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Cellular Communications in Early Brain Development Using Human Brain Organoids

Brain development encompasses a significant portion of our lives, from embryonic stages through approximately two decades of our lives. Within this intricate process lie the keys to understanding the onset of neurodevelopmental disorders, which can arise from genetic mutations and/or environmental factors profoundly impacting brain development.

Our laboratory has largely contributed to the identification of molecular and cellular mechanisms that contribute to a group of neurodevelopmental disorders called "synaptopathies" such as autism spectrum disorder (ASD) and Fragile X Syndrome (FXS). The goal of the proposed project is to investigate the contribution of the impaired cortico-striatal signaling to ASD and FXS, identify biomarkers for a future personalized medicine and provide a proof-of-concept therapeutical approach.

Taking advantage of a newly established Faculty platform https://wp.unil.ch/scof/ starting from iPSCs of typically developing individuals and individuals with ASD and FXS we have developed brain-region-specific organoids that recapitulate the early stages of brain development. The project develops around two main axes: understanding the contribution of the cortico-striatal signaling while the brain develops and the impact of an early RNA-based therapy to correct brain wiring. Specifically, we will generate dorsoventral cortical assembloids, by fusing dorsal and ventral brain organoids, and study the development, migration and molecular signature of human interneurons in health, ASD and FXS conditions. To reveal the spatiotemporal dynamics of identified dysregulated mRNAs we will use spatial transcriptomic (MERFISH technology) and electrophysiology on an array with > 25.000 electrodes (CMOS). Next, we will use RNA-based therapy to correct the observed affected developmental processes.

The multidisciplinary expertise – one of the strengths of our laboratory – and the access to cutting-edge technologies present in our department and at the faculty level, places this proposal in an excellent position to contributing to the understanding of neurodevelopmental disorders and paving the way for interventions and treatments. Together, we can make a profound impact on the lives of those affected by these conditions and shape the future of neuroscience.

The PhD candidate will be exposed to and acquire various techniques to develop an innovative project and be supervised by senior researchers and collaborate with clinicians - receiving therefore an exceptional training. Commitment to science, proactivity and curiosity are mandatory requirements to develop this project.