Hans Kornberg

1928–2019

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by Antonio Gotto

NATIONAL ACADEMY OF SCIENCES

HANS KORNBERG

January 14, 1928–December 16, 2019

Elected to the NAS, 1986

By Antonio Gotto

Hans Kornberg, a 1939 refugee from Nazi persecution at the age of 11, established a distinguished career in the United Kingdom as a leading pioneer in the study of the processes of biochemical metabolism at the micro-organic level, elucidating many hitherto unknown findings about fundamental life mechanisms operating in the Krebs cycle of animals and plants.

After completing his primary education, Kornberg won a scholarship to Sheffield University, where he earned a bachelor's degree and then a Ph.D. He then received a two-year fellowship for further study and research at Yale. Upon his return to England, he joined the research faculty at Oxford University, working with Nobel Laureate Sir Hans Krebs. In 1960 he took on the task of developing and heading up a new biochemistry department at Leicester University. He moved on in 1975 to the chairmanship of biochemistry at Cambridge University, where he remained until mandatory retirement at age 67. He then returned to the United States, accepting a professorship at Boston University, teaching and researching until his death at age 91.

I first met Hans Kornberg in the spring of 1958 at Oxford University, where I was a medical student. Several months later I was having dinner with Hans in the elegant Rathaus Cellar Restaurant, in Vienna. He then filled me in on his life story. Born in Herford, Germany, in 1928, he escaped to the United Kingdom in 1939 and was reared by a beloved uncle in Yorkshire. Hans' parents were victims of the Holocaust. He told me he had never returned to Germany and that, at that time, he had no intention of doing so.

After graduating from grammar school, at age 17, he began working in the biochemistry laboratory of Hans Krebs, at Sheffield University. Krebs helped Hans get a scholarship at Sheffield, where he subsequently received his undergraduate degree (1949) and a Ph.D. (1953) in biochemistry.

Hans did postdoctoral research with noted English biochemist Robert Davies. Hans often referred to this period, which shows that early successful research experience bodes well for subsequent research and an academic career. Hans was able to show that the source of gastric unease was bacterial, using germ-free animals in the course of his research. In later years, he would reminisce that it was too bad this all happened before the discovery of the bacterium Helibacter pylori, now known to be the primary cause of stomach ulcers.

At this junction in his career, Hans received a two-year fellowship to gain research experience in the United States. While the fellowship was to be based at Yale, Professor Joseph Fruton allowed him to gain research experience elsewhere. Hans was able to spend time in the laboratory of Melvin Calvin at Berkeley, where he learned the technique of radiocarbon labelling to measure early downstream metabolites. He also, at different times, worked with Ephraim Racker and Bernard Horecker at the Public Health Institutes of New York. There he participated in research on enzymes of the pentose phosphate pathway.

After these two years of valuable experience in the United States, Hans returned to England and joined the Medical Research Center (MRC) Laboratory in Oxford University's Biochemistry Department. The department was chaired by Hans Krebs, who had been knighted and had received the Nobel Prize for his discovery of the citric acid cycle. Krebs, who had also escaped from Nazi Germany, resumed his role as lifelong friend, mentor, and colleague of Hans. Before he left Germany, Krebs had already described, with his assistant, Dr. Kurt Henseleit, the urea cycle. Thus, the MRC unit at Oxford was acutely aware of cycles in metabolic pathways. In 1957, shortly after he returned to the UK, Hans coauthored with Krebs a book, *Energy Transformations in Living Matter*. This book became my Bible when I became a student in Hans' lab.

Soon after coming to Oxford, Hans met and married Monica King, a radiology technician, and they had four children. I came to know Monica very well, and she was a wonderful partner to Hans in all aspects of his career and in whom he took great pride until her passing in 1989.

At Oxford, Hans undertook addressing the question of how the intermediates of the Krebs cycle are replenished. He obtained *E. coli*, a strain of bacteria called *Pseudomonas ovalis* chester, and other microorganisms for his ensuing research. He began by exploring how microorganisms could grow on acetate as their sole source of carbon. There had to be a mechanism for converting the 2-carbon compounds in acetate to 3-,4-, and higher

carbon compounds in order to sustain growth. He discovered a new enzyme, isocitratase, which catalyzes the cleavage of isocitric acid, forming glyoxylate and succinate. Then malate synthetase, previously described by biochemist Samuel Ayl, catalyzes the formation of malate from glyoxylate and acetate. Malate is then oxidized to oxaloacetate, and the citric acid cycle continues.

