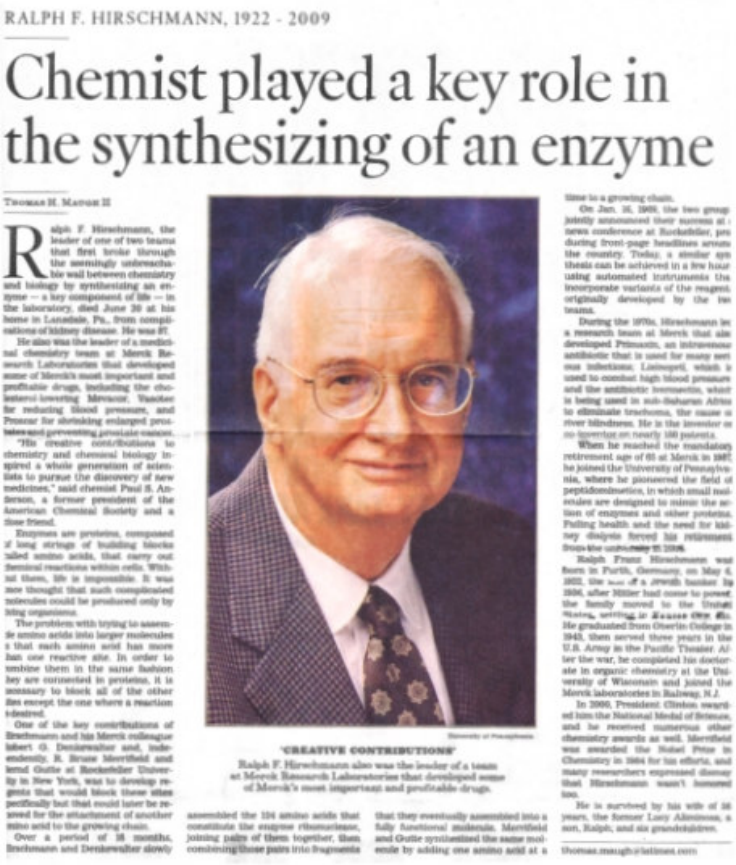
Prof. Dr. Ralph F. Hirschmann

(6.5.1922 in Fürth - 20.6.2009 in Lansdale, Pennsylvania, USA)



RALPH F. HIRSCHMANN, 1922 - 2009

Chemist played a key role in the synthesizing of an enzyme

THOMAS H. MAUGH II

Ralph F. Hirschmann, the leader of one of two teams that first broke through the seemingly unbreachable wall between chemistry and biology by synthesizing an enzyme — a key component of life — in the laboratory, died June 20 at his home in Lansdale, Pa., from complications of kidney disease. He was 87.

He also was the leader of a medicinal chemistry team at Merck Research Laboratories that developed some of Merck's most important and profitable drugs, including the cholesterol-lowering Mevacor, Vasotec for reducing blood pressure, and Proscar for shrinking enlarged prostates and preventing prostate cancer.

"His creative contributions to chemistry and chemical biology inspired a whole generation of scientists to pursue the discovery of new medicines," said chemist Paul S. Anderson, a former president of the American Chemical Society and a close friend.

Enzymes are proteins, composed of long strings of building blocks called amino acids, that carry out chemical reactions within cells. Without them, life is impossible. It was once thought that such complicated molecules could be produced only by living organisms.

The problem with trying to assemble amino acids into larger molecules is that each amino acid has more than one reactive site. In order to combine them in the same fashion they are connected in proteins, it is necessary to block all of the other sites except the one where a reaction is desired.

One of the key contributions of Hirschmann and his Merck colleague Robert G. Denkewalter and, independently, R. Bruce Merrifield and Bernd Gutte at Rockefeller University in New York, was to develop reagents that would block these sites specifically but that could later be removed for the attachment of another amino acid to the growing chain.

Over a period of 18 months, Hirschmann and Denkewalter slowly assembled the 124 amino acids that constitute the enzyme ribonuclease, joining pairs of them together, then combining those pairs into fragments that they eventually assembled into a fully functional molecule. Merrifield and Gutte synthesized the same molecule by adding one amino acid at a time to a growing chain.

On Jan. 16, 1969, the two groups jointly announced their success at a news conference at Rockefeller, producing front-page headlines across the country. Today, a similar synthesis can be achieved in a few hours using automated instruments that incorporate variants of the reagents originally developed by the two teams.

