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Epigenetic Gene Regulation in Biology and Medicine

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Course Overview

The eukaryotic cell nucleus is a three-dimensional mosaic of individual chromosomes suspended in the nuclear milieu. Chromosomes are macromolecular polymers composed primarily of DNA and proteins. The DNA sequence of chromosomes codes for the unique genetic makeup of individuals and genes are segments of chromosomal DNA that usually code for RNA and proteins. During development and differentiation, totipotent cells give rise to the vastly different cell types in the adult. Each cell type has the same DNA sequence but different gene expression patterns such that only a subset of genes is active in any given cell at any particular time. The variable expression of genes is due to specific activation and silencing of genes in a cell type specific manner. Most importantly once these expression patterns are established they are stably maintained as cells grow and divide throughout the life span of the individual. Epigenetics is the field that studies the factors and mechanisms involved in the stable but differential expression of genes in cells undergoing growth and division.

Given the centrality of proper differentiation, development and growth to the life of the organism understanding the complex interplay between chromatin structure and gene activity is critical for modern medicine and biotechnology. This lecture course will aim to impart the basics of this young developing field to advanced students and research scientists in biology, molecular medicine and biotechnology.

The DNA in chromosomes is bound by various structural and enzymatic proteins to form chromatin. Active genes use DNA sequences called enhancers and enzymes to open chromatin-allowing genes to synthesize RNA while silent genes use silencers and bind repressor proteins to condense chromatin and inactivate genes. Chromosomes are therefore organized into alternating segments of open chromatin domains juxtaposed next to condensed domains. While the basic constituents of chromatin were discovered and elucidated in the 1970s and 1980s, the role of specific factors in epigenetics and the molecular mechanisms underlying these processes were only elucidated over the last decade or so. The structure of chromatin is dynamic and constantly changes in response to cues. Composition of chromatin proteins as well as modifications to these proteins altering the structure of chromatin and chromosomes cumulatively resulting in completely different expression programs and cell identities.

Modern epigenetics investigates the stable heritable expression patterns of genes, as cells divide, without any change in the underlying sequence of the DNA. The methods used are a combination of genetic, biochemical, microscopic and genomic. The aim of this course will be to inculcate in the students an appreciation of the role of chromatin in stable gene regulation. The course will not comprehensively list all examples of epigenetic gene regulation but focus on using well-characterized systems to highlight the different factors and distinct mechanisms that underlie various epigenetic phenomenon. In the process of these lectures and discussions students will become familiar with and appreciate the strengths and weaknesses of the research approaches and methods employed to dissect epigenetic phenomenon and will be able to use similar approaches and methods in their own research studies.

The structure of this course will be a lecture on a topic coupled with a discussion of three to four papers in detail on that topic. The papers discussed will be both key "historically important" papers that were considered paradigm shifting, coupled with important recent papers that build on the historic work and will thus allow the student to visualize the journey that has been accomplished. Participants will read the papers prior to each discussion section and will be expected to engage in an active discussion of the findings in the papers. The discussion will focus on the hypothesis/question being addressed, the methods used and their strengths and weaknesses as well as the key findings and future experiments.

Dates	**28th November to 2nd December, 2016** **Maximum Number of participants: 50.**
You Can Attend if	• Graduate students, M.Sc, M.Tech, M.Phil/ PhD, PDFs from biological, pharmaceutical and medical sciences • Students studying Medical Sciences • Limited merit based seats can be offered to undergraduate students. • Faculty members from University departments, institutes and colleges • Researchers from national research laboratories, Pharmaceutical industry
Fees	**One-Time GIAN Registration:** Visit http://www.gian.iitkgp.ac.in/GREGN/ **Course Fees:** Those affiliated to Savitribai Phule Pune University or affiliated colleges: **No fee, but registration is must.** Those affiliated to Academic Institutions, Research Institutes : **₹1000.** Those from industry: **₹5000.** Those from abroad: **US $ 150.** Fees include tea with light snacks, any instructional material provided by the expert faculty, Out-station candidates need to arrange for transport and accommodation on their own. Appearing for evaluations/examinations during the course is necessary for certificate of grades in the course.

Prof. Rohinton Kamakaka is Professor at University of California, and is focused on understanding how the packaging of DNA in the nucleus affects various processes in a cell. As a graduate student he was the first to utilize ChIP in vertebrate cells to map proteins on active and inactive genes and show that active genes were depleted of histone H1 and packaged in an open configuration. As a post-doc he developed novel transcription and chromatin assembly extracts to directly test the inter-relationships between replication, chromatin assembly and gene regulation. He also purified and characterized chromatin assembly factors and described some of the steps involved in chromatin remodeling during gene activation. As an independent research professor, initially at NIH and then at UCSC, he continued this focus, identifying and characterizing insulators in yeast, purifying Sir repressor protein complexes as well as investigating the molecular mechanisms by which these proteins interacted with nucleosomes to mediate repression and silence genes. His research is currently focused on understanding how active and repressed chromatin domains are packaged in the nucleus and interface with each other, the mechanism by which insulators organize chromatin domains in the nucleus and the role of repair proteins in the three dimensional organization of the nucleus.

Course Coordinator

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