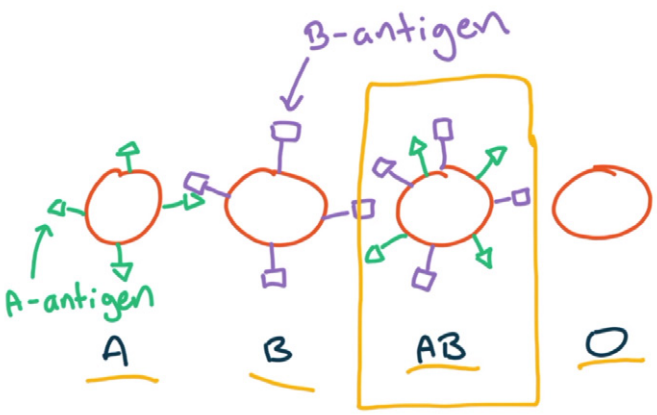
GENETICS

Section I - Genetics Overview

Term	Definition	Example
Codominance	Multiple alleles associated with a gene are simultaneously expressed	Blood groups
Incomplete penetrance	Individuals who carry the mutant genotype but do not express the mutant phenotype	BRCA1 may cause breast cancer in one individual but the other individual may remain cancer free
Variable expressivity	Variability in the phenotype expressed by individuals with the same genotype	Patients with neurofibromatosis type I (NF1) may have cutaneous neurofibromas covering the entire body or only a small part of the body (all patients have 100% penetrance) (Figure 2.4.2)
Pleiotropy	One gene is responsible for multiple phenotypic manifestations	Homocystinuria causes multiple symptoms affecting multiple organs (lens dislocation, DVTs, Marfanoid habitus, and intellectual disability)
Anticipation	The tendency of a disease to occur earlier or to be more severe in succeeding generations	Huntington disease
Loss of heterozygosity	Refers to the idea that tumor suppressor genes must develop mutations in both alleles before cancer will develop	Retinoblastoma (Figure 2.4.3)
Germline mosaicism	The presence of multiple, genetically distinct cell lines in the gametes	(Figure 2.4.4)
Somatic mosaicism	The presence of multiple, genetically distinct cell lines within the cells that form the body	Turner syndrome McCune-Albright syndrome (Figure 2.4.5)
Locus heterogeneity	The same phenotype can be caused by mutations at different loci	Albinism
Allelic heterogeneity	The same phenotype can be caused by mutations in the same locus	β-thalassemia
Heteroplasmy	The presence of both mutated and normal mitochondrial genomes within a single cell	Mitochondrial disorders (Figure 2.4.6)
Dominant negative mutation	The mutation results in a dominant effect	A nonfunctional protein prevents another normal protein from functioning properly

Table 2.4.1 - Genetic terms



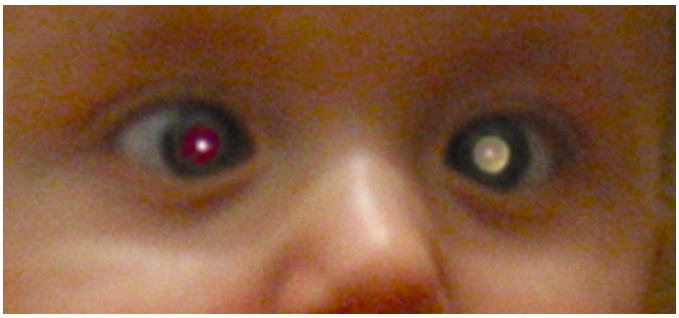


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Figure 2.4.2 - Retinoblastoma

