LEUKEMIA & LYMPHOMA SOCIETY®

PROVIDING THE LATEST INFORMATION
FOR PATIENTS & CAREGIVERS

Understanding Genetics

Revised **2020**

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A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/ happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.

Discover what thousands already have at **www.LLS.org/Community**

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find:

- **Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff**
- **Accurate and cutting-edge disease updates**
- **The opportunity to participate in surveys that will help improve care**

Inside This Booklet

Acknowledgement

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Introduction

Cancer is a disease that is caused by abnormal changes (mutations) to the genetic material inside of cells. This genetic material is called DNA (deoxyribonucleic acid). When cells divide to create new cells, the DNA is passed to the new cells. Therefore, mutated DNA may cause the new cells to develop into cancer cells.

Cancer cells behave differently than normal cells. They multiply uncontrollably even though they are not needed in the body, and evade the immune system. DNA damage and mutations happen more commonly than one might think but the immune system usually identifies these abnormal cells and eliminates them. Some of these abnormal cells that avoid immune detection go on to become cancerous cells. These cancer cells can spread to surrounding areas and form tumors. The cancer cells can build up in the blood, the bone marrow (the spongelike tissue in the center of most bones), the lymph nodes and other areas of the body.

Genetics and Genomics. Each person's cancer has a unique combination of genetic mutations. Genetic materials are examined in two different, but complementary, fields of study, namely genetics and genomics.

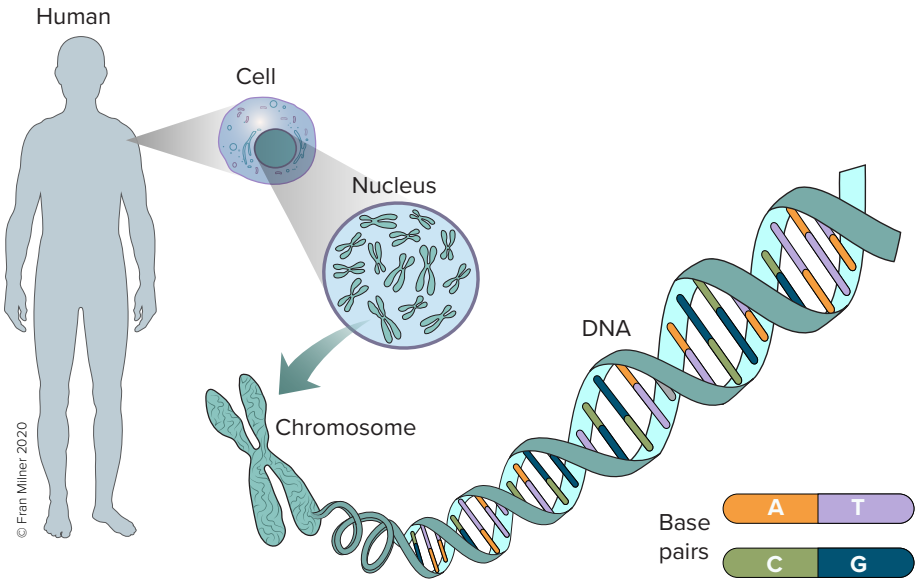
"Genetics" is the study of genes and their roles in inheritance—the ways in which traits or conditions are passed down from one generation to the next. "Genomics" is the study of the complete set of DNA of a person's genome; the genome is made up of *all* of a person's genes. Genomics also examines how the genes interact with each other and how, or if, they are affected by environmental factors. Researchers are learning that the genetic changes that occur in one person's cancer may not occur in other people who have the same type of cancer. Specific information about a person's own genes and/or proteins is used to prevent, diagnose, or treat cancer in an approach to a type of care known as "precision medicine."

Genetic and genomic testing provides doctors with the individualized information (based on specific genetic changes and the genomic makeup of abnormalities within the cancer tissue) that they need to develop specific targeted treatments for their patients.

- Genetic testing: These tests examine changes in an individual gene and/or set of genes that may account for the likelihood of a particular disease process; however, a test may not pick up every change in a gene. This type of information is useful if a particular drug is known to work for certain gene/protein variants. It allows for targeted therapies (for example, Tibsovo® [ivosidenib], which is approved for treatment of acute myeloid leukemia in patients who have an *IDH1* gene mutation).

- Genomic testing: These tests assess an individual's genome (all of a person's genes, rather than a specific gene or set of genes). The scope of genomic testing includes gene alterations (mutations) and/or harmful changes in the genetic code—however they are caused. Researchers hope that, one day, testing cancer cells for mutations this way will help doctors match each patient with the most effective treatment for his or her disease.

Cells, Chromosomes, and DNA



Highlights. In this booklet you will learn that

- The human body is made up of trillions of cells.
- In almost every cell, there is a nucleus that contains your genome (all of your genetic material), which is essentially a blueprint for your body to develop and grow.
- In the nucleus of most cells, your genetic material is packaged into thread like structures called "chromosomes."
- Chromosomes are made of DNA (deoxyribonucleic acid) that is wrapped around specialized proteins called "histones."
- DNA is the hereditary material that passes from one generation to the next. Nearly every cell in your body has the same DNA.
- Cancer is a disease that is caused by abnormal changes (mutations) to the genetic material inside of cells.

- Each person's cancer has a unique combination of genetic mutations. Precision medicine is an important approach to patient care that allows doctors to select treatments that are tailored to specific genetic changes of each person's cancer.

Feedback. Visit www.LLS.org/PublicationFeedback to give suggestions about this booklet.

Cells

Cells are considered the basic units of life. The human body is made up of trillions of cells that carry out essential functions allowing the body to survive. Each type of cell plays a specific role in the body. For example, red blood cells carry oxygen throughout your body; nerve cells send electrical messages that create thoughts and movement; and heart cells contract to pump blood. Cells also make products that your body needs such as sweat, saliva, and hormones.

