know error®

Know Error and DNA Specimen Provenance Assignment Testing for Prostate Biopsies

DNA testing that assures patient safety and diagnostic accuracy throughout the biopsy evaluation process

STRAND DIAGNOSTICS™

*The **person** in personalized medicine.®*

The Clinical Problem

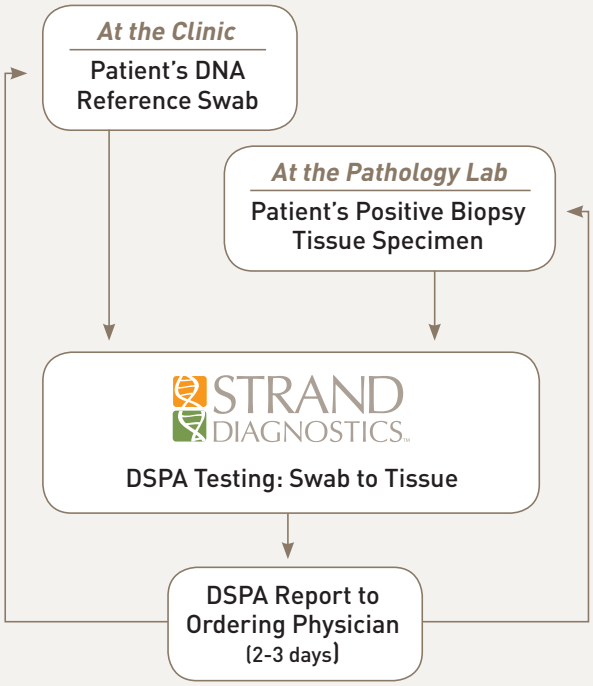
The biopsy testing cycle for cancer can involve 18 different steps[1] performed at different locations each of which creates an opportunity for a switching or contamination error. Many of the steps are outside the control of a clinician and can lead to a Specimen Provenance Complication (SPC). If undetected the result may lead to the clinician assigning a cancer diagnosis to and treating the wrong patient. Thankfully, many of these SPCs can be discovered early and corrected before iatrogenic harm befalls the patient.

DSPA Test

DNA Specimen Provenance Assignment (DSPA) testing is used to definitively assign specimen identity to the patient being evaluated. Patient misidentification, specimen transposition, and foreign cell contamination can be identified and resolved with Strand's DNA Specimen Provenance Assignment (DSPA) testing.

The DSPA process

The patient's DNA is collected via cheek swab at the clinic and sent to Strand. The biopsy tissue specimen(s) is sent to Strand from the pathology laboratory. Strand performs the DSPA test by comparing the DNA profiles of the cheek swab to the biopsy tissue specimen. A report is then issued to the physician confirming a match or non-match of each specimen tested.



Expect the Unknown

Data from Washington University published in the A*merican Journal of Clinical Pathology* indicate that **up to 3.5% of biopsies**[2] may be subject to **undetected** (occult) specimen provenance complications (SPCs) which could lead to a cancer diagnosis being assigned to the wrong patient. SPCs **occurred in every urology practice and pathology laboratory** evaluated in the study, concluding that **no one setting is immune from this problem** of **occult** errors.

The Prospective Solution

Strand's patented **know error® system** can detect both suspected and unsuspected (occult) specimen provenance complications. The system includes a tissue collection kit which utilizes bar coding and forensic chain of custody principles in an effort to reduce errors in the sample collection process as well as incorporating the DSPA test to confirm that the biopsy specimen diagnosis is truly matched to the patient being evaluated. When used as part of routine clinical practice, it protects the entire diagnostic test cycle from otherwise occult errors and helps prevent adverse patient outcomes. Over 6% of prostate biopsies in U.S. are performed using the **know error® system** .

1. Bronner MP. DNA fingerprint analysis for specimen identification. *Clinical and Translational Pathology Research*. Div. of Pathology and Laboratory Medicine, Cleveland Clinic. 2006; Fall:5-7.
2. Pfeifer JD, Liu J. Rate of occult specimen provenance complications in routine clinical practice. Table 3. *Am J Clin Pathol.* 2013;139:93-100.

The know error® system

The **know error® system**, provided at no charge, includes a biopsy collection kit with patient identification bar codes; cheek swabs for patient DNA collection; biopsy specimen, formalin-filled containers; and microcentrifuge tubes for pathology lab submission of biopsy tissue to Strand. Once the DSPA test is complete, a report for each patient is issued to the physician confirming a match or non-match of each specimen tested. The average turn-around-time for prostate biopsy samples is 2 to 3 days.

Prostate Biopsy Kit Components

Reference Swab Return Envelope
A prepaid shipping envelope for swabs.

Pathology Lab Components
This box contains the vials to transport tissue scrolls (taken from positive specimens) and a prepaid shipping mailer to send them to Strand for analysis.

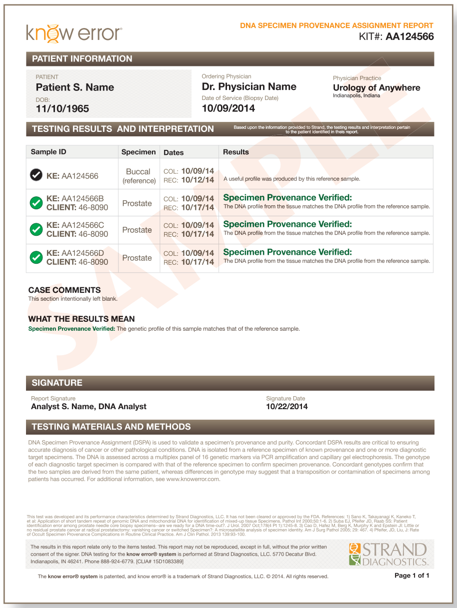
Biopsy Specimen Collection Jars
Collect the patient's tissue sample(s) and send bar-coded jars to pathology lab.

