Angelman Syndrome

1. Introduction

Angelman Syndrome is a neuro-genetic disorder caused due to loss of function of the maternal UBE3A gene on chromosome 15q11–q13. It affects the nervous system and leads to developmental delay, speech problems, and characteristic behavior.

2. Genetic Basis

Angelman Syndrome occurs because UBE3A gene is active only on the maternal chromosome in certain brain cells. The paternal UBE3A is normally imprinted (silenced).

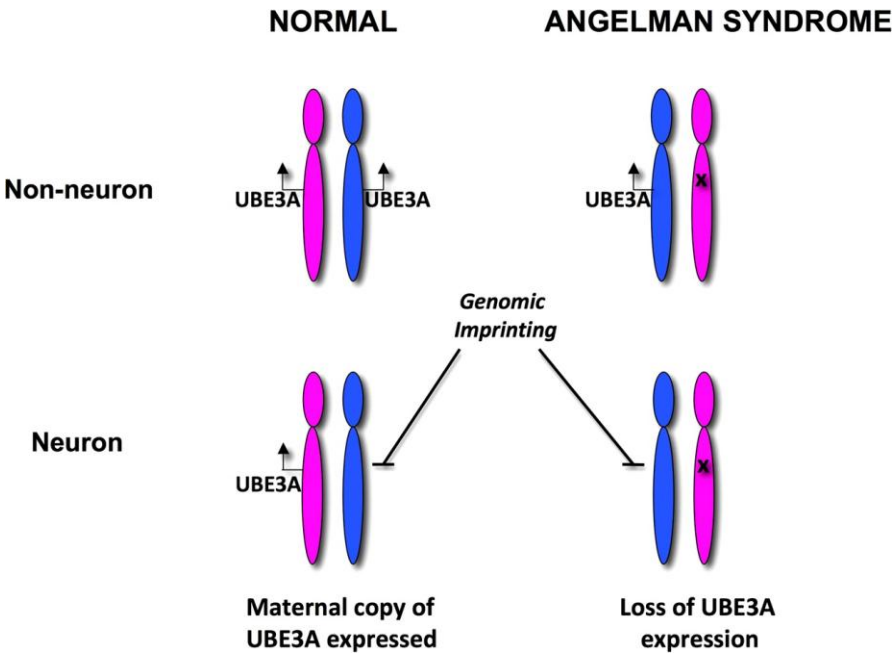
Mechanisms that cause AS:

1. Maternal deletion (70%) – Deletion of maternal 15q11–q13 region.

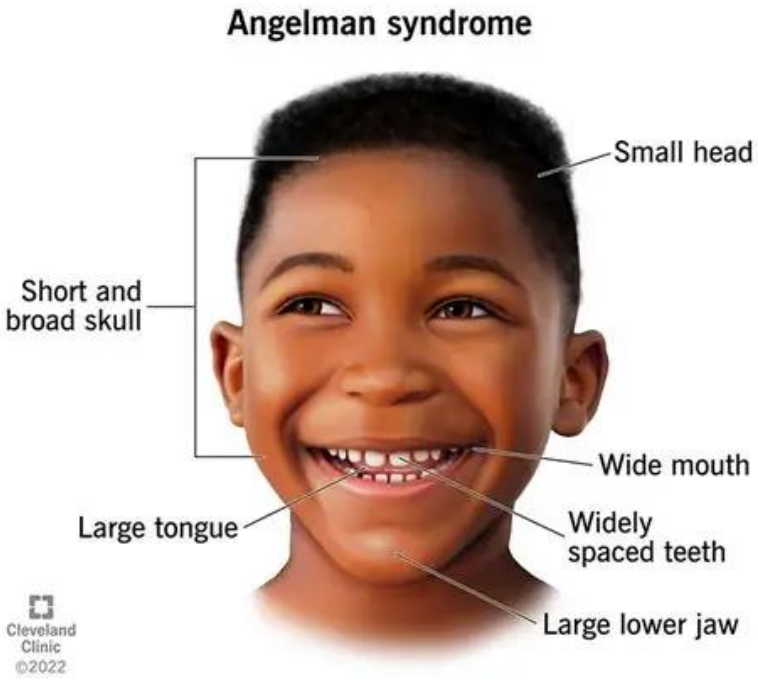
2. Paternal uniparental disomy (UPD) (2–5%) – Child inherits both chromosome 15 copies from father.

3. Imprinting defect (3–5%) – Maternal chromosome present but imprinting control region is defective.

4. UBE3A gene mutation (10%) – Mutation in maternal UBE3A.



3. Key Features / Symptoms



Neurological:

- Severe developmental delay
- No or minimal speech
- Ataxia
- Seizures
- Tremors

Behavioral:

- Happy disposition
- Frequent smiling and laughter
- Hyperactivity

Physical Features:

- Microcephaly
- Wide mouth, protruding tongue
- Strabismus
- Sleep disturbances
- Fair skin and light-colored hair (in deletion cases)

Other:

- Feeding difficulty
- Constipation

4. Diagnosis

- DNA methylation test

- FISH for deletion of maternal 15q11–q13

- UPD testing

- UBE3A gene sequencing

- EEG shows high-amplitude slow waves with spikes.

5. Inheritance Pattern

Usually not inherited (de novo). If caused by UBE3A mutation or imprinting defect, may show autosomal dominant inheritance with imprinting effect.

6. Difference Between Angelman Syndrome and Prader–Willi Syndrome

Angelman Syndrome:

- Maternal gene lost

- UBE3A affected

- Happy behavior, laughter, ataxia, severe speech impairment

Prader–Willi Syndrome:

- Paternal gene lost

- Multiple genes affected

- Hyperphagia, obesity, short stature, hypotonia in infancy