






The Cancer Cell: Changes That Lead to Cancer

Myriads of molecular changes occur inside of a cell that result in the initiation and progression of cancer. These changes can occur in the genetic material, but also in how that material is copied and read. In order to understand how to treat cancer, researchers seek to understand what these changes are, how they come about, and how they affect cellular function. Emerging studies such as those listed below highlight how these changes can be different in population groups with different genetic ancestries.

STUDY	EXAMPLE OF ANCESTRY-RELATED DIFFERENCE
 <p>DNA Mutations</p> <p>Alterations in the DNA sequence, referred to as mutations, alter the message that is read by the cell to make proteins, and result in new proteins, altered versions of normal proteins, or loss of protein function, which can lead to cancer.</p>	<p>Fifty percent of patients with lung cancer who were of Asian ancestry had a mutation in the <i>EGFR</i> gene compared to only 10 percent of patients who were of European or African ancestry.</p>
 <p>Epigenetic Modifications</p> <p>Epigenetic modifications determine whether a gene is accessible for reading but do not alter the genetic message itself. These modifications can be influenced by factors such as stress, diet, and pollution.</p>	<p>Among patients with a specific subtype of breast cancer, those who were of African ancestry had different epigenetic marks on several genes important for slowing down cell replication as compared to those who were of primarily European ancestry.</p>
 <p>Genetic/Chromosomal Aberrations</p> <p>Unlike base changes, larger parts of a gene or chromosome, including the gene or chromosome itself, can be duplicated, multiplied, rearranged, or deleted. Genetic/chromosomal aberrations can generate increased quantities of proteins, entirely new proteins, or loss of proteins and change how a cell grows and divides leading to cancer.</p>	<p>Hispanic/Latino/a individuals have higher incidence and mortality of acute lymphoblastic leukemia (ALL) compared to all other racial groups (excluding American Indians/Alaska Natives). A key genetic aberration called the <i>IGH-CRLF2</i> fusion is associated with poor prognosis in ALL. This arises when two normal genes (<i>IGH</i> and <i>CRLF2</i>) are rearranged and the alteration occurs four times more often in Hispanic patients than in non-Hispanic White patients. This may explain why ALL occurs more often in this population.</p>
 <p>Cancer-Related Alternative Splicing</p> <p>Normal cells copy the information from DNA in pieces of RNA that are assembled in a process called splicing to complete the message. In cancer cells, this process can be altered to generate abnormal proteins which fuel uncontrolled cell proliferation and growth.</p>	<p>In prostate cancer patients “skipping” of certain parts of the <i>PIK3CD</i> gene promotes this cancer’s aggressiveness; this phenomenon occurs more often in those of African ancestry than in European American patients with prostate cancer.</p>
 <p>Changes in RNA Levels</p> <p>Comparing the levels of thousands of RNA molecules within a tumor or even a single cancer cell can help researchers build a molecular profile of the cancer. This profile can be compared to profiles that have been documented in other cancers or normal cells. This comparison can inform the health care team about prognosis and best course of treatment.</p>	<p>In an analysis of 1,152 U.S. patients with prostate cancer, substantial gene expression differences were found between men of African and European ancestries, with a reduced expression of genes that prevent DNA damage seen more frequently in those of African ancestry. These observed differences could explain why this group experiences higher rates of aggressive prostate cancer and could prove useful in tailoring treatments to patients of African ancestry.</p>