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Inhibition of Salmonella Motility and SPI-1 Mediated Entry into Epithelial Cells by a Protective Anti-Lipopolysaccharide Monoclonal IgA

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Secretory IgA (SIgA) antibodies directed against the O-antigen of lipopolysaccharide (LPS) are the primary determinants of mucosal immunity to gram-negative enteric pathogens, although the underlying mechanisms by which these antibodies interfere with colonization and invasion remain largely unknown. In this study, we report that Sal4, a protective, anti-O5 specific monoclonal IgA antibody, is a potent inhibitor of the flagellum-based motility of *Salmonella enterica* serovar Typhimurium (*S. Typhimurium*). Sal4, at concentrations previously shown to block bacterial attachment to, and invasion of, epithelial cells, completely immobilized ("paralyzed") *S. Typhimurium*, within 15 min. Sal4-mediated motility arrest occurred independently of agglutination, and was distinct from anti-flagellum (H) antibody-mediated arrest. Polyclonal anti-LPS IgG antibodies and F(ab')₂ were as effective as was Sal4, in impeding bacterial swimming, whereas monovalent Fab fragments were 5-10 fold less effective. To test whether motility arrest accounts for Sal4's protective capacity *in vitro*, we performed epithelial cell invasion assays, in which the requirement for motility in the entry process was by-passed by centrifugation of antibody-treated bacteria onto cell monolayers. Under these conditions, Sal4-treated *S. Typhimurium* adhered to epithelial cells as capably as did the control bacteria, yet they remained non-invasive. Sal4 did not inhibit *S. Typhimurium* uptake into mouse macrophages, revealing that Sal4 interferes specifically with SPI-1-dependent -- and not SPI-1-independent -- entry of *S. Typhimurium* into host cells. We conclude that Sal4 inhibits *S. Typhimurium*'s flagellum-based motility and SPI-1-mediated entry into epithelial cells, two processes essential for colonization and invasion of the intestinal mucosa.