Residents news

Residents present their research work at USCAP 2024 (check the pictures in the next slides)

-Dr. Dilara Akbulut wins the ISUP Stipend Award 2024 (https://ccr.cancer.gov/laboratory-of-pathology#news)

-Dr. Evsen Apaydin Arikan is elected Chief Resident 2024-2025

-Dr. Dilara Akbulut shares her experience as a LP clinical fellow (check the 2023/2024 Winter issue of the CCR-FYI newsletter online here)

-Dr. Khaled Bin Satter presents his research work at the AACR 2024

Evaluation of novel neuroendocrine transcription factor expressions (ASCL1, NEUROD1, POU2F3) in well differentiated neuroendocrine tumors

Dilara Akbulut, Niharika Shah, Maria Del Carmen Rodriguez Pena, Markku M Miettinen
Laboratory of Pathology, National Cancer Institute, NIH, Bethesda, MD

NIH NATIONAL CANCER INSTITUTE

Background

- ASCL1, NEUROD1 and POU2F3 are novel transcription factors that play role in neuroendocrine differentiation.
- Their expression has been recently identified in high grade neuroendocrine carcinomas (NEC) in lung, with potential therapeutic and prognostic implications.
- A differential expression pattern with different subtypes have been shown in the tissue via immunohistochemistry.
- Different mutation profiles, hence reflecting the possible different biologic evolution between well-differentiated neuroendocrine tumors (NET) and high-grade neuroendocrine carcinomas were reported.
- In this study, we evaluate these novel markers' expression in a large group of NET, which has not been fully elucidated yet.

Design

- Total of 270 cases were assessed in 7 multi-tissue tumor blocks.
- The cohort included 199 well differentiated NET:
- 40 thoracic, 79 GI, 80 pancreatic NET.
- 29 NEC and 42 medullary thyroid carcinoma constituted the comparison group.
- ASCL1, NEUROD1 and POU2F3 immunostaining was performed and evaluated with external controls.
- Cases were considered positive with nuclear staining, weak to strong staining intensity. Staining percentages were also noted.

Results

	Well differentiated NET, THORACIC (n=40)	Well differentiated NET, GI (n=79)	Well differentiated NET, PANCREAS (n=80)	High grade NEC (n=71)
ASCL1 % (n)	23% (9)	1% (1)	1% (4)	21% (15)
NEUROD1 % (n)	0	0	4% (3)	0
POU2F3 % (n)	0	0	0	0

- ASCL1 was expressed in 14 out of 199 (7%) NET, with the following distribution:
  - 7 lung, 4 pancreatic, 2 thymic and 1 appendix NET.
- 7 of 42 (17%) medullary thyroid carcinoma and 8 of 29 (28%) NEC showed ASCL1 expression.
- Fisher's Exact Test was performed to compare ASCL1 expression between NET and NEC and showed significance with p<0.0025. (Figure 1)

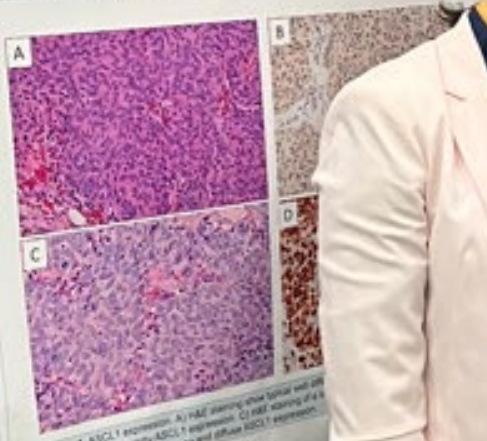

Figure 1. ASCL1 expression. A) H&E staining small tumor cells with B) weak and patchy ASCL1 expression. C) H&E staining of a high grade features and D) strong and diffuse ASCL1 expression.

