

New Biomarker Tests for Prostate Cancer

By Dean James Foster, MD



Dr. Dean Foster

Biomarker Tests Guide PCa Treatment

A bio-revolution is taking shape in the rational treatment of prostate cancer. It is being led by the rapid development of biomarker tests for prostate cancer.

This article will cover paraffin fixed tissue biomarker tests. Other tests of blood and urine are also being developed and will be covered in the future. These tests can accurately inform men with indolent prostate cancer that they can safely enter active surveillance, keeping them from the harm of over-treatment. In addition, biomarker tests are helping determine when there is aggressive disease that does need treatment.

Molecular Profiling

These biomarkers are detected molecular signatures, profiling the cell's metabolic processes. They change when progressive mutations sequentially derange normal processes and lead to cancer. These sequential changes in the cancer cell can now be detected in the blood, urine, semen, and from within the cancer biopsy or surgery tissue itself. By molecularly profiling these changes with the clinical behavior of the tumor, these tests improve accuracy of PCa detection and prediction of treatment outcome. These tests require tissue, so check beforehand how much is required. Also, more recent biopsies are preferred, so check about time limits for specimens.

Proving the Value of New Biomarkers

As promising as all this sounds, new biomarker tests are just getting off the ground. They will need time/testing to work out the bugs. This happened with the PSA. A widely used biomarker, the PSA has taught us valuable lessons about the pros and cons of biomarkers in general. For example, one drawback of PSA screening is that it has led to overtreatment of low risk disease. In fact, this is one of the motivations for the biotech industry to develop more sensitive and specific biomarker tests.

Tests That Improve the Accuracy of a Negative Biopsy

Prostate Cancer Mitomic Test (PCMT)

A recent publication from the Sunnybrook Division of Urology has found that the PCMT test can accurately predict when a biopsy is truly negative or if it missed the tumor (1,2). Mitomics predicts if tumor is present by detecting mitochondrial DNA deletions commonly found in the tumor *or around the tumor*. Thus, if the biopsy needle misses the tumor, this test can clarify that the PCa was missed and confirm the need for a second biopsy.

Pros: Very sensitive in detecting prostate cancer and if both the biopsy and PCMT are negative it predicts that there is no need for a second biopsy with 91% accuracy.

Cons: If it does detect a nearby tumor, it cannot determine its aggressiveness and does not help predict risk. It therefore requires the need for a repeat biopsy.

The test is available now through QDX Pathology Services as the "QPredict PCMT". It must be ordered by

your physician by calling (866) 909-7284 or online at <http://www.qdxpath.com/QPredict.pdf>.

Confirm MDx Test

In two recently published studies, researchers in Johns Hopkins Brady Urologic Institute and U. of Edinburgh Urological Cancer Group confirm that epigenetic changes (cellular changes other than DNA mutation) can accurately predict if the biopsy needle missed cancer. These studies found that the levels of GSTP1, APC and RASSF1 in “normal” tissue surrounding the cancer can determine if there truly is no cancer nearby with a 90% predictive value (3,4). This test helps men avoid a repeat biopsy (with the 1 in 1000 + risk of infection and even death) and confirms the absence of cancer in the prostate.

Pros: This test on biopsy tissue is designed to help men with a negative biopsy avoid a repeat biopsy by confirming the absence of PCa with 90% accuracy.

Cons: If it does detect a nearby tumor, it does not determine its aggressiveness or predict risk. It therefore requires the need for a repeat biopsy.

The test is restricted to tissue submitted within 24 months of biopsy. It is available now and is physician ordered by phone (866) 259 5644 and online at <http://www.mdxhealth.com>. Costs start at ~ \$2,000.

Tests That Improve the Accuracy of Pathologic Grading of a Positive Biopsy or Radical Prostatectomy Specimen

OncotypeDX Test (Genomic Prostate Score)

Researchers analyzed RNA from 17 genes across multiple biological pathways (3 stromal response, 4 cellular organization, 3 androgen, 1 proliferation, and 5 reference genes) in radical prostatectomy and prostate biopsy specimens and found a gene signature that helps predict prostate cancer aggressiveness. To simplify reporting, the test result is rendered as a number: the Genomic Prostate Score. It ranges from between 0 (low) to 100 (high). The number is then added to the CAPRA Score (CAPRA-S for RP specimens), significantly improving the Score's predictive accuracy.

