The Next Generation in Cancer Screening

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The global community, women’s health, and regular screenings for cervical and breast cancer for prevention and early detection are more than words to pathologists and laboratory professionals. Those phrases are integral to delivering patient-centered care every day and to moving beyond the laboratory—metaphorically and geographically.

From Jack Andraka, the 15-year-old scientific whiz kid, to four dynamic keynote sessions, the 2012 ASCP Annual Meeting, held Oct. 31–Nov. 3 in Boston, was a tour de force that delivered critical scientific knowledge and engaged attendees’ empathy for patients worldwide. The keynote speakers—Donald M. Berwick, MD; Ashley Judd; Laura W. Bush; and Giuliana and Bill Rancic—are cultural change agents who illuminated how they have turned their visions for a better world into plans of action. Their insights morphed how pathologists and laboratory professionals consider diagnostic medicine and the U.S. healthcare system, as well as our responsibility for improving global health. See pages 37-39 for photos and in-depth coverage of the 2012 ASCP Annual Meeting.

Throughout the year, ASCP has been steadfast in its involvement in changing perceptions about the role of pathologists and laboratory professionals amongst clinicians and patients worldwide, while continuing our commitment to improving patient care all over the globe. While our initiatives happen throughout the year, the ASCP Annual Meetings accelerate our progress toward moving out of the medical laboratory to join our clinical partners and the entire healthcare team.

Journey to Genomics

In this issue, ASCP President Joel M. Shilling, MD, FASCP, discusses how pathologists and laboratory professionals need to redefine themselves as consultants and ensure their role on the multidisciplinary healthcare team. Council of Laboratory Professionals Chair Barbara S. Caldwell, MS, MT(ASCP)SH, lauds the importance of regularly scheduling cancer screenings while acknowledging that healthcare professionals are as guilty of procrastination as other patients.

Mindful of the lack of knowledge about the crucial role of pathologists in patient diagnosis, Resident Council Chair Evelyn T. Bruner, MD, urges pathology residents nationwide to educate medical students and residents in other specialties about the pivotal part pathologists play to ensure accurate diagnoses of disease.

By pooling the results of a national network of research and technology teams, The Cancer Genome Atlas improves pathologists’ understanding of how mutations function and the identification of biomarkers that show which specific drugs work for individual patients. To date, cancer genome studies have shown that it is less important to determine the organ system in which the cancer originated than to treat the underlying driving mutations. According to Richard L. Haspel, MD, FASCP, pathologists must have a keen understanding of genomic medicine, and all pathology resident programs must teach genomics-related concepts.

Molecular pathologists point to two types of biomarkers: prospective risk of disease and post-diagnostic biomarkers. For prospective biomarkers, the pathologist asks which clinical outcome corresponds to the presence of a specific biomarker. In other instances, a biomarker may show that a cancer will be slow growing or may indicate metastatic disease.

Alan Dove, PhD, reports that advances in medical imaging diagnostics increase the importance of the pathologist’s role in diagnosing cancer and in advising clinicians on the best options for treating their patients. As the treatment options expand rapidly, three authors give their own fascinating perspectives on the pharmaceutical industry and companion diagnostics.

As always, I thank you for your support of ASCP. Remember, we are in fact Stronger Together. Please remember to send your suggestions or comments to me at Blair.Holladay@ascp.org. My best to you in the New Year.

Dr. Holladay is Executive Vice President of ASCP.
The Cancer Genome Atlas: What Will Its Legacy Be?

According to the project website, TCGA began as a three-year pilot in 2006 with investments from the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI). “The TCGA pilot project confirmed that an atlas of changes could be created for specific cancer types,” the website states. “It also showed that a national network of research and technology teams worked together to achieve this goal.”

By James Netterwald, PhD, MT (ASCP)

Cancer researchers define The Cancer Genome Atlas and its current and future applications.

The Director shall “collect, analyze, and disseminate information…useful in the prevention, diagnosis, and treatment of cancer, including the establishment of an international cancer research data bank…(for) cancer research undertaken in any country for the use of any person involved in cancer research in any country.”—National Cancer Act, Section 404 (a) (1), 1971
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Fifteen-year-old Jack Andraka has already accomplished what many pathologists dream about by discovering an inexpensive early detection method for pancreatic cancer. His innovative method involves carbon nanotubes; mesothelin, a biomarker for detecting cancer; and antibodies interacting with changes to electrical flow measured by a $50 home electrical meter purchased at Home Depot. What’s more, Jack believes that with access to the Internet, the support of an excellent mentor, and use of a medical laboratory, pathologists and laboratory professionals can develop groundbreaking ideas like his.

Jack impressed his peers and older colleagues in science at the 2012 ASCP Annual Meeting in Boston. On Nov. 2, he made a presentation to 100 high school students and several ASCP
Career Ambassadors and was interviewed about his discovery before an audience of pathologists and laboratory professionals. With his openness to ideas, his scientific mindset, and his poise and sense of humor, this high school sophomore shattered our notions of what we expect to learn from the most advanced scientists and physicians, much less from a teenager.

Yet his message is simple and down-to-earth. If pathologists and laboratory professionals believe that they can change the world for the better, they will. Scientists have the resources, the intelligence, the perseverance, and the adaptability to make a difference for their patients.

Redefinition and Skill Enhancement

That concept fits perfectly with how pathology and laboratory medicine are changing. Each pathologist or laboratory professional needs to redefine who they are and their role on the multidisciplinary healthcare team. That’s the path toward improving diagnosis and treatments for patients, resulting in the best patient outcomes.

At the 2012 ASCP Annual Meeting, patient-centricity became the new mantra for pathologists. In his Scientific Address, Donald M. Berwick, MD, presented examples of how pathologists can implement innovations for new results. In addition to emphasizing multidisciplinary teamwork, Dr. Berwick focused on continuous improvement through lean production; applied technology such as electronic health records; newly skilled workforce; expanding scope of practice; and patient-centered design.

His principles for pathologists include placing patients first, protecting the disadvantaged, starting at scale, returning the money, and acting locally. “There has never been a better time, or a more important role, for healthcare professionals to lead the reform and improvement of American health care as a system,” Dr. Berwick said.

How can pathologists begin to implement such changes? To start, they can evaluate their entire practice. How can patients become more central to their diagnosis of diseases? Where can they reduce costs for patients while improving care? What recommendations can pathologists give to clinicians to limit unnecessary tests? How can their laboratory teammates help them enhance their skills?

For example, in the medical laboratory where I work, four pathologists and 40 laboratory professionals conduct weekly discussions about patient diagnoses, laboratory tests, and treatments. We learn from each other; 44 minds are better than one. Pathologists know a lot about diagnoses, but laboratory professionals understand more about the laboratory tests.
Message from the President

Stronger Together

Moving beyond a pathologist’s laboratory, ASCP is building an infrastructure for pathologists and laboratory professionals to make the transition to personalized medicine. This new initiative, called Stronger Together, connects two distinct sides of the laboratory—pathologists and laboratory professionals.

As part of this initiative, ASCP is forging alliances with like-minded organizations such as the Society for Hematopathology (see page 37) and encouraging pathologists and laboratory professionals to join multidisciplinary healthcare teams to ensure the optimum patient outcomes.

At the crux of these endeavors is science and research. For example, Ossama Tawfik, MD, FASCP, recently led a team of physicians and scientists who analyzed how the behavior of the Ki-67 protein tumor marker predicts when breast cancer in the lymph nodes will turn more aggressive. Their research gives pathologists another method to use when advising clinicians on the most appropriate treatment for individual patients.

This is only the beginning. More follow up studies will look at tumor cells on the molecular level to see which ones have mutated, so they can stop them from growing in patients, ultimately saving lives. Pathologists and laboratory professionals require multiple forums in which to share their discoveries with ASCP colleagues.

Soon ASCP will implement virtual communities for members with similar clinical, demographic, geographic, and content interests to network, collaborate, and exchange best practices. Based on the recent report from the Task Force on ASCP Governance, these online forums will provide more interaction between ASCP and our members, resulting in more engagement by spring 2013.

Four virtual interest communities will be created:

- Clinical Interest Content Groups will operate as incubators for rapid and nimble program development.
- Content Interest Groups will serve as another resource for the swift creation of new products.
- Demographic Interest Groups will provide a general point of entry to exchange information, discuss results, and evaluate best practices.
- Geographic Interest Groups will supply more information on licensure, ASCP certification (nationally and internationally), and trends shaping the future for the entire laboratory team.

This is another example of how ASCP is responding proactively and nimbly to changes in health care and technology that affect patients and future generations. These communities will assist our Society to recruit future thought leaders in high school to become pathologists and laboratory professionals.

ASCP may have found one already. Jack Andraka, the scientific whiz kid, said that he wants to be a pathologist.

I welcome any comments, questions, or suggestions you may have. Please email them to me at President@ascp.org.

Dr. Shilling is the Medical Director, Radiation Safety Officer, and Technical Director of Toxicology at Quest Diagnostics, Portland, Ore.
As one of the world’s leading healthcare companies, Roche recognizes Cervical Health Awareness Month.

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Message from the Chair of the Council of Laboratory Professionals

By Barbara S. Caldwell, MS, MT(ASCP)SH

Prioritizing Cancer Screenings

Health screenings should be conducted routinely as preventive measures to detect early signs of disease. The Latin phrase “minima maxima sunt” translates, “the smallest things are most important.” We understand that any form of cancer and its possible treatment could have a major impact on our lives. And yet, how many of us procrastinate getting those necessary screening tests done?

Consider our daily routines. We make sure to tune into the weather report each day. Some people check sports team scores, while others tune into the most current stock market data, entertainment, or political news. Many other tempting diversions exist as well: surfing the Web, texting our colleagues, downloading and using apps.

Yet we postpone the vital cancer checks for our bodies that could identify a problem before we show any symptoms. Just like the plumber with the leaky faucets in his own home, or the physician who does not pay attention to that old axiom, “physician, heal thyself,” many of us delay getting recommended health checkups and cancer screening tests.

