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POU4F3 with Keratin AE1/AE3 or Pan-Keratin: An Optimal Sentinel Lymph Node Protocol for Merkel Cell Carcinoma

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62nd Annual Meeting of the American Society for Dermatopathology
7 Nov 2025

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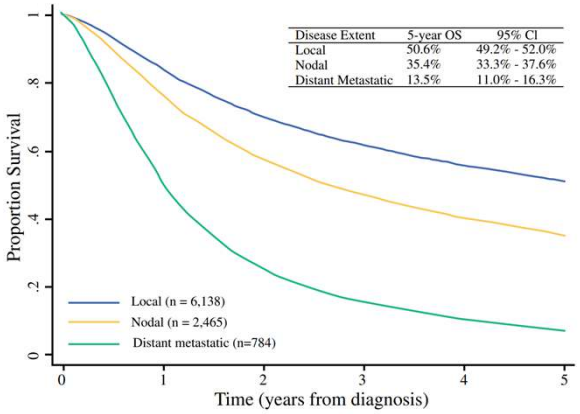
Disclosures

We do not have any relevant financial relationships to disclose.

2

Sentinel lymph node metastases are a cornerstone of staging for Merkel cell carcinoma

- MCC often spreads to sentinel and non-regional lymph nodes
- Nodal metastases portend worse overall survival
- Nodal metastases upstage patients to AJCC 8th stage III



Harms et al. Ann Surg Oncol, 2016

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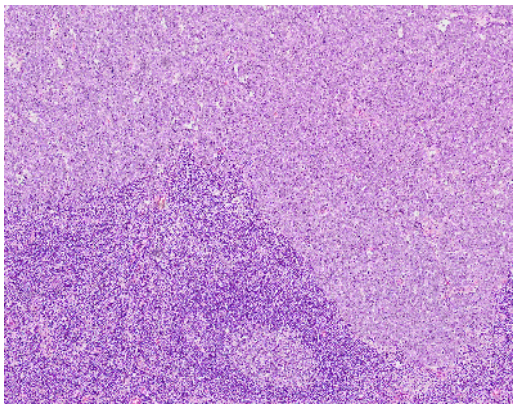
Detecting MCC in SLN remains a challenge



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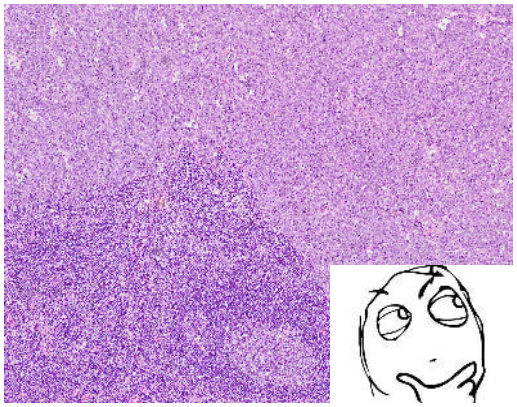

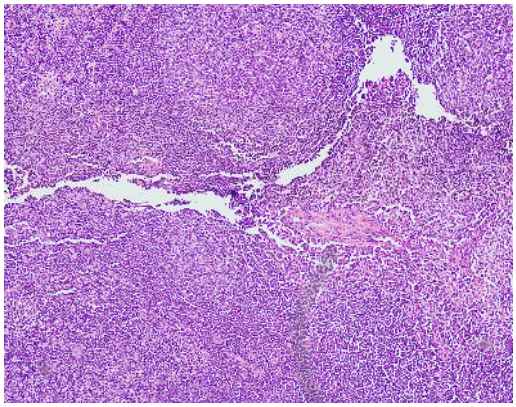

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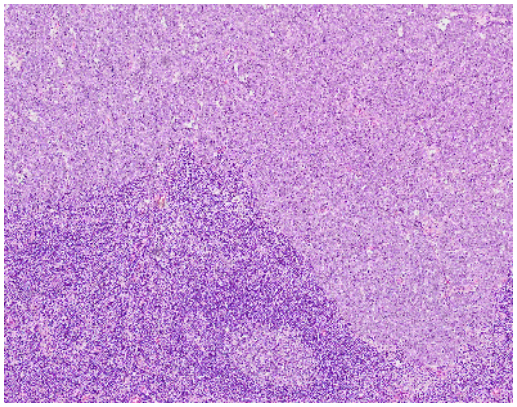

