Optical Genome Mapping service

Take advantage of our expertise in the detection of genome-wide structural variations in an unbiased manner, offering considerably higher sensitivities when compared to sequencing-based technologies (Next Generation Sequencing, NGS) and classic cytogenetic techniques.

Introduction

The Optical Genome Mapping (OGM) method finds widespread applications among genomics laboratories, research institutions, and biotechnology companies. It serves various research purposes, including:

- **Constitutional Genetic Disorders**: OGM excels in detecting genome-wide Structural Variations (SVs) at a resolution over 10,000 times higher than karyotyping. This makes it a valuable tool for studying and understanding genetic disorders.
- **Hematologic Malignancies**: OGM is employed to detect genome-wide Copy Number Variations (CNVs) and fusions in hematologic malignancies, including identification of fusion partners. This aids in the comprehensive analysis of genetic abnormalities associated with blood cancers.
- **Gene Discovery and Therapy**: OGM plays a crucial role in gene discovery and therapy development by identifying genes of interest, determining their locations, and assessing the impact of SVs on them. This information is vital for the effective development of therapeutic interventions.
- **Cell Bioprocessing Quality Control**: OGM is utilized for quality control in cell bioprocessing, enabling the detection of transgenes and identification of undesired genomic changes introduced during cell culturing. This ensures the integrity of cell lines used in biotechnological processes.
- **Solid Tumor Research**: OGM facilitates the detection of somatic rearrangements in heterogeneous tumors at a variant allele fraction as low as 5 %. This capability is essential for advancing research in understanding and treating solid tumors.

In summary, Optical Genome Mapping is a versatile method that contributes significantly to advancing genomic research and applications across various domains, offering high-resolution insights into genomic structures and variations.

IAB Expertise

Numerous successfully executed service projects enabled us to be number one in the sample preparation for Optical genome mapping, its labeling, and optimizations proceeding in close cooperation with the customers. Using second-generation Bionano Kits, with robust enhancements and optimizations to OGM workflow allows us to extract and label ultra-high molecular weight (UHMW) DNA for analysis with the Saphyr system.

Material and Methods

Protocol

Sample preparation

The most recent Bionano SP DNA preparation kits demonstrate the ability to extract (UHMW) DNA from a variety of sources, including tissue, tumors, bone marrow aspirate (BMA), blood, cells, as well as plant and animal tissues.

To initiate the process with Bionano's SP kits, 1.5 * 10^6 cells (applicable to blood, cell lines, and BMA) or 10–30 mg of tissue is required as input. The isolation of UHMW DNA takes approximately four hours and involves a lyse, bind, and wash procedure utilizing innovative paramagnetic disks.

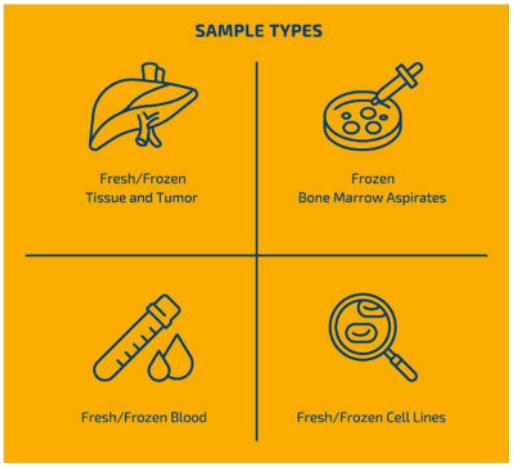

Figure 1: Important sample types for isolation of HMW DNA

Sample QC

- Quantification HMW DNA (QUBIT dsDNA BR Assay kit): typical gDNA concentration is 45-90 ng/µl with a Coefficient of Variation (CV) of ≤ 0.30 (recommended).

Labelling of UHMW DNA

During the labeling process, the fluorescent labels are affixed to a 6-base pair sequence motif. This motif appears, on average, 20 times per 100 kb pairs in the human genome. The attachment of fluorescent labels employs direct label and stain technology (DLS), a nondestructive process that preserves the integrity of DNA samples. The outcome is a distinct genome-specific labeling pattern that facilitates de novo map assembly, the anchoring of sequencing contigs, and the identification of structural variations, with resolution of 500 base pairs.

- Quantification labeled DNA (QUBIT dsDNA HS Assay kit): The labeled gDNA concentration should ideally fall between 4-16 ng/µl with a Coefficient of Variation (CV) of ≤ 0.30 (recommended).

