Test could detect early colorecral cancer-causing genetic biomarkers with high sensitivity

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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.

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