**DOTTORATO DI RICERCA IN BIOLOGIA CELLULARE E DELLO SVILUPPO**

**39th CYCLE**

**Project proposal for a PhD scholarship financed by an external institution**

**Title: Development of 3D human brain cell models for studying the molecular pathogenesis of leukodystrophies caused by astrocyte cell dysfunction**

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The objective of the present project is to generate human cerebral 3D models from inducible pluripotent stem cells (iPSC) derived from healthy subjects and patients affect by rare leukodystrophies caused by astrocyte dysfunctions, such as Megalencephalic leukoencephalopathy with subcortical cysts (MLC) and Alexander’s disease (AxD). Both MLC and AxD are highly disabling and incurable disease whose pathomechanisms are still unknown. The 3D models developed during the project will be used to study the dysfunctional molecular mechanism causing brain damages, possible biomarkers of disease progression and molecular targets for astrocyte functional rescuing. Moreover, in accordance with the results obtained above, specific functional assays will be set up to use the 3D brain models for the screening and repurposing of drugs with therapeutic potential.