STANDARDIZATION FOR REPORTING CANCER BIOMARKER TEST DATA

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Challenges with Reporting Biomarker Data

- Lack of standardization (inconsistent terminologies, test names, etc. used across laboratories)
- Differences in what is included in the reports (genes tested, probes used, qualitative data, quantitative data, etc.)
- Variation among College of American Pathologist (CAP) Cancer Protocols regarding tumor markers
- Time delay between diagnosis and molecular test results
- Difficulties in aggregating and analyzing data due to
  - Disparate reporting practices
  - Lack of structured data
## Comparison of Hormone Receptor Test Results from 4 National Laboratories

<table>
<thead>
<tr>
<th>Lab</th>
<th>% staining reported</th>
<th>Scoring criteria</th>
<th>Fixative and fixation time reported</th>
<th>Clone reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Yes</td>
<td>&gt;4% Positive</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-4% Weakly positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1% Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Yes</td>
<td>≥1% Positive</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1% Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Yes</td>
<td>≥1% Positive</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1% Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Yes</td>
<td>≥1% “Favorable”</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1% “Unfavorable”</td>
<td></td>
<td></td>
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</tbody>
</table>
JAK2 Tests provided by Laboratory A

**Search For Tests**

[By Keyword] [By Condition]

JAK2

**Your Search:** Search Terms: "JAK2*"

**Found:** 7 Tests

<table>
<thead>
<tr>
<th>Test Number</th>
<th>Test Name</th>
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<tbody>
<tr>
<td>489230</td>
<td>JAK2 V617F Mutation Analysis, Qualitative, With Reflex to JAK2 Exon 12 Mutation Analysis</td>
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<tr>
<td>489200</td>
<td>JAK2 V617F Mutation Analysis, Qualitative</td>
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<tr>
<td>489212</td>
<td>JAK2 Exon 12 Mutation Analysis</td>
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<tr>
<td>489470</td>
<td>JAK2 V617F Mutation Analysis, Quantitative</td>
</tr>
<tr>
<td>150330</td>
<td>CML FISH Reflex to Qualitative JAK2 V617F Mutation Analysis</td>
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<tr>
<td>150340</td>
<td>CML FISH Reflex to Qualitative JAK2 V617F Reflex to JAK2 Exon 12 Mutation Analysis</td>
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<tr>
<td>489150</td>
<td>MPL Mutation Analysis</td>
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</table>

Displaying results 1 - 7 of 7
JAK2 Tests provided by Laboratory B

- JAK2 V617F Mutation Analysis
- JAK2 Exon 12-14 Mutation Analysis
Multiple LOINC Codes for JAK2 Test

<table>
<thead>
<tr>
<th>Score</th>
<th>LOINC</th>
<th>Component</th>
<th>Property</th>
<th>Timing</th>
<th>System</th>
<th>Scale</th>
<th>Method</th>
<th>exUC</th>
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<tbody>
<tr>
<td>35.29</td>
<td>53761-3</td>
<td>JAK2 gene.p.V617F mutanthonormal</td>
<td>RelRto</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Qn</td>
<td>Molgen</td>
<td>%</td>
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<td>28.81</td>
<td>55300-8</td>
<td>JAK2 gene exon 12 mutations</td>
<td>Prid</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Nar</td>
<td>Molgen</td>
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<td>63421-2</td>
<td>JAK2 gene exon 12 mutations tested for</td>
<td>Prid</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Nom</td>
<td>Molgen</td>
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<tr>
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<td>Prid</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Nar</td>
<td>Molgen</td>
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<tr>
<td>28.81</td>
<td>43399-5</td>
<td>JAK2 gene.p.V617F</td>
<td>Arb</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Ord</td>
<td>Molgen</td>
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<td>JAK2 gene mutation analysis</td>
<td>Prid</td>
<td>Pt</td>
<td>Bld/Tiss</td>
<td>Nar</td>
<td>Molgen</td>
<td></td>
</tr>
</tbody>
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Search generated 6 hits in 0.006 secs.
College of American Pathologists (CAP) Cancer Biomarker Reporting Committee

- CAP awarded a Centers for Disease Control and Prevention (CDC) grant to assist with:
  - Coordinating expert panels
  - Identifying and/or developing standardized terminology for cancer biomarker data
  - Developing a standardized transmission format for reporting cancer biomarker data to state cancer registries
  - Implementing a pilot with a national lab as a proof of concept

- Charge: Develop stand-alone reporting templates for cancer biomarkers (predictive and prognostic) that would replace the “Ancillary Studies” section of the CAP Cancer Protocols
Biomarker Template Development

