

Chromosomal aberrations in cancer cells

One of a hallmark feature of cancer cell is the presence of significant rearrangements of the genome.

Chromosomal aberrations appear on the **somatic level** and somehow give selective advantage for the cancerous tissue to overgrow its surroundings. The karyotype appearance is rather heterogeneous presenting aberrant number and/or structure, with both gains and losses of specific genomic regions. **Cancer chromosome rearrangements** mainly include translocations, deletions, and duplications (amplifications), but all types of structural aberrations are possible.

Chromosomal instability (CIN) refers to the lack of capacity to maintain the same chromosome number or structure from one cell generation to the next. Cancer cells often manifest CIN, but somehow advantageous for the specific cell clone. Chromosome instability is viewed as a consequence of mutations in genes involved in DNA integrity mechanisms (telomere structures), replication, chromosome segregation and cell cycle checkpoints. Aneuploidy (changed number of chromosomes, thus changed amount of gene products) might be the causative agent for further chromosomal rearrangements that eventually may lead to new hybrid genes (newly formed fusions between two genes that make a new product) or cause dysregulation of other genes involved.

Some cytogenetic findings are random, but some are non-random and can act as driver mutation for cancer formation. Those non-random karyotype findings serve as a diagnostic tool. Patients having the same aberrant karyotype in their tumor tissue form a specifically treated group.

Among the **non-random cancer cytogenetic findings** belong:

- **Philadelphia chromosome** t(9;22) – reciprocal translocation between 9 and 22, causing fused gene bcr-abl, balanced translocation, diagnostic marker in chronic myelogenous leukemia (90% of CML patients have Philadelphia chromosome).
- **t(8;14)** – reciprocal translocation between chromosomes 8 and 14, by fusion between proto-oncogene MYC on chromosome 8 and massively expressed immunoglobulin heavy chain locus (TCR alpha or delta) on chromosome 14 which causes overexpression of MYC, often found in Burkitt lymphoma.
- **Breast cancers with HER2 gene amplification** (thousands of copies of HER2 gene per cell): HER2-positive breast cancer patients form a specifically medically treated group. Their cancers tend to grow faster and are more likely to spread, but with a suitable medicine, there is good response for treatment.

Many methods of molecular diagnostic departments apply in chromosome aberrations inspections. For example, classic karyotyping, comparative genomic hybridization (plus arrayCGH), FISH and m-FISH, immunohistochemistry (IHC), NGS massive parallel sequencing, qPCR, MLPA and other...