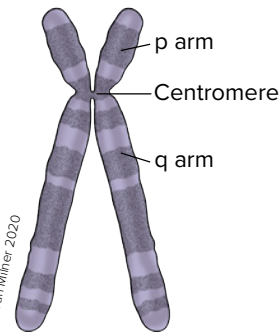
In almost every cell, there is a nucleus that contains your genome (all of your genetic material). Your genome is essentially a blueprint for your body to develop and grow.

Chromosomes

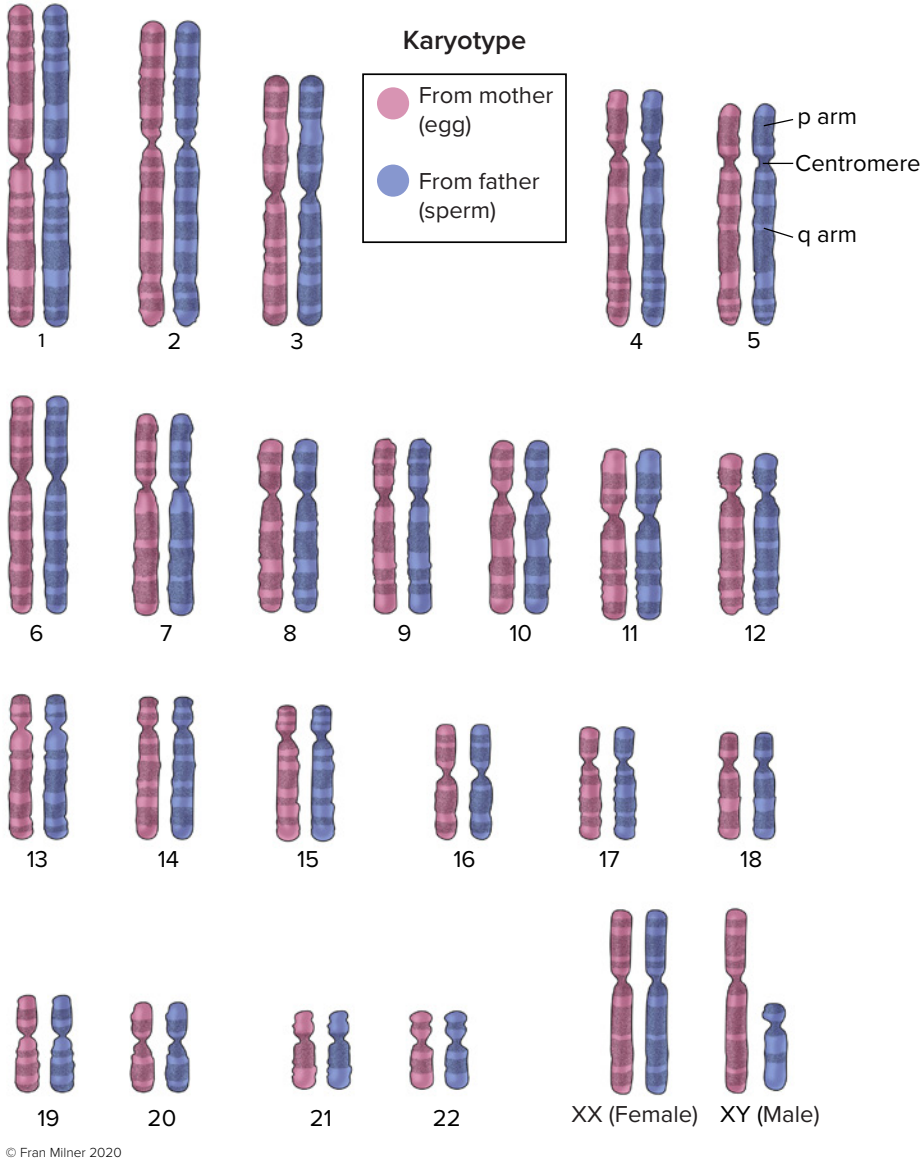
In the nucleus of most cells, your genetic material is packaged into threadlike structures called "chromosomes." Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes. Chromosomes are passed from the parents to a child. You inherit 23 chromosomes from your mother's egg cell, and you inherit the other 23 chromosomes from your father's sperm cell.

Under the microscope, you can see that chromosomes come in different lengths and striping patterns. The first 22 of these pairs are called "autosomes," and they are the same in males and females. The 23rd pair is the sex chromosomes; female and male sex chromosomes are different. Females have two copies of the X chromosome, whereas males have one X chromosome and one Y chromosome.

Somewhere between one-third and two-thirds of the way down the chromosome is the centromere, a narrow region that divides the chromosome into two sections, or "arms." The short arm of the chromosome is called the "p arm," and the long arm of the chromosome is called the "q arm." Geneticists use the names of the arms to describe the position of a specific section of the chromosome. For example, 13q describes the long arm of chromosome 13, while 17p describes the short arm of chromosome 17.



This image of normal human chromosomes lined up in pairs is called a “karyotype.”



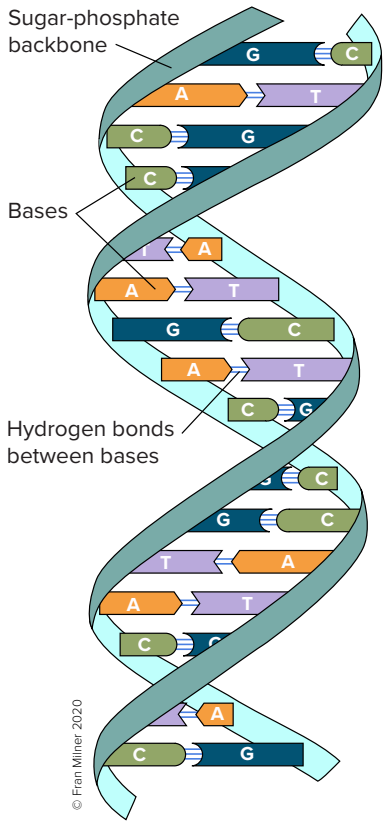
DNA (deoxyribonucleic acid)

Chromosomes are made of DNA. The DNA molecule is the hereditary self-replicating material that passes genetic information from one generation to the next. Chromosomes are made up of DNA that is wrapped around specialized proteins called “histones.”

