0 a 10.

Peso Global (%)	Criterio	Peso Específico (%)	Subcriterio
60%	CV	34%	Educación y training
		34%	Experiencia profesional
		16%	Resultados de investigación: publicaciones, conferencias, méritos, patentes, movilidad, enseñanza, otros logros, ayudas recibidas
		16%	Carta de motivación
40%	Entrevista		

2.1. Fase I: Evaluación remota de las candidaturas

   a) Las candidaturas que sean elegibles serán valoradas por un panel de evaluación científico formado por dos miembros del consorcio (una persona de la entidad de investigación básica y una persona de la entidad de investigación sanitaria).
   b) Cada panel evaluará el CV de cada candidatura de acuerdo a los criterios de la tabla anterior.

c) El panel elaborará una clasificación preliminar de todas las candidaturas en base a la puntuación obtenida. Las **dos candidaturas con mayor puntuación pasarán a la fase de entrevistas (Fase II)**, y el resto quedará en una lista de reserva de Fase I. En el caso que no sea posible contactar con las candidaturas seleccionadas, se notificará a la siguiente persona en la lista.

2.2. Fase II: Entrevistas a las candidaturas finalistas

a) El panel científico y una persona de Recursos Humanos (HR) del IBEC llevarán a cabo entrevistas telemáticas con las dos candidaturas finalistas para cada posición. La entrevista tendrá un peso del 40% en la puntuación final.

b) Las entrevistas evaluarán la motivación y las competencias de las personas candidatas (como, por ejemplo, comunicación, trabajo en equipo, compromiso, proactividad, integridad, pensamiento crítico y analítico, trabajo en equipo y colaborativo, compromiso y proactividad). Las personas candidatas recibirán un documento guía para preparar la entrevista.

c) La selección final se llevará a cabo en una reunión de consenso. Se contactará a la persona finalista y en caso de que ésta deniegue, la siguiente persona (candidato/a reserva) será contactada. En el supuesto que la persona candidata de reserva también rechazara la posición, el panel de evaluación contactaría con las dos candidaturas mejor puntuadas de la Fase I para someterse a la Fase de Entrevistas.

3. Confirmación de aceptación

Tras la decisión final, el IBEC comunicará a las personas seleccionadas su selección **entre el 1 y el 3 de marzo de 2023**, y se les solicitará la firma de una carta de aceptación.

Sexto. – Condiciones de contratación

1. Tipo de contratación: contrato de trabajo temporal asociado al Plan de Recuperación, Transformación y Resiliencia (PRTR) con fondos Next Generation. La persona estará contratada directamente por el IBEC con doble adscripción a la entidad coordinadora del proyecto.
2. Duración: la contratación tendrá una duración de 18 meses no prorrogables. Los contratos deberán iniciarse entre el **1 de abril y el 16 de junio de 2023**, excepto por causas debidamente justificadas y con la aprobación del director científico del Plan Complementario (en cualquier caso, no más tarde del 30 de junio de 2023).
3. Ubicación: dada la naturaleza colaborativa, el personal investigador podrá estar ubicado en cualquiera de las instituciones participantes del proyecto (ver Anexo B).
4. Salario bruto anual: 32.400 €
5. 23 días de vacaciones y 9 de asuntos propios.

Séptimo. – Cronograma

1. Presentación de solicitudes: del 22 de noviembre al 22 de diciembre de 2022 a las 23:59 horas (hora peninsular)
2. Verificación de elegibilidad: del 23 al 30 de diciembre de 2022.

3. Evaluación Fase I:
   a. Evaluación científica (CV): del 3 al 24 de enero de 2023.
   b. Comunicación a las candidaturas no seleccionadas: 25 de enero de 2023
   c. Comunicación a las candidaturas seleccionadas Fase I: 26 de enero de 2023
4. Evaluación Fase II:

   Periodo de entrevistas: del 6 al 24 de febrero de 2023
5. Comunicación a las candidaturas: Entre el 1 y el 3 de marzo de 2023
6. Inicio de los contratos: entre el 1 de abril y el 16 de junio de 2023

Octavo. – Detalles de contacto

Para dudas sobre el proceso de selección, enviar un correo a jobs@ibecbarcelona.eu (asunto: Dudas PPCC-PI + referencia posición)

Para dudas relacionadas con los proyectos o con el Plan Complementario, enviar un correo a planescomplementariossalud@ibecbarcelona.eu (asunto: Dudas PPCC-PI + referencia posición)

ANEXO A: "PROYECTOS COLABORATIVOS" SELECCIONADOS

A continuación, se listan los "Proyectos Colaborativos" priorizados por el Comité Científico Estatal según la Línea de Actuación (LA).

Para cada uno de estos proyectos, se indica la siguiente información: el título y acrónimo, entidad coordinadora, y entidades participantes.

LÍNEA DE ACTUACIÓN 2:

IMPLEMENTACIÓN Y ANÁLISIS DE BASES DE DATOS EN MEDICINA DE PRECISIÓN

1. **Proyecto IA4DT2**: Development and implementation of integrated artificial intelligence models for Type 2 Diabetes risk prediction

   - **Abstract**: A large part of the health care burden in developed countries is devoted to the treatment and follow-up of patients with complex diseases, such as Type 2 Diabetes (T2D). For this reason, the identification of treatments, but above all of protocols for their prediction and prevention, have become priorities for research in biomedicine and for their translation into clinical practice. These diseases have a complex etiology, with a significant genetic burden and a strong dependence on external, environmental and lifestyle variables, the exposome.

     Numerous genetic studies have identified hundreds of variations in the genome associated with the risk of developing this type of disease, with the promise and hope that their results would allow the identification of pharmacological targets, and the possibility of predicting the risk of suffering the disease. However, although they have targeted specific genes, the translation of this genetic information into predictive models with clinical validity is currently very limited. This is due to the poor predictive power of reductionist approaches, such as Polygenic Risk Scores, and the limited possibilities of integrating other clinical, environmental and lifestyle variables, which are potential risk modifiers in this type of pathology.

     For this reason, in this project we propose the construction of prediction models for T2D, based on more integrative approaches using artificial intelligence (machine learning models), for the identification of genetic, clinical (variables and associated pathologies) and environmental determinants, and for the construction of prediction and classification models for T2D patients. With these combined models, we can not only propose new therapeutic targets, but also robust predictors that allow the development and implementation of lifestyle-based clinical prevention protocols for each individual.

   - **Entidad Coordinadora:** Barcelona Supercomputing Center (BSC)
   - **Entidades Participantes:**
     - Institut de Recerca Germans Trias i Pujol (IGTP)
     - Universidad del País Vasco

2. **Proyecto MITOCANCER**: Targeting a mitotic polyglutamylation enzyme - a novel strategy for cancer therapy

   - **Abstract**: Breast cancer is the most common cancer in women worldwide and the second leading cause of cancer related death. In half of the cases cancer reoccurs within the first five years and acquire resistance, which is a major clinical challenge in the management of this disease. New targets and approaches are therefore needed to successfully treat this type of cancer. We have preliminary evidence that an enzyme involved in microtubule polyglutamylation in the mitotic spindle, may provide a new interesting target as an alternative to taxanes. This enzyme is downregulated in human tumours including breast cancers, and this favours aneuploidy and CIN (Chromosome Instability) a hallmark of cancer, but at the same time its activity appears to be essential for survival. Indeed, eliminating its expression in zebrafish embryos results in embryo death. Our hypothesis is that decreasing the activity of this enzyme below a certain threshold in cancer cells may send them into mitotic catastrophe, triggering micronuclei formation and generating inflammatory responses thereby cell death and tumor size reduction.

