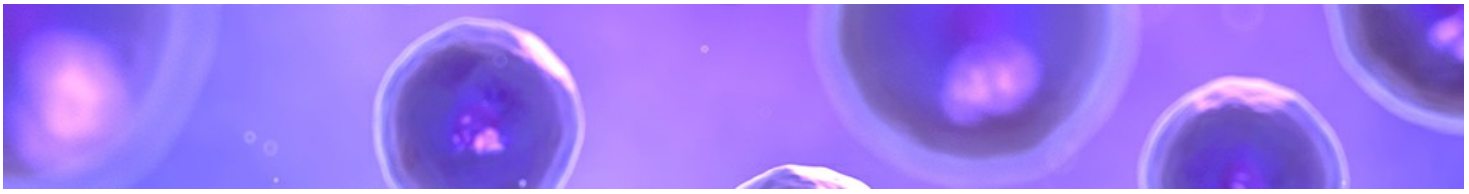
Single cancer cell analysis



Key genomic alterations of cancer cells can be structural, including deletions, translocations, or amplification of genes/portions of the genome, or can affect the DNA sequence itself, as with mutations. Cancer progression can be caused by clonal expansion and selection of these driver mutations, resulting in a plethora of malignant alterations characterizing the tumoral DNA. Recent advances in NGS have made it possible to profile the genomes of single tumor cells, allowing systematic documentation of cancer cells' mutational DNA makeup; tracking of clonal and subclonal heterogeneity, generation, and phylogeny; and monitoring of the effects of anticancer therapies at a single-cell level (Van Loo and Voet, 2014). The complexity and heterogeneity of tumor cells also translate at the transcriptomic level, where genomic heterogeneity is mirrored by single-cell variations within the transcriptomes of cancer cells, cancer persister cells, and circulating tumor cells (CTCs).

Studying single cells from precious samples such as cancer persister cells and CTCs requires extraordinarily sensitive and reproducible methodologies. Therefore, the accurate capture and quantification of RNA transcript variations from single tumor cells remains a significant challenge, but would allow researchers to gain insights into tumor complexity and ultimately help in the development of tailored anticancer therapies (Zhu et al. 2017).

Highlighted products

Single-cell genome sequencing

PicoPLEX WGA and DNA-Seq kits, as well as the new PicoPLEX Gold Single Cell DNA-seq Kit, use our patented PicoPLEX technology for single-cell whole genome amplification, which uses multiple cycles of quasi-random priming for reproducible library construction, suitable for sequencing on Illumina platforms. Indeed, our PicoPLEX technology allows the precise and impartial analysis of the genome for many applications in cancer research, including the study of chromosomal aneuploidies, copy number variations (CNVs), single nucleotide variations (SNVs), and the detection of insertions/deletions (Figure 1). Many publications have cited the use of the PicoPLEX technology for high-performance CNV analysis, and the genomic profiling of single cells from FFPE tumor tissues and CTCs. Moreover, our PicoPLEX technology is a vital component of the recently developed single-cell Genome & Transcriptome-seq approach (G&T-seq; Babayan et al. 2017, Cayrefourcq et al. 2015, Lieselot et al. 2017, Macaulay et al. 2015, Morrow et al. 2016, Premasekharan et al. 2016, and Williamson et al. 2016).

