Title: “Update on the genetics of pituitary and adrenocortical tumors: beyond MENs and Carney complex”

Speaker: Dr. Constantine A. Stratakis did predoctoral work in Athens and Paris, France, before joining the Developmental Endocrinology Branch of the National Institute of Child Health & Human Development (NICHD) at the National Institutes of Health (NIH), Bethesda, MD. At Georgetown University Medical School, Washington, D.C., he finished a residency in Pediatrics and two fellowships, in Pediatric Endocrinology, and Medical Genetics. Between 2002 and 2014, he was the Director of the NIH Pediatric Endocrinology Fellowship Program. From 2003 to 2011 he served in various leading positions at NICHD, NIH. His research focuses on the genetic defects leading to pituitary and adrenal diseases, and his laboratory has identified a number of genes involved in pituitary adenoma formation, adrenocortical hyperplasias and other tumors. He is the author of more than 500 publications and is currently serving in the Editorial Boards of several leading journals. Dr. Stratakis has received from the Endocrine Society the 1999 Award for Excellence in Published Clinical Research and the 2009 Ernst Oppenheimer Award, a number of NIH Merit Awards, and from a variety of Institutions a number of other honors, including an Honorary PhD from the University of Liege, Belgium. He has also been named Visiting Professor in several academic centers around the world. Dr. Stratakis is now the Scientific Director of NICHD, one of the largest Institutes of NIH.

Abstract: The goal of my work has been to understand the genetic and molecular mechanisms leading to disorders that affect the adrenal cortex, with emphasis on those that are developmental, hereditary and associated with adrenal hypoplasia or hyperplasia, multiple tumors and abnormalities in other endocrine glands (especially the pituitary gland and to a lesser extent the thyroid gland). We have studied congenital adrenal hypoplasia caused by triple A syndrome and other defects, other multiple endocrine deficiencies, familial hyperaldosteronism, adrenocortical and thyroid cancer, pituitary tumors and multiple endocrine neoplasia (MEN) syndromes affecting the pituitary, thyroid and adrenal glands, and Carney complex (CNC), an autosomal dominant disease. CNC is a MEN syndrome affecting the pituitary, adrenal cortex, thyroid, and the gonads, and is associated with a variety of other tumors, including myxomas and schwannomas, and skin pigmentation defects (lentigines, cafeaulait spots, and nevi). We have identified the regulatory subunit type 1A of protein kinase A (PKA), which is coded by the PRKAR1A gene as the gene responsible for most CNC patients. Thus, a significant part of our work is now focused on PKA-stimulated signaling pathways, PKA effects on tumor suppression and/or development, the cell cycle and chromosomal stability. Prkar1a-specific animal models have also been created to address the tumorpromoting effects of this gene and serve as models for possible therapies. In addition, genes that are mutated in patients with CNClike and other forms of inherited adrenal tumors are being investigated. Most recently, mutations in PRKACA, PRKACB and ARMC5, as well as in phosphodiesterase genes phosphodiesterase 11A (PDE11A) and PDE8B were identified in patients with various forms of bilateral adrenocortical hyperplasias. Mouse models of PDE11A and PDE8B deficiency are being studied, and mutations of these genes are being sought in other endocrine tumors. We have also elucidated the causative genetic defects in Carney-Stratakis syndrome (CSS) and we continue our search for genes that are related to tumors that develop in association with CSS and a similar condition (Carney Triad). Finally, in 2014, we identified a genetic defect that explains most cases of early pediatric gigantism in humans on chromosome Xq26. The responsible gene is most likely GPR101, that is the subject of intense work in the Stratakis lab.