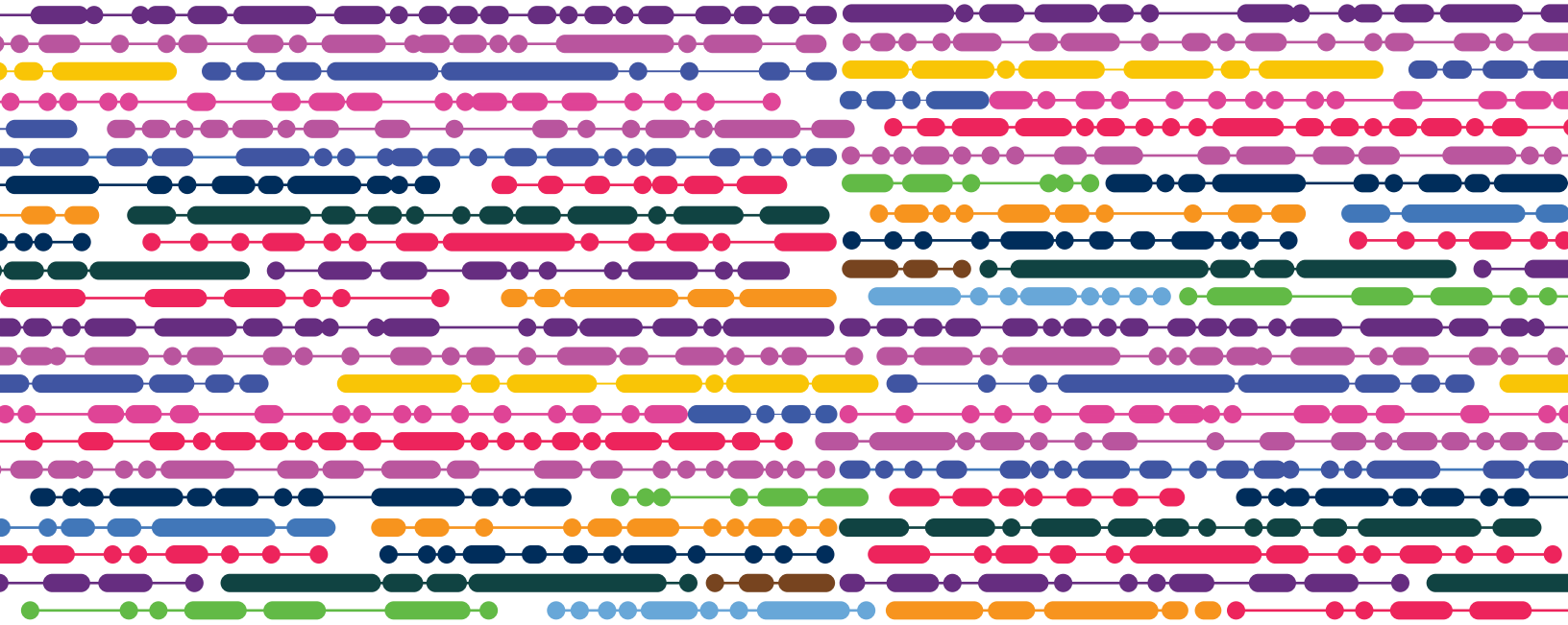
Product Brochure



CHROMIUM™

Genome Solution

10xGenomics.com/genome

CHROMIUM™

Genome Solution

Discover What You Have Been Missing

- Long-range information from a short-read Illumina sequencer
- High-quality libraries from as little as 1 ng of genomic DNA
- Turn-key analysis pipeline and visualization tools
- Call and phase major classes of structural variants (SVs) like deletions, inversions, and translocations, even in genes inaccessible to short-read sequencers
- Phase SNVs, indels and SVs across >10 Mb haplotype blocks

Introduction

The Chromium Genome Solution uses the power of Linked-Reads to fully resolve genic phasing, structural variation, and detect variants in previously inaccessible and complex regions of the genome.

