

Exercise walk-through

6.3

Non-Mendelian inheritance

University Medicine

Non-Mendelian: three extra layers

- 1 **mtDNA** Maternal line only; all children of an affected mother at risk; heteroplasmy = severity lottery.
- 2 **Imprinting** Same 15q deletion: paternal → Prader-Willi, maternal → Angelman - parent of origin IS the disease.
- 3 **Repeats Anticipation**: CAG/CGG repeats expand each **meiosis** - earlier, more severe (fragile-X premutation 55-200 → full >200).

Non-Mendelian - the figure

three signatures Mendel never saw

mitochondrial

maternal line only — ALL children of an affected mother

imprinting (15q)

same deletion: paternal → Prader-Willi; maternal → Angelman

repeat expansion

anticipation: repeats grow — earlier and more severe

heteroplasmy · parent-of-origin · instability

Mitochondrial, imprinting, repeat-expansion signatures compared.

Exercises 2.1-2.3

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]

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2.1

- Mitochondrial inheritance.

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

2.2

- Maternal (UBE3A region).

2.3 Define anticipation. [3]

2.3

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

Exercise 3.1

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]

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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.

Exercise 3.2

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).

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3.2

- Repeats expand through female transmission: 70 → 150 → >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.