Serum miR-1290 as a marker of pancreatic cancer - Letter

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We have read with interest the study by Li and colleagues (1) on serum miRNAs in pancreatic ductal adenocarcinoma (PDAC). These data add to the evidence for the feasibility of using circulating cell-free miRNAs for screening and early detection of PDAC, as well as risk stratification for treatments. MiR-1290, a relatively unknown miRNA, emerged as a blood-based biomarker for diagnosing and prognosing PDAC patients. Accordingly, sera from nude mice implanted with human PDAC xenografts have high levels of circulating miR-1290 compared to controls (2). However, additional key points should be discussed in more detail.

Firstly, debate still exists over whether miR-16 is suitable as an endogenous control. miR-16 is a red blood cell expressed miRNA, and variations in blood cell count and/or sample hemolysis could have important implications for biomarker interpretation (3). Furthermore, high circulating cell-free miR-16 discriminate PDAC from healthy individuals and those with benign disease (4). A serum miRNA with the least change in expression across the various tissues should have been chosen as a normalizer, and if miR-16 is indeed the ideal candidate, this should be highlighted in order to implement the measurement of circulating non-coding-RNAs in PDAC patients.

Secondly, miR-1290 and miR-486-3p need to be validated in independent cohorts, but only miR-1290 was evaluated by RT-qPCR and LNA-FISH in 46 PDACs. Importantly, the analysis of a publically available dataset (GSE24279) confirmed its up-regulation in samples from stage-II/III/IV PDAC (n=136), showing that miR-1290 is related to a malignant, rather than an inflammatory process and expressed during disease progression (Figure 1A). Although the majority of PDAC patients do not develop jaundice until locally advanced or metastatic stages, the prognostic value of serum miR-1290 would need to be tested in a cohort of patients with obstructive jaundice in order to...
assess its performance, since hyperbilirubinaemia can affect miRNA levels (5). Furthermore, miR-486-3p was neither validated by Li and colleagues, nor by our analysis (Figure 1B), suggesting that the source of this miRNA is unlikely to be derived from tumor cells.

Thirdly, these data differ from prior analyses, including a recent study on correlation of high serum miR-21 with worse survival (6). Li and colleagues found that high expression of both miR-1290 and miR-486-3p had independent prognostic value, but did not report the univariate analyses for other 16 candidates, including miR-21.

Finally, in the attempt to combine miR-1290 and miR-486-3p expression to see if their prognostic value was improved, high levels of either miRNA were compared to low levels of both, but we wonder whether the comparison of survival rates for patients with high levels of both miRNAs to low levels of both might have proved better this hypothesis.

In conclusion, we are indebted to Li and collaborators for their study, but additional parameters may strengthen the value of miR-1290 in clinics beyond already available PDAC biomarkers.
References


Figure legend

Figure 1 – miR-1290 is up-regulated in PDAC compared to normal pancreas and chronic pancreatitis. Using a publically available dataset (GSE24279) we examined miR-1290 and miR-486-3p expression in a large cohort of PDAC patients and compared it to chronic pancreatitis (CP) and normal pancreas (Normal) samples. This dataset contains miRNA expression profiling results from tissue samples: PDAC (n = 136), chronic pancreatitis (n=27) and normal pancreas (n=22). Due to an approximate normal distribution, the non-parametric Kruskal–Wallis one-way analysis of variance (ANOVA) was used to compare miRNA levels between tissue-types, followed by Dunn's multiple comparison test. Patients included in this study were of stages II, III and IV. Scatterplots are shown for each miRNA and the horizontal line represents the median expression level and inter-quartile range (**p<0.01; ***p<0.001; ns, non-significant).
Figure 1

A

B

Relative miR-1290 expression

Tissue type

Normal

CP

PDAC

Relative miR-486-3p expression

Tissue type

Normal

CP

PDAC

Figure 1
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