Oxidation-sensitive adhesion

Cross-linking of the T cell receptor (TCR) can induce production of reactive oxygen species (ROS). Yet, how TCR-mediated ROS generation links to downstream signaling pathways remains unknown. In the *EMBO Journal*, Kwon *et al.* show that reversible oxidation of a cysteine residue in the active site of the protein tyrosine phosphatase SHP-2 occurs after TCR ligation. This modification inhibits SHP-2 catalytic activity. As a result, an increased abundance of signaling complexes containing phosphorylated Vav1 and ADAP (adhesion and degranulation adaptor protein), a regulator of inside-out β-integrin activation, associates with the adaptor SLP-76. Cells with SHP-2 mutants that mimic the ROS-mediated oxidative enzyme inactivation show increased adhesive properties. Thus, TCR-generated ROS increases T cell adhesion by reversible inhibition of SHP-2. ***LAD***
***EMBO J.* 24, 2331–2341 (2005)**

CD28's other talent

Ligation of the T cell receptor (TCR) and the co-stimulatory molecule CD28 results in phosphorylation of intracellular molecules, which leads to T cell activation. In the *Journal of Experimental Medicine*, Blanchet *et al.* identify arginine methylation of signaling proteins as another level of control of T cell activation. CD28 signaling, with only minor contribution from TCR signaling, induces arginine methylation of the signaling molecule Vav1 through the methyltransferase enzyme PRMT. Studies of the kinetics of protein modification suggest that Vav1 is methylated in the nucleus. Inhibition of the methyltransferase activity results in a decrease in interleukin-2 production by the activated T cells, indicating the importance of this CD28 signaling pathway. *PTL*
J. Exp. Med. **202**, 317–377 (2005)

SLAPping down zeta

How Src-like adaptor protein (SLAP) dampens T cell receptor (TCR) signaling via Src-family kinases is not well understood. In the *Journal of Cell Biology*, Myers *et al.* find that SLAP binds directly to phosphorylated TCRζ found in TCR-CD3 complexes on internalized, recycling clathrin-coated vesicles. The association of SLAP and TCRζ leads to lysosomal degradation of TCRζ and hence decreased TCR-CD3 recycling to the plasma membrane. The functional consequence is reduced steady-state TCR-CD3 available for signaling. The mechanism by which SLAP affects TCRζ degradation seems to require Lck and probably ubiquitination via c-Cbl. This regulatory pathway may provide insight into why SLAP is most highly expressed in double positive thymocytes, where the strength of TCR-CD3 signals is thought to be crucial for subsequent thymocyte development. ***DCB***
***J. Cell Biol.* 170, 285–294 (2005)**

Nipah virus receptor

Nipah virus is an emerging neurotrophic pathogen that causes substantial mortality and infects multiple mammalian species. In *Nature*, Negrete *et al.* report the identification of the receptor used by Nipah virus to infect human cells as EphrinB2. The host receptor, which is a signaling ligand for ephB tyrosine kinase receptors, was identified using immunoglobulin fusion proteins containing viral envelope glycoproteins. Transfection of ephrinB2, but not the closely related ephrinB1, into nonpermissive cells conferred susceptibility to Nipah virus syncytium formation, a hallmark of infection by this virus. Countermeasures can now be pursued that are aimed at blocking viral entry via the EphrinB2 interaction. *LAD*
Nature **436**, 401–405 (2005)

Janus-faced dendritic cells

Using dendritic cells (DCs) as antigen-loaded mediators of vaccination is in vogue. Exactly which subtype of DCs promotes the most effective immunity, however, is still under investigation. In the *Proceedings of the National Academy of Sciences,* Radhakeishnan *et al.* describe a unique population of DCs that show both the avid antigen-uptake potential of immature DCs and the strong co-stimulatory activity of mature DCs. Concomitant stimulation of mature DCs with both Toll-like receptor agonists and a unique antibody to B7-DC, a recently described member of the B7 family of co-stimulatory molecules, results in DCs with the dual-function phenotype. This synergistic outcome is associated with an anti-B7-DC–dependent increase in *Cdc42* mRNA, a Rho family GTPase involved in endocytosis. This unique method of producing dual-function DCs may aid the quest for optimal DC-based vaccination. *DCB*
Proc. Natl. Acad. Sci. USA **102**, 11438–11443 (2005)

Class II cytotoxic T cells

Competing models of thymocyte lineage determination remain actively disputed. Sarafova *et al.*, in *Immunity*, offer a powerful volley in favor of the 'kinetic signaling' model. This model postulates that CD4-CD8 lineage fate is determined by differences in TCR signal strength due to the kinetics of *Cd4* and *Cd8* gene expression during positive selection. By transiently suppressing *Cd4* transgene expression via the known *Cd8* enhancer $E8_{III}$, they show that parallel downregulation of $E8_{III}$-*Cd4* and endogenous *Cd8* during positive selection results in major histocompatibility complex (MHC) class I and MHC class II expressing peripheral T cells with cytotoxic CD8-lineage properties. They conclude that TCR and co-receptor signals, required to initiate positive selection, do not dictate lineage. Instead, the crucial factor determining lineage fate is duration of co-receptor signaling during positive selection. *DCB*
Immunity **23**, 75–87 (2005)

NK traffic

Natural killer (NK) cells are among the earliest cells to be activated during an infection. However, the precise early responses of these cells, such as the site of proliferation and trafficking pattern, are unclear. In the *Journal of Immunology*, Prlic *et al.* find that NK cells accumulate rapidly at the site of infection, whereas their numbers decrease in the spleen. The accumulation of NK cells at the infection site is primarily due to migration rather than local proliferation. In contrast, NK cells proliferate extensively in the spleen during infection. The trafficking of NK cells to the site of infection, but not to other tissues, is dependent on signaling via a G protein–coupled receptor. Thus, NK cells trafficking appears to mimic that of memory T cells. ***PTL***
***J. Immunol.* 175, 2152–2157 (2005)**

Written by Douglas C. Braaten, Laurie A. Dempsey, and Peter T. Lee.