A Science Scoop by China

Peking Biologists Complete Britisher's Work in Synthesis of Insulin Protein

By Joshua Lederberg

Science and Man

UNDER THE impetus of strong support for basic research, the last 20 years have seen one epochal achievement after another in biological chemistry. "Unraveling the DNA Code" is, by now, a well-known headline for this progress, but one must look more deeply into each of the advances to assess our present situation and understand its human significance.

One of the most startling successes, outstripping the most daring imaginations of prior years, has been the analysis of protein structures. Then, as if to show that confident attack can surpass the most unthinkable challenges, we have recent confirmation of the laboratory synthesis of a protein, insulin.

This announcement by a group of chemists from the Chinese Academy of Sciences, corroborated by their rivals in the United States and Germany, is a pointed reminder that scientific culture is available to, and embraced by, all the world, allies and antagonists alike.

INSULIN HAS long played a central role in the application of biochemistry to medicine. Many people now living by the grace of this knowledge should recall its discovery 44 years ago as the hormone that the diabetic has lost the ability to make in his own pancreas.

At that time, no scientist would admit to the fantasy that such a protein hormone might some day be synthesized—well, perhaps by the 25th century, along with space travel and atomic energy. That the Chinese should have scooped the rest of us adds to the science-fictional flavor of the reality.

Insulin is far simpler than growth hormones. Its first analysis, reported about ten years ago by Dr. Fred Sanger, a British biochemist, was simplified by its being made up of two fairly short chains of amino acids. The chains can be symbolized as YWVGOC * C * ESWC *SUTQUGNTC * and FVNQHUC * YSHUVGLUTLVC * YGRYFFTEPIE.

The two chains are readily separated from natural insulin, so the analytical problem could be divided into two more easily manageable parts. Each chain in turn could be dissected by various chemical reagents into smaller pieces until recognizable fragments were obtained. There was then a reassembly of the jigsaw puzzle to prove the whole structure, a fascinating game for which Sanger was awarded a Nobel Prize in 1958.

AMONG THE insights we get from such studies, a characteristic difference between man and cow is in the structure of the midsection of one chain, C*ESWC* in contrast to C*LSVC*. The difference in insulin is not the essence of humanity; too many people live with the help of the bovine protein to allow such a thought. But the evolution of many analogous differences in the structure of important proteins, say of the brain, may be the central clue.

Each of the two chains had been synthesized, once Sanger had shown the structures, by some three years ago. The problem then was to put the whole molecule together, which involves joining the pairs of C* (cysteine) groups of the chains in one particular way.

There would be hundreds of incorrect ways in which two or, even worse, more than two chains might be joined by these — C**C — links, only one of which would result in proper insulin. The trick was a controlled method of joining that would encourage the right combination, and this was the Chinese success in this puzzle.

TO WORK out the structures of proteins is one of the most direct routes of attack on many fundamental questions of evolution, cellular processes and disease. It is arduous but, by now, rather routine work.

There could be great economy in applying automated equipment and specially trained technicians to building a library of analytical information. The same approach would apply even more to the routine synthesis of proteins. The actual work of analysis and synthesis is really no longer basic research; that would rather lend itself to more highly directed and managed technology.

The realization of these technological possibilities is an example of the imperfect technique we have evolved so far to bring about the quickest practical applications of basic discovery. Private enterprise might be expected to exploit the opportunities. However, by the vagaries of patent law, natural materials like proteins make hazardous private investments. Several million dollars might be committed to analyze the first protein examined by an industrial laboratory with no assurance of specific return to the investor.

On the other hand, the efficient prosecution of coordinated projects on a large scale is beyond the proper role of the academic laboratory. Even the cooperation of academic scientists with industry has perils for the investor because of the Government's jealously kept proprietary interest in patents supported in any way by Federally funded research, and most basic work in this field is funded by the NIH. Policy rather than scientific insight is already the limiting factor in further exploitation of protein chemistry for human advantage.

WE MUST make a clearer choice of one or another policy in each case: to provide adequate inducements to private enterprise, even at the expense of reversing moralistic commitments to the concept of public ownership of assets vital for health; or to subsidize the development process by letting Government contracts to industry, as has been so successful in military and space efforts, or to organize publicly owned development laboratories.

A foolish policy would steal the funds for application-development from basic research. Why should a commitment proven to have such vast potential be the most vulnerable in seeking how to finance new enterprises? We should rather reorient our priorities of social action over the whole sphere of our existing and wished-for balance of commitment.