Guidelines from WHO, NCCN and others, for the genetic analysis of hematological malignancies included structural variation analysis. Traditionally, this has relied on a combination of three cytogenetic technologies for structural variation analysis: karyotyping, FISH, and microarray. These methods are also applied for mutation analysis but have not been successful for structural variation analysis. These traditional methods have many very manual aspects and require extensive expertise. Optical genome mapping (OGM) consolidates assays into a single laboratory assay in which the output provides the visualization of structural and copy number variants at one time.

OGM is able to comprehensively detect structural variations genome wide down to 5% variant allele fraction for CNVs, inversions, and translocations from blood and bone marrow aspirates making it an attractive choice for hematologic malignancy genomic analysis. Preanalytical and analytical steps require approximately 4-5 days from sample to processed data with structural variation calls. Dynamic filtering in the user interface can be configured to remove most polymeric variants and prioritize relevant variants. In addition, the OGM graphical user interface software, Bionano Access 1.7, allows for the user to assign classification/relevance to the variants for each case. For example, an ALL sample with t(9;22), deletion of CDKN2A, and whole chromosome gains of 4, 6, and 10 can easily be visualized with the Circos plot and, then, can be further examined and annotated as needed. A second analyst can repeat the process blind to the first analysis and a supervisor can adjudicate the classifications. A variety of cases with hallmark abnormalities from various leukemias will be presented with the filtering and prioritization workflow used to derive them. This comprehensive technology allows for a quicker, more reliable output than traditional cytogenetic approaches.

**Virtual Panels**

All classes of structural variations can be detected by OGM in a single assay. Above, deletions, amplifications, inversions, and translocations are shown to represent all variants recommended by the National Comprehensive Cancer Network (NCCN).

### Acute Myelogenous Leukemia

**Chr5, 5q**
- **CfDL deletion seen through copy number loss indicated by red shaded box covering 5p13.1-5p15.1.** In addition, the fusion across the deletion is shown through alignment of the fusion map to 5p15.1 and 5q13.1 (circled).

**Chr7, 7q**
- **EDN deletion seen through copy number loss indicated by the red shaded box covering 7q36.3-q31.2.** The fusion across the deletion is shown through alignment of the fusion map to 7q36.3 and 7q31.2 (circled).

**t(11q23) (KMT2A/MLL)**
- **M新鲜A/MLL is amplified in this case, the CN profile shown a copy number gain (circled).**

**t(8;21) (RUNX1/RUNX1T1)**
- **Amplified** in this case, the CN profile shown a copy number gain (circled).

### Chronic Myelogenous Leukemia

**BCR/ABL**
- **Fusion between BCR and ABL1 is seen by the blue case's map aligning to ABL1 on the right/top and BCR on the bottom/left.**

**Trisomy8**
- **Trisomy 8 is called with whole genome CNV profile based on molecule counts across the genome. This case also has +8, +14.**

### Acute Lymphocytic Leukemia

**IGH**
- **Fusion between BCR and ABL1 is seen by the blue case's map aligning to ABL1 on the right/top and BCR on the bottom/left.**

**Trisomy8**
- **Trisomy 8 is called with whole genome CNV profile based on molecule counts across the genome. This case also has +8, +14.**

**Publications**

- OGM allows for the detection of all classes of structural variations occurring in the human genome
- Removes the need for tiered testing as part of a clinical work-up
- OGM can pick up all actionable SVs as per NCCN/WHO guidelines
- Bionano’s Access software solution - ease of use
- Graphical user interface allows filtering and manual evaluation on a per SV basis including access to raw data support
- Fast TAT (sample to answer in 4 days)
- Multiple studies have demonstrated 100% concordance with cytogenetic methods (karyotype, microarray, FISH) for constitutional and hematologic malignancy
- Multiple studies showing increase in diagnostic yield against the standard of care in pediatric and heme