In a UCSF study of 395 prostatectomy and biopsy specimens, the genetic patterns reclassified low risk men into a very low risk category suitable for active surveillance 35% of the time. Ten percent of the time low-risk men were reclassified into a higher risk category (5).

Pros: Helps determine the risk of pursuing active surveillance. Improves CAPRA risk assessment accuracy on biopsy and improves the CAPRA-S score for risk of progression free survival determined by prostatectomy pathological grading.

Cons: For biopsy tissue, the accuracy of the test depends on accuracy of the biopsy.

The test is available through your physician by phone (877) 622 6897 and online at <http://www.oncotypedx.com>. They help with costs (~\$3,800) and insurance billing.

Prolaris Test (Score)

The Polaris Score (PS) measures the average RNA expression of 31 cell cycle genes that reflect frequency of cell division. The more aggressive the PCa, the faster is the rate of cell division/proliferation and the higher the PS.

Researchers at UCSF found combining the Polaris score (PS) with the CAPRA score improved predictive risk assessment for biochemical recurrence and mortality (6).

Pros: This test, which is performed on biopsy tissue, helps men decide between active surveillance and local treatment. When the test is performed on prostate tissue after surgery, it helps men determine if postoperative treatment is indicated.

Cons: For biopsy tissue, the accuracy of the test depends on accuracy of the biopsy and may add unnecessary expense in following very low risk PCa.

The test is available through your physician by phone (801) 584 1175 and online at <http://www.prolaristest.com>. They help with costs (~ \$3,400) and insurance billing.

Decipher Test (Genomic Prostate Cancer Classifier)

Researchers at both Johns Hopkins and Mayo have collaborated and confirmed the Decipher “Genomic Prostate Cancer Classifier” can significantly enhance prediction of biochemical recurrence and metastases following radical prostatectomy. The test uses paraffin embedded tissue from the RP specimen to check on 22 genomic biomarkers. It reports a low to high probability of rapid metastatic progression and potential disease specific mortality.

Decipher testing helps high-risk men identify who really needs radiation and/or androgen deprivation therapy. For example, Decipher reclassified 60% of high-risk category men into low risk. They had 2.5 times less risk of metastases. These men could wait before having radiation. Another subgroup in this high-risk category was four times more likely to have rapid metastatic progression and would have elected to receive treatment (7). In another study, when presented Decipher data, 31% of physicians changed their recommendation from treatment to observation in this high-risk group. Decipher has been shown to improve CAPRA prediction of risk (8).

Pros: Helps men who have had surgery decide on need/timing of further treatment. Improves prediction of biochemical recurrence after surgery and whether it will lead to subsequent life threatening rapid metastatic progression.

Cons: Only used on RP specimens. Currently not available unless approved in a trial, available by the end of 2013.

The test will be available by 2014. Follow it online at <http://www.genomedx.com/decipher/overview>.

QuadVysion and ProstaVysion Tests

QuadVysion

Pathologists don't always agree on Gleason grade or even on whether or not cancer is present.(9) Having a pathology second opinion can improve accuracy. Bostwick Labs uses the QuadVysion IS report to help clarify uncertain biopsies by immunohistochemical staining with 4 antibodies (AMACR, C-myc, HMW P63 and Cytokeratin).

ProstaVysion

ProstaVysion provides a score on biopsy material that helps determine the cancer's aggressiveness and long-term prognosis. Immunohistochemical staining for two biomarkers (ERG gene fusions and PTEN deletion) are graded and the score is summarized with clinical relevance needed for guiding patient treatment decisions.

Pros: QuadVision can help determine presence of cancer when the pathology report is equivocal. ProstaVysion can help determine PCa aggressiveness.

Cons: Does not check surrounding tissue for PCa biomarkers, therefore a negative biopsy may not preclude the presence of cancer.

Both tests are available through your physician by phone (877) 865 3262 and online at <http://www.prolaristest.com>. Cost for QV, ~\$600; PV, ~\$1,350.

OurView Prognostic Panel

This panel incorporates clinical factors, Gleason grade, PTEN, proliferation Ki67 and DNA Ploidy in a pathology second opinion report on your biopsy that improves risk assessment and treatment decision-making.

