XXV Congreso Nacional SEAP
Zaragoza 18-21 Mayo, 2011

hospital universitario
VIRGEN MACARENA Y ÁREA

Inmunohistoquímica en el diagnóstico de las neoplasias cutáneas basaloides.

Aspectos prácticos

J. J Ríos Martín
H. Virgen Macarena
Sevilla

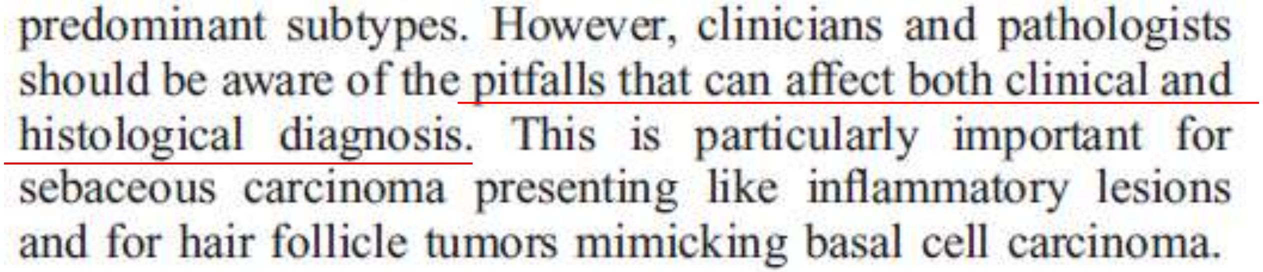
CIVDAD
DEL
BETIS

CLINICOPATHOLOGIC CORRELATION

Clinicopathological Features of Eyelid Skin Tumors. A Retrospective Study of 5504 Cases and Review of Literature

Manuel Deprez, MD, PhD† and Sylvie Uffer, MD, PhD**

Am J Dermatopathol • Volume 31, Number 3, May 2009



predominant subtypes. However, clinicians and pathologists should be aware of the pitfalls that can affect both clinical and histological diagnosis. This is particularly important for sebaceous carcinoma presenting like inflammatory lesions and for hair follicle tumors mimicking basal cell carcinoma.

J Cutan Pathol 2007: 34: 612–619
doi: 10.1111/j.1600-0560.2006.00674.x
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Journal of
Cutaneous Pathology

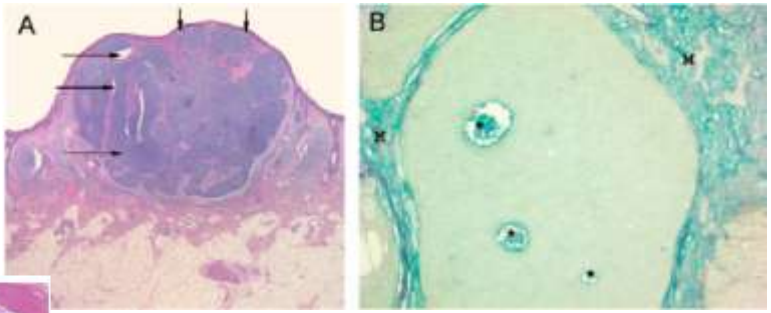
Merkel cell carcinoma frequently shows histologic features of basal cell carcinoma: a study of 30 cases

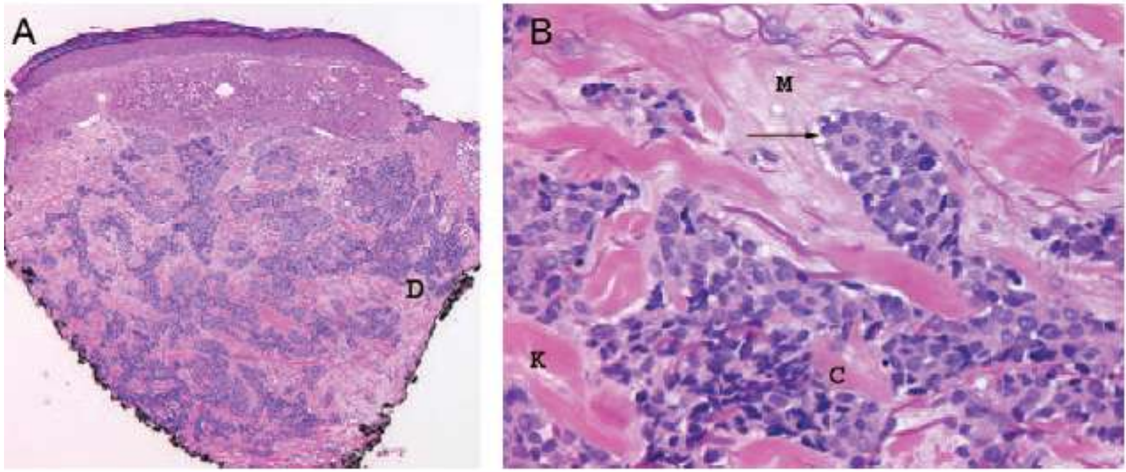
Background: Merkel cell carcinoma (MCC) is a basaloid cutaneous neoplasm that may be mistaken for basal cell carcinoma (BCC).
Methods: Thirty MCCs were examined for areas that histologically resembled BCC.
Results: One of the histologic features of BCC (either a mucinous stroma or stromal artifactual retraction) was identified in all MCCs. A mucinous stroma was found in 28 MCCs (93%), stromal artifactual retraction in 27 (90%), mucin-containing gland-like spaces within

