Reconstruction and computational modelling of dopaminergic neuronal metabolism

https://neurodegenerationresearch.eu/survey/reconstruction-and-computational-modelling-of-dopaminergic-neuronal-metabolism/

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Country

Luxembourg

Title of project or programme

Reconstruction and computational modelling of dopaminergic neuronal metabolism

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FNR

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15/09/2013

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4

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Research Abstract

A computational model of dopaminergic metabolism could be used for interpretation of experimental data, queried to suggest new experiments and ultimately guide the development of drugs targeted toward the aetiology of Parkinson’s disease. However, at present, there exists no such computational model tailored to represent dopaminergic neuronal metabolism.The applicant shall reconstruct and computationally model the salient biochemistry of normal and diseased dopaminergic neurons. Firstly, omics data will be combined with published algorithms to generate a draft dopaminergic specific reconstruction, to obtain a subset of the biochemical reactions in the recently published cell type unspecific reconstruction of human metabolism.

Secondly, extensive manual curation of literature will be used to reconcile this draft reconstruction with known biochemical features of normal dopaminergic neurons. Using standard procedures, the reconstruction will be converted into a constraint-based computational model of dopaminergic metabolism. Iterative rounds of reconstruction, model prediction and reconciliation with existing experimental data shall create a computational model which is formal synthesis of current knowledge on dopaminergic neuronal metabolic function.The applicant shall test the accuracy of the dopaminergic neuronal metabolic model by qualitatively comparing predicted active pathways with pathways established experimentally to be active, using mass spectrometry to intracellularly trace isotopic labels added to in vitro models of dopaminergic neurons. This effort will be facilitated by algorithmic tabulation of the mapping between substrate and product atoms in each reaction of the dopaminergic metabolic model.The applicant shall conduct a computational sensitivity analysis of metabolic reactions in the model that energetically support normal neurophysiological activity. By comparison of predicted sensitive reactions, with literature on reactions known to be involved with the pathogenesis of Parkinson’s Disease, we shall test the hypothesis that dopaminergic neurons are particularly sensitive to neurodegeneration due to negative energy balance.

Further information available at:

https://www.findaphd.com/search/projectdetails.aspx?PJID=53275#

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Luxembourg

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