Technology Assessment

Technology Assessment Program

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

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

Technology Assessment Report

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Tufts Evidence-based Practice Center

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

This report is based on research conducted by the Tufts Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHSA 290 2007 10055 I). The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. No statement in this article 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.

The information in this report is intended to help health care decision-makers; patients and clinicians, health system leaders, and policymakers, make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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

Peer Reviewers

We wish to acknowledge individuals listed below for their review of this report. This report has been reviewed in draft form by individuals chosen for their expertise and diverse perspectives. The purpose of the review was to provide candid, objective, and critical comments for consideration by the EPC in preparation of the final report. Synthesis of the scientific literature presented here does not necessarily represent the views of individual reviewers.

Diane Allingham-Hawkins, PhD
Director, Genetic Test Evaluation Program
Hayes, Inc
157 South Broad Street
Lansdale, PA 19446-3853

David Dotson, PhD
Office of Genetics and Disease Prevention
Centers for Disease Control and Prevention
4770 Buford Highway
Atlanta, GA 30341-3724

Marta Gwinn, MD, MPH
Office of Genetics and Disease Prevention
Centers for Disease Control and Prevention
4770 Buford Highway
Atlanta, GA 30341-3724

Ira Lubin, PhD
Office of Genetics and Disease Prevention
Centers for Disease Control and Prevention
4770 Buford Highway
Atlanta, GA 30341-3724

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Executive Summary

Introduction

The Coverage and Analysis Group at the Centers for Medicare and Medicaid Services (CMS) is interested in an update report of genetic tests for cancer conditions and the accompanying database to serve as a ready reference for their internal discussions in this area as well as the source for decisions on future topics for systematic reviews. CMS requested that the Technology Assessment Program (TAP) of the Agency for Healthcare Research and Quality (AHRQ) conduct an update of genetic tests for cancer conditions that were identified since the 2006 horizon scan report on Genetic Testing for Cancer. 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 main objective of this report is to provide succinct information along with a preliminary estimate on the amount of published literature available on each identified genetic test through grey literature search since 2006. Systematic review of selected tests will be the subject of future focused reviews. The contents in the database and in this report reflect the data of genetic tests that were obtained from manufacturers' Web sites or other commercial Web sites, and should not be construed as definitive clinical evidence or as recommendations for their routine clinical use.

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. We used the terminologies and definitions from the 2008 Report of the Secretary's

Advisory Committee on Genetics, Health, and Society (SACGHS) available at http://oba.od.nih.gov/.

Inclusion criteria

We considered genetic tests that have applications in the common 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 with more applicability to the Medicare age group. We included genetic tests that are performed to aid in diagnosing, treating, predicting, prognosticating, monitor patient status and detect cancer recurrence. We also included genetic tests based on any one of the following selection 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 exclusively result in early death before reaching adulthood. We also excluded tests performed for the purpose of identifying noncancer conditions.

Clinical Applications of Genetic Tests

Genetic tests were further classified into diagnostic, prognostic, predictive, recurrence, 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) Predictive: information from the test can be used to determine or predict the response of the disease or overall outcome of the disease with treatment.
4) Recurrence: to detect disease recurrence in a patient who has already been diagnosed and treated for cancer.
5) Monitoring: test used to monitor tumor and/or patient response to treatment.

Description of grey literature sources

The contents in this section were obtained directly from manufacturers' Web sites or other commercial Web sites, and should not be considered as verified information. Some examples of grey literature sources include: GeneTests (genetests.org), Google News (news.google.com), Commercial diagnostic laboratories in the United States such as Roche Diagnostics®, Quest Diagnostics®, and LabCorp®, PHG Foundation (phgfoundation.org), EGAPP Reviews (egappreviews.org), and Association for Molecular Pathology (amp.org), and PharmGKB Web site (pharmgkb.org)

Individual test summaries

Once the list of current genetic tests was identified, 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 following items are included in the one-page

summary: Test name, Description, Purpose, Availability, Specimen, Diseases, Clinical uses, Source, Marker (Medline Search Terms), Organ (Medline Search Terms), and Exploratory PubMed search.

Description of the electronic database

We developed an in-house electronic database for efficient storage and retrieval of the aforementioned information on eligible genetic tests. We have created a My Structured Query Language (MySQL) (http://mysql.com/) database to store the collected genetic test information. The MySQL database created for this review stores and indexes all of the genetic tests. 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. 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 interfaced with PubMed so as to automatically generate the number of hits a search in PubMed turns up for a gene test over time.

Updating of the database

The horizon scanning has been ongoing as a continuous process since 2007 and the database is being continuously updated. The results of grey literature along with one-pagers are sent to AHRQ quarterly. The relevance of the genetic tests and their evolution are assessed biannually.

Results

Currently, the Gene Test Tracker database contains 112 different genetic tests logged into 161 test-disease combinations that are used in a variety of solid tumors and hematological cancers. We identified 50 new genetic tests for common cancer conditions since the 2006 report, with the largest number of tests being utilized for breast cancer, colorectal cancer, multiple cancers, lung cancer, and prostate cancer. Of these, 16 tests were identified through internet searches alone, 21 tests matured to clinical use of the 104 that were identified as tests "in development" in our 2006 report; and 13 tests were identified by experts during the peer review process. The one-page description for these newly identified genetic tests for cancer conditions can be found in Appendix A. Of the 104 tests that were identified as tests in development in our 2006 report, only 21 tests matured to full clinical use. One test (PyloriProbe) has been voluntarily withdrawn from the market, two tests that were identified as those used in the context of aspiration of cervical or breast specimens were excluded, and one test was excluded since it was identified as evaluating genetic material of infectious agent (digene High-Risk HPV HC2 DNA Test). The remaining 79 tests are currently being tracked as tests in development or in research. In addition, one test (PreGen Plus) which was identified as a test in clinical use in our 2006 report has also been withdrawn voluntarily from the market.

Discussion

We identified 50 new genetic tests available for clinical use in cancer conditions since 2006. Of these, 16 tests were identified through internet searches alone, 21 tests matured to clinical use of the 104 tests "in development" in our 2006 report; and 13 tests were identified by experts during the peer review process. 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. Potential limitations of our report include lack of empirical structure providing guidance on how to conduct optimal grey literature searches of the Internet and Internet searches are not strictly reproducible. When compared to our previous 2006 report, the methodology of grey literature search is different, in that recent horizon scanning rely only on Internet searching without further contact with the companies. Currently, this process limits our ability to identify a test with multiple commercial names (for example, a test that has been licensed from one company to another company, but carries a different commercial name for the same test) or if changes are made to a test that retains the same name (for example, when additional single-nucleotide polymorphisms are added to a test).

This report of horizon scan for genetic tests for cancer conditions, with biannual updates, adds important information on emerging tests. Currently, there are attempts by different national agencies to summarize information on genetic tests. Until the NIH registry is fully effective, the current report is a valuable source of genetic tests that are in clinical use with specific applicability to older adults. Genetic testing is a rapidly emerging field with the potential to dramatically influence clinical decision-making. Health care providers, patients, payers, decision-makers, and consumers can benefit from staying abreast of newly-released tests.