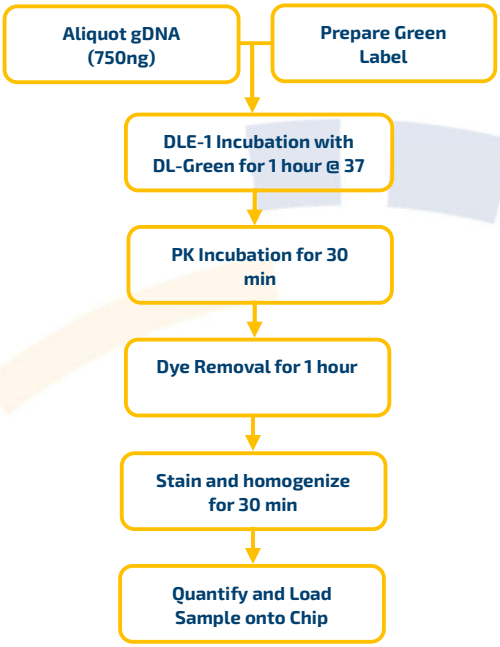

Figure 2 Bionano Prep DLS-G2 Overview

Linearizing of UHMW DNA for single-molecule Imaging

Bionano Saphyr Chip consumables utilize hundreds of thousands of parallel nanochannels that linearize long, labeled DNA molecules, allowing the Saphyr system to directly image your samples.

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Molecule Quality report

- Automatically generated by the Saphyr system
- Defined run quality metrics: average label density per 100kbp, DNA throughput per scan, average map rate, estimate effective coverage, average N50 (≥150kbp).

Figure 3 Saphyr Chip's Nanochannels Linearize UHMW DNA for Single-molecule Imaging

Results

When your high-resolution genomic mapping service is completed, data are delivered through the Bionano Access software. Raw molecular data, assemblies, and variant annotations are uploaded to a Bionano Access server. Genome mapping technology interactively visualizes, filters, classifies, and curates variants of interest, as well as generates reports.

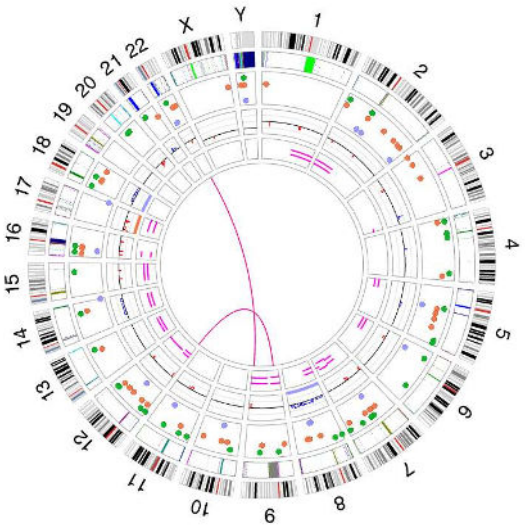

Figure 4 Circos plot from OGM indicating Philadelphia chromosome

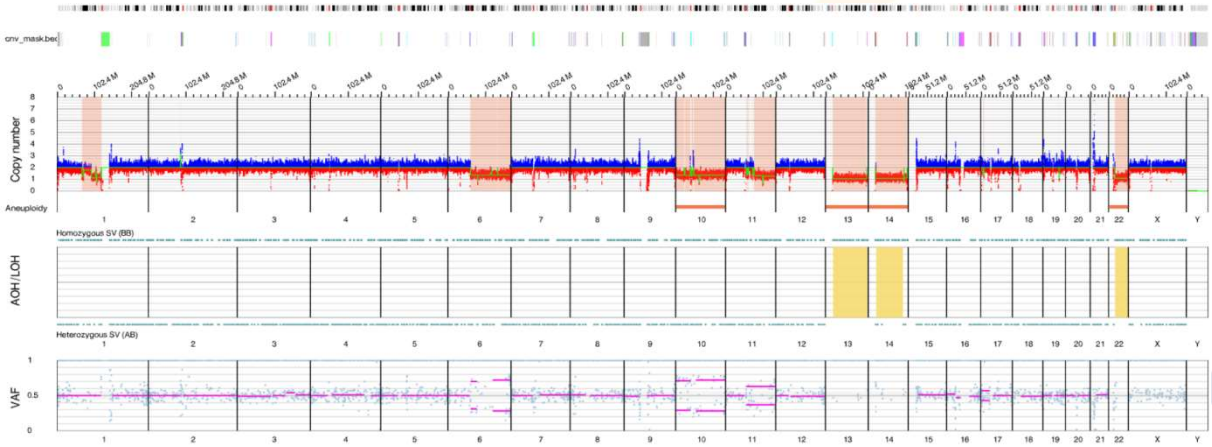

Figure 5 Visualisation of OGM results with BionanoAccess Software; copy number track indicating aneuploidy on chr 10, 13, 14 and 22. AOH/LOH track visualize Loss of Heterozygosity on chr 13 and 14

Conclusion

The genomic coverage achieved with the Saphyr system is flexible and allows for the detection of heterozygous variants or rarer variants found in mosaic samples and heterogeneous tumors. Running samples at 400X coverage provides SV detection down to 5 % VAF.

By combining of OGM with sequencing, researchers achieve more comprehensive variant calls. This approach involves using sequencing for single nucleotide variants and indels alongside OGM for whole genome SV detection, providing a multidimensional genomic analysis.

IAB Laboratories provide access to Optical Genome Mapping (OGM) services for researchers, clinicians, and pharmaceutical companies with a variety of applications. Each service project includes a presentation on OGM data review and a demonstration of the Bionano Access software. If you require additional training on the analysis software, our team is ready for further guidance and support. You are also welcome to our facility to take part in processing of your samples as a hand-on workshop.