Structural and Functional Characterization of a Novel Bacterial Glycosyltransferase Family Involved in Pathogenesis

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Bacterial pathogens have evolved distinct ways of colonizing host cells and promote infection. Many human intestinal bacterial pathogens such as *Salmonella, Shigella* and enteropathogenic/ enterohemorrhagic *Escherichia coli* utilize type III secretion systems to deliver virulence effector proteins into the host to promote colonization and interfere with antimicrobial host response. Among the type III effectors, the NleB protein has been shown to be essential for virulence of enteric pathogens. NleB is a glycosyltransferase that has been shown to interact with host cell death-domain-containing proteins, GlcNAcylate a specific arginine on these and thereby inhibiting death receptor signalling and preventing host cell apoptosis.

Preliminary data suggest a phage origin for NleB protein with up to two isoforms present in *E. coli* cells, *nleb* wt that codifies for NleB1 and *nleb* V2 that codifies for NleB2 whose target is unknown. According with the activity tests, the transfer of glucose by recombinant NleB1 seems to be restricted to the death domain of the FAD protein. This finding is supported with the observation of a soluble stable complex of NleB1 with FADD-DD domain that produce promising crystals under crystallization assays. However, this data is very preliminary thus more effort is required to structurally characterize NleB1 catalytic mechanism as a model and extrapolate this knowledge to the whole new family of NleB orthologues. Furthermore, the proposed research over arginine GlcNAcylation constitutes a complete new research field in cell signalling and bacterial virulence.