IN THIS ISSUE

The red scaly skin of patients with psoriasis is caused by a complex circuit of inflammatory cells and cytokines. Zaba et al. (page 3183) now find that switching off one type of T helper (Th) cell is enough to break the circuit and heal the lesions.

Th1 cells that secrete interferon (IFN)-γ were initially thought to be the main villains within psoriatic plaques—build-ups of overproliferating skin cells. In animal models of psoriasis, IFN-γ thickens plaques by further increasing the proliferation of skin cells and enhancing their production of chemokines that recruit inflammatory cells.

But cytokines other than IFN-γ may be more to blame. Inhibitors of tumor necrosis factor (TNF)—originally given to patients to treat Crohn’s disease and other inflammatory illnesses—have been shown to alleviate psoriasis-like lesions. How they work, however, was unclear.

Zaba et al. now find that blocking TNF prevents psoriasis by inactivating Th17 cells. Th17 cells are normally activated by TNF-stimulated dendritic cells (DCs) and induce epithelial cell proliferation by secreting IL-22. But fewer DCs and lower levels of IL-22 were found in treated plaques, which disappeared after two weeks of treatment with the TNF blocker.

Immediate relief from psoriasis might thus be made possible by getting rid of Th17 cells. Future studies might therefore benefit from focusing on Th17 cells rather than on Th1 cells, which survive in the plaques weeks longer than Th17 cells but fail to perpetuate disease.

Skin DCs go deeper

Skin dendritic cells (DCs), called Langerhans cells (LCs), reside in the epidermis, where they express a lectin called langerin. Although DCs were also known to reside in the dermis, these cells were not thought to express langerin. But three reports by Bursch et al. (page 3147), Poulin et al. (page 3119), and Ginhoux et al. (page 3133) now show that a subset of langerin-expressing DCs call the dermis home.

The new cells were discovered in mice whose own bone marrow had been eliminated by irradiation and replaced with donor bone marrow. The irradiation eliminates all immune cells except for epidermal LCs. Six weeks after bone marrow transplant, Bursch et al. found that epidermal LCs were primarily from the host, as expected. But they also found donor-derived DCs that expressed langerin in the dermis and lymph nodes. These new DCs were also spotted circulating in the blood by Ginhoux et al. and in the lung and liver by Poulin et al. The latter group showed that the dermal langerin+ DCs expressed surface markers distinct from those expressed by classic LCs.

The dermal DCs repopulated the skin more rapidly than LCs after toxin-induced DC depletion, according to Bursch et al. This finding may explain prior DC depletion studies, which showed that allergic skin reactions—thought to require T cell activation by epidermal LCs—occurred before the LCs could repopulate the skin.

The precise role of the new langerin+ DCs is not yet clear. They have been seen clustering around hair follicles in the upper dermis, which may give them access to antigens that do not penetrate more deeply. Their rapid renewal and trafficking to lymph nodes might also be important in protecting the dermis against infection when the epidermis is injured. What these cells are doing in the lung and the liver, however, is a bigger mystery.

Th17 blockade reduces the itch

The red scaly skin of patients with psoriasis is caused by a complex circuit of inflammatory cells and cytokines. Zaba et al. (page 3183) now find that switching off one type of T helper (Th) cell is enough to break the circuit and heal the lesions.

Th1 cells that secrete interferon (IFN)-γ were initially thought to be the main villains within psoriatic plaques—build-ups of overproliferating skin cells. In animal models of psoriasis, IFN-γ thickens plaques by further increasing the proliferation of skin cells and enhancing their production of chemokines that recruit inflammatory cells.

But cytokines other than IFN-γ may be more to blame. Inhibitors of tumor necrosis factor (TNF)—originally given to patients to treat Crohn’s disease and other inflammatory illnesses—have been shown to alleviate psoriasis-like lesions. How they work, however, was unclear.

Zaba et al. now find that blocking TNF prevents psoriasis by inactivating Th17 cells. Th17 cells are normally activated by TNF-stimulated dendritic cells (DCs) and induce epithelial cell proliferation by secreting IL-22. But fewer DCs and lower levels of IL-22 were found in treated plaques, which disappeared after two weeks of treatment with the TNF blocker.

Immediate relief from psoriasis might thus be made possible by getting rid of Th17 cells. Future studies might therefore benefit from focusing on Th17 cells rather than on Th1 cells, which survive in the plaques weeks longer than Th17 cells but fail to perpetuate disease.

Skin DCs go deeper

Skin dendritic cells (DCs), called Langerhans cells (LCs), reside in the epidermis, where they express a lectin called langerin. Although DCs were also known to reside in the dermis, these cells were not thought to express langerin. But three reports by Bursch et al. (page 3147), Poulin et al. (page 3119), and Ginhoux et al. (page 3133) now show that a subset of langerin-expressing DCs call the dermis home.

The new cells were discovered in mice whose own bone marrow had been eliminated by irradiation and replaced with donor bone marrow. The irradiation eliminates all immune cells except for epidermal LCs. Six weeks after bone marrow transplant, Bursch et al. found that epidermal LCs were primarily from the host, as expected. But they also found donor-derived DCs that expressed langerin in the dermis and lymph nodes. These new DCs were also spotted circulating in the blood by Ginhoux et al. and in the lung and liver by Poulin et al. The latter group showed that the dermal langerin+ DCs expressed surface markers distinct from those expressed by classic LCs.

The dermal DCs repopulated the skin more rapidly than LCs after toxin-induced DC depletion, according to Bursch et al. This finding may explain prior DC depletion studies, which showed that allergic skin reactions—thought to require T cell activation by epidermal LCs—occurred before the LCs could repopulate the skin.

The precise role of the new langerin+ DCs is not yet clear. They have been seen clustering around hair follicles in the upper dermis, which may give them access to antigens that do not penetrate more deeply. Their rapid renewal and trafficking to lymph nodes might also be important in protecting the dermis against infection when the epidermis is injured. What these cells are doing in the lung and the liver, however, is a bigger mystery.

Th17 blockade reduces the itch

The red scaly skin of patients with psoriasis is caused by a complex circuit of inflammatory cells and cytokines. Zaba et al. (page 3183) now find that switching off one type of T helper (Th) cell is enough to break the circuit and heal the lesions.

Th1 cells that secrete interferon (IFN)-γ were initially thought to be the main villains within psoriatic plaques—build-ups of overproliferating skin cells. In animal models of psoriasis, IFN-γ thickens plaques by further increasing the proliferation of skin cells and enhancing their production of chemokines that recruit inflammatory cells.

But cytokines other than IFN-γ may be more to blame. Inhibitors of tumor necrosis factor (TNF)—originally given to patients to treat Crohn’s disease and other inflammatory illnesses—have been shown to alleviate psoriasis-like lesions. How they work, however, was unclear.

Zaba et al. now find that blocking TNF prevents psoriasis by inactivating Th17 cells. Th17 cells are normally activated by TNF-stimulated dendritic cells (DCs) and induce epithelial cell proliferation by secreting IL-22. But fewer DCs and lower levels of IL-22 were found in treated plaques, which disappeared after two weeks of treatment with the TNF blocker.

Immediate relief from psoriasis might thus be made possible by getting rid of Th17 cells. Future studies might therefore benefit from focusing on Th17 cells rather than on Th1 cells, which survive in the plaques weeks longer than Th17 cells but fail to perpetuate disease.