The information in DNA is stored as a code that is made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T). The order of the bases encodes the information available for creating and maintaining your body’s functions.

The DNA bases pair up with each other (A always pairs with T and C always pairs with G) forming units called “base pairs.” Each base pair is connected to a sugar molecule and coupled to a phosphate molecule. Together, a base pair (along with its linked sugar and phosphate molecules) is called a “nucleotide.”

Nucleotides are arranged on two long strands called a “double helix.” A double helix resembles a twisted ladder. One base pair (the bases linked with a hydrogen bond) forms the “rungs” of the ladder, and the sugar and phosphate molecules form the “side rails” of the ladder.



When cells divide, the DNA molecule can make copies of itself; this process is called “mitosis.” It is important to note that when cells divide, each new (daughter) cell has the same exact DNA as the original (parent) cell. Everything in the parent cell is duplicated: the two new daughter cells have the same DNA, functions, and genetic code as the parent cell.

Mitosis is the mechanism that supplies complex organisms with necessary new cells.

Genes

A gene is a section of DNA that is passed down through generations from a parent to a child. Genes contain instructions for individual characteristics, such as eye and hair color. They also contain instructions for making specific proteins that determine how the cell functions.

Genes are arranged, one after another, on the chromosomes. The four bases of DNA (A, G, C and T) are organized in different ways to form thousands of genes. Just as the letters of the alphabet are strung together to form words, the sequence of the four bases creates a gene. Some genes are short, maybe just a few hundred base pairs. Other genes are long, made up of thousands of base pairs.

Genes control how cells function by making proteins. Proteins do much of the work in cells and the body. Some proteins give cells their shape and structure. Other proteins help cells perform biological functions such as carrying oxygen throughout the body or digesting food. Genes also ensure that cells grow and divide in an orderly and controlled manner.

Mutations

A gene mutation is a permanent change in the DNA sequence of a cell. It occurs when there are changes in the sequences of bases, A, G, C and T.

Mutations vary in size; they can affect a single DNA building base or a large segment of a chromosome that includes many genes. Gene mutations affect your health in different ways, depending on where they occur and whether they alter the function of important proteins. Mutations can have a positive effect, negative effect, or no effect on your health.

There are two types of gene mutations: hereditary (germline) mutations and acquired (somatic) mutations. Hereditary mutations are inherited from a parent. They occur before conception and are present throughout a person’s life in almost every cell in the body.

Acquired mutations occur after conception, during a person's life, and are only present in certain cells. They are not present in every cell in the body.

Acquired mutations can be caused by environmental factors such as exposure to specific chemicals or radiation. These agents can damage DNA. If the cell cannot repair the DNA so it returns to its original sequence, and it remains slightly different from the original DNA, a mutation has occurred.

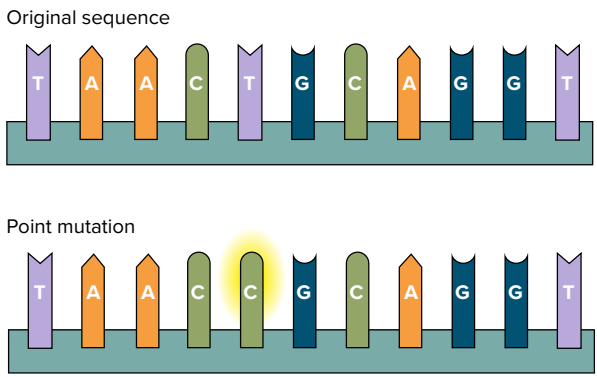
Acquired mutations can also occur if a mistake is made during DNA replication. DNA replication is the process by which DNA copies itself and then divides to form two identical cells. However, sometimes the DNA makes a mistake when copying itself; the result is a mutation.

Mutations occur randomly and frequently throughout a lifetime. Typically, a cell detects the mutation and repairs it. If the cell cannot be repaired, the cell receives a signal telling it to die (a process called "apoptosis"). This process is one way in which the immune system rids itself of abnormal or unneeded cells. A cell that is not repaired and does not die may become cancerous.

A single mutation will likely not cause cancer but, over time, the damage may build up. Usually, cancer is the outcome of multiple gene mutations that have occurred over many years. The accumulation of mutations accounts for the onset of cancer in many older people. Cancer can also occur through several rounds of replication, as is the case in cancers of the blood cells, such as leukemia.

Changes in Genes. Our genome changes throughout our lifetime. Genes change (mutate) in different ways and for different reasons. Gene changes include

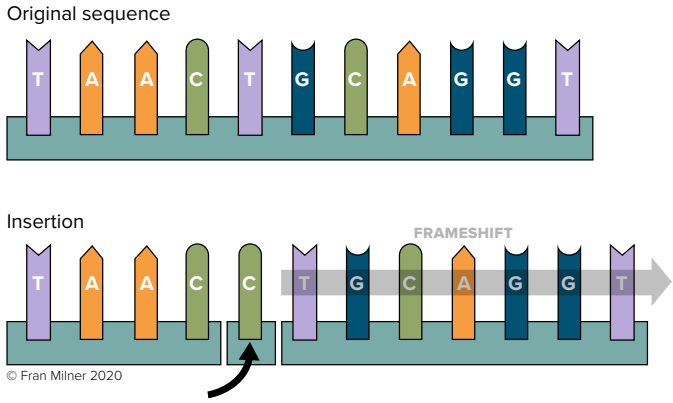
A point mutation: A point mutation is a change within a gene in which one base pair in the original DNA sequence is altered.



