DOWNLOAD PDF EPIGENETICS AND CHROMATIN

Chapter 1 : Histone Modifications | What is Epigenetics?

Epigenetics & Chromatin is a peer-reviewed, open access journal that publishes research, and reviews, providing novel insights into epigenetic inheritance and chromatin-based interactions. The journal aims to understand how gene and chromosomal elements are regulated and their activities maintained during processes such as cell division.

Histone Modifications Schematic representation shows the organization and packaging of genetic material. N-terminal histone tails blue are shown protruding from H3 and H4. Histone proteins act to package DNA, which wraps around the eight histones, into chromosomes. In most species, histone H3 is primarily acetylated at lysines 9, 14, 18, 23, and 56, methylated at arginine 2 and lysines 4, 9, 27, 36, and 79, and phosphorylated at ser10, ser28, Thr3, and Thr Histone H4 is primarily acetylated at lysines 5, 8, 12 and 16, methylated at arginine 3 and lysine 20, and phosphorylated at serine 1. Thus, quantitative detection of various histone modifications would provide useful information for a better understanding of epigenetic regulation of cellular processes and the development of histone modifying enzyme-targeted drugs. The process of histone acetylation is tightly involved in the regulation of many cellular processes including chromatin dynamics and transcription, gene silencing, cell cycle progression, apoptosis, differentiation, DNA replication, DNA repair, nuclear import, and neuronal repression. The modifying enzymes involved in histone acetylation are called histone acetyltransferases HATs and they play a critical role in controlling histone H3 and H4 acetylation. More than 20 HATs have been identified which can be classified into five families: Histone deacetylaces HDACs catalyze the hydrolytic removal of acetyl groups from histone lysine residues. An imbalance in the equilibrium of histone acetylation has been associated with tumorigenesis and cancer progression. Detecting whether histone H3 is acetylated at its lysine residues would provide useful information for further characterization of acetylation patterns or sites, thereby leading to a better understanding of epigenetic regulation of gene activation as well as the development of HAT-targeted drugs. So far, at least 4 classes of HDACs have been identified. HDAC inhibition displays significant effects on apoptosis, cell cycle arrest, and differentiation in cancer cells. HDAC inhibitors are currently being developed as anticancer agents. N-terminal tail modifications of H3 and H4. HMTs control or regulate DNA methylation through chromatin-dependent transcriptional repression or activation. In the cell nucleus, when histone methylation occurs, specific genes within the DNA complexed with the histone may be activated or silenced. G9a and polycomb group enzymes such as EZH2 are histone methyltransferases that catalyze methylation of histone H3 at lysine 27 H3-K27 in mammalian cells. Increased global H3-K27 methylation is also found to be involved in some pathological processes such as cancer progression. Roles of histone acetyltransferases and deacetylases in gene regulation. Bioessays, August 20 8: Molecular Cancer Research, Oct;5 Nature Reviews Genetics, 13, Posttranslational Modifications of Histones by Methylation. Proteins in eukaryotic transcription. Advances in Protein Chemistry

Chapter 2 : Keystone Symposia | Scientific Conferences on Biomedical and Life Science Topics

You are cordially invited to participate in the fourth Cold Spring Harbor Laboratory meeting on Epigenetics & Chromatin. The opening session will begin at pm on Tuesday, September 11 and the meeting will end after lunch on Saturday, September 15,

