

# Yeast Engineered to Produce Hepatitis B Coat

Gene-splicing scientists are moving into a second generation of genetic engineering attempts to make large amounts of valuable biological materials. Not content to move genes into laboratory bacteria for production of potential drugs and vaccines, several groups of scientists have gone a step further: They are moving genes of interest from their bacterial "foster homes" into a slightly more complex organism, a yeast. Results reported this week at the International Conference of Virology in Strasbourg by William Rutter and colleagues at the University of California at San Francisco indicate that the yeast, as a higher organism, does have skills bacteria lack. When endowed by scientists with the gene for the coat protein of the hepatitis B virus, the yeast synthesizes not the simple protein, but a complex biochemical structure. The structure resembles the immunizing particle, containing protein, sugar and fat-like molecules, found in the blood of hepatitis B patients.

The hepatitis gene is the second gene of clinical interest reported to be expressed in yeast. Last March, scientists from Genentech, Inc. reported yeast production of a human interferon (SN: 3/7/81, p. 148). Both the Genentech and the more recent UCSF projects were done in collaboration with yeast geneticists Benjamin Hall and Gustave Ammerer of the University of Washington.

The gene for the hepatitis B surface protein had previously been moved from the virus into bacteria, where it is active (SN: 3/21/81, p. 180), but its product appears to be degraded by bacterial enzymes, explains Pablo Valenzuela, a member of the UCSF group who is now at the Chiron Corp. in San Francisco. To transfer the hepatitis gene into yeast, it was taken from bacterial cells and linked with a control region of DNA that normally promotes the yeast enzyme called alcohol dehydrogenase. The combined genes were spliced into a ring of DNA, which was then inserted into yeast cells. The yeast produces more than 10,000 molecules of hepatitis B surface protein per cell, the scientists report. They predict that a more powerful promoter region could induce even greater production.

The complex structure produced by the genetically engineered yeast has the same size, shape and sedimentation properties as the immunizing particles from hepatitis B patients, Valenzuela says. He warns, however, that further experiments are needed to confirm that it contains the appropriate sugar and fat-like molecules. "Right now the sugar is just a hypothesis," he says.

Immunizing particles are of great interest because they have been effective as a vaccine against hepatitis B in a clinical

trial (SN: 10/11/80, p. 231). The current method of producing the potential vaccine for clinical testing is slow and costly; the material is purified from the serum of hepatitis B patients. The immunizing particle from patient serum is more effective than pure hepatitis B surface protein for creating an immune system response. Valenzuela says that tests on mice are currently underway, in collaboration with Merck & Co., Inc., to see whether the particles produced by the genetically engineered yeast can act as an effective vaccine. Merck partially sponsored the earlier UCSF-University of Washington research.

In addition to yeast's ability to add sugars to proteins and thus produce complex biochemical structures, yeast have other advantages over bacteria for large-scale production of biologicals. The tech-

niques for growing large quantities of yeast for commercial use have been developed thoroughly by bread, beer and wine producers. Furthermore, yeast do not produce the toxic chemicals, known as endotoxins, that are a concern in fermentation of bacteria.

