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Abstract Title:- MedGenome-DNAScar : An accurate and cost effective solution to predict HRD Status

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Aims:-Homologous Recombination Repair (HRR) is one of the key mechanisms where cells harbour in repairing double strand breaks. As can be noted in different solid cancers, alterations in key regulators of HRR pathway mainly BRCA1/2 can lead to deficiency in HRR pathway (HRD) causing genome instability. Clinical findings from ovarian cancer patients with HRD show sensitivity towards PARP inhibitors (PARPi). HRD status is used as a biomarker for targeted therapy. Many commercial assays are currently available for predicting HRD status but a cost effective solution with in-depth insights is still a challenge.

Methods:- Here, we present MedGenome-DNAScar, an accurate HRD status prediction solution that has been validated on a large number of clinical samples (N=170) including several samples with low input material. We have developed an comprehensive SNP backbone valid across multiple ethnicities along with 15 HRR genes and CCNE1 for predicting HRD status.

Results:- We evaluated DNAScar with other existing solutions (AmoyDx HRD Focus/SOPHiA HRD). Overall, our solution achieved 96.39% Positive Percent Agreement (PPA), 98.3% Negative Percent Agreement (NPA) and 97.05% Overall Percent Agreement (OPA). On reference standard our assay achieved 100% concordance. Along with 15 HRR genes our assay also predict amplifications in CCNE1 which is increasingly considered for their chemotherapy resistance. Our assay predicted 6% of ovarian cancer patients with CCNE1 amplification.

Conclusions:- Overall, our assay provided one of the best performance metrics in the industry with minimal assay failure rate on clinical samples.

Keywords:- HRD, BRCA1/2, HRR, Ovarian cancer, NGS