Neoplastic Chromosome Analysis – Bone Marrow, Peripheral Blood, Bone Core or Tumors

Chromosome Analysis for Neoplastic Disorders

Clinical Background

- Clonal genetic abnormalities are a hallmark of malignant neoplasms and a wide range of these abnormalities can be identified by cytogenetic studies.
- Chromosome abnormalities have been reported in many human neoplasms.
- In hematologic disorders, chromosomal abnormalities play an important role in the pathogenesis, prognosis, diagnosis, treatment selection and in monitoring treatment response and remission in patients.
- Cytogenetic analysis to identify an abnormal clone consistently associated with a neoplasm is used in determining the staging of solid tumors.
- Chromosomal abnormalities are used to classify various neoplastic disorders.
- Companion fluorescence \textit{in-situ} hybridization (FISH) testing with appropriate probe sets may further delineate chromosome abnormalities and assess minimal residual disease.

Epidemiology

Table 1. Incidence of representative neoplastic disorders.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence (Worldwide)</th>
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<tbody>
<tr>
<td>Chronic Myeloid Leukemia (CML)</td>
<td>1-2/100,000</td>
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<tr>
<td>Polycythemia vera</td>
<td>0.7-2.6/100,000 (increases with age)</td>
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<td>Myelodysplastic Syndromes</td>
<td>5/100,000</td>
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<tr>
<td>Acute Myeloid Leukemia (AML)</td>
<td>3/100,000 (adults); 0.7/100,000 (children)</td>
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<tr>
<td>Chronic Lymphocytic Leukemia (CLL)</td>
<td>2-6/100,000</td>
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<tr>
<td>Acute Lymphoblastic Leukemia (ALL)</td>
<td>1-4.75/100,000</td>
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<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>~ 70,000 diagnosed annually</td>
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<tr>
<td>Monoclonal Gammapathy Undetermined Significance (MGUS)</td>
<td>1-2/100 in patients &gt; 50 years</td>
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<tr>
<td>Plasma Cell Myeloma (Multiple Myeloma)</td>
<td>3-9/100,000</td>
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<tr>
<td>Neuroblastoma</td>
<td>10.5/100,000</td>
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<tr>
<td>Ewing Sarcoma</td>
<td>4/100,000</td>
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<tr>
<td>Rhabdomyosarcoma</td>
<td>2-4/100,000</td>
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</table>
Genetics

- Chromosome abnormalities are acquired during the neoplastic process. These abnormalities are found in the tumor cells. Abnormalities may be associated with chromosome rearrangement and include structural changes such as translocations, deletions, duplications or other abnormalities.
- Abnormal segregation during mitosis as a result of nondisjunction or other errors in cell division may produce monosomies, trisomies or ploidy changes.
- Certain acquired abnormalities are indicative of specific diseases.

Indications for Ordering

- Newly diagnosed hematopoietic disorders
- Follow up of hematopoietic disorders
- Newly diagnosed neoplastic disorders
- Staging of other neoplastic disorders

Interpretation

- A range of chromosome abnormalities are specifically associated with certain types of cancers.
- Presence of a normal karyotype however does not eliminate the possibility of an underlying neoplastic mutation. Submicroscopic abnormalities may be present which cannot be detected by chromosome analysis.
- In a small number of cases, a chromosomal abnormality may be associated with a congenital disorder which may not be related to the neoplastic process. Consultation with a medical genetics professional is recommended in these cases.
- Availability of clinical information facilitates in determining the appropriate type of cytogenetic study to be performed and ensures an accurate interpretation of the test.
- **Limitations:** This analysis does not eliminate the possibility of low frequency mosaicism or small structural abnormalities. Living cells are required for chromosome analysis. As such, sample quality can affect the turnaround time.

Methodology
- Tissue culture of neoplastic cells in appropriate culture medium, followed by metaphase chromosome preparation, G-banding of chromosomes and microscopic or computer analysis of available metaphases at 400-500 band level are performed.
- Additional staining techniques may be utilized.
- Results of companion FISH testing (if requested) are reported along with the chromosome analysis.

**References**