PathGroup
Physician Centered. Patient Focused.

SmartGenomics™ Colon Profile

Oncology Services

Clinical to Genomic

Advanced Standard of Care

PathGroup SmartGenomics: Colon is designed for ***use at diagnosis*** in suspected or proven metastatic colon adenocarcinoma to uncover therapeutic options and aid in treatment planning to improve patient outcomes.

- **Includes expanded RAS testing recommended by the National Comprehensive Cancer Network (NCCN)**
- Clinically actionable genomic information for 7 genes, DNA MMR (IHC), and MSI
- Fully integrated testing with gold standard technologies for a complete patient picture

Next Generation Sequencing

Medically responsible, targeted sequencing with meaningful results.

- All selected genes have at least one targeted therapeutic available
- Clinical indications, prognostic data and potential therapies presented in a comprehensive report
- Full results in 7 to 10 days

Tailored Genomic Colon Profile

Next Generation Sequencing (NGS)	
BRAF	Lack of response to EGFR monoclonal antibody therapy
CTNNB1	EGFR resistance, mutations associated with Lynch Syndrome
KRAS	Associated with lack of response to EGFR monoclonal antibody therapy
NRAS	Associated with lack of response to EGFR monoclonal antibody therapy
PIK3CA	Adjuvant therapy response, prognostic markers and potentially improved survival with aspirin use
PTEN	Predictive of shorter overall survival; decreased sensitivity to EGFR monoclonal antibody therapy
TP53	Negative prognostic factor
Immunohistochemistry (IHC)	
DNA MMR	Lynch Syndrome screening test - recommended by NCCN
Polymerase Chain Reaction (PCR)	
MSI	Adjuvant therapy response; prognostic marker; potential implications for immuno-therapy

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NGS COLON REPORT

Original Procedure Date: 12/31/2014, Sample Type: Colon, Block Information: 2A, Original Accession number:
Tumor Percentage: 51-80%
Original Diagnosis: Adenocarcinoma

Results from all technologies integrated into a single report

RESULTS

BRAF S465Y, CTNNB1 A43V, TP53 S269R and R306X mutations were detected by NGS.

NO KRAS or NRAS mutation was detected.

Microsatellite instability was detected by separate IHC and PCR studies.

SEE COMMENT IN INTERPRETATIVE SUMMARY.

Pertinent negatives highlighted

Personalized interpretive summary provided for each patient

INTERPRETATIVE SUMMARY

***Comment:* Given the genomic profile (detailed below) and especially in light of the PCR and IHC findings, genetic counseling is strongly recommended to exclude a hereditary cancer predisposition syndrome such as Lynch Syndrome.**

Review of the accompanying pathology report indicates a history of colorectal cancer. Microscopic examination confirms adenocarcinoma corresponding to the above referenced accession number. Sufficient tumor tissue is present for molecular analysis. Excellent gene coverage was achieved, which passed our internal quality checks. **BRAF S465Y, CTNNB1 A43V,TP53 S269R and R306X mutations were detected** by targeted next generation sequencing. No other mutations were detected by targeted next generation sequencing interrogating the 7 genes summarized in the NGS technical table. Please also see the NGS technical table for a summary of single nucleotide polymorphisms (SNPs).

The *BRAF* gene encodes a protein belonging to the raf/mil family of serine/threonine protein kinases. In the setting of colorectal cancer, BRAF mutations are associated with an aggressive clinical course, sporadic tumor (virtually excludes Lynch Syndrome) and a less likely response to EGFR monoclonal antibody therapy. However, it must be noted that the prognostic and therapeutic significance of non-V600E BRAF mutations is not entirely clear. Early studies have demonstrated success utilizing BRAF inhibitors in combination with other therapeutics such that target MEK, EGFR and/or PIK3CA.

CTNNB1 mutations have been described in a variety of solid tumors, and investigational therapeutic regimens targeting the ß-catenin/Wnt signalling pathway may be available. In colon cancers, certain CTNNB1 mutations have been associated with Lynch Syndrome.

Mutations in TP53 are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome, and are generally associated with a poor prognosis. Therapies directly or indirectly targeting TP53 may be available in an investigational context.

electronically signed on

Decisions regarding patient care and/or treatment should not be based on the results of this test alone or the information contained in this report, but upon the independent medical judgment of the treating physician in the context of the patient's condition and other factors in accordance with the applicable standard of care. The selection of agents identified in this report, whether none, in part, or in entirety, is at the discretion of the treating physician. Additionally, agents listed in this report, along with indicated clinical trials, are not ranked in order of potential efficacy, predicted efficacy, or level of evidence which may vary from the patient's indicated tumor type.

THERAPEUTIC ASSOCIATIONS

	Potential Therapeutic Response / Drug Class	Disease Association	Gene	Alteration
✓	Increased likelihood of response to anti-EGFR monoclonal therapy	Colon cancer	KRAS and NRAS	WILD TYPE (NO MUTATION)
📋	Targeted therapies (i.e. MEK/PI3K/RAF/EGFR inhibitors may be available in an investigational context	Colon cancer	BRAF	p.S465Y

No therapeutic associations for other diseases at this time.

Therapeutic guidance in an easy to read format