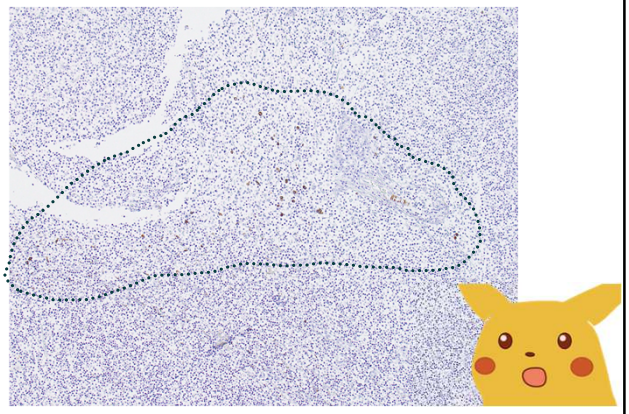

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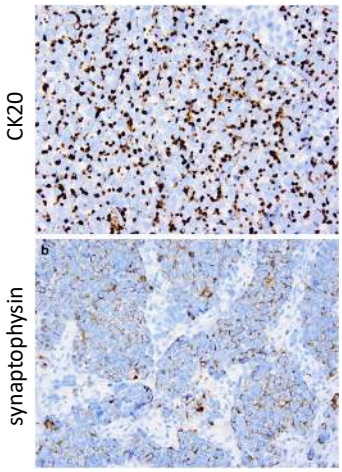
Immunohistochemistry has improved detection of MCC in SLN – but an optimal panel is lacking



- Several markers have been proposed to aid in detection of metastatic MCC
- CK20 and keratins AE1/AE3 and pan-keratin have been widely used, as well as synaptophysin and chromogranin
- INSM1, SATB2, SOX2 are more recent markers proposed to help identify metastatic MCC

Pan et al. Mod Path, 2014

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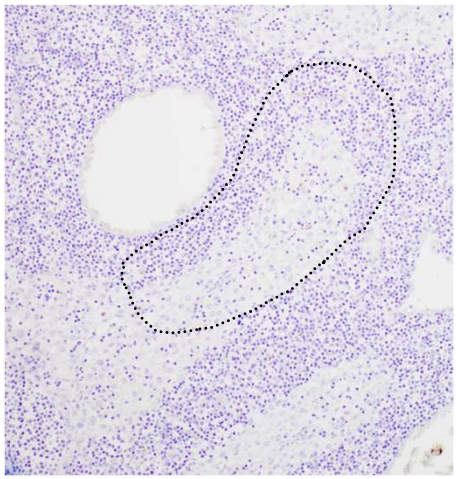

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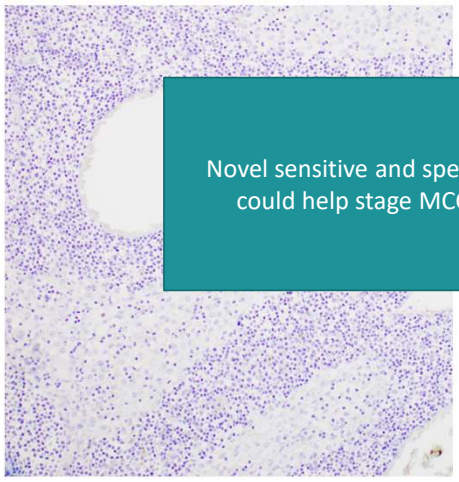

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Novel sensitive and specific Merkel cell carcinoma markers could help stage MCC more accurately and efficiently

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POU4F3 is a novel highly sensitive and specific immunohistochemical marker of Merkel cell carcinoma