     Combining the expertise of the Vernos group (Catalonia) in cell division and the microtubule cytoskeleton with the expertise of clinicians in breast cancer (Ramon y Cajal group, Catalonia) together with a collaboration with a top institute for chemical screening (Loza Group, Galicia) as well as for genomic analysis (Carracedo group, Galicia), we aim at obtaining a full characterization of the transcriptomic landscape of different types of breast tumours at a single cell level at the CRG facility to evaluate the heterogeneity of expression levels of the enzyme in different tumours and within a single tumour. In parallel, we will identify inhibitory compounds against the enzyme and test their potential to promote breast cancer cell death.

   - **Entidad Coordinadora:** Fundació Centre de Regulació Genòmica (CRG)
   - **Entidades Participantes:**
     - Vall Hebron Institut de Recerca (VHIR)
     - Centro Singular de Investigación en Medicina Molecular e Enfermedades Crónicas (CiMUS) (Galicia)
   - **Línea de Actuación complementaria**: LA3

3. **Proyecto InMaM**: New immunotherapeutic opportunities in metastatic breast cancer: CDK4/6 inhibitors and their impact on the immune system

   - **Abstract**: The treatment of advanced breast cancer has undergone a revolution with the approval of a new class of drugs targeting CDK4/6 function. Increasing evidence indicates that the antitumor immune response represents a key factor in determining the efficacy of CDK4/6 inhibitors, which would have immunomodulatory properties of great therapeutic interest. The objective of the project is to define and characterize the molecular mechanisms responsible for the immunomodulatory effects of CDK4/6 inhibitors, with the ultimate goal of providing a biological basis for the development of treatment response biomarkers and new immunotherapeutic strategies.

     To this end, we will use single-cell transcriptomic techniques to identify and characterize the effect of CDK4/6 inhibitor treatment on the immune system and its regulatory pathways in vivo.

In-depth characterization of peripheral immune function in a well-described cohort of patients with metastatic breast cancer will identify putative biomarkers of response to treatment with CDK4/6 inhibitors, but also has the potential to set up the basis for the monitoring of antitumor immune response in blood. In addition, the increased knowledge on immunomodulatory properties of CDK4/6 inhibitors will enable to propose novel immunotherapeutic strategies that will be subsequently tested in 3D heterotypic cell models, providing preclinical proof of concept of its efficacy and putative clinical use.

Overall, the project will contribute to a better understanding of the complexity of breast cancer, but specifically of the interactions between the tumor and host immune cells. Solving the tumor-immune system interface will certainly open the door to radical improvements in anti-cancer therapy.

- **Entidad Coordinadora:** Institut de Recerca de la SIDA-Caixa (Irsi-Caixa)
- **Entidades Participantes:**
  - Institut de Recerca Germans Trias i Pujol (IGTP)
  - Instituto de Investigación Sanitaria Biocruces Bizkaia – Hospital Universitario de Basurto (País Vasco)
- **Línea de Actuación complementaria**: LA4

LÍNEA DE ACTUACIÓN 3:

PLATAFORMA DE CRIBADO DE FÁRMACOS Y ANÁLISIS INTERACCIONES FÁRMACO-DIANA

4. **Proyecto STOP-DMG**: Identification and validation of therapeutic targets for Diffuse Midline glioma (DMG) based on high-throughput screen screening
   - **Abstract**: Diffuse Midline glioma (DMG) is an aggressive brain tumor primarily arising in the pons, which affects children between 6-12 years of age who rapidly and invariably demise from the disease. Nearly 80% of DMGs harbor mutations in histone H3 genes, which affect how histone H3 are epigenetically modified by the Polycomb group of proteins. This is turn reverberate not only on the overall tissue organization and growth, but also it affects chromatin architecture, genome-wide epigenetic landscape, transcriptome, and chromatin composition. We plan to: i) validate several of the identified targets; ii) perform a chemical screening using patient-derived cells.
   - **Entidad Coordinadora:** Fundació Centre de Regulació Genòmica (CRG)
   - **Entidades Participantes:**
     - Pediatric Cancer Center Barcelona (PCCB) – Hospital Sant Joan de Déu
     - Centro Singular de Investigación en Medicina Molecular e Enfermedades Crónicas (CiMUS) (Galicia)

5. **Proyecto ABPATHFINDER**: Screening of new precision antibiotics for the treatment of multiresistant infections

   - **Abstract**: The emergence of antibiotic-resistant pathogens has become a serious public health threat. Conventional screening platforms tend to rediscover the same compounds, showing clear signs of depletion. In this context, we need to devise new approaches to discover new drugs. In addition to being effective, new antibiotics should be selective to preserve the host's microbiota. Broad-spectrum antibiotic treatments reduce the overall diversity of gut microbiota species, causing metabolic changes, increasing intestinal susceptibility to colonization, and stimulating the development of bacterial resistance.

     For these reasons, it is essential to develop new screening approaches to find alternative treatments to broad-spectrum antibiotics that also act selectively against pathogens, preserving the structure of the patient's microbiota. In this project, we will design precision antibiotics against essential bacterial complexes that are conserved in gram-negative pathogens but absent in most gut microbiota taxa. We will use a combination of experimental and computational screening assays to discover new inhibitors. Also, we will measure the antimicrobial activity of these molecules, the ability to generate resistance in bacteria, and the effect on the gut microbiota.

     The possibility of generating compounds that inhibit essential complexes in bacteria will allow us to create antibiotics with a completely new mechanism of action that preserves the richness of the host microbiota, thus avoiding dysbiosis and recurrence in infections.

   - **Entidad Coordinadora:** Universitat Autònoma de Barcelona (UAB)
   - **Entidades Participantes:**
     - Vall Hebron Institut de Recerca (VHIR)
     - Hospital Reina Sofía (Andalucía)

6. **Proyecto FANCONI-CURE**: Precision Medicine in Fanconi anemia

   - **Abstract**: Fanconi anemia (FA) is a rare disease characterized by bone marrow failure (BMF), malformations, and cancerpredisposition, especially leukemia and head and neck carcinomas in children and young adults due to their lack of DNA repair. Protein products of genes mutated in FA patients constitite a DNA repair pathway that is essential in DNA damage response. Our aim is to use a newly developed cell model to perform a pharmacological screening to identify drugs targeting this pathway. This project involves genomic-based personalized precision medicine, drug screening, and development of novel cell-based models for drug screening andadvanced therapeutics.

   - **Entidad Coordinadora**: Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau (HSCSP)
   - **Entidades Participantes:**
     - Institut de Recerca contra la Leucèmia Josep Carreras (IJC)
     - Universidad de Sevilla CABIMER (Andalucía)
   - **Línea de Actuación complementaria**: LA4

7. **Proyecto OsteoMetTherapy**: Search for new therapeutic options in metastatic osteosarcoma using patient derived tumor cell lines

   - **Abstract**: This project aims to look for new therapeutic options for metastatic osteosarcoma using patient derived cellular models and high throughput drug screening technologies. Osteosarcoma is the most common kind of bone cancer, occurring preferentially in children, teens, and young adults. Lung metastasis affects about 30% of these patients and is the major hurdle for their survival.

     The first line treatment for localized osteosarcoma consists on a combination of methotrexate, adriamycin and cisplatin, which is also given to metastatic cases. However, these tumors tend to be highly resistant to chemotherapy and patients with metastasis have a very poor prognosis. Since there are barely no current alternatives to this chemotherapy regimen, and no advances have been described in the last decades, there is an urgent need to find new therapeutic options for osteosarcoma patients. Our approach will involve the generation of patient derived metastatic cell lines and searching for new therapeutic agents using chemical screenings.

