Funded PhD project at IGBMC – Strasbourg – France

Topic : Identification and functional characterization of novel genes for myopathies

Project :
Skeletal muscle represent half of the dried body weight and is key for many physiological functions including metabolism and movement. A plethora of muscle diseases are known, including severe congenital myopathies associated to life-threatening muscle weakness. Main bottlenecks are that half of patients lack a genetic diagnosis, the pathological mechanisms are not understood, and there is no specific cure for most of them. Thus we aim to identify novel myopathy genes that will represent novel therapeutic targets.
To this goal, the PhD student will use next generation sequencing strategies, exome and genome sequencing of patients DNA, and RNAseq/transcriptome from patient muscles, and process these big datasets through bioinformatics pipelines to identify mutated genes in patients with myopathies. The functional impact of mutations will be confirmed by in vitro assays with recombinant proteins and transfected and differentiated muscle cells followed by confocal and video microscopies. The importance of these new myopathy genes for muscle function will be evaluated in vivo in an animal model (zebrafish or mice depending on the gene conservation) with CRISPR/Cas9 genome editing, RNA interference and adeno-associated virus. Animals will be phenotyped with simple motor tests, histology, electron microscopy and confocal imaging. This will also provide faithful laboratory models in which therapies may be later tested.
The success of this project will lead to a better diagnosis and patient care, and the identified genes will increase our understanding of the pathomechanisms and represent novel therapeutic targets.

Keywords : Genetics, myopathy, sequencing, informatics, cell, mouse, mutation

Location : IGBMC is one of the main European research center in Biomedicine, located in Strasbourg, close to Germany and less than 2hrs train from Paris, within a nice and typical countryside near the Vosges mountains. 750 persons from 40 nationalities work at IGBMC which houses a large number of state-of-the-art scientific platforms/services.

References : (*PhD student)
-Lornage X* et al. ACTN2 mutations cause "Multiple structured Core Disease" (MsCD). Acta Neuropathol. 2019 Mar;137(3):501-519.
-Lionello VM* et al. Amphiphysin 2 (BIN1) modulation rescues MTM1 centronuclear myopathy and prevents focal adhesion defects. Sci Transl Med. 2019 Mar 20;11(484).

Application : please send your CV, letters of recommendation and Master results to J Laporte and J Bohm (jocelyn@igbmc.fr; johann@igbmc.fr). www.igbmc.fr/laporte