**The Biology of Leukemia: The Cancer of the Blood**

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**Abstract:** Thousands of people die from cancer each year. Although scientists and doctors have worked endlessly to find cures for various cancers, there is currently not an absolute cure for leukemia. Leukemia can be diagnosed in almost all age ranges and can be quite deadly due to its tendency to be asymptomatic for long periods of times. This disease attacks the human bodies defense system, the white blood cells. Not only are white blood cells attacked, but bone marrow and other blood made tissues are harmed as well. Over the last few years, health professionals have made great improvement in their knowledge towards treating the various types of leukemia. Doctors have used chemotherapy for years to treat cancer, however, stem cell transplants have recently shown great significance towards the curing of deadly diseases. The pathogenesis of a disease such as leukemia can be incredibly complex, but modern technology has allowed human genes to be analyzed at microscopic levels to help health professionals grasp a greater understanding of how these diseases form and take over our bodily systems so rapidly.

**Introduction**

Over the last several decades, thousands of people have died from cancer. Today, the trend is still ongoing as there are various types of cancer, some of which do not have cures. Although there are several incurable cancers, leukemia is being diagnosed more frequently today. Leukemia is a cancer that is found in the blood marrow, lymphoid system, and in the blood formed tissues of the human body. Leukemia, as well as other cancers, generally occurs due to mutations in cells, however leukemia targets white blood cells’ genetic material. Both children and adults can be diagnosed with this cancer, however the body’s white blood cells are almost always affected. White blood cells are crucial in the human body’s defense against illnesses, but patients who have leukemia often produce an excess of white blood cells that malfunction. The disease causes cells to continuously grow and divide, causing blood cell production to become unrestrained. This results in the mutated cells overcrowding healthy blood cells in the bone marrow, which lessens the population of healthy white blood cells. Treatment for leukemia is extremely intricate, and it has yet to be sufficient to cure the disease. The treatment process varies depending on the class of Leukemia one is diagnosed with. Leukemia is seen in four major types: Acute Myeloid, Chronic Myeloid, Acute Lymphocytic, and Chronic Lymphocytic.

**Recent Progress**

Acute myeloid leukemia (AML) is often found in patients above the age of 45 but is rarely seen in adolescents. This form of cancer is a “hematopoietic malignancy characterized by a complex interplay of aberrations at different levels of the genome” and the complexness is evident through both the pathogenesis and treatment of this disease (Šestáková). AML is an extremely serious disease that can merely be diagnosed by the microscopic analyzation of bone marrow. In this form of leukemia, the bone marrow of the body is affected and can only be treated by chemotherapy, along with bone marrow infusions. Although there is temporary treatment for this cancer, there is currently no permanent cure. Recent studies have been conducted on clinically performing DNA methylation and whether it would be significant to AML pathogenesis and treatment. DNA methylation happens to be one of the longest-studied epigenetic mechanisms and has been reported to be relatively easy to measure (Šestáková). DNA methylation is the process of screening a patient’s genes to discover if an additional methyl group being added to an epigenetic mechanism, which can result in the modification of the gene function and expressions. Doctors and scientists are hopeful to use this new technology to recognize genetic changes that could be a harmful to the body’s blood system.

Another common type of leukemia is chronic myeloid leukemia (CML). This class of leukemia is mostly diagnosed in adults. It is not uncommon for patients with CML to go months without experiencing symptoms of the disease. In fact, patients usually show symptoms once their body enters a phase where leukemia cells grow rapidly. Scientists have narrowed down the biology of CML to the fact that the disease is merely caused by unregulated signal transduction by a tyrosine kinase (Sawyers). In addition, this disease is almost always found in patients who have a defect in the hematopoietic stem cells. The stem cells in this case contain a malignant clonal disorder which results in increased levels of myeloid cells, erythroid cells, platelets in peripheral blood, and marked myeloid hyperplasia found in the bone marrow (Sawyers). The symptoms of CML can include fatigue, anorexia, and bulimia; however nearly 40 percent of patients are asymptomatic (Sawyers). This disease can increase at an extremely fast pace, but health professionals typically use high doses of hydroxyurea or busulfan. These two drugs are known to halter or stop the growth of cancer cells. Doctors typically diagnose CML by analyzing and detecting the Philadelphia chromosome but is referred to as chromosome 22 when it is diagnosed as an abnormal chromosome (Sawyers). When cases of CML are too aggressive for common chemotherapies, cytoreductive therapy is commonly required to prevent thrombotic complications. Many patients with CML can go into remission because CML cells are sensitive to several oral chemotherapeutic drugs (Sawyers). Common to other types of leukemia, blood marrow transplants are often a treatment choice as well, however, CML treatment requires the transplant to be from allogeneic marrow.

