Publication wherein FolC-Ugd interaction published

**Global landscape of cell envelope protein complexes in Escherichia coli.**

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Bacterial cell envelope protein (CEP) complexes mediate a range of processes, including membrane assembly, antibiotic resistance and metabolic coordination. However, only limited characterization of relevant macromolecules has been reported to date. Here we present a proteomic survey of 1,347 CEPs encompassing 90% inner- and outer-membrane and periplasmic proteins of Escherichia coli. After extraction with non-denaturing detergents, we affinity-purified 785 endogenously tagged CEPs and identified stably associated polypeptides by precision mass spectrometry. The resulting high-quality physical interaction network, comprising 77% of targeted CEPs, revealed many previously uncharacterized heteromeric complexes. We found that the secretion of autotransporters requires translocation and the assembly module TamB to nucleate proper folding from periplasm to cell surface through a cooperative mechanism involving the β-barrel assembly machinery. We also establish that an ABC transporter of unknown function, YadH, together with the Mla system preserves outer membrane lipid asymmetry. This E. coli CEP 'interactome' provides insights into the functional landscape governing CE systems essential to bacterial growth, metabolism and drug resistance.

Publication with FolC structure (in complex with ADP+DHFS (1W78 – used for docking) and in complex with only ADP (1W7K)

Mathieu, M., Debousker, G., Vincent, S., Viviani, F., Bamas-Jacques, N. and Mikol, V., 2005. Escherichia coli FolC structure reveals an unexpected dihydrofolate binding site providing an attractive target for anti-microbial therapy. *Journal of Biological Chemistry*, *280*(19), pp.18916-18922.

## Abstract

In some bacteria, such as Escherichia coli, the addition of l-glutamate to dihydropteroate (dihydrofolate synthetase activity) and the subsequent additions of l-glutamate to tetrahydrofolate (folylpolyglutamate synthetase (FPGS) activity) are catalyzed by the same enzyme, FolC. The crystal structure of E. coli FolC is described in this paper. It showed strong similarities to that of the FPGS enzyme of Lactobacillus casei within the ATP binding site and the catalytic site, as do all other members of the Mur synthethase superfamily. FolC structure revealed an unexpected dihydropteroate binding site very different from the folate site identified previously in the FPGS structure. The relevance of this site is exemplified by the presence of phosphorylated dihydropteroate, a reaction intermediate in the DHFS reaction. L. casei FPGS is considered a relevant model for human FPGS. As such, the presence of a folate binding site in E. coli FolC, which is different from the one seen in FPGS enzymes, provides avenues for the design of specific inhibitors of this enzyme in antimicrobial therapy.