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EPIGENETICS

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ABSTRACT

Epigenetics is the study of heritable changes in gene function that do not involve changes in the sequence. The Greek prefix *epic-* (ἐπι- "over, outside of, around") in *epigenetics* implies features that are "on top of" or "in addition to" the traditional genetic basis for inheritance. Epigenetics most often denotes changes in a chromosome that affect gene activity and expression, but can also be used to describe any heritable phenotypic change that does not derive from a modification of the genome, such as prions. Such effects on cellular and physiological phenotypic traits may result from external or environmental factors, or be part of normal developmental program. The standard definition of epigenetics requires these alterations to be heritable,[3][4] either in the progeny of cells or of organisms. The term also refers to the changes themselves: functionally relevant changes to the genome that do not involve a change in the nucleotide sequence. Examples of mechanisms that produce such changes are DNA methylation and histone modification, each of which alters how genes are expressed without altering the underlying DNA sequence. Gene expression can be controlled through the action of repressor proteins that attach to silencer regions of the DNA. These epigenetic changes may last through cell divisions for the duration of the cell's life, and may also last for multiple generations even though they do not involve changes in the underlying DNA sequence of the organism, instead, non-genetic factors cause the organism's genes to behave (or "express themselves") differently. One example of an epigenetic change in eukaryotic biology is the process of cellular differentiation. During morphogenesis, totipotent stem cells become the various pluripotent cell lines of the embryo, which in turn become fully differentiated cells. In other words, as a single fertilized egg cell – the zygote – continues to divide, the resulting daughter cells change into all the different cell types in an organism, including neurons, muscle cells,

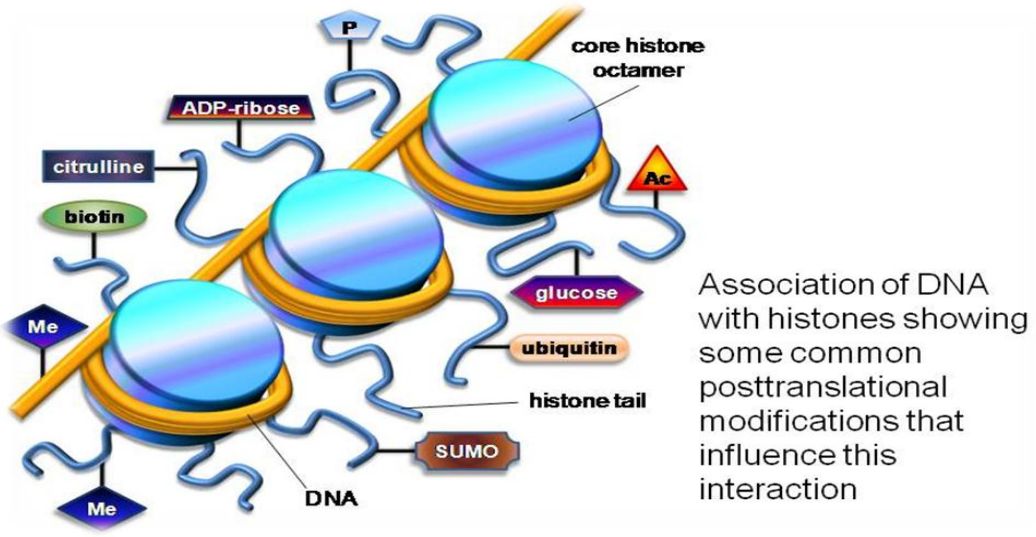
epithelium, endothelium of blood vessels, etc., by activating some genes while inhibiting the expression of others.

KEYWORDS: Epigenetics is the study expression of others.

INTRODUCTION

The term epigenetics in its contemporary usage emerged in the 1990s, but for some years has been used in somewhat variable Meanings. A consensus definition of the concept of *epigenetic trait* as "stably heritable phenotype resulting from changes in a Chromosome without alterations in the DNA sequence" was formulated at a Cold Spring meeting in 2008, although Alternate definitions that include non-heritable traits are still being used.

