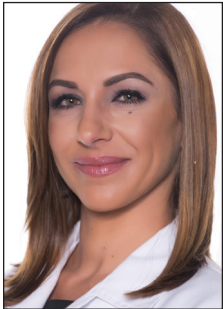


boards fodder

Important immunohistochemical stains in dermatology

by Sheila M. Valentín-Nogueras, MD, and Oswald Y. Carrasquillo, MD, MPH



Sheila M. Valentín-Nogueras, MD, is an associate professor in the department of dermatology at the University of Puerto Rico.



Oswald Y. Carrasquillo, MD, MPH is a recent graduate, working in private practice in San Juan, Puerto Rico.

<i>Angiosarcoma</i>	CD31+ CD34+ ERG+ (most sensitive and specific) FLI-1+	c-MYC amplifications are positive in radiation-induced angiosarcoma
<i>Atypical fibroxanthoma</i>	Vimentin+ CD99+ CD10+ Pro-collagen-1+ LN-2 (CD74)- MNF116-	CD68+ (57-62%) α1 anti-trypsin and α1 anti-chymotrypsin + in >50%
<i>Malignant fibrous histiocytoma</i>	LN-2 (CD74)+	Weak staining for CD99
<i>Basal cell carcinoma (BCC)</i>	bcl-2+ (diffuse staining) peanut agglutinin+ (band-like peritumorous reaction) Ber-Ep4+ Androgen receptor+ CD34-	Clinically aggressive BCCs have low labeling with <i>bcl-2</i>
<i>Trichoepithelioma (TE)</i>	bcl-2+ (only in basal layer) peanut agglutinin- Ber-Ep4+ (~75% of desmoplastic TE) Androgen receptor- CD34+ (peritumoral fibroblasts)	Desmoplastic trichoepitheliomas are CK20+ due to the presence of Merkel cells (uncommon in BCC)
<i>Basaloid squamous cell carcinoma</i>	Cytokeratin 5/6+ HMWK 34βE12 + bcl-2- Ber-Ep4+/-	CK 5/6 → distinguishes primary cutaneous adnexal CA (+) from metastatic adenocarcinoma from internal organs (-)
<i>Basosquamous Carcinoma</i>	Pan-cytokeratin AE1/AE3+ Proliferative Cell Nuclear Antigen (PCNA)+ Ber-Ep4+	p16+/-
<i>Sarcomatoid or spindle cell squamous cell carcinoma</i>	MNF116+ Pan-cytokeratin AE1/AE3- (in high grade variant)	
<i>Dermatofibroma</i>	CD34- FXIIIa+ Stromelysin-3+ D2-40+	
<i>Dermatofibrosarcoma protuberans</i>	CD34+ FXIIIa- Stromelysin-3- D2-40-	
<i>Epithelioid sarcoma</i>	Cytokeratin (CK8, CK19)+ EMA+ Vimentin+	~50% are CD34+
<i>Granular cell tumor</i>	S100+ NSE+ Granules are: PAS+ PTAH+	Myelin basic protein staining variable

Important immunohistochemical stains in dermatology

by Sheila M. Valentín-Nogueras, MD, and Oswald Y. Carrasquillo, MD, MPH

<i>Hemangioma of infancy</i>	GLUT-1+	
<i>RICH</i> <i>NICH</i> <i>Vascular malformations</i> <i>(capillary, lymphatic, venous,</i> <i>and arteriovenous)</i>	GLUT-1-	
<i>Infantile digital fibromatosis</i>	Eosinophilic cytoplasmic inclusion bodies are: PTAH+ Masson's trichrome+ (stains red) Actin+ PAS-	
<i>Kaposi's sarcoma</i>	LANA-1 of HHV-8+ (nuclear staining)	Variable staining for CD31, CD34, <i>Ulex Europeans</i> , and factor VIII-related antigen
<i>Langerhans cell histiocytosis</i>	S100+ CD1a+ Langerin (CD207)+ Factor XIIIa- CD68- HAM56-	BRAF V600E mutation in 60%
<i>Non-Langerhans cell histiocytosis</i>	S100- in all <u>except</u> in Rosai-Dorfman and Indeterminate cell histiocytosis CD1a- in all <u>except</u> Indeterminate cell histiocytosis Langerin (CD207)- Factor XIIIa +/- CD68+	
<i>Leiomyosarcoma</i>	Vimentin+ Desmin+ Smooth muscle actin+	
<i>Lymphangioma circumscriptum and Cystic hygroma</i>	LYVE-1+ D2-40 (podoplanin)+	
<i>Lymphomatoid papulosis</i>	CD3+ CD30+ CD8- except type D	CD2 +/- CD5 +/- CD7 +/-
<i>Mastocytosis</i>	Giemsa+ Touline blue+ Leder (chloracetate esterase)+ c-kit (CD117)+	CD25+ on cutaneous mast cells from adult patients with UP is predictive of systemic mastocytosis
<i>Melanoma</i>	S100+ HMB-45+ MART-1+ MITF+	Desmoplastic melanoma: SOX-10+ S100+ p75 Neurotrophin receptor (p75 NTR)+ HMB-45- MART-1- MITF-
<i>Merkel cell carcinoma</i>	CK20+: paranuclear dot staining CK7- Thyroid transcription factor (TTF-1) -	neuron-specific enolase (NSE), EMA, synaptophysin, and chromogranin + CD44+ may indicate metastatic potential

