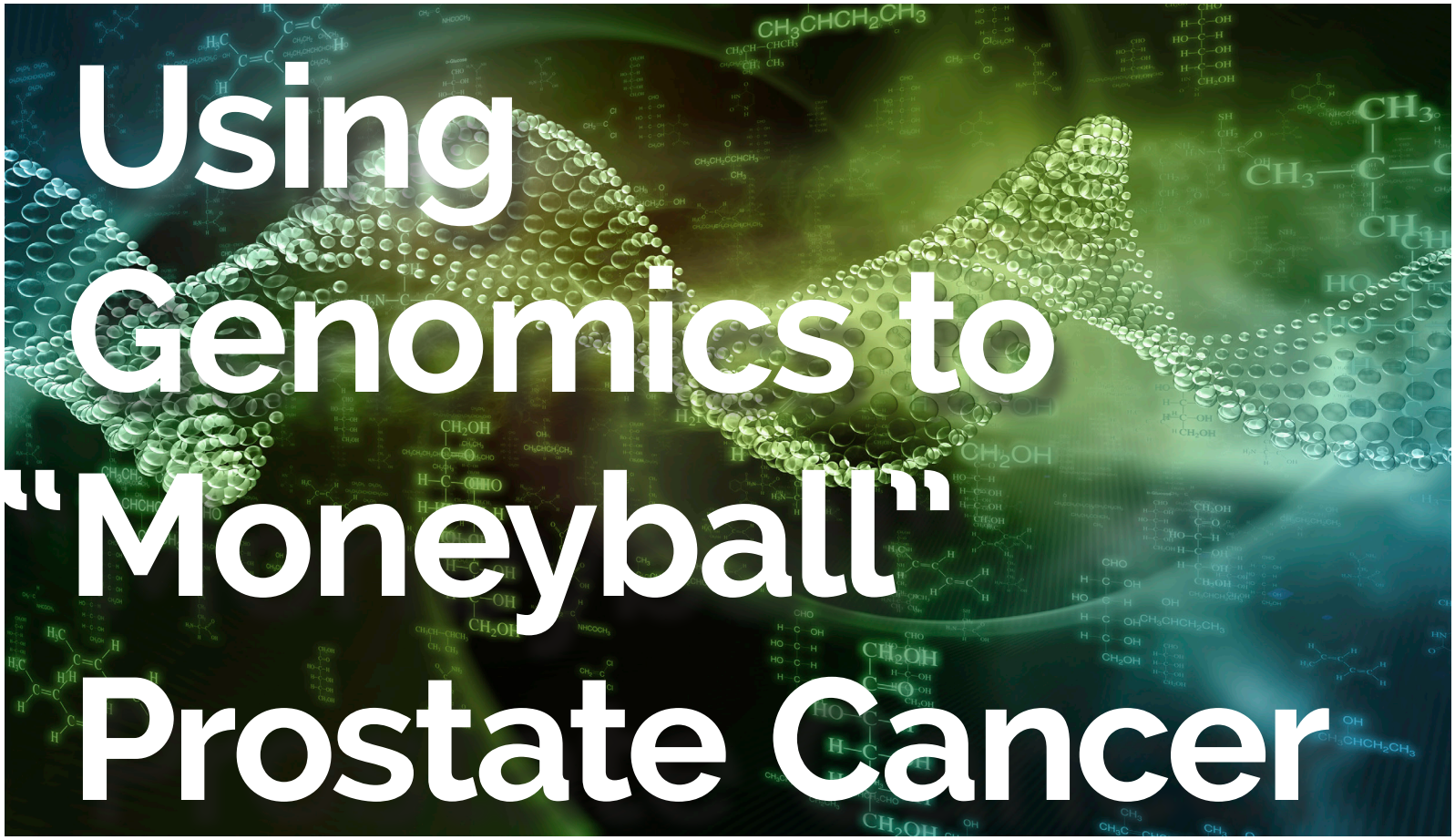


Using Genomics to "Moneyball" Prostate Cancer

By Sarah Neumann & Elai Davicioni

Decipher® prostate cancer classifier

Moneyball, by Michael Lewis, tells the true story of how Billy Beane, the general manager of baseball's Oakland Athletics, forms a winning team by analyzing individual player's statistics. Instead of investing in one or two of the most well known players in the league, he scans through them all, using advanced statistical algorithms to pick out the ones who are perfect for a certain spot on the roster, but who otherwise would never be picked. This is how a San Diego based company, GenomeDx Biosciences, uses its Decipher platform to look at the genes in the genome. →

WHO IT'S FOR:
Men at risk of prostate cancer metastasis after surgery.

WHAT IT DOES:
Predicts probability of metastasis:
5 yrs after radical prostatectomy (RP)[3]
& 3 years after a PSA rise after RP (Biochemical recurrence)[4]

THE TECHNOLOGY:
Microarray, which provides a read-out of over 1.4 million segments of expressed (activated) DNA from one archived tumor sample. Decipher reports on 22 of these expressed DNA segments.

Where to get more information:
Web: www.deciphertest.com
Email: client.service@genomedx.com
Phone: 1-888-792-1601
Corresponding author contact: sarah@genomedx.com

Sarah received her BSc in Cell Biology and Genetics at the University of British Columbia, Canada, and spent four years working as a scientist and lab manager in the field of epigenetics before joining GenomeDx Biosciences.