Acute lymphocytic leukemia (ALL) is another familiar type of leukemia that is seen by health professionals today. This form of leukemia is most found in young adolescents but can also be diagnosed in adults as it is the second most common acute leukemia found in older individuals (Mayo Clinic, Terwilliger). The prognosis is typically much worse for elderly individuals; however, adults often have a higher response to chemotherapy treatment than children. High responses to chemotherapy is always a positive sign because it can result in remission. This dangerous type of leukemia is caused by malignant transformation and proliferation of lymphoid progenitor cells found in the bone marrow, blood, and extramedullary sites (Terwilliger). Doctors have analyzed the pathogenesis of this leukemia and have discovered that the first biological signs of this illness are abnormal proliferation and differentiation of lymphoid cells. In a study over the pathophysiology of ALL, scientists claimed that chromosomal aberrations are considered a hallmark of ALL (Terwilliger). However, these aberrations are not always sufficient to cause the disease to form. Symptoms of ALL can include severe anemia, fever, weight loss, fatigue, dyspnea, infection, and more. As previously mentioned, chemotherapy is typically the best treatment option as health professionals use the intense chemicals in attempt to achieve normal hematopoiesis with the goal of remission. After the four-week chemotherapy treatment period, many patients experience remission, however, it is not uncommon for them to relapse again in their lifetime. Furthermore, health professionals and scientists are currently studying the process of targeting of several antibodies that are related to this disease.

Furthermore, chronic lymphocytic leukemia (LLC) is also seen by many physicians today. LLC harshly affects the lymphoid cells in the body. These cells are responsible for making lymphoid tissue, which is crucial to our health as these tissues make up our immune system. This disease can begin and grow very slowly, leaving people symptomless for years. While chemotherapy and radiation are popular forms of treatment for this form of leukemia, leukapheresis has been a groundbreaking discovery for this disease. Leukapheresis is the process of circulating a patient’s blood through a machine that removes the white blood cells completely, returning the red blood cells and plasma. This form of treatment allows the body to generate new, healthy white blood cells, while ridding the body of the mutated and cancerous cells. In addition to this form of treatment, other cellular therapies are being used to treat this form of leukemia. Treatments such as stem cell transplants, as well as chimeric antigen receptor T cells (CAR-T) cell injections (Terwilliger). CAR-T cells are genetically engineered cells that can be used in immunotherapy. CAR-T has been proven to be a safe treatment; however, doctors are still unsure on how effective it is because not all patients have shown a response to the treatment. In addition, a drug called Ibrutinib is now being used in B-cell cancers, like LLC. This prevents B-cell receptors pathway, which can aid halting of proliferation of cancerous cells.

**Discussion**

Over the last decade, scientists and doctors have made significant progress toward the cure of leukemia. This disease is extremely complex and targets very delicate components of the body. As previously mentioned, chemotherapy and radiation are often used as treatment, but health professionals are active in studying the complexness of molecular and genetic alteration. In addition to these treatments, antibody targeting is rarely used, however, scientists are researching ways to make this form of treatment more effective to patients. Overall, effectiveness is the primary issue of treatment in all types of leukemia. Patients who have received forms of genetic alteration have had little effectiveness or haven’t experienced any improvement at all. Stem cell injections have proven to be more successful in patients and have even resulted in remission, but not a complete cure. Every form of leukemia is intricate and can be fatal to people of all ages. Today, scientists and doctors are working collectively to find a cure for this complex disease.

**References**

“Leukemia.” *Mayo Clinic*, Mayo Foundation for Medical Education and Research, 13 Jan. 2021, https://www.mayoclinic.org/diseases- conditions/leukemia/symptoms- causes/syc-20374373.

Sawyers, Charles L., and Author AffiliationsFrom the Division of Hematology and Oncology. “Chronic Myeloid Leukemia: Nejm.” *New England Journal of Medicine*, 2 Sept. 1999.

Šestáková, Š., Cerovská, E., Šálek, C. *et al.* A validation study of potential prognostic DNA methylation biomarkers in patients with acute myeloid leukemia using a custom DNA methylation sequencing panel. *Clin Epigenet* **14,**22 (2022). https://doi.org/10.1186/s13148-022- 01242-6

Terwilliger, T, and M Abdul-Hay. “Acute lymphoblastic leukemia: a comprehensive review and 2017 update.” *Blood cancer journal* vol. 7,6 e577. 30 Jun. 2017.