For decades, cytogenetic testing has identified disease causing structural variation in the genome. However, some cases remain clinically ambiguous due to limitations in precisely characterizing the structural nature of the identified abnormality. Mate-pair sequencing is a next-generation sequencing technology that can aid in the further characterization of chromosome abnormalities by sequencing the entire genome and bioinformatically mapping these sequences to create a comprehensive structural map.

Mate-pair’s unique library preparation method utilizes large genomic fragments that are more likely to span chromosomal breakpoints at low sequencing depth. This technique enables detection and precise mapping of chromosome rearrangements, allowing identification of genes at or near the breakpoints.

Many hematologic malignancies and solid tumors have a subset of common and/or well-characterized acquired chromosome abnormalities. However, sometimes a patient’s neoplasm is found to have one or more acquired chromosome abnormalities of uncertain significance for which no additional clinical testing is available. Mate Pair sequencing can clarify submicroscopic gene disruption or dysregulation, which may lead to better understanding of the pathogenicity and prognostic implications as well as identification of treatment options.

**USEFUL FOR:**

- Second-tier testing:
  - To clarify position, orientation, and likelihood of gene disruption of clinically ambiguous copy number gains identified by chromosomal microarray
- Determining the size, precise breakpoints, gene content, orientation, and/or any unappreciated complexity of abnormalities identified by other methodologies
- Providing important diagnostic, prognostic, and therapeutic information critical to proper patient management

**FEATURED TEST**

- MatePair, Targeted Rearrangements, Hematologic (Mayo ID: MTRBM)
- MatePair, Targeted Rearrangements, Oncology (Mayo ID: MTRTI)
CASE EXAMPLE

In this case, a patient with B-cell ALL in relapse was first tested by chromosome/karyotyping studies as well as fluorescence in-situ hybridization (FISH). Interphase FISH identified three signals for ETV6, while metaphase FISH demonstrated that the third ETV6 signal appeared to be located on chromosome 15, indicating a possible 12;15 translocation disrupting ETV6. This translocation was not identified by karyotyping and is therefore “cryptic,” and no additional FISH probes were available to attempt to determine the partner gene. MTRBM was performed and indicated an ETV6/NTRK3 rearrangement. This finding allowed the use of novel, targeted chemotherapeutic agents (tyrosine kinase inhibitors such as crizotinib) in this patient’s treatment regimen.

SAMPLE REQUIREMENTS

MTRBM
- Specimen Type: Whole blood or bone marrow
  - Container/Tube: Green top (sodium heparin)
  - Specimen Volume: 1-2 mL bone marrow or 7-10 mL whole blood

MTRTI
- Specimen Type: Tumor biopsy, lymph node, skin biopsy, snap frozen tissue, cryo-frozen tissue, cultured cells
  - Container/Tube: Green top (sodium heparin)
  - Specimen Volume: > 3cm³ (biopsy), >1cm³ (lymph node), >4mm diameter (skin biopsy),

LIMITATIONS

- This testing is not amenable to detection of single nucleotide variants (SNVs)
- Analysis and interpretation are limited to the previously identified variant (targeted)
- Low-level acquired abnormalities (present in less than approximately 20% of cells) may not be detectable by current Mate Pair methods
- In rare instances, some rearrangements, particularly those involving highly repetitive regions, may not be detectable by current Mate Pair methods

CLINICAL REFERENCES


For additional information, please contact a genetic counselor in the Genomics Laboratory, Cytogenetics area at 507-284-1668 or gccytogenetics@mayo.edu with any additional questions. Genetic counselors are available Monday through Friday from 8 am to 5 pm CST.

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