

Arthur Kornberg 1918-2007

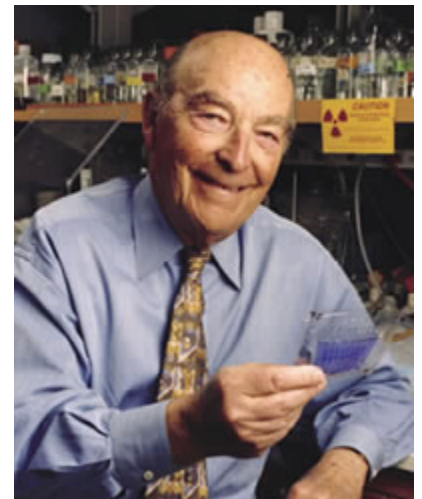
November 9, 2007

Named University buildings typically recognize and honor the philanthropy of a major donor. The Kornberg Medical Research Building of the University of Rochester is different – it recognizes and honors the life and scientific achievements of Arthur Kornberg, MD, Class of 1941 and 1959 Nobel Laureate in Medicine and Physics. "Kornberg" our shorthand name for this research facility, inspires those who work within it to reach for path-breaking, paradigm-shifting science worthy of its namesake. Dr. Kornberg died on October 26, 2007, at age 89. Two weeks earlier, he was working in his lab and playing tennis.

Arthur Kornberg was born on March 3, 1918, the son of Joseph and Lena Kornberg, who immigrated to the United States from Austrian Galicia (now part of Poland) at the turn of the century to escape religious oppression. They raised their family in Brooklyn, and Joseph commuted for almost 30 years to the sweat shops of the Lower East Side of Manhattan to work as a sewing machine operator. When his health faltered, Joseph opened a small hardware store in Brooklyn, where Arthur assisted customers. Arthur's father spoke six languages although he had no formal education.

Arthur attended the public schools in Brooklyn. He developed an early interest in chemistry and was a gifted student, scoring 100% on the New York State Regents Exam in Chemistry. Despite his academic achievements, college may not have been financially feasible were it not for the tuition-free City University system in New York City. He attended City College, earning a B.Sc. in 1937 at age 19, followed by an M.D. from the University of Rochester in 1941. During medical school, he discovered that he had mildly elevated bilirubin and he conducted assays of fellow students to determine the prevalence of this condition. The results were published in 1942 – Dr. Kornberg's first research paper.

After medical school, Dr. Kornberg completed an internship at Strong Memorial Hospital, and then joined the U.S. Coast Guard as a Lieutenant, serving as a ship's doctor in 1942. At that point, one of those transformational events that aren't appreciated as such at the time occurred in Dr. Kornberg's life. According to family, as a result of his paper on jaundice in medical school, Arthur was transferred by the Coast Guard from his ship to the NIH. His paper on jaundice was one of the few on the subject at the time and NIH wanted him to study the jaundice outbreak that was occurring among troops, and its linkage to the yellow fever vaccine that they were receiving. The story that he recounted to his sons was that this reassignment changed his career from clinical medicine to research.



Arthur Kornberg, MD

Thus, Dr. Kornberg moved to NIH and worked in the Nutrition Laboratory. In addition to studying jaundice, he was asked to join a research team focused on vitamins. Although he made several fundamental discoveries about the actions of vitamins, he gradually became fascinated by enzymes. During this period, he also became fascinated with Sylvy Ruth Levy, whom he married in 1943. Sylvy was a double-alumna of the University of Rochester, receiving a B.A. from the College in 1938 and a M.S. in Biochemistry from the School of Medicine and Dentistry in 1940. Sylvy also became a biochemist of note, and on the day that Dr. Kornberg was awarded the Nobel prize, she was quoted in a newspaper as saying "I was robbed!"

In 1946, Dr. Kornberg joined the laboratory of Severo Ochoa (with whom he later shared the Nobel Prize), where he learned more about enzymology. During that year, he took graduate courses in organic and physical chemistry and learned the techniques of enzyme purification that would be so important in his later work. From 1947-1953, Dr. Kornberg was Chief of the Enzyme and Metabolism Section at NIH. His purification of the enzyme NAD gained him recognition from his peers and set him on course for the many discoveries he was to make about the enzymes that assemble DNA, genes and chromosomes.

In 1953, he moved to St. Louis to become Professor and Chair of the Department of Microbiology at Washington University. It was in St. Louis that he conducted his Nobel prize-winning work, isolating a DNA polymerizing enzyme, the first enzyme to take direction from a template, now known as DNA polymerase I. (Arthur's son, Thomas B. Kornberg, discovered DNA polymerases II and III in 1970. All three polymerases are needed for DNA replication. Another son, Roger Kornberg, was the 2006 Nobel Laureate in Chemistry for unraveling the 3-dimensional structure of RNA polymerase at atomic resolution. Extending these studies, he created an actual picture of how transcription works at a molecular level.)

