Reviewer’s report

Title: Pre-diagnostic metabolite concentrations and prostate cancer risk in 1077 cases and 1077 matched controls in the European Prospective Investigation into Cancer and Nutrition

Version: 0 Date: 27 Feb 2017

Reviewer: Daniel Raftery

Reviewer’s report:

The authors describe a very thorough study of prostate cancer risk in over 4000 subjects from the EPIC study using quantitative metabolomics.

The carefully matched, case-control nested study design is excellent, and the metabolomics data and statistical analysis are also of very high quality. The work sets a benchmark for future studies in terms of design and execution. It’s a pity that no very strong biomarkers were found, but then careful studies such as the present are needed in order to settle such questions.

One request I have is for the authors to provide the actual quantitative data (i.e., metabolite concentrations) on the metabolites that they measured. It is extremely useful for other researchers to be able to compare their results in terms of concentration means and SD for both the cases and controls, and also to know whether there is some skew in the metabolite distributions. A clear listing of the metabolites with missing values or that were too low to measure would be helpful, although this can be figured out from the text with some detective work. This information is probably best supplied as supplemental tables.

It would also be useful for the authors to comment on the use of citrate blood collection tubes, which some metabolomics researchers have observed effects on metabolite extraction or metabolite signal suppression. See, for example, Metabolomics (2013) 9:337-348, or Analytica Chimica Acta 2013-03-20.

With these relatively minor changes, the article should be published.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.


Yes

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I am able to assess the statistics

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