of IFNγ-secreting T cells. These data indicate that distinct TLRs might differentially regulate the T_H1/T_H2-cell balance (which, in turn, influences the induction of humoral and cell-mediated immunity).

In addition to improving our understanding of YF-17D, unravelling the mechanism of action of such a successful vaccine might help in the design of vaccines against other microorganisms. The authors conclude that the efficacy of YF-17D is associated with the presence of multiple TLR ligands and therefore postulate that incorporating different combinations of TLR ligands into vaccine candidates might allow the stimulation of strong, appropriate immune responses.

Davina Dadley-Moore

ORIGINAL RESEARCH PAPER Querec, T. *et al.* Yellow fever vaccine YF-17D activates multiple dendritic cell subsets via TLR2, 7, 8, and 9 to stimulate polyvalent immunity. *J. Exp. Med.* **203**, 413–424 (2006)

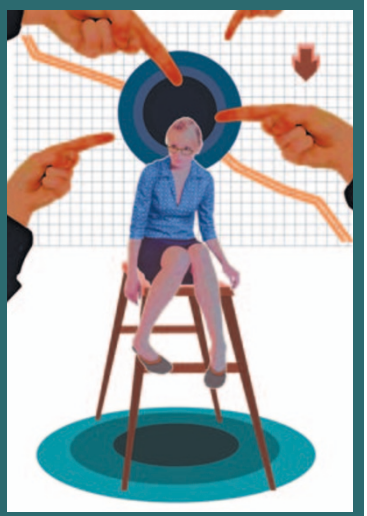
WEB SITE

Bali Pulendran's homepage: http://www.vaccines.emory.edu/scientists/pulendran.shtml

antibodies are required to prevent allograft rejection and that treatment with CD154-specific antibodies has been associated with thromboembolic complications.

Karen Honey

ORIGINAL RESEARCH PAPER Xu, H., Zhang, X., Mannon, R. B. & Kirk, A. D. Platelet-derived or soluble CD154 induces vascularized allograft rejection independent of cell-bound CD154. *J. Clin. Invest.* 23 Feb 2005 (doi:10.1172/JCI127155)



T-CELL MEMORY

Location, location, location

Can the tissue microenvironment influence memory CD8⁺ T-cell differentiation? Recent research published in *The Journal of Immunology* indicates that the anatomical location directly influences the differentiation of memory CD8⁺ T cells.

Two subsets of memory CD8⁺ T cells have previously been identified: CD8⁺ central memory T (T_{CM}) cells, which express CD62L and traffic through the blood, spleen and lymph nodes; and CD8⁺ effector memory T (T_{EM}) cells, which lack CD62L and circulate through the parenchyma of non-lymphoid tissue. It is unclear, however, whether pathogen-specific CD8⁺ T cells that persist in the intraepithelial compartment of the intestinal mucosa following clearance of infection fit neatly into the T_{CM}- or T_{EM}-cell subsets. This study compared the phenotype of these three CD8⁺ T-cell populations and showed that virus-specific CD8⁺ T cells from the gut do not resemble either the T_{CM}- or T_{EM}-cell populations found in the blood or spleen.

By transferring naive CD8⁺ T cells from the spleen of P14 transgenic mice — that is, T cells specific for an immunodominant epitope of lymphocytic choriomeningitis virus (LCMV) — to recipient mice that are then infected with LCMV, Masopust and colleagues could track a monoclonal homogeneous starting population of CD8⁺ T cells at all stages of the response.

A comparison of CD8⁺ T cells from the spleen and gut 85 days after infection showed a marked difference in phenotypic and functional properties. Gut CD8⁺ T cells expressed large amounts of granzyme B, CD69 and CD103 but small amounts of CD62L and Ly6C, whereas splenic CD8⁺ T cells showed the opposite phenotype. In addition, gut CD8⁺ T cells produced less interleukin-2 (IL-2) and lacked expression of the IL-15 receptor β-chain, and a smaller proportion of these cells produced the antiviral cytokines interferon-γ and tumour-necrosis factor than did splenic CD8⁺ T cells. Interestingly, although gut CD8⁺ T cells are $CD62L^{low}$, none of the phenotypic characteristics resembles those of T_{EM} cells (or T_{CM} cells), showing that a unique population of memory CD8⁺ T cells resides in the gut.

To examine the role of the microenvironment on the development of memory CD8⁺ T cells, memory T cells isolated from the spleen and gut of infected mice were transferred to naive mice, which were then challenged with LCMV. Examination of phenotypic characteristics following restimulation and migration of these transferred cells showed that both spleen and gut memory CD8⁺ T cells largely adopted the characteristics of their new environment. For example, gut memory CD8⁺ T cells remained $Ly6C^{low}$ within the gut but became $Ly6C^{hi}$ CD8⁺ T cells when localized in the spleen, similar to T_{CM} or T_{EM} cells, whereas spleen CD8⁺ T cells had reduced expression of Ly6C when they localized in the gut following secondary infection.

These data show that a unique population of memory CD8⁺ T cells, distinct from CD8⁺ T_{CM} or T_{EM} cells, is found in the gut. They also indicate that the microenvironmental location directly influences the differentiation of memory CD8⁺ T cells, but the mechanism involved has yet to be described.

Olive Leavy

ORIGINAL RESEARCH PAPER Masopust, D., Vezys, V., Wherry, E. J., Barber, D. L. & Ahmed, R. Gut microenvironment promotes differentiation of a unique memory CD8 T cell population. *J. Immunol.* **176**, 2079–2083 (2006)