Microbiome May Predict Colon Cancer Tumor Mutational Status

Neil Osterweil | October 13, 2015

BALTIMORE — Analysis of the microbiome surrounding colon cancer tumors could be used as a noninvasive screening test that is more sensitive and specific than fecal occult blood testing, according to the results of a new study.

"This is something that could be critical in colon cancer, because each tumor may have a different mutational landscape with different genes mutated, and that might have an effect on the microbiome," said Ran Blekhman, PhD, from the University of Minnesota in Minneapolis.

The results of the study were presented here at the American Society of Human Genetics 2015.

Dr Blekhman and his colleagues looked at the genetic differences between healthy colon cells and tumor cells from adults with colorectal cancer, and found that specific tumor mutations are associated with the presence of specific bacteria in the gut.

For example, in people with an *APC* gene mutation, there is a strong association between familial adenomatous polyposis, a hereditary cancer syndrome, and an abundance of *Fusobacterium*, said Dr Blekhman.

He pointed out that his lab is the first to analyze the correlation between specific tumor mutations and the composition of the tumor microbiome.

More Mutations, More Diversity

The investigators used whole-exome sequencing to assess the protein-coding regions of tumors and microbiome profiling to characterize the microbiota in tumor biopsy specimens and normal colon tissue samples from 44 adults with colon cancer.

They found that the more mutations, the more varied the bacterial species in the tumor microbiome.

And for certain genes, there was a correlation between somatic mutations and changes in the abundance of specific microbes.

Other evidence of the correlation between bacteria and tumor was seen at the pathway level.

Loss-of-function mutations were detected in tumor glucose transport pathways and were strongly correlated with higher levels of energy utilization in the microbiome, said Dr Blekhman. This suggests that the tumor and the bacteria in its neighborhood are competing for bodily resources.

The investigators created a risk index that evaluated the correlation between microbes and each of several known tumor driver mutations. The index was able to accurately predict the presence of a loss-of-function mutation in *ZFN717*, a gene encoding for a zinc finger nuclease, part of a family of enzymes involved in DNA repair.

These findings suggest that it is possible to genetically classify tumors from fecal samples alone. Theoretically, this means that manipulation of the tumor microenvironment could be used to prevent or treat colon cancer, Dr Blekhman explained.

This study addresses, in part, the problem of "hidden heritability," said Chris Gunter, PhD, from Emory University School of Medicine in Atlanta.

"If you look at cancer-sequencing studies now, they identify something like 10 possible driver mutations. We have not yet managed to predict what all the drivers and passengers will be," she told *Medscape Medical News.*

"If this type of work can help us narrow down the list, that should add to our understanding of how cancer develops," she said.

Dr Blekhman and Dr Gunter have disclosed no relevant financial relationships.

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