Testing a combination therapy with Ras-ERK and mTor inhibitors for L-DOPA induced dyskinesia

https://neurodegenerationresearch.eu/survey/testing-a-combination-therapy-with-ras-erk-and-mtor-inhibitors-for-ldopa-induced-dyskinesia/

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United Kingdom

Title of project or programme

Testing a combination therapy with Ras-ERK and mTor inhibitors for L-DOPA induced dyskinesia

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Parkinson's UK

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€ 203,370

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01/12/2014

Total duration of award in years

2

Keywords

Research Abstract

L-DOPA remains the most effective treatment for alleviating Parkinson's disease (PD) symptoms but causes currently untreatable severe motor side effects, collectively known as levodopa-induced dyskinesia (LID). Recent evidence indicates that a key pathogenic factor for LID, linked to abnormally high dopamine-mediated responses, is the hyperactivation in the striatum of both the Ras-ERK and the mTor signalling pathways. Previous work by the

applicant, funded by Parkinson's UK, identified a clinically relevant Ras-ERK inhibitor that, given systemically, is not only able to block cell signalling in a mouse model of PD and LID but also to partially revert already established dyskinesia. Since the inhibition of LID with maximal doses of this Ras-ERK inhibitor is incomplete, we hypothesise that a combination approach with a selected mTor inhibitor may provide a better therapeutic outcome. Hence, in this project we will test 5 distinct mTor inhibitors, already in advanced stage of clinical development for cancer treatment, for their ability to prevent in mice abnormal involuntary movements (AIMs), the rodent correlate of LID.

Further information available at:

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Investments < €500k

Member States:

United Kingdom

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Years:

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