The Chromium™ Genome Solution

Powered by the GemCode™ Technology, the Chromium™ Genome Solution massively partitions and molecularly barcodes DNA using microfluidics, producing sequencing-ready libraries with >1,000,000 unique barcodes. After molecular barcoding, fragments are pooled and undergo standard library preparation. Final libraries are compatible for sequencing on most Illumina systems, including the HiSeq X. The Chromium Software Suite, which includes the Long Ranger™ software package and the Lariat™ Aligner, provides turn-key analysis pipelines and visualization tools utilizing Linked-Read data.

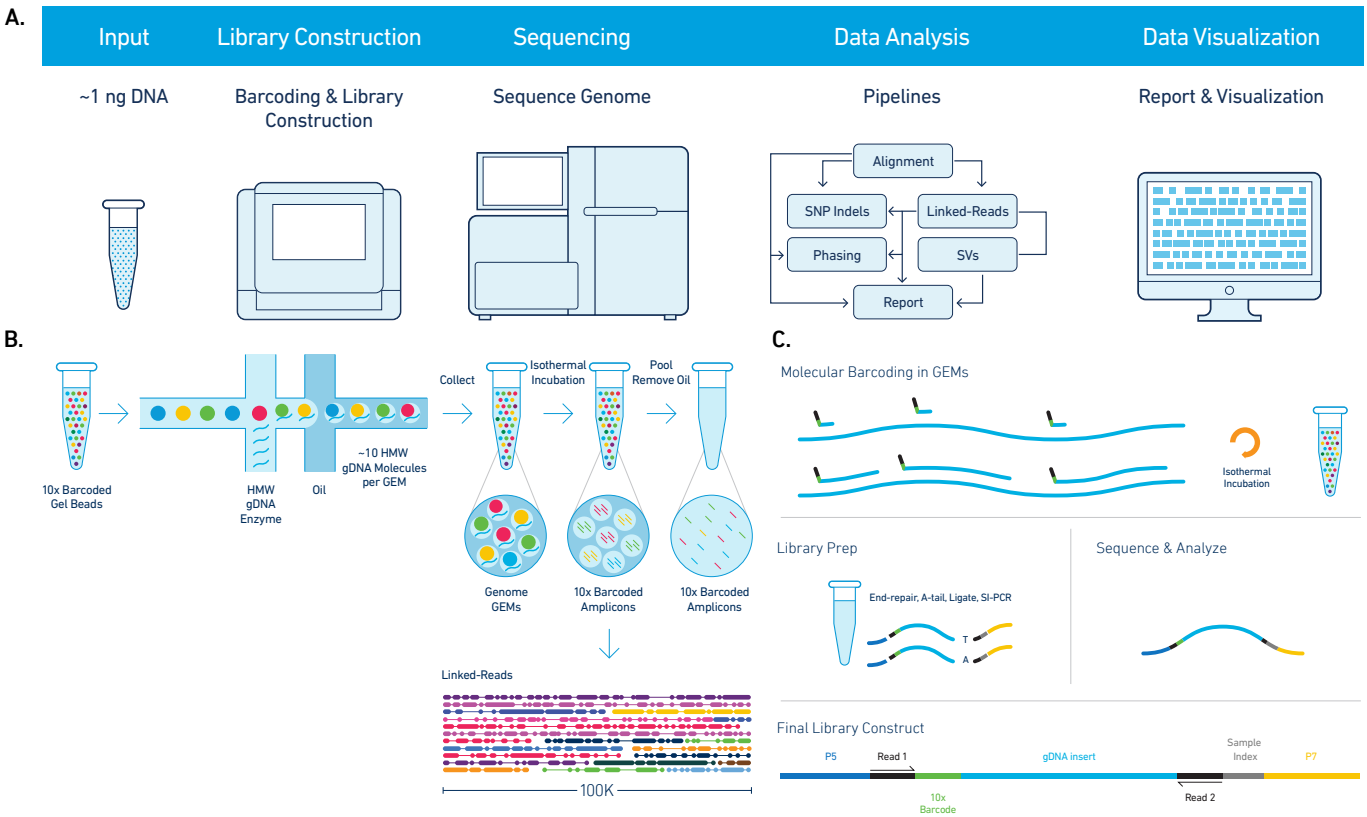


Figure 1. Chromium™ Genome Solution. (a) The Chromium Genome Solution provides a streamlined workflow and easy-to-use informatics pipeline and software for whole genome analysis. (b) An automated microfluidic system allows for functionalized gel beads to be combined with high molecular weight DNA (HMW gDNA) and oil to form a 'Gel Bead in Emulsion (GEM)'. Each GEM contains ~10 molecules of HMW gDNA and primers with unique barcodes. Isothermal incubation allows for the addition of a unique barcode to all DNA within the GEM. (c) Assay schematic overview.

