The period between mitotic divisions - that is, G1, S and G2 - is known as interphase.

Mitosis

Mitosis is a form of eukaryotic cell division that produces two daughter cells with the same genetic component as the parent cell. Chromosomes replicated during the S phase are divided in such a way as to ensure that each daughter cell receives a copy of every chromosome. In actively dividing animal cells, the whole process takes about one hour.

The replicated chromosomes are attached to a 'mitotic apparatus' that aligns them and then separates the sister chromatids to produce an even partitioning of the genetic material. This separation of the genetic material in a mitotic nuclear division (or **karyokinesis)** is followed by a separation of the cell cytoplasm in a cellular division (or **cytokinesis**) to produce two daughter cells.
In some single-celled organisms mitosis forms the basis of asexual reproduction. In diploid multicellular organisms sexual reproduction involves the fusion of two haploid gametes to produce a diploid zygote. Mitotic divisions of the zygote and daughter cells are then responsible for the subsequent growth and development of the organism. In the adult organism, mitosis plays a role in cell replacement, wound healing and tumour formation.

Mitosis, although a continuous process, is conventionally divided into five stages: prophase, prometaphase, metaphase, anaphase and telophase.

and mammals. In addition, some regulators are absent in single cell eukaryotes, including the pRb and E2F families, and nearly all regulatory genes have expanded into subfamilies with multiple members in mammals. Studies over the last decade have shown that cell-cycle control in *C. elegans* uses well-recognizable homologs of nearly all mammalian regulators, often represented by just a single member (Table 1). As an exception to the rule, the pINK family of Cdk4/6 kinase inhibitors has not as yet been identified in *C. elegans*. Genetic studies have placed the *C. elegans* cell-cycle genes into pathways that resemble those in mammals, and novel regulatory elements have been discovered.

Table 1. *C. elegans* cell-cycle mutants (for references: see text)

Gene name	**Alternate**	**Homolog**	**Presumed function**	**Cell-cycle phenotype (loss of function)**
Cyclin-dependent kinases				
cdk-1	*ncc-1*	Cdk1	Promotes M phase entry/progression	G_2 arrest, starting in L1. RNAi: one-cell arrest
cdk-4		Cdk4/Cdk6	Promotes Progression through G_1	G_1 arrest, starting late embryogenesis
cdk-7		Cdk7	CDK activating kinase/Pol II CTD kinase	*cdk-7*(ax224 *RNAi*): one-cell arrest
Cyclins				
cyd-1		Cyclin D1/D2/D3	G_1 Cyclin, promotes progression through G_1	G_1 arrest, starting late in embryogenesis
cye-1	*evl-10*	Cyclin E1/E2	G_1/S Cyclin	Late larval defects. (RNAi: 100-cell arrest)
Inhibitors				
cki-1		Kip1	Cip/Kip family CDK inhibitor. Inhibits G_1/S transition.	Extra cell division (failure to arrest)
CDK inhibitory phosphorylation				

Gene name	Alternate	Homolog	Presumed function	Cell-cycle phenotype (loss of function)
mat-1	*pod-5*	APC3, Cdc27	Component APC E3 Ubiquitin ligase	Arrest at metaphase-to-anaphase transition meiosis
mat-2	*pod-3, evl-22*	APC1	Component APC E3 Ubiquitin ligase	Arrest at metaphase-to-anaphase transition meiosis
mat-3	*pod-4*	APC8, Cdc23	Component APC E3 Ubiquitin ligase	Arrest at metaphase-to-anaphase transition meiosis
emb-27	*pod-6*	APC6, Cdc16	Component APC E3 Ubiquitin ligase	Arrest at metaphase-to-anaphase transition meiosis
emb-30		APC4	Component APC E3 Ubiquitin ligase	Arrest at metaphase-to-anaphase transition
DNA damage/DNA replication checkpoint				
mrt-2		Rad1	DNA-damage checkpoint protein	Deficient in apoptosis in response to DNA damage
clk-2	*rad-5*	Tel2p	DNA-damage checkpoint protein	Deficient in apoptosis in response to DNA damage
hus-1		Hus1	DNA-damage checkpoint protein	Deficient in apoptosis in response to DNA damage
cep-1		*p53*	Transcription factor DNA-damage checkpoint	Deficient in apoptosis in response to DNA damage
Spindle assembly checkpoint				
mdf-1		MAD1	Spindle assembly checkpoint protein	Mitotic arrest defective in nocodazole. Lethal, sterile

