The EGF signaling cascade (Figure 1) is a primary target of new cancer therapies. The assessment of KRAS and/or EGF mutations are formal guidelines in identifying colorectal cancer (CRC) and lung cancer patients most likely to benefit from EGF-targeted therapy. Additionally, BRAF and RAS mutation testing is included in the 2009 Revised ATA Thyroid Cancer Guidelines to improve preoperative FNA diagnosis of thyroid cancer. The Signature® Platform Technology offers rapid and sensitive detection of common mutations associated with cancer and response to treatment.

RESULTS

A. KRAS and BRAF Analytical Sensitivity

B. BRAF/KRAS+5 Analytical Sensitivity and Specificity

C. FFPE Specimen Testing

Figure 3. Signature® KRAS/BRAF Preliminary Sensitivity, Specificity and Detection of FFPE Samples. A) Analytical sensitivity of the Signature® KRAS/BRAF assay. The log10 values were calculated by testing genomic DNA isolated from FFPE tissues containing 3% KRAS mutant positive cell line (HCT-116 or HT29) diluted in a background of WT HCT-116 cells at 20, 10, 5, 2, 1, or 0.5%. The mean MFI values were calculated by testing genomic DNA isolated from FFPE blocks containing 3% KRAS mutants in a background of WT DNA, each at 0.5% input. NTC and cell line negative controls are shown. The results indicate detection to at least 1% target mutation.

Figure 4. EGR Targets with Preliminary Detection Sensitivity and Specificity. A) Schematic of the EGR gene showing complexity of DNA variations and high-frequency mutations. B) Detection of EGR targets in a population of two cell lines (H1299) is a double mutant from 100% to 0.5% input. NTC and two false negative controls are shown. The results indicate detection at or above 15% target mutation.

*Research Use Only. Not For Use In Diagnostic Procedures.

**Preliminary Research Data. The performance characteristics of this assay have not yet been established.

**Limit of detection was 1% input of each mutant DNA with both cell line and clinical samples representing a range of specimen sources.

**CONCLUSION

• The Signature® Technology Platform™ enables the specific and sensitive detection of codon variants within multiple gene targets associated with targeted cancer therapies.

• This highly multiplexed approach can be scaled to accommodate modular mutation panels, and enable flexibility in variant detection.

• This simple and rapid workflow is amenable to processing 96 samples for one panel or 24 samples across all panels in a single-plate within 5 hours.

• The limit of detection was 1% input of each mutant DNA with both cell line and clinical samples representing a range of specimen sources.

• Personalized medicine is the forefront of new cancer therapies. Determination of the unique genetic characteristics of the tumor or the individual with cancer can contribute to improved patient care.