B·DEBATE International Center for Scientific Debate BARCELONA

CRG Centre for Genomic Regulation

DANNY REINBERG

CV

PARTICIPANT AT:

CODING AND NON-CODING FUNCTIONS OF THE GENOME
BARCELONA CONFERENCE ON EPIGENETICS AND CANCER

October, 29th-30th, 2015, Barcelona

Danny Reinberg, Investigator, NYU Langone School of Medicine at Smilow Research Center, New York, USA

Our current focus is on the molecular mechanisms of epigenetics, that is, the extra-genetic information that gives rise to the different patterns of gene expression that distinguish different cells of an organism. Since all the cells of an individual contain identical DNA, the different patterns of genes they express come about, in part, by how tightly the different regions of the DNA are packaged. This packaging of the DNA can either be an obstacle to gene expression or can be a loose assemblage that allows RNA polymerase access to the DNA to be transcribed. Different regions of the genome are packaged differently to give rise to distinct tissues and this occurs during development. These patterns of gene expression are then maintained in adult cells and, importantly, this extra-genetic information is transferred to daughter cells after cell division so that the tissue specificity is again maintained. One critical aspect of how this packaging is regulated involves specific modifications placed on the histone proteins around which the DNA is wrapped. The histones can be modified at their N-terminal tails and these modifications include acetyl-groups, phosphates and methyl-groups. In fact, some of these modifications can affect other modifications being placed on the same histone protein demonstrating the intricacies and dynamics inherent to the regulation of this process. Of particular interest for our studies are the enzymes responsible for placing methyl modifications on lysine residues of histone proteins. Some methyl modifications appear to be very stable and therefore their presence might account for the heritability of patterned gene expression. We are studying the factors required to achieve higher-order genome structures as well as the regulation and capabilities of the enzymes that place methyl groups, and how and when they are targeted to different histones on the DNA. Given that tumorigenesis is a prime example of misregulated gene expression patterns, studies of the molecular basis of epigenetics would pertain to aberrant as well as normal cellular identity. As an example, the levels of one of the histone lysine methyltransferases under study are up-regulated in later stages of prostate cancer, specifically when the cancer becomes metastatic. We are currently investigating the function of this histone lysine methyltransferase using mouse-model systems.

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ABSTRACT

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Keynote: Polycomb Complexes in Development and Disease

Epigenetics encompasses changes in gene expression profiles that occur without alterations in the genomic DNA sequence of a cell. This arises from the dynamic processes that structure regions of chromosomal DNA through a range of compaction in eukaryotes. The altered pattern of gene expression is pivotal to cellular differentiation and development and is inherited by daughter cells thereby maintaining the integrity, specifications, and functions for a given cell type. Aberrancies in this epigenetic process give rise to perturbations that are also inherited and disruptive to normal cellular properties. The histone proteins that package DNA into chromatin are subject to post-translational modifications generating different chromatin structures. The polycomb repressive complexes play pivotal functions in maintaining cellular identity through alteration of chromatin domains. Functions of these complexes will be discussed.

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