"In any given month you'll see another report of another marker. But none of them come from strong enough study design that they're ready for prime-time."Many experts say that EPCA-2, for instance, doesn't live up to the hype it's generated.

As soon as he read the 2007 paper in *Urology*, biochemist Eleftherios Diamandis says that he "was 100% sure that the assay would have never worked for measuring any protein, let alone the EPCA-2."

He argues that Getzenberg's team, according to their published methods, used 100,000 times too much serum to coat the standard assay plate. This made it impossible to for minute quantities of specific proteins, such as EPCA-2, to bind the plate. "What they thought was binding to the plate would have never bound because of other proteins competing for [the space]," says Diamandis, whose lab at the University of Toronto is also searching for biomarkers of aggressive cancers.

Diamandis spelled out these objections in a letter that he submitted to the journal *Clinical Biochemistry*, which published it in December 2007[11]. "I'm totally convinced that my critique is valid," he says.

"People say these aren't the greatest assays," Getzenberg says. But "we're not assay development people; we are biomarker discovery people." His lab's job is to identify the biomarkers detectable in the blood of key patient groups, he says. After that, they "hand them off" to a company to develop more rigorous assays for the clinic.

"You tell me: how could somebody discover a biomarker without measuring it?" Diamandis says, incredulously. When asked about the merit of the lawsuit, he says, "I don't think it's fraud; I think it's incompetence."

Diamandis adds that over the past few years, many companies have invested in biomarker research, and many have come away disappointed.

On 14 September, Onconome submitted to the Baltimore court system a partial transcript from a videotaped deposition from one of Getzenberg's former senior lab members. Eddy Leman, who had run the EPCA-2 assay on the samples published in the 2007 *Urology* paper, admitted that he was the only person in Getzenberg's lab to ever get the EPCA-2 assay to work, and that it only worked for him once. He also acknowledged that he forgot to document that particular run in his lab binder.

That's contrary to the published study, which states that the researchers ran the assay three times on a pilot data set of 30 samples and that the variation across the three runs did not exceed 10%.

Prostate clues in the genome

Genetic association studies, involving tens of thousands of men with prostate cancer, have identified about 30 gene variants that are mildly associated with the disease (*Nat. Genet.* **41**, 1116–1121; 2009).

But whereas these discoveries may eventually help point to biochemical pathways underlying cancer, they don't do much for predicting risk. That's because most of the variants are common, present in at least 5% of the population. Carrying one only slightly increases an individual's risk.

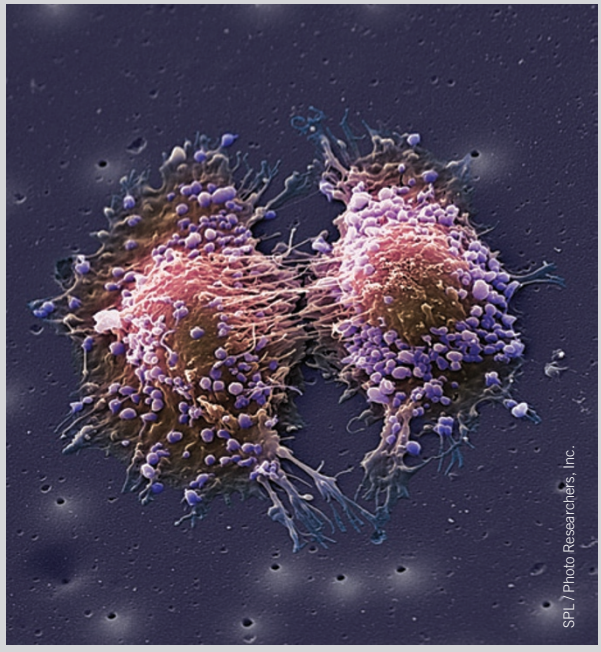
In 2005, Arul Chinnaiyan found a genetic signature that could be more useful. Analyzing genes that are overexpressed in prostate cancer tissue, he found that more than half of tumors harbor an abnormal chromosomal fusion between the *TMPRSS2* gene and that encoding a specific transcription factor, ERG (*Science* **310**, 644–648; 2005).

"It's our belief that certainly this fusion is an initiating event in prostate cancer," says Chinnaiyan, director of the University of Michigan's Center for Translational Pathology. "Our goal is to develop it into some sort of relatively economical screening test."

But the fusion marker and the variants pinpointed in the genetic association studies suffer from one of the same problems as PSA: they reveal men who have, or are likely to develop, any kind of prostate cancer, rather than only the aggressive forms.

At Johns Hopkins, Bill Isaacs' group is now screening men who have aggressive tumors and comparing their genetic makeup to men who have nonthreatening cancers. He says he's found the first common risk variant that confers risk of the aggressive kind but has not yet published the data.

Meanwhile, in October, engineers and biochemists from the University of Toronto unveiled a crude prototype of a $10, handheld silicon chip device that screens urine samples for *TMPRSS2* fusions in 30 to 60 minutes (*ACS Nano.* **3**, 3207–3213; 2009). The device could be adapted to screen for multiple genetic or protein biomarkers, says lead investigator Ted Sargent. "The entire premise of our approach is that there will not be a silver bullet."



Deadly division: Two prostate cancer cells

Virginia Hughes, New York