

## Obituary

# Seymour Kaufman

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Seymour Kaufman, a long-time Fellow of the ACNP, renowned for his research on the enzymatic hydroxylation of the aromatic amino acids phenylalanine and tryptophan, key reactions in the synthesis of the neurotransmitters, dopamine, norepinephrine, and serotonin passed away on 23 June 2009.

Seymour was born in Brooklyn, NY on 13 March 1924. Artistically talented, he attended the New York High School for Music and Art, but reading Paul DeKruif's *Microbe Hunters*, redirected his interest to biochemistry. After learning of the outstanding reputation of the University of Illinois' Department of Chemistry and reasoning that a background in chemistry would be valuable in biochemistry, he enrolled there in 1941. He took there most of the available courses in chemistry and biochemistry and acquired extensive experience in organic and synthetic chemistry that proved to be so invaluable later in his research. After receiving a BS degree in chemistry in 1945 and an MS degree in biochemistry in 1946, he enrolled as a PhD candidate under Hans Neurath in the Department of Biochemistry at Duke University where he worked on proteolytic enzymes and earned his PhD in 1949. He then joined Severo Ochoa's Department of Pharmacology in New York University, first as a postdoctoral fellow and then as an assistant professor. In his 5 years there he matured into an outstanding enzymologist and biochemist and made his first major contribution to biochemistry, the discovery of substrate phosphorylation in the conversion of  $\alpha$ -ketoglutarate to succinate in the tricarboxylic acid cycle.

Seymour joined the Laboratory of Cellular Pharmacology of NIMH in 1954, but on arrival found his laboratory still under construction. He used the delay to deliberate on choosing a research project that was consistent with his strong background and interest in organic chemistry and enzymology, his ambition to contribute to biomedical research, and his desire to contribute to brain research. All three considerations were satisfied by his choice to study

the enzymatic hydroxylation of phenylalanine to tyrosine because: (1) as an organic chemist he was curious about how nature achieved such a reaction; (2) the reaction was a fundamental one in biochemistry and the first step in the synthesis of the neurotransmitters dopamine and norepinephrine; and (3) failure in this reaction was believed to be the basis of phenylketonuria, an inherited mental disorder characterized by mental deficiency.

He developed a soluble *in vitro* enzyme system that converted phenylalanine to tyrosine. It required molecular oxygen, NADPH, and a boiled rat liver extract (ie, 'Kochsaft'), which indicated the requirement of an essential nonprotein cofactor. He, subsequently, identified the cofactor as tetrahydrobiopterin and showed that it was formed from 7,8-dihydrobiopterin in the presence of NADPH. He later found that tetrahydrobiopterin was also an essential cofactor in the hydroxylation of tryptophan to hydroxytryptophan, the rate-limiting step in the biosynthetic pathway of serotonin, another major neurotransmitter.

In 1968, Seymour was appointed Chief of NIMH's Laboratory of Neurochemistry where he concentrated on phenylketonuria. In examinations of biopsied liver tissue from patients, he proved that classical phenylketonuria was indeed due to deficient activity of the phenylalanine hydroxylase enzyme, but he also identified other variants of phenylketonuria that were not because of insufficient phenylalanine hydroxylase activity, but because of other enzymes involved in the synthesis of the essential cofactor tetrahydrobiopterin.

Seymour was honored by his selection to serve two terms on the editorial board of the *Journal of Biochemistry*, election to the National Academy of Sciences, and the American Academy of Arts and Sciences, the Meritorious Presidential Rank Award, and the Hillebrand Prize of the American Chemical Society.

Though he chose science over art, Seymour never lost his interest in art and acquired an impressive collection of artworks, some by Toulouse-Lautrec, whose work he particularly admired. He also owned several sculptures by his daughter Emily, a successful sculptor with one of her works on display in the Hirshhorn Museum. Other interests to which he was passionately devoted were tennis and good food, the latter acquired after dining at some outstanding French restaurants during trips to Europe.

Seymour retired from NIMH in 1999 and passed away on 23 June 2009 after several years of ill health. He is survived by his wife Elaine; son Allan; daughters Emily and Leslie Kaufman; three grandchildren, Lisa, Joshua, and Amanda Kaufman; and two sisters, Lilly Wolfe and Dottie Laiserin. He will be greatly missed by them, his friends and associates, and by all in the neuroscience community.

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