ONCOGENES

An **oncogene** is a gene that when mutated or expressed at abnormally-high levels converts a normal cell into a cancer cell. Many cells normally undergo a programmed form of death (apoptosis). Activated oncogenes can cause those cells to survive and proliferate instead. Most oncogenes require an additional step, such as mutations in another gene, or environmental factors, such as viral infection, to cause cancer. Since the 1970s, dozens of oncogenes have been identified in human cancer.

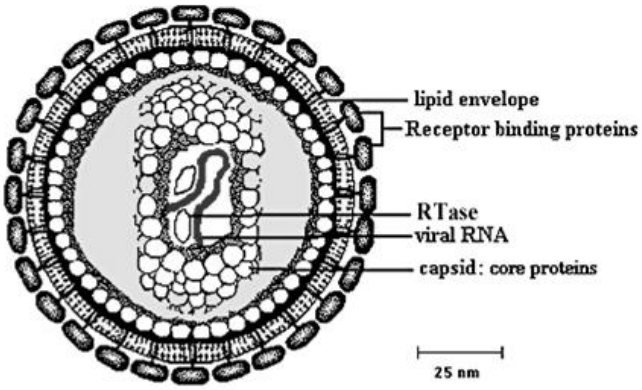
A **proto-oncogene** is a normal gene that can become an oncogene due to mutations or increased expression. Proto-oncogenes code for proteins that help to regulate cell growth and differentiation. Examples of proto-oncogenes include RAS, WNT, MYC, ERK, and TRK. The proto-oncogene can become an oncogene by a relatively small modification of its original function. There are three basic activation types:

- A mutation within a proto-oncogene can cause a change in the protein structure, causing
    - an increase in protein (enzyme) activity
    - a loss of regulation
- An increase in protein concentration, caused by
    - an increase of protein expression
    - an increase of protein stability
    - a gene duplication resulting in an increased amount of protein in the cell
- A chromosomal translocation causing
    - an increased gene expression in the wrong cell type or at wrong times
    - the expression of a constitutively active hybrid protein. This type of aberration in a dividing stem cell in the bone marrow leads to adult leukemia

RETROVIRUSES

A **retrovirus** is an RNA virus that is replicated in a host cell via the enzyme reverse transcriptase to produce DNA from its RNA genome. The DNA is then incorporated into the host's genome by an integrase enzyme. The virus thereafter replicates as part of the host cell's DNA. Retroviruses are enveloped viruses that belong to the viral family *Retroviridae*.

Structure



Retroviruses are infectious particles consisting of an **RNA genome** packaged in a protein **capsid**, surrounded by a **lipid envelope**. This lipid envelope contains polypeptide chains including **receptor binding proteins** which link to the membrane receptors of the host cell, initiating the process of infection.

Retroviruses contain RNA as the hereditary material in place of the more common DNA. In addition to RNA, retrovirus particles also contain the enzyme reverse transcriptase (or **RTase)**, which causes synthesis of a **complementary DNA molecule (cDNA**) using virus RNA as a template.

When a retrovirus infects a cell, it injects its RNA into the cytoplasm of that cell along with the reverse transcriptase enzyme. The cDNA is produced from the RNA template and the viral RNA degrades. The cDNA synthesises its complementary strand and becomed doble-stranded, gets integrated into host genome and directs the synthesis of viral RNA and proteins. Thus new viral particles are produced inside the host cell.

The virus that causes AIDS (*acquired immune deficiency syndrome*) **is a retrovirus**. It is called **HIV** for *human immunodeficiency virus*. Retroviruses are proving to be valuable research tools in molecular biology and have been used successfully in gene delivery systems

TRANSPOSONS

Transposons are segments of DNA that can move around to different positions in the genome of a single cell. In the process, they may cause mutations and increase (or decrease) the amount of DNA in the genome. These mobile segments of DNA are sometimes called **"jumping genes"**. Transposons were first discovered by Barbara McClintock.

There are three distinct types of transposons:

- **Class II Transposons** consisting only of DNA that moves directly from place to place. They move by a "cut and paste" process: the transposon is cut out of its location and inserted into a new location. This process requires an enzyme - **transposase** - that is encoded within some of these transposons.

- **Class III Transposons**; also known as **M**iniature **I**nverted-repeats **T**ransposable **E**lements or **MITE**s. They contain recurring motif consisting of almost identical sequences of about 400 base pairs flanked by characteristic **inverted repeats** of about 15 base pairs

- **Retrotransposons** (Class I) that first transcribe the DNA into RNA and then use reverse transcriptase to make a DNA copy of the RNA to insert in a new location.

Transposons have been an especially useful tool in plant molecular biology. Researchers use transposons as a means of mutagenesis. Sometimes the insertion of a transposon into a gene can disrupt that gene's function in a reversible manner; transposase-mediated excision of the transposon restores gene function. This produces plants in which neighboring cells have different genotypes. This feature allows researchers to distinguish between genes that must be present inside of a cell in order to function (cell-autonomous) and genes that produce observable effects in cells other than those where the gene is expressed.

Nif GENES

The nif genes are genes encoding enzymes involved in the fixation of atmospheric nitrogen. The primary enzyme encoded by the nif genes is the nitrogenase complex which is in charge of converting atmospheric nitrogen to other nitrogen forms such as ammonia which the plant can use for various purposes. Besides the nitrogenase enzyme, the nif genes also encode a number of regulatory proteins involved in nitrogen fixation. The nif genes are found in both free living nitrogen fixing bacteria and in symbiotic bacteria in various plants. The expression of the nif genes is induced in response to low concentrations of fixed nitrogen and oxygen concentrations.

Activation of the nif genes transcription takes place in times of nitrogen stress. In most plants, activation of nif genes transcription is done by the nitrogen sensitive NifA protein. When there isn't enough fixed nitrogen factor for available for the plant's use, NtrC which is a RNA polymerase triggers NifA's expression, and NifA activates the rest of the nif genes transcription. If there is a sufficient amount of reduced nitrogen or oxygen is present, another protein is activated – NifL, and NifL inhibits NifA activity resulting in the inhibition of nitrogenase forming. NifL is regulated by glnD and glnK gene products. The nif genes can be found on bacteria's chromosomes, but a lot of the times they are found on bacteria's plasmids with other genes related to nitrogen fixation (such as the nod genes).

Nif gene transfer to plants

An efficient way to help N_2 fixation by higher plants is the transfer of nif genes and its expression in higher plants. Genetic transformation with nif genes should not only ensure their expression but also must provide for the protection of nitrogenase from inactivation by oxygen and for the supply of energy for its functioning. Chloroplasts appear to provide the most suitable environment for nif gene expression in a plant cell. But, for effective transcription of nif genes in chloroplast, it may be necessary to substitute each nif gene promoter with an appropriate promoter recognised by chloroplast RNA polymerase. Also, inorder to avoid deactivation of nif genes by oxygen, it may be necessary to establish temporal separation of N_2 fixation and photosynthesis by limiting nif gene expression to dark periods.