Overview

Useful For
Establishing a diagnosis of a plasma cell proliferative disorder

Providing prognostic information for newly diagnosed multiple myeloma and other plasma cell proliferative disorders

Assessing response to therapy and detecting disease relapse and progression in treated plasma cell proliferative disorder patients

Determining plasma cell DNA content and proliferation

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCINT</td>
<td>Flow Cytometry Interp, 2-8 Markers</td>
<td>No, (Bill Only)</td>
<td>Yes</td>
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Testing Algorithm
When this test is ordered, flow cytometry interpretation will always be performed at an additional charge.

The following algorithms are available in Special Instructions:

- Laboratory Screening Tests for Suspected Multiple Myeloma
- Laboratory Approach to the Diagnosis of Amyloidosis

Special Instructions

- Laboratory Approach to the Diagnosis of Amyloidosis
- Laboratory Screening Tests for Suspected Multiple Myeloma

Method Name
Flow Cytometry/DNA Content/Cell Cycle Analysis

NY State Available
Yes

Specimen

Specimen Type
Bone Marrow

Advisory Information
This test should be ordered at diagnosis of Multiple Myeloma. However, if wanting MPCPD / mSMART, Plasma Cell Proliferative Disorder (PCPD), FISH to be performed at Mayo, order MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report. The Laboratory Screening Tests for Suspected Multiple Myeloma algorithm will allow plasma cell FISH to be reflexed based on the PCPRO flow results.
Necessary Information
1. Include patient's disease state (untreated, treated, monoclonal gammopathy of undetermined significance, stable).
2. Indicate if patient is on anti-CD38 therapy.

Specimen Required
Specimen Type: Redirected bone marrow

Preferred: Yellow top (ACD)
Acceptable: EDTA or heparin

Specimen Volume: 4 mL

Specimen Stability Information: <72 hours

Forms
If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
2 mL

Reject Due To

<table>
<thead>
<tr>
<th>Hemolysis</th>
<th>Mild OK; Gross reject</th>
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<tbody>
<tr>
<td>Lipemia</td>
<td>NA</td>
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<tr>
<td>Icterus</td>
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<tr>
<td>Other</td>
<td>Fully clotted or frozen specimen</td>
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Specimen Stability Information

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<tr>
<th>Specimen Type</th>
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<th>Time</th>
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<tr>
<td>Bone Marrow</td>
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Clinical and Interpretive

Clinical Information
Plasma cell proliferative disorders are a group of plasma cell derived clonal hematologic neoplasms that exhibit a wide range of biologic activity ranging from monoclonal gammopathy of uncertain significance (MGUS), a usually indolent disorder with a low rate of disease progression, to multiple myeloma (MM), a disease that is often aggressive with poor long-term survival. Detecting plasma cell clonality through demonstrating immunoglobulin (Ig) light chain restriction (ie, the presence of either predominately kappa or predominately lambda light chains), supplemented by the plasma cell immunophenotype and DNA index, is an important element in establishing the diagnosis.
It is important to correctly classify patients with plasma cell proliferative disorders as the various disease entities are treated differently. A number of factors are used for this classification including the proportions of clonal bone marrow plasma cells, the DNA index of the clonal plasma cells, and their proliferative activity. The plasma cell DNA index and proliferation assessment by flow cytometry are rapid and reliable. This information can be used to distinguish patients with overt active MM from less aggressive diseases such as MGUS and smoldering MM.

Furthermore, in combination with other laboratory data, the results of these studies can be used as a measure of disease aggressiveness in newly diagnosed MM and also to determine therapeutic efficacy and detect disease relapse in treated MM patients.

See Laboratory Screening Tests for Suspected Multiple Myeloma in Special Instructions.

**Reference Values**

**Plasma Cell Clonality:**

Normal bone marrow

No monotypic clonal plasma cells detected

**DNA Index:**

Normal polytypic plasma cells

DNA index (G0/G1 cells): Diploid 0.95-1.05

**Interpretation**

**Plasma Cell Clonality:**

Plasma cell populations with a kappa to lambda ratio of either greater than 3.9 or less than 0.5 will be considered either kappa or lambda immunoglobulin light chain restricted (monotypic), respectively. As, in rare instances, immunoglobulin light chain restricted plasma cell populations may be polyclonal at the genetic level, the term monotypic rather than monoclonal plasma cells will be used.

In addition to immunoglobulin light chain expression, other data collected will be used to supplement the detection of abnormal plasma cell populations. In plasma cells, CD19 expression is associated with the presence of benign, polytypic cell populations. Therefore CD19 expression will be used as a secondary element in detecting clonal plasma cells. While loss of plasma cell CD45 expression is associated with neoplasia, CD45 is expressed by both normal and neoplastic plasma cells. Therefore, absence of plasma cell CD45 expression will be used as an aid in detecting abnormal plasma cells. In some plasma cell proliferative disorders there are both CD45-positive and CD45-negative subsets within the clonal cell population, therefore inclusion of antibodies to this antigen allows for more sensitive detection of both subtypes. In addition, as DNA content will be simultaneously assessed, the detection of plasma cell aneuploidy will also serve as a tool for identifying abnormal plasma cell populations. These additional phenotypic tools for identifying abnormal plasma cells will increase the sensitivity of the method beyond examining light chain expression; particularly in biclonal plasma cell proliferative disorders in which there are both kappa and lambda immunoglobulin light chain expressing subsets.

