Allergy-free rodents lack a key receptor

Genetic manipulation of laboratory mice has demonstrated a pivotal step in the development of allergic reactions.

The sneezing, wheezing, itching, and other miseries elicited in susceptible people by pollen and other allergens come down to a particular docking site, or receptor, on certain cells in the body, says Jean-Pierre Kinet, an immunologist at the National Institute of Allergy and Infectious Diseases in Rockville, Md.

Scientists have long known that the body responds to allergens by producing a family of antibodies – immunoglobulin E, or IgE. IgE interacts with two kinds of white blood cells to set off the cascade of reactions responsible for the allergic response. The white cells, called mast cells and basophils, contain at least three kinds of receptors for IgE, Kinet says.

Researchers seeking to develop drugs to block allergic responses need to know the roles of these different receptors in activating the white blood cells. To find this out, Kinet and his colleagues teamed up with Beverly H. Koller at the University of North Carolina at Chapel Hill. Koller's group created a strain of mice lacking the high-affinity IgE receptor.

Those mice show no evidence of allergic response, the two teams report in the Dec. 3 CELL. "The mice are protected against these reactions," says Kinet.

D. Dombrowicz *et al.*/CELL

Blue ears (center) reveal allergic mouse.

To produce the mice, Koller's group began with cells removed from very early mouse embryos. They made a piece of the gene that codes for the high-affinity receptor defective by inserting another gene in the middle of it. When inserted properly, this interloper gene also makes the early cells, called embryonic stem cells, resistant to the killing effects of an antibiotic.

Of 600 cells treated, nine took up the gene and multiplied in a test tube containing the antibiotic. Researchers added cells from three of these test tubes to developing mouse embryos. They then mated the resulting mice that had incorporated these transferred cells into their bodies. Some of the offspring inherited two copies of the defective, or knockout, gene. As a result, their cells lacked the high-affinity IgE receptor.

The scientists then assessed the mice's ability to show an allergic reaction. In one test, they injected both normal and knockout mice with IgE antibodies. The next day, the researchers injected the same mice with allergen and blue dye.

The normal mice started to go into shock: Their blood pressure dropped and their blood vessels became leaky. This leakiness allowed the molecules of blue dye to escape from the blood into the surrounding tissue, so the mice undergoing this allergic reaction turned blue in a matter of minutes. "If the mice are protected, they stay white," Kinet explains.

These experiments demonstrate that the high-affinity receptor is the predominant docking site enabling IgE to set off allergic reactions, he adds. Finding ways to block this docking may prevent such reactions from occurring.

Kinet and his colleagues are now developing mice with human instead of mouse IgE receptors. These mice will enable scientists to test drugs aimed at blocking IgE docking, he adds. *– E. Pennisi*

Astronauts snare Hubble, repair flaws

Photos: NASA

A team of specialists paid a call on the ailing Hubble Space Telescope this week, hoping their ministrations would sharpen the telescope's cloudy vision and improve its overall health. Featuring an unprecedented series of space walks, the mission began after a two-day chase in which the space shuttle Endeavour came within 30 feet of Hubble. Astronaut Claude Nicollier, using a mechanical arm, reached out, grabbed the orbiting observatory, and secured Hubble in the shuttle's cargo bay.

"Houston, Endeavour has a firm handshake with Mr. Hubble's telescope," radioed shuttle commander Richard O. Covey.

Although Hubble's blurry vision has become the telescope's most notorious flaw, astronauts addressed other problems during the mission's first two space walks (SN: 11/6/93, p.296). Floating out into the cargo bay for the first walk, Jeffrey Hoffman and Story Musgrave replaced two pairs of gyroscopes (top photo), three of which had failed. Had a fourth gyroscope died before the repair, Hubble could no longer have pointed accurately enough to observe astronomical targets.

During the second walk, Kathryn Thornton and Tom Akers replaced Hubble's two wing-like solar arrays, which flapped unacceptably each time the telescope passed in and out of Earth's shadow. Ground controllers had earlier commanded the arrays to roll up like window shades so the crew could stow them for a return trip to Earth. But one of the 400-pound, 5-meter arrays, badly warped during its 3.5 years in space, retracted only partially, making it impossible to store. Thornton first attached a handle to the warped array as she perched on the end of the mechanical arm. She then jettisoned the array, which drifted into space (bottom photo) as the shuttle gently sped away.

It will take some seven weeks to determine whether the crew's optical repairs have improved Hubble's ability to see faint objects.