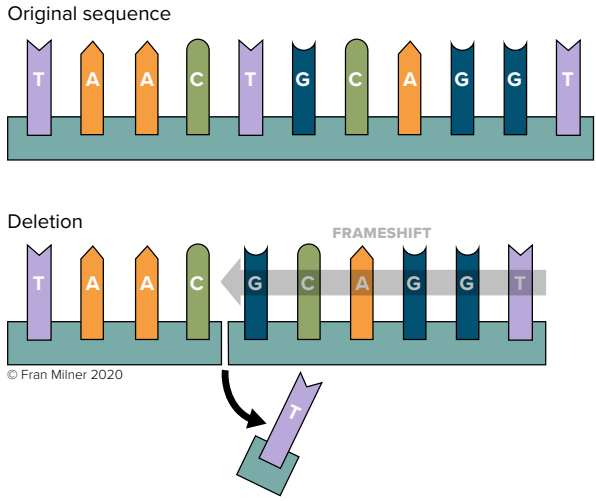
A frameshift mutation: A genetic mutation caused by an insertion (addition) or deletion (loss) in a DNA sequence that shifts the way the sequence is read. This is referred to as a "reading frame." It consists of groups of three bases, each of which code for one amino acid (one of several molecules that join together to form proteins). A frameshift mutation shifts the grouping of these bases and changes the code for amino acids. The resulting protein is usually nonfunctional. Insertions, deletions, and duplications can all be frameshift mutations.

The mutations shift the reading frame of the genetic message (remember that the reading frame is in sets of three). So if a base is either added to or deleted from the reading frame, the genetic code is shifted. In the following example, a letter is deleted, so the other letters shift and spell different words. Example: "The dog can run." When the letter T is deleted, this sentence reads as "hed ogc anr un."

- **An insertion:** An insertion changes the number of DNA bases in a gene by adding a piece of DNA.



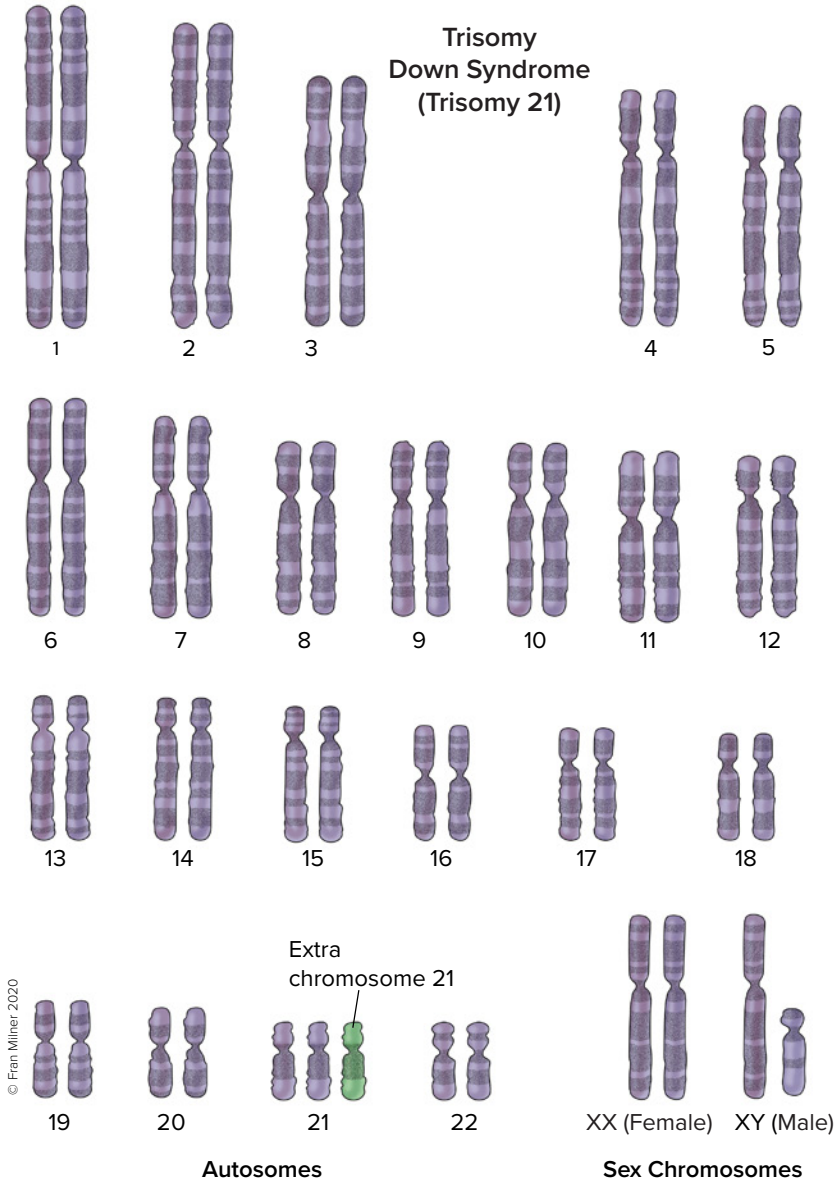
- **A deletion:** A deletion changes the number of DNA bases by removing a piece of DNA. Small deletions may remove one or a few base pairs within a gene whereas larger deletions can remove an entire gene.



Changes in Chromosomes. Most chromosomal abnormalities occur when there is an error in cell division. These changes can occur during the formation of reproductive cells (eggs and sperm), in early fetal development, or in any cell after a person is born.

There are two types of chromosomal changes, numerical abnormalities and structural abnormalities.

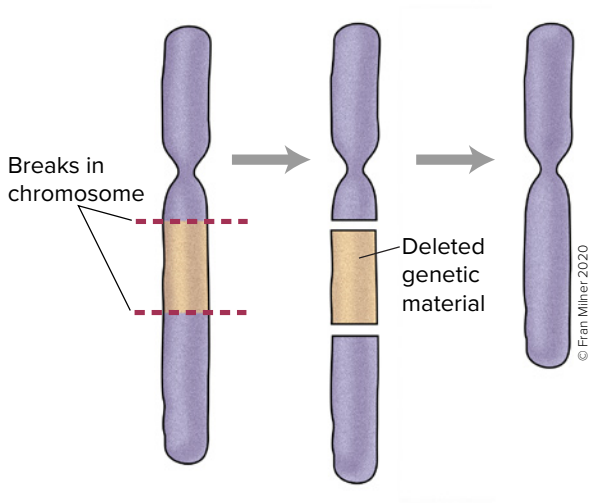
Numerical abnormalities: Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes. A numerical abnormality is the gain or loss in the number of chromosomes from the normal 46. Trisomy, the presence of an extra chromosome in the cells, is a common numerical abnormality. Down syndrome is a condition caused by trisomy. People with Down syndrome typically have three copies of chromosome 21 in each cell (trisomy 21), for a total of 47 chromosomes in each cell.