     The consortium assembled for this project includes clinicians, molecular oncologists, and medicinal chemists, whose combined expertise covers all the steps of the drug discovery process including the identification of real clinical needs, the development of reliable and informative screenings systems, the selection and optimization of potential hits, and their validation using pre-clinical models.

   - **Entidad Coordinadora:** Institut de Recerca Biomèdica de Barcelona (IRB Barcelona)
   - **Entidades Participantes:**
     - Hospital Sant Joan de Déu (SJD)
     - Universidad de Santiago de Compostela (USC)
   - **Línea de Actuación complementaria**: LA4

8. **Proyecto DRUG4-COXPD1**: Generation of therapies and biomarkers for the treatment of mitochondrial dysfunction driven neurodegenerative diseases

   - **Abstract**: The growing incidence of neurodegenerative diseases represents a huge challenge, and the understanding of this group of conditions requires multidisciplinary approaches. Neurodegenerative disorders include a heterogeneous group of diseases characterised by a progressive loss of neurons. The clinical consequence is the loss of previously acquired motor, sensory and cognitive functions. The mechanisms by which various neurodegenerative conditions develop are not yet completely understood, and increasing evidence implicates mitochondrial dysfunction as key in the development and progression of various forms of neurodegeneration.In this proposal, we plan to identify efficacious therapies in the treatment of a specific mitochondrial disease that cause hepatoencephalopathy, named COXPD1.

     We propose the generation of a consortium oriented to search for therapies, and biomarkers in one neurodegenerative (and mitochondrial) disorder, referred to as COXPD1. This disease is caused by mutations in the nuclear gene GFM1, which encodes the mitochondrial translation elongation factor G1 (EFG1). There is no treatment for this disease and patients often die during the first months of life.

The approach will involve three interrelated activities:

a) Search for therapies through the screening in human fibroblasts with a library of 50,300 compounds to rescue the alterations driven by GFM1 mutations, followed by delineation of a preclinical path.

b) Generation of a gene therapy study that ameliorates brain damage in a mouse model of COXPD1. Initial studies performed by one of the teams are very promising, and ameliorate liver damage after a single injection of a viral vector.

c) Identification of plasma biomarkers by metabolomics in COXPD1 patients, in order to and monitor disease status, and drug response. In all,we propose a transformative research that will permit the generation of therapies and biomarkers under conditions of mitochondrial dysfunction secondary to GFM1 mutations

- **Entidad Coordinadora:** Institut de Recerca Biomèdica (IRB Barcelona)
- **Entidades Participantes:**
  - Vall d'Hebron Institut de Recerca (VHIR)
  - Hospital Sant Joan de Déu (SJD)
  - Universidad de Zaragoza (UNIZAR) (Aragón)
- **Línea de Actuación complementaria**: LA4

LÍNEA DE ACTUACIÓN 4:

DESARROLLO DE MODELOS BIOLÓGICOS PARA CRIBADO Y ESTUDIO DE LA ACTIVIDAD DE MOLÉCULAS TERAPÉUTICAS

9. **Proyecto B-Org**: Patient-derived liver biopsy-organoids for personalized medicine in NAFLD (Non-Alcoholic Fatty Liver Disease): towards real time assessment of drug response

- **Abstract**: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease with a prevalence of 25% in the general population. NAFLD is a multifactorial disease caused by genetic factors, lifestyle and diet leading to increased lipotoxicity and activation of liver inflammation and fibrogenesis. Although there are multiple ongoing clinical trials, currently no drug treatment is available, and drugs proven to be effectives in animal models have shown poor translation to the clinical setting.

  The main reasons explaining this failure are the lack of human-based preclinical models to mimic the heterogeneity of the disease, and the difficulties in assessing early therapeutic response. Thus, there is an urgent need to develop relevant preclinical models recapitulating the heterogeneity and pathophysiology of NAFLD as well as means for assessing early treatment response. Hence, B-ORG aims to generate a platform of patient-derived liver biopsy-organoids (b-Orgs) mimicking the full spectrum of NAFLD and to develop strategies for non-invasive real time assessment of drug response.

To achieve this goal, B-ORG will combine the expertise of six partners to 1- generate a collection of patient-derived b-Orgs recapitulating the different stages, pathophysiology and heterogeneity of NAFLD; 2- develop strategies for non-invasive real-time assessment of drug response by using hyperpolarisation-enhanced nuclear magnetic resonance (HP-MR) as an imaging strategy to assess NAFLD metabolism in b-Orgs and drug response; 3- to build a platform of b-Orgs for drug testing, as a proof of concept that organoids are suitable for assessing drug response and mechanism of action.

By combining clinical expertise in NAFLD with technologies to generate patient-derived b-Orgs, biomimetic matrices, bioinformatics and HP-MR we will develop an ideal platform to test new therapeutic drugs and their mechanisms, and thus to help to implement future personalized strategies for NAFLD patients.

- **Entidad Coordinadora:** Consorci Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)
- **Entidades Participantes:**
  - Institut de Bioenginyeria de Catalunya (IBEC)
  - Vall d'Hebron Institut de Recerca (VHIR)
  - Universitat de Barcelona (UB)
  - Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau (HSCSP)
  - School of Engineering TECNUN de la Universidad de Navarra (UNAV) (País Vasco)
- **Línea de Actuación complementaria**: LA3

10. **Proyecto MnkImmunOnco**: <u>Overcoming therapy resistance and immune evasion with a novel MNK inhibitor</u>

- **Abstract**: Therapy resistance remains a main cause of therapeutic failure in cancer treatment. Immunotherapy has opened a new avenue in oncology but is only effective in a small fraction of patients. Therapy resistance and immune evasion critically rely on the activation of stress response pathways. Those pathways activate the kinases MNK1/2 which uniquely regulate eIF4E. Phosphorylation of eIF4E is associated worse prognosis in several tumors and targeting MNKs has evolved as strategy in oncology.

  We have identified with EB1 the first in-class Type-II inhibitor of MNKs and have demonstrated its superior mode of action. Ongoing work for the use of EB1 in vivo demonstrates its oral and intraperitoneal applicability. For the clinical application of EB1, proof of concept studies have revealed increased sensitivity to anti-hormonal treatments in castration resistant prostate cancer (CRPC) cells. Drug interaction in CRPC is found in the synergistic inactivation of androgen receptor (AR) and the splice variant AR-V7. The AR-V7 variant is insensitive to anti-androgen therapies and EB1 therefore represent a novel therapeutic opportunity for AR-V7 positive patients.

  Targeting of MNK activity has been proposed to increase the efficacy of immune therapy. In this context, we can demonstrate that EB1 promotes a favorable tumor immune environment by regulating cytokines and PD-L1 without adverse effects on immune cells. Consequently, EB1 strongly increases the efficacy of CAR-T cells in a breast cancer model in vitro.

In summary, our data support the use of EB1 as a novel strategy to increase the efficacy of conventional- and immunotherapies. Our technology is in TLR3/4 and patent protected (PCT for Europe, USA and Japan). The here proposed project focuses on the application of EB1 in mouse models in vivo and mode of action studies by single cell sequencing combined with patient stratification and pharmacodymic lead optimization to initiate IND-enabling studies and future clinical trials.

