

A Novel Platform for the Genomic Characterization of Cell Lines



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Abstract

NewBiologix Xcell™ Genomic Analytical Platform is a newly developed proprietary workflow specifically designed for the in-depth genomic and transcriptomic characterization of cell lines, using a combination of optical genome mapping (OGM), high-fidelity (HiFi) long reads and high-throughput short reads sequencing technologies.

This platform allows for reliable characterization of cell lines, including accurate transgene integration site detection, assessment of genomic stability and identification of genetic alterations, all of which support quality control and long-term monitoring of engineered cells^[1, 2].

Here, we illustrate the use of our platform to characterize NewBiologix Eng-HEK293 cell line. OGM was used to assess cells genome architecture and ploidy estimates compared to a parental polyclonal HEK293 cell line, while short reads sequencing was conducted to identify differentially expressed genes. Whole-genome assembly was performed using HiFi long reads and subsequently coupled with OGM to obtain annotated chromosome-scaled scaffolds which included localization of genes and transcripts, 5mC methylation status as well as calling of SNVs, InDels and more complex structural alterations. Finally, integration site analysis provided sequence integrity and precise loci of integrated transgenes.

Our platform is an innovative and complete support in characterizing cells used in Gene and Cell Therapies or for biologics production.

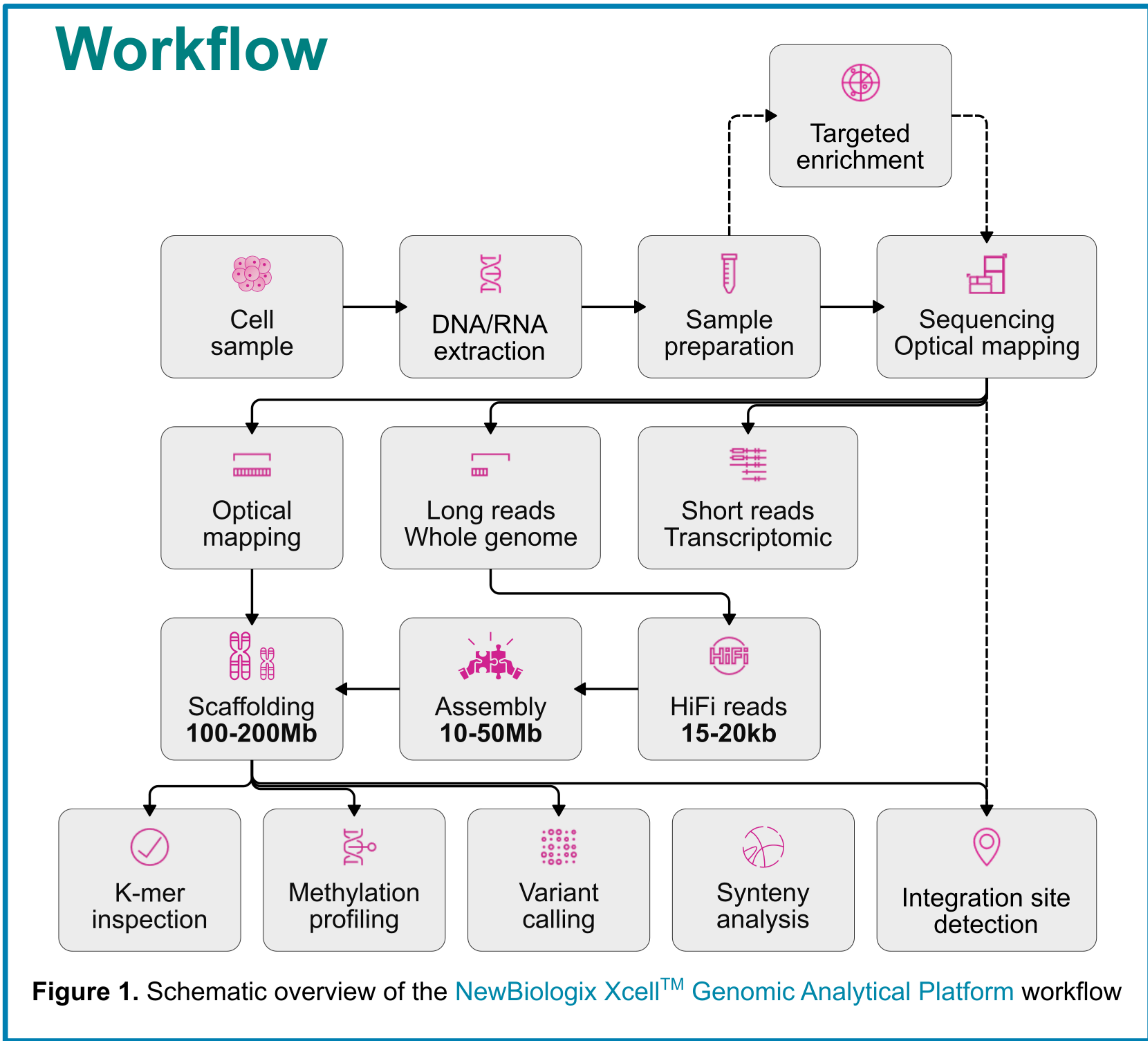


Figure 1. Schematic overview of the NewBiologix Xcell™ Genomic Analytical Platform workflow

References

- Vockley J, et al. *Whole-genome sequencing holds the key to the success of gene-targeted therapies*. Am J Med Genet C Semin Med Genet, 193 (2023)
- Jain MD, et al. *Whole-genome sequencing reveals complex genomic features underlying anti-CD19 CAR T-cell treatment failures in lymphoma*. Blood, 140 (2022)