Important immunohistochemical stains in dermatology

by Sheila M. Valentín-Nogueras, MD, and Oswald Y. Carrasquillo, MD, MPH

<i>Metastatic small cell lung carcinoma</i>	CK20- CK7+ TTF-1+	
<i>Microcystic adnexal carcinoma</i>	CEA+ EMA+ Ber-Ep4-	Morpheaform BCC and desmoplastic trichoepithelioma are Ber-Ep4+
<i>Mycosis fungoides</i>	CD2, CD3, CD4, and CD45RO+ CD8- CD30-	Loss of CD7 (most common, non-specific), CD5 and CD2 (least common, more specific) Hypopigmented variant usually CD4-/CD8+
<i>Mammary Paget's disease</i>	CK7, CEA, EMA, low molecular weight cytokeratins (CAM 5.2), PAS, Alcian blue, and mucicarmine +	
<i>Primary extra-mammary Paget's disease</i>	CK7+/CK20-/GCDFP-15+	Both are CEA, EMA, low molecular weight cytokeratins, PAS, Alcian blue, and mucicarmine +
<i>Secondary extra-mammary Paget's disease</i> (Associated with an underlying visceral carcinoma)	CK7+/CK20+/GCDFP-15-	CK7+ associated with malignancies above diaphragm (breast, lung) CK20+ associated with malignancies below diaphragm (colon, stomach)
<i>Sebaceous carcinoma</i>	Adipophilin+ Androgen receptor+ EMA+ Ber-EP4-	Ocular tumors usually express CK7
<i>Spitz nevus</i>	S100A6+ p16+	vs Melanoma: weak staining with p16 and S100A6 Most Spitz nevi exhibit a distinct mutation profile from common nevi and melanoma, featuring more HRAS, rather than BRAF or NRAS mutations

References

- Hartel PH, Jackson J, Ducatman BS, Zhang P. CD99 immunoreactivity in atypical fibroxanthoma and pleomorphic malignant fibrous histiocytoma: as useful diagnostic marker. *J Cutan Pathol.* 2006; 33: 24-28.
- de Feraudy S, Mar N, McCalmont TH. Evaluation of CD10 and Procollagen 1 expression in atypical fibroxanthoma and dermatofibroma. *Am J Surg Pathol.* 2008; 32: 1111-1121.
- Lazova R, Moynes R, May D, Scott G. LN-2(CD74): A marker to distinguish atypical fibroxanthoma from malignant fibrous histiocytoma. *Cancer.* 1997; 79: 2115-2124.
- Krahl D, Sellheyer K. Monoclonal antibody Ber-EP4 reliably discriminates between microcystic adnexal carcinoma and basal cell carcinoma. *J Cutan Pathol.* 2007; 34: 782-787.
- Cribier B, Noacco G, Peltre B, Grosshans E. Stromelysin 3 expression: A useful marker for the differential diagnosis dermatofibroma versus dermatofibrosarcoma protuberans. *J Am Acad Dermatol.* 2002; 46: 408-413.
- Taskin WB, Miettinen M. Epithelioid sarcoma: new insights based on an extended immunohistochemical analysis. *Arch Pathol Lab Med.* 2003; 127: 1161-1168.
- Leon-Villapalos J, Wolfe K, Kangesu L. GLUT-1: an extra diagnostic tool to differentiate between hemangiomas and vascular malformations. *Br J Plast Surg.* 2005; 58: 348-52.
- Hollmann TJ, Brenn T, Hornick JL. CD25 expression on cutaneous mast cells from adult patients presenting with urticaria pigmentosa is predictive of systemic mastocytosis. *Am J Surg Pathol.* 2008; 32: 139-145.

