Seminar Title:

Lsr2: a novel global regulator and role in Mtb latent infection

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Abstract:

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), is one of the ‘Big Three’ infectious diseases (AIDS, TB, Malaria) that are major threat to public heath. In 2012, TB causes 1.4 million deaths and 8.8 new infections worldwide. The success of Mtb as a deadly pathogen lies in its ability to establish latent infection that can last for decades in the host, and to reactivate upon host immune suppression. How Mtb reprograms itself to adapt to the changing host environment to cause latent infection and reactivation remains poorly understood. Lsr2 is a protein of unknown function present in all mycobacterial species. Recent work from my laboratory reveals that Lsr2 is a nucleoid-associated protein and a functional analog of H-NS of gram-negative bacteria. We show that Lsr2 is a global regulator that silences AT-rich DNA in Mtb genome. Structure-function analysis indicate although Lsr2 and H-NS exhibits little sequence homology, both proteins have employed a similar mechanism to specifically target AT-rich DNA, which represents a novel paradigm of DNA recognition. We further found that Lsr2 is involved in genetic regulation of Mtb latent infection, which opens new avenues for elucidating the molecular mechanisms underlying Mtb latent infection and offer attractive targets for drug intervention.