Technology Assessment

Update on Horizon Scans of Genetic Tests Currently Available for Clinical Use in Cancers

Prepared for: Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, Maryland 20850

Draft
November 03, 2010
Update on Horizon Scans of Genetic Tests Currently Available for Clinical Use in Cancers

Technology Assessment Report
Project ID: GEND0508

November 03, 2010

Tufts Medical Center
Evidence-based Practice Center

Gowri Raman, MD, MS
Byron Wallace, MS
Kamal Patel, MPH, MBA
Joseph Lau, MD
Thomas A. Trikalinos, MD, PhD
Disclaimer

This draft technology assessment is distributed solely for the purpose of peer review. It has not been otherwise disseminated by AHRQ. It does not represent and should not be construed to represent an AHRQ determination or policy.

This report is based on research conducted by the Tufts Medical Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Project ID: GEND0508). The findings and conclusions in this document are those of the authors who are responsible for its contents. The findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

None of the investigators has any affiliations or financial involvement related to the material presented in this report.
# Table of Contents

Disclaimer .................................................................................................................. 4
Table of Contents ...................................................................................................... 5
Table of Contents for Tables ..................................................................................... 6
Table of Contents for Figures ................................................................................... 6
Table of Appendices ................................................................................................ 6
Introduction ............................................................................................................... 7
Methods .................................................................................................................... 8
  Terminologies and definitions ................................................................................... 9
    Genetic test ......................................................................................................... 9
  Eligibility criteria .................................................................................................. 10
Clinical Applications of Genetic Tests ..................................................................... 11
Literature searches .................................................................................................... 12
  Description of grey literature sources .................................................................. 12
Individual test summaries ....................................................................................... 15
Description of the electronic database ................................................................... 16
  MySQL database .................................................................................................. 16
  Front end ............................................................................................................. 17
Results ..................................................................................................................... 19
Discussion ............................................................................................................... 23
References .............................................................................................................. 25
Table of Contents for Tables
Table 1. Websites that were systematically perused to identify new genetic tests for cancers............................................................................................................................................. 14
Table 2: Genetic tests for cancer found between January, 2006 and October, 2010....... 20

Table of Contents for Figures
Figure 1. The front end to GeneTestTracker, the electronic database that lists genetic and genomic tests............................................................................................................................................. 18
Figure 2. Number of genetic tests addressing different cancer types, from 2006-2010.. 22

Table of Appendices
Appendix A. One-page summaries of the genetic tests for cancers ................................. 26
Introduction

Greater knowledge about the human genome has been gained through the completion of the Human Genome Project (1) and by the International Haplotype Map (HapMap) project. In addition, recent technical advances have resulted in the rapid proliferation of lower cost and more efficient genomic technologies. (2) The number of available genetic tests that can be used in every day clinical practice is increasing, and the rapid dissemination of these tests directly to consumers is already occurring through the Internet. The genetic tests are used for a variety of purposes that may include screening, diagnosis, risk stratification, and therapeutic management. In addition, the genetic tests can be used as a clinical decisionmaking tool to aid disease monitoring and prognosis of patients.

Genetic tests for cancer differ from genetic tests for noncancer conditions in the relatively larger number of tests for somatic mutations. Somatic mutations are genetic mutations that occur in somatic cells after conception. As cancer develops, somatic mutations are common if growth regulators in the cell are damaged by toxins, radiation, random error in cell division, and other factors. Somatic mutations cannot be inherited and only affect the lineage of cells derived from mutated cells. In contrast, mutations in germ cells will affect all the cells in the body, and are often the result of acquired mutations from a parent.

The Coverage and Analysis Group at the Centers for Medicare and Medicaid Services (CMS) requested the Technology Assessment Program (TAP) of the Agency for Healthcare Research and Quality (AHRQ) to conduct an update of the horizon scan of genetic tests for cancer and non-cancer diseases/conditions, and for alternate year update
reports on cancer and non-cancer conditions. AHRQ assigned this project to the Tufts Medical Center Evidence-based Practice Center (Contract Number: HHSA 290 2007 10055 I, Task Order #3, work assignment #3). The current report presents an update of genetic tests for cancer conditions that were identified since the 2006 horizon scan report on Genetic Testing for Cancer. (3) CMS would like the report and the accompanying database to be a ready reference for their internal discussions in this area and for decisions on future topics for systematic reviews. The main objective of this report is to provide a broad overview with sufficient information on each identified genetic test, and to provide a preliminary estimate on the amount of published literature available on each genetic test. This report is not meant to be an in-depth review of each test. Systematic review of selected tests will be the subject of future focused reviews. The contents in the database reflect the data obtained from manufacturers’ Web sites or other commercial Web sites, and should not be construed as definitive clinical evidence.

**Methods**

We adopted the 2006 horizon scan report *Genetic Testing for Cancer Conditions* (by the Tufts-EPC) as a model for this report. We adopted all the terminologies used in the previous report. The current report updates the database of genetic tests for cancer conditions, and provides concise summaries for all newly identified tests since 2006. For readers’ convenience, some sections from the 2006 horizon scan report on *Genetic Testing for Cancer* are reproduced in the Methods section. The items that are bold-faced and italicized pertain to new entries in the Methods section.
Terminologies and definitions

Genetic test

We adopted specific sections of the updated genetic test definition from the 2008 Report of the Secretary’s Advisory Committee on Genetics, Health, and Society (http://oba.od.nih.gov/).(4)

“A genetic test is an analysis performed on human DNA, RNA, genes, and/or chromosomes to detect heritable or acquired genotypes, mutations, phenotypes, or karyotypes that cause or are likely to cause a specific disease or condition. A genetic test also is the analysis of human proteins and certain metabolites, which are predominantly used to detect heritable or acquired genotypes, mutations, or phenotypes. The purposes of these genetic tests include predicting risks of disease, screening of newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations.”

This definition includes genetic variations, panels of genetic markers, measurements of gene expression and transcription products, biochemical biomarkers, topographic genotyping, and cytogenetic tests. The terms “genetics” and “genomics” are often used interchangeably in the literature, and both can refer to tests for molecular or biochemical biomarkers, as well as cytogenetic and gene-based tests. In general, the genetic tests for cancer conditions have no specific names and are usually named after the disease/condition and/or by the gene and methodology of the specific genetic test. Thus, the name of a genetic test can vary from one laboratory to another. Therefore, the types of genetic tests in this report also include genomic, pharmacogenomic, proteomic, and other
tests as reported by the individual manufacturers or laboratories. We summarized all genetic tests that we found can be used to provide diagnostic and prognostic information, monitor patient status, or detect disease recurrence.

**Eligibility criteria**

**Inclusion criteria**

We considered genetic tests that have applications in the solid tumors (breast, lung, colorectal, pancreas, etc.) as well as tests that are used in hematologic cancers (leukemia, lymphoma). We included genetic tests that are already in clinical practice. The population of interest was adults in the Medicare age group in which a genetic test result would directly impact health outcomes. We included genetic tests that are performed to aid in diagnosing, treating, and prognosticating cancers that commonly occur in adult patients. In addition, we also included tests that were utilized to monitor patient status and detect disease recurrence. The included genetic tests were selected using any one of the following criteria:

1) Genetic tests that have been cleared by FDA or pending clearance by FDA.
2) Genetic tests that are conducted in Clinical Laboratory Improvement Amendments (CLIA) certified labs and require a physician order.
3) Genetic tests offered by Internet sites that specifically require a physician order.

**Exclusion criteria**

We excluded tests that are performed for conditions that result in early death before reaching adulthood, such as metabolic or heritable disorders. We also excluded tests performed for the purpose of identifying noncancer conditions.
Clinical Applications of Genetic Tests

For the clinical applications of genetic tests that are covered in this report, we adapted the Tufts-EPC 2006 horizon scan report, *Genetic Testing for Cancer*. The following categories were used to describe the different applications for various genetic tests:

i. Prevention (primary or secondary): to detect inherited susceptibility to cancer in persons who do not have cancer in order to initiate appropriate interventions, or to detect cancer in persons who have early stage (asymptomatic) cancer.

ii. Diagnosis and management: includes confirming, classifying, and predicting typical course of cancer, choosing type of treatment (e.g. surgery alone or with adjuvant chemotherapy), monitoring response to therapy, choosing right drug in right dose at right frequency (pharmacogenomics).

Tests were further classified into diagnostic, prognostic, and monitoring categories:

1) Diagnostic: used to confirm or aid in the diagnosis of the particular disease.

2) Prognostic: information from the test can be used to determine or predict the aggressiveness of the disease or overall outcome of the disease at the time of initial diagnosis and prior to initiation of treatment. Prognostic information can then be used to determine a particular or individualized treatment plan.

3) Recurrence: to detect disease recurrence in a patient who has already been diagnosed and treated for cancer.
4) Monitoring: test used to monitor tumor and/or patient response to treatment.

Literature searches

Our previous experience suggests that systematic searches of the published scientific literature are not a practical way to identify new genetic tests for the following reasons: 1) there are no specific pre-defined search strategies to identify genetic tests that are currently available in clinical use; 2) the large volume of publications on genetic, genomic, proteomic, and related molecular markers and panels makes review too resource intensive; 3) typically publications referring to specific patented technologies may not be indexed by their genetic test names, as the main focus may be to study molecular expression patterns or gene-disease associations; 4) even if a test is currently in clinical use and there are studies that pertain to the test of interest, there may still be a time lag until their publication; and 5) many potentially evaluated gene-disease associations may not have matured to a clinically useful genetic test.