Results

- Staining intensity was higher in NEC, compared to NET.
  - Mean staining percentage for high grade NEC was 40% and 17% for NET.
  - A t-test was utilized to compare staining percentages among high grade NEC and NET, with a p value of <0.0001. (Figure 2)
- NEUROD1 was expressed in only 3 out of 80 pancreatic NET and was negative in the rest of the cases.
- POU2F3 expression was not detected in any of the cases.


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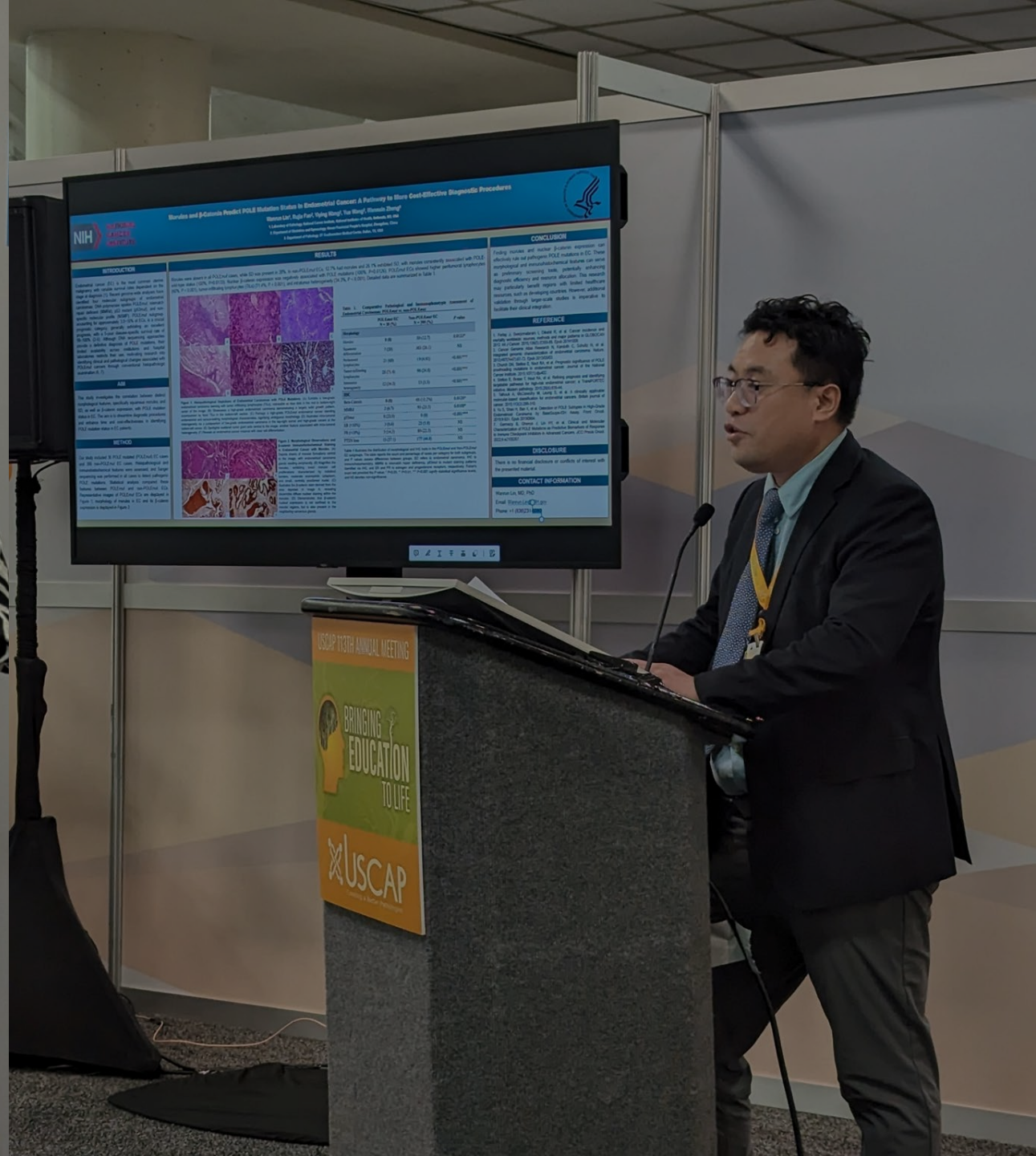
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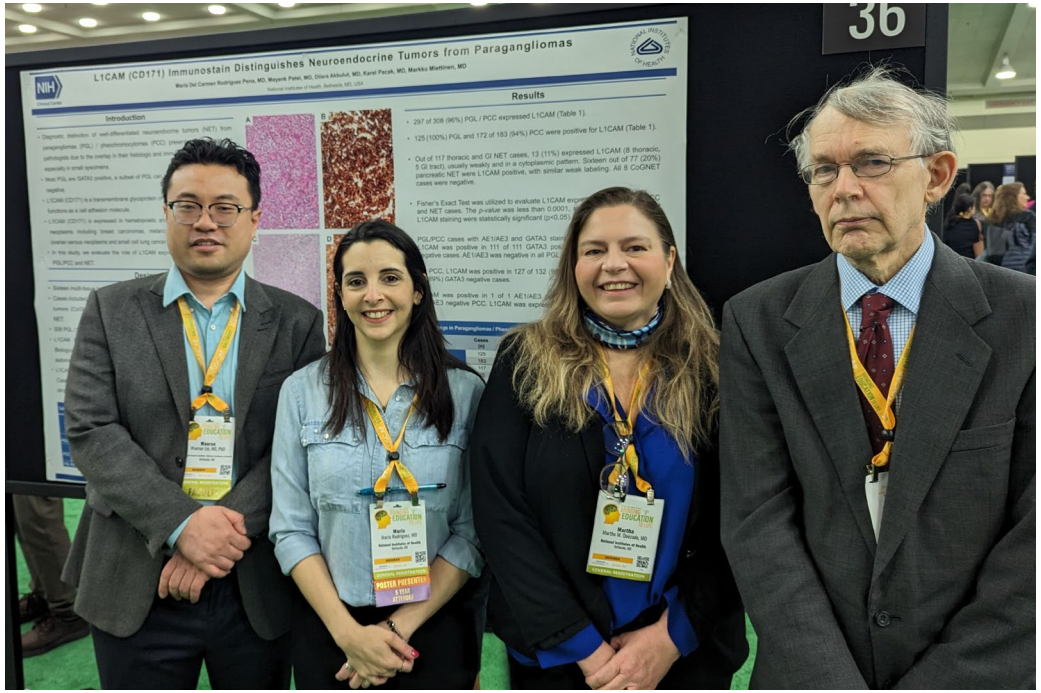

