

# Programmed Cells from Basic Neuroscience to Therapy

Studies of human brain and neuronal function in phenotypically normal as well as neurological and psychiatric patients have been performed using noninvasive imaging methods. However, the spatial and temporal limitations do not permit single cell/neuron resolution. In addition, genomic and molecular studies of neurological and psychiatric patients are conducted on postmortem tissues often representing the end-stage of life and disease or from peripheral tissues and biopsies, and blood. The recent advances in programming somatic cells (PSC), including induced pluripotent stem cells (iPS) and induced neuronal phenotypes (iN), have changed the experimental landscape and opened new possibilities. These advances have provided an important tool for the study of human neuronal function as well as neurodegenerative and neurodevelopmental diseases in live human neurons in a controlled environment. Researchers are just beginning to take advantage of the many implications of studying developing neurons from living humans in vitro. For example, reprogramming cells from patients with neurological diseases allows the study of molecular pathways particular to specific subtypes of neurons, such as dopaminergic neurons in Parkinson's disease, motor neurons for amyotrophic lateral sclerosis, or myelin for multiple sclerosis. In addition, because PSC technology allows for the study of human neurons during development, disease-specific pathways can be investigated prior to and during disease onset. Detecting disease-specific molecular signatures in live human brain cells opens possibilities for early intervention therapies and new diagnostic tools. Importantly, it is now feasible to obtain gene expression profiles from neurons that capture the genetic uniqueness of each patient. Importantly, once the neurological neural phenotype is detected in vitro, the so-called disease-in-a-dish approach allows for the screening of drugs that can ameliorate the disease-specific phenotype. New therapeutic drugs could either act on generalized pathways in all patients or be patient-specific and used in a personalized medicine approach. However, there are a number of pressing issues that need to be addressed and resolved before PSC technology can be extensively used for clinically relevant modeling of neurological diseases. Among these issues are the variability in PSC generation methods, variability between individuals, epigenetic/genetic instability, and the ability to obtain

disease-relevant subtypes of neurons. Current protocols for differentiating PSC into specific subtypes of neurons are under development, but more and better protocols are needed. Understanding the molecular pathways involved in human neural differentiation will facilitate the development of methods and tools to enrich and monitor the generation of specific subtypes of neurons that would be more relevant in modeling different neurological diseases. The meeting of Fondation IPSSEN on “Programmed cells: from basic neuroscience to therapy” held in Paris, April 2, 2012, is well captured in this volume and reflects the cautious optimism exhibited by the participants of the meeting.

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