

IBEC-SJD INTERNATIONAL PhD PROGRAMME

Position

1. Project Title/ Job Position title:

New tools and physiological models to assess the efficacy of gene-editing-based therapies for Collagen VI-related congenital muscular dystrophies

2. Research project/ Research Group description:

Research project description: Collagen VI-related congenital muscular dystrophies (COL6-RD) are a set of rare congenital neuromuscular conditions for which there is no effective treatment. They are caused by mutations in one of the three major COL6 genes, resulting in the deficiency or dysfunction of the COL6 incorporated into the ECM of connective tissues, affecting the assembly and structural integrity of the entire fibrillar network. The clinical features of COL6-RDs are secondary to ECM disruption and include muscle weakness, proximal joint contractures and distal hyperlaxity. Although some features have been identified in patients' ECMs, no direct correlation between them and the clinical phenotype has been established, mainly due to the lack of predictive models of pathology. Recently, the Nanobioengineering group at IBEC in collaboration with the group of Applied research in neuromuscular diseases at SJD, developed a personalized preclinical model of the disease based on cell-derived matrices (CDMs) from COL6-RD patients' cells, which show distinctive features of the patient's phenotypes. More recently, in collaboration with the Nanoprobes and Nanoswitches group at IBEC, we conducted the nanomechanical analysis of the CDMs from patients with atomic force microscopy-force spectroscopy (AFM-FS), which allowed us to define a healthy range for the Young's modulus, from which the phenotypes of the disease are excluded and distinguished. A proof of concept assay with genetically edited cells showed that the mechanical properties of the CDMs are restored after editing. Based on these promising results, the current project aims to evaluate the most recent gene therapies developed by SJD, based on nucleic acids, such as CRISPR/Cas9, base editors or antisense oligonucleotides in CDMs from patients by AFM-FS and biomolecular characterization.

3. Job position description:

The Nanobioengineering and Nanoprobes and Nanoswitches groups at IBEC are looking for a PhD candidate to join a multidisciplinary team to work on the development of in vitro models for the diagnosis and prognosis of musculoskeletal diseases. In particular, the work will focus on the development of new tools and physiological models to evaluate the efficacy of gene editing-based therapies for collagen VI deficiency muscular dystrophy, in close collaboration with the Hospital Sant Joan de Déu and within the framework of the project “Ajuts per a projectes de recerca i innovació Torrons Vicens-RAC 1”. The candidate will join a translational and multidisciplinary team with extensive experience in training researchers at postgraduate, predoctoral and postdoctoral levels. The research groups, located at IBEC, are in close contact with international and national teams, and belong to CIBER-BBN (Instituto de Salud Carlos III).

The main tasks and responsibilities include culturing of patient cells (edited and unedited), fabrication of physiologically relevant in vitro models of diseases with patient cells, mainly cell-derived matrices (CDMs), biomolecular characterization of the models and image processing, as well as micro- and nanomechanical characterization of the models with atomic force microscopy (AFM) and data analysis. A bachelor's and master's degree in areas such as biology, biochemistry, chemistry, biotechnology, biomedical engineering, biomedicine, nanotechnology or any related field is required. In addition, the candidate should have experience in cell culture and basic molecular biology techniques, image acquisition techniques (e.g. confocal microscopy or life imaging) and previous experience in scanning probe microscopy, especially AFM. Skills in communication, teamwork, proactivity, integrity, critical thinking and a high level of English are also required. Previous experience in materials science and international experience would be an asset.

Group Leaders at IBEC

1. Title: Dr.
2. Full name: Anna Lagunas Targarona
3. Email: alagunas@ibecbarcelona.eu
4. Research Group: Nanobioengineering

1. Title: Dr.
2. Full name: Marina Inés Giannotti
3. Email: migiannotti@ibecbarcelona.eu
4. Research Group: Nanoprobes and nanoswitches

Group Leader at SJD

1. Title: Dr.
2. Full name: Arístides López Márquez
3. Email: aristides.lopez@sjd.es
4. Research group: Applied research in neuromuscular diseases