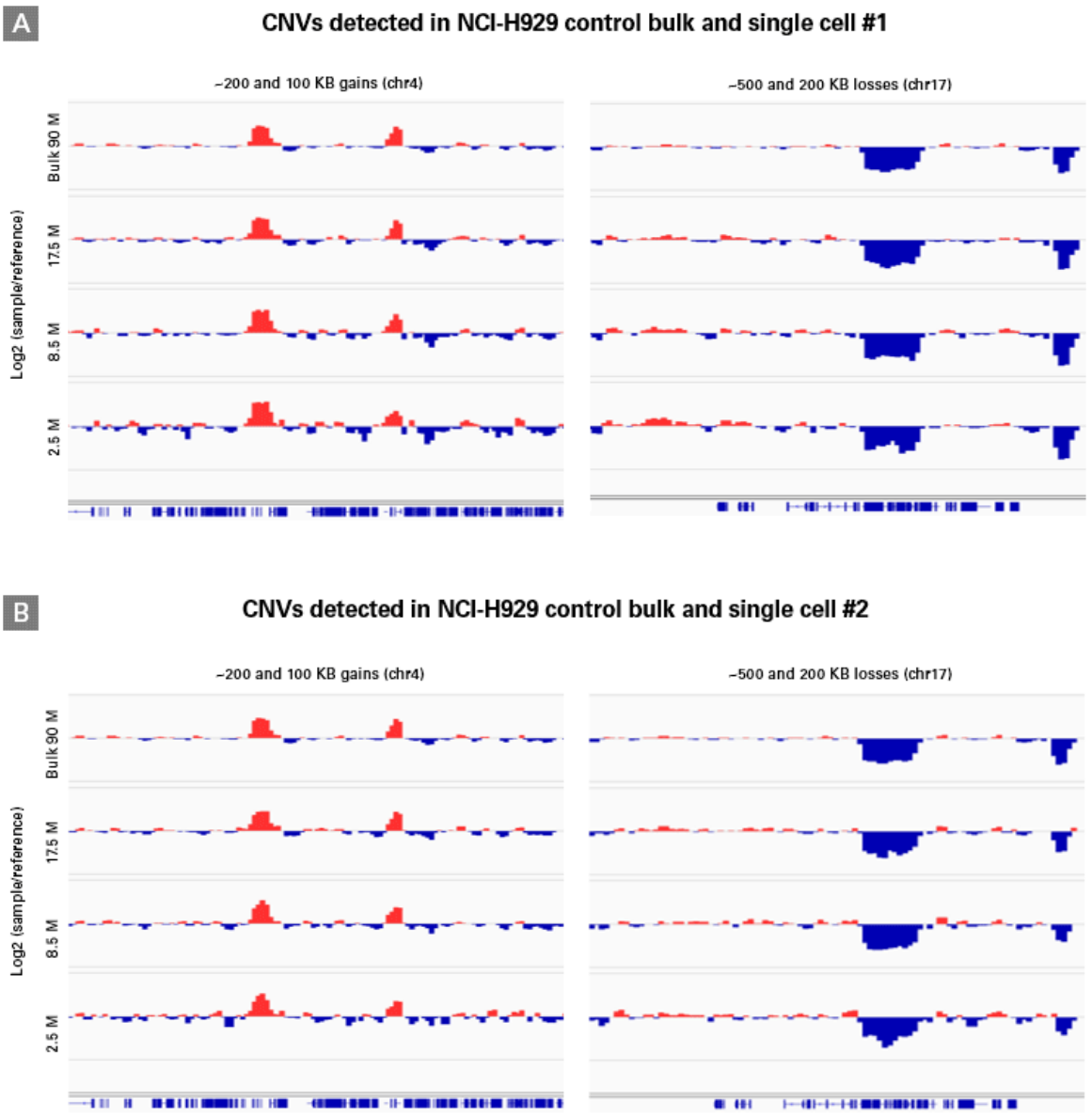


Figure 1. CNVs detected in two individual cells using the PicoPLEX Gold Single Cell DNA-seq Kit. Log_2 ratio of the total number of reads in 50-kb bins from single NCI-H929 cells, shown as one cell in Panel A and a second cell in Panel B. Red bars represent copy-number gains while blue bars represent losses. The top row of the graphs in each panel depicts the control bulk sample sequenced to a depth of 90 million read pairs. The highly reproducible coverage of the PicoPLEX Gold kit enables the accurate detection of structural variants as small as 100 kb, even at shallow sequencing depths (2.5–8.5 million read pairs).

We have always been at the forefront of single-cell mRNA-seq research by leveraging our patented SMART-Seq technology to provide NGS kits with the capability to obtain full-length mRNA sequence information, including splice junction/alternative transcript information, from single cells. Our fourth-generation SMART-Seq v4 Ultra Low Input RNA Kit for Sequencing and the high-throughput SMART-Seq HT Kit represent our most sensitive mRNA-seq solutions for single cells, a few cells, and ultra-low inputs of RNA. These kits rely on oligo(dT) priming and proprietary SMART (Switching Mechanism at 5' end of RNA Template) technology to ensure full-length, unbiased mRNA coverage. Intact cells can be used directly as input for these kits, guaranteeing high-quality input RNA and full-length cDNA coverage. Our SMART-Seq v4 technology is now also fully integrated into the Apollo Library Prep System and the ICELL8 Single-Cell System, our advanced automation platform for high-throughput single-cell analysis. Moreover, many publications have cited the use of our SMART-Seq solutions for single-cell RNA-seq in various cancer applications, including profiling tumor cells and tumor-infiltrating immune cells, analyzing cancer stem cell heterogeneity, identifying tumor cell clones resistant to therapy, and simultaneous sequencing of genome and transcriptome in cancer cells (Chung et al. 2017, Chiu et al. 2018, Han et al. 2018, Kim et al. 2015, and Zheng et al. 2018).

Finally, the SMART-Seq Stranded Kit enables the generation of stranded Illumina-compatible sequencing-ready libraries at the single-cell level. This kit combines features of our SMART-Seq v4 technology with the unique features of our referenced SMARTer Stranded Total RNA-Seq Kit v2 - Pico Input Mammalian Kit, suitable for library preparation from picogram input amounts of tumor total RNA including very degraded FFPE samples from tumor samples.

References and publications citing the use of SMART-seq solutions for single-cell RNA-seq and PicoPLEX solutions for single-cell DNA-seq in various cancer applications

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