

New Hope for Millions of Men

Dr. William Oh's research aims to end the uncertainty over prostate cancer testing – and greatly reduce the number of deaths from the disease.

By Philip Berroll

Every year, across the United States, millions of men go into their doctors' offices for a blood screening – the Prostate-Specific Antigen (PSA) test – to see if they are at risk for prostate cancer. The need for the test is clear: prostate cancer is the tenth-leading cause of cancer death in the U.S.; close to 200,000 men each year are found to have the disease, and more than 27,000 will die from it. One man in six will get prostate cancer during his lifetime, and for one man in 35 it will be fatal.

But the test's reliability has increasingly been in dispute. A finding of high levels of PSA in the blood is often followed by a biopsy – a painful, invasive procedure with some risk of complications – to detect cancerous cells; yet in nearly two-thirds of biopsies, no such cells are found. This high rate of “false positive” test results underscores the need for a more accurate method for detecting prostate cancer.

That is the central focus of Dr. William Oh's work.

Dr. Oh, who came to Mount Sinai last year after 12 years at Boston's Dana-Farber Cancer Institute and Brigham and Women's Hospital, is continuing a groundbreaking project that he began at Dana-Farber: the development of a new blood test which in combination with the PSA screening could sharply increase the accuracy of prostate cancer diagnoses – and eliminate tens of thousands of unnecessary biopsies.

“If you are biopsying 100 men and only finding cancer in a third of them, that's a pretty poor hit rate,” he points out. “And when you multiply 100 times thousands – because there are 200,000 cases a year, which means that there are at least 600,000 biopsies a year, in the U.S. alone – we're talking about a substantial cost to society and to individuals. So if you could reduce the number of unnecessary biopsies, it would improve quality of life, decrease health care costs and make many people happier.”

The upbeat, energetic Dr. Oh has a wide range of responsibilities at Mount Sinai – he is Chief of the Division of Hematology and Medical Oncology in the Department of Medicine, Co-Director of the Prostate Cancer Program, Associate Director for Clinical Research for the Tisch Cancer Institute, Ezra M. Greenspan, MD Professor in Clinical Cancer Therapeutics and Professor of Medicine and Urology. A native New Yorker, he returned to his home town for “the opportunity to build a program that could lead the world in developing new therapeutics for cancer patients.”

As Dr. Oh explains it, the problem with the current test lies in its focus on PSA levels rather than cancer. “It’s not a *prostate cancer*-specific antigen test, it’s a *prostate*-specific antigen test,” he notes. “So other things like infection or inflammation or enlargement of your prostate can make your PSA rise. And that decreases what we call the specificity of the test. Basically, it’s less specific for prostate cancer alone, and this leads to false positives.”

In addition, he says, the test fails to distinguish between “aggressive cancers that will prematurely end someone’s life” and slow-growing cancers that pose no threat during a patient’s natural lifespan. “We’re finding cancers in older men who are being over-treated because the cancers grow so slowly,” he says. “Let’s say a healthy man in his eighties is diagnosed with prostate cancer – the cancer is predicted, if left alone with nothing done about it, to potentially be lethal in 30 years, when he would be 110 years old. The problem is our tests right now don’t help us make those distinctions.”

The Genes Are the Key

Dr. Oh’s original study measured the accuracy of a blood test developed at Source MDx, a medical research company in Boulder, CO, which isolated six genes that, as a group, were highly sensitive in predicting which patients had prostate cancer and which were disease-free. Dr. Oh and his team found that the new test produced a dramatic jump in accuracy – especially when PSA measurements were added.

“What we found,” says Dr. Oh, “was that using the six-gene model combined with PSA, we were able to determine – more than 90 percent of the time – whether or not somebody had cancer. (Earlier studies had found that the PSA test by itself is 60 to 70 percent accurate.) So we were able to greatly reduce the number of what we predict would be false positives.”

At Mount Sinai, Dr. Oh is joining researchers at other leading U.S. medical centers to determine if these findings remain valid – using a clinical trial which will involve almost 1,000 men. To date, more than 200 have enrolled in the study.

“In this trial,” the doctor explains, “men who are about to get a prostate biopsy – usually because of an elevated PSA – are going to get a blood test similar to the one in our earlier study to determine whether we can more accurately predict whether the biopsy will be positive or negative. In other words, we want to see whether or not our test will be better than the PSA test, either alone or in combination, at predicting whether somebody’s going to get a positive biopsy. We believe that we can use a test like this to get a more accurate prediction.”

For now, Dr. Oh rejects what he calls the “nihilistic” view that because of the PSA test’s shortcomings, men should avoid having it. “Our findings are very encouraging,” he says, “but until we can verify them, it is important to recognize that the PSA test, despite its limitations, is still the best test available for diagnosing prostate cancer at this time.”

But looking to the future, Dr. Oh predicts, “We will look at prostate cancer the same way we now look at certain infectious diseases such as tuberculosis or syphilis” – illnesses that a century ago were often fatal, but were conquered when doctors “figure[ed] out ways of diagnosing them early and then figuring out how to treat them or at least control them.”

And what Dr. Oh has learned about the complexities of prostate cancer can be applied, he feels, to other forms of the disease. “People have spoken of a ‘war’ on cancer, but it is much more like battling terrorists – you can’t always see them, they’re all over the place, and they may use different techniques to fight you,” he says. “The mistake that was made 40 or 50 years ago was to think of cancer as one disease; what we’ve learned is that there isn’t a single thing driving most cancers – there are many different pathways that the cancers can take to grow. Armed with that understanding, I think that we are really making progress. And I believe that in the future, this will continue – we’ll be able to cure more people, keep them alive longer and give them a better quality of life.”

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