Pros: Helps to resolve equivocal pathology and Gleason grading on the PCa biopsy and helps predict need for treatment. Cost of test is \$350.

Cons: For biopsy tissue, the accuracy of the test depends on accuracy of the biopsy.

This test is available by physician at (888.868.7522) and https://www.ourlab.net/OURView_Prognostic_Panel.asp

Tests that Improve PCa Treatment Selection and Efficacy

Caris Molecular Intelligence Profile and Profile Plus Tests

The Caris MI Profile tests are done on tumor tissue from any source. The MI Profile test offers a comprehensive test of over 30 cancer biomarkers to profile PCa and determine the likelihood of

response to therapy from its universe of 46 different FDA approved cancer drugs. The MI Profile Plus test adds the Next Generation Sequencing Panel, testing an additional 44 biomarkers.

The Caris tests are part of a service that is especially helpful in difficult to treat cancers like neuroendocrine (small cell) PCa. They suggest novel medications to try that have a high likelihood of helping. In addition, they offer individual tests like P-glycoprotein, an accurate predictor of resistance to chemotherapies like Docetaxel.

Pros: Very flexible and custom biomarker testing platform. Helps oncologist to work “outside the box” for treatment of difficult PCa by suggesting novel medications. The company will help match patients with ongoing clinical trials.

Cons: Because the treatments and biomarkers for PCa are rapidly evolving, clinical trial confirmation of efficacy is limited. Costs are high but insurance is

reimbursing.

Both tests are available by physician at (866) 771 8946 and at <http://www.carislifesciences.com>. The company will help with insurance billing. Charges are accepted and reimbursed by Medicare. The MI Profile costs \$6,500, the MI Profile Plus \$10,000.

Conclusion:

Like other new technologies, the biomarker industry is rapidly evolving/improving. Although expensive, insurances like Medicare have seen their value in guiding men in the difficult decisions they face and are beginning to authorize coverage/payment. The realization of personalized care for a very complicated disease has begun. The implications for improving treatment are profound. The PCRI is committed to reporting this bio-revolution and making its latest advances available to you. □

Annual Conference attendees can visit these exhibitors for more information on these tests.

(references available online)

THE PROSTATE CANCER WORLD HAS LOST A BRIGHT SHINING LIGHT

By Mark Scholz, MD

Tom Brodzeller passed away May 14th from complications of a stroke that occurred while he was in the hospital for heart problems. Tom and Ralph Valle have been leading an amazingly vibrant and successful prostate cancer support group in Phoenix for many years. While I have not been privy to the inner workings of the group, I have seen Tom serving as an indefatigable booster and a tremendous force for public relations. Ralph brings tremendous depth of knowledge about prostate cancer, giving unbiased direction to men seeking answers. Tom also worked tirelessly helping fellow prostate cancer survivors and was very well versed in the disease.

I knew Tom as a prostate cancer patient. He had one of those confusing “in between” types of prostate cancer that seem to threaten, but even after many years of off and on treatment, never actually led to any direct health problems. At the time Tom died, he was off all therapy with a low PSA.

Tom would come and visit me in Los Angeles every six months. Despite his bigger than life personality and in-depth knowledge of prostate cancer he was always deferential. At least as deferential as a gigantic ball of energy can be. He would time his doctor visits to coincide with the need to pass through Los Angeles on the way to taking one of the frequent cruises he so enjoyed.

A very brief synopsis of Tom’s life history has kindly been provided by Ken Cantrell. “Tom was born in Wisconsin in 1937. He attended college at St. Norbert’s in De Pere, Wisconsin. He was a detail man for McNeil Labs prior to starting his own pest control business. Tom was an avid trap and skeet shooter in his younger years and enjoyed bird hunting and fishing. He is survived by his brother, a retired Jesuit priest.”

Tom was one of those rare individuals who are so much fun to be around you always felt badly when he had to go. I know that hundreds of men who have been touched by Tom’s enthusiastic generosity and wisdom will feel exactly the same way. Ralph, who helped start the “Lunch Bunch” support group, has asked Us Too to rename the group, “The Tom Brodzeller Lunch Bunch Support Group.” How appropriate. By the reminder of his name, Tom’s inspiring presence will continue to encourage us all each time the Lunch Bunch is mentioned.