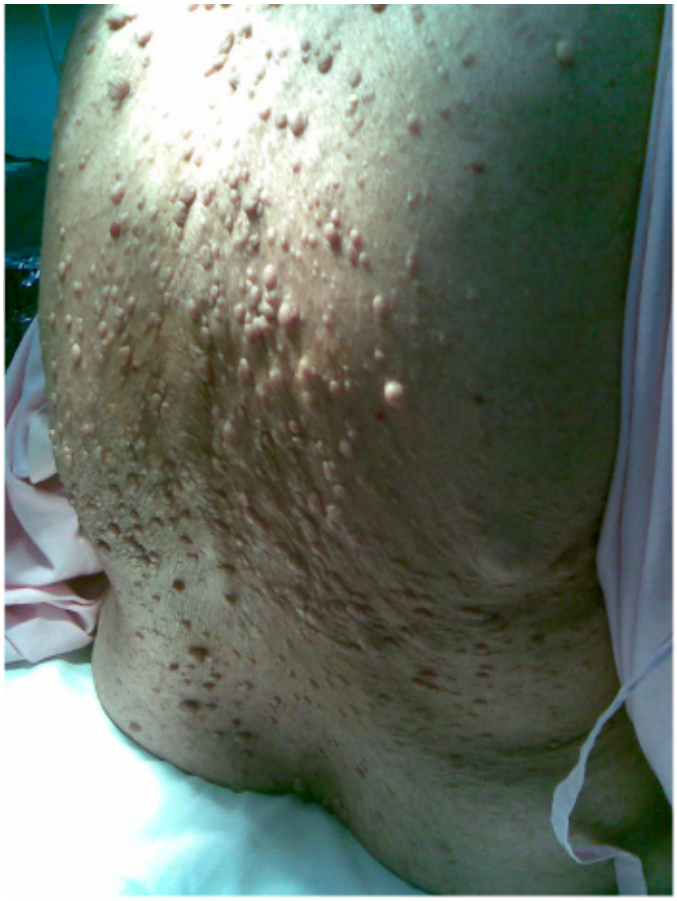

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Figure 2.4.1 - Neurofibromas

