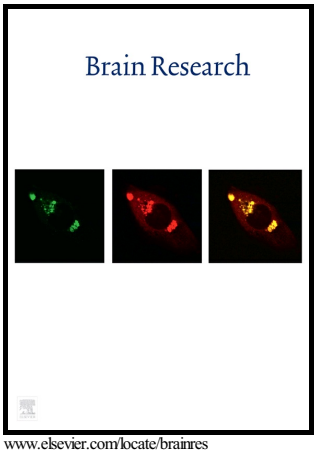

Studying human disease using human neurons

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PII: S0006-8993(16)30189-5
DOI: http://dx.doi.org/10.1016/j.brainres.2016.03.051
Reference: BRES44817

To appear in: *Brain Research*

Received date: 3 September 2015
Revised date: 8 March 2016
Accepted date: 31 March 2016

Cite this article as: Tim Ahfeldt, Nadia K. Litterman and Lee L. Rubin, Studying human disease using human neurons, *Brain Research* http://dx.doi.org/10.1016/j.brainres.2016.03.051

Working Title: Drug discovery using neurons derived from patients

Publication Title: Studying Human Disease Using Human Neurons

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Abstract

Utilizing patient derived cells has enormous promise for discovering new drugs for diseases of the nervous system, a goal that has been historically quite challenging. In this review, we will outline the potential of human stem cell derived neuron models for assessing therapeutics and high-throughput screening and compare to more traditional drug discovery strategies. We summarize recent successes of the approach and discuss special considerations for developing human stem cell based assays. New technologies, such as genome editing, offer improvements to help overcome the challenges that remain. Finally, human neurons derived from patient cells have advantages for translational research beyond drug screening as they can also be used to identify individual efficacy and safety prior to clinical testing and for dissecting disease mechanisms.

Drug discovery for neuronal disorders - why traditional approaches have failed

A patient diagnosed with Parkinson's disease (PD) in 1967 would have been introduced to the first symptomatic treatment, namely dopamine replacement therapy with Levodopa. A PD patient diagnosed in 2015 would receive the same treatment. Even as basic neurobiology research has yielded tremendous advances in understanding of the brain, disorders of the central nervous system (CNS) remain pervasive, debilitating, and largely without effective therapeutic options. PD is only one example of a neurological disorder but CNS diseases, which include neurodevelopmental, psychiatric, and neurodegenerative disorders, represent a large and growing disease burden, with few effective treatments (Bloom, 2011; Insel et al., 2013; Organization, 2006). Indeed, the prevalence of neurological disease is increasing due especially to the aging population. There is an urgent need to develop new drugs that can do more than treat the symptoms of a disease. Rather, we need to identify therapeutics that can cure disease, or at least halt disease progression. It is necessary to gain a detailed understanding of the mechanisms underlying disease in order to develop effective intervention strategies.