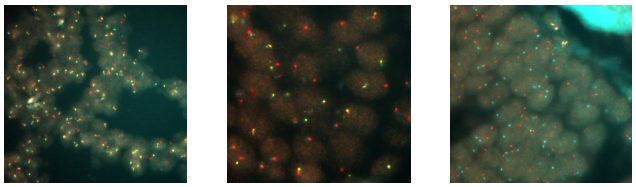
GOPATH® LABORATORIES
Global Pathology Services

GoProDx™
Prostate Cancer Prognostics

What is GoProDx™?

GoProDx™ is a prostate cancer prognostic test that uses fluorescence in situ hybridization (FISH) technology to analyze critical biomarkers that are most indicative of a patient's outcome for prostate cancer.

By testing for PTEN/ERG mutations, GoProDx™ provides clinicians with important data about a cancer's aggressiveness. Furthermore, GoProDx™ can be an essential tool for risk stratification and treatment selection for patients with Gleason scores of 6 or 7, an atypical prostate cancer diagnosis, and HGPINs.



Normal Pattern | Hemizygous Loss | Homozygous Loss

These images show normal PTEN patterns and hemizygous and homozygous deletions, which are associated with more aggressive tumors and increased risk of metastasis.

Why order GoProDx™?

- **Two Biomarkers Are Better Than One:** Analyzing PTEN and ERG together gives the clearest picture regarding prognosis including clinical outcome and prediction of recurrence.
- **Rapid Turnaround:** 3-5 day TAT allows for quicker decisions for patients with a more aggressive cancer.
- **Low QNS Rate:** GoProDx™ can be run with as few as 50 cancer cells, which makes our QNS rate significantly lower than our competitors' rate.
- **GoPath's FISH Expertise:** We have several years of experience in FISH testing, which is why GoPath offers the most comprehensive and accurate diagnostics available.
- **Guides Treatment Decisions:** GoProDx™ provides insight on a cancer's responsiveness to treatments. For example, prostate cancer patients with ERG overexpression have shown radiotherapy resistance in early studies and patients may benefit with the addition of androgen deprivation therapy.[1,2,3] Also, when PTEN loss is exhibited, a patient may respond to Rapamycin (p13K-pathway targeted) therapy.[4,5]
- **Helps Predict Prognosis:** Knowing PTEN/ERG status can help when determining a prognosis. For example, in one study, patients with ERG rearrangement and PTEN deletion demonstrated significantly worse relapse-free survival rates compared to those with ERG or PTEN wild type.[1]
- **Disease Progression:** GoProDx™ gives clinicians an assessment of how their patient's cancer is progressing. *(See Risk Stratification Chart below).*

GoProDx™ Risk Stratification Chart:

PTEN and ERG by FISH Scenarios Low Grade Gleason Score: 6 and 7 in Needle Biopsies	
Scenarios	**Prediction**
PTEN intact ERG not rearranged	Favorable (slow) progression
PTEN deletion and/or ERG rearrangement	Unfavorable prognosis/aggressive
PTEN intact and ERG rearranged	Intermediate to less than favorable outcome
PTEN deleted and ERG not rearranged	Intermediate to aggressive outcome

For a list of all molecular tests, visit our website at www.gopathlabs.com

855.GOPATH9

Why GoPath?

- **Cutting Edge Lab:** We are a state-of-the-art, CAP-accredited, CLIA-certified laboratory staffed by molecular diagnostic-trained specialist pathologists.
- **Billing:** We treat ALL patients as in-network regardless of their insurance company's contracted status. **Cancer does not only affect the well-insured.** For this reason, we have created a comprehensive indigent and financial hardship plan to ensure that your patients have access to the tests they need.
- **In-House Pathology:** On-site pathologists available for consultation on any case.
- **Specimen Handling:** We are experienced at retrieving tissue blocks (FFPE) from in-house facilities or the hospital where the specimen was stored. Simply indicate the facility name and address/city/state on the test requisition and GoPath will do the rest.
- **Connectivity:** Customizable access to test results via fax, e-mail, online and interface.
- **Comprehensive Test Menu:** We offer an extensive list of molecular diagnostics including liquid biopsy, FISH, ddPCR, flow cytometry and microarray analysis.

