

# Decipher Protein Structure

Roswell Park scientists believe in cancer link to disturbed atomic order

The scientists who have deciphered the complex assembly of atoms that make up the enzyme ribonuclease believe that alterations of the atomic structure of such proteins may have a relationship to cancer.

The structural analysis of ribonuclease was made by scientists at Roswell Park Memorial Institute in a \$2 million project that lasted 16 years. It was the first time atomic structure of a protein so critical in the life process had been analyzed, though earlier protein work in England laid the base.

**Ribonuclease is a protein** that degrades, or breaks down RNA, short for ribonucleic acid, the important go-between in the cell.

Instructions from DNA, or deoxyribonucleic acid, the bearer of genetic information located in the cell nucleus, are carried to the rest of the cell by RNA.

The messenger RNA tells the cell what proteins to make and in general how to grow and conduct its life processes.

Ribonuclease becomes active when it is necessary to break down or eliminate some RNA, either during the life of the cell or when it dies. The enzyme can be considered not only a type of control mechanism but a kind of house-cleaner.

Ribonuclease contains more than 1,000 atoms arranged as a chain of 124 amino acid units that have been cross-linked. In the course of the investigation the Roswell Park researchers determined the molecular structure of 24 other simpler substances, having only 25 to 50 atoms in the molecule, including hormones and drugs.

**Dr. David Harker** drew on the techniques of two Nobel Prize winners in chemistry at Cambridge University, England. Austrian-born Dr. Max F. Perutz and Dr. J. C. Kendrew shared the Prize for deciphering the structure of myoglobin, or muscle hemoglobin, from sperm whales. Dr. Perutz had earlier made a partial analysis of hemoglobin in horses.

Also in Britain, Dr. D. C. Phillips and his colleagues at the Royal Institute reported in 1965 finding the structure of lysozyme, another enzyme in the body, approximately one-third more complex than ribonuclease.

Dr. Harker of Roswell Park used a computer because of the enormous number of mathematical calculations

required, and in the past two years, calculations for the ribonuclease structure project have utilized one-third of the time of Roswell Park's IBM 7040 as well as moderate amounts of time of the 7044 at the State University of New York at Buffalo. He believes that other proteins can be analyzed in much less time through automation.

Dr. Harker is director of the Center for Crystallographic Research at Roswell Park, the New York State Health Department's cancer research and treatment facility. He headed the research reported at an international meeting at Madras, India, by Dr. Gopinath Kartha, a colleague.

The amazingly complex compounds called proteins cause us to go through the cycle called life, Dr. Harker says.

**"The life process depends** upon the orderly behavior of complex forces acting within protein molecules, and their interactions and reactions with neighboring molecules," he explains.

"It is possible that when the atomic structures of proteins are altered in some manner, there may be a relationship to cancer. Now that we have the structure of ribonuclease, we will be better able to determine the structures of other proteins as well as see precisely how ribonuclease works—especially since we now know where its active site of combination with RNA is located."

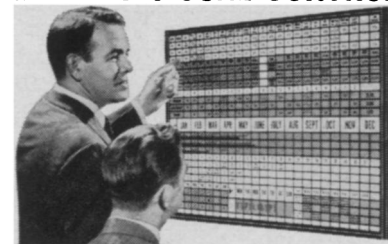
The techniques of the branch of science called X-ray crystallography were required to clarify the ribonuclease structure. Crystallography generally is concerned with the arrangement of atoms within substances and how their properties are related to these arrangements.

**To be studied by X-ray bombardment** the ribonuclease first had to be put into crystalline form, a task undertaken by the third colleague, Dr. Jake Bello. After the crystals had formed they were put into an automated X-ray diffraction unit controlled by a computer.

The Center for Crystallographic Research has been in existence since August 1965. It was the first of its kind in the United States.

Dr. Harker came to the institute with his co-workers seven years ago. The enzyme project was begun July 1, 1950, at the Polytechnic Institute of Brooklyn where it took up 2,500 square feet of bare floor space and was supported by a \$250,000 grant from the Dean Langmuir Foundation.

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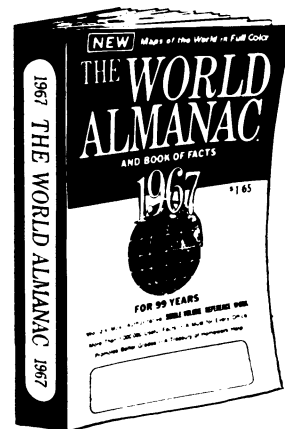
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