Introduction

Greater knowledge about the human genome has been gained through the completion of the Human Genome Project and by the International Haplotype Map (HapMap) project.(1) 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 decision-making tool to aid disease monitoring and prognosis of patients.

Genetic tests are now increasingly being used for the screening and diagnosis of both cancer and noncancer conditions. Those 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 that the Technology Assessment Program (TAP) of the Agency for Healthcare Research and Quality (AHRQ) 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 serve as a ready reference for their internal discussions in this area as well as the source 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 and in this report reflect the data of genetic tests that were obtained from manufacturers' Web sites or other commercial Web sites, and should not be construed as definitive clinical evidence or as recommendations for their routine clinical use.

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 (SACGHS) (http://oba.od.nih.gov/).

> "A genetic or genomic test involves an analysis of human chromosomes, deoxyribonucleic acid, ribonucleic acid, genes, and/or gene products (e.g., enzymes and other types of proteins), which is predominately used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease and health. The purpose of genetic tests includes predicting risk of disease, screening newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or populations. Excluded from the definition are tests conducted exclusively for forensic and identity purposes as well as tests conducted purely for research. Also excluded are tests that are used primarily for other purposes but that may contribute to diagnosing a genetic disease or disorder (e.g., blood smears, certain serum chemistries). For example, cholesterol screening in the general population is not considered a genetic test, but it may reveal a genetic disorder such as an inherited form of hypercholesterolemia".

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 provide diagnostic and prognostic information, monitor patient status, or detect disease recurrence.

Eligibility criteria

Inclusion criteria

Similar to the criteria listed in the 2006 horizon scan report *Genetic Testing for Cancer Conditions* (by the Tufts-EPC), we considered genetic tests that have applications in the common 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 with more applicability to the Medicare age group. We included genetic tests that are performed to aid in diagnosing, treating, predicting, 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. More recently, in consultation with the AHRQ and CMS, we included genetic tests based on any one of the following selection 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 exclusively result in early death before reaching adulthood. 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 the right drug in the right dose at the right frequency (pharmacogenomics).

Tests were further classified into diagnostic, prognostic, predictive, recurrence, 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) Predictive: information from the test can be used to determine or predict the response of the disease or overall outcome of the disease with treatment.
4) Recurrence: to detect disease recurrence in a patient who has already been diagnosed and treated for cancer.
5) 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 noncancer conditions, 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

The contents in this section were obtained directly from manufacturers' Web sites or other commercial Web sites, and should not be considered as verified information.

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 GeneTests.org reports that 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, clinical uses, and other resources from the GeneReviews section of the GeneTests.org 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 the following: “gene, genetic, genomic, pharmacogenomic, 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 weekly. We also visited the relevant laboratories that appeared in the news items to identify any new genetic tests. The Web links that identify potentially eligible tests are stored in a spreadsheet.

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 selected list of systematically queried laboratories and their Web sites can be found in Table 1. The websites of the major laboratories are visited once quarterly every year. 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. Selected list of Websites that were reviewed to identify new genetic tests for cancers

Description	*URL*
Quest Diagnostics®	http://www.questdiagnostics.com/
LabCorp®	http://www.labcorp.com/
Roche Diagnostics®	http://www.roche-diagnostics.us/
Athena Diagnostics, Inc	http://www.athenadiagnostics.com
GeneDx	http://www.genedx.com
Abbott Molecular Laboratories	http://www.abbottmolecular.com
Google News	http://news.google.com
FDA News	http://FDAnews.com
Genelex Corporation	http://www.healthanddna.com/
deCODE Genetics Inc.	http://www.decode.com/
Medical Solutions Ltd. (Nottingham)	http://www.medical-solutions.co.uk/default.aspx
PreMD, Inc. (formerly IMI International Medical Innovations)	http://www.premdinc.com/
DiagnoCure	http://www.diagnocure.com/en/index.php
Epigenomics	http://www.epigenomics.com/
Correlogic	http://www.correlogic.com/
Matritech, Inc.	http://www.matritech.com/
Agendia	http://www.agendia.com/
Caris Life Sciences	http://www.molecularprofiling.com/
Monogram Biosciences	http://www.monogrambio.com/
Bostwick Laboratories	http://www.bostwicklaboratories.com/home/
Genzyme Genetics	http://www.genzymegenetics.com/
Arup Laboratories	http://www.aruplab.com/
Wako Chemicals USA, Inc	http://www.wakousa.com/
Veridex, LLC	http://www.veridex.com/
CeMines, Inc.	http://www.cemines.com/
Dako (formerly DakoCytomation)	http://www.dako.com/
Ambrilia Biopharma Inc.	http://www.ambrilia.com/en/index.php
Clarient, Inc	http://www.clarientinc.com/

4) Other internet sites: At the direction of experts in the field of genetics, we included tests available at the following Web sites PHG Foundation (phgfoundation.org), EGAPP Reviews (egappreviews.org), and Association for Molecular Pathology (amp.org).

5) The two currently developing fields of pharmacogenetics (focuses on single genes) and pharmacogenomics (focuses on multiple genes) may provide insights into the inter-individual

variability in drug responses. We identified genetic tests from the PharmGKB Web site (pharmgkb.org) maintained by Stanford University.

Individual test summaries

Once the list of current genetic tests was identified, 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, predictive, recurrence, monitoring, and therapeutic management.

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 (Medline Search Terms): A PubMed search parameter; included the list of possible genetic test names, genes, and biomarkers that were used for Medline search strategy.

10) Organ (Medline Search Terms): A PubMed search parameter; 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 1/01/2011. 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 in-house 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 My Structured Query Language (MySQL) (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 interfaced with PubMed so as to automatically generate the number of hits a search in PubMed turns up for a gene test over time.

Updating of the database

The horizon scanning has been ongoing as a continuous process since 2007 and the database is being continuously updated. The results of grey literature along with one-pagers are sent to AHRQ quarterly. The relevance of the genetic tests and their evolution are assessed biannually. In the results section, we describe more on the evolution of previously identified genetic tests for cancer conditions.