Epigenetic is the study of heritable change in gene expression (active versus inactive genes) that do not involve changes to the underlying DNA sequence a change in phenotype without a change in genotype which in turn affects how cells read the genes. Epigenetic change is a regular and natural occurrence but can also be influence by several factor including age the environment lifestyle, and disease state .epigenetic modification can manifest as commonly as the manner in which cell terminally differentiate can manifest as commonly as the manner in which cells terminally differentiate to end up as skin cells liver cells brain cell.etc. or epigenetic change can have more including DNA methylation histone modification and non-coding RNA ncRNA associated gene silencing are currently considered to initiated and sustain epigenetic change new and ongoing research is continuously uncovering the role of epigenetics in a variety of human disorder and fatal diseases.



Association of DNA with histones showing some common posttranslational modifications that influence this interaction

The term "epigenetic" has also been used in developmental psychology to describe psychological development as the result of an ongoing, bi-directional interchange between heredity and the environment Interactivist ideas of development have been discussed in various forms and under various names throughout the 19th and 20th centuries. 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 2003. This view encompasses all of the possible developing factors on an organism and how they not only influence the organism and each other, but how the organism also influences its own development.

The developmental psychologist Erik Erikson wrote of an *epigenetic principle* in his book *Identity: Youth and Crisis* (1968), 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.

Molecular basis

Epigenetic changes modify the activation of certain genes, but not the genetic code sequence of DNA. The microstructure (not code) Of DNA it 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. Most epigenetic changes only occur within the course of one individual organism's lifetime; However, these epigenetic changes can be transmitted to the organism's offspring through a process called transgene rational Epigenetic inheritance. 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 Specific epigenetic processes include permutation, bookmarking, imprinting, gene silencing, X chromosome inactivation, position Effect, DNA methylation reprogramming, transection, maternal effects, the progress of carcinogenesis, many effects of teratogens, Regulation of histone modifications and heterochromatin, and technical limitations affecting parthenogenesis and cloning.

DNA methylation: is process by which by which methyl group are added to the DNA molecule. Methylation can change the activity of a DNA segment without changing the sequence when location in a gene transcription. DNA methylation is essential for normal development and is associated with a number of key processes including genomic impairing –x chromosome inactivation, repression of transposable elements aging and carcinogenesis.

