Suitability of combined immunohistochemistry analysis of CPA1 and CELA3B for diagnosing acinar cell carcinoma of the pancreas.

Ria Uhlig[1], Hendrina Contreras[1], Nina Bröker[1], Sören Weidemann[1], Natalia Gorbokon[1], Anne Menz[1], Maximillian Lennartz[1], Niclas C. Blessin[1], Viktor Reiswich[1], Guido Sauter[1], Waldemar Wilczak[1], Sarah Minner[1], Stefan Steurer[1], Eike Burandt[1], David Dum[1], Ronald Simon[1], Till Krech[1], Till S Clauditz[1], Frank Jacobsen[1]

[1]Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Universität Hamburg — Universitätsklinikum Hamburg-Eppendorf

Introduction and Objectives

Carboxypeptidase A1 (CPA1) and chymotrypsin-like elastase family member 3B (CELA3B) are pancreatic enzymes with specific roles for nutrient digestion. Immunohistochemistry analyses suggest that both proteins are secreted from pancreatic acinar cells. This study was undertaken to estimate the suitability of combining immunohistochemistry analysis of CPA1 and CELA3B for diagnosing acinar cell carcinoma of the pancreas.

Materials and Methods

Tissue microarrays from human normal and neoplastic tissues were studied by immunohistochemistry. The normal tissue array contained 608 samples of 64 normal tissues (8 samples per organ), and the tumor tissue arrays contained 13,618 samples from 129 different tumor types.

Immunostaining protocol and controls CPA1
- Antibody: MS validated antibodies, clone MSVA-601M, Mouse IgG, Dilution: 1:150
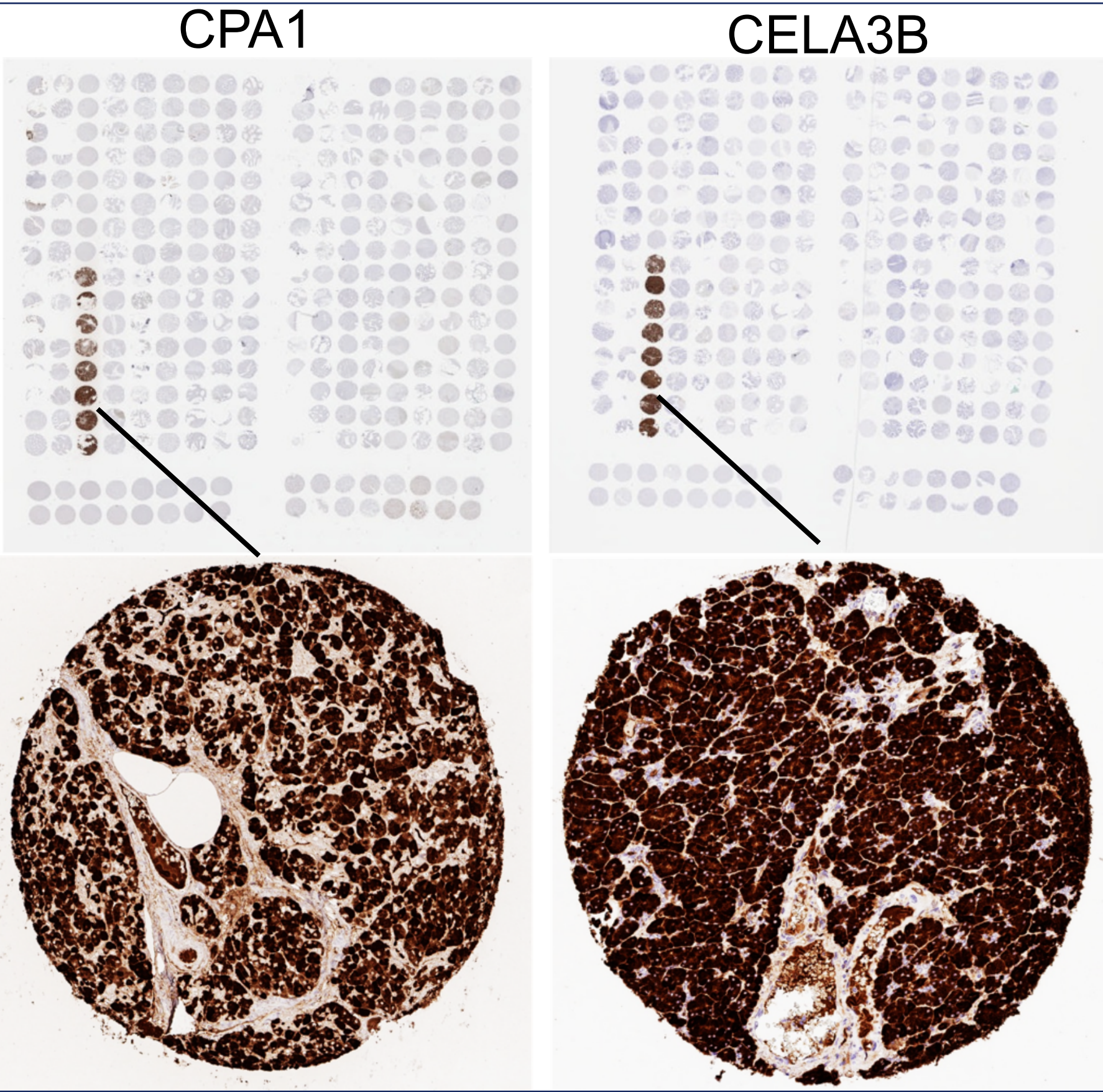- Antigen retrieval: 5 min at 121°C (autoclave) in pH 7.8 buffer

