

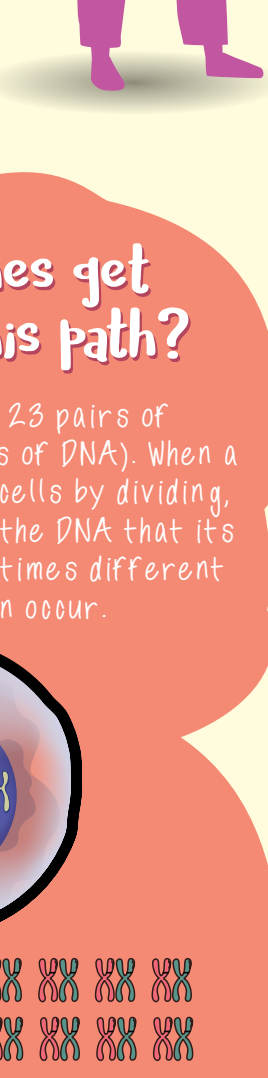
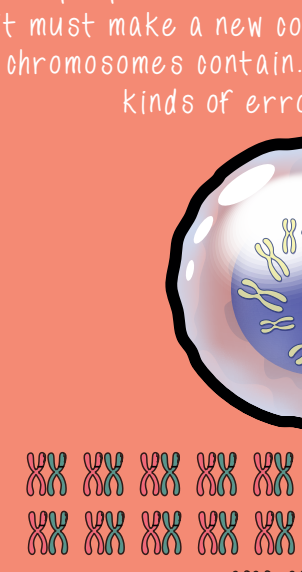
# WHAT CAUSES CML?



CML is the result of a change that occurs in our DNA—the chemical that carries our genes. DNA provides the recipe for how our cells function.

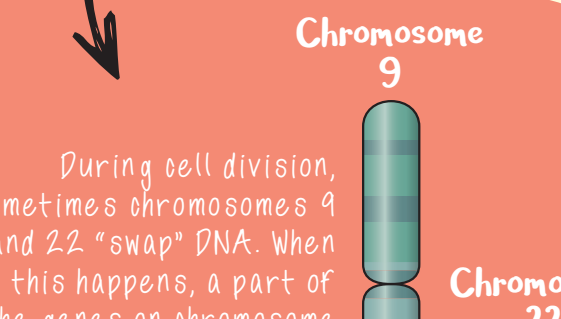
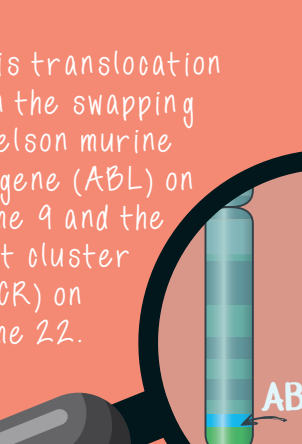


In most cases of CML, our genes become rearranged in a way that codes for a recipe telling healthy cells to not function the way they should in our bodies and to become cancerous.

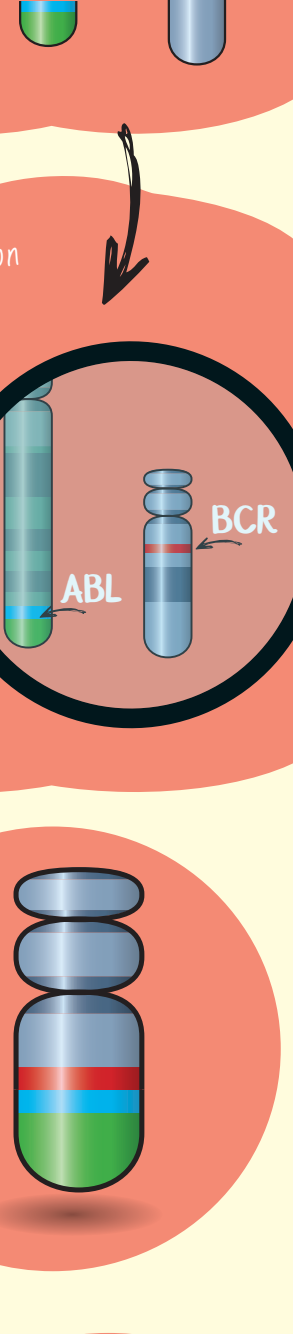


## How do our genes get directed down this path?

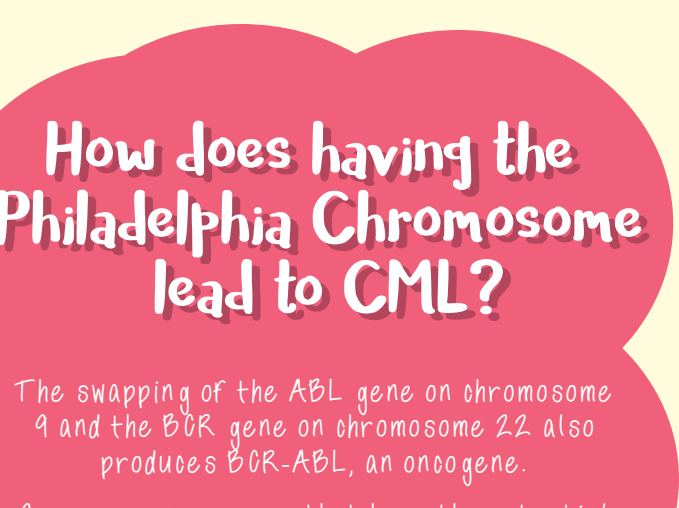
Each human cell houses 23 pairs of chromosomes (long molecules of DNA). When a cell prepares to make new cells by dividing, it must make a new copy of the DNA that its chromosomes contain. Sometimes different kinds of errors can occur.