Definitions[edit] The term epigenetics in its contemporary usage emerged in the s, but for some years has been used in somewhat variable meanings. It has been used in English since the 17th century. Waddington held that cell fates were established in development canalisation much as a marble rolls down to the point of lowest local elevation. An early version was proposed, among the founding statements in embryology , by Karl Ernst von Baer and popularized by Ernst Haeckel. A radical epigenetic view physiological epigenesis was developed by Paul Wintrebert. Another variation, probabilistic epigenesis, was presented by Gilbert Gottlieb in The developmental psychologist Erik Erikson wrote of an epigenetic principle in his book Identity: Youth and Crisis , encompassing the notion that we develop through an unfolding of our personality in predetermined stages, and that our environment and surrounding culture influence how we progress through these stages. This biological unfolding in relation to our socio-cultural settings is done in stages of psychosocial development , where "progress through each stage is in part determined by our success, or lack of success, in all the previous stages. The more recent usage of the word in science has a stricter definition. For example, Adrian Bird defined epigenetics as "the structural adaptation of chromosomal regions so as to register, signal or perpetuate altered activity states. Such redefinitions however are not universally accepted and are still subject to dispute. The "epigenome" is a parallel to the word "genome", referring to the overall epigenetic state of a cell, and epigenomics refers to more global analyses of epigenetic changes across the entire genome. Taken to its extreme, the "epigenetic code" could represent the total state of the cell, with the position of each molecule accounted for in an epigenomic map, a diagrammatic representation of the gene expression, DNA methylation and histone modification status of a particular genomic region. More typically, the term is used in reference to systematic efforts to measure specific, relevant forms of epigenetic information such as the histone code or DNA methylation patterns. Molecular basis[edit] Epigenetic changes modify the activation of certain genes, but not the genetic code sequence of DNA. The microstructure not code of DNA itself or the associated chromatin proteins may be modified, causing activation or silencing. This mechanism enables differentiated cells in a multicellular organism to express only the genes that are necessary for their own activity. Epigenetic changes are preserved when cells divide. Moreover, if gene inactivation occurs in a sperm or egg cell that results in fertilization, this epigenetic modification may also be transferred to the next generation. These damages are largely repaired, but at the site of a DNA repair, epigenetic changes can remain. In one study, markers for oxidative stress, such as modified nucleotides that can result from DNA damage, were decreased by a 3-week diet supplemented with soy. Covalent modifications[edit] Covalent modifications of either DNA e. Therefore, the word "epigenetics" is sometimes used as a synonym for these processes. However, this can be misleading. Chromatin remodeling is not always inherited, and not all epigenetic inheritance involves chromatin remodeling. Because the phenotype of a cell or individual is affected by which of its genes are transcribed, heritable transcription states can give rise to epigenetic effects. There are several layers of regulation of gene expression. One way that genes are regulated is through the remodeling of chromatin. Chromatin is the complex of DNA and the histone proteins with which it associates. If the way that DNA is wrapped around the histones changes, gene expression can change as well. Chromatin remodeling is accomplished through two main mechanisms: The first way is post translational modification of the amino acids that make up histone proteins. Histone proteins are made up of long chains of amino acids. If the amino acids that are in the chain are changed, the shape of the histone might be modified. DNA is not completely unwound during replication. It is possible, then, that the modified histones may be carried into each new copy of the DNA. Once there, these histones may act as templates, initiating the surrounding new histones to be shaped in the new manner. By altering the shape of the histones around them, these modified histones would ensure that a lineage-specific transcription program is maintained after cell division. The