Based on our experience with two prior technology assessment reports on genetic tests for cancer and non-cancer, focused searches of the grey literature are preferable to searches of the published scientific literature for the identification of new genetic tests.

Description of grey literature sources

1) GeneTests (www.genetests.org) is a Web site funded by the National Institutes of Health and sponsored by the University of Washington in Seattle. The current Web site includes links to the International Laboratory Directory, the International Genetics Clinic Directory, GeneReviews, and Educational Materials. The purpose of this Web site is to
provide medical genetics information to physicians, other healthcare providers, and researchers. GeneTests.org is available free of charge to all interested persons. GeneReviews is authored and reviewed by experts in the field of genetics, updated and/or revised periodically as clinically relevant material emerges. GeneReviews allows searches to be conducted by disease name, gene symbol, chromosomal locus, protein name, feature, Online Mendelian Inheritance in Man (OMIM) number, author, or title. The International Laboratory Directory is a voluntary listing of laboratories offering molecular genetic testing, specialized cytogenetic testing, and biochemical testing for inherited disorders. We obtained information related to testing, gene reviews, and other resources from the GeneReviews section of the Web site. We also utilized the links to commercial diagnostic laboratories that were provided by testing sources to explore the specimen collection methods, methodology, and genetic disease/condition descriptions.

2) We searched Internet Web sites using the following algorithm. We first searched Google News (http://www.news.google.com) for “gene OR genetic OR genomic test OR epigenetic”, and “FDA cleared genetic test.” The news items with their links were automatically deposited into an email system to generate daily email alerts. Periodically, we visited Web links listed in the news items. We also visited the relevant laboratories that appeared in the news items to identify any new genetic tests.

3) Commercial diagnostic laboratories’ Web sites were screened to identify genetic tests that are available for routine clinical use. We also identified the Web pages of companies or major commercial laboratories in the United States, such as Roche Diagnostics®, Quest Diagnostics®, and LabCorp®. A complete list of systematically queried laboratories and their Web sites can be found in Table 1. For any potential genetic tests that were
mentioned in these Web sites, we conducted focused Internet searches by including the specific test names to find more information, including other manufacturers, suggested uses, and press releases.

Table 1. Websites that were systematically perused to identify new genetic tests for cancers

<table>
<thead>
<tr>
<th>Description</th>
<th>URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quest Diagnostics®</td>
<td><a href="http://www.questdiagnostics.com/">http://www.questdiagnostics.com/</a></td>
</tr>
<tr>
<td>LabCorp®</td>
<td><a href="http://www.labcorp.com/">http://www.labcorp.com/</a></td>
</tr>
<tr>
<td>Roche Diagnostics®</td>
<td><a href="http://www.roche-diagnostics.us/">http://www.roche-diagnostics.us/</a></td>
</tr>
<tr>
<td>Athena Diagnostics, Inc</td>
<td><a href="http://www.athenadiagnostics.com">http://www.athenadiagnostics.com</a></td>
</tr>
<tr>
<td>GeneDx</td>
<td><a href="http://www.genedx.com">http://www.genedx.com</a></td>
</tr>
<tr>
<td>Abbott Molecular Laboratories</td>
<td><a href="http://www.abbottmolecular.com">http://www.abbottmolecular.com</a></td>
</tr>
<tr>
<td>Google News</td>
<td><a href="http://news.google.com">http://news.google.com</a></td>
</tr>
<tr>
<td>FDA News</td>
<td><a href="http://FDAnews.com">http://FDAnews.com</a></td>
</tr>
<tr>
<td>Genelex Corp</td>
<td><a href="http://www.healthanddna.com/">http://www.healthanddna.com/</a></td>
</tr>
<tr>
<td>Medical Solutions (Nottingham) Ltd.</td>
<td><a href="http://www.medical-solutions.co.uk/default.aspx">http://www.medical-solutions.co.uk/default.aspx</a></td>
</tr>
<tr>
<td>PreMD, Inc. (formerly IMI International Medical Innovations)</td>
<td><a href="http://www.premdinc.com/">http://www.premdinc.com/</a></td>
</tr>
<tr>
<td>Epigenomics</td>
<td><a href="http://www.epigenomics.com">http://www.epigenomics.com</a></td>
</tr>
<tr>
<td>Correlogic</td>
<td><a href="http://www.correlogic.com">http://www.correlogic.com</a></td>
</tr>
<tr>
<td>Agendia</td>
<td><a href="http://www.agendia.com">http://www.agendia.com</a></td>
</tr>
<tr>
<td>Caris Life Sciences</td>
<td><a href="http://www.molecularprofiling.com">http://www.molecularprofiling.com</a></td>
</tr>
<tr>
<td>Monogram Biosciences</td>
<td><a href="http://www.monogrambio.com">http://www.monogrambio.com</a></td>
</tr>
<tr>
<td>Bostwick Laboratories</td>
<td><a href="http://www.bostwicklaboratories.com/home/">http://www.bostwicklaboratories.com/home/</a></td>
</tr>
<tr>
<td>Genzyme Genetics</td>
<td><a href="http://www.genzymegenetics.com">http://www.genzymegenetics.com</a></td>
</tr>
<tr>
<td>Arup Laboratories</td>
<td><a href="http://www.aruplab.com">http://www.aruplab.com</a></td>
</tr>
<tr>
<td>Wako Chemicals USA, Inc</td>
<td><a href="http://www.wakousa.com">http://www.wakousa.com</a></td>
</tr>
<tr>
<td>Veridex, LLC</td>
<td><a href="http://www.veridex.com">http://www.veridex.com</a></td>
</tr>
<tr>
<td>Dako (formerly DakoCytomation)</td>
<td><a href="http://www.dako.com/">http://www.dako.com/</a></td>
</tr>
</tbody>
</table>
Individual test summaries

Once the list of current genetic tests was updated, one-page summaries of each test in the database were completed using data extracted from various sources, including laboratory Web sites and test manufacturer Web sites. Data included in these summaries are a more detailed description of the test and its clinical use. The “one-page summary” included the following items:

1) Test name: The majority of the clinically available genetic tests were identified either by the disease/conditions or by the disease causing genes without any specific test name. Hence the gene names, protein, and disease/conditions served as the surrogate for the genetic testing identifier. When available, we recorded the specific test name.

2) Description: Included a brief summary of the genetic or genomic test and its association with the cancer condition.

3) Purpose: The clinical applications of genetic tests included primary or secondary prevention, diagnostic, prognostic, recurrence, and monitoring.

4) Availability: Included a brief list of laboratories including commercial and academic laboratories in the U.S. and other countries.

5) Specimen: The specimen was utilized to evaluate the gene-disease condition, which included whole blood, serum, tumor tissue, etc.

6) Diseases: Included a list of disease conditions for which the genetic test was utilized.

7) Clinical uses: Included genetic test applications in a clinical setting (e.g. routine use, investigational use, etc.).

8) Source: A list of additional sources that were typically consulted for information about the genetic test application.
9) Marker: Included the list of possible genetic test names, genes, and biomarkers that were used for Medline search strategy.

10) Organ: Included a list of specific organ(s) affected by the gene-disease association.

11) Exploratory PubMed search: The exploratory PubMed search included the name of the genetic or molecular marker, the disease, and the terms “cancer condition [MeSh]”. For tests that use a panel of genetic or molecular markers, we used the brand name of the panel crossed with the search terms. All searches were repeated on 11/01/2010. These search strategies are exploratory and the number of citations returned is an estimate of the scientific literature available on each test-disease condition. However, this number is preliminary and would be subject to change from the use of a more fully developed search strategy and the application of specific screening criteria.

**Description of the electronic database**

We developed an electronic database for efficient storage and retrieval of the aforementioned information on eligible genetic tests. For convenience, we developed a user-friendly front end (interface) that allows browsing and searching of the database without the need to use low-level programming commands.

**MySQL database**

We have created a MySQL ([http://www.mysql.com/](http://www.mysql.com/)) database to store the collected genetic test information. MySQL is a relational database management system that is free, open-source, well documented, extremely robust, and widely used. It is often held to be a *de facto* standard for databases. Furthermore, the embedded SQL query language allows for quick and flexible querying of the stored data. For example, the end
user can easily request information for all tests related to a specific cancer, with an arbitrarily complex set of limits. MySQL databases can be exported to a myriad of other formats, including Microsoft© Excel readable Comma Separated Values (CSV) format.

In the genetic test database, data is separated into cancer and non-cancer genetic tests. For each, we kept a record of all the data needed for one-page summaries of genetic tests. In particular, for cancer-related genetic tests, the used fields corresponded to the items described in the “Individual test summaries” section.

**Front end**

The MySQL database created for this review stores and indexes all of the genetic tests. However, it is not necessarily straightforward for those unfamiliar with MySQL (and the SQL query language), limiting access to this data once collected. The Tufts-EPC is therefore developing a user-friendly interface to interact with the database, dubbed the ‘GeneTestTracker.’. The front end is Web-based, and written in the Python programming language (http://python.org/), using the Pylons (http://pylonsHQ.com/) Web framework. Having a Web-based program is advantageous because it theoretically allows remote access to the database (via any standard internet browser), is platform independent, and software updates need only be dropped on to the server (rather than installed manually by end users).

