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

hepatitis C cases in the early, acute stages because the antibody takes months to develop, notes molecular virologist Daniel W. Bradley of the Centers for Disease Control's Hepatitis Branch in Atlanta. Bradley says he and his coworkers are working to develop other assays for the acute disease as well as a vaccine.

To make the test, the Chiron researchers stitched together three hepatitis C viral clones and inserted them into yeast, which then began making a viral protein from the foreign genetic material. Antibodies to the virus bind to the protein and become visible after a color-producing reaction with another antibody, enabling scientists to use the manufactured viral protein to test blood samples for the hepatitis C virus, the team reports.

The test gave a positive result in six out of seven blood samples known to cause non-A, non-B hepatitis in chimpanzees and a negative result in all seven control samples, demonstrating that it detects antibody in infectious samples, Houghton says. And when mixed with blood from 10 prospectively studied transfusion recipients diagnosed with non-A, non-B hepatitis, the test showed that all developed antibodies within a year after infection; for nine, the test picked out a positive blood donor. No such antibodies were detected in blood from 43 people infected with other known hepatitis viruses, he says.

Further use of the test should shed light on whether other agents can cause non-A, non-B hepatitis, Houghton says. Other studies already indicate that a significant portion of the cases may be caused by mutant forms of the hepatitis B virus (SN: 1/28/89, p.52).

The test is now in clinical trials, which should be completed by June, and Chiron plans to apply to the Food and Drug Administration to market the test by the end of the summer, says company spokesman Larry Kurtz. *– I. Wickelgren*

Recent ocean warming: Are satellites right?

Satellites have detected a significant warming in Earth's oceans between 1982 and mid-1988 that conventional methods have underestimated, reports Alan E. Strong from the National Environmental Satellite Data Information Service in Suitland, Md. But another researcher who works with the same measurements sees the purported warming as a largely artificial one created by biases in the satellite information and by the brevity of the record.

According to Strong, who presents his analysis in the April 20 NATURE, "The global ocean is undergoing a gradual but significant warming of [approximately] 0.1°C per year, whereas the trend obtained for the same period from conventional data sources (ships and buoys) is about half that magnitude."

Satellite measurements for ocean temperature go back no farther than 1982. While this relatively short observation period makes it premature to use satellite data to detect long-term trends, such as a greenhouse warming, "we may just be beginning to witness the onset of this warming through satellite surveillance of ocean-surface temperature," says Strong.

Yet Richard W. Reynolds of the Climate Analysis Center in Camp Springs, Md., says he is "flabbergasted" by the reported warming in the satellite data. "I think this whole thing is an error."

The controversy revolves around data taken by thermal sensors aboard several satellites run by the National Oceanic and Atmospheric Administration. These instruments measure infrared radiation emitted by the ocean, which can give an indication of sea-surface temperature once researchers perform difficult corrections for water vapor and clouds in the atmosphere.

By checking the satellite observations against measurements taken by drifting buoys, Strong says he has corrected for the important biases in the satellite data. (Bias is a consistent tendency to overestimate or underestimate.)

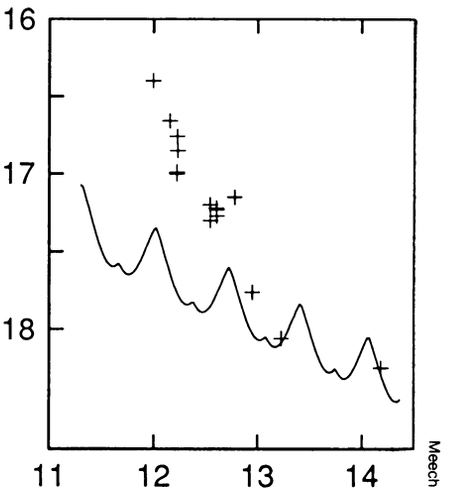
But Reynolds says significant biases remain in the satellite data. The 1982 eruption of the Mexican volcano El Chichón skewed the record by flooding the stratosphere with dust particles that absorbed infrared radiation. For the first two years of the observation period, these particles made the oceans seem cooler than they were. Other biases can affect certain regions of the globe. Right now, satellite instruments consistently indicate the Western Pacific is 0.5°C colder during day than during night, which poses a clear problem, Reynolds says.

In his paper, Strong reports that eliminating the El Chichón years of 1982 and 1983 only slightly reduces the observed warming. But Reynolds contends that these biases introduce a substantial artificial warming into the record. In his own analysis of global ocean temperatures, Reynolds mathematically blends satellite measurements with those taken by both ships and buoys, a technique he says removes the satellite biases. The blended record shows almost no temperature rise between 1982 and 1988.

Reynolds notes that ending the record in mid-1988 exaggerated the satellite errors because the record includes the hot El Niño of 1987 but misses much of the cool La Niña of 1988. Because of such natural fluctuations, he and other researchers caution against using a six-year-long record to talk about temperature trends. *– R. Monastersky*

Chiron's brightening hints it's a comet

When astronomer Charles Kowal in 1977 discovered the object now called Chiron between the orbits of Saturn and Uranus, it was known enigmatically as "Object Kowal." Astronomers could not tell whether it was an asteroid or a comet, since it orbited farther from the sun than most known asteroids but for years failed to show a comet's fuzzy "coma." Now Chiron may have revealed its true identity.



Solid line shows how a typical asteroid brightens as it nears the sun, compared with additional brightening of "Comet" Chiron. Horizontal axis represents distance from sun in astronomical units; vertical axis shows visual magnitude.

Astronomers had speculated that the object might never warm enough to release the frozen surface material that would give it a coma. But as early as November 1987, as it approached the sun, Chiron seemed to brighten more rapidly than would be expected of a bare, rocky object. Now Karen J. Meech of the University of Hawaii Institute for Astronomy in Honolulu and Michael J.S. Belton of Kitt Peak National Observatory in Tucson, Ariz., report a coma around Chiron in images made with the Kitt Peak 4-meter telescope when the object was about 11.8 astronomical units from the sun (1 astronomical unit equals about 92.9 million miles). Chiron is expected to get no closer than about 8.5 astronomical units, but the brightening is apparently due to "sunlight reflected from an extended dust atmosphere," they say, "indicating that it is a very large comet."

The researchers note that Chiron appears about 112 miles in diameter, 10 to 20 times the size of Comet Halley. Ices such as carbon dioxide, which evaporate at much lower temperatures, may have been freed in what could be Chiron's first trip this close to the sun. *– J. Eberhart*