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On to the Finish Line

By Laura Pratt
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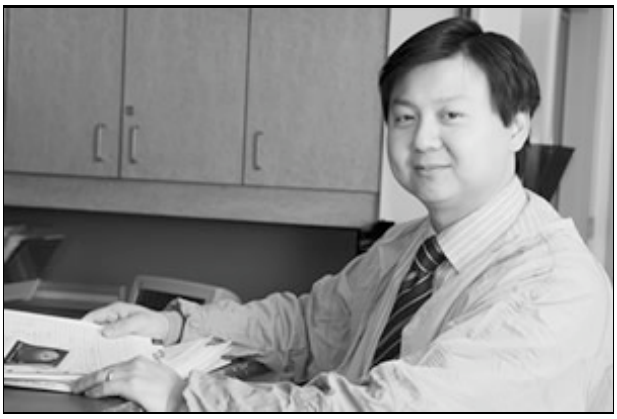
Dr. Robert Nam is in a race. It's an important race, and an extremely invigorating one. What's more, it's a contest for which he feels nothing but confidence. "We're 100% hopeful," he says of his chances of finishing at the front of the pack. "It's very realistic." Indeed, this associate scientist at Sunnybrook Research Institute and urologic oncologist at Sunnybrook Health Sciences Centre has barely broken a sweat.

His is a pursuit of the gene that will allow researchers to predict more accurately who is most at risk for developing prostate cancer. Technology is powering forward the chase with a just-five-year-old bio-tech system that allows researchers to analyze hundreds of thousands of genes where conventional PCR methods (polymerase chain reaction, a biochemistry and molecular biology technique for enzymatically replicating DNA without using a living organism, allows a small amount of DNA to be amplified exponentially) once facilitated the study of a single gene at a time. The old way was labour intensive, says Nam, and tedious. Now every last gene can be scrutinized, from chromosome one through chromosome 22.

Identifying the prostate cancer gene

This work was made official last January, when Nam, who is also an assistant professor in the department of surgery at the University of Toronto, was awarded $700,000—the second-highest amount awarded in that competition by the Canadian Institutes of Health Research operating grant competition. The project—which began in April and will span three years—is to do genome-wide association studies for prostate cancer genetics. While some putative prostate cancer genes have been found, consistency and validation are lacking, and none is yet in clinical use. Nam and his team will analyze blood samples on gene chips for genetic mutations, right across the genome. It is expensive work—about $1,000 a sample—but very detailed and precise. All told, Nam will look at the tissues of some 600 patients, drawing extensively on the University of Toronto's impressive repository of over 3,000 DNA samples from prostate cancer patients, created by Dr. Nam.



Dr. Robert Nam works to cultivate a better method for predicting susceptibility to prostate cancer.
- Photo by Doug Nicholson

"The human genome project is complete, which means many genes, and mutations of genes, have been described," says Nam. "And because we know what the human genome is, we can look at changes in prostate cancer patients to see what's different. That's exciting."

This work dovetails nicely with Nam's other recent occupation: research to evaluate a new prostate cancer screening instrument, called a nomogram.

A nomogram is a statistical model that evaluates a person's risk for disease—in this case, prostate cancer—based on a range of factors, including age, family history and race, along with a rectal exam and the standard prostate-specific antigen (PSA) test. The problem with the latter, says Nam, is its imprecision. "We have learned that there are many things that can falsely elevate PSA," he says, "and that there are many cancers that [a PSA test] can miss." For example, both benign

prostatic hypertrophy, which is a benign growth of the prostate gland; and prostatitis, an inflammation of the prostate gland, can raise PSA levels. Indeed, PSA testing—which has been in widespread use for the last decade—has clocked such an alarming record of false negatives (25%) and false positives (50%) that, says Nam, it is simply not acceptable for reliable application.

Just the same, it's the only prostate-cancer testing method currently on offer. "No one," says Nam, "has been able to replace it." Until—perhaps—now.

Adding to the screening toolbox

The National Cancer Institute of Canada grant—awarded in May 2006—dedicates $460,000 to Nam's research to develop a new screening tool for prostate cancer that has better accuracy than PSA alone. The grant is for three years. The study started in July 2006.

The nomogram method was developed by Dr. Michael Kattan, who is chair of Quantitative Health Sciences at the Cleveland Clinic, in the 1990s. Today, there are nomograms in use for various clinical applications, including prediction of the likelihood of other cancers developing, their recurrence and their response to treatment. Nam is working in collaboration with Kattan in this research, which is multi-institutional in its scope, including six institutes across Canada (one each in Vancouver, London, Montreal and Halifax, and two in Toronto: (Sunnybrook and the University Health Network)).

"This is highly innovative for prostate cancer," says Nam, because we've had nothing for the last 10 years."

This research, coupled with the genetic findings of his biomarker program study, will, says Nam, create a scenario in which doctors will be able to predict who is at risk for developing prostate cancer with 100% accuracy. In the next three years, he declares, the world will benefit from the combination of this groundbreaking work and men everywhere will be spared the damage of falsely declared diagnoses, the discomfort of unnecessary biopsies and the despair of not assuredly knowing the condition of their prostates.

"What excites me is the ability to help the increasing proportion of men who are aging and who will be able to have their prostate cancer cured because it was identified early, thanks to our nomogram and genetics assessment."

And so the race continues.

But the winner's circle should be reserved, Nam believes, for only those with the purest of motivation. "Everybody's trying to find the next biomarker to make them millionaires," he says. "They don't realize that we have all the information we need in front of us already."

Laura Pratt is a writer with Sunnybrook Research Institute.