After 15 years at Leicester, he moved to Cambridge University, where he continued research using bacterial mutants to study metabolism, primarily of carbohydrates, and became the chair of the Biochemistry Department. Subsequently he became the master of Christ's College,where he finished his remarkable career in the UK, owing to Cambridge's mandatory retirement age. Before leaving the University, and the country, for the United States, Hans married Donna Haber in the first Jewish wedding ever held in Christ's College at Cambridge.

But his professional work was far from over. Hans once again returned to the United States to become a distinguished professor at Boston University, where he worked in the laboratory with graduate students and postdoctoral fellows, continuing his research and teaching until near the end of his life at age 91.

After the discovery of the glyoxalate cycle, Hans elucidated how microorganisms grow on other 2-carbon compounds—glycolate, which was my project, and glycine and oxalate, which were pursued by others. Hans used genetic mutants to study the uptake of carbohydrates by bacteria. With *E. coli* he demonstrated alternate paths for fructose metabolism and used mutants to identify different pathways supporting fructose metabolism. He continued productive research at Leicester, Cambridge, and Boston University until near the end of his life. Always staying close to the bench, Hans modestly described himself as a simple "hod carrier" in the overall scheme of research. This, of course, vastly underestimates his contributions.

Personal Remembrances

When I first met Hans Kornberg in the spring of 1958, I had just completed my first year of medical school at Oxford in the "Final Honors School of Animal Physiology." Hans had just become a tutor in biochemistry at Worcester College, Oxford, where I was a student. Hans apologized that he had been away during the year, giving lectures in the United States on the recently elucidated glyoxylate cycle. He invited me to spend the summer in his lab at the MRC so I could learn some biochemistry. As he had been away, I had had no biochemistry tutorials, which was the classic way of teaching at Oxford. I

jumped at the offer and began to work immediately. My project was to show that when microorganisms were shifted from a glucose environment to an acetate environment, they induced isocitratase prior to growth. I worked closely with Hans and a superb technician, Patricia Lund, who spent many years with Hans and subsequently with Krebs, after Hans left Oxford.

By the end of the summer Hans and I had sufficient data to publish a paper in *Nature,* my first scientific publication. The World Congress in Biochemistry was being held in Vienna that year, and Hans was scheduled to present a talk on our research. He graciously invited me to attend the Congress and introduced me to many world-famous biochemists. He always made sure to give me a complimentary introduction to whoever was around. As soon as I began working in Hans' lab, Sir Hans Krebs, who was known as "the Prof," would come around at 8:00 sharp each morning and ask me what I was doing. These encounters were brief, but what a wonderful learning experience they were.

At my dinner with Hans in Vienna, which I referred to at the beginning of this piece, Hans told me that he and Krebs wished to meet with me while we were in Vienna. With great trepidation I came to the meeting. Krebs opened by saying he thought it would be a waste of my time to spend another year studying animal physiology, that unless I wanted to be a politician, rather than a scientist, it would be to my advantage to become a graduate student in biochemistry under Hans' direction. The Prof then pointed out that there was no guarantee that my work would qualify for a doctorate, or D.Phil., in the Oxford terminology, but that they thought I had enough promise to undertake it. Krebs was always very cautious and never overstated anything. I had a lot of balls in the air at the time, was very flattered by the offer, thanked them, and told them I would let them know. I was scheduled to return to the United States after 2 years, enter Vanderbilt as a medical student, and marry my fiancée, Anita Safford. My physiology tutor advised me against making any change in those plans, but the Warden of Rhodes House, Bill Williams, said it was too good an offer to turn down. I accepted his recommendation and became an Oxford predoctoral student in biochemistry.

I was assigned the project of how the microorganism, *Pseudomonas ovalis* chester, was able to grow on glycolate as its sole carbon source. Hans was an extraordinary mentor. He was extremely bright, instructed me in strict principles of research, and was both encouraging and critical. I cannot imagine a more ideal supervisor. He was also an extremely social individual and included me in on many social occasions. He was always witty, a great conversationalist and raconteur. Some of the stories he told me, I heard him repeat many

years later. We had a parade of notable biochemists visit during my doctorate period; to mention a few: Boris Magasanik, I.C. Gunsalus, Samuel Ayl, Clint Fuller, Clarke Gray, and Lowell Hager. I was often asked to escort them around Oxford, giving me more exposure to them. While I was traveling on the continent, awaiting my recall to Oxford for my oral exam, Hans arranged for me to meet Howard Hiatt and Jacques Monod at the Pasteur Institute in Paris.

