Chromosomal aberrations in the etiology of neoplasms

Chromosome aberation we mean mainly chromosome aberrations in the sense of their disruption. hey are determined by cytogenetic examination. In addition to chromosomal changes in neoplasms, aberrations are also seen in some congenital diseases. The introduction of more detailed banding techniques has The introduction of more detailed banding techniques has . The malignant cells of most tumors have chromosomal changes, many of which are stable. Typical are **deletions**, **balanced translocations** (one chromosome is affected regularly, i the breakpoint; na on this chromosome is permanent, but the other chromosome involved may always be different) and less frequent are **trisomies** of some chromosomes.

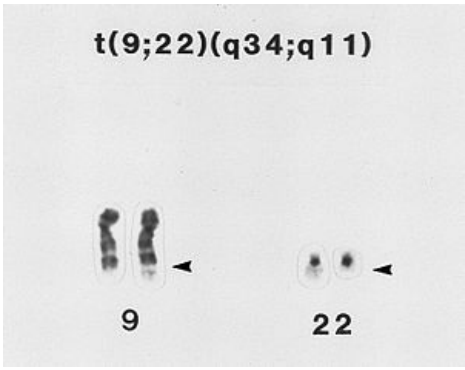
Permanent changes diagnosed in human tumors

Chronic myeloid leukemia

Reciprocal translocation between chromosome 22 and 9 – **t(9;22)(q34;q11)** occurs in about 95% of adult **chronic myeloid leukemia** . This aberration is called the **Philadelphia chromosome** (according to the place of discovery).

Burkitt's lymphoma

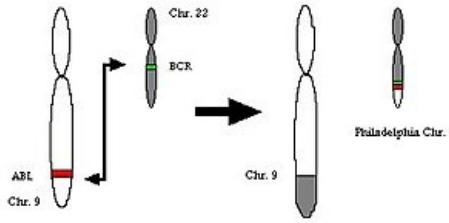
Tumor-transformed B-lymfocytes are removed by immunological mechanisms with the crucial involvement of T cells.T-lymphocytes on their surface recognize virus -induced TSTA *tumor-specific transplant antigens* (TSTA) presented by MHC molecules.In the absence of T-cells or in the suppression of their activity, tumor growth develops rapidly. Most patients have a stable **reciprocal translocation between chromosomes 8 and 14** – most commonly t(8;14)(q24;q32). Malignancy occurring in Central Africa; and typical is osteolytic jaw lesion.



Philadelphia chromosome, t(9;22)(q34;q11)

Retinoblastoma

Its an **embryonic retinal tumor**, that occurs in hereditally form and in isolated form. In the hereditary form, more tumors develop (multifocal onset), usually in both eyes (bilateral onset), and there is an increased risk of other primary malignancies - such as osteosarcoma (tumor multiplicity). The deletion on chromosome 13 in the 13q14 region affects the genr **Rb1** (OMIM: 180200 (https://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=180200)). Familial retinoblastoma is one of the hereditary tumor syndromes, segregating in families as an AD trait.



Scheme of the Philadelphia chromosome. The formation of the BCR-ABL fusion gene is shown.

Lung karcinoma

Deletion or translocation of part of chromosome 3, namely the p14-23 region.

Asociation of Aniridia and Wilms' tumor

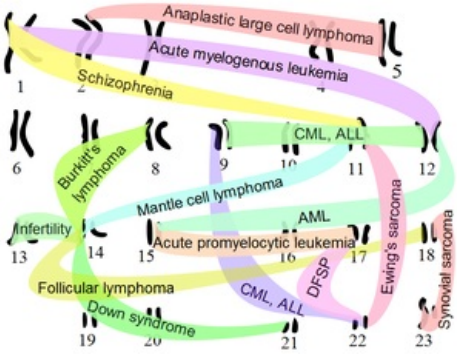
Deletion of section of chromosome 11, in the region **11q15**. **Wilms' tumor** is a malignant tumor of the kidney that usually manifests in early childhood or even prenatally. **Aniridia** (lack of iris) and Wilms' tumor can manifest independently of each other. Many patients often have other malformations, **mental retardation**, genital malformations, and developmental delays (**WAGR snydrome** - a mikrodeletion syndrome). In many patients with this association, a deletion of the 11q region is evident and one of the oncogenes, the so-called – tzv. *c-Ha-ras* , is located at the site of the deletion .

Secondary chromosome changes

During the development of neoplasias, their cells may acquire different chromosomal changes, which may not be accidental. E.g. in chronic myeloid leukemia , patients in the terminal stage of the disease have excessive Philadelphia chromosomes, trisomy 8, or the isochromosome of the long arms of chromosome 17, while men lose the Y chromosome. These abnormalities are associated with the selection and proliferation favor of malignant clones. Changes often occur in solid tumors, where homogeneously staining regions (HSR – Homogeneously Staining Regions) and acentric fragments are formed; its most probably **gene amplification**. Multiplying the gene dose may be important for the loss of control over tumor growth and aggression.

Relationship of oncogenes to chromosomal aberrations

Onkogenes form a group of many genes. These genes are **structurally and functionally heterogeneous** and are important in the transformation of a cell into a malignant one. They occur in the cell in the form of proto-oncogenes and are activated either by association with a retrovirus or by mutations. Oncogene names are **abbreviations** erived from their origin - for example, ***c-myc*** was originally found in **B-cells of avian myelocytoma .** Throughout evolution , oncogenes have been conserved and are thought to be present in at least one copy in the human genome. he most well-known relationship between oncogene and chromosome aberration is the **association of *c-myc* with t(8;14)** in case os Burkitt's lymfoma. In humans, *c-myc* is located in the region of lane 8q24, which is involved in **translocation**. The translocation thus brings the *c-myc* close to the 14q32 region with the gene encoding the imunoglobulin heavy chain. In some cases, translocation results in up to a 20-fold **increase transcription of** c-myc; in others, an abnormal gene product is formed.



Scheme of various chromosomal translocations and their relation to selected diseases

Links

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- Structural chromosomal aberrations
- Numerical chromosomal abnormalities
- Tumor cytogenetics
- Characteristics of tumor-transformed cels
- Oncogenes
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- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 2009]. <http://www.stefajir.cz>.