

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 microRNA (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 patients with PDAC. Accordingly, sera from nude mice implanted with human

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 to implement the measurement of circulating noncoding-RNAs in patients with PDAC.

Second, miR-1290 and miR-486-3p need to be validated in independent cohorts, but only miR-1290 was evaluated

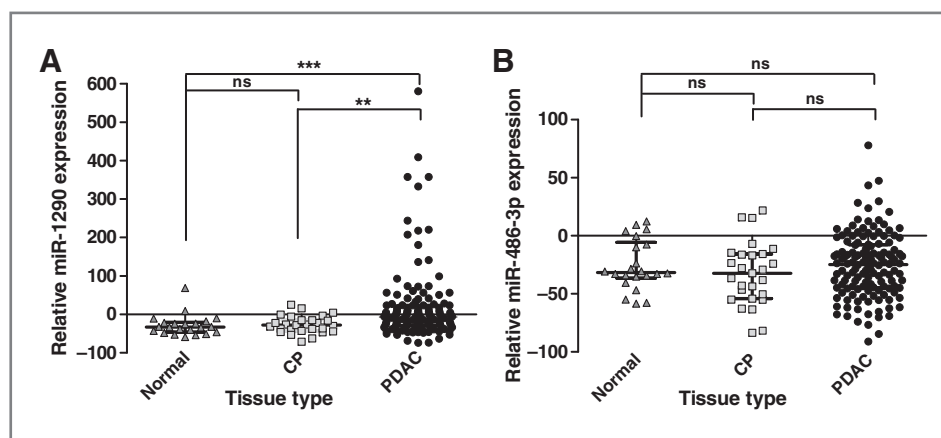


Figure 1. miR-1290 is upregulated in PDAC compared with normal pancreas and chronic pancreatitis. Using a publicly available dataset (GSE24279), we examined miR-1290 and miR-486-3p expression in a large cohort of patients with PDAC and compared it with chronic pancreatitis (CP) and normal pancreas (Normal) samples. This dataset contains miRNA expression profiling results from tissue samples: PDAC ($n = 136$), chronic pancreatitis ($n = 27$) and normal pancreas ($n = 22$). Because of an approximate normal distribution, the nonparametric Kruskal–Wallis one-way analysis of variance (ANOVA) was used to compare miRNA levels between tissue-types, followed by Dunn 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 (***, $P < 0.001$; **, $P < 0.01$; ns, nonsignificant).

PDAC xenografts have high levels of circulating miR-1290 compared with controls (2). However, additional key points should be discussed in more detail.

First, 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

by qRT-PCR and LNA-FISH in 46 PDACs. Importantly, the analysis of a publicly available dataset (GSE24279) confirmed its upregulation 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 (Fig. 1A). Although the majority of patients with PDAC 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 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 (Fig. 1B), suggesting that the source of this miRNA is unlikely to be derived from tumor cells.

Third, 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

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independent prognostic value, but did not report the univariate analyses for other 16 candidates, including miR-21 (1).

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 with 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 colleagues for their study, but additional parameters may strengthen the

value of miR-1290 in clinics beyond already available PDAC biomarkers.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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