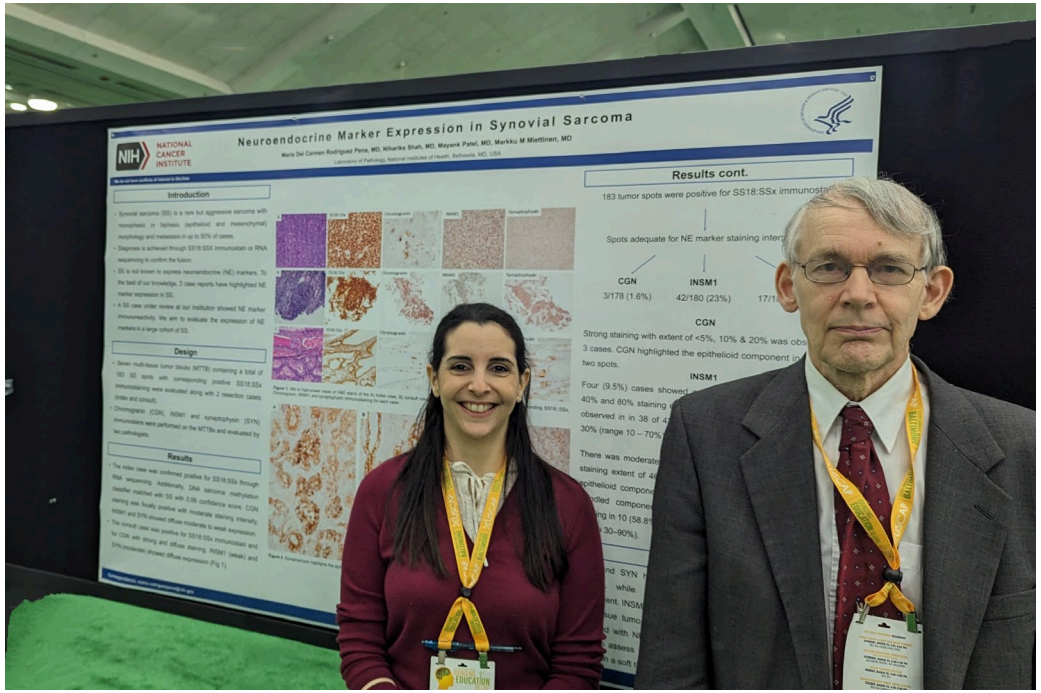

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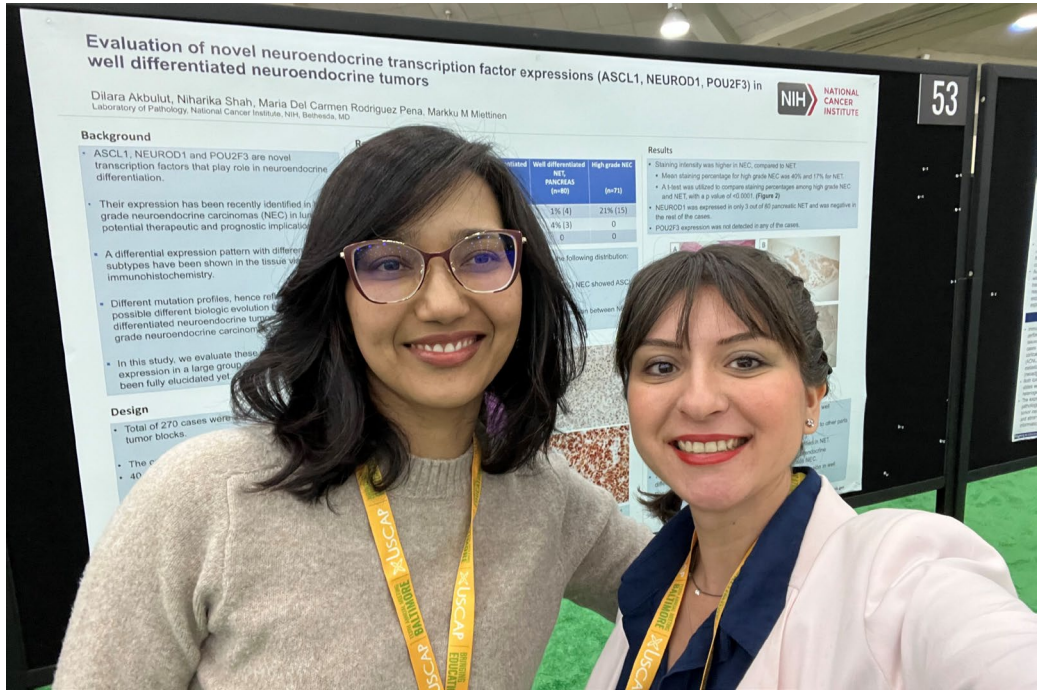

