

Protooncogenes

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Protooncogenes are genes that code for proteins responsible for proliferation. Mutations in protooncogenes can lead to an increase in protein expression, hyperactivity (i.e. gain-of-function) and/or loss of regulation. This mutated form is called **oncogene**.

Another mechanism leading to tumor proliferation is a mutation of antiproliferative *tumor-suppressor genes*. Usually, both copies of tumor-suppressor gene have to be mutated so the effect is manifested (two-hit hypothesis). Protooncogenes, however, differ in that area – mutation of one copy of the protooncogene to oncogene is often sufficient to induce cancer. There are several possible ways of protooncogene activation:

- **point-mutation;**
- **amplification** (many copies of normal oncogene);
- **translocation to a transcriptionally active site** (e.g. Burkitt lymphoma due to translocation of *MYC* oncogene into immunoglobulin locus);
- **chimeric (fusion) gene creation due to chromosomal rearrangement** (e.g. Philadelphia chromosome).

Protooncogenes can encode a wide variety of proteins with multiple functions (cell differentiation genes, signaling molecules, surface receptors, cell cycle regulatory genes, secreted growth factors ...). The functional consequences of protooncogene activation include situations when:

- protein begins to be formed in cells in which they normally do not form;
- protein is made in appropriate cells, but in excessive amounts;
- protein is formed in a form that can not be regulated by normal mechanisms.

Examples of (proto)Oncogenes

Currently, about **40 genes are known to be protooncogenes**. In 16 of them direct correlation with tumor proliferation was shown, such as:

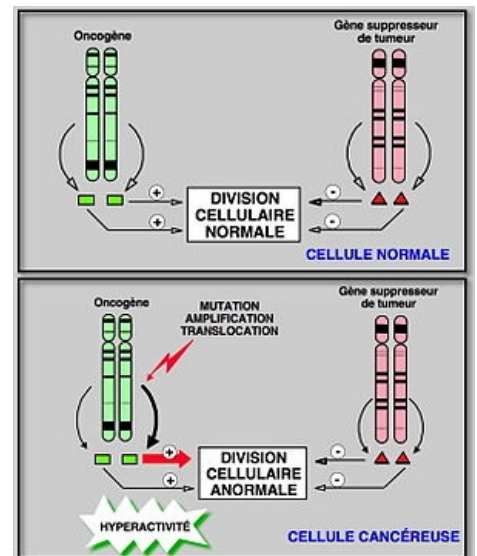
- *ERBB2 (HER2)*: breast cancer, by amplification;
- *KRAS*: tumors of the esophagus, colon, pancreas, by point mutation;
- beta-Catenin: Pancreatic cancer;
- Cyclin E: liver tumors;
- *BRAF*: melanomas;
- *BCR-ABL*: chronic myeloid leukemia.

Cellular and Viral Oncogenes

Oncogenes were originally identified in viruses causing cancers. These are called *transformation viruses* (often retrovirus) as they change the growth pattern of cells from normal to tumor-like. The viral oncogenes are designated with an "**v-**" prefix, such as **v-src gene**. The viral oncogenes originated as copies of cellular protooncogenes, designated with an "**c-**" prefix. So the *v-myc* is the viral homologue of *C-MYC* (i.e. *MYC* gene, as is reflected in its official gene name: v-myc myelocytomatosis viral oncogene homolog (avian)).

Viral oncogenes - normal function of protooncogene - tumors caused by mutations:

- *v-abl* – Tyr-specific protein kinase – pre-B-lymphocytic leukemia;
- *v-erbB* – epidermal growth factor receptor (*EGFR*) – erythroleukemia;
- *v-fos*, *v-jun*, *v-myc* – gene regulation (DNA-binding protein)– osteosarcomas, fibrosarcomas;
- *v-src* – Tyr-specific protein kinase – sarcomas.



Difference between normal cell and cancerous cell.

Links

Related articles

- Mutation

External links

- What are Proto-Oncogenes (<http://www.news-medical.net/health/What-are-Proto-Oncogenes.aspx>)
- Proto-Oncogenes to Oncogenes to Cancer (<http://www.nature.com/scitable/topicpage/proto-oncogenes-to-oncogenes-to-cancer-883>)

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