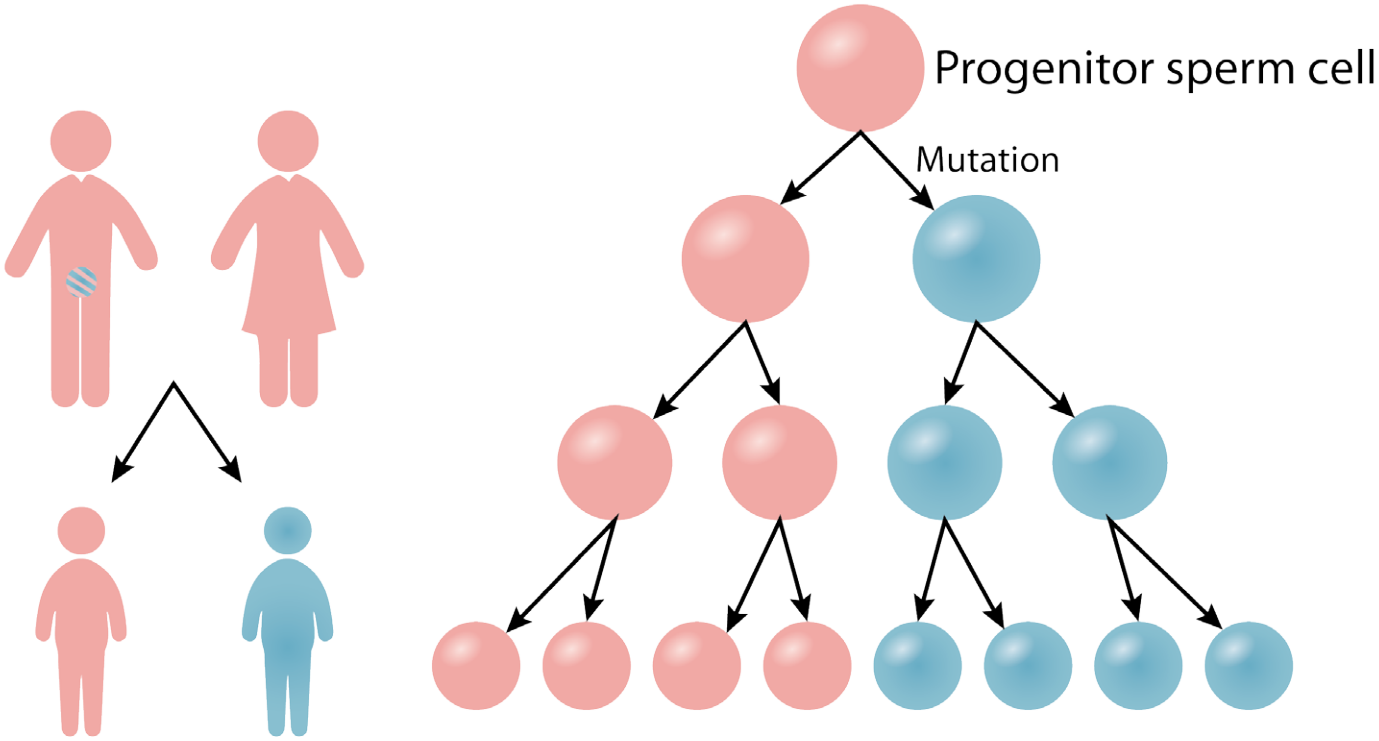


Figure 2.4.3 - Germline mosaicism

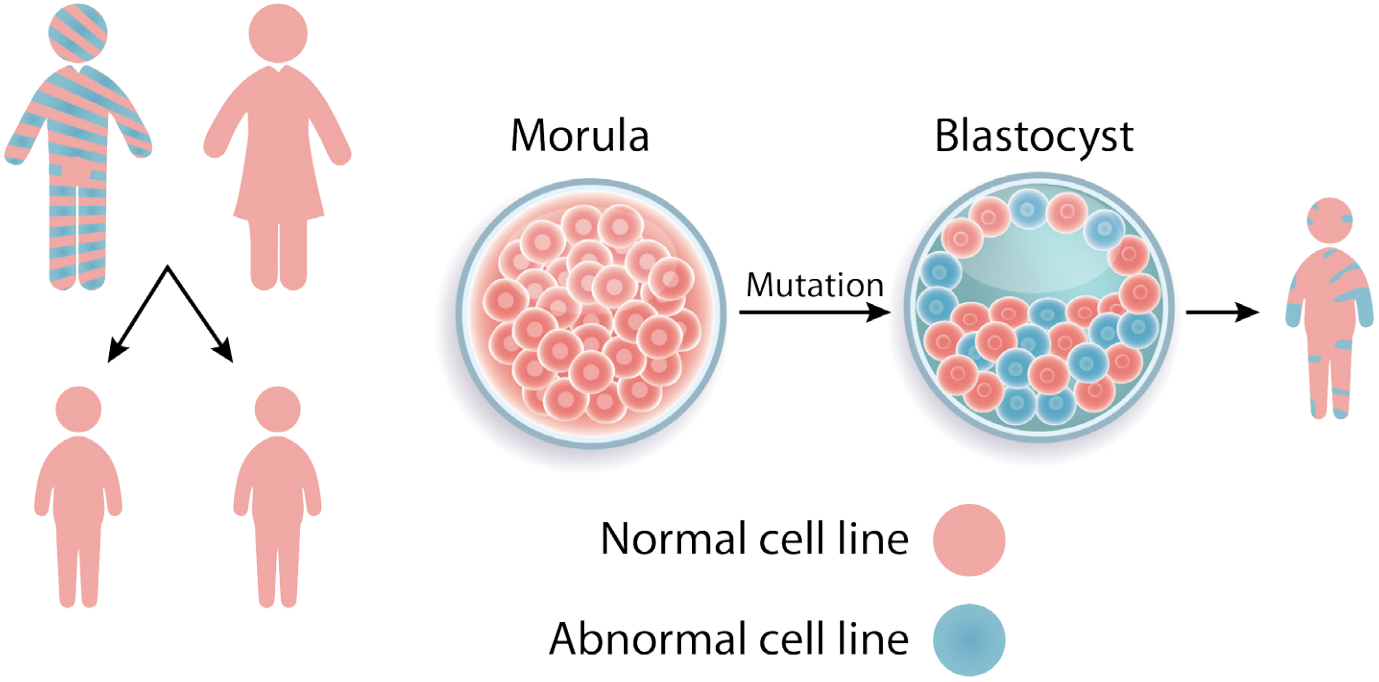
