18 - Mitochondrial inheritance

Mitochondrial inheritance

© SPMM Course of the sons will be affected, and half of the daughters will be carriers. e.g. haemophilia A/B, Duchene muscular dystrophy, and androgen insensitivity syndrome. X-linked dominant disorders These are rare. Similar to X-linked recessive pattern, male-male transmission of the disease-causing mutation is not seen. Because females have higher gene frequency for X chromosomes compared to males, females have twice as much chance than males to inherit an X-linked disease-causing mutation. Vitamin D-resistant rickets is the best-known example. Females who are heterozygous for the mutant gene and males who have one copy of the mutant gene on their single X chromosome will manifest the disease. As in autosomal dominant inheritance, the disease phenotype is seen in multiple generations making ‘skipped generations’ relatively unusual. If the affected male mates with homozygous normal female, none of the sons will be affected but all of the daughters will be affected. Heterozygous female mating a normal male will result in 50% of sons being affected and 50% of daughters being affected. An atypical pervasive developmental disorder called Rett’s syndrome is inherited in X-linked dominant fashion. B. Non Mendelian inheritance Mitochondrial inheritance, mosaicism, trinucleotide expansions and genomic imprinting do not follow normal Mendelian principles and so are called non-Mendelian inheritance. Polygenic and multifactorial disorders too, do not obey Mendelian principles in strict sense. Mitochondrial inheritance Mitochondrial DNA is wholly inherited from the ovum. The sperm has no mitochondria in its ‘head’; ‘head’ is made of nuclear material and acrosomal cap. The ‘body’ of sperm has many mitochondria that provide energy in propelling the ‘tail’. The ‘body’ and ‘tail’ are shed on entry of sperm into the ovum. Hence the mitochondria of an embryo are completely maternal-derived. The mitochondrial chromosome has no introns in the genes. Therefore any mutation has a high chance of having an effect. Most mitochondrial diseases are myopathies and neuropathies. This is important in clinical genetics as mitochondrial DNA abnormalities result in various diseases such as MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and recurrent stroke syndrome) and Leber hereditary optic neuropathy. X-LINKED MENTAL RETARDATION (XLMR) Learning disability is significantly more common in males than in females. So X linked genes are a suspect in their aetiology.

XLMR is a heterogenous condition - subdivided into syndromic (1/3rd) and nonsyndromic (2/3rd) forms, depending on the presence of further abnormalities.

The most common form of XLMR is the Fragile X syndrome.

Mutations in MECP2 gene in X chromosome give rise to a wide range of disorders, including female-specific Rett syndrome. MECP2 mutations also lead to other phenotypes such as severe encephalopathy, progressive spasticity, Angelman and PraderWilli like phenotypes and nonsyndromic XLMR in males

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