Microbiome analysis complements fecal occult blood test for improved detection of colonic lesions

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Colorectal cancer is the third leading cause of death among cancers in the United States1. Although individuals diagnosed early have a greater than 90% chance of survival, more than one-third of individuals do not adhere to screening recommendations partly because the standard diagnostics, colonoscopy and sigmoidocsopy, are expensive and invasive1–4. Thus, there is a great need to improve the sensitivity of non-invasive tests to detect early stage cancers and adenomas. Numerous studies have demonstrated a causal linkage between the formation of colonic lesions and the activity of the gut microbiota in tissue culture and animal models5–8. These findings have been complemented by studies in human populations identifying shifts in the composition of the gut microbiota associated with the progression of colorectal cancer9–12. These results suggest that the gut microbiota may represent a reservoir of biomarkers that would complement existing non-invasive methods such as the widely used fecal immunochemical test (FIT). Using stool samples from 490 patients we developed a cross-validated random forest classification model that detects colonic lesions using the relative abundance of gut microbiota and the concentration of hemoglobin in stool. The microbiome-based random forest model detected 95.0% of cancers and 61.1% of adenomas while FIT detected 75.0% and 15.7%, respectively. Of the colonic lesions missed by FIT, the model detected 80.0% of cancers and 53.9% of adenomas. To date this is the largest study to characterize alterations in the microbiota associated with colorectal cancer and the first to demonstrate a method by which microbiome analysis improves upon existing screening methods. With a negative predictive value of 99.98%, our model could be used to accurately identify those patients for whom a colonoscopy is unnecessary, potentially reducing healthcare costs and complications due to invasive screening while decreasing the incidence and mortality of colorectal cancer.

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