Procrastinators Abound

“Procrastination is the bad habit of putting off until the day after tomorrow what should have been done the day before yesterday,” according to Napoleon Hill.¹
For example, do you think you will have time to get tested—some day in the future—but don’t have time right NOW? If you are nodding your head (or hanging your head), then you are most likely being honest about procrastinating.

Procrastination is a huge problem, and some scientists say it is getting worse. A Canadian industrial psychologist postulated in a large research study that not only is procrastination increasing, but it also makes people less wealthy, less healthy, and less happy.²

According to University of Calgary Professor Piers Steel, PhD, only about 5 percent of the American public thought of themselves as chronic procrastinators in 1978. Now, according to Dr. Steel, 95 percent admit to procrastinating, with about 26 percent indicating that it is a chronic condition.³ And if you think your best work is done under pressure, you should know that last-minute work has been shown to contain more mistakes.

Minds are wonderful rationalizers for all manner of things. For example, if we have no evidence of cancer and are in good health, then certainly problems will not crop up in the future. That test can be postponed for a bit longer, right? Well, not necessarily.

When it comes to “getting around to it,” Dr. Steel said that men are slightly more guilty than women (men represent about 54 out of 100 chronic procrastinators), and a younger person is more likely to procrastinate than an older person.³ Some see procrastination as a response to the modern world; we used to have to respond immediately to tasks because our livelihood depended on it. Now we may be inclined to procrastinate because the task is not mandatory at this moment. But with modern technology handing us the tools to practice preventive medicine, shouldn’t we be paying attention to the importance of our own health screenings?

**In the Driver’s Seat**

There are few excuses for rationalizing procrastination on cancer screenings, given that procrastinators tend to be among the least healthy of us. The definition of a good screening test is that it is low cost, widely available, and has the ability to assist early diagnosis to change long-term outcome. The U.S. Preventive Services Task Force and U.S. Centers for Disease Control and Prevention support
Leadership Messages

breast, cervical, and colorectal cancer screening. Screening intervals depend on individuals’ ages and family history, but overall recommendations are as follows:

- Breast cancer—Mammograms are the best way to find breast cancer early.
- Cervical cancer—The Pap and HPV tests can detect abnormal cervical cells, which may transform into cancer cells. Pap and HPV tests also can find cervical cancer early, when the chance of being cured is very high.
- Colorectal cancer—Screening tests can find precancerous polyps, which can be removed before turning cancerous. Screening tests also can find colorectal cancer early, when treatment works best.

Medical tests, particularly something as important as a colonoscopy, should not be postponed because of fear, discomfort, or embarrassment. Colon cancer is the second most common cause of death but is treatable and even preventable if identified early. Make it a goal to get into the driver’s seat, overcome your procrastination urges and modern-day technological temptations, and elevate cancer screening to an important health management responsibility.

Reward for Foresight

Just as the Thanksgiving turkey that has been fed every day trusts that this will continue to be the case, we should not be lulled into a false sense of security. With today’s easy-access, high-tech, and increasingly sensitive testing, there is no excuse not to put your health before less important daily routines. Don’t procrastinate in things that matter; the time will never be just right. So take advantage of today’s advanced technology and make that appointment to get your preventive screening tests done today!

I welcome your feedback. Please send your questions or comments to me at CLP@ascp.org.

References


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I asked my 12-year-old son the other day if he knew what cancer was. His reply was simply, “It’s like an infection; it’s a tumor.”

I’m not sure he knows exactly what a tumor is, but his answer was fairly accurate. Cancer is an infectious tumor; it starts growing and spreads like a toxic infection if it’s not caught early enough. My son understands even less about what I do on a day-to-day basis. I have tried to explain on several occasions and even offered to speak to his science class about being a pathologist. He curtly responded, “No way, Mom.”

The reality is that even our physician colleagues do not entirely understand what we, as pathologists, do. This is certainly not true of all physicians. But I am always surprised when I get a random page on call from a resident to that effect. For example, an internal medicine resident recently asked, “Don’t you guys do biopsies?” Well, no, not exactly.

I am also surprised by the second-year medical students I have encountered in a small group setting for the last four years. At the beginning of the year they simply ask, “What does a pathologist do?” They seem to be like the rest of the public in that, when they hear the title pathologist, they automatically think forensics. I am delighted to clarify that misconception and tell them that pathologists wear many hats.

I emphasize these points: We are part of the patient’s team. Like the physicians in any other specialty, we provide the best in patient care. I use an example of a patient with a newly discovered mass and take them through the biopsy, resection with intraoperative consultations, and staging to point out all of the critical phases in which the pathologist is involved. As a result, I expect these budding physicians to go through their careers with a better understanding of pathology.

Admittedly, I am slightly biased and usually focus primarily on what a surgical pathologist does. In fact, pathologists are involved in so many important facets of patient care that it would be too time consuming for me to explain them all to my medical students. Nevertheless, I genuinely want them to have more knowledge and appreciation of our role in medicine. This is intended not only to promote pathology as a subspecialty, but also perhaps to persuade a few students to perform a pathology rotation during their third or fourth year so they can experience firsthand what pathologists do.

I implore residents across the country to do the same: educate others about pathology. We are on the front lines, whether it is teaching medical students, participating on tumor boards, or answering physicians’ inquiries and requests. Each encounter is an opportunity. By making the most of these moments, we are ultimately improving patient care.

Furthermore, it is vitally important for our colleagues to understand the many components of the pathology profession. One day, a pathologist may encounter a patient with a newly found mass. The next day, a pathologist may have a patient who is experiencing unexplained tiredness. We are in the critical position of making an early diagnosis of a type of cancer or leukemia that can save lives. There are no longer solo practitioners. Health care is a team effort, and the pathologist is a critical member of the team.
Collaborative Endeavor

In addition, it is important to remember that the team is not made up only of physicians. Medical laboratory scientists, medical transcriptionists, pathologists’ assistants, nurses, social workers, clinical coordinators, and many others are part of the patient’s healthcare team. It is a true collaboration of care for each patient who seeks medical attention. Like any team, in sports or medicine, performance is always at its best when it’s a coordinated effort, with each member contributing individual skills and knowing when to rely on others for their expertise.

The further I have gotten into my training, the more I have come to this realization. When I explain to others what a pathologist does, it often begins with descriptions of how pathologists help other physicians and patients. For example, through our diagnoses, we help assist the clinician in giving patients the right treatments; we help interpret laboratory tests; and the list goes on.

Simply put, I am passionate about pathology. I want to pass this along to my colleagues, medical students, and those outside of medicine. In educating others about what pathologists do, we are not only promoting our specialty, but also providing better patient care through collaboration, education, and understanding.

Right now, my 12-year-old son may not completely understand what I do or want to follow in my footsteps, but he sees and hears the enjoyment I get from my job. One day, I might just have a budding pathologist in the family. And one day, I am going to speak to his science class, whether he likes it or not!

If you would like more information on how to get involved on a national level or how to become an ASCP resident representative, contact us at ResidentCouncil@ascp.org.

Dr. Bruner is a fourth-year pathology resident at the Medical University of South Carolina, Charleston, S.C.
Think back to the early days of cancer research, when the disease was treated as a monolithic condition; that is, all cancers were thought to have a single etiology and were assumed to have a common cure. But research has unveiled an increasingly sophisticated and complex picture of cancer. We now understand that cancers are not all alike. Breast cancer is different from skin cancer is different from colon cancer and so on. What’s more, not all breast cancers are alike—in fact, not all cancer cells from an individual tumor are identical.

This molecular heterogeneity has become a driving force in the search for therapeutics that target specific variants of cancer, even specific genes. Likewise, diagnostic and prognostic tools are becoming increasingly targeted. The ultimate hope is to identify a biomarker—a molecule or morphological feature easily and noninvasively detected from tissue samples that can determine the risk of developing disease, distinguish between disease variants, or provide diagnostic and prognostic information as well as guide treatment decisions.
Biomarker Prognostics

Cancer biomarkers generally consist of genomic alterations in one or more proteins that are present in a tissue or body fluid, but they can also be morphological changes in a tissue. Whatever the molecule or tissue, the essence of the biomarker is that its presence correlates highly with and is somewhat predictive of a risk for developing a particular clinical condition.

Molecular pathologists generally speak of two main types of biomarkers: prospective and post-diagnostic biomarkers. For the prospective biomarkers, the physician asks the question, “What clinical outcome is associated with the presence of a specific biomarker?” Some biomarkers may indicate that a patient is at risk for developing a certain cancer. In other cases, a biomarker may help signal that a cancer will be slow growing, while still others may presage metastatic disease.

Certain biomarkers may also help determine the course of treatment by indicating whether a cancer patient should receive a specific cancer drug. Alternatively, biomarkers may also help assess whether a patient’s tumor will be sensitive or resistant to the treatment.

Among the useful and well-established molecular biomarkers are the oncogenic GTPase, KRAS, and microsatellite instability for colorectal cancer, as well as oncogenic epidermal growth factor receptor (EGFR), KRAS, and anaplastic lymphoma kinase (ALK) for lung cancer. In another example, the presence or absence of the human epidermal growth factor receptor 2 (HER2) on tumor cells will guide decisions about the course of treatment for breast cancer.

Molecular Pathology Evolves

Molecular biomarkers for cancer have not always been commonplace in cancer diagnosis and treatment decision making. Before the advent of molecular testing for cancer biomarkers, the pathologist relied mostly on tumor samples stained with Hematoxylin and Eosin (H&E) to detect morphological changes indicative of cancer.

"However, there is much more to learn about tumors than from looking at an H&E slide, and that is why molecular diagnostics is becoming more and more dominant in the field of pathology and will be even more dominant in
the next decade for sure,” says Shuji Ogino, MD, PhD, MS (epidemiology), associate professor of pathology at Harvard Medical School; associate professor in the Department of Epidemiology at the Harvard School of Public Health; and molecular pathologist at Brigham & Women’s Hospital and Dana-Farber Cancer Institute, all in Boston.

