LEUKEMIA & LYMPHOMA SOCIETY OF CANADA®

TREATING BLOOD CANCERS

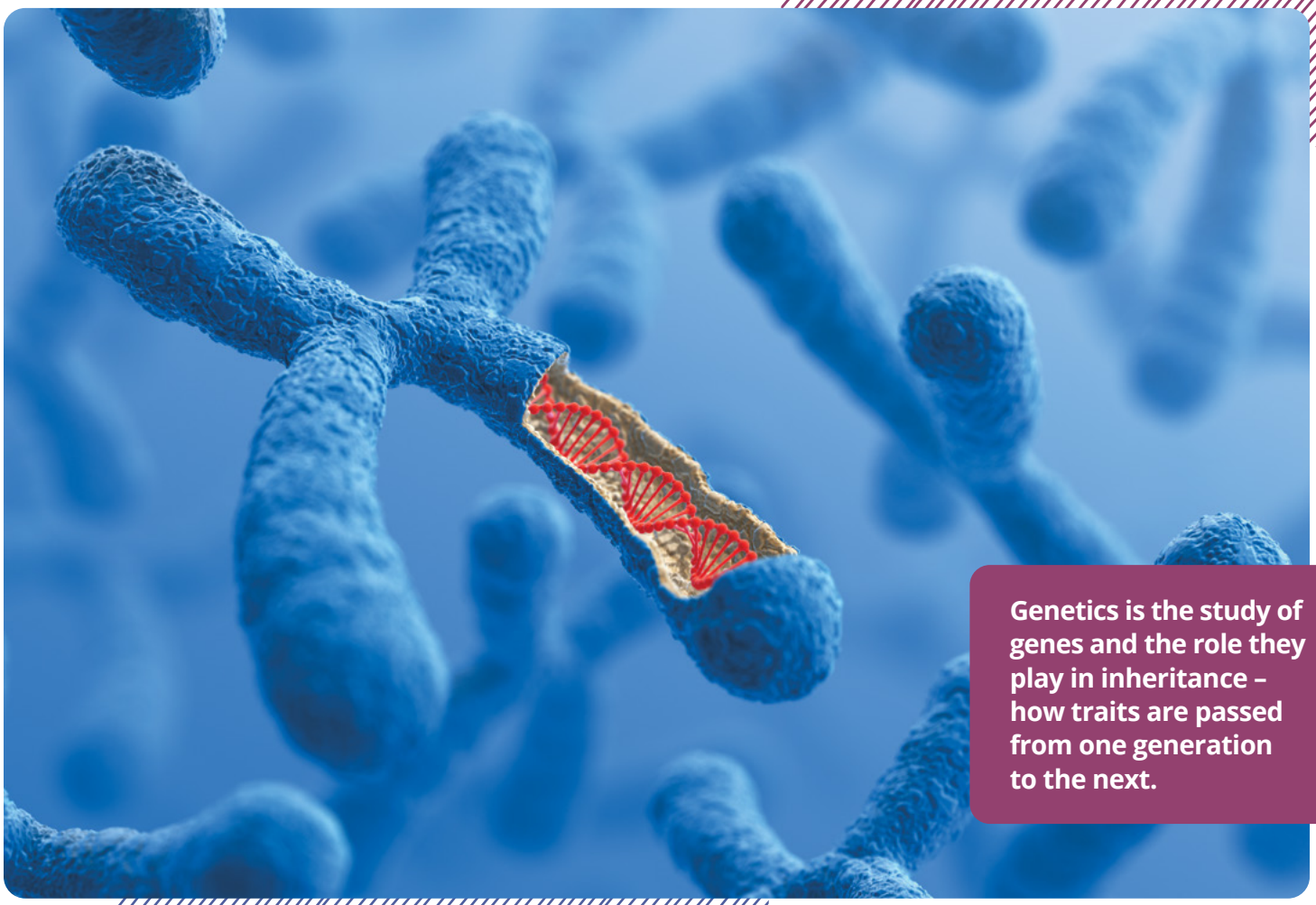
Understanding GENETICS

WHAT YOU NEED TO KNOW

You or your loved one has been diagnosed with a type of blood cancer. Genetics plays an important role in understanding cancer and treatments for cancer. What is genetics and how is it involved in cancer?

