(lacking IL-12 and IL-23) and p19-deficient mice (lacking IL-23 only) were resistant to EAE. Introduction of IL-23 into the CNS of mice lacking IL-23 using gene-transfer vectors reconstituted susceptibility to EAE, although the mice lacking both IL-12 and IL-23 had delayed onset and severity of disease. Supplying p40-deficient mice with either IL-12 (from day 0), or IL-12 (from day 0) plus IL-23 (from day 8), during the induction of EAE showed that IL-12 alone did not lead to EAE but that the combined cytokine treatment did, which indicates that IL-23 is important for inflammatory events that follow the induction of $T_H1$ cells.

The authors then took a closer look at T-cell responses compared with macrophage responses. Mice lacking IL-23 alone generated MOG-specific T-cell responses, but IL-12-deficient mice could only develop $T_H2$-cell responses. MOG-specific T cells and inflammatory macrophages ($CD4^-CD11b^+CD45^{hi}$) could migrate to the CNS in IL-12-deficient mice, but this did not lead to the further recruitment of T cells or macrophages, and the resident macrophages (or microglia) were not activated.

Using real-time quantitative PCR to assess the expression of cytokine and cytokine-receptor genes, the authors observed that IL-23 is produced by inflammatory macrophages and microglial cells, but that only the former cells can respond to IL-23. By contrast, IL-12 is produced mainly by inflammatory macrophages, but both cell types can respond to it.

So, previous data from studies involving p40 might need to be re-interpreted with regard to the role of IL-12. This study shows that IL-23 mediates the later inflammatory events that follow the induction of $T_H1$ cells. As IL-23 seems to be important for chronic inflammation, it could be a good therapeutic target for many autoimmune inflammatory diseases.

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**References and links**

**ORIGINAL RESEARCH PAPER** Cua, D. J. *et al.* Interleukin-23 rather than interleukin-12 is the critical cytokine for autoimmune inflammation of the brain. *Nature* **421**, 744–748 (2003)

# IN BRIEF

INNATE IMMUNITY

## Impairment of dendritic cells and adaptive immunity by Ebola and Lassa viruses.

Mahanty, S. *et al. J. Immunol.* **170**, 2797–2901 (2003)

Ebola and Lassa viruses cause haemorrhagic fevers. Early infection seems to be associated with the release of pro-inflammatory mediators. But people who survive Lassa-virus infection show signs of immune suppression and delayed adaptive immune responses. The role of dendritic cells (DCs) in Ebola and Lassa virus infections is not known. The results of this study show that both viruses can infect and replicate in human monocyte-derived DCs. Infected DCs did not secrete several pro-inflammatory cytokines and co-stimulatory molecules were not upregulated. Furthermore, these DCs failed to induce T-cell proliferation in mixed-lymphocyte reaction assays. These results indicate that DCs do not become activated after virus infection, either because of active suppression of DCs or failure of DC maturation.

SIGNAL TRANSDUCTION

## Vav1 transduces TCR signals required for LFA-1 function and cell polarization at the immunological synapse.

Ardouin, L. *et al. Eur. J. Immunol.* **33**, 790–797 (2003)

T-cell receptor (TCR)-triggered rearrangement of the actin cytoskeleton is crucial for T-cell activation. It was suspected that Vav1, a guanine nucleotide exchange factor for the Rho-family GTPases, is involved in these processes as Rho-family proteins are important regulators of the actin cytoskeleton and Vav1-deficient T cells have defective TCR-signal transduction. As *Vav1*$^{-/-}$ TCR-transgenic mice lack mature T cells, $CD4^+CD8^+$ thymocytes from these mice were examined for cytoskeleton-dependent TCR-driven events. Although Vav1 was not required for the clustering of proteins at the immunological synapse, it was essential for 'inside-out' signals that lead to the activation of the integrin LFA1 and for the polarization of the microtubule-organizing centre towards the immunological synapse.

DENDRITIC CELLS

## Compartmentalized production of CCL17 *in vivo*: strong inducibility in peripheral dendritic cells contrasts selective absence from the spleen.

Alferink, J. *et al. J. Exp. Med.* **197**, 585–599 (2003)

Several chemokines have been implicated in the attraction of T cells by dendritic cells (DCs), including CCL22 and CCL17, which bind to the chemokine receptor CCR4 on activated T cells. To clarify the role of CCL17, mice were created in which a green fluorescent protein reporter gene was inserted into the *Ccl17* locus. The highest expression level of CCL17 was by mature myeloid DCs, including the Langerhan's cells of the skin and the DCs of the Peyer's-patch subepithelial dome. Exposure to Toll-like receptor ligands was found to upregulate the expression of CCL17 by these peripheral DCs. But, strikingly, splenic DCs never expressed CCL17, even after systemic microbial challenge.