Poster Presentation

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Structure of pneumococcal GtfA reveals a novel prokaryotic O-GlcNAc transferase

W. Shi[1], Y. Jiang[1], F. Zhu[2], H. Wu[2], C. Zhou[1], Y. Chen[1]

[1]School of Life Sciences, University of Science and Technology of China, Hefei, Anhui, China, [2]Departments of Pediatric Dentistry and Microbiology, University of Alabama at Birmingham, Schools of Dentistry and Medicine, Birmingham, AL, USA

Protein glycosylation is increasingly recognized as an important process for bacterial physiology and pathophysiology. Glycosylation of serine-rich repeat (SRR) glycoprotein PsrP is essential for the pathogenesis of Streptococcus pneumoniae, one of the most common human pathogens. This glycosylation process is initiated by a glycosyltransferase complex comprising two components, a core enzyme GtfA and a co-activator GtfB. Here we report the 2.0-Å crystal structure of GtfA in complex with GlcNAc and UDP. The structure possesses a core domain of GT-B fold and an unprecedented "add-on" domain of DUF1975, which adopts a β-meander structure. This novel DUF1975 domain is critical for the intact glycosyltransferase activity of GtfA–GtfB complex via mediating their self-recognition and the binding to the acceptor protein PsrP. The glycoproteomic analysis revealed a novel pattern of protein O-linked glycosylation at the serine residue cluster. The findings suggest that GtfA is a new glycosyltransferase and provide a structural basis for the future design of inhibitors against the biogenesis of bacterial SRRPs.

Keywords: O-linked glycosylation, Streptococcus pneumoniae, serine-rich repeat glycoprotein