“As a molecular pathologist, I spend about 20 percent of my time in a clinical molecular diagnostics laboratory, where molecular biomarkers can aid in familial risk assessments as well as treatment decision making for cancer patients,” Dr. Ogino says. “We have to take action to improve training for our current and future pathologists. When I teach pathology to my students, I focus on molecular pathology, in addition to morphology.’

The limited role of the pathologist in prognosis and tumor staging is in the past. Dr. Ogino notes that today’s molecular pathologist can actually help oncologists take more effective treatment action by determining the particular molecular subtype of the cancer, which offers information that can guide very specific treatment decisions. “Thus, molecular testing has become an essential part of treatment decision making,” Dr. Ogino says. “That is a huge paradigm shift in the last five to 10 years. These are the predictive biomarkers because they can predict treatment response or non-response.”

Mark Boguski, MD, PhD, associate professor in the Center for Biomedical Informatics at Harvard Medical School and in the Department of Pathology at Beth Israel Deaconess Medical Center in Boston, stressed the importance of educating today’s pathologists for the future. “We realized that pathologists needed to learn about molecular medicine,” Dr. Boguski says. “So, more than three years ago, we started a mandatory training module in a residency program called the Genomic Medicine Initiative. When we designed the course, we could have spent a lot of time talking about technology. But, with technologies changing so rapidly, they would be obsolete even before the residents finished their training.”

Instead, Dr. Boguski and his colleagues made data analytics and interpretation the focus of the residency training. “We are training our residents to operate in the future, which is going to be dominated by molecular testing,” says Dr. Boguski, who adds that more continuing medical education is also needed to train practicing pathologists to perform molecular pathology.

“I think in this Internet age, patients are becoming better informed and more savvy about off-label treatment options for cancer. And although their physician might not be aware of these treatment options, patient demand will supersede physician acceptance,” explains Dr. Boguski, who recently launched a new company, Genome Health Solutions, to accelerate the transition to personalized genomic medicine as the new standard of care. “As physicians, we have to shed the role of learned intermediaries and actually become co-managers with our patients in the application and interpretation of these molecular tests. That will make a big change in how pathologists interact with their patients directly.” [See sidebar on the TRIG project.]

**Biomarkers for Glioblastoma**

Moving the role of the molecular pathologist into a future replete with genomic medicine approaches will take not only education, but also research, both basic and translational.

Defining cancer types by their molecular phenotype is the primary goal of many research projects that study cancers. “The importance of molecular pathology has grown dramatically in recent years, and this is likely to be the critical link that guides treatment for patients,” says Paul Mischel, MD, a member and head of the Laboratory of Molecular Pathology at the Ludwig Institute for Cancer Research and professor of pathology at the University of California at San Diego. “The understanding of [biomarker] function becomes more important for using the information to guide and develop better care for patients.”

Driving this understanding will likely be in-depth research into the function of novel cancer biomarkers following their discovery through the mining of data output from The Cancer Genome Atlas, a large initiative of the National Cancer Institute and other cancer genome projects.

In his own work, Dr. Mischel and his colleagues are exploring molecular pathways of glioblastoma in three different studies. The first research project focuses on the EGFR/PI3-K/mTOR signaling pathway, which is mutation-activated in glioblastoma and required for tumor growth and maintenance (note: PI3–K is an abbreviation for phosphoinositide 3-kinase). Dr. Mischel’s work aims to understand the biology of this highly drug-targetable signaling network, including understanding how it becomes rewired to dodge the effects of some of the current treatments and maintain tumor growth. Developing such an understanding may lead to better inhibition of the pathway and suppress drug resistance.

“This is a highly targetable pathway, but when one goes to the clinic with small-molecule inhibitors, there has not been great success,” he says.

The second area of research is focused on tumor metabolism to understand the biochemical consequences of specific mutations in cancer. Dr. Mischel’s laboratory is interested in how biochemical changes resulting from cancer-causing mutations render tumors sensitive to drugs that block specific metabolic enzymes, thus suggesting an alternative approach to treating cancer.

His third area of research is tumor heterogeneity. “Cancers are not only heterogeneous between two individuals with
How Can We Teach Genomic Medicine to Pathology Professionals?

By Richard L. Haspel, MD, PhD, FASCP

As experts in clinical diagnostics, pathology professionals must understand genomic medicine. Genomic testing is now part of patient care. Tumors are analyzed at multiple loci and even at the whole-genome level to identify treatment targets. Next-generation sequencing is used to assess fetal risk for Down syndrome and has determined the genetic makeup of microorganisms responsible for major outbreaks. This technology has entered or is poised to enter almost every subspecialty within pathology. However, a 2010 survey administered through the Program Directors Section (PRODS) of the Association of Pathology Chairs (APC) showed that only about 30 percent of residency programs currently teach genomics-related concepts. Pathologists are not prepared for this new era in medicine.

As a response to this clear educational need, the Training Residents in Genomics (TRIG) Working Group was formed through PRODS in 2010. This group is made up of residency directors, molecular pathologists, and genetic counselors, with ASCP providing administrative support. Members include representatives from several major pathology organizations, past presidents of the Association for Molecular Pathology (AMP), and the executive director of the National Coalition for Health Professional Education in Genetics (NCHPEG). The group is focused on three major goals: creating learning tools; disseminating information related to genomic medicine; and assessing the degree of integration of genomic medicine training into pathology residency programs.

Toward creating learning tools, the TRIG Working Group released a series of four educational PowerPoint lectures in 2012. Although primarily designed for residents, these lectures provide an excellent introduction to genomic medicine for any pathology professional. Based on a curriculum first created at Beth Israel Deaconess Medical Center in Boston (genomic-medicineinitiative.org), the topics covered include next-generation sequencing technology, clinical interpretation of genomic data, and ethical issues in the genomic era. These lectures, with notes and a booklet of references, are available for free on the Intersociety Council for Pathology Information website (www.pathologytraining.org/trig_lecture.htm).

With the assistance of the TRIG Working Group, genomics-related questions are now included on the pathology Resident In-Service Exam (RISE). This exam, administered by ASCP, is taken by almost all pathology residents in the United States. Using this exam, the TRIG Working Group will be able to track progress related to integrating genomic pathology into resident education.

To further disseminate information on genomic medicine to pathology professionals, the TRIG Working Group has also been involved in presentations at major pathology meetings. At the 2012 United States and Canadian Academy of Pathology Annual Meeting, the TRIG curriculum was first introduced as part of a joint session of ASCP, AMP, and the American Society for Investigative Pathology. Given the popularity of and interest in the session, the three organizations also collaborated for a session titled “Genomic Testing: What Pathologists Need to Know” for the 2012 ASCP Annual Meeting in Boston. Although based on the TRIG curriculum, this session was designed for any pathology professionals interested in how to integrate genomics into their practice. There have also been presentations at the Annual Meetings of APC, NCHPEG, the National Society of Genetic Counselors, and the Academy of Clinical Laboratory Physicians and Scientists. Aside from conferences, a review titled “TRIG on TRACK: Training pathology residents in genomic medicine” was recently published (Pers Med. 2012; 9: 287–293). This peer-reviewed article described the approach of the TRIG Group as a model for teaching healthcare professionals about novel technologies.

The TRIG Group hopes to continue providing educational resources to pathologists. Recently, the chair of the TRIG Group received an R25 grant from the National Institutes of Health to further develop a genomics curriculum for pathology residents. Totaling approximately $1.3 million over five years, the funding will be used to assist in carrying out the goals of the TRIG Working Group. ASCP will leverage its educational design infrastructure to create online modules as well as surveys and exams to assess the curriculum.

In the two years since its formation, the TRIG Working Group has made considerable progress in promoting education in genomic pathology. With grant funding, the group will not only be able to continue but also will be able to expand its mission. As such, the TRIG Working Group welcomes additional input from pathology professionals who may want to join in this effort. Please contact Dr. Richard Haspel at rhaspel@bidmc.harvard.edu.

Dr. Haspel is an Assistant Professor of Pathology at Beth Israel Deaconess Medical Center and Harvard Medical School in Boston.
the same cancer, but also within an individual’s tumor. Individual tumor cells may differ profoundly in their genetic and epigenetic constitution and evolve in response to therapy,” he explains. “We are trying to understand how tumor heterogeneity occurs, how it’s maintained, and how it facilitates drug resistance, with the hope of developing ways to suppress it.”

These research programs integrate multidisciplinary studies performed in cancer cell cultures, mouse models of cancer, and in humans. The patient data come from state-of-the-art Phase 1 clinical trials.

“The traditional approach to translational medicine has been to go from discovery to preclinical models, and finally to clinical trials, but we have a very high failure rate using that approach,” Dr. Mischel says. His team’s research involves discovery at the clinical trial stage to understand whether a drug is actually hitting the target, blocking its intended pathways, and how these events affect patient outcome. “All that information can be gleaned by integrating studies of preclinical and clinical trials,” he adds. Work like this helps link potential biomarkers with the diagnostic and prognostic information that may one day inform clinical decisions.

From Biomarkers to Diagnostics

Biomarkers can also help inform the design of diagnostic assays for cancer.

Determining that a specific molecule is associated with a particular disease or disease state requires researchers to measure the presence or absence of that molecule in tissue samples representing different forms and stages of a disease compared with tissue from individuals without the disease. State-of-the-art molecular detection tools are becoming exquisitely precise, as they must distinguish between molecular variants that exist in vanishingly small quantities in a highly heterogeneous mix of molecules. To accomplish this, one researcher is using a tried-and-true biochemical approach in his brand of cancer biomarker discovery.

“We use mass spectrometry to identify and quantify protein-based cancer biomarkers,” says Tim Griffin, PhD, associate professor of biochemistry at the University of Minnesota in Minneapolis. The identification of the biomarker is based on comparative studies of pooled, noninvasively collected saliva samples from “normal” patients versus those from cancer patients. These samples are analyzed for differences in either the presence/absence or quantity of a specific protein. If any difference is determined in a given protein in the cancer patient versus the patient without cancer, then that protein is a potential biomarker.

