

Seminar Series of the
CIHR Training Grant in

Protein Folding and Interaction Dynamics

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Modulation of small GTPase activities by pathogenic bacteria

Posttranslational modification (PTM) of proteins is a versatile cellular process to regulate the activities of proteins. These modifications are mostly brought about by enzymes that regioselectively introduce a not-genetically encoded functionality at one or several specific proteins. Very interestingly, PTMs are also utilized by bacterial pathogens to manipulate the activities of such host proteins that could potentially interfere with the survival and replication of infectious agents. Since small GTPases are major regulators of intracellular signaling, they are not surprisingly targeted frequently by pathogenic proteins in order to divert cellular defense mechanisms. In this respect, the recent discovery of reversible adenylylation and phosphocholination of the Rab1 subfamily of small GTPases by *Legionella pneumophila* has been very insightful since these PTMs differently affect Rab biology. Also, adenylylation of the Rho family by enzymes from *Histophilus somni* and *Vibrio parahaemolyticus* affect intracellular signaling by modulating Rho activities. Phosphocholination and adenylylation of small GTPases by bacterial enzymes have been observed in the regulatorily relevant switch I and switch II regions. Since the switch loops are important for discriminatory interactions with regulatory proteins and downstream effectors depending on the activity state of the GTPase, the PTMs may interfere with binding partner interaction by sterically blocking access or altering the conformations of these regions. Here, we analyze the potential consequences of GTPase adenylylation and phosphocholination for the conformations of the switch regions. Our findings may implicate that PTMs can also modulate protein-protein interactions by specifically altering switch conformations. Also, we discuss potential applications of these posttranslational modifications.

Host: Dr. Cordula Enenkel

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