- Form expert panel
- Review evidence and current recommendations (e.g. ASCO, NCCN)
- Draft standardized, structured report templates modeled after the College of American Pathologists (CAP) Cancer Protocols
  - Report template to include results and methods
  - Explanatory Notes
- Expert review
- Open public comment period
- Publish and maintain
Cancer Biomarker Expert Panel Representation

- College of American Pathologists
- North American Association of Central Cancer Registries
- Association of Molecular Pathology
- Centers for Disease Control and Prevention
- American Society of Clinical Oncology
- National Comprehensive Cancer Network
- Cancer Care Ontario, Canada
- American Joint Committee on Cancer
- National Cancer Registrars Association
Goals of Cancer Biomarker Reporting Committee

- Standardize terminology and report elements
- More efficient template update
- Facilitate electronic transmission of structured data using a standardized transmission format
  - Improve data aggregation and analysis
Status of Template Development

- Four templates have been developed and published on the College of American Pathologists (CAP) website:
Cancer Biomarker Templates

Template for Reporting Results of Biomarker Testing of Specimens From Patients With Carcinoma of the Breast

Template web posting date: December 2013

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For the Members of the Cancer Biomarker Working Group, College of American Pathologists
RESULTS

+ **EGFR Mutational Analysis (Note B)**
  + ___ No mutation detected (wild-type EGFR allele)
  + ___ Mutation identified (select all that apply)
    + ___ Exon 18 Gly719#
    + ___ Exon 19 deletion#
    + ___ Exon 20 insertion##
    + ___ Exon 20 Thr790Met###
    + ___ Exon 21 Leu858Arg#
    + ___ Other (specify)####:________________________
  + ___ Cannot be determined (explain):________________________

* This EGFR activation mutation is associated with response to EGFR tyrosine kinase inhibitors.

## This form of EGFR activating mutation is generally associated with resistance to EGFR tyrosine kinase inhibitors although insertions at or before position 768 can be associated with sensitivity.

### This mutation is typically secondary to other EGFR activating mutations and is associated with acquired resistance to tyrosine kinase inhibitor therapy. If seen in untreated/pretreated patients, may be present in the germline and indicate a hereditary cancer syndrome, in which case genetic counseling is suggested.

#### There is limited data on response to EGFR tyrosine kinase inhibitors for many of the uncommon EGFR activating mutations.
Lung Biomarker Template
Methods Section

+ METHODS

+ EGFR Exons Assessed (select all that apply)
  +  [ ] 18
  +  [ ] 19
  +  [ ] 20
  +  [ ] 21

+ EGFR Mutational Analysis Testing Method (select all that apply)
  +  [ ] Direct (Sanger) sequencing
  +  [ ] Pyrosequencing
  +  [ ] High-resolution melting analysis
  +  [ ] Polymerase chain reaction (PCR), allele-specific hybridization
  +  [ ] Real-time PCR
  +  [ ] Next-generation (high-throughput) sequencing
  +  [ ] Other (specify): __________________________

Note: Please specify in Comments section if different testing methods were used for different exons.
Electronic Reporting of Biomarker Templates

- All paper templates will be converted into electronic, computer-readable format to be incorporated into laboratory information systems that will result in the capture of structured data with minimal textual data.

- College of American Pathologists (CAP) electronic Cancer Checklists (eCCs) will include biomarker reporting templates.
Issues with Templates

- Length of paper templates
- Maintenance (frequency of updates)
- Rapidly changing environment that will require development of new templates for new tests
- Harmonization across templates
- Differences between solid and hematolymphoid neoplasms
Challenges with Reporting Biomarker Data

- One standardized terminology needed for reporting biomarker data (paper and electronic versions)

- Laboratories need to be able to map appropriate reference terminologies for cancer registries
  - LOINC codes exist for some tests but not all
  - Multiple LOINC codes exist for similar tests
  - No LOINC/SNOMED codes exist for results from cancer biomarker tests
Challenges with Reporting Biomarker Data

- Different report outputs
  - EGFR T790M mutation
    - EGFR Exon 20 Thr790Met Human Readable
    - NM_005228.3: c.2369C>T HGVS name*
    - Chr.7 55249071 Genome location

*Nomenclature of Human Genome Variation Society*
Current Activities

- Work with Regenstrief Institute to extend the existing LOINC model to accommodate reporting of biomarker test names and results
- Work with Integrating the Healthcare Enterprise (IHE) and a national lab to implement and test the College of American Pathologists (CAP) electronic Cancer Checklist (eCC) and biomarker reporting templates ~ to show proof of concept
  - Health Information and Management Systems Society (HIMSS) Conference
  - American Society of Clinical Oncologist (ASCO) Annual Meeting
- Map CAP biomarker reporting template data elements to NAACCR Volume V Standard for Electronic Pathology
Thank you!

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.