Achieve Equivalent Performance with Only ~1 ng of High Molecular Weight DNA

10x libraries demonstrate equivalent performance to standard short-read libraries with more than 100-fold lower DNA input amounts.

	10x Genomics Chromium™ Genome	Standard PCR-Free Library
Input DNA	1.25 ng	200 ng
Sequencing	130 Gb	100 Gb

Technical Performance

The Chromium Genome Solution provides comparable coverage evenness to standard PCR-free libraries. Moreover, sensitivity and positive predictive value (PPV) for small variant (SNP) calling is approximately 99%.

Coverage Evenness

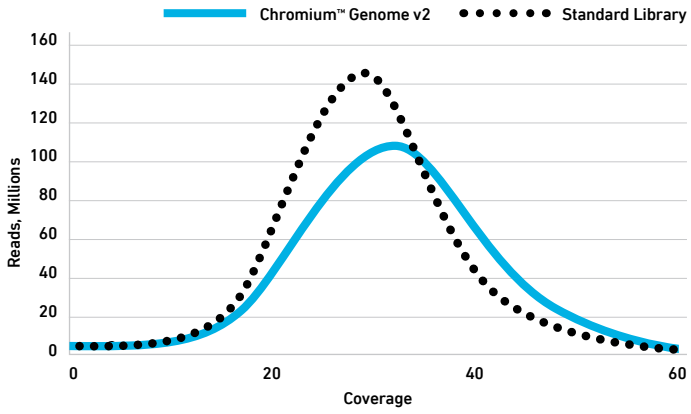


Figure 2. Coverage of NA12878 for 128Gb Chromium™ Genome v2 Solution library versus 100 Gb standard PCR-Free library. Calculations were performed using Genome in a Bottle (GIAB) confident regions calculated on the NA12878 genome.

Chromium™ Genome Variant Calling

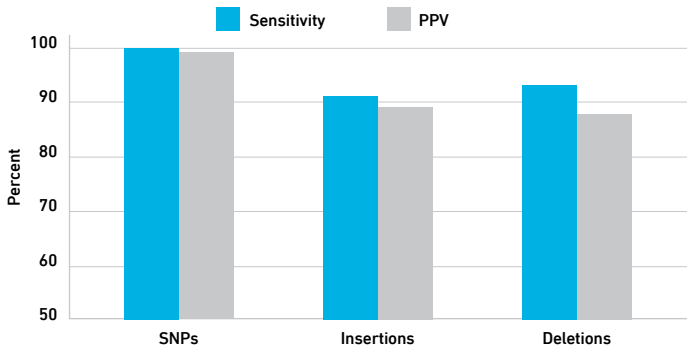


Figure 3. Sensitivity and positive predictive value (PPV) metrics for Chromium™ Genome Solution libraries. Calculations were performed using Genome in a Bottle (GIAB) confident regions calculated on the NA12878 genome.