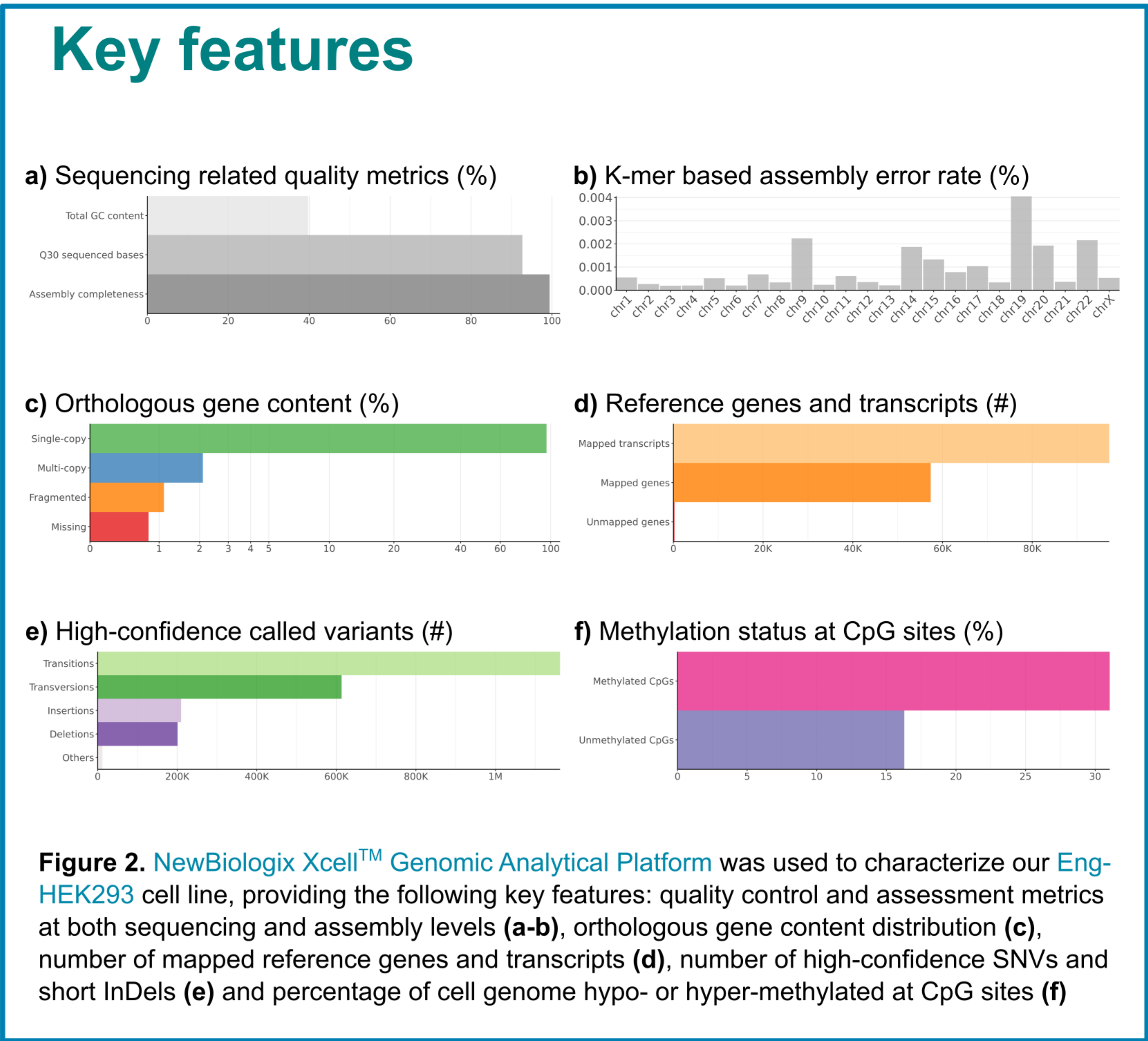


Figure 2. NewBiologix Xcell™ Genomic Analytical Platform was used to characterize our Eng-HEK293 cell line, providing the following key features: quality control and assessment metrics at both sequencing and assembly levels (a-b), orthologous gene content distribution (c), number of mapped reference genes and transcripts (d), number of high-confidence SNVs and short InDels (e) and percentage of cell genome hypo- or hyper-methylated at CpG sites (f)

