

Open Letter to the Editor

C. Mel Wilcox, MD, Editor,

Clinical Gastroenterology and Hepatology,

AGA, 4930 Del Ray Avenue, Bethesda, Maryland 20814-3015;

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Referring to: The Stool DNA Test is More Accurate than the Plasma Septin 9 Test in Detecting Colorectal Neoplasia. Clin Gastroenterol Hepatol. 2011 Oct 19.

Author(s): Ahlquist DA, Taylor WR, Mahoney DW, Zou H, Domanico M, Thibodeau SN, Boardman LA, Berger BM, Lidgard GP. Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester MN.

Sir,

In the referenced article, a plasma-test for methylated Septin9 is compared to a stool DNA test, with results inconsistent with those previously reported for the ARUP Septin9 LDT . We developed and licensed the Septin9 technology to ARUP Laboratories and the results reported in the article are inconsistent with our experience of the Septin9 biomarker as well. Careful review of study methodology indicates systemic flaws in the reporting, including missing information and incomplete authorship with a bias potentially originating from the first author's financial interest in the success of the stool DNA test.


An explanation of the selection process for CRC cases tested in the study is lacking and is described as "selected if they had participated in a recent multicenter evaluation of a prototype next generation sDNA test". A selection process rather than a more unbiased design of testing all subjects with both tests indicates that bias could have been introduced particularly if a inordinate number of sDNA test positive subjects were chosen. The use of a different set of colonoscopy normal

control patients for each test makes any comparison illusive. The choice of the controls for the blood test seems to be inadequate, with both the unusually high false positive rate and the occurrence of 8% (4/49) other cancers in the plasma control group casting doubt whether they represent average risk individuals.

The study employed archived samples although little information is provided on sampling procedures, blood collection tubes used or timing of blood collection – all of which have a significant impact on Septin9 performance. The authors conceded that plasma sample preparation was only “similar” to the test commercialized by ARUP Laboratories. An accurate comparison can only be achieved when both tests have been performed according to procedures that would occur in routine clinical practice. Finally, it seems telling that no co-author from ARUP has been involved in manuscript preparation. This incomplete authorship further supports the grave concern that the article presents a methodologically flawed and biased study. We have knowledge of a letter dated April 15th, 2011 and addressed by ARUP to the first author objecting to a publication. In this letter, an ARUP co-investigator of the study formally raised concerns on the validity of the data.

In summary, the lack of complete protocol information, the lack of a shared set of colonoscopy-normal controls, the nebulous clinical history of the plasma control patients and the incomplete study authorship casts serious doubts about this study as a sincere, scientific comparison between Dr Ahlquist’s stool DNA test and a Septin9 plasma test.

Sincerely yours,



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