This fact sheet will help you:

- Learn about how genetics plays a role in cancer
- Understand what genetics is
- Get an overview of genetics terms
- Learn about mutations in cancer
- Understand the types of testing for mutations



Genetics is the study of genes and the role they play in inheritance – how traits are passed from one generation to the next.

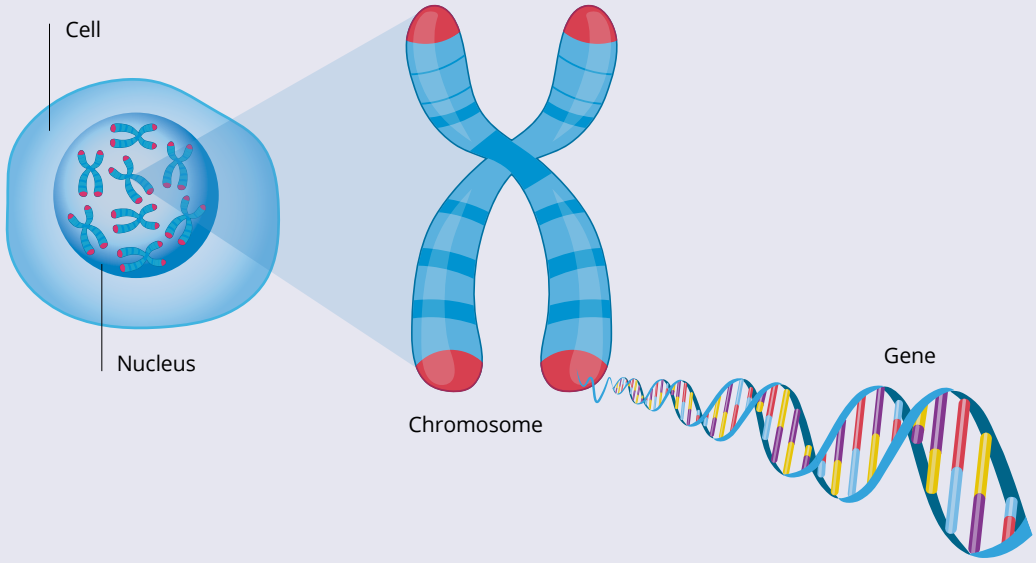
Genetics and blood cancers

To understand your cancer, it helps to know about genetics. Cancer is a disease caused by abnormal changes (mutations) to our genes that control how our cells work, grow, and divide. Each person's cancer has a unique combination of genetic mutations.

About cancer cells

- They behave differently from normal cells
- They can multiply uncontrollably even when they are not needed
- Abnormal cells survive when they should die, and new cells form when they are not needed
- These extra cancer cells can spread and form a tumour
- In blood cancers, uncontrolled growth can lead to cancer cells being in the blood, bone marrow, lymph nodes, and other parts of your body

Most blood cancers do not have a proven genetic predisposition. This means there is no evidence that the genes a person inherits from their parents give them a higher chance of getting blood cancer. We still don't understand the causes of most blood cancers.



Genetics 101

Genetics is the study of genes and family traits and how they are passed on through generations.

Key terms include cells, chromosomes, DNA, and genes.

What are cells?

- Cells are basic units of life. Human bodies have more than 30 trillion cells
- Each type has a different job. For example, red blood cells carry oxygen and heart cells contract to pump blood
- Most cells have a nucleus that contains your genetic material: a blueprint of how your body will develop and grow

What are chromosomes?

