

Analysis of Proteomic and Metabolomic Patterns for Early Detection or Assessing Risk of Cancer

Effective: October 1, 2018

Next Review: November 2018

Last Review: September 2018

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Proteomics is known as protein expression profiling, while metabolomics is the assaying of substrates and by-products of enzymatic reactions. Both of these types of tests are currently being used in an effort to improve screening and early detection of cancer or assess the risk of cancer development.

MEDICAL POLICY CRITERIA

Note: This policy does not address proteomic and metabolomic tests for ovarian cancer, prostate cancer, or lung nodules, or urinary biomarker tests (see Cross References section).

Analysis of proteomic and metabolomic patterns for screening and detection of cancer or for assessing risk of cancer development is considered **investigational** for all indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. [Detection of Circulating Tumor Cells in the Management of Patients with Cancer](#), Laboratory, Policy No. 46
2. [Proteomics-based Testing Related to Ovarian Cancer](#), Laboratory, Policy No. 60
3. [Protein Biomarkers for Screening, Detection, and/or Management of Prostate Cancer](#), Laboratory, Policy No. 69
4. [Urinary Biomarkers for Cancer Screening, Diagnosis, and Surveillance](#), Laboratory, Policy No. 72
5. [Molecular Testing in the Management of Pulmonary Nodules](#), Laboratory, Policy No. 73

BACKGROUND

The genetic basis of cancer has been the focus of intense research; however, genetic mutations do not reflect the complicated interactions between individual cells, tissue, and organs. Proteins are the functional units of cells and represent the end product of the interactions among the underlying genes, and substrates and by-products of enzymatic reactions are indicators of cellular metabolic status. As such, research interest has been increasing in the fields of proteomics and metabolomics, in an effort to improve on screening and early detection efforts for malignancies.

SERUM PROTEIN BIOMARKERS

Current diagnostic and follow-up serum biomarkers in clinical oncology (e.g., prostate specific antigen [PSA, prostate cancer], CA-125 [ovarian cancer]), involve identifying and quantifying specific proteins, but limitations may include non-specificity and elevation in benign conditions.

Ovarian cancer is the leading cause of death from gynecologic malignancy in the United States; most patients present with advanced disease, which has a five-year survival rate from 15%–45%. If the disease is diagnosed in Stage I, survival rates are 95%. Therefore, there is great interest in using a biomarker to detect ovarian cancer in its earliest stages, as current screening methods are inadequate.

Serum measurements of PSA are used as a screening method for detecting prostate cancer. Very low or very high serum PSA results are most reliable in determining cancer risk. However, values often fall within a range that is nonspecific, and thus many patients end up undergoing biopsy for benign disease. Proteomics has been proposed as a technique to further evaluate cancer risk in this diagnostic gray zone.

PROTEOMICS

Proteomics involves the use of mass spectrometry to study differences in patterns of protein expression. While patterns of protein expression have been proposed to yield more biologically relevant and clinically useful information than assays of single proteins, many limitations in the use of proteomics exist.

METABOLOMICS

Metabolomics is a newly emerging field that involves the characterization of small molecule metabolites in biological systems, primarily substrates and by-products of enzymatic reactions. It can provide information regarding the metabolic status and global biochemical events associated with a cellular or biological system.

In contrast to genomics, in which amplification techniques like polymerase chain reaction (PCR) allow for the investigation of single cells, no technology is available at the protein or

metabolite level. Another issue with proteomics and metabolomics is that studies involving these methods as screening or diagnostic tools have lack of uniform patient inclusion and exclusion criteria, small patient numbers, absence of standardized sample preparations, and limited analytical reproducibility.

REGULATORY STATUS

None of the tests addressed in this policy have been submitted to the U.S. Food and Drug Administration (FDA) for marketing clearance but, if available, are offered as laboratory-developed tests by Clinical Laboratory Improvement Amendments (CLIA) licensed laboratories.

EVIDENCE SUMMARY

The potential role for proteomics and metabolomics for cancer screening and detection has undergone considerable discussion^[1-4]; however, data in the peer-reviewed literature are inadequate to permit scientific conclusions regarding colon cancer or other malignancies.

Metabolomics is still considered an emerging field and all of the published studies focus on improving the analytical and clinical validity of these tests for various oncological indications. To date, there have been no studies published on actual clinical utility of any metabolomic test.

SYSTEMATIC REVIEWS OF PROTEOMIC AND METABOLOMIC ANALYSES FOR VARIOUS TYPES OF CANCER

In 2013, Liesenfeld conducted a systematic review of mass spectrometry-based metabolomics in cancer research, including 106 studies reporting on 21 different types of cancer in seven different sample types.^[5] Only 15 out of 106 studies (14%) investigated samples from more than 100 cancer patients. Seventy-seven studies (73%) of the included studies examined the use of blood or urine with the intent of early diagnosis of cancer, with 20 studies on colon cancer, and thirteen on breast, lung and liver. The reviewers concluded that metabolomics is at a developmental stage and large-scale studies including prospective validation are needed.

A number of preliminary proteomic studies are available for many cancers including breast, lung, colorectal, gastric, pancreatic, liver, cervical, endometrial, renal, bladder, lymphoma/leukemia, melanoma, neuroblastoma, meningiomas, nasopharyngeal carcinomas, and astrocytomas.^[6-20]

PRACTICE GUIDELINE SUMMARY

AMERICAN COLLEGE OF RADIOLOGY (ACR)^[21]

The 2012 ACR guidelines on ovarian cancer screening state that although there is increased interest in proteomic screening “there is currently insufficient evidence available for determining the value of biomarkers in population-level ovarian cancer screening”.

SUMMARY

The use of proteomic and metabolomic pattern analysis for the early detection of cancer is currently in the early research phase. There is no research showing that the use of proteomic or metabolomic analysis for screening, detection, or assessing risk of disease

improves clinical outcomes compared to standard screening and diagnostic tools. In addition, there are no research-based practice guidelines that recommend proteomic or metabolomic analysis for this purpose. Therefore, the use of proteomic or metabolomic pattern analysis for the early detection of cancer or for assessing risk of cancer development is considered investigational.

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CODES

Codes	Number	Description
CPT	83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
	84999	Unlisted chemistry procedure
	0067U	Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYAL1], highly expressed in cancer protein [HEC1]), formalin-fixed paraffin-embedded precancerous breast tissue, algorithm reported as carcinoma risk score
HCPCS	None	

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