

New Colorectal Cancer Test Could Detect Early Cancer-causing Genetic Biomarkers with High Degree of Sensitivity

PHILADELPHIA —An investigational test that screens for colorectal cancer could detect genetic mutations that are indicative of the disease with a high degree of sensitivity and specificity, according to results of a study presented at the [AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics](#), held Oct. 26-30.

“Early detection of colorectal cancer dramatically increases rates of patient survival,” said the study’s lead author, Michael J. Powell, PhD, C. Chem, MRSC, chief scientific officer of DiaCarta Inc., based in Richmond, California, with operations in Shanghai and Nanjing, China. “Currently, available molecular tests for colorectal cancer do not detect early cancer or adenomas with enough sensitivity and specificity.”

Colorectal cancer is the second leading cause of [cancer death](#) in the United States, according to federal estimates. Current [guidelines](#) suggest that patients of average risk get screened regularly from age 50 to age 75. Colonoscopy and fecal occult blood tests are the most common screening tools.

The ColoScape assay can be used as a screening assay, however, Powell said its primary use is as a triage, recurrence, and monitoring assay. The ColoScape assay uses xenonucleic acid (XNA) molecular clamping technology to detect multigene mutation biomarkers in colorectal cancer. Powell explained that XNAs are novel synthetic analogs of nucleic acids that help suppress the amplification of normal DNA sequences and allow selective amplification of mutated DNA sequences using real-time polymerase chain reaction (qPCR).

In this validation study, researchers analyzed a total of 324 clinical samples from tissue biopsies and plasma. For all tissue samples, ColoScape detected mutations with 95 percent specificity and 91 percent sensitivity. For tissue samples that excluded adenomas, ColoScape detected mutations with 96 percent specificity and 100 percent sensitivity.

For plasma samples that excluded adenomas, ColoScape detected mutations with 92 percent specificity and 86 percent sensitivity. In tests that combined tissue and plasma, with adenomas excluded, specificity and sensitivity were both 93 percent.

Powell added that a previous study, led by DiaCarta's collaborators at the University of Potsdam in Germany, from which the biomarker panel was licensed, indicated that the panel could detect precancerous lesions with over 65 percent accuracy in stool samples.

If the ColoScape test is approved, it would be available commercially as an "in vitro" diagnostic kit, which could be used in a local hospital setting or laboratory with qPCR capabilities. Powell said that since the test can be performed in local hospitals or labs, it could potentially make molecular testing more accessible to patients. ColoScape can be used to study tissue, stool, or plasma samples. Results can be obtained in three to four hours, compared with about two weeks for competing screening technology, according to Powell.

Powell said that if ColoScape is approved by the U.S. Food and Drug Administration (FDA), it would typically be administered after a patient had a positive fecal hemoglobin test or at the recommendation of a physician. If the patient tested positive for the mutations that can indicate colorectal cancer, he would receive a follow-up colonoscopy.

DiaCarta anticipates that the assay could also be used to monitor patients following surgery or chemotherapy, as the presence of certain biomarkers could suggest a recurrence of colorectal cancer.

Powell said that by identifying the mutations associated with colorectal cancer, ColoScape could help clinicians determine how to treat each patient. For example, he noted, a patient with a BRAF mutation might receive a targeted therapy that has shown benefit in patients with that specific mutation.

Powell said that further research is necessary to evaluate ColoScape's effectiveness in triage and detecting recurrence and monitoring treatment response.

DiaCarta is currently seeking further clinical validation for the ColoScape assay in the United States and China, and intends to seek regulatory approvals for the test in all those markets. ColoScape currently is approved for in vitro diagnostic use in Europe (CE-IVD).

This study was funded by DiaCarta.

Abstract: LB-B11

Presentation Session: [LBPO.B05 – Other Topics](#); Sunday, Oct. 29; 12:30-4 p.m. ET; Session B, Hall E

Title: Development and Validation of ColoScape™ - A New Colorectal Cancer Mutation Detection Assay™

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Introduction: Colorectal cancer is a highly preventable disease as early detection increases rates of patient survival to near 100%. Herein we report the development and validation of ColoScape™, a highly sensitive test powered by XNA technology to detect novel multigene mutation biomarkers in CRC by real-time PCR. The assay allows the sensitive detection of the presence or absence of mutations in the targeted regions of the genes interrogated in tissue biopsy (FFPE) and plasma samples.

Methodology: The high sensitivity of this multigene biomarker assay is achieved due to xenonucleic acid (XNA) probe technology. XNA probes are novel backbone modified oligomers with natural nucleoside bases (A, T, C and G) that hybridize by Watson-Crick base pairing to natural DNA and RNA with much higher binding affinity. XNA probes are designed that bind to the selected wild-type sequences at the respective genetic loci in the target genes. These XNA probes cannot be extended by DNA polymerase thus suppress amplification of WT DNA templates and only allow amplification of the target mutant DNA templates in the sample. For each of the selected mutation sites, primers and FAM-labeled TaqMan probes were designed and tested together with the selected XNA oligomers. An internal PCR control selected in the Human -Actin (ACTB) gene was employed utilizing an HEX-labeled TaqMan probe.

Results: The ColoScape™ kit was demonstrated to have robust analytical performance and clinical accuracy for FFPE, stool and plasma samples. The rapid, precise and sensitive molecular assay for mutation detection in colon cancer has key benefits listed below. The assays showed a sensitivity of as low as 0.1% mutation in 5-10 ng of WT DNA/well. No cross-reactivity was observed with wild-type up to 320ng purified gDNA and up to 20ng FFPE DNA per reaction demonstrating high specificity of the ColoScape™ assay. Intra-assay, inter-assay, lot-to-lot and operator variation comparison showed CV% between 3% and 8%. Excluding pre-cancer samples, the assay clinical specificity and sensitivity were 95% and 100%, respectively. Pre-cancer detection sensitivity was 60% and 62.5% for stool samples. For tested FFPE clinical samples, the assay specificity and sensitivity were 95% and 91% respectively while the assay clinical specificity and sensitivity were both 100% for plasma samples.

Conclusion: The ColoScape™ Colorectal Cancer Mutation Detection qPCR assay is shown to be a sensitive tool intended to aide in the early detection of colorectal cancer, disease monitoring and therapeutic interventions.

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Hosted by the American Association for Cancer Research (AACR), the National Cancer Institute (NCI), and the European Organisation for Research and Treatment of Cancer (EORTC), the 2017 Molecular Targets and Cancer Therapeutics conference will bring together more than 1,500 academics, scientists, and pharmaceutical industry representatives from across the globe to discuss innovations in drug development, target selection, and the impact of new discoveries in molecular biology. For more about the AACR, visit www.AACR.org. For more about the NCI, visit www.cancer.gov. For more about the EORTC, visit www.eortc.org.