Goldilocks Principle and Monoallelic Expression

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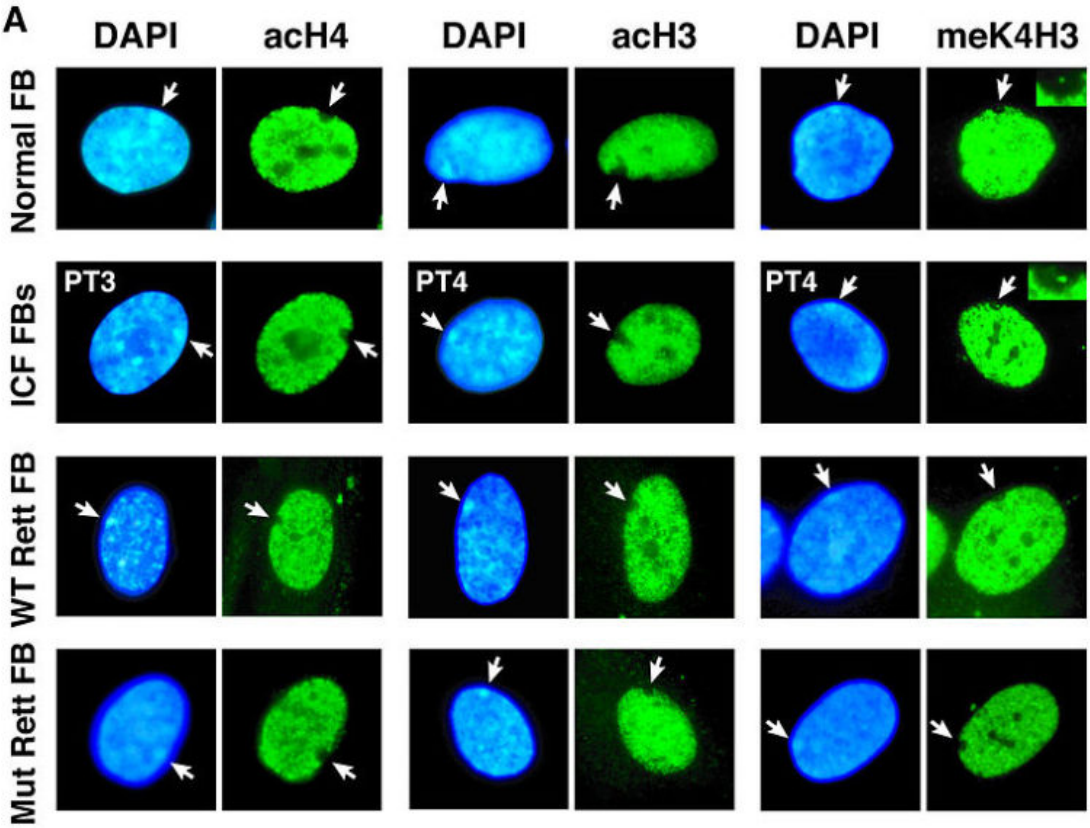
Monoallelic gene expression refers to the allele-specific expression of genes. Only one allele of the gene is actively transcribed. It can occur in different ways, such as genomic imprinting, random choice of one allele, and X-inactivation. Other allele expressions are balanced and unbalanced expressions. Balanced expressions have both alleles equally expressed, whereas unbalanced ones do not express each allele equally. Goldilocks principle states that everything should fit in a certain margin; neither too much nor too less. When the amount of gene product changes, it no longer follows the “just right” principle of Goldilocks.



Introduction

An **allele** is the variant form of a gene as detected by various phenotypes say a color variation of white and purple petals as demonstrated by Gregor Mendel.

Apart from some notable exceptions, diploid organisms express both alleles at a given locus in the normal state. However, a monoallelic expression is much more widespread

thus need to study it to describe various disease processes.

Monoallelic Expression

Monoallelic gene expression is the type of gene expression in which **one copy of the gene is active, and the other copy is silent**. Once it is initiated early in the development of an organism, the monoallelic expression is stably maintained after that. The more prevalent form of gene expression is a **biallelic expression**. It is the transcription of both alleles of a gene.

Unbalanced expression

Each allele is not expressed equally. An allelic imbalance is exhibited in 5 – 20% of the autosomal genes.

Balanced expression

An equal amount of each allele is expressed.

The monoallelic expression can occur in a number of ways:

- Genomic imprinting
- Random choice of one allele
- X-inactivation

Genomic Imprinting

Different **epigenetic marks** are placed in the male and female germline during gametogenesis.

Genomic imprinting is a type of monoallelic expression that is determined by these epigenetic marks; thus, the copies of imprinted genes of the fertilized egg that came from the paternal and maternal contributions have different marks.

