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Robust and comprehensive target sequencing method comparison for the detection of actionable cancer-driver somatic mutations

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Somatic mutations emerge as superior biomarkers for rationalized drug selection in combating cancer. To trace the full cancer heterogeneity and detect mutations in cancer cells within DNA preparation that includes neighboring normal stromal cells, multiple target enrichment tools were developed to allow sequencing of the most relevant area of the genome at the deepest possible. We assessed seven platforms for sensitivity and specificity over a common genomic area encompassing all frequently mutated exons of over 150 cancer causing genes; Fluidigm® Access Array, Raindance®, Life Technology® AmpliSeq-Ion Torrent, Illumina® TruSeq and Nextera rapid capture and Agilent® HaloPlex and SureSelect (all but the first sequenced on IlluminaMiSeq and HiSeq2500). Although these technologies were relatively comparable and capable of identifying clinically relevant mutations at high level of reproducibility and at least 90% specificity and sensitivity, one method emerged as superior. It had advantage when the cancer cells were a minority of the sample and had unique capability to detect gene fusions. Detecting low frequency mutations is important due to the dynamic selection that occurs when treating with anti-cancer drug. Therefore, we analyzed a number of samples from before and after acquired resistance and indeed found partial evidence to support the hypothesis that resistant cells are present in the onset of treatment. These results suggest that clinically driven tumor sequencing should read the samples at relatively high depth to allow the identification of rare resistant variants and attempt to treat in accordance to their presence in the first line of treatment.

Biography

Izhak Haviv has completed his PhD at the age of 32 years from Weizmann Institute of Science and Postdoctoral studies from University of California, Berkeley (c/o Tjian lab, Head, HHMI). He is the Director of Cancer Research Center of excellence in the Faculty of Medicine in the Galilee of Bar Ilan University, an academic clinical and translational research organization. He has an Affiliate Position in the University of Melbourne for 11 years and at Peter MacCallum Cancer Centre, Australia for 16 years. He has published more than 59 papers in reputed journals.

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