How do UNC45B mutations lead to cardiac and skeletal muscle diseases?

The labs of Julien Ochala and Pia R. Lundegaard are looking to recruit an ambitious master student to undertake a project in understanding the consequences of mutations in genes involved in muscle fiber development and function. The project will involve the usage of several different techniques with the field of biochemistry, molecular biology and biophysics.

Aim: To better understand the pathogenesis of UNC45B-related muscle disorders.

Brief description: UNC45B is a molecular chaperone essential for myosin and muscle homeostasis[1]. What remains unknown is how mutations in the UNC45B gene modify myosin structure/function and induce severe incurable diseases characterized by deleterious cardiac and skeletal muscle pathologies[1].

Specific aim 1: Create a zebrafish model: We will use CRISPR/Cas9 genome editing to generate one genetically modified zebrafish model with a mutation in UNC45Ba/b[2-4]. The mutant will be generated by CRISPR-cas9 with gRNA target selecting for point mutation and/or truncation.

Specific aim 2: Characterize early changes in cardiac and skeletal muscles: After having designed a model, we will explore the early developmental consequences at the myosin/muscle levels at different time points. The specific myosin structure/function will be assessed using super-resolution microscopy in combination with biophysical assays (eg Mant-ATP chase experiments) whilst the overall muscle growth will be evaluated by using state-of-the-art immuno-histochemical techniques[5-7].

Interested in during this project?

Please contact either associate professor Julien Ochala (julien.ochala@sund.ku.dk) or assistant professor Pia Rengtved Lundegaard (plundegaard@sund.ku.dk) for further information.

References: **1**. Lee CF et al. Int Rev Cell Mol Biol 2014. **2**. Collins MM et al. PNAS 2019. **3**. Skarsfeldt MA et al. Acta Physiol (Oxf) 2018. **4**. Sokol AM et al. PLoS Genet 2018 **5**. Levy Y et al. JCI Insight 2018 **6**. Lindqvist J et al. Ann Neurol 2016 **7**. Ross JA et al. Acta Neuropathol 2019