- **Entidad Coordinadora:** Vall d'Hebron Institut de Recerca (VHIR)
- **Entidades Participantes:**
  - Institut Químic de Sarrià (IQS)
  - Centro de Investigación Cooperativa en Biociencias (CIC bioGUNE) (País Vasco)
- **Línea de Actuación complementaria**: LA3

11. **Proyecto WORMVUS**: Rapid in vivo characterization of the functional impact and vulnerabilities for PTEN tumor suppressor gene variants

- **Abstract**: The avalanche of data from sequencing cancer cells is provoking a bottleneck in the understanding of the functional impact of gene mutations or variants. Importantly, these variants would also determine vulnerabilities that can provide therapeutic advantages. With this proposal, we intend to establish C. elegans as a preclinical model for rapid functional studies to determine the influence of gene variants in cancer-related processes and therapies. In particular, we will focus on some variants of unknown significance (VUS) for the tumor suppressor gene PTEN.

  PTEN is frequently altered in solid tumors and about 50% of its variants are VUS. These variants, which are missense mutations in conserved amino acids, will be mimicked in C. elegans by CRISPR. When a specific PTEN cancer mutation was reproduced in the C. elegans ortholog daf-18, we observed a synthetic phenotype with a gain-of-function mutation in cdc-25.1, ortholog of CDC25 oncogenes. Since CDC25 proteins are targetable, we will investigate if other PTEN VUS could potentially benefit from the use of CDC25 inhibitors. These inhibitors have not reached the clinic yet.

  We hypothesise that a sensitive background and the combination with other therapeutic agents would help CDC25 inhibitors to reach the clinic. To determine these other therapeutic agents, we plan a drug screen and low input RNA-seq of double mutant PTEN-CDC25 animals with the more penetrant phenotype.
- **Entidad Coordinadora:** Instituto de Investigación Biomédica de Bellvitge (IDIBELL)
- **Entidades Participantes:**
  - Fundació Centre de Regulació Genòmica (CRG)
  - Instituto de Investigación Sanitaria Biocruces Bizkaia (País Vasco)
  - Universidad de Sevilla (Andalucía)
- **Línea de Actuación complementaria**: LA3

LÍNEA DE ACTUACIÓN 5:

DESARROLLO DE NANOFÁRMACOS, BIODISTRIBUCIÓN, TOXICIDAD Y ACCIONES TERAPÉUTICAS EN MODELOS DE PATOLOGÍA

12. **Proyecto ADNano**: Alzheimer's disease-modifying Nanomedicines

- **Abstract**: We propose here a completely new Alzheimer's disease (AD) nanomedicine based on synergistic therapies that are combined into multifunctional platforms that cross the brain vasculature, also known as the blood-brain barrier (BBB) and act on the different AD facets. We will focus our design on clinically-tested materials to expedite translation.

  Here we will optimise and test our nanomedicines using state-of-the-art animal models and in vitro models to study the nanomedicine effects on BBB transport of misfolded proteins (Battaglia, Samitier, and Del Rio labs at the IBEC), brain inflammation and glia cells modulation (Matute Labs at the Achucarro Basque Center for Neuroscience), effect on synaptic dysfunction and cognition (Saura Labs at UAB). We will mirror animal and in vitro work with pre-clinical evaluation of the BBB markers and misfolded proteins in clinical samples (Lleo and Fortea labs at the Sant Pau Memory Unit).

- **Entidad Coordinadora:** Institut de Bioenginyeria de Catalunya (IBEC)

- **Entidades Participantes:**
  - Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau (HSCSP)
  - Universitat Autònoma de Barcelona (UAB)
  - Universidad del País Vasco (EHU)

13. **Project EVBRAINTARGET**: Validation of BP-EVs as a next-generation compound delivery platform for targeted release within the Central Nervous System

- **Abstract**: Extracellular vesicles (EVs) conform an excellent platform of nanocarriers for drug delivery. However, scalable obtention and use of EVs for that aim still faces important challenges being safety, availability and cost the most relevant. Researchers of the team in this proposal have recently uncovered and protected by European patent (EP21382983.1) the potential applications of EVs obtained from food industry by products, asset dubbed as BP-EVs. BP-EVs represent a leap forward in front of current EVs-oriented nanocarrier available options improving the crucial aspects of safety, availability and cost. Furthermore, these vesicles show excellent oral bioavailability and organ targeting capacity within the central nervous system (CNS).

  Based on these facts, here we aim to specifically determine: i) The ability of BP-EVs to improve central nervous system (CNS) bioavailability of drugs and their optimal oral administration dosage; ii) capacity of BP-EVs to improve drug efficacy by in turn reducing adverse effects. As a proof-of-concept, BP-EVs will be edited to encapsulate the commercial psychotropic drug clozapine (CLZ), the best available antipsychotic if its adverse effects are minimized. Intestinal absorption, blood brain barrier crossing ability and neuronal mechanisms of delivery of CLZ loaded into BP-EVs (CLZBP-EVs) will be assessed by in vitro and in vivo studies following oral administration of CLZBP-EVs in a murine model of psychotic symptomatology. In vivo toxicity of CLZBP-EVs, as well as CLZ performance enhancing capacity exerted by BP-EVs will also be

investigated in vivo. Completion of the research actions detailed here seek to move forward BP-EVs closer to its prospective clinical licensing.

- **Entidad Coordinadora:** Institut d'Investigació Biomèdica de Lleida (IRBLLEIDA)
- **Entidades Participantes:**
  - Universitat de Lleida (UdL)
  - Universidad del País Vasco (EHU)
- **Línea de Actuación complementaria**: LA6

LÍNEA DE ACTUACIÓN 6:

TÉCNICAS Y PROCESOS PARA TERAPIAS AVANZADAS Y DIRIGIDAS, FORMACIÓN QUIRÚRGICA Y ROBÓTICA MÉDICA

14. **Proyecto LENTI-UP**: Optimization of the lentiviral vector manufacturing for the production CAR-T or other cell therapies

- **Abstract**: Immunotherapy promotes an immune response against tumor cells which has been a paradigm shift in cancer treatment. Specifically, adoptive cell therapy based on T cells modified to express Chimeric Antigen Receptors (CAR) has proven to be a successful strategy for the treatment of hematological cancers.

  Our academic group has developed CAR Ts against CD19 antigen (ARI0001) for B-cell cancers. We have obtained the authorization of use by the Spanish Agency for Medicines and Health Products (AEMPS) and for the first time for an academically developed product, the PRIME designation of the EMA (European Medicines Agency). More recently, CART-BCMA (ARI0002) cells have also been successfully developed for multiple myeloma (MM) and other mature B-cell malignancies.

  The production process of CAR T cells is performed by transduction of autologous T cells with viral vectors containing the CAR sequence. The currently authorized production protocol for the different CAR (ARI001, ARI002) is carried out under GMP (Good Manufacturing Practices) conditions within clean room facilities and consists of obtaining small-scale batches using multi-layer culture flasks. Considering the current demand and the future perspective, due to the success of these therapies, it is necessary scale-up the current lentiviral production process to enable the treatment of a greater number of patients.

  Our principal aim is to implement a lentivirus production system in GMP bioreactors, validated, and authorized by the AEMPS for CAR-T therapy. As a result, in addition to allowing the treatment of a greater number of patients, the process will be easily adapted for future developed CAR T or other gene therapies using lentivirus. Consequently, we hope to have a positive impact on society by benefiting a large number of patients, while saving costs to the national health system due to the optimization of the production process of these therapies.