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

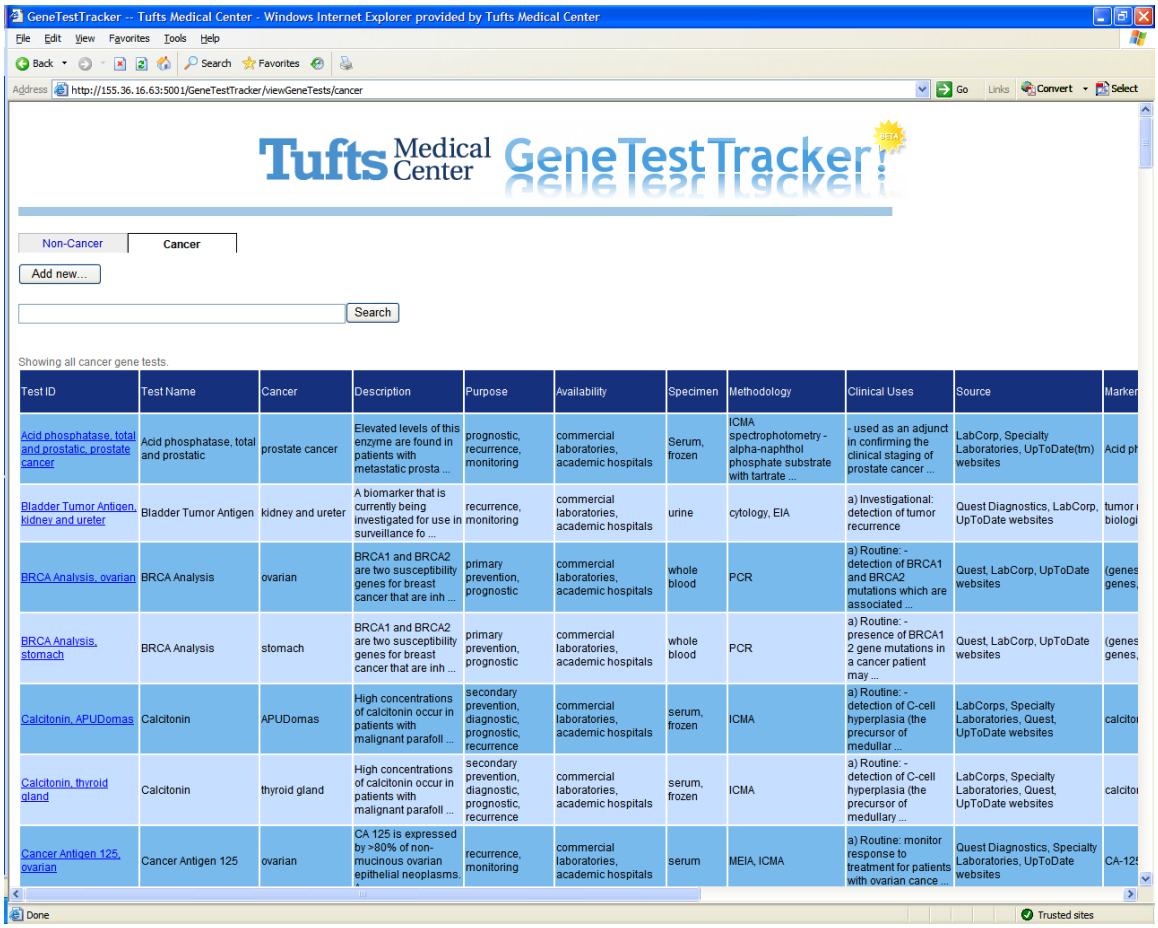

Figure 1 is a snapshot of Gene Test Tracker, the front end to the electronic database that lists genetic and genomic tests. After logging in the password-protected site, the user sees an html page depicting a table. Each row pertains to a specific test. The columns list the test name, cancer and description 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 112 different genetic tests logged into 161 test-disease combinations. We identified 50 new genetic tests for common cancer conditions since the 2006 report, with the largest number of tests being utilized for breast cancer, colorectal cancer, multiple cancers, lung cancer, and prostate cancer (Table 2). Of these, 16 tests were identified through internet searches alone, 21 tests matured to clinical use of the 104 that were identified as tests "in development" in our 2006 report; and 13 tests were identified by experts during the peer review process. 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 the 104 tests that were identified as tests in development in our 2006 report, only 21 tests matured to full clinical use (Appendix B). One test (PyloriProbe) has been voluntarily withdrawn from the market, two tests that were identified as those used in the context of aspiration of cervical or breast specimens were excluded, and one test was excluded since it was identified as evaluating genetic material of infectious agent (digene High-Risk HPV HC2 DNA Test). The remaining 79 tests are currently being tracked as tests in development or in research. In addition, one test (PreGen Plus) which was identified as a test in clinical use in our 2006 report has also been withdrawn voluntarily from the market.

Table 2: Genetic tests for cancer found between January, 2006 and February 2011

Test Name	Purpose						
	Prognostic / Predictive	Diagnostic	Monitoring	Recurrence	Therapeutic management	Primary prevention	Secondary prevention
Breast							
Breast Profile					x		
deCODE BreastCancer™	X	X					
GeneSearch™ BLN Assay	X	X					
Her2 Neu Overexpression					X		
Her2 Pro™		X			X		
MammaPrint®	X	X					
SPOT-Light ®HER2 CISH Kit					X		
Tamoxitest™					X		
TOP2A FISH pharmDx™ Kit	X		X				
Colorectal							
BRAF mutation	X	X			X		
ColonSentry™						X	
Colopath®/ColorectAlert™		X					
Cytokeratin 20(CK 20)		X					
KRAS Mutation Analysis	X						
Oncotype DX® colon cancer assay				X			X
Septin-9 DNA methylation biomarker		X					
UGT1A1 Molecular Assay™					X		
Genitourinary							
ImmunoCyt™/uCyt+™			X				
NMP22®BladderChek®		X					
Hematologic							
G6PD					X		
Heme Profile	X						
JAK2		X			X		
KIT Asp816Val Mutation Analysis		X			X		
Lung							
CellCorrect KvA-40 Lab® Kit		X					
EGFR Mutation Analysis					X		

Test Name	Purpose						
	Prognostic / Predictive	Diagnostic	Monitoring	Recurrence	Therapeutic management	Primary prevention	Secondary prevention
ELSA-CYFRA 21-1	X	X					
ERCC1					X		
KRAS Mutation Analysis	X				X		
MESOMARK®		X			X		
Ovarian							
OVA1™	X						X
OvaCheck™		X					
OvaSure™		X					
Prostate							
Bayer Immuno 1™Complexed PSA		X	X				
deCODE Prostate Cancer		X					
Hybritech Tandem-R free PSA test		X				X	
Progensa® PCA3 Assay	X	X			X		
Prostate-63						X	
uPM3™ test; PCA3Plus™ test	X	X					
*Other***							
DakoCytomation's c-Kit (9.7) pharmDx™		X			X		
LBA®AFP-L3						X	
MGMT methylation testing					X		
*Multiple****							
CellSearch®	X		X	X			
CupPrint		X					
DPD deficiency					X		
EGFR™ assay					X		
miRview™		X					
Pathwork® Tissue of Origin test		X					
PI3K	X						
TheraGuide™					X		
Tumor Profile	X						

** Other includes brain, liver, and upper gastrointestinal, respectively
*** Tests used for multiple cancers including breast, colorectal, lung, ovarian, prostate

Discussion

We performed Internet-based grey literature searches and added 50 new genetic tests available for clinical use in cancer conditions. Of these, 16 tests were identified through internet searches alone, 21 tests matured to clinical use of the 104 tests "in development" in our 2006 report; and 13 tests were identified by experts during the peer review process. 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* and many other sites identified through Google News searches. Our list encompasses both gene associations of potential biomarkers and pharmacogenomic tests using a broad definition of genetic tests put forth by the 2008 SACGHS Report. 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 within the sources we evaluated for the disease-conditions and for the population of interest.

