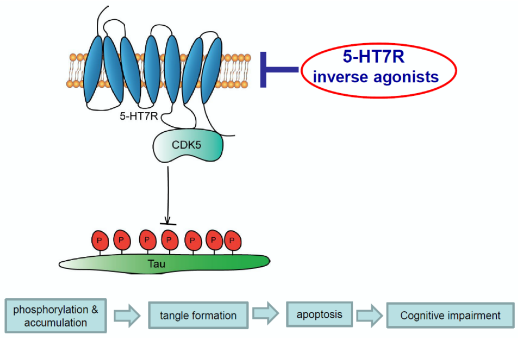
Technology Offer

Novel treatment of dementia-associated taupathies

Reference Number 23-00065

Challenge

One of the main causes of dependency and disability among the elderly worldwide is dementia. In 60-70% of the cases, the underlying condition of dementia is Alzheimer's disease (AD). At present, only 5 medications for the treatment of AD are approved, all of which treat symptoms. The mechanism of pathogenicity in tauopathies has been shown to be the hyperphoshorylation of tau protein which in turn results in the formation of tau tangles in nerve cells and leads to network malfunctions and neuronal death. The challenge is to target the pathogenic mechanism pharmaceutically.



Impact of 5-HT7R inverse agonist on Tau-mediated pathology.

Technology

Candidate molecules are serotonin 5-HT7 receptor inverse agonists for use in preventing or treating tauopathies. The inverse agonist prevents hyperphosphorylation of the tau protein. In the neuroblastoma cell line model expressing mutated human tau, an inverse agonist reversed accumulation tau, p-tau and tau aggregates. Immunfluorescence confirmed the prevention of tau tangle formation. Blockade of constitutive receptor activity in neurons that overexpressed pathological Tau prevented Tau hyperphosphorylation, aggregation, and neurotoxicity. Moreover, receptor knockdown in prefrontal cortex fully abrogated Tau-induced LTP deficits and memory impairments. Application of approved drugs possessing inverse agonism towards the 5-HT7R demonstrate similar favorable effects both *in vitro* and *in vivo*.

Commercial Opportunity

In-licensing and/or co-development.

Development Status

In vivo data. Preclinical development.

Patent Situation

Priority 2018.

Further Reading

Hogendorf et al., 2019. Fluorinated indole-imidazole conjugates: Selective orally bioavailable 5-HT7 receptor low-basicity agonists, potential neuropathic painkillers. EJMC.
Bijata et al., 2017. Synaptic remodeling depends on signaling between serotonin receptors and the extracellular matrix. Cell Reports.
Speranza et al., 2017. Serotonin 5-HT7 receptor increases the density of dendritic spines and facilitates synaptogenesis in forebrain neurons. J of Neurochem.
Wirth et al., 2017. How serotonin receptors regulate morphogenic signalling in neurons. Prog Neurobiol.
Butzlaff and Ponimaskin, 2016. The role of Serotonin Receptors in Alzheimer's disease. Opera Med et Physiol.

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