

P054 *Salmonella* evades early innate immune recognition by the intestinal epithelium

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Innate immune receptors like Toll-like receptor (TLR) 4 recognize conserved microbial structures and mediate cellular stimulation and host defence activation. Here we analyzed the stimulation kinetic of TLR4-positive intestinal epithelial mIC_{cl2} cells exposed to the gram-negative enteropathogenic bacterium *Salmonella* Typhimurium. Chemokine secretion, NF- κ B reporter activity, and p65/RelA nuclear translocation were significantly delayed but not reduced after exposure to *S. Typhimurium* as compared to a commensal *E. coli* isolate. This difference was also noted using heat-killed bacteria but abolished in isogenic *S. Typhimurium* mutants carrying a reduced length of the lipopolysaccharide (LPS) O-Antigen (Ag). A similar delay in recognition was noted between purified smooth (long O-Ag) as compared to rough (short O-Ag) LPS. LPS release from wt or mutant *Salmonella* or *E. coli* in the culture supernatant was comparable. Co-stimulation of wildtype (wt) *S. Typhimurium* and rough LPS resulted in early recognition, whereas addition of smooth LPS to *E. coli* was not able to inhibit early cellular stimulation indicating a structural impairment of the smooth LPS TLR4 interaction. Indeed, over expression of the TLR4 co-receptor CD14 enhanced early recognition of smooth LPS or wt *Salmonella*. Thus, expression of smooth LPS protects *S. Typhimurium* from early recognition by CD14^{low} intestinal epithelial cells, which may facilitate invasion of the epithelial layer and infiltration into the subepithelial space prior to activation of mucosal antibacterial host defences.