Investigation of the effect of *Salmonella* on the Ubiquitin-Proteasome System

Cells constantly adapt to ever-changing environment through the alteration of their biological processes enabled by the manipulation of their proteomes. Post-translational modifications (PTMs) of the existing protein pool allow for a timely reaction to the encountered signal. Ubiquitination is a reversible PTM that involves the covalent addition of a small protein called ubiquitin (Ub) to the target substrate protein. This modification is a result of an enzymatic cascade consisting of the E1 Ub-activating enzyme, the E2 Ub-conjugating enzyme (E2), and E3 Ub ligase (E3). The E3 is a scaffold, often composed of multiple subunits, that bridges the substrate and the Ub-charged E2, catalyzing the Ub transfer onto the substrate. Protein ubiquitination often marks proteins for degradation by the Ubiquitin-Proteasome System, a machinery responsible for the majority of protein degradation in the cell. Importantly, by recognizing and ubiquitinating hundreds of cellular substrates, E3s effectively control their level and therefore play a key role in virtually every aspect of cellular biology (i.e. cell division, oncogenesis, signal transduction, transcription, metabolism, and others).

Salmonella enterica serovar Typhimurium is an intracellular pathogen causing gastroenteritis in humans and a more invasive disease in immunocompromised patients. This bacterium translocates around 30 different effector proteins into the host cell to manipulate its immune responses and facilitate bacterial replication. We identified a previously unknown interaction between one S. *enterica* effector protein an E3 component. Our long-term goal is to determine the mode of recognition of these proteins through structural studies and to understand the effect of this interaction on the function of this E3. These studies will deepen our knowledge of the mechanism of action of this E3 which will contribute to opening new avenues for rational drug design of this critical for oncogenesis Ub ligase system.