Upon logging in to the password-protected site, users can see all of the genetic tests in a tabular format; the non-cancer tests are displayed on one tabbed page, while the cancer tests are displayed in Figure 1. From this screen, users can add a new genetic test by simply clicking the “add new” button. Furthermore, users can click on an existing gene test to bring up the corresponding one-page summary. This summary can then be
edited or deleted by the user. Additionally, a Microsoft® Word-friendly Rich Text Format (RTF) document can be automatically generated from the summary page, which the user can download to their computer locally, or print out.

We have also been working on interfacing with PubMed so as to automatically generate plots showing the number of hits a search in PubMed turns up for a gene test over time. This is partially implemented, but not yet complete.

Figure 1. The front end to GeneTestTracker, the electronic database that lists genetic and genomic tests.

Figure 1 is a snapshot of Gene Test Tracker, the front end to the electronic database that lists genetic and genomic tests. After logging in the password-protected site, the user sees
an html page depicting a table. Each row pertains to a specific test. The columns list the
test name, cancer and description of disease, purpose of the test, availability, specimen,
methodology, clinical use, sources, marker, organ, and PubMed search strategies. Above
the columns is a search window in which the user may search the database for any
genetic test within two categories, cancer and non-cancer. The database may be searched
using the test name, gene symbol, disease, or laboratory as keywords to find a specific
test or any number of tests currently available for a specific disease.

Results

Currently, the Gene Test Tracker database contains 100 different genetic tests
logged into 149 test-disease combinations. We identified 38 new genetic tests for 48
different cancer conditions since the 2006 report,(3) with the largest number of tests
being utilized for breast cancer, colorectal cancer, and multiple cancers (Table 2). The
one-page description for these newly identified genetic tests for cancer conditions can be
found in Appendix A. These tests are used in a variety of solid tumors and hematological
cancers. Of these, breast cancer(s) is the type with the largest number of new tests in the
database (Figure 2). The Gene Test Tracker database also compiles one-page summaries
for each of the genetic tests. The one-page summaries provide additional detail on the
individual genetic tests, including further discussion on their clinical use and a graphic
plot of exploratory literature search yields as listed in Appendix A. This graphic plot may
be informative for identifying tests for future focused reviews.
Table 2: Genetic tests for cancer found between January, 2006 and October, 2010

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Purpose*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast</strong></td>
<td></td>
</tr>
<tr>
<td>AmpliChip p53 Test</td>
<td>T, P</td>
</tr>
<tr>
<td>deCODE BreastCancer™</td>
<td>D, P</td>
</tr>
<tr>
<td>Estrogen Progesterone Receptor Assay</td>
<td>D, P</td>
</tr>
<tr>
<td>GeneSearch™ BLN Assay</td>
<td>D</td>
</tr>
<tr>
<td>Her2 Neu Overexpression</td>
<td>PGx</td>
</tr>
<tr>
<td>MammaPrint®</td>
<td>D, P</td>
</tr>
<tr>
<td>SPOT-Light @HER2 CISH Kit</td>
<td>PGx</td>
</tr>
<tr>
<td>Tamoxitest™</td>
<td>PGx</td>
</tr>
<tr>
<td>TOP2A FISH pharmDx™ Kit</td>
<td>P, M</td>
</tr>
<tr>
<td><strong>Colorectal</strong></td>
<td></td>
</tr>
<tr>
<td>ColonSentry™</td>
<td>Pp</td>
</tr>
<tr>
<td>Colopath®/ColorectAlert™</td>
<td>D</td>
</tr>
<tr>
<td>Cytokeratin 20(CK20)</td>
<td>D</td>
</tr>
<tr>
<td>Oncotype DX® colon cancer assay</td>
<td>R, S</td>
</tr>
<tr>
<td>Septin-9 DNA methylation biomarker</td>
<td>D</td>
</tr>
<tr>
<td>UGT1A1 Molecular Assay™</td>
<td>PGx</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td></td>
</tr>
<tr>
<td>Digene HC2 High-Risk HPV DNA Test</td>
<td>Pp, D</td>
</tr>
<tr>
<td>ImmunoCyt®</td>
<td>M</td>
</tr>
<tr>
<td>NMP22®BladderChek®</td>
<td>D</td>
</tr>
<tr>
<td><strong>Hematologic</strong></td>
<td></td>
</tr>
<tr>
<td>G6PD</td>
<td>PGx</td>
</tr>
<tr>
<td>KIT Asp816Val Mutation Analysis</td>
<td>D, T</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td></td>
</tr>
<tr>
<td>CellCorrect KvA-40, LAb® clinical Dx</td>
<td>D</td>
</tr>
<tr>
<td>ELSA-CYFRA 21-1</td>
<td>D, P</td>
</tr>
<tr>
<td><strong>Ovarian</strong></td>
<td></td>
</tr>
<tr>
<td>Test Name</td>
<td>Use</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>OVA1™</td>
<td>S, P</td>
</tr>
<tr>
<td>OvaCheck™</td>
<td>D</td>
</tr>
<tr>
<td>OvaSure™</td>
<td>D</td>
</tr>
</tbody>
</table>

### Prostate

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bayer Immuno 1™ Complexed PSA</td>
<td>D, M</td>
</tr>
<tr>
<td>Hybritech Tandem-R free PSA test</td>
<td>Pp, D</td>
</tr>
<tr>
<td>Progensa™ PCA3 Assay</td>
<td>D, P, T</td>
</tr>
<tr>
<td>uPM3(TM) test; PCA3Plus™ test</td>
<td>D, P</td>
</tr>
</tbody>
</table>

### Other**

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>DakoCytomation’s c-Kit (9.7) pharmDx™</td>
<td>D, T</td>
</tr>
<tr>
<td>LBA(R)AFP-L3</td>
<td>Pp</td>
</tr>
<tr>
<td>MGMT methylation testing</td>
<td>PGx</td>
</tr>
</tbody>
</table>

### Multiple***

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>CellSearch™</td>
<td>P, R, M</td>
</tr>
<tr>
<td>CupPrint</td>
<td>D</td>
</tr>
<tr>
<td>DPD deficiency</td>
<td>PGx</td>
</tr>
<tr>
<td>EGFRx™ assay</td>
<td>PGx</td>
</tr>
<tr>
<td>miRview™</td>
<td>D</td>
</tr>
<tr>
<td>Pathwork® Tissue of Origin test</td>
<td>D</td>
</tr>
</tbody>
</table>

* P = prognostic, D = diagnostic, M = monitoring, R = recurrence, T = therapeutic management,
Pp = primary prevention, PGx = pharmacogenetic, S = secondary prevention
** Other includes brain, liver, and upper gastrointestinal, respectively
*** Tests used for multiple cancers including breast, colorectal, lung, ovarian, prostate
Figure 2: Number of genetic tests addressing different cancer types, from 2006-2010
Discussion

We performed Internet-based grey literature searches and added 38 new genetic tests for cancer conditions found since 2006. Recent grey literature searches indicate that the largest numbers of new tests were found in the breast, colorectal, and multiple cancer categories. Most of the information for each of the genetic tests was gathered from various public and proprietary Web sites. The laboratories offering genetic testing services provided most of the information on the description of the gene involved with the disease. We searched sites that were identified from our 2006 horizon scan report, *Genetic Testing for Cancer Conditions* (3) and many other sites identified through Google News searches. Our list encompasses both gene associations of potential biomarkers, and pharmacogenomic tests. In terms of tests of gene associations, only few biomarkers ever make it to the clinical application stage. Thus, the list of tests we identified in this report along with genetic tests identified in our 2006 report are fairly comprehensive with regard to the diseases/conditions for which currently a clinical genetic testing is available for the Medicare population.

Potential limitations of our report include lack of empirical structure providing guidance on how to conduct optimal grey literature searches of the Internet. The following are caveats to our grey literature searches. Internet searches in Google are not strictly reproducible. This has been partially overcome by storing Web links along with access dates in our database. However, for searches conducted within a reasonably short time period, the Web pages will be more or less the same. To overcome such limitations related to searches conducted in Google, we supplemented Internet searches with periodic
review of Web sites of major companies that manufacture genetic and molecular tests, and by searching the FDA Web site.

Our report indicates that there has been an increase in the number of genetic tests for specific cancerous conditions, and there is inherent subjectivity in identifying emerging genetic tests. Many genetic and molecular markers and panels are being associated with cancerous conditions. We have selected those that are available for clinical applications in screening, diagnosis, prognosis, disease management, or patient monitoring as tests for cancerous conditions. In addition to grey literature searches, our discussion with local experts as well as the external panel of reviewers helped us to identify this comprehensive list of genetic tests.

This horizon scan for genetic tests for cancerous conditions, with biannual updates, adds important information on emerging tests. Genetic testing is a rapidly emerging field with the potential to dramatically influence clinical decisionmaking. Health care providers, patients, payers, decisionmakers, and consumers can benefit from staying abreast of newly-released tests.
References


Appendix A. One-page summaries of the genetic tests for cancers.