Immunostaining protocol and controls CELA3B
- Antibody: MS validated antibodies, clone MSVA-410M, Mouse IgG, Dilution: 1:150
- Antigen retrieval: 5 min at 121°C (autoclave) in pH 7.8 buffer

CPA1 and CELA3B in normal tissues

CPA1   CELA3B

Overview of the normal tissue array. Eight spots of acinar parenchyma in one row show strong staining of CPA1 and CELA3B (one spot each magnified).

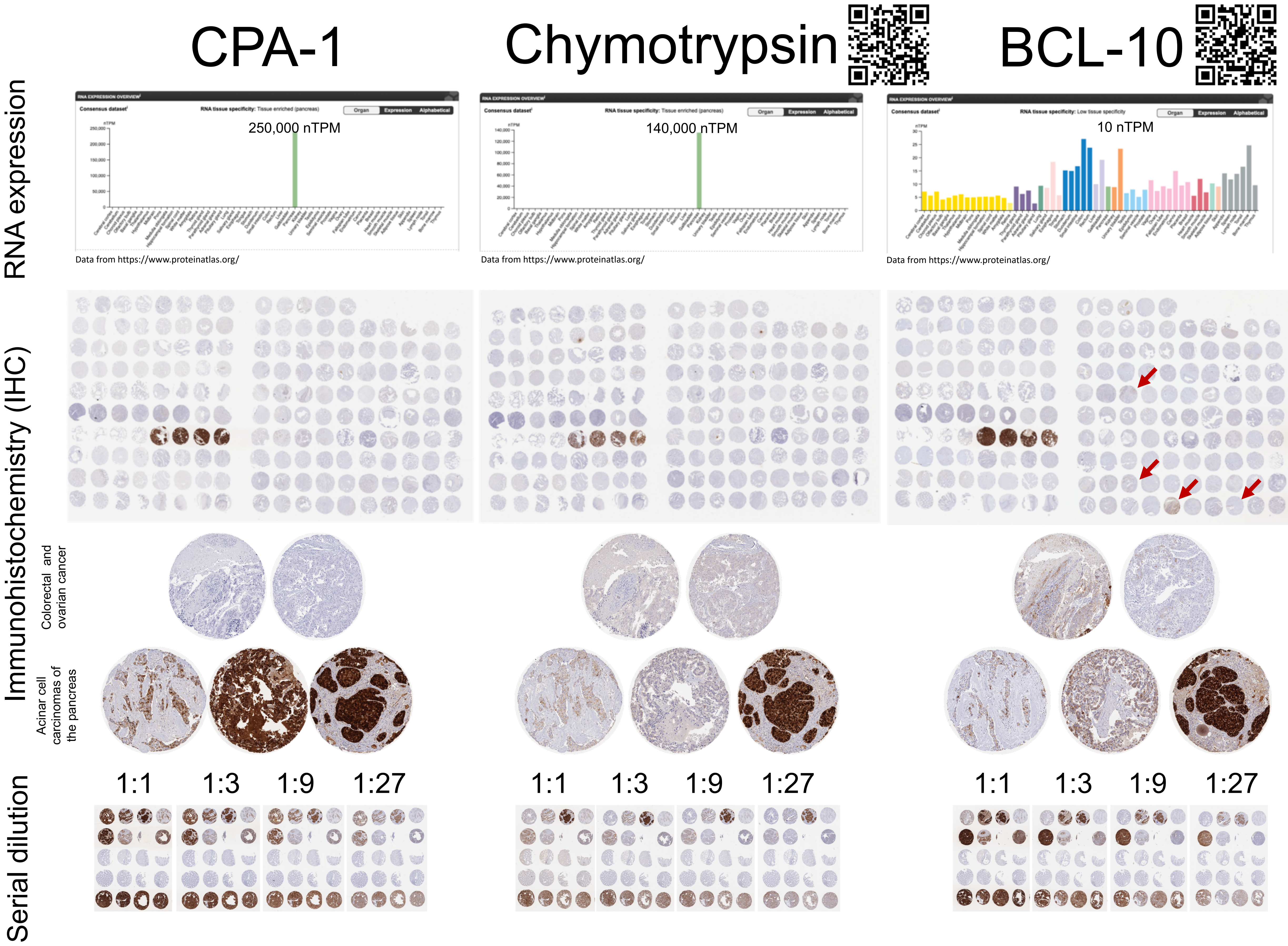## CPA1 and CELA3B in cancer tissues

Details of 19 tumors with positive staining on CPA1 and/or CELA3B

Tumor #	Tumor type	CPA1	CELA3B
1	Acinar cell carcinoma of the pancreas	positive	positive
2	Acinar cell carcinoma of the pancreas	positive	positive
3	Acinar cell carcinoma of the pancreas	positive	positive
4	Acinar cell carcinoma of the pancreas	positive	positive
5	Acinar cell carcinoma of the pancreas	positive	positive
6	Acinar cell carcinoma of the pancreas	positive	positive
7	Acinar cell carcinoma of the pancreas	positive	positive
8	Acinar cell carcinoma of the pancreas	positive	positive
9	Acinar cell carcinoma of the pancreas	positive	positive
10	Acinar cell carcinoma of the pancreas	positive	positive
11	Acinar cell carcinoma of the pancreas	positive	positive
12	Acinar cell carcinoma of the pancreas	positive	positive
13	Acinar cell carcinoma of the pancreas	positive	negative
14	Acinar cell carcinoma of the pancreas	positive	negative
15	Adenocarcinoma of the colon	negative	positive
16	Adenocarcinoma of the colon	negative	positive
17	Mucoepidermoid carcinoma of the salivary gland	positive	positive
18	Mucoepidermoid carcinoma of the salivary gland	positive	positive
