**Engineering Connections: Combining stem cells, bioengineering, microfabrication and imaging technologies to model the nervous system in health and disease –**

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Neurodegenerative disorders are hereditary or sporadic diseases characterized by chronic, progressive loss of specific neuronal populations, and are generally incurable. This lack of available treatments stems directly from a lack of understanding of the molecular pathways involved: in many cases the genetic causes of neurodegeneration are known, but how they translate into the symptoms, and how to stop that remains unresolved. Induced pluripotent stem cells (iPSCs) and stem cell differentiation technologies allow to perform disease modelling directly on the cell subtype that is degenerating in a patient, and are able to recapitulate the disease phenotype, discover novel molecular pathways involved and even serve as drug discovery platforms. However, neurodegeneration often is the result of breakdowns in the interplay between different cell types. Therefore, reductionist models focusing one cell type cannot not fully capture the interactions that give rise to the disease. Moreover, conventional analysis techniques –such as end-point fluorescent imaging on fixed cells- fails to capture important aspects of the disease molecular process in vitro.

My research focuses on developing "neural-tissue-on-a-chip" modelling platforms, capable of capturing the complexity of neural circuits in vivo using patient iPSC cells, within controllable systems, coupled with more advanced imaging technologies that can fully capture the complexity of cellular interactions occurring in the model. Using a combination of topographical patterning, soft lithography and cell confinement plating it is possible to control cellular positioning and axonal sprouting with iPSC-derived disease relevant neuronal populations, opening the possibility to create oriented circuits. The tailoring of the cellular environment allows to perform both basic neurobiology studies focused on the response of neural cells to topography and stiffness, as well as easily highlighting disease-relevant phenotypes. In parallel, I am also developing new imaging approaches to be used together with the in vitro modelling platforms.