Six-Gene Cluster Stratifies Need for Colonoscopy

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — The probability of colorectal cancer in asymptomatic patients can be fairly accurately stratified by RNA expression profiling of six genes detectable in whole blood, researchers reported at the annual meeting of the American Association for Cancer Research.

The finding may enable clinicians to prescreen and risk stratify reluctant candidates for screening colonoscopy, poster presenter Dr. Wayne Marshall, president/CEO of GeneNews Corp. of Richmond Hill (Ont.), suggested in an interview at the meeting.

The company has announced plans to launch a laboratory test, ColonSentry, based on the six-gene panel, by the third quarter of this year in Canada.

Fewer than half of Americans comply with recommended colorectal cancer screening guidelines, with far lower compliance—about 15%—in Canada and Western Europe, Dr. Marshall noted.

The ColonSentry pattern of molecular blood markers was developed by the company's chief scientist, Dr. Choon-Cin Liew, who was formerly a researcher in microarray technology aimed at bladder cancer and heart disease at Brigham and Women's Hospital and Harvard Medical School, both in Boston. Dr. Liew cofounded GeneNews with Dr. Marshall, an orthopedic surgeon and joint neurophysiology researcher.

Research identified six genes whose expression could discriminate between blood samples provided by colorectal cancer patients and controls.

Preliminary research identified six genes (ANXA3, CLEC4D, LMNB1, PRRG4, VNN1, and IL2RB) whose expression could meaningfully discriminate between blood samples provided by 116 patients with colorectal cancer and 127 control subjects. The six genes had an accuracy of 74.6% (area under the receiver operating characteristic [ROC] curve, 0.79; 95% confidence interval, 0.73-0.84)

A confirmatory, blinded, independent study of samples from 166 colorectal cancer patients and 171 controls confirmed the area under the curve and found the panel was 70.3% accurate, including 127 true-positive, 39 false-positive, 110 true-negative, and 61 false-positive results (Clin. Cancer Res. 2008;14:455-60.)

These data were then combined with the known colorectal prevalence rate of 0.5% in an average-risk population to create a three-tier probability matrix:

► Based on their six-gene profiles, an estimated 18% of this population would receive a "high probability" designation, suggesting a 1.5% risk of colorectal cancer, a threefold increase over baseline risk.

► Another 20% of this population would be at average risk, with a 0.62% probability of having colorectal cancer.

► Finally, 62% of this population would fall into the "low probability" designation, with a 0.16% risk of colorectal cancer, a threefold decreased risk from baseline.

Receiving news of a "high probability" designation would place a patient at approximately the same risk as a person with a first-degree relative with colorectal cancer, Dr. Marshall said. "They are no longer an average-risk person. I think very few folks armed with that information would not undergo screening," he said.

At the other end of the spectrum are the majority of patients who learn they have a lower than average risk for colorectal cancer. In this case, unless symptoms arise, the risk of complications from colonoscopy would likely outweigh the risk of cancer, Dr. Marshall said.

"As a front-line screening tool [for lower than average risk patients], colonoscopy is arguably overkill," he added. "Information that is clinically actionable occurs at both ends of the scale."

Although a price has not been set for the ColonSentry test, it will cost more than a prostate-specific antigen test and far less than a colonoscopy, Dr. Marshall said.

At first, the test will be performed in a designated laboratory. The company intends to pursue Food and Drug Administration certification so the test can be performed by laboratories meeting criteria of the Clinical Laboratory Improvement Amendment approved by the Centers for Medicare and Medicaid Services. ■