Nigel J. Ball[1] and Grace Tanhuanco-Kho[2]

[1]Departments of Pathology and Dermatology, The University of British Columbia and Vancouver General Hospital, Vancouver, British Columbia, Canada and
[2]The Department of Laboratory Medicine, Royal Jubilee Hospital, Victoria, British Columbia, Canada

Immunohistochemical staining		
Cam5.2	+	+
Ber-EP4	+	+
Neuron-specific enolase	+	+/−
Chromogranin A	+	+/−
Cytokeratin 20	+	−





The vanishing biopsy: the trend toward smaller specimens.

Fernández EM, Helm T, Ioffreda M, Helm KF.

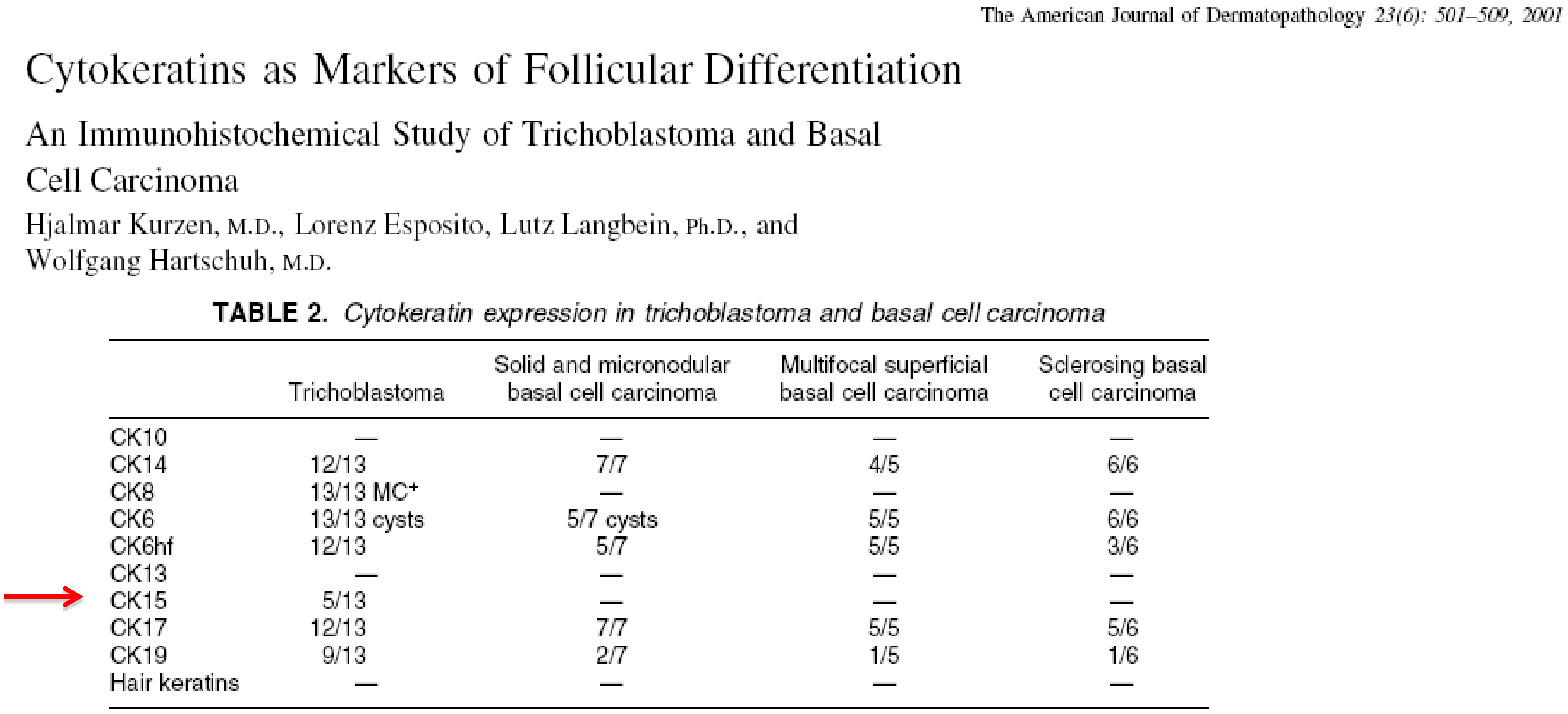
Cutis 2005; 76:335.