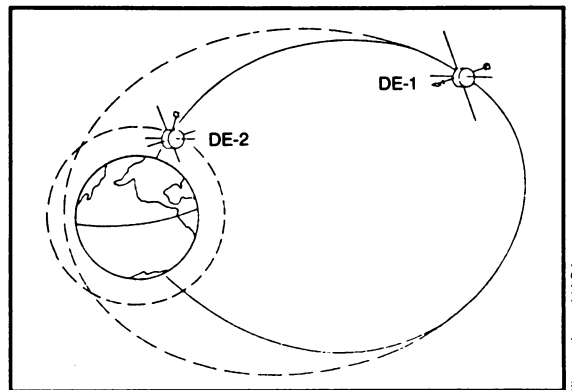
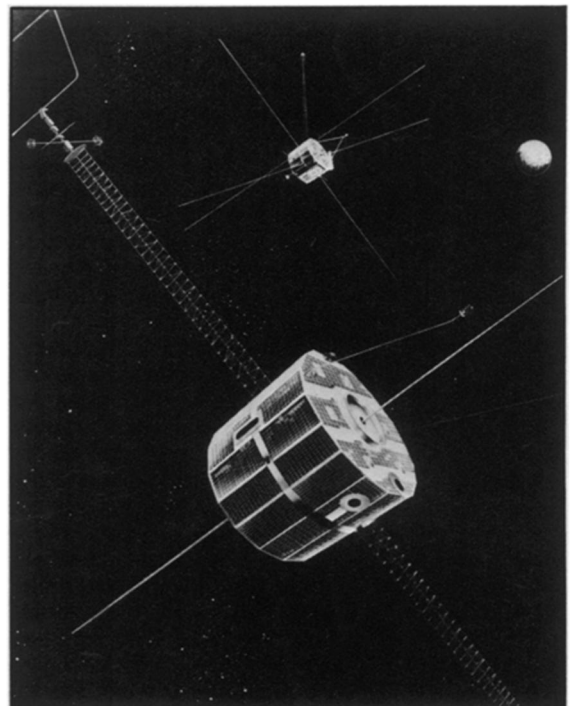
Hepatitis B, the most dangerous strain of liver-infecting virus, affects more than half a billion people throughout the world. Approximately 200 million carry the virus in their blood and can pass on the infection through intimate contact, via blood transfusion or from mother to fetus. In addition, the virus has been implicated in a type of liver cancer common in Asia and Africa. It is hoped that an effective vaccine against the hepatitis B virus would eradicate both the liver disease and the cancer. □

## DE-1, 2: The high road and the low

The microscope gave early biologists far more than just a closer look at their subjects. It revealed the cell, together with a host of structures and processes that affect living things in ways not only unimagined, but unimaginable from a coarser-scale view. Similarly fundamental surprises are around each turn in studying the details of the earth's responses to the energy outpourings of the sun. Different regions of the magnetic field, ionosphere and atmosphere hold the keys to phenomena whose consequences often belie their subtlety. Scientists transmitting weak radio signals along geomagnetic field lines, for example, have found them to trigger emissions 1,000 times stronger than the original impulses — and suggesting similarly energetic natural processes.

Satellites play a major part in such studies, but the developing picture of the sun-earth link has required researchers to go to increasing lengths to place the probes where they are needed. To study the ionosphere and ozone layer at the altitudes where they are pro-

*Bristling with antennas, the two Dynamics Explorer satellites orbit the earth at different heights but in the same plane.*



Illustrations: NASA

duced by solar ultraviolet radiation, the National Aeronautics and Space Administration several years ago sent three Atmospheric Explorer satellites into deep-dipping orbits that would carry them within 120 kilometers of the ground, where atmospheric drag leads to short working lifetimes. In order to follow the effects of the solar wind as it strikes the sun-facing part of earth's magnetosphere and slides around and out down the planet's extended magnetic tail, two International Sun-Earth Explorer satellites were launched to follow each other around a huge ellipse, varying in altitude from barely 480 to nearly 145,000 km. A third ISEE probe was placed at a libration point between the earth and sun, to record the earthbound solar flow in its "raw" form. ISEE-3's problem was made still more difficult because the libration point is directly on the sun-earth line, where solar interference would drown out its data transmissions; instead of being exactly on the point, it was placed in a bizarre "halo" orbit around the point, requiring periodic corrective maneuvers to keep the plane of the halo properly aligned.

The latest additions to this orbiting task force follow similarly exotic paths. Launched Aug. 3, Dynamics Explorers 1 and 2 are designed to investigate a diverse domain that extends all the way from earth's outer magnetosphere down into the depths of the ionosphere where it begins to mix with the fringes of the atmosphere beneath. Both probes are in pole-crossing orbits so that they can follow the magnetic field lines that are the natural "power grid" for the incoming solar-wind particles. DE-1 ranges from about 570 km above the earth to 23,000, while DE-2 takes the low road from 1,000 km down to perhaps 310. But the unique aspect of the arrangement is that the two orbits are in the same plane, often enabling the satellites to study different points on the same field line simultaneously.

