

Alzheimer's Disease & Dementia

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The place of tau in the pathology, treatment and prevention of Alzheimer's disease and frontotemporal dementia

Claude M Wischik TauRx Therapeutics, UK

In Alzheimer's disease (AD), the microtubule associated protein Tau, is implicated in a self-amplifying aggregation cascade which kills nerve cells and transmits the pathology to otherwise healthy neurons, spreading the disease throughout the brain in manner that is quantitatively linked to the degree of clinical dementia. A similar process occurs for Synuclein in PD.

The Tau Aggregation Inhbitors (TAIs) we have developed block this process in cell models and reduce Tau pathology in transgenic mouse models. The first of these (methylthioninium, MT) to be tested in a large Phase 2 clinical trial in AD reduced the rate of disease progression by 90% over 12 months on clinical and imaging endpoints. The brain concentration required for clinical efficacy is the same as that required for TAI activity in model systems. Phase 3 trials in mild and moderate AD are currently underway globally (including Canada) aiming to confirm the Phase 2 results, using an improved version of the drug (LMTX*). We are also conducting a Phase 3 trial in FTD, where either Tau or TDP-43 proteins aggregate, both blocked by LMTX*. The initial results will be available in the first half of 2016.

If the Phase 3 trials are successful, LMTX^{*} could be used preventatively, since Tau aggregation affects about 50% of the over-45 population, but progresses slowly at the early stages. LMTX^{*} also reduces pathology in a Synuclein mouse model of PD, so we aim to conduct trials with LMTX^{*} in PD in the future.

Biography

Claude M Wischik holds the Chair in Old Age Psychiatry at the University of Aberdeen in Scotland, and is Executive Chairman of TauRx Pharmaceuticals. He studied medicine in Australia, completed his PhD at the Laboratory of Molecular Biology in Cambridge, and also higher psychiatric training in Cambridge. He was the first to identify Tau protein as the main constituent of the Alzheimer tangle and developed the first Tau Aggregation Inhibitors. He has published 121 papers and holds 11 patent groups based on his work with over 40 individual patents.

cmw@taurx.com

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