**PhD program:** Cellular and Molecular Physiopathology

**Scientist in charge:** Carla Taveggia

**Unit:** Axo-Glial Interaction

**Title:** Role of L-PGDS in PNS myelin maintenance

Myelin is a multilamellar spiral membrane surrounding the axons in peripheral (PNS) and central nervous system (1,2). In the PNS myelin is synthesized by Schwann cells and we previously identified in axonal Neuregulin 1 (NRG1) type III the key signal controlling PNS myelination and Schwann cell development (3). All NRG1 are activated by proteases-mediated cleavage. In particular, NRG1 type III is cleaved in the extracellular region by the α-secretase TACE and the β-secretase BACE1. We previously demonstrated that in the PNS the α-secretase TACE cleaves NRG1 type III and inhibits its activity (4).

NRG1 type III intracellular domain is also processed by the γ-secretase complex. We recently showed that upon cleavage, NRG1 type III intracellular domain translocates into the nucleus to upregulate the prostaglandin D2 synthase (L-PGDS) gene. L-PGDS catalyzes the enzymatic conversion of prostaglandin H2 to prostaglandin D2, one of the major lipid mediator synthesized in the nervous system. Further, we showed that specific inhibition of L-PGDS activity impairs in vitro myelination and causes myelin damage. Accordingly, myelin in nerves of L-PGDS−/− mice is noticeably thinner and aberrant, thus suggesting that L-PGDS is a novel modulator of PNS myelination (5).

A PhD project is available to investigate the role of L-PGDS in myelin maintenance. The project includes genetic manipulation of L-PGDS activity and levels in vivo in transgenic animals already developed in the laboratory. We will also investigate how L-PGDS influences myelin maintenance in vitro in a neuronal-Schwann cells coculture system, by using a combination of live-imaging, immunohistochemistry and biochemical analyses.

**References:**


**HSR website:**