“Identifying potential proteins in noninvasively collected samples like saliva could help us distinguish between patients with a premalignant oral lesion from patients with oral cancer, and detect the cancer earlier,” Dr. Griffin says. “The ultimate goal of this research is to define protein biomarkers that could be non-invasively collected and then develop a very simple, cheap, easy cancer diagnostic test that can be used to monitor patients over time.”

This diagnostic test is still in the developmental stages in which the protein biomarkers are being defined and validated. The next steps will be to assay saliva samples from a relatively large population of patients in order to generate adequate data for statistical analysis as well as to determine the sensitivity and specificity of the test.

“It could be 10 years before we acquire enough patient samples because one of the limitations is that the cancer type we are studying contains such a small population with these premalignant lesions … so there is not great infrastructure to recruit these patients and gather samples in large numbers to really do those next validation steps,” Dr. Griffin explains. “If the right infrastructure could be put in place and done pretty well, we could speed up the process.”

Evolving Role for Pathologists

The fields of molecular pathology and genomic medicine have co-evolved and grown dramatically into the driving forces of change in diagnosis and the treatment of cancer. In this new era of precision diagnostics, the molecular pathologist will increasingly collaborate with the treating physician to make better treatment decisions at earlier stages of the cancer. This vision of the future, notes Dr. Boguski, puts pathologists in the driver’s seat.

Additional resources:
http://genomicmedicineinitiative.org/

Dr. Netterwald is a freelance science writer based in New Jersey.
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The Cancer Genome Atlas: What Will Its Legacy Be?

Cancer researchers define The Cancer Genome Atlas and its current and future applications.

The National Cancer Act of 1971, which launched what Americans have come to know as the "War on Cancer," anticipated an international repository of all the information derived from the research the Act promoted. But it was not until genome-based science became a reality that such a repository was made possible in the form of The Cancer Genome Atlas (TCGA), a storehouse of cancer-related genetic sequence and associated data.

According to the project website, TCGA began as a three-year pilot in 2006 with investments from the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI). "The TCGA pilot project confirmed that an atlas of changes could be created for specific cancer types," the website states. "It also showed that a national network of research and technology teams working on distinct but related projects could pool
the results of their efforts, create an economy of scale, and develop an infrastructure for making the data publicly accessible. Importantly, it proved that making the data freely available would enable researchers anywhere around the world to make and validate important discoveries.” The initial pilot focused on glioblastoma and ovarian cancer, but the success of those projects led the National Institutes of Health to commit additional resources to TCGA to collect and characterize more than 20 additional tumor types.

For the TCGA, the most significant achievement to date has been the development of a program that “brings together many different kinds of data and allows users to collaborate with all of it in essentially real time,” says Kenna Shaw, PhD, director of The Cancer Genome Atlas Program for the NCI.

TCGA provides the mutational landscape of cancer. “The Cancer Genome Atlas is a large database that is based on primary tumors from patients. TCGA has sequenced, characterized, and analyzed genomic changes within matched sample pairs of tumor and normal tissues,” says Fang Tian, PhD, a senior scientist for American Type Culture Collection (ATCC) in Manassas, Va. A nonprofit biological resource and research center, ATCC authenticates microorganisms and cell lines and manages logistics of long-term preservation and distribution of cultures for the scientific community. Dr. Tian manages ATCC’s cell biology general collection.

Collecting that kind of data is facilitated by using the cell lines maintained in biorepositories such as ATCC. “People want to gain information on the driver mutations and passenger mutations involved in cancer development,” Dr. Tian says. “So, we are developing next-generation tumor cell line panels which are based on the top genetic alterations indicated by TCGA and other genomic databases. Those cell lines could be very useful tools for both basic and translational cancer research.”

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<tr>
<th>Cancer Type</th>
<th>Sample Collection</th>
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<td>Central Nervous System (Brain)</td>
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<td>Uterine Corpus Endometrial Carcinoma</td>
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The Cancer Genome Atlas: Cancers Selected for Study
Paul Mischel, MD, head of the Laboratory of Molecular Pathology at the Ludwig Institute for Cancer Research and a professor of Pathology at the University of California in San Diego, anticipates that there are a number of lessons to be gleaned from the Atlas. One key lesson is the existence of core mutational pathways that are frequently activated across different types of cancer. But the manner in which those pathways become activated varies among different cancer types and among patients with the same type of cancer. This illustrates the importance of those pathways for cancer, Dr. Mischel explains. He adds that The Cancer Genome Atlas improves the diagnostic landscape of cancer by providing a list of these core mutations that can be used for cancer diagnosis, including a wide range of specific mutations that can be detected in each cancer type.

Since different tumors—maybe even different cancer types—may share common genetic targets, researchers like Mark Boguski, MD, PhD, expect drugs effective for one type of cancer may have utility in treating other cancers, the discovery of which is facilitated by information found within the Atlas.

“By determining the location of driver mutations, you have more opportunities for off-label use of various cancer drugs,” says Dr. Boguski, who is an associate professor in the Center for Biomedical Informatics at Harvard Medical School and in the Department of Pathology at Beth Israel Deaconess Medical Center, both in Boston.

**Beyond One Legacy**

Not only is TCGA (and similar cancer genome projects) useful in identifying changes within gene sequences, it is also useful for analyzing epigenetic changes that affect when, how, and at what level a gene is expressed—alterations in methylation patterns, chromosomal coiling, or genetic copy number, for example.

“We are using these large data sets to determine how tumors develop, and how they behave, but we are looking at more than just genome [sequence] data as most people do,” says Shuji Ogino, MD, MD, PhD, MS (epidemiology), associate professor of pathology at Harvard Medical School, associate professor of Epidemiology at the Harvard School of Public Health, and molecular pathologist at Brigham and Women’s Hospital and the Dana Farber Cancer Institute, all in Boston. Dr. Ogino further explains that his lab is exploring the exposome, which represents various environmental, dietary, lifestyle, behavioral, and genetic factors, and how those factors contribute to the changes in the cancer genome and epigenome.

“Understanding how these mutations function can help us identify biomarkers that can be used to determine whether or not the drug that is designed to target specific mutations is actually interacting with its intended molecular target and limiting its downstream activities,” Dr. Mischel says. “Such biomarkers can also help determine whether or not a patient is responding to a drug, and whether or not they are likely to develop resistance to the therapy.”

“One of the big take-home messages of these cancer genome studies is that it is becoming less important these days to determine the organ system from which the cancer originated, and it is really important to treat the underly-
It’s hardly news that the field of medical imaging, especially for cancer diagnosis, has experienced explosive growth in recent years. Radiologists can analyze smaller tumors faster and more precisely than ever, endoscopists can extract unprecedented amounts of diagnostic information from ever-more-compact probes, and pathologists can see cellular structures and tissue architectures that their predecessors didn’t even know existed.

The steady stream of new technologies has driven a persistent increase in expectations, with oncologists and their patients continuing to demand earlier, more definitive answers to pressing medical questions: Is this growth malignant? Did the surgeon remove all of it? Is the chemotherapy working?

This trend shows no signs of abating, as a quick survey of some of the new cancer imaging techniques now in development show; researchers are still extending the limits of current tumor imaging technologies, and also creating entirely new ones. And as the field continues to evolve, traditional boundaries in medicine are beginning to blur and tough new questions are being raised.

The Doctor Will See Inside You Now

The leading edge of cancer imaging is perhaps easiest to see in the endoscopy suite, where a technique called optical endomicroscopy, first approved for clinical use two years ago, lets physicians observe microscopic structures inside patients’ bodies. Currently, endoscopists are often interpreting the microscopic views from these systems themselves, but that may not be the best approach.

“Especially as it pertains to cancer diagnosis and also dysplasia and other pre-malignant conditions, pathologists are trained to study and understand these patterns that we’re now seeing from living patients, so I’ve always felt that pathologists have to play a major role in this field for it to be successful,” says Gary Tearney, MD, PhD, professor of pathology at Harvard Medical School in Boston.

A pathologist’s eye will become even more important as optical endomicroscopy continues to evolve. Systems that are now in clinical use rely on one of two technologies. Confocal endomicroscopy works like a standard benchtop confocal microscope, which scans light across points in a sample to obtain detailed images. The second technology, optical coherence tomography (OCT), monitors the interference pattern between a beam of light that goes into a tissue and one that does not, in order to generate a cross-sectional view. For both systems, fiber optic cables carry the light in and out of the patient, and the rest of the image processing occurs in an adjacent work station. “From a pathologist’s perspective ... OCT sees architectural morphology and confocal sees cellular morphology,” Dr. Tearney says.

Though OCT and confocal endomicroscopy systems are currently separate, each with distinct strengths and weaknesses, Dr. Tearney expects that to change. “Developments for each technology are happening that will allow, for instance, confocal to see much larger areas and OCT to see at much higher resolution, so at some point these technologies may converge somewhat,” he says.

Other techniques for analyzing cells and tissues, such as monitoring subcellular chemical changes with fluorescence spectroscopy, are also migrating from the laboratory bench to the endoscope probe. Ultimately, Dr. Tearney and his colleagues hope to assemble a suite of tools that essentially will allow for a complete pathology laboratory to be inserted into a patient: “What we are trying to do is develop
these technologies that allow for molecular and chemical compositional imaging,” he says, “and we’re also merging that with the structural imaging techniques so that you can get both from the same location at the same time.”

Lighting the Way Through Oncology

Besides speeding cancer diagnoses, new imaging techniques could also help monitor treatment, especially as researchers discover new biomarkers that correlate with tumor prognosis. The human epidermal growth factor receptor 2 (HER2) receptor, which appears on a subset of breast and ovarian tumors, illustrates how this new “image and treat” strategy is evolving.