- Biopsias “shave”
  - 36,8% - 77,6% (1988-2003)
- Biopsias “punch”
  - 32,2% - 63,2% (1988-2003)
  - Volumen de los “punch”: 65,0 – 33,9 mm^3

CCB. Subtipos histológicos

- Nodular
- Micronodular
- Infiltrativo
- Queratósico
- Basoescamoso (metatípico)
- Superficial
- Con diferenciación anexial
- Adenoide
- Morfeiforme (esclerosante)
- Pigmentado
- Otros:
  - Pleomórfico
  - Células claras
  - Células granulares
  - Infundíbuloquístico
  - Metaplásico (carcinosarcoma)
  - Con diferenciación matricial
  - Queloideo
  - Con empalizada tipo “neural”

Carc células basales vs Tricoblastoma



The American Journal of Dermatopathology 23(6): 501–509, 2001

Cytokeratins as Markers of Follicular Differentiation

An Immunohistochemical Study of Trichoblastoma and Basal Cell Carcinoma

Hjalmar Kurzen, M.D., Lorenz Esposito, Lutz Langbein, Ph.D., and
Wolfgang Hartschuh, M.D.

TABLE 2. *Cytokeratin expression in trichoblastoma and basal cell carcinoma*

	Trichoblastoma	Solid and micronodular basal cell carcinoma	Multifocal superficial basal cell carcinoma	Sclerosing basal cell carcinoma
CK10	—	—	—	—
CK14	12/13	7/7	4/5	6/6
CK8	13/13 MC^{+}	—	—	—
CK6	13/13 cysts	5/7 cysts	5/5	6/6
CK6hf	12/13	5/7	5/5	3/6
CK13	—	—	—	—
CK15	5/13	—	—	—
CK17	12/13	7/7	5/5	5/6
CK19	9/13	2/7	1/5	1/6
Hair keratins	—	—	—	—

No es posible diferenciarlos por el patrón de expresión de citoqueratinas.

ORIGINAL ARTICLE

Cytokeratin Profile in Basal Cell Carcinoma

Elvio Alessi, MD, Luigia Venegoni, BSc,* Daniele Fanoni, BSc,* and Emilio Berti, MD†*

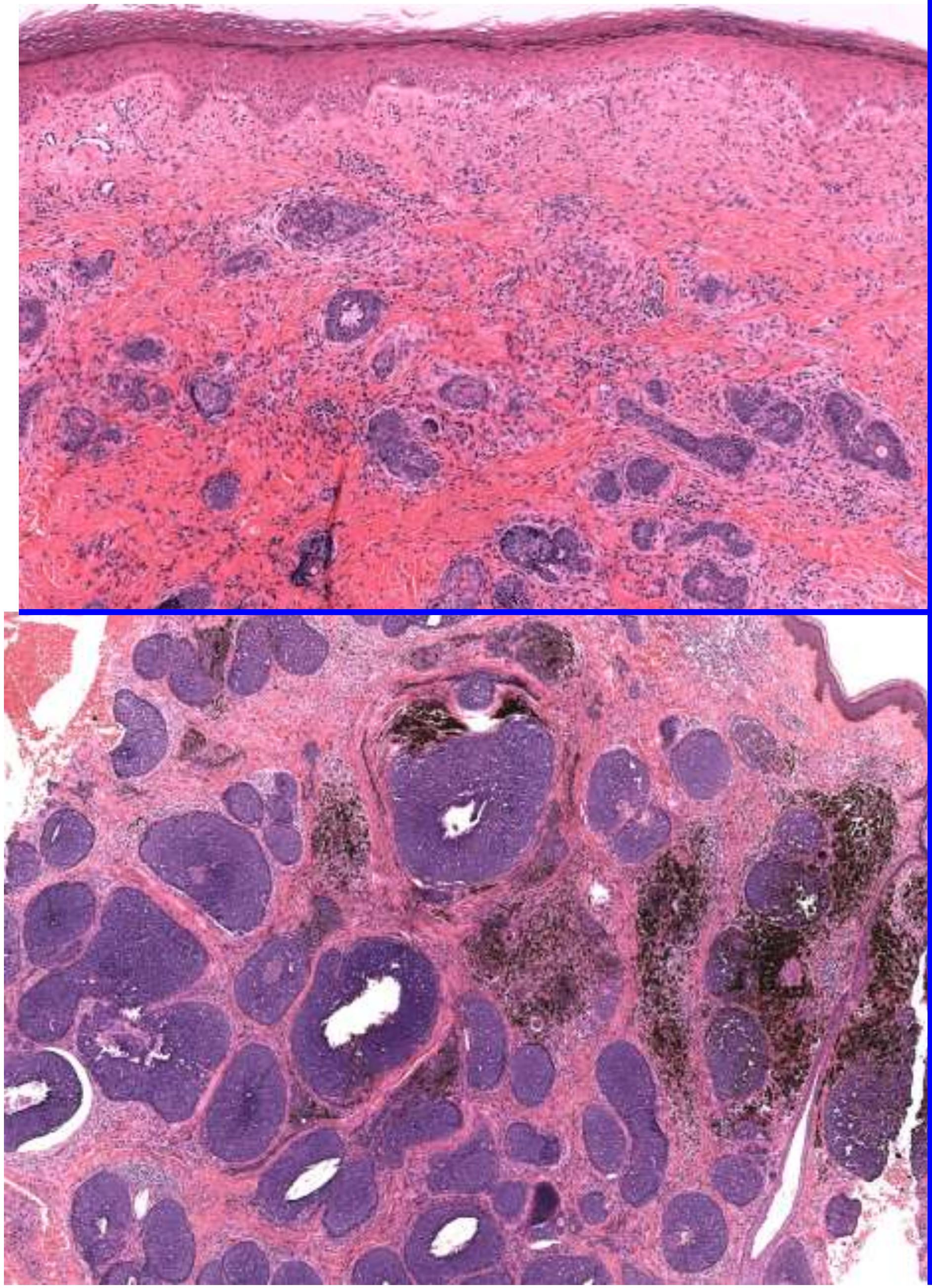
(*Am J Dermatopathol* 2008;30:249–255)

