Chemical Biology Seminar

"Trehalose glycopolymer as an excipient for insulin stabilization: safety, mechanism, optimization, and fluid properties"

Abstract: Biopharmaceutics are widely used to treat serious diseases, but the architectural and chemical complexity that makes proteins good therapeutics renders them susceptible to degradation and aggregation during manufacturing, transportation, and storage. Loss of intact biopharmaceutics causes patient under-dosing as well as adverse reactions. With the growth of biopharmaceuticals coming to market, the need increases for benign excipients to stabilize proteins against environmental stresses without posing a safety concern. A class of glycopolymers bearing a pendant trehalose, a natural sugar, were developed by our group and demonstrated the ability to stabilize a range of biopharmaceuticals. However, this research area had not yet explored the trehalose polymer for safety, mechanism of stabilization, physical properties, or potential optimization. This talk focuses on the ongoing efforts to expand our knowledge base in applying the methacrylate trehalose polymer as an excipient to formulate biopharmaceuticals. In particular, I will highlight the glycopolymer's benign immunogenic, excretion, and biodistribution behaviors as well as how proteins are unaffected *in vivo* by the polymer. Next, because the mechanism by which proteins are stabilized as well as the conformation in which they are stabilized affects their onset of activity, I will show how the glycopolymer stabilizes insulin. Due to the importance of patient comfort and compliance, I will finally present my research into the fluid properties of the glycopolymer, optimization of insulin formulations, and optimized formulations properties. Altogether, this work shows specifically how insulin is stabilized by the methacrylate trehalose polymer and, more broadly, that the glycopolymer can be broadly applied as an excipient to stabilize therapeutic macromolecules safely and without significantly changing the *in vivo* response or physical properties.

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