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Research
The isoform B of inositol 1,4,5-trisphosphate 3-kinase (ITPKB) generates inositol 1,3,4,5-tetrakisphosphate (IP4). IP4 is considered as a potential modulator of calcium signalling and is implicated in the modification of intracellular localization of protein containing a PH (Plekstrin Homology) Domain in competition with PIP_3.
In 2006, a microarray study has shown that ITPKB mRNA is increased in brain tissue of Alzheimer's disease (AD) patients. AD is the most common form of dementia and is characterised by two types of neuropathological lesions: intracellular neurofibrillary tangles (NFT), composed by aggregated hyperphosphorylated Tau, and senile plaques mainly composed of extracellular amyloid Aβ peptide.
To determine if the hypothesis that ITPKB dysfunction might play a role in AD, the expression of ITPKB was studied in brain tissue of AD patients and in transgenic models of AD.
We observed that, physiologically, ITPKB mRNA and protein are expressed by neurons and astrocytes in human and mouse brain. A higher expression of ITPKB was found by western blotting in the cerebral cortex of AD patients. By immunocytochemistry, a strong ITPKB immunoreactivity was observed in dystrophic neurites surrounding the amyloid Aß deposits in senile plaques in AD patients. Identical results were obtained in APP/PS1 transgenic mice, a model of AD by overexpression of mutant APP and PS1 proteins. An ITPKB immunoreactivity was not directly associated to the NFT in AD and in Tau transgenic mice, another model of AD and tauopathies by overexpression of mutant Tau protein.
To further investigate the implication of ITPKB in Alzheimer's Disease, new strains of mice, APP mice overexpressing specifically ITPKB in neurons or in astrocytes, have been generated and are being studied.

Selected publications
Stygelbout, V., Leroy, K., Pouillon, V., Schurmans, S. and Brion, J. P. (2008) Expression of inositol 1,4,5-trisphosphate 3-kinase B in Alzheimer's disease and in transgenic models. In: *11th International Conference on Alzheimer Disease (ICAD)*. Suppl. to Alzheimer's & Dementia, vol. 4, pp T185., Chicago (USA).