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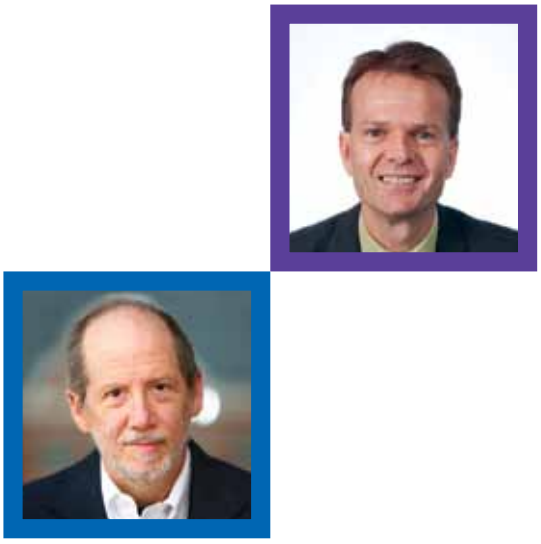
Pathway to prevention

Two Ludwig scientists imagine a future in which a blood test could detect signs of early tumors.



PHOTOS
From left
Bert Vogelstein
Baltimore, USA

Peter Gibbs
Melbourne, Australia

When Peter Gibbs finally managed to meet Bert Vogelstein, at a Ludwig-sponsored meeting in October 2010, he did not know how their encounter would go. Still, he knew it was a great opportunity. Although the researchers worked as part of the Ludwig community on different continents, and their research branched out in different directions, they both studied colorectal cancer, the topic of the meeting.

Neither scientist imagined the meeting would spark a collaboration that would draw millions of dollars in funding from outside the Institute, and that could have a major impact on cancer detection and treatment.

Gibbs, a Ludwig scientist in Melbourne, Australia, is a clinician. He sees patients regularly and knows how to run human studies. Vogelstein, a Ludwig scientist based at Johns Hopkins University in Baltimore, is a self-described "lab rat" known for his seminal research discoveries on key cancer genes. In their many years studying cancer, the researchers had never crossed paths.

When Vogelstein gave his presentation at the Ludwig meeting on the Johns Hopkins campus, Gibbs sat up in his seat. Vogelstein's group was making fast progress on developing a novel technology to detect signs of colon cancer in blood samples, based on measuring the presence of DNA from tumors. Such a biomarker indicates the presence of cancer.

"Putting our clinical and scientific expertise together really works very well. The combination is powerful," says Peter Gibbs.

Vogelstein also had preliminary results from a small pilot study. In that study, he looked for cancer DNA in the blood of patients who had undergone surgery for advanced metastatic cancer that had spread to the liver. Patients with the highest levels of the biomarker were most likely to experience recurrence. Such information could potentially help doctors make decisions about treatment strategies. But the findings were preliminary, and Vogelstein needed more patients.

Vogelstein explained that his pilot studies, like many done by other researchers, were not enough. The field needs "definitive studies," he says, that "must show beyond question that the markers are useful for clinicians and can guide treatment decisions."

Gibbs knew he had what Vogelstein needed—access to hundreds of patients who could be enrolled in prospective protocols, with a structure in place to collect and store their tumor and blood samples for analysis, combined with comprehensive data on their treatment and outcomes. "It became obvious both of us should work together," says Gibbs.

The two researchers are now conducting large-scale confirmatory studies on DNA biomarkers that, if successful, will make a difference in the lives of people with cancer.

The first of these large-scale confirmatory studies is similar to Vogelstein's pilot study—testing whether the presence of cancer DNA in the blood can predict which patients will suffer disease recurrence after removal of metastatic lesions from the liver. Gibbs' group collects samples from patients, processes them and then ships them to Vogelstein's group for analysis. The researchers enrolled their first patients in September 2011, and they expect results to emerge in late 2012 or early 2013.

The research underway is a first step to finding biomarkers that can detect tumors before they develop in the first place. With that goal in mind, the scientists are already designing additional studies to look at DNA biomarkers in earlier stages of colorectal and pancreatic cancer—work that has drawn the financial support of multiple Australian funding bodies and the Conrad N. Hilton Foundation.

Vogelstein and Gibbs imagine a future in which people who have developed early tumors could be flagged by detection of a biomarker in their blood. Then they could be treated with conventional surgery and chemotherapeutic agents, which nearly always cure patients as long as the cancers haven't widely spread when detected.

"The fundamental idea is that we are not likely to conquer cancer simply by treating advanced cancers, which is what the majority of directed cancer research is now aimed at," says Vogelstein. "Maybe we can do what has been done with other diseases and rely on prevention and early detection approaches."

Vogelstein and Gibbs acknowledge that such an approach is many years in the future. But both give credit to Ludwig for enabling them to take steps to make that possibility come alive.

"We would not have met unless both of us had had that Ludwig connection," says Gibbs. "Putting our clinical and scientific expertise together really works very well. The combination is powerful."

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