Important immunohistochemical stains in dermatology

by Sheila M. Valentín-Nogueras, MD, and Oswald Y. Carrasquillo, MD, MPH

9. Radfar A, Stefano CM, Ghosn S, Bhawan J. NGFR-Positive desmoplastic melanomas with focal or absent S-100 staining: Further evidence supporting the use of both NGFR and S-100 as a primary immunohistochemical panel for the diagnosis of desmoplastic melanomas. *Am J Dermatopathol.* 2006; 28: 162-167.
10. Leech SN, Kolar AJO, Barrett PD, Sinclair SA, Leonard N. Merkel cell carcinoma can be distinguished from metastatic small cell carcinoma using antibodies to cytokeratin 20 and thyroid transcription factor 1. *J Clin Pathol.* 2001; 54: 727-729.
11. Penneys NS, Shapiro S. CD44 expression in Merkel cell carcinoma may correlate with risk of metastasis. *J Cutan Pathol.* 1994; 21: 22-26.
12. Nowak MA, Guerriere-Kovach P, Pathan A, Campbell TE, Deppisch LM. Perianal Paget's disease: Distinguishing primary and secondary lesions using immunohistochemical studies using gross cystic disease fluid protein-15 and cytokeratin 20 expression. *Arch Pathol Lab Med.* 1998; 122: 1077-1081.
13. Ribé A, McNutt NS. S100A6 protein expression is different in Spitz nevi and melanoma. *Mod Pathol.* 2003; 16: 505-511.
14. Hillard NJ, Krahl D, Sellheyer K. p16 expression differentiates between desmoplastic Spitz nevus and desmoplastic melanoma. *J Cutan Pathol.* 2009; 36: 753-759.
15. Luo S, Sepehr A, Tsao H. Spitz nevi and other Spitzoid lesions: Part I. Background and Diagnoses. *J Am Acad Dermatol.* 2011 Dec; 65(6): 1073-1084.
16. Boyd AS, Stasko TS, Tang YW. *J Am Acad Dermatol.* 2011 Jan;64(1):144-51.
17. Carrasquillo OY, Cruzval-O Reilly E, Sánchez JE, Valentín-Nogueras SM. Differentiation of Basal Cell Carcinoma and Trichoepithelioma: An Immunohistochemical Study. *Am J Dermatopathol.* 2020 Aug 17. Online ahead of print.
18. Katano H. Pathological Features of Kaposi's Sarcoma-Associated Herpesvirus Infection. *Adv Exp Med Biol.* 2018;1045:357-376.
19. Bologna JL, Callen JP, Jorizzo JL, Schaffer JV. *Dermatology.* 4th ed. Elsevier; 2018.
20. Alikhan A, Hocker TLH, Chavan R. *Review of Dermatology.* Edinburgh: Elsevier; 2017.
21. Kumari K, Haragannavar VC, Kumar KV, Prasad K, Nambiar S. Basaloid Squamous Cell Carcinoma of Tongue: A Report with Emphasis on Immunohistochemistry. *J Clin Diagn Res.* 2017 Mar;11(3):ZD16-ZD18.
22. TW Beer, P Shepherd, JM Theaker. Ber EP4 and epithelial membrane antigen aid distinction of basal cell, squamous cell and basosquamous carcinomas of the skin. *Histopathology.* 2000 Sep;37(3):218-23.
23. Ramos-Herberth FI, Karamchandani J, Kim J, Dadras SS. SOX10 immunostaining distinguishes desmoplastic melanoma from excision scar. *J Cutan Pathol.* 2010 Sep;37(9):944-52.
24. Sramek B, Lisle A, Loy T. Immunohistochemistry in ocular carcinomas. *J Cutan Pathol.* 2008 Jul;35(7):641-6.
25. Winters R, Naud S, Evans MF, Trotman W, Kasznica P, Elhosseiny A. Ber-EP4, CK1, CK7 and CK14 are useful markers for basaloid squamous carcinoma: a study of 45 cases. *Head Neck Pathol.* 2008;2(4):265-271. doi:10.1007/s12105-008-0089-7 "Ber-EP4 is a useful diagnostic marker for BSCC, positive in 82% (37/45) of the cases."