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Aldehyde Dehydrogenases as novel therapeutic targets for metabolic diseases and cancer stem cells

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Abstract

The aldehyde dehydrogenase (ALDH) super family comprises NADP-dependent enzymes that catalyze the oxidation of aldehydes to their corresponding carboxylic acids. To date, 19 ALDH genes have been identified in the human genome. In addition to aldehyde metabolizing capacity, ALDHs have additional catalytic (e.g. esterase and reductase) and non-catalytic activities. The latter include functioning as structural elements in the eye (crystallins) and as binding molecules to endobioticsand xenobiotics. Mutations in human ALDH genes are the molecular basis of several diseases, including gamma-hydroxybutyricaciduria, type II hyperprolinemia, Sjögren-Larsson syndrome, pyridoxine-dependent epilepsy as well as osteoporosis andgout. ALDH enzymes also play important roles in embryogenesis and development, neurotransmission, oxidative stress and cancer. One of the most exciting recent discoveries regarding ALDHs is their identification as markers of cancer stem cells and their involvement in cancer cell resistance to chemotherapy and radiotherapy. Thus, therapeutic targeting of ALDHs may represent a novel means of more effectively treating patients with cancer or metabolic disease and improving clinical outcomes.

Biography

Vasilis Vasiliou is Professor of Molecular Toxicology & Pharmacogenetics at the Departments of Pharmaceutical Sciences and Ophthalmology at the University of Colorado Anschutz Medical Campus. He is also Director of the Toxicology Graduate Program at the University of Colorado Denver since 2001. Vasiliou graduated from the University of Ioannina, Greece with a BS in Chemistry (1979-1983) and a Ph.D. in Biochemical Pharmacology (1983-1988). After a two-year mandatory service n the Greek Army, he trained in Molecular Toxicology and Pharmacogenetics with Dan W. Nebert at the Department of Environmental Health of the University of Cincinnati School of Medicine (1990-1995) with two years (1992-1994) as Fogarty Fellow. Finally, Vasiliou spent his one-year Sabbatical as a Guest Scientist at the National Eye Institute, National Institutes of Health (NIH 2005-2006) in the laboratory of Molecular and Developmental Biology with Joram Piatigorsky. Vasiliou's major research interest has been the cellular responses to oxidative stress induced by physical agents (e.g., UV radiation), metabolism and toxicity of both endogenous and foreign chemicals. He is a Specialist Advisor for the Human Gene Nomenclature Committee of the Human Genome Organization (HUGO). Vasiliou is a world leader in the field of ALDHs and is widely recognized for his many contributions to understanding the role of corneal crystallins in the physiology and pathophysiology of the cornea, lens and, more recently, in the retina. His laboratory is focused on the cellular responses to oxidative stress generated by ultraviolet radiation and endogenous metabolism. During the last three years, Vasiliou's laboratory has been conducting drug discovery focused on ALDHs with the intention of developing therapeutic strategies targeting cancer stem cells. Vasiliou's research program has been constantly funded since 1997 from NEI/NIH and NIAAA/NIH. He is the author of more than 140 original scientific papers and review articles published in peer reviewed international journals. Vasiliou is the editor of the journal *Human Genomics* and he is a member of the Editorial Board of the *Cutaneous and Ocular Toxicology*, Experimental Eye Research, and *The Ocular Surface*.