BHARATHIDASAN UNIVERSITY

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Programme: M.Sc. Biochemistry

Course Title : Chromatin and Epigenetics
Course Code : BC205DCE

Unit-5
Epigenetics and Diseases

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Unit-5 Overview

- Predisposition to disease
- Imprinting based disorders
- Epigenetics of memory, neurodegenaration and mental health
- Kidney, diabetes and cardiovascular disorders

Animal models in Epigenetic research

epigenetic mechanisms that regulate phenotypic expression

basic mechanisms of conditional transcriptional regulation

is not limited to any single phase of an organism's life course and can have acute, chronic and multigenerational, significance.

address across the entire lifespan, including conception through birth, growth, maturation, and senescence.

Most of the animal models currently used is rodents

Yellow Agouti Mouse Model

pheomelanin and eumelanin pigment proteins are expressed in hair follicles to give yellow coat color.

Hypomethylation characteristic yellow coat color

Hypermethylation appear completely brown pseudoagouti mouse

this to be an exceptional model for environmental and nutritional factors that induce methylation.

https://www.youtube.com/watch?v=IYJ_nd9glvw

Axin1-Fused (Axin1Fu) Mouse Model

Axin1Fu allele code for a regulatory protein that controls Wnt signaling, transforming growth factor beta, signal transduction pathways including mitogen-activated protein kinases, and the transformation-related protein 53

Mice that contain the *Axin1*^{Fu} allele exhibit a range of tail abnormalities such that axial duplications

minor wavy appearance to severe kinking of the tail

Complete hypomethylation results in the most severe kinked tail morphology

normal tails when complete hypermethylation is achieved

Genomic imprinting in mammals

In diploid organisms, the maternal and paternal alleles are expressed at similar levels,

and thus contribute equally to the phenotype

However, in eutherian mammals parental alleles are not functionally equivalent

By embryological studies in mice: nuclear transfer experiments using pronuclear stage embryos showed that reconstituted embryos with two maternal genomes and no paternal complement

Those with two paternal genomes and no maternal complement never survive beyond mid-gestation

parental genomes are functionally non-equivalent and marked or imprinted differently during male and female gametogenesis

genetic experiments using chromosome translocations in mice showed that specific chromosomal segments, but not the entire genome, function differently depending on the parental origin

mouse *Igf2r* was identified as the first imprinted gene

It was expressed only from the maternal allele.

To date, more than 100 imprinted genes have been identified in mice and many of them are also in humans.

All imprinted genes show either maternal-specific or paternal-specific mono-allelic expression, and their proper expression is essential for normal development, fetal growth, nutrient metabolism and adult behavior.

https://www.youtube.com/watch?v=g1XASDr-NWM

Multiple layers of Epigenetic regulations

Covalent Modifications
DNA and Histone modifications

Non covalent modifications
Histone variants, RNA trancripts – MiRNA, SiRNA

Genome wide analysis of analysis markers