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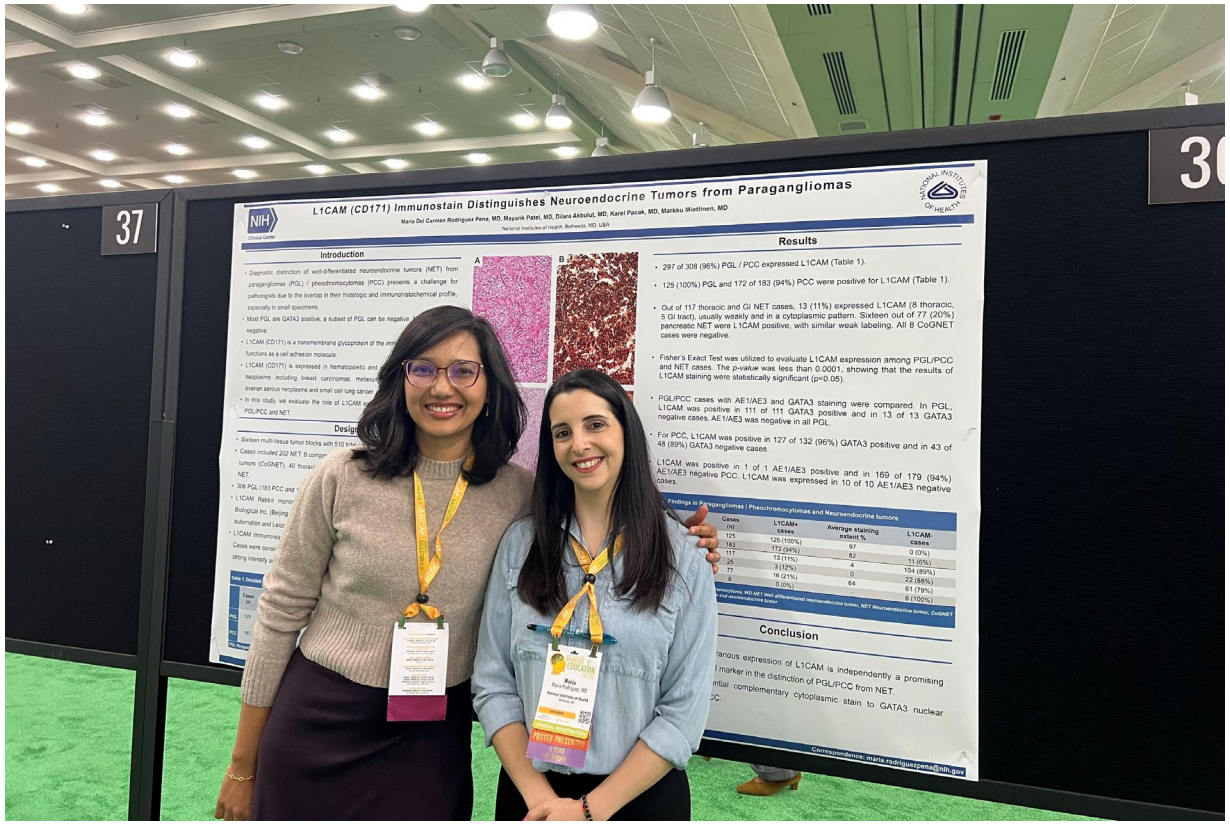

