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MicroRNA Profiling of a Familial Primary Pulmonary Enteric Adenocarcinoma

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- pulmonary enteric adenocarcinoma (PEAC) is a rare lung adenocarcinoma with a predominant component (>50%) of intestinal differentiation and tumor cells positive for at least one intestinal marker (CDX2, CK20, MUC2)

- only 31 cases in literature and occurrence in two family members has never been reported before

- PEAC should be distinguished from metastatic colorectal carcinoma because of the different treatment strategy and prognosis

- due to its rarity and pecularity, no specific guidelines for therapy exist

Aim of the study

- molecular and histological characterization of a PEAC from a patient with another family member affected by the same tumor

Methods

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ORIGINAL PAPER

MicroRNA profiling for the identification of cancers with unknown primary tissue-of-origin

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The molecular characteristics of proband's PEAC were evaluated applying a previously validated 47-miRNA diagnostic classifier to predict tumor primary origin.

It has high overall accuracy of 100% for primary cancers and 78% for metastases.

Results

Characteristic	Proband	His sister
General		
Age at diagnosis (years)	68	71
Smoking habit	Yes	Yes
Primary localization	lung: right/lower lobe	lung: right/lower lobe
Colonoscopy	multiple benign polyps (N<10), diverticulosis	multiple benign polyps (N<10), diverticulosis
Radical surgery (R0)	Yes	Yes
Metastases/DFS (months)	bone / 1.5	lung, adrenal glands / 12
Histological findings		
Histology	PEAC	PEAC
Stage (pTNM)	pT2apN1	pT2apN0
IHC analyses		
TTF-1	NEG	NEG
Napsin A	NEG	NA
CK7	POS	NEG
CK20	NEG	POS
CDX2	POS	POS
MUC1	POS	NA
MUC2	NEG	NA
MUC5A	POS	NA
MUC6	NEG	NA
Genetic aberrations		
EGFR	wild type	wild type
K-RAS	Gly12Asp mutation	Gly12Asp mutation
ALK	wild type	wild type

Familial aggregation of PEAC was associated with:

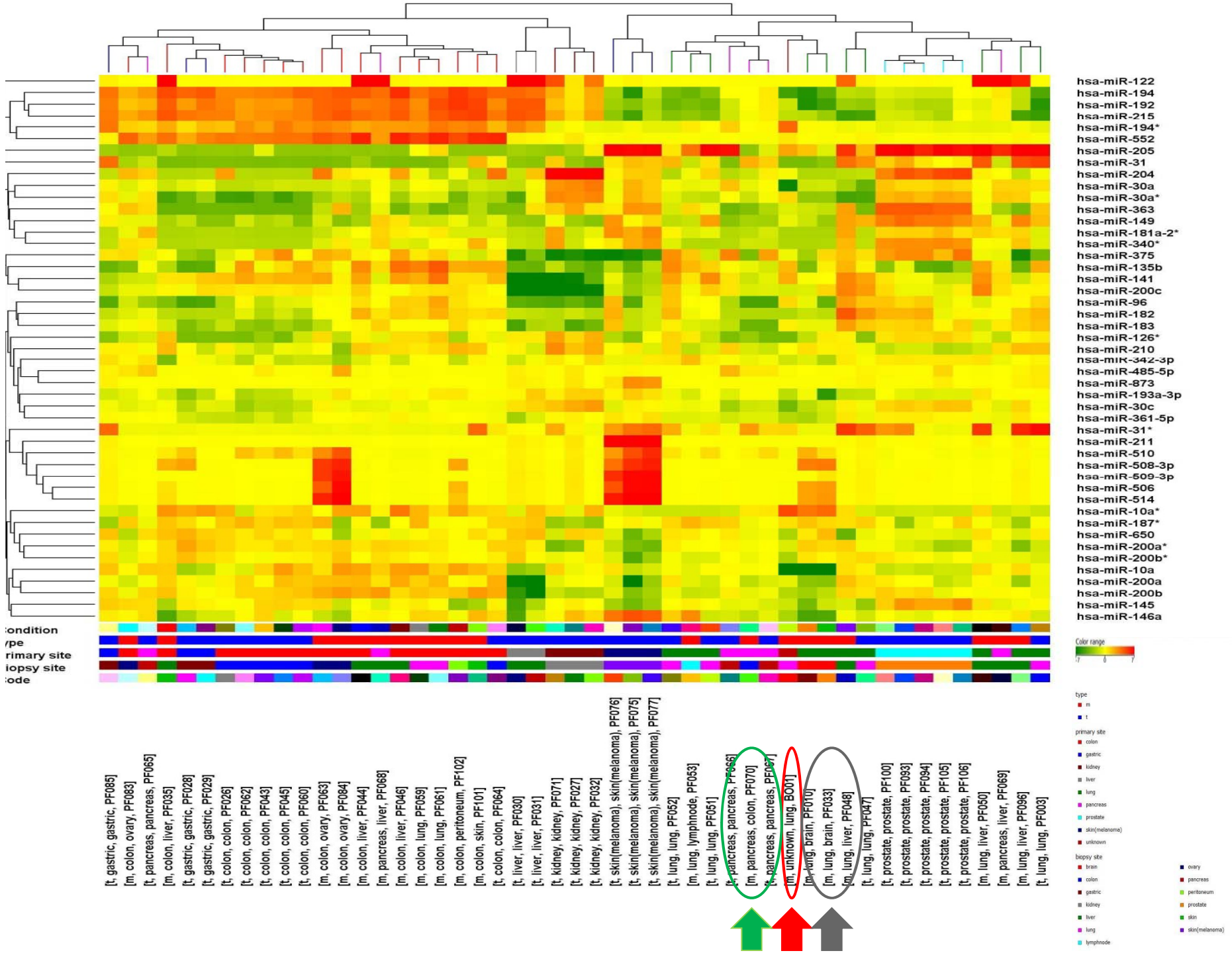
- **similar clinicopathological features**
- age at diagnosis
- smoking-habit
- tumor localization
- multiple benign colon polyps

- **histologic findings**
- TTF-1 negativity
- CDX2 positivity

- **genetic findings**
- K-RAS(Gly12Asp) mutation
- no EGFR/ALK aberrations

- miRNA profiling revealed main similarities with **lung cancer** (75.98%), and partial overlap **with pancreatic cancer** (23.34%), but not with colorectal cancer (less than 0.5%)

- PEAC shares with pancreatic cancer key miRNAs associated with tumor aggressiveness:
  - miR-31
  - miR-126
  - miR-506
  - miR-508-3p
  - miR-514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hsa-miR-194
hsa-miR-192
hsa-miR-215
hsa-miR-194*
hsa-miR-552
hsa-miR-205
hsa-miR-31
hsa-miR-204
hsa-miR-30a
hsa-miR-30a*
hsa-miR-363
hsa-miR-149
hsa-miR-181a-2*
hsa-miR-340*
hsa-miR-375
hsa-miR-135b
hsa-miR-141
hsa-miR-200c
hsa-miR-96
hsa-miR-182
hsa-miR-183
hsa-miR-126*
hsa-miR-210
hsa-miR-342-3p
hsa-miR-485-5p
hsa-miR-873
hsa-miR-193a-3p
hsa-miR-30c
hsa-miR-361-5p
hsa-miR-31*
hsa-miR-211
hsa-miR-510
hsa-miR-508-3p
hsa-miR-509-3p
hsa-miR-506
hsa-miR-514
hsa-miR-10a*
hsa-miR-187*
hsa-miR-650
hsa-miR-200a*
hsa-miR-200b*
hsa-miR-10a
hsa-miR-200a
hsa-miR-200b
hsa-miR-145
hsa-miR-146a
condition
type
primary site
biopsy site
code
Color range
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[m, colon, ovary, PF083]
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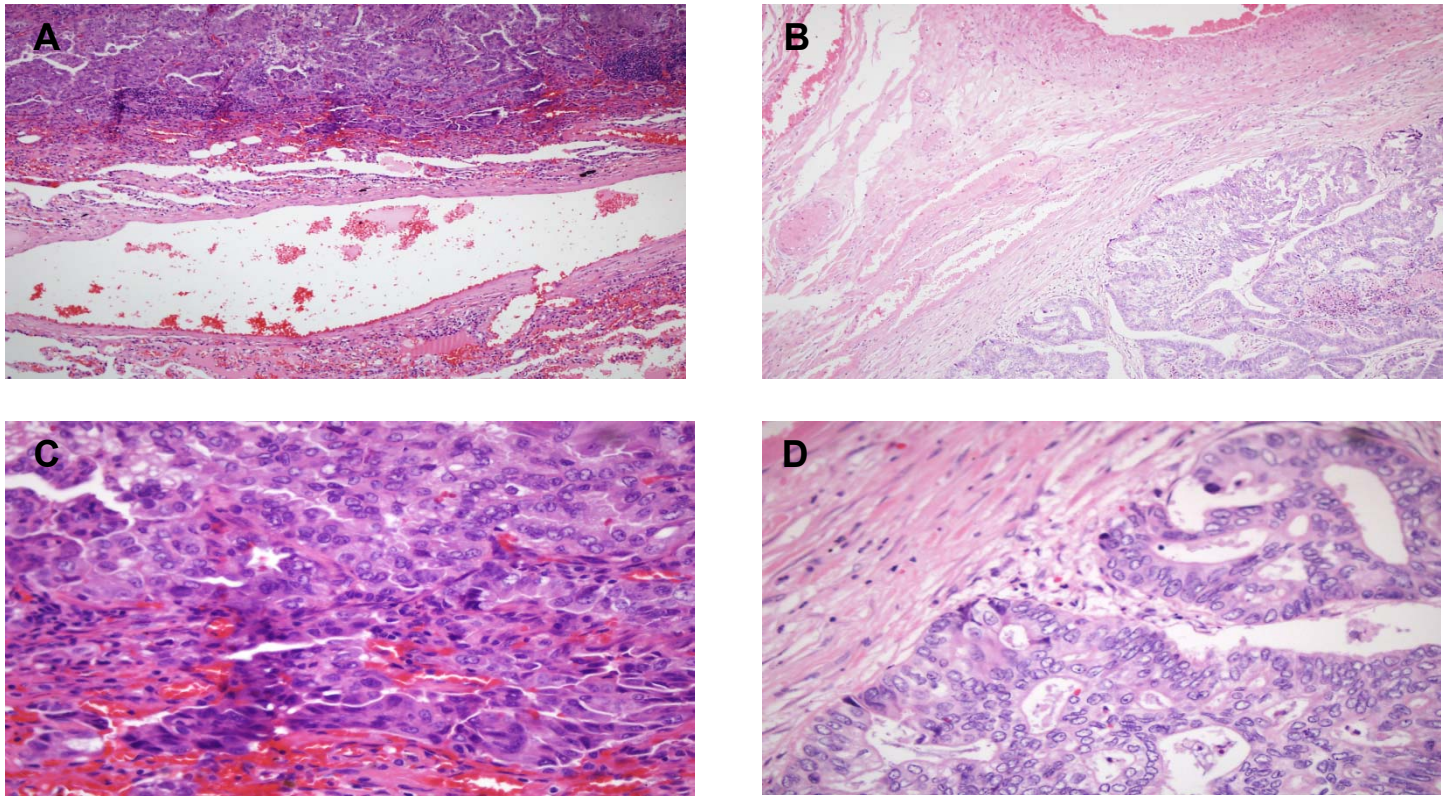
[m, lung, liver, PF050]
[m, pancreas, liver, PF069]
[m, lung, liver, PF096]
[t, lung, lung, PF003]
type
m
t
primary site
colon
gastric
kidney
liver
lung
pancreas
prostate
skin(melanoma)
unknown
biopsy site
brain
colon
gastric
kidney
liver
lung
lymphnode
ovary
pancreas
peritoneum
prostate
skin
skin(melanoma)