MODERN PATHOLOGY

USCAP

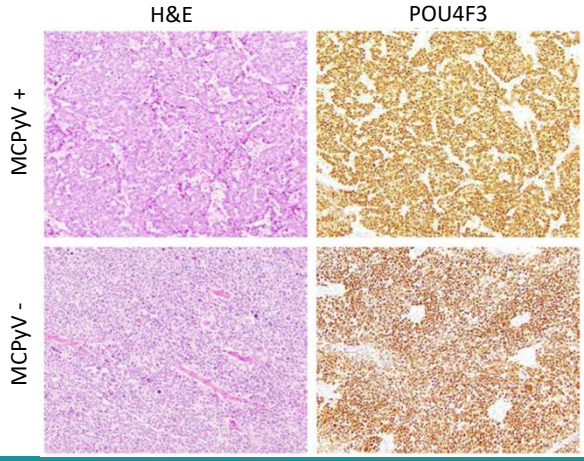
Journal homepage: https://modernpathology.org/

Research Article

POU4F3 Is a Sensitive and Specific Marker of Merkel Cell Carcinoma

Paweł Karpinski[a,*], Javier E. Mendez-Pena[b], Cheng-Lin Wu[c], Ali Akalin[d], Kristine M. Cornejo[b], Yin P. Hung[b], Mai P. Hoang[b,*]

[a] Department of Genetics, Wroclaw Medical University, Wroclaw, Poland; [b] Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [c] Department of Pathology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [d] Department of Pathology, UMass Medical Center, Worcester, Massachusetts



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- Widely and uniformly expressed in MCC (98.7% sensitivity, 98.3% specificity)
- Not expressed in other cutaneous malignancies or NE tumors
- Independent of MCPyV/CK20 status

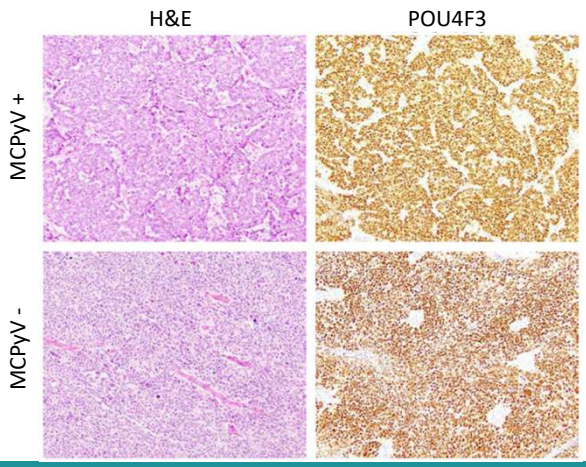

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Table 1
Summary of POU4F3 expression in Merkel cell carcinomas and histologic mimics

Tumor type	N	POU4F3			
		Positive	3+	2+	Negative
Merkel cell carcinoma	153	151/153 (98.7%)	149	2	2
MCPyV-positive	82	82/82	81	1	0
MCPyV-negative	71	69/71	68	1	2
Keratin 20-negative	10	9/10	9	0	1
Keratin 20 focally positive	12	12/12	12	0	0
TTF1-positive	8	8/8	8	0	0
Non-Merkel cell carcinoma cases	180	3/180 (1.7%)			
Small cell carcinoma, total	95	3/95 (3.2%)	0	2	92
Small cell carcinoma of lung	55	2/55	0	2	53
Small cell carcinoma of cervix	12	0/12	0	0	12
Small cell carcinoma of vagina	3	1/3	1	0	2
Small cell carcinoma of endometrium	3	0/3	0	0	3
Small cell carcinoma of salivary gland/head and neck	6	0/6	0	0	6
Small cell carcinoma of bladder	11	0/5	0	0	11
Small cell carcinoma of prostate	3	0/1	0	0	3
Small cell carcinoma of pancreas	1	0/1	0	0	1
Small cell carcinoma of gallbladder	1	0/1	0	0	1
Ewing sarcoma	3	0/3	0	0	3
Rhabdomyosarcoma, alveolar	1	0/1	0	0	1
Synovial sarcoma, poorly differentiated	4	0/4	0	0	4
Lymphoblastic lymphoma	2	0/2	0	0	2
NUT carcinoma	3	0/3	0	0	3
Trichoblastoma	3	0/3	0[a]	0	3
Basal cell carcinoma	36	0/36	0	0	36
Metastatic melanoma	22	0/22	0	0	22
Malignant peripheral nerve sheath tumor	11	0/11	0	0	11

