Few diseases instill greater fear than cancer, which strikes Americans of both sexes and all ethnic and socio-economic backgrounds with equal fury. The risk of developing cancer rises with age, but children and young adults are not spared, and the disease touches every family at some time.

Cancer is not a single condition but a diverse group of diseases with the hallmark of uncontrolled cell growth. Some cancers can be cured in their early stages with an operation, but in only a minority of cases are they detected early enough. More often, cancers spread to other organs before producing any symptoms. By this time, billions of cancer cells have spread extensively, with entrenched malignant features that resist conventional attacks from surgery, radiation, or chemotherapy. There is an urgent need to understand cancer’s root causes and to devise new strategies to detect cancer early as well as treatments that destroy cancer cells late in the disease course, when they produce the most suffering.
Targeting Cancer Stem Cells

Among the trillions of cells in our bodies, cancer represents the clonal outgrowth of a single errant cell. Even as tumors expand, however, only a small fraction of all the cells—the cancer stem cells—are responsible for producing new cells and sustaining tumor growth. Harvard Stem Cell Institute (HSCI) scientists aim to discover the properties and unique vulnerabilities of cancer stem cells, whose eradication is the surest road to long-term cures.

Genetic Mutations in Cancer

A revolution in DNA sequencing technology, combined with a number of large, international collaborative efforts, have resulted in the sequencing of thousands of cancer genome samples, revealing the full set of mutations that cause various cancers.

Many of the recently identified genes that are mutated in cancer occur in regulators of the “epigenome.” These factors govern the activity of genes, turning some genes on and silencing others. These switches are hereditary, copied from a cancer cell to its progeny when a cell divides.

Cancer stem cells, in particular, have specific epigenetic states that are distorted, pathological counterparts of normal stem cells. HSCI investigators are making important contributions in the field of epigenetics and so are perfectly positioned to develop the next generation of cancer treatments: drugs that will alter cells’ epigenetic features and force cancer stem cells to cease cloning themselves indefinitely.

Many new drugs have already been developed that successfully target epigenetic regulators, and the development of additional agents is proceeding rapidly. This class of therapies represents one of the most promising approaches to improve the treatment of cancer.

Modeling Cancer

Mimicking cancer in experimental model systems is a pre-requisite for genuine progress, both to understand basic biology of the disease and to test novel treatments. Growing cell clones on plastic dishes has been a mainstay of research for decades, but the technique limits the ability to study distinct sub-populations such as cancer stem cells, which requires propagation of human tumors in animals. It was only by creating cancer models in mice and studying these models in detail that scientists could demonstrate the role of cancer stem cells and begin to investigate their properties.

HSCI investigators are at the forefront of research using animal models to reproduce cancer accurately in the laboratory. They have played leading roles in modeling some of the commonest and deadliest cancers: those of the bone marrow (leukemia), colon, breast, lung, prostate, brain, and ovaries.

These models have proven to be especially effective for drug screening. One scientist used leukemia mouse models to test many possible drugs at a time, increasing the odds of finding one that eliminates cancer cells and not healthy blood cells. In a related study, using a specific mouse leukemia model to better understand how the cancer forms identified a new set of therapeutic targets, while a parallel in vitro chemical screen found novel therapeutic compounds with potential for clinical trial. HSCI provides a perfect environment for our cancer biologists to collaborate in new and highly productive ways.