Chromosomal aberrations in etiology of neoplasms

By Chromosomal aberrations we mean mainly deviations of chromosomes in the sense of their disruption. They 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 led to detailed knowledge about chromosomal changes in cancer. The malignant cells of most tumors have chromosomal changes, many of which are stable. **Deletions, balanced translocations** (one chromosome is affected regularly, the site of a break on this chromosome is permanent, but the other chromosome involved may always be different) and less frequent **trisomies** of some chromosomes are typical.

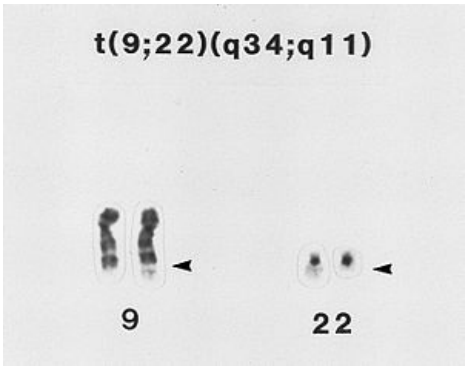
🔎 *For more information see chromosomal aberrations.*

Permanent changes in human cancers diagnosed

Chronic myeloid leukemia

Reciprocal translocation between chromosomes 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).

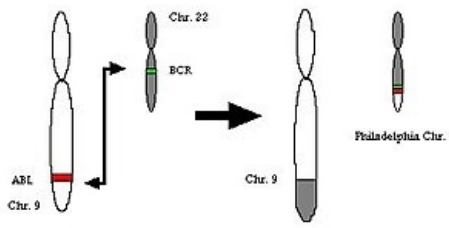
🔎 *For more information see Chronic myeloid leukemia.*



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

Burkitt's lymphoma

Tumor-transformed B-lymphocytes 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; an osteolytic jaw lesion is typical.



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

Retinoblastoma

It is an **embryonic retinal tumor** that occurs hereditarily and in isolation. In the hereditary form, more tumors arise (multifocal onset), usually in both eyes (bilateral onset), and there is an increased risk of other primary malignancies - such as osteosarcoma (tumor multiplicity). Deletions of chromosome 13 in region 13q14 engages gene **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.

Lung cancer

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

Association of Aniridie and Wilms' tumor

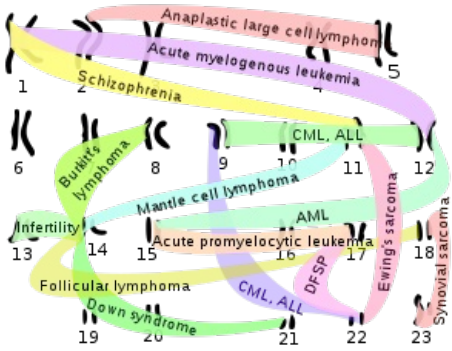
Deletion of a region of chromosome 11, in the region **11q15**. **Wilms' tumor** is a malignant tumor of the kidney that usually manifests itself in early childhood or even prenatally. **Aniridia** (absence of the iris) and Wilms' tumor can manifest independently of each other. Many patients often have other malformations, **mental retardation**, genital malformations, and delayed physical development (**WAGR syndrome** - a microdeletion syndrome). In many patients with this association, deletion of the 11q region is evident 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 neoplasias, their cells may acquire different chromosomal changes, which may not be random. E.g. in chronic myeloid leukemia, patients in the terminal stage of the disease show excessive Philadelphia chromosomes, trisomy 8, or the isochromosome of the long arms of chromosome 17, in men the Y chromosome is lost. These abnormalities are associated with the selection and proliferative advantage of malignant clones. Changes often occur in solid tumors, with homogeneously staining regions (HSRs) and acentric fragments; rather, they are sites of **gene amplification**. Multiplying the gene dose may be important for loss of control over tumor growth and aggression.

Oncogenes' relationship 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 retrovirus or by mutations. The names of oncogenes are **abbreviations** derived from their origin - for example, ***c-myc*** was originally found in **B-cells of avian myelocytoma**. Throughout the evolution oncogenes have been conserved, and each is thought to have atleast one copy in the human genome. The best known relationship between oncogene and chromosomal aberration is the **association of** *c-myc* **st (8;14)** in the case of Burkitt's lymphoma. In humans, ***c-myc*** is located in the region of the 8q24 band, which is involved in **translocaation**. The translocation thus brings the ***c-myc*** gene close to the 14q32 region with the gene encoding immunoglobulin heavy chain. In some cases translocation results in up to a 20-fold **increase in** *c-myc* **transcription**; in others, an abnormal gene product is formed.



Scheme of various chromosomal translocations and their relationship to selected diseases

References

Related articles

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

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