Karpinsky et al. Mod Path, 2025

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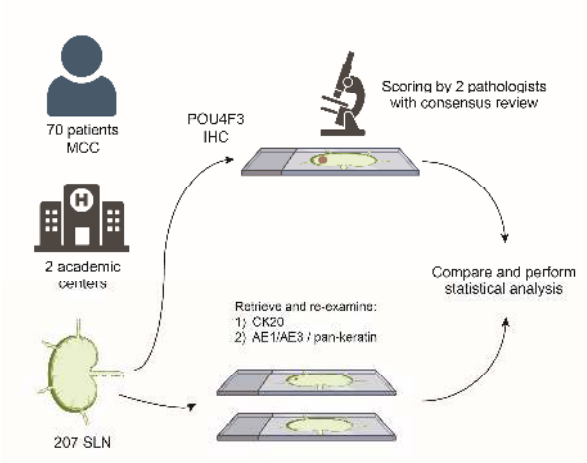
A retrospective study to improve accuracy of MCC SLN metastasis detection using POU4F3



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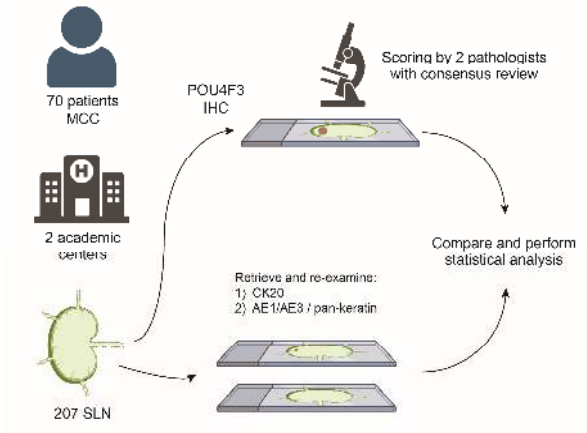

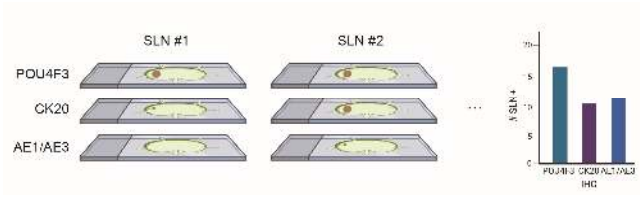

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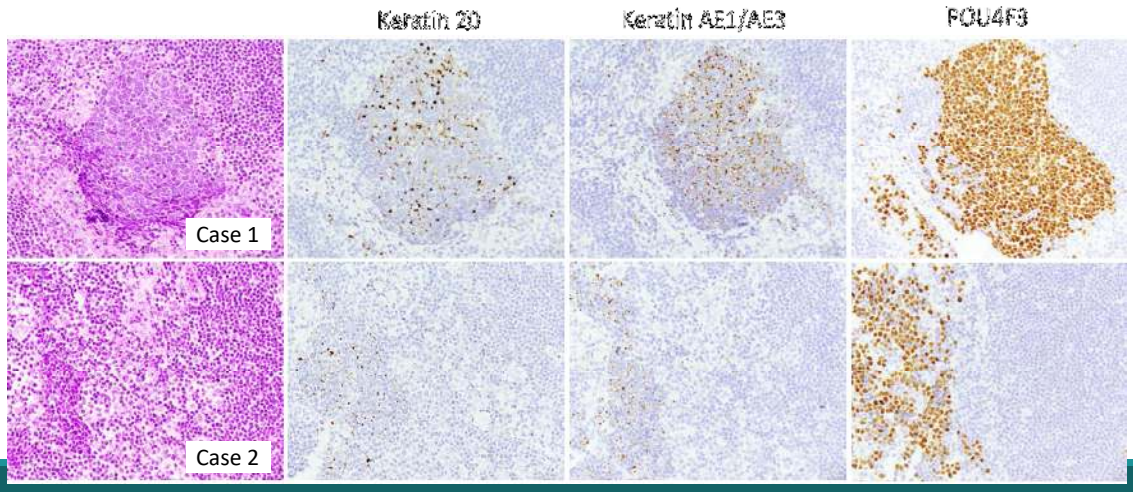
POU4F3 highlights SLN micro- and macro-metastases



