Reviewer's report

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

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Reviewer: Juergen Schrezenmeir

Reviewer's report:

The manuscript RN Sharaf et al. is interesting, but still has some drawbacks which require major compulsory revisions.

The methodology of search for candidates resulting in FABP1 should be described more precisely to enable understanding the process of data analysis and the results of this search should be given in detail to enable understanding the basis of candidate selection. What was the scoring of FABP1 (between the given range of +1.0 and -1.0) compared to other genes, what was the ranking compared to other genes?

To further elucidate, whether diabetes may have been more or less likely to be associated with FABP1 expression by tumor tissue, the duration of diabetes in the 13 diabetes cases (based on patient’s histories) would be interesting to know.

Furthermore the grade of infiltration of the pancreas of the cases without compared to the cases with diabetes would be of interest, since diabetes might be due to the grade of infiltration, which may be related to the grade or kind of differentiation (that may be related to FABP1 expression).

FABP1 is suggested to be involved in the pathogenesis of diabetes via facilitating fat uptake, cellular trafficking, and chylomicron/VLDL production. This seems unlikely to take place to a significant extent in pancreatic tumor tissue, which is supplied by the nutrients via the portal vein. Therefore a secondary mechanism should be suggested in case the findings may be confirmed in later studies.

Pg. 6
Which microarrays were used? (human genome wide? Which supplier?).

The authors state that a measure ranging from +1.0 (highest value found in pathologic tissue) to -1.0 (lowest value in normal tissue) was used to rank the genes expressed in diseased samples.

This score should be given in the results as well as the scores of the other 10 genes ranking close to (higher and/or lower than) FABP1.

It is confusing that this measure evidently was not used as stated, but a comparison with pancreatitis and type 1 diabetes samples was used for selection.

The sentence “we crossed the list” should be rephrased more precisely. Down to
which RR or OR was this “crossing” done?

Pg 7
The first sentence “given the beta cell …” is not clear.
Were all genes associated with DM or only those which were associated with beta-cell function and insulin resistance in pancreatic carcinoma?
Why are type 2 diabetes susceptibility genes separately mentioned?

Pg 15
Last sentence: “to have”

Pg 16
Better rephrase:
“Only one pathologist scored immunohistochemistry. He, however, has several years of experience.”

Table 1
The diabetes prevalence of 21% is in contrast to published data (45-65%). This should be discussed by the authors.