Arginine reverses T cell defects

An amino acid might help fight chronic hepatitis, according to a study by Das et al. (page 2111). The amino acid arginine is indispensible for the host’s T cell response against tumors or chronic infection. Without arginine, a T cell receptor (TCR) component cannot be produced efficiently, thus dampening TCR signaling. As a result, the cells do not proliferate normally or produce the survival cytokine IL-2, although they still make inflammatory cytokines such as IFN-γ and TNF.

Das et al. now find that CD8+ T cells in the livers of patients with chronic hepatitis B infections show signs of arginine starvation. Despite proliferating poorly, the cells’ production of IFN-γ and TNF might explain the liver damage seen in these patients. The amino acid deficiency stemmed from the activity of the arginine-destroying enzyme arginase, which was elevated in inflamed livers. The arginase source is still unknown but seems to be confined to the liver, as T cells elsewhere in the patients were less affected.

Culturing patients’ liver-derived CD8+ T cells with arginine corrected their defects. Whether arginine supplements can help cure hepatitis B remains to be seen.

Ticks’ evasion cocktail

On page 2019, Déruaz et al. find that ticks might prefer to take on immune cells one at a time rather than brave the whole lot at once.

Some worms and viruses fend off immune cells by neutralizing the chemokines that attract them. These species make one chemokine-blocking protein that covers all the bases. But ticks don’t use this one-for-all strategy, the authors now find. Instead, they made at least three single-chemokine blockers, which probably prevent host immune cells from swarming into the bite site and clogging up the ticks’ food pipeline. These anti-chemokines, called evasins, each had a unique shape that might contribute to their selectivity.

Ticks might have evolved this selectivity to counter the host’s step-wise immune response to the Lyme disease parasite they carry. In parasite-infected hosts, neutrophils usually arrive first to the bite site, followed by eosinophils and monocytes, and finally other immune cells. Tick saliva has different anti-chemokine activity at different times during feeding, suggesting that having several evasins might somehow better counter this staggered cell influx. Viruses, on the other hand, do not have the luxury of combating one cell type at a time and might therefore depend on a single multi-purpose protein.

Spreading tolerance by converting

Unlike some religious leaders, suppressive T cells need more than just charisma to spread messages of tolerance: the cells rely on a cell surface cytokine complex to convert others, according to Andersson et al. (page 1975).

Regulatory T (T reg) cells suppress other T cells in part via the cytokine TGF-β, which can convert naïve CD4+ T cells into suppressor cells. Andersson et al. now find that naïve CD4+ T cells turn into suppressor cells only when they bump into T reg cells that have an inactive TGF-β complex on their surface. Proteolysis of the inactive complex, which liberates soluble protein, was required for conversion. Inhibiting the protease or swamping the cells with inactive complex prevented cleavage and thus conversion. The converted cells could suppress gut inflammation when transferred into mice suffering from colitis.

Other immune cells also secrete soluble TGF-β, but they do not seem to force conversion—at least in this system. Previous experiments showed that naïve T cells cultured with T reg cell-depleted spleen cells, which secrete TGFβ, fail to convert. Non-T reg cells don’t express the inactive surface complex, so perhaps its cleavage is needed to trigger other conversion-supporting signals.

The latent TGF-β complex was present only on T reg cells that had been stimulated via their T cell receptors. This specificity might allow T reg cells to limit conversion by delivering the TGF-β signal only to T cells bound to the same antigen-presenting cell and thus on the verge of being activated. “We wouldn’t want T reg cells to run amok and convert all naïve T cells,” says lead author Ethan Shevach. How often T reg cells rely on this mechanism and its impact on the induction of tolerance in vivo are unknown.