

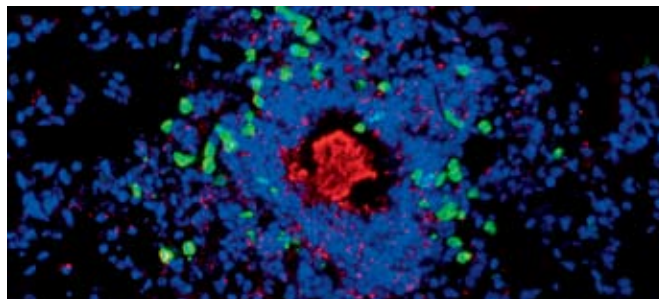
Ubiquitous Allergen

ONE OF THE MOST COMMON BIOPOLYMERS ON EARTH MAY SOMETIMES CAUSE ASTHMA.

The culprit for some forms of asthma may not be blowing in the wind but rather swimming in the sea or pushing through the soil. HHMI investigator Richard M. Locksley of the University of California, San Francisco, and colleagues have identified it as chitin—nature’s second-most-abundant biopolymer—which is found, for example, in the exoskeletons of shellfish, the powerful inner grinders of worms, and the cell walls of fungi and insects.

Many of these organisms, including cockroaches and dust mites, are associated with allergies. And a sizeable percentage of asthma—as high as 25 percent—has been detected in previously asymptomatic workers in shellfish-processing plants. While humans and other vertebrates do not produce chitin, our immune systems innately recognize and eliminate it from the body. When this response goes awry, the result could be inflammation of airways that sets off asthma.

To pinpoint the exact molecular mechanism, Locksley’s team infected mice with common parasitic worms called helminths. These mice were genetically engineered with fluorescent probes in their immune systems that would light up when activated. The researchers then observed that the mice responded by producing interleukin-4 and interleukin-13, which are the immune-cell chemicals typically dispatched to attack an allergen invader.



Upon encountering the allergen chitin (red), immune cells release interleukin-4 (green) and interleukin-13, causing an allergic reaction. Host cells (blue) may release the enzyme chitinase to preempt the immune response.

Locksley and colleagues also increased the expression of a gene coding for the enzyme, acidic mammalian chitinase (AMCase), that normally breaks chitin down. When the mice expressed more AMCase than normal, the immune response to chitin was greatly reduced. Similarly, mice exposed to purified chitin that was pretreated with AMCase had attenuated allergic reactions. The team’s results were published in the May 3, 2007, issue of *Nature*.

“It’s been an intriguing finding that we’re continuing to follow up on,” says Locksley, who is now looking at human lung cells to see whether asthma patients have less of the enzyme or a weaker form. ■ –JACQUELINE RUTTIMANN

IN BRIEF

RESEARCHERS LEARN WHAT SPARKS PLANT GROWTH

How plants “decide” to grow, a secret long held by plants, has been revealed by HHMI investigator Joanne Chory and others at the Salk Institute for Biological Studies.

The findings, published March 8, 2007, in *Nature*, put to rest a century-old debate over how tissue systems in plants coordinate cell growth.

The scientists examined the three tissue layers that make up the shoots of the mustard plant *Arabidopsis*: the epidermis, which is the waxy, protective skin; the mesophyll tissue, which contains the plant’s chloroplasts—cell organelles that conduct photosynthesis; and the vascular tissue through which water and nutrients are transported.

Chory’s team looked at the expression of plant hormones called brassinosteroids in the outer and inner layers. Dwarf plants grew to full size when brassinosteroid was expressed and taken up by receptors in the epidermis, whereas the plant’s growth was restricted when a gene was expressed in the epidermis that inactivated brassinosteroid. Thus, cell signaling began in the epidermis and followed into the inner

layers of tissue, directing those cells to grow or to restrict growth.

“This knowledge will ultimately lead to our ability to increase yield, while decreasing the need for fertilizer and pesticides,” says Chory.

SLEEPING SICKNESS PARASITE CAN’T LIVE WITH STRESS

Research from HHMI international research scholar Shulamit Michaeli at Bar-Ilan University in Ramat-Gan, Israel, and colleagues, shows that the African sleeping sickness parasite’s natural response to stress is enough to kill it, a weakness that researchers may be able to exploit.

African sleeping sickness is caused by the parasite *Trypanosoma brucei*, which lives in tsetse flies. After a person is bitten by an infected fly, the parasite crosses into the brain, where it disrupts neurological function and leads to death if not treated.

Understanding how proteins move across the parasite’s internal membranes led to the discovery. Before they leave the ribosome where they are created, certain newly synthesized proteins are given a molecular tag, called a signal peptide, that allows them to cross the cell’s membranes.

The tags are noted by the signal recognition particle (SRP) complex, which interacts with a membrane receptor and directs the proteins to unbind from the ribosome and go there.

When Michaeli’s team knocked out the membrane receptor, the SRP complex had no place to dock, causing it to stick to ribosomes with the newly synthesized tagged protein. This “stress” causes the parasite cells’ nuclei to shut down a small RNA molecule called the spliced leader RNA, which is responsible for all mRNA production in the cell. Protein production then stops and the organism dies. This novel stress-induced mechanism, described in the April 2007 issue of *EMBO Reports*, is termed spliced leader RNA silencing.

SHAKING UP HIV’S FAMILY TREE

In the battles that rage between the human immunodeficiency virus (HIV) and an infected patient’s T cells, the rules of engagement are always changing. The T cells adapt continuously to recognize HIV proteins and alert the immune system to attack. But, with its exceptional capacity to mutate to forms that can escape immune surveillance, the virus perseveres.