Behind the Name

Bruce Weller

OUR NAME—THE HOWARD HUGHES MEDICAL INSTITUTE—CAN be puzzling. Every day we hear from people with questions about medical conditions that affect them or family members. These inquiries, whether they come via telephone, e-mail, or handwritten letter, express a desire for information filled with hope and sometimes desperation: Do you offer clinical trials for my disease? What new therapies are available? Can you help me?

HHMI is not a medical center with a full roster of doctors and nurses. We don't see patients or manage clinical trials here at our headquarters in Chevy Chase, Maryland. Therefore, our responses may discourage those who turn to us for immediate, direct help. At our host institutions, our scientists focus primarily on the basic biological processes that underlie human diseases. They rely on worms, flies, mice, and other model systems to probe the functions of specific genes or to deconstruct complex biochemical pathways that are important to understanding human biology.

Yet the medical part of our name represents a critical part of our mission and our work. HHMI's mission is not only "the promotion of human knowledge within the field of the basic sciences (principally the field of medical research and education)" but also "the effective application thereof for the benefit of mankind." Finding the effective application for our knowledge can take time. Indeed, it may take decades to make the definitive connection between the lab and our ultimate aim: benefiting humanity.

Some HHMI physician-scientists are actively engaged in translating the discoveries in their laboratories into new therapies or diagnostic tools. I was particularly struck by the *medical* impact of HHMI science during a recent gathering of investigators at HHMI headquarters. These periodic meetings—each of our 350-plus scientists attends one a year—are always exciting because we hear about new work and share ideas. This particular meeting focused on translational medicine and the talks covered the gamut of human disease—from coronary artery disease and cancer to Alzheimer's disease, tuberculosis, and HIV/AIDS.

For example, Helen Hobbs at the University of Texas Southwestern Medical Center at Dallas focuses her research on the genetic factors that influence an individual's blood cholesterol levels and risk for heart disease. As leader of the Dallas Heart Study, she and her colleagues are combining population-based research with the powerful tools of reverse genetics to tease out the genetic basis for complex traits. Already, Hobbs' research has generated an important hypothesis—that early intervention to lower "bad" LDL cholesterol can substantially reduce the risk of heart disease, even among individuals who have other significant risk factors.

Like Hobbs, Bert Vogelstein of the Johns Hopkins University School of Medicine works with large pools of data collected from patients—in his case, patients with cancer. Studying tumors of the pancreas, brain, colon, and breast, Vogelstein and his colleagues have built complex maps to chart gene mutations and the biochemical pathways they alter. The results may change how new drugs are developed. The researchers found 280 genes mutated in breast and colon cancers—a daunting array of potential targets for any scientist seeking to develop new therapies—but the mutated genes were involved in only 15 pathways. Vogelstein hopes to use this knowledge to create tools to detect cancer early and prevent it from progressing.

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> THOMAS CECH

Cancer remains one of the most challenging clinical problems—in part because it is so closely tied to normal cell function—and HHMI scientists are approaching it from many different angles. Robert Darnell of The Rockefeller University works with small numbers of patients whose bodies mount a powerful immune response to cancer. These rare individuals—only one in 10,000 patients with breast or ovarian cancer—fend off the cancer but in the process produce antibodies that cause serious neurological problems. Darnell is now taking knowledge he's gained from studying these individuals to devise customized vaccines for brain tumor patients. The approach is now being tested in a phase 2 clinical trial at Rockefeller.

The common thread that connects these scientists—and dozens of others in the HHMI community—is their dedication to directing the tools of modern biology toward alleviating human suffering. And the common refrain we hear from the people who contact HHMI—even when we cannot give them what they most want, a cure or a treatment—is sincere gratitude. For each of us at HHMI, our challenge is to repay that gratitude by living up to the Institute's bold mission by supporting the very best science, from the most basic studies through translational research. My recently named successor, Professor Robert Tjian of the University of California, Berkeley, will undoubtedly find new ways to advance that commitment when he becomes president of HHMI in April 2009.