However, the contribution of *lin-35* Rb to negative regulation of G_1 progression became apparent in double mutant combinations. Inactivation of *lin-35* substantially rescues the larval arrest of cell division in mutants that lack the positive G_1 regulators *cyd-1* and *cdk-4* (Boxem and van den Heuvel, 2001). In addition, *lin-35* inactivation synergistically increases the number of extra cell divisions when combined with negative G_1 regulators, such as *cki-1* Cip/Kip, *cdc-14* Cdc14 and *fzr-1* Cdh1/FZR (Boxem and van den Heuvel, 2001; Fay et al., 2002; Saito et al., 2004). Together, such results indicate that *lin-35* acts redundantly to inhibit G_1 progression, likely downstream of *cyd-1* and *cdk-1* and parallel of *cki-1*,*fzr-1* and *cdc-14* (Figure 3).

Examination of additional double mutant combinations revealed that some of the other synMuv class B genes also contribute to G_1 control (Boxem and van den Heuvel, 2002;Fay et al., 2002). Specifically, *efl-1* E2F negatively regulates cell-cycle entry, while *dpl-1* DP appears to act both as a positive and negative regulator. In addition, a negative G_1regulatory function was identified for *lin-9* Mip130/TWIT, as well as *lin-15B* and *lin-36*, which encode novel proteins. Class A synMuv genes and class B genes that encode NURD components have not been observed to affect the cell cycle.

Candidate targets of Rb/E2F regulation in *C. elegans* include *cye-1* Cyclin E and *rnr-1*, which encodes the ribonucleotide reductase large subunit. These genes have multiple E2F-binding sites within their promoter regions (Brodigan et al., 2003; Hong et al., 1998) and are regulated by E2F in other species. Several genetic observations are also consistent with *lin-35* acting upstream of *cye-1* to repress its transcription (Boxem and van den Heuvel, 2001; our unpublished observations).

Cell division is a physiological process that occurs in almost all tissues and under many circumstances. Under normal circumstances, the balance between proliferation and programmed cell death, usually in the form of apoptosis, is maintained by regulation of both processes to ensure the integrity of tissues and organs. Mutations and epimutations in DNA that lead to cancer (only certain mutations and epimutations can lead to cancer and the majority of potential mutations and epimutations will have no such effect) disrupt these orderly processes by disrupting the programming regulating the processes.

Carcinogenesis is caused by mutation and epimutation of the genetic material of normal cells, which upsets the normal balance between proliferation and cell death. This results in uncontrolled cell division and the evolution of those cells by natural selection in the body. The uncontrolled and often rapid proliferation of cells can lead to benign tumors; some types of these may turn into malignant tumors (cancer). Benign tumors do not spread to other parts of the body or invade other tissues, and they are rarely a threat to life unless they compress vital structures or are physiologically active, for instance, producing a hormone. Malignant tumors can invade other organs, spread to distant locations (metastasis) and become life-threatening.

More than one mutation is necessary for carcinogenesis. In fact, a series of several mutations to certain classes of genes is usually required before a normal cell will transform into a cancer cell.[1] On average, for example, 15 "driver mutations" and 60 "passenger" mutations are found in colon cancers.[2] Mutations in those certain types of genes that play vital roles in cell division, apoptosis (cell death), and mutations and epimutations (see article Genome instability) in DNA repair genes will cause a cell to lose control of its cell proliferation.

Oncovirinae, viruses that contain an oncogene, are categorized as oncogenic because they trigger the growth of tumorous tissues in the host. This process is also referred to as viral transformation.

Cancer is fundamentally a disease of regulation of tissue growth. In order for a normal cell to transform into a cancer cell, genes that regulate cell growth and differentiation must be altered.[3] Genetic and epigenetic changes can occur at many levels, from gain or loss of entire chromosomes, to a mutation affecting a single DNA nucleotide, or to silencing or activating a microRNA that controls expression of 100 to 500 genes.[4][5] There are two broad categories of genes that are affected by these changes. Oncogenes may be normal genes that are expressed at inappropriately high levels, or altered genes that have novel properties. In either

miR-137 can cause downregulation of expression of 491 genes, and miR-137 is epigenetically silenced in 32% of colorectal cancers>[5]