Human organisms are diploid in nature and all somatic cells have two copies of a genome derived from the mother and another from the father. In genomic imprinting, however, it is only from the paternal allele that some imprinted genes are expressed, while others are expressed only from the maternal allele.

Same active allele is present in all cells in which a given gene is imprinted. This active allele is determined by the parent of origin of the allele. Genomic imprinting is also known as **parent of origin imprinting**.

All imprinted genes encode a protein. Different proteins have different and a wide variety of functions within the cells.

The difference between genomic imprinting and random forms of monoallelic expression is that, in genomic imprinting, the choice is non-random for the allele which is to be expressed and is determined totally by the parental origin.

During the process of imprinting, there is an introduction of epigenetic marks at specific locations in the genome. This occurs in the germline of one parent and results in monoallelic expression of one or multiple genes that are present within the imprinted region.

More than 100 genes that have a function in development are affected by genomic imprinting. Imprinting marks certain genes to have come from the mother or father. This happens during **gametogenesis** and before fertilization. Imprinting is maintained throughout development and adulthood.

Random Choice of One Allele (Random Monoallelic Expression)

In this type, **differential epigenetic regulation of two alleles** results in monoallelic expression. This leads to a **unique cell identity** for each cell. Some of the genes that are subjected to random monoallelic expression include:

- Pheromone receptor genes
- Interleukin genes
- Genes encoding receptors on natural killer cells

Allelic silencing: in this process, only one allele of a gene is expressed, while the other allele is silenced.

Somatic rearrangement: in this type, there is a change in DNA organization to produce functional gene at one allele, but not at the other. Genes affected by this type of random monoallelic expression are:

- T-cell receptor genes
- Immunoglobulin genes

Developmental origin of somatic rearrangement is B and T cell lineage.

X-inactivation

It is the best known and most widely studied form of monoallelic expression. Usually, the genetic makeup of all male individuals comprises of a Y chromosome and an X chromosome while that of a female individual is made up of two X chromosomes. However, the expression of X linked phenotypic features is equal or mildly different in these individuals and not more in the female counterpart as it would be thought to be. This is achieved via a phenomenon described as **dosage compensation** where the genes on one of the X chromosome are inactivated in every cell.

This **epigenetic silencing** of one or more alleles in the imprinted region is achieved via cis-regulatory elements and non-coding RNAs interactions in a region called the X-inactivation center. The developmental origin of X-inactivation is early embryogenesis during the blastocyst stage. There is a random choice of one X chromosome and when one is selected, all cells of that lineage have X phenotype inactivation. However, sometimes there is a skewing of X inactivation.

Some of the epigenetic marks that are associated with the X-inactivation are as follows:

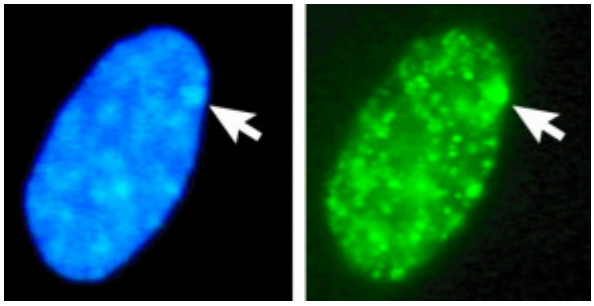


Image: “The interphase inactive X chromosome: macroH2A1 association. Photomicrograph example of normal fibroblast that was FITC-labeled using antisera to histone macroH2A1. Arrow points to sex chromatin in DAPI-stained cell nucleus, and to the corresponding sex chromatin site in the FITC-labeled photo.” by Stanley M Gartler, Kartik R Varadarajan, Ping Luo, Theresa K Canfield, Jeff Traynor, Uta Francke and R Scott Hansen – BMC Biology 2004, 2:21 doi:10.1186/1741-7007-2-21. License: CC BY 2.0

- Late replication
- DNA methylation at CpG islands
- Hypoacetylation of histones
- Unusual histone subunit deposition
- Dosage compensation

Barr body: a heterochromatic mass seen during interphase is known as a Barr body.

Dosage compensation

Dosage compensation is a term that describes the processes by which organisms equalize the expression of genes between members of different biological sexes. It results in **random epigenetic silencing of one X chromosome**.

Often, changes in the level of gene expression go unnoticed; however, sometimes even a small change can have severe clinical consequences.

Goldilocks Principle

Goldilocks principle states that something must fall within certain margins, as opposed to reaching extremes. It is derived from an initial analogy of a child named Goldilocks who chose a bowl of porridge that was neither too hot nor too cold as the preferred choice. This principle of just the right amount is applied in genetics indicate that something must be **just right**, neither too much, nor too less. Many genetic principles involve changes in the amount of gene product. When the amount of gene product changes, it no longer follows the ‘just right’ principle of Goldilocks.

References

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Notes