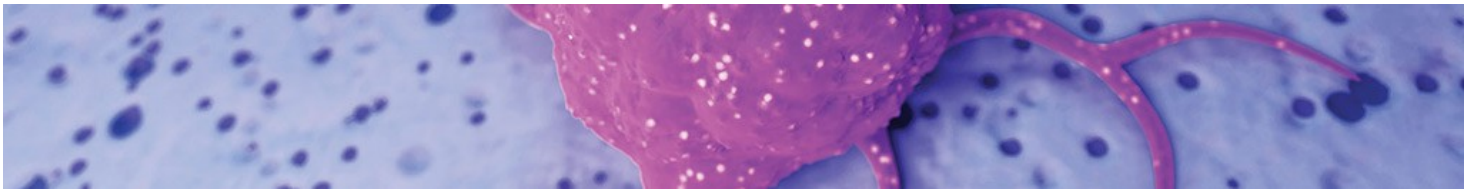
Cancer genomics and epigenomics



Genome alterations such as mutations, copy number variations, and structural variations, in parallel with dysregulations within the epigenetic landscape (i.e., DNA methylation status), are hallmarks of cancer. Whole genome sequencing and targeted sequencing approaches, mainly focused on the detection of somatic variants and CNVs, allow cancer researchers to obtain a comprehensive picture of genomic alterations. Targeted approaches such as exome or panel sequencing focus on specific regions or genes of interest and allow deeper sequencing for increased sensitivity in variant detection with respect to whole genome sequencing. Epigenetic approaches, on the other hand, have proven useful in describing cancer-specific DNA binding proteins, histone modifications, and the DNA methylation makeup of cancer cells. Understanding how these epigenetic changes act in concert with genomic alterations in tumor onset and progression, and in tumor resistance to therapy, is extremely important for improving cancer care.

Highlighted products

We provide many innovative technologies to speed up your whole-genome and targeted sequencing workflow for somatic variant and CNV discovery, including our patented SMARTer ThruPLEX technology. All of our SMARTer ThruPLEX kits are designed to reduce user error, sample loss, and contamination with a single-tube, two-hour, three-step workflow (Figure 1). The highly sensitive SMARTer ThruPLEX DNA-Seq Kit allows the construction of NGS libraries from picogram amounts of DNA, including FFPE samples and ChIP DNA. The SMARTer ThruPLEX Plasma-Seq Kit has been specifically designed for use with cell-free DNA (cfDNA) and circulating tumor DNA (ctDNA). Lastly, the SMARTer ThruPLEX Tag-seq kits contain more than 16 million unique sequences that are used to tag individual DNA fragments prior to amplification, allowing the tracking of fragments through the library preparation, target enrichment, and data analysis processes to detect low-frequency alleles or to count individual fragments.

SMARTer ThruPLEX technology is also compatible with and has been validated for use with significant target enrichment platforms such as Agilent SureSelect, Roche Nimblegen SeqCap EZ, and IDT xGen Lockdown probes. Moreover, SMARTer ThruPLEX technology has been successfully utilized and cited for whole genome sequencing, targeted sequencing, CNV analysis, and ChIP-seq studies in various types of cancers.