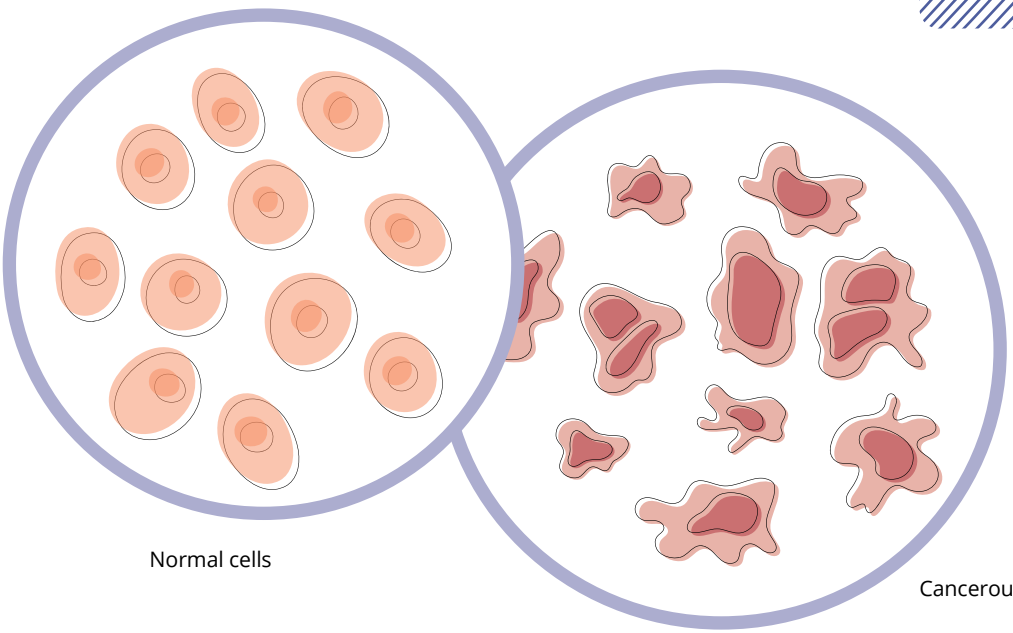
- Inside most cells, your genetic material is packed into threadlike structures
- Human cells usually contain 23 pairs of chromosomes
- Chromosomes are passed (inherited) from parents to the child
- Chromosomes are made up of DNA

What is DNA?

- DNA (deoxyribonucleic acid) carries genetic information from one generation to the next
- Nearly every cell in your body has the same DNA

What are genes?

- A gene is a section of DNA that carries the traits you inherit from your parents, such as eye and hair colour
- Genes contain instructions that tell the cell how quickly to grow, how often to divide, and how long to live



Normal cells

Cancerous cells

Mutations and cancer

A gene mutation is a permanent change in the DNA sequence (order) of a cell. Mutations affect your health in different ways depending on where they happen in your body and if they change the function of important proteins. Proteins help cells perform functions in your body, such as carrying oxygen through your body or digesting food.

About mutations

- They vary in size
- They occur often and randomly during your lifetime
- Your body usually detects the mutation: the cell is repaired or it dies
- A cell that is not repaired and does not die may become cancerous
- Cancer can occur over time as mutations build up
- Cancer can occur with many rounds of replications: this is the case in blood cells (for example, leukemia)

Why do gene mutations happen?

There are two kinds of genetic mutations: ones you inherit from your parents and ones where the damage happens during your lifetime.

- **A hereditary mutation** (also known as germline) is inherited from a parent. These mutations are present during your lifetime in most cells in your body.
- **An acquired mutation** (also known as somatic) occurs during your life and is not found in every cell in your body. With this type of mutation, your DNA becomes damaged. Causes can include environmental factors such as exposure to radiation or certain chemicals, as well as lifestyle factors such as smoking, age, and diet. They can also happen if a mistake is made when DNA copies itself (replicates).

How do mutations cause cancer?

The genes in our cells are mutating all the time. Usually, the change is detected and is repaired, or the cell dies. A single mutation will not likely cause cancer, but over time, the damage can build up. For this reason, cancer happens more often in older people.

