URO-GEN DX™
A NEW Biopsy-based tool for bladder cancer management

Examines three major mechanisms of carcinogenesis

P-TEN

LOSS OF TUMOR SUPPRESSOR GENE

FGFR3

GENE DELETION/ TRANSLOCATION

P53

LOSS OF TUMOR SUPRESSOR GENE

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

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

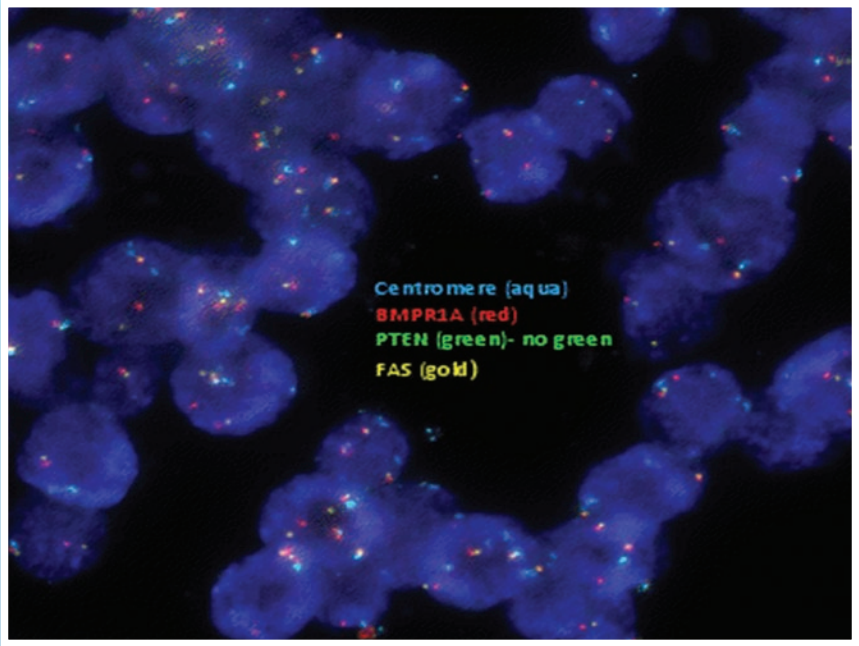
MOLECULAR

- 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.

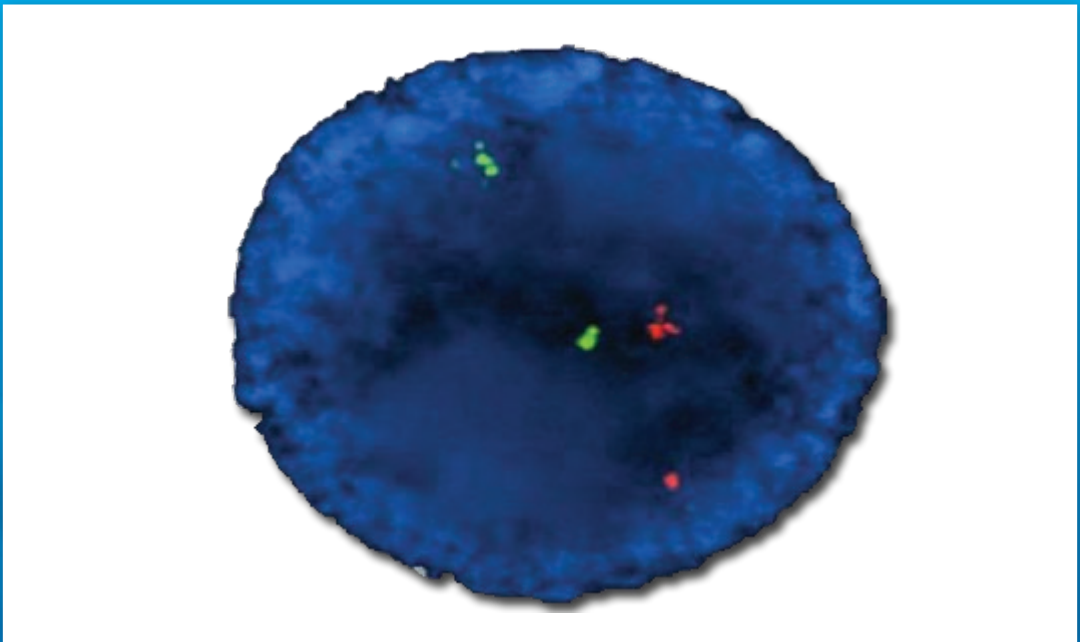
PTEN



- 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.

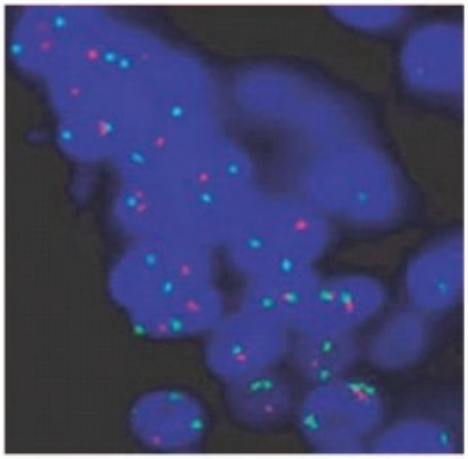
FGFR3

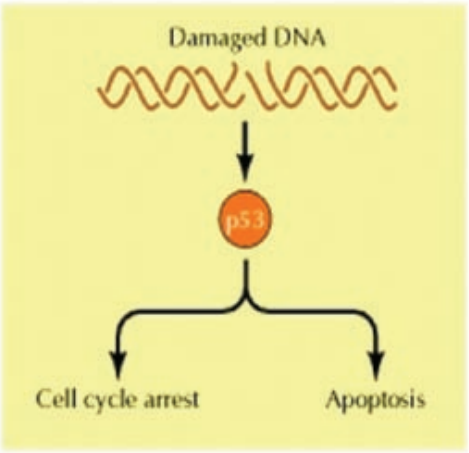


- FGFR3 is an epithelial growth factor found in Chromosome 4p16.3. Its presence, absence, or mutation has prognostic implications in tumor behavior. FGFR3 is translocated from the cytoplasm to the nucleus.

- Non-muscle invasive bladder cancers (NMI-BCs) represent 75% of bladder cancers upon presentation. Mutations in the FGFR3 oncogene are common in NMI-BCs and are associated with a lower change of progression to muscle-invasive disease. FGFR3 mutations are equally prevalent in primary and recurrent tumors (63%). The FGFR3 assay is used to detect lower stage/grade bladder cancers which have been difficult to detect with other biomarkers.

p53





- The p53 gene is tumor suppressor gene found on chromosome 17 and its product, the p53 protein, is responsible for the death of DNA damaged cells.

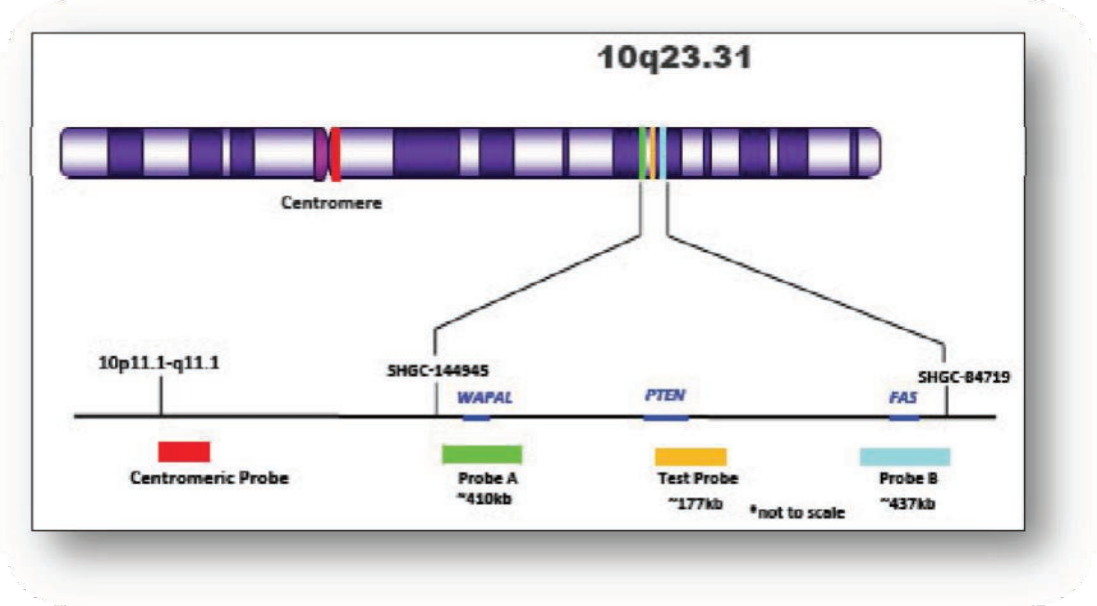
- Cells lacking p53 fail to undergo apoptosis (cell death) in response to agents that damage DNA, including radiation and many of the drugs used in cancer chemotherapy. This failure to undergo apoptosis in response to DNA damage contributes to the resistance of many tumors to chemotherapy. In addition loss of p53 appears to interfere with apoptosis induced by other stimuli, such as growth factor deprivation and oxygen deprivation. These effects of p53 inactivation on cell survival are thought to account for the high frequency of p53 mutations in tumors.