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. The attempt to horizon scan genomic testing through Web searching has been applied by other groups.(4) When compared to our previous 2006 report, the methodology is different, in that recent horizon scanning rely only on Internet searching without further contact with the companies. Currently, this process limits our ability to identify a test with multiple commercial names (for example, a test that has been licensed from one company to another company, but carries a different commercial name for the same test) or if changes are made to a test that retains the same name (for example, when additional single-nucleotide polymorphisms are added to a test).

Our report indicates that there has been an increase in the number of genetic tests for specific common cancer conditions, and there is inherent subjectivity in identifying emerging genetic tests. Many genetic and molecular markers and panels are being associated with cancer conditions. We have selected those that are available for clinical applications in screening, diagnosis, prognosis, prediction, disease recurrence, therapeutic management, or patient monitoring as tests for cancer 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 list of genetic tests.

This report of horizon scan for genetic tests for cancer conditions, with biannual updates, adds important information on emerging tests. Currently, there are attempts by different national agencies to summarize information on genetic tests.(4;5) Until the NIH registry is fully effective, the current report is a valuable source of genetic tests that are in clinical use with specific applicability to older adults. Genetic testing is a rapidly emerging field with the potential to

dramatically influence clinical decision-making. Health care providers, patients, payers, decision-makers, and consumers can benefit from staying abreast of newly-released tests.

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

BREAST CANCER

Gene Test Information: Breast Profile (TM), Breast

Test Name: Breast Profile (TM)

Description: Breast Profile (TM) identifies a patient's HER2 status and in addition, can risk-stratify patients according to their cancer's molecular subtype association (Luminal A, Luminal B, ERBB2, Basal, Unclassified) to aid in therapeutic management. The test evaluates the tumor's overall genomic stability vs. instability for additional risk stratification of patients into Low vs. High Risk groups.

Purpose: Therapeutic management

Availability: CombiMatrix Diagnostics

Specimen: Paraffin-embedded tumor tissue block

Methodology: DNA array-based comparative genomic hybridization (aCGH) and molecular subtyping

Diseases: Breast

Clinical Uses: Detects HER2 gene status along with cancer's molecular subtyping. The test identifies an independent marker of high risk disease and poor prognosis. The potential side effects of trastuzumab and response to treatment increase the importance of identifying HER2 gene and other molecular subtypes.

Sources: combimatrix.com

Marker (Medline Search Terms): (array-comparative genomic hybridization OR DNA copy number alteration)

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND (array-comparative genomic hybridization OR DNA copy number alteration) AND Breast
Medline hits=521.

FDA Approved: No

Gene Test Information: deCODE BreastCancer, Breast cancer

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 predictive, 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 (Medline Search Terms): rs13387042 OR rs4415084 OR rs889312 OR rs13281615 OR rs1219648 OR rs3817198 OR rs3803662

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND rs13387042 OR rs4415084 OR rs889312 OR rs13281615 OR rs1219648 OR rs3817198 OR rs3803662 AND Breast
Medline hits=38.

FDA Approved: No

Gene Test Information: GeneSearch BLN Assay, Metastatic Breast cancer

Test Name: GeneSearch BLN Assay

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

Purpose: Prognostic, Predictive, 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 (Medline Search Terms): GeneSearch BLN Assay

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND GeneSearch BLN Assay AND Breast
Medline hits=8.

FDA Approved: Yes

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 ErbB 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: Therapeutic management

Availability: Commercial laboratories, including HercepTest (Dako Corp, Carpinteria, Calif), Subsequently Pathway (Ventana Medical Systems, Tucson, Ariz), Her2 Pro (TM) from Combimatrix

Specimen: Tumor tissue

Methodology: Molecular: PCR, FISH, Northern blot, or protein overexpression via ELISA, Western blot on cytosols or IHC

Diseases: Breast cancer

Clinical Uses: The potential side effects of Herceptin 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 Herceptin.

Sources: www.medscape.com

Marker (Medline Search Terms): Trastuzumab AND HER2 neu

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND Trastuzumab AND HER2 neu AND Breast
Medline hits=264.

FDA Approved: Yes

Gene Test Information: HER2 Pro(TM), Breast

Test Name: HER2 Pro(TM)

Description: HER2 Pro (TM) identifies a patient's genomic copy number changes at the DNA level. The test evaluates a complete genomic analysis of each patient's unique tumor DNA. Every breast cancer has a unique genomic aberration pattern that is associated with distinct prognostic and therapeutic characteristics. Genomic subtyping of the patient's tumor can provide significant value in the overall treatment planning and also provide additive risk assessment measures to conventional testing.

Purpose: Diagnostic, therapeutic management

Availability: CombiMatrix Diagnostics

Specimen: Paraffin-embedded tissue block, non-fragmented total DNA

Methodology: DNA array-based comparative genomic hybridization (aCGH)

Diseases: Breast

Clinical Uses: The DNA array-based karyotyping detects aneusomy of chromosome 17, which is proven to be an independent marker of high risk disease and poor prognosis. The potential side effects of trastuzumab and response to treatment increase the importance of identifying HER2 gene status.

Sources: combimatrix.com

Marker (Medline Search Terms): Array-based karyotyping OR Her2 Pro

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND (Array-based karyotyping OR Her2 Pro) AND Breast Medline hits=3.

FDA Approved: No

Gene Test Information: MammaPrint(R), Breast cancer

Test Name: MammaPrint(R)

Description: The MammaPrint test uses 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 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: Prognostic predictive, diagnostic

Availability: Commercial laboratories

Specimen: Breast tissue

Methodology: Molecular: microarray analysis

Diseases: Breast cancer

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

Sources: FDA, Agendia

Marker (Medline Search Terms): MammaPrint

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND MammaPrint AND Breast
Medline hits=40.

FDA Approved: Yes

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: Invitrogen

Specimen: Tumor tissue from breast

Methodology: Chromogenic in situ hybridization (CISH)

Diseases: Breast cancer

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

Sources: www.invitrogen.com; www.FDA.gov

Marker (Medline Search Terms): HER2 CISH

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND HER2 CISH AND Breast
Medline hits=67.

FDA Approved: Yes

Gene Test Information: Tamoxitest, Breast

Test Name: Tamoxitest

Description: About 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 increases their chance of breast cancer recurrence.

Purpose: Therapeutic management

Availability: Genelex and other 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: www.Genelex.com

Marker (Medline Search Terms): Cytochrome P-450 OR CYP2D6

Organ (Medline Search Terms): Tamoxifen

Medline Searches: neoplasm AND Cytochrome P-450 OR CYP2D6 AND Tamoxifen Medline hits=351.

FDA Approved: No

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: Prognostic predictive, monitoring

Availability: Dako

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: www.FDA.gov; www.dako.com

Marker (Medline Search Terms): TOP2A or (Topoisomerase 2A)

Organ (Medline Search Terms): Breast

Medline Searches: neoplasm AND (TOP2A or topoisomerase 2A) AND Breast
Medline hits=87.