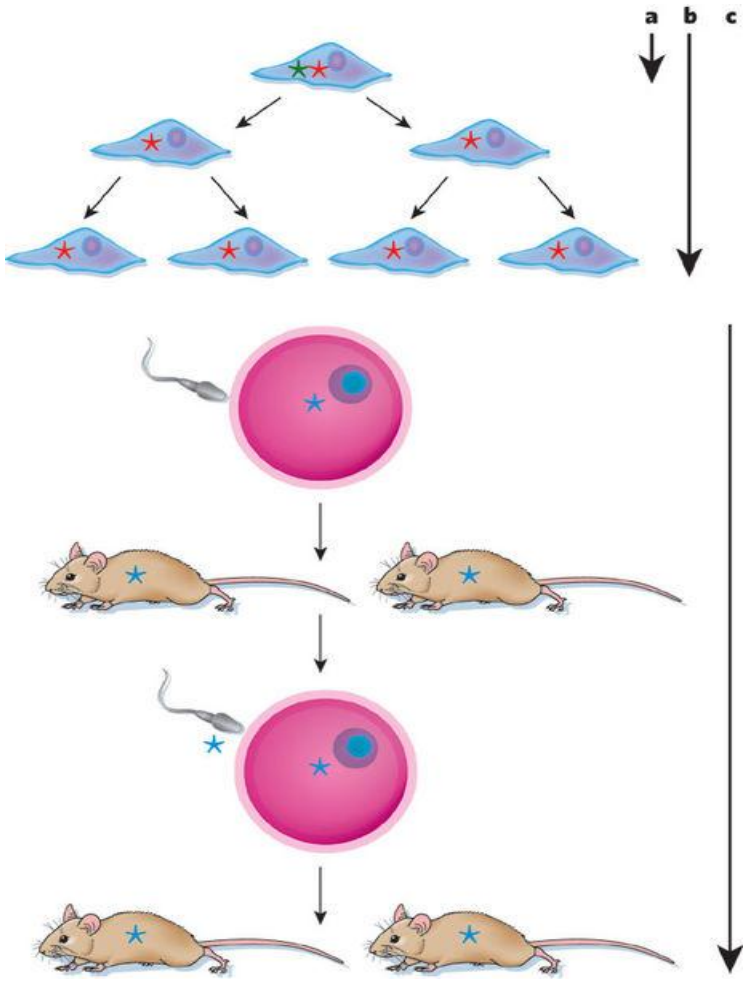
Epigenetic in bacteria

While epigenetics is of fundamental importance in eukaryotes, especially metazoans, it plays a different role in bacteria. Most Importantly, eukaryotes use epigenetic mechanisms primarily to regulate gene expression which bacteria rarely do. However, bacteria Make widespread use of post replicative DNA methylation for the epigenetic control of DNA-protein interactions. Bacteria also use DNA adenine methylation (rather than DNA cytosine methylation) as an epigenetic signal. DNA adenine methylation is important in Bacteria virulence in organisms such as Escherichia coli, Salmonella, Vibrio, Yersinia, Hemophilic, and Brucella. In Alphaproteobacteria, methylation of adenine regulates the cell cycle and couples gene transcription to DNA replication. In Gammaproteobacteria, adenine methylation provides signals for DNA replication, chromosome segregation, mismatch repair, packaging of bacteriophage, transposes activity and regulation of gene expression. There exists a genetic switch controlling Streptococcus pneumonia (the pneumococcus) that allows the bacterium to randomly change its characteristics into six alternative states that could pave the way to improved vaccines. Each form is randomly generated by a phase variable methylation system. The ability of the pneumococcus to cause deadly infections different in each of these six states. similar system existing other bacterial genera.

Epigenetics and inheritance

Should heritability be mandatory in a contemporary view of epigenetics? The requirement that epigenetic characters should be transmissible through mitosis or meiosis has the virtue of clarity but can be a liability. To explain why, it is necessary to introduce a third, somewhat informal, 'definition' of epigenetics that has crept into widespread use. This incarnation of epigenetics encompasses the biology of chromatin, including the complex language of chromatin marks, the transcriptional effects of RNA interferon and, for good measure, the effects of the higher-order structure of chromosomes and the nucleus The attraction of this usage is that it brackets together some of the most exciting contemporary work in biology. Its drawback is that it does not sit easily with the prevailing textbook definitions. One reason for

this is that many chromatin marks are short-lived. For example, phosphorylation of the variant histone H2AX (also known as H2AFX) after a double-strand break11 would qualify as an epigenetic mark under the emerging definition, but it is too transient to qualify as a heritable epigenetic mark. Histone modifications associated with transcription are also ambiguous with respect to heritability. On the one hand, DNA methylation affects histone acetylation and histone methylation, so these modifications can be viewed as heritably epigenetic, albeit indirectly12. On the other hand, these histone marks can also result from events that seem to involve neither DNA methylation nor Holcomb group proteins, and the marks are not necessarily transmissible between generations. Therefore, a single histone modification could, in principle, be rated as either epigenetic or not epigenetic according to the heritability credentials of its origin. Such a complicated classification system would have limited utility.



Alterations that last less than one cell cycle (green asterisk, **a**) do not qualify as epigenetic under the definition that strictly requires heritability, whereas non-mutational changes that are

transmitted from one cell to its daughters (red asterisk, **b**) or between generations of an organism (blue asterisk, **c**) do qualif.

The issue of replicative accuracy is also relevant when considering heritability. DNA synthesis is spectacularly accurate, making only 1 'unforced' error for every 107–108 bases copied. But DNA methylation has an apparent accuracy of ~96%, which is ~1 error for every 25 methylated sites copied. Because of this error rate, cloning from a single cell quickly results in a population of cells in which DNA methylation patterns are diverse. Methylated domains are more stably maintained, even though the detailed location of methylated sites varies within them. But even the peloric variant of toadflax, which is an otherwise perfect example of heritable epigenetics in action, shows considerable instability as the plant grows. So how accurately transmitted should an epigenetic mark be? Variation due to faulty copying is compounded by current evidence that all histone modifications, as well as DNA methylation itself, can be abruptly removed during development, thereby preventing the persistence of these modifications in a heritable epigenetic sense. The restrictiveness of the heritable view of epigenetics is perhaps best illustrated by considering the brain. A growing idea is that functional states of neurons, which can be stable for many years, involve epigenetic phenomena, but these states will not be transmitted to daughter cells because almost all neurons never divide.

