A genomic test for metastatic potential in colon cancer – progress and potential

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Background. This year, 103,000 people in the U.S. will be diagnosed with colon cancer and over 50,000 people will die of colorectal cancer. Patients are treated with surgery, radiation therapy or systemic chemotherapy based on macroscopic traits of the tumor, and the tumor stage. Chemotherapy is recommended for patients with stage III or IV tumors, or stage II tumors with at least 10 positive lymph nodes. While chemotherapy is of some benefit for stage II colon cancers [1], 82% of these patients will survive for 5 years without further treatment. At the same time, 10% of the patients who do not receive chemotherapy will die of the disease within 5 years. A method of identifying the patients who can safely avoid chemotherapy and the patients who may benefit from chemotherapy, will save lives, relieve thousands of people from the toxic side effects of unnecessary chemotherapy, and save the nation millions in healthcare expense.

Progress. Dr. Buechler and Dr. Hummon have advanced understanding of colon cancer by showing that different processes dominate disease progression in left-side colon cancer (LCC) and right-side colon cancer (RCC); i.e., LCC and RCC must be treated as separate diseases [3]. The right side of the colon includes the ascending and transverse colon, while the left side encompasses the descending colon to the sigmoid. Applying this principle and the algorithm in [2] to publicly available microarray data results in separate panels of genes for RCC and LCC that identify large sets of good prognosis colon cancer patients (Fig.1). There are numerous other genes that can replace the four genes in the model with little loss of significance, so this should be viewed as a family of equivalent tests. No external funds were used in this project. A provisional patent application has been filed for this invention.

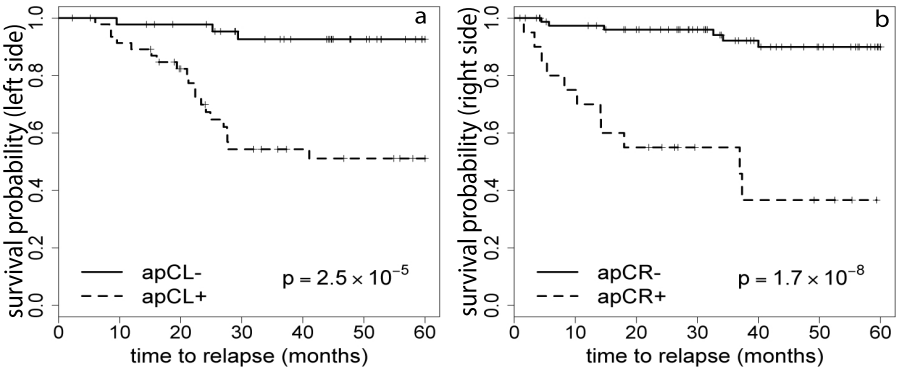

Fig. 1 Survival plots for models of metastasis in LCC & RCC in microarray dataset with ~ 100 samples per group. **ap-Colon test** definition:

Left	
apCL-	low NOX4 & high MMP3
apCL+	high NOX4 or low MMP3
Right	
apCR-	high CDX2 & low FAM69A
apCR+	low CDX2 or low FAM69A

Development of clinical version. Due to current practices in surgery and pathology, a clinically applicable version of this test must measure mRNA obtained from formalin-fixed, paraffin-embedded (FFPE) tissue. Development of the clinical test and subsequent validation in archival tissue will likely be completed by the end of 2011.

Commercial potential. The potential annual U.S. revenue for RL-COLON is $285M, based on an estimated 75,000 non-metastatic colon cancer cases and a sale price of $3,800. Genomic Health is marketing a diagnostic test that is predictive of the need for chemotherapy, however there is no prognostic test currently available.

References

[1] Quasar Collaborative Group, Adjuvant chemotherapy versus observation in patients with colorectal cancer: a randomised study, *Lancet*, 2007, **370** (9604) 2020-9.

[2] S. Buechler, Low expression of a few genes indicates good prognosis in estrogen receptor positive breast cancer, *BMC Cancer*, 2009, **9** (1) pp243.

[3] K. Bauer, A Hummon, S. Buechler, Right-side and left-side colon cancer follow different pathways to relapse, *Molecular carcinogenesis*, to appear.