TREAT-AD
TaRget Enablement to Accelerate Therapy Development for AD

IUSM-Purdue TREAT-AD Center Target Enabling Report
LYN, Src family tyrosine-protein kinase: Protein Constructs, Cryo-EM, and Biochemical Assay

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SUMMARY OF PROJECT

Alzheimer's Disease (AD) is a neurodegenerative disease that progresses with age and is one of the most common forms of dementia. This disease is also associated with cognitive impairment due to the result of neural death in the various areas of the brain [1]. The pathogenesis of AD is associated with neural death caused by Amyloid-beta 1-42 ($A\beta_{1-42}$) and tau hyperphosphorylation [2][3]. The hyperactivity of a non-receptor tyrosine kinase Lyn was observed in the brains of AD patients [4]. Also, Lyn was associated with promoting brain cell death by exposure to $A\beta_{1-42}$ [5]. Lyn is a member of the *Src* family kinases (SFKs) that are well-known for their implication in cell transformations and cancer progression [6]. Recent studies also implicate the role of the Lyn in the progression of the neural death promoted by the $A\beta_{1-42}$ peptide. One such reported interaction is the hyperactivity of Lyn which results in the phosphorylation of Fcγ receptor IIb2 (FcγRIIb2). Such studies implicate that Lyn has a crucial role in AD and therefore targeting Lyn with small molecule compounds has potential for new-age treatment options. The goal of this project are to structurally enable Lyn for structure-based drug design and to biochemically and biophysically characterize the interaction of inhibitors with Lyn.