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Genomic Profiling of Tumors for Targeted Therapy Matching Using Novel Liquid Biopsy Platform (SMSEQ)

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Purpose: Cell-free tumor DNA (cftDNA) in blood circulation harbors genomic alterations originated from tumor cells. Genomic profiling of cftDNA from blood (liquid biopsy) can be used as a non-invasive method in real time to select personalized therapies for metastatic or refractory patients. The major challenge of using NGS to analyze cftDNA is the extremely small fraction of cftDNA present within background levels of normal cell-free DNA (cfDNA). Standard NGS is too error prone to reliably detect mutations at low tumor fraction. We have developed a novel liquid biopsy platform (SMSEQ) that dramatically improves detection sensitivity and specificity at low tumor DNA presence. The SMSEQ platform allows confident calling of variants down to 0.1% tumor fraction with analytical specificity > 99.999%.

Materials & Methods: We performed a clinical study using SMSEQ platform with 35 Colorectal Cancer (CRC) patients and 28 healthy individuals from Chang Gung Memorial Hospital, Taoyuan, Taiwan. All cancer patients had metastatic colorectal cancer confirmed by tissue biopsy.

Results: Somatic mutations were identified in 34 CRC cases, yielding a clinical sensitivity of 97% (34/35). No mutations in our cancer panel were detected in the healthy cohort giving 100% specificity. The most frequently mutated genes were TP53, APC, and KRAS. 87% of CRC patients had at least one mutation in a gene known to have an effect on treatment efficacy. Three patients were identified with wild-type KRAS and mutated BRAF. Mutated BRAF, which occurs in 5%-10% of wild-type KRAS patients and is not commonly tested in mCRC, may confer resistance to anti-EGFR treatment.

Conclusion: cftDNA analysis with SMSEQ platform is shown to be a reliable method of detecting tumor mutations for metastatic CRC. Liquid biopsy's non-invasiveness as compared to tissue sampling, and ability to track mutations in real time expands the treatment options for patients without sufficient tissue sample.