Genetic Imprinting and Uniparental Disomy

Course instructor: Jibril H. Yusuf PhD.

E-mail: jibril.habib@tiu.edu.iq

Course: Genetics II (MA 206)

Summer class

Week 3

Date 16-08-2026

Outline

- What is Genetic Imprinting
- Mechanism of Imprinting.
- Disorders Associated with Genetic Imprinting
- Uniparental Disomy
- Mechanisms of UPD
- Diagnostic Approaches

Objectives

- To understand and explain the fundamental principles of Genetic Imprinting and Uniparental Disomy.

❑ What is Genetic Imprinting

- The concept of was discovered by **Metz (1938)** and **Crouse 1960**, who coined the term.

- Is an **epigenetic process** where certain genes are expressed in a **parent-of-origin-specific manner**.

- Imprinted genes are either **silenced** or **activated** depending on whether they are inherited from the **mother or the father**.

❖ Main Features of Genetic Imprinting:

- **Monoallelic expression**: Only one allele (either maternal or paternal) is expressed, while the other is silenced.

❖ **Imprinted genes are crucial for**:

✓ Regulating growth

✓ Development

✓ Metabolism.

❑ Mechanism of Imprinting

1. DNA Methylation:

- ✓ Addition of methyl groups to cytosine bases leads to the repression of one allele.

2. Histone Modifications:

- ✓ Changes in chromatin structure regulate gene expression.

3. Long Non-Coding RNAs :

- ✓ These can mediate gene silencing and activation.

❑ Examples of Imprinted Genes:

- **IGF2 (Insulin-like Growth Factor 2):**

❖ Paternally expressed and promotes fetal growth.

- **H19:**

❖ Maternally expressed and regulates growth suppression.

- **UBE3A:**

❖ Maternally expressed in the brain.

- **CDKN1C (Cyclin-Dependent Kinase Inhibitor 1C):**

❖ Maternally expressed and regulates **cell cycle progression** and is involved in **embryonic development**.

- **SNRPN (Small Nuclear Ribonucleoprotein Polypeptide N):**

❖ Paternally expressed and Involved in **RNA processing** and is crucial for **normal brain function**.

- **GRB10 (Growth Factor Receptor-Bound Protein 10):**

❖ Maternally expressed and Regulates **insulin signaling** and **glucose metabolism.**

- **PEG3 :**

❖ Paternally expressed and involved in **placental development**.

- **MEST :**

❖ Paternally expressed and Involved in **embryonic development and cell differentiation**.

- **DLK1 :**

❖ Paternally expressed and **development of various tissues** .

❑ Disorders Associated with Genetic Imprinting:

- Genetic imprinting plays a crucial role in development, and disruptions in imprinting can cause disorders such as:

1. Prader-Willi Syndrome (PWS):

- Cause: Loss of paternal expression of genes (**SNRPN, NDN, MAGEL2**) in the 15q11-q13 region.

- Symptoms:

- Hypotonia (low muscle tone), obesity, intellectual disability, and short stature.

2. Angelman Syndrome (AS):

- ✓ Cause: Loss of maternal expression of the **UBE3A gene** in the **15q11-q13 region**.

- Symptoms:

- ➢ Severe intellectual disability, seizures, ataxia, and a happy demeanor.

3. Beckwith-Wiedemann Syndrome (BWS):

✓ Cause: Abnormal imprinting of genes on chromosome 11p15 (e.g., **IGF2**).

- Symptoms:

➢ Overgrowth, increased risk of tumors, and organomegaly.

❑ Uniparental Disomy (UPD):

Definition: It occurs when both copies of a **chromosome are inherited from the same parent**, instead of one copy from each parent.

Types of UPD:

1. Heterodisomy: Two different homologous chromosomes from the same parent.

2. Isodisomy: Two identical copies of a chromosome from one parent.

❑ Mechanisms of UPD

1. Trisomy Rescue:

- ✓ A fertilized zygote with three copies of a chromosome loses one copy, potentially leading to UPD.

2. Monosomy Rescue: :

- ✓ Duplication of a single chromosome in a monosomic zygote.

3. Gamete Complementation:

- ✓ Union of a disomic gamete with a nullisomic gamete.

Consequences of UPD

1. **Imprinting Disorders**: If the affected chromosome contains imprinted genes, UPD can lead to disorders such as PWS, AS, and BWS.

2. **Recessive Disease Manifestation**: In cases of isodisomy, a recessive mutation inherited from one parent may be expressed, leading to a genetic disorder.

❑ Diagnostic Approaches

A. **DNA Methylation Analysis**:

- ✓ Detects abnormal imprinting patterns, Used to diagnose conditions like PWS and AS.

B. **Chromosomal Microarray (CMA)**:

- ✓ Identifies chromosomal deletions or duplications associated with imprinting disorders.

C. **Molecular Testing for UPD**:

- ✓ Microsatellite analysis or SNP array can confirm the parent-of-origin of chromosomal regions.

❑ Clinical and Research Implications:

1. Importance in Development:

❖ Imprinted genes regulate critical processes like growth, placental function, and brain development.

2. Assisted Reproductive Technologies (ART):

❖ ART may increase the risk of imprinting disorders due to epigenetic changes during embryo culture.

3. Personalized Medicine:

- Understanding imprinting and UPD can inform therapeutic approaches for genetic and epigenetic disorders.

4. Research in Epigenetics:

- Imprinting disorders provide a model for studying epigenetic regulation and inheritance.

❖ Quiz:

Fill in the blanks

1. **Genetic imprinting is an _____ process that causes parent-of-origin-specific gene expression.Answer: epigenetic**
2. **The human gene IGF2 is normally expressed predominantly from the _____ allele.Answer: paternal**
3. **The gene UBE3A is predominantly expressed from the _____ allele in neurons.Answer: maternal**
4. **Uniparental disomy occurs when both copies of a chromosome are inherited from _____ parent.Answer: one**
5. **Prader–Willi syndrome is associated with abnormal expression of imprinted genes on chromosome _____.Answer: 15.**
6. **Genetic imprinting changes the DNA nucleotide sequence of an imprinted gene.**
7. **IGF2 is a classic example of a paternally expressed imprinted gene.**
8. **Angelman syndrome can result from loss of maternal UBE3A function in neurons.**
9. **Define genetic imprinting.**
10. **Give two examples of imprinted genes.**
11. **Differentiate between maternal and paternal UPD.**

References

1. Reik, W., & Walter, J. (2001). Genomic imprinting: parental influence on the genome. Nature Reviews Genetics, 2(1), 21-32.

2. Cassidy, S. B., & Driscoll, D. J. (2009). Prader-Willi syndrome. European Journal of Human Genetics, 17(1), 3-13.

3. Kotzot, D. (2008). Complex and segmental uniparental disomy updated. Journal of Medical Genetics, 45(9), 545-556.

Thanks