Bacteria Coerced to Produce Insulin

Boston researchers have sped past a major milestone in the race to engineer bacteria to produce medically valuable substances. Walter Gilbert of Harvard University announced last week that gene transplant techniques have induced bacteria to produce a form of rat insulin. Within a few months several U.S. research groups hope to have bacteria making human insulin.

Rat genes for insulin were successfully transported into bacteria by California scientists more than a year ago (SN: 5/28/77, p. 340), but did not produce detectable hormone. Last November, a simpler human hormone, somatostatin, was manufactured in bacteria directed by a laboratory-synthesized gene (SN: 11/12/77, p. 310).

In the recent Boston work, the strategy for obtaining genetic material was similar to the other insulin gene transfer, but a novel trick induced hormone production and excretion. The insulin gene was synthesized in the laboratory, not piece by piece as in the somatostatin research, but copied off a template of insulin messenger RNA, abundant in special rat tumor cells. DNA back-copied from messenger RNA is equivalent to the original gene.

The successful trick is linkage of the synthesized DNA with a natural bacterial gene whose product is routinely exported from cells. The gene selected is one that codes for penicillinase, an enzyme that breaks down penicillin and makes the bacteria resistant to that drug. The penicillinase gene is found on plasmids, DNA rings independent of the bacterial chromosome.

The researchers inserted the insulin-coding DNA into the penicillinase gene on a plasmid. The new DNA had to link up in the right orientation and reading frame, so its message could tag onto that sent from the penicillinase gene to the bacterium's protein-making machinery. When the altered plasmids entered bacteria (*Escherichia coli*) they functioned, churning out hybrid penicillinase-insulin protein molecules. Because the bacteria normally excrete penicillinase, the tagged-on insulin portion of the molecule also left the cells. William Chick and Stephen Naber of the Joslin Diabetes Foundation in Boston, who supplied the original rat tumor cells, used antibodies to measure the proinsulin excreted. They found about 100 molecules of proinsulin per bacterial cell.

The researchers don't yet know a simple way to separate proinsulin from the penicillinase portion of the hybrid, although proinsulin can be converted to insulin easily enough. Such subsequent treatment is of minor importance, they believe. They see the major achievement as the successful direction of protein production and excretion. The results show that plasmid construction can lead to expression of fused protein. The procedure can now be repeated with minor changes to get different hybrids of the proteins or perhaps just proinsulin linked to bacterial control signals.

The research was funded by the National Institutes of Health and carried out in recombinant DNA safety facilities at the Massachusetts Institute of Technology. Other members of the Boston team are Lydia Villa-Komaroff, Argiris Efstratiadis, Stephanie Broome, Peter Lomedico, Richard Tizard and Greg Sutcliffe. Gilbert has filed a patent application for portions of the procedure, according to another Harvard researcher.

Bacterial production of human insulin would be important for the millions of diabetics who take daily injections of insulin, a hormone that is currently being isolated from the pancreatic glands of cows and pigs in a relatively expensive procedure. With increasing numbers of diabetics, a shortage of available animal insulin is feared. In addition, some diabetics are allergic to the cow and pig hormones, which are slightly different from the human form.

The researchers anticipate that bacterial production of human insulin can be developed following the same rationale as the production of rat insulin. The gene might be copied from human insulin-producing tumors or from normal pancreas cells. At present, the NIH guidelines on recombinant DNA research strictly limit work with human genes. The experiments aimed at producing human insulin in bacteria may be performed only in the NIH P-4 facility at Fort Detrick, Md. (SN: 3/25/78, p. 180). A revision of the guidelines, now waiting the approval of Health, Education and Welfare Secretary Joseph A. Califano Jr., would allow laboratories with different safety facilities to work on transplanting the human insulin gene.

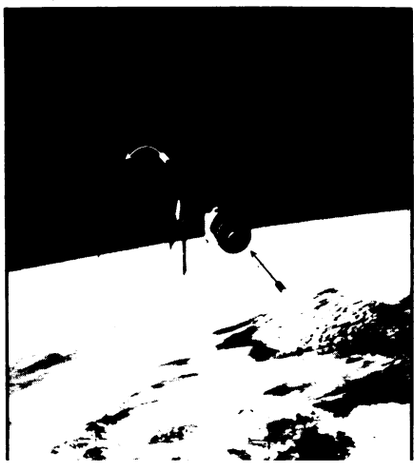
In all the arguments about the safety and desirability of recombinant DNA research, bacterial production of insulin has been offered as an important, although uncertain, benefit. Numerous scientists imagined vats of bacteria synthesizing commercial quantities of the hormone and have competed toward that end. Now little doubt remains that the finish line is in sight. □

Skylab shifted to low-drag position

Skylab has done *its* part, maneuvering in response to a series of commands that occupied flight controllers at the NASA Johnson Space Center in Houston from just before midnight on June 8 to the early hours of June 11. Now the space agency groundlings can only wait, hoping that the move has given Skylab a new lease on life by extending its orbital lifetime until space shuttle astronauts can attach a rocket to send the massive laboratory beyond the atmosphere's grasping fingers.

The corrective maneuver was a multi-step affair, designed to reorient Skylab to a less drag producing position that essentially resembles the one it had when it was a working space station more than four years ago. At that time, the axis of the cylindrical workshop was maintained parallel to the ground beneath and aligned with the direction of travel in orbit. The observatory section, called the Apollo Telescope Mount or ATM, was at the leading end.

Skylab, photographed by astronauts in 1973, is now in similar orientation.



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When the station was "turned off" on Feb. 9, 1974, following the departure of its third crew of astronauts, it began to drift into what NASA calls a "gravity-gradient" position, with the main axis radial to the earth, the more massive aft end of the workshop "down" and the ATM at the top. It was also rolling slowly on its axis, a motion made more complex by mass-distribution assymetries that caused it to turn in a narrow-angle cone. The workshop's one "wing" of solar cells, source of electricity to charge Skylab's batteries, stuck out from the cylinder like a flag from a pole; the ATM's separate set of solar panels, an X-shaped array, was in the same plane as the wing.

On the evening of Thursday, June 8, in the first step of the maneuver sequence, the NASA flight controllers commanded Skylab's computer to stop the rolling when a sensor indicated that the solar panels were facing the sun. At this point, the workshop was no longer turning on its axis, but the axis itself was still going