second way is the addition of methyl groups to the DNA, mostly at CpG sites , to convert cytosine to 5-methylcytosine. However, some areas of the genome are methylated more heavily than others, and highly methylated areas tend to be less transcriptionally active, through a mechanism not fully understood. Methylation of cytosines can also persist from the germ line of one of the parents into the zygote, marking the chromosome as being inherited from one parent or the other genetic imprinting. Mechanisms of heritability of histone state are not well understood; however, much is known about the mechanism of heritability of DNA methylation state during cell division and differentiation. Heritability of methylation state depends on certain enzymes such as DNMT1 that have a higher affinity for 5-methylcytosine than for cytosine. If this enzyme reaches a "hemimethylated" portion of DNA where 5-methylcytosine is in only one of the two DNA strands the enzyme will methylate the other half. Although histone modifications occur throughout the entire sequence, the unstructured N-termini of histones called histone tails are particularly highly modified. These modifications include acetylation , methylation , ubiquitylation , phosphorylation , sumoylation , ribosylation and citrullination. Acetylation is the most highly studied of these modifications. For example, acetylation of the K14 and K9 lysines of the tail of histone H3 by histone acetyltransferase enzymes HATs is generally related to transcriptional competence. Because it normally has a positively charged nitrogen at its end, lysine can bind the negatively charged phosphates of the DNA backbone. The acetylation event converts the positively charged amine group on the side chain into a neutral amide linkage. This removes the positive charge, thus loosening the DNA from the histone. This is the "cis" model of epigenetic function. In other words, changes to the histone tails have a direct effect on the DNA itself. In this model, changes to the histone tails act indirectly on the DNA. For example, lysine acetylation may create a binding site for chromatin-modifying enzymes or transcription machinery as well. This chromatin remodeler can then cause changes to the state of the chromatin. It may be that acetylation acts in this and the previous way to aid in transcriptional activation. The idea that modifications act as docking modules for related factors is borne out by histone methylation as well. Methylation of lysine 9 of histone H3 has long been associated with constitutively transcriptionally silent chromatin constitutive heterochromatin. It has been determined that a chromodomain a domain that specifically binds methyl-lysine in the transcriptionally repressive protein HP1 recruits HP1 to K9 methylated regions. One example that seems to refute this biophysical model for methylation is that tri-methylation of histone H3 at lysine 4 is strongly associated with and required for full transcriptional activation. Tri-methylation in this case would introduce a fixed positive charge on the tail. This enzyme utilizes a catalytically active site called the SET domain Suppressor of variegation, Enhancer of zeste, Trithorax. The SET domain is a amino acid sequence involved in modulating gene activities. This domain has been demonstrated to bind to the histone tail and causes the methylation of the histone. Also, multiple modifications may occur at the same time, and these modifications may work together to change the behavior of the nucleosome. The idea that multiple dynamic modifications regulate gene transcription in a systematic and reproducible way is called the histone code , although the idea that histone state can be read linearly as a digital information carrier has been largely debunked. Epigenetic changes of this type thus have the potential to direct increased frequencies of permanent genetic mutation. This recently identified enzyme has a catalytically active site called the Jumonji domain JmjC. The demethylation occurs when JmjC utilizes multiple cofactors to hydroxylate the methyl group, thereby removing it. JmjC is capable of demethylating mono-, di-, and tri-methylated substrates. Epigenetic control is often associated with alternative covalent modifications of histones. Small interfering RNAs can modulate transcriptional gene expression via epigenetic modulation of targeted promoters. For example, Hnf4 and MyoD enhance the transcription of many liver- and muscle-specific genes, respectively, including their own, through the transcription factor activity of the proteins they encode. RNA signalling includes differential recruitment of a hierarchy of generic chromatin modifying complexes and DNA methyltransferases to specific loci by RNAs during differentiation and development. Descendants of the cell in which the gene was turned on will inherit this activity, even if the original stimulus for gene-activation is no longer present. These genes are often turned on or off by signal transduction , although in some systems where syncytia or gap junctions are important, RNA may spread directly to other cells or nuclei by diffusion. A large amount of RNA and protein is contributed to the zygote

