Ilse Dewachter

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Alzheimer dementia

Ir Bio-engineering, KUL, 1993
PhD Bio-Medical Science, KUL, 2000

Current Position

FNRS Permanent Researcher
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Current Project Members

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Keywords
Alzheimer Disease-Amyloid Precursor Protein-Tau Protein-synaptic and cognitive function-Transgenic mice.

Science

Research is focused on the study of the pathological mechanisms of amyloid and Tau and the identification of their modifiers as potential therapeutic targets. Using in vivo models that recapitulate features reminiscent for AD including amyloid pathology, cognitive and synaptic dysfunction, we previously analysed the modulatory role of α, β, and γ-secretase, and of different anti-amyloid directed therapeutic strategies. In this context, we identified, in collaboration with F. Fahrenholz, ADAM10 as alpha-secretase exerting enzyme in vivo in neurons. Lack of success of anti-amyloid directed clinical trials in diagnosed AD patients, has emphasized the preventive nature of anti-amyloid directed therapies, the need for models with combined amyloid and Tau-pathology, and the need for combined therapies aiming at amyloid and Tau concomitantly. We have generated mice with robust combined amyloid and Tau-pathology. This model not only recapitulates amyloid induced Tau-pathology, but also demonstrates the contribution of

amyloid induced Tau-pathology in cognitive and synaptic dysfunction. This model is used to further study the link between amyloid and Tau-pathology with an emphasis on the role of dysregulated kinases. We investigate the pathogenetic and physiological role of Tau, by identification and mechanistic analysis of Tau-modifiers in vitro and in vivo, based on high-throughput screening and a Tau-interactome map. This analysis includes the study of mechanisms and functional repercussions of prion-like spreading of Tau-pathology.

Recent Research Projects

IWT Feasibility Studies (x2) Analysis and validation of Tau-interacting targets identified by Tau-interactome mapping - Period: 2011-2013 - Role: PI

IWT/O&O:Towards an integrated drug discovery platform for Tau-pathogenesis - Period: 2013 – 2015- Role: PI

FNRS Impuls-financing (MIS) + prolongation : Identification of Tau and Amyloid-Tau modifiers - Period: 2012-2015 - Role: PI

Convention du Fonds National de la Recherche Scientifique FRSM n° 3.4579.12 - Le rôle du précurseur du peptide amyloïde dans la maladie d'Alzheimer - Period: 2012 – 2015 - Role: co-P.I.

Convention de la Fondation Médicale Reine Elisabeth FMRE - Alteration of cholesterol turnover in Alzheimer disease: molecular mechanisms and therapeutic applications- Period: 2014 – 2016 - Role: co-P.I.

Selected Publications

Stancu IC, Ris L, Vasconcelos B, Marinangeli C, Goeminne L, LaPorte V, Haylani LE, Couturier J, Schakman O, Gailly P, Pierrot N, Kienlen-Campard P, Octave JN, **Dewachter I.** Tauopathy contributes to synaptic and cognitive deficits in a murine model for Alzheimer's disease. FASEB J. 2014 Mar 6 (I.F.: 5.704)

Chapuis J et al. Increased expression of BIN1 mediates Alzheimer genetic risk by modulating tau pathology. Mol Psychiatry. 2013 Nov;18(11):1225-34. (I.F.: 14.897)

Jaworski T*, **Dewachter I***, Lechat B*, Gees M, Kremer A, Demedts D, Borghgraef P, Devijver H, Kügler S, Patel S, Woodgett JR, Van Leuven F. GSK-3α/β kinases and amyloid production in vivo. Nature. 2011 Dec 7;480(7376) (I.F.: 38.597)

Postina R*, Schroeder A*, **Dewachter I**.*, Bohl J, Schmitt U, Kojro E, Prinzen C, Endres K, Hiemke C, Blessing M, Flamez P, Dequenne A, Godaux E, van Leuven F, Fahrenholz F. A disintegrin-metalloproteinase prevents amyloid plaque formation and hippocampal defects in an Alzheimer disease mouse model. J Clin Invest. 2004 May;113(10):1456-64. (I.F.: 12.812)

Dewachter I, Van Leuven F. Secretases as targets for the treatment of Alzheimer's disease: the prospects. Lancet Neurol. 2002 Nov;1(7):409-16. (I.F.: 23.917)

Dewachter I, Reversé D, Caluwaerts N, Ris L, Kuipéri C, Van den Haute C, Spittaels K, Umans L, Serneels L, Thiry E, Moechars D, Mercken M, Godaux E, Van Leuven F. Neuronal deficiency of presenilin 1 inhibits amyloid plaque formation and corrects hippocampal long-term potentiation but not a cognitive defect of amyloid precursor protein [V717I] transgenic mice. J Neurosci. 2002 May 1;22(9):3445-53. (I.F.: 6.908)

All publications