Comprehensive Reporting

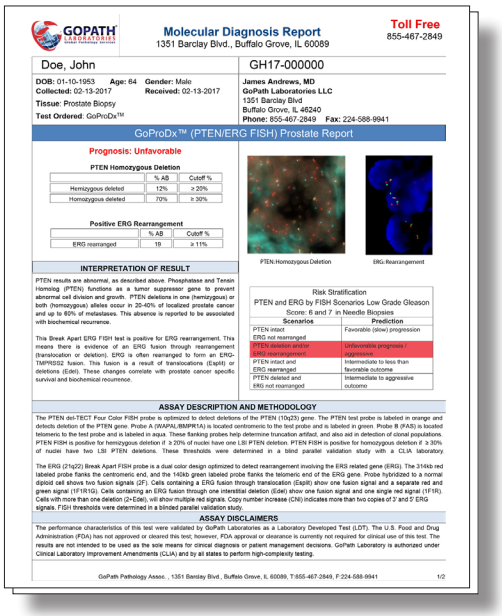
With each GoProDx™ report, you will receive:

- An easy-to-read, color-coded prognosis/risk stratification
- Interpretation of results from our on-site pathologist
- High-resolution PTEN & ERG FISH images
- Separate charts indicating percentages of abnormal & cutoff

GoProDx™- Specimen Requirements

FFPE tissue blocks are preferred. Blanks at 4µm for 10 slides or at 8 µm for 5 slides are acceptable when blocks cannot be provided. Specimen types include: endoscopic biopsies, excisional biopsies, core needle biopsies, surgical resections and cell blocks (pleural effusions, ascites).

GoProDx™ Sample Report and Requisition



GOPATH LABORATORIES

Molecular Diagnosis Report
1351 Barclay Blvd., Buffalo Grove, IL 60089

Toll Free
855-467-2849

Doe, John — GH17-000000

DOB: 01-10-1953 **Age:** 64 **Gender:** Male
Collected: 02-13-2017 **Received:** 02-13-2017
Tissue: Prostate Biopsy
Test Ordered: GoProDx™

James Andrews, MD
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Buffalo Grove, IL 46240
Phone: 855-467-2849 **Fax:** 224-588-9941

GoProDx™ (PTEN/ERG FISH) Prostate Report

Prognosis: Unfavorable

PTEN Homozygous Deletion

	% AB	Cutoff %
Hemizygous deleted	12%	≥ 20%
Homozygous deleted	70%	≥ 30%

Positive ERG Rearrangement

	% AB	Cutoff %
ERG rearranged	19	≥ 11%

PTEN Homozygous Deletion — ERG Rearrangement

INTERPRETATION OF RESULT

PTEN results are abnormal, as described above. Phosphatase and Tensin Homolog (PTEN) functions as a tumor suppressor gene to prevent abnormal cell division and growth. PTEN deletions in one (hemizygous) or both (homozygous) alleles occur in 20-40% of localized prostate cancer and up to 60% of metastases. This absence is reported to be associated with biochemical recurrence.

This Break Apart ERG FISH test is positive for ERG rearrangement. This means there is evidence of an ERG fusion through rearrangement (translocation or deletion). ERG is often rearranged to form an ERG-TMPRSS2 fusion. This fusion is a result of translocations (Esptl) or deletions (Edel). These changes correlate with prostate cancer specific survival and biochemical recurrence.

Risk Stratification
PTEN and ERG by FISH Scenarios Low Grade Gleason Score: 6 and 7 in Needle Biopsies

Scenarios	Prediction
PTEN intact ERG not rearranged	Favorable (slow) progression
PTEN deletion (eHot) ERG rearrangement	Unfavorable prognosis / aggressive
PTEN intact and ERG rearranged	Intermediate to less than favorable outcome
PTEN deleted and ERG not rearranged	Intermediate to aggressive outcome