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EXHIBIT HALL HOUR
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Tuesday, March 26
9:30 AM-5:00 PM
Wednesday, March 27
9:00 AM-4:00 PM
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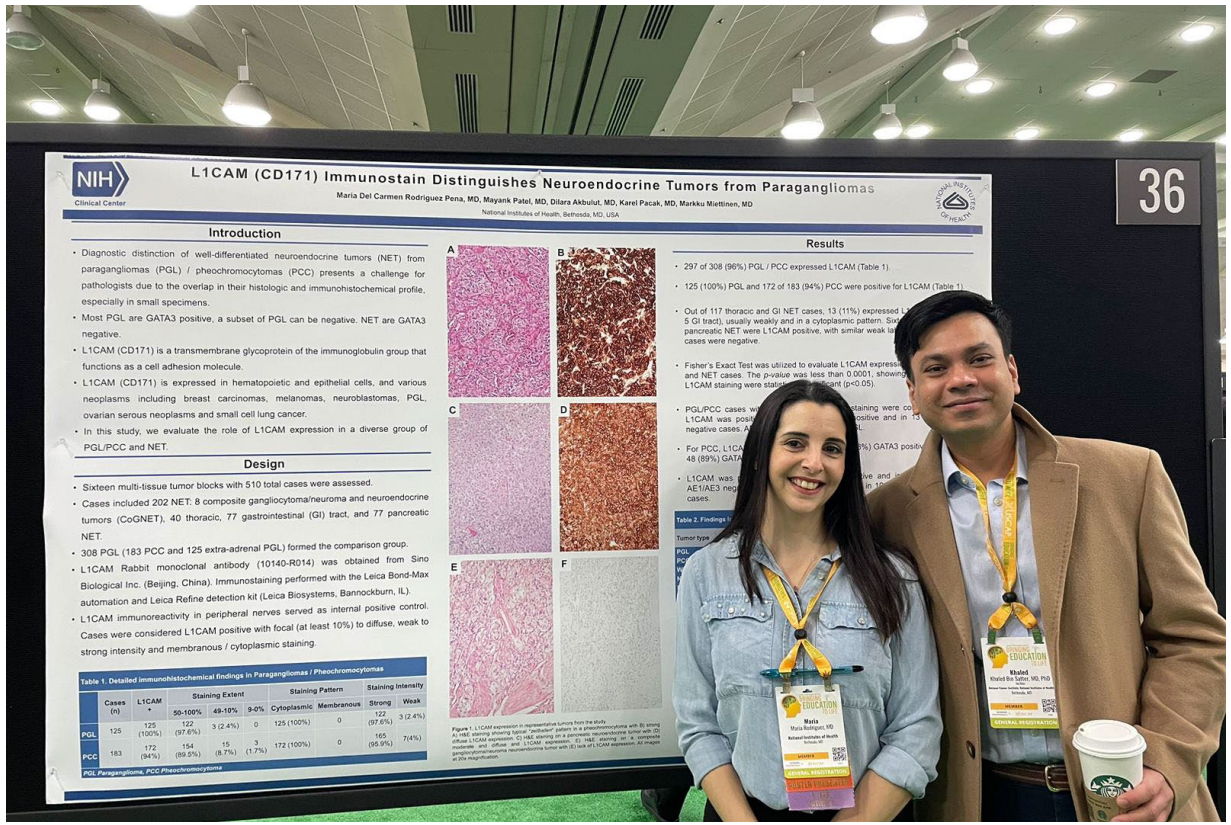