- **Entidad Coordinadora:** Consorci Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS)

- **Entidades Participantes:**
  - Leitat Technological Centre (LEITAT)
  - Fundació per a la Recerca Sant Joan de Déu (SJD)
  - Complejo Hospitalario y Universitario de Santiago-Galaria (CHUS-Galaria) (Galicia)

15. **Proyecto BIOMOD**: Development of advanced biomechanical models for the planning and improvement of surgical practice applied to cleft lip and palate maxillofacial surgery

- **Abstract**: Cleft lip and palate is the most frequent congenital malformation of the head and neck, with an incidence of 1 in 700-1100 newborns. Surgical reconstruction of the different anatomical structures is performed by implanting an alveolar graft, an aggressive procedure that is not exempt from complications that in some cases must be repeated due to the lack of osseointegration of the implant. The project focuses on studying how the different biomechanical parameters present in the mandibular region play an active role during the osseointegration of alveolar implants used in maxillofacial surgery for cleft lip and palate cases.

  The objectives of the project consist of establishing a correlation between the biomechanical parameters of the maxillofacial scenario and the osseointegration of the implant through the development of an advanced finite elements based biomedical model. Once this relationship has been established it will be possible to design cleft lift implants that provides the appropriate degree of biomechanical signaling to promote osseointegration, ensuring the performance of the implant and improving the success of the clinical practice.

- **Entidad Coordinadora**: Institut Químic de Sarrià (IQS-URL)
- **Entidades Participantes:**
  - Fundació per a la Recerca Sant Joan de Déu (SJD)
  - Hospital Universitario Virgen de las Nieves de Granada (Andalucía)
- **Línea de Actuación complementaria**: LA4

16. **Proyecto 3DSurgHELP**: Virtual and augmented reality and 3D printing for surgical planning of complex surgeries in paediatric oncology and creation of surgical simulation models for training

- **Abstract**: Paediatric surgery is the medical speciality responsible for the diagnosis and management of surgical pathology in children and adolescents. Paediatric oncological surgery aims to achieve complete resection of the tumour being operated on, which can be very difficult when the disease is located in areas of the body with noble structures. Paediatric oncological cases need to be carefully studied and planned, using all the information that diagnostic imaging can provide.
  Today, materials engineering and advanced production processes such as additive manufacturing make it possible to produce products with defined textures, colours and mechanical behaviour in a short time and at the point of demand. On the other hand, advances in diagnostic imaging technologies and medical image post-processing, coupled with the integration of medical-technical disciplines, allow the rapid and accurate production of virtual anatomical models. All this represents a new paradigm for advancing towards personalised and precision medicine and makes it possible to consider new models of surgical learning and

training, wherever they are needed (distance learning), which will increase the safety, efficacy and efficiency of training and improve results.

Considering all of the above, our proposal for training and simulation of surgical skills for complex paediatric oncological surgery cases is a valuable contribution for many expert paediatric surgeons in need of skills training or complex cases and surgeons in distant places, with small but equally active units, where children with complex pathologies may arrive, who do not have the option of moving to another centre or to another country in search of therapeutic alternatives, and where their only hope is the local highly complex hospital

- **Entidad Coordinadora:** Fundació per a la Recerca Sant Joan de Déu (SJD)
- **Entidades Participantes:**
  - Fundació CIM-UPC
  - Hospital Regional Universitario Carlos Haya (Andalucía)
- **Línea de Actuación complementaria**: LA5

ANEXO B: PERFIL Y FUNCIONES DEL PERSONAL INVESTIGADOR POR PROYECTO

1. **Proyecto IA4DT2**

Posición (Ref. PPCC-IA4DT2): Postdoctoral Researcher on the Development and implementation of integrated artificial intelligence models to predict the risk of Type 2 Diabetes

a) Requirements for candidates:

Essential:

- PhD in Biomedicine, Biotechnology, Biostatistics or related discipline.
- Proven experience in the creation of artificial intelligence and machine learning models, and the use of statistical models.
- Experience in managing, organising, preparing, and analysing genetic data in large cohorts.
- Good programming skills in different languages including Python and R, and to be familiarised with HPC environments.
- Experience in the genomic analysis of complex diseases and to know the main factors predisposing to disease development (crucial).

Advantageous:

- Candidates with previous knowledge of Type 2 Diabetes will be positively valued

b) Main tasks and responsibilities

Under the supervision of Dr. David Torrents (ICREA Professor), the applicant will carry out the following research activities:

- In charge of getting access and preparing the clinical and molecular data required for the different analyses planned within the project.
- Creation and implementation of the necessary machine learning models for 1) discovering the variables affecting disease development and 2) predicting the risk.
- The candidate must be capable of applying the models in different populations and of generating protocols to evaluate and ensure the reliability of the outcomes.
- Elaboration of periodical reports to facilitate the follow up by the different collaborators.
- Promotion of the dissemination of the findings obtained within the project with the research community.

c) Location

The selected candidate will perform the work at the department of Computational Genomics group of BSC.

2. **Proyecto MITOCANCER**

Posición (Ref. PPCC-MITOCANCER): Postdoctoral Researcher on Targeting a mitotic polyglutamylation enzyme in cancer

a) Requirements for candidates:

Essential:

- PhD in Cell and/or Cancer biology
- Previous solid experience in cell and molecular biology methods.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Previous experience with handling primary tumour tissue will be very positively evaluated
- Experience in bridging fundamental research with clinical research.
- A solid knowledge in bioinformatics would be desirable

b) Main tasks and responsibilities

Under Prof Isabelle Vernos at the CRG, the selected candidate will carry out the following research activities:

- Coordination of the collection of tumour samples from patients at the hospital and processing for single cell sequencing at the CRG.
- Participation in the analysis of the sequencing data after their initial analysis at the CRG with the group of Prof Carrecedo in Galicia.
- Perform experiments in breast cancer cell lines to investigate the role of the enzyme in cancer progression
- In addition, the candidate will perform experiments to test the activity of the purified enzyme in vitro and help with the setting up of the high throughput screening protocol for the identification of inhibitory compounds. Further test and validation of potential hits may also be required.

c) Location

The candidate will work mainly at the CRG in the Vernos group. The candidate will visit the department of Anatomía Patológica of the Hospital de la Vall d'Hebron headed by Dr Santiago Ramon y Cajal for discussions on the project and to collect and process primary tumor tissue for single cell sequencing at the CRG.

3. **Proyecto InMaM**:

Posición (Ref. PPCC- InMaM): Research Assistant on Immunotherapeutic Strategies in Breast Cancer

a) Requirements for candidates:

Essential:

- Master's degree in the biomedicine field.
- Experience in cell culture (primary and cell lines), evaluation of immunomodulatory factors (cytokines, chemokines, soluble factors…), flow cytometry and basic molecular biology techniques (PCR, isolation of DNA/RNA, western blot, etc).
- Knowledge on the mechanisms of antitumor immune response.
- At least one publication in an international peer-reviewed journal as first author
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking High level of English
- High level of English

Advantageous:

- PhD in the biomedicine field

b) Main tasks and responsibilities

Under the direction of the principal investigators the applicant will carry out the following research activities:

- Updating and recording of clinical data from the study cohort, with the support of the ICO-Badalona clinical trials unit.
- Processing and storage of blood samples from patients with breast cancer.
- Participation in the experimental design and analysis of single cell transcriptomics data (selection of patients, sample preparation…)
- Experimental validation of the results obtained in additional cohorts of patients.
- Development of in vitro models aimed at evaluating new therapeutic combinations.

c) Location

The selected candidate will be located at the Irsicaixa and IGTP facilities, in Can Ruti campus in Badalona (IrsiCaixa-IGTP).