FDA Approved: yes

COLORECTAL CANCER

Gene Test Information: BRAF Mutation Test, Colorectal cancer

Test Name: BRAF Mutation Test

Description: In colorectal adenocarcinomas and in certain other cancers, BRAF V600E acts as an oncogene driving tumor cell proliferation. Patients whose colon cancer harbored BRAF mutation had poor response to anti-EGFR therapy (e.g. panitumumab or cetuximab). BRAF mutation is found in about 14% of KRAS wild type cancers. Patients whose colon cancer harbors BRAF mutation also have a worse prognosis based on time to progression and survival data, especially when the cancer is microsatellite stable (MSS).

Purpose: Diagnosis, Prognosis, therapeutic management

Availability: Academic and Commercial laboratories

Specimen: Paraffin block of tumor cells

Methodology: Molecular: PCR

Diseases: Colorectal cancer

Clinical Uses: Useful in patients with colorectal adenocarcinoma and absent KRAS mutation, who are candidate for anti-EGFR therapy. Also is useful in the work-up of Lynch syndrome in patients with colorectal carcinomas who are having microsatellite instability (MSI-H) or loss of MLH1 protein expression.

Sources: www.unchealthcare.org; www.genzymegenetics.com

Marker (Medline Search Terms): BRAF mutation

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND BRAF mutation AND colorectal
Medline hits=365.

FDA Approved: No

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: Diagnostic

Availability: Commercial labs

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 (Medline Search Terms): (plasmalogen or colopath or colorectAlert)

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND (plasmalogen or colopath or colorectAlert) AND colorectal
Medline hits=1.

FDA Approved: No

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 (Medline Search Terms): (genes and biological markers)

Organ (Medline Search Terms): colorectal

Medline Searches: neoplasm AND (genes and biological markers) AND colorectal
Medline hits = 1122
FDA Approved: No

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: Diagnostic

Availability: Commercial Laboratories

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

Marker (Medline Search Terms): Cytokeratin 20 or CK20

Organ (Medline Search Terms): Colorectal

Medline Searches: neoplasm AND (Cytokeratin 20 or CK20) AND Colorectal
Medline hits=266.

FDA Approved: No

Gene Test Information: KRAS mutation analysis, Colorectal cancer

Test Name: KRAS mutation analysis

Description: Individuals respond differently to chemotherapeutic and targeted biologic agents. The evaluation of therapeutic markers, such as KRAS can help patients individualize cancer therapy for their patients. Recent studies have shown that assessing KRAS gene mutational status in tumor tissue can help identify patients who may not benefit from cetusimab or panitumab treatment.

Purpose: Prognostic Predictive

Availability: Genzyme genetics; other Commercial Labs

Specimen: Tumor tissue

Methodology: Single nucleotide primer extension

Diseases: Colorectal cancer

Clinical Uses: KRAS Mutation Analysis provides additional guidance in therapeutic treatment decisions for patients with metastatic colorectal cancer.

Sources: Commercial Labs

Marker (Medline Search Terms): Codons 12 and 13 of the KRAS gene

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND Codons 12 and 13 of the KRAS gene AND Colon Medline hits=8.

FDA Approved: No

Gene Test Information: Oncotype DX(R) colon cancer assay, Colon cancer

Test Name: Oncotype DX(R) colon cancer assay

Description: The Oncotype DX Colon Cancer Assay is clinically available for patients with newly diagnosed stage II colon cancer. The Oncotype DX Colon Cancer Assay is a clinically validated diagnostic assay based on an individual patient's colon tumor expression of 12 genes (seven cancer-related, five reference), which quantifies the likelihood of recurrence in stage II colon cancer in the three years following surgery. This test provides physicians with a precise assessment of the underlying tumor biology for this gene panel, and provides value beyond currently available clinical and pathological tools to quantify the risk of recurrence for each individual patient. Use of this test allows clinicians and patients to make more appropriate decisions regarding adjuvant chemotherapy, which will help maximize the benefits of treatment while minimizing the risk.

Purpose: Prognosis

Availability: Genomic Health, Inc.

Specimen: Paraffin-embedded breast tumor tissue

Methodology: RT-PCR

Diseases: Colon cancer

Clinical Uses: Oncotype DX is a prognostic assay that assesses the likelihood of cancer recurrence.

Sources: www.genomichealth.com

Marker (Medline Search Terms): Oncotype DX

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND Oncotype DX AND colon
Medline hits = 3

FDA Approved: Yes

Gene Test Information: Septin 9 DNA methylation biomarker, Colorectal center

Test Name: Septin 9 DNA methylation biomarker

Description: This test is a molecular-based laboratory test that can help physicians detect colorectal cancer based on a patients 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: The Septin 9 DNA methylation test acts as a supplement to conventional methods of colorectal cancerscreening, including colonoscopy and fecal occult blood tests (FOBTs)

Sources: www.epigenomics.com

Marker (Medline Search Terms): DNA methylation

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND DNA methylation AND Colon
Medline hits=774.

FDA Approved: No

Gene Test Information: UGT1A1 Molecular Assay(TM), Colorectal cancer

Test Name: UGT1A1 Molecular Assay(TM)

Description: The 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: Recurrence

Availability: Genzyme Genetics; other commercial labs

Specimen: Blood

Methodology: In vitro nucleic acid hybridization assay

Diseases: Colorectal cancer

Clinical Uses: The assay identifies 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 (Medline Search Terms): UGT1A1

Organ (Medline Search Terms): Colon

Medline Searches: neoplasm AND UGT1A1 AND Colon
Medline hits=20.
FDA Approved: No

GENITOURINARY

Gene Test Information: ImmunoCyt™/uCyt+™, Bladder cancer

Test Name: ImmunoCyt™/uCyt+

Description: ImmunoCyt™/uCyt+ 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: Immunocytofluorescence

Diseases: Bladder cancer

Clinical Uses: 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 increases the sensitivity to over 80% for high-grade cancers and 67% for low-grade cancers.

Sources: scimedx.com

Marker (Medline Search Terms): Immunocyt

Organ (Medline Search Terms): Bladder

Medline Searches: neoplasm AND Immunocyt AND Bladder cancer
Medline hits=29.

FDA Approved: Yes

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: Diagnostic

Availability: Commercial laboratories and academic laboratories

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 (Medline Search Terms): NMP22

Organ (Medline Search Terms): Bladder

Medline Searches: neoplasm AND NMP22 AND Bladder
Medline hits=187.

FDA Approved: Yes

HEMATOLOGICAL

Gene Test Information: G6PD deficiency, Hematologic cancers

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: Therapeutic management

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 (Medline Search Terms): Glucose-6-phosphate dehydrogenase

Organ (Medline Search Terms): Blood

Medline Searches: neoplasm AND Glucose-6-phosphate dehydrogenase AND Rasburicase
Medline hits=5.

FDA Approved: No

Gene Test Information: Heme Profile (TM), Hematological

Test Name: Heme Profile (TM)

Description: This is a DNA array-based test for detecting chronic lymphocytic leukemia (CLL) and myelodysplastic syndromes. Since tumor burden is high in the peripheral blood, CLL can be evaluated with array-based karyotyping that also detects 11q deletion. Heme Profile combines the high resolution of FISH with the genome-wide copy number assessment found in traditional cytogenetics testing.

Purpose: Prognostic

Availability: Combimatrix

Specimen: Blood or bone marrow

Methodology: Microarray and FISH analysis

Diseases: Hematological

Clinical Uses: The test delineates key genome-wide gains and losses, which equates detailed prognostic portrait of patient's tumor. It aids in monitoring for clonal evolution and disease progression.

Sources: Combimatrix.com

Marker (Medline Search Terms): array-comparative genomic hybridization

Organ (Medline Search Terms): Leukemia

Medline Searches: neoplasm AND array-comparative genomic hybridization AND Leukemia
Medline hits=390.

FDA Approved: No

Gene Test Information: JAK2, Chronic myeloproliferative disorder

Test Name: JAK2

Description: The JAK2 V617F mutation is specifically associated with chronic myeloproliferative disorders. It has been reported in approximately 97% of polycythemia vera, 57% of essential thrombocythemia and 50% chronic idiopathic myelofibrosis.

Purpose: Diagnosis, Therapeutic Management

Availability: Academic, commercial laboratories

Specimen: Bone marrow or blood

Methodology: Polymerase chain reaction (PCR), gel electrophoresis

Diseases: Chronic myeloproliferative disorder

Clinical Uses: Confirms diagnosis in individuals with clinical suspicion of myloproliferative disorders.

Sources: www.ohsu.edu pathology wardman forms jak2infosheet.pdf, www.genzymegenetics.com

Marker (Medline Search Terms): JAK2

Organ (Medline Search Terms): myeloproliferative disorder

Medline Searches: neoplasm AND JAK2 AND myeloproliferative disorder
Medline hits=421.

FDA Approved: No

Gene Test Information: KIT Asp816Val Mutation Analysis, Resistance to Imatinib therapy in chronic myeloid leukemia

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 is associated with resistance to treatment with imatinib.

Purpose: Diagnostic, therapeutic management

Availability: Commercial labs

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

Clinical Uses: Aids with diagnosing systemic mastocytosis and guiding imatinib therapy in chronic myeloid leukemia.

Sources: PharmGKb; Mayo medical Lab

Marker (Medline Search Terms): KIT Asp816Val

Organ (Medline Search Terms): Imatinib

Medline Searches: neoplasm AND KIT Asp816Val AND Imatinib
Medline hits=4.

FDA Approved: No

Lung

Gene Test Information: CellCorrect KvA-40 Cell Correct Lab clinical Dx, Lung cancer

Test Name: CellCorrect KvA-40 Cell Correct Lab Clinical Dx

Description: The test uses a bioinformatics platform, with a profiling library of 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: Commercial labs

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, the test is utilized for lung cancer diagnosis. Other potential applications include the detection and diagnosis of breast, colon, and stomach cancer.

Sources: www.medscape.com, CeMines, Inc

Marker (Medline Search Terms): Molecular fingerprinting

Organ (Medline Search Terms): Lung

Medline Searches: neoplasm AND Molecular fingerprinting AND Lung
Medline hits=32.

FDA Approved: No

Gene Test Information: EGFR Mutation Analysis, Non-Small Cell Lung Cancer

Test Name: EGFR Mutation Analysis

Description: Epidermal growth factor receptor (EGFR) mutation analysis detects EGFR gene mutations in tumor specimens of patients with non-small cell lung cancer (NSCLC) using microdissection of tumor tissue. EGFR, when activated, plays a role in cellular tumor growth and proliferation and is the target of tyrosine kinase inhibitors (TKI). Clinical studies have found that up to 20% of NSCLC tumors harbor the EGFR mutation, and that ~85% of patients with these mutations respond to TKI treatment. The molecular diagnostic procedure incorporates PCR amplification and bidirectional gene sequencing of exons 18 through 21 of the tyrosine kinase domain of the EGFR gene.

Purpose: Therapeutic management

Availability: www.genzymegenetics.com

Specimen: Tumor tissue

Methodology: Molecular: DNA sequencing

Diseases: Non-Small Cell Lung Cancer

Clinical Uses: To guide the use of EGFR-targeted tyrosine kinase inhibitor (TKI) therapy.

Sources: www.genzymegenetics.com

Marker (Medline Search Terms): (EGFR gene OR erbb-1 genes)

Organ (Medline Search Terms): Non-Small Cell Lung Cancer

Medline Searches: neoplasm AND (EGFR gene OR erbb-1 genes) AND Non-Small Cell Lung Cancer
Medline hits=736.

FDA Approved: No

Gene Test Information: ELSA-CYFRA 21-1, Non-small cell lung cancer

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: Prognostic, prognostic predictive

Availability: Cisbio Bioassays

Specimen: Serum

Methodology: Solid-phase sandwich immunoradiometric assay

Diseases: Non-small cell lung caner

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 (Medline Search Terms): Antigen CYFRA21.1

Organ (Medline Search Terms): Lung

Medline Searches: neoplasm AND Antigen CYFRA21.1 AND Lung
Medline hits=200.

FDA Approved: No

Gene Test Information: ERCC1, Non-Small Cell Lung Cancer

Test Name: ERCC1

Description: The ERCC1 (Excision Repair Cross-Complementing Rodent Repair Deficiency, Complementation Group 1) polypeptide is required for nucleotide excision repair (NER) of damaged DNA. Elevated levels have also been reported in cisplatin-resistant cells.

Purpose: Therapeutic management

Availability: Commercial laboratories

Specimen: Formalin-fixed paraffin-embedded tumor tissue samples

Methodology: Immunohistochemical staining

Diseases: Non-Small Cell Lung Cancer

Clinical Uses: ERCC1 may guide the use of plantinum-based (for e.g., cisplatin or oxaliplatin) therapy.

Sources: www.clarientinc.com; www.genzymegenetics.com

Marker (Medline Search Terms): ERCC1

Organ (Medline Search Terms): Non-Small Cell AND Lung

Medline Searches: neoplasm AND ERCC1 AND Non-Small Cell AND Lung
Medline hits=161.

FDA Approved: No

Gene Test Information: KRAS Mutation Analysis, Non-Small Cell Lung Cancer (NSCLC)

Test Name: KRAS Mutation Analysis

Description: Mutations with KRAS gene have been associated with poor prognosis, are reported in approximately 15-30% of lung carcinoma, and are associated with resistance to tyrosin kinase inhibitor treatment. KRAS Mutation Analysis analyzes codons 12 and 13 of the KRAS gene by allele-specific primer extension.

Purpose: Diagnostic, prognostic, predictive, and therapeutic management

Availability: www.Genzymegenetics.com

Specimen: Tumor tissue in fixed paraffin block with corresponding H&E slide

Methodology: Molecular:Allele-specific primer extension

Diseases: Non-Small Cell Lung Cancer (NSCLC)

Clinical Uses: The determination of KRAS mutational status of a tumor may guide therapeutic decision making for patients with NSCLC and aid in prognosis.

Sources: www.Genzymegenetics.com

Marker (Medline Search Terms): KRAS mutations or RAS oncogene

Organ (Medline Search Terms): Lung

Medline Searches: neoplasm AND (KRAS mutations or RAS oncogene) AND Lung Medline hits=2015.