For tests included in the previous report, please visit http://www.ahrq.gov/clinic/ta/gentests/gentestsdata2.htm.

**Test Name:** AmpliChip p53 test

**Description:** The AmpliChip p53 test enables rapid detection of p53 mutations among patients with breast cancer. Tumor suppressor gene p53 influences cellular proliferation, survival, and genomic integrity in breast cancer. Disruption of p53 function results in uncontrolled proliferation of damaged cells. The relationship between p53 and patient outcome suggests that p53 mutation status may be a prognostic indicator and could predict response to therapy.

**Purpose:** treatment management, prognosis

**Availability:** Roche Diagnostics, in development

**Specimen:** tumor tissue

**Methodology:** DNA microarray-based sequencing

**Diseases:** Breast cancer

**Clinical Uses:** The AmpliChip p53 test may help physicians select the anticancer medicines best suited to their patients need.

**Sources:** 2007 Breast Cancer Symposium abstract (Distribution of p53 mutations by AmpliChip assay in patients receiving neoadjuvant capecitabine (C) plus docetaxel (D) with or without trastuzumab (T) for newly diagnosed breast cancer (BC))

**Marker:** p53 gene

**Organ:** Breast

**Medline Searches:** neoplasm AND p53 gene AND Breast
2. Gene Test Information: Bayer Immuno 1(TM) Complexed Prostate Specific Antigen, Prostate

**Test Name:** Bayer Immuno 1(TM) Complexed Prostate Specific Antigen  
**Description:** Human prostate specific antigen (PSA) is a glycoprotein. PSA forms complexes with protease inhibitors such as alpha.sub.1 -antichymotrypsin (ACT) to form complexed PSA (cPSA). Concentrations of cPSA above 3.6 ng mL (nanograms per milliliter) are considered abnormally high, which indicates the possibility of prostate cancer.  
**Purpose:** diagnosis and monitoring  
**Availability:** Commercial laboratories, academics  
**Specimen:** Blood  
**Methodology:** Immunoassay  
**Diseases:** Prostate  
**Clinical Uses:** The test is used in addition to a digital rectal examination (DRE). cPSA in combination with DRE detects significantly more cancer cases than DRE alone.  
**Sources:** FDA  
**Marker:** Complexed Prostate Specific Antigen  
**Organ:** Prostate cancer  
**Medline Searches:** neoplasm AND Complexed Prostate Specific Antigen AND Prostate cancer
3. Gene Test Information: CellCorrect KvA-40 Cell Correct Lab (R) clinical Dx, Lung cancer

**Test Name:** CellCorrect KvA-40 Cell Correct Lab (R) clinical Dx

**Description:** The test uses a bioinformatics platform, which a profiling library with more than 1500 key biomarkers and an additional 700 biomarkers that may be relevant in determining certain characteristics related to the reproduction stage of cancer cells.

**Purpose:** Diagnosis

**Availability:** European Union countries

**Specimen:** Whole blood

**Methodology:** Molecular finger printing

**Diseases:** Lung cancer

**Clinical Uses:** The test detects molecular fingerprints of disease-related autoantibodies in the bloodstream. Currently utilized for lung cancer diagnosis. Other potential applications include the detection and diagnosis of breast, colon, and stomach cancer.

**Sources:** [www.medscape.com](http://www.medscape.com), CeMines, Inc

**Marker:** Molecular fingerprinting

**Organ:** Lung

**Medline Searches:** neoplasm AND Molecular fingerprinting AND Lung
4. Gene Test Information: CellSearch(TM), Breast colorectal and prostate cancer

**Test Name:** CellSearch(TM)

**Description:** The CellSearch(TM) System identifies and counts circulating tumor cells (CTC) of epithelial origin (CD45-, EpCAM+, and cytokeratins8, 18+, and or 19+) in whole blood to predict progression-free survival and overall survival in patients with metastatic breast, colorectal or prostate cancer, and can do so earlier than the current standard of care.

**Purpose:** prognostic, recurrence, monitoring

**Availability:** Veridex, LLC

**Specimen:** whole blood

**Methodology:** Immunomagnetic labeling and immunofluorescent identification of cells

**Diseases:** Breast, colorectal, and prostate cancer

**Clinical Uses:** The results of serial testing for CTCs with the CellSearch(TM) System provide additional information to the oncologist and does so earlier than other currently approved diagnostic modalities, thereby allowing the oncologist to make more-informed patient care decisions.

**Sources:** Medical News Today (http: www.medicalnewstoday.com articles 98810.php); Veridex (http: www.veridex.com pdf MKG1982PanCancerGTWshortPresentationFINAL.pdf)

**Marker:** (CellSearch or Circulating tumor cells)

**Organ:** (breast or colorectal or prostate)

**Medline Searches:** neoplasm AND (CellSearch or Circulating tumor cells) AND (breast or colorectal or prostate)
5. Gene Test Information: Colopath(R) or ColorectAlert(TM), colorectal cancer

**Test Name:** Colopath(R) or ColorectAlert(TM)

**Description:** Colopath(R) screens for a phospholipid analyte (plasmalogen) in rectal mucus of individuals with colorectal pathology, whereas ColorectAlert(TM) screens for the T-antigen, a complex sugar in rectal mucus. Both tests involve the application of a rectal mucus sample to a test strip, and a positive negative result is based on a Schiffs aldehyde reaction.

**Purpose:** Diagnosis

**Availability:** Commercial labs in the US and Canada

**Specimen:** rectal mucus

**Methodology:** not documented

**Diseases:** colorectal cancer

**Clinical Uses:** Highly sensitive and minimally invasive screening and monitoring test strip for colorectal cancer.

**Sources:** Procyon Biopharma Inc., www.ambriliabiopharma.com

**Marker:** (plasmalogen or colopath or colorectAlert)

**Organ:** colorectal

**Medline Searches:** neoplasm AND (plasmalogen or colopath or colorectAlert) AND colorectal
6. Gene Test Information: ColonSentry(TM), Colorectal cancer

**Test Name:** ColonSentry(TM)  
**Description:** The ColonSentry(TM) test measures the expression of seven genes in whole blood, which serve as biomarkers to detect colorectal cancer.  
**Purpose:** primary prevention  
**Availability:** GeneNews(TM) Corporation  
**Specimen:** whole blood  
**Methodology:** microarray and quantitative RT-PCR (qRT-PCR)  
**Diseases:** Colorectal cancer  
**Clinical Uses:** The ColonSentry test is a risk stratification tool that will enable better physician-patient dialogue and decisionmaking as part of the colorectal cancer screening process.  
**Sources:** ColonSentry (www.colonsentry.com)  
**Marker:** (genes and biological markers)  
**Organ:** colorectal  
**Medline Searches:** neoplasm AND (genes and biological markers) AND colorectal
7. Gene Test Information: CupPrint, Cancer of Unknown Primary Origin

**Test Name:** CupPrint

**Description:** Using a database of 51 different tumor types, the CupPrint test can be applied to determine the gene expression profiling of the specimen and identify the tissue of origin. Prior studies have demonstrated that the cells of a distant majority retain vast majority of the gene expression characteristics of their originating site.

**Purpose:** Diagnostic

**Availability:** Europe

**Specimen:** Tumor tissue

**Methodology:** Gene expression profiling

**Diseases:** Cancer of Unknown Primary Origin

**Clinical Uses:** Aids in identifying primary tumor origin and thereby assists in the adequate treatment for tumors of unknown primary origin. Prior studies have shown that the tumor response varies substantially based on the tumor’s site of origin

**Sources:** www.ferrerincode.com

**Marker:** CupPrint

**Organ:** Unknown Primary

**Medline Searches:** neoplasm AND CupPrint AND Unknown Primary
8. Gene Test Information: Cytokeratin 20 (CK20), Colorectal and gastrointestinal carcinomas

**Test Name:** Cytokeratin 20 (CK20)

**Description:** Cytokeratin 20 is 46 kDa intermediate filament protein that has been identified with expression primarily restricted to gastric and intestinal epithelium, urothelium, and Merkel cells. Cytokeratin 20 is a unique type I keratin that is expressed in adenocarcinomas of the colon, stomach, pancreas and bile system. It is also expressed in mucinous ovarian tumors, transitional cell carcinomas of the urinary tract, and Merkel cell carcinomas. CK20 is essentially non-reactive in squamous cell carcinomas and adenocarcinomas of the breast, lung, and endometrium, as well as non-mucinous tumors of the ovary and small cell carcinomas. CK20 was formerly known as "protein IT".

**Purpose:** diagnosis for the primary site of a carcinoma

**Availability:** Many manufacturers

**Specimen:** Tumor tissue

**Methodology:** Immunohistochemistry

**Diseases:** Colorectal and gastrointestinal carcinomas

**Clinical Uses:** Cytokeratin 20 is often used in conjunction with CK7 and other antibodies in distinguishing colon carcinomas (CK20+) from ovarian, pulmonary, and breast carcinomas.

