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.

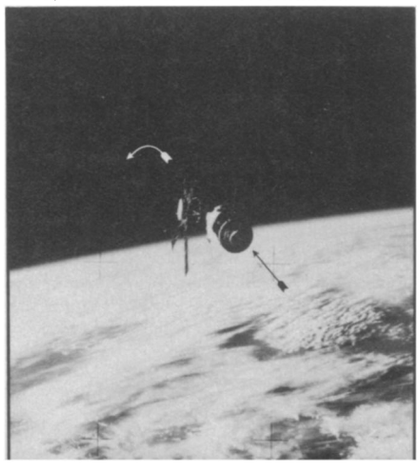
In all the arguments about the safety and desirability of recombinant DNA research, bacterial production of insulin has been offered as an important, although uncertain, benefit. Numerous scientists imagined vats of bacteria synthesizing commercial quantities of the hormone and have competed toward that 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 multistep 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.



NASA

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

through its conical oscillation. Next, the attitude-control jets were used to reduce the "coning" until the solar panels were staying within 6° of being pointed directly at the sun. The guidance system was then switched to "solar inertial" mode, in which the panels would face permanently sunward. Part of that command also tilted Skylab down so that it was parallel to the earth and aligned with its orbital motion. The command did not specify which way it was to tilt, however, and the move ended up with the ATM to the rear. Since the ATM offers a smaller drag-producing cross-section to the rarified atmosphere than does the station's other end, the controllers on the ground ordered a 180° turn, to which Skylab responded perfectly.

Early this week the controllers were fine-tuning the space station's orientation to minimize some residual coning, in order to effectively reduce the atmospheric drag still further. Officials estimated that it will take about six weeks of radar tracking by NASA and by the North American Air Defense Command (NORAD) to confirm that the maneuver has indeed slowed Skylab's rate of descent enough to provide the hoped-for six to 12 months of extra time in orbit. Even this week, however, NASA was already feeling out members of Congress about the prospect of freeing funds to begin building the auxiliary rocket that would be shuttled up and attached to the station to kick it into a still longer lasting orbit. □

Children of gays: Sexually 'normal'

Whether or not homosexuals make inappropriate schoolteachers — as some antigay activists claim — is unresolved, but preliminary psychiatric data now indicate that as parents, gays and transsexuals do not adversely affect their own children's sexual identity.

A study of 37 children being reared by either female homosexuals or by parents who have changed sex reveals that 36 of the youngsters are heterosexually oriented—those who have reached adolescence are attracted to the opposite sex, and the younger children display behaviors that indicate they are on the road to developing "normal" sexual preferences.

Aside from their social significance, the results appear to punch some holes in psychoanalytic theory, Richard Green of the State University of New York at Stony Brook reports in the June AMERICAN JOURNAL OF PSYCHIATRY. "Both psychoanalytic and social reinforcement or role-modeling views would predict that having a transsexual or homosexual parent should have a striking effect on a child's sexual identity development," says Green. "Penis envy, castration fear and resolution of family romance (oedipal conflict) are pivotal for normal psychosexual maturation of the child, according to psychoanalytic theory.

"Thus, a father without a penis or a mother or father with a same-sex partner preference serving as the identification object during the resolution phase of the oedipal period should profoundly influence psychosexual development," Green says. But the psychiatrist's results do not suggest such an influence. "What one can say is at this time, based on the best indicators of emerging sexual identity, psychosexual development appears to be typical in at least 36 of the 37 children described in this paper."

Green studied the children — 18 males and 19 females, ages 3 years to 20 years (mean age 11.3) — over a two-year period. Twenty-one were being reared by homosexual parents and 16 by transsexual parents; several of the children of transsexuals remembered their parent in his or her original sexual state before the transformation. The younger children were evaluated on their toy and game preferences, peer group composition (which is typically same-sex during grade school), clothing preference, roles played in fantasy games, vocational aspiration and the Draw-A-Person test (in which boys typically draw males first and girls draw females). For adolescents, information was obtained on romantic crushes, erotic fantasies and sexual behavior.

With one questionable exception, the children's responses suggested they were heterosexually inclined. None exhibited homosexual or transsexual fantasies, adolescents had romantic inclinations toward the opposite sex and young children preferred to play with same-sex playmates. Vocational choices reflected standard, if somewhat chauvinistically flavored preferences, with boys designating positions such as doctors, engineers, firemen, scientists and policemen and girls opting for nurses and teachers. Only two girls, however, chose "housewife" or "mommy" and one set her sights on "popsicle lady."

While there is no definitive explanation of the apparent normality of the group — even among older children who have been living under such circumstances for much of their lives — Green suggests outside influences may be critical. "Children do not live in a universe composed entirely of their home environment," he says. School, peer group members and their families and even much-maligned television programming expose the child to "conventional family styles and conventional patterns of... development," he says.

The psychiatrist currently is studying matched control groups of heterosexual and homosexual divorced mothers and their children, which he says will yield more detailed data. "At this stage I tentatively suggest that children being raised by transsexual and homosexual parents do not differ appreciably from children raised in more conventional family settings...," he says. □

A quasar sat unnoticed nearby

Quasars are usually considered to have cosmological connections. Most of them are extremely far away — the most distant objects known are quasars — and so they are expected to give an idea of conditions on the edge of the observable universe. Distance in space is also distance in time, and so the astrophysical phenomena that account for the quasars' appearance and their extremely large energy output for their size are widely believed to belong to an early epoch in the universe.

Now comes a nearby quasar, a very nearby quasar. It was found by Bruce Margon of the University of California at Los Angeles and is reported in the June 8 NATURE. Designated 0241+622 (these designations come from an object's coordinates on a sky map, in case anybody was wondering), this quasar is only 800 million light years from the earth. In 800 million years a lot has changed on the surface of the earth, but that is something less than a tenth of the distance of the most distant known quasars, which go as far as 15 billion years. The difference represents a lot of the universe's development time. The new quasar is thus in "familiar territory," Margon says.

The discovery came as Margon and his graduate student Karen B. Kwitter were trying to identify a binary star system with a source of X-rays that had been noted by a group led by Hale V. Bradt and Richard Dower of the Massachusetts Institute of Technology. X-ray sources are another topic of wide interest in astronomy these days. They are often found in binary star systems in which one member is an ordinary star and one a compact dark object.

Binary stars are Margon's particular interest, so he and Kwitter were searching for an optical counterpart to the X-ray source found by Bradt, Dower and company. They used the 120-inch telescope at the Lick Observatory on Mt. Hamilton near San Jose to look in the direction specified by the X-ray astronomers, which is in the constellation Cassiopeia. In the spectrum they obtained they found emission lines not characteristic of a binary star. From the redshift, Margon deduced that they were seeing a quasar that was some distance outside our galaxy rather than a binary star that would have been inside our galaxy. If this quasar didn't happen to be lined up with the obscuring dust in the plane of our galaxy, it would look like an 11th magnitude star. The discovery of quasars might have come decades before.

The discovery of a quasar so near is sure to be injected into the continuing debate over their cosmological significance. Theories that assign the quasar phenomenon to the early days of the universe will have to make room for more contemporary possibilities. □