Reviewer's report

Title: Validation of podocalyxin-like protein as a biomarker of poor prognosis in colorectal cancer

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Reviewer: Dermot Leahy

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In this paper the authors confirm their previously published finding that overexpression of PODXL is associated with poor prognosis in colorectal cancer. While this validation in two large independent cohorts is useful, the potentially novel aspect of the paper lies in their examination of the correlation between PODXL mRNA and protein levels in a subset of tumours.

In general the paper is well written but there are some points that need to be clarified before I could recommend acceptance.

Major Compulsory Revisions

1. The immunohistochemical staining was dichotomised as low and high staining. Low staining included complete absence of staining and cytoplasmic staining while high staining is membranous. How many cases showed complete lack of staining? Was there any significance in “absence of staining” versus “any positivity in cytoplasm or membrane”.

2. Membranous staining was seen mainly at the invasive tumour front. In the construction of the TMA, was at least one core taken from the invasive front? Is it possible that some positive cases were missed due to this localisation of staining? Were some full face sections analysed to control for this potential problem with the TMA method?

3. The authors report that no significant correlation was found between mRNA levels and protein expression of PODXL. Similar to No.1, were a group with complete lack of expression compared to a group with any degree of expression.

4. Did the authors consider microdissection of a strongly staining area from a frozen section to provide a definitive answer to the question of correlation with mRNA.

Minor issues not for publication

In "Evaluation of PODXL staining" the symbol for "less than or equal" should be corrected.

In fourth paragraph of Discussion "molocular" should be "molecular".

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