Patient Information Card
This card provides the patient facts about Know Error.

Labels and Security Seals
Bar code labels can be placed on patient files as needed. An orange label is provided for placement on the requisition to request Know Error testing.

Reference Swabs
Buccal swabs are used to collect a patient DNA reference sample before the biopsy procedure.

The DNA Report
A DSPA report is issued for each patient to summarize the test results. A Know Error representative will attempt to contact the appropriate parties immediately if a non-match is detected.



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DNA SPECIMEN PROVENANCE ASSIGNMENT REPORT
KIT#: **AA124566**

PATIENT INFORMATION

PATIENT
Patient S. Name
DOB:
11/10/1965

Ordering Physician
Dr. Physician Name
Date of Service (Biopsy Date)
10/09/2014

Physician Practice
Urology of Anywhere
Indianapolis, Indiana

TESTING RESULTS AND INTERPRETATION Based upon the information provided to Strand, the testing results and interpretation pertain to the patient identified in theis report.

Sample ID	Specimen	Dates	Results
KE: AA124566	Buccal (reference)	COL: **10/09/14** REC: **10/12/14**	A useful profile was produced by this reference sample.
KE: AA124566B **CLIENT:** 46-8090	Prostate	COL: **10/09/14** REC: **10/17/14**	**Specimen Provenance Verified:** The DNA profile from the tissue matches the DNA profile from the reference sample.
KE: AA124566C **CLIENT:** 46-8090	Prostate	COL: **10/09/14** REC: **10/17/14**	**Specimen Provenance Verified:** The DNA profile from the tissue matches the DNA profile from the reference sample.
KE: AA124566D **CLIENT:** 46-8090	Prostate	COL: **10/09/14** REC: **10/17/14**	**Specimen Provenance Verified:** The DNA profile from the tissue matches the DNA profile from the reference sample.

CASE COMMENTS
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WHAT THE RESULTS MEAN
Specimen Provenance Verified: The genetic profile of this sample matches that of the reference sample.

SAMPLE

SIGNATURE

Report Signature
Analyst S. Name, DNA Analyst

Signature Date
10/22/2014

TESTING MATERIALS AND METHODS

DNA Specimen Provenance Assignment (DSPA) is used to validate a specimen's provenance and purity. Concordant DSPA results are critical to ensuring accurate diagnosis of cancer or other pathological conditions. DNA is isolated from a reference specimen of known provenance and one or more diagnostic target specimens. The DNA is assessed across a multiplex panel of 16 genetic markers via PCR amplification and capillary gel electrophoresis. The genotype of each diagnostic target specimen is compared with that of the reference specimen to confirm specimen provenance. Concordant genotypes confirm that the two samples are derived from the same patient, whereas differences in genotype may suggest that a transposition or contamination of specimens among patients has occurred. For additional information, see www.knowerror.com.

This test was developed and its performance characteristics determined by Strand Diagnostics, LLC. It has not been cleared or approved by the FDA. References: 1) Sano K, Takayanagi K, Kaneko T, et al: Application of short tandem repeat of genomic DNA and mitochondrial DNA for identification of mixed-up tissue Specimens. Pathol Int 2000;50:1-6. 2) Suba EJ, Pfeifer JD, Raab SS: Patient identification error among prostate needle core biopsy specimens--are we ready for a DNA time-out?. J Urol. 2007 Oct;178(4 Pt 1):1245-8. 3) Cao D, Hafez M, Berg K, Murphy K and Epstein JI: Little or no residual prostate cancer at radical prostatectomy: vanishing cancer or switched Specimen?: A microsatellite analysis of specimen identity. Am J Surg Pathol 2005; 29: 467. 4) Pfeifer, JD, Liu, J: Rate of Occult Specimen Provenance Complications in Routine Clinical Practice. Am J Clin Pathol. 2013 139:93-100.

The results in this report relate only to the items tested. This report may not be reproduced, except in full, without the prior written consent of the signer. DNA testing for the **know error® system** is performed at Strand Diagnostics, LLC. 5770 Decatur Blvd. Indianapolis, IN 46241. Phone 888-924-6779. [CLIA# 15D1083389]

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The cost of using the know error® system

Know Error collection kits are provided at no charge (including all shipping costs) along with training of medical professionals and staff. The test is run only when an ordering physician requests a DSPA test. Strand bills third-party payers for the DSPA testing and, should the non-government payer refuse to pay, the maximum out-of-pocket expense for a patient is $295. Patients covered by a government payer will never receive a bill.

Further, in a recent study, researchers examined the costs to health care associated with the use of DSPA testing on positive samples even when no errors were suspected, that is, in routine clinical practice via the **know error® system**. The study concluded that DSPA testing is cost effective.[3]

DSPA testing for use with a biomarker test

When ordering tests such as OncoType® Dx, Prolaris®, etc. it is important to request DSPA testing not only to confirm the test is matched to the correct patient, but that the biomarker test is performed on non-contaminated tissue. Strand has procedures in place with most biomarker companies for DSPA testing which can eliminate potential for block exhaustion.

3. Pfeifer JD, Singleton MN, et al. Development of a decision-analytic model for the application of STR-based provenance testing of transrectal prostate biopsy specimens. *Value in Health.* 2012; 15 (6): 860-867.

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