Vitamin B3 and Neurodevelopment in Parkinson's Disease

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Session Information

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Session Time: 1:45pm-3:15pm

Session Title: Therapy in Movement Disorders: Gene and Cell-Based Therapies

Location: Hall 3FG

Objective: This study aimed to investigate the potential of vitamin B3 to promote the conversion of stem cells to mature central nervous system (CNS) neurons.

Background: Vitamin B3 has been shown to play an important role during embryogenesis. Specifically, there is growing evidence that nicotinamide, the biologically active form of vitamin B3, plays a critical role as a morphogen in the differentiation of stem cells to mature cell phenotypes, including those of the CNS. Nicotinamide levels must be tightly regulated, with excess leading to neural damage, and deficiency leading to the condition, Pellagra, which manifests in a number of neural symptoms similar to Parkinson's. Detailed knowledge of the action of small molecules during neuronal differentiation is not only critical for uncovering mechanisms underlying lineage-specification, but also to establish more effective differentiation protocols to obtain clinically relevant cells for regenerative therapies for neurodegenerative conditions such as Parkinson's disease.

Methods: Nicotinamide was applied to developing mouse embryonic stem cells (mESCs) during their conversion towards a neural fate. Cells were assessed for survival, proliferation, differentiation and maturation.

Results: In the presence of an optimal dose of nicotinamide (10 mM), mESCs showed accelerated neural and neuronal differentiation, to yield higher numbers of dopamine neurons. Nicotinamide was shown to act in a dose-dependent manner in a defined time-window – with high doses (20mM) however causing toxicity. The mechanism of nicotinamide's action was through reduction in cell proliferation (i.e. cell cycle exit), rather than increased survival of neural progenitors. Nicotinamide alone was sufficient to generate dopaminergic neurons in similar numbers to current cell culture additives that have been used in previously published methods.

Conclusions: Our results show that, within an optimal dose range, nicotinamide is able to positively influence the conversion of embryonic stem cells to dopamine neurons, and therefore may be a critical factor for normal brain development. Thus, nicotinamide may offer a simple effective alternative supplement to enhance the use of stem cells as therapeutics for Parkinson's. An optimal maternal to foetal dietary dosage of nicotinamide – neither too low nor too high – could also be linked to protection from Parkinson's disease later in life.

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