

Polysaccharide A: An Immunomodulatory Molecule having Therapeutic Potential against Inflammatory Gut Diseases

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The human gut is colonized by tons of microorganisms but it is still not known how the immune system distinguishes between beneficial and pathogenic microbes. The recent findings from the laboratory of Sarkis K. Mazmanian from California Institute of Technology, Pasadena, CA published in Science [1], provides clue by which our immune system differentiates between the microbiota and enteric infections using *Bacteroides fragilis*. *B. fragilis* is an anaerobic gram negative bacillus and is a human gut commensal bacteria [2]. This bacterium is common in the terminal ileum, and prolific in the colon. Earlier it has been demonstrated that *B. fragilis* uses polysaccharide A (PSA) to prevent activation of immune responses [3-6]. In this study it has been shown that *B. fragilis* in the absence of PSA (*B. fragilis* ΔPSA) is unable to colonize the colon of the animals. Further, *B. fragilis* ΔPSA mounts an inflammatory immune response as indicated by elevation IL-17 immune responses, which can be detrimental to the gut and can cause tissue damage. Treatment of *B. fragilis* mono-associated animals with PSA prevented T_H17 responses suggesting that PSA suppress inflammatory immune responses. The suppression of immune responses by PSA was dependent on toll like receptor-2 (TLR2) expression on T lymphocytes leading to production of IL-10. The results of this study also suggest that Foxp3+ T_{reg} are responsible for the downregulation of T_H17 immune responses. These workers suggested that “unlike pathogens that trigger inflammatory responses through TLRs to clear infections, symbiotic colonization by *B. fragilis* is actually enhanced via the TLR pathway”. It was concluded that “PSA evolved to engender host-bacterial mutualism by inducing mucosal tolerance through TLR2 activation of T_{reg} cells”.

Taken together the results of this study provide us with a molecule (PSA) by which *B. fragilis* colonizes the gut. This study provides clue by which immune system discriminates between beneficial and virulent microorganisms. Since PSA has earlier been shown to protect against intestinal inflammation in a mouse model of experimental colitis [7], therefore, this molecule can be of immense therapeutic potential in down regulating intestinal inflammation observed in gut diseases like inflammatory bowel disease (IBD).

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