MUCOSAL IMMUNOLOGY

Setting up camp

Many millions of bacteria colonize our intestines but they are mainly confined to the colon and are kept at low levels in the small intestine. Several host mechanisms have been implicated in preventing bacteria from colonizing the small intestine, and now Nieuwenhuis *et al.* show that the MHC class I-like molecule CD1d — which is recognized by natural killer T (NKT) cells — also contributes to this process by influencing Paneth cell function.

Given that CD1d-restricted NKT cells are important for antimicrobial defence and that CD1d is constitutively expressed by various cells in the intestine, the authors investigated whether CD1d is involved in regulating bacterial colonization of the intestine using mice raised under specific pathogen-free (SPF) or germ-free conditions. They found that oral inoculation of *Cd1d*$^{-/-}$ SPF mice with the pathogenic bacterium *Pseudomonas aeruginosa* led to an overgrowth of bacteria specifically in the small intestine, with much higher levels of *P. aeruginosa* detected in the faeces of these mice than in those of wild-type SPF mice. Other strains of bacteria (including the commensals *Escherichia coli* and *Lactobacillus gasseri* and the Gram-positive bacterium *Staphylococcus aureus*) could also more efficiently and rapidly colonize the small intestines of *Cd1d*$^{-/-}$ mice than those of wild-type mice. A role for CD1d in preventing bacterial colonization was also supported by the finding that administration of the CD1d ligand α-galactosylceramide to wild-type SPF and germ-free mice prior to inoculation with bacteria limited the ability of *E. coli* to establish normal intestinal colonization.

Further comparison of the intestines of *Cd1d*$^{-/-}$ and wild-type mice revealed differences in the composition of the commensal microbiota, with increased quantities of adherent bacteria found in *Cd1d*$^{-/-}$ mice. Moreover, the authors noted profound differences in the morphology and degranulating function of Paneth cells, which are found only in the crypts of the small intestine and are the main source of various antimicrobial proteins; Paneth cells in *Cd1d*$^{-/-}$ SPF mice failed to release the antimicrobial protein lysozyme from intracellular granules in response to microbial colonization. Finally, the finding that Paneth cell degranulation could be induced *in vitro* by incubating wild-type intestinal crypts with NKT cells and α-galactosylceramide led the authors to conclude that CD1d-restricted mechanisms regulate intestinal colonization by acting on Paneth cells.

Lucy Bird

ORIGINAL RESEARCH PAPER Nieuwenhuis, E. E. S. *et al.* Cd1d-dependent regulation of bacterial colonization in the intestine of mice. *J. Clin. Invest.* 6 Apr 2009 (doi:10.1172/JCI36509)