MS11-01 **Serial femtosecond crystallography provides new approaches to structural enzymology.** Ilme Schlichting,[ab] [a]*Max Planck Institute for Medical Research, Heidelberg,* [b]*Max Planck Advanced Study Group, Center of Free Electron Laser Science, Hamburg, Germany*
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Serial femtosecond crystallography (SFX) is an emerging technique for structure determination beyond the limits imposed by radiation damage using conventional data collection approaches. SFX is based on a "diffraction-before destruction" approach [1] that uses highly intense x-ray pulses provided by a x-ray free-electron laser (XFEL) that are so brief that they traverse the sample before the onset of significant radiation damage, producing usable diffraction signal. Since the demonstration of the concept at the Linac Coherent Light Source (LCLS) , the first operational hard X-ray FEL, for protein micro- and nanocrystals , our international collaboration has demontrated that high resolution data can be collected that compare well with low dose synchrotron data [4]. This establishes SFX as a very valuable high-resolution complement to existing macromolecular crystallography techniques. In addition to enabling the analysis of very radiation sensitive systems, such as tiny crystals, SFX may provide new approaches to structural enzymology e.g. by fast mixing, and by facilitating the study of irreversible reactions [5]. Recent experiments and results will be described.

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MS11-02 **Advances in bacterial cell-wall remodeling enzymes. Implications in virulence and antibiotics resistance.** Juan A. Hermoso,[a] [a]*Department of Crystallography and Structural Biology. Institute of Physical-Chemistry Rocasolano. CSIC. Madrid. Spain*
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The bacterial cell wall is comprised of cross-linked strands of peptidoglycan (PG), which encase the entire cytoplasm. A healthy cell wall is critical for survival of bacteria and serves as a docking station for bacterial surface proteins, some of them representing key players in adhesion, colonisation and virulence. Therefore cell wall remodeling is critical in host-pathogen interactions, cell division, virulence, PG recycling and antibiotics resistance. Four families of proteins decorate the cell surface of the human pathogen *Streptococcus pneumoniae* many of them displaying different enzymatic activities. This talk reviews recent progress in the investigation of the three-dimensional structures of enzymatic surface-exposed pneumococcal proteins. The modular nature of some of them produces a great versatility and sophistication of the virulence functions that, in most cases, cannot be deduced by the structural analysis of the isolated modules. The three-dimensional structure of Phosphoril-choline esterase, Pce (70 KDa) [1] showed that Pce hydrolyses PAF, a potent lipidic first messenger of inflammatory processes. Besides, Pce selectively remodels the bacterial surface impairing the ability of host proteins to efficiently bind the bacteria, and would provide a mechanism for pneumococci escaping attack by the host defense system [1].

CbpF (38 KDa) [2] inhibit the activity of autolysin LytC, a critical protein involved in the virulence mechanism of fratricide. We have reported the functional characterization of the key effector of pneumococcal fratricide CbpD [3] and the crystal structure of LytC [4] that explain the activation of LytC by CbpD in fratricide and provide the first structural insights into the critical and central function that LytC plays in pneumococcal virulence.

During homeostasis, including growth, cell wall is simultaneously biosynthesized and degraded. Lytic transglycosylases (LTs) initiate the degradative events on cell wall. The products of LTs are internalized to the cytoplasm, and hydrolised by glucosaminidase NagZ and amidase AmpD. The reaction products of AmpD play roles in both PG recycling events and in an induction event that leads to the expresion of β-lactamase, a key β-lactam antibiotic resistance enzyme. We have observed that AmpD undergoes an activation mechanism without precedent for a single domain protein [5].

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