19	Acinic cell carcinoma of the salivary gland	negative	positive

Legend: positive (red), negative (green)

Of 10,334 interpretable tumors, 5 (0.05%) were positive only for CELA3B, 2 (0.02%) only for CPA1, and 12 (0.12%) for both proteins. Of these 19 tumors, 14 (75%) were acinar cell carcinomas of the pancreas, 1 (5%) was an acinar cell carcinoma of the salivary gland, and 2 (10%) each were mucoepidermoid carcinomas of the salivary gland and adenocarcinomas of the colon. Of the 14 pancreatic acinar cell carcinomas, 12 were positive for CPA1 and CELA3B, and 2 were positive for CPA1 only.

	CPA1 alone	CELA3B alone	CPA1 and CELA3B combined
Sensitivity ...	100	85.7	100
Specificity ...	100	100	99.99

... to detect acinar cell carcinoma of the pancreas

Comparison of 3 IHC markers for pancreatic acinar cell carcinoma

CPA-1   Chymotrypsin   BCL-10

RNA expression

250,000 nTPM — Data from https://www.proteinatlas.org/

140,000 nTPM — Data from https://www.proteinatlas.org/

10 nTPM — Data from https://www.proteinatlas.org/

Immunohistochemistry (IHC)

Colorectal and ovarian cancer

Acinar cell carcinomas of the pancreas

Serial dilution

1:1   1:3   1:9   1:27

	CPA1	Chymotrypsin	BCL-10
Sensitivity	very good	good	good
Specificity	excellent	very good	limited
Signal to noise	excellent	poor	very good

Summary and Conclusions

➢ CPA1 immunohistochemistry greatly facilitates the otherwise often difficult diagnosis of pancreatic ACC.

➢ CELA3B can be used as a complement diagnostic marker - together with CPA1 - for confirming the difficult diagnosis of pancreatic acinar cell carcinoma.

Contact: n.blessin@uke.de