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Antibacterial toxin binding to receptor lipids revealed by neutron reflection

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Escherichia coli bacteria secrete colicins, a class of antibacterial proteins to kill closely related competing strains. This relies on the surprising ability of these toxins to cross the Gram-negative outer membrane (OM), a robust, impermeable, asymmetric lipid bilayer comprising an outer leaflet of lipopolysaccharide (LPS) and an inner leaflet of phospholipid. Colicins attach to their target cells by interacting with specific outer membrane protein receptors but colicin N (ColN) attaches to the core oligosaccharide of LPS. Here, we identify an exposed loop region at the end of the R-domain which is critical for ColN toxicity. Mutants which showed reduced in vivo toxicity also displayed lower binding to LPS in vitro, confirming the correlation between toxicity and LPS recognition. Using neutron reflectometry and in vitro models of the OM, we show that the inner core oligosaccharide of LPS must be exposed for colicin N to bind specifically. Since such exposure naturally occurs next to the outer membrane protein receptor for colicin N (OmpF), the combined results suggest how this non-canonical LPS-binding region may guide the initial steps of ColN OM-translocation.

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