Repositioning Gliptins for Parkinsons Disease Treatment

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Contact information of lead PI
Country

USA

Title of project or programme

Repositioning Gliptins for Parkinsons Disease Treatment

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 956,851.38

Start date of award

30/09/2015

Total duration of award in years

2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

gastric inhibitory polypeptide receptor, SERPINA4 gene, glucagon-like peptide, exenatide, Parkinson Disease

Research Abstract

? DESCRIPTION (provided by applicant): Dipeptidyl protease-4 (DPP-4) inhibitors – also known as gliptins – are widely used in the effective treatment of type 2 diabetes to safely regulate bloo

glucose levels. DPP-4 is the key enzyme responsible for the metabolism of the endogenous incretins, glucagon-like peptide-like-peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) whose elevated levels in brain, we hypothesized, would provide neurotrophic/neuroprotective actions in cellular and in vivo rodent models of Parkinson’s disease (PD). On evaluating several DPP-4 inhibitors, brain and plasma incretin levels were, indeed, substantially elevated in rodents, and this resulted in amelioration of Parkinsonism and elevations in brain dopamine levels in a well- characterized acute rodent PD model as well as reducing toxicity in vitro cellular model. Our proposed studies will extend our evaluation of dipeptidyl protease-4 (DPP-4) inhibitors as a new treatment strategy for Parkinson’s disease by assessing the DPP-4 inhibitor sitagliptin in chronic toxin and genetics rodent PD models. In these chronic rodent PD models, we will evaluate neurorestorative activity of sitagliptin by measuring behavioral, biochemical, and immunocytochemical parameters. In addition, mechanistic studies will be carried out to correlate sitagliptin efficacy with analysis of ER stress/unfolded protein responses, mitochondrial function and neuroinflammation.

Lay Summary
PUBLIC HEALTH RELEVANCE: Our initial dipeptidyl protease-4 (DDP-4) inhibitor studies defined this drug class as beneficial in well characterized cellular and rodent acute Parkinson’s disease (PD) models. Our aim is to evaluate whether the beneficial actions of clinically relevant and doses of DPP-4 inhibitors to elevate incretin GIP and GLP-1) levels will translate to chronic rodent PD models as a key step to de-risk clinical translation. If successful, our proposed studies will lay the essential groundwork for a clinical trial of the DPP-4 inhibitor sitagliptin i PD – by defining a drug dose for central incretin actions.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

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