Subtelomeric rearrangements of chromosomes

Subtelomeric chromosome rearrangements are submicroscopic or cryptic aberrations in the subtelomeric regions of various chromosomes. With the greatest frequency, these aberrations appear on chromosomes **1, 2, 5, 6, 8, 9, 12, 16, 18p** and **22q**. The most common are deletions, but translocations and duplications are not rare either. In almost 50 percent of cases of patients with subtelomeric deletions, the same rearrangement is also found in one of the parents, but it is a balanced form.

Analysis

Subtelomeric rearrangements were hidden from scientists until the invention of fluorescence in situ hybridization (FISH) and other modern **molecular cytogenetic methods**, such as chromosome CGH or array CGH. Classical cytogenetic methods cannot identify these aberrations. The most common analysis is performed by the FISH method using locus-specific subtelomeric probes. However, due to the small number of affected individuals, the investigation must be performed on a considerably large set of patients, in whom the subtelomeric regions of all chromosomes must be analyzed. Another problem is that these are very small-scale rebuilds. Beyond the telomere, which in all human chromosomes consists of several kilobase-long blocks containing characteristic repetitive sequences (**TTAGGG**)$_n$, there are gene loci that alternate with **TAR** (z angl. telomere associated repeats) regions. TAR regions are repetitive sequences associated with telomeric regions of chromosomes. However, most probes only hybridize to loci located beyond the TAR region toward the centromere. Sections in the TAR area are mostly examined using array CGH.

Clinical significance

Analysis of subtelomeric rearrangements may help clarify the cause of a significant proportion of mental retardation, for which there is no obvious cause (previously they were referred to as idiopathic). Mental retardation is defined as a condition where the patient's IQ does not exceed 70. According to the severity of the mental disorder, mental retardation is divided into 4 degrees: mild (IQ 50-70), moderate (IQ 35-50), severe (IQ 25-35) and profound (IQ 20–25) mental retardation. The first stage is characterized by limited educability, persons affected by the last stage are not able to live without constant supervision. Currently, the cause of mental retardation can only be explained in 50-60 percent of patients. In some of them, cryptic aberrations were found in the subtelomeric regions of certain chromosomes. For successful research, it is very important to select a suitable sample of patients affected by mental retardation for further examination. They should meet certain criteria, which are summarized in the professional literature in the abbreviations MR, DD, NDF, which means: Mental Retardation, Developmental Delay, Nonspecific Dysmorphic Features. It is also important to carefully consider whether mental retardation is really caused by genetic factors and not by other influences (e.g. degenerative disease of the central nervous system).

Links

related articles

- Chromosomal abnormalities
- Structural chromosomes aberrations
- Telomeres and telomerase
- Chromosome

References

- KOČÁREK, Eduard – PÁNEK, Martin. *Klinická cytogenetika I : úvod do klinické cytogenetiky.* 2. edition. Praha : Karolinum, 2010. ISBN 978-80-246-1880-7.