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Cancer Genomics Promises to Revolutionize Patient Care

When the National Cancer Act was passed in 1971, a diagnosis of cancer was considered a death sentence. Cancer was often diagnosed only after the disease was advanced, having spread to distant parts of the body—when it is most difficult to treat. Doctors had no way of knowing why a treatment might work for one patient but not for another.

For many cancers, treatments still involve surgery to remove the tumor, plus radiation or chemotherapy to kill any remaining cancer cells. Each can result in serious side effects. Many common chemotherapy drugs, for example, cause hair loss, severe nausea and dangerous drops in red and white blood cells. But tremendous progress in medical research—much of it done at U.S. medical schools and teaching hospitals with support from the National Institutes of Health (NIH) and especially, the NIH's National Cancer Institute (NCI)—has led to better and earlier detection of cancer, more targeted and effective treatment, and improved management of side effects.

Cancer Survival Rates are Increasing

- In 1976, just half of all cancer patients survived more than five years after their diagnosis. Today, closer to two-thirds (64 percent) are alive five years after they learn they have the disease.
- Deaths rates for the four most common cancers—breast, lung, prostate, and colorectal—began dropping in the late 1990s and continue to do so. Today, almost eight out of 10 women with breast cancer are alive 10 years after their diagnosis, according to data from the NCI.
- The five-year survival rate for children with cancer is now more than 75 percent—a vast improvement over the early 1960s, when childhood cancers were nearly always fatal.

Testicular cancer is a striking example of the great progress made. Men diagnosed with metastatic testicular cancer in the 1970s had a five percent cure rate. In 1977, researchers at the Indiana University School of Medicine developed a new chemotherapy regimen that boosted cure rates for the advanced form of this disease to 80 percent. Today, the overall five-year survival rate for testicular cancer is 96 percent.

Cancer still remains a formidable foe. Yet, breathtaking research within the field of cancer genomics has the medical community predicting revolutionary changes in the way cancer is understood, diagnosed and treated. Researchers are working to interrupt cancer at many stages—to prevent it from developing, eliminate it early when it does occur, and diminish its devastating effects.

While genetics is the study of single genes in isolation, genomics is the study of all the genes in the genome and the interactions among them and their environments. Cancer genomics has brought about a fundamental shift in the way scientists think about cancer. Cancers that appear on the surface to be the same disease, when analyzed for their "genetic fingerprint," show important differences that determine how aggressive the cancer will be and how it will respond to certain treatments.

Using genomics technology, researchers are discovering the genetic causes of cancer. By focusing on the genes responsible for the growth and spread of various cancers, researchers can identify leads to future drug targets, and design new treatments to zero in on cancer cells without harming healthy tissue.

Prevention
Finding the genetic triggers of cancer gives scientists a chance to try to prevent the disease altogether.

- In 2005, NIH-supported researchers at multiple institutions worked together to show how women with higher levels of an antibody to a protein called human mucin, or MUC1, are less likely to develop ovarian cancer. The findings may lead to a vaccine to prevent ovarian cancer. The institutions involved in this important discovery included **Brigham and Women's Hospital in Boston, New Hampshire's Dartmouth Medical School and the University of Pittsburgh School of Medicine.**

- In 1997, researchers at the **Columbia University College of Physicians and Surgeons** in New York identified a tumor suppressor gene involved in a large percentage of brain, breast, and prostate cancers.

- At **Stanford University School of Medicine** in 1996, NIH funding helped researchers isolate the gene for basal cell carcinoma, a form of skin cancer that affects about 750,000 Americans each year.

Diagnostics and Screenings
Diagnostic tools based on genomics will help doctors improve accuracy of cancer detection and lead to better screening tests.

- In 2002, NIH-supported researchers at the **Johns Hopkins University School of Medicine** identified a new genetic culprit that may serve as an early marker for prostate cancer and may also help identify new dietary or chemical means of preventing the disease. They used DNA microarray technology, first developed by **Stanford University School of Medicine** in 1995, to analyze more than 6,500 genes and found that one gene was overexpressed in prostate cancer. When they examined 168 prostate cancer tumors, more than 95 percent of the tumors showed overexpression of the gene, making it one of the most consistent biological markers known for prostate cancer.

