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Structural variant analysis of a cancer reference cell line sample using multiple sequencing technologies

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Abstract

Background: The cancer genome is commonly altered with thousands of structural rearrangements including insertions, deletions, translocation, inversions, duplications, and copy number variations. Thus, structural variant (SV) characterization plays a paramount role in cancer target identification, oncology diagnostics, and personalized medicine. As part of the SEQC2 Consortium effort, the present study established and evaluated a consensus SV call set using a breast cancer reference cell line and matched normal control derived from the same donor, which were used in our companion benchmarking studies as reference samples.

Results: We systematically investigated somatic SVs in the reference cancer cell line by comparing to a matched normal cell line using multiple NGS platforms including Illumina short-read, 10X Genomics linked reads, PacBio long reads, Oxford Nanopore long reads, and high-throughput chromosome conformation capture (Hi-C). We established a consensus SV call set of a total of 1788 SVs including 717 deletions, 230 duplications, 551 insertions, 133 inversions, 146 translocations, and 11 breakends for the reference cancer cell line. To independently evaluate and cross-validate the accuracy of our consensus SV call set, we used orthogonal methods including PCR-based validation, Affymetrix arrays, Bionano optical mapping, and identification of fusion genes detected from RNA-seq. We evaluated the strengths and weaknesses of each NGS technology for SV determination, and our findings provide an actionable guide to improve cancer genome SV detection sensitivity and accuracy.



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The Cancer Reference

Jiyuan Zhang



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