IUSM-Purdue TREAT-AD Center Target Enabling Report
Proline-rich Tyrosine Kinase 2 beta (PTK2β): Protein Constructs, Cryo-EM, Biophysical Assay, and Biochemical Assay

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SUMMARY OF PROJECT

Alzheimer's Disease (AD) is associated with the progressive memory loss and cognitive impairment that occurs as age progresses. The amyloid beta (Aβ) plaque-induced neuron death in the aging brain is believed by many to be the primary cause and diagnosis of AD [1]. To date, there is a paucity in therapeutic interventions that can slow or halt the AD progression. A non-receptor proline-rich protein tyrosine kinase (PTK2b) is a calcium-dependent kinase highly enriched in forebrain neurons [2]. It is also a signaling protein involved in various pathways resulting in contrasting functions [3]. Traditionally, PTK2b has been considered an oncogene and targeted for development of anti-cancer drugs. Its diversity in function and recent bioinformatic analysis has revealed a potential role of PTK2b in the risk for late-onset AD [4]. Based on existing studies, the complex mechanisms of PTK2b are hypothesized to contribute to amyloid toxicity and tauopathy that may lead to a neuronal functional deficits in the microglia [5]. Thus, the implication that PTK2b activity contributes to the development of AD at various stages supports the hypothesis that novel therapeutics that selectively inhibit PTK2b may be developed to treat AD.