My summary of Arthur Kornberg's isolation and discovery of DNA polymerase I is based on a recent conversation with Robert Lehman, PhD., to whom I am most grateful for his patient and compelling recounting of the story. Every word was full of admiration for Dr. Kornberg and his genius. (Some material was also gleaned from Dr. Kornberg's 1989 book, "For the Love of Enzymes: The Odyssey of a Biochemist.") Dr. Lehman, now Emeritus Professor of Biochemistry at Stanford (and early mentor to Robert Bambara, PhD), knew Arthur for 52 years. He first learned of Dr. Kornberg's work at the 1955 meeting of the Federation of the American Society of Biology in Atlantic City. He was so taken by a 10-minute presentation on the discovery of phosphoribosyl pyrophosphate and its role in pyrimidine nucleotide biosynthesis by one of Dr. Kornberg's students (Irving Leiberman, PhD), that he immediately decided he should switch the direction of his work from the protein chemistry he had completed at Hopkins to this fascinating new field. Later that summer, Dr. Lehman moved to St. Louis to begin a post-doc with Dr. Kornberg.

Upon arriving at Washington University, Dr. Lehman learned that Dr. Kornberg was not satisfied with unraveling the chemistry of how nucleotides are made. Rather, he wanted to solve a puzzle that was more grand – he wanted to go from understanding ribonucleotides "up" to DNA. One of Dr. Kornberg's post-docs, Uriel Littauer (later, an eminent biochemist at the Weizmann Institute of Science), spent months making labeled nucleotide extracts of *E. coli* to assist this work. Dr. Kornberg asked Dr. Lehman if he would like to join the group in its DNA odyssey – how can DNA be made from DNA? During the next 3 years, the Kornberg laboratory discovered DNA polymerase I from *E. coli*, and showed that it was a template-directed enzyme. In effect, they showed how DNA self-replicates, and also laid the groundwork for much of the genetic technology in common use today, from the development of polymerase chain reaction (PCR) techniques to amplify DNA in research or forensics to drug development to DNA sequencing. Later in life, Dr. Kornberg became a public advocate for the funding of basic science research. At the end of the video we made on the occasion of the ribbon-cutting for the Kornberg Building, he was asked about the high cost of research, to which he replied, "If you think research is expensive, try disease."

Of note, while it is clear that Dr. Kornberg's work is fundamental to contemporary "genetic engineering" and other medical applications, it is also clear that, to Kornberg, the miracle of genetic engineering is not its enormous impact on agriculture, medicine, industry and even Wall Street, but its illumination of biology: how the individual subunits of an enzyme work, are assembled and function, and therefore how the biochemical process of nature can be controlled.

To address the question of how an enzyme can foster DNA self-replication, Kornberg made use of fundamental biochemistry principles and methods that had served the field well for decades – make extracts and purify the relevant proteins and enzymes with great care to reveal the story of how they work together and in sequence. In this case, he used a radiolabeled nucleotide substrate of high specific activity and incubated it with ATP and extracts of *E. coli*, an organism that reproduces itself every 20 minutes. There was conversion of only a very small fraction of the acid-soluble (nucleotide) fraction into an acid-insoluble (i.e., DNA) fraction (about 50 counts out of a million). "While this represented only a few pmoles of reaction," he said in his Nobel speech, "it was something. Through this tiny crack we tried to drive a wedge, and the hammer was enzyme purification." Starting with this "tiny crack," Dr. Kornberg and his group went on to show that DNA functions not only as a primer in the manner of glycogen polymerization but also as a template in directing the synthesis of exact copies of itself. The enzyme purified from this extract – DNA polymerase I – was the first enzyme discovered that takes instructions from a template. It adds the particular purine or pyrimidine substrate which will form a hydrogen-bonded pair with a base on the template.

What kind of man was Dr. Kornberg? Listen to Bob Bambara, who was a postdoctoral fellow with Bob Lehman in 1975 and 1976, and therefore shared lab rooms with Dr. Kornberg's group: "Arthur was totally devoted to science, and spent a lot of time talking to people in the group about their results. He participated in the lunch student seminar in the departmental library and also taught in courses. He tended to leave administrative work to other faculty, but it appeared that everyone at Stanford asked his advice on every issue. Arthur was not ostentatious in any way at work. He had a small office in the middle of the department. It had little decoration or fancy furniture. It had a tiny table with three legs and three chairs that he used for discussing data with the students. The door was unadorned and there was no name tag. From the hall, it easily could have been the janitor's closet. I suspected that calling attention to his office would only have led to a lot more people seeking his advice and distractions from his science. Arthur expected scientific excellence from his students, and he wanted them to be positively competitive. He had a gentle way of expressing this, but the message was very clear. No one wanted to disappoint him with a less than outstanding performance. I once gave a student seminar on molecular mechanisms of Epstein Barr virus infection. It was a subject that I had to learn for the seminar. He said 'Interesting talk, but I could tell that was not your field.' I was very excited when he came to visit us three years ago to talk about his research. When I asked a question from deep in the audience, he joked 'What are you doing here?' I had the brief feeling that I should have been back at my bench in Stanford doing an experiment."

