Characterization of spatiotemporal organization of the brain lipidome

Neural cells produce thousands of different lipids, each endowed with peculiar structural features and contributing to specific biological functions. Lipid composition affects neuron firing properties influencing vesicle fusion and fission processes, membrane conductivity, and ion fluxes. Nonetheless, a systematic and fine-grained characterization of lipid composition in the different brain regions is not available.

Lipids also play a fundamental role in brain development. For example, some lipids, such as glycosphingolipids, mediate cell-cell recognition, others like steroid hormones, and phosphoinositides, have a role in stimulating cell growth and signaling. Furthermore, exposure to teratogenic agents, during development, is associated to cognitive or sensory impairments that might be mediated by interference of these teratogens with lipid biogenesis and metabolism. However, little is known about how the regional specificity of lipids is developmentally established and maintained throughout adulthood.

The doctoral candidate will aim at filling this gap by collecting systematic data necessary to construct a high spatially resolved atlas of the lipidome of the adult and developing mouse brain. We expect this resource to provide numerous cues of the underlying regulation mechanisms; the most interesting observations will be experimentally followed up by the candidate and related to function.

The project offered jointly by the La Manno and D'Angelo labs will allow the candidate to:

- Use super-resolved Imaging Mass Spectrometry (IMS) to reconstruct the spatial lipidome in serial brain sections from adult and developing mice.

- Assess the lipid deregulation resulting from the exposure of different teratogenic conditions.

- Investigate the relation between the lipidome of different stem cell populations and their neural progeny.

- Investigate how perturbation to genes involved in lipid metabolism affects brain development.

- Assess how direct perturbations of lipid composition affect morphogenesis and adult brain structure and composition.