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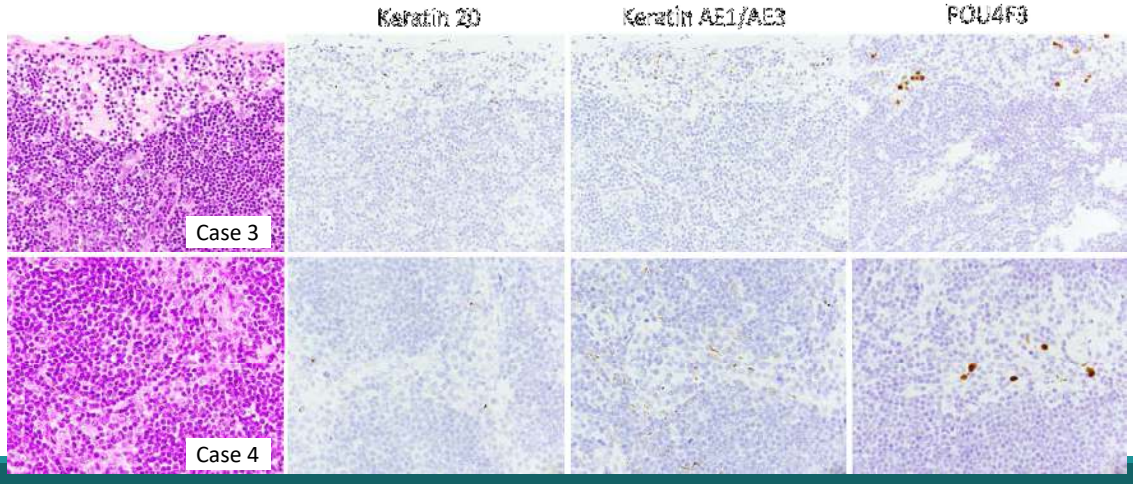

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MCC SLN immunophenotypes

POU4F3	Keratin 20	Keratin AE1/AE3 or Pan-keratin	N SLN	Percentage SLN
+	+	+	61	29.5%
+	-	-	27	13.0%
+	-	+	5	2.4%
+	+	-	5	2.4%
-	+	+	2	1.0%
-	-	+	2	1.0%
-	+	-	0	0%
-	-	-	105	50.7%
			207	

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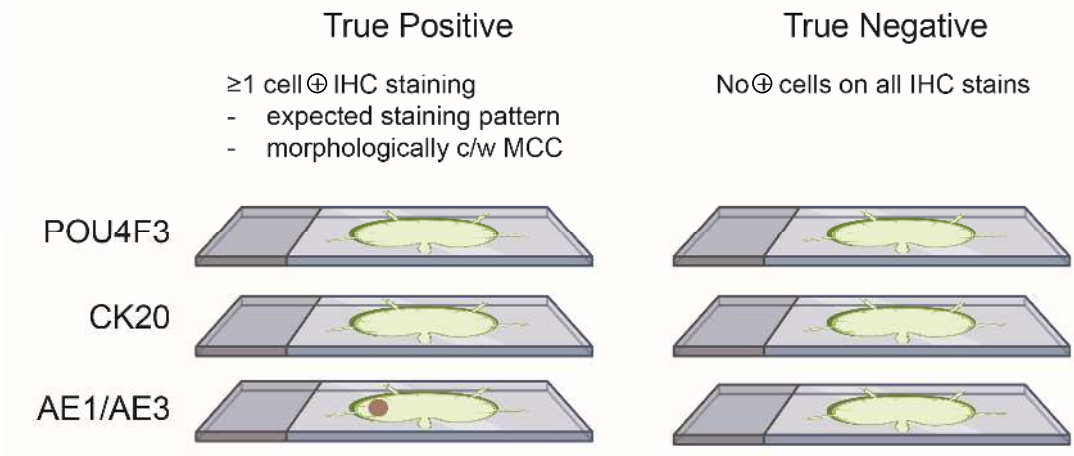
Establishing sensitivity of POU4F3 in detecting MCC SLN metastasis