TABLE 2. Focal or Diffuse Expression for 12 CKs in Some BCC Subtypes

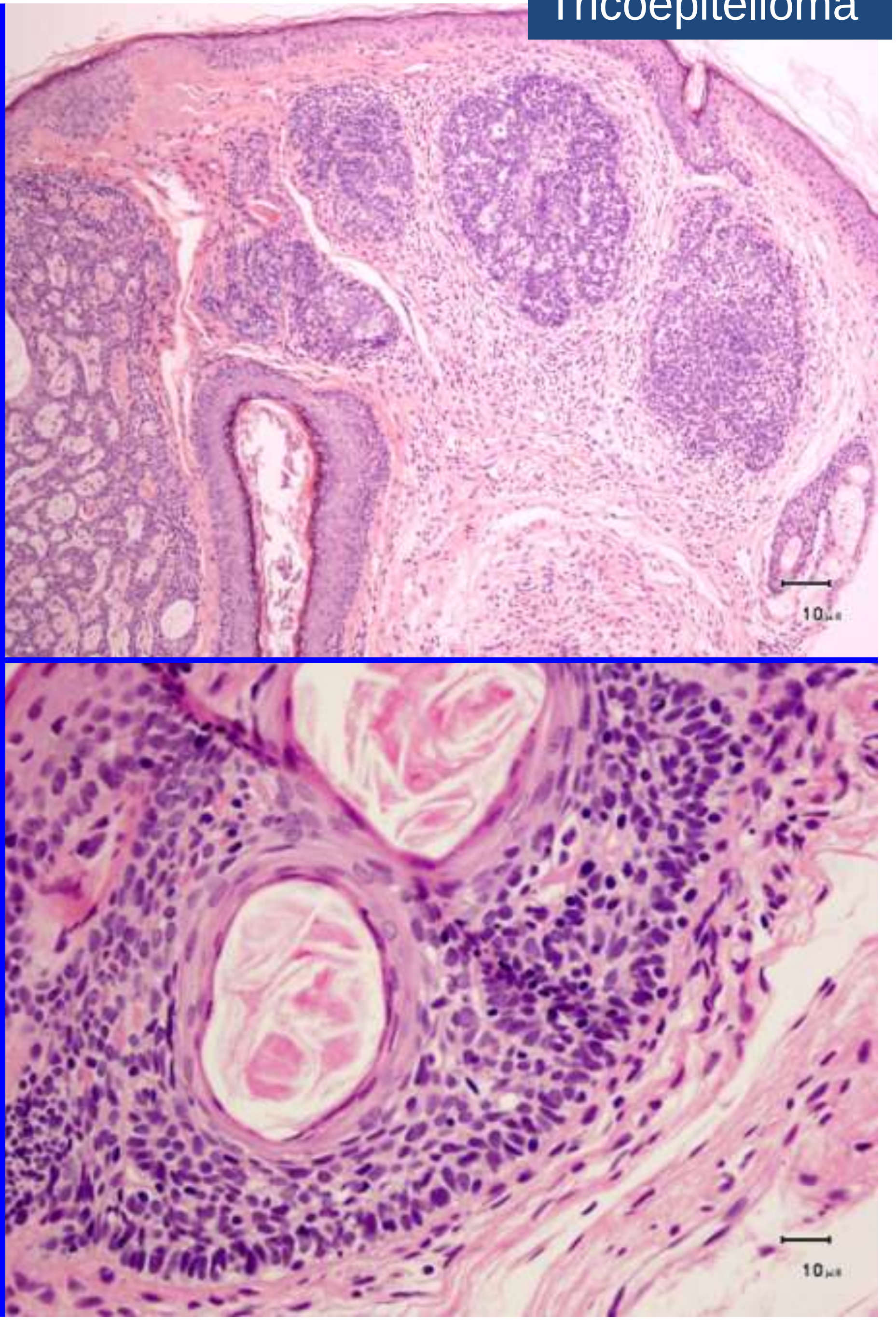
	CK											
	1	**5**	**6**	**7**	**8**	**10**	**14**	**15**	**16**	**17**	**18**	**19**
Superficial BCC	7/10*	10/10	0/10†	7/10	4/10	0/10	0/10	0/10	6/10¶	10/10	7/10	2/10
Nodular BCC	4/10*	10/10	2/10	2/10	7/10	0/10	0/10	0/10	4/10	10/10	8/10	2/10
Micronodular BCC	3/4*	4/4	1/4	3/4	2/4	0/4	1/4	0/4	2/4	4/4	3/4	1/4
Morpheiform BCC	0/2	2/2	0/2	0/2	1/2	0/2	0/2	0/2	0/2	2/2	1/2	0/2
Fibroepithelial BCC	5/5	5/5	0/5†	2/5‡	2/5	0/5	1/5§	0/5	1/5¶	5/5	4/5	2/5
Nodulocystic BCC	4/4	4/4	0/4	1/4	3/4	0/4	2/4	0/4	2/4	4/4	3/4	1/4
BCC with adnexal diff.	17/17	17/17	7/17†	15/17	14/17	0/17	3/17§	0/17	13/17¶	17/17	16/17	6/17