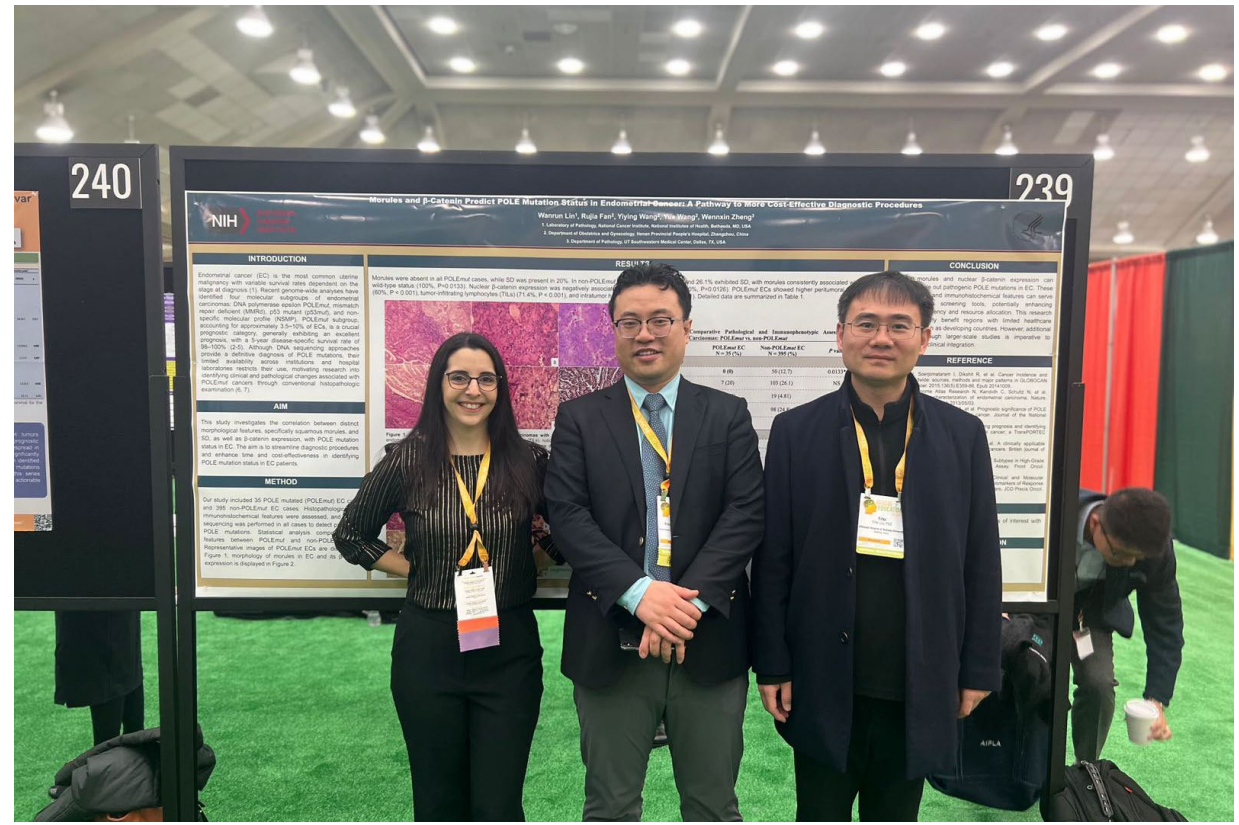

L1CAM (CD171) Immunostain Distinguishes Neuroendocrine Tumors from Paragangliomas

Maria Del Carmen Rodriguez Pena, MD, Mayank Patel, MD, Dilara Akbulut, MD, Karel Pacak, MD, Markku Miettinen, MD

National Institutes of Health, Bethesda, MD, USA

NIH Clinical Center

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Introduction

- Diagnostic distinction of well-differentiated neuroendocrine tumors (NET) from paragangliomas (PGL) / pheochromocytomas (PCC) presents a challenge for pathologists due to the overlap in their histologic and immunohistochemical profile, especially in small specimens.
- Most PGL are GATA3 positive, a subset of PGL can be negative. NET are GATA3 negative.
- L1CAM (CD171) is a transmembrane glycoprotein of the immunoglobulin group that functions as a cell adhesion molecule.
- L1CAM (CD171) is expressed in hematopoietic and epithelial cells, and various neoplasms including breast carcinomas, melanomas, neuroblastomas, PGL, ovarian serous neoplasms and small cell lung cancer.
- In this study, we evaluate the role of L1CAM expression in a diverse group of PGL/PCC and NET.

Design

- Sixteen multi-tissue tumor blocks with 510 total cases were assessed.
- Cases included 202 NET: 8 composite gangliocytoma/neuroma and neuroendocrine tumors (CoGNET), 40 thoracic, 77 gastrointestinal (GI) tract, and 77 pancreatic NET.
- 308 PGL (183 PCC and 125 extra-adrenal PGL) formed the comparison group.
- L1CAM Rabbit monoclonal antibody (10140-R014) was obtained from Sino Biological Inc. (Beijing, China). Immunostaining performed with the Leica Bond-Max automation and Leica Refine detection kit (Leica Biosystems, Bannockburn, IL).
- L1CAM immunoreactivity in peripheral nerves served as internal positive control. Cases were considered L1CAM positive with focal (at least 10%) to diffuse, weak to strong intensity and membranous / cytoplasmic staining.

