

A team of scientists from four institutions have found a cancer gene that is related to a gene with a known function in human cells. The scientist from UCSD is Dr. Russell F. Doolittle

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CANCER GENE FOUND TO HAVE "STRIKING SIMILARITY" TO GENE ENCODING NORMAL HUMAN GROWTH FACTOR

For the first time, a known cancer gene has been identified that is apparently related to a gene with a known function in human cells, a team of scientists from four institutions has found.

One of the scientists was Dr. Russell F. Doolittle, professor of chemistry at the University of California, San Diego, who used his personally compiled computer data bank of protein sequences to make the key link between separate research efforts by teams of scientists at the Center for Blood Research in Boston and the National Cancer Institute in Washington, D.C.

The study was cited at the symposium on the "Role of Oncogenesis in Carcinogenesis" at the 74th annual meeting of the American Society of Biological Chemists in San Francisco, June 5-9, 1983. It will be published in the July 15 issue of Science.

The scientists-from UCSD, Caltech, the National Cancer Institute, and the Center for Blood Research-discovered that the protein produced by a cancer-causing virus in monkeys has "striking similarity" to a wound-healing protein found in human serum and in blood platelets. This important blood protein, called platelet-derived growth factor (PDGF), begins the healing process after injury by triggering cells around the wound site to begin multiplying.

The finding may offer an important new understanding of how cancer genes transform normal cells into wildly dividing cancer cells. According to the scientists, the cancer gene they studied may act to permanently turn on the same potent growth-promoting process that is normally activated only temporarily during wound-healing.

Although the cancer virus was of the type that affects only monkeys, expression of a similar cancer-causing gene has also been detected in certain human tumors of bone and connective tissue.

Authors of the Science article, "A Simian Sarcoma Virus onc Gene, v-sis, is derived from the Gene(s) Encoding a Platelet-Derived Growth Factor," are:--Russell F. Doolittle, University of California, San Diego,--Michael W. Hunkapiller and Leroy E. Hood, California Institute of Technology,--Sushilkumar G. Devare, Keith C. Robbins, and Stuart A. Aaronson, National Cancer Institute, and--Harry N. Antoniades, Center for Blood Research, Boston, and the Harvard University School of Public Health.

For the past several years, scientists have known that certain viruses harbor genes called oncogenes that can cause cancers, probably by altering normal genes in the cell. Scientists also knew that the effects of oncogenes on cells closely resembled the effects of normal growth-promoting hormones and other proteins. However, researchers had been unable to show that cancer genes closely resembled any human genes with a known physiological function.

In the Science paper, the scientists reported a comparison of PDGF with the protein made by the oncogene v-sis, which is found in simian sarcoma virus, a cancer virus affecting monkeys.

PDGF was first isolated and purified by Dr. Antoniades and his associates. This research began in 1973 with funding from the National Cancer Institute. The American Red Cross Blood Services Northeast Regional Office supplied the blood serum and many thousands of units of clinically outdated human platelets over the course of the research.

Drs. Antoniades and Hunkapiller, using a highly sensitive protein-sequencing machine at Caltech, derived the amino acid sequence of purified PDGF and its subunits and reported their findings in the May 27, 1983 issue of Science. Proteins like PDGF are composed of strings of amino acid units, and their properties are determined by the identities of those units.

Dr. Doolittle read this report in Science and, using his home terminal linked to UCSD, entered the PDGF sequence into a computer data bank of protein sequences he maintains at UCSD. He discovered an 87.1 percent sequence match between PDGF and the v-sis protein.

The discovery and analysis of the v-sis gene and its protein product had been made by doctors Devare, Robbins, Aaronson and their colleagues at the NCI.

With Dr. Doolittle's computer sequence correlation, more than 10 years of research culminated in a 20-minute computer search. The Science report by the scientists on the PDGF/v-sis relationship was prepared after Dr. Doolittle wrote Drs. Antoniades and Hunkapiller of his findings.

In their paper, the scientists called for a major effort to match cancer gene proteins with normal growth proteins:

"Other oncogenes, perhaps as yet uncharacterized, may code for growth regulatory proteins whose primary structures have not been determined," they wrote. "Therefore, any proteins that are suspected in regulation of normal cell growth and all oncogenes should be scrutinized rigorously by computer analysis as soon as their sequences are known."

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