Changes to your genes

Genes change (mutate) in different ways and for different reasons. Some examples include:

- **Point mutation,** when a pair in the DNA sequence is altered (for example, with some forms of myelodysplastic syndromes)
- **Frameshift mutation**, when there is an insertion (addition) or deletion (loss) in the DNA

Changes to your chromosomes

Most chromosome abnormalities happen when there is an error as a cell is dividing. There are two types:

- **Numerical abnormalities**, when you gain chromosomes or lose the usual number of chromosomes
- **Structural abnormalities**, when the change affects the structure of the chromosome and impacts the growth, development, and function of your body. This can include:
  - deletion (a section of the chromosome is missing)
  - duplication (a chromosome is present too many times)
  - inversion (a piece of a chromosome breaks, turns upside down, and reattaches)
  - translocation (a piece of one chromosome breaks off and attaches to another)

Types of testing for mutations in cancer cells

The type of cancer you have has a unique combination of genetic changes. These can be inherited, but most occur randomly over your lifetime. It can often help to know the genetic mutations of your cancer cells to determine the best treatment plan. Various tests are used to get this genetic information.

Name of test	Description
Biopsy	The doctor removes a sample of the cancer cells to determine the changes to the DNA.
Deoxyribonucleic acid (DNA) sequencing	These lab tests examine the sequence (order) of DNA. This helps to determine the genetic changes in cancer cells that may be causing the cancer to grow.
Cytogenetic analysis (karyotyping)	This test looks for abnormal changes in the chromosomes of cancer cells.
Fluorescence *in situ* hybridization (FISH)	This lab test detects certain abnormal changes in the genes and chromosomes of cancer cells.
Polymerase chain reaction (PCR)	This lab test detects and measures some genetic mutations and chromosome changes that are too small to be seen with a microscope.

Treating your cancer with precision medicine

Precision medicine allows doctors to select therapies tailored to your unique genetic mutations.

Identifying your type of cancer (diagnosis)

Some types of genetic mutations are common in certain blood cancers. Finding them can confirm a diagnosis. For example:

Chronic myeloid leukemia (CML)	Most cases of CML are caused by the BCR-ABL fusion gene. This gene usually needs to be present for CML to be diagnosed.
Hairy cell leukemia (HCL)	Most cases have a mutation of the BRAF gene. The presence of this gene is a marker of this type of leukemia.

Predicting your outcome (prognosis)

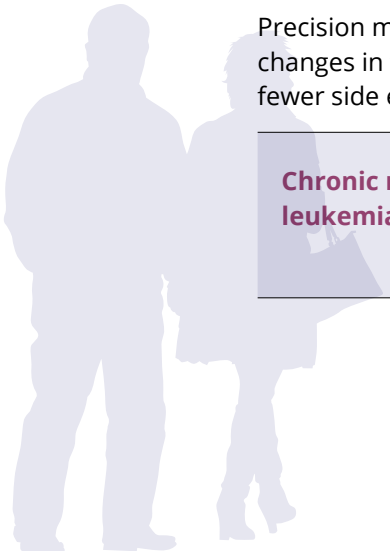
Doctors often look for specific changes in genes to help predict how a disease will progress and what the outcome will be. This can help them make decisions about your treatment. For example:

Acute myeloid leukemia (AML)	People with AML whose cancer cells have an NPM1 gene mutation often have a better prognosis (outcome) than people who don't have this gene.
Myelodysplastic syndromes (MDS)	People with MDS whose cancer cells have a specific mutation (TP53, EZH2, ETV6, RUNX1, ASXL1) often have a poorer prognosis (outcome) than people who don't have these mutations.

Testing and treating your cancer

Precision medicine allows some people with cancer to get specific treatment based on the genetic changes in their cancer cells. These new therapies can do a better job of eliminating cancer, with fewer side effects. For example:

Chronic myeloid leukemia (CML)	A successful precision treatment for CML is the drug Imatinib mesylate. For many people with CML, this drug has helped change the disease from potentially fatal to one that can be controlled.



Every new drug treatment goes through a series of studies called clinical trials before it becomes standard. Talk to your doctor to see if a clinical trial is an option for you.

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