When physicians treat a patient with the HER2-targeting monoclonal antibody Herceptin (trastuzumab), they need to track the tissue’s subsequent expression of HER2 in order to determine whether the treatment is working. “If you can accurately assess the status of the receptors at a very early point, then that can help save lives and also costs,” says Amir Gandjbakhche, PhD, senior investigator at the National Institute of Child Health and Human Development in Bethesda, Md.

Currently, the standard techniques for HER2 monitoring are immunohistochemistry and enzyme-linked immunosorbent assays (ELISA). Immunohistochemistry provides only a qualitative measure of HER2 expression, while ELISA yields quantitative results. Both, however, require excisional biopsies, severely limiting the frequency with which a physician can sample the tissue.

Dr. Gandjbakhche and his colleagues decided to take a different approach. “Our strategy was actually trying to send an imaging probe to the receptors … to obtain noninvasively the expression of HER2,” he says. The scientists used small fluorescently labeled antibody-like molecules called affibodies to target HER2. One crucial difference between the affibodies and many standard anti-HER2 antibodies is that the affibodies don’t interfere with trastuzumab binding to the receptor. That’s important for imaging tumors in patients during treatment, as the drug generally saturates its epitope on HER2 when given at the proper dose.

With the label in hand, Dr. Gandjbakhche’s team was able to track HER2 expression quantitatively in live mice with xenograft tumors, using a relatively inexpensive fluorescence imaging setup. The system is as accurate and quantitative as ELISA, without requiring a biopsy. However, Dr. Gandjbakhche cautions that imaging human tumors will be substantially harder. In addition to requiring clinically approved reagents, human trials will also involve more complex image processing. “What we are doing now is xenografts, and they are on the skin of the mouse … however, if you want to go and image the breast, the tumors are inside, deeper in the tissue,” Dr. Gandjbakhche says.

One if Benign, Two if Malignant

While HER2 provides a convenient and very specific tumor marker, in most cancers physicians must rely on less definitive measures for diagnosis. A small, contrast-enhancing area on a radiologist’s scans could reveal that a patient’s colon tumor has come back, for example, or it could merely indicate a local inflammation or beginning scar that doesn’t need treatment. In theory, the two processes would be easy to distinguish if there were detectable general-purpose biomarkers that could identify multiple types of cancer.

Two leading candidates for such biomarkers are cathepsins and matrix metalloproteinases, enzymes that many tumor cells tend to overexpress as they invade surrounding tissue. To pinpoint these enzymes, Jan Grimm, MD, PhD, and his colleagues at Memorial Sloan-Kettering Cancer Center in New York City are developing new classes of enzymatically activated probes for optical and magnetic resonance
imaging. In the optical system, Dr. Grimm’s team links a pair of fluorescent molecules that can transfer energy between themselves and quench each other, so they do not fluoresce. The linkage, however, is a target site for one of the tumor-specific enzymes. “If they’re cleaved from each other ... no energy transfer can occur because now they’re too far apart from each other, and you get a signal,” says Dr. Grimm, a radiologist at Memorial Sloan-Kettering Cancer Center and assistant professor of radiology at Weill Cornell Medical College in New York City. The enzymatically activated probes can therefore highlight tumors while leaving other types of tissue anomalies dark.

For magnetic resonance imaging (MRI), researchers have developed probes with chemical groups that physically block water exchange in a gadolinium-based MRI contrast agent, preventing the agent from emitting a signal on the scan unless an enzyme cleaves away the blocking group. Though enzymatically activated MRI contrast agents have worked in preclinical studies, Dr. Grimm expects the optical strategy to get to the clinic first. “For MRI it might be a little bit more difficult, because the particles [have] certain side effects, and there are very few approved,” he says. Indeed, the difficulty of getting new injected dyes approved for clinical use may be one of the biggest barriers to using them. “It’s very difficult to get diagnostic agents through the FDA,” says Dr. Grimm, adding that, “regulations are very strict, much stricter than for any cancer therapy for various reasons.”

Working in a Data Mine

One way to avoid the difficulty of getting new reagents approved is to pull more data out of existing techniques. That’s the concept behind a strategy some proponents are labeling “radiomics,” which brings the same data-mining techniques used in genomic research to medical imaging. “The purpose of the whole endeavor is to extract as much information as we can from biomedical images, working right now with standard-of-care images,” explains Robert Gillies, PhD, chair of Cancer Imaging and Metabolism at the H. Lee Moffitt Cancer Center & Research Institute in Tampa, Fla.

In a typical application of the technique, Dr. Gillies and his colleagues collect digital imaging data from computed tomography (CT), MRI, and positron emission tomography (PET) scans, identify a potential tumor, and then segment the tumor into sub-regions based on measurable parameters such as shape, texture, and size. Though the system is still in development, Dr. Gillies envisions future radiologists reading scans in the usual way while simultaneously feeding data into an automated system that generates its own report. “What we are attempting to do is develop a system that fits completely within a typical radiologist’s workflow,” Dr. Gillies says.

The approach relies heavily on radiological images, but Dr. Gillies says that it can easily incorporate data from histopathology, which is itself already heavily dependent on data mining. “Digital pathology is essentially predicated on the same hypothesis, that if you extract some of these more subtle features from images, that might improve the pathology diagnostic power,” he says.

For example, the investigators have developed the ability to identify each individual cell within a stained section and generate cellular-level pathology reports that include dozens of individual measurements. The next step is to determine how to apply this trove of information to improve diagnosis and treatment. That will require running analyses on thousands of patients to identify useful diagnostic features that weren’t previously apparent, a task that calls for extensive collaboration between specialists. “There are a lot of commonalities between pathology and radiology, and we would like to see these disciplines become more integrated,” Dr. Gillies says.

The Price of Progress

As imaging technologies get more sensitive and sophisticated, though, they also run the risk of feeding spiraling medical costs, a problem that already afflicts the field. “What’s happened is that we have had a pretty big explosion in ... technologies which we can use to look inside the body,” says Larry Kessler, ScD, chair of the Department of Health Services at the University of Washington in Seattle. That explosion has had both benefits and drawbacks. “People are saying, ‘If I can see more and diagnose more accurately, I can treat more appropriately, maybe even treat less,’ and so I think that’s been a good thing.” However, he argues that several factors have driven hospitals, clinics, and physicians to overpurchase and overuse many of the new imaging technologies, especially for heavily publicized and litigated diseases such as breast cancer, which drives up medical costs without improving diagnostic accuracy.

Hospitals and physician groups in the United States compete fiercely for patients, prompting many to purchase the latest imaging systems regardless of medical need. “There’s the need to buy it because the guys down the street have it,” Dr. Kessler says. One result is a vast surplus of imaging systems that spend much of their time idle or performing clinically uninformative scans, driving up costs. In countries with more tightly regulated medical systems, such as the United Kingdom and other European nations, government officials determine the appropriate number of imaging systems for the population, drastically reducing costs and limiting overuse while still ensuring appropriate care. Instead of scanning every patient, doctors in these countries are more selective in using the technology.

A new focus on cost-control research could bring a similar streamlining to the U.S. healthcare system. “Before we subject people to a bunch of examinations where we’re not sure what we’re going to get, let’s make sure we understand whether the juice is worth the squeeze,” Dr. Kessler says. “I think this decade we’re going to ask a lot of those questions.”

Indeed, even researchers at the preclinical stage are starting to ponder the potential costs and benefits of their systems. As Dr. Gandjbakhche says, “You should not think only that you have an imaging system, [but] does this imaging system change the practice of medicine in the future?”

Originally trained as a microbiologist, Dr. Dove is now a science journalist based in western Massachusetts.

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Pharmaceutical companies have traditionally had little interest in clinical diagnostics. The province of most of these companies had always been high-margin, one-size-fits-all therapeutics (drugs and biologics). The high costs associated with developing drugs, executing clinical trials, and obtaining regulatory approvals makes pharmaceuticals a risky business. Success required a high degree of focus on relatively few products. The complexities of the diagnostic business—the need to sell instrument platforms, service contracts, buffer solutions, and disposable cuvettes in addition to hundreds of chemistry, immunoassay, coagulation, hematology, and microbiology tests—just did not seem like a very attractive business. Superimpose the relatively low margins associated with diagnostics, at least compared with therapeutics, and it becomes easy to understand why most pharmaceutical companies have not been interested.

The pharmaceutical business has changed. In many respects, the industry is a victim of its past success. Inexpensive generic versions of innovative drugs that have come off patent are available for many of the maladies that can be treated by the one-size-fits-all approach. The unmet medical needs must now be addressed by specialty pharmaceuticals. Fortunately, the industry is armed with new tools that can help it fill these needs. The Human Genome Project has facilitated discovery of new drug targets: enzymes, signaling proteins, and receptors that play an important role in the pathogenesis of various diseases.
Perhaps the greatest impact has been in the area of oncology. Compared with many other therapeutic areas, progress in the development of anti-cancer drugs historically has been rather poor. More recently, cancer biologists have made great progress in elucidating what makes a cancer cell a cancer cell. Overexpression of receptors such as human epidermal growth factor receptor 2 (HER2), activating mutations of receptors such as epidermal growth factor receptor (EGFR), and activating mutations of signaling proteins such as KRAS are a few of the more well-known mechanisms by which cell replication becomes uncontrolled. The advances in cancer biology at the basic science level have created a paradigm shift in cancer therapeutics. It is no longer possible to view non-small cell lung carcinoma (NSCLC), for example, as a single disease that can be treated with a single one-size-fits-all drug. The therapeutic approach to treating NSCLC differs greatly depending on whether the tumor cells harbor the EGFR mutation, the KRAS mutation, or neither. This explains why the one-size-fits-all approach has produced such little progress in oncology. It also explains why diagnostics that stratify diseases such as NSCLC are becoming essential for treatment. And it further explains pharmaceutical companies’ newfound interest in diagnostics, especially in the area of oncology.