Elai received his PhD in pathobiology from the University of Southern California and worked in oncology biomarkers at a computational biology company before launching GenomeDx Biosciences.

Genomic data can provide another layer of information that is independent from pathological analysis of cancer tissue. Pathologists examine sections of tissue under a microscope to assess certain factors such as the Gleason score and the status of surgical margins. In the genomics lab, the readout of DNA (gene expression, or RNA) from a small piece of tissue provides additional information.

The physician receives a report of the Decipher results in the same way that he would receive results from the pathology lab. A sample report can be found at www.PCRI.org.

Genetic Profiling for Patients

The ability to collect over 1.4 million data points per patient tumor means that researchers are not restricted to the information provided by a few genes common to some cancer tests. Instead, Decipher is able to "moneyball" a winning team of cancer biomarkers customized for each clinical scenario. The Decipher test reports on the activity of 22 small sections of the human genome that are extracted from your prostate after it has been surgically removed. Analysis of these genetic sections provide a forecast of future risk of metastasis after radical prostatectomy.

If you are among the many men considering salvage radiation after surgery, the first thing that needs to be determined is the probability of the prostate cancer recurring. Genomic tests such as Decipher, help to provide a clearer picture.

Health care providers counseling patients in this situation face a dilemma. After surgery, they know that only 1 out of 10 men will develop distant metastasis without radiation treatment[1], but clinical practice guidelines recommend that all these patients be considered for radiotherapy[2]. Risk factors like Gleason score, clinical stage and PSA do not provide doctors with an accurate enough prediction as to what may or may not happen with a patient's cancer after RP. With this uncertainty, doctors tend to recommend radiation – not a pleasant undertaking for a patient on the road to recovery (e.g., from urinary incontinence and decline in sexual function) after surgery.

Collecting "Stats" on Tumors

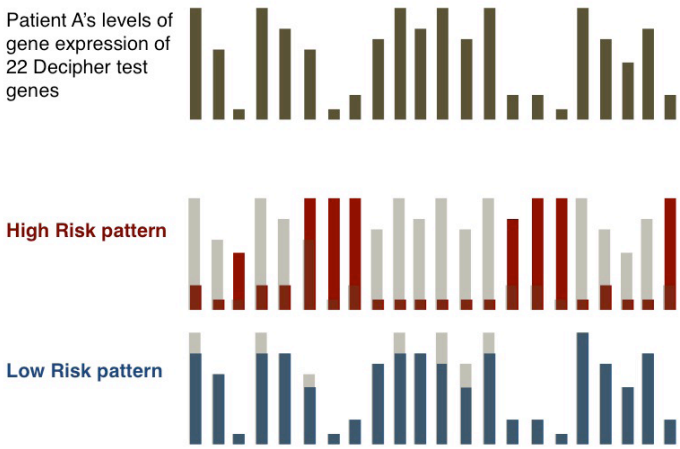
Genetic technology now available to health care providers allows them to collect and interpret genomic information to get a more accurate 'biological read' on a patient's tumor and it's future ability to grow and spread. Expression 'profiling' technology takes a snapshot of the activity of all of the genes in the genome from just a tiny sample of tumor tissue removed by RP. Cloud computing and advanced data analytics allow researchers to gather, store and rapidly analyze patterns for an individual patient which can finely characterize the biology of the tumor inside. The combination of millions of data points and the high-performance computing means that researchers can use algorithms to "Moneyball" prostate cancer to create accurate, clinically predictive tests.

A simplified schematic of what it means to use gene activity (measurement represented by vertical bars) to predict metastatic risk is depicted in Figure 1. In this case, Patient A's gene expression pattern more closely matches the pattern of gene expression for the average low risk patient studied. Patient A's Decipher probability of developing metastasis might therefore be around 2%.

Validation by Scientific Studies

How do we know that these genes will actually predict relapse? The genetic markers discussed above have been scientifically validated.[4] A study published by researchers at Thomas Jefferson University shows that when Decipher suggested a higher risk of future relapse, the patients who received immediate ('adjuvant') radiation had better outcomes.[12] Researchers also found that when Decipher indicated a lower risk of future relapse, delaying radiation did not compromise future cancer outcome.

Figure 1



Accurate Predictions Improve the Odds of Winning

What is important for patients and physicians making a clinical decision is whether their results indicate the presence of aggressive tumor cells that, given time, will spread, or if they indicate that the tumor has already been effectively cured with the surgery.

The test result from Decipher is presented in a report format that gives a prediction conveyed to you as a percentage risk of future relapse.

The Decipher Prostate Cancer Classifier is available to US patients through their physicians and as part of GenomeDx's ongoing program of clinical studies. It has been validated to predict metastasis in men at risk of prostate cancer recurrence after surgery. □

By running the Decipher test on patients, information on the activity of 1.4 million gene segments within each sample of tumor is collected. If a patient consents to let academic researchers use their their tumor's gene activity data for further study it will be used to advance research on new drug targets and additional tests. This data may be used to help make future treatment decisions for the patient himself, or at least, it may benefit prostate cancer patients of the future - potentially his sons and grandsons.

References can be found online at PCRI.org