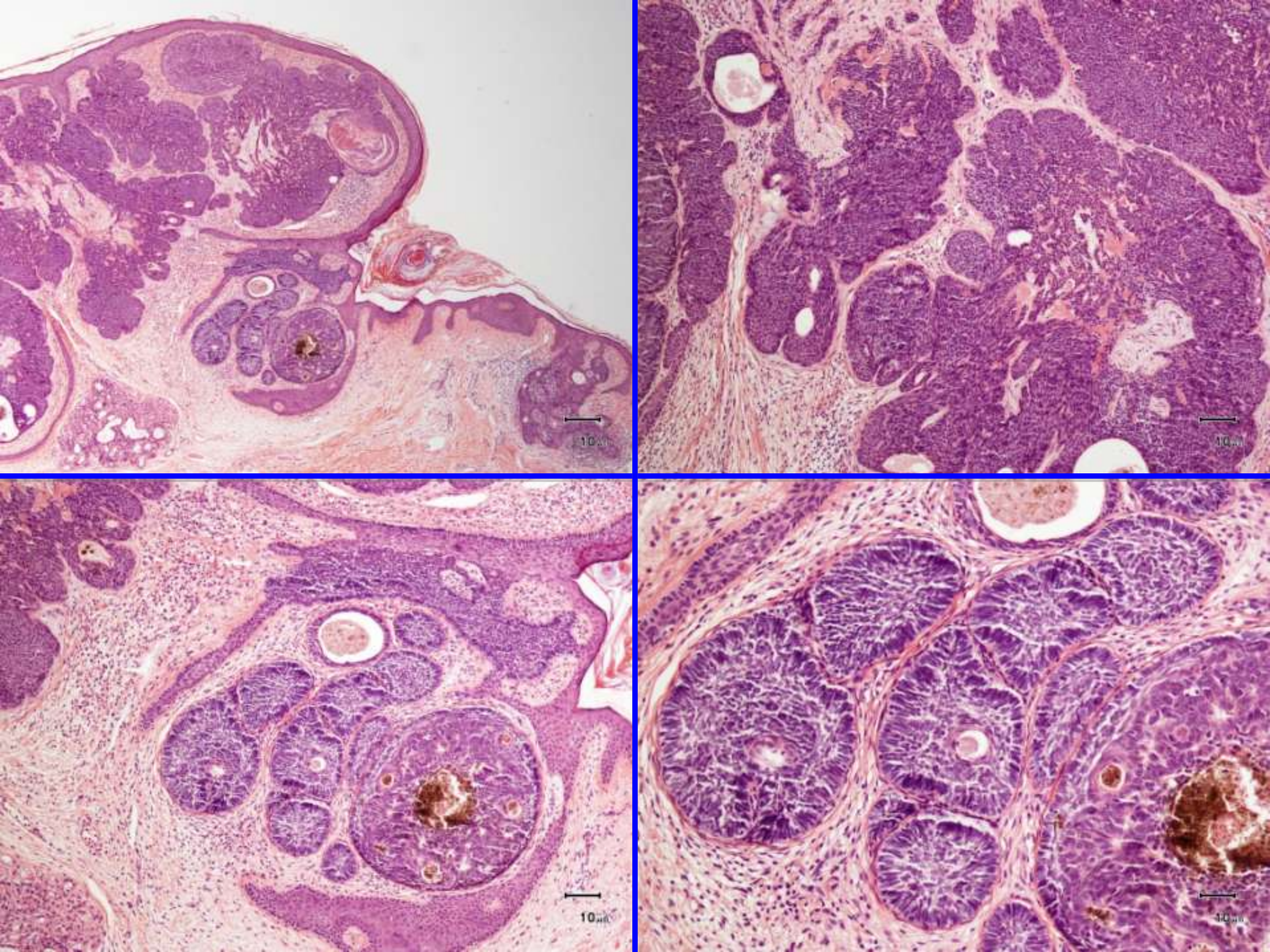
In conclusion, our study confirmed the suggested close relationship between BCC cells and hair follicle epithelial cells. It was in favor of tumor differentiation toward follicular outer root sheath cells and, in most cases, also toward the glandular components of the pilosebaceous–apocrine unit. It also showed that no significant difference in the CK profile among the BCC subtypes exists.