An in vitro diagnostic (IVD) test that is essential for safe and effective use of a therapeutic is considered to be a companion diagnostic by the U.S. Food and Drug Administration (FDA). Generally, FDA approval of the therapeutic drug or biologic is contingent on simultaneous approval of the companion diagnostic. So far, all FDA-approved companion diagnostics are for oncology therapeutics: each identifies a subset of tumors likely to respond to a particular therapeutic. However, FDA has made it clear that therapeutics outside the realm of oncology may also require companion diagnostics. A companion diagnostic may be necessary either to individualize dose, to monitor response, to identify patients likely to have untoward effects, or to predict response to therapy. Many regulatory agencies outside of the United States have become equally interested in the role of diagnostics for ensuring the safe and effective use of therapeutics and are taking steps to regulate companion diagnostics appropriately.

**Practicing Diagnostics**

Physicians, particularly those practicing in academic medical centers, are not, of course, waiting for pharmaceutical companies to translate advances in basic sciences into clinical practice. Hence the field of “personalized medicine” has emerged. Clinical laboratories have developed a plethora of tests designed to help physicians choose the right therapy for the right patient at the right time. This signifies an important trend for pharmaceutical companies: diagnostic tests drive the choice of therapeutics. Physicians are no longer willing to employ a trial-and-error approach. The commercially
successful therapeutic of the future is likely to have a companion diagnostic that identifies patients who are likely to benefit from that therapeutic.

Thus, basic science, regulatory agencies, and the marketplace have sparked a keen interest in diagnostics by pharmaceutical companies. This interest does not, however, translate into a rush by pharmaceutical companies to diversify and to get into the diagnostics business. Pharmaceutical companies still see diagnostics as a very complex, relatively low-margin business that falls outside their core competencies. In fact, the diagnostics business is so complex that it is probably not practical even for the largest of pharmaceutical companies to internally develop all of its companion diagnostics. The technologies used in clinical diagnostics are so diverse—they include immunohistochemistry (IHC), in situ hybridization (ISH), gene mutation tests, RNA-based gene expression profiles, and proteomics—that none of the existing diagnostics companies offer all of these technologies. Thus, most pharmaceutical companies seem to be pursuing a strategy of developing partnerships with diagnostics companies.

Novartis is the outlier. It formed a molecular diagnostics unit a few years ago, although more recently the company merged its diagnostics business into its oncology franchise. Roche remains a major player in both the pharmaceutical and diagnostics industries. Bayer, on the other hand, sold its diagnostics business to Siemens a few years ago, and Abbott plans to spin off its pharmaceutical division but keep its diagnostics businesses. Most big pharmaceutical companies—Bristol-Myers Squibb, Glaxo SmithKline, Merck, and Pfizer, to name a few—appear to be employing the partnership strategy.

This is certainly not a novel approach. Dako developed and commercialized the first-ever companion diagnostic, Herceptest, an IHC test for HER2, as a requisite step for Genentech (now part of Roche) to obtain FDA approval for Herceptin (trastuzumab). Dako subsequently developed IHC tests for EGFR overexpression as a companion diagnostic for ImClone's cetuximab (Erbitux) and for c-KIT overexpression as a companion diagnostic for Novartis' imatinib (Gleevec). More recently, Abbott Molecular developed a fluorescent in situ hybridization (FISH) test for the ALK gene rearrangement as a companion diagnostic for Pfizer's crizotinib (Xalkori), and Qiagen developed a KRAS mutation test as a second companion diagnostic for cetuximab. Herceptest has also become a companion diagnostic for Pfizer's crizotinib (Xalkori), and Qiagen developed a fluorescent in situ hybridization (FISH) test for the ALK gene rearrangement as a companion diagnostic for Pfizer's crizotinib (Xalkori), and Qiagen developed a KRAS mutation test as a second companion diagnostic for cetuximab. Herceptest has also become a companion diagnostic for Pfizer's crizotinib (Xalkori), and Qiagen developed a fluorescent in situ hybridization (FISH) test for the ALK gene rearrangement as a companion diagnostic for Genentech's pertuzumab (Perjeta). Roche began developing the BRAF V600E mutation test as a companion diagnostic for Genentech's vemurafenib (Zelboraf) before acquiring the company.

**Getting Down to Business**

Diagnostics companies are experiencing a renaissance of sorts, but they still face a challenging business model that justifies the reluctance of the pharmaceutical industry to diversify into this area. Developing a companion diagnostic is a very expensive and very risky endeavor. The expense of development stems from two factors. First, FDA sees companion diagnostics, for the most part, as high-risk medical devices, and thus subjects these devices to the highest level of premarket review and post-market controls. Second, many companion diagnostics employ the newest and most demanding technologies. Superimposed on this high development cost, a companion diagnostic is anything but a sure thing. If the therapeutic goes bust, so does the diagnostic. Even if the diagnostic makes it to market, it is difficult, if not impossible, for a diagnostics company to recover development costs. One or two thousand dollars might seem pricey compared with most other diagnostic tests (especially to a payer), but it may not be enough for a diagnostics company to recover development costs. Compounding the problem is the fact that a diagnostics company cannot expect market exclusivity for the companion diagnostic test it develops because patent protection for the analyte is either lacking or virtually impossible to enforce. Even if there is rapid market uptake of both the therapeutic and diagnostic tests, the diagnostic company is likely to see rapid market and price erosion as less expensive laboratory-developed tests (LDTs) appear.

It might seem like the economics of companion diagnostics simply do not work, but this is true in many areas of health care. The solution to this dilemma—as is always the case in medical economics—is cost shifting. The pharmaceutical company typically pays the development costs for the diagnostics company. The pharmaceutical company must then recover the development costs for the diagnostic along with its own development costs for the therapeutic. These must all be built into the margin of the therapeutic, much to the dismay of pharmaceutical companies.

**Regarding Regulations**

FDA is not concerned with the economic dilemma created by diagnostic-pharmaceutical partnerships. The agency is, however, quite concerned about clinical laboratories substituting their own LDTs for FDA-approved companion diagnostic tests. This concern, along with the proliferation of other tests that purport to help physicians choose the right therapeutic for the right patient at the right time, ranks high among the many reasons why FDA feels the need to regulate LDTs (also known as "home brew" tests). Whereas most tests performed by clinical laboratories in the United States are manufactured and sold as complete kits by diagnostics companies and subject to FDA regulation, an LDT is developed in-house by a clinical laboratory for its own use. Whereas the laboratories are regulated under federal law by the Clinical Laboratories Improvement Amendments of 1988 (CLIA), individual tests—including LDTs—are subject to the Medical Device Amendment to the Food, Drug, and Cosmetic Act—at least according to FDA. The key question is whether or not an LDT is interchangeable with an FDA-approved companion diagnostic test. FDA contends that CLIA lacks the necessary premarket review and ongoing post-market controls to ensure that an LDT is interchangeable with an FDA-approved test. Thus, FDA intends to regulate LDTs, and implementation is likely to begin with companion diagnostics and other areas of personalized medicine.

Whether FDA really has the authority to regulate LDTs is a matter of considerable debate and controversy. However, FDA’s authority to regulate drugs and biologics is without question. This regulatory authority means that FDA ultimately decides what goes into the label of the therapeutic. When FDA decides that safe and effective use of the therapeutic requires a companion diagnostic,
the labeled indication for the drug will specify the use of an “FDA-approved test.” This implies that a physician who prescribes the therapeutic based on something other than the FDA-approved companion diagnostic (or no test at all, for that matter) is technically using that therapeutic off-label. FDA does not regulate medical practice, and physicians have every right to use a drug or biologic off-label. However, payers, particularly Medicare and Medicaid, may choose not to reimburse for off-label use, or may demand repayment from providers for reimbursed services that were represented as on-label. Off-label use can also become tasty fodder for malpractice attorneys. So far, these issues are only theoretical, but the threats to physicians and laboratories are there.

Sustaining Interest

With all of the complexity, business challenges, and controversies that come along with co-development of companion diagnostics, is there enough of a business case to sustain the pharmaceutical industry’s interest in diagnostics? From a pure business perspective, does it make sense for a pharmaceutical company to limit its potential market to a subset of patients? Yes, it does. Sometimes segmenting a market can be a very successful strategy, as the following simple, hypothetical example demonstrates.

Consider a situation in which there are three drugs (A, B, and C) for a particular oncology indication. Approximately 20 percent of tumors respond to each drug, and the toxicity is similar for all three drugs. Drug C is the newcomer to the market. Drug C can expect to achieve a market share of approximately 33 percent at best. In reality, as the third drug for the indication, Drug C will probably get a much lower market share. Oncologists tend to stick with familiar drugs unless there is good reason to switch. Further suppose that approximately 50 percent of tumors overexpress a particular membrane receptor, and that 35 percent of these tumors respond to Drug C. In a logical world, Drug C should get 50 percent market share; i.e., oncologists should use Drug C for all tumors that overexpress the membrane receptor. In the real world, Drug C probably will not do this well, but the point is that the best-case market share for Drug C is higher (50 percent) if the indication is limited to overexpressing tumors than if it is for all tumors (33 percent).

Trastuzumab is a market success, and probably is still the best example of how it makes sense for a pharmaceutical company to narrow its potential market with a companion diagnostic. On the flip side, gefitinib is an extreme example of what can happen when a pharmaceutical company fails to take this approach. Gefitinib is a tyrosine kinase inhibitor “with clear activity against a proportion of lung cancers with genomic anomalies of the EGFR.” However, U.S. approval of the drug was withdrawn because AstraZeneca failed to confirm clinical benefit of the drug. Many experts believe that a companion diagnostic for EGFR mutations to identify the subpopulation of patients likely to benefit from gefitinib would have saved U.S. approval.

Panitumumab (Vectibix from Amgen) is a less extreme example of how the lack of a companion diagnostic (and a wider potential market) can hurt commercial success. Panitumumab is unlikely to be effective in tumors harboring KRAS mutations, yet it was developed without a companion diagnostic to exclude patients with such tumors. FDA approved this therapeutic, but the observed efficacy rate was lower than it would have been with a companion diagnostic. This probably reduced the overall commercial revenues for this therapeutic, since efficacy observed during premarket clinical trials is a main driver of price. Similarly, premarket co-development of a KRAS companion diagnostic (as opposed to the post-market development mentioned above) probably also would have enhanced the commercial success of cetuximab.