During cell division, sometimes chromosomes 9 and 22 “swap” DNA. When this happens, a part of the genes on chromosome 9 are transferred to chromosome 22, and a part of the genes on chromosome 22 are transferred to chromosome 9. This process is called a **translocation**.



In CML, this translocation results in the swapping of the Abelson murine leukemia gene (ABL) on chromosome 9 and the breakpoint cluster region (BCR) on chromosome 22.



The result: a shorter than normal chromosome 22, called the **Philadelphia Chromosome**.



The Philadelphia chromosome has been detected in either:

**Bone Marrow**



**cells circulating in the blood**



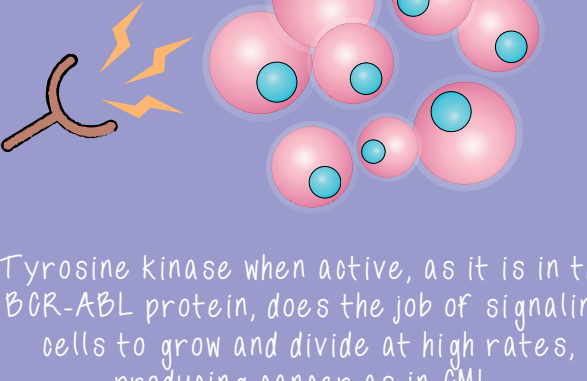
**95% of patients with CML.**

## How does having the Philadelphia Chromosome lead to CML?

The swapping of the ABL gene on chromosome 9 and the BCR gene on chromosome 22 also produces BCR-ABL, an oncogene.

Oncogenes are genes that have the potential to turn a normal cell into a cancerous one.

**Normal cell** → **Oncogenic event** → **Cancer cells**



The BCR-ABL oncogene makes the BCR-ABL protein, which directs cells to behave in abnormal ways.

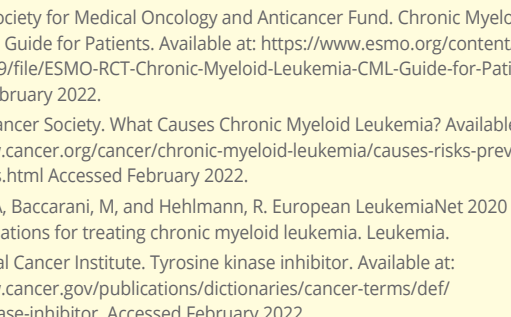
These include abnormal cell maturation, increasing cell turnover and proliferation (speeding up the time it takes for new cells to develop and making them multiply in number), and immortalizing cells (making them live forever).

All of these changes cause CML cells to develop and divide uncontrollably.



## Since CML develops when our genetics are altered, can you inherit it from your parents or other family members?

No, CML is not something that you can inherit before you are born. It is not a disease that runs in families either. The changes in DNA that are related to CML occur after a person is born and during their lifetime.



## How do genetics affect CML treatments?

The BCR-ABL protein that BCR-ABL oncogene makes is a type of protein called a tyrosine kinase. The first-line treatment for CML, tyrosine kinase inhibitors (TKIs) use the very knowledge of this type of protein and target it.



Tyrosine kinase when active, as it is in the BCR-ABL protein, does the job of signaling cells to grow and divide at high rates, producing cancer as in CML.

**TYROSINE KINASE INHIBITOR**

Tyrosine kinase inhibitor drugs that block the BCR-ABL protein from working. As a result, tyrosine kinase inhibitors stop CML cancer cells from continuing to grow and divide, causing the CML cells to die.



One of the benefits of these therapies is that they zero in on their target. TKIs attack specific types of cancer cells while causing less damage to the body's healthy cells.

If you have any questions about your treatment, please speak to your healthcare team.



# THE END!

References:  
 European Society for Medical Oncology and Anticancer Fund. Chronic Myeloid Leukemia: A Guide for Patients. Available at: <https://www.esmo.org/content/download/6597/114989/file/ESMO-RCT-Chronic-Myeloid-Leukemia-CML-Guide-for-Patients.pdf> Accessed February 2022.  
 American Cancer Society. What Causes Chronic Myeloid Leukemia? Available at: <https://www.cancer.org/cancer/chronic-myeloid-leukemia/causes-risks-prevention/what-causes.html> Accessed February 2022.  
 Hochhaus, A, Baccarani, M, and Hehlmann, R. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. Leukemia.  
 NIH, National Cancer Institute. Tyrosine Kinase Inhibitor. Available at: <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/tyrosine-kinase-inhibitor>. Accessed February 2022.  
 Leukemia & Lymphoma Society. Tyrosine Kinase Inhibitor (TKI) Therapy. Available at: <https://www.lls.org/leukemia/chronic-myeloid-leukemia/treatment/tyrosine-kinase-inhibitor-tki-therapy#:~:text=TKIs%20come%20as%20pills%2C%20taken,the%20CML%20cells%20to%20die>. Accessed February 2022.