BIOCHEMISTRY

Human Insulin Made

Human insulin has been synthesized for the first time and although there is no need now for its commercial production, it may be necessary in the future.

➤ HUMAN INSULIN has been synthesized for the first time. It is the first human protein man has made artificially, and only the third protein ever made.

The synthesis of effective human insulin was achieved by Dr. Panayotis G. Katsoyannis and his co-workers at Brookhaven National Laboratory, Upton, N.Y.

Although there is no need now for commercial production of artificial insulin, it may be necessary in the future since supplies of natural insulin are limited and diabetes is on the increase.

Dr. Katsoyannis told SCIENCE SERVICE that the success of his step-by-step research has inspired him to further work. He is looking for higher yields of the synthetic protein so that enough can be produced to study insulin's role in diabetes. This will be done through the use of radioactive insulin and chemically altered forms of the compound, called analogs.

The first artificial protein, sheep insulin, was synthesized by Dr. Katsoyannis with a University of Pittsburgh research team two years ago. German and Chinese chemists independently have made sheep and beef insulin, respectively. Although the three proteins differ only slightly, creation of human insulin required the development of new methods.

The synthesis of a human protein marks a high point in the efforts of chemists to understand body processes, such as enzyme and hormone action, through the study of protein structure.

Insulin is a protein hormone made by the pancreas. In some unknown way insulin stimulates the body's burning, or oxidation, of sugar. When insulin is not produced, as in diabetics, sugar accumulates in the muscles and bloodstream, ending in death unless insulin or a hypoglycemic drug is given.

Between one and two percent of the U.S. population is afflicted with diabetes. Natural beef and pork insulins are now used to treat diabetics.

The use of radioactive insulin or of analogs may help answer several questions about the cause of diabetes, Dr. Katsoyannis said, such as whether or not the pancreas is producing imperfect insulin and whether or not the insulin is destroyed outside the pancreas by an enzyme.

The synthesis of human insulin was reported in the Journal of the American Chemical Society Jan. 5, 1966, by Dr. Katsoyannis, Dr. Andrew Tometsko and Clyde Zalut of Brookhaven National Laboratory.

Only about two percent of the possible amount of insulin was produced in the process, but recent work indicates that the yield may be increased to as much as 55%.

A molecule of insulin is a complex affair, composed of two chains of smaller molecules, called amino acids. The "A" chain consists of 21 amino acids, and the "B" chain 30; the two chains are held together by two crosslinks of sulfur atoms.

Human insulin differs from sheep insulin in that it has some different types of amino acids in its molecular chains—three in the A chain and one in the B chain.

The synthesis of the A chain, which contains the three new amino acids located between a "bridge" of sulfur atoms, was especially difficult because one of the amino acids, serine, can react in several different ways, Dr. Katsoyannis said.

The B chain also required a new approach because the one different amino acid, threonine, located at the head of the chain, also is extremely reactive.

Dr. Frederick Sanger of England received the Nobel Prize in Chemistry in 1958 for determining the structure of a protein, beef insulin, for the first time. The structure of human insulin was discovered in 1960 by Dr. D. S. H. W. Nicol and Dr. L. F. Smith of England.

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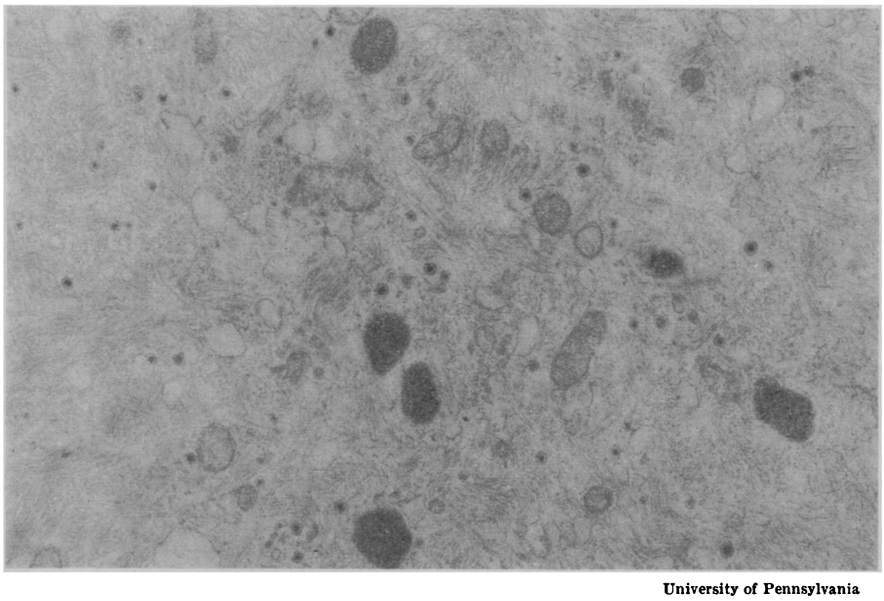

University of Pennsylvania

VIRUS-LIKE PARTICLES IN BRAIN—The small, virus-like cells with dark centers surrounded by light margins and membranes were found in the brain of a child suffering from sub-acute sclerosing encephalitis by Dr. Nicholas K. Gonatas of the University of Pennsylvania.

MEDICINE

Virus-Like Particles Seen In Photographs of Brain

➤ THE FIRST KNOWN pictures of brain cells containing virus-like particles have been taken at the University of Pennsylvania.

The pictures were made from biopsied material from the brain of a nine-year-old child who for the preceding 15 months had been deteriorating mentally, Dr. Nicholas K. Gonatas told SCIENCE SERVICE.

The girl had trouble holding objects in her hands, and walked with a noticeably abnormal gait. Her speech was slurred, she wet the bed, had tremors and generalized seizures, and for 10 months had been developing sexually in a precocious way, including early breast development. She could not respond to light or to any stimulus except pain.

The patient was suffering from sub-acute sclerosing encephalitis, Dr. Gonatas said, a fatal disease of uncertain origin, attacking the central nervous system and usually affecting children and adolescents.

Under the electron microscope, Dr. Gonatas and his co-worker, Dr. G. Milton Shy, found a large number of virus-like particles in the cytoplasm of star-shaped cells called astrocytes in the brain's white matter. They saw no such particles in the cytoplasm of neurons in the gray matter.

"Our problem is that the identity of the virus, if it is a virus, has not been established," Dr. Gonatas noted. Even if it is proved to be one, it remains to be seen whether it is actually causing the disease or is only a "bystander."

Viruses have already been found in animals suffering from chronic nervous system diseases of degenerative or demyelinating nature, such as scrapie, Visna and Aleutian disease of mink, making the present discovery in a human disease of special interest.

The University of Pennsylvania research was done under a U.S. Public Health Service grant, and reported in Nature 208:1338, 1965.

The probable role of a slow virus in the cause of chronic disease of the central nervous system of man should be reinvestigated in view of the findings now reported, the researchers said.

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