The cells in which all these DNA alterations accumulate are difficult to trace, but two recent lines of evidence suggest that normal stem cells may be the cells of origin in cancer.[13][14] First, there exists a highly positive correlation (Spearman's rho = 0.81; P < 3.5 × 10−8) between the risk of developing cancer in a tissue and the number of normal stem cell divisions taking place in that same tissue. The correlation applied to 31 cancer types and extended across five orders of magnitude.[15] This correlation means that if the normal stem cells from a tissue divide once, the cancer risk in that tissue is approximately 1X. If they divide 1,000 times, the cancer risk is 1,000X. And if the normal stem cells from a tissue divide 100,000 times, the cancer risk in that tissue is approximately 100,000X. This strongly suggests that the main reason we have cancer is that our normal stem cells divide, which implies that cancer originates in normal stem cells.[14] Second, statistics show that most human cancers are diagnosed in aged people. This means that most cancers occur because our cells accumulate damage as we age. DNA is the only cellular component that can accumulate damage during our whole life, and stem cells are the only cells that can transmit our DNA from the zygote to the cells we have when we die. The rest of the cells cannot keep our DNA from the beginning of life until a possible cancer occurs. This implies that most cancers arise from normal stem cells.[13][14]

CANCER AND FORMS

It's important for doctors to know what type of cancer a person has. The type of cancer is generally based on the part of your body and the type of cell where the cancer first developed.

The most common places for cancer to develop are the skin, lungs, breasts, prostate, colon and rectum.

There are three main types of cell where cancer develops:

- **Epithelial cells.** Cancers that develop in this type of cell are called carcinomas. About 80-90% of cancers are this type.
- **Cells of the blood and lymphatic system.** Cancers that develop in this type of cell are called leukaemias and lymphomas. About 7% of cancers are this type.

Cancer can also be described according to the type of cell it started in. This can be just as important in how a cancer behaves and responds to treatment as the site where it started.

Cells

Our body is made up of millions of cells. The cells, organised together, make up all of our tissues and organs. There are different types of cells to carry out different functions in the body. Some types are very common and are found in almost all the organs in our body. Other types, such as the brain cells, are very specialised and only found in one part of our body.

The main types of cells in our body are:

- **Epithelial cells** These cover the outside of our body (as skin) and make up tissues that line the inside of our bodies and cover our organs.
- **Cells of the blood and lymphatic system** These are found in our blood, in the bone marrow (where blood cells are made) and in the lymphatic system (which fights infection).
- **Connective tissue cells** These cells are found in supportive and connective tissues in our body such as the muscles, bones and fatty tissue.

Cancers that start in each of these types of cells have different names.

Carcinomas

Cancers that start in epithelial cells are called carcinomas. They are the most common type of cancer in adults and make up 80-90 out of every 100 (80-90%) cancers. Most lung, breast, prostate and bowel cancers are carcinomas.

There are different types of epithelial cells:

- **Squamous cells** are found in the skin and cover the surface of many parts of the body including the mouth, gullet (oesophagus) and the airways.
- **Adeno cells** form the lining of all the glands in the body including those in the breast, bowel, stomach, ovaries and prostate.
- **Urothelial (transitional) cells** line the bladder and parts of the urinary system.

- Translocation events that lead to a fusion between a proto-oncogene and a 2nd gene (this creates a fusion protein with increased cancerous/oncogenic activity)
- The expression of a constitutively active *hybrid protein*. This type of mutation in a dividing stem cell in the bone marrow leads to adult leukemia
- Philadelphia Chromosome is an example of this type of translocation event. This chromosome was discovered in 1960 by Peter Nowell and David Hungerford, and it is a fusion of parts of DNA from chromosome 22 and chromosome 9. The broken end of chromosome 22 contains the "BCR" gene, which fuses with a fragment of chromosome 9 that contains the "ABL1" gene. When these two chromosome fragments fuse the genes also fuse creating a new gene: "BCR-ABL". This fused gene encodes for a protein that displays high protein tyrosine kinase activity (this activity is due to the "ABL1" half of the protein). The unregulated expression of this protein activates other proteins that are involved in cell cycle and cell division which can cause a cell to grow and divide uncontrollably (the cell becomes cancerous). As a result, the Philadelphia Chromosome is associated with Chronic Myelogenous Leukemia (as mentioned before) as well as other forms of Leukemia.[13]

The expression of oncogenes can be regulated by microRNAs (miRNAs), small RNAs 21-25 nucleotides in length that control gene expression by downregulating them.[14] Mutations in such microRNAs (known as oncomirs) can lead to activation of oncogenes.[15] Antisense messenger RNAs could theoretically be used to block the effects of oncogenes.

Classification

There are several systems for classifying oncogenes,[16][17] but there is not yet a widely accepted standard. They are sometimes grouped both spatially (moving from outside the cell inwards) and chronologically (parallelling the "normal" process of signal transduction). There are several categories that are commonly used:

Category	Examples	Cancers	Gene functions

How are tumor markers used in cancer care?

