Department of Biochemistry

2015 Axelrod Distinguished Lectures

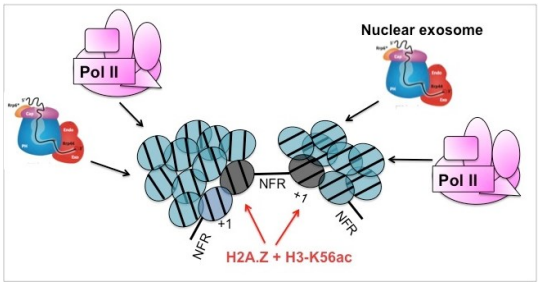
Craig Peterson

Program in Molecular Medicine
University of Massachusetts Medical School

Tuesday, March 24
3:30 - Deans Auditorium (PFEN 241)
Chromatin remodeling machines: Connecting the epigenome to nuclear functions

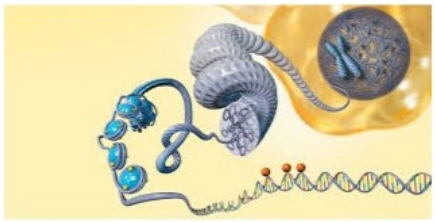
Wednesday, March 25
4:00 - Deans Auditorium (PFEN 241)
Chromatin dynamics: Regulation of transcriptional homeostasis

Chromatin remodeling machines: Connecting the epigenome to nuclear functions



A typical eukaryotic cell contains over three linear feet of DNA squeezed into a tiny nucleus of about 20 μm in diameter. Such compaction is achieved by wrapping DNA around histones proteins to form nucleosomes, the basic unit of chromosome structure. Although these condensed structures solve the packaging problem, they essentially hide the genetic information contained within DNA. Furthermore, very early studies indicated that these nucleosomal structures serve a regulatory function, controlling which genes are ON or OFF in different cells. This has led to the view that nucleosomes are the foundation of the "epigenome" which controls cell function independent of DNA sequence. Work over the past 20 years has led to the discovery of a large family of "chromatin remodeling" enzymes that can be targeted to particular genomic locations to unwrap or re-wrap nucleosomes, providing exquisite control over genome functions. Chromatin remodeling enzymes are essential for development and cell identity, control many basic cellular functions, and their dysfunction leads to human diseases, especially cancers.

Chromatin dynamics: Regulation of transcriptional homeostasis



www.celgene.com/content/uploads/2013/12/Therapeutic_Possibilities_Epigenetics.jpg

The histone variant H2A.Z is a hallmark of nucleosomes flanking the promoters of many protein coding genes, and it is often found in concert with acetylation of histone H3 at lysine 56 (H3-K56Ac). Here we report that inactivation of the nuclear RNA exosome uncovers global roles for H2A.Z and H3-K56Ac in expression of both noncoding RNAs (ncRNAs) and protein coding genes. Furthermore, we find that the INO80c chromatin remodeling enzyme counteracts H2A.Z and K56Ac, preventing extensive ncRNA expression that can impede genome stability pathways. We also describe roles for H2A.Z and H3-K56Ac in promoting formation of genome-wide, chromosome interaction domains (CIDs). We suggest a model in which CIDs control transcription by integrating transcription initiation and RNA degradation events, controlling transcriptional noise and poising genes for proper regulation.

About the Axelrod Lectures:

Dr. Bernard Axelrod served as Head of the Department of Biochemistry. His efforts were instrumental in founding the biochemistry program at Purdue University. On the occasion of his 70th birthday, colleagues and friends established this lectureship in honor of Dr. Axelrod's many contributions to the field of biochemistry and its community of scientists. Dr. Axelrod passed away in 2011 at the age of 97.