In the course of my research we discovered a new enzyme and were fortunate enough to crystallize it. I remember calling Hans late one Saturday night to tell him I had successfully separated the two key enzymes of the glycolate pathway, using a DEAE-c (diethylaminoethyl cellulose) column. He was ecstatic, even more enthusiastic than I. The second enzyme, we called tartronic semialdehyde reductase, and I was fortunate enough to crystallize it with ammonium sulfate. When convinced the crystals were the enzyme, I made a fresh preparation and had it under a phase-contrast microscope when Krebs came by at 8 a.m. I told him that I had something to show him. As he viewed the crystals under the microscope he asked me to explain what he was seeing. After a few minutes of viewing, he stood up, said "quite satisfactory," and walked off. As soon as he left, Hans came over and asked, "What did the Prof think?" I said I don't think he was much impressed, as he had just said, "quite satisfactory," and left. Hans replied, "When I told him my discovery of the glyoxylate cycle, he only said 'satisfactory.' Quite satisfactory is the highest praise you will ever get from The Prof." My D.Phil. examiners were Krebs, as the internal examiner, and F. Dickens, one of the early researchers on the pentose phosphate pathway. as the external one.

As one final gesture of kindness, when Hans purchased a new car, he lent his old one to my wife, Anita, and me. Fortunately, I was able to sell it for a profit, and Hans appeared astounded at our final meeting when I presented him with a healthy sum of pounds.

Sir Hans Krebs and Sir Hans Kornberg (knighted in 1978) continued as my friends and advisers. They visited me a number of times in the United States, and I visited them in the UK. I last saw Hans Kornberg at the Festschrift held in his honor at Boston University on the occasion of his 80th birthday. I joined several of his former and present colleagues with presentations. He was as sharp and eloquent as ever. I had the pleasure of meeting Donna, who was a wonderful partner to him. The day ended with a celebratory dinner. We then stayed in touch with emails and calls. We were both happy about the recent growing interest in metabolic pathways in both cancer and cardiac research. We discussed the role of isocitric acid and its metabolism in certain cancers and the appli-

cation to an inhibitor of ATP-citrate lipase in hyperlipidemia. Most recently, Hans had sent an outstanding young postdoc to meet with me in New York.

I will miss Hans as will many colleagues, friends, and family. His influence on my life and career was extraordinary, and I will be forever grateful.

SELECTED BIBLIOGRAPHY

1950 With R. E. Davies. Gastric urease and HCl secretion. *Biochem J.* 47(1):ii-iii.

1951 With R. E. Davies. The role of gastric urease in acid secretion. *Biochem J.* 50(1):119-22.

1957 With N. B. Madsen. Synthesis of C4-dicarboxylic acids from acetate by a glyoxylate bypass of the tricarboxylic acid cycle. *Biochimica Et Biophysica Acta* 24(3):651-3.

With H. Beevers. A mechanism of conversion of fat to carbohydrate in Castor beans. *Nature* 180(4575):35-6.

With H. A. Krebs. *Energy Transformations in Living Matter*. Springer-Verlag Ohg. Berlin, Gottingen, Heidelberg.

1958 With A. M. Gotto and P. Lund. Effect of growth substrates on isocitratase formation by Pseudomonas ovalis Chester. *Nature* 182(4647):1430-1.

1959 With A. M. Gotto. Biosynthesis of cell constituents from C2-compounds: Formation of malate from glycollate by pseudomonas ovalis Chester. *Nature* 183:1791-3.

1961 With A. M. Gotto. The metabolism of C2 compounds in microorganisms. 7. Preparation and properties of crystalline tartronic semialdehyde reductase. *Biochem. J.* 81(2):273-84.

With A. M. Gotto. The metabolism of C2 compounds in microorganisms. 6. Synthesis of cell constituents from glycollate by Pseudomonas sp. *Biochem. J.* 78(1):69-82.