Jay Stein, MD, who re-established Rochester's connection with Dr. Kornberg at the time that Dr. Stein was Senior Vice President for Health Affairs, remembers Dr. Kornberg this way: "Shortly after I arrived in Rochester, a senior development officer, Roger Latham, came to see me and urged me to go meet Arthur Kornberg. Up to that point, I hadn't even realized that Arthur was a University of Rochester graduate and had no idea of the early stories of how our most famous alumnus had been shunned because he was Jewish. We now had Goldsmith, Goldstein and Stein in charge of the University of Rochester Medical Center, i.e., things have changed. I went out to Palo Alto and had lunch with Arthur who arrived in his green Jaguar convertible. What a guy! This began a wonderful friendship with this remarkable man. The culmination was his agreement to have the first new research building in the medical center named for him. He was so thrilled that he reached into his drawer and handed me his Nobel medal that he was awarded in 1959. He then asked us to put the medal in a nice place for the public to see and it resides in the foyer of the Kornberg Building today."

Phillip Pizzo, MD '70, Dean of the Stanford University School of Medicine has this to say about Dr. Kornberg's impact: "Arthur Kornberg's work has left an enduring and indelible mark on science and the foundations of modern molecular biology and genetics. But he also left an indelible mark on Stanford University and its School of Medicine as well as other institutions. When he was recruited to establish a department of Biochemistry at Stanford University School of Medicine in 1959, triggered by the school's move from San Francisco to the Stanford campus in Palo Alto, he brought his entire department from Washington University with him, which included Dr. Lehman along with other notable luminaries. Dr. Kornberg and his colleagues helped lay the foundation for a school that was committed to scientific excellence commensurate with his devotion and vision. He helped recruit many of the school's leading faculty, played a role in shaping its mission and direction, and catalyzed numerous research discoveries that created the path to the future of bioscience. He was a remarkable man whose life never wavered from his commitment to knowledge – and as he was fond of saying, "curiosity driven investigation." Arthur Kornberg was a towering figure who will be remembered for the remarkable discoveries he made, the generations of young scientists he trained and developed, the institutions he helped shape, the new fields he helped open and define, and for the strongly ethical and moral life he led - for which he will be long remembered as well as deeply admired and appreciated."

I had a distant connection to Dr. Kornberg through my father. It turns out that they were born weeks apart and attended the same High School in Brooklyn, Abraham Lincoln. When Dr. Kornberg won the Nobel Prize in 1959, I was 7 years old. I still remember my father telling me: "I'm not surprised. He was the smartest kid in the class." At the time, Lincoln was a brand-new school, and my father always told me that his was Lincoln's first graduating class. When I met Dr. Kornberg, I related this story and he smiled, correcting me: "I finished High School early," he said. "Actually, I was the first graduating class, a class of 1."

Dr. Kornberg's first wife, Sylvy, died in 1986. He married Carolyn Dixon in 1998. Carolyn tells a story that conveys a charming side of Dr. Kornberg that may not have been widely appreciated: "When my mother met Arthur, it didn't take long for her to fall in love with him. She told me 'you be nice to him, he's a keeper'." In describing her late husband, Carolyn emphasized his marvelous love of life, his brilliance, and his sense of humor. She said that as he became more "seasoned" in his later years, he "became universal. He always had time for everyone – students, sons, grandchildren, faculty, friends, post-docs. Sometimes faculty who wanted to see Arthur had to wait in line while he would be chatting with someone in his office who was 'unscheduled,' but this is who he was. His door was always open."

As a final measure of the man, here is the remembrance of his son, Kenneth Kornberg, who now runs an architectural firm (Kornberg Associates) specializing in the design of research buildings: "Arthur was as remarkable at being a supportive and conscientious father as he was as a scientist. I cannot remember an occasion in my life when he did not give me his absolute and full attention when I saw him or talked to him. In spite of his busy schedule and far ranging activities, whenever I called or saw him he responded caringly and with undivided attention to my inquiries and thoughts. He did not seem to have priorities that superseded my concerns. From the comments we have received from so many around the world over the last two weeks, he seems to have provided that concern and attention universally."

Meliora,

David S. Guzick, MD, PhD
Dean, School of Medicine and Dentistry

