Structural Insights on Regulation of Lytic Machineries in the Pneumococcal Divisome

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Separation of daughter cells during bacterial cell division requires that the septal cross wall be split by peptidoglycan hydrolases. In *Streptococcus pneumoniae* D,D-carboxypeptidase DacA and L,D-carboxypeptidase DacB function in a sequential manner while essential endopeptidase PcsB is regulated by the transmembrane FtsEX complex. The crystal structure of DacB, radically different to that of DacA, contains a mononuclear Zn^{2+} catalytic center located in the middle of a large and fully exposed groove. Two different conformations were found presenting a different arrangement of the active site topology. The critical residues for catalysis and substrate specificity were identified. The crystal structure of full-length PcsB shows an unprecedented dimeric structure in which the unique V-shaped coiled-coil domain of each monomer acts as a molecular tweezers locking down the catalytic domain of its dimeric partner in an inactive configuration. This finding strongly suggests that the release of the catalytic domains requires an ATP-driven conformational change in the FtsEX complex, which is most likely conveyed towards the catalytic domains through a set of coordinated movements of the α-helices forming the coiled-coil domain of PcsB. Recent findings on regulation of the different lytic machineries in this system will be discussed.