Reviewer's report

Title: Integrative genome-wide expression profiling identifies three distinct molecular subgroups of renal cell carcinoma with different patient outcome

Version: 1 Date: 26 March 2012

Reviewer: Annika Fendler

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In this study Beleut et al. identified distinct molecular subtypes of renal cell cancer that are independent of histological classification and tumor stage. It is surprising that ccRCC, pRCC and chrRCC are not clustering in different molecular subgroups, although they are morphologically distinct and partially have differing cells of origin.

The author's state that molecular patterns of cancers do not reflect copy number alterations, which clearly highlights the importance of other mechanisms of gene regulation.

I think the study is well composed and of interested for researchers with related research fields.

Discretionary revisions:

1) The author's selected two genes as well as MVD to distinguish the three subtypes at the protein level and performed survival analysis. Interestingly, this gene pattern was able to identify highly aggressive tumors when tumor staging failed to do so. Nevertheless, survival analysis on gene level has not been performed. It would be interesting to see, whether this would identify even more suitable genes for prognosis, which could then be reevaluated on protein level.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests.