Reviewer's report

Title: Genomic expression and single-nucleotide polymorphism profiling discriminates chromophobe renal cell carcinoma and oncocytoma

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Reviewer: Jason Herschkowitz

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Tan et al. pose the question of whether chromophobe renal cell carcinoma (chRCC) and renal oncocytoma, two closely related but clinically disparate entities, can be distinguished based on genomic profiling. They developed a 14 probe-set signature that was able to classify the tumors with 93% accuracy. This was validated on an external data-set with 94% accuracy. The authors also identified areas of copy number alterations also corresponding to expression biases differentiating the two entities. Loss of chromosome 1p was a common event to both chRCC and renal oncocytoma. Importantly, they were able to use the gene expression comparison to identify a set of novel immunohistochemical markers that may be useful clinically.

The authors pose a well-defined question and the methods they use to address it are appropriate and well described.

The 14 probe-set signature derived using PAM was able to classify the tumors with 93% accuracy compared to a diagnosis based on histology. The predictor called all the oncocytomas correctly but misclassified some of the chRCC as oncocytomas. The authors need to discuss whether the gene expression signature could be more accurate. AQP6 mRNA was lower in chRCC than in oncocytomas yet the immunohistochemistry showed the opposite. AQP6 was also shown to mark oncocytomas by IHC in a recent study (Yusenko et al. Int J Biol Sci 2009) which should be discussed. What is the reason for this discrepancy? Overall, the discussion and conclusions are well balanced and adequately supported by the data.

Major Compulsory Revisions - None

Minor Essential Revisions - It is a journal policy that authors should adhere to the standards proposed by the Microarray Gene Expression Data Society and must deposit microarray data in one of the public repositories, such as ArrayExpress, Gene Expression Omnibus (GEO) or the Center for Information Biology Gene Expression Database (CIBEX). All genomic data should be deposited if it has not been already in one of these databases before acceptance for publication.

Discretionary Revisions – The distinction between chRCC and renal oncocytoma is very important clinically with chRCC usually being malignant and oncocytomas usually being benign. The number of samples used in this paper is small. It would be very informative to be able to validate the identified markers on a large set of
samples with accompanying patient clinical data. Are these markers predictive of clinical outcome and can they be used to make informed treatment decisions? How does this compare to current diagnosis?

**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.

**Declaration of competing interests:**

I declare that I have no competing interests