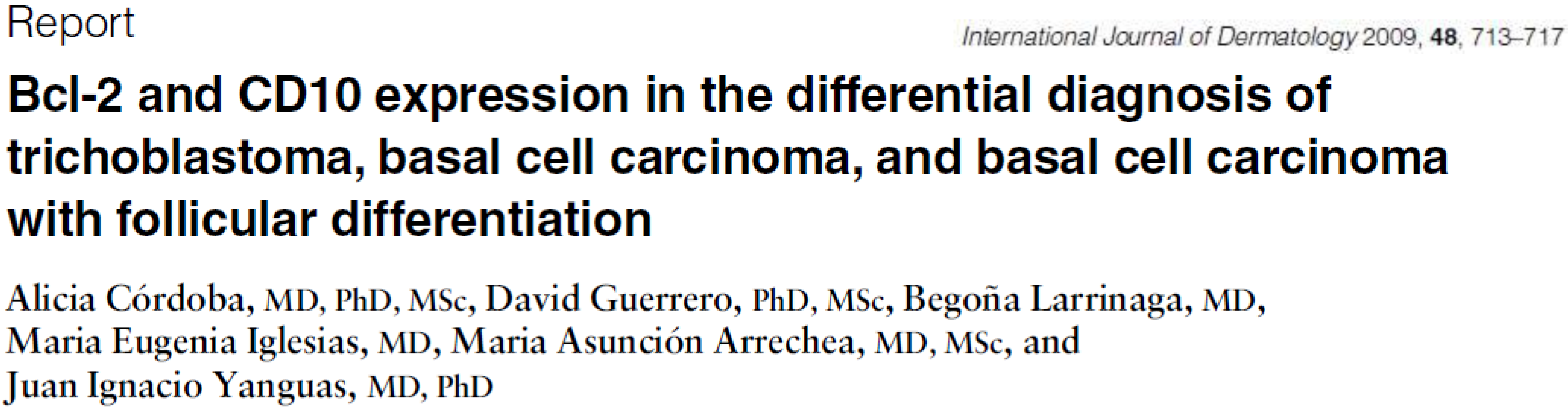
Tricoblastoma



Tricoepitelioma




10㎛
10㎛
10㎛
10㎛

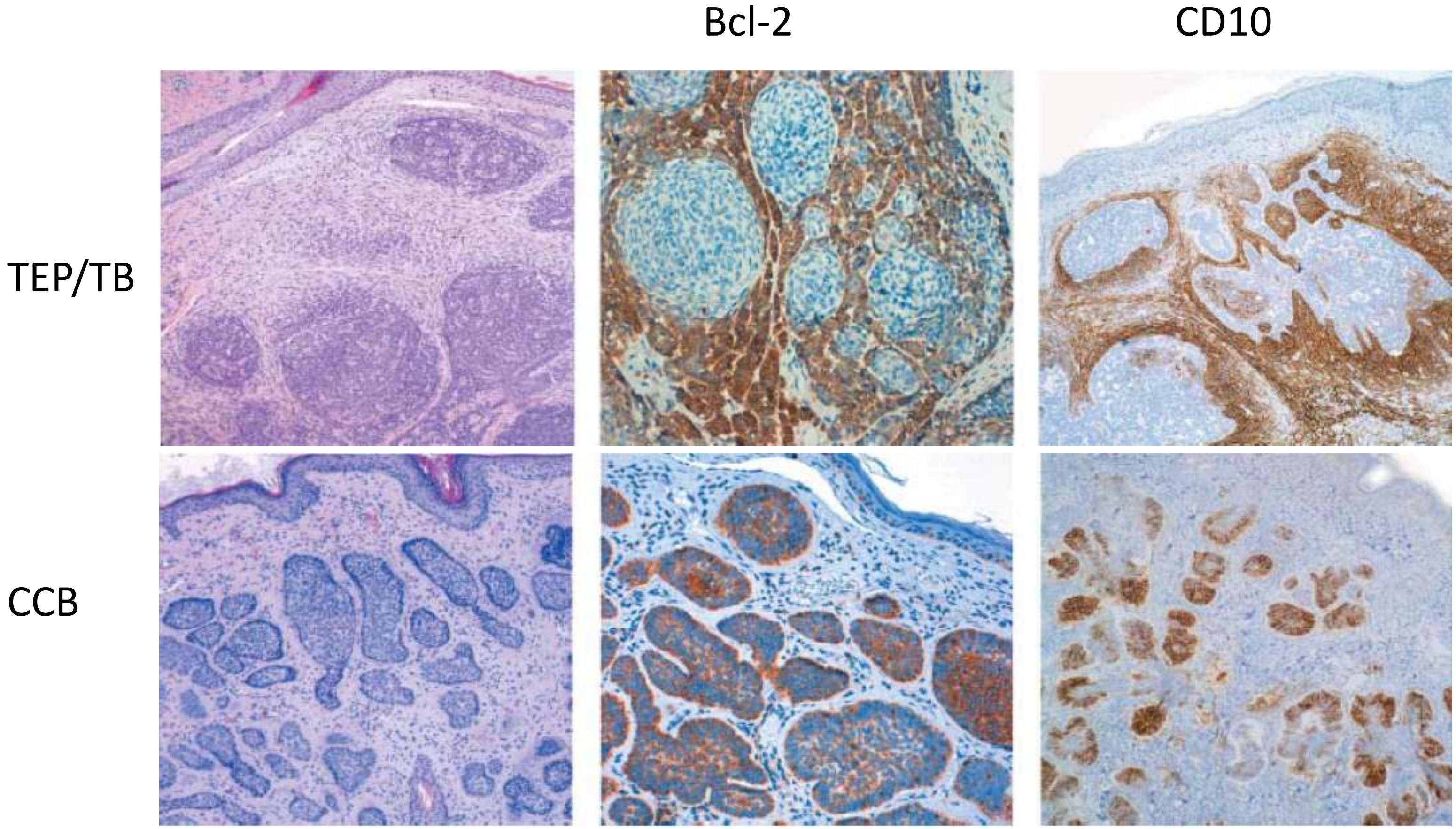


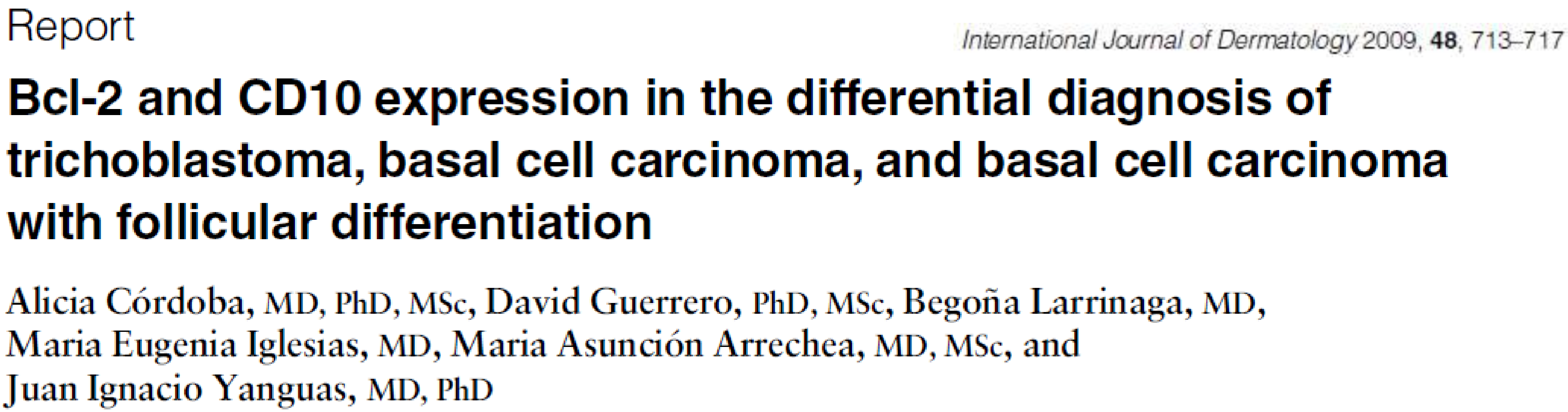
Report

International Journal of Dermatology 2009, **48**, 713–717

Bcl-2 and CD10 expression in the differential diagnosis of trichoblastoma, basal cell carcinoma, and basal cell carcinoma with follicular differentiation