by the mother during oogenesis or via nurse cells , resulting in maternal effect phenotypes. A smaller quantity of sperm RNA is transmitted from the father, but there is recent evidence that this epigenetic information can lead to visible changes in several generations of offspring. Transcription from methylated CpG islands is strongly and heritably repressed. They control gene expression including virulence genes in pathogens and are viewed as new targets in the fight against drug-resistant bacteria. Their phylogenetic analyses, for example through sRNAâ€”mRNA target interactions or protein binding properties , are used to build comprehensive databases. Fungal prions Prions are infectious forms of proteins. In general, proteins fold into discrete units that perform distinct cellular functions, but some proteins are also capable of forming an infectious conformational state known as a prion. Although often viewed in the context of infectious disease , prions are more loosely defined by their ability to catalytically convert other native state versions of the same protein to an infectious conformational state. It is in this latter sense that they can be viewed as epigenetic agents capable of inducing a phenotypic change without a modification of the genome. Structural inheritance In ciliates such as Tetrahymena and Paramecium , genetically identical cells show heritable differences in the patterns of ciliary rows on their cell surface. Experimentally altered patterns can be transmitted to daughter cells. It seems existing structures act as templates for new structures. The mechanisms of such inheritance are unclear, but reasons exist to assume that multicellular organisms also use existing cell structures to assemble new ones. Nucleosome position is not random, and determine the accessibility of DNA to regulatory proteins. This determines differences in gene expression and cell differentiation. It has been shown that at least some nucleosomes are retained in sperm cells where most but not all histones are replaced by protamines. Thus nucleosome positioning is to some degree inheritable. Recent studies have uncovered connections between nucleosome positioning and other epigenetic factors, such as DNA methylation and hydroxymethylation. Predetermined epigenesis is a unidirectional movement from structural development in DNA to the functional maturation of the protein. Probabilistic epigenesis on the other hand is a bidirectional structure-function development with experiences and external molding development. Thus, as individuals develop, morphogens activate or silence genes in an epigenetically heritable fashion, giving cells a memory.

Chapter 3 : Epigenetics and Chromatin Clinic | Johns Hopkins Institute of Genetic Medicine

Join leading scientists from within chromatin and epigenetics research on April , in Munich. Talk and poster abstracts are invited.

This factor turned out to have essential roles in embryonic development and cell division Diekwisch and Luan , Luan and Diekwisch Currently, we are defining the role of this factor in chromatin segregation and craniofacial syndromes. The essential function of chromatin in early development prompted us to ask how epigenetic factors contribute to the differentiation of dental tissues. Here we focused on histone modifications as early marks in tissue differentiation. Our studies identified a switch from active to repressive histone marks during periodontal differentiation Dangaria et al. We also reported that dentin-related genes such as DSPP and DMP are repressed in dental follicle progenitors while they are active in dental pulp lineage Gopinathan et al. CP27 localization in a fibroblast nucleus. Today, the gene is called CFDP1 craniofacial development protein 1. As a chromatin complex member, it plays an important role in the regulation of transcription. Contributions to Journals Luan, X. MicroRNAs and periodontal homeostasis. MicroRNA inhibits periodontal progenitor differentiation under inflammatory conditions. Novel approaches toward managing the micromanagers: Cyclic stretch and compression forces alter microRNA expression of human periodontal ligament cells. Epigenetic marks define the lineage and differentiation potential of two distinct neural crest-derived odontogenic progenitors. Differentiation of neural crest-derived intermediate pluripotent progenitors into committed periodontal population involves unique molecular signature changes, cohort shifts, and epigenetic modifications. Stem Cells and Development 20, CP27 localization in the dental lamina basement membrane and in the stellate reticulum of developing teeth. CP27 affects viability, proliferation, attachment, and gene expression in embryonic fibroblasts. Cell Proliferation 35, CP27 function is necessary for cell survival and differentiation during tooth morphogenesis in organ culture. Cloning, gene expression, and characterization of CP27, a novel gene in mouse embryogenesis. Epigenetic regulation of dentin-related genes in neural crest progenitors. Dental follicle and dental papilla are neural crest derived odontogenic progenitors giving rise to periodontal tissues dental follicle and the dentin-pulp complex dental papilla. These data demonstrate the significant role of histone lysine methylation in progenitor fate determination.

