IN BRIEF

T CELLS

The junctional adhesion molecule JAML is a costimulatory receptor for epithelial γδ T cell activation

Witherden, D. A. *et al. Science* **329**, 1205–1210 (2010)

The molecular interaction of CAR and JAML recruits the central cell signal transducer PI3K

Verdino, P. *et al. Science* **329**, 1210–1214 (2010)

γδ T cells in the skin provide a rapid response to environmental insults and are important for maintaining epithelial integrity, but little is known about what activates them to carry out these functions. In these two papers, junctional adhesion molecule-like protein (JAML) is identified as a co-stimulatory receptor for epithelial γδ T cells and the interaction with its ligand Coxsackie and adenovirus receptor (CAR) is subject to structural analysis, providing evidence that the JAML–CAR interaction on γδ T cells has an equivalent co-stimulatory function to the B7–CD28 interaction on αβ T cells. JAML was found to be expressed at a low level by resting γδ T cells from the skin and was upregulated following stimulation of the cells with a mitogen. Ligation of JAML with a specific monoclonal antibody induced proliferation and cytokine production by skin γδ T cells, but had no stimulatory effect on splenic γδ T cells or $CD8^+$ αβ T cells, despite their expression of JAML. Moreover, CAR ligation of JAML led to rapid binding of phosphoinositide 3-kinase (PI3K) to a YMxM motif in the JAML intracellular domain, a motif that is also present in CD28. In addition, co-ligation of the γδ T cell receptor and JAML increased JNK activation compared with ligation of each receptor alone. A requirement for JAML-mediated co-stimulation *in vivo* was confirmed by the finding that blockade of the JAML–CAR interaction immediately after wounding of mouse skin was associated with reduced activation of skin γδ T cells and delayed wound closure. It is thought that γδ T cells in the skin receive this co-stimulatory signal from neighbouring keratinocytes that express CAR.

T CELL SIGNALLING

Differential effects of STAT5 and PI3K/AKT signaling on effector and memory CD8 T-cell survival

Hand, T. W. *et al. Proc. Natl Acad. Sci. USA* 7 Sep 2010 (doi:10.1073/pnas.1003457107)

Several studies indicate that contraction of the effector $CD8^+$ T cell response after viral infection is not stochastic, but what determines the cell fate decision between effector cell death or survival as a long-lived memory cell? This study supports the hypothesis that intrinsic differences between effector and memory $CD8^+$ T cells modulate their responsiveness to the pro-survival cytokines interleukin-7 (IL-7) and IL-15. Memory-precursor cells had greater activation of the phosphoinositide 3-kinase (PI3K)–AKT pathway in response to IL-15 than short-lived effector $CD8^+$ T cells. However, constitutive activation of AKT in effector $CD8^+$ T cells did not increase their survival and was associated with decreased expression of the receptors for IL-2, IL-7 and IL-15, thus preventing downstream phosphorylation of signal transducer and activator of transcription 5 (STAT5) in response to these cytokines. STAT5 signalling downstream of IL-7 and IL-15 receptors was required for the survival of both effector and memory T cells, indicating that STAT5 signalling is somehow limiting in effector T cells after infection.