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BACTERIAL PATHOGENESIS

Message in a bottle

Jennie Vallis/NPG

> outer membrane vesicles ... promote colitis in susceptible mice

The intestinal epithelial barrier is covered by a thick layer of stratified mucus that physically separates commensal bacteria from the epithelial cells and underlying immune cells. Now, a new study shows that the symbiont *Bacteroides thetaiotaomicron* releases antigen-containing outer membrane vesicles (OMVs) that traverse these barriers and access intestinal immune cells in a sulfatase-dependent manner to promote colitis in susceptible mice.

B. thetaiotaomicron is a commensal bacterium that can trigger colitis in CD4-dn*Tgfbr2*;*Il10rb*$^{-/-}$ mice (referred to as dnKO mice), which carry mutations that are associated with disease susceptibility in humans. The authors generated a panel of monoclonal antibodies specific for *B. thetaiotaomicron*, one of which stained the periphery of the bacterial cells and another that labelled small particles that were not associated with bacterial DNA. Using these two antibodies, the authors found that, surprisingly, the whole bacteria remained in the intestinal lumen of diseased dnKO mice that had been pretreated with antibiotics followed by gavage with *B. thetaiotaomicron*. By contrast, small particles, which they subsequently characterized to be OMVs, were present in macrophages around the epithelial crypt base, where inflammation is typically initiated.

One way that OMVs could traverse the host barriers is through the production of sulfatases that degrade sulfated mucin glycans in the mucus layer. So, the authors generated a mutant bacterial strain deficient in sulfatase activity (Δ*anSME* strain). Although Δ*anSME* bacteria colonized the host at levels similar to wild-type *B. thetaiotaomicron* and produced OMVs of similar appearance to wild-type OMVs, these sulfatase-deficient bacteria did not elicit disease in dnKO mice. Indeed, OMVs were rarely observed in intestinal macrophages in dnKO mice colonized with Δ*anSME* bacteria. Furthermore, only colonic macrophages isolated from mice colonized by wild-type *B. thetaiotaomicron*, and not those isolated from mice colonized by the Δ*anSME* strain, expressed mRNA for the pro-inflammatory molecules COX2, TNF and IL-1β.

These data show that OMVs from *B. thetaiotaomicron* access mucosal macrophages in a sulfatase-dependent manner, where they initiate an inflammatory response in susceptible hosts.

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ORIGINAL RESEARCH PAPER Hickey, C. A. *et al.* Colitogenic *Bacteroides thetaiotaomicron* antigens access host immune cells in a sulfatase-dependent manner via outer membrane vesicles. *Cell Host Microbe* **17**, 672–680 (2015)