The Effects of Phenylalanine Mutants on the Aggregation of Amylin

Ayanna Stewart, Natasha Charles & Ranjit Singh
Mentor(s): Professor Ruel Desamero & Adam Profit
CUNY York College

Amylin aggregation plays a crucial role in the formation of amyloid deposits associated with type 2 diabetes, which contributes to pancreatic β-cell dysfunction and disease progression. This project investigates the synthesis and characterization of the pentapeptide FLPN-Xaa and its phenylalanine mutants to assess their potential in inhibiting this aggregation. Studies indicate that the pentapeptide FLPNF interacts with human islet amyloid polypeptide (hIAPP) to reduce amyloid formation. The pentapeptide FLPNF is derived from residues 11-15 (RLANF) of human islet amyloid polypeptide (hIAPP) (Yue Shi, Wu Lv et al., 2019). This region falls within the critical amyloidogenic sequence 8-20 of hIAPP, which is known to lead to amyloid aggregation. By introducing mutations at the phenylalanine position, we aim to investigate how structural modifications affect amyloid formation. To explore this, FLPNW, FLPNY, FLPN Phe-NH_2, FLPN-Phe-(4-NO_2), FLPN-Phe-(4-CN), FLPN-Phe-(4-guanidino) and FLPN-Phe-4-NH have been synthesized using solid-phase peptide synthesis (SPPS). These peptides were cleaved, purified, and analyzed using high-performance liquid chromatography (HPLC) and mass spectrometry (MS) to confirm their purity. Further analysis will use turbidity assays, Thioflavin T fluorescence, circular dichroism (CD), and molecular dynamics (MD) simulations to assess the structural properties of the peptides and their ability to inhibit fibril formation. These analyses will also evaluate how polarity modifications at the phenylalanine position influence the propensity for amyloid aggregation.