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Glycobiology of *Salmonella typhimurium* Lipopolysaccharide Biosynthesis: Invasive Potential and Antibiotic Resistance

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The antibacterial mechanism and invasiveness of enterobacter *Salmonella typhimurium* was studied. The *rfa* (*Waa*) gene cluster of *S. typhimurium* encodes the core oligosaccharide biosynthesis of lipopolysaccharide (LPS). Among *rfa* gene cluster, our group have first cloned the *rfaE* gene, which is involved in ADP-L-*glycero*-D-*manno*-heptose biosynthesis (Jin U-H *et al.*, 2001). The *rfaE* mutant synthesizes heptose-deficient LPS, which consists of only lipid A and 3-deoxy-D-*manno*-octulosonic acid (KDO), and mutants. This makes an incomplete LPS, and is a rough mutant. *S. typhimurium* deep-rough mutants in the heptose region of the inner core show a reduced growth rate, sensitivity to high temperature and hypersensitivity to hydrophobic antibiotics. The cloned *rfaE* gene was added to the into *S. typhimurium rfaE* mutant strain SL1102 (*rfaE543*), which makes heptose-deficient LPS and has a deep rough phenotype. The complementation created a smooth phenotype in the SL1102 strain. The sensitivity of SL1102 to bacteriophages was recovered to wild-type strain, indicating that LPS is used as the receptor for bacteriophage infection. The permeability barrier of SL1102 to hydrophobic antibiotics such as novobiocin and baicalin was restored to that of the wild-type, suggesting that antibiotic resistance of the wild type strain is highly correlated with their LPS. LPS produced by the *rfaE*-complemented SL1102 strain was indistinguishable from LPS biosynthesis of smooth strains. Infection experiments in vitro demonstrated that the mutant could not invade human Chang epithelial cells despite of a genetically defined invasion-promoting salmonella protein. These data imply that the LPS phenotype is a critical factor for salmonella invasiveness