IFN-γ than wild-type cells. Together with the observation that IL-27 induced the phosphorylation of STAT1 (signal transducer and activator of transcription 1), these results led the authors to suggest that WSX1 signalling is required for STAT1 activation, and subsequent T_H1-cell differentiation, only when IL-12 is limiting, and that in situations in which IL-12 is plentiful — such as during *T. gondii* infection — WSX1 is not required for the generation of a T_H1-cell response and is, in fact, required to prevent overproduction of cytokines.

Using Wsx1-deficient mice these two studies have revealed a new role for WSX1 as a negative regulator of the cytokine response to intracellular pathogens, making it a potential therapeutic target for the treatment of inflammatory diseases.

Karen Honey

References and links

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T-CELL MEMORY

Staying alive with IL-7

The generation and survival of memory T-cell populations are crucial for prolonged protective immunity following infection. Although the factors involved in $CD8^+$ memory T-cell homeostasis are well defined, an important role for interleukin-7 (IL-7) in the generation and maintenance of $CD4^+$ memory T cells has only recently been clarified by two groups, reporting in *The Journal of Experimental Medicine*.

Activated effector cells are highly susceptible to apoptosis; factors that rescue cells from programmed cell death or activation-induced cell death are crucial for the transition of effector T cells to persistent memory cells. The common γ chain receptor cytokines IL-7 and IL-15 have previously been shown to be important for the survival of naive T cells and $CD8^+$ memory T cells. The survival of naive T cells depends on stimulation through the T-cell receptor (TCR) and is usually accompanied by cell division, whereas the survival of memory populations seems to be independent of TCR ligation and division. Previous *in vivo* and *in vitro* studies on the role of IL-7 in the homeostasis of $CD4^+$ T-cell memory have produced conflicting data.

Both reports start by showing that addition of low doses of IL-7 to $CD4^+$ memory cells *in vitro* promotes cell survival in the absence of cell division. Increased survival was concomitant with the upregulation of expression of the anti-apoptotic protein Bcl-2 and memory cell markers. Using different approaches, they then went on to see whether the same was true *in vivo*.

JiChu Li *et al.* generated activated $CD4^+$ effector T cells *in vitro* from wild-type and IL-7 receptor (IL-7R)-deficient mice and co-transferred them to wild-type mice or MHC class-II-deficient mice to assess the dependency of effector–memory transition on IL-7 signalling and TCR ligation *in vivo*. After only two days, the survival of the transferred *IL-7R*$^{-/-}$ cells was markedly lower than wild-type cells, which expressed increased levels of Bcl-2. Recovery of transferred cells was also IL-7 dependent in MHC class II$^{-/-}$ hosts.

Kondrack *et al.* generated resting memory cells *in vivo* by transferring naive $CD4^+$ T cells specific for ovalbumin (OVA)-derived peptide (OT-II cells) to intact or lymphopaenic recipients, which were then immunized with OVA. *In-vivo*-induced resting memory cells were repurified and transferred to wild-type or *IL-7*$^{-/-}$ hosts. Few OT-II memory cells could be recovered from the *IL-7*$^{-/-}$ mice after one week, whereas those in control mice persisted for extended periods of time. They also showed that both central memory (lymph-node homing, $CD62L^+$) and effector memory cells ($CD62L^-$), which reside in the non-lymphoid organs, require IL-7 for persistence. When memory OT-II cells were generated in OVA-immunized *IL-7*$^{-/-}$ hosts, cells initially proliferated, as in *IL-7R*$^{-/-}$ hosts; however, OT-II cells were no longer detectable by day 21 in lymphoid or non-lymphoid organs.

Finally, both groups confirmed the requirement of IL-7 for $CD4^+$ memory T-cell generation and persistence in recipient mice that were rendered deficient in IL-7 by antibody blocking.

Lucy Bird

References and links

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