BioMS Seminar 191107

Welcome to our seminar on protein structure and biological mass spectrometry. We have two interesting presentations from Umeå Centre for Microbial Research (UCMR) and The Laboratory for Molecular Infection Medicine Sweden (MIMS). The seminar will be held on Thursday **7 th** of November **10.30 – 12.00** in lecture room **BMC I 1345**. No registration or access card is needed.

Johan Malmström node manager BioMS.

Panacea: A master antitoxin domain for neutralisation of any protein toxin?

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Toxin-antitoxin systems (TAs) are typically comprised of two closely linked genes encoding a toxic protein or RNA and its antidote, the antitoxin - also protein or RNA. TAs provide a regulatory mechanism of severe but reversible growth rate reduction, and while specific functions are often unknown, roles have been documented for certain TA pairs in plasmid maintenance and resistance to bacteriophages. TAs are most common in bacteria, but are also found in genomes of archaea and bacteriophages. Using our computational tool FlaGs, standing for Flanking Genes, which detects conservation of gene neighbourhood over large evolutionary distances, we are uncovering a vast network of combinations of different toxin and antitoxin protein domains. Most strikingly, we have discovered an antitoxin protein domain that can be paired with hundreds of different toxin domains, and is present in many lineages across the bacterial tree of life with additional representatives in phages and archaea. The list of toxin domains includes some well-known toxins such as mRNA endonucleases MazF and MqsR, but most are currently unknown. Using toxin neutralisation microbiological assays, we have confirmed 12 predicted novel TA pair types as bona fide TA systems involving a common antitoxin domain and novel toxins. Given its apparent function as a universal antidote, we have named this domain Panacea. We are now working to understand the mechanism of action of Panacea, and the many novel toxins it neutralises, while also analysing the evolutionary processes of TA partner swapping.

Structure-functional studies of bacterial and yeast ribosome-associated protein factors: key players in protein synthesis, stress response and antibiotic resistance

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The ribosome is the hub of translation, binding numerous protein factors that assist protein synthesis during the translation cycle and stress conditions. These protein factors can protect the ribosome from antibiotics, sense the metabolic state of the cell, and resolve non-productive stalled ribosomal complexes. In the Hauryliuk lab we work on a number of different ribosome interacting proteins from bacteria and eukaryotes. I will discuss our work on the RelA-SpoT Homolog (RSH) and ATP binding cassette family F (ABCF) proteins. RSH factors sense nutrient starvation in bacteria, and when activated overproduce the alarmone molecule (p)ppGpp that rewires bacterial physiology, rendering bacteria virulent and tolerant to antibiotics. The most well-studied RSH factor, Escherichia coli RelA, is activated upon amino acid starvation by the presence of deacylated tRNA in the ribosomal A-site. Another group of proteins, the ribosome-associated ABCF ATPases are evolutionally ubiquitous, but poorly understood on the molecular level. In eukaryotes, they regulate the ribosomal cycle (e.g. eEF3) and alert the cell when translation encounters problems, such as amino acid deprivation (Gcn20). In bacteria, antibiotic resistance (ARE) ABCFs mediate antibiotic resistance in numerous pathogens, including Staphylococcus, Streptococci and Enterococcus. Using a combination of microbiology, biochemistry and ribosome profiling supported by collaborative cryo-EM reconstructions, we uncover the molecular mechanisms of ribosome-associated ABCF ATPases and RSH factors.