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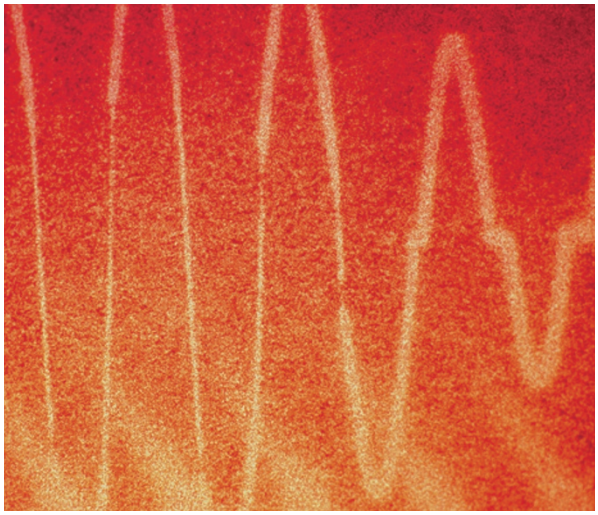
T CELLS

New regulator of calcium signalling



A protein known as SLAT (SWAP70-like adaptor of T cells) was recently identified, but elucidation of its function awaited further study. Now, reporting in *The Journal of Clinical Investigation*, Bécart *et al.* show that SLAT is required for T-cell development, activation and effector function, and it does this by controlling calcium signalling.

SLAT (also known as IBP) is a guanine-nucleotide-exchange factor that is known to be activated following ligation of the T-cell receptor (TCR). To investigate the physiological role of SLAT in T cells, Bécart *et al.* studied T-cell development in SLAT-deficient mice. Their analysis revealed that there was a defect at an early stage of thymocyte development in *Slat*$^{-/-}$ mice, such that proliferation of thymocytes at the double negative 1 (DN1) stage was impaired. As a result, fewer CD4^{+} T cells and, to a lesser extent, CD8^{+} T cells were present in the periphery of *Slat*$^{-/-}$ mice compared with wild-type mice.

Moreover, those CD4^{+} T cells that did populate the periphery in *Slat*$^{-/-}$ mice showed markedly reduced proliferation and interleukin-2 production in response to TCR and CD28 ligation, although they proliferated normally in response to PMA (phorbol 12-myristate 13-acetate) plus ionomycin (stimuli known to bypass the TCR).

Previous studies had suggested that SLAT might be involved in T helper 2 (T_H2)-cell differentiation, so the authors next tested the ability of *Slat*$^{-/-}$ mice to mount T_H2-cell-mediated lung inflammation. As expected, there was a marked reduction in T_H2-cell-mediated lung inflammation in *Slat*$^{-/-}$ mice; unexpectedly, however, *Slat*$^{-/-}$ mice also failed to mount T_H1-cell-mediated lung inflammatory responses, indicating that SLAT is involved in responses by both T_H1- and T_H2-cell subsets.

Further investigation into the activation defect in T cells from *Slat*$^{-/-}$ mice indicated that the most marked defect was in the nuclear translocation of NFAT (nuclear factor of activated T cells) following TCR and CD28 stimulation. Consistent with this, the initial rise in the free intracellular Ca^{2+} concentration that should occur following TCR ligation to promote NFAT translocation was severely reduced in the absence of SLAT. This, the authors show, most likely reflects a defect in the release of Ca^{2+} from endoplasmic reticulum stores.

So, by controlling TCR-induced Ca^{2+} and NFAT signalling, SLAT is required for proper T-cell development and effector function.

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ORIGINAL RESEARCH PAPER Bécart, S. *et al.* SLAT regulates Th1 and Th2 inflammatory responses by controlling Ca^{2+}/NFAT signaling. *J. Clin. Invest.* **117**, 2164–2175 (2007)
FURTHER READING Feske, S. Calcium signalling in lymphocyte activation and disease. *Nature Rev. Immunol.* **7**, 690–702 (2007)