PgmNr 2445: High accuracy NGS platform based on electrical impedance detection: Applications for oncology research.

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Next Generation Sequencing (NGS) technologies have made rapid strides in the throughput and accuracy of DNA sequencing in recent years. These advances have revolutionized biomedical and clinical research, especially in oncology. NGS cancer panels are used to determine cancer predisposition, detect early cancer, identify tumor mutations, and develop personalized therapies. Here, Genapsys presents a novel, scalable, low cost, and high accuracy NGS platform, and demonstrates its applications to oncology research.

The GenapSys NGS platform is based on accurate detection of electrical impedance changes resulting from single base incorporations during sequencing-by-synthesis. We show that impedance changes measure a steady state dNTP incorporation signal, leading to higher accuracy. The core of the technology is a CMOS-based electronic chip that enables scalability and low instrument and consumable costs. Chips with 1M, 16M and 144M sensors can be run on the same GenapSys instrument, giving a lab flexibility in NGS assay design and sample multiplexing. We demonstrate that a single run with a 16M sensor chip generates 1.5 Gb of data, with greater than 99% raw accuracy and up to 175 bp read lengths.

We tested hybrid-capture and amplicon-based cancer panels on a range of DNA sources, including oncology reference standards derived from cell line DNA, as well as clinical FFPE and blood sample DNA. Reference DNA standards from Horizon Discovery included the Quantitative Multiplex (HD701), EGFR Gene-Specific Multiplex (HD802) and Oncospan (HD827). For hybrid-capture libraries, we tested the IDT xGen Pan Cancer Panel v1.5 (800 Kb target region, 127 genes) and the IDT xGen Exome Research panel (39 Mb target region, 19,396 genes). We detected low frequency mutations in the range of 1%-24.5% across multiple standards with the Cancer panel, with mean coverage of >600x in a single run. Whole exome sequencing of clinical FFPE and blood samples showed high concordance (F1 score > 95%) of SNV mutation calling with industry standard technology. For amplicon panels, we used the Ion AmpliSeq Cancer Hotspot Panel v2 (207 amplicon pairs, 50 genes) with Horizon reference standards. We demonstrate detection of low frequency mutations (>1%) and a high correlation (R squared > 0.99) with expected allele frequencies. Thus, we demonstrate that the GenapSys NGS platform is an accurate, scalable, and low cost solution for oncology research on a wide range of sample types and NGS assays.