The Lariat™ Aligner

Roughly 5% of the genome is contained in segmental duplications that are often problematic for accurate short-read mapping and variant calling. The Chromium Genome Solution includes the Lariat™ Aligner, which leverages 10x Linked-Reads to resolve many of these problematic genomic areas. The Lariat Aligner links reads in difficult regions that share a barcode with those in flanking confident regions to anchor them. This capability greatly increases the ability to accurately assign a read to the correct region and allows for the calling of SNPs, indels, and structural variants in these regions, while maintaining comparable performance in currently accessible genomic regions.

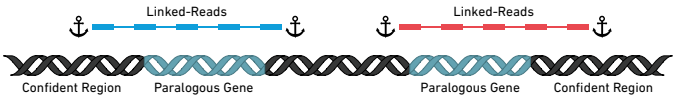


Figure 4. The Lariat™ Aligner. Long Ranger's Lariat Aligner is able to recover new genomic content by anchoring short reads to confident regions and using Linked-Reads to reach into difficult regions.

Analyze More of the Genome

Segmental duplications are typically inaccessible to short-read sequencing due to read homology to multiple genomic positions. By leveraging 10x's molecular barcodes and Linked-Read data, the Lariat Aligner is able to confidently map reads into these regions.

Segmental Duplications Rescued by Lariat™ Aligner

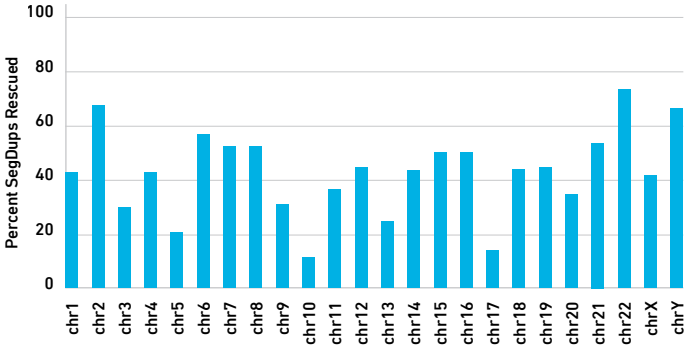


Figure 5. The Lariat™ Aligner unlocks new genomic content. Long Ranger's Lariat™ Aligner rescued approximately 50% of segmental duplications in the human genome. These regions are lost with standard short-read sequencing.

Chromium™ Genome Solution Datasets Available for Download:

- HCC1954 Normal whole genome
- HCC1954 Tumor whole genome
- NA12878 Germline whole genome

More files available at: http://support.10xgenomics.com/genome-exome/datasets

Improved Access to Medically-Relevant Genes

The Lariat™ Aligner improves access to medically relevant genes. For example, the SMN1 gene (below), which is associated with spinal muscular atrophy, differs from its homologue SMN2 by only 8 nucleotides (3 exonic). The high degree of similarity between the two genes makes it difficult to confidently map reads in this region with standard alignment methods. The Lariat™ Aligner was able to accurately place reads in SMN1 over BWA, resulting in increased coverage in this difficult, medically relevant region and improved variant calling.

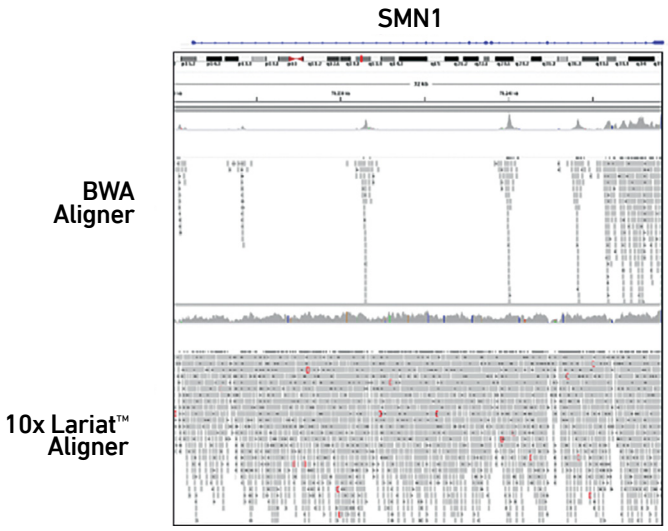


Figure 6. Mapping into previously inaccessible regions using the Lariat™ Aligner improves access to medically relevant genes. Comparison between BWA aligner and 10x's Lariat™ Aligner in SMN1 gene. Only reads containing a MAPQ score of >20 are shown.

Call and Phase Genetic Variants

Using traditional short-read sequencing approaches, the identification of the full range of genetic variation can be challenging. Linked-Reads provide a combination of long range information and haplotype information, which facilitates the detection of both balanced and unbalanced structural rearrangements as well as compound heterozygotes. Fanconi-Anemia is an autosomal recessive disorder characterized by chromosome instability. As shown below, we are able to identify two damaging single nucleotide variants from a single individual that are phased in trans.

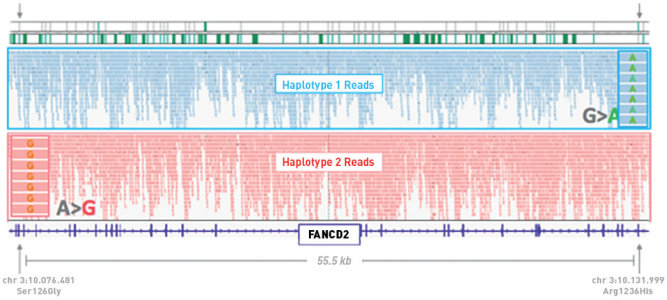


Figure 7. Chromium™ Genome Solution can detect variants in FANCD2 gene that are 55 Kb apart, and the entire region is contained within a 17.5 Mb phase block.

Identify Gene Fusions

The Chromium Genome Solution allows for identification of gene fusions such as the EML4-ALK translocation using whole genome sequencing.

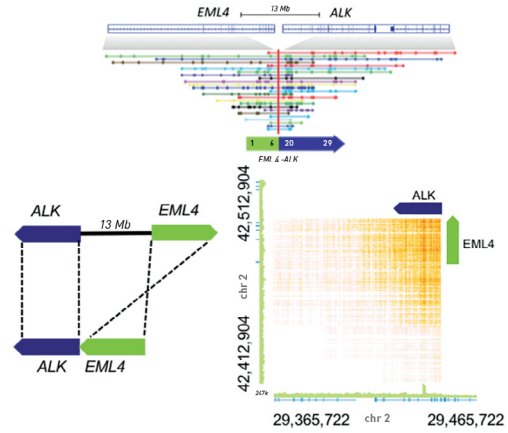


Figure 8. Chromium™ Genome Solution detects the EML4-ALK translocation using whole genome sequencing. (Top) Linked-read plot for reads over the EML4-ALK translocation colored by barcode. (Bottom) Schematic of ALK-EML4 translocation and 10x Loupe matrix plots of EML4-ALK barcode overlap in Whole Genome library.

Summary of Variant Classes Called and Phased Using the Chromium™ Genome Solution

Variant Type	Called and Phased
SNVs	Yes
Indels	Yes
Balanced structural variants >30 Kb	Yes
Deletions > 50 bp (including single exon to single gene deletions)	Yes

Conclusion

The Chromium Genome Solution, with the Long Ranger software package and Lariat Aligner, provides a transformative upgrade to existing short-read data, enabling confident interrogation of critical but difficult areas of the genome. This approach provides vastly improved resolution and variant calling in these important areas. 10x Genomics' molecular barcoding further enables phasing and resolution of compound heterozygotes, and unique delineation of translocations and other structural events.

Literature Cited: Ingelman-Sundberg *et al.* (2007) Pharmacol Ther 116(3):496-526.
Zheng *et al.* (2016) Nat Biotechnol 34(3):303-11.

All Publications are Available at:

10xgenomics.com/resources

Additional Resources:

support.10xgenomics.com/genome-exome

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