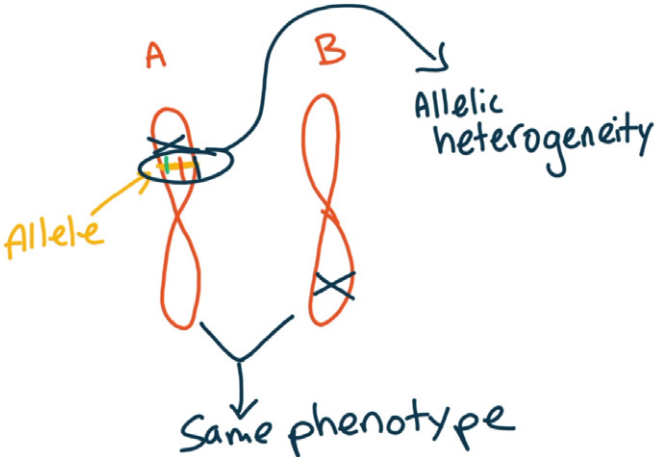
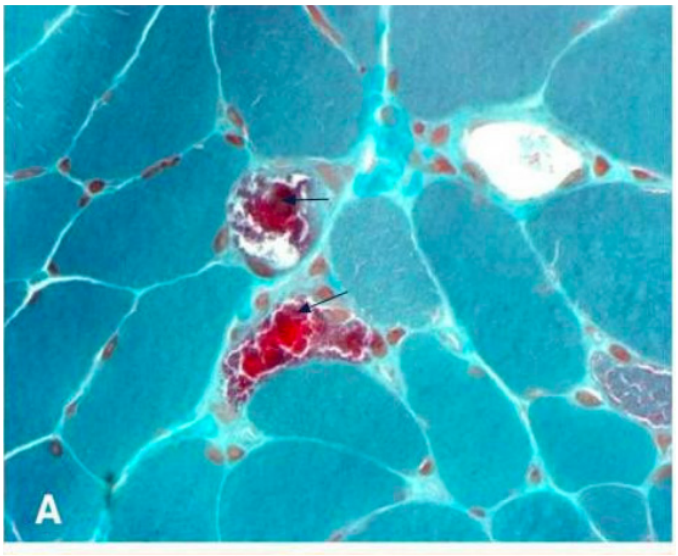


Figure 2.4.4 - Somatic mosaicism





By Modified_Gomori_trichrome_stain_showing_several_ragged_red_fibers_.jpg: Abu-Amero KK, Al-Dhalaan H, Bohlega S, Hellani A, Taylor RW.derivative work: CopperKettle [CC BY 2.0 (https://creativecommons.org/licenses/by/2.0)], via Wikimedia Commons

Figure 2.4.5 - Gomori trichrome stain of ragged-appearing muscle fibers

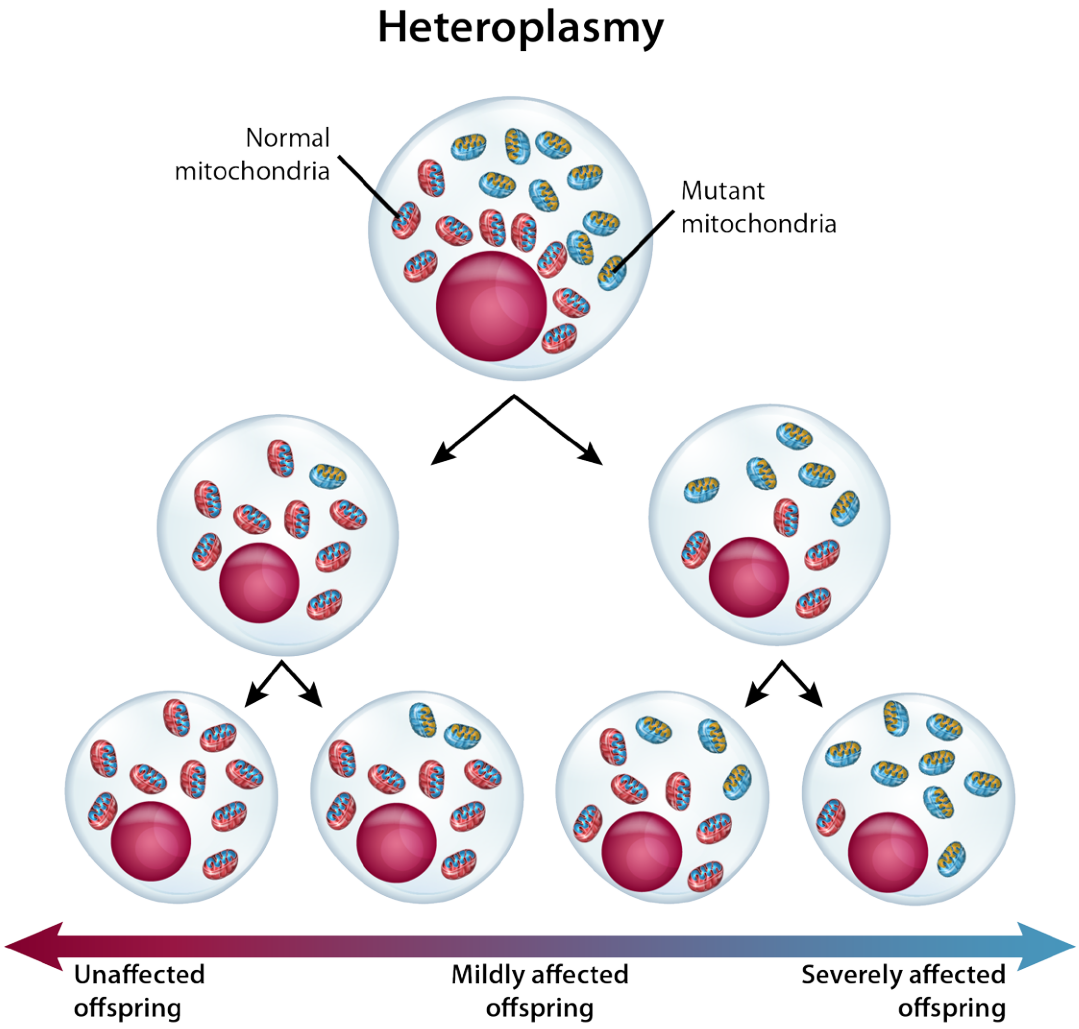


Figure 2.4.6 - Heteroplasmy

REVIEW QUESTIONS

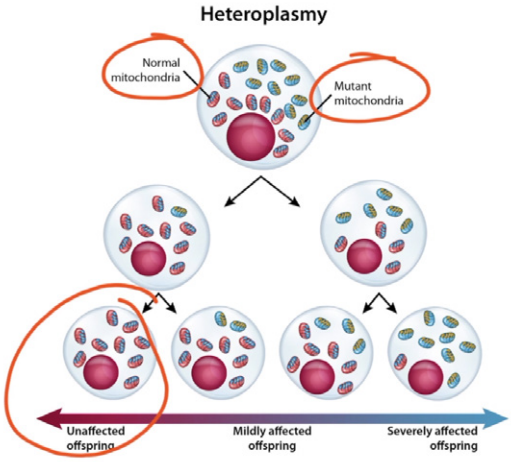
1. A 1-day-old boy is born to a healthy 25-year-old female at term. On exam the boy is noted to have upslanting palpebral fissures, a single palmar crease bilaterally, and prominent epicanthal folds. FISH analysis on cultured fibroblasts shows that 70% of the cells have 47 chromosomes while 30% of the cells have 46 chromosomes. What genetic principle most likely explains these findings?

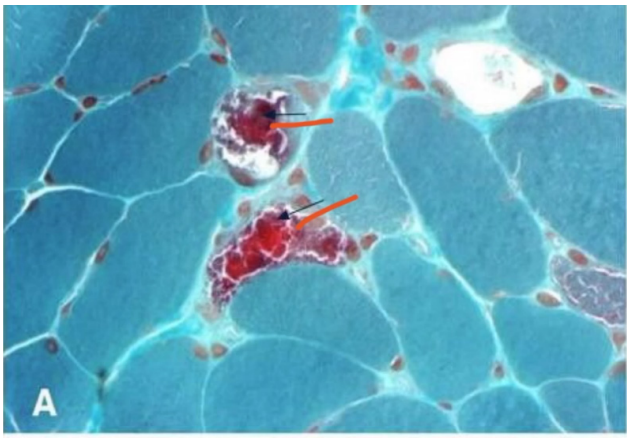
    A) Meiotic nondisjunction
    B) Germline mosaicism
    C) Somatic mosaicism
    D) Loss of heterozygosity
    E) Variable expressivity

- **Correct answer is C**
- **Upslanting palpebral fissures, a single palmar crease bilaterally, and prominent epicanthal folds → Down syndrome**
- **FISH reveals two distinct cell lines (70% of the cells have 47 chromosomes while 30% have 46 chromosomes) → somatic mosaicism**

2. A 41-year-old female presents to the physician for chronic muscle weakness. A skeletal muscle biopsy reveals ragged-appearing muscle fibers. DNA analysis reveals a mutation in 70% of the mitochondrial DNA. The physician is concerned about the possibility of the disease affecting the patient's children. However, the patient states that none of her children have any symptoms. What genetic principle most likely explains the absence of symptoms in this patient's children?

- **Heteroplasmy**
- **The patient has chronic muscle weakness and a mutation in 70% of her mitochondrial DNA yet none of her children have symptoms**
- **The 30% of her normal mitochondria can be passed onto her children resulting in unaffected offspring**
- **Mitochondrial diseases usually present with muscle weakness and a biopsy will reveal ragged-appearing muscle fibers**





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