FA1-MS12-T01

Structure and role in pathogenesis of pneumococcal cell-wall associated proteins. Juan A. Hermoso[a], Inmaculada Pérez-Dorado[a], Martín Martínez-Ripoll[a].
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S. pneumoniae displays on its surface numerous proteins, the majority of which are virulence factors that contribute to the pathogenesis of this organism. Such proteins participate in specific interactions with human host tissues, thereby facilitating bacterial survival, helping the organism spread within host tissues, and concealing the bacterial surface from the host's defense mechanism. Pneumococcal choline-binding proteins (CBPs) share an N- or C-terminal choline-binding module made up of homologous repeats of about 20 amino acid residues, allowing them to anchor to the cell envelope through non-covalent interactions with cell surface-located choline residues. The complete 3D structures of pneumococcal CBP, the phosphorylcholine esterase Pce [1] and the choline-binding protein CbpF [2] revealed strong implications in pneumococcal pathogenesis. Now the first structure of a pneumococcal autolysin, that of LytC, has been solved in a ternary complex with choline and a pneumococcal peptidoglycan fragment [3]. Due to the unusual hook-shaped conformation of the multimodular protein, it is only able to hydrolyze non-crosslinked peptidoglycan chains for steric reasons, an assertion validated by additional experiments. These results explain the activation of LytC by CbpD in fratricide, a competence-programmed mechanism of predation of noncompetent sister cells. The results provide the first structural insights into the critical and central function that LytC plays in pneumococcal virulence and explain a long-standing puzzle of how murein hydrolases can be controlled to avoid self-lysis during bacterial growth and division.

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Keywords: pneumococcal surface proteins, virulence, fratricide

FA1-MS12-T02

Molecular mechanisms of fungal cell wall assembly Alex Schuettelkopf, Daan van Aalten, Helge Dorfmueller. *College of Life Sciences, University of Dundee, Scotland.*
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The fungal cell wall is a dynamic and multi-layered structure, containing a core of crosslinked chitin and glucan. Despite decades of work, there are huge gaps in our knowledge of the enzymes responsible for cell wall synthesis, modification and crosslinking. This is particularly pressing given the significant rise in fatal fungal infections of immunocompromised patients, and thus the need for novel, properly genetically/chemically validated, drug targets. I will present data from a multidisciplinary approach (covering genetics, biochemistry, structural biology, high throughout screening, synthetic chemistry and cell biology) that furthers our understanding of the function, biochemistry, inhibition and genetic/chemical validation of A. fumigatus/C. albicans enzymes involved in fungal cell wall biogenesis. Aspects of cell wall synthesis, sugar nucleotide biosynthesis, cell wall modification/hydrolysis and crosslinking/transglycosylation will be covered.

Keywords: cell wall, fungi, inhibitors

FA1-MS12-T03

Crystal structure of the mammalian cytosolic chaperonin CCT in complex with tubulin. Inés G. Muñoz[a#], Hugo Yébenes[b#], Min Zhou[c], Pablo Mesa[a,b], Marina Serna[b], AhYoung Park[c], Elisabeth Bragado-Nilsson[a], Ana Beloso[b], Carol V. Robinson[c], José M. Valpuesta[b*], Guillermo Montoya[a*]. [a]*Macromolecular Crystallography Group, Structural Biology and Biocomputing Programme, Spanish National Cancer Research Centre (CNIO), Melchor Fdez. Almagro 3, 28029 Madrid, Spain.* [b]*Centro Nacional de Biotecnología, CSIC, Campus de la Universidad Autónoma de Madrid, Darwin, 3, 28049 Madrid, Spain.* [c]*Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK; Department of Chemistry, Physical and Theoretical Chemistry Laboratory, South Parks Road, Oxford OX1 3QZ, UK.*
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Protein folding in the cell is assisted by a large group of proteins termed molecular chaperones[1], one of the most important members being the chaperonins or Hsp60s (Heat Shock Proteins of 60 kDa). The eukaryotic cytosolic chaperonin CCT[2] (chaperonin containing TCP-1, also known as TRiC) is the most complex of all chaperonins, a 1 MDa oligomer built by two identical rings, each composed of single copies of eight different 60kDa subunits called α, β, γ, ζ, ε, δ, θ and η. This macromolecular complex has crucial relevance in several essential biological processes, emerging as a key molecule due to its role in the folding of many important proteins including actin, α and β tubulins [3]. An electron density map at 5 Å resolution has enabled us to build the CCT complex, revealing the presence of a substrate in the inner cavities of both octagonal rings. Here we present the crystal structure of this protein machine in complex with tubulin, providing information about the molecular mechanism by which this macromolecular complex aids the tubulin folding process. Our data provide the structural basis for understanding the function of this molecular machine.

Keywords: macromolecular complexes, protein folding, mitosis