Refining a definition

Given that there are several existing definitions of epigenetics, it might be felt that another is the last thing we need. Conversely, there might be a place for a view of epigenetics that keeps the sense of the prevailing usages but avoids the constraints imposed by stringently requiring heritability. The following could be a unifying definition of epigenetic events: the structural adaptation of chromosomal regions so as to register, signal or perpetuate altered activity states. This definition is inclusive of chromosomal marks, because transient modifications associated with both DNA repair or cell-cycle phases and stable changes maintained across multiple cell generations qualify. It focuses on chromosomes and genes, implicitly excluding potential three-dimensional architectural tempting of membrane systems and prions, except when these impinge on chromosome function. Also included is the exciting possibility that epigenetic processes are buffers of genetic variation, pending an epigenetic (or mutational) change of state that leads an identical combination of genes to produce a different developmental outcome17.

An implicit feature of this proposed definition is that it portrays epigenetic marks as responsive, not proactive. In other words, epigenetic systems of this kind would not, under normal circumstances, initiate a change of state at a particular locus but would register a change already imposed by other events. Such events could be, for example, the collision of DNA with ionizing radiation or a developmental switch in gene expression. It could be argued that the responsive nature of epigenetic processes is a unifying feature, because classic epigenetic systems such as the DNA methylation system and the Polycomb/Trithorax systems seem to respond to previous switches in gene activity in this way. Therefore, their sophisticated feature is the ability, in the 'darkness' of the nucleus, to sense and mark changes in the chromosomal status. For example, transcriptional activation through sequence-specific DNA-binding proteins brings in histone acetyl transferees, which then epigenetically adapt the promoter region for transcription (for histone acetyl groups, although ephemeral, would now be epigenetic). Similarly, elongating polymerases carry enzymes that restrain the spurious transcriptional initiation that might arise within the temporarily disrupted chromatin of an active gene. Without such epigenetic mechanisms, hard-won changes in genetic programming could be dissipated and lost; transient disruptions of chromosomal organization might go uncompensated; and DNA damage mightescape repair.

Psychology and psychiatry

Early life stress

In a groundbreaking 2003 report, Capsid and colleagues demonstrated that in robust cohort of over one-thousand subjects assessed Multiple times from preschool to adulthood, subjects who carried one or two copies of the short allele of the serotonin transporter Promoter polymorphism exhibited higher rates of adult depression and sociality when exposed to childhood maltreatment when compared to long allele homozygotes with equal ELS exposure. Parental nutrition, in utero exposure to stress, male-induced maternal effects such as attraction of differential mate quality, and Maternal as well as paternal age, and offspring gender could all possibly influence whether a germ line permutations is ultimately Expressed in offspring and the degree to which intergenerational inheritance remains stable throughout posterity.

Addiction

Addiction is a disorder of the brain's reward system which arises through transcriptional and neuroepigenetic mechanisms and occurs over time from chronically high levels of exposure

to an addictive stimulus (e.g., morphine, cocaine, sexual intercourse, gambling, etc.). Transgenerational epigenetic inheritance of addictive phenotypeshas been noted to occur in preclinical studies.

Anxiety

Transgenerational epigenetic inheritance of anxiety-related phenotypes has been reported in a preclinical study using mice. In this investigation, transmission of paternal stress-induced traits across generations involved small non-coding RNA signals transmitted via the male germline.

Depression

Epigenetic inheritance of depression-related phenotypes has also been reported in a preclinical study. Inheritance of paternal stress-induced traits across generations involved small non-coding RNA signals transmitted via the paternal germline.

Fear conditioning

Studies on mice have shown that certain conditional fears can be inherited from either parent. In one example, mice were conditioned to fear a strong scent, acetophenone, by accompanying the smell with an electric shock. Consequently, the mice learned to fear the scent of acetophenone alone. It was discovered that this fear could be passed down to the mice offspring. Despite the offspring never experiencing the electric shock themselves the mice still display a fear of the acetophenone scent, because they inherited the fear epigenetically by site-specific DNA methylation. These epigenetic changes lasted up to two generations without reintroducing the shock.

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