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Biochemistry & Molecular Biophysics **Seminar**

Molecular mechanism of proteostasis in *Mycobacterium tuberculosis*

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Tuberculosis (TB) is the leading cause of death from a bacterial infection. During infection, *Mycobacterium tuberculosis* (Mtb) encounters several types of stress in the host cells, such as reactive oxygen species, reactive nitrogen species, and chemotherapy. These stresses impair protein integrity and result in protein aggregation. The impaired or aggregated proteins have to be either degraded and recycled or else resolved and repaired. Protein degradation and recycling in Mtb is mainly carried out by the Pup-proteasome system. Protein rescue in Mtb, i.e., resolving toxic protein aggregates to a native folded state, is carried out by the ATP-powered ClpB/DnaK bi-chaperone system. Therefore, the proteasome and the ClpB/DnaK systems are the yin and yang of cellular proteostasis in Mtb. In my seminar, I will discuss our structural and mechanistic studies of the Mtb Pup-proteasome and the ClpB/DnaK protein refolding systems. Interestingly, proteasome is absent in most bacteria; yet essential to Mtb's survival inside the host, providing an ideal target for the development of anti-TB agents. I will also discuss our collaboration with chemical biologist on the development of inhibitors that are selective against Mtb proteasome while sparing the human proteasomes.