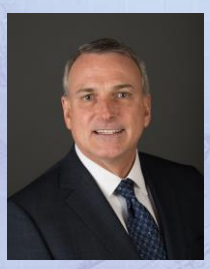
Dr. Herbert and Nicole Wertheim Leadership in Healthcare and Medicine Lectureship

Disease-Related Genetic Polymorphisms in the Aromatic Amino Acid Hydroxylases



Dr. Kent E. Vrana
Elliot S. Vesell Professor and Chairperson
Department of Pharmacology
The Pennsylvania State University College of Medicine

Date: May 16, 2018
Time: 12:00pm - 1:00pm
Venue: AHC 2 453

Biography

Kent E. Vrana, PhD, FAAAS has served as Elliot S. Vesell Professor and Chair of Pharmacology at the Penn State College of Medicine and Milton S. Hershey Medical Center since 2004. He received Ph.D. in Biochemistry from Louisiana State University Medical Center. He completed his postdoctoral training at the Carnegie Institution of Washington. Dr. Vrana has served as chair and/or a member of over 110 scientific review panel meetings including the National Institutes of Health, the Veterans Administration, and the US Department of Defense. He has co-authored more than 175 scientific articles, book chapters, and monographs (including two textbooks). His research is focused on molecular neurobiology of substance abuse, neurotransmitter biosynthesis, stem cells and neurodegenerative disease. He currently serves as co-director of the Problem-Based Learning courses for the first and second years of the Penn State medical curriculum. In 2009, he was named an honorary professor of the School of Medicine of the Peruvian University of Applied Science in Lima, Peru, and was inducted into the Society of Distinguished Educators at the Penn State College of Medicine. In 2017, he received the Outstanding Research Mentor Award from the College of Medicine.

Abstract

The aromatic amino acid hydroxylases (phenylalanine hydroxylase, tyrosine hydroxylase) and dopamine-β-hydroxylase play essential roles in the biosynthesis of the catecholamine neurotransmitters and neurohormones (dopamine, norepinephrine, and epinephrine). Growing evidence, from our laboratory, is implicating single nucleotide polymorphisms (SNPs) within the genes for these hydroxylases in disease processes, particularly in the gut-brain axis. Data will be presented describing genetic polymorphisms that are associated with Parkinson's disease and inflammatory bowel disease. Moreover, we will also describe how these coding-region SNPs affect enzyme function. Specifically, we find that a common polymorphism in tyrosine hydroxylase (V81M) impacts enzyme kinetic parameters and alters both motor and non-motor symptoms of Parkinson's disease. In addition, a fortuitous deep-sequencing project has illuminated a single dopamine-β-hydroxylase SNP (R549C) that is over-represented in both Parkinson's disease and inflammatory bowel disease and dramatically reduces levels of the enzyme.