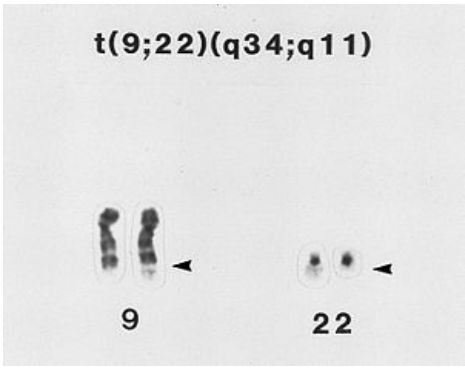
Chromosome aberrations in the etiology of neoplasia

By chromosomal aberrations we mean in particular deviations of chromosomes in sense of their disruption. They are detected during a cytogenetic examination. In addition to chromosomal changes in neoplasias, aberrations are also demonstrated in some congenital diseases. The introduction of more detailed banding techniques led to detailed knowledge of chromosomal changes in cancer . Malignant cells of most tumors have chromosomal changes, many of which are permanent. Typical are **deletions**, **balanced translocations** (one chromosome is regularly affected, even the break point on this chromosome is constant, but the next involved chromosome can always be different) and less frequent **trisomies** of some chromosomes.

Permanent changes diagnosed in human tumors

Chronic myeloid leukemia

A 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).



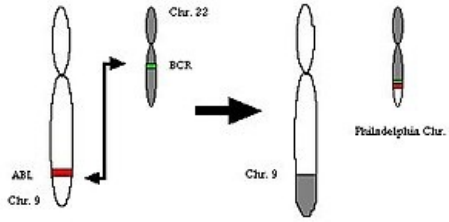
Philadelphia_chromosome,_t(9;22)_translocati

Burkitt's lymphoma

Tumor-transformed B-lymphocytes are eliminated by immunological mechanisms with the decisive participation of T-cells. T-lymphocytes on their surface recognize virus-induced TSTA *tumor-specific transplantation antigens* (TSTA) presented by MHC molecules. In the absence of T-cells or when their activity is suppressed, rapid development of tumor growth will occur. Most patients have a stable **reciprocal translocation between chromosomes 8 and 14** – most often t(8;14)(q24;q32). A malignancy occurring in central Africa; an osteolytic lesion of the jaw is typical.

Retinoblastoma

It is an **embryonic tumor of the retina**, which occurs both hereditary and isolated. In the hereditary form, multiple tumors arise (multifocal onset), usually in both eyes (bilateral onset), while there is also an increased risk of other primary malignancies – e.g. osteosarcoma (tumor multiplicity). A deletion on chromosome 13 in the 13q14 region affects the Rb1 gene **Rb1** (OMIM: 180200 (https://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=180200)). Familial retinoblastoma is one of the hereditary tumor syndromes,it segregates in families as an AD trait.



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

Lung carcinoma

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

Association of Aniridia and Wilms Tumor

Deletion of a section of chromosome 11, namely in the **11q15**. **Wilms tumor** is a malignant tumor of the kidney that usually manifests itself in early childhood or even prenatally. Both **Aniridia** (lack of iris) and Wilms tumor can manifest independently. Many patients often have other malformations, **mental retardation**, genital malformations and delayed physical development (**WAGR snydrom** - belongs to microdeletion syndromes). Many patients with this association have a demonstrable deletion of the 11q section, and one of the oncogenes - the so-called c-Ha-ras - is located at the site of the deletion.

Secondary chromosomal changes

During the development of neoplasia, their cells can acquire different chromosomal changes, which, however, may not be random. E.g. in chronic myeloid leukemia, in patients in the terminal stage of the disease, supernumerary Philadelphia chromosomes, trisomy 8 or the isochromosome of the long arms of chromosome 17 appear, in males the chromosome Y is lost. These abnormalities are related to the selection and proliferative advantage of malignant clones. Changes often occur even in solid tumors, homogeneously staining regions (HSR - Homogeneously Staining Regions) and acentric fragments are formed; these are probably places of **gene amplification**. Multiplication of gene dosage may be important for loss of control over tumor growth and aggressiveness.

Relationship of oncogenes to chromosome aberrations

Oncogenes 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. The names of oncogenes are **abbreviations** derived from their origin – for example,***c-myc*** was originally found in the **B-cells of avian myelocytoma .**.Oncogenes have been conserved throughout evolution, and each is thought to be present in at least one copy in the human genome. The most well-known relationship between an oncogene and a chromosomal aberration is **the *c-myc* st(8;14) association**in the case of Burkitt's lymphoma. In humans *c-myc* is localized to the 8q24 stripe region, which is involved in **translocation**. The translocation thus brings the *c-myc* gene close to the region of 14q32 with the gene that encodes the immunoglobulin heavy chain. In some cases, the translocation leads to up to a 20-fold **increase** in c-myc transcription; in others, an abnormal gene product is formed.

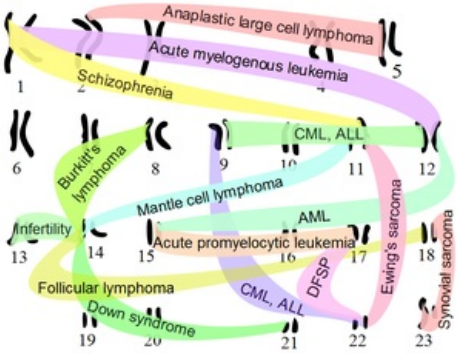


Diagram of various chromosomal translocations and their relationship to selected diseases

Links

related articles

- Chromosomal abnormalities
- Structural chromosomal aberrations
- [Numerical chromosomal abnormalities]]
- Tumor cytogenetics
- Characteristics of tumor-transformed cells
- Oncogenes
- Hereditary tumor syndromes

Source

- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 2009]. <http://www.stefajir.cz>.