MS04 P01

Structural and functional studies of the probiotic organism *Lactobacillus salivarius* Mario Bumann[a], Heinz Gut[a], F. Fang[b], Paul O'Toole[b], & Martin A. Walsh[a]
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Keywords: Probiotics, Bacterial Adherence, Structural proteomics

Probiotics are live bacterial strains in foods which upon ingestion in certain amounts are beneficial to health beyond inherent basic nutrition. They have been shown to have a positive effect in the prevention and treatment of specific gastrointestinal disorders and in counteracting gut barrier dysfunction associated with inflammation and infection. Accordingly, specific probiotic strains have been shown to prevent diarrhea, shorten the duration of diarrheal episodes, and alleviate inflammatory responses. Other studies have shown that probiotics may alleviate lactose intolerance; have a positive influence on the intestinal flora of the host; competitively exclude pathogens; possess anti-colon cancer effects; reduce the clinical manifestations of atopic dermatitis, Crohn's disease, constipation, candidiasis, and urinary tract infections [1]. The mechanisms behind favourable clinical outcome from the use of probiotics are still largely unknown. As a first step, understanding the basis of gastric survival and colonization is being pursued at both the structural and functional level for the probiotic bacterium *Lactobacillus salivarius* that colonizes the human gastrointestinal tract.
An important trait for potential probiotic strains is their ability to adhere to the intestinal mucosa. The adherence of microorganisms to host tissues is often presented by surface proteins like fibronectin.
Here, we will present results from the structural analyses of the fibronectin binding protein of *L. salivarius*. Moreover, these studies are being complemented by work on a fibronectin binding protein from the pathogen *Streptococcus pneumoniae*. The sequence identity of these proteins is 44%. This protein plays a direct role in the pathogenesis of pneumococcal infections and has been identified as a potential vaccine candidate.

[1] Mercenier A, Pavan S, Pot B: Probiotics as biotherapeutic agents: present knowledge and future prospects. *Current pharmaceutical design* 2003, 9(2):175-191.

MS04 P02

Bone Morphogenetic Protein Type II Receptor Structure in Two Crystal Forms. Sue Cutfield, John Cutfield, Peter Mace. *Biochemistry Department, University of Otago, Dunedin, New Zealand.*.
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Keywords: fertility, SAD, ligand-binding

BMPRII is a type II TGF-ß serine threonine kinase receptor integral to the bone morphogenetic protein (BMP) signalling pathway. It is known to bind BMP and growth differentiation factor (GDF) ligands, and has overlapping ligand specificity with the activin type II receptor, ActRII. BMP signalling is important in many growth and development pathways as well as in mammalian reproduction.
Crystals of the human BMPRII ectodomain were grown in two different forms from the same crystallization conditions. The structures retain the basic three-finger toxin fold of other TGF- ß receptor ectodomains, and share the main hydrophobic patch used by ActRII to bind various ligands. However, they present different conformations of the A-loop at the periphery of the proposed ligand-binding interface, as a result of Cys94 'switching' between two rotamers. Evidence is presented that the two crystal forms represent ligand bound and free conformations of BMPRII.

MS04 P03

Interaction of SRP54 GTPase and SRP RNA in the free signal recognition particle Tobias Hainzl, Shenghua Huang & A. Elisabeth Sauer-Eriksson *Umeå Center for Molecular Pathogenesis, Umeå University, SE-901 87 Umeå, Sweden.* E-mail: tobias.hainzl@ucmp.umu.se

Keywords: ribonucleoproteins, protein-RNA crystal structures, RNA-protein interactions

The signal recognition particle (SRP) is a ubiquitous protein-RNA complex which targets proteins to cellular membranes for insertion or secretion. A key-role in SRP-mediated protein targeting has the conserved core consisting of the S domain of SRP RNA and the multi-domain protein SRP54. The SRP54 M domain anchors SRP54 on the SRP RNA and recognizes signal sequences of nascent polypeptide chains while the SRP54 GTPase domain, comprising the N and G domains, binds to the SRP receptor. In free SRP a direct interaction of SRP RNA with the GTPase domain has been proposed, but has never been structurally verified. Here we present the crystal structure at 2.5 Å resolution of the SRP54-SRP19-SRP RNA complex of *Methanococcus jannaschii* SRP. The structure shows that the SRP54 GTPase domain interacts with the SRP RNA in a domain arrangement in which the GTPase domain is spatially well separated from the signal peptide binding site. Given the association of both the N and G domains with SRP RNA, the restricted SRP54 inter-domain communications in free SRP suggest a regulatory function for SRP RNA. The assembly of SRP is a hierarchical process where SRP19 binding to SRP RNA precedes SRP54 binding. The previously solved structures of the SRP RNA of *M. jannaschii* in its free form and bound to SRP19 together with the present structure disclose the structural changes in SRP RNA which ultimately lead to high affinity binding of SRP54.

MS04 P04

Structure and function of Survivin-Borealin-INCENP Core Complex in mitosis A. A. Jeyaprakash[a], U. R. Klein[b], E. A. Nigg[b], E. Conti[ab] [a]*European Molecular Biology Laboratory (EMBL), Meyerhofstrasse 1, D-69117 Heidelberg, Germany.* [b]*Max-Planck-Institute of Biochemistry, Am Klopferspitz 18, D-82152 Martinsried, Germany.*. E-mail: jeyaprak@embl.de

Keywords: protein-protein interaction, mitosis, Chromosomal Passenger Complex

Survivin, Borealin, INCENP and the kinase Aurora-B are the members of the Chromosomal Passenger Complex