At diagnosis

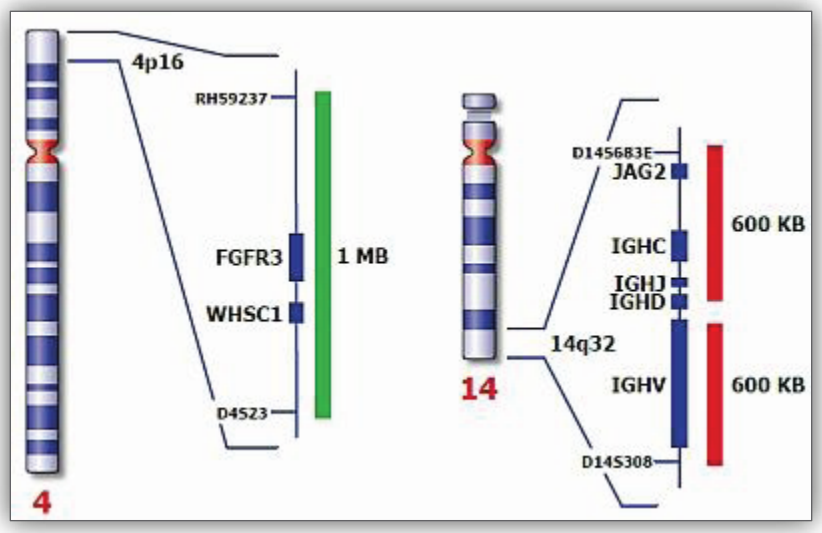
We have used multiple scientific disciplines to predict disease progression at the time of diagnosis.

- Three 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 resource.
- Provides physicians and patients with enhance insights for treatment decisions.

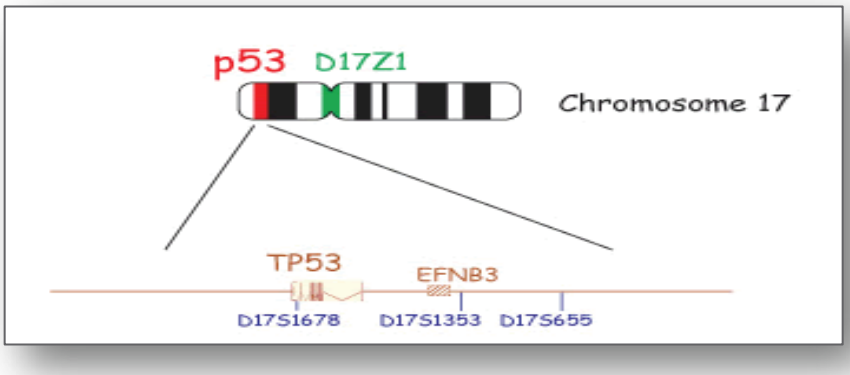
PTEN



FGFR3



P53



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