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

Keyur Talsania<sup>1,2†</sup>, Tsai-wei Shen<sup>1,2†</sup>, Xionglong Chen<sup>1,2†</sup>, Erich Jaeger<sup>3†</sup>, Zhipan Li<sup>4†</sup>, Zhong Chen<sup>5</sup>, Wanqiu Chen<sup>5</sup>, Bao Tran<sup>6</sup>, Rebecca Kusko<sup>7</sup> , Limin Wang<sup>8</sup>, Andy Wing Chun Pang<sup>9</sup>, Zhaowei Yang<sup>10</sup>, Sulbha Choudhari<sup>1,2</sup>, Michael Colgan<sup>11</sup>, Li Tai Fang<sup>12</sup>, Andrew Carroll<sup>13</sup>, Jyoti Shetty<sup>6</sup>, Yuliya Kriga<sup>6</sup>, Oksana German<sup>6</sup>, Tatyana Smirnova<sup>6</sup>, Tiantain Liu<sup>7</sup>, Jing Li<sup>10</sup>, Ben Kellman<sup>9</sup>, Karl Hong<sup>9</sup>, Alex R. Hastie<sup>9</sup>, Aparna Natarajan<sup>3</sup>, Ali Moshrefi<sup>3</sup>, Anastasiya Granat<sup>3</sup>, Tiffany Truong<sup>3</sup>, Robin Bombardi<sup>3</sup>, Veronika Mankinen<sup>14</sup>, Daoud Meerzaman<sup>15</sup>, Christopher E. Mason<sup>16</sup>, Jack Collins<sup>1,2</sup>, Eric Stahlberg<sup>7</sup>, Chunlin Xiao<sup>17</sup>, Charles Wang<sup>7\*</sup> , Wenming Xiao<sup>11\*</sup> and Yongmei Zhao<sup>1,2\*</sup> 

<sup>†</sup>Keyur Talsania, Tsai-wei Shen, Xionglong Chen, Erich Jaeger, Zhipan Li contributed equally

\*Correspondence: cchwang@fda.hhs.gov; Yongmei.Zhao@nih.gov

<sup>2</sup>Bioinformatics and Computational Science Directorate, Frederick National Laboratory for Cancer Research, Frederick, MD, USA

<sup>11</sup>Center for Genomics, Loma Linda University School of Medicine, Loma Linda, CA, USA

<sup>17</sup>Center for Drug Evaluation and Research, FDA, Silver Spring, MD, USA

Full list of author information is available at the end of the article

## 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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# Cancer Reference

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