Will the interest in diagnostics by pharmaceutical companies be sustained? Or is it just a passing fad? It all depends on whether the science pans out. If patient care can be improved by pairing targeted therapeutics with companion diagnostics, diagnostics will become an integral component of pharmaceutical development.

References


Dr. Kenneth Emancipator, MD, FASCP, is Director of Companion Diagnostics at Merck Research Laboratories and a Member-at-Large of the ASCP Board of Directors.
Ellen V. Sigal, PhD, is the chairperson and founder of Washington, D.C.-based Friends of Cancer Research (Friends). She has worked with federal health agencies, congressional leadership, academic research institutions, and private sector industry to bring safe treatments to cancer patients.

On Sept. 14, 2012, Friends co-sponsored a conference on drug and diagnostic co-development, which included voices that spanned the research enterprise, among them drug and device officials from the the Food and Drug Administration (FDA), industry representatives, and patient advocates. The forum added to the momentum created by the 2011 draft guidance from FDA on the basics of developing targeted therapies with companion diagnostics.

“It’s not about altering standards,” Dr. Sigal notes, “but rather about examining different approaches for successful drug and diagnostic co-development.” Here, Dr. Sigal talks with Critical Values about the increasing interest in developing companion diagnostics, and the effect it may have on patients.

Critical Values: Health care is becoming more personalized, based on an individual patient’s needs. But simultaneously, health insurance is moving toward universal cover-
age. How can these ideas work in concert? Can we afford to do personalized medicine if our end goal is for the greater good?

Ellen Sigal: In addition to the goal of the Affordable Care Act, which takes significant steps to provide increased access to care, there is the need in tandem to better understand which interventions can produce the best outcomes for the individual. Personalized medicine suggests that a subset of the population has been shown to experience greater benefit from a particular treatment, and that they can be identified in advance of receiving the therapy. This actually results in a cost-optimization of services by tailoring treatment options, which also can reduce the use of treatments that are unlikely to work for certain individuals. Additionally, the question of “Are we spending more?” doesn’t take into account the clear benefits of significantly improving the lives of patients.

CV: There is a concern that by getting into companion diagnostics, drug companies would shrink their margins. Are there benefits—for patients and companies alike—of the pharmaceutical industry working to develop companion diagnostics?

ES: For diseases like cancer, where new drugs are being developed that differentiate the cancerous cells from the normal ones, [shrinking margins] seem to be inevitable. The challenge is that not all cancers are driven by the same cellular malfunctions. If that were the case, one drug would have the potential of working for all patients. Looking at this purely from an economic standpoint, it is true that the sheer number of patients could be quite small compared to all individuals with a particular disease in this model. However, if the drug is capable of shifting treatment of the disease to more of a chronic condition, this was the experience with Gleevec for chronic myelogenous leukemia. The disease occurs in a relatively small population, but the drug is taken for extensive periods of time and has been shown to be a profitable investment financially. And it revolutionized how a once deadly disease is managed. Furthermore, if the population is enriched with those patients highly likely to respond, the effect size observed will be larger. This could allow for smaller and shorter trials and enable a drug to get onto the market sooner and have a longer exclusivity period to recoup the initial investment. The economic models are slightly different than with traditional drug development, but this is the direction that science is heading, so new models are needed.

CV: The Food and Drug Administration Safety and Innovation Act (FDASIA) of 2012 established a Breakthrough Therapy designation that expedites the development and review of drugs for serious and life-threatening diseases that show major improvement in Phase 1 or Phase 2 trials. Will this designation have any effect on the development of companion diagnostics?

ES: The Breakthrough Therapy designation established under FDASIA could have a positive impact on drugs with companion diagnostics. As Friends of Cancer Research developed the concept of the Breakthrough Therapy designation, we conducted a retrospective review of drugs that may have qualified for such a designation had it previously existed. That assessment revealed multiple potential breakthrough drugs that had a companion diagnostic. Presumably, with a companion diagnostic, the selected population is likely to be high responders and substantial clinical activity can be detected earlier. One hallmark of the Breakthrough designation is the use of multidisciplinary review teams. FDA is signaling that when unprecedented effects are seen early, they want to meet with the sponsor sooner to collaborate on the future development plan of the drug—and this can include early coordination with the device center at FDA.

CV: Are there any ethical pitfalls inherent in the advanced, molecular-based screening methods?

ES: Strong public policy has been enacted to help safeguard against potential misuse of genetic information. The Genetic Information Nondiscrimination Act of 2008 prohibits discrimination in healthcare coverage or employment on the basis of genetic information. To further strengthen this, the Affordable Care Act requires insurance companies to offer the same premium to all applicants of the same age and geographical location without regard to pre-existing conditions. Still, with these policies, challenges exist to widespread molecular screening. Advancing technologies may help address these challenges in the future. For example, new common platforms are beginning to alleviate some logistical challenges of testing a single biopsy for multiple different markers that could influence treatment decisions. It remains to be seen how rapidly these types of technologies will be adopted into routine clinical practice and to what extent insurers will pay for such an approach.

CV: In your role as advocate for the cancer patient, what are the other benefits of the new cancer diagnostics?

ES: A patient’s diagnosis with cancer is an overwhelming experience filled with seemingly endless questions. But what patients value most is knowing what treatment option will provide the best chance to improve their life. Developing new diagnostics to help understand which patients should receive which treatments is playing a promising role in directly linking complex science to clinical decisions. We have a long way to go toward improving health care in this country, but as I see how exciting discoveries are ultimately improving patients’ lives, it provides great hope that we are on the right path to improving healthcare decisions, delivery, and efficacy.

Ms. Strzelecki is Senior Editor of Critical Values.
A decade ago, the register of the top 15 selling drugs was the pharmaceutical industry’s equivalent of the Hollywood A-list: if your product was on it, then you were raking in at least $1 billion in sales for your blockbuster drug. But a look at today’s top 15 list reveals the slots are not filled only by the likes of Lipitor or Cymbalta, which tout multibillion-dollar sales to the masses, but also by biologics such as Herceptin and Gleevec, which, while still quite profitable, have a much smaller prescription population.

These biologics, along with their growing number of companion diagnostics, says Joshua Cohen, PhD, a senior research fellow of Health Economics at Tufts University in Boston, are proving that the traditional blockbuster drug definition is changing, and fast.

“The blockbuster model has changed in a qualitative way,” Dr. Cohen explains. “We’re no longer seeing Lipitors and Claritins as much as we used to. Instead we’re seeing specialized pharmaceuticals targeting relatively small populations that cost more money per patient.”

As pharmaceutical companies move into an era of personalized medicine, markets will become increasingly more segmented. As a result, pharmaceutical companies are taking a more active role in developing companion diagnostics for targeted therapeutics to push their profitability. They’re looking for the win-win situation, Dr. Cohen says, where the outcomes for a smaller population are much better, and therefore the drug’s cost-effectiveness numbers are improved.

“It’s the scenario where the pharmaceutical companies believe there’s a lot of market uptake potential,” Dr. Cohen notes, “especially if you can co-develop therapeutics and diagnostics.” Although few companion diagnostics currently on the market can claim true co-development—having been developed simultaneously with the therapeutic, from
Phase 1 testing on up—a recent study by Cohen’s colleague Christopher Milne, DVM, MPH, JD, director of research at the Tufts Center for the Study of Drug Development, found that many pharmaceutical companies are investing heavily in pharmacogenomics.

“Personalized medicine has a lot to offer, but the science of it is difficult,” Dr. Cohen says. “With so much investment going on there will be more co-developed therapies and diagnostics.” And co-developed combinations are already starting to crop up. In 2011, two drugs and their companion diagnostics were approved. The first was Zelboraf (vemurafenib), a treatment for melanoma, and its companion diagnostic cobas 4800 BRAF V600 Mutation Test, which helps determine if a patient’s melanoma cells have the BRAF V600E mutation. The second was Xalkori (crizotinib), a treatment for non-small cell lung cancer, and its companion diagnostic, Vysis ALK Break Apart FISH Probe Kit, which can determine if a patient has the abnormal ALK gene. Dr. Cohen adds that going forward it is possible the industry could start to see two to three drug/diagnostic combinations approved by the Food and Drug Administration each year.

The current picture looks a little different. The majority of the companion diagnostics on the market today were developed, as Dr. Cohen says, “post hoc,” or after the drug was already on the market. These post-hoc companion diagnostics are also a boon for the pharmaceutical industry.

“If the companion diagnostic is stratifying the populations right way, but it was developed 10 years after the drug was approved, it can be a renaissance for these drugs,” Dr. Cohen says. “That’s where companion diagnostics have a huge future, because we’re finding more and more biomarkers, and therefore whoever is making the diagnostic has a very good value proposition if they can prove that by using their diagnostic they’re going to save the payer a lot of money, and they’re also going to improve outcomes. It’s an area where there is a lot of upside.”

Knock and the Door Will Open

As development continues, many of the companion diagnostics that will hit the marketplace will come through a cancer entry point. While there is research and development being done in other areas, including cardiovascular
disease, diabetes, and depression, the longstanding interest in oncology and the search for biomarkers to stratify populations into positive and negative responders to therapeutics have put cancer in a particularly advantageous position for developing companion diagnostics, Dr. Cohen says.

“Biomarkers are not exclusively the domain or terrain of oncology,” Dr. Cohen says. “In other areas, they know about linkages and associations, but they are statistical associations, and there is no causation, or at least none that they can find yet. They know the causation with oncology.”

Cancer also makes a wise entry point for new companion diagnostics thanks to the high rate of reimbursement for cancer therapeutics.

