Upcoming Discovery Lecture:

Vanderbilt Cutting-Edge Discovery Lecture: Vanderbilt Scholars

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208 Light Hall / 4:00 P.M.
VARYING THE TERRAIN OF EPIGENETIC LANDSCAPES: IMPLICATIONS FOR GENE REGULATION, DEVELOPMENT, AND CANCER

Although every gene exists within every cell in the human body, only a small percentage of genes are activated in any given cell or tissue type. In eukaryotes, nature has evolved a sophisticated indexing system that facilitates access to specific genes when needed. This system relies on a DNA-histone protein complex called chromatin to efficiently package the genetic information that exists within each cell type, giving rise to ‘epigenomes’. This packaging system makes certain expressed genes, or genes to be expressed, more readily accessible to transcription factors and other machinery that must engage our genetic template. The Allis laboratory is perhaps best known for deciphering regulatory mechanisms that impinge upon chromatin and for identifying the responsible enzyme systems that govern the covalent modifications of histone proteins. The regulation of the enzyme systems responsible for adding or subtracting modifications from histones and DNA, or for reading them, are taking center stage in the study of cancer in the current post-genomic or epigenomic era.

Recent studies are centered upon histone mutations (‘oncohistones’), representing a previously unrecognized mechanism to alter epigenetic states in a variety of pathologies through inhibition of a wide range of histone methyltransferases. In turn, oncohistone mutations exert their oncogenic effect by reprogramming the cellular epigenome and transcriptome, thereby disrupting the highly coordinated epigenetic programs required for cell-specific differentiation. Implications of this research for human biology and human disease, notably cancer, are far-reaching and continuing at a remarkable pace.

Dr. David Allis is the Joy and Jack Fishman Professor and Head of the Laboratory of Chromatin Biology and Epigenetics at The Rockefeller University. He received his Ph.D. in 1978 from Indiana University and performed postdoctoral work with Martin Gorovsky at the University of Rochester. Before he joined Rockefeller in 2003, Dr. Allis held several academic positions at the Baylor College of Medicine, Rochester, and the University of Virginia School of Medicine.

Dr. Allis is a member of the National Academy of Sciences and the American Academy of Arts and Sciences. Among his many honors are the 2015 Breakthrough Prize in Life Sciences, the 2014 Japan Prize, the 2011 Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Science, the 2008 ASBMB-Merck Award, the 2007 Gairdner Foundation International Award, the 2004 Wiley Prize in Biomedical Sciences, the 2003 Massry Prize, and the 2002 Dickson Prize in Biomedical Sciences.

He is best known for the ‘histone code’ hypothesis of epigenetics, which proposes that post-translational modifications to histones on chromatin provide information about how neighboring genes should be expressed. ‘Writers’ are enzymes that create these modifications, while ‘readers’ detect and respond to them. The concept of the histone code arose from his discovery of the critical link between histone acetylation and gene-specific transcriptional activation, and later the link between histone phosphorylation and mitosis. His recent studies suggest a new model in which histone mutations (‘oncohistones’) represent a novel and previously unrecognized mechanism to alter epigenetic states in a variety of pathologies through inhibition of a wide range of histone methyltransferases.