Bacterium Is Used in Producing Insulin

By Robert Cooke
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A team of biologists at Harvard University has found a way to use a common bacterium to manufacture the medically valuable hormone insulin.

The unprecedented scientific achievement appears to open the way to eventual mass production of almost any protein—including human hormones—by microscopic "factories" of bacteria.

Led by Prof. Walter Gilbert, the Harvard team used scientifically elegant gene-splicing techniques to induce the bacteria to turn out a precursor to rat insulin, a mammalian hormone vital in the metabolism of sugar. The precursor, called pro-insulin, can be converted to insulin once outside the bacterium. The researchers report their bacteria churn out about 100 molecules of rat pro-insulin per cell. Multiplied by billions of bacteria, a large amount of rat insulin could be produced.

Several U.S. research teams are believed to be within months of getting bacteria to produce the human form of insulin, a step that would have important practical significance for the millions of diabetics whose lives depend on daily insulin injections. Currently medical insulin is derived from the pancreas glands of slaughtered cows and pigs, but a 6 percent annual increase in the incidence of diabetes may eventually create a shortage of the hormone.

In addition, some diabetics do not tolerate the animal insulin, which is slightly different chemically from the human hormone.

The intense scientific competition to engineer an insulin-producing bacterium is based less on its immediate practical usefulness than on the desire to demonstrate that a lower organism can be induced to manufacture complex human proteins. This step would have immense scientific and medical implications; there are many human proteins unavailable for medical use or study that might become available through the same techniques that the Harvard group had used in the pioneering rat-insulin work.

The Harvard experiments were done in an especially secure laboratory at the Massachusetts Institute of Technology under guidelines formulated in 1976 by the National Institutes of Health.

Under those guidelines, the critical final experiments toward producing human insulin in bacteria could not be performed in any American laboratory outside the NIH's own top-security lab in Maryland. However, a revision of those rules, now on the desk of Health, Education and Welfare Secretary Joseph A. Califano Jr., would open up the human insulin experiments to dozens of U.S. laboratories.

The Harvard team used an ingenious strategy to "trick" the bacterium to produce insulin, a complex protein for which the bacterium has no use. First they made an artificial copy of the rat genes for insulin—the code that specifies how to assemble the molecules of insulin. Then they spliced the artifical gene into a small ring of genes called a plasmid.

They used a well-known plasmid containing the genes for penicillinase, an enzyme that enables bacteria to resist the antibiotic effects of penicillin.

Then they inserted the remodeled plasmid into a living bacterium, an enfeebled strain of a ubiquitous organism called Escherichia coli. The bacterium obediently began excreting complete insulin molecules attached to molecules of the penicillinase enzyme.

The penicillinase plasmid was used because it was known that the bacterium normally excretes the enzyme rather than keeping it within the cell. So the researchers figured—accurately, as it turned out—that the insulin would be piggybacked on the enzyme.

In order to make sure that the insulin would come out attached to the penicillinase molecule, they had to use a technique called "sequencing" to locate the genes for penicillinase so they could insert the insulin genes in the midst of the enzyme gene.

Sequencing was also used to make sure the spliced-in insulin genes were in the correct orientation (frontwards instead of backwards) and "in frame," meaning that the gene was copied accurately by the bacterium.

Aiding the Harvard team in the insulin work were researchers from the Joslin Clinic, a Boston diabetes research center. The team plans to publish a report in August in the Proceedings of the National Academy of Sciences.

Today's Activities in Congress

Senate

Meets at 10 a.m. on the labor law bill.
Committees:

Agriculture Subcomite. on Nutrition—9 a.m. Open. Hearings on diet-cancer relationship. 324 Russell Office Bldg.

Banking—9:30 a.m. Open. Hearings on N.Y. city financial aid. 5302 Dirksen Office Bldg.

Commerce—10 a.m. Open. Nomination hearings on members to the U.S. Metric Board. 235 ROB.

Environment—9:30 a.m. Open. Comte to mark-up S. 1493, energy impact legislation, and building perspectus legislation. 4200 DOB.

Governmental Affairs—10:30 a.m. Open. Mark-up on S. 2640, civil service bill. 3302 DOB.

Judiciary Subcomite. on Administrative Practice—10 a.m. Closed. Hearing on application and enforcement of the proposed FBI charter. 2228 DOB.

Energy—10 a.m. Open. Mark-up continues on DOE energy bill, S. 2693 and other comte. business. 3110 DOB.

House

Meets at noon on a resolution condemning violations of human rights by Uganda.
Committees:

Appropriations—10 a.m. Open. Treas., Postal Serv., Genl. Govt. Subc. on Postal Serv. suppl. H-164 Capitol.

Government Operations—9:30 a.m. Open. Environ., Energy & Natural Res. Subc. Cont. hrngs. on solar energy. 2154 Rayburn Office Bldg.

Interior—9:45 a.m. Open. Energy & Environ. Subc. Cont. hrngs. on Nuclear Siting & Licensing Act. 1324 Longworth House Office Bldg.

International Relations—2 p.m. Open. Europe & Mid. East Subc. on recent developments in Mideast. H-236 Cap.

Commerce—10 a.m. Open. Health & Environ. Subc. Cont. hrngs. on drug regulation reform. 2322 RHOB.

Commerce—10 a.m. Open. Energy & Power Subc. Oversight hrngs. on energy dept. entitlement prog. 2123 RHOB.

Judiciary—10:30 a.m. Open. Admin. Law & Govt. Rel. Subc. Mark-up pending legis. 2226 RHOB.

Merchant Marine—10 a.m. Open. Oceanography & Fish. & Wildlife Conserv. & Environ. Subcs. on NOAA Organic Act. 1334 LHOB.

Small Business—10 a.m. Open. SBA & SBIC Auth. Subc. Cont. hrngs. on meat marketing. 2359 RHOB.

Conferees—2 p.m. Open. HR 5289—Natural gas legis. 2123 RHOB.