**Sources:** Biocare Medical (http://www.biocaremed.com/antibodies/Cytokeratin_20__CK20_.html)

**Marker:** (Cytokeratin 20 or CK20)

**Organ:** colorectal

**Medline Searches:** neoplasm AND (Cytokeratin 20 or CK20) AND colorectal
9. Gene Test Information: DakoCytomation c-Kit pharmDx(TM), Gastro-intestinal stromal tumors (GIST)

**Test Name:** DakoCytomation c-Kit pharmDx(TM)

**Description:** The antibody is used to identify c-KIT tyrosine kinase protein, a protein in the body that stimulates cancerous tissue cell growth. The presence of this protein establishes a diagnosis of GIST. The c-Kit pharmDxTM assay is a qualitative immunohistochemical (IHC) kit system used for the identification of c-kit protein CD 117 antigen (c-kit protein) expression in normal and neoplastic formalin-fixed paraffin-embedded tissues for histological evaluation. The c-kit pharmDxTM rabbit polyclonal antibodies specifically detect the c-kit protein in CD 117 antigen-expressing cells.

**Purpose:** diagnosis and therapeutic management

**Availability:** Commercial and academic labs

**Specimen:** Tumor tissue

**Methodology:** qualitative immunohistochemical (IHC) kit system with c-kit pharmDxTM rabbit polyclonal antibodies

**Diseases:** Gastro-intestinal stromal tumors (GIST)

**Clinical Uses:** Along with other pathological and clinical information establishes a diagnosis of GIST and indicates eligibility for treatment of GIST with the FDA-approved drug, Gleevec (imatinib mesylate)

**Sources:** FDA

**Marker:** c-kit tyrosine kinase

**Organ:** Gastro-intestinal stromal tumors

**Medline Searches:** neoplasm AND c-kit tyrosine kinase AND Gastro-intestinal stromal tumors

**Test Name:** deCODE BreastCancer

**Description:** The deCODE BreastCancer test determines the genotypes for 7 known single-nucleotide polymorphisms (SNPs) that have been linked to genetic predisposition to female breast cancer. The variants are located on chromosomes 2q35 (rs13387042), 5p12 (rs4415084, near the MRPS30 gene), 5q11 (rs889312, near the MAP3K1 gene), 8q24 (rs13281615), 10q26 (rs1219648, near the FGFR2 gene), 11p15 (rs3817198, near the LSP1 gene), and 16q12 (rs3803662, near the TNRC9 TOX3 gene). Based on an individual's genotypes for these SNP markers, lifetime genetic risk of being diagnosed with breast cancer can be determined and related to the general risk of breast cancer in the population.

**Purpose:** prognostic, diagnostic

**Availability:** deCODE diagnostics

**Specimen:** blood, buccal

**Methodology:** ND

**Diseases:** breast cancer

**Clinical Uses:** The test may indicate a use for preventative therapy. The test is also useful in parallel with BRCA1 and BRCA2 testing since it may reinforce that patients who are negative for BRCA1 and BRCA2 may still be at increased risk for later-onset breast cancer.

**Sources:** deCODE diagnostics

**Marker:** rs13387042 OR rs4415084 OR rs889312 OR rs13281615 OR rs1219648 OR rs3817198 OR rs3803662

**Organ:** breast

**Medline Searches:** neoplasm AND rs13387042 OR rs4415084 OR rs889312 OR rs13281615 OR rs1219648 OR rs3817198 OR rs3803662 AND breast
11. Gene Test Information: DPD 5-FU GenotypR (TM), Multiple

**Test Name:** DPD 5-FU GenotypR (TM)

**Description:** Capecitabine is a chemotherapy drug that is given as a treatment for many types of cancer, including bowel cancer, breast cancer, stomach cancer and esophageal cancer. As a prodrug, capecitabine is selectively activated by tumor cells to its cytotoxic moiety, 5-fluorouracil (5-FU). Dihydropyrimidine deshydrogenase (DPD) is the main enzyme involved in the degradation of 5-FU. Decrease in DPD activity results in toxicity to 5-FU in cancer patients. An estimated 3-8% of patients have a genetic variation that leads to a deficiency of DPD. Patients with this variation have severe toxic reactions that may be fatal with even small doses and often the very first dose of 5-FU.

**Purpose:** pharmacogenetic

**Availability:** commercial laboratories

**Specimen:** buccal swab

**Methodology:** PCR

**Diseases:** Multiple

**Clinical Uses:** The DPD test for 5-FU is considered appropriate for any person who is taking or considering 5-FU based chemotherapy. It is recommended that this screening be accompanied by direct measurement of DPD activity prior to 5-FU treatment in cancer patients

**Sources:** PharmGKB

**Marker:** Dihydropyrimidine deshydrogenase deficiency

**Organ:** 5-Fluorouracil

**Medline Searches:** neoplasm AND Dihydropyrimidine deshydrogenase deficiency AND 5-Fluorouracil
12. Gene Test Information: EGFRx(TM) assay, multiple cancers

**Test Name:** EGFRx(TM) assay

**Description:** A new class of anti-cancer drugs selectively targets cells within the body that have a specific molecular defect that is believed to cause dangerous cell behaviors such as uncontrolled proliferative growth and high metastatic potential behaviors that typically are associated with aggressive cancer. The defect occurs within the interior of the cell in a region that is called the tyrosine kinase domain and it involves a complicated chemical process called EGFR signaling. The drugs are called anti-EGFR drugs or tyrosine kinase inhibitors. When the drugs work, they can be highly beneficial, causing tumor shrinkage or promoting stable disease and extending survival. However, as with most of the newer, targeted therapy drugs, tyrosine kinase inhibitors only work for a small percentage of the patients who receive them. In various studies, response rates in single agent and combined anti-EGFR drug therapy ranged from around 10% to 66%, depending upon the cancer type and the patient population involved. Further, the drugs are expensive and have been associated with toxic side effects. Finally, to make matters worse, no molecular (gene-based) test has been proven to tell reliably who will benefit from anti-EGFR treatment. In contrast, the Weisenthal Cancer Group EGFRx profile has been shown to correlate highly with patient response to anti-EGFR treatment and with overall patient survival. Reported prospectively, EGFRx profile results reliably identified patients who did or did not respond to treatment with anti-EGFR drugs and also those who achieved superior survival after treatment.

**Purpose:** pharmacogenetic

**Availability:** Weisenthal Cancer Group

**Specimen:** tumor cells

**Methodology:** "Whole Cell Profiling" in which living tumour cells are removed from an individual cancer patient and exposed in the laboratory to the new drugs

**Diseases:** multiple cancers

**Clinical Uses:** The EGFRx targeted therapy profile includes analysis of the following targeted drugs: erlotinib (Tarceva), gefitinib (Iressa), sorafenib (Nexavar), and sunitinib (Sutent). For certain types of cancer, a drug called imatinib (Gleevec), which works in a very different way, may be tested. The finding is important because the EGFRx test, which can also be applied to many emerging targeted cancer drugs, could help to help to solve the growing problem of knowing which patients should receive costly, new treatments that can have harmful side-effects and which work for some but not all cancer patients who receive them.

**Sources:** http: www.weisenthalcancer.com Patient%20Pages EGFRXPatients.htm

**Marker:** tyrosine kinase

**Organ:** pharmacogenomics

**Medline Searches:** neoplasm AND tyrosine kinase AND pharmacogenomics

**Test Name:** ELSA-CYFRA 21-1  
**Description:** CYFRA 21-1 is a cytokeratin 19 fragment found in serum of cancer patients. Precise recognition of this fragment is made with two monoclonal antibodies (BM 19-21 and KS 19-1)* which were obtained after immunisation of mice with MCF-7 cells. Cytokeratin 19 (CK19) is a member of the intermediate filament group of proteins, whose physiological role remains unclear.  
**Purpose:** diagnostic, prognostic  
**Availability:** Cisbio Bioassays - France  
**Specimen:** serum  
**Methodology:** solid-phase sandwich immunoradiometric assay  
**Diseases:** non-small cell lung cancer  
**Clinical Uses:** Preliminary clinical studies of bronchial cancer patients sera have shown that CYFRA 21-1 assay is useful in the diagnosis and follow-up of non-small cell lung carcinoma and particularly of squamous cell carcinoma of the lung.  
**Sources:** Cisbio Bioassays  
**Marker:** antigen CYFRA21.1  
**Organ:** lung  
**Medline Searches:** neoplasm AND antigen CYFRA21.1 AND lung

Test Name: G6PD deficiency

Description: Rasburicase has recently been approved for the management of reduction of uric acid due to tumor lysis syndrome in hematologic malignancies. Patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency who are treated with rasburicase are at risk of severe hemolysis. Rasburicase is contraindicated for such patients. Patients deficient in G6PD have reduced ability to reduce the hydrogen peroxide formed as a major byproduct of the rasburicase-catalyzed oxidation of uric acid to allantoin.

Purpose: pharmacogenetic

Availability: Commercial laboratories

Specimen: Blood

Methodology: direct DNA testing and or sequencing of the G6PD gene

Diseases: hematologic cancers

Clinical Uses: The FDA recommends, but does not require, genetic testing prior to initiating treatment with rasburicase. It is recommended that patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) be screened prior to starting rasburicase therapy.

Sources: PharmGKB

Marker: glucose-6-phosphate dehydrogenase

Organ: rasburicase

Medline Searches: neoplasm AND glucose-6-phosphate dehydrogenase AND rasburicase
15. Gene Test Information: GeneSearch BLN Assay, Metastatic Breast cancer

**Test Name:** GeneSearch BLN Assay

**Description:** Detects the presence of breast tissue in nodal tissue using 2 tissue specific RNA molecules as biomarkers. The two biomarker RNA’s are transcribed from genes expressed at high levels in breast cancer tissue but only at low or background levels in nodal tissue.

