Technical advances in plasma genomic biomarkers for mutation detection and monitoring in cancer patients

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A sea-change is imminent for cancer medicine, due to the use of non-invasive genomic biomarkers in blood to inform screening, diagnosis and the selection of treatment. This technology may be used routinely in oncology within five years. Although numerous studies, including work in our laboratory, have shown that genomic analysis of blood can detect the presence and even the type of cancer, researchers have only scratched the surface of what this technology can do. There are still many technical challenges that need to be addressed before these biomarkers can be used routinely in the clinic. In our laboratory, we are generating new methods to improve the sensitivity and accuracy of non-invasive tests mutation detection in cancer patients.

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Introduction

Firstly, we are using a custom amplicon next generation sequencing panel – DNA QiaTarget, to screen for specific mutational hotspots or genes (Fig. 1 and 2). This strategy is useful when common mutations are absent, such as in Neuroendocrine Cancer, or to identify mutations in cancer types that have several genes mutated. Secondly, we are using Droplet Digital PCR (ddPCR) which allows the specific detection of a mutation of interest through a competitive probe assay. This method is particularly useful in cancers such as Melanoma, where discrete mutations such as BRAF V600E, are present in up to 40% of Melanomas. However, this requires the presence of each mutation to be screened for individually, and each assay requires optimisation (Figs 3 and 4).

Methods

Sensitivity of ddPCR assays for detection of BRAF V600E melanoma mutation

Future Directions

We will continue the development of non-invasive technologies in our laboratory to further investigate the limits of detection for diagnosis of mutations in cancer, and the roles these technologies may play in the monitoring for relapse in cancer patients.