Identifying genomic markers

Oncology SNP array karyotyping
Oncology molecular karyotyping

The importance of identifying chromosome abnormalities in cancer, especially in hematolymphoid disorders, has long been well established as they provide diagnostic, prognostic, and therapeutic information critical to proper patient management. Furthermore, the identification by both conventional karyotyping and FISH of recurrent balanced or unbalanced chromosome changes in specific disorders has permitted the elucidation of the genetic mechanisms that underlie their malignant origins, thus providing the basis for the development of specific treatments. FISH panels are now routinely utilized in evaluation of hematological disorders including myelodysplastic syndrome, acute myeloid leukemia, chronic lymphocytic leukemia, pediatric acute lymphoblastic leukemia, and plasma cell myeloma. Recent advances in chromosome array technology have provided an opportunity to examine the whole genome of cancer cells at a level of resolution far greater than what is achievable by previous methods including FISH. A single nucleotide polymorphism (SNP) DNA array can detect genomic gain or loss at a very high level of resolution and can also provide genotype information which permits detection of copy number neutral loss of heterogeneity (acquired uniparental disomy or aUPD).

Clinical Utility

In the last several years, a number of different neoplastic conditions have been studied using SNP array analysis. These conditions include chronic lymphocytic leukemia, myelodysplastic syndromes, acute myeloid leukemia (especially with a normal karyotype), plasma cell myeloma, B-cell lymphomas, and solid tumors. These studies have demonstrated a greater sensitivity compared with traditional FISH studies for identifying unbalanced chromosome abnormalities. SNP array can detect complex genomic changes not apparent by either karyotype or FISH, changes which have been correlated with a poorer prognosis in most cases. As a demonstration of the clinical importance of SNP analysis in patients with hematological malignancies, Dougherty et al (2011), performed array analysis on 180 samples from children with a suspected or confirmed hematological malignancy. Of these 180 bone marrow or lymph node biopsies, 130 (72 percent) revealed aberrations not seen by karyotype. SNP array analysis has also provided valuable, and previously unattainable in a high throughput fashion, information in renal cell carcinoma, neuroblastoma and glial tumors. At the present time, there is strong supporting data to recommend the use of SNP-array karyotyping in all newly diagnosed cases of CLL, MDS, AML negative for karyotype abnormalities as well as for FLT3 and NPM1 mutations, renal cell carcinomas with equivocal histology and neuroblastoma.

Test limitations CMA cannot detect:

1. balanced chromosome rearrangements such as translocations, balanced insertions, or inversions
2. low-level mosaicism
3. an abnormality in a region not represented on the array

Patients *(Children and adults)*

Applications of SNP array analysis in oncology:

- chronic lymphocytic leukemia
- myelodysplastic syndrome/myeloproliferative neoplasm
- plasma cell myeloma
- acute lymphoblastic leukemia
- acute myeloid leukemia
- renal cell carcinoma
- neuroblastoma
- evaluate equivocal tumor histology - is the tumor benign or malignant?
- subclassify tumors based on their characteristic chromosomal gains or losses
- monitor tumor progression by identifying whether a tumor is accumulating additional chromosomal lesions over time

References

1. Dougherty, MJ (2011): Implementation of High Resolution Single Nucleotide Polymorphism Array Analysis as a Clinical Test for Patients with Hematologic Malignancies. Cancer Genet 204, 26-38.
2. Yi, JH et al (2011): Adverse Prognostic Impact of Abnormal Lesions Detected by Genome-Wide Single Nucleotide Polymorphism Array-Based Karyotyping Analysis in Acute Myeloid Leukemia with Normal Karyotype. J Clin Oncol 29(35), 4702-4708.
3. Ouillette, P et al (2011): Acquired Genomic Copy Number Aberrations and Survival in Chronic Lymphocytic Leukemia. Blood 118(11):3051-3061.

Beaumont Laboratory
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Principle of the test

At Beaumont, the CMA test utilizes the Affymetrix CytoScan HD single nucleotide polymorphism (SNP) array which can reliably detect 25-50 kb copy number changes across the genome. With more than 2 million copy number markers, including 750,000 SNPs, the Beaumont CytoScan Array offers high-density resolution of the entire genome. The Beaumont SNP array can also provide genotype information that allows for detection of copy number neutral loss of heterozygosity (uniparental disomy).

Specimen collection

One green-top (Sodium Heparin) tube. Collect 2-3 mL bone marrow (minimum: 1.0 mL) OR 5-7 mL peripheral blood (minimum: 3.0 mL). Gently invert tube to mix specimen.

Rejection criteria:

- improperly labeled specimens
- frozen specimens
- cracked or compromised specimen tubes
- specimens received greater than 72 hours past the time of collection

Test code: GSNPG

Specimen storage

Room temperature (20-25°C or 68-77°F): 24 hours

Refrigerated (2-8°C or 36-46°F): 72 hours

Frozen (-20°C/-4°F or below): Unacceptable

Physician office /draw site specimen preparation
Do not freeze specimen. Store bone marrow or peripheral blood at room temperature (20-25°C or 68-77°F) prior to courier pickup. For delays in transport (greater than 24 hours from the time of collection), refrigerate (2-8°C or 36-46°F) specimen.

Transport

Preparation for courier

Room temperature (20-25°C or 68-77°F): 24 hours

Refrigerated (2-8°C or 36-46°F): 72 hours

Frozen (-20°C/-4°F or below): Unacceptable

FedEx shipping instructions

Transport 2-3 mL bone marrow (minimum: 1 mL) or 5-7 mL whole blood (minimum: 3 mL) at room temperature. If the specimen will not be received at the testing laboratory within 48 hours of collection, transport refrigerated. Do not fix or freeze the specimen. A pathology report for the patient must be provided.

Advantages of SNP array karyotyping in oncology

- identify characteristic genomic signatures of various tumors
- helps to confirm diagnosis, predict prognosis and inform therapy decisions
- one assay - whole genome copy number and loss of heterozygosity (LOH) status
- does not require culture, can be performed on tumor samples
- creates a high-resolution picture of the tumor genome
- per chromosomal arm resolution is increased by several thousand fold when compared to FISH
- detects abnormalities missed by other techniques
- acquired uniparental disomy (UPD)/copy-number neutral LOH
- can accurately detect genomic complex malignancies

- test performed Monday through Friday
- results available within seven to 14 days
- additional time may be needed for reflex testing of abnormal results
- positive or negative for chromosome abnormality; a comprehensive interpretative report will be provided

For more information or questions about SNP Array, please contact Mark Micale, Ph.D. at 248-898-9063, or a Customer Service Agent at 800-551-0488.

Beaumont Cytogenomics Laboratory is an approved Children's Oncology Group (COG) Laboratory capable of performing all cytogenetic testing for children on COG protocols.

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