Reviewer’s report

**Title:** Gene expression profiling supports the hypothesis that human ovarian surface epithelia are pluripotent and capable of serving as ovarian cancer initiating cells

**Version:** 1  **Date:** 31 August 2009

**Reviewer:** Karin Sundfeldt

**Reviewer’s report:**

Comments to author;

In the manuscript entitled “Gene expression profiling supports the hypothesis that human ovarian surface epithelia are pluripotent and capable of serving as ovarian cancer initiating cells” by authors Bowen et al human ovarian surface epithelium and ovarian serous adenocarcinoma epithelial cells were analysed by gene expression analysis (Affymetrix) and compared with analysis algorithms. A few genes were confirmed on protein level by immunohistochemistry.

General comment:
Overall this is a well performed study. The collection of material, choice of method and analysis of results is elegantly designed. The results suggest that the hypothesis of the “uncomitted” normal ovarian surface epithelial cell could be true. That an OSE cell can move into different lineages of differentiation when turning neoplastic, as an explanation to the great heterogeneity of ovarian cancer. I have only minor comments.

Background:
Interesting and well written.

Material and methods:

Methods for tissue collection;
What was the indication for operation in the 12 OSE brushings? How did you retrieve the cells from the Cytobrush? Did you pool your OSE and CPI cells or did you analyze them individually (12+12 expression profiles)? How many were fertile and how many were menopausal? Did hormonal status make any difference in your comparative analysis (that is if you didn´t pool all your OSE)? Did you put your tumour tissue in RNA later as well?
You state that RNA quality was verified, which is good. How was the quality of your RNA? What did you considered to be good or of acceptable quality?
In the amplification step, how many amplifications did you do? What control steps did you do to minimize the risk of overamplification?
Why did you in the IHC chose the three specific proteins that you chose?
Results:
This part is too expansive and speculative and more like a review or a discussion and should be shortened along with the reference list.
In the results you discuss several pathways differentially expressed in OSE and CPI. This tends to be very speculative. IHC analysis of a couple of proteins from each pathway discussed would make the gene ontology algorithms more credible.

Discussion:
In the discussion the interesting hypothesis that OSE is a stem cell niche of its own is carefully introduced. However this is the only thing discussed here.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.