FDA Approved: No

Gene Test Information: MESOMARK (R), Mesothelioma

Test Name: MESOMARK (R)

Description: The test measures soluble mesothelin related peptides in serum that may aid in the management of patients diagnosed with epithelioid or biphasic mesothelioma. Epidemiologic studies have established exposure to asbestos fibers as the primary cause of malignant mesothelioma.

Purpose: Diagnosis and therapeutic management

Availability: Arup Laboratory

Specimen: Blood (serum, plasma, or whole)

Methodology: Enzyme-Linked Immunosorbent Assay

Diseases: Mesothelioma

Clinical Uses: The test can aid in the management of patients diagnosed with epithelioid or biphasic mesothelioma.

Sources: www.aruplab.com

Marker (Medline Search Terms): Mesothelin

Organ (Medline Search Terms): Mesothelioma

Medline Searches: neoplasm AND mesothelin AND mesothelioma
Medline hits=125.

FDA Approved: Yes

OVARIAN

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 predictive

Availability: Commercial labs

Specimen: Blood

Methodology: ND

Diseases: Ovarian

Clinical Uses: OVA1 is the first FDA-cleared lab test for ovarian cancer that can indicate before biopsy or exploratory surgery, the likelihood of a highly sensitive cancer. 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 (Medline Search Terms): Proteomics

Organ (Medline Search Terms): OVA1

Medline Searches: neoplasm AND proteomics AND OVA1
Medline hits=1.

FDA Approved: Yes

Gene Test Information: OvaCheck(TM), Ovarian cancer

Test Name: OvaCheck(TM)

Description: OvaCheck is 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

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 test's 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 is classified 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. OvaCheck was developed as an additional tool for physicians for use in assessing women at high risk of ovarian cancer.

Sources: Lab Test Online (labtestsonline.org); www.correlogic.com

Marker (Medline Search Terms): OvaCheck

Organ (Medline Search Terms): (ovary or ovarian)

Medline Searches: neoplasm AND OvaCheck AND (ovary or ovarian)
Medline hits=3.

FDA Approved: No

Gene Test Information: OvaSure(TM), Ovarian Cancer

Test Name: OvaSure(TM)

Description: OvaSure(TM), also known as the Yale Ovarian Cancer Test, is a six-marker ovarian cancer assay to identify candidate biomarkers to assess early stage ovarian cancer in high-risk women. The test includes leptin, prolactin, osteopontin, insulin-like growth factor II, macrophage inhibitory factor (MIF), and CA-125 in a multiplex immunoassay, as well as a calculated risk index. Each biomarker is weighted differently in the equation previously 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 Techinal 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 (Medline Search Terms): Yale Ovarian Cancer Test or Ovasure

Organ (Medline Search Terms): Ovary or ovarian

Medline Searches: neoplasm AND (Yale Ovarian Cancer Test or Ovasure) AND (ovary or ovarian)
Medline hits=77.

FDA Approved: Yes

PROSTATE

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: Diagnostic, 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 (Medline Search Terms): Complexed Prostate Specific Antigen

Organ (Medline Search Terms): Prostate

Medline Searches: neoplasm AND Complexed Prostate Specific Antigen AND Prostate cancer
Medline hits=242.

FDA Approved: Yes

Gene Test Information: deCODE Prostate Cancer, Prostate Cancer

Test Name: deCODE Prostate Cancer

Description: deCODE Prostate Cancer analyzes 25 genetic markers that have been associated with risk of prostate cancer in published, peer-reviewed studies involving tens of thousands of patients and control subjects from multiple populations (1-48). The risk conferred by each marker compared to that of the general population has been separately derived, replicated and validated. deCODE Prostate Cancer results apply only to men of European and African-American descent as the necessary scientific information to interpret the genetic risk for individuals of other ethnicities is not available. The website only mentions about two of the 25 markers.

Purpose: Diagnostic

Availability: deCODE diagnostics

Specimen: Buccal swab

Methodology: DNA amplification, hybridization and fluorescent detection

Diseases: Prostate Cancer

Clinical Uses: deCODE Prostate Cancer is a one time test that measures genetic risk of prostate cancer and can thereby help to establish an individual's baseline risk.

Sources: deCODE diagnostics

Marker (Medline Search Terms): rs2710646 and rs1447295

Organ (Medline Search Terms): Prostate

Medline Searches: neoplasm AND rs2710646 and rs1447295 AND Prostate
Medline hits=1.

FDA Approved: No

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: Primary prevention, 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 (Medline Search Terms): Free PSA

Organ (Medline Search Terms): Prostate

Medline Searches: neoplasm AND Free PSA AND Prostate
Medline hits=2753.

FDA Approved: Yes

Gene Test Information: Progensa(TM) PCA3 Assay, Prostate cancer

Test Name: Progensa(TM) PCA3 Assay

Description: Progensa(TM) PCA3 Assay 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: Diagnostic, prognostic prediction, therapeutic management

Availability: Commercial laboratories

Specimen: First urine collection 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 (Medline Search Terms): 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])

Organ (Medline Search Terms): 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
Medline hits=60.

FDA Approved: No

Gene Test Information: Prostate-63, Prostate

Test Name: Prostate-63

Description: Monoclonal Mouse Anti-Human p63 Protein, Clone 4A4, antibody labels the nuclei of basal or progenitor cells in a variety of epithelia. The test may be a useful tool for the differential diagnosis of benign versus malignant prostatic lesions and for the identification of squamous cell carcinomas. Differential identification is aided by the results from a panel of antibodies.

Purpose: Primary prevention

Availability: Asymmetrxmedical and other commercial laboratories

Specimen: Liquid suspension of a cervical cell sample

Methodology: Immunocytochemistry

Diseases: Prostate cancer

Clinical Uses: Prostate-63 differentiates between benign and malignant prostatic lesions.

Sources: www.asymmetrxmedical.com

Marker (Medline Search Terms): Monoclonal Mouse Anti-Human p63 Protein

Organ (Medline Search Terms): Prostate

Medline Searches: neoplasm AND Monoclonal Mouse Anti-Human p63 Protein AND Prostate
Medline hits=0.

FDA Approved: No

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: Prognostic predictive, therapeutic management

Availability: Bostwick Laboratories, DiagnoCure Inc

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 contains 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 (Medline Search Terms): PCA3

Organ (Medline Search Terms): Prostate

Medline Searches: neoplasm AND PCA3 AND Prostate
Medline hits=89.

FDA Approved: No

Other

Gene Test Information: LBA(R)AFP-L3, Hepatocellular Cancer

Test Name: LBA(R)AFP-L3

Description: LBA AFP-L3 is a lab test that helps determine the risk of developing liver cancer in patients with chronic liver disease (CLD). AFP is a glycoprotein with a single glycosylation site at a specific argininne 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: Primary prevention

Availability: Wako diagnostics; other Commercial Laboratories

Specimen: Serum

Methodology: Liquid-phase binding assay

Diseases: Hepatocellular Cancer

Clinical Uses: LBA(R)AFP-L3 is used in the assessment of risk for the development of hepatocellular carcinoma (HCC) in patients with chronic liver diseases.