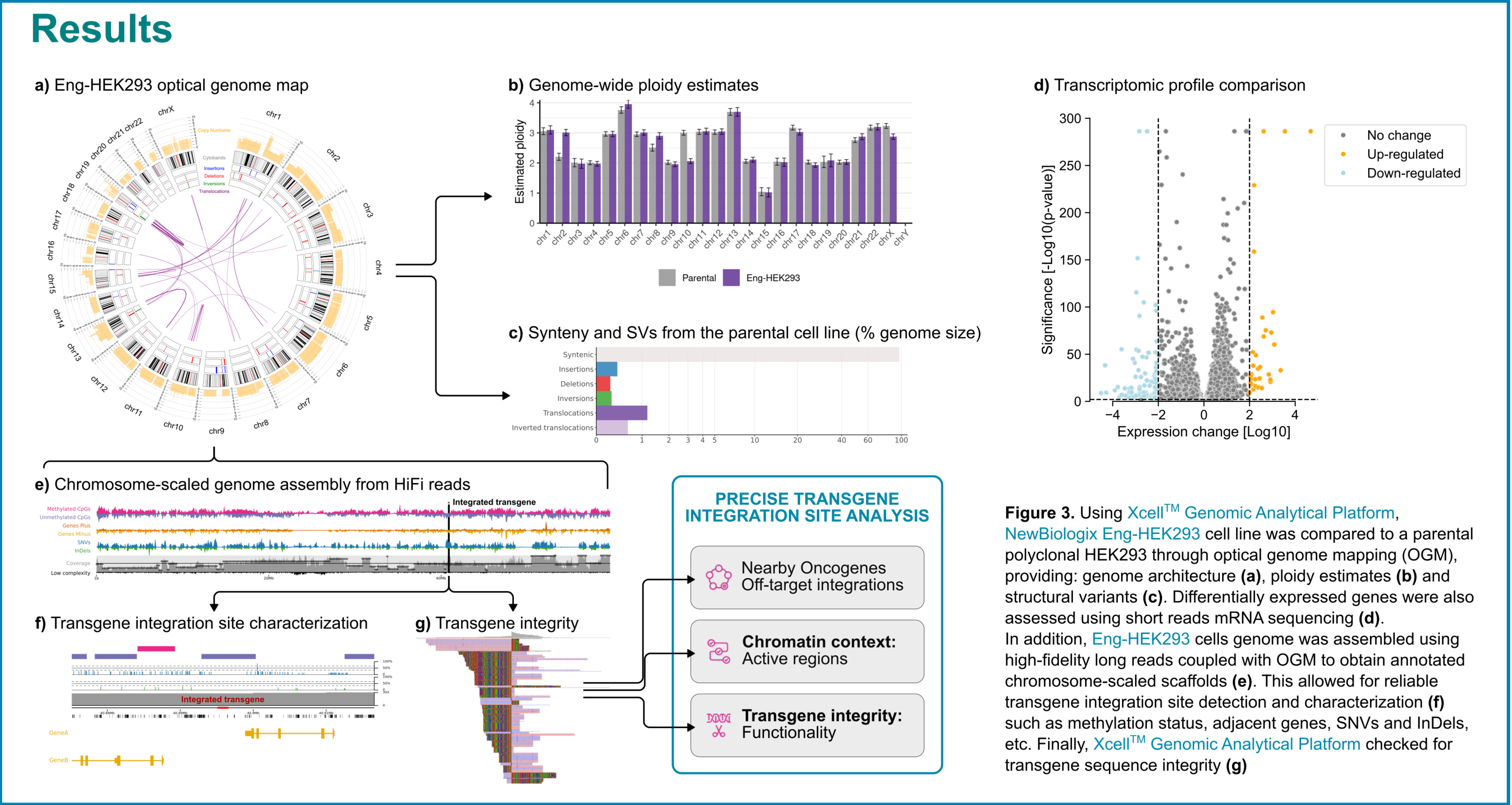


Figure 3. Using Xcell™ Genomic Analytical Platform, NewBiologix Eng-HEK293 cell line was compared to a parental polyclonal HEK293 through optical genome mapping (OGM), providing: genome architecture (a), ploidy estimates (b) and structural variants (c). Differentially expressed genes were also assessed using short reads mRNA sequencing (d). In addition, Eng-HEK293 cells genome was assembled using high-fidelity long reads coupled with OGM to obtain annotated chromosome-scaled scaffolds (e). This allowed for reliable transgene integration site detection and characterization (f) such as methylation status, adjacent genes, SNVs and InDels, etc. Finally, Xcell™ Genomic Analytical Platform checked for transgene sequence integrity (g)

Conclusions

A novel pipeline
A novel pipeline has been developed for the characterization of cells used in Gene or Cell Therapies and biomanufacturing. Our pipeline uses a combination of state-of-the-art technologies and performs both accurate whole-genome assembly and reliable integration site analysis through an automated bioinformatics procedure. We also provide genomic stability testing using optical genome mapping as well as transcriptomic data analysis using short reads sequencing

Optical genome mapping
Bionano technology helps to assess transgene integration site analysis commonly used in LVV, CRISPR and transposon-mediated integration

Integration site analysis
A proprietary approach allows for precise transgene integration site analysis commonly used in LVV, CRISPR and transposon-mediated integration

Detection of DNA methylation
PacBio technology provides 5mC methylation in CpG contexts within high-fidelity long sequenced genomic DNA molecules

High-quality control
Quality control and assessment are performed continuously at both sequencing and analysis levels, providing unparalleled data quality

Reliably Produce your Gene Therapy vectors with our Advanced Technology Platform and Custom Solutions
SWISS PRECISION AND QUALITY CONTROL AT EVERY STAGE

Xcell™ Eng-HEK293 Cell Line
Xcell™ Genomic Analytical Platform
Xcell™ rAAV Production & Analytical Platform

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