A Series of Fortunate Events

In the world of scientific research, methodical approaches, driven by logic, reign. Some of the most influential and lasting contributions to science, however, are the result of unexpected twists in experiments, serendipitous "accidents." Penicillin, for example, was discovered in 1928 by Alexander Fleming after he neglected to properly clean bacteria cultures and left them in his lab. The renowned 19th century chemist and biologist Louis Pasteur once said, "Chance favors the prepared mind." Rather than relying solely on methods or on chance, however, truly visionary scientific discovery can only be achieved through a balance of both. **Nancy E. Davidson, M.D.**, *former Medical Staff Fellow at CCR, now President of the American Society of Clinical Oncology and Director of the Breast Cancer Research Program at Johns Hopkins University's Sidney Kimmel Comprehensive Cancer Center, offers her thoughts on how that balance has affected her career as a breast cancer clinician and researcher.*

As a high school student growing up in Potomac, Md., near the National Institutes of Health, I attended a program at the National Naval Medical Center. While there, I was drawn to biology, an interest that shifted to molecular biology during my undergraduate and medical studies. Through a series of serendipitous events, I spent part of my undergraduate years working part time in a laboratory that was focused on liver cancer, an experience that sparked my interest in cancer.

As a student at Harvard Medical School, I again found myself working in a lab during the summer, this time in a breast cancer laboratory at NCI. It was here that serendipity yielded to passion and planning. That summer was life-defining for me, as it helped me realize that I wanted to focus on breast cancer. This realization not only gave me a clear path for my training, but it ultimately led me back to NCI as a Medical Staff Fellow from 1982–1985, and then to Johns Hopkins, where I have been a faculty member for over 20 years.

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Good science is generally a combination of reason and providence, and translational breast cancer research requires a mix of laboratory insight and clinical observation. Investigation at the interface between the bench and bedside drives my research, even today, and it was a key factor in my development as an independent physician-scientist. Early in my career, I was given the opportunity to lead a large NCI-sponsored clinical trial focused on premenopausal women with breast cancer. At this critical early time, I was—and still am—fortunate to participate in the cooperative group process as a committee member and chair involved in the conduct of a number of clinical trials that examined optimal treatment for women with breast cancer. These collaborations have helped advance the standard of care in breast cancer by establishing appropriate kinds of chemotherapy and hormone treatments, and they instilled in me a lasting fascination with the concept of hormones in breast cancer and why some types of cancer do not respond to estrogen-related therapies while others do.

In addition to my early clinical research experiences, the collaborative environment of the laboratory also influenced my work. When I first joined the faculty at Johns Hopkins, my research centered on the roles of oncogenes in breast cancer growth. A laboratory colleague of mine at the time, Johns Hopkins scientist John Isaacs, Ph.D., pointed out a disconnect between my research focus and my clinical practice. "As a physician," he noted, "you work with patients to destroy the cancer invading their bodies. But as a researcher, you devote your time to discovering how to make breast cancer cells *grow*."

This chance conversation had a transformative effect on my research. I turned from studying the proliferation of breast cancer cells to studying their death, refocusing my work on apoptosis in breast cancer cells. Over time, my focus shifted again to bring my laboratory research back in line with my abiding clinical interest in the unique biological connections between hormones and breast cancer.

These connections have been a common theme in the field for many years. The estrogen receptor (ER) has long been the target of therapies aimed at reducing the growth-promoting influence of estrogen on breast cancer cells; the first hormone therapies for breast cancer were actually used over 100 years ago. While this is not a new arena for us, it is kept vital by the strides that researchers have made in recent years toward understanding the biology of hormones and breast cancer and its clinical exploitation.

But about 25 percent of human breast cancers lack ER expression, a trait that makes them resistant to hormonal therapies. Our current research focus on the epigenetics of ER expression is aimed at understanding one mechanism by which ER expression may be silenced in some breast cancers. With this knowledge in hand, we can work to develop a way to reverse this process, perhaps making it possible to treat these endocrine-resistant forms of cancer with traditional hormonal treatments.

As a new breast cancer researcher in the 1980s and 1990s, I had the good fortune to enter the field in a time of great change and promise, a feeling that persists even today. The advent of modern molecular biology techniques, advances in our knowledge of the human genome, engagement of breast cancer patients, and a shift toward very scientifically-based clinical trials should put us even closer to achieving our goal of reducing the burden of cancer.

This optimism, however, is tempered by the reality of the research and healthcare environment that both researchers and clinicians face on a daily basis. Though we have made a number of inroads, we are still confronted by challenges that make it difficult to take advantage of these opportunities in the current research and clinical climates. Reduced research funding, increasing healthcare costs, and a population of approximately 47 million uninsured Americans[1] make it more difficult to use our growing knowledge about cancer to improve the well-being of all patients.

To overcome these research and clinical challenges, it is important that we not only remain open to those serendipitous moments that present themselves but also utilize them in the most efficient way possible. In addition, we must recognize the benefit of collaboration in our work. The true power of a team can only come from listening and interacting with other researchers, clinicians, and advocates, all committed to advancing research and helping patients.

As a researcher, I am ever more interested in working at the interface between the lab and the clinic. My lab science grows more reflective of questions that I see in the clinic, and I like to think that my clinical research and clinical practice are ever more driven by good science and rigorous evidence. Of course all of the techniques and methods used in breast cancer research can be applied to different types of cancer as well. I believe that all cancer researchers can make focused and practical choices while staying receptive to the unexpected moments that can help drive truly beneficial science forward.

[1]*National Coalition on Health Care. "Health Insurance Coverage." http://www.nchc.org/facts/coverage.shtml. Accessed February 27, 2008.*

(*Photo: Courtesy of N. Davidson*)

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