Tomorrow’s Treatments

Interview from Pictures of the Future, Spring 2007

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Ralph Weissleder M.D., PhD, is Professor of Radiology at the Harvard Medical School, and Director of the Center for Molecular Imaging Research at Massachusetts General Hospital in Boston. A leader in the emerging field of molecular imaging research, Weissleder has developed methods for detecting cancer cells using magnetic resonance imaging, positron emission tomography, and new, optical technologies.

Tomorrow's Treatments

What are the major trends behind advances in molecular medicine?
Weissleder: The primary trend is that as imaging and in vitro technologies improve, we will detect diseases earlier and ensure that they won't turn into something life threatening further down the line. Other major trends are that diagnostics and therapeutics will gradually be combined and that therapies will become less and less invasive. Much of this is in turn being driven by what we call systems biology. This is an emerging research field that aims at understanding how cells work together in complex environments.

In other words, analyzing the molecular mechanisms that drive them?
Weissleder: Yes. If you were a cancer researcher and you wanted to know what makes a cancer cell different from a normal cell, you would look at differences in molecules. But cancers are much more complex than that. Their constituent molecules change over time and are related to each other. So what systems biology attempts to do is to understand all of the 20,000 to 30,000 types of molecules related to a cancer cell — in other words, its entire physiology. By the way, this approach has implications for cardiovascular diseases, neurological conditions, degenerative diseases, autoimmune diseases, and of course cancers. The bottom line is that eventually this field will allow us to develop drugs much more efficiently.

What are the most promising fields of R&D in molecular medicine?
Weissleder: Nanotechnology and related imaging agents and diagnostic agents and sensors. Many new compounds and applications are in the pipeline. Optical imaging and sensing are also really hot because we can now do in vivo pathology. So, for example, we can now put a fiber optic line into a mouse colon, peritoneum or lungs, and get pathology-grade images without having to resect anything.

How does that work?
Weissleder: It functions essentially like a microscope at the tip of a fiber optic catheter. The device sees cells based on the application of a fluorescent imaging agent that differentiates cancer cells from normal cells. Such generic imaging agents bind to whatever makes a cancer cell different from a normal cell — things like growth factor receptors or signaling molecules on the cell surface. The good news is that these compounds already exist. The bad news is that it may take years for them to reach clinical practice.

A minute ago you mentioned the ability to do in vivo pathology. Will there eventually be probes that will be able to deliver the kind of information now available only with a biopsy?
Weissleder: Yes. In the future, an option will be to insert a needle into a cancer. The needle will have 20 or so multiplexed sensors on it. The sensors will be able to describe the molecular makeup of the cancer in terms of multiple channels. We've all heard of the lab-on-a-chip concept; but this is a lab-on-the-point-of-a-needle concept. The sensors will tell you things like whether the cancer will respond best to therapy X or Y.

What are you working on with Siemens?
Weissleder: One project is a data mining product called the Molecular Imaging Portal. It is a platform to archive, integrate, and ultimately make optimal use of experimental and clinical data, including gene expression data. We are also working on next-generation molecular markers for combined PET/CT imaging. On the MR side, we are working on refinements — in particular the detection of magnetic nanoparticles with improved spatial resolution and diagnostic sensitivity. One of the most exciting projects is a fluorescent probe that could be used in combination with an intraoperative imaging system that Siemens has developed. This could help surgeons to detect cancer cells that might otherwise be left behind. The probe is a molecule that is taken up exclusively by cancer cells. It appears to be generic and therefore does not need to be designed for a specific cancer cell type. Once the probe has been injected, it basically lights up any cancer cells. The surgeon then uses a handheld device that allows him to see the area of interest at a different wavelength, which shows any residual cancer cells. The resolution is close to a millimeter — good enough for brain surgery. It is still a year or two from clinical trials, but it's revolutionary.

What will molecular imaging and treatment look like by 2025?
Weissleder: Number one, we will be able to detect diseases much, much earlier than is possible today. For example, with Alzheimer's, we will be able to detect it when the first signs of memory loss occur, and be able to slow its progression. With type 1 diabetes, we will be able to detect it when the initial inflammation occurs and before loss of islet cells takes place. With cancers, we will be able to detect them when they are less than five millimeters — in other words when they are still curable. There will be a shift toward earlier detection and much more successful treatment. Number two, we will be able to tailor treatments to the patient. We will be able to determine if a given drug works for a given patient, and if so, at what dose level. Today, we do one size fits all. The capability to personalize treatment will result from a growing body of genetic and imaging knowledge. Tests will be developed to figure out whether a certain drug actually inhibits a certain target.

Will all of this add up to a healthcare revolution?
Weissleder: Over the last ten years we focused on the development of the technology that allows us to profile the entire genome. Now we need to create an atlas of what the genome looks like in different cohorts of patients and with different diseases — that's where our Molecular Imaging Portal fits in. And then we will have to figure out what all of it means clinically. But somewhere down the road we will see a healthcare revolution, and it will be characterized by early detection, personalized care, and some pretty amazing new treatments.

■ *Interview conducted by Arthur F. Pease.*

In Brief

■ The field of molecular medicine deals with health and disease on the cellular and molecular levels. It helps to improve diagnoses and treatments, while cutting healthcare costs at the same time. The three pillars of molecular medicine — in vitro and in vivo diagnostics, and knowledge-based IT — influence all stages of healthcare, from disease prevention and diagnosis to treatment and aftercare. Through the acquisition of Diagnostic Products Corporation and Bayer Diagnostics, Siemens has brought these three pillars of molecular medicine together under one roof, making it the first company in the world to offer integrated diagnostics. (p. 50, 54)

■ In vitro diagnostics: In the future, lab tests will increasingly rely on analyses of the human genome, making it possible to determine a person's genetic predisposition toward many diseases. Diseases could then be averted by treating patients with a customized disease-prevention programs. With the help of biomarkers, lab tests will, for example, discover cancers, infections and cardiovascular diseases at an early stage. In addition, biopsies may be replaced by "needle-tip labs" (p. 50, 54, 74).

■ In vivo diagnostics: New types of biomarkers, contrast agents, and ultra-high-field MR and MR-PET tomographs make it possible to detect initial changes in cell metabolism. It may be possible, for example, to identify and treat Alzheimer's years before any memory loss occurs. In addition, the effects of medications on the human body could be viewed in greater detail than is the case today, and treatment adapted accordingly. (p. 57, 65, 68, 74)

■ Knowledge-based IT: Among other things, Siemens' GeneSim platform is designed to help uncover key relationships in databases throughout the world. Examples include finding out which genes play a role in cancer and how they interact, thereby simplifying the development of effective medications. Researchers will also benefit from the Molecular Imaging Portal, which links all pre-clinical and clinical data. (p. 70)

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