Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, Jan. 27, 2017 in SSC 1511 @ 12 noon

presented by:

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In silico discovery and substrate recognition of bacterial mono-ADP-ribosyltransferase toxins

Mono-ADP-ribosyltransferases (mARTs) are enzymes that catalyze the transfer of ADP-ribose from NAD^+ to a target macromolecule in order to modify its activity. Important bacterial pathogens secrete mART toxins to interfere with essential host cellular functions in debilitating diseases such as cholera, diphtheria, and whooping cough. Although mART toxins possess low overall sequence homology, their catalytic domains share key conserved residues and structural similarities. An *in silico* data mining approach exists in which toxins are discovered by screening bacterial genomic data. This strategy originated with basic comparative sequence alignments and secondary structure predictions, and has evolved to include fold recognition algorithms and structural modelling. The increasing quality and accessibility of bioinformatics software, coupled with an unprecedented availability of sequence data and abundance of mARTs in bacterial genomes, creates an environment where new mARTs are now ripe for discovery. Modern remote homology detection methods will be used to scan bacterial genome databases to generate a list of putative novel mART toxins. Homology-based structural models and ligand docking simulations will be used to predict mART function. Potential toxins will then be expressed in yeast to assess their cytotoxicity and validate computer predictions. Finally, as target prediction is currently a major challenge with regards to toxin discovery, electrostatic properties of known mART structures will be examined in order to develop a similarity index corresponding to substrate specificity. As antibiotic resistance becomes increasingly problematic, the continued discovery of novel mART toxins will diversify our repertoire of virulence factors for the design of inhibitors with therapeutic potential as an alternative to antibiotics.