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BMS

Judging Dept.

Stephen Forbes

Student

BMS

2

Nicholas J. Mantis

Dept or Program Years in program

Mentor

Novel Mechanism of IgA-Mediated Immunity to *Salmonella typhimurium*

Author (s)

Stephen Forbes, Marisa Eschmann, Richard Cole, William Samsonoff, Nicholas J. Mantis

The monoclonal IgA antibody Sal4 protects intestinal epithelial cells from infection by the enteric pathogen *Salmonella typhimurium*, although the mechanism(s) by which this mAb functions remains unknown. Sal4 recognizes a carbohydrate epitope within the bacterial lipopolysaccharide (LPS) layer and induces bacterial agglutination. We confirmed that Sal4 is neither bacteriocidal nor bacteriostatic. However, using video light microscopy we observed that Sal4 (but not a control IgA) caused a rapid and dose-dependent arrest in bacterial motility that preceded agglutination. Motility of a *S.typhimurium oafA* mutant, which lacks the Sal4 epitope, was not affected under similar experimental conditions. Polyclonal anti-LPS antiserum (anti-O antigen) was as potent as Sal4 in stopping bacterial movement, and, surprisingly, more effective than antiserum directed against the bacterial flagella. Although we have yet to uncover the mechanism by which antibodies against LPS affect flagella function, these data clearly explain, in part, the protective capacity of Sal4, as bacterial motility is required for infection of intestinal epithelial cells *in vitro* and *in vivo*. We also observed by scanning electron microscopy that Sal4-mediated agglutination of *S. typhimurium* induces cell-cell 'fusion' events that we hypothesize may impair secretion of proteins and other molecules across the outer membrane, thereby further attenuating the invasion process. This hypothesis is further supported by evidence indicating that *S. typhimurium* is unable to invade cell monolayers after growth in the presence of Sal4, even when bacterial motility is bypassed via centrifugation. We conclude that Sal4 protects the intestinal epithelium by at least one novel and previously unrecognized mechanism.