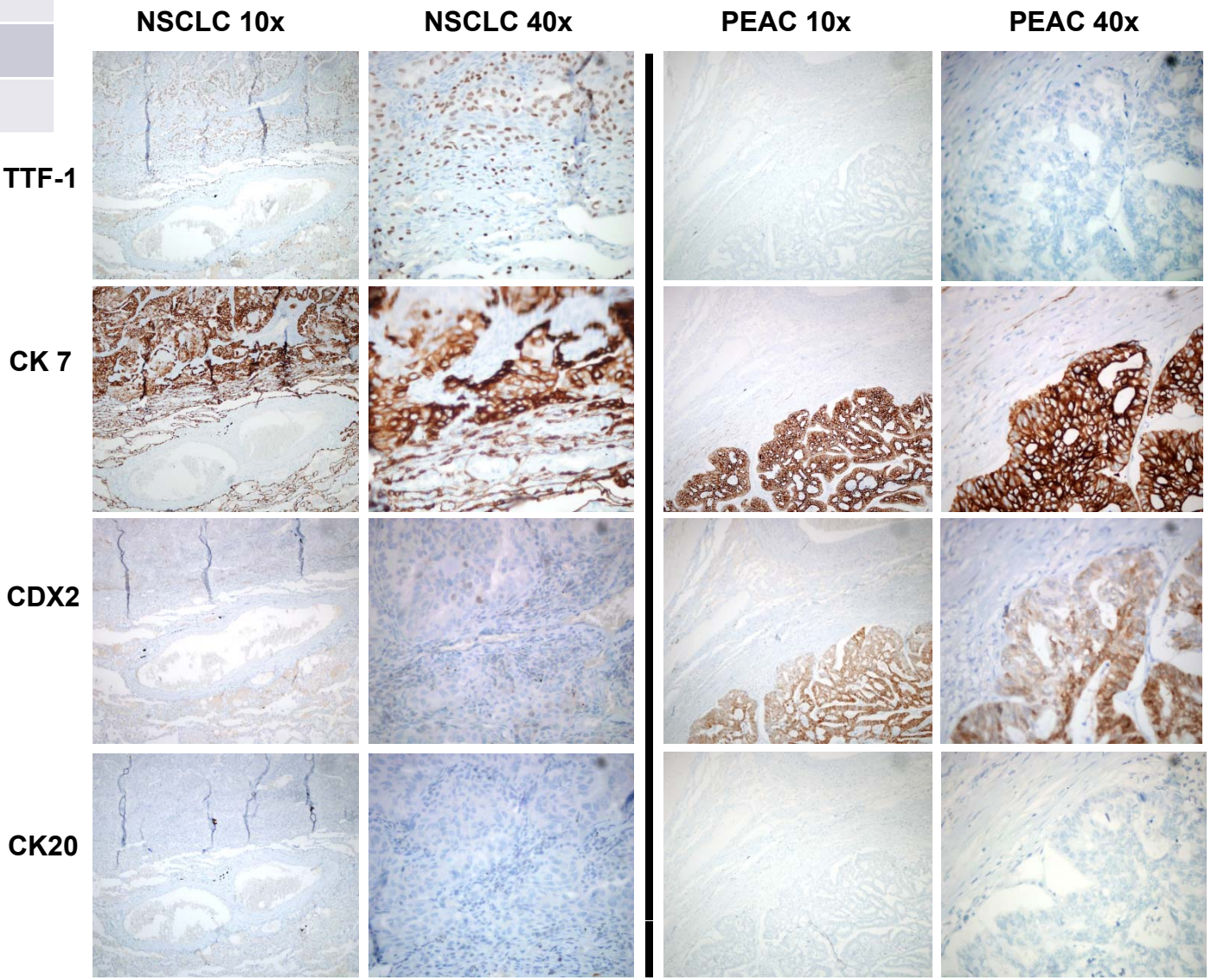
Histological analyses revealed the presence of two different phenotypes in the lung lesion of the proband: NSCLC (30%) and PEAC (70%).

NSCLC

PEAC



IHC Marker	NSCLC Phenotype	PEAC Phenotype
TTF1	+	-
CK7	+	+
CDX2	-	+
CK20	-	-



Conclusions

- we described, for the first time, a case of PEAC in two members of the same family, associated with similar clinicopathological feature and histological/genetic findings

- miRNA profiling of PEAC resembled mostly NSCLC, with a partial overlap with PDAC's pattern that could explain:
  - aggressive behavior compared to most NSCLC
  - guide future tailored-therapy approaches

Thank you for your attention!

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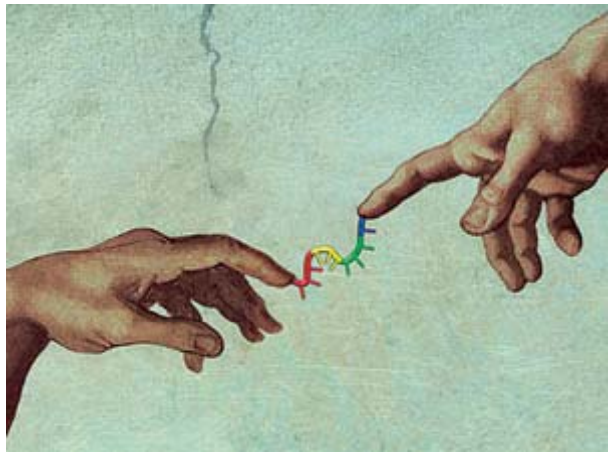
(Bologna)



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