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Scientists pair blood test and gene sequencing to detect cancer

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Scientists at the Johns Hopkins Kimmel Cancer Center have combined the ability to detect cancer DNA in the blood with genome sequencing technology in a test that could be used to screen for cancers, monitor cancer patients for recurrence and find residual cancer left after surgery.

"This approach uses the power of genome sequencing to detect circulating tumor DNA in the blood, providing a sensitive method that can be used to detect and monitor cancers," says Victor Velculescu, M.D., Ph.D., professor of oncology and co-director of the Cancer Biology Program at Johns Hopkins.

A report describing the new approach appears in the Nov. 28 issue of *Science Translational Medicine*. To develop the test, the scientists took blood samples from late-stage colorectal and breast cancer patients and healthy individuals and looked for DNA that had been shed into the blood.

The investigators applied whole-genome sequencing technology to DNA found in blood samples, allowing them to compare sequences from cancer patients with those from healthy people. The scientists then looked for telltale signs of cancer in the DNA: dramatic rearrangements of the chromosomes or changes in chromosome number that occur only in cancer cells.

No signs of cancer-specific chromosome changes were found in the blood of healthy individuals, but the investigators found various cancer-

specific alterations in the blood of all seven patients with colon cancer and three patients with breast cancer. Using specialized bioinformatic approaches, they were able to detect these alterations in a small fraction of the millions of DNA sequences contained in the blood sample.

"This is proof of the principle that genome sequencing to identify chromosomal alterations may be a helpful tool in detecting cancer DNA directly in the blood and, potentially, other body fluids," says Rebecca Leary, a postdoctoral fellow at Johns Hopkins. "But larger clinical trials will be needed to determine the best applications of this approach."

The investigators note that there may be less circulating DNA in early stage cancers, and, thus, these would be more challenging to detect without more extensive sequencing. As sequencing costs decrease, the investigators expect that detecting earlier-stage cancers may become more feasible.

Velculescu says that additional research will focus on determining how the new test could help doctors make decisions on treating patients. For example, the blood test could identify certain chromosomal changes that guide physicians to prescribe certain anti-cancer drugs or decide patient enrollment in clinical trials for drugs that target specific gene defects. Currently, physicians use cellular material biopsied from the original tumor to make these decisions, but tumor material can often be inaccessible or unavailable.

The Johns Hopkins study builds on the team's earlier work using genomic sequencing of DNA in the blood to find rearrangements of chromosomes. The previous work required samples of the original tumor and knowledge of DNA changes in that tumor to find those same changes in the blood. This new test has no need for original tumor samples and includes an analysis of changes in the copy number of chromosomes.

"It's an evolution of technologies we're developing for cancer diagnosis, and, by combining our knowledge, we can build better ways to detect disease," says Luis Diaz, M.D., an oncologist and director of the Swim Across America laboratory at Johns Hopkins.

Provided by Johns Hopkins University School of Medicine