ASSAY DESCRIPTION AND METHODOLOGY

The PTEN del-TECT Four Color FISH probe is optimized to detect deletions of the PTEN (10q23) gene. The PTEN test probe is labeled in orange and detects deletion of the PTEN gene. Probe A (NVAPAL/BMPR1A) is located centromeric to the test probe and is labeled in green. Probe B (PAS) is located telomeric to the test probe and is labeled in aqua. These flanking probes help determine truncation artifact, and also aid in detection of clonal populations. PTEN FISH is positive for hemizygous deletion if ≥ 20% of nuclei have one LSI PTEN deletion. PTEN FISH is positive for homozygous deletion if ≥ 30% of nuclei have two LSI PTEN deletions. These thresholds were determined in a blind parallel validation study with a CLIA laboratory

The ERG (21q22) Break Apart FISH probe is a dual color design optimized to detect rearrangement involving the ERG related gene (ERG). The 314kb red labeled probe flanks the centromeric end, and the 140kb green labeled probe flanks the telomeric end of the ERG gene. Probe hybridized to a normal diploid cell shows two fusion signals (2F). Cells containing a ERG fusion through translocation (Esptl) show one fusion signal and a separate red and green signal (1F1R1G). Cells containing an ERG fusion through one interstitial deletion (Edel) show one fusion signal and one single red signal (1F1R). Cells with more than one deletion (2+Edel), will show multiple red signals. Copy number increase (CN) indicates more than two copies of 3' and 5' ERG signals. FISH thresholds were determined in a blinded parallel validation study.

ASSAY DISCLAIMERS

The performance characteristics of this test were validated by GoPath Laboratories as a Laboratory Developed Test (LDT). The U.S. Food and Drug Administration (FDA) has not approved or cleared this test; however, FDA approval or clearance is currently not required for clinical use of this test. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions. GoPath Laboratory is authorized under Clinical Laboratory Improvement Amendments (CLIA) and by all states to perform high-complexity testing.

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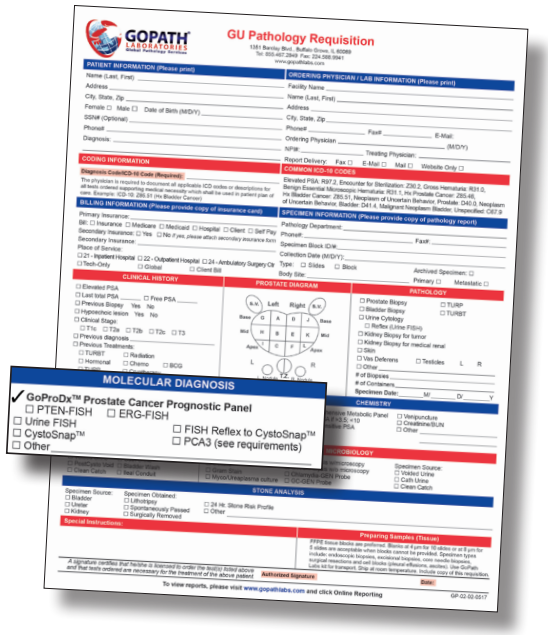

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GU Pathology Requisition
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PATIENT INFORMATION (Please print)
ORDERING PHYSICIAN / LAB INFORMATION (Please print)
CODING INFORMATION
BILLING INFORMATION (Please provide copy of insurance card)
SPECIMEN INFORMATION (Please provide copy of pathology report)
CLINICAL HISTORY
PROSTATE DIAGRAM
PATHOLOGY
CHEMISTRY
MOLECULAR DIAGNOSIS
✓ GoProDx™ Prostate Cancer Prognostic Panel
☐ PTEN-FISH ☐ ERG-FISH
☐ Urine FISH
☐ CytoSnap™
☐ Other
☐ FISH Reflex to CytoSnap™
☐ PCA3 (see requirements)
UROLOGY
STONE ANALYSIS
Special Instructions:
Preparing Samples (Tissue)
Authorized Signature
Date:
To view reports, please visit www.gopathlabs.com and click Online Reporting
GP-02-02-0517

References

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2. Han S, Brenner JC, Sabolch A, et al. Targeted radiosensitization of ETS fusion-positive prostate cancer through PARP1 inhibition. Neoplasia. 2013 Oct;15(10):1207-17.
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5. Bitting RL, Armstrong AJ. Targeting the PI3K/Akt/mTOR pathway in castration-resistant prostate cancer. Endocr Relat Cancer. 2013 May 20;20(3):R83-99. doi: 10.1530/ERC-12-0394. Print 2013 Jun.