“The binary choice—Do we cover [cancer drugs] or not?—is not really a choice in the United States,” Dr. Cohen explains. “Almost all drugs are covered by almost all payers. When they’re not covered, it’s usually because of a regulatory issue or safety issue, not a cost or even an effectiveness issue.”

He notes that while the majority of companion diagnostics are also reimbursed, the system for reimbursing them is essentially outdated. Temporary reimbursement codes are in place, but these lack the level of specificity necessary for diagnostics manufacturers to feel they are being reimbursed at prices that reflect the current reality. To date, the guidelines for reimbursement are under revision, and new protocols are being developed by Medicare for companion diagnostics.

“Companion diagnostics are a qualitatively different kind of diagnostic—to be used in conjunction with a therapy, both of which can be very expensive,” Dr. Cohen says. “But there is a lot to gain from knowledge about a patient to whom you’re going to prescribe a very expensive drug. If you have a drug that will target a specific tumor, and you have a test that will target the right patient type, that’s the win–win, and that’s what they’re trying to do in Washington: Update the diagnostic’s coding to reflect that.”

Additionally, a diagnostic that is properly stratifying populations can help drive down the overall cost of care for patients by adding an improved value proposition. Dr. Cohen points to Gleevec and Herceptin, two popular cancer therapeutics that each have well-tested and highly beneficial companion diagnostics. “A drug’s conditions of reimbursement can be lowered, and the cost sharing can be lowered if indeed you find a diagnostic that is pointing out those who will benefit from the drug,” Dr. Cohen explained. “The patient doesn’t have to be subjected to conditions of reimbursement like prior authorization or step edits because we know it’s a cost-effective solution.”

**Regulations Follow Suit**

Reimbursement codes aren’t the only thing that needs updating. FDA is also updating its protocols for the development of companion diagnostics. Recognizing their value, FDA released a draft guidance in 2011 outlining the new pathways for developing therapeutics and diagnostics. The agency, Dr. Cohen notes, recognizes the issues involved in development—such as when can something be called a companion diagnostic, or what if it’s developed 20 years after the original drug—and addresses those concerns in the revised protocols.

The blockbusters of the pharmaceutical industry are changing, and the development of companion diagnostics, particularly for cancer, is pushing that change. The conventions that were in place are falling away as the combination of therapeutics and diagnostics proves to be not only beneficial for patients but also for the companies that manufacture them.

“There was a fear 15 years ago that the industry shouldn’t steer away from the blockbuster model because they’d be left with mini-blockbusters that cost just as much to develop as a regular drug,” Dr. Cohen says. “But looking at the top drug list today, who would have thought 15 years ago Herceptin would be on that list? So the fear isn’t entirely founded.

“Providers and patients aren’t dumb. They’re taking these drugs because they work, and therefore, these drugs are blockbusters, too.”

**Additional resources:**


Ms. Strzelecki is Senior Editor of *Critical Values*. 
2012 ASCP Annual Meeting Sizzles with Energy and Advocacy

More than 1,300 guests from around the world were inspired by illuminating keynote speakers, a 15-year-old scientific genius, and groundbreaking discoveries at the 2012 ASCP Annual Meeting, Oct. 31–Nov. 3, in Boston.

The energy and excitement at the 2012 ASCP Annual Meeting was palpable, as attendees heard poignant and personal stories shared by distinguished speakers—all of them agents of change and advocates for access to quality health care globally. Actress and global healthcare advocate Ashley Judd captivated her audience when she spoke about her humanitarian work as a global ambassador for YouthAIDS, traveling to countries including Kenya, Rwanda, and Cambodia. Witnessing firsthand the impact of deprivation and illness has propelled her to advocate for social change and to promote awareness of the need for improved health care.

In a conversation with ASCP Executive Vice President Dr. Blair Holladay, former First Lady Laura W. Bush emphasized the importance of raising awareness of women's health issues around the world, particularly for breast and cervical cancer and heart disease. Since the launch of Pink Ribbon Red Ribbon for breast and cervical cancer prevention and early detection, she has promoted efforts to include cervical cancer testing and treatment for women receiving antiviral drugs for AIDS through the President's Emergency Plan for AIDS Relief.

Celebrity couple Giuliana and Bill Rancic spoke about the important role that their pathologist played when Giuliana was diagnosed with early stage breast cancer. The pathologist, they said, acted in a consultative role that helped the couple determine what treatment to pursue. The couple urged women to be proactive about their own health.

Dr. Donald M. Berwick, former Administrator of the Centers for Medicare and Medicaid Services, shared his professional experiences of health care as a pediatrician, which reinforced his commitment to improve inefficiencies and reduce high costs. He said ASCP is uniquely positioned to take a leadership role in the implementation of healthcare reform in the United States.

The collective message of these diverse speakers was clear, says Lee Hilborne, MD, FASCP, DLM[ASCP]SM, “The laboratory community has been traditionally inward focused, and we’ve started to look outside of ourselves and acknowledge that we are part of a much bigger world,” he says. “It’s important for us if we are going to have the greatest impact on health care, domestically and internationally. We heard that from Ashley Judd, Laura Bush, and the Rancics. Don Berwick emphasized that health care is changing, and what we’re doing and the way we’re doing it is not sustainable.

“For us to be relevant, we need to think very differently. It’s really very exciting.”

Excitement permeated other activities at the Annual Meeting as well. Fifteen-year-old scientific whiz kid Jack Andraka, winner of the $75,000 grand prize at the 2012 Intel Science and Engineering Fair, mesmerized his audiences—from high school students to pathologists and laboratory professionals—as he described his remarkable discovery of a method for early detection of pancreatic cancer. He proudly announced that he would like to become a pathologist.

Overall, the 2012 ASCP Annual Meeting generated 420 news articles and broadcast segments that reached more than 45 million people. ASCP member Sujatha Balija, MD, FASCP, made the news when she went to extraordinary lengths to travel from Philadelphia to Boston, where she was scheduled to present a course at the ASCP Annual Meeting. When her flight was canceled, she took a $750 taxi ride to Boston, landing her in the Boston Globe and on the news of ABC-TV’s Boston affiliate station.

ASCP and Society for Hematopathology Announce Collaboration

At the 2012 ASCP Annual Meeting, 2011–2012 ASCP President C. Bruce Alexander, MD, FASCP, emphasized the importance of collaboration as one of the Society’s core values. He announced that ASCP and the Society for Hematopathology have signed a Memorandum of Understanding (MOU), effective in January 2013, which will enhance education initiatives, membership services, and advocacy to benefit the members of both Societies.

This partnership will strengthen both Societies’ shared missions of interdisciplinary education, scientific discovery, and advocacy; leverage their respective resources and membership benefits; and create administrative efficiencies while allowing each Society to maintain its own identity and governance, he said. ASCP will provide concierge staff support to the Society for Hematopathology leadership, conduct membership campaigns, and coordinate member communications and meetings. Beginning in 2015, the Society for Hematopathology’s biennial hematology workshop will be held in tandem with the ASCP Annual Meeting.

As the ASCP Annual Meeting came to a close, the Society welcomed 2012–2013 ASCP President Joel M. Shilling, MD, FASCP, President-Elect Steven H. Kroft, MD, FASCP, and new Board members, and expressed its gratitude for Dr. Alexander’s leadership and service over the past year. Fifteen pathologists and laboratory professionals were also honored for their extraordinary contributions to their profession and the Society.

Save the dates of Sept. 18–21 for the 2013 ASCP Annual Meeting in Chicago!
Displaying poise and intelligence, former First Lady Laura W. Bush discussed her advocacy for patients globally through the Pink Ribbon Red Ribbon program for the prevention and early detection of breast and cervical cancer with Dr. Blair Holladay, Executive Vice President at ASCP.

Celebrity couple Bill and Giuliana Rancic (left and center) spoke about the pivotal role their pathologist played when Giuliana was diagnosed with early stage breast cancer. After the couple’s presentation, ASCP emcee Jennifer Lopez (right) asked them a few questions.

Fifteen-year-old Jack Andraka captured the hearts and minds of his audiences in describing his invention of an early detection method for pancreatic cancer.

Dr. Donald M. Berwick presented a persuasive case for pathologists and laboratory professionals to implement innovations in their practices locally to achieve better results.
Displaying poise and intelligence, former First Lady Laura W. Bush discussed her advocacy for patients globally through the Pink Ribbon Red Ribbon program for the prevention and early detection of breast and cervical cancer with Dr. Blair Holladay, Executive Vice President at ASCP.

The grand opening of the ASCP Exhibit Hall took place immediately following Ashley Judd’s Keynote session.

One hundred sophomores from the Edward M. Kennedy Academy for Health Careers were impressed with the demonstrations by several ASCP Career Ambassadors.

ASCP Resident Chair Dr. Evelyn Bruner (center) presented Resident Representative Leadership Awards to Dr. Feriyl Bhaijee (left) and Dr. Rebecca Sonu (right).

2011–2012 ASCP President Dr. Bruce Alexander presented Keynote Speaker Ashley Judd with the 2012 ASCP Humanitarian Award for Global Health. Ms. Judd related how her work as a global humanitarian since 2006 has changed and expanded her empathy for humanity and enriched her life.

The grand opening of the ASCP Exhibit Hall took place immediately following Ashley Judd’s Keynote session.

Jeff Jacobs, Senior Vice President at ASCP, presented Ms. Bush with the ASCP Patients’ Advocate Award for her work as an exemplary global health advocate.

2011–2012 ASCP President Dr. Alexander (right) introduced 2012–2013 ASCP President Dr. Joel Shilling (left) during the transition of the presidency.
My New Year’s Resolutions for 2013

1. Keep my practice on the cutting-edge – earn CE and stay up-to-date on what’s next for pathology and laboratory medicine.

2. Meet more colleagues – attend face-to-face ASCP gatherings.

3. Make a difference – explore ASCP volunteer opportunities to make an impact outside my own lab.

New Year. New You. New ASCP.

Go to ascp.org/renew to join 100,000 of your peers committed to improving patient outcomes.