Manipulation of the Direct/Indirect-Pathway Neurons in Striatum by Use of Genetically Reengineered Receptors to Restore Motor Function in Parkinsonian Mice

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Denmark

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Manipulation of the Direct/Indirect-Pathway Neurons in Striatum by Use of Genetically Reengineered Receptors to Restore Motor Function in Parkinsonian Mice

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1

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Research Abstract

Parkinson’s disease (PD) is the most common neurodegenerative movement disorder characterized by progressive loss of dopaminergic neurons in the substantia nigra (SN) with unknown etiology and affects approximately 1% of the elderly population. Clinical manifestations

include motor phenotypes such as tremor, bradykinesia and rigidity. Progressive loss of dopaminergic neurons in SN attenuates dopamine receptor activation in striatum which compromises dopaminergic signaling by shifting the balance between the direct- and indirect-pathway. The prevailing model of basal ganglia function states that the direct- and indirect pathway neurons show bidirectional control of movement in which activation of direct pathway facilitates movement while activation of indirect-pathway inhibits movement. Recent approaches using optogenetics have though questioned the opposing roles in motor function but this technique might not be ideal for probing activation of subcortical structures in motor function. Genetically reengineered G-protein coupled receptors (DREADDs) more closely mimic native in vivo signaling by influencing intracellular signaling cascades and can be used to understand dysfunctional dopaminergic signaling in PD.

Further information available at:

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