Generation and characterization of a human dopamine producing cell system

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Country

Luxembourg

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Generation and characterization of a human dopamine producing cell system

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Research Abstract

Parkinson’s disease is a common neurodegenerative disorder characterized by the death of dopaminergic neurons.Current in vitro systems to study dopaminergic neurons have been derived from animal and human cells. The assessment of the dopamine (DA) status of these models is based on the presence of the key enzyme tyrosine hydroxylase (TH) or the DA transporter. However, preliminary data from our Metabolomics group showed that DA could not be detected by gas chromatography coupled to mass-spectrometry (GC-MS) in LUHMES and SH-SY5Y cells, both are commonly used models for dopaminergic neurons. This means, the presence of these enzymes does not necessarily mean DA is present in physiological levels.DA

production is a fundamental feature of dopaminergic neurons given its high impact on cell metabolism and its involvement in oxidative stress, one of the causes suspected to induce cell death in Parkinson’s disease.Another substantial aspect of a dopaminergic neuron model is its human origin. Indeed, the enzymes involved in DA synthesis and degradation as well as their regulation are species and tissue specific.To our knowledge, a human cellular model of dopaminergic neurons producing DA does not exist. Thus, the goal of this project is to analyze and understand the underlying regulatory network responsible for DA production, using the LUHMES cell line. First we will check for the presence of all components involved. Secondly, we will stimulate the system using different factors such as BH4 (a TH cofactor), hypoxia, methamphetamine and KCl which have been found to induce TH activity in other cell systems. Once this DA-producing system is established, we will use GC-MS and high performance liquid chromatography (HPLC)-MS to study the effects of DA on the metabolism of these DA-producing cells.

Further information available at:

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