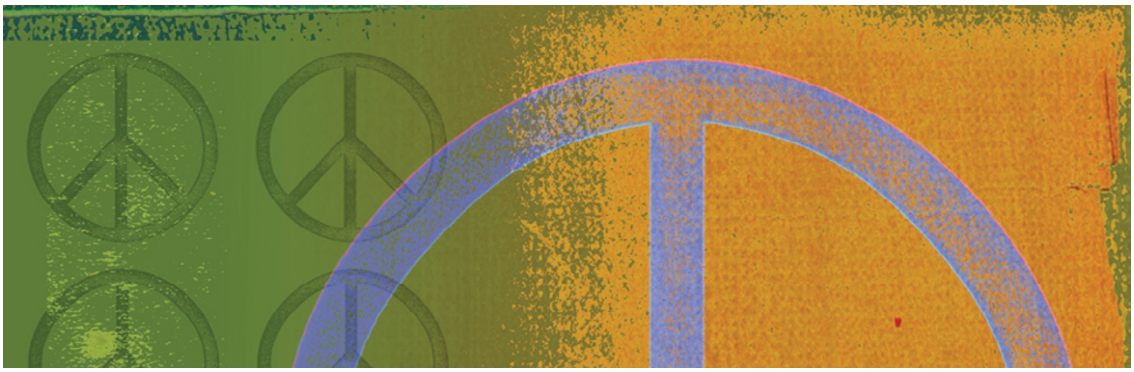
HOST RESPONSE

IgA — peacemaker in the gut



Using a novel gnotobiotic mouse model in which the diverse gut microbiota is reduced to a single bacterial species, and the antibody repertoire to a single monoclonal immunoglobulin A (IgA) antibody that is directed against the bacterium's capsular polysaccharide, Jeffrey Gordon and colleagues provide evidence that supports a role for IgA in the gut as a mediator of tolerance.

The IgA antibody response has a key role in establishing and maintaining a non-inflammatory relationship between the host and microbiota in the gut. Germ-free mice that are colonized with normal gut microbiota develop bacteria-specific IgA antibody responses, but the effects of these responses on the biology of the host and microbiota are not well defined. Peterson *et al.* developed a gnotobiotic mouse model to study these effects.

As their model symbiont, they chose the bacterium *Bacteroides thetaiotaomicron*, which is a prominent, obligately anaerobic, Gram-negative member of the human distal intestinal ecosystem that also efficiently colonizes the intestines of adult germ-free C57BL/6J mice. *B. thetaiotaomicron* was introduced into germ-free, recombination-activating-gene-1-deficient (*Rag1*$^{-/-}$) mice (which lack mature B and T cells) or germ-free *Rag1*$^{-/-}$ mice that had been injected under their dorsal skin with *B. thetaiotaomicron*-primed IgA-producing hybridoma cells.

An inverse relationship was found between IgA antibody levels and the levels of its *B. thetaiotaomicron* epitope in the intestinal lumen — that is, infected mice with IgA secreted by the hybridoma cells had lower levels of epitope expression than mice without IgA. In the absence of IgA, *B. thetaiotaomicron* elicited a more robust innate immune oxidative response, and adapted to this response by inducing genes that are involved in the metabolism of oxidative products of the host response. The presence of IgA, however, reduced intestinal pro-inflammatory signalling (by downregulating signal transducer and activator of transcription 3 and interferon regulatory factor 8, for example), and bacterial epitope expression.

Therefore, these results suggest that it is the IgA antibody response that establishes a quiescent relationship between *B. thetaiotaomicron* and its host. They are also consistent with a model in which a set of adaptations that involve both the symbiont and its host lead to co-evolved homeostasis.

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ORIGINAL RESEARCH PAPER Peterson, D. A. *et al.* IgA response to symbiotic bacteria as a mediator of gut homeostasis. *Cell Host Microbe* **2**, 328–339 (2007)