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NIH in History: Christian B. Anfinsen

Celebrating the Life and Work of Nobel Laureate Christian B. Anfinsen

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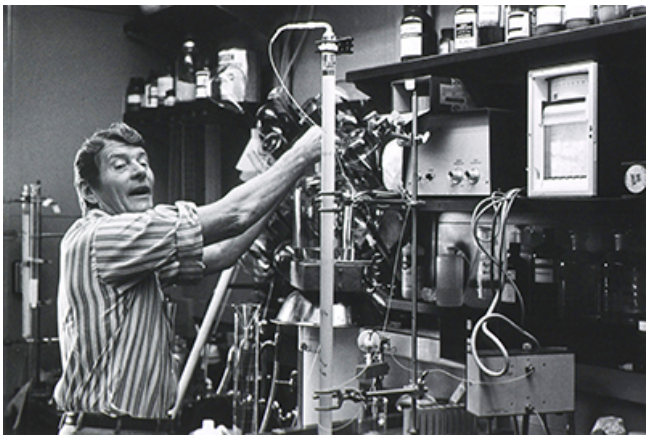
He won a Nobel Prize in chemistry in 1972, and his work still influences research being done today. He was a beloved mentor to dozens of scientists at the NIH. And he worked tirelessly to promote human rights for scientists around the world.



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Christian Anfinsen's research "continues to underlie new work in biochemistry," said **Alan Schechter** at a symposium he organized on October 15, 2018, to commemorate his mentor and former colleague, who died in 1995 at the age of 79. Anfinsen is also featured in an NIH exhibit that opened earlier this year in the central first-floor corridor of Building 10.

Christian Anfinsen working with chemical apparatus in a laboratory.

In his introductory remarks, **Griffin P. Rodgers**—director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and a former member of Anfinsen's Laboratory of Chemical Biology (NIDDK), in the 1980s—talked about the advice the Nobel laureate had given him about how to succeed in science as a physician. In fact Anfinsen played a key role in establishing NIH's Foundation for Advanced Education in the Sciences (FAES) in 1959, which "was particularly needed back in the '60s," said Rodgers. Many physicians came to the NIH "to do both their research training [and] their clinical training in an era before there was a general availability of M.D.-Ph.D. programs."

Anfinsen's "work, unlike that of many other Nobel Prize winners, is continuing to attract interest and development of his ideas in new science," said Schechter, currently chief of NIDDK's Molecular Medicine Branch. "What I've tried to do in choosing the three main lecturers today is highlight the new science that has been based upon Chris Anfinsen's work of 60 years ago." Schechter recounted that citations of Anfinsen's key papers, including the Nobel Lecture in Science in 1973, have increased greatly over the years, suggesting that this work is still central to much research that goes on now.

Background. After earning his undergraduate degree from Swarthmore College (Swarthmore, Pennsylvania) and a master's degree in organic chemistry from the University of Pennsylvania (Philadelphia), Anfinsen received a fellowship from the American Scandinavian Foundation in 1939 to work on micromethods for metabolic studies at the famed Carlsberg Laboratory (Copenhagen, Denmark). But in 1940, soon after World War II started, he returned to the United States and entered a biochemistry Ph.D. program at Harvard Medical School (HMS) in Boston. From 1943 to 1950 he served as an HMS faculty member and conducted research in the fledgling field of biochemistry. His personal experiences in Europe—seeing and understanding the horrors of war–may have stimulated his sense of social responsibility. Throughout his life, he continued to engage scientists in social and political issues such as nuclear disarmament, environmental degradation, and human-rights abuses against scientists in foreign nations.

NIH. In 1950, NIH's National Heart Institute (now the National Heart, Lung, and Blood Institute) recruited Anfinsen to be chief of its Laboratory of Cellular Physiology and Metabolism. In addition to working on lipoproteins, protein synthesis, and several other subjects, he began studies on the amino-acid

sequence of pancreatic ribonuclease. In 1962, he briefly left NIH but in 1963 he returned to what is now NIDDK to create the Laboratory of Chemical Biology. His work on ribonuclease, especially making and breaking its disulfide bonds, eventually led to his thermodynamic hypothesis that proteins could spontaneously fold in vitro to their active conformation. In 1972, Anfinsen shared the Nobel Prize in Chemistry with Stanford Moore and William Howard Stein for this groundbreaking "work on ribonuclease, especially concerning the connection between the amino acid sequence and the biologically active conformation."

The Importance of His Work. Three scientists—Stephen Kent, **Bruce Furie,** and Arthur Horwich—gave presentations that highlighted the continued importance of Anfinsen's achievements. Kent, a professor of chemistry at the University of Chicago (Chicago), told how his research on the total chemical synthesis of proteins was influenced by Anfinsen's thermodynamic hypothesis, which "turns out to be key," said Kent. "If you wanted to make proteins by total chemical synthesis, you needed to have Chris Anfinsen come up with this insight."

Furie, a former member of the Laboratory of Chemical Biology and now a professor of medicine at HMS, described his recent work on protein disulfide isomerase (PDI), a protein whose existence was first postulated and identified by Anfinsen. Furie has shown that PDI is essential in blood clotting and other extracellular processes.

Lastly, Horwich, a professor of genetics and pediatrics at the Yale School of Medicine (New Haven, Connecticut) and one of the discovers of the chaperonin proteins (which help maintain favorable conditions for protein folding within the cell), also shared the personal and scientific experiences he'd had with Anfinsen. Horwich named the cavity within certain chaperonins the "Anfinsen cage" in recognition of the processes first described by the Nobel laureate.

After the scientific talks, several other people shared their more personal memories of the Nobel laurate. Laboratory of Chemical Biology alumni **Kathryn Zoon** and **David Sachs** described their experiences with Anfinsen as their mentor; Carol Crafts, his daughter, told stories about their family interactions; and **Buhm Soon Park**, who worked at the Office of NIH History for several years, described Anfinsen's role in the development of FAES and other education programs at NIH.

"All of you here carry on his work, his talents, his passions, his philosophy, his optimism, his sense of justice," said Anfinsen's daughter Carol. "For all of that, he will be remembered through you."

To watch a videocast of "The Legacy of Christian B. Anfinsen and His Thermodynamic Hypothesis: From Total Chemical Synthesis to the Folding of Proteins In and Out of the Cell," which took place on October 15, 2018, go to https://videocast.nih.gov/launch.asp?26114 (https://videocast.nih.gov/launch.asp?26114). To learn more about Anfinsen's life, visit the exhibit on the long first-floor corridor of Building 10, just across the corridor from the FAES bookstore, or see the exhibit online at https://history.nih.gov/exhibits/anfinsen/ (https://history.nih.gov/exhibits/anfinsen/).