Centre de recherche
CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant

Université de Montréal

PROGRAMME DE STAGES D'ÉTÉ
Initiation à la recherche biomédicale
au Centre de recherche du CHU Sainte-Justine
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Modelling MPSIIIC through human induced pluripotent stem cells

Numéro de l'offre de stage : No. 34

Équipe de recherche

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Responsable de la supervision du stagiaire

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Programmes d'études ciblés

Neuroscience, Cell Biology, Biochemistry

Description du projet (max 1 page)

Lysosomal storage disorders (LSDs) are caused by genetic defects in lysosomal catabolism. Although rare, they constitute a heavy burden for the health care in Canada and worldwide. Most LSDs affect the CNS of children and result in severe neurodegenerative decline leading to disability and death. The main challenge in developing therapies for neurological LSDs is to deliver the missing catabolic enzymes into the brain.

Our major objective is to develop therapies for neurological LSDs using Mucopolysaccharidosis III (MPSIII) as a template model. MPSIII shares a common pathological mechanism with other neurological LSDs and manifests with neuropsychiatric problems, mental retardation and dementia. Using mouse models of the disease we have demonstrated that the pathophysiological mechanism of MPSIIIC involves both neurodegeneration and functional pathological changes in neurons affecting in particular excitatory glutamatergic synapses. To mimic disease specific mutations as seen in patients, we aim to use neurons derived from induced pluripotent stem cells

(iPSCs) from MPSIII patient skin fibroblasts and test if a similar form of neurodegeneration and synaptic dysfunction also exist in these neurons.

To enable this, the candidate will first generate cortical neurons from the iPSCs. The candidate will then characterize, in these neurons, synaptic and other cellular deficits using different neuronal and cellular markers respectively. The study should clarify CNS pathophysiology of MPSIII and suggest novel therapeutic approaches. It may also provide a paradigm for treating other neurodegenerative lysosomal diseases affecting synaptic transmission.

Modeling MPSIII through human induced pluripotent stem cells will not only generate significant patient specific insights into the neurobiology of the disease but also pave the path for tailoring future therapeutics by using them for high throughput screening of potential small molecules.

Rôle du stagiaire

The candidate will be involved in generation and characterization of cortical neurons from iPSCs derived from MPSIII patient skin fibroblasts.

Mots clés

iPSCs derived neurons, cell culture,MPSIII