Investigating the process of fibril formation in novel human lysozyme variants

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Project Proposal:

Aggregation in vivo is associated with a wide range of human disorders including Alzheimer’s disease, systemic amyloidosis and type II diabetes. Due to the prevalence of these disorders, it is crucial to increase our understanding, on a molecular basis, of the mechanism by which peptides and proteins linked with disease misfold. Here we focus on the misfolding pathways associated with human lysozyme, a globular protein with genetic variants that cause a rare, but fatal systemic amyloidosis. Using a variety of biophysical techniques, we have looked at the structural dynamics of mutational variants of lysozyme to try and understand how these mutations influence fibril formation (Ahn et al. 2016). This project will further characterise recently discovered naturally occurring lysozyme variants to broaden our understanding as to what triggers the manifestation of disease and it will investigate in vitro lysozyme aggregation using an established kinetics analysis approach (Habchi et al, 2017) to probe the microscopic processes involved with lysozyme fibril formation.

References: