When Persistence Pays Off

As important as innovation, depth of expertise and determination are often key to great advances in biomedicine.

Some say that breakthroughs happen when people with a fresh, even naïve, perspective look at an old problem. But in science, particularly in the complex and detail-intense world of biomedicine, sustained work and investment in a particular set of problems, coupled with an open and creative mind, is often the most fruitful path to scientific advancement.

In this issue of *CCR connections*, we see several examples of researchers that have tackled the hard problems of a particular field for decades and consistently reaped great rewards. In "It's All About the Client," we learn how Len Neckers, Ph.D., identified the ubiquitous heat shock protein Hsp90 as an anti-cancer target 15 years ago. Defying conventional wisdom, he worked within NCI to develop the first clinical trial of an Hsp90 inhibitor and paved the way for the 13 Hsp90 inhibitors currently in clinical trials. Neckers and his team are continuing to establish the basic mechanisms of Hsp90 function and doing the preclinical work to optimize this therapeutic strategy.

Along with other NIH intramural colleagues, Gordon Hager, Ph.D., studied the role of chromatin structure in gene regulation long before most scientists believed it had any relevance and before the advent of research tools such as modern gene cloning technologies. Our feature, "Don't Throw Out the Packing Materials," explains how Hager's work has led to fundamental insights into the dynamic nature of gene regulation that have direct implications for understanding and overcoming the gene dysregulation associated with cancer.

One of our newest tenure-track Investigators, Christina Annunziata, M.D., Ph.D., has been studying the subtleties of a single molecular pathway—NF-κB—since she was a graduate student. As an inaugural participant in our Clinical Investigator Development Program, she had the opportunity to apply her insights and knowledge of this pathway from prior research in multiple myeloma and create a strong preclinical ovarian cancer program to evaluate NF-κB pathway inhibitors. "One Molecule, Multiple Cancers: The Devil is in the Details," describes her plans to translate this research into better treatment for patients.

We are also pleased to have an article from Joyce O'Shaughnessy, M.D., who developed a passion for clinical research in breast cancer during her years at NCI in the late 1980s. She brought that passion with her to Texas Oncology and Baylor College of Medicine, and in "Breast Cancer: The Triple-Negative Problem," O'Shaughnessy talks about the most recent fruits of her research—results of a very exciting phase 2 trial recently published in the *New England Journal of Medicine*, on the use of PARP inhibitors for the treatment of triple-negative breast cancer.

(*Photo:* B. Branson)

Robert Wiltrout, Ph.D.

At CCR, we are proud of the role we have played in selecting and supporting scientists who have the commitment and fortitude it takes to brave uncharted territories, and who stay the course and get answers from their scientific investigations. Without this kind of sustained effort and determination to grapple with the complex and sometimes very basic questions in biomedical research, clinical breakthroughs would simply not be possible.