Is war necessary (for transplant success)?

If immune cells are an army, then a graft transplant is a foreign invasion. New work by Yu et al. on page 1851 shows that antigen-presenting cells (APCs) from the graft are rapidly killed by the host’s first line of defense: natural killer (NK) cells. But far from hindering the chance of graft survival, this battle actually improves it.

NK cells are known to improve the chance of graft survival, but how they do this was unknown. Li’s team wanted to know what happens to graft APCs when NK cells are absent.

NK cells, donor APCs could roam free in the host, as confirmed by their presence in spleen, liver, and lung. In the presence of NK cells, however, injected or graft-derived APCs were completely eliminated from the host.

The team reasoned that immediate destruction of the APCs by NK cells was preventing a more vigorous anti-APC response by host lymphocytes. To confirm this, they restored the T lymphocyte population of the mice and showed that, in the absence of NK cells, APCs activated robust and persistent T cell proliferation and IFN-γ production—marks of a ferocious immune response. But in the presence of NK cells this T cell activation was, as predicted, markedly reduced.

The daily immunosuppressants that transplant patients must take “are designed to suppress T cells,” says lead researcher Xian Li, “but we don’t know if they are also suppressing NK cells.” Drugs that specifically suppress T cells but boost host NK cells might therefore improve the outcome for transplant patients. JEM

Don’t overreact

Response to microbial infection must be perfectly balanced to kill off the bugs but not the surrounding host tissue. Wirtz et al. (page 1875) report that in sepsis this balance fails. By attempting to prevent an overzealous innate immune response, the cytokine IL-27 prevents efficient bacterial clearance.

IL-27 is strongly induced by microbial stimuli in vitro, but its response to microbes in vivo was unclear. In a mouse model of septic peritonitis, microbial invasion from the gut triggered IL-27 production. IL-27 was produced earlier than cytokines of the adaptive immune response, IL-12 and IL-23, indicating that IL-27 induction was, in this case, part of the innate response.

In earlier studies, IL-27 was shown to promote T cell proliferation and thus positively regulate adaptive immunity. In the present study, however, IL-27 displayed a negative effect on the innate response: mice lacking functional IL-27 cleared bacteria more efficiently and were more likely to survive than their wild-type counterparts. The authors attribute this increased survival to a corresponding increase in the number and the oxidative burst activity of granulocytes found in the abdomen.

How IL-27 suppresses myeloid cell activation remains to be determined. Furthermore, “the normal physiological role [of IL-27] is still unclear,” says Wirtz. Its role in innate immunity, at least, is probably to limit inflammation and thus protect body tissues from damage. In the case of sepsis, however, this control goes too far. JEM

Why lymph nodes grow

At the initiation of an immune response, lymph nodes can double in size in a day and can be ten times their original size in five to seven days. Webster and colleagues report on page 1903 that dendritic cells, quite distinct from their function in antigen presentation, stimulate endothelial cell proliferation and vascular growth in the growing lymph node.

Peripheral challenge (such as immunization) induces dendritic cells to mature and migrate to the lymph nodes. But what is their role once there? Dendritic cells are well known for their role in B and T cell lymphocyte stimulation but, surprisingly, Lu’s team found that without lymphocytes (in Rag−/− mice) dendritic cells could activate lymph node growth and endothelial cell proliferation almost as effectively.

Vascular endothelial growth factor (VEGF) has been implicated in lymph node growth, and the team found that dendritic cells could increase VEGF levels in the lymph node, again, without the need for lymphocytes. Increased VEGF and increased endothelial cell proliferation required dendritic cell–mediated recruitment of cells from the circulation. Either these recruited cells or other lymph node cells (but not the dendritic cells) are then thought to produce the VEGF. Determining how VEGF levels are up-regulated is the subject of ongoing study.

Enlargement of the lymph nodes is a normal step in combating infection, but it also occurs during autoimmune responses. One possibility for combating lymph node growth during autoimmunity is antiangiogenic drugs, which were developed to combat tumors. JEM