- Researchers at the medical schools at **University of California campuses in San Diego and Davis** have worked collaboratively, with NIH support, to develop the first new breast CT scanner to reach clinical testing in a generation. This new technology may have the ability to detect tumors much earlier than conventional mammography and is easier on patients since it does not require compression of breast tissue.

- In 1998, NIH-funded research conducted at **University of California, Irvine, College of Medicine**, identified a protein that holds the key to more reliably warning women about early cell abnormalities in the cervix before cancer develops, leading to the development of an improved standardized screening test for cervical cancer.

Prognosis
Cancer researchers are using genomics information to accurately predict which cancers are likely to spread aggressively and which cancers are most likely to respond to current therapies or require different approaches.

- Researchers at the National Surgical Adjuvant Breast and Bowel Project (led by a researcher from the **University of Pittsburgh Medical Center**) have developed a "recurrence score" for women with breast cancer that helps determine whether these women will need chemotherapy after surgery. The research suggests that almost half of the 50,000 U.S. women diagnosed annually with this form of the disease are at low risk of recurrence and can be spared chemotherapy and its harmful side effects. NSABP is a clinical trials cooperative group supported by the NCI.

- NIH-supported researchers at **Stanford University Medical School** used genetic profiling to identify tumors with gene expression signatures suggestive of active wound healing. The signature they found appeared early in the disease, persisted during treatment and predicted increased risk of metastasis and death in breast, lung, and gastric cancers. This research provides a possible link between cancer progression and wound healing and may be a powerful predictor of the clinical course of several common cancers.

NIH-Supported Networks

U.S. medical schools and teaching hospitals play integral roles in several NIH-supported networks, including the NCI-supported Comprehensive Cancer Centers. Networks and consortia usually focus on the development or validation of new interventions, ranging from new therapies to genetic-risk counseling to outreach. More than 40 Comprehensive Cancer Centers exist today as unique venues for integrating laboratory, clinical and basic research with health care delivery. All but one is directly affiliated with medical schools and teaching hospitals, and together, they serve as a model of the collaboration between the NIH and the nation's medical schools and teaching hospitals.

The NCI's Specialized Programs of Research Excellence (SPOREs) initiative is an example of the federal government's expanding support for translational research. Most of the 60 SPOREs, which cover 14 different cancers, are located at medical schools, teaching hospitals and affiliated cancer centers. For example, the University of North Carolina SPORE in Breast Cancer's unique goals emphasize multidisciplinary translational research that encompasses the population, clinical, and basic sciences, and examines health disparities between African-American and Caucasian populations.

Treatment

The ultimate goal of pharmacogenomics—the study of how genes affect the way people respond to medicines—is to tailor medicines to people's unique genetic make-ups. Several targeted drugs are already available, and were either developed at U.S. medical schools or tested in clinical trials through networks of medical schools and teaching hospitals around the country. For example:

- In 2004, **Pennsylvania State University College of Medicine** researchers found that a booster dose of a substance already found in the body appears to be a safe, non-toxic treatment for pancreatic cancer and shows signs of arresting pancreatic cancer cell growth in patients.

- In 2003, the Food and Drug Administration approved a new drug, Velcade, a potent new treatment for an often-fatal bone marrow cancer. The drug was developed based on research by scientists at **Harvard Medical School** who wanted to learn how, when and why cells destroy their own proteins. Their research identified a proteasome, a kind of garbage disposal that chews up abnormal or damaged proteins and can also control cell growth and affect other processes by destroying regulatory proteins. In working to develop drugs that will inhibit the proteasome, these researchers discovered one inhibitor, Velcade, that would block growth of cancer cells and shrink tumors in mice.

- In 1988, researchers at the **David Geffen School of Medicine at University of California, Los Angeles** discovered the relationship between a certain gene and an aggressive form of breast cancer, which led to the development of an antibody called Herceptin. Two years later, scientists at **University of Pennsylvania School of Medicine** unraveled the basic science behind Herceptin, which was added to the chemotherapy treatments for women who have aggressive, early stage breast cancer. Herceptin cut the risk of recurrence of the disease for these patients in half.

Genomics is moving us away from a one-size-fits-all model of patient care. Researchers are using genomic technology to gather a wealth of new information that should aid cancer diagnosis and ultimately therapy. Researchers also hope to pair genomics with imaging to monitor cancer at the molecular level, enabling earlier diagnosis and the ability to measure treatment effects before the cancers are clinically apparent, and make more timely treatment decisions.