SLAM: measles virus receptor

In *Nature*, Tatsuo *et al.* further our understanding of measles virus (MV) pathogenesis. The Edmonston strain of MV, and vaccine strains derived from it, use CD46 as a cellular receptor. However, most clinical isolates cannot use this receptor. This group identified human SLAM (signaling lymphocyte–activation molecule) as the cellular receptor for MV. Nonsusceptible cell lines can bind MV, support viral replication and develop cytopathic effects when transfected with SLAM cDNA. SLAM is constitutively expressed on immature thymocytes, memory T cells and a proportion of B cells, and can be induced on T and B cells following activation. Therefore, the tissue distribution of SLAM, unlike CD46, which is ubiquitously expressed, is consistent with the pathology of MV infection in humans.

Nature **406**, 893–97 (2000)

Cytotoxic Vav-2

In the *Journal of Experimental Medicine,* Billadeau *et al.* identified Vav-2 as a specific RhoA family guanine nucleotide exchange factor (GEF) that regulates cell-mediated cytotoxicity. After cross-linking activating receptors on CTLs, Vav-2 is phosphorylated on tyrosine. Cellular cytotoxicity can be enhanced by overexpression of Vav-2 and is dependent on the Dbl homology and Src homology 2 domains. In addition, the pleckstrin domain is required for activation of Vav-2 by certain activating receptors on NK cells. Unlike Vav, another GEF family member, Vav-2 is unable to regulate NFAT AP-1–mediated gene transcription after TCR cross-linking. Thus, Vav-2 differs from Vav and plays a role in the regulation of the development of cell-mediated cytotoxicity.

J. Exp. Med. **192**, 381–91 (2000)

CD1 presentation pathways

CD1b and CD1c are known to present mycobacterial lipid and glycolipid antigens to specific T cell subsets. Two articles shed light on the trafficking pathways of CD1b and CD1c. In the *Journal of Immunology,* Geho *et al.* engineered GPI-modified variants of CD1 molecules. Although the GPI-modified CD1c was equally efficient at presenting antigen as the unmodified form, the same was not true for the GPI-modified CD1b, suggesting that the two molecules have non-overlapping antigen presenting pathways. In the *Journal of Experimental Medicine,* Briken *et al.* found that unlike CD1c, CD1b antigen presentation is affected by the presence of drugs inhibiting endosomal acidification, suggesting that that CD1b, but not CD1c, is localized in acidic vesicles.

J. Immunol. **165**, 1272–77 (2000)
J. Exp. Med. **192**, 281–87 (2000)

ICOS and costimulation

Complete immune activation requires costimulatory signals in addition to those delivered to the TCR by MHC-peptide complexes. In *Immunity*, Coyle *et al.* investigated the role of a CD28-related molecule, ICOS, in immune activation. Functionally, ICOS regulates cytokine production (IL-2, IL-4, IL-5 and IFN-γ) from recently activated T cells but not naïve T cells. T cell–dependent B cell activation in a secondary immune response is at least in part ICOS-dependent *in vivo*. However, ICOS only contributes to highly differentiated T_H2 but not T_H1 effector function *in vitro*, and ICOS blockade selectively inhibits T_H2- but not T_H1-mediated inflammation and altered airway responsiveness. These data suggest that ICOS is an important molecule for T cell–dependent immune responses.

Immunity **13,** 95–105 (2000)

Role of CD30 on γδ T cells

CD30 is a member of the TNFR superfamily. It is expressed on Hodgkin's lymphoma cells and activated lymphocytes. In the *European Journal of Immunology,* Biswas *et al.* show that CD30 is highly expressed on recently activated human γδ T cells, and elevated CD30 levels persist in long-term cultures of these cells without further stimulation. On CD3 stimulation, engagement of CD30 enhanced the expression of IL-4, IFN-γ, IL-8 and certain other chemokines. However, expression of IL-10 was not enhanced, and secretion of MCP-1 was not detected. The study shows that triggering of CD30 may modulate the expression of certain γδ T cell cytokines to shape the outcome of an immune response.

Eur. J. Immunol. **30**, 2171–80 (2000)

Complementing SLE

C1q is known to bind to surface blebs of apoptotic cells, and common SLE autoantigens have been localized on the surfaces of apoptotic cells. These observations have led to the hypothesis that C1q deficiency may predispose to autoimmunity as a consequence of impaired clearance of apoptotic cells. In the *Journal of Experimental Medicine*, Taylor *et al.* used complement (C)-deficient mice to determine the relative contribution of different C proteins to the phagocytosis of apoptotic cells using an *in vitro* murine peritoneal model of apoptotic cell clearance. Clearance of human apoptotic cells in this system required both C1q and C4, indicating that opsonization with C3 was the most likely pathway of clearance. However, clearance of apoptotic syngeneic murine cells was much more severe in the C1q-deficient mice compared to the C4-deficient animals. This result shows a hierarchy of importance of C proteins in the phagocytic clearance of apoptotic cells.

J. Exp. Med. **192**, 359–66 (2000)

Control of endocytosis in DCs

Highly endocytic immature dendritic cells (DC) capture large amounts of antigen efficiently unlike mature DCs, which are poorly endocytic. In the August edition of *Cell*, Garret *et al.* unravel the mechanisms that control endocytosis during DC maturation. They show that endocytosis in immature DCs can be abrogated by inhibition of Cdc42 using Toxin B or microinjection of dominant-negative inhibitors of Cdc42. Injection of constitutively active Cdc42 or *S. typhimurium* delivery of a Cdc42 nucleotide exchange factor reactivated endocytosis in mature DCs. In addition, endogenous levels of Cdc42-GTP are reduced in mature versus immature DCs. Thus, levels of Cdc42 appear to play a role in the developmental regulation of endocytosis in DC.

Cell **102**, 325–34 (2000)