Table 1. Detailed immunohistochemical findings in Paragangliomas / Pheochromocytomas

	Cases (n)	L1CAM +	Staining Extent			Staining Pattern		Staining Intensity	
			50-100%	49-10%	9-0%	Cytoplasmic	Membranous	Strong	Weak
PGL	125	125 (100%)	122 (97.6%)	3 (2.4%)	0	125 (100%)	0	122 (97.6%)	3 (2.4%)
PCC	183	172 (94%)	154 (89.5%)	15 (8.7%)	3 (1.7%)	172 (100%)	0	165 (95.9%)	7(4%)

PGL Paraganglioma, PCC Pheochromocytoma

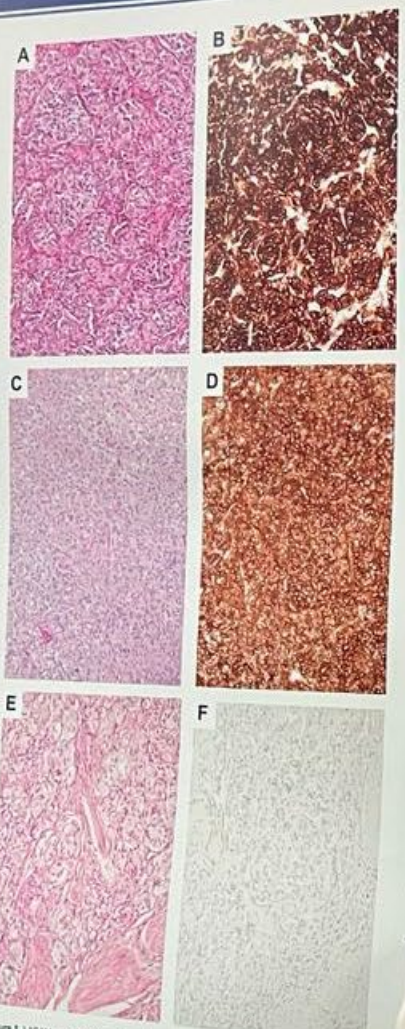

Figure 1. L1CAM expression in representative tumors from the study. A) H&E staining showing typical "zellballen" pattern in a pheochromocytoma with B) strong diffuse L1CAM expression. C) H&E staining on a pancreatic neuroendocrine tumor with (D) moderate and diffuse and L1CAM expression. E) H&E staining on a composite gangliocytoma/neuroma neuroendocrine tumor with (E) lack of L1CAM expression. All images at 20x magnification.

Results

- 297 of 308 (96%) PGL / PCC expressed L1CAM (Table 1).
- 125 (100%) PGL and 172 of 183 (94%) PCC were positive for L1CAM (Table 1).
- Out of 117 thoracic and GI NET cases, 13 (11%) expressed L1CAM (8 thoracic, 5 GI tract), usually weakly and in a cytoplasmic pattern. Sixteen out of 77 (20%) pancreatic NET were L1CAM positive, with similar weak labeling. All 8 CoGNET cases were negative.
- Fisher's Exact Test w… L1CAM expression among PGL/… and NET cases. T… 0001, showing that the res… L1CAM staining w… 0.05).
- PGL/PCC cases … ning were compared. L1CAM was pos… tive and in 13 of 13… negative cases. A…
- For PCC, L1CAM w… %) GATA3 positive and… 48 (89%) GATA3 neg…
- L1CAM was positive i… ositive and in 169 of 17… AE1/AE3 negative PCC, … ad in 10 of 10 AE1/AE3… cases.

Table 2. Findings in Parag… tumors

Tumor type	
PGL	
PCC	
WD…	
NE…	
Pa…	
Co…	
P…