Brain Diseases

BATTEN'S DISEASE

Background

Batten`s disease is a genetic, rare, and fatal lysosomal storage disorders. One of the main characteristic of Batten`s disease is the neurodegeneration of a brain area due to neuroinflammation. In fact, abnormal interaction between neurons and microglia, the resident immune cells within the central nervous system, has been identified as a crucial step in the onset of the pathology. Currently, microglia's role in the onset, development, and therapy of Batten`s disease remains unfortunately unknown. This is a critical issue since activated microglia not only may either positively or negatively influence neuronal survival, via the production of growth factors or pro-inflammatory mediators, but it may also act as an ideal target for early diagnosis.

Pathology Model

By culturing microglia, astrocytes and neurons on separated microchambers interconnected by microfluids, it is possible to recreate in vitro the different combinations of intercellular crosstalk in different pathophysiological scenarios, and thus understand in detail the specific contribution of each cell type in the complex biological crosstalk of a specific disease scenario such as Batten's disease.

Microglia, astrocytes and neurons from different brain areas (i.e. cortex and hippocampus) of either Cln3-/- or wt animal models will be cultured in separate chambers in the microfluidic platform.

.

Readouts

All cell types in separate chambers of the microfluidic platform will be monitored for viability and oxidative stress, in order to compare standard culturing conditions on glass coverslips with culturing of cells on microdevices, as previously reported for wt neurons.

In particular, all cell types in separate chambers of the microfluidic platform will be monitored for proliferation, activation state (i.e. membrane permeability), motility, phagocytic activity, microvesicle shedding, mitochondrial damage (i.e. HCS assay) and inflammatory cytokine production (multiplex ELISA). The most physiologically relevant conditions as well as more relevant readouts for the evaluation of Batten disease model in vitro will be identified by comparing wt and KO data.