**Purpose:** Diagnostic

**Availability:** Commercial labs and Academic hospitals

**Specimen:** Sentinel lymphnode

**Methodology:** reverse transcriptase polymerase chain reaction assay

**Diseases:** Metastatic Breast cancer

**Clinical Uses:** During a lumpectomy or mastectomy to remove a breast tumor, surgeons commonly remove the sentinel node for examination under a microscope. Results of this rapid test are available while patients are on the operating table, helps to avoid a second operation

**Sources:** FDA, Veridex

**Marker:** GeneSearch BLN Assay

**Organ:** Breast

**Medline Searches:** neoplasm AND GeneSearch BLN Assay AND Breast
16. Gene Test Information: SPOT-Light (R) HER2 CISH Kit, Breast cancer

**Test Name:** SPOT-Light (R) HER2 CISH Kit

**Description:** Patients with breast cancer may have more copies of HER2 gene, prompting them to overproduce HER2 protein so that more signals are sent to breast cells. As a result, the cells grow and divide much too quickly. This gene regulates the growth of cancer cells. The SPOT-Light HER2 CISH kit is a test that measures the number of copies of the HER2 gene in tumor tissue.

**Purpose:** Therapeutic management

**Availability:** Commercial laboratories

**Specimen:** Tumor tissue from breast

**Methodology:** Chromogenic in situ hybridization (CISH)

**Diseases:** Breast cancer

**Clinical Uses:** SPOT-Light HER2 CISH kit - a genetic test for determining whether patients with breast cancer are good candidates for treatment with the drug Herceptin (trastuzumab)

**Sources:** Invitrogen, FDA

**Marker:** HER2 CISH

**Organ:** Breast

**Medline Searches:** neoplasm AND HER2 CISH AND Breast
17. Gene Test Information: Her2 neu overexpression, breast cancer

**Test Name:** Her2 neu overexpression

**Description:** HER2 neu (also known as ErbB-2, ERBB2) stands for "Human Epidermal growth factor Receptor 2" and is a protein giving higher aggressiveness in breast cancers. It is a member of the ErB protein family, more commonly known as the epidermal growth factor receptor family. HER2 neu has also been designated as CD340 (cluster of differentiation 340) and p185. Because anti-HER2 neu therapy benefits only patients with invasive breast carcinomas overexpressing HER2 neu, testing is used to identify those patients most likely to respond to anti-HER2 neu therapies.

**Purpose:** pharmacogenetic

**Availability:** commercial laboratories, including HercepTest (Dako Corp, Carpinteria, Calif), Subsequently Pathway (Ventana Medical Systems, Tucson, Ariz)

**Specimen:** tumor tissue

**Methodology:** PCR, FISH, Northern blot, or protein overexpression via ELIZA, Western blot on cytosols or IHC

**Diseases:** breast cancer

**Clinical Uses:** The potential side effects of trastuzumab and the cost of therapy increase the importance of identifying HER2 neu overexpression. Given the latter considerations and the fact that the majority of patients with carcinoma overexpressing HER2 neu do not benefit from trastuzumab, testing may also be conceptualized as a mode of selecting patients who lack HER2 neu overexpression and thus should not be treated with anti-HER2 neu therapy.


**Marker:** trastuzumab AND HER2 neu

**Organ:** breast

**Medline Searches:** neoplasm AND trastuzumab AND HER2 neu AND breast
18. Gene Test Information: digene High-Risk HPV HC2 DNA Test, Cervical cancer

**Test Name:** digene High-Risk HPV HC2 DNA Test

**Description:** The test detects 13 high-risk human papillomavirus (HPV) types. HPV infection is associated with increased risk for cervical cancer

**Purpose:** Primary prevention, diagnostic

**Availability:** QIAGEN technologies

**Specimen:** Cervical specimens

**Methodology:** in vitro nucleic acid hybridization assay

**Diseases:** Cervical cancer

**Clinical Uses:** Diagnosis of HPV infection and risk assessment for cervical cancer

**Sources:** www1.qiagen.com

**Marker:** High-Risk HPV HC2

**Organ:** cervical

**Medline Searches:** neoplasm AND High-Risk HPV HC2 AND cervical
19. Gene Test Information: Hybritech(R) free PSA Test, Prostate cancer

**Test Name:** Hybritech(R) free PSA Test  
**Description:** In the early 1990s, it was discovered that measuring the ratio of "free" to "total" PSA could further help in distinguishing prostate cancer from benign prostate disease. The Hybritech(R) free PSA test helps determine the percent of free PSA. The measurement of percent free PSA improves the accuracy of prostate cancer detection. The free PSA test is used following a non-suspicious DRE (digital rectal examination) and a total PSA test that shows moderately elevated PSA levels (between 4 and 10 ng mL) in men aged 50 years and older.  
**Purpose:** screening, diagnostic  
**Availability:** Beckman Coulter, Inc.  
**Specimen:** Serum  
**Methodology:** Immunochemistry, dual monoclonal antibodies  
**Diseases:** Prostate cancer  
**Clinical Uses:** The manual version of the Hybritech Total PSA test was the first to be approved by the FDA for monitoring patients diagnosed with prostate cancer. Then, FDA also approved for differentiating between cancer and benign conditions in men aged 50 years and older with total PSA between 4 and 10 ng mL and negative DREs.  
**Sources:** Beckman Coulter, Inc. (http://www.beckmancoulter.com products testdetail access freepsa.asp)  
**Marker:** Free PSA  
**Organ:** Prostate  
**Medline Searches:** neoplasm AND Free PSA AND Prostate
20. Gene Test Information: ImmunoCyt(R), Bladder cancer

**Test Name:** ImmunoCyt(R)

**Description:** ImmunoCyt uses a cocktail of 3 monoclonal antibodies to detect bladder cancer cells in the urine. When combined with routine cytology, the detection rate for bladder cancer is high.

**Purpose:** monitoring of recurrent bladder cancer

**Availability:** Commercial labs

**Specimen:** Urine

**Methodology:** immunocytochemistry assay

**Diseases:** Bladder cancer

**Clinical Uses:** ImmunoCyt combines immunofluorescence method with morphological evaluation via urine cytology provides a noninvasive, highly sensitive tool for the early detection of bladder cancer recurrence. The ImmunoCyt™ test detected low-grade as well as high-grade cancers with a sensitivity ranging from 60% to 76%. Combining the two tests increased the sensitivity to over 80% for high-grade cancers and 67% for low-grade cancers.

**Sources:** FDA news, LabCorp

**Marker:** Immunocyt

**Organ:** Bladder cancer

**Medline Searches:** neoplasm AND Immunocyt AND Bladder cancer

**Test Name:** KIT Asp816Val Mutation Analysis

**Description:** Imatinib is an inhibitor of the BCR-ABL tyrosine kinase that is created by the Philadelphia chromosome rearrangement in chronic myeloid leukemia. Imatinib also inhibits the kinases encoded by the PDGFRB and KIT genes. The KIT:D816V mutation, found in many patients with aggressive systemic mastocytosis, and is associated with resistance to treatment with imatinib.

**Purpose:** Diagnosis and therapeutic management

**Availability:** Commercial labs in the US

**Specimen:** Bone marrow; whole blood

**Methodology:** allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) with fragment analysis

**Diseases:** Resistance to Imatinib therapy in chronic myeloid leukemia (pharmacogenetic test)

**Clinical Uses:** Diagnosing systemic mastocytosis and guiding imatinib therapy in chronic myeloid leukemia.

**Sources:** PharmGKb; Mayo medical Lab

**Marker:** KIT Asp816Val

**Organ:** Imatinib

**Medline Searches:** neoplasm AND KIT Asp816Val AND Imatinib
22. Gene Test Information: LBA(R)AFP-L3, Hepatocellular Cancer

**Test Name:** LBA(R)AFP-L3  
**Description:** AFP is a glycoprotein with a single glycosylation site at a specific arginine residue. AFP-L3 fraction (the glycosylation variant that binds strongest to LCA) is produced predominantly by malignant cells. Liver cancer cells that express AFP-L3 have been shown to have an increased tendency for early vascular invasion and development of intrahepatic metastasis.  
**Purpose:** Risk Assessment; Predictor  
**Availability:** Commercial Laboratories  
**Specimen:** Serum  
**Methodology:** Liquid-phase binding assay  
**Diseases:** Hepatocellular Cancer  
**Clinical Uses:** Use in the assessment of risk for the development of hepatocellular carcinoma (HCC) in patients with chronic liver diseases  
**Sources:** FDA, Labcorp  
**Marker:** alpha-Fetoproteins  
**Organ:** hepatocellular  
**Medline Searches:** neoplasm AND alpha-Fetoproteins AND hepatocellular
23. Gene Test Information: MammaPrint(R), Breast cancer

**Test Name:** MammaPrint(R)

**Description:** The MammaPrint test uses the latest in molecular technology to predict whether existing cancer will metastasize (spread to other parts of a patient's body). The MammaPrint test measures the level of activity of each of these genes in a sample of a woman's surgically removed breast cancer tumor, then uses a specific formula, known as an algorithm, to produce a score that determines whether the patient is deemed low risk or high risk for spread of the cancer to another site.