Where the high-speed stream of charged particles called the solar wind strikes earth's magnetosphere, a shock wave is formed, much like that in the airflow around a supersonic jet. Almost all of the wind is deflected around this "bow shock" and down the magnetic tail, but a tiny fraction of the particles—perhaps 0.1 percent, says program scientist E.R. Schmerling of NASA—leak through, forming a hot but tenuous plasma that is carried around the planet by convection. Meanwhile, down at the top of the atmosphere, the colder, more dense plasma of the ionosphere is also swept around, but this time by the rotation of the magnetic field, which turns with the earth. A major goal of the Dynamics Explorer project is to learn more about how these two plasmas interact—a fundamental step in understanding the complex energetics of the whole system.

How do they couple together? Both plasmas contain electric fields, but the

patterns of the fields in the ionosphere have turned out to be poor predictors of the patterns to expect in the convecting plasma overhead. Localized electric fields aligned with the magnetic field lines seem to be a factor, but the problem is far more complex. Even the wind—the non-solar kind—plays a part, seemingly out of place among so many electromagnetic interactions. At near-polar latitudes, says DE project scientist Robert A. Hoffman of the NASA Goddard Space Flight Center in Maryland, winds are set up largely by collisions between convecting ions and the particles of the neutral atmosphere; the inertia of the winds prevents rapid changes of direction at convection boundaries, thus causing the winds in turn to drag the ions and generate electric fields.

The two satellites are packed with instruments and bristle with antennas up to 100 meters long for their elaborate study. Besides carrying magnetometers, plasma sensors and mass spectrometers, DE-1, says Schmerling, is the first NASA satellite to be equipped with a camera especially for photographing the aurora. Designed to make images in as little as a few minutes, the camera will be able to record the development of auroral effects that typically

evolve over half an hour or more. The lower-flying DE-2 is equipped for its role with devices to measure the composition, winds and temperature structure of the neutral atmosphere, as well as ion behavior and electric fields in the ionosphere.

Many instruments on the two probes directly complement one another, such as the suites of long antennas designed to pick up very low frequency (VLF) radio waves. Past studies with signals injected onto magnetic field lines from a VLF transmitter at Siple, Antarctica, have showed that emissions 1,000 times stronger could be triggered in response. Now transmissions will be sent from Siple when the DE's are in position to monitor their effects both from low altitude, where the field lines are nearly vertical, and from higher up, where the processes causing the amplification effect may be taking place. In the future, the space shuttle will be able to carry equipment that can inject VLF signals onto whatever field lines are in the proper locations for satellite-borne and earth-based receivers. And NASA also plans to launch a set of four satellites called OPEN—for Origin of Plasmas in Earth's Neighborhood—to take a yet more detailed look at what happens as the earth encounters the sun. □

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## Life after a death: Widows' advantage

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The anguish that often follows the death of a spouse may make the surviving partner especially susceptible to disease and early death, many researchers believe, but a study from Johns Hopkins University indicates that such a loss hits men harder than women. By following 4,000 widowed persons aged 18 years or older through 12 years of census records, scientists found that widowers died sooner than married men of the same age and race, and similar home environment. Widows, however, showed an annual mortality rate that was indistinguishable from that of their married counterparts.

Unlike most previous studies of survival after bereavement that simply compared death rates, the data examined by Knut J. Helsing, Moyses Szklo and George W. Comstock included information about each individual's smoking history, years of schooling, and number of housemates—all factors that affect mortality rates. Each widowed person was "paired" in the study with a similar individual whose spouse remained alive. Despite the difference in their death rates, widowed men and married men generally died of the same natural causes and diseases, the researchers say.

While a demographic survey could never "prove" that losing a husband or wife shortens one's lifespan, one finding from the study, published in the August AMERICAN JOURNAL OF PUBLIC HEALTH, hints that the effects of marriage on longevity might be strong: Mortality rates

among widowed men who remarried were very much lower than among those who did not remarry. In fact, for most of the age ranges studied, remarried widowers actually had mortality rates lower than those in the married control group. (Too few widows in the study remarried to make a similar comparison in women, the researchers report.)

The jump in the widowers' death rate did not appear until several years after the wives died, reports Helsing, suggesting that it is the absence of his spouse rather than the immediate trauma of her death that most affects a man's health. Helsing, the study's principal investigator, speculates that the social support that marriage provides might stave off death for married men by providing them with partners to share their daily stresses who can also help during a medical emergency. Why women suffer less from the same loss can only be explained through further research, he adds, though other studies indicate that "women are better adapted to survival than men to start with." □

