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A Lecture Series Focused on Induced Pluripotent Stem Cells

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HUMAN CELLULAR MODELS OF NEURODEVELOPMENT AND PSYCHIATRIC DISORDER – NOVEL INSIGHTS INTO MECHANISMS AND POTENTIAL THERAPEUTIC AVENUES

The aetiology of neurodevelopmental and psychiatric conditions such as autism spectrum disorders (autism) and schizophrenia are thought to arise from a complex interaction between environmental and genetic factors. This has presented researchers with a number of challenges when trying to dissect mechanisms that underlie these disorders. Human induced pluripotent stem cells (hiPSCs) offer a unique opportunity to examine how environmental factors may both contribute to the underlying pathophysiology of conditions such as autism and schizophrenia, as well as understanding their potential therapeutic potential. Importantly, the use of patient-derived hiPSCs allow us to study the impact of environmental factors whilst being able to account for the complex genetic background associated with conditions such as autism or schizophrenia.

In this seminar I will discuss findings from 2 recent studies from our lab. In the first study I will discuss the impact of elevated levels of the cytokine interferon-gamma (IFNg) on the development of human forebrain neurons. Specifically, I will discuss how IFNg induces long-lasting cellular changes via a mechanism involving in increased expression of major histocompatibility complex (MHC) class I molecules, and alters gene expression changes similar to those seen in the brains of autistic and schizophrenic individuals. I will then go on to discuss preliminary findings from work aimed at providing mechanistic insight complimenting recent clinical studies showing that estrogen-based compounds exert beneficial effects in male and female schizophrenic patients. Here, we use a combination of patient-derived hiPSCs as well as drug-repurposing studies, to examine whether estrogen-based compounds can modulate the expression of synaptic proteins in hiPSC-neurons generated from healthy or schizophrenic male individuals.

These studies exemplify how hiPSC-based cellular models can be used to further understand the mechanisms underlying the impact of environmental factors in disorders with complex genetic components.