**Purpose:** Diagnosis and Prognosis

**Availability:** Commercial laboratories

**Specimen:** Breast tissue

**Methodology:** microarray analysis

**Diseases:** Breast cancer

**Clinical Uses:** Prognostic tests like the MammaPrint can measure the activity of these genes, and thus help physicians understand their patients' odds of the cancer spreading.

**Sources:** FDA, Agendia

**Marker:** MammaPrint

**Organ:** Breast

**Medline Searches:** neoplasm AND MammaPrint AND Breast
24. Gene Test Information: MGMT methylation testing, glioblastoma

**Test Name:** MGMT methylation testing

**Description:** MGMT is an enzyme found in many normal tissues, including brain. It is responsible for ensuring the quality of cellular DNA, by repairing specific types of DNA injury. Several of the common treatments for gliomas, including alkylating agents such as temozolamide and carmustine, kill cancer cells by causing selective damage to tumor DNA. If the tumor is one which expresses MGMT, this damage may be undone, and the treatment will then be less effective or completely ineffective.

**Purpose:** pharmacogenetic

**Availability:** OncoMethylome Sciences; LabCorp

**Specimen:** blood or tumor tissue

**Methodology:** immunohistochemistry

**Diseases:** glioblastoma

**Clinical Uses:** Studies have shown that brain tumors lacking MGMT (either by IHC or by assessing promoter methylation) respond better to chemotherapy than those expressing MGMT.

**Sources:** oncomethmgmt.com home MGMT_Leaflet.pdf

**Marker:** MGMT

**Organ:** brain

**Medline Searches:** neoplasm AND MGMT AND brain
25. Gene Test Information: miRview, multiple cancers

**Test Name:** miRview

**Description:** miRview mets is the a microRNA-based molecular diagnostic test designed to identify the origin of metastatic tumors, designed with Cancer of Unknown Primary (CUP) patients in mind. miRview mets identifies 25 different tumor types, including lung, ovarian, testis, and prostate cancer.

**Purpose:** diagnosis

**Availability:** Rosetta Genomics

**Specimen:** formalin-fixed paraffin-embedded (FFPE), fresh frozen, serum, saliva, urine, and other body fluid samples

**Methodology:** microRNA

**Diseases:** multiple cancers

**Clinical Uses:** Better identification of primary origin can: 1) Inform proper treatment selection 2) Spare patients unnecessary exposure to ineffective therapy

**Sources:** www.mirviewdx.com; promets.html; http://www.mirviewdx.com innerData pdf mirvie_mets.pdf

**Marker:** microRNA

**Organ:** Cancer of Unknown Primary

**Medline Searches:** neoplasm AND microRNA AND Cancer of Unknown Primary
26. Gene Test Information: NMP22(R) test kit or NMP22(R)BladderChek(R), Bladder cancer

**Test Name:** NMP22(R) test kit or NMP22(R)BladderChek(R)

**Description:** Test detects elevated levels of NMP22 protein. Healthy individuals generally have very small amounts of NMP22 protein in the urine. However, the level of NMP22 protein is often elevated in the urine of patients with bladder cancer, even at early stages of the disease.

**Purpose:** Diagnosis of early and recurrent disease

**Availability:** Commercial laboratories, urologists clinic

**Specimen:** Urine

**Methodology:** microplate enzyme immunoassay

**Diseases:** Bladder cancer

**Clinical Uses:** The test is a quantitative tool that identifies hidden or rapidly recurring disease. The test can be performed in a physician’s office with results delivered during the patient visit, allowing a rapid, accurate and cost-effective way to aid in the detection of bladder cancer in patients at risk.

**Sources:** www.matritech.com, Wampole Laboratories, FDA

**Marker:** NMP22

**Organ:** Bladder

**Medline Searches:** neoplasm AND NMP22 AND Bladder
27. Gene Test Information: Oncotype DX(R) colon cancer assay, Colon cancer (stage II)

Test Name: Oncotype DX(R) colon cancer assay

Description: The genes that are included in the Oncotype DX colon cancer assay were selected from among 760 candidate genes that were tested in more than 1,800 colon cancer patients. Oncotype DX colon cancer assay after development was further tested in 1,200 patients.

Purpose: Recurrence; secondary prevention

Availability: limited availability via Genomic Health, Inc.

Specimen: tumor tissue

Methodology: tumor tissue RNA

Diseases: Colon cancer (stage II)

Clinical Uses: Use of the Oncotype DX colon cancer assay gene expression test may allow for more accurate identification of these higher-risk patients.

Sources: genomichealth.com; google

Marker: Oncotype[All Fields] AND DX[All Fields]

Organ: colon

28. Gene Test Information: OVA1, Ovarian

**Test Name**: OVA1

**Description**: OVA1 uses a blood sample to test for levels of five proteins that change because of ovarian cancer. OVA1 then uses proprietary computer software to calculate a single numerical score based on the five protein levels. The test combines the five separate results into a single numerical score between 0 and 10 to indicate the likelihood that the pelvic mass is benign or malignant.

**Purpose**: secondary prevention, prognostic

**Availability**: commercial labs

**Specimen**: blood

**Methodology**: ND

**Diseases**: Ovarian

**Clinical Uses**: First FDA-cleared lab test for ovarian cancer that can indicate before biopsy or exploratory surgery the likelihood that the cancer is highly sensitive. The OVA1 test identifies some women who will benefit from referral to a gynecological oncologist for their surgery, despite negative results from other clinical and radiological tests for ovarian cancer. If other test results suggest cancer, referral to an oncologist is appropriate even with a negative OVA1 result. (FDA) OVA1 is only intended for women aged 18 and older who are already selected for surgery because of their pelvic mass. Interpreting test results requires knowing whether the woman has gone through menopause.

**Sources**: WebMD; Vermillion

**Marker**: proteomics

**Organ**: OVA1

**Medline Searches**: neoplasm AND proteomics AND OVA1
29. Gene Test Information: OvaCheck(TM), low-molecular-weight serum protein pattern recognition

**Test Name:** OvaCheck(TM)

**Description:** OvaCheck based on the discovery that certain diseases, like ovarian cancer, are associated with a distinct protein pattern that can help in their detection. It looks for subtle changes in patterns among the tens of thousands of proteins, protein fragments and metabolites in the blood. It then employs an artificial intelligence-based computer technology to identify these hidden patterns.

**Purpose:** diagnostic

**Availability:** Correlogic Systems, Inc.

**Specimen:** blood sample taken from a fingerstick

**Methodology:** low-molecular-weight serum protein pattern recognition

**Diseases:** Ovarian cancer

**Clinical Uses:** Despite some promising findings, many health professionals still have concerns. They would like to see more published results of the tests accuracy, and the labs that will perform the OvaCheck analyses still need to complete their own validation studies. Consequently, it will still be some time before it becomes available. Update 8 30 04:The FDA recently decided that the software used with the OvaCheck test classifies as a medical device and therefore is subject to its premarket review process. As a result, it will still be some time before OvaCheck becomes available.

**Sources:** Lab Test Online (http://labtestsonline.org news ovacheck040606.html); Correlogic (http://www.correlogic.com research-areas ovarian-cancer-faqs.php)

**Marker:** OvaCheck

**Organ:** (ovary or ovarian)

**Medline Searches:** neoplasm AND OvaCheck AND (ovary or ovarian)
30. Gene Test Information: OvaSure(TM), Ovarian Cancer

**Test Name:** OvaSure(TM)

**Description:** Synonym: Yale Ovarian Cancer Test. A six-marker ovarian cancer assay to identify candidate biomarkers to assess early stage ovarian cancer in high-risk women. Test includes leptin, prolactin, osteopontin, insulin-like growth factor II, macrophage inhibitory factor (MIF), and CA-125 in a multiplex immunoassay, and calculated risk index. Each biomarker is weighted differently in the equation, that had been validated by clinical studies. A calculated risk index of 0.50 or greater indicates a positive reading, which is suggestive of ovarian cancer.

**Purpose:** diagnostic

**Availability:** LabCorp (Laboratory Corporation of America)

**Specimen:** Serum, frozen

**Methodology:** Multiplex, bead-based immunoassay

**Diseases:** Ovarian Cancer

**Clinical Uses:** The OvaSure assay may be used as a tool to identify high-risk women who might have ovarian carcinoma. OvaSure is not indicated for a patient who is currently undergoing chemotherapy, who has had both ovaries removed, who is pregnant, or who is lactating.

**Sources:** LabCorp, OvaSure Technical Review (https://www.newlabcorp.com wps wcm connect 7e0575004abea8aa8d9cbdce2e728548 L6367.pdf?MOD=AJPERES); LabHorizons, Volume VIII, No. 6, June 2008 (http://www.labcorp.com pdf LH6_2008.pdf)

**Marker:** (Yale Ovarian Cancer Test or Ovasure)

**Organ:** (ovary or ovarian)

**Medline Searches:** neoplasm AND (Yale Ovarian Cancer Test or Ovasure) AND (ovary or ovarian)

**Test Name:** Pathwork Tissue of Origin test  
**Description:** The Pathwork Tissue of Origin test compares the genetic material of a patient’s tumor with genetic information on malignant tumor types stored in a database. It uses a microarray technology to analyze thousands of pieces of genetic material at one time. The test considers 15 common malignant tumor types, including bladder, breast, and colorectal tumors.