Tumor markers are used to help detect, diagnose, and manage some types of cancer. Although an elevated level of a tumor marker may suggest the presence of cancer, this alone is not enough to diagnose cancer. Therefore, measurements of tumor markers are usually combined with other tests, such as biopsies, to diagnose cancer.
Tumor marker levels may be measured before treatment to help doctors plan the appropriate therapy. In some types of cancer, the level of a tumor marker reflects the stage (extent) of the disease and/or the patient's prognosis (likely outcome or course of disease). More information about staging is available in the NCI fact sheet Cancer Staging.

Tumor markers may also be measured periodically during cancer therapy. A decrease in the level of a tumor marker or a return to the marker's normal level may indicate that the cancer is responding to treatment, whereas no change or an increase may indicate that the cancer is not responding.

Tumor markers may also be measured after treatment has ended to check for recurrence (the return of cancer).

How are tumor markers measured?

A doctor takes a sample of tumor tissue or bodily fluid and sends it to a laboratory, where various methods are used to measure the level of the tumor marker.

If the tumor marker is being used to determine whether treatment is working or whether there is a recurrence, the marker's level will be measured in multiple samples taken over time. Usually these "serial measurements," which show whether the level of a marker is increasing, staying the same, or decreasing, are more meaningful than a single measurement.

Does NCI have guidelines for the use of tumor markers?

NCI does not have such guidelines. However, some national and international organizations do have guidelines for the use of tumor markers for some types of cancer:

- The American Society of Clinical Oncology (ASCO) has published clinical practice guidelinesExit Disclaimer on a variety of topics, including tumor markers for breast cancer, colorectal cancer, lung cancer, and others.
- The National Academy of Clinical Biochemistry publishes laboratory medicine practice guidelines, including *Use of Tumor Markers in Clinical Practice: Quality RequirementsExit Disclaimer*, which focuses on the appropriate use of tumor markers for specific cancers.

What tumor markers are currently being used, and for which cancer types?

A number of tumor markers are currently being used for a wide range of cancer types. Although most of these can be tested in laboratories that meet standards set by the Clinical Laboratory Improvement Amendments, some cannot be and may therefore be considered experimental. Tumor markers that are currently in common use are listed below.

ALK gene rearrangements and overexpression

- Cancer types: Non-small cell lung cancer and anaplastic large cell lymphoma
- Tissue analyzed: Tumor
- How used: To help determine treatment and prognosis

Alpha-fetoprotein (AFP)

- Cancer types: Liver cancer and germ cell tumors
- Tissue analyzed: Blood
- How used: To help diagnose liver cancer and follow response to treatment; to assess stage, prognosis, and response to treatment of germ cell tumors

Beta-2-microglobulin (B2M)

- Cancer types: Multiple myeloma, chronic lymphocytic leukemia, and some lymphomas
- Tissue analyzed: Blood, urine, or cerebrospinal fluid
- How used: To determine prognosis and follow response to treatment

Beta-human chorionic gonadotropin (Beta-hCG)

- Cancer types: Choriocarcinoma and germ cell tumors
- Tissue analyzed: Urine or blood
- How used: To assess stage, prognosis, and response to treatment

Reducing cancer risk in our communities

Adopting a healthier lifestyle is easier for people who live, work, play, or go to school in an environment that supports healthy behaviors. Working together, communities can create the type of environment where healthy choices are easy to make.

We all can be part of these changes: Let's ask for healthier food choices at our workplaces and schools. For every junk food item in the vending machine, ask for a healthy option, too. Support restaurants that help you to eat well by offering options like smaller portions, lower-calorie items, and whole-grain products. And let's help make our communities safer and more appealing places to walk, bike, and be active.

The bottom line

It has been estimated that as much as one-third of all cancer deaths in the US are related to diet and activity factors. Let's challenge ourselves to lose some extra pounds, increase our physical activity, make healthy food choices, limit alcohol, and look for ways to make our communities healthier places to live, work, and play.

How can cancer be detected early?

In many cases, the sooner cancer is diagnosed and treated, the better a person's chance for a full recovery. If you develop cancer, you can improve the chance that it will be detected early if you have regular medical checkups and do certain self-exams. Often a doctor can find early cancer during a physical exam or with routine tests, even if a person has no symptoms. Some important medical exams, tests, and self-exams are discussed on the next pages. The doctor may suggest other exams for people who are at increased risk for cancer.

Ask your doctor about your cancer risk, problems to watch for, and a schedule of regular checkups. The doctor's advice will be based on your age, medical history, family history, and other risk factors. The doctor also can help you learn about self-exams. (More information and free booklets about self-exams are available from the National Cancer Institute's Cancer Information Service).

Many local health departments have information about cancer screening or early detection programs. The Cancer Information Service also can tell you about such programs.