Beyond Structures: Deciphering the Regulatory Interplay between Cell-Wall Degrading Machineries and Bacterial Cell Division

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The bacterial cell wall is an essential gigantic macromolecule that defines the shape of the bacterium and enables the bacterium to resist lysis as a result of its high intracellular osmotic pressure. The main component of the cell wall is peptidoglycan (PG) which consists of repeating linear polymers of N-acetylglucosamine (NAG) and N-acetylmuramic acid (NAM) linked together via short oligopeptide chains. The steps involved in its regulation are the targets of antibiotics like beta-lactams that represent >50% of the available contemporary antibiotic arsenal. Growth, division, and morphogenesis, and in some cases antibiotic resistance, are intimately linked to the synthesis of this exoskeleton but also its hydrolysis. The enzymes that cleave the PG meshwork require careful control to prevent aberrant hydrolysis and loss of envelope integrity. Bacteria employ diverse mechanisms to control the activity, localization, and abundance of these potentially autolytic enzymes.
A paradigmatic example is bacterial cell division, a central process that requires delicate regulation of PG hydrolases to prevent aberrant cell lysis and to allow the final separation of viable daughter cells. Recently [1-5] we provided structural insights on how this regulation is performed in bacterial cell division by the addition of modules capable of specific recognition of the septal PG, or by the interaction with regulatory protein complexes or with surface polymers. Remarkably, the regulation of these autolytic enzymes incorporates more than one of these control mechanisms to finely tune activity and provide spatial and temporal control during this essential process. Details of these regulatory mechanisms will be provided in the talk.
References:
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[5] Martínez-Caballero et al Cell Reports (2023) 42, 112756