Designing Peptide Inhibitors to Prevent Amyloid Beta Aggregation

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In Alzheimer's disease, a progressive neurodegenerative disease, a key pathological feature of the is the accumulation of amyloid-ß peptides in the brain, which aggregate to form plaques that disrupt neuronal function and contribute to cognitive decline. Current therapeutic strategies have largely focused on small molecule inhibitors; however, these compounds often struggle to effectively bind the large protein interfaces involved in amyloid aggregation. Peptide inhibitors offer a promising alternative due to their higher specificity and ability to interact with larger binding surfaces on target proteins. In this project, I aimed to identify the potential of short peptide inhibitors to bind amyloid-ß and disrupt its aggregation process. Peptides were designed and structurally modeled using UCSF ChimeraX. The amyloid-ß structure was obtained from the Protein Data Bank and prepared through hydrogen addition and energy minimization. Protein–peptide docking simulations were then conducted using the HDOCK to predict binding interactions between amyloid-ß and candidate peptide inhibitors. Docking scores and predicted binding interfaces were analyzed to identify peptides with the strongest affinity for aggregation-prone regions of amyloid-ß. The results of this study aim to identify peptide sequences with strong predicted binding to amyloid-ß that may inhibit fibril formation. By using computational structural biology tools to screen potential inhibitors, this research demonstrates an accessible method for early-stage therapeutic discovery and contributes to ongoing efforts to develop treatments targeting protein aggregation in neurodegenerative diseases.

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