Chapter 4 : EMBO Conference - Chromatin and Epigenetics - 3 - 6 May

Chromatin remodeling is the rearrangement of chromatin from a condensed state to a transcriptionally accessible state, allowing transcription factors or other DNA binding proteins to access DNA and control gene expression. Chromatin is the complex of DNA and proteins that are packed within the nucleus of mammalian cells.

Representation of condensed heterochromatin and relaxed euchromatin. Acetylation of histones, for example, can impact chromatin accessibility and alter gene expression. Chromatin remodeling is the rearrangement of chromatin from a condensed state to a transcriptionally accessible state, allowing transcription factors or other DNA binding proteins to access DNA and control gene expression. Chromatin is the complex of DNA and proteins that are packed within the nucleus of mammalian cells. To form chromatin, DNA is tightly condensed by being wrapped around nuclear proteins called histones. This repeating DNA-histone complex, which consists of base pairs of double-stranded DNA wrapped around eight histone proteins, is called a nucleosome. In general, the more condensed the chromatin, the harder it is for transcription factors and other DNA binding proteins to access DNA and perform their duties. When chromatin is tightly packed, and not actively being transcribed it is called heterochromatin. When chromatin is more loosely packed, and therefore accessible for transcription it is called euchromatin Fig. Chromatin remodeling is highly implicated in epigenetics. The interaction of these DNA and proteins is critical for cellular functions such as signal transduction, gene transcription, chromosome segregation, DNA replication and recombination, and epigenetic silencing. It can be used for determining if a specific protein binds to a particular sequence of a gene, such as the target sequence of a transcription factor or to compare the level of histone methylation associated with a specific gene promoter region between normal and diseased tissue. Identifying the genetic targets of DNA binding proteins and revealing the mechanism of protein-DNA interaction is crucial for understanding cellular processes. For a ChIP assay, chromatin is extracted, sheared and then added into a microwell where protein-DNA complexes are captured by affinity antibodies. The captured DNA is then released and purified. The chromatin can then be used in PCR, microarray, or sequencing applications. These histone proteins are involved in structural organization of chromatin in eukaryotic cells and can undergo various posttranslational modifications which can alter their interaction with DNA and nuclear proteins. The H3 and H4 histones for example, have long tails protruding from the nucleosome which can be covalently modified at several sites. Modifications of the histone tails include methylation, acetylation, phosphorylation, ubiquitination, sumoylation, citrullination, and ADP-ribosylation occuring on the N-terminal tail domain, which result in remodeling of the nucleosome structure into an open conformation more accessible to transcription complexes H2A can also be modified. Ready to learn about another epigenetic mechanism? Histone Modifications Baylin S. The language of covalent histone modifications.

Chapter 5 : EMBO Workshop - Chromatin and Epigenetics - 1 - 4 May

Renowned speakers will cover the latest advances in the field, including chromatin regulation, chromatin dynamics, signalling to chromatin, nuclear architecture and dynamics, developmental epigenetics, epigenomics, epigenetics and human diseases, genome stability, environmental epigenetics, and transgenerational inheritance.

Chapter 6 : Epigenetics and Chromatin

The Epigenetics and Chromatin Clinic provides treatment for patients with either classical epigenetic disorders or mutations of the epigenetic machinery.

Chapter 7 : Epigenetics & Chromatin | CSHL

The worlds largest Epigenetics Conference and Gathering for the Research Community,Join the Epigenetics

Conference ICEC at Vienna, Austria during August ,

Chapter 8 : Epigenetics & Chromatin Clinic | Johns Hopkins Institute of Genetic Medicine

The Conference on Cancer Genetics and Epigenetics will focus on newly emerging aspects of the field including the genetic heterogeneity of cancer, the "long tail" of less frequent cancer mutations and the importance of intratumoral heterogeneity as assayed by single cell technologies.

Chapter 9 : Chromatin Remodeling | What is Epigenetics?

Epigenetic modifications of histones can be described as biochemical marks within histones that result in changes to chromatin conformation and thus affect chromatin accessibility to transcription factors.