Deciphering the diagnostic potential of non-coding rnas for the detection of pancreatic ductal adenocarcinoma through liquid biopsies

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Abstract

Background & Objectives

Pancreatic Ductal Adenocarcinoma (PDAC) is highly lethal due to late diagnosis and limited treatment options. Current diagnostic methods lack adequate sensitivity and specificity. This study identifies an ensemble of unique circulating cell-free non-coding RNA (ncRNA) signatures for PDAC detection through advanced sequencing, bioinformatics, and machine learning (ML) approaches.

Methods

We analyzed plasma samples from 79 controls and 43 PDAC patients. Cell-free small RNAs were isolated and sequenced using Next Generation Sequencing. An innovative stepwise mapping strategy and bioinformatics pipeline were developed to quantify diverse ncRNA species, including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), piwi-interacting RNAs, and other small RNA subtypes. Differential expression analysis identified ncRNAs significantly altered between PDAC patients and controls. ML algorithms ranked gene importance to select key ncRNAs, and a gradient boosting classifier was trained using the top-segregating ncRNAs to evaluate diagnostic accuracy. Gene set enrichment and pathway analyses validated the biomarkers' biological relevance to PDAC.

Results

Twenty ncRNAs were identified as significant discriminators between PDAC patients and controls. Our integrated bioinformatics and ML approach achieved a classification accuracy of 87% and an area under the receiver operating characteristic curve of 91%, surpassing existing diagnostic methods focusing on a single subtype. Top ncRNAs encompassed various classes, including multiple microRNAs, lncRNAs, and Y_RNA transcripts, each exhibiting distinct expression patterns associated with PDAC. Gene set enrichment and pathway analyses revealed that these ncRNAs are involved in critical pancreatic cancer-related pathways, such as cell proliferation, MAPK signaling and cellular senescence, underscoring their biological significance and potential roles in PDAC pathogenesis.

Conclusion

The combined analysis of multiple ncRNA subtypes using stepwise mapping bioinformatic approach and integration of ML methods presents an advancement in the non-invasive diagnosis of PDAC. Unlike traditional methods that focus on a single RNA subtype, our ensemble ncRNA strategy leverages collective diagnostic potential. We identified key ncRNA signatures that are intricately involved in PDAC-specific pathways. This comprehensive approach not only enhances detection capabilities but also provides biological evidence into PDAC pathogenesis. Our work demonstrates the effectiveness of combining multi-class ncRNA profiling with ML to improve diagnostic precision, and for the development of more effective non-invasive diagnostic assays.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.