During the 1970s, Hirschmann led a research team at Merck that also developed Primaxin, an intravenous antibiotic that is used for many serious infections; Lisinopril, which is used to combat high blood pressure and the antibiotic ivermectin, which is being used in sub-Saharan Africa to eliminate trachoma, the cause of river blindness. He is the inventor or co-inventor on nearly 100 patents.

When he reached the mandatory retirement age of 65 at Merck in 1987, he joined the University of Pennsylvania, where he pioneered the field of peptidomimetics, in which small molecules are designed to mimic the action of enzymes and other proteins. Failing health and the need for kidney dialysis forced his retirement from the university in 1998.

Ralph Franz Hirschmann was born in Fürth, Germany, on May 6, 1922, the son of a Jewish banker. In 1936, after Hitler had come to power, the family moved to the United States, settling in Kansas City, Mo. He graduated from Oberlin College in 1943, then served three years in the U.S. Army in the Pacific Theater. After the war, he completed his doctorate in organic chemistry at the University of Wisconsin and joined the Merck laboratories in Rahway, N.J.

In 2000, President Clinton awarded him the National Medal of Science, and he received numerous other chemistry awards as well. Merrifield was awarded the Nobel Prize in Chemistry in 1984 for his efforts, and many researchers expressed dismay that Hirschmann wasn't honored too.

He is survived by his wife of 58 years, the former Lucy Altenmoos, a son, Ralph, and six grandchildren.

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"CREATIVE CONTRIBUTIONS"

Ralph F. Hirschmann also was the leader of a team at Merck Research Laboratories that developed some of Merck's most important and profitable drugs.

Nachruf auf Prof. Hirschmann in der *Los Angeles Times*

Prof. Dr. Hirschmann stammte aus einer Fürther Bankiersfamilie. Sein Großvater Friedrich hatte nach seiner Rückkehr von einem mehrjährigen Aufenthalt in den USA in seiner Heimatstadt das Bankhaus Hirschmann und Kitzinger gegründet, wo er sein Gastland seit 1880 konsularisch vertrat. Diese Verbindung, die auch unter dem Sohn Karl nicht abriss, nutzte die Familie 1936, als sie der Druck der Nazis zur Auswanderung in die Vereinigten Staaten zwang. Dort diente Ralph Franz, der jüngste von drei Söhnen, ab 1943 drei Jahre bei der US-Armee auf dem pazifischen Kriegsschauplatz, bevor er an der Universität des Bundesstaates Wisconsin 1950 seinen Doktortitel in organischer Chemie erwarb und anschließend eine Anstellung in der Forschungsabteilung des Pharmakonzerns Merck erhielt.

Hirschmanns Beiträge zur Entwicklung neuer Medikamente, die ein Fachkollege anlässlich seines Todes als „Inspiration für eine ganze Generation von Wissenschaftlern“ bezeichnete, beinhalten die wichtigsten Präparate seiner Firma zur Prävention von Krankheiten, die durch Cholesterin oder hohen Blutdruck verursacht werden. Bahnbrechend nicht nur für die Pharmatechnik war das Verfahren, das eine von ihm und Robert G. Denkewalter geleitete Arbeitsgruppe zur künstlichen Herstellung von Enzymen fand, den Proteinen, die den Stoffwechsel als Voraussetzung organischen Lebens ermöglichen. Mit seinen zahlreichen Innovationen erwarb Hirschmann im Laufe seines Berufslebens insgesamt 150 Patente als Allein- oder Mitinhaber.

Nach Erreichen der Altersgrenze wandte sich der unermüdliche Wissenschaftler seit 1987 an der University of Pennsylvania der Molekularforschung zu. Für seine Entdeckungen erhielt Hirschmann 2000 vom US-Präsidenten die höchste nationale Auszeichnung für Leistungen in den Naturwissenschaften. Erst im Jahre 2006 zwangen ihn gesundheitliche Probleme zum Rückzug aus dem universitären Betrieb.

Die Nachricht von seinem Tod verbreiteten führende Blättern, u.a. die berühmten drei „Times“ in London, New York und Los Angeles, in mehrspaltigen Artikeln, ein weiterer Beweis dafür, welches geistige Potenzial Fürth und ganz Deutschland durch die Vertreibung und Vernichtung seiner jüdischen Bevölkerung verloren hat.

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Quellen

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