INSTITUT PARIS DESCARTES NEUROSCIENCES COGNITION

FÉDÉRATION DE RECHERCHE EN NEUROSCIENCES

Neuroscience Seminar Series

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Salle des Conférences (R229)
Centre Universitaire des Saints-Pères
45 rue des Saints-Pères, 75006 Paris

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Investigating the pathophysiology of Amyotrophic Lateral Sclerosis using human induced pluripotent stem cell technology

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease for which a greater understanding of early disease mechanisms is needed to reveal novel theraputic targets. We are therefore investigating the pathophysiology of ALS using human induced pluripotent stem cell (iPSCs) technology. Utilising whole-cell patch-clamp recordings we have revealed a dysfunctional phenotype in MNs derived from iPSCs of ALS patients (harbouring TARDBP or C9ORF72 mutations). This phenotype is characterised by an initial period of hyperexcitability followed by a progressive loss of voltage-activated currents and action potential output. We are currently investigating the potential role of perturbed glial-neuronal interactions in these pathological changes. Our findings to date implicate early dysfunction or loss of ion channels as a convergent point that may contribute to the initiation of downstream degenerative pathways in ALS and highlight the importance of addressing MN function, perhaps by targeting ion channels, when designing new treatment strategies for ALS. In addition, the sensitive but robust pathophysiological phenotype we have revealed in this human MN-based model provides an invaluable tool for the screening of emerging ALS therapeutics.

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