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MUCOSAL IMMUNOLOGY

We seek him here...

Just as the rulers of the French Revolution were unable to discern the identity of the Scarlet Pimpernel in Emmuska Orczy's novel, the function of T cells in the intestinal epithelial layer (intraepithelial lymphocytes; IELs) remains elusive. Two recent studies that investigated the gene-expression profile of IELs provide new insight into the function of these cells.

Reporting in *Proceedings of the National Academy of Sciences*, Fahrner and colleagues used DNA microarrays to compare the gene-expression profiles of $\gamma\delta$ IELs (those expressing a $\gamma\delta$ T-cell receptor) with conventional lymph node CD8 $^{+}$ $\alpha\beta$ T cells in a *Yersinia pseudotuberculosis* infection model. Surprisingly, they found that nearly all of the highly expressed genes, which included granzymes A and B, and the inflammatory chemokine RANTES (CCL5), were expressed at the same level in $\gamma\delta$ IELs from uninfected and infected mice. This implied that, in contrast to lymph node CD8 $^{+}$ $\alpha\beta$ T cells, which must be activated to become cytotoxic effectors, $\gamma\delta$ IELs constitutively transcribe cytotoxic genes. $\gamma\delta$ IELs also expressed natural-killer-inhibitory receptors, which might keep their effector functions under control, but allow them to be rapidly activated against a wide range of pathogens without transcriptional delays.

A second report, by Shires and colleagues in *Immunity*, presents an extensive serial analysis of gene expression (SAGE) of IELs. This

study allowed for the direct comparison of gene-expression patterns of the four main subsets of IELs ($\gamma\delta^{+}$ CD8 α^{-} , $\gamma\delta^{+}$ CD8 α^{+} , $\alpha\beta^{+}$ CD8 α^{+} and $\alpha\beta^{+}$ CD8 $\alpha^{+}\beta^{+}$) from the same anatomical location. An amazing 15,574 distinct transcripts expressed by IELs were identified and categorized depending on their abundance. Granzymes A and B, Fas ligand and CCL5 were highly expressed, whereas homeostatic cytokines and their receptors were expressed at low levels, leading the authors to define them as 'activated-yet-resting' cells. This report also provides insight into how IELs function and respond to growth factors in contrast to peripheral T cells.

To identify functional differences, the authors looked for differential gene expression among the IEL subsets. Preliminary analysis showed that genes were expressed at similar levels in $\gamma\delta$ and $\alpha\beta$ IELs, and $\gamma\delta$ IEL-specific genes were difficult to identify. A number of differences in gene expression were identified in the $\alpha\beta^{+}$ CD8 $\alpha^{+}\beta^{+}$ subset in comparison with other IELs, therefore showing heterogeneity among the $\alpha\beta$ IELs.

These studies have provided further clues as to the function and regulation of these mysterious cells, and the information

generated in these studies will form the basis of much future work.

Jenny Buckland

References and links

ORIGINAL RESEARCH PAPERS Fahrner, A. M. *et al.* Attributes of $\gamma\delta$ intraepithelial lymphocytes as suggested by their transcriptional profile. *Proc. Natl Acad. Sci. USA* **98**, 10261–10266 (2001) | Shires, J., Theodoridis, E. & Hayday, A. C. Biological insights into TCR $\alpha\beta^{+}$ and TCR $\gamma\delta^{+}$ intraepithelial lymphocytes provided by serial analysis of gene expression (SAGE). *Immunity* **15**, 419–434 (2001)

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