# 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.

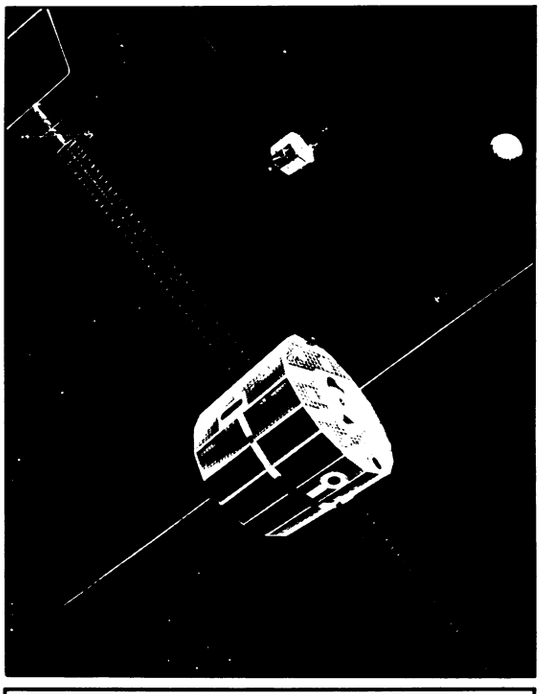
In addition to yeast's ability to add sugars to proteins and thus produce complex biochemical structures, yeast have other advantages over bacteria for large-scale production of biologicals. The techniques for growing large quantities of yeast for commercial use have been developed thoroughly by bread, beer and wine producers. Furthermore, yeast do not produce the toxic chemicals, known as endotoxins, that are a concern in fermentation of bacteria.

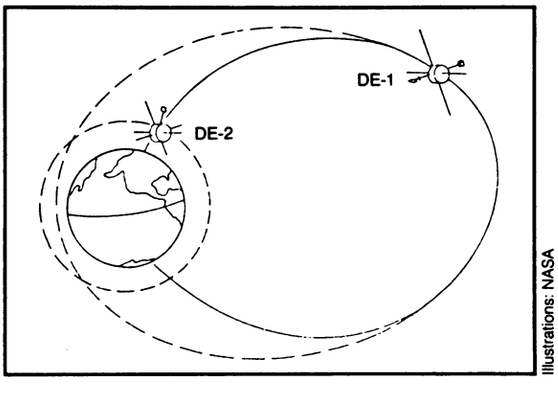
Hepatitis B, the most dangerous strain of liver-infecting virus, affects more than half a billion people throughout the world. Approximately 200 million carry the virus in their blood and can pass on the infection through intimate contact, via blood transfusion or from mother to fetus. In addition, the 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