SCIENCE

THE EDGE
AACR

We are at a critical moment in the history of cancer research. Recent discoveries in science and technology have dramatically altered and increased our understanding of the biological events that lead to cancer. This new knowledge paves the way for improving diagnosis as well as developing better therapies and preventive strategies.

Targeting cancer at the nano-level

Cancer cells differ from normal cells in part by displaying unique surface markers and by creating a cellular environment that supports malignant growth. These differences can be targeted, directing therapy to the malignant cells while sparing healthy ones. With increasing knowledge of the genes expressed in tumor versus normal cells and with advances in targeting and nanoparticle technology, the prospects of success are rapidly improving. In addition, there are new therapeutic agents that could be delivered directly to the cancer cells by targeted approaches, such as small protein molecules that can silence cancer-causing genes. Drugs that effectively kill cancer cells but cause debilitating side effects can also be improved through targeted delivery to tumor cells. The challenge becomes one for engineers and cell biologists - how to couple these drug molecules and therapeutic nanoparticles to cell surface markers in such a way that they cause cancer cell death.

Finding a needle in the haystack

In order to accurately diagnose cancer at its earliest stages and effectively treat the disease, doctors must be able to monitor a patient's cells to determine the type of tumor cell and its genetic composition. Researchers are exploring the potential of a new breakthrough technology in which circulating cancer cells are recovered from a small sample of a patient's blood. Such technology has the potential to detect tumors when they are small and more easily treatable, and to detect tumor cells that have spread to another part of the body. Genetic analysis of such samples could offer valuable information about how or whether a tumor is responding to treatment, helping physicians and patients make treatment decisions. Technologies developed through research that explores the interface of engineering and cancer biology could enhance the efficacy of clinical trials and offer new hope for advancing the treatment of patients in the near term.

Stopping cancer in its tracks

Cancer research has advanced to the point that many cancers are now treatable -- even curable -- if caught early, before the disease spreads. However, metastatic disease - cancer that has spread beyond the primary tumor site - remains one of the biggest challenges and is the major cause of treatment failures. Researchers are urgently seeking better ways of diagnosing and treating metastatic disease, which will come from advances in the understanding of the molecular and biological mechanisms underlying metastasis.

Taking a personalized approach to cancer

Most currently available cancer medicines are aimed at large groups of cancer patients, making them optimal for some but ineffective or even harmful for others. Advances in genetics are enabling researchers to identify people at high risk for cancer based on their individual genetic makeup long before the disease has a chance to form, and to develop more powerful prevention strategies and treatments that target cancer at the molecular level.

Unmasking infectious causes of cancer

Researchers currently estimate that approximately 20 percent of all human cancers are associated with viruses, including cervical, gastric, head and neck cancers as well as Hodgkin's lymphoma. However, there may be many more, as well as cancers associated with other infectious agents, such as bacteria. Given the nascent and promising field of cancer vaccine development, which has yielded an HPV vaccine that prevents cervical cancer, the association of viral agents to cancer is an area well worth exploring. The development of gene-based screening technologies to detect viral agents will be a powerful tool in our arsenal of weapons for diagnosis and could lead to breakthroughs in the treatment of Hodgkin's disease and other cancers that are caused by infectious agents.

Combining therapies for maximum impact

There are many new therapeutic agents for potential use in treating cancer, and they attack tumor cells in different ways. For example, targeted therapies disrupt specific cell signaling pathways that the cancer cells use to grow, anti-angiogenic agents prevent the formation of new blood vessels that provide tumors with oxygen and nutrients, and immunotherapies stimulate a patient's immune system to kill the tumor cells. Researchers are focused on determining precisely how all of these different therapies work so they can develop effective combinations of drugs with which to treat patients.

Approaching cancer from a fresh perspective

The identification of several classes of genes that undergo mutations and contribute to cancer has increased our understanding of the origins and causes of cancer. Research teams in laboratories all over the world have uncovered this information one gene at a time, a slow and laborious approach that has nonetheless identified several plausible mutational targets for drug therapy. Now, the opportunity to accelerate cancer research lies in a "systems biology" approach to integrate and digest the vast amount of knowledge about these mutated genes, such as how they are expressed in normal cells and how their interaction with environmental, nutritional and other factors leads to

cancer. It requires the combined expertise of cancer biologists, clinicians, statisticians, mathematicians and physicists to create large data sets of information, interpret them, and extract useful information that will impact the prevention, diagnosis, and treatment of cancer.

Cancer Epigenetics

Cancer is a genetic disease initiated by alterations in genes that regulate cell proliferation. In cancer cells, genes are either modified by mutations, which alter the function of the proteins they encode, or through epigenetic processes, which are modifications to chromosomes that alter gene expression patterns. A major effort is underway to map the entire human epigenome, to identify and understand all of the chemical changes and chromosomal relationships which provide function to the genetic code. Such information could potentially lead to breakthroughs in our understanding of both normal and disease states.

The buzz about biomarkers

Detecting molecular and biological changes in a patient's blood, urine, and tissues can help identify individuals who have cancer or who are at a high risk for developing cancer. Many such "biomarkers" have been identified and others will be discovered as our understanding of the genes and biological processes involved in cancer increases. These markers are used to help diagnose cancer, predict a patient's response to particular therapies, check a patient's response to treatment, and determine if cancer has returned.

Inflammation and cancer

Inflammation is the body's normal response to tissue damage, resulting from physical injury, exposure to toxins and other types of trauma. Although it can play a role in tumor suppression by stimulating an anti-tumor immune response, research is showing that the damage caused by inflammation increases the likelihood that genes will mutate and take on the properties of cancer-promoting genes. Scientists are beginning to suspect inflammation is a culprit in promoting tumor development and growth.

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The Edge was written by the experts at the AACR, the world's oldest and largest professional organization dedicated to advancing cancer research. The membership includes nearly 27,000 basic, translational, and clinical researchers; health care professionals; and cancer survivors and advocates in the United States and more than 70 other countries.

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