Alicia Córdoba, MD, PhD, MSc, David Guerrero, PhD, MSc, Begoña Larrinaga, MD,
Maria Eugenia Iglesias, MD, Maria Asunción Arrechea, MD, MSc, and
Juan Ignacio Yanguas, MD, PhD





Report

International Journal of Dermatology 2009, **48**, 713–717

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Juan Ignacio Yanguas, MD, PhD

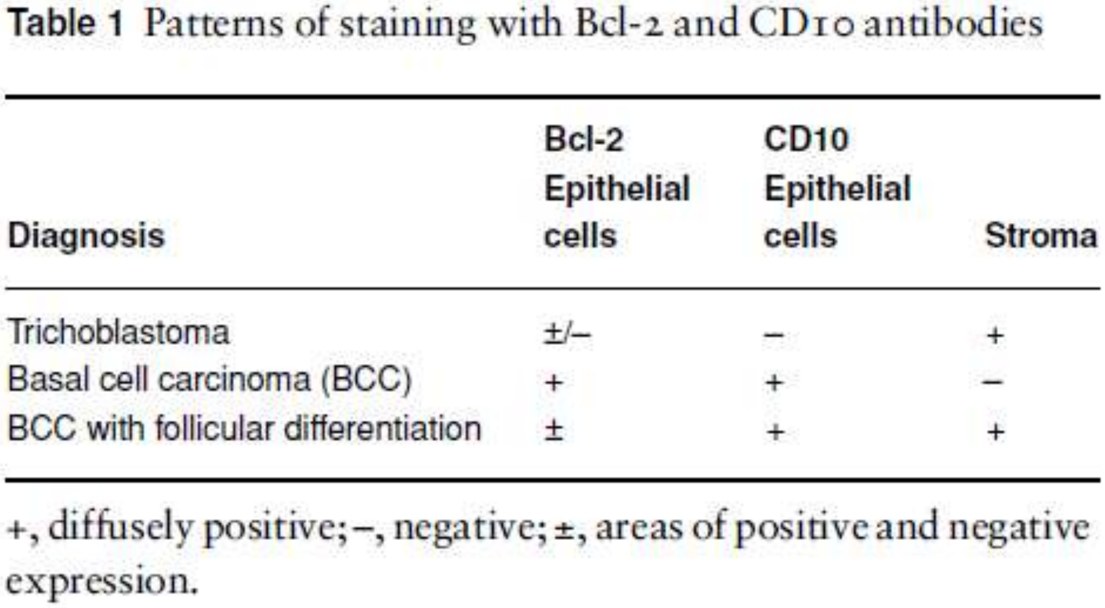