4. **Proyecto STOP-DMG**:

Posición (Ref. PPCC-STOP-DMG): Postdoctoral Researcher on the Identification and validation of therapeutic targets for Diffuse Midline glioma

a) Requirements for candidates:

Essential:

- PhD in Biology, Bioinformatics, or related topics.
- Mastered several techniques, such as general DNA and RNA manipulation techniques purification, cloning, mutagenesis, PCR, RT-PCR, qPCR, chromatin Immunoprecipitation,

proteomic techniques (protein extraction, subcellular fractionation, western blot, protein-protein interaction techniques) as well as in bioinformatic analysis.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English).

Advantageous:
- We provide a highly stimulating environment with state-of-the-art infrastructures, and unique professional career development opportunities.

b) Main tasks and responsibilities

Under the direction of Dr Di Croce, the applicant will carry out the following research activities:
- Responsible to generate patient-derived neuorospheres
- Responsible to analyse biopsies from PDX mice.
- Participation in the design and execution of a chemical screening

c) Location

The selected candidate will be located at the CRG Epigenetic events in cancer group, directed by Dr. Di Croce, at the Barcelona Biomedical Research Park (PRBB).

5. **Proyecto ABPATHFINDER**

Posición (Ref. PPCC-ABPATHFINDER): Postdoctoral Researcher on Screening of new precision antibiotics for the treatment of multiresistant infections

a) Requirements for candidates:

Essential:
- PhD. in Biochemistry, Molecular Biology, Biotechnology, Microbiology, or related disciplines.
- Accredited experience in research, mainly in the design and evaluation of antimicrobial compounds
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:
- Experience in the determination of antimicrobial activities (MIC) and cytotoxicity assays
- Previous experience in (i) screening of compound libraries, especially in bacteria, (ii) experience in cloning and protein expression, and (iii) biophysical techniques
- Knowledge of bioinformatics and statistics in the field of life sciences, especially in the management of R and/or Python languages

b) Main tasks and responsibilities

The selected candidate will join the laboratory of Biology of Infection Systems, belonging to the Department of Biochemistry and Molecular Biology of the Universitat Autònoma de Barcelona (UAB), under the supervision of Dr. Marc Torrent.

He/she is expected to conduct high-quality research, including the following responsibilities (i) writing research project proposals, (ii) preparing, writing, and reviewing scientific articles, and (iii) supervising undergraduate, master's, and doctoral students, as appropriate to their experience.

The main tasks to be performed within the project will be:

- Design and develop a new screening platform for antimicrobial compounds against specific targets.
- Supervise the screening of chemical libraries in bacterial systems and analyze the results obtained.
- Determine compound binding affinities using biophysical techniques.
- Determine antimicrobial activities and cellular cytotoxicity

c) Location

The selected candidate will perform the work mainly at the Universitat Autònoma de Barcelona. He/she may stay for short periods at the Vall d'Hebrón Hospital in Barcelona or at the Reina Sofía Hospital in Córdoba.

6. **Proyecto FANCONI-CURE**:

Posición (PPCC-FANCONI-CURE): Postdoctoral Researcher on Drug Screening for Precision Medicine in the Fanconi anemia pathway

a) Requirements for candidates:

Essential:

- PhD degree in the field of life sciences and biomedicine (Genetics, Biotechnology, Pharmacy, Medicine, Biomedical Sciences, etc...)
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

b) Main tasks and responsibilities

Under the direction of Prof. Dr. Jordi Surrallés, the applicant will carry out the following research activities,

- Execution of a drug discovery project using a defective DNA repair pathway as a therapeutic target in patients with Fanconi anemia.
- Application of techniques of genetics, biotechnology, molecular biology and cell biology for the validation of targets and drugs arising from pharmacological screenings.

c) Location

The work site will be the Joint Unit of Genomic Medicine of the Research Institute of the Hospital de Sant Pau-IIB Sant Pau.

7. **Proyecto OsteoMetTherapy**

Posición (Ref. PPCC-OsteoMetTherapy): Research Assistant on New therapeutic options in metastatic osteosarcoma

a) Requirements for candidates:

Essential:

- Graduate in Health Sciences (Biochemistry, Biotechnology, Medicine...), ideally with knowledge in molecular oncology.
- At least 4 years of laboratory experience using cell and molecular biology techniques.
- Demonstrable experience working with primary cell cultures and cell lines, virus infection and transfection techniques, cell proliferation and death assays.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- Organizational and problem-solving skills to work with minimal supervision
- High level of English

Advantageous:

- A PhD in the field of cell and molecular biology techniques will be highly valued.
- Experience in genetic manipulation using CRISPR-Cas9 technology.
- Previous experience in Drug Discovery processes and/or in experimentation with mice.

b) Main tasks and responsibilities

The applicant will carry out the following research activities:

- Generation and characterization of new cellular models
- Genetic manipulation of cells using both virus and CRISPR-Cas9 technology
- Design, optimization and validation of HTS assays
- Implementation of viability and cell death assays, as well as other cellular assays

c) Location

The selected candidate will be at the Signaling and Cell Cycle laboratory at IRB Barcelona. Occasionally, he/she will have to go to the Sant Joan de Déu Hospital.

8. **Proyecto DRUG4-COXPD1**:

Position 1 (Ref. PPCC-DRUG4-COXPD1_1): Research Assistant on the Generation of therapies and biomarkers for the treatment of mitochondrial dysfunction driven neurodegenerative diseases

a) Requirements for candidates:

Essential:

- Bachelor's and master's degree in a discipline in the field of biomedicine (biology, biochemistry, biotechnology, biomedicine, chemistry, or similar). The marks obtained in the bachelor's and in the master's degree will be valued.
- Official title to be able to work with experimental animals.
- Three or more years of experience in biomedical laboratory research.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English).

Advantageous:

- Experience in work handling rodents
- Knowledge and experience in evaluating mitochondrial function and/or mitochondrial genetics.
- Knowledge and experience in general methods of molecular biology (quantitative PCR, sequencing techniques, western blot, etc.).
- Knowledge of Catalan and Spanish.

b) Main tasks and responsibilities

Under the direction of Dr Ramon Martí Seves, the applicant will carry out the following research activities:

- Management and care of a colony of genetically modified mice.
- Phenotypic characterization (biochemical, molecular, survival, etc.) of the animals.
- Design and execution of gene therapy application experiments in animals.
- Other research tasks derived from the results and evolution of their research.
- Contribution to shared general management tasks of the laboratory and the research group.
- Preparation of manuscripts and presentation of results in national and international scientific meetings.

c) Location

The selected candidate will perform the work at, at the Laboratories of the Vall d'Hebron Research Institute (VHIR), in Barcelona.

Position 2 (Ref. PPCC-DRUG4-COXPD1_2): Postdoctoral Researcher on the Generation of therapies and biomarkers for the treatment of mitochondrial dysfunction driven neurodegenerative diseases

a) Requirements for candidates:

Essential:

- PhD in a discipline in the area of biomedicine (biology, biochemistry, biotechnology, biomedicine, chemistry, or similar).
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Extensive experience in cell culture and immortalization.
- Accreditation and experience to be able to work with experimental animals.
- Knowledge and experience in evaluating mitochondrial function.
- Knowledge and experience in general methods of molecular biology (quantitative PCR, sequencing techniques, western blot, etc.).
- Experience in international teams.

b) Main tasks and responsibilities

Under the direction of Dr Antonio Zorzano Olarte, the applicant will carry out the following research activities

- Fibroblasts in culture, and cellular immortalization.
- Phenotypic characterization of cells in culture and analysis of the response to mitochondrial stress.
- Other tasks related to the "screening" of molecules through the use of human cells.
- Execution of pharmacological therapy application experiments in animal models.
- Other research tasks derived from the results and evolution of their research.
- Contribution to shared general management tasks of the laboratory and the research group.
- Preparation of manuscripts and presentation of results in national and international scientific meetings.

c) Location

The selected candidate will perform the work at the Laboratories of the Institute for Research in Biomedicine (IRB Barcelona) in Barcelona.

