



IN MEMORIAM

Ernest P. Noble

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Champion of the biological underpinnings
of alcoholism
ACNP Fellow Emeritus

Ernest (Ernie) P. Noble, M.D., Ph.D. died on 17 October 2017 at age 88. He was an ACNP Fellow Emeritus.

Dr. Noble was the Pike Chair of Alcohol Research and Distinguished Professor of Psychiatry and Biobehavioral Sciences at UCLA. Of note, he had also served as the second Director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) from 1976 to 1978. He was most known for expanding the role of systematic and especially neurobiologically oriented research into the causes of alcoholism, and for providing an early, strong voice to the government and general public about alcohol-related birth defects, and fetal alcohol syndrome in particular. He also played a critical role in the team that established the first gene variant consistently associated with an increased likelihood of developing alcoholism, other drug abuse, and related impulse disorders.

Ernie was born to an American family living in Baghdad, Iraq. His father, a physician-scientist, had worked with Madam Curie, then went to Iraq to bring radiological diagnostic and cancer treatment methods to that country. With the outbreak of WW-II, the Noble family was unable to escape to the West, and fled to India.

After the war, they settled first in New Jersey, then moved to Berkley, CA. At UC-Berkley, Ernie majored in Chemistry, then did fellowships in biochemistry at Oregon State and The Sorbonne. During a NIH-sponsored fellowship at Case Western Reserve University, he met his soon-to-be wife, Birgitta; they were married for over 50 years and had three children. While at Case Western, he had a productive research career studying carbohydrate metabolism, while also completing his M.D.

It was during an internship at Stanford University that he became interested in alcohol abuse, and with the support of David Hamburg, Chair of Psychiatry, did a full residency while also

appointed as Assistant Professor. He studied a mouse model of alcohol abuse, and then went for a year to work with Julius Axelrod at NIH. Subsequently he was on faculty at UC Irvine 1969–1981, ultimately as Professor of Psychiatry, Psychobiology and Pharmacology, before being recruited to UCLA.

Besides his advocacy of public awareness of fetal alcohol syndrome, Ernie was most known for his research to determine genetically directed vulnerabilities to alcoholism. In July 1991, he and colleagues reported in *Archives of General Psychiatry* that a variant in a gene related to D2 dopamine receptors, labeled the DRD2 A1 allele, produced reduced numbers of D2 receptors, whether a person was alcoholic or not, and had an increased likelihood of becoming alcoholic. They hypothesized that this A1 allele led to a state of “reward deficiency,” and subsequently provided evidence suggesting that it could also be involved in nicotine, opiate, and cocaine addictions, and even in over-eating. Although there was much resistance to this evidence for genetic, biological factors in addictions from those adamant that these are moral and/or socially induced afflictions, subsequent research in other laboratories has supported this notion that having this A1 allele increases the likelihood of addictions, as well as impulse-control problems. Dr. Noble and colleagues also published in *Nature Medicine* in 1995 a study showing that the dopamine agonist, bromocriptine, reduced craving and anxiety in alcoholics with this DRD2 A1 allele. Thus, Ernie and his many colleagues were among the first to provide evidence that led to the explosion of research and general interest in genetic factors in addictions, leading in turn to the promise of new, improved treatments.

Ernie always credited the phenomenal mentorship he had in developing his career, and it is no fluke that he paid the debt back by mentoring and sponsoring many students. Although never doing direct research with him, I frequently sought his advice about a number of research and academic/political issues and quandaries, and he was always available to listen and give his best-considered and principled advice. I always found him of remarkable good humor, and quite self-effacing. Indeed, few knew that in addition to all his other credits, Ernie was an accomplished opera singer, having sung in Carnegie Hall as a youth, and later while on a sabbatical in France, as the lead baritone role in *Carmen* and *Aida* at the Strasbourg Opera House.

Ernie is missed as one of such diverse talents, drive, and dedication, now increasingly rare, but memorialized as a physician-scientist who accomplished a variety of feats of considerable significance and lasting importance.

¹Gainesville, FL, USA