Reviewer's report

Title: A combined blood based gene expression and plasma protein abundance signature for diagnosis of epithelial ovarian cancer - A study of the OVCAD consortium

Version: 2 Date: 23 November 2012

Reviewer: Ian Cree

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This is an interesting paper representing a considerable workload and is a major study in the field. However, it could be improved, particularly with regard to the potential clinical significance of the results and how these tests might be used in practice. In my view there is a requirement for a prospective real world study to show whether such extraordinary accuracy of discrimination between patients and controls can be translated to an unselected population. The UKCTOCS study is a design that should be considered, and it may of course be feasible to go back to some of the UKCTOCS and similar studies to obtain samples to show that this is worthwhile.

Discretionary revisions

- The supplementary files are tables that should be part of the main paper - this is an online journal and the few kilobytes this would take are insignificant. The histological make up of the group should be stated in the paper and whether histology was centrally reviewed.
- The list of proteins tested should be clearly stated earlier in the paper - it was not until opening the supplementary table 2 that they were obvious. Reference in the methods section to a table of the genes and proteins tested would help.
- The authors correctly state that they did not look at other disease states and this could be discussed further: it is important in my view.
- Figure 3 is the only place in the paper which I could begin to work out whether protein or genes should be tested - and the difference between protein alone v. protein + genes seems small. Is this truly the case, are the tests completely independent, and which would you test first in patients? Could one develop a clinical decision rule for testing to avoid the costs involved in testing large numbers of women with both methods?
- There are occasional minor typographical errors - for instance, 'seeked' instead of 'sought' in the first paragraph of the abstract.

Level of interest: An exceptional article

Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests