



CarciKnow News

the voice of Carcinogenesis Foundation



<http://www.carciknowgenesis.org>

June 2009

Miracle drug against chronic myeloid leukaemia

Gleevec (Imatinib) is a small molecule drug belonging to a class of chemicals known as phenyl-aminopyrimidines and is used to treat chronic myeloid leukemia (CML).

In 1992 researchers from Swiss drug company Ciba-Geigy (currently Novartis) discovered imatinib mesylate while attempting to develop a drug for inflammation.

A team of doctors led by Dr. Brian J. Druker of Oregon Health and Science University Cancer Institute in Portland tested the drug in CML patients and found that Gleevec is well tolerated by patients and is very effective in inducing remission. The majority of chronic phase CML patients treated with gleevec can expect to have durable responses with good quality of life.

The drug was approved by the US Food and Drug Administration in 2001. Gleevec is the first small molecule targeted therapeutic heralding the era of molecularly targeted therapies with high efficacy and low toxicity. Gleevec is also effective in the treatment of solid tumors of gastrointestinal tract known as Gastrointestinal stromal tumors (GISTs).

Gastrointestinal Stromal Tumors (GIST)s

Gastrointestinal tumors appear in stomach or intestine of human body. The stomach is a sac-like organ that holds food and begins the digestive process by secreting gastric juice. The small intestine, the longest part of gastrointestinal (GI) tract, further breaks down food and absorbs most of the nutrients. The small intestine joins the colon, a muscular tube, which serves as a storage place for waste. The waste left after this process goes into the rectum.

Gastrointestinal stromal tumors (GISTs) are fairly rare tumors of the GI tract. These tumors are in fact not true muscle or nerve tumors. They start in special cells found in the wall of the GI tract, called the interstitial cells of Cajal (ICCs), or in very early cells that can develop into ICCs.

ICCs are part of the autonomic nervous system, which sends signals to the GI tract. The nerve signals they send cause muscles of the digestive organs to contract, which helps to move food and liquid through the GI tract.

Not all GISTs are cancerous. Some are benign -- they don't invade into other areas or spread to other parts of the body.

GISTs are different from these more common GI tract cancers, as they start in different types of cells. Most cancers in the GI tract start in glandular cells lining the GI tract. GISTs are also quite different in their prognosis (outlook for survival) and their treatment.

Inside this issue:

GASTROINTESTINAL TUMORS

SOFT TISSUE TUMOR

CAUSES OF LEUKEMIAS

LEUKEMIA AROUND THE —

BONE-MARROW

PLANT CHEMICALS

TYPES OF LEUKEMIAS—

Anti-viral Drug Tames Cancer

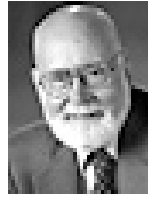
Ribavirin, a common anti-viral drug has shown promise to be an effective antidote to cancer. This drug has been shown to suppress the activities of eIF4E gene, which is dysregulated in 30 per cent of cancers including breast, prostate, head and neck, colon and stomach cancer.

This result of a Canada-wide clinical trial led by Dr. Katherine Borden at the Institute for Research in Immunology and Cancer (IRIC) of the Universite de Montreal has appeared in the May 11 2009 online issue of journal Blood.

These results are first to show that targeting the gene in humans is clinically beneficial. The drug blocks the gene effectively, without producing any side effects in patients. The next challenge for this team is to overcome the resistance that develops over time to ribavirin.

Researchers are also interested to test whether ribavirin is as effective in the treatment of other cancers with dysregulated eIF4E.

Bone-marrow Transplant to Cure Leukemia



There was a time when chances of survival for leukemia were little more than zero. Thanks to a team of pioneering scientists led by Dr. E. Donnall Thomas at Fred Hutchinson Cancer Research Center, tens of thousands of leukemia patients now lead productive lives.

A medical visionary with persistence and conviction, Dr. E. Donnall Thomas received the 1990 Nobel Prize in physiology or medicine for this lifesaving work.

Laboring in the basement of temporary facilities in Seattle four decades ago, Thomas sought to do what others were convinced would never work. He ventured to cure leukemia and other cancers of the blood by destroying a patient's diseased bone marrow with near-lethal doses of radiation and chemotherapy and then rescuing the patient by transplanting healthy marrow. The

goal of this approach is to establish a fully functioning and cancer-free blood and immune system.

Today, the success of bone-marrow transplantation stands among the world's most significant medical advances. The technique has transformed leukemia and related cancers, once thought incurable, into highly treatable diseases with survival rates as high as 90 percent.

Sarcoma: Adult Soft Tissue Tumor

A sarcoma is a type of cancer that develops from certain tissues, such as bone or muscle. There are 2 main types of sarcoma: osteosarcoma, which develops from bone, and soft tissue sarcomas. Soft tissue sarcomas can develop from soft tissues such as fat, muscle, nerves, fibrous tissues, blood vessels, or deep skin tissues.

They can emerge in any part of the body. Most of them develop in the arms or legs. They can also be found in the trunk, head and

neck area, internal organs, and the area in back of the abdominal cavity.

There are about 50 different types of soft tissue sarcomas.

There are tumors of fat tissue. Lipomas, lipoblastomas, and hibernomas are benign tumors of fat tissue. Liposarcomas are malignant tumors of fat tissue. Leiomyomas are benign tumors of smooth muscle (or involuntary muscle). Leiomyosarcomas are malignant tumors of smooth muscle.

Like leiomyomas, they can grow almost anywhere in the body. They are most often found in the retroperitoneum (area in back of the abdominal cavity), the internal organs, and blood vessels.

Causes of Leukemia

A **chromosome** is an organized structure of DNA and protein that is found in cells. A chromosome is a single piece of coiled DNA containing many genes and other genetic material.

Some genes (packets of our DNA) contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called oncogenes. Others that slow down cell division or cause cells to die at the appropriate time are called tumor suppressor genes.

Cancers can be caused by DNA mutations (gene defects) that turn on oncogenes or turn off tumor suppressor genes.

Leukemia can be caused by chromosomal translocations in which some of the DNA from one chromosome becomes attached to a different chromosome. This cancer can also be caused by exposure to radiation or cancer-causing chemicals such as those in tobacco smoke.

Translocations that develop during life are quite common in

chronic leukemias. People exposed to very high levels of radiation are much more likely than others to get acute myeloid leukemia, chronic myeloid leukemia, or acute lymphocytic leukemia.

Exposure to benzene in the workplace can cause acute myeloid leukemia. It may also cause chronic myeloid leukemia or acute lymphocytic leukemia. Benzene is used widely in the chemical industry. It's also found in cigarette smoke and gasoline.

Global Leukemia incidence

Leukemia is a malignancy of blood-forming tissues — bone marrow, lymph nodes and the spleen. According to the World Health Organization, the global incidence of leukemia is about 8 to 9 per 100,000 people each year. Approximately 250,000 new cases occur annually worldwide. The disease appears as uncontrolled multiplication of abnormal white blood cells. Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in the U.S. and Europe, with an incidence of close to 3 cases per 100,000 people, and occurs particularly in the elderly. Leukemia rates are higher in Americans of European descent than among those of any other race or ethnicity.

History of leukemias

In 1845, Edinburgh pathologist John Hughes and Rudolf Virchow from Berlin published two very similar cases of death, which probably represent the first descriptions of leukemia that later became known as chronic myeloid leukemia (CML). Bennet thought that the patient had an infection, Virchow suspected a neoplastic disorder that he soon called white blood disease or leukemia.

In 1872, Ernst Neumann observed that leukemia cells originated in the bone marrow. The next decades saw the differentiation into myeloid versus lymphoid and acute versus chronic leukemias.

A real quantum leap in the leukemia research was the discovery in 1960 by Philadelphia cytogeneticists Peter Nowel and David Hungerford of an abnormally small G-group chromosome that is now called the Philadelphia chromosome (Ph).

Thirteen years later Janet Rowley recognized that Ph was the product of a reciprocal translocation between chromosomes 9 and 22 giving rise to chimeric BCR-ABL gene, whose protein product is a tyrosine kinase.

History of Leukemia Treatment

Historically, one of the most common treatments for leukemia was arsenic. This cure is mentioned in the ancient Ramayana of India, and was used by Hippocrates (460-370 BC), who gave cancer its name. In the 18th century, Thomas Fowler created what became known as "Fowler's Solution," a combination of arsenic trioxide and potassium bicarbonate, which "became a standard remedy to treat anemia, Hodgkin's disease, and leukemia.

Until after World War II, there were no adequate treatments for leukemia. One of the most important treatments for cancer, chemotherapy, actually developed from an agent of chemical warfare used by the Germans during WWI, mustard gas, which attacks rapidly-dividing white blood cells. Scientists discovered the tumor-fighting effects of mustard gas when a group of soldiers during WWII accidentally came in contact with mustard gas and "were later found to have very low white blood cell counts"

George Hitchings (1905-1998) and Gertrude Elion (1918-1999) used rational drug design to create 6-mercaptopurin, the first truly effective leukemia drug.

Therapies for leukemias was slow to develop. Interferon- α was found to induce durable complete cytogenetic responses and long-term survival, although in only a small fraction of patients.

We are in an era when biology is driving targeted therapies, especially in the field of oncology. Gleevec is an example of such a promising therapy that selectively blocks BCR-ABL protein in CML patients and checks abnormal cellular growth. In the USA, incidence rates for leukemia have shown the greatest decline in American Indian or Alaska natives between 1995 to 2004.

Plant Chemicals to Protect against Cancer

The term 'phytochemicals' refers to a wide variety of compounds produced by plants. They are found in fruits, vegetables, beans, grains, and other plants. There is some evidence that a diet rich in fruits, vegetables, and whole grains reduces the risk of certain types of cancer and other diseases.

There is some evidence that certain phytochemicals may help prevent the formation of potential carcinogens (substances that cause cancer), block the action of carcinogens on their target organs or tissue, or act on cells to suppress cancer development.

Flavonoids are plant chemicals found in a broad range of fruits, grains, and vegetables. They are being studied to find out whether they can prevent chronic diseases such as cancer and heart disease.

Other polyphenols (including some flavonoids) act as antioxidants. These are thought to rid the body of harmful molecules known as free radicals, which can damage a cell's DNA and may trigger some forms of cancer and other diseases. These compounds are commonly found in vegetables such as broccoli, brussels sprouts, cabbage, and cauliflower and in teas.





Research-Awareness-Care-Education

CARCINOGENESIS FOUNDATION

<http://www.carciknowgenesis.org>

Editor

Gopala Kovvali Ph.D.

gopala@carciknowgenesis.org

Research Editor

Biplab Das

biplab@carciknowgenesis.org

Mission of the Carcinogenesis Foundation

The mission and activities of Carcinogenesis Foundation can be summarized by an acronym PRIME (Prevention-Research-Innovation-Medicine-Education). Prevention is the best medicine for any disease, especially cancer. CF believes that innovative research and development of medicinal agents coupled with education will be the key to the global vision of eradicating cancer incidence. The Foundation will catalyze and support innovations in carcinogenesis research and education.

Please contact us for further details and opportunities to get involved.

Publish your research in the Journal of Carcinogenesis

Journal of Carcinogenesis is a peer-reviewed, online journal designed to bring together many aspects of research to develop the understanding of carcinogenesis.

Edited by Dr. Gopala Kovvali, Journal of Carcinogenesis is supported by an international Editorial Board.

Journal of Carcinogenesis considers manuscripts in many areas of carcinogenesis and Chemoprevention. Primary areas of interest to the journal include: physical and chemical carcinogenesis and mutagenesis; processes influencing or modulating carcinogenesis, such as DNA repair; genetics, nutrition, and metabolism of carcinogens; the mechanism of action of carcinogens and modulating agents; epidemiological studies; and, the formation, detection, identification, and quantification of environmental carcinogens. Manuscripts that contribute to the understanding of cancer prevention are especially encouraged for submission.

Please contact us at editor@carcinogenesis.com for further details.

Types of Leukemias

Not all leukemias are the same. Depending on the growth (maturation) of bone marrow cells, leukemias can be acute or chronic.

Leukemia: Acute or Chronic

In acute leukemia, the bone marrow cells cannot mature properly. Immature leukemia cells continue to grow and build up. Untreated, most patients with acute leukemia would live only a few months.

In chronic leukemia, the cells can mature partly but not completely. These cells are not really normal. They generally do not fight infection as well as do normal white blood cells. Chronic leukemias

tend to develop over a longer period of time, and most patients can live for many years an acute leukemias.

Myeloid Leukemia versus Lymphocytic Leukemia

Leukemias that start in early forms of myeloid cells-white blood cells (other than lymphocytes), red blood cells, or platelet-making cells (megakaryocytes)-are myeloid leukemias.

If the cancer starts in lymphocytes, it is called lymphocytic leukemia (also known as lymphoid leukemia).

By considering whether they are acute or chronic, and whether

they are myeloid or lymphocytic, leukemias can be divided into 4 main types: acute myeloid (or myelogenous) leukemia (AML), chronic myeloid (or myelogenous) leukemia (CML), acute lymphocytic (or lymphoblastic) leukemia (ALL), chronic lymphocytic leukemia (CLL).

In addition to these, there are other rarer forms of leukemias – Prolymphocytic leukemia (immature forms of B lymphocytes), Large granular lymphocyte leukemia (large cancer cells) and Hairy cell leukemia (cancer of lymphocytes but different from CLL).