**Purpose:** Diagnosis  
**Availability:** Commercial Labs  
**Specimen:** Tumor tissue  
**Methodology:** Microarray or gene expression array  
**Diseases:** malignant tumor  
**Clinical Uses:** Different types of cancers are classified based on the organs in which the tumors develop. With the help of microarray technology, they will be able to classify these types of cancers in a standardized non-reader dependent manner based on the patterns of gene activity in the tumor cells

**Sources:** FDA  
**Marker:** Pathwork  
**Organ:** Tissue of origin test  
**Medline Searches:** neoplasm AND Pathwork AND Tissue of origin test
32. Gene Test Information: Progensa(TM) PCA3 Assay, Prostate cancer

Test Name: Progensa(TM) PCA3 Assay

Description: Detects overexpression of the PCA3 gene in prostatic cells in urine sample, by means of mRNA quantification. Prostatic cells enter the urine stream and are collected in the first urine stream. Overexpression of the PCA3 gene has been associated with malignancy. The test results are theorized to be independent of prostate volume. It is suggested that this test is more specific than the serum PSA antigen.

Purpose: diagnosis, prognosis and management


Specimen: Collect first urine after digital rectal exam with or without prostatic massage.

Methodology: TMA - transcription mediated amplification

Diseases: Prostate cancer

Clinical Uses: a) Routine: None. b) Investigational: add-on after digital rectal exam or PSA

Sources: www.pca3.org; www.gen-probe.com

Marker: pca3 gene

Organ: prostate

Medline Searches: neoplasm AND pca3[All Fields] AND ("research design"[MeSH Terms] OR ("research"[All Fields] AND "design"[All Fields]) OR "research design"[All Fields] OR "test"[All Fields] OR "laboratory techniques and procedures"[MeSH Terms] OR ("laboratory"[All Fields] AND "techniques"[All Fields] AND "procedures"[All Fields]) OR "laboratory techniques and procedures"[All Fields]) AND prostate
33. Gene Test Information: Septin 9 DNA methylation biomarker, Colorectal center

**Test Name:** Septin 9 DNA methylation biomarker

**Description:** A molecular-based laboratory test that can help physicians detect colorectal cancer based on a patient's blood specimen. This technology aims at detecting DNA based on specific DNA methylation patterns in blood plasma samples or other body fluids. The Septin 9 gene encodes a protein involved in cell division and is thought to play a role in the onset of cancer.

**Purpose:** diagnostic

**Availability:** Epigenomics, Quest Diagnostics

**Specimen:** blood

**Methodology:** portfolio of proprietary DNA methylation technologies and biomarkers

**Diseases:** Colorectal center

**Clinical Uses:** Septin 9 DNA methylation test acts as a supplement to conventional methods of colorectal cancer screening, including colonoscopy and fecal occult blood tests (FOBTs)

**Sources:** Epigenomics press release (http://www.epigenomics.com en Newsroom Press_Releases 2008 datednews 080219_Quest_PM.html)

**Marker:** Septin 9 DNA methylation

**Organ:** Colon

**Medline Searches:** neoplasm AND Septin 9 DNA methylation AND Colon

![Graph showing Medline hits over time](Image)
34. Gene Test Information: Tamoxitest, Breast

**Test Name:** Tamoxitest

**Description:** 7-10% of women with breast cancer may not receive the full medical benefit from taking tamoxifen due to having a version of Cytochrome P450 2D6 (CYP2D6), which reduces the effectiveness of tamoxifen and increase their chance of breast cancer recurrence.

**Purpose:** pharmacogenetic

**Availability:** Commercial laboratories

**Specimen:** buccal swab

**Methodology:** ND

**Diseases:** Breast

**Clinical Uses:** The CYP2D6 test for tamoxifen is considered appropriate for women who are taking or considering taking tamoxifen to prevent the recurrence of breast cancer. It is especially important if the patient is also taking or considering co-administration with SSRIs.

**Sources:** Genelex

**Marker:** Cytochrome P-450 OR CYP2D6

**Organ:** Tamoxifen

**Medline Searches:** neoplasm AND Cytochrome P-450 OR CYP2D6 AND Tamoxifen
35. Gene Test Information: TheraGuide 5FU (TM), Multiple

**Test Name:** TheraGuide 5FU (TM)

**Description:** Nearly 85% of 5-FU administered is metabolized by dihydropyrimidine dehydrogenase (DPD), rendering about 15% of the dose active. Variations in either the DPYD or TYMS genes that will increase the risk up to 60% during 5-FU treatment. TheraGuide 5FU (TM) comprehensive test for predisposition to 5-FU toxicity caused by variations in the DPYD and TYMS genes.

**Purpose:** Pharmacogenetic test

**Availability:** www.myriadtests.com

**Specimen:** Blood

**Methodology:** PCR

**Diseases:** Multiple

**Clinical Uses:** Identifying patients with an increased risk for toxicity to 5-FU and capecitabine

**Sources:** www.myriadtests.com

**Marker:** DPYD OR TYMS

**Organ:** capecitabine

**Medline Searches:** neoplasm AND DPYD OR TYMS AND capecitabine
36. Gene Test Information: TOP2A FISH pharmDx, Breast cancer

**Test Name:** TOP2A FISH pharmDx

**Description:** The TOP2A gene plays a role in DNA replication. The TOP2A FISH pharmDx test uses fluorescently labeled DNA probes to detect or confirm gene or chromosome abnormalities. The recurrence of cancer depends partly on certain genes whose activity may be altered by changes in the number of gene copies in the tumor. Changes in the TOP2A gene in breast cancer cells mean there is an increased likelihood that the tumor will recur or that long-term survival will be decreased.

**Purpose:** Prognosis, monitoring

**Availability:** Manufacturer: Dako Denmark A S

**Specimen:** Tumor tissue

**Methodology:** Fluorescent in situ hybridization (FISH)

**Diseases:** Breast cancer

**Clinical Uses:** The test helps in assessing the risk of tumor recurrence and long-term survival for patients with relatively high-risk breast cancer.

**Sources:** FDA news

**Marker:** (TOP2A or topoisomerase 2A)

**Organ:** Breast

**Medline Searches:** neoplasm AND (TOP2A or topoisomerase 2A) AND Breast
37. Gene Test Information: UGT1A1 Molecular Assay(TM), colorectal cancer

**Test Name:** UGT1A1 Molecular Assay(TM)

**Description:** UGT1A1 Molecular Assay is an in-vitro diagnostic test that detects two genetic polymorphisms in the UGT1A1 gene. The enzyme produced by UGT1A1 is responsible for the metabolism of irinotecan (Camptosar), a drug used in combination with standard chemotherapeutic agents in the first-line treatment of patients with metastatic colorectal cancer. The UGT1A1 Molecular Assay detects the *1 (TA6) and *28 (TA7) alleles of the UGT1A1 gene in genomic DNA. This test will help identify patients with a greater risk for irinotecan toxicity.

**Purpose:** pharmacogenetic

**Availability:** Genzyme Genetics; other commercial labs

**Specimen:** Blood

**Methodology:** in vitro nucleic acid hybridization assay

**Diseases:** colorectal cancer

**Clinical Uses:** A pharmacogenetic test for identifying patients with specific genetic mutations that have been associated with an increased risk of neutropenia after use of Camptosar (irinotecan), the antineoplastic agent used to treat metastatic colorectal cancer. The active form of irinotecan is metabolized by the polymorphic enzyme UGT1A1. UGT1A1 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as the UGT1A1*28 polymorphism. Approximately 10% of the North American population is homozygous for the UGT1A1*28 allele. Patients with reduced UGT1A1 activity are at an increased risk of experiencing grade 4 neutropenia when treated with irinotecan.

**Sources:** FDA insert: http://www.ons.org fda documents FDA93005insert.pdf

**Marker:** UGT1A1

**Organ:** colon

**Medline Searches:** neoplasm AND UGT1A1 AND colon
38. Gene Test Information: uPM3(TM) test; PCA3Plus test, Prostate cancer

**Test Name:** uPM3(TM) test; PCA3Plus test  
**Description:** uPM3(TM) is based on PCA3, a specific gene that is profusely expressed in prostate cancer tissue (on average, 34 times greater than in benign prostate tissue). No other human tissues have ever been shown to produce PCA3.  
**Purpose:** diagnostic and therapeutic application  
**Availability:** Bostwick Laboratories, DiagnoCure Inc. of Quebec  
**Specimen:** Urine  
**Methodology:** immunocytofluorescent assay and Gene expression profiling  
**Diseases:** Prostate cancer  
**Clinical Uses:** PCA3Plus(TM) tests for prostate cancer cells that are shed into the urine. The rectal exam causes cells from the patients prostate to be shed into the urine, and the urine sample, containing the released cells. If the sample is positive for PCA3, then the patient has a very high likelihood of having prostatic adenocarcinoma.  
**Sources:** www.biospace.com  
**Marker:** PCA3  
**Organ:** Prostate  
**Medline Searches:** neoplasm AND PCA3 AND Prostate