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Identification of the donor molecules for phosphorylcholine modification of pilin in Neisseria meningitidis

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Background

Neisseria meningitidis is gram-negative bacteria that can causes acute bacterial meningitis and life-threatening sepsis. Pili of N. meningitidis are a major virulence factor and are subject to several different post-translational modifications. Among these modifications, ChoP modification on pili is crucial for early colonization of the airway epithelium, as it mediates adherence via binding to the platelet activating factor receptor expressed on airway epithelial cells. The presence of phosphorylcholine (ChoP) is phase-variable due to frequent frame-shifting events in the poly-guanine (G) tract of the phosphorylcholine transferase A (PptA) coding sequence. Interestingly, unlike bacteria that possess ChoP-linked glycoconjugates, N. meningitidis does not contain any of the characterized ChoP biosynthetic pathways. PptA is the only known protein involved in the addition of ChoP to C-terminus of pilin in N. meningitidis. The pathway(s) required for ChoP production prior to pilin post-translational modification is still unknown.

Aim/Methods

In this study, we aim to identify the donor molecules for ChoP synthesis in N. meningitidis by screening ChoP donor molecule candidates using surface plasmon resonance (SPR) to determine their affinity to PptA.

Results

We found that PptA-soluble domain binds to the target C-terminus peptide receptor for ChoP, 53CRDASDAS160, and that phosphatidylcholine binds with the highest affinity to PptA among the candidate donor molecules tested (KD [equilibrium dissociation constant]. 377±53.6nM). Additionally, the increased ChoP expression was observed due to the phosphatidylcholine supplementation and interruption of phospholipid homeostasis in N. meningitidis. The presence of phosphatidylcholine in meningococci was detected using lipidomic analysis.

Conclusions

These findings suggest that phosphatidylcholine may be the donor molecule for ChoP conjugate synthesis

and PptA is responsible for transferring ChoP from phosphatidylcholine to the C-terminus of pilin. N. meningitidis has a novel ChoP biosynthetic pathway.