9. **Proyecto B-ORG**:

Posición 1 (PPCC-B-Org_1): Postdoctoral Researcher on Bioengineering for patient-derived organoids for personalized medicine in NAFLD

a) Requirements for candidates:

Essential:

- PhD in bioengineering, biochemistry o related disciplines
- Experience in 3D cell culture and molecular biology techniques
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Experience in bioinformatics/computing
- Experience in biomaterials manipulation (hydrogels)

b) Main tasks and responsibilities

Under the supervision of Pau Sancho-Bru from IDIBAPS, the applicant will carry out the following research activities:

- Generate and characterize organoids derived from biopsies of patients at different stages of the disease. The organoids will be characterized at phenotypic and functional level and their cellular heterogeneity will be evaluated by single cell RNASeq.
- Mimic the pathophysiology of the disease in biopsy organoids by developing biomaterials and disease mediators.
- Use organoids to understand drug response mechanisms.
- Evaluate biopsy organoids as a platform for real-time drug screening.

c) Location

The activity will be developed mainly at the Liver Cell Plasticity and tissue repair research group at IDIBAPS, with close collaboration with the Molecular Imaging for Precision Medicine research group from IBEC and the Translational Lung Mechanobiology at UB.

Position 2 (PPCC-B-Org_2): Postdoctoral Researcher on Bioengineering / Biophysics for patient-derived organoids for personalized medicine in NAFLD

a) Requirements for candidates:

Essential:

- PhD in in physics, chemistry, bioengineering or related disciplines.
- Experience in experimental techniques (preferably in the field of biomechanics and micro-copying) and data analysis with specialized software (Matlab, R, Python or similar).
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Experience in nuclear magnetic resonance
- Experience in manipulation of biomaterials (hydrogels)

b) Main tasks and responsibilities

Under the supervision of Irene Marco-Rius from IBEC and Jordi Alcaraz from UB, the candidate will carry out the following research activities:

- Generation of biomaterials for modeling NAFLD pathophysiology in organoids. The investigator will be responsible for the development and characterization of bioscaffolds and materials for organoid growth, disease modeling and organoid evaluation by HP-MR.
- Technical development and optimization of samples for HP-MR.
- Development of hardware and software for quantitative assessment by HP-MR to provide day/week time course data for non-invasive assessment of metabolite flux in organoids.

c) Location

The activity will be developed at both the Molecular Imaging for Precision Medicine research group at IBEC and the Translational Lung Mechanobiology at UB.

10. **Proyecto MnkImmunOnco**

Posición (PPCC-MnkImmunOnco): Postdoctoral Researcher on Therapy resistance and immune evasion on a novel MNK inhibitor

a) Requirements for candidates:

Essential:

- PhD in the area of biomedical sciences to lead the project.
- Experience in a research laboratory
- Extensive knowledge in the area of small molecule inhibitors and their further development.
- Experience in the design of experiments for the research project
- Experience in guidance of personal (PhD and Master students) involved in the project.
- Previous experience of at least 5 years in a molecular biology research laboratory
- Postdoctoral experience abroad of at least 2 years.
- Implementation and standardization of new laboratory techniques.

b) Main tasks and responsibilities

Under the direction of Dr. Santiago Ramón y Cajal, the main tasks of the selected person are the supervision and guidance of the personal to perform the experiments for the proposed project:

- Design of experiments to prepare samples for pharmacodynamic analysis of EB1 in vitro and in vivo. Analysis and interpretation of results and test of new formulations to optimize EB1 for the use in vivo.
- Setup of animal models of AR-V7 positive CRPC and breast cancer model for CAR-T cell-based therapy.
- Performance of efficacy studies combing EB1 with standard of care in CRPC models and with CAR-T cell-based therapy.

- Adapt existing in vitro models for compatibility with downstream analysis by single cell sequencing.
- Assistance in data analysis, interpretation of the results as well as plan and execute validation experiments for the obtained data.
- Coordinate with clinicians (pathologist) sample collection and IHC analysis for patient stratification.
- Write reports and scientific publications resulting from the work.

c) Location

The selected candidate will coordinate the proposed project at the VHIR Translational Molecular Pathology, located at the Vall de Hebron Institute of Research (VHIR) in Barcelona.

11. **Proyecto WORMVUS**

Posición (Ref. PPCC-WORMVUS): Postdoctoral Researcher on Rapid in vivo characterization of the functional impact and vulnerabilities for PTEN tumor suppressor gene variants

a) Requirements for candidates:

Essential:

- Bachelor and PhD in disciplines related to biology or biomedicine.
- Experience in Molecular Biology techniques.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English.

Advantageous:

- Previous experience in C. elegans, R and bioinformatic analysis of RNA-sequencing assays will be positively valued.
- Competitive CV and interest in applying for scholarships or contracts to extend the postdoctoral period.

b) Main tasks and responsibilities

Under the direction of Dr Julián Cerón (IDIBELL) and Dr Nicholas Stroustrup (Center for Genomic Regulation CRG), the applicant will carry out the following research activities:

- Editing of the C. elegans genome using CRISPR technology, to introduce mutations and humanize genes.
- Genotypic and phenotypic analyzes in C. elegans.
- Design and coordinate a drug screen on the IRB Drug Screens platform.
- State-of-the-art transcriptomic analysis (single worm/low input), generation of libraries for sequencing, analyses of RNA-sequencing using R.
- Making reports and writing scientific articles.

c) Location

The selected candidate will perform the work mainly in the "Genes, Disease and Therapy" department of IDIBELL (Bellvitge Biological Research Institute), in the "Models of Disease in *C. elegans*" group, with temporary stays in the Regulation Center Genomics (CRG), in the Dynamics of Living Systems Group.

12. **Proyecto ADNano**

Position 1 (Ref. PPCC-ADNano_1): Postdoctoral Researcher on the Synthesis of Alzheimer's disease-modifying nanomedicines

a) Requirements for candidates:

Essential:

- PhD in Polymer Chemistry, Nanomedicine, Bioengineering, Materials Science, or related discipline
- Prior experience in step and controlled polymerizations
- Previous experience in micelles or vesicle characterization
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking,
- High level of English

Advantageous:

- Prior experience with block copolymer micelles for drug delivery and biomedical applications
- Experience with blood-brain barrier in vitro models

b) Main tasks and responsibilities

Under the direction of Prof Giuseppe Battaglia, the applicant will carry out the following research activities:

- Synthesis of sequenced controlled polyesters
- Self-assembly and characterization of micelles
- Conjugations and characterization of LRPs ligands to micelles.
- Assessment of BBB crossing and anti-inflammatory activity.

c) Location

The candidate will work at IBEC Molecular Bionics group facilities (Parc Científic de Barcelona).

Position 2 (Ref. PPCC-ADNano_2): Postdoctoral Researcher on the Neurobiological assessment of Alzheimer's disease-modifying nanomedicines

a) Requirements for candidates:

Essential:

- PhD in Neuroscience, Nanomedicine, Bioengineering, or related discipline
- Prior experience in neurodegeneration and Alzheimer's disease models
- Prior experience in neuro-inflammation
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking.
- High level of English

Advantageous:

- Prior experience in brain vasculature and transport
- Prior experience in nanomedicine.

b) Main tasks and responsibilities

Under the direction of Prof Giuseppe Battaglia, the selected candidate will carry out the following research activities:

- Blood-brain barrier crossing and LRPs modulation
- AD animal models
- In vitro and in vivo microglia anti-inflammatory activity assays
- Behavioral studies

c) Location

The candidate will work at IBEC Molecular Bionics group facilities (Parc Científic de Barcelona).