Structural abnormalities: Changes that affect the structure of chromosomes can affect growth, development, and the functioning of the body. These changes can impact genes on the chromosome and disrupt the proteins made from those genes. The effects of structural abnormalities depend on their size and location and whether any genetic material is lost or gained. There are several chromosomal rearrangements that can change the structure of a chromosome.

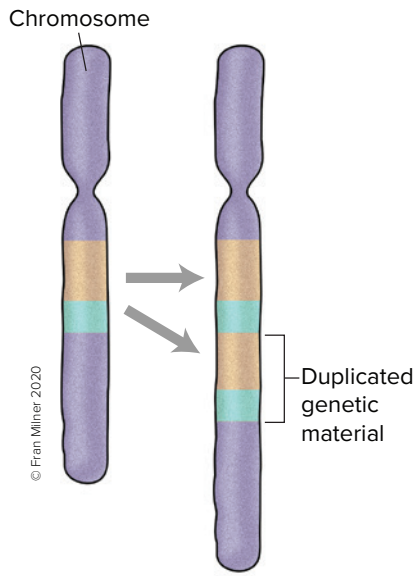
- **A deletion:** A deletion occurs when a portion of the chromosome is missing or deleted.

Chromosomal Deletion



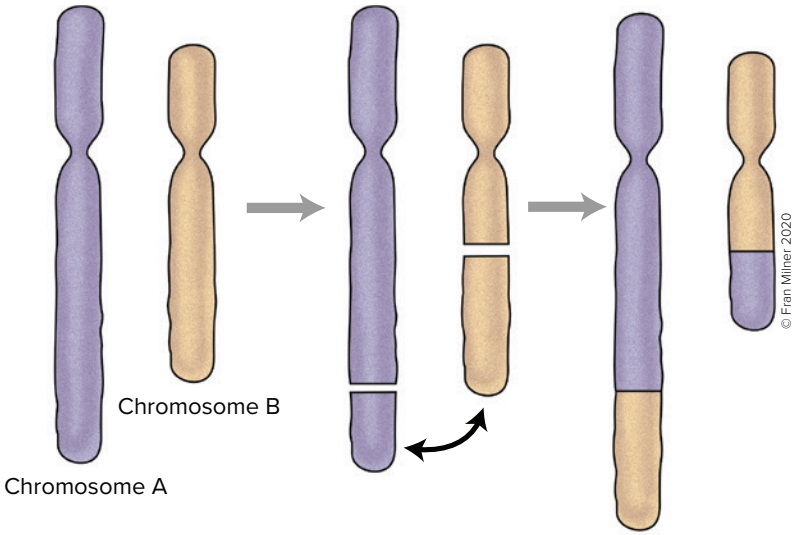
- **A duplication:** A duplication occurs when a portion of a chromosome is duplicated too many times, resulting in too many copies of that genetic material within a cell.

Chromosomal Duplication



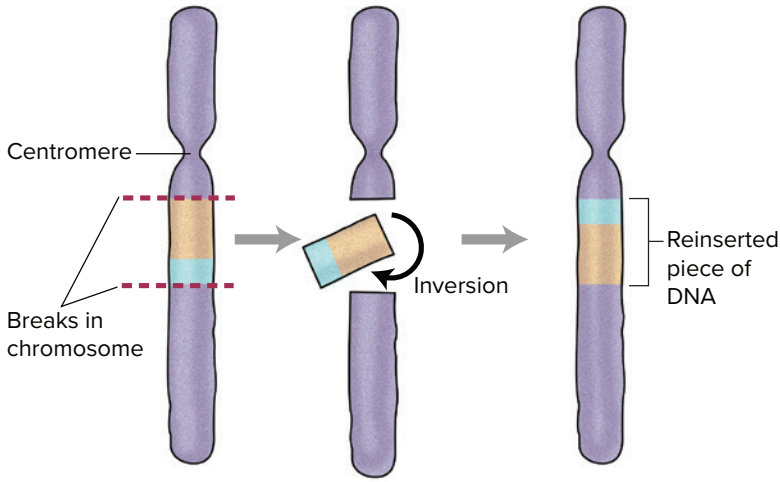
- **A translocation:** A translocation occurs when a piece of one chromosome breaks off and attaches to another chromosome. The location at which the break occurs can affect nearby genes.

Balanced Translocation

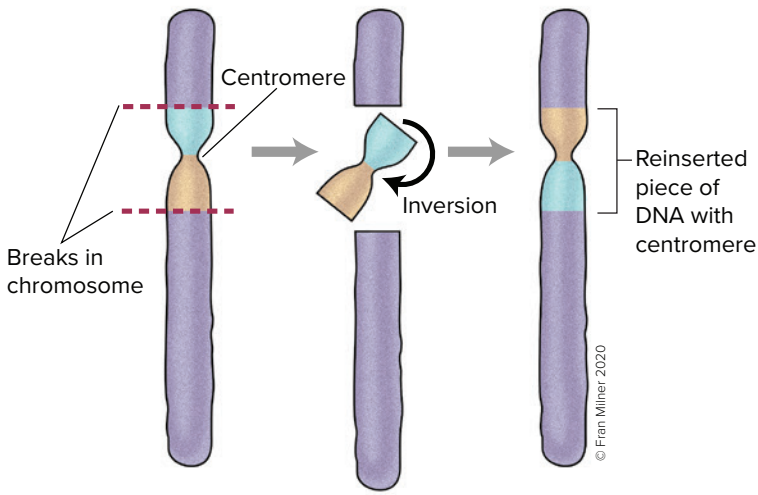


- **An inversion:** An inversion occurs when a portion of a chromosome breaks off, turns upside down, and reattaches. As a result, the genetic material is inverted, and is now in a different order. Inversions can result in the loss of a gene or genes because the cell can no longer read its instructions. A paracentric inversion is an inversion that does not include the centromere and both breaks occur in one arm of the chromosome. A pericentric inversion is an inversion that includes the centromere and there is a breakpoint in each arm.

