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T-CELL RESPONSES

NK cells set a prime example

The priming of naive T cells is mainly mediated by mature dendritic cells (DCs) in secondary lymphoid organs; however, now Sallusto and colleagues show that, after stimulation with mature DCs or certain adjuvants, natural killer (NK) cells are rapidly recruited to lymph nodes, where they produce interferon- γ (IFN- γ), which promotes T helper 1 (T_H1)-cell polarization.

Under steady-state conditions, NK cells circulate in the blood but are largely excluded from the lymph nodes. So, to determine whether NK cells could be involved in T-cell priming during an immune response, the authors injected mice subcutaneously with lipopolysaccharide (LPS)-matured DCs and analysed the cellular composition of the draining lymph nodes. As expected, the total cellularity of the 'DC-draining' lymph nodes increased, but surprisingly, they observed a marked increase in the number of NK cells in DC-draining lymph nodes compared with control lymph nodes. This increase in NK-cell number did not result from cell proliferation but from the rapid recruitment of activated NK cells from the blood.

The recruitment and co-localization of mature DCs and T cells in the T-cell areas of the lymph nodes depends on expression of the chemokine receptor CCR7. However, NK cells in the DC-draining lymph nodes expressed only low levels of CCR7 (unlike T cells, which express high levels). And CCR7-deficient NK cells

were equally efficient at migrating to DC-draining lymph nodes as wild-type NK cells. By contrast, NK cells deficient in CXCR3 did not migrate to the lymph nodes in response to injection of mature DCs, indicating a previously unknown CXCR3-dependent pathway of NK-cell migration.

So, do NK cells in the lymph nodes have an impact on T-cell priming? To test this, fluorescently labelled ovalbumin (OVA)-specific T cells were adoptively transferred to mice, and the mice were then injected with OVA-pulsed DCs or soluble OVA in the presence of various adjuvants (R848, Ribi, CpG1826 and complete Freund's adjuvant). Although all conditions induced comparable T-cell proliferation, only R848 and Ribi induced the recruitment of NK cells to the lymph nodes (and these were as efficient as LPS-matured DCs). But, T cells primed using these adjuvants

were biased towards T_H1 cells compared with those primed using adjuvants that did not recruit NK cells. Consistent with a role for NK cells in inducing T_H1 -cell polarization, depletion of NK cells impaired differentiation to effector T_H1 cells. Moreover, when NK-cell-depleted mice were reconstituted with IFN- γ -deficient NK cells, T_H1 -cell priming did not occur, indicating that the effect on T-cell polarization is mediated by the production of IFN- γ by the NK cells.

In light of these results, adjuvants that promote NK-cell-mediated T_H1 -cell polarization could be used to enhance the efficacy of vaccines that rely on T_H1 -cell responses.

Lucy Bird

References and links

ORIGINAL RESEARCH PAPER

Martin-Fontecha, A. *et al.* Induced recruitment of NK cells to lymph nodes provides IFN- γ for T_H1 priming. *Nature Immunol.* **5**, 1260–1265 (2004).