OMICS International
conferenceseries.com
3rd International Conference on
Predictive, Preventive and Personalized Medicine & Molecular Diagnostics
September 01-03, 2015 Valencia, Spain

J Pharmacogenomics Pharmacoproteomics 2015, 6:3
http://dx.doi.org/10.4172/2153-0645.C1.007

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

Izhak Haviv[1,2,3], Sebastian Lunke[1], Roi Feingersh[2], Ayala Lagzuel[2], Shani Carmi[3], Neta Moskovitz[2], Salomon Stemmer[4], Barney Rudzki[1] and **Paul Waring[1]**
[1]Melbourne University, Australia
[2]GeneSort®, Israel
[3]Bar Ilan University, Israel
[4]Rabin Medical Center, Israel

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 development 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.

Izhak.Haviv@biu.ac.il

NGS sounds really good. But, what kind of NGS-based test might be offered to my patient?

Javier Garcia-Planells
Instituto de Medicina Genomica, Spain

NGS is being established as a new alternative for the diagnosis of genetic diseases in the clinical practice. The great advantages of this promising technology have been duly demonstrated in research. But some considerations need to be taken into account before being implemented as a clinical routine. NGS is a great technology, or better said, a set of technologies and different applications, but more important than the technology itself is the use that is made of it. We have developed different NGS based strategies for the analysis of genetic conditions. An accurate and highly sensitive approach based on a PCR specific design, which we have called NextGeneDx®. This approach was extensively validated to be used for diagnostic applications. An exome analysis focused only to the genes associated to clinical phenotypes according to OMIM (Clinical Exome). And a phenotype driven or Ad Hoc Exome focused to the genes associated to a specific condition or phenotype. Specific bioinformatics pipelines and interpretation algorithms were implemented for all these strategies. NGS technology enables to address the genetic diagnosis more efficiently, reducing costs and times. Depending on the clinical needs we can choose between two types of NGS strategies: High accuracy or high amount of data. NextGeneDx® is a highly accurate NGS strategy suitable for the diagnosis of genetically heterogeneous diseases. Highest diagnostic yield is obtained when a definite group of genes or genomic regions can be selected and analyzed through a precise clinical orientation.

javier.garcia@imegen.es