1964 With J. M. Ashworth. The role of isocitrate lyase in *Escherichia coli*. *Biochimica Et Biophysica Acta* 89:383-4.

1967 With R. A. Cooper. The direct synthesis of phosphoenolpyruvate from pyruvate by *Escherichia coli*. *Proceedings of the Royal Society of London. Series B. Biological Sciences* 168(1012):263-80.

1968 H. A. Krebs: a pathway in metabolism. *Biochemical Society Symposium* 27:3-9.

1969 With J. Smith. Genetic control of hexose phosphate uptake by *Escherichia coli*. *Nature* 224(5226):1261-2.

With M. J. Morgan. Regulation of sugar accumulation by *Escherichia coli*. *Febs Letters* 3(1):53-56.

1970 The role and maintenance of the tricarboxylic acid cycle in *Escherichia coli*. *Biochemical Society Symposium* 30:155-71.

1971 With T. Ferenci. Pathway of fructose utilization by *Escherichia coli*. *Febs Letters* 13(2):127-130.

1972 With J. Smith. Genetic control of glucose uptake by *Escherichia coli*. *Febs Letters* 20(3):270-272.

With R. E. Reeves. Inducible phosphoenolpyruvate-dependent hexose phosphotransferase activities in *Escherichia coli*. *Biochem. J.* 128(5):1339-44.

1973 Carbohydrate transport by microorganisms. *Proceedings of the Royal Society of London. Series B. Biological Sciences* 183(1071):105-23.

1975 With R. C. Essenberg. Energy coupling in the uptake of hexose phosphates by *Escherichia coli. J. Biol. Chem.* 250(3):939-45.

1978 With P. D. Watts. Roles of crr-gene products in regulating carbohydrate uptake by *Escherichia coli*. *Febs Letters* 89(2):239-32.

1983 With F. Parra and M. C. Jones-Mortimer. Phosphotransferase-mediated regulation of carbohydrate utilization in *Escherichia coli* K12: the nature of the iex (crr) and gsr (tgs) mutations. *Journal of General Microbiology* 129(2):337-48.

1986 The roles of HPr and FPr in the utilization of fructose by *Escherichia coli*. *Febs Letters* 194(1):12-5.

1987 With H. F. Bramley. Sequence homologies between proteins of bacterial phosphoenolpyruvate-dependent sugar phosphotransferase systems: identification of possible phosphate-carrying histidine residues. *Proc. Natl. Acad. Sci. U. S. A.* 84(14):4777-80.

With C. M. Elvin. Location and function of fruC, a gene involved in the regulation of fructose utilization by *Escherichia coli*. *Journal of General Microbiology* 133(2):341-6.

1989 Travelling to, and along, the glyoxylate bypass: a commentary on Synthesis of C4-Dicarboxylic Acids from Acetate by a 'Glyoxylate Bypass' of the Tricarboxylic Acid Cycle. *Biochimica Et Biophysica Acta* 1000:271-4.

1992 With L. T. Lambourne. Role of the phosphoenolpyruvate-dependent fructose phosphotransferase system in the utilization of mannose by *Escherichia coli*. *Proc. Biol. Sci.* 250(1327):51-5.

With L. T. Lambourne. Role of the phosphoenolpyruvate-dependent fructose phosphotransferase system in the utilization of mannose by *Escherichia coli*. *Proc. Biol. Sci.* 250(1327):51-5.

2000 With L. T. Lambourne and A. A. Sproul. Facilitated diffusion of fructose via the phosphoenolpyruvate/glucose phosphotransferase system of *Escherichia coli. Proc. Natl. Acad. Sci. U. S. A.* 97(4):1808-12.

Krebs and his trinity of cycles. *Nat. Rev. Mol. Cell Biol.* (3):225-8.

2001 Routes for fructose utilization by *Escherichia coli*. *J. Mol. Microbiol. Biotechnol*. 3(3):355-9.

2002 If at first you don't succeed em leaderfructose utilization by *Escherichia coli*. *Adv. Enzyme Regul.* 42:349-60.

2003 Memoirs of a biochemical hod carrier. *J. Biol. Chem.* 278(12):9993-10001.

2006 With C. Lourenco. A route for fructose utilization by *Escherichia coli* involving the fucose regulon. *Proc. Natl. Acad. Sci. U. S. A.* 103(51):19496-9.

Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.