

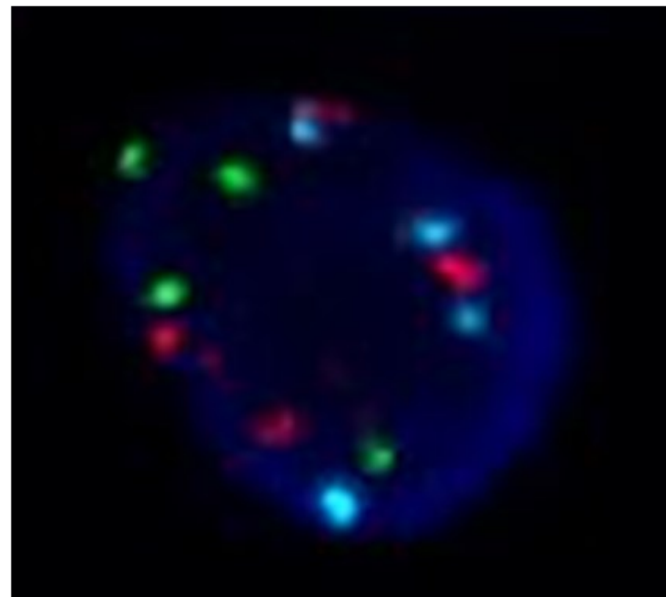
References

- Yoshimoto M, et al. "Absence of TMPRSS2:ERG fusions and PTEN losses in prostate cancer is associated with favorable outcome." *Mod Pathol*. 2008 Dec;21(12):1451-60. Epub 2008 May 23.
- Berger MF, Lawrence, et al. "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: 10.1111/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 cancer?" *Br J Cancer* 2008;99:1296-301.
- Rubin MA, Gerstein A, Reid K, Bostwick DG, Cheng L, Parsons R, Papdopoulos N. "10q23.3 loss of heterozygosity is higher in lymph node-positive (pT2-3,N+) versus lymph node-negative (pT2-3,N0) prostate cancer." *Hum Pathol* 2009 Apr;31(4):504-8.
- Van Rhijn et al., *J Clin Oncol* 21(10):1912-1921, 2003. "...patients with an FGFR3 mutation have a significantly better prognosis than those without the FGFR3 mutation."
- Kompier et al, *J pathol* 218:104-112, 2009. "Recurrences in this (FGFR3 mutant) patient group were of lower stage and grade than those of patients with wild-type primary tumor."
- Hernandez et al, *J Clin Oncol* 24(22):3664-3671, 2006. "FGFR3 mutations characterize a subgroup of bladder cancers with good prognosis."
- Burger et al, *European Urology* 54:8335-44, 2008. "Presence of FGFR3 mutation was associated with a lower risk of progression."
- Van Oers JM, et al. "FGFR3 mutations and a normal CK20 staining pattern define low-grade noninvasive urothelial bladder tumors."
- Puzio-Kuter Anna M., et al. "Inactivation of p53 and PTEN promotes invasive bladder cancer". *Genes & Development* 2009 Mar4;23:675-680.

Disclaimer: This laboratory test was developed and its performance determined by multiple laboratories among them Predictive Biosciences and SunCoast Pathology Associates. This test has not been cleared or approved by the US FDA, although such approval is not required for clinical implementation. SunCoast Pathology Associates is CLIA certified to perform high complexity testing.



URO-GEN-DX™ *Personalized genomic testing for bladder cancer*



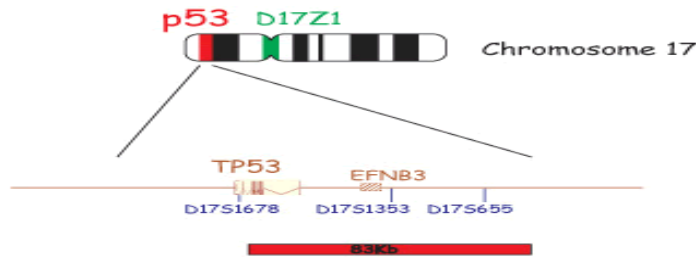
SunCoast Pathology Associates
3030 Venture Lane, Ste 108
Melbourne, FL 32934
Phone: 321 253-5197

URO-GEN-DX™ is a proprietary test to detect genomic indicators for risk assessment for progression and prognosis of bladder cancer. The test uses fluorescence-in-situ hybridization (FISH) to examine specific genetic information in your chromosomes that has been correlated with increased progression of your disease.

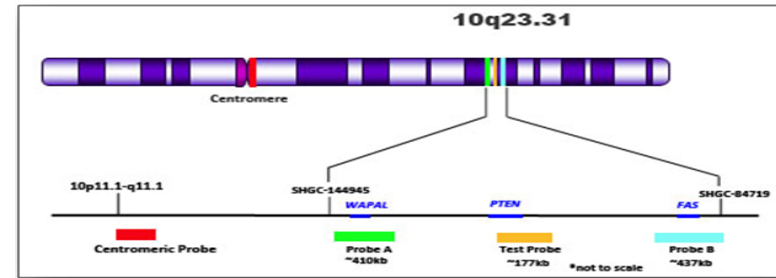
The genomic information obtained by URO-GEN-DX™, in addition to the histopathology of your biopsy, and use of immunohistochemical studies for Ki67 and CK20, assists in the treatment and management of your cancer. This combination of tests complements the pathologic diagnosis, eliminates variability of assessment, and provides a new tool to aid in the management of bladder cancer.

By using FISH, URO-GEN-DX™ looks at specific chromosomes for p53 and PTEN (tumor suppressor genes), and FGFR-3 (an epithelial growth factor) give specific and personal genomic information.

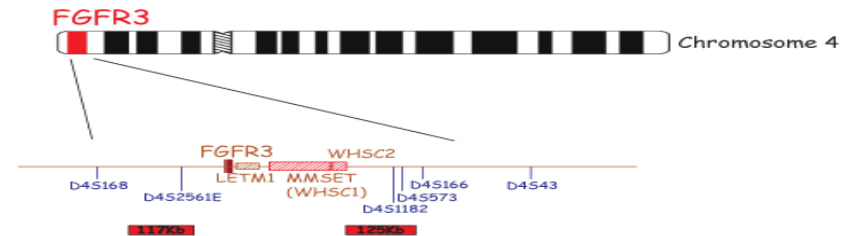
The p53 gene is a tumor suppressor gene found on chromosome 17 and its product, the p53 protein, is responsible for the death of DNA damaged cells. In the absence of p53 activity, cells that cannot be repaired will continue to proliferate in their damaged state. The mutation or loss of p53 is associated with tumor recurrence and progression.



PTEN encodes a phosphatase that regulates a critical cell cycle involved in cell proliferation. When PTEN is deleted or otherwise inactivated, cell division continues unchecked, causing progression of cancer.



FGFR3 is an epithelial growth factor found in chromosome 4. Its presence, absence, or mutation has prognostic implications in tumor behavior.



Ki67 and CK20 are immunohistochemical tests also associated with tumor progression and are assessed using computer assisted image analysis. These tests improve traditional pathology results which are based on morphology alone.

Marker Status	Prognosis	Pathologic Grade
FGFR3 mutation, low Ki67, no loss of p53, PTEN or CK20	Favorable	Low Malignant Potential
FGFR3 mutation, high Ki67, loss of either p53 or PTEN, slight loss of CK20	Intermediate	Low Grade
FGFR3 mutation, high Ki67, loss of p53 or PTEN, and loss of CK20	Poor Prognosis	High Grade