BiophysTO Lunchtime Talks

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Formation of an Amyloid State by a Bacterial Chaperone: Structure and Consequences

Protein misfolding underlies many human diseases such as Alzheimer's or Type 2 diabetes, where the conversion of proteins into an amyloid structure is associated with toxicity. Amyloids are stable structures, which have a cross-ß fibrillar architecture that is perpendicular to the fibril axis. However, the precise mechanisms of amyloid formation remain to be elucidated. Surprisingly, we discovered that a bacterial Escherichia coli chaperone-like protein that we are investigating termed Regulatory ATPase Variant A (RavA), and specifically the LARA domain within RavA, can also form amyloids under acidic and thermal stress conditions. RavA has been implicated in modulating the proper assembly of inner membrane respiratory complexes and is found to interact with the acid stress protein, the lysine decarboxylase (LdcI). The LARA domain of RavA is responsible for the RavA-LdcI protein-protein interaction. Structurally, the LARA domain contains an N-terminal flexible loop region followed by a folded core which mainly consists of ß-sheets. Several biochemical, biophysical, and theoretical approaches were used that revealed a possible mechanism of amyloid formation by the LARA domain. The LARA domain was found to have an amyloidogenic core that is protected by the N-terminal loop region. During acid and thermal stress, the N-terminal loop is destabilized allowing the fibrillization process to begin. The physiological relevance of amyloid formation of RavA is currently being investigated and will be discussed.

Host: Dr. Anton Zilman

(Refreshments and pizza will be provided)

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Thursday, December 17, 2015 – 12:00 pm, noon
Davenport Room, Chemistry Building
(and via streaming to Davis Building 4001 UTM)