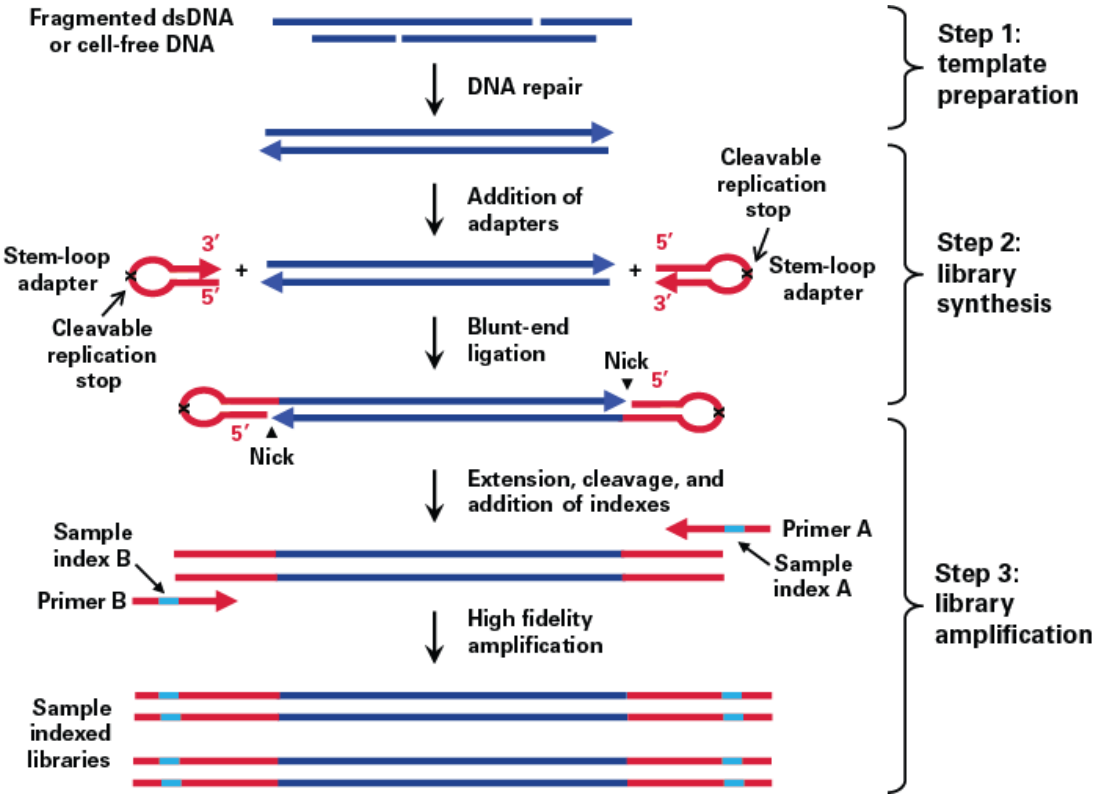


Figure 1. SMARTer ThruPLEX technology workflow.

References and publications citing the use of SMARTer ThruPLEX technology for whole genome sequencing, targeted sequencing, CNV analysis, and ChIP-seq studies in various types of cancer include the following:

Cato, L. *et al.* Development of Bag-1L as a therapeutic target in androgen receptor-dependent prostate cancer. *eLife* **6,** e27159 (2017).

Jeselsohn, R. *et al.* Allele-specific chromatin recruitment and therapeutic vulnerabilities of ESR1 activating mutations. *Cancer Cell* **33,** 173–186 (2018).

Jin, X. *et al.* Targeting glioma stem cells through combined BMI1 and EZH2 inhibition. *Nature Med.* **23,** 1352–1361 (2017).

Klevebring, D. *et al.* Evaluation of exome sequencing to estimate tumor burden in plasma. *PLoS One* **18,** e104417 (2014).

Markus, H. *et al.* Evaluation of pre-analytical factors affecting plasma DNA analysis. *Sci. Rep.* **8,** 7375 (2018).

McNair, C. *et al.* Differential impact of RB status on E2F1 reprogramming in human cancer. *J. Clin. Invest.* **128,** 341–358 (2018).

Murtaza, M. *et al.* Non-invasive analysis of acquired resistance to cancer therapy by sequencing of plasma DNA. *Nature* **497,** 108–112 (2013).

Patel, K. M. *et al.* Association of plasma and urinary mutant DNA with clinical outcomes in muscle-invasive bladder cancer. *Sci. Rep.* **7,** 5554 (2017).

Wang, X. *et al.* Purine synthesis promotes maintenance of brain tumor-initiating cells in glioma. *Nature Neurosci.* **20,** 661–673 (2017).

Weiss, G. J. *et al.* Tumor cell-free DNA copy number instability predicts therapeutic response to immunotherapy. *Clin. Cancer Res.* **23,** 5074–5081 (2017).

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