caBIG™: The Power Of Connection

Introduction

Dr. John Niederhuber: In just three years since the announcement of this initiative, caBIG™ has progressed from a concept, a vision of where we needed to be…to a robust grouping of more than 40 software products that enhance our ability to manage data and interface patient research with clinical practice.

caBIG™ will drive clinical trials of the future. It will be the way we bring genomics, proteomics and clinical data together for each patient in a clinical trial.

Narrator: Cancer. It has afflicted us throughout history. We know more today about cancer than ever before. Yet, despite advances in science and medicine, cancer continues to take our lives and those of our loved ones.

But in the future, we will be able to detect cancer earlier, diagnose each cancer type and select the most effective treatment.

By unlocking the molecular mysteries of cancer, we will be better able to understand different forms of cancer and treat each form with greater precision than we ever imagined.

But solving this mystery is a challenge greater than any one scientist or any single institution.

So the National Cancer Institute is working with *thousands* of scientists and *hundreds* of institutions to meet this challenge. The cancer Biomedical Informatics Grid, or C-A-Big, will link together the entire cancer community, forming a network in which information flows freely from researcher to researcher to physician to patient.

Dr. Anna Barker: Our vision is an unprecedented network that will tie the cancer community together in a way that will allow us to leverage what we've already done, speed up the processes of discovery, development, and delivery, and ultimately ensure that this all reaches patients.

Narrator: In this video series you will see how the caBIG™ initiative is connecting the entire cancer community and accelerating the process by which new therapies are discovered and delivered to the patient.

Chapter 1: History of Cancer Treatment

Narrator: Cancer has been with us – and mystified us – throughout the ages. Egyptian physicians were the first to treat cancer by performing surgery. Thousands of years later, the discovery of the microscope helped scientists see cancer up close, but its origins remained a mystery.

What scientists did know was that cancer resulted when the normal process of cell division shifted into overdrive and cells reproduced again and again and again. Treatments were developed to stop this process of endless cellular replication.

Radiation, for example, was introduced in the late 19th Century as a tool in the fight against cancer. Years later, chemotherapy was introduced as another effective treatment. Both methods of treating cancer worked similarly: they destroyed cancer cells or prevented them from reproducing.

Despite their benefits, both chemotherapy and radiation have their drawbacks. Chemotherapy, for example, can kill healthy cells along with cancer cells, which can lead to unpleasant and potentially serious side effects. Better treatments, however, required a better understanding of the disease.

Why did some people develop cancer while others did not? Why did some cells quit functioning normally and shift into an endless cycle of division? These questions continued to puzzle scientists.

In the 1980s, in what would become a watershed moment in cancer research, scientists made an important discovery about how cancer might get its start. It appeared to scientists that some cancers begin in response to messages encoded in our genetic material, or DNA. When an otherwise healthy cell has certain mutations in its DNA, it can trigger a response of endless replication, and grow into a tumor.

Using an expanding set of new technologies, scientists were able to explore many of the molecular pathways that lead to cancer. These pathways are comprised of interactions among proteins and genes and they can lead to a number of biological outcomes. For example, some pathways create blood vessels that feed the tumor; other pathways tell the cell to keep making copies of its DNA; and still other pathways signal the cell to wander off and start new tumors.

By exploring cancer's molecular mechanisms, scientists hoped to develop a new generation of treatments. Treatments based on molecular pathways are often referred to as "targeted therapies" and are considered to be more precise than traditional methods of treatment, including chemotherapy and radiation.

Early versions of targeted therapies included monoclonal antibodies. Introduced in the 1990s, these antibodies are laboratory versions of the molecules that the immune system produces in response to foreign invaders. Unlike chemotherapy's broad-based attack, monoclonal antibodies are much more precise – limiting their effect exclusively to cancer cells.

Several targeted drugs led to remarkable results, with relatively few side effects. One such drug, Imatinib Mesylate, works to fight certain types of cancer by turning off an enzyme that causes cells to become cancerous and multiply.

Today, physicians continue to rely on traditional methods of treatment such as surgery, radiation, and chemotherapy, while more and more targeted therapies are emerging as important weapons in the fight against cancer. Even with these targeted therapies, individual response varies greatly. What works for one person doesn't work for another.

Understanding those variations was only possible with new levels of insight brought about by the next scientific breakthrough – the decoding of the human genome, which is ushering in a new era in cancer treatment, an era of personalized, molecular medicine.

Chapter 2: New Era of Molecular Medicine

Narrator: The Human Genome. The completion of this project in 2003 marked the beginning of the age of molecular, or targeted, medicine.

Dr. Anna Barker: We're now entering a new age of medicine, in which we are beginning to identify and classify disease at its most fundamental level: the molecular level.

Narrator: Decoding the genome made it possible to look at specific genetic variations to understand why people are so different…and why they respond to the same treatments so differently.

Dr. Howard Fine: We treat these tumors very much as a single type of tumor. Yet we know that these tumors behave very differently in different patients, and we believe the difference really lies in the fact that these tumors aren't just a few different tumors types but rather represent many different tumor types.

Narrator: Defining these different tumor types requires studying the molecular activity of genes, and proteins, and their interactions, which generates a huge and continually growing amount of data. Whether it's genetic patterns gleaned from biospecimens, or measurements of the tens of thousands of proteins that make up the Human Proteome, or the clinical data from patient medical histories and the results from their laboratory tests; all this information needs to be integrated, analyzed, and interpreted.

And for our knowledge to grow, this information must be *shared.*

At present, there are few common vocabularies by which to describe findings, few common standards for reporting research results, no infrastructure to share tumor samples from one lab to another, and no way to combine patient histories from one medical institution to another, which means that valuable information, knowledge, and resources are cut off from those that need them.