Paracentric Inversion



Pericentric Inversion



The Genetics of Cancer

Cancer is a disease caused by mutations in genes that control the way our cells work, especially how they grow and divide. The human body is made up of trillions of cells. Usually, we have the right number of each type of cell in our body. Our cells grow and divide to form new cells as we need them (mitosis). When cells become old or damaged, they die and, in most cases, new cells take their place.

Genes carry instructions that make specific classes of proteins that tell the cell when to grow and divide. These specialized proteins control how quickly a cell grows, how often it divides, and how long the cell lives.

Some mutations occur in genes that make the proteins that control cell growth. When these mutations occur, they can cause cells to grow and multiply uncontrollably, which can lead to cancer.

When cancer develops, abnormal cells survive when they should die, and new cells form when they are not needed. These extra cells can form solid tumors. In blood cancers, such as leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms, uncontrolled growth can lead to the presence of cancer cells in the blood, bone marrow, lymph nodes and other parts of the body.

Types of Testing for Mutations in Cancer Cells

Your cancer has a unique combination of genetic changes. These changes can be inherited (hereditary), but most occur randomly during your lifetime (somatic). In some cases, knowing the genetic mutations of your cancer cells can help determine the best treatment plan. Some treatments, particularly some targeted therapies, are effective only for people whose cancer cells have specific genetic mutations.

To determine the changes to the DNA in your cancer cells, you will need a biopsy. A biopsy is a procedure in which your doctor removes a sample of the cancer cells. Your doctor may examine your blood, bone marrow and/or lymph node cells.

The following tests can be done to obtain information about the genetic changes to your cancer cells:

Cytogenetic Analysis (Karyotyping). In this test, a hematopathologist (a doctor who has had special training in identifying blood diseases by studying cells and tissues) uses a microscope to examine the chromosomes inside of cells. This test is used to look for abnormal changes in the chromosomes of the cancer cells. The cancer cells in the sample are allowed to grow in the laboratory and then

they are stained with a special dye to allow visualization of the chromosomes. The stained sample is examined under a microscope and then photographed to show the arrangement of the chromosomes. This image is called a "karyotype." The karyotype shows if there are any abnormal changes in the size, shape, structure or number of chromosomes in the cancer cells. See image on page 5.

Fluorescence in Situ Hybridization (FISH). Doctors use FISH to detect certain abnormal changes in the chromosomes and genes of cancer cells. Pieces of DNA that contain special fluorescent dyes are made in the laboratory and added to the cells on a glass slide. When the pieces of DNA bind to specific genes or areas of chromosomes on the slide, they light up when viewed under a fluorescent microscope. FISH testing is able to detect changes that are too small to be seen on basic cytogenetic tests. A FISH test is not, however, a general screening tool because the doctor must select specific chromosomes or genes to examine before running the test.

Polymerase Chain Reaction (PCR). This test is a very sensitive genetic laboratory technique that is used to detect and measure some genetic mutations and chromosomal changes that are too small to be seen with a microscope. Polymerase chain reaction testing essentially increases (amplifies) small amounts of specific pieces of DNA so that they are easier to detect and measure. This test can find a single cancer cell among more than 500,000 to one million normal cells.

Deoxyribonucleic Acid (DNA) Sequencing. "Sequencing" refers to a number of different laboratory tests that examine the exact sequence (order) of the four bases (A, C, G and T) of DNA. By comparing the sequence of DNA in cancer cells with the DNA in normal cells, doctors can find genetic changes in cancer cells that are unique to the cancer cells and may be driving the growth of the patient's cancer.

There are targeted DNA sequencing tests (also called "multigene panels") that look for specific mutations in a sample. The test focuses on specific sets of genes or areas of DNA.

There are also broad DNA sequencing tests (genomic screening tests) that analyze the sequence of large regions of DNA rather than looking for mutations of specific genes. Doctors may also order sequencing of all of the DNA in your entire genome. This test is known as "whole genome sequencing."

The term "next-generation sequencing (NGS)" is a catch-all term used to describe a number of different modern sequencing technologies. These technologies allow for sequencing of DNA and ribonucleic acid (RNA) much more quickly and cheaply than the previously used sequencing methods. Consult your doctor to discuss the possibility of next-generation sequencing as part of your care. Next-generation sequencing is commonly used for patients with cancers that can be treated with a targeted therapy.

In addition, some doctors may recommend next-generation sequencing for patients with advanced cancer that is not responding to standard treatment. This approach may help doctors to identify other treatments that may be effective given the cancer's genetic makeup.

Precision Medicine

Each person's cancer has a unique combination of genetic mutations. Precision medicine is a specific treatment approach that lets doctors select therapies that are tailored to the genetic mutations in each person's cancer.

Diagnosing Patients. Some genetic mutations are commonly found in certain blood cancers. Finding these mutations can confirm a diagnosis. For example,

- Most cases of chronic myeloid leukemia (CML) are caused by the *BCR-ABL* fusion gene. The *BCR-ABL* gene is formed by a translocation (see page 13) between parts of chromosomes 9 and 22. For most CML patients, the presence of the *BCR-ABL* gene is needed to diagnose the disease.
- In almost all cases of hairy cell leukemia, the leukemia cells have a mutation of the *BRAF* gene. The *BRAF-V699E* gene mutation serves as a reliable marker of the disease, and it distinguishes hairy cell leukemia from other B-cell leukemias and lymphomas.

