Immunosuppressive viral proteins

Measles virus (MV) can cause profound immunosuppression, however, the mechanisms behind this remain elusive. In *Immunity*, Marie *et al.* use a mouse model to investigate the role of MV proteins in the generation of immunosuppression *in vivo*. MV proteins, in the absence of MV replication, could induce systemic immunosuppression *via* two pathways. One requires MV-nucleoprotein and its cellular receptor FcγR on dendritic cells (DCs) and the other involves virus envelope glycoproteins and the MV-hemagglutinin receptor, CD46. The MV proteins ablated hypersensitivity responses, decreased IL-12 production by DCs and impaired antigen-specific T cell proliferation. Thus, MV proteins can modulate DC function and affect the priming and effector phase of hypersensitivity, making them candidates for therapeutic use.

Immunity **14**, 69–79 (2001)

Unoccupied stable β dimer

The cytokines GM-CSF, IL-3 and IL-5 use unique α subunit receptors but share a common β_c receptor subunit. In *Cell,* Young and colleagues report the structure of the complete extracellular domain of the βc subunit at a 3 Å resolution. These cytokines are involved in the regulation of hematopoiesis and inflammation. GM-CSF and IL-3 are both broad-acting growth regulators, whereas IL-5 plays a unique role in the regulation of eosinophils. The subunit structure is unlike any class I cytokine receptor described previously. It forms a unique interlocking dimer structure and gives new insights into the mechanism of receptor activation.

Cell **104**, 291–300 (2001)

PPARγ cholesterol efflux

The nuclear receptor PPARγ has been implicated in macrophage uptake of oxidized LDL. In *Molecular Cell*, Tontonoz and colleagues provide evidence that, in addition to lipid uptake, PPARγ regulates a cholesterol efflux pathway. This occurs *via* a transcriptional cascade mediated by nuclear receptor LXRα. Ligand activation of PPARγ induces LXRα, which leads to induction of the transporter protein ABCA1. Transfer of PPARγ-deficient bone marrow into $LDLR^{-/-}$ mice results in a significant increase in atherosclerosis. The authors propose that macrophage PPARγ coordinates a complex physiological response to oxidized LDL and cholesterol removal through ABCA1.

Mol. Cell **7**, 161–171 (2001)

Mgat5, a negative regulator

Specific glycan structures play a role in lymphocyte adhesion, recirculation and maturation. The enzyme Mgat5 catalyzes the addition of β1,6GlcNAc to N-glycans. Magt5-modified glycans bind galectins, proteins that restrict TCR mobility. In *Nature*, Demetriou *et al.* examined the role of Mgat5 in T cell immunity using Mgat5-deficient mice. These mice displayed kidney autoimmune disease, enhanced delayed hypersensitivity and an enhanced susceptibility to experimental autoimmune encephalomyelitis. Mgat5-deficient T cells showed enhanced ligand-dependent TCR recruitment, signal transduction, microfilament reorganization and proliferation. Pretreatment of wild-type T cells with lactose, a galectin competitor, also induced TCR clustering. These results suggest that the absence of Mgat5-modified glycans can lower T cell activation thresholds by enhancing TCR clustering. Thus, Mgat5-dependent galectin-glycoprotein lattice may act as a negative regulator of T cell activation. Dysregulation of Magt5 may increase susceptibility to autoimmune disease.

Nature **409**, 733–739 (2001)

Exosomes help reject tumors

T cell–mediated anti-tumor responses require DC presentation of tumor-antigen peptides on MHC class I. A study by Wolfers *et al*. in the March issue of *Nature Medicine* identifies a new source of tumor antigens available for DCs. They show that exosomes, small membrane vesicles secreted by cells, isolated from tumor cells are taken up by DCs. Exosomes display a discrete set of molecules involved in antigen presentation, including MHC class I and II and costimulatory molecules. DCs, loaded with tumor-derived exosomes, induce potent $CD8^+$ T cell–dependent anti-tumor responses to established syngeneic and allogeneic tumors. Exosomes from tumor cells may represent a source of tumor-rejection antigens relevant for immunotherapy.

Nature Med. **7**, 297–303 (2001)

MHC signaling through Igα-Igβ

Paired molecules on T and B cells mediate adhesion and signal transduction events during cognate T-B interactions. The TCR-pMHC class II interaction is central among these interactions, transducing signals that lead to Src family kinase activation, $Ca2^+$ mobilization and proliferation. In *Science*, Cambier and colleagues. investigate the mechanism by which TCR-pMHC class II interaction leads to B cell activation. MHC class II molecules associate with Igα-Igβ heterodimers after antigen stimulation of resting B cells and function as signal transducers upon MHC class II aggregation by TCR. Class II MHC-associated Igα-Igβ heterodimers are derived, but distinct, from BCRs. Thus, these data show that Igα-Igβ heterodimers are sequentially used to transduce both antigen and cognate T helper cell signals.

Science 291 (2001)

IKKα and B cells

IκB kinase (IKK) α and β phosphorylate IκB proteins resulting in NF-κB activation. These highly homologous kinases play differential roles *in vivo*. In the *Journal of Experimental Medicine*, Akira and colleagues analyze the *in vivo* role of IKKα in hematopoietic cells by generating bone marrow chimeras with a transfer of fetal liver cells from mice obtained by intercrossing $IKK\alpha^{+/-}$ mice. $IKK^{-/-}$ chimeras exhibited a decrease in mature B cells, serum immunoglobulin and impaired antigen-specific immune responses. The splenic microarchitecture, including germinal center formation, was disrupted. $IKK\alpha^{-/-}$ B cells exhibited enhanced cell death, impaired mitogenic responses and reduced NF-κB activity *in vitro*, whereas B cell turnover rate was increased *in vivo*. Bcl-2 expression could only partially rescue impaired B cell development. Thus, IKKα is critical for mature B cell development and function.

J. Exp. Med **193,** 417–426 (2001)