PROSTA-GEN DX™ A NEW Biopsy-based tool for prostate cancer management

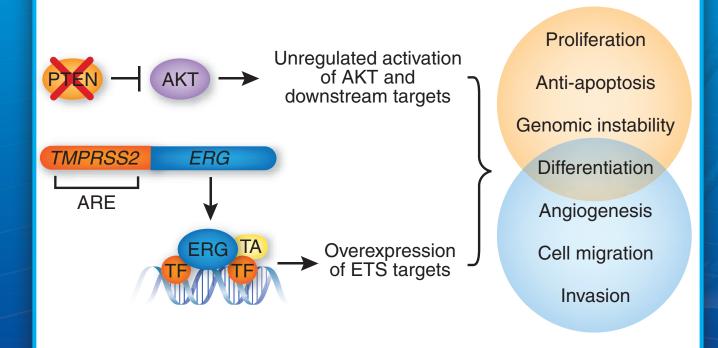
Examines two major mechanisms of carcinogenesis

P-TEN

LOSS OF TUMOR SUPPRESSOR GENE TMPRSS2:ERG

GENE FUSION/ TRANSLOCATION ANEUPLOIDY

PROSTATE CANCER PROGRESSION



ONLY TECHNOLOGY THAT COMBINES HISTOLOGIC, MOLECULAR AND CLINICAL PARAMETERS TO PREDICT DISEASE PROGRESSION

HISTOLOGIC

- Quantitatively captures and analyzes cellular features
- Pathologist selects the most representative tumor area for analysis

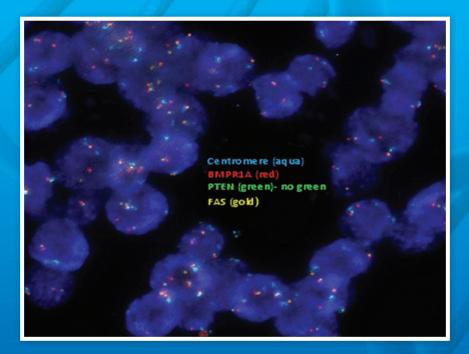
MOLECULAR

- Fluorescent in-situ hybridization captures loss or translocation of gene.
- Computer digital imaging quantifies and captures biologic results.

CLINICAL

- Incorporates clinical features to complete patient analysis.
- Biopsy Gleason Score

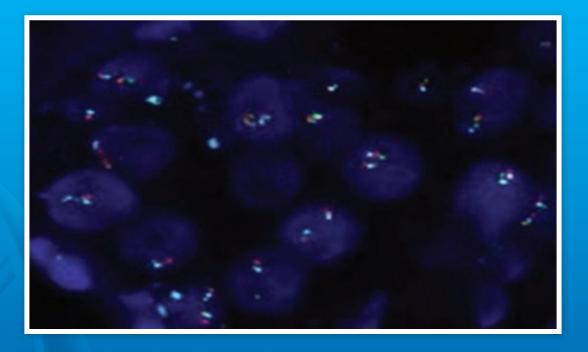




• The PTEN (phosphatase and tensin) gene encodes a phosphatase which counteracts the PI3K/Akt signaling pathway, one of the most critical cancer-promoting pathways identified to date. It is involved in the regulation of DNA repair, genomic instability, stem cell self-renewal, cellular senescence, and cell migration (metastasis).

• Studies published, correlate PTEN deletion with poor clinical outcome in cases of hormone refractory prostate cancer¬, with 42.6% of tumors displaying the PTEN deletion. In addition, it has been observed that the frequency and type of PTEN deletion is correlated to disease progression and early biochemical recurrence.

TMPRSS2:ERG



• TMPRSS2-ERG gene rearrangements are present in 30-50% of prostate cancer and lead to over expression of a truncated ERG protein. The presence of the rearrangement may have prognostic significance and assist in patient stratification to guide therapy.

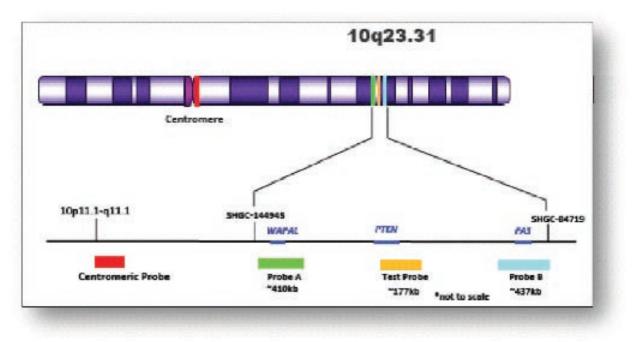
• Hormonally treated PCa patients having an ERG rearrangement have a significantly increased risk of becoming castration resistant compared to patients without the rearrangement. This is a sign of more aggressive disease and could potentially be used to identify patients less likely to respond to hormone treatment.

