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mGluRpatho: Group III metabotropic glutamate receptors (mGluRs): from new molecules to therapeutic development for the treatment of Parkinson's disease

Project Description

Restoring the balance between excitatory and inhibitory circuits in the basal ganglia, following the loss of dopaminergic (DA) neurons of the substantia nigra pars compacta in Parkinson's disease (PD), represents a major challenge to treat Parkinsonian patients and avoid long-term L-DOPA induced dyskinesia. Recent studies have focused on the modulatory action of metabotropic glutamate receptors (mGluRs) on neurodegenerative diseases including PD and subtypes 4 and 7 mGluRs (belonging to group III) are largely expressed in the basal ganglia. The objectives of the project are to gather the expertise of five different international teams and use their individual skills in chemistry, pharmacology, behaviour, quantitative morphology and molecular biology to achieve a complete picture of "candidate" molecules for PD treatment that have agonist action at mGluR4 and 7, from their chemical structure-based design to their physiological action. Analyzing the functional and cellular impact of treatments activating these receptors will be essential to identify the best pharmacological anti-glutamate neuroprotective and neurorestorative strategy alternative to surgery in PD treatment.

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