

Centre de Neurosciences Psychiatriques CNP SEMINAR

ANNOUNCEMENT

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"Novel anti-inflammatory drugs for the treatment of neurodementing diseases?"

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Deregulation of the immune system plays a critical role for the pathogenesis of neurodementing diseases. We have recently provided evidence that the tetravalent guanylhydrazone CNI-1493, an inhibitor of proinflammatory cytokines, works in animal models of neurodegeneration such as Alzheimer's (AD) and Parkinson's disease. In both models, we achieved neuroprotective effects by peripheral administration of CNI in the absence of detectable transport of the compound across the blood brain barrier (BBB). Subsequently, a hydrolysis resistant derivative of CNI-1493 has recently been developed which displays improved transport across the BBB. In a further project we are evaluating the effects of a new inhibitor for the cytokine macrophage migration inhibitory factor (MIF) for the possible future treatment of AD patients. The immune modulator MIF has recently been described to be elevated in the CSF of mild cognitive impairment (MCI) and AD patients.

Selected Publications:

- 1. Bacher M, Dodel R, Aljabari B, Keyvani K, Marambaud P, Kayed R, Glabe C, Goertz N, Hoppmann A, Sachser N, Klotsche J, Schnell S, Lewejohann L, Al-Abed Y: CNI-1493 inhibits Abeta production, plaque formation, and cognitive deterioration in an animal model of Alzheimer's disease. J Exp Med 205:1593-9, 2008
- 2. Popp J, Bacher M, Kölsch H, Noelker C, Deuster O, Dodel R, Jessen F: Macrophage migration inhibitory factor in mild cognitive impairment and Alzheimer's disease. J Psychiatr Res. 2009 May;43(8):749-53.
- 3. Dodel RC, Balakrishnan K, Keyvani K, Deuster O, Neff F, Andrei-Selmer LC, Roskam S, Balzer-Geldsetzer M, Al-Abed Y, Du Y, Bacher M: Naturally occurring autoantibodies against beta-amyloid: Their role in Alzheimer's disease. J Neuroscience, 31:5847-54, 2011
- 4. Noelker C, Stuckenholz V, Reese JP, Alvarez-Fischer D, Sankowski R, Rausch T, Oertel WH, Hartmann A, van Patten S, Al-Abed-Y, Bacher M: CNI-1493 attenuates neuroinflammation and dopaminergic neurodegeneration in the acute MPTP mouse model of Parkinson's disease. Neurodegener Dis. 12:103-10, 2013

