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Multivalent polymer conjugate inhibits aggregation of beta amyloid and disassembles amyloid fibrils – potential for a polymer therapeutic

Beta-amyloid (Aβ) is a member of a class of proteins that are intrinsically unstable. Aβ normally exist as random coil polypeptide. However, the protein will rearrange to the beta-sheet structure resulting in aggregation followed by fibril formation in the brain. Fibrils become the plaques that are observed in Alzheimer's patients. In patients that develop Alzheimer's disease, abnormal levels of Aβ protein accumulate in the brain and aggregate. Aβ protein aggregates and fibrils are believed to be neurotoxic leading to neurodegeneration and cell death. We demonstrated (Y. Song, et.al. JACS, 2014, 136:5233-5236) that a multivalent polymer-peptide conjugate (mPPC) is a very potent inhibitor of Aβ aggregation. The polymer consists of a linear N-(2-hydroxypropyl)-methacrylamide backbone appended with multiple copies of a pentapeptide. As a monomeric strand, this pentapeptide is known to bind to the beta sheet region of the Aβ protein. The enhanced local concentration of the pentapeptide in mPPC dramatically enhances the interference of beta-sheet formation with Aβ. Moreover, mPPC also disassembles amyloid fibrils leaving nanoparticle complexes of mPPC and Aβ aggregates (Y. Song, et.al. JACS, 2017, 139:4298-4301). Synthetic polymers, like mPPC, represent an untapped class of therapeutic agents. Polymers offer potential benefit as therapeutic agents when designed with specific binding agents and other selective functionality. To realize this potential further research and development is needed to provide discrete chemical entities with defined molecular weights and uniquely positioned functional moieties. Precision polymers are evolving to create a new class of discrete chemical entities to further enhance medical applications.

Biography

Edwin Moore has 40 years of biopharmaceutical, pharmaceutical, and clinical diagnostic industry experience from global companies, Baxter Healthcare Corp and Abbott Laboratories, in R&D product development. Since retiring he has enjoyed research, teaching, and mentoring startup companies at University of Illinois, Champaign-Urbana campus, and consulting with BioPhia Consulting, Inc. He was a postdoc at University of Michigan, and received his PhD from Cornell University in Biochemistry, B.S. from University of Illinois in Biochemistry.

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