**Plasma Cell Proliferation:**

The proportion of plasma cells in S-phase will be determined by measuring the proportion of cells with DNA content between the G0/G1 and G2/M peaks. In some instances, plasma cell proliferation will not be able to be determined by this method, including when there are fewer than 300 abnormal plasma cell events and when there are multiple aneuploid plasma cell populations. In newly diagnosed multiple myeloma, a plasma cell labeling index (PCLI) of
Test Definition: PCPRO
Plasma Cell Proliferation, Marrow

greater than or equal to 3.0 is associated with a more aggressive disease course.(1,2) As there was a 100% concordance between a PCLI of greater than 3.0 and an estimated S-phase of greater than 1.5%, and this value is published standard for identifying plasma cell neoplasms with a high proliferative rate, it will be noted in the report if the estimated S-phase exceeds this value.(3,4)

DNA Index:

Processed cells are stained with DAPI to determine the DNA index of the abnormal plasma cells. This will be determined by dividing the measured DNA content of the G0/G1 abnormal plasma cells by the DNA content of the normal G0/G1 plasma cells present. For this determination, normal plasma cells are the optimal control cell population due to similarities in nuclear and overall cell size. Plasma cells with a G0/G1 DNA content index of less than 0.95 will be considered hypodiploid (worst prognosis); those with a G0/G1 DNA content index of greater than 1.05 will be considered hyperdiploid (favorable prognosis). Plasma cells with a DNA index of 1.9 to 2.1 will be considered tetraploid (nonfavorable prognosis) if a confirmatory G2/M population with a DNA index of 4 is identified. As noted above, since normal plasma cells are neither hyper- nor hypodiploid, DNA index will be used as a supplemental tool in detecting clonal plasma cells.

Percent Polyclonal Plasma Cells in Total Plasma Cells:

It has been shown that higher percent polyclonal plasma cells in total plasma cells can mean longer progression-free survival, higher response rates, and lower frequency of high-risk cytogenetics abnormalities. Studies have also shown a higher incidence of polytypic plasma cells in monoclonal gammopathy of uncertain significance and smoldering myeloma in comparison to multiple myeloma.

Caution

In order to provide an adequate specimen, it is important that the marrow specimen be from a "redirect" marrow aspirate. The marrow needle should be redirected so the marrow can be aspirated from a previously unsampled site.

Clinical Reference


Performance

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**Method Description**

Flow cytometric immunophenotyping of bone marrow is performed using the following antibodies; CD19, CD38, CD45, CD138, cytoplasmic kappa and lambda immunoglobulin, and DAPI. Plasma cell clonality is detected through demonstrating CD38 and CD138 positivity along with immunoglobulin light chain restriction (ie, the presence of either predominately kappa or predominately lambda light chains) and abnormality of CD19 and/or CD45 expression. DNA index of clonal plasma cells and their proliferation activity is determined through staining of double-stranded DNA using DAPI.

Plasma cells (monoclonal/monotypic and polyclonal/polytypic) are detected by immunoglobulin light chain restriction, surface immunophenotype, and DNA content. If present, the light chain expressed by the monotypic plasma cells is indicated. The percentage of clonal plasma cells estimated by flow cytometry is affected by specimen processing and antigen loss with specimen aging. Manual differential counting remains the accepted standard for determining the bone marrow plasma cell percentage. The percentage of monotypic plasma cells in S-phase of the cell cycle is determined by quantitative DNA analysis. The DNA index is a calculated value. The presence of more than 1 value indicates the presence of cell populations with differing DNA contents within the monotypic plasma cells.(Orfao A, Garcia-Sanz R, Lopez-Berges MC, et al: A new method for the analysis of plasma cell DNA content in multiple myeloma samples using a CD38/propidium iodide double staining technique. Cytometry 1994 Dec 1;17(4):332-339)

**PDF Report**

No

**Day(s) and Time(s) Test Performed**

Specimens are processed Monday through Sunday and reported Monday through Friday.

**Analytic Time**

1 day

**Maximum Laboratory Time**

4 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Rochester

**Fees and Codes**

**Fees**

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

**Test Classification**

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

88182-Flow cytometry, cell cycle or DNA analysis
Test Definition: PCPRO
Plasma Cell Proliferation, Marrow

88184-Flow cytometry; first cell surface, cytoplasmic or nuclear marker

88185 x 5-Flow cytometry; additional cell surface, cytoplasmic or nuclear marker (each)

88187-Flow cytometry interpretation, 2 to 8 Markers (added as FCINT)

**LOINC® Information**

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<td>Plasma Cell Proliferation, Marrow</td>
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<td>Monotypic Plasma Cells S-phase</td>
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