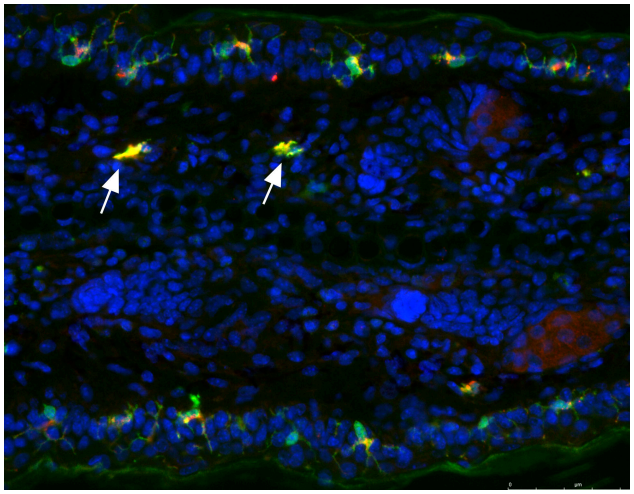


A new subset of dendritic cells (arrows) is found in the dermis.

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 Bursch et al. Poulin et al. 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 elimination, 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. **RR**

Th17 blockade reduces the itch

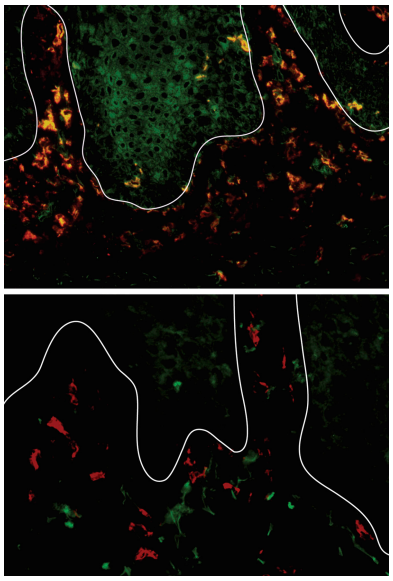
The red scaly skin of patients with psoriasis is caused by a complex circuit of inflammatory cells and cytokines. Zaba et al. (page 3183) now find that switching off one type of T helper (Th) cell is enough to break the circuit and heal the lesions.

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. **HB**



TNF (green) stimulates dendritic cells (red) that cause psoriasis-like lesions (top). Lesions can be relieved by a TNF blocker (bottom).

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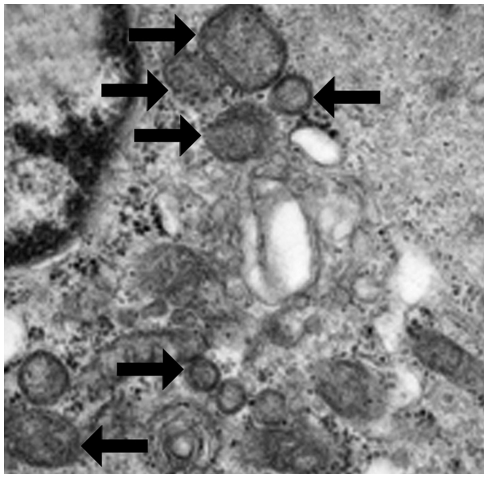
Choking on mitochondria



Smooth muscle cells from patients with asthma have increased numbers of mitochondria (arrows).

In patients with asthma, airway smooth muscle cells make too many mitochondria, say Trian et al. on page 3173. Instead of easing breathing, these mitochondrial masses trigger cell division, leading to a choking build-up of smooth muscle cells.

Many chronic lung diseases, such as asthma and chronic obstructive pulmonary disease (COPD), are characterized by an increased mass of smooth muscle in the bronchi, which causes the airways to constrict. Although bronchial dilators ease acute asthma attacks, they have no effect on the muscle build-up.

In patients with asthma, these muscle cells were known to divide excessively, but what prompted this cell division was unclear. Trian et al. now show that an overdose of calcium influx triggers the expression of mitochondria-building transcription factors in the cells.

The resulting construction of new mitochondria—and subsequent burst in ATP production—gave the cells the energy boost needed for proliferation. This pathway was specific to patients with asthma, as mitochondria numbers and activity were not increased in cells from patients with COPD. Smooth muscle cell proliferation in COPD patients, by contrast, was driven by anaerobic glycolysis.

Calcium channel blockers, which have been shown to relieve asthma attacks and block tumor cell proliferation, might thus also reverse the smooth muscle cell accumulation that perpetuates chronic disease. **RR**

Antibody-driven psychosis

Psychotic episodes in lupus patients can be triggered by an antibody attack on brain cells, according to Matus et al. (page 3221).

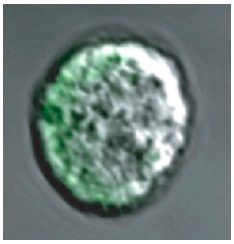
The psychosis that occurs in a small subset of lupus patients is associated with an antibody that recognizes a trio of ribosomal phosphoproteins. It was assumed that this antibody binds to the cell surface version of one of the phosphoproteins and somehow penetrates cells to cause damage. But how the interaction between the antibody and its targets leads to a breakdown in neuronal function was a mystery.

Matus et al. now find that the antibody also recognizes a novel, nonribosomal protein on the surface of neurons. In rat brains, this protein was concentrated in regions that control cognition and emotion—the functions that go awry during lupus-related psychosis. Treating cultured neurons with the antibody or injecting it directly into rat brains caused increased intracellular calcium levels, thereby causing neuronal death. The kind of ion channel opened by antibody binding and the mechanism involved is still unknown.

The team also found these antibodies in lupus patients who showed no signs of psychosis. Antibodies that attack neurons can only cause damage if they are allowed to sneak through a breach in the blood–brain barrier. The authors therefore suspect that only patients who for some reason have such a breach experience the psychosis.

The function of the neuronal surface protein is unknown. Its associations with clathrin and protein domains that are characteristic of ubiquitin ligases suggest that this protein may regulate the trafficking and degradation of surface receptors in neurons. **HB**

Antibodies, hold the light chain



A B cell produces functional antibodies (green) that lack light chains.

Antibodies don't always need light chains to function, according to Zou et al. (page 3271).

In mammalian antibodies, two heavy chains link together to form a Y-shaped complex, with each arm of the Y linked to a light chain. In mice and humans, lone heavy chains are usually prevented from being secreted by a chaperone that associates with the heavy chain's constant region—the same region that links to the light chain. But the new report shows that an unusual set of fully functional heavy chain–only antibodies do get secreted.

The anomalous antibodies escaped to the cell surface because they lacked the chaperone-binding region. The secretion of these antibodies was discovered in mutant mice that lack light chain genes, but the authors also found that smaller amounts were produced in the spleen of normal mice, probably as a result of gene deletion errors during B cell development. The odd antibodies appeared to bind antigen normally and display the normal range of heavy chain diversity.

The discovery has precedence—camels and their relatives produce heavy chain–only antibodies in abundance. Light chain–deficient mice might allow the ready production of heavy chain–only monoclonal antibodies, whose smaller size lets them recognize antigen structures that elude standard antibodies. Humans might also make these antibodies in small amounts, but their relevance in vivo remains a mystery. **RR**