IN BRIEF

MUCOSAL IMMUNOLOGY

RORγt is dispensable for the development of intestinal mucosal T cells.

Naito, T. *et al. Mucosal Immunol.* **1**, 198–207 (2008)

Intraepithelial lymphocytes (IELs) of the gut and other body surfaces comprise the largest peripheral T-cell pool in the body. Whereas about half of IELs originate from the thymus, the origin of the rest has been a subject of debate. Gut cryptopatches — small organized structures containing immature $LIN^{-}CD25^{+}$ $IL\text{-}7R^{+}KIT^{+}$ haematopoietic cells — could be a potential source of local IEL precursors. But other groups suggest instead that cryptopatch cells are the adult counterparts of RORγt (retinoic-acid-receptor-related orphan receptor-γt)$^{+}$ fetal lymphoid-tissue-inducer (LTi) cells that promote lymphoid organogenesis. Now, Naito *et al.* reveal the unappreciated complexity of cryptopatches and suggest that LTi-like cells support the development of cryptopatch T-cell progenitors that are RORγt independent. In support of this model, the expression of RORγt by cryptopatch cells was heterogeneous, RORγt^{-} (and some RORγt^{+}) cryptopatch cells had hallmarks of T-lineage cells and near normal numbers of intestinal IELs were found in RORγt-deficient mice.

IMMUNOGENETICS

Genetic determinants of ulcerative colitis include the *ECM1* locus and five loci implicated in Crohn's disease.

Fisher, S. A. *et al. Nature Genet.* 27 April 2008 (doi:10.1038/ng.145)

Replication of signals from recent studies of Crohn's disease identifies previously unknown disease loci for ulcerative colitis.

Franke, A. *et al. Nature Genet.* 27 April 2008 (doi:10.1038/ng.148)

These two studies identify several new genetic risk variants associated with the inflammatory bowel disease ulcerative colitis. Several of these (*IL23R*, *IL12B*, *HLA*, *NKX2-3* and *MST1*) are already known to be associated with the related disorder Crohn's disease. But others, such as the candidate gene *ECM1*, which is expressed in the intestine and known to activate nuclear-factor-κB signalling, were found to be unique to ulcerative colitis. In addition, Franke *et al.* report evidence for associations of *PTPN2*, *HERC2* and *STAT3* with ulcerative colitis. So, these studies extend our understanding of the genetic relationship between the two disorders and provide exciting avenues for future research.

MUCOSAL IMMUNOLOGY

MR1 uses an endocytic pathway to activate mucosal-associated invariant T cells.

Huang, S. *et al. J. Exp. Med.* **205**, 1201–1211 (2008)

Mucosal-associated invariant T (MAIT) cells are similar to CD1d-restricted NKT cells but are unique in that they preferentially localize to the intestine and require MHC-class-I-related protein (MR1) for their activation and expansion. Antigen presentation by CD1d molecules has been characterized, but the pathway of endogenous antigen presentation by MR1 molecules was not previously known. Here, the authors show that MAIT hybridoma cells were activated by MR1-expressing cells deficient in the MHC class I chaperone proteins and under conditions of proteasome inhibition. By contrast, overexpression of the MHC class II chaperone invariant chain (Ii) augmented MR1-dependent MAIT-cell activation by facilitating MR1 endosomal trafficking. So, similar to MHC class II molecules, MR1 uses an endocytic pathway for presentation of as yet unknown MAIT-cell ligands.