Dr. Kenneth Buetow: The current cancer community is broken up into small and fragmented units and we need to have effective means by which we can bring the important, disparate parts of the community together so that the whole can be more than the sum of the parts.

Dr. Rebecca Crowley: Data is locked up in institutions, and tissue is locked up in institutions, and individuals don't have the tools they need to really do things quickly, in an automated fashion.

Dan Pelino: Standards is about how we transmit information. We must have building blocks. We must build to share information, from research to clinical trials to treatments.

Dr. Laura Esserman: Unfortunately in medicine, to get a lot of good information is very, very hard. A lot of the electronic medical records that we have are often just scanned documents, so it's not information that we can analyze and understand.

Dr. Janet Woodcock: It's very confusing. It's not standardized. There's not a coherent, efficient, and seamless system.

Narrator: But it's all about to change.

Dr. Anna Barker: We're building an infrastructure that will provide the tools, that will allow our investigators to share information immediately and in a meaningful way that will allow us to really deliver new therapies, new diagnostics, new preventives to patients.

Chapter 3: Understanding the caBIG™ Initiative

Narrator: Cancer research is now a sophisticated, multifaceted effort.

The research is taking place in government, biotech, pharmaceutical, and academic laboratories across the country.

Over the past 30 years, NCI has supported the building of a number of databases to store all kinds of information – clinical trials information from the Clinical Trials Working Group, Genomics data from the Cancer Genome Anatomy Project, and much more.

These databases form the pillars of our understanding of cancer. Among the goals of caBIG™ is to CONNECT those existing databases to maximize the knowledge, as well as integrating new sources of data that are now emerging, such as data from The Cancer Genome Atlas project, studies from the Clinical Proteomic Technologies Initiative, and findings from the NCI Alliance for Nanotechnology in Cancer.

There is a vast amount of information being generated and we are learning so much – but we could be learning so *much more*…

Despite technological advances, it is difficult, if not impossible right now, to easily and rapidly connect research in one location with resources in another and with clinical trials in a third and fourth and 10th and 100th location. The caBIG™ initiative will change that.

Let's take a closer look at how the tools and systems developed by the caBIG initiative will help translate research discoveries into patient care…

A patient is diagnosed with breast cancer. She undergoes surgery and donates a tissue sample, known as a biospecimen, from her tumor. This biospecimen, along with her medical history, is stored in a biorepository with thousands of other biospecimens.

Dr. Mark Watson: The one key thing that will really accelerate research and our ability to leverage all of these biospecimens is to put them into an information network, where scientists as a group can know what's available for research purposes

Narrator: The stored biospecimens can be labeled and tracked with a software suite called caTISSUE, one of the many software tools developed for caBIG™.

Dr. Michael Becich: So now one of our researchers decides that they want to identify a cohort of patients to do a study on in a biologically meaningful way. They then do a query against the system and it returns the number of specimens that match those criteria.

Narrator: Researchers require hundreds or thousands of biospecimens to identify the important characteristics that differentiate one cancer from another and to identify a molecular signature comprised of particular mutations or abnormalities in the patient's DNA.

caTISSUE is just one example of dozens of tools and software being developed and adopted at cancer centers across the country. Other tools such as REMBRANDT, caMatch, caARRAY, and many more will help to accelerate the discovery of new molecular signatures and the development of diagnostics to identify them.

Armed with this knowledge, patients and physicians can choose the best treatment. A particular molecular signature may lead to surgery for one individual.

For another, the signature may help determine that surgery isn't necessary because that particular form of cancer is not aggressive.

In yet another patient, the molecular signature may lead to the use of a particular drug, such as tamoxifen or herceptin for the treatment of breast cancer. Diagnostic tests that screen multiple genes can now be used to inform a patient whether they can safely avoid chemotherapy altogether.

This knowledge about molecular signatures can be shared throughout the caBIG™ network so that one researcher may use this information as the starting point for developing a new drug and a different researcher may look for new molecular categories of breast cancer so that patients can be diagnosed and treated more precisely.

Yet another researcher may use that data to help study other types of cancer – colon or lung or pancreatic – which might share common molecular characteristics.

As the caBIG™ network continues to grow...as more cancer research centers become part of the grid, as more and more biotech, pharmaceutical, and IT companies build caBIG™ compliance into their software and technical infrastructure, and as the amount of shared data increases, the caBIG™ initiative will create an unprecedented opportunity to translate knowledge into better ways to detect, diagnose and treat and even prevent the many diseases that constitute cancer.

Chapter 4: caBIG™ in the Future

Narrator: The National Cancer Institute and the entire cancer community are working together to usher in a new age of cancer care.

Dr. Kenneth Buetow: caBIG™ is a reality and the reality is captured in the people participating in it. We have more than 800 active participants. People willing to roll up their sleeves and do the hard work of collaborations.

Dr. Rebecca Crowley: caBIG™ is really going to help us make that jump from one institution to many institutions.

Dr. Janet Woodcock: caBIG™ is kind of the cutting edge.

Dr. Mark Watson: The true mission of caBIG™ is to provide the network to put all these pieces together.

Dr. Howard Fine: That is the idea of caBIG™: to be more than just a place to put data but a way of actually using data.

Dr. Laura Esserman: What could be more important than sharing information?

Dan Pelino: caBIG™ as a catalyst for what we're doing with cancer is a tremendous role model for what we can do in the future.

caBIG™ cancer Biomedical Informatics Grid ™

Dr. Anna Barker: caBIG™ is, I believe, the most important initiative undertaken by the cancer research enterprise in the entire history of the war on cancer. It will, in fact, change everything.

As a community, we are united by our mission, we are enabled by cancer research and we are connected by caBIG™.

For more information, please visit http://cabig.cancer.gov