Fragile X syndrome

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Fragile X Syndrome (Fragile X Chromosome Syndrome, Martinuv-Bell syndrome) is a disease that got its name from a specific chromosomal abnormality -**fragility** in the subterminal part of the long arms X chromosome (band Xq27.3 – **FRAXA**), which occurs in a part of cells under special culture conditions (low serum content, reduced folic acid content in the medium).

Fragile X syndrome is characterized by an elongated face, large ears, prominent chin.

Pathogenesis

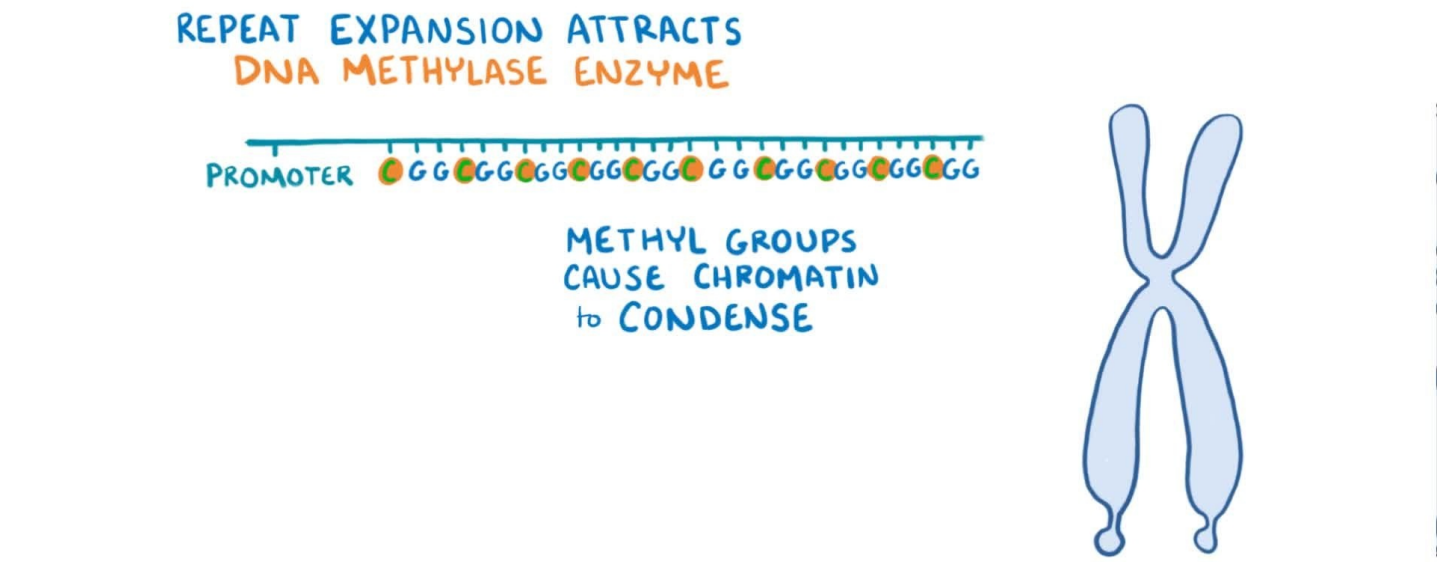
In affected mentally retarded men, there is an amplification of trinucleotide sequences in the promoter of the FMR1 gene located in this region of the X chromosome. **CCG / CGG**. This mutation arises from a so-called **premutation** occurring in the mothers of affected men who have this amplification to a lesser extent (50-200 copies). Normal individuals also have some repeats of this sequence, but to a much lesser extent than individuals with the premutation (6–50 copies). The transformation of an unstable premutation into a full mutation (i.e. an increase in the length of the amplificate to more than 200 copies) occurs **only during transmission by a woman**, no elongation occurs when the element passes through spermiogenesis. A **full mutation**, i.e. an increase in the trinucleotide repeat above 200 copies leads to methylation of this element, and since it is located in the promoter of the gene, arrest of transcription of the gene occurs and the '"mental retardation"' and other clinical manifestations. It is assumed that amplification of the amplification can occur only in early embryogenesis (but it is determined in gametogenesis), which is evidenced by somatic heterogeneity in the length of the repeat, degree of methylation, and also the existence of individuals - mosaics full of mutation and premutation.

"New mutations" have *not been described* in this disease, i.e. the emergence of a full mutation in the offspring of a person with a normal number of repeats. The formation of a full mutation always happens by gradually increasing the element through premutation. The length of the repeat sequences **correlates with the degree of mental retardation** and with cytogenetic expression.

There is an **other fragile site** (FRAXE) on the X chromosome associated with mild mental retardation.

Clinical signs

- **mental retardation**,
- elongated face,
- rough features,
- big ears,
- macroorchidism.



Links

Related Articles

- Instability of repetitive sequences
- Chromosomal Abnormalities
- Huntington's disease
- Mutation

References

- THOMPSON, James Scott – THOMPSON, Margaret Wilson – NUSSBAUM, Robert L. *Klinická genetika: Thompson & Thompson.* 6. edition. Triton, 2004. 426 pp. ISBN 80-7254-475-6.
- NUSSBAUM, R. – MCINNES, R. R. – WILLARD, H. F. *Thompson & Thompson: Genetics in Medicine.* 7. edition. Saunders, 2007. 600 pp. ISBN 1416030808.