Colorectal cancer (CRC) is one of the major causes of global cancer mortality. Until recently, KRAS has been the only predictive biomarker for anti-EGFR therapy for metastatic CRC, and yet predicting prognosis in clinical practice is still poor. Therefore, a more accurate method for prognosis of CRC patients is needed.

Gene expression profiling has shown great promise in predicting prognosis of individual patients in diverse cancers. The development of RNA-sequencing has greatly facilitated identification of biomarkers that can be used to stratify patients for targeted therapies. Despite the decrease in cost of sequencing in the last few years, the time and the resources needed for analysis limits its use in clinical trials for patient selection. Targeted gene expression technologies like iPlex® NanoString enable highly customizable assays that can be conveniently performed for patient recruitment.

The aim of this study was to investigate potential alternatives for gene profiling using a novel NanoString PlexSet technology. The PlexSet system comes with pre-packaged and custom code sets in identifying genetic markers. Up to 8 samples can be pooled to each NanoString cartridge lane, enabling a total of 36 samples per run, thus lowering cost.

For this study, gene expression signature was developed using RNA-Seq data where we have profiled 74 CRC samples, 20 of which have matching normal samples. A RAS signature score based on expression profile was calculated and used for each sample to look for potential gene signatures, differential gene expression analysis was performed between the following groups: (a) samples with high versus those with low RAS signature scores in the 54 CRC (b) KRAS mutant vs wildtype samples and (c) tumor versus normal samples in the clinical study.

We hypothesized that our genes of interest is most likely significantly differentially expressed in one of these groups. The count of significantly expressed gene for the groups (a-c) are 1560, 34 and 24, respectively.

Therefore, significantly differentially expressed genes between groups were selected and ranked based on frequency of occurrence. These genes of interest were analyzed using NanoString PlexSet to evaluate the potential of using NanoString PlexSet system for targeted gene expression profiling. Results of these analyses are presented here.

Conclusion

This study shows that the newly developed NanoString PlexSet technology can be a good choice as a potential alternative for gene profiling. Leveraging on previous data, we selected genes that were expressed significantly to build a panel and test for reproducibility. The standard RNA-Seq data was further compared to Nanostring, HTG EdgeSeq Oncology Biomarker panel data and were seen to have high correlation scores across platforms. NanoString PlexSet data and RNA Sequencing data for 32 samples had high correlation for the genes compared. We are in process of designing TDLA card to compare other low throughput technologies.

References


#3418. Cross-Comparison of Targeted Gene Expression Technologies for Patient Stratification

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