Sources: FDA, Labcorp

Marker (Medline Search Terms): Alpha-Fetoproteins

Organ (Medline Search Terms): Hepatocellular

Medline Searches: neoplasm AND alpha-Fetoproteins AND Hepatocellular
Medline hits=2976.

FDA Approved: Yes

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 (Medline Search Terms): c-kit tyrosine kinase

Organ (Medline Search Terms): Gastro-intestinal stromal tumors

Medline Searches: neoplasm AND c-kit tyrosine kinase AND Gastro-intestinal stromal tumors
Medline hits=17.

FDA Approved: Yes

Gene Test Information: MGMT methylation testing, Glioblastoma

Test Name: MGMT methylation testing

Description: O^6-Methylguanine-DNA methyltransferase (MGMT) is an enzyme found in many normal tissues, including the 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: Therapeutic management

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: www.oncomethmgmt.com

Marker (Medline Search Terms): MGMT

Organ (Medline Search Terms): Brain

Medline Searches: neoplasm AND MGMT AND Brain
Medline hits=363.

FDA Approved: No

MULTIPLE

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 predictive, diagnostic, monitoring

Availability: Veridex, LLC

Specimen: Whole blood

Methodology: Immunomagnetic labeling and immunofluorescent identification of cells

Diseases: Breast colorectal and prostate cancer

Clinical Uses: The CellSearch(TM) System identifies and counts circulating tumor cells in a blood sample 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. 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: www.medicalnewstoday.com; www.veridex.com

Marker (Medline Search Terms): CellSearch or Circulating tumor cells

Organ (Medline Search Terms): Breast or colorectal or prostate

Medline Searches: neoplasm AND (CellSearch or Circulating tumor cells) AND (breast or colorectal or prostate)
Medline hits=1960.
FDA Approved: Yes

Gene Test Information: CupPrint, Cancer of Unknown Primary

Test Name: CupPrint

Description: Using a database of 51 different tumor types, 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: Commercial laboratories

Specimen: Tumor tissue

Methodology: Gene expression profiling

Diseases: Cancer of Unknown Primary

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

Sources: www.ferrerincode.com

Marker (Medline Search Terms): CupPrint

Organ (Medline Search Terms): Unknown Primary

Medline Searches: neoplasm AND CupPrint AND Unknown Primary
Medline hits=2.

FDA Approved: No

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: Therapeutic management

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 (Medline Search Terms): Dihydropyrimidine deshydrogenase deficiency

Organ (Medline Search Terms): 5-Fluorouracil

Medline Searches: neoplasm AND Dihydropyrimidine deshydrogenase deficiency AND 5-Fluorouracil
Medline hits=2.

FDA Approved: No

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: Therapeutic management

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 (Medline Search Terms): Tyrosine kinase

Organ (Medline Search Terms): Multiple organs

Medline Searches: neoplasm AND Tyrosine kinase AND Multiple organs
Medline hits=54.

FDA Approved: No

Gene Test Information: miRview, Multiple cancers

Test Name: miRview

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

Purpose: Diagnostic

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 (Medline Search Terms): microRNA

Organ (Medline Search Terms): Cancer of Unknown Primary

Medline Searches: neoplasm AND microRNA AND Cancer of Unknown Primary Medline hits=33.

FDA Approved: No

Gene Test Information: Pathwork Tissue of Origin test, malignant tumor

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: Diagnostic

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, these types of cancers can be classified in a standardized non-reader dependent manner based on the patterns of gene activity in the tumor cells.

Sources: FDA

Marker (Medline Search Terms): Pathwork

Organ (Medline Search Terms): Tissue of origin test

Medline Searches: neoplasm AND Pathwork AND Tissue of origin test
Medline hits=4.

FDA Approved: Yes

Gene Test Information: PI3K, Multiple

Test Name: PI3K

Description: Activation of the phosphatidylinositol 3-kinase (PI3K)-AKT pathway, regulates many normal cellular processes which include cell proliferation, survival, and motility. PI3K signaling pathways can be deregulated by a variety of mechanisms in human tumors. Activation of the PI3K signaling pathway is frequently found in common human cancers, brought about by oncogenic receptor tyrosine kinases acting upstream, PTEN loss, or activating mutations of PI3K itself. Mutations in PI3K occur in a significant fraction of colorectal, breast, brain, lung and other tumor types. PI3K plays an essential role in tumor cell proliferation in adverse conditions as well as in invasion and metastasis.

Purpose: Prognostic and predictive

Availability: Clarient and other commercial laboratories

Specimen: Formalin-fixed paraffin-embedded tumor tissue

Methodology: Molecular: PCR

Diseases: Multiple

Clinical Uses: The test results suggest patients with tumors containing PI3K mutations may ultimately benefit from therapy directed at mutant PI3K or its downstream targets.

Sources: www.clarientinc.com

Marker (Medline Search Terms): PI3K oncogene

Organ (Medline Search Terms): neoplasm AND PI3K oncogene AND
Medline hits=1968.

FDA Approved: No

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 increase the risk up to 60% during 5-FU treatment. TheraGuide 5FU (TM) is a comprehensive test for predisposition to 5-FU toxicity caused by variations in the DPYD and TYMS genes.

Purpose: Therapeutic management

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 (Medline Search Terms): DPYD OR TYMS

Organ (Medline Search Terms): capecitabine

Medline Searches: neoplasm AND DPYD OR TYMS AND capecitabine
Medline hits=13.

FDA Approved: No

Gene Test Information: Tumor Profile, Multiple

Test Name: Tumor Profile

Description: The Tumor profile test allows identifying key amplifications and deletions across the genome. This can yield important information on key therapeutic oncogenes.

Purpose: Prognostic and predictive

Availability: Combimatrix

Specimen: Formalin fixed paraffin embedded tumor tissue

Methodology: Molecular: DNA array

Diseases: Multiple

Clinical Uses: The test is useful in a wide variety of tumors to yield prognostic and predictive information, which can further help in personalizing treatment for each individual patient.

Sources: www.combimatrix.com

Marker (Medline Search Terms): Oligonucleotide array sequence analysis OR DNA array

Organ (Medline Search Terms): Oncogene

Medline Searches: neoplasm AND (oligonucleotide array sequence analysis OR DNA array) AND Oncogene
Medline hits=2420.

FDA Approved: No

Appendix B. Tests that matured to clinical use since 2006

Name	Breast	Prostate	Lung	Colorectal	Pancreas	Ovarian	Esophagus	Liver	Lymphoma	Leukemia	Other
AFP-L3								x			
BladderChek											x
CeMines CellCorrect Lab			x								
c-Kit pharmDx											x
Colorectalert				x							
cPSA		x									
CupPrint											x
Cyfra 21-1			x								
DNA methylation (oncomethylome)		x	x			x					x
DNA methylation (second code)		x	x	x							
EGFR			x								
Immunocyt/ uCyt											x
K-ras			x	x							
MammaPrint	x										
MESOMARK											x
MGMT				x							
NMP22											x
Ovacheck						x					
Prostate 63		x									
TUO test											x
uPM3		x									