

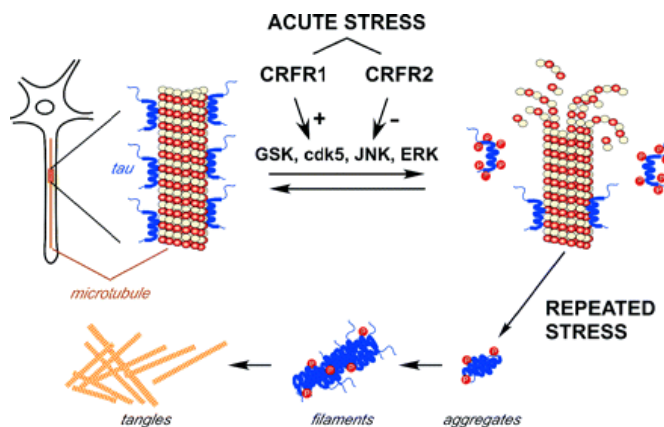
## CRFR1 antagonists: Therapeutic for Alzheimer's Disease and related tauopathies

Alzheimer's Disease and related neurodegenerative disorders are characterized by the formation of neurofibrillary tangles and  $\beta$ -amyloid plaques in the brain. Tangles consist of hyperphosphorylated forms of the microtubule-associated protein tau. Because of the key role that excessive tau phosphorylation plays in Alzheimer's neuropathology, understanding the mechanisms resulting in tau phosphorylation may be key towards identifying a cure.

Studies with rodent models suggest that stress induces tau phosphorylation. The corticotropin-releasing factor (CRF) signalling system plays an essential role in initiating pituitary-adrenal, behavioral and autonomic responses to stress. Indeed, acute stress increases tau phosphorylation, and situations of repeated stress promote the development of tangle pathology as depicted below. Upon specifically inhibiting the CRF Receptor 1 (CRF-R1) pathway, stress-induced tau phosphorylation is eliminated. Recent studies implicate this same signaling system in the development of amyloid plaques in mouse models of Alzheimer's Disease.

Several CRF-R1 selective antagonists are currently in clinical development for various disorders including anxiety, depression, alcoholism and ischemia.

Dr. Sawchenko of the Clayton Foundation Laboratories for Peptide Biology at the Salk Institute, has demonstrated through exciting results in animal studies that these antagonists may be highly effective therapeutic agents to treat tauopathies including Alzheimer's Disease.



J Neurosci. 2007 Jun 13;27(24):6552-62.

### Intellectual Property

Intellectual property protection (US, EP and CA) for this technology is owned by Research Development Foundation:

US12/663805 METHODS FOR TREATMENT AND PREVENTION OF TAUPATHIES AND AMYLOID BETA AMYLOIDOSIS BY MODULATING CRF RECEPTOR SIGNALING

*Methods for treating or preventing tauopathies and/or A-beta amyloidosis by modulating CRF receptor signaling. Accumulation of hyperphosphorylated tau protein in the CNS may be reduced by administration of CRF-R1 selective antagonists and/or CRF-R2 selective agonists. For example, in some aspects, methods for preventing the onset of disease by administration of CRF-R1 selective antagonist are provided.*

*Available for licensing*

**For more information, please contact our business development unit:**

Dr. Alexandra Richardson +41-22-382-3802 or +41-76-342-7147 - arichardson@claytonbiotech.com