Regulation of penicillin-binding protein Pbp2a in *Streptococcus pneumoniae*

Streptococcus pneumoniae is an extracellular human pathogen that encodes a unique eukaryotic-type Ser/Thr protein kinase StkP in its genome. This enzyme is involved in other cellular processes, such as cell division and cell wall synthesis, through phosphorylation with its substrates.

A transmembrane protein MacP has been identified as a substrate of StkP. It is an activator of penicillin-binding protein PBP2a, which is involved in the synthesis of peptidoglycan with its transpeptidase and transglycosylase activities. We found that MacP is phosphorylated by the protein kinase StkP at positions T32 and T56.

We confirmed that proteins MacP and PBP2a interact with each other and that phosphoablative and phosphomimetic mutations of the major phosphorylated residues of the MacP protein do not affect the interaction with PBP2a and do not fundamentally affect the function of MacP *in vivo*. Furthermore, we showed that the Δ*macP* mutation is synthethically lethal with the Δ*pbp1a* mutation, confirming that MacP is an activator of the PBP2a protein. MacP is located in the cell septum and interacts with a number of *S. pneumoniae* cell division proteins.

Keywords:

Streptococcus pneumoniae, cell division, MacP, PBP2a, phosphorylation