At diagnosis

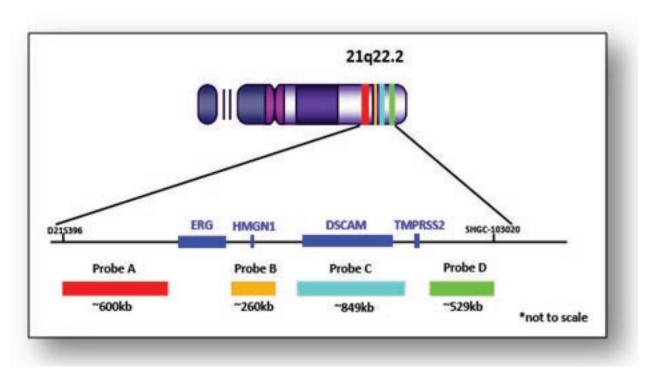
We have used multiple scientific disciplines to predict disease progression at the time of diagnosis.

- Two major mechanisms of carcinogenesis are examined.
- Generates a personalized prediction of risk of disease progression.
- Determines patients' genetic prognosis for serious disease progression.
- Delivers clinically proven, reliable results.
- Provides physicians and patients with enhance insights for treatment decisions.

P-TEN



TMPRSS2:ERG



PROSTA-GEN DXTM REFERENCES

- Yoshimoto M, Joshua AM, Cumha IW, Coudry RA, Fonseca FP, Ludkoski O, Zielensk M, Soares FA, Squire JA. "Absence of TMPRSS2:ERG fusions and PTEN loses in prostate cancer is associated with favorable outcome." Mod Patho. 2008 Dec;21(12):1451-60. Epub 2008 May 23.
- Berger MF, Lawrence MS, Demichelis F, Drier Y, Cibulskkis K, Sivachenko AT, Sboner A, Esgueva R, Pflueger D, Sougnez C, Onofrio R, Carter SL, Park K, Habegger L, Ambrogio L, Fennell T, Parkin M, Saksena G, Voet D, Ramos AH, Pugh TJ, Wilkinson J, Fisher S, Wincler W, Maha S, Ardlie K, Balswin J, Simons JW, Kitabayashi N, MacDonald TY, Kantoff PW, Chin L, Gabriel SB, Gerstein MB, Golub TR, Meyerson M, Tewari A, Lander ES, Getz G, Rubin MA, Grarraway LA,. "The genomic complexity of primary human prostate cancer." Nature 2011 Feb 10;470(7333):214-20.
- Bismar TA, Yoshimoto M, Vollmer RT, Duan Q, Firszt M., Corcos H, Squire JA. "PTEN genomic deletion is an early event associated with ERG gene rearrangements in prostate cancer." BJU Int 2011 Feb;107(3):477-85. Doi: 10.111/j.1464-410X.2010.09470.x
- Carver BS, Tran J, Gopalan A, Chen Z, Shaikh S, Carracedo A, Alimonti A, Nardella C, Varmeh S, Scardino PT, Cordon-Cardo C, Gerald W, Pandolfi PP. "Aberrant ERG expression cooperates with loss of PTEN to promote cancer progression in the prostate." Nat Genet 2009 May;41(5):619-24 Epub 2009 Apr 26
- Liu S, Yoshimoto M, Trpkov K, Duan Q, Firszt M, Corcos J, Squire JA, Bismar TA. "Detection of ERG gene rearrangements and PTEN deletions in unsuspected prostate cancer of the transition zone." Cancer Biol Ther. 2011 Mar15:(11(16).
- McCall P, Witton CJ, Grimsley S, Nielsen KV, Edwards J. "Is PTEN loss associated with clinical outcome measures in human prostate cnacer?" Br J Cancer 2008;99:1296-301.
- Rubin MA, Gerstein A, Reid K, Bostwick DG, Cheng L, Parsons R, Papdoupoulos N. "10q23.3 loss of heterozygosisty is higher in lymph node-positive (pT2-3,N+) versus lymph nodenegative (pT2-3,N0) prostate cancer." Hum Pathol 200 Apr;31(4):504-8.
- Torres CH, Soares FA, Squire JA. "FISH analysis of 107 prostate cancers shows that PTEN genomic deletion is associated with poor clinical outcome." Br J Cancer. 2077 Sep 3;97(5):678-85.
- Sircar K, Yoshimoto M, Monzon FA, Koumakpayi IH, Katz RL, Khanna A, Alvarez K, Chen G, Darnel AD, Aprikian AG, Saad F, Bismar TA, Squire JA. "PTEN genomic deletion is associated with p-Akt and AR signaling in poorer outcome, hormone refractory prostate cancer." J Pathol Aug 2009;218(4):505-13.