Lecture 4. Epigenomics.

Learning outcomes:
1. Explain the difference between the terms “genetics” and “epigenetics”, “genomics” and “epigenomics”.
2. Explain the term “gene expression” and different mechanisms of inheritance.
3. Describe the mechanisms of gene expression regulation on the transcriptional and post-transcriptional level in procaryotes and eucaryotes.
4. Characterize the histone modifications and their influence on gene expression.
5. Explain the mechanisms of environmental influence on gene expression.

In biology, **epigenetics** is the study of **heritable phenotype changes** that do not involve alterations in the DNA sequence. The Greek prefix **epi-** (ἐπι- "over, outside of, around") in epigenetics implies features that are "on top of" or "in addition to" the traditional genetic basis for inheritance. **Phenotype** (from Greek pheno- 'showing', and type 'type') is the term used in genetics for the composite observable characteristics or traits of an organism. **Epigenomics** is the study of the complete set of **epigenetic modifications** on the genetic material of a cell, known as the **epigenome**. The field is analogous to genomics and proteomics, which are the study of the genome and proteome of a cell. Epigenetic modifications are reversible modifications on a cell's DNA or histones that affect **gene expression** without altering the DNA sequence. Epigenomic maintenance is a continuous process and plays an important role in stability of eukaryotic genomes by taking part in crucial biological mechanisms like **DNA repair**. Plant flavones are said to be inhibiting epigenomic marks that cause cancers. Two of the most characterized epigenetic modifications are **DNA methylation** and **histone modification**. Epigenetic modifications play an important role in gene expression and regulation, and are involved in numerous cellular processes such as in differentiation/development and tumorigenesis. The study of epigenetics on a global level has been made possible only recently through the adaptation of genomic high-throughput assays.
DNA methylation is the process by which a methyl group is added to DNA. The enzymes responsible for catalyzing this reaction are the DNA methyltransferases (DNMTs). While DNA methylation is stable and heritable, it can be reversed by an antagonistic group of enzymes known as DNA de-methylases. In eukaryotes, methylation is most commonly found on the carbon 5 position of cytosine residues (5mC) adjacent to guanine, termed CpG dinucleotides.
In eukaryotes, genomic DNA is coiled into protein-DNA complexes called **chromatin**. **Histones**, which are the most prevalent type of protein found in chromatin, function to condense the DNA; the net positive charge on histones facilitates their bonding with DNA, which is negatively charged. The basic and repeating units of chromatin, nucleosomes, consist of an octamer of histone proteins (H2A, H2B, H3 and H4) and a 146 bp length of DNA wrapped around it. **Nucleosomes** and the DNA connecting form a 10 nm diameter chromatin fiber, which can be further condensed. **Chromatin remodeling** occurs via post-translational modifications of the N-terminal tails of core histone proteins. The collective set of **histone modifications** in a given cell is known as the histone code. Many different types of histone modification are known, including: **acetylation, methylation, phosphorylation, ubiquitination, SUMOylation, ADP-ribosylation, deamination and proline isomerization**; acetylation, methylation, phosphorylation and ubiquitination have been implicated in gene activation whereas methylation, ubiquitination, SUMOylation, deamination and proline isomerization have been implicated in gene repression.
Gene expression means how the genes are “expressed” (showed) themselves in the phenotype of the organism. There are many **mechanisms of inheritance**: **full dominance, incomplete dominance, co-dominance, polymeria, epistasis, complexive gene interactions** and etc. Gene expression is regulated in **procaryotes** and **eucaryotes** on the transcriptional and post-transcriptional level by different ways. Many procaryotic genes are organized as so-called

“**operons**”. Each operon is the **set of genes** responsible for one metabolic pathway that are **regulated and transcribed together** (for example, lactose operon of *E. Coli*). Each protein-coding gene is called “**cistron**” so this genome organization is called “**polycistronic**”. Eucaryotes have “**monocistronic**” genome organization. This means that individual genes are located, transcribed and regulated **separately** from each other.

The questions for self - control:

1. What are the “genetics” and “epigenetics”, “genomics” and “epigenomics”.
2. “Gene expression” and different mechanisms of inheritance.
3. How the gene expression are regulated on the transcriptional and post-transcriptional level in procaryotes and eucaryotes?
4. What are the histones and what are their functions?
5. How the environmental conditions can influence on gene expression?

Recommended readings:

1. Dupont C, Armant DR, Brenner CA (September 2009). "Epigenetics: definition, mechanisms and clinical perspective". Seminars in Reproductive Medicine. 27 (5): 351–7. doi:10.1055/s-0029-1237423. PMC 2791696. PMID 19711245.
2. Rutherford, Adam (19 July 2015). "Beware the pseudo gene genies". The Guardian.
3. Russell PJ (2010). iGenetics: A Molecular Approach (3rd ed.). San Francisco: Pearson Benjamin Cummings. ISBN 978-0-321-56976-9.
4. Alabert C, Groth A (February 2012). "Chromatin replication and epigenome maintenance" (PDF). Nature Reviews. Molecular Cell Biology. 13 (3): 153–67. doi:10.1038/nrm3288. PMID 22358331.
5. Ghosh S, Sinha JK, Raghunath M (September 2016). "Epigenomic maintenance through dietary intervention can facilitate DNA repair process to slow down the progress of premature aging". IUBMB Life. 68 (9): 717–21. doi:10.1002/iub.1532. PMID 27364681.
6. "The Potential Epigenetic and Anticancer Power of Dietary Flavones". 2016-10-11.
7. Zhu J, Adli M, Zou JY, Verstappen G, Coyne M, Zhang X, et al. (January 2013). "Genome-wide chromatin state transitions associated with developmental and environmental cues". Cell. 152 (3): 642–54. doi:10.1016/j.cell.2012.12.033. PMC 3563935. PMID 23333102.
8. Laird PW (March 2010). "Principles and challenges of genomewide DNA methylation analysis". Nature Reviews. Genetics. 11 (3): 191–203. doi:10.1038/nrg2732. PMID 20125086.
9. Barski A, Cuddapah S, Cui K, Roh TY, Schones DE, Wang Z, et al. (May 2007). "High-resolution profiling of histone methylations in the human genome". Cell. 129 (4): 823–37. doi:10.1016/j.cell.2007.05.009. PMID 17512414.
10. Kouzarides T (February 2007). "Chromatin modifications and their function". Cell. 128 (4): 693–705. doi:10.1016/j.cell.2007.02.005. PMID 17320507.