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Establishing sensitivity of POU4F3 in detecting MCC SLN metastasis

Single marker	Positivity	Sensitivity
POU4F3	98/102	96%
Keratin 20	68/102	67%
Keratin AE1/A3 or pan-keratin	70/102	69%

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First marker	Second marker	Positivity	Sensitivity
POU4F3	ø	98/102	96%
Keratin 20	ø	68/102	67%
Keratin AE1/A3 or pan-keratin	ø	70/102	69%
POU4F3	Keratin 20	102/102	100%
POU4F3	Keratin AE1/A3 or pan-keratin	102/102	100%
Keratin 20	Keratin AE1/A3 or pan-keratin	76/102	74%

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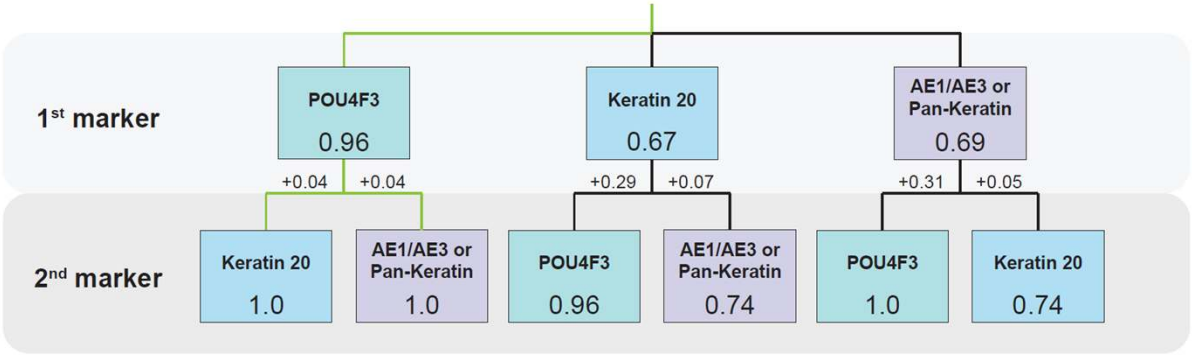
An optimal IHC panel for SLN MCC detection



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Advantages and limitations of a POU4F3-based IHC panel for MCC SLN

Advantages

- Sensitivity superior to conventional MCC markers in SLN
- Nuclear marker with solid staining pattern and low background staining
- High specificity of staining in SLN and primary tumors
- A panel of POU4F3 and AE1/AE3 or pan-keratin could be implemented as a routine SLN panel in MCC patients

Limitations

- Not widely available yet in many IHC labs (but commercially available)
- Benefits from additional keratin staining for maximum sensitivity
- Lack of gold standard for presence of metastatic MCC in SLN limits specificity calculation

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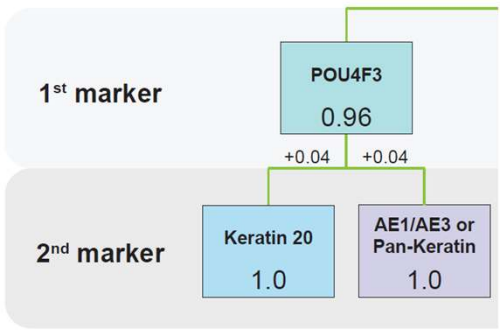
Take home messages

- POU4F3 is a very sensitive and specific nuclear marker of MCC with low LN background staining
- An IHC panel combining POU4F3 and keratin AE1/AE3 or pan-keratin achieves very high sensitivity and specificity in MCC SLN detection
- Adoption of a standardized POU4F3-based IHC panel may improve MCC staging accuracy and efficiency



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