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A Multi-Gene Transcript Blood Molecular Signature for the Detection and Treatment of Gut Neuroendocrine Tumors

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Background: Gastroenteropancreatic (GEP) neuroendocrine neoplasms (NENs) or NETs ("carcinoids") are problematic to treat as delays in diagnosis are common and culminate in late-stage disease. This reflects the lack of specific blood biomarker tests both to detect tumors as well as to measure treatment responsiveness. We report the utility of a 51 marker peripheral blood signature in comparison to chromogranin A (CgA).

Methods: The candidate signature was validated for detecting NETs in two sets (n=115 and n=120) and for measuring treatment responses in a third set (n=133, including complete remission: n=4, clinically stable disease: n=82 and non-responders/clinically progressive disease: n=47). Comparison with CgA (ELISA) was undertaken. The effects of acid suppressive medication, age, sex and race were also determined for the PCR test.

Results: The PCR test detects tumors with high sensitivity (85-98%) and specificity (93-97%). It identifies pancreatic and gastrointestinal NETs with similar efficacy (>85%) as well as metastatic and non-metastatic lesions. PCR score was significantly reduced (p<0.004) following surgery or RFA and was significantly higher in clinically progressive disease compared to stable disease (5.8±0.3 versus 0.6±0.1, p<0.002). The performance metrics for differentiating stable and progressive disease were sensitivity: 91% and specificity: 91%. The score was robust (reproducibility: Coefficient of Variation<2%).Long-term PPI use (>1yr), age, sex and ethnicity did not alter the PCR values. The PCR score was significantly (p<0.0005) more accurate than CgA for identifying NETs and was elevated in 91% of NETs when CgA (DAKO) was normal.

Conclusion: A multi (51)-gene NET panel is both sensitive and specific for detecting NETs and is capable of differentiating clinically stable from progressive disease. The test is robust and significantly more sensitive and specific (accurate) than CgA measurement. Application of this PCR-based blood test will permit accurate disease detection, and facilitate identification of disease progress thereby enabling assessment of treatment efficacy.