Reviewer's report

Title: Reduction of novel circulating long-chain fatty acids and colorectal cancer patients is independent of tumor burden and correlates with age.

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Reviewer: Patrizia P. Ferroni

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The manuscript by Ritchie and colleagues reports the clinical significance of hPULCFA C28H46O4 (CRC-446) in colorectal cancer (CRC). The main findings of the study are that CRC-446 levels are not affected by conventional CRC treatment and inversely correlate with age, which suggest that reduced serum CRC-446 levels likely exist prior to the development of CRC. Authors conclude that extrapolating their results to a screening scenario it would imply a significant reduction of colonoscopies and an increase in CRC detection rates over the life of the subject. Overall, the article is complete, fully comprehensive to the reader and conveys a clear-cut message. The aim is interesting and well defined, methods are well documented without being over-detailed, data are sound, the discussion and conclusions are well balanced and adequately supported by the data presented. Limitations of the work are clearly stated. I have no major comments on this well presented paper, except few discretionary revisions:

Abstract
- Report the number of patients in the American cohort
- Report on the distribution of CRC-446 in CRC vs. control subjects

Results
- Although CRC-446 levels were already reported to be reduced in pre-treatment CRC patients compared to disease-free subjects, I believe it would be useful to have a brief description of pre-treatment values in comparison with controls (Caucasian vs. Japanese). I acknowledge this is only a confirmatory finding, but a direct comparison, instead of single reference to Figures 1 and 2 might increase clearness for the reader.

Discussion
- Reference to other previously reported hPULCFAs, CRC-448 and CRC-450, is redundant.
- Do the Authors have any information in terms of cost-benefit?

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests