Allergy-triggering receptor made *en masse*

Scientists this week reported coaxing cultured monkey cells to sprout millions of the cell-surface receptors that serve as docking sites for the immune protein triggering allergic reactions in humans. The successful mass production of the so-called IgE receptor on living cells gives researchers their first chance to experiment with rationally designed molecules that can block those receptors. Such experiments may lead to the development of drugs that singlehandedly could prevent the entire gamut of allergic reactions, say the researchers and others.

In humans, two types of cells have IgE receptors – basophils, which circulate in the blood, and mast cells, which reside in tissues such as the lungs and skin. But these cell types are rare and difficult to purify, slowing research on IgE-blocking drugs for the one out of six people in the United States who suffer from allergies. Rather than blocking IgE binding, today's drugs interfere with the later stages of an IgE-triggered biochemical cascade that leads to sneezing, itching and the life-threatening reaction called anaphylaxis. They do so with only partial success and often cause a variety of side effects such as drowsiness or insomnia.

Jean Pierre Kinet and his colleagues at the National Institutes of Health in Bethesda, Md., performed the latest experiments in cultured monkey kidney cells – a line of cells that can be genetically manipulated with relative ease. They used a gene-altered virus to inject into these cells pieces of DNA coding for the production of a critical portion of the human IgE receptor. They also injected genes coding for the remaining two portions of the three-component receptor, but used rat genes because no one has yet cloned the human genes for these two portions.

Once fed the three genes, the monkey cells made millions of human-rat receptors that bound human IgE just as normal human IgE receptors do, report Kinet, Larry Miller, Henry Metzger and Ulrich Blank in the April 21 SCIENCE.

"I'd say this is one of the holy grails of immunology of allergy – to understand the hook by which IgE attaches to cells," says Philip Askenase, an allergy researcher at Yale University in New Haven, Conn. He says scientists have yet to characterize many other immune system receptors. "But from the point of view of human disease, this is the one. IgE allergies are tremendously important and common diseases."

Kinet says his team has partially succeeded in expressing the IgE receptor in a more stable line of cells taken from hamster ovaries, and is "very close" to cloning the human versions of the remaining two subunits of the receptor. The researchers are collaborating with Hoffmann-La Roche Inc., a pharmaceutical company based in Nutley, N.J.

Kinet and others say that IgE, mast cells and basophils probably play some useful, but perhaps not critical, roles in the body. Mast-cell-deficient mice suffer no apparent signs of immunological deficiency.

Says Kinet: "Maybe these cells are involved in some immunological defense, but maybe not so critically that if you inhibited that receptor you'd have any real problem." – *R. Weiss*

Crossing the 'borderline' of child abuse

Boston researchers report that child abuse often lurks in the background of adults with borderline personality disorder, a controversial diagnosis applied to about 20 percent of hospitalized psychiatric patients and people seeking psychotherapy.

Child abuse alone does not cause borderline personality disorder, say psychiatrist Judith L. Herman and her colleagues at Harvard Medical School, but it appears to play an influential role in many cases.

"Borderlines" are characterized by intense and unstable relationships, self-destructive and impulsive behavior (such as drug abuse), fears of abandonment, suicide attempts aimed at manipulating others, feelings of emptiness, and rage alternating with a childish dependency on others. Many borderlines slip into a temporary psychosis under stress or the influence of drugs.

Herman and her co-workers conducted intensive interviews with 21 individuals meeting diagnostic criteria for borderline personality disorder, 11 falling short of the diagnosis but possessing several "borderline traits" and 23 with related diagnoses such as antisocial personality disorder (persistent violence and lawbreaking).

The great majority of the borderlines – 17 of 21 – reported a history of trauma before age 18, including physical abuse, sexual abuse and witnessing serious domestic violence. Childhood trauma was reported by 8 of 11 individuals with borderline traits and 12 of 23 subjects with related disorders, the researchers note, but their abusive experiences were less frequent and less severe than those of the borderlines.

Multiple episodes of abuse before age 6 were almost exclusively reported by subjects with borderline personality disorder, the scientists say.

The psychological vulnerability imposed by child abuse may help explain why women borderlines outnumber men 2.5 to 1, they maintain. Girls are at far greater risk for sexual abuse than boys, and their sexual abuse apparently is more common and longer in duration than the physical abuse boys are more likely to experience.

The findings have significant treatment implications, the researchers conclude in the April AMERICAN JOURNAL OF PSYCHIATRY. Many borderline patients may need to confront traumatic memories and explore the intense emotions surrounding childhood abuse before they can develop rewarding relations with others.

– *B. Bower*

Path to hepatitis C yields test, clues

Last May, researchers announced they had identified and cloned parts of the genetic material of a new virus, which they suggested causes most of the world's cases of non-A, non-B hepatitis (SN: 5/14/88 p.308). The researchers have now disclosed the molecular method that led to the discovery and that has since allowed them to characterize more than 90 percent of the viral genome. They also report developing a test for the virus, designated hepatitis C, which they hope will soon win approval for large-scale blood screening and patient diagnosis, says study leader Michael Houghton of Chiron Corp. in Emeryville, Calif.

The Chiron group's approach to characterizing the hepatitis C virus could prove useful in finding pathogens for other diseases – such as Alzheimer's or multiple sclerosis – in which "an infectious agent might be implicated but is not proven [to cause or abet the illness]," Houghton says. "I think several new infectious agents will be discovered."

More than 90 percent of the hepatitis transmitted through blood transfusions represents the non-A, non-B type, an ill-defined ailment diagnosed when nonspecific biochemical tests indicate liver injury but the blood bears no indicators of any known hepatitis-causing virus, Houghton says.

The researchers have already used the newly developed hepatitis C test to survey non-A, non-B patients for circulating antibodies to the virus. In a U.S. study, 17 of 24 transfusion-acquired cases and 34 of 59 cases of unknown origin tested positive. "Thus, it appears that hepatitis C virus is a major cause of community-acquired non-A, non-B hepatitis as well as post-transfusion non-A, non-B hepatitis," the researchers write in the April 21 SCIENCE. In addition, they report that 78 percent of chronic cases studied in Japan and 84 percent in Italy tested positive for hepatitis C.

The test probably doesn't pick up all