Prognosis and Testing. A prognosis is a prediction of the outcome of a disease. In some cancers, doctors look for specific gene changes to predict outcomes. Knowing your prognosis can help you and your doctor make decisions about treatment. For example,

- For patients with acute myeloid leukemia (AML) whose cancer cells have a *NPM1* gene mutation (without a *FLT3-ITD* gene mutation) seem to have a better prognosis than people without the *NPM1* mutation.
- For patients with myelodysplastic syndromes (MDS), several studies have shown that cancer cells with mutations of the *TP53, EZH2, ETV6, RUNX1* and *ASXL1* genes predict a decrease in overall survival.

For patients diagnosed with high-risk disease, doctors may recommend a different treatment such as a targeted therapy, more intense treatments or enrollment in a clinical trial.

Testing and Treatment. Before precision medicine, most people with a specific type and stage of cancer received the same treatment. Certain treatments, however, worked better for some patients than for others. After decades of research, scientists now understand that genetic differences in tumor cells may explain why patients have different responses to treatment.

Doctors are now offering some patients treatment that is based on the genetic changes in their cancer cells. These new therapies can work better to eliminate cancer and may have fewer side effects. One of the first successful precision treatments has been the drug imatinib mesylate (Gleevec®) approved by the Food and Drug Administration (FDA) for the treatment of patients with CML. Patients with CML have a gene mutation that produces an abnormal protein that signals blood stem cells to produce too many immature white blood cells. Imatinib mesylate blocks these signals and stops the body from producing the cancer cells. For most patients, imatinib mesylate has changed CML from a potentially fatal disorder to a disease that can be controlled.

Scientists see a future where testing for genetic mutations in cancer cells can help doctors match each patient with the most effective treatment for his or her disease.

Research and Clinical Trials

Clinical trials are essential in making progress against cancer. Today, people are living longer because of successful cancer treatments that are the result of past clinical trials.

New approaches are being studied in clinical trials for the treatment of blood cancers using precision medicine. Many of these trials are supported by LLS research programs and hold the promise of increasing the rates of remission and finding cures for all blood cancers.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called "clinical trials" before it becomes part of standard therapy. Clinical trials are carefully designed and reviewed by expert clinicians, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time you discuss your treatment with your doctor. Patient participation in past clinical trials has resulted in the Food and Drug Administration (FDA)-approved therapies we have today.

The Leukemia & Lymphoma Society (LLS) Information Specialists, available at (800) 955-4572, offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Diversity in Clinical Trials. Diversity in clinical trials is critical to public health. Researchers now know that a patient's response to a treatment can vary due to a number of factors including race and ethnic origin. These differences can play a role in the safety and effectiveness of a medication. When clinical trials include a diverse group of patients, the results of the study may be much more relevant to the general population.

While researchers are sequencing millions of human genomes in the hopes of finding new, targeted therapies and personalized drugs, most participants in studies and genetic databases are white people of European descent. This limitation prevents people of color from benefitting from precision medicine.

In order to deliver healthcare recommendations that are tailored to individuals, researchers need to better understand the biology of ancestry and ethnicity. If a person's genetic background is not represented in the genetic databases, he or she could potentially miss out on certain cures. Making precision medicine available to all people means research studies must include diverse populations. Joining a clinical trial may not only benefit you but your community as well.

Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of the knowledge and skills of the members of your healthcare team.

For Help and Information

Consult With an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 am to 9 pm ET)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

Clinical Trials Support Center (CTSC). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Please visit www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support booklets that can be either read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial assistance to individuals with blood cancer. Please visit www.LLS.org/finances for more information.

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for eligible patients. For more information, please

- Call: (877) 557-2672
- Visit: www.LLS.org/copay

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Please visit www.LLS.org/HealthManager to download for free.

One-on-One Nutrition Consultations. Access free one-on-one nutrition consultations with a registered dietitian who has experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management, and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Podcast. The *Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other health care professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Please visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Please visit www.LLS.org/SuggestedReading to find out more.

Continuing Education. LLS offers free continuing education programs for health care professionals. Please visit www.LLS.org/ProfessionalEd for more information.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Please visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients to reach out and share information. Please visit www.LLS.org/chat to join.

LLS Chapters. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to obtain our directory.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

Additional Help for Specific Populations

Información en español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let members of your healthcare team know if you need a language interpreter or other assistance, such as a sign language interpreter. Often, these services are free.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information please

- Call: the VA (800) 749-8387 (select option 4)
- Visit: www.publichealth.va.gov/exposures/AgentOrange

World Trade Center (WTC) Survivors. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be eligible for help from the World Trade Center (WTC) Health Program. People eligible for help include

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area, lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA, crashes.

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People Suffering From Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a 2-week period. For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov. Enter “depression” in the search box.

Other Resources

Clinical Trials Support Center

www.LLS.org/CTSC

Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help them to find clinical trials and personally assist them throughout the entire clinical trial process.

Genetics Home Reference

https://ghr.nlm.nih.gov/

Genetics Home Reference is a consumer health website from the National Library of Medicine, which is part of the National Institutes of Health. The website provides information for members of the general public about the effects of genetic variations on human health.

Health Terms

Acquired (somatic) Mutation. These mutations occur at some time during a person's life and are present only in certain cells, not in every cell in the body. These changes can be caused by environmental factors or can occur if an error is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed to the next generation.

Amino Acid. One of several molecules that join together to form proteins.

Apoptosis. A type of cell death in which a series of molecular steps in a cell lead to its death. This is one method the body uses to get rid of unneeded or abnormal cells. The process of apoptosis may be blocked in cancer cells. Also called "programmed cell death."

Arm. Each chromosome has a constriction point called the "centromere," which divides the chromosome into two sections, or "arms." The short arm of the chromosome is labeled the "p arm." The long arm of the chromosome is labeled the "q arm." The location of the centromere on each chromosome gives the chromosome its characteristic shape, and can be used to help describe the location of specific genes.

Base Pair. A base pair is two chemical bases bonded to one another forming a "rung of the DNA ladder." The DNA molecule consists of two strands that wind around each other like a twisted ladder. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases—adenine (A), cytosine (C), guanine (G), or thymine (T). The two strands are held together by hydrogen bonds between the bases, with adenine forming a base pair with thymine, and cytosine forming a base pair with guanine.

