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Structural studies of the *B. pertussis* extracytoplasmic solute receptor DctP7

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The global transport capacities of bacteria generally correlate with their ecological niche as well as their metabolic properties. In Gram negative bacteria, substrate transport is in part attributed to *tr*ipartite *A*TP independent *p*eriplasmic (TRAP) transporters [1]. Such transport systems are composed of 2 inner-membrane proteins DctQ and DctM and an extracytoplasmic solute receptor DctP [1].
Bordetella pertussis, the whooping cough agent, encodes for a dozen such TRAP transporters [2]. The genes encoding one of these TRAP transport systems (TRAP7) are located in a region flanking three virulence factors (FhaB, FhaC and FimD) which are regulated at the transcriptional level by the BvgAS two-component system. Given the proximity of TRAP7 to the above virulence locus, studies have been initiated in order to determine whether the substrate it transports could be involved in the modulation of the BvgAS system. In this view, DctP7, the extracytoplasmic solute receptor component of TRAP7, has been crystallized and its three-dimensional structure has been determined to a 1.95 Å resolution using the *s*ingle-wavelength *a*nomalous *d*ispersion (SAD) method.
The three-dimensional structure of *B. pertussis* DctP7 has shown that the protein possesses a fold related to that of periplasmic substrate binding proteins. $2f_o$-f_c and f_o-f_c electron density maps have indicated that DctP7 was crystallized in its liganded form, and have enabled the identification of the bound ligand as pyroglutamic acid.
This study will allow further investigation into the potential modulation effects of pyroglutamic acid on the BvgAS two-component system and on *B. pertussis* metabolism.

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The penicillin-binding proteins of class C1

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Bacteria produce several penicillin-binding proteins (PBPs) that are involved in the synthesis and remodeling of the peptidoglycan, a highly cross-link mesh that protects the bacterium from osmotic shock and helps maintaining cell shape. They generally produce a unique PBP belonging to class C1, characterized by a molecular mass of circa 50kDa, a high sensitivity to penicillin and an endopeptidase activity not encountered in the other classes of PBPs. The precise role of these PBPs remains unclear. Under laboratory growth conditions, they are dispensable and unlike most PBPs, they are not anchored in the membrane. We have solved the structures of two PBPs of class C1, the PBP4a from *Bacillus subtilis* and a PBP from *Actinomadura R39* (R39). The structure of these PBPs is composed of three domains: a penicillin-binding domain similar to the penicillin-binding domain of *E. coli* PBP5 and two domains of unknown function. In most multimodular PBPs, additional domains are generally located at the C- or N-termini of the penicillin-binding domain. In PBP4a and R39, the other two domains are inserted in the penicillin-binding domain, between the SXXK and SXN motifs, in the way of ''Matryoshka dolls''. These domains could be involved in protein-protein interactions or metabolite recognition for the localization of the protein in the cell wall. Recently, We have solved a series of complex-structures of PBP4a and R39, using several modified penicillins, cephalosporins and a peptidoglycan mimetic peptide. The covalent binding of penicillins and cephalosporins to the active site serine reveals the absence of active site conformational change upon binding the beta-lactams while binding of the peptidoglycan mimetic peptide reveals near the active site a binding pocket that can accommodate the H_3N^+-CH-COO^--group of the diaminopimelic acid, the third residue of the peptidoglycan stem peptide.