13. **Proyecto EVBRAINTARGET**

Posición (PPCC-EVBRAINTARGET): Postdoctoral Researcher for validation of BP-EVs as a next-generation compound delivery platform

a) Requirements for candidates:

Essential:

- PhD in Biotechnology, Biomedicine or related fields.
- Accredited experience, through scientific publications in journals indexed by the Journal Citation Reports (preferably as leading author), in the tasks described in the offer (or most of them).
- Experience in animal experimentation (murine models).
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Experience in mass spectrometry techniques, mainly proteomics.
- Experience in omics data analysis.
- Experience in supervising predoctoral students.
- Experience independently writing scientific articles.
- Interest in progressing independently in the research career.

b) Main tasks and responsibilities

The successful postdoctoral researcher hired through this position will lead and actively participate in the achievement of the following tasks:

- Optimization of the loading of antipsychotic compounds in BP-EVs nanocarriers.
- Evaluation of the conditions of preservation and conservation of the loaded nanocarriers.
- In vitro and in vivo studies to evaluate the cell targeting capacity of loaded nanocarriers in the CNS and their associated drug releasing mechanisms.
- Scientific dissemination tasks (preparation and publication of scientific articles, participation in scientific conferences, conducting seminars, etc.) preferably with a moderate/high degree of independence.
- Active and creative participation in the design of experiments and the preparation of scientific projects.

c) Location

The successful candidate will have the support of a predoctoral researcher to carry out the tasks described. All described tasks will be carried out at the +PPRG laboratory at IRBLleida or the University of Lleida, both institutions located in the city of Lleida, Catalonia, Spain.

14. **Proyecto LENTI-UP**

Posición 1 (Ref. PPCC-LENTI-UP_1): Research Assistant on Bioprocesses for the development of viral vector production in bioreactors

a) Requirements for candidates:

Essential:

- Bachelor's and MSc in biotechnology, bioengineering and/or health sciences.
- Experience in bioprocess development to produce viral vectors in bioreactors.
- Experience in concentration and diafiltration processes for viral vectors.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- PhD in biotechnology, bioengineering and/or health sciences.
- Experience in purification by chromatography.
- Experience in carrying out and analysing the results of analytical tests with biochemical and/or molecular biology methods

- Experience in plasmid bioreactor production
- Work experience in clean rooms and knowledge of GMP processes

b) Main tasks and responsibilities

Under the direction of Dr. Hugo Calderón, the applicant will carry out the following research activities:

- Design, planning and execution of tests and activities related to the project.
- Management of documentation and resources associated with the project activity.
- Fine-tuning of medium-scale plasmid productions.
- Execution of cell culture assays in suspension and adherence to produce viral vectors.
- Commissioning of viral vector production in small and medium scale bioreactors.
- Analysis of results and preparation of reports

c) Location

The selected candidate will perform the work at Leitat Medical, Centro Tecnológico Leitat, located in Barcelona.

Posición 2 (Ref. PPCC-LENTI-UP_2): Research Assistant in Gene and cell therapies developments

a) Requirements for candidates:

Essential:

- Bachelor's and MSc in health sciences, favourable if it is in immunology and/or oncology.
- At least 3 years of laboratory work experience.
- Experience in performing and evaluating analytical tests with biochemical, molecular biology and immunoassay-based methods.
- Experience in performing and analysing functional assays in immunology.
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- PhD in health sciences, favourable if it is in immunology and/or oncology
- Experience in cell production in GMP bioreactors.
- Knowledge in preparation of quality and regulatory documentation

b) Main tasks and responsibilities

Under the direction of Dr. Manel Juan Otero, the applicant will carry out the following research activities:

- Design, planning and execution of tests and activities related to the project.
- Preparation and management of documentation and resources associated with the project activity
- Carrying out immunology and analytical tests
- Cellular and functional assays in immunology

- Analysis of results and preparation of reports

c) Location

The selected candidate will perform the work at IDIBAPS.

15. **Proyecto BIOMOD**

Posición (Ref. PPCC-BIOMOD): Postdoctoral Researcher on Biomechanical Models

a) Requirements for candidates:

Essential:

- PhD in Biomedical Engineering, Mechanical Engineering, Industrial Technology Engineering or Industrial Engineering
- Experience calculating structures using finite elements (ANSYS or similar).
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English

Advantageous:

- Experience in fields related to biomechanics or health sciences will be appreciated.
- Experience with post processing tools such as Hypermesh or Ansa will be assessed positively
- Experience with medical image processing (3D Slicer, Mimics, 3Matic, MeshLab) will be appreciated.
- Experience in conducting mechanical tests and materials characterization tests will be appreciated.

b) Main tasks and responsibilities

Under the direction of Robert Texidó (IQS) and Arnau Valls (HSJD), the main tasks to be performed within the project by the selected person will be:

- Participation in the development of biomechanical models through medical image processing, finite elements / post-processing tools, DICOM image segmentation and CAD reconstruction
- Work with a physical model for the evaluation of biomechanical models through mechanical testing (traction, compression, among others)
- Characterization of biological materials (elastic and viscoelastic properties of biological tissue samples
- Participación en el desarrollo de modelos biomecánicos mediante tratamiento de imagen

c) Location

The selected person will be part of a team made up of members of IQS and HSJD. He/she will perform the activity at both locations.

16. **Proyecto 3DSurgHELP**

Posición (Ref. PPCC-3DSurgHELP): Postdoctoral Researcher on Medical 3D printing and planning bioengineering

a) Requirements for candidates:

Essential:

- PhD in Biomedical Engineering, Mechanical Engineering, Industrial Technology Engineering or Industrial Engineering or Telecom Engineering.
- Experience with CAD/CAM technologies.
- Experience in the post-processing of the medical image (segmentation of DICOM, surgical planning…).
- Competencies and skills: Communication, Teamwork and collaboration, Commitment, Proactivity, Integrity, Critical and Analytical thinking
- High level of English).

Advantageous:

- Experience in fields related to biomechanics, materials or health sciences will be appreciated.
- Experience with medical image processing (3D Slicer, Mimics, 3Matic, MeshLab) will be appreciated.
- Experience with virtual and augmented reality image processing software (Unity, Mimics, other) will be appreciated.
- Experience in 3D printing technologies will be appreciated.

b) Main tasks and responsibilities

Under the direction of Lucas Krauel (HSJD) as PI and technical supervision of Arnau Valls (HSJD), the main tasks to be performed within the project by the selected person will be:

- Participation in the development of virtual (CAD) and physical simulation models of complex paediatric cancer cases (neuroblastoma, hepatoblastoma…).
- Segmentation of the medical image (DICOM), pots-processing, and CAD reconstruction.
- Work with virtual reality and augmented tools and software to generate virtual simulators for the training of skills of oncologic surgeons.
- Work with 3D printing, moulage techniques and manufacturing techniques for the production of a physical simulation model for the training and evaluation of skills of oncologic surgeons.
- Organize and participate on the clinical validation of the simulators (digital and physical) developed in training sessions with oncologic surgeons in HSJD and HRUM.

c) Location

The selected person will be part of a team made up of members of the HSJD and CIM UPC. He/she will perform the activity at HSJD and will interact with CIM UPC and HRUM.