Reviewer's report

Title: microRNA-99a acts as a tumor suppressor and is down-regulated in bladder cancer

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Reviewer: Ross M Drayton

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This article uses appropriate and well-defined methods to answer a clearly defined question, namely whether microRNA-99a is downregulated in bladder cancer tissue, and whether this alteration is detectable in plasma. The data generated is sound and in the main supports the conclusion.

Justification for the study of microRNA-99a in bladder cancer is given by reference to a single paper (Han et al 2011), however, there are papers published before this that have identified this dysregulation (for example Catto et al, Cancer Research 2009).

The manuscript adheres to the relevant standards for reporting.

The authors understand the limitations of their data and the conclusions drawn are appropriate. The paper would benefit from some discussion of the potential limitations of detecting microRNA-99a downregulation in the blood. For example, presumably the rest of the (healthy) bladder (and many other tissues and organs) continue to deposit high/background levels of microRNA-99a into the plasma. How likely is it that a modest downregulation in a relatively small number of cells (ie, the tumour) is going to have a measurable effect on plasma microRNA-99a levels? Other possible explanations could be offered and should be discussed.

The writing on the borderline of reaching an acceptable standard. There are several spelling and grammatical errors that do not detract from the overall meaning.

Minor Essential Revisions
1. Re-write Background section to acknowledge work on microRNA-99a in bladder cancer that pre-dates this study.
2. Add further discussion on limitations of plasma-based microRNA biomarkers for detecting downregulated molecules in tumour cells as mentioned above.
3. Further additional Proof-read

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published.

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

Declaration of competing interests:
I declare I have no competing financial interests.