Digital Pathology: Gateway to Personalized Medicine

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Disclosures

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Whenever science makes a discovery, the devil grabs it while the angels are debating the best way to use it.

~Alan Valentine
Digital Pathology : 
Gateway to Personalized Medicine

- The media is filled with reports that personalized medicine will revolutionize the practice of medicine and that genomics may replace traditional diagnostic pathology and cytology.

- The real promise in personalized medicine will have as its foundation tools, digital pathology and image analysis.

- Genotype and phenotype are not the same. The “gold standard” of disease is based on over 100 years of tissue-based study.

- Specific biomarkers and image analysis has added new methods that leverage the information we have gained from the tissue.

- The role of well-documented biobanks in research also ensures a renewed focus on the value of traditional histological specimens.

- To obtain new information “opening the window” into the tissue itself, will require the power of image analysis of digitized tissue.
Now the Question is Why and Why Now?

- Advances in technology
- Advances in scientific knowledge
- Increasing complexity of analysis
- Desire to connect drug development to specific patient and specific patient's medical problem
- Desire and/or belief can improve outcomes and lower costs of healthcare
- Analog images must transition to digital
Digital Pathology Will Usher in a New Era of Personalized Medicine

5 comments | June 14, 2010 | includes: AFFY, AMGN, AZN, BIO, CVD, DQX, GENZ, GHDX, ILMN, LH, LLY, MYRX, QGEN, RHHBY, FK, SQNM

The Human Genome Project (HGP) was a 13-year project coordinated by the U.S. Department of Energy and the National Institutes of Health in cooperation with genetic bio-sciences giants Celera Genomics (CRA), Incyte (NCY), and Human Genome Sciences (HGS1). The Human Genome Project aimed to tell us what the sequence of the average person's genetic code is "supposed" to be, and gave the necessary information for publicly funded research as well as for-profit research to begin understanding how the differences between individual DNA affect health and disease. Indeed, this information gave rise to the concept of "personalized medicine", which seeks to use precise genetic information about individual patients to customize their mode of therapy for a disease. This concept of personalized medicine has fueled the growth of multi-billion dollar companies like Myriad Genetics (MYGN), Sequenom (SQNM), Illumina (ILMN), and Affymetrix (AFFY).

We have been hearing about the promise of "personalized medicine" for over a decade now, but what has come of it? It has long been predicted that diagnostics based on genetic information brought forward by the human genome project would bring more targeted and cost-effective therapies. However, to date, almost 20 years later, there are only a few examples that have come to fruition. In general, large pharma has been slow to implement useful companion tools to apply the concept of personalized medicine to their clinical drugs. The idea seems simple:
Digital Pathology and Biomarkers Help Pave the Way to Personalized Medicine

Advances in biomarker technology are aiding researchers in identifying the right treatments for the right patient.

Posted on 01 January 2010 by Christopher Ung, VP, Strategic Business & Operations, Oncology, Quintiles

The biopharmaceutical industry is adapting to shrinking pipelines, increased market access barriers, significant financial strains and advances in technology. Companies must employ certain tools to bring life-saving medicines to market sooner and remain competitive in the rapidly changing arena of drug development.

 Among the technological advances that can shorten drug development...
“Digital Pathology is a bridge to improved patient care in era of Personalized Medicine”

LIS Vendor 2010
Patients Want More Pathology Information

Breastcancer.org launches its first-ever mobile app
September 22, 2010 | Diana Manos, Senior Editor

ARDMORE, PA — The nonprofit Breastcancer.org has launched its first-ever iPhone application for breast cancer patients, allowing them to receive customized research news based on their diagnosis.

The Breast Cancer Diagnosis Guide is a free mobile app that walks users through the breast cancer pathology report -- a vital report that sets the patient's treatment path.

In addition to educating users on the terms in their pathology report and other tests, Breastcancer.org's Breast Cancer Diagnosis Guide allows them to input their own pathology report results so they can receive research news, information, and articles specific to their diagnosis.

"This is truly groundbreaking," said Marisa Weiss, MD, director of breast radiation oncology at Lankenau Hospital and president and founder of Breastcancer.org. "There is no 'one size fits all' treatment plan. A breast cancer patient's pathology report helps each patient customize her treatment course to the exact nature and extent of her specific cancer diagnosis ... from deciding on what kind of surgery to evaluating the role of radiation, chemotherapy, hormonal, and targeted therapies, and potential participation in clinical trials."

"What's particularly exciting about the Breastcancer.org Breast Cancer Diagnosis Guide is that it takes the understanding a step further by allowing patients to get background information and research news that is directly relevant to her particular diagnosis and situation," Weiss said. "This is profoundly important as..."
Factoid

Dr. W. W. Mayo, the founder of the Mayo Clinic and the father of the 'Mayo Brothers', needed a microscope for his medical practice. At a cost of $600 (in the early 1900's) would mean he and his wife would have to put a mortgage on their house to obtain the microscope. His wife decided the issue by saying if the microscope would help him give greater service to his patients, he should have it.

"The difficulty of securing the microscope and its value as an aid to the practice of medicine gave it unusual value in our eyes and, perhaps for that reason, Charles and I, even as children, became expert in its use."

~ Dr. William J. Mayo, 1930.
Digital Pathology – Revolution or Evolution

Today    Digital Pathology

- Advanced Visualization
- Digital Diagnostics
- Slide Sharing
Despite countless people (including royalty who paid tribute to early microscopists), the medical world, practicing clinicians, and academic physicians generally ignored or ridiculed them. The microscope was not appreciated as a useful scientific instrument by leaders in morbid anatomy such as Morgagni (1682-1771), John Hunter (1728-1793), and Mettew Baillie (1761-1823). The first atlas of pathology, written by Baillie and published in 1799, does not contain even one microscopic illustration among more than 100 engravings.

Clinical microscopy had a slow beginning; more than two centuries passed before the value of microscopes began to be appreciated by clinical and laboratory scientists.

In 1800, Bichat (1771-1802), a young pathologist, published a book in which, for the first time, morbid anatomic and histopathologic changes of various organs of the body were discussed and illustrated.
First illustration of the microscope in use for clinical examinations in medicine. 1686.

Fig. 1. This is the first illustration of the microscope in use for clinical examinations in medicine. The microscope designed by Joseph Campani of Bologna is standing on a table (in an enlarged form, left of the picture); and a hand-held microscope is shown in actual use to examine a wound on the leg of the recumbent patient. Note the woman who holds a candle and a mirror for optimal illumination. A second observer with a microscope (standing on the left) seems confused about whether he is using a microscope or a telescope. (Figure from page 372 of Acta Eruditorum, 1686, ref. [4]).

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He is an optician, daily having to deal with the microscope, telescope, and other inventions for sharpening our natural sight, thus enabling us mortals (as I once heard an eccentric put it) liberally to enlarge the field of our essential ignorance.

Herman Melville, *Inscription Epistolary to W.C.R.*
Why am I Confident that Pathologists Will Adopt Digital Pathology as One of Tools to Enable Us to be Personal with Precision Medicine?
Grind the Tumor and Put in Sequencer: Maybe it’s More Complicated?

DNA vs Protein

Same Genome – Different Proteome

Slide Thanks To Dr David Rimm
Morphologic Diversity in Ocular Melanoma Case Highlights Heterogeneity of Many Tumors

Conjunctival Melanoma with orbital invasion

Staghorn pattern
Signet-ring cells
Rosettoid pattern

MN Burnier, AN Odashiro, BF Fernandes. Conjunctival Melanoma with orbital invasion. Ocular Pathology Course, IAP meeting, Sao Paulo 2010
Morphologic Diversity

- Architecture
- Size & shape of cells
- Cytoplasmic features
- Vasculature

Conjunctiva & Orbital Melanoma
- May simulate other neoplasms
- Poorly differentiated carcinoma
- Fibrohistiocytoma
- Metastatic adenocarcinoma
- Neuroendocrine tumor

MN Burnier, AN Odashiro, BF Fernandes. Conjunctival Melanoma with orbital invasion. Ocular Pathology Course, IAP meeting, Sao Paulo 2010
Heterogeneity of Angiogenesis and Blood Vessel Maturation in Human Tumors: Implications for Antiangiogenic Tumor Therapies

Anne Eberhard, Sebastian Kahler, Valentin Goede, Bernhard Hemmerlein, Karl H. Plate, and Hellmut G. Augustin

Abstract

Microvessel density (MVD) counting techniques have been widely used to assess the vasculature in tumors. MVD counts assess the presence of blood vessels but do not give an indication of the degree of angiogenesis and the functional status of the tumor neovasculature. To analyze angiogenesis and the functional status of the tumor vascular bed, we have quantitated endothelial cell proliferation and the recruitment of pericytes in human tumors [glioblastomas (n = 30), renal cell carcinomas (n = 23), colon carcinomas (n = 18), mammary carcinomas (n = 24), lung carcinomas (n = 15), and prostate carcinomas (n = 19)]. These findings were compared to the physiological angiogenesis in the cyclic bovine ovarian corpus luteum. Tissue sections were examined applying double-labeling immunohistochemical techniques to detect proliferating endothelial cells and to localize endothelial cells and pericytes. The following parameters were quantitated: (a) MVD count; (b) proliferating endothelial index...
Pathologists are Writing the Prescriptions In this New Era of Personalized Medicine
Barriers to Adoption: Information Technology/ $$$ Justification / Regulatory/ Risk Management & Liability Issues/ Leadership Issues
With every tool, man is perfecting his own organs, whether motor or sensory, or is removing the limits to their functioning... by means of the microscope he overcomes the limits of visibility set by the structure of his retina.

~Sigmund Freud, Civilization and its Discontents, 1930.
Pfizer, Medco Team on 'Precision Medicine' Effort

October 26, 2011

Pfizer, Medco Team on 'Precision Medicine' Effort

By a GenomeWeb staff reporter

NEW YORK (GenomeWeb News) – Pfizer will collaborate with Medco Health Solutions and its United BioSource subsidiary in a research effort based on Pfizer's "precision medicine" approach, which integrates genomic and phenotypic information to help identify patients that may benefit from a new drug.

The partners aim to identify and evaluate patient subgroups in which both investigational and marketed drugs have been shown to be most effective. The firms, which have collaborated previously on product-specific programs, said that they are in the process of identifying collaborative opportunities to apply the precision medicine approach.

According to a statement issued by Pfizer after the close of the market Wednesday, the drivers of precision medicine include "a critical focus on human biology and pathogenic — or disease-causing — mechanisms; effective interpretation and application of genomic information about groups of patients with the same disease; the ability to identify unique information that emerges from patient studies to shed light on treatment responses; and new application of all of this knowledge to every stage of drug discovery and development."

Further details of the collaboration, which was announced at the TEDMED Conference in San Diego, were not disclosed.

Related Stories

- Cancer Research UK Close to Launching $28.5M Cancer Genetic Testing Program
  September 12, 2011 / GenomeWeb Daily News
- Medco, Sanofi Partner on PGx, Comparative Effectiveness
  June 23, 2011 / GenomeWeb Daily News
- Decode, Pfizer Collaborate on Sequence Variants for Lupus
Always walk through life as if you have something new to learn and you will. ‘ Fortune Cookie
Anton Leeuwenhoek was Dutch.
He sold pincushions, cloth, and such.
The waiting townsfolk fumed and fuzzed
As Anton's dry-goods gathered dust.

He worked, instead of tending store,
At grinding special lenses for
A microscope. Some of the things
He looked at were:

Mosquitoes' wings
The hairs of sheep, the legs of lice,
The skin of people, dogs, and mice;
Ox eyes, spiders' spinning gear,
Fishes' scales, a little smear
Of his own blood.

And best of all,
The unknown, busy, very small
Bugs that swim and bump and hop
Inside a simple water drop.

Impossible! Most Dutchmen said.
This Anton's crazy in the head.
We ought to ship him off to Spain.
He says he's seen a housefly's brain.
He says the water that we drink
Is full of bugs. He's mad, we think!

They called him dumkopf,
Which means dope.
That's how we got the microscope.