6.3 Non-Mendelian inheritance

Name: _____ Class: _____ Date: _____ **Total: 23 marks**

KEY WORDS genomic imprinting

Objective

Recognise the non-Mendelian signatures and reason about parent-of-origin and repeat instability.

1 Key knowledge and worked examples

■ **The three layers**

mtDNA: maternal-only, heteroplasmy lottery. Imprinting (15q): paternal deletion → Prader–Willi, maternal → Angelman ✓. Repeat expansion: anticipation (CAG/CGG grow per meiosis).

■ **Worked example: one region, two syndromes**

Only one parental copy of 15q is active (methylation): delete the WORKING copy → disease, so the parent of origin decides the syndrome ✓.

2 Practice

2.1 Which non-Mendelian pattern affects all children of an affected mother? [3]

2.2 What parental-origin deletion gives Angelman? [3]

2.3 Define anticipation. [3]

3 Exam-style questions

3.1 A family has affected mothers, affected children of both sexes, and no male transmission over three generations (fictional).

Identify the pattern. Explain the severity spread (heteroplasmy and the meiotic bottleneck). Predict the risk to an affected woman's next child. [7]

3.2 A fragile-X family: the grandmother has a 70-CGG premutation; her daughter 150; her grandson >200 with the full syndrome (fictional).

Explain the expansion trend (premutation range 55–200; full >200). Explain why daughters of premutation carriers are at expanding risk. State the Huntington contrast (paternal CAG expansions → juvenile onset). [7]

Solutions

2.1

- Mitochondrial inheritance.

2.2

- Maternal (UBE3A region).

2.3

- Earlier and/or more severe disease in successive generations as the repeat expands.

3.1

- Mitochondrial (MELAS-pattern) inheritance.
- Each child samples a different fraction of mutant mtDNA at the meiotic bottleneck: severity varies from deafness/diabetes to encephalopathy.
- Each child is at risk; the probability of severe disease depends on the mother's mutant load and the sampled bottleneck.

3.2

- Repeats expand through female transmission: $70 \rightarrow 150 \rightarrow >200$ crosses from premutation to full mutation.
- Expansion risk rises with maternal repeat length; daughters inherit the expanded allele.
- Huntington: paternal CAG expansion gives juvenile onset – the parent-of-sex direction differs by disease.