POSTDOCTORAL FELLOW

Université catholique de Louvain, Brussels, Belgium

We are seeking to recruit a Postdoctoral Fellow (international mobility) to join the Alzheimer dementia research group at the Institute of Neuroscience.

Description of the project

Alzheimer's disease (AD), the most frequent cause of dementia in the elderly, is characterized by loss of autonomy due to significant ***cognitive impairment***, associated with the presence of typical lesions, resulting from the deposition of abnormal proteins in the brain. Intraneuronal hyperphosphorylated protein tau accumulates in neurofibrillary tangles, and extracellular deposits of senile plaques contain aggregated amyloid peptide Aβ derived from the amyloid precursor protein APP. The exclusive focus on established lesions has not been very successful so far in developing effective therapies susceptible to alter the disease course.

Regulation of cognitive processes depends on the fine-tuning between excitatory and inhibitory neurotransmission. Gamma-amino-butyric acid (GABA) is the primary inhibitory neurotransmitter. Binding of GABA to $GABA_A$ receptors leads to the flow of negatively charged Cl^- ions into the cell, resulting in hyperpolarization. While GABA is inhibitory in the mature brain, it is primarily excitatory in the developing brain. ***Since $GABA_A$ receptors predominantly conduct Cl^- ions, the state of GABAergic transmission, excitatory versus inhibitory, is essentially determined by the electrochemical Cl^- gradient, which depends on the intracellular concentrations of Cl^-. In neurons, the intracellular concentration of Cl^- is controlled by expression levels of NKCC1, a Cl^- importer, and KCC2, a neuronal Cl^- extruder.***

The present project is based on our recent observation that ***APP regulates expression of KCC2 in neuronal networks in culture.*** Therefore, our working hypothesis is that APP could affect GABAergic neurotransmission by modifying the electrochemical Cl^- gradient. Such modifications could have an important impact on cognition and, in particular, on memory functioning in AD patients, in which we observed a down-regulation of KCC2 expression in post-mortem brains**.** ***We aim to characterize in depth the signature of GABAergic neurotransmission in vitro, in animal models, in patients at early stages of AD, and in asymptomatic individuals carrying a high risk of developing AD.***

Additional information

The contract duration is for 2 years with the possibility of an extension up to 3 years

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