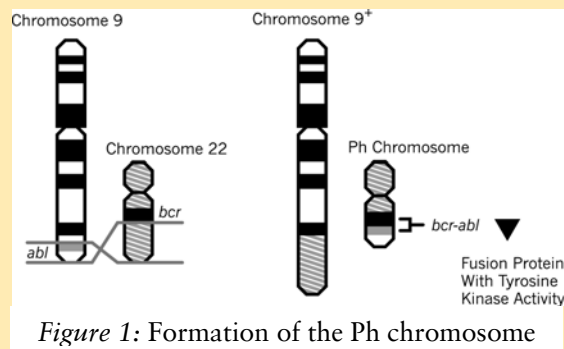


Chronic Myeloid Leukemia (CML)

What is Chronic Myeloid Leukemia (CML)?

Chronic myeloid leukemia (CML), also known as chronic myelogenous leukemia, is one of the four most common types of leukemia. The American Cancer Society estimates that 4,570 new cases of CML will be diagnosed and approximately 490 deaths from CML will occur in 2007.¹ CML usually affects the middle-age population, and the average age of people with CML is 66.² About 2% of cases are diagnosed in children.²

CML is a hematologic malignancy in which white blood cells do not mature and become too numerous. It is characterized by the presence of an abnormality called the Philadelphia (Ph) chromosome. The Ph chromosome is created by an exchange of genetic material between chromosomes 9 and 22. A detached portion of chromosome 9 shifts to chromosome 22, and a section of chromosome 22 shifts to chromosome 9 in a phenomenon known as "translocation." The shortened chromosome 22 is referred to as the Philadelphia chromosome. (Figure 1)



The Ph chromosome produces an abnormal protein, known as Bcr-Abl tyrosine kinase, which is responsible for blocking the normal signal that tells the body to stop producing white blood cells.

Diagnosis and Stages of CML

Diagnosis The Ph chromosome is detected in the bone marrow of approximately 95% of patients with CML and is the hallmark of the disease. At the time of diagnosis, CML patients typically have a significantly elevated white blood cell count. CML typically progresses slowly over several years, and in its early stages patients often do not have symptoms. Nonspecific symptoms typical of leukemia, such as tiredness that will not go away, a lack of energy, fever, lack of appetite, night sweats or an enlarged spleen, may be present.

Stages Once CML has been diagnosed, further testing defines the stage or extent of disease and helps in developing a treatment plan. The stages of CML include:

Chronic Phase: There are few immature (blast) cells in the blood and bone marrow and symptoms may or may not be present. This stage may last from several months to several years. The majority of patients present to their physician at this stage.³

Accelerated Phase: More blast cells are present in the blood and bone marrow with fewer normal cells. Symptoms are often present.

Blast Phase: Greater numbers of blast cells are found in the blood or bone marrow and may form tumors outside of the bone marrow in the bone or lymph nodes. May be referred to as "blast crisis" (a situation in which the excessive numbers of blast cells produce life-threatening infections, bleeding or risk of stroke).

Therapy and Response

A Primary Goal of Therapy: The Elimination of the Ph Chromosome

Controlling the signs and symptoms of CML, reducing the number of white cells and preventing the progression of CML to the terminal phases are important treatment objectives. As Ph+ CML is caused by a genetic abnormality, the Ph chromosome, elimination of the chromosome is a primary goal of therapy.

Complete elimination of the Ph chromosome from the bone marrow is considered a complete cytogenetic response (CCR). A direct association between cytogenetic response and prolonged survival has been demonstrated for various Ph+ CML therapies. The efficacy of Ph+ CML treatment is measured by two standard criteria: hematologic response and cytogenetic response.

<i>Hematologic Response</i>	A complete hematologic response refers to the normalization of blood counts, lasting for at least four weeks, effectively identifying the degree to which the most apparent abnormality in CML (i.e., proliferation of white blood cells) is controlled. During a hematologic response, the Ph chromosome-positive (Ph+) cells may still be present.
<i>Cytogenetic Response</i>	A cytogenetic response, traditionally regarded by researchers as compelling evidence that a particular treatment is effective, is the disappearance or reduction of the number of Ph+ cells detectable by standard lab methods. This is an indicator of the degree to which the underlying cause of the disease itself is controlled.

There can still be evidence of Bcr-Abl transcripts even when CCR is attained. While attaining CCR is important, many researchers believe that a better result may be when patients with CML achieve a molecular response (MR).

<i>Molecular Response</i>	In CML, an MR is the disappearance or reduction in quantities of Bcr-Abl, the abnormal protein responsible for proliferation of white blood cells that occurs in Ph+ CML patients. A complete molecular response (CMR) indicates that Bcr-Abl levels are undetectable. Molecular response may prove a possible new benchmark for further evaluating effectiveness of drug therapy and disease prognosis. MR can be measured with a relatively new technique, called polymerase chain reaction (PCR), which measures the levels of Bcr-Abl transcripts.
---------------------------	---

References:

¹ American Cancer Society. Cancer Facts and Figures, 2007. Atlanta: American Cancer Society; 2007.

² American Cancer Society. Overview: Leukemia – Chronic Myeloid (CML).

http://www.cancer.org/docroot/CRI/content/CRI_2_2_1x_How_Many_People_Get_Chronic_Myeloid_Leukemia.asp?nav=crl. Last accessed Jan 22, 2007.

³ Faderl S; Talpaz M; Estrov Z; O'Brien S; Kurzrock R; Kantarjian HM. The biology of chronic myeloid leukemia. N Engl J Med 1999 Jul 15;341(3):164-72.