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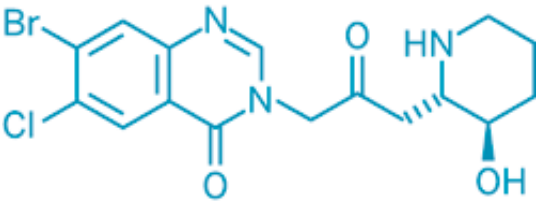
Immunology

Blocking Wayward Immune Cells

Small molecule prevents differentiation of cell involved in autoimmune diseases

Sarah Everts



Halofuginone

The creation of a badly behaved cell type called T_H17, which is linked with such autoimmune diseases as multiple sclerosis, inflammatory bowel disease, and psoriasis, can be prevented with a small molecule called halofuginone, researchers have found.

A team led by Malcolm Whitman, Tracy Keller, and Anjana Rao of Harvard Medical School report that halofuginone blocks the generation of T_H17 cells from precursor $CD4^+$ immune cells. And it does this without preventing $CD4^+$ cells from differentiating into other cell types such as T_H1 and T_H2, which are necessary for fighting bacteria and parasites (*Science* **2009,** *324,* 1282).

T_H17 is "arguably the most exciting cell in the immune system these days" because of its role in autoimmune diseases, note Julie Magarian Blander of Mount Sinai School of Medicine, in New York City, and Derk Amsen of the Academic Medical Center, in Amsterdam, in a commentary about the work.

Blander and Amsen note that halofuginone's ability to selectively block differentiation will help researchers understand how the immune system produces T_H17 cells but that the molecule may not end up as a drug. That's because by the time autoimmune disease symptoms appear, T_H17 has already wreaked havoc. Thus, giving halofuginone therapeutically could only prevent further damage at best.

Whitman points out that drugs currently in use or in development for the treatment of autoimmune disease don't repair existing damage either. "Autoimmune inflammation is, in general, an ongoing, often relapsing process. Halofuginone, like other strategies to modulate the immune system during autoimmune disease, would have the potential to prevent new damage triggered by T_H17 cells but not to repair preexisting damage."

Blander and Amsen add that halofuginone prevents differentiation of T_H17 cells in an "intriguing" manner. The molecule

activates a pathway that cells typically trigger only when amino acids are scarce. This so-called amino acid starvation response selectively modifies DNA transcription and translation so only essential proteins are produced. The consequence is that genes involved in T_H17 differentiation are also turned off, preventing differentiation of the wayward cell type.

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