Reviewer's report

Title: Computational Prediction and Experimental Validation Associating FABP-1 and Pancreatic Adenocarcinoma with Diabetes

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Reviewer: David Morse

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The article uses a previously reported database containing human disease-related expression changes generated from publicly available DNA microarray data to initially identify a set of genes with increased expression in pancreatic cancer compared to expression in acute pancreatitis and type I diabetes mellitus (DM). The list was then filtered using a list of genes known to be genetically associated with DM. The resulting list was again filtered for a biofluid database containing proteins known to be detected in blood or urine. This is a thorough, well presented study demonstrating the potential for this approach to identify useful diagnostic markers for pancreatic adenocarcinoma associated with diabetes. However, the potential utility for FABP-1 as a diagnostic marker is questionable (as detailed below).

Major Essential Revisions:

1) Although FABP-1 is expressed in renal proximal tubule cells which shed into the urine, it is doubtful that cells from PaC will also shed into the urine by this mechanism. However, circulating tumor cells (CTCs) in the blood have been found to express FABP-1 after enriching the sample for CTCs extracting and detecting FABP-1 mRNA, and has thus been proposed as a marker for CTCs (study not-referenced in the manuscript). Unfortunately, CTCs are only associated with metastatic disease and thus could only be used for diagnosis of advanced stages of cancer. Otherwise, being that FABP-1 is cytoplasmic and not found on the cell-surface, it is difficult to see the utility of FABP-1 as a diagnostic marker because it would be difficult to develop a targeted imaging probe against it. The authors should more clearly state/justify the proposed method that will be used for detection of this diagnostic marker in patients.

Minor Essential Revisions:

2) Figure 2 would be better presented in the results section.

3) Page 12, 3rd paragraph - There is a typo, FABP1-1 should be FABP-1.

Discretionary revisions:

4) Based on the representative images provided for Figure 2, a score of 1 represents weak staining (expression). Hence, only 20% of ‘PaC-DM’, 10% of all ‘PaC’ and 5% of ‘PaC no DM’ have moderate to strong expression of FABP-1.
Since it is not clear that weak expression could be detected relative to expression in normal tissues in the blood or urine, the reported 50% expression of FABP-1 in PaC-DM possibly overstates the potential for diagnostic utility (although 20% coverage is not bad). As reported, this marker is not an absolute marker of diabetes associated pancreatic cancer, e.g. 5% of PaC with no DM moderately or strongly express this marker. Based on these numbers, 4 out of 5 (80%) of tumors expressing this marker will have associated DM (which is not bad). The authors may choose to use a more stringent, and thus more relevant, cutoff for IHC data when reporting the percentage of tumors covered by the FABP-1 marker.

**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