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Sialylation of outer membrane porin protein D impedes β-lactam antibiotic entrance in Pseudomonas aeruginosa

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Sialic acids (Sias) are typically present as terminal sugars in oligosaccharide moieties attached to glycoproteins. *Pseudomonas aeruginosa* (PA), a gram-negative bacterium infects immuno-suppressed patients. We have established the presence of linkage-specific Sias on PA. Sialic acid-binding immunoglobulin-type lectins (Siglecs) are present on all immune cells. Sialylated PA (PA^{+Sias}) binds to neutrophils through Sias-siglecs interactions. We have observed reduced oxidative burst, release of elastase and decrease NETs formation thus indicating subversion of host innate immunity. Next, we have affinity purified and sequenced twenty six sialoglycoproteins from PA^{+Sias}. One such identified sialoglycoprotein is outer membrane porin protein D (OprD), a beta-barrel shaped channel-forming protein. To establish the role of Sias on OprD proteins, they are purified from sialylated (PA^{+Sias}) and non-sialylated (PA^{-Sias}) and their sialylation status are established. Profiling of glycan structures reveals the presence of sialylated N- and O-glycans in OprD^{+Sias}. Bioinformatics studies reveal that amongst four N-glycosylation sites of OprD, Asn311 is present in the extracellular loop region having high solvent accessibility for its proper glycosylation. Core glycan moieties can properly fit into Asn311 site with no spatial overlaps with suitable glycosidic conformations. Molecular modeling studies suggest the presence of glycan structure with terminal bulky sialic acid hinders the channel passage of OprD towards β-lactam antibiotic permeabilization. This might be one of the new mechanisms for β-lactam antibiotic resistance of PA and thereby facilitating their survival in host. Our findings might help to open new avenue to design latest drug which can enter cells freely even in presence of sialic acids.

Biography

Chitra Mandal completed her PhD at the age of 28 years from Indian Institute of Science, Bangalore and Post-Doctoral studies at University of Pennsylvania. She is the Director of CSIR-Indian Institute of Chemical Biology, Kolkata, India and Sir J C Bose National Fellow, Head CSIR-Innovation Complex. She has published 150 research papers and holds 10 patents, guided 26 PhD students and transferred three technologies. She is an elected fellow of 'The World Academy of Sciences, main four academies in India. Main theme of her group is to understand the mystery of glycosylation of biomolecules and their potential applications in health and diseases.

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