Biomarker. A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called "molecular marker" and "signature molecule."

Cells. In biology, the smallest unit that can live on its own and that makes up all living organisms and the tissues of the body. The basic units of life. The human body has more than 30 trillion cells.

Chromosome. The DNA molecule that is packaged into thread like structures in the nucleus of each cell. Each chromosome is made up of DNA tightly coiled many times around proteins called "histones" that support its structure.

DNA. The molecules inside cells that carry genetic information and pass it from one generation to the next. Also called "deoxyribonucleic acid."

Gene. The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein.

Gene Expression. The process by which a gene gets turned on in a cell to make RNA and proteins. Gene expression may be measured by looking at the RNA, or the protein made from the RNA, or what the protein does in a cell.

Genetics. Having to do with genes. Most genes are sequences of DNA that contain information for making specific RNA molecules or proteins that perform important functions in a cell. The information in genes is passed down from parent to child. Sometimes, certain changes in genes can affect a person's risk of disease. These changes may be inherited or they may occur with age or exposure to environmental factors, such as diet, exercise, drugs, and chemicals.

Genetic Testing. The process of analyzing cells or tissue to look for changes in genes, chromosomes, or proteins that may be a sign of a disease or condition, such as cancer. These changes may also be a sign that a person has an increased risk of developing a specific disease or condition. Genetic testing may be done on tumor tissue to help diagnose cancer, plan treatment, or find out how well treatment is working.

Genome. The complete set of DNA (genetic material) in an organism. In people, almost every cell in the body contains a complete copy of the genome. The genome contains all of the information needed for a person to develop and grow. Studying the genome may help researchers understand how different types of cancer form and respond to treatment. This may lead to new ways to diagnose, treat, and prevent cancer.

Genomics. The study of the complete set of DNA (including all of its genes) in a person or other organism. Almost every cell in a person's body contains a complete copy of the genome. The genome contains all the information needed for a person to develop and grow. Studying the genome may help researchers understand how genes interact with each other and with the environment and how certain diseases, such as cancer,

diabetes, and heart disease, form. This may lead to new ways to diagnose, treat, and prevent disease.

Genomic Screening. Assesses an individual's genome (all of a person's genes, rather than a specific gene or set of genes).

Hereditary Mutation. Inherited from a parent and are present throughout a person's life in virtually every cell in the body. These mutations are also called "germline mutations" because they are present in the parent's egg or sperm cells, which are also called "germ cells."

Histone. A protein that provides structural support to a chromosome. In order for very long DNA molecules to fit into the cell nucleus, they wrap around complexes of histone proteins, giving the chromosome a more compact shape. Some variants of histones are associated with the regulation of gene expression.

Karyotype. An individual's collection of chromosomes. The term also refers to a laboratory technique that produces an image of an individual's chromosomes. The karyotype is used to look for abnormal numbers or structures of chromosomes.

Marker. A DNA sequence with a known physical location on a chromosome. Markers can help link an inherited disease with the responsible genes. DNA segments close to each other on a chromosome tend to be inherited together. Markers are used to track the inheritance of a nearby gene that has not yet been identified but whose approximate location is known. The marker itself may be a part of a gene or may have no known function.

Molecule. The smallest particle of a substance that has all of the physical and chemical properties of that substance. Molecules are made up of one or more atoms. If they contain more than one atom, the atoms can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms.

Molecular Marker. See Biomarker.

Mutation. A change in a DNA sequence. Mutations can result from DNA copying mistakes made during cell division, exposure to ionizing radiation, exposure to chemicals called "mutagens," or to infection by viruses. Germ line mutations occur in the eggs and sperm and can be passed on to offspring, while somatic mutations occur in body cells and are not passed on.

Nucleotide. A nucleotide is the basic building block of nucleic acids. RNA and DNA are polymers made of long chains of nucleotides. A nucleotide consists of a sugar molecule (either ribose in RNA or deoxyribose in DNA) attached to a phosphate group and a nitrogen-containing base. The bases used in DNA are adenine (A), cytosine (C), guanine (G), and thymine (T). In RNA, the base uracil (U) takes the place of thymine.

Precision Medicine. A form of medicine that uses information about a person's own genes or proteins to prevent, diagnose, or treat disease. In cancer, precision medicine uses specific information about a person's tumor to help make a diagnosis, plan treatment, find out how well treatment is working, or make a prognosis. Examples of precision medicine include using targeted therapies to treat specific types of cancer cells or using tumor marker testing to help diagnose cancer. Also called "personalized medicine."

Personalized Medicine. See Precision medicine.

Protein. A molecule made up of amino acids. Proteins are needed for the body to function properly. They are the basis of body structures, such as skin and hair, and of other substances such as enzymes, cytokines, and antibodies.

Tumor Markers. A substance found in tissue, blood, bone marrow, or other body fluids that may be a sign of cancer or certain benign (noncancer) conditions. Many tumor markers are proteins made by both normal cells and cancer cells, but they are made in higher amounts by cancer cells. Genetic changes in tumor tissue, such as gene mutations, patterns of gene expression, and other changes in tumor DNA or RNA, are also being used as tumor markers. A tumor marker may be used with other tests to help diagnose cancer. It may also be used to help plan treatment, give a likely prognosis, and find out how well treatment is working or if cancer has come back.

NOTES

NOTES

LEUKEMIA & LYMPHOMA SOCIETY®

Get support. Reach out to our **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individual clinical-trial searches

Contact us at
800-955-4572 or
www.LLS.org/InformationSpecialists
(Language interpreters can be requested)

LEUKEMIA & LYMPHOMA SOCIETY®

For more information, please contact our Information Specialists **800.955.4572** (Language interpreters available upon request).

BEATING CANCER IS IN OUR BLOOD.®

National Office 3 International Drive, Suite 200 Rye Brook, NY 10573

The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at **www.LLS.org**.

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