Entity: Vall d'Hebron Institut de Recerca (VHIR)

Research group, Unit or Department: Pediatric Neurology

Student's tutor: María José Pérez/ Francina Munell

Positions available: 1

Project description/ Research lines:

Spinal Muscular Atrophy

SMA is a devastating disease; patients affected by severe forms of the disease usually do not live past the age of three. SMA is characterized by degeneration of alpha motor neurons in the spinal cord, resulting in progressive proximal muscle weakness and paralysis (D'Amico et al., 2011). Patients with SMA type I, II and III are intellectually normal but develop progressive muscle weakness involving limbs as well as other muscle-related functions such as breathing and swallowing. Respiratory failure is the main cause of death in patients with SMA.

SMA is clinical classified into four phenotypes based on age of onset and motor function achievement. Spinal muscular atrophy 0 is a very severe spinal muscular atrophy with respiratory failure at birth. SMA type I is characterized by onset before the age of 6 months and failure to achieve the ability to sit without support; life expectancy is less than 2 years. SMA type II is usually symptomatic between ages 6 and 18 months but may manifest earlier. Patients with SMA type III become symptomatic after the age of 18 months, and all achieve the ability to walk independently.

The severity of the phenotype in SMA is mainly due to the number of copies of the highly homologous SMN2 gene, which is present in all patients, being the main modifier of SMA and the primary target for therapy. Although the correlation of SMN2 copy number and severity of the phenotype is strong, it is not absolute and should not be used for the prediction of the SMA subtypes or for prognosis (Wirth et al., 2013). Most type I patients carry two copies of SMN2, type II three SMN2 copies, type III three to four SMN2 copies and type IV four to six SMN2 copies. In this feature, our objectives are to understand the genetic modifiers and to find new biomarkers of prognosis.

Neuromuscular Junctions (NMJ) are the sites of synapses that connect the motor nerve and muscle fibers. One of the functional alterations found in SMA is in α-MNs at the NMJ

(Hamilton and Gillingwater, 2013). The development of the NMJ in SMA patients is severely arrested, which impairs the maturation of Acetylcholine receptors (AChR) (Kariya et al., 2008).The working hypothesis is that NMJ dysfunction is contributing to SMA. Therefore one of the aspects of this research line is study the dysfunction of NMJ in SMA samples.

All together, our aims are:

1. To understand the genetic modifiers in SMA.

2. To find new biomarkers of prognosis in this pathology.

3. To understand the dysfunction of NMJ in SMA and find specific molecules that can restore the NMJ functionality.

4. Role of autophagy in SMA (in collaboration with IRBlleida, PI: Dr Rosa M Soler)

All our effort is for improve the quality of the life of SMA patients.

Period for the internship: master practicum

Requirements:

- Degree in Life Sciences
- Good academic records (preferably above 2)
- Fluently in English
- Motivation in research career

Where to apply: Interested candidates please send a letter of intention, CV and academic records to María José Pérez (maria.perez@vhir.org)
