



# Differential Expression of miR-196a and miR-216a in Cholangiocarcinoma and Pancreatic Ductal Adenocarcinoma



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## Introduction:

- Cholangiocarcinomas (CC) and pancreatic ductal adenocarcinomas (PDAC) are virtually indistinguishable histologically and have overlapping immunohistochemical profiles.
- MicroRNAs (miRNAs) are short non-coding RNAs involved in post-transcriptional regulation of gene expression.
- Dysregulation of miRNAs (miR-21, 10b, 196a and 216a) and their cognate targets are increasingly implicated in many cancers.
- Use of miRNA in diagnostic applications has been limited by inability to determine expression patterns in situ, as profiling-based strategies using tissue homogenates may not adequately identify differential expression between normal and abnormal tissue.

## Aim:

To detect the expression of miR-21, 10b, 196a and 216a in CCs and PDACs

## Material and Methods:

- 13 cases of CCs (12 intrahepatic and 1 extrahepatic) and 18 cases of PDACs were used in the study.
- Cases were subjected to in situ hybridization (ISH) using FAM-labeled miRNA probes (BioGenex) for miR-21, miR-10b, miR-196a and miR-216a followed by super sensitive ISH Detection Kit (BioGenex, DF400-YAX).
- Nuclear staining was evaluated semi-quantitatively by intensity (low: no or weak stain; high: moderate to intense stain).
- Statistical analysis was performed using Fisher's exact two-tailed test.

## Results:

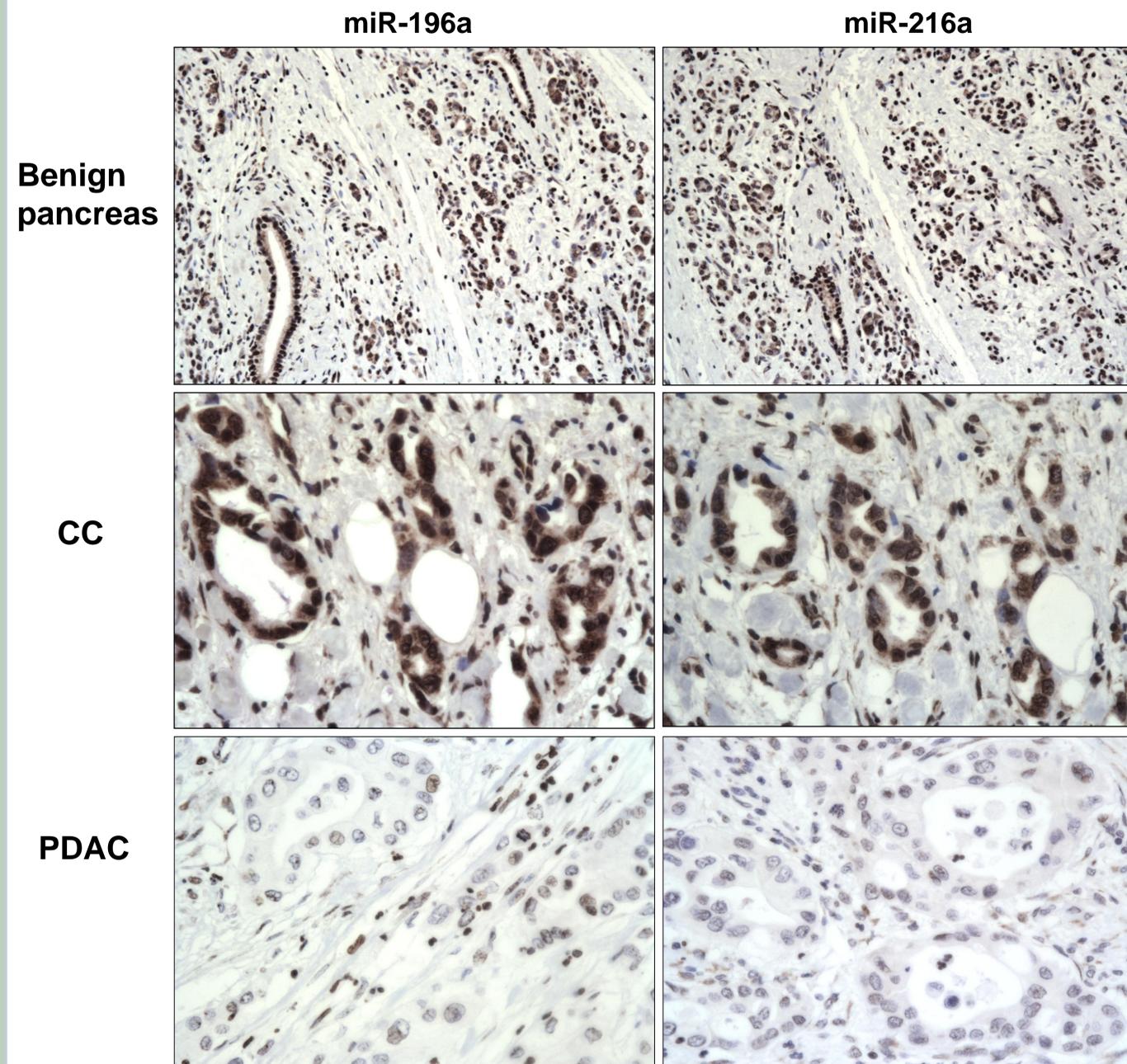


Figure 1: Expression of the miR-196a and 216a in benign pancreatic tissue, cholangiocarcinoma and pancreatic ductal adenocarcinoma. miR-196a and 216a are over-expressed in majority of CC, but are negative to weak focal positive in PDAC

Table 1. Comparison of levels of miR-10b, 21, 196a and 216a between cholangiocarcinoma (CC) and pancreatic ductal adenocarcinoma (PDAC)

miRNA levels	CC (n=13)	PDAC (n=18)	p value
miR-10b			
Low	9	10	0.484
High	4	8	
miR-21			
Low	4	5	1.000
High	9	13	
miR-196a			
Low	2	14	0.001
High	11	4	
miR-216a			
Low	2	13	0.003
High	11	5	

Table 2. Sensitivities and specificities of miR-196a and 216a expression in distinguishing cholangiocarcinoma (CC) from pancreatic ductal adenocarcinoma (PDAC)

miR (high level)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
miR-196a	85 (72-98)	78 (63-93)
miR-216a	85 (72-98)	72 (56-88)

## Conclusions:

- miR-196a and miR-216a expression are downregulated in PDACs compared to CCs.
- No significant differences in the expression of miR-21 and miR-10b are identified between the CCs and PDACs.
- This study demonstrates the feasibility of in situ evaluation in paraffin-embedded tissue where the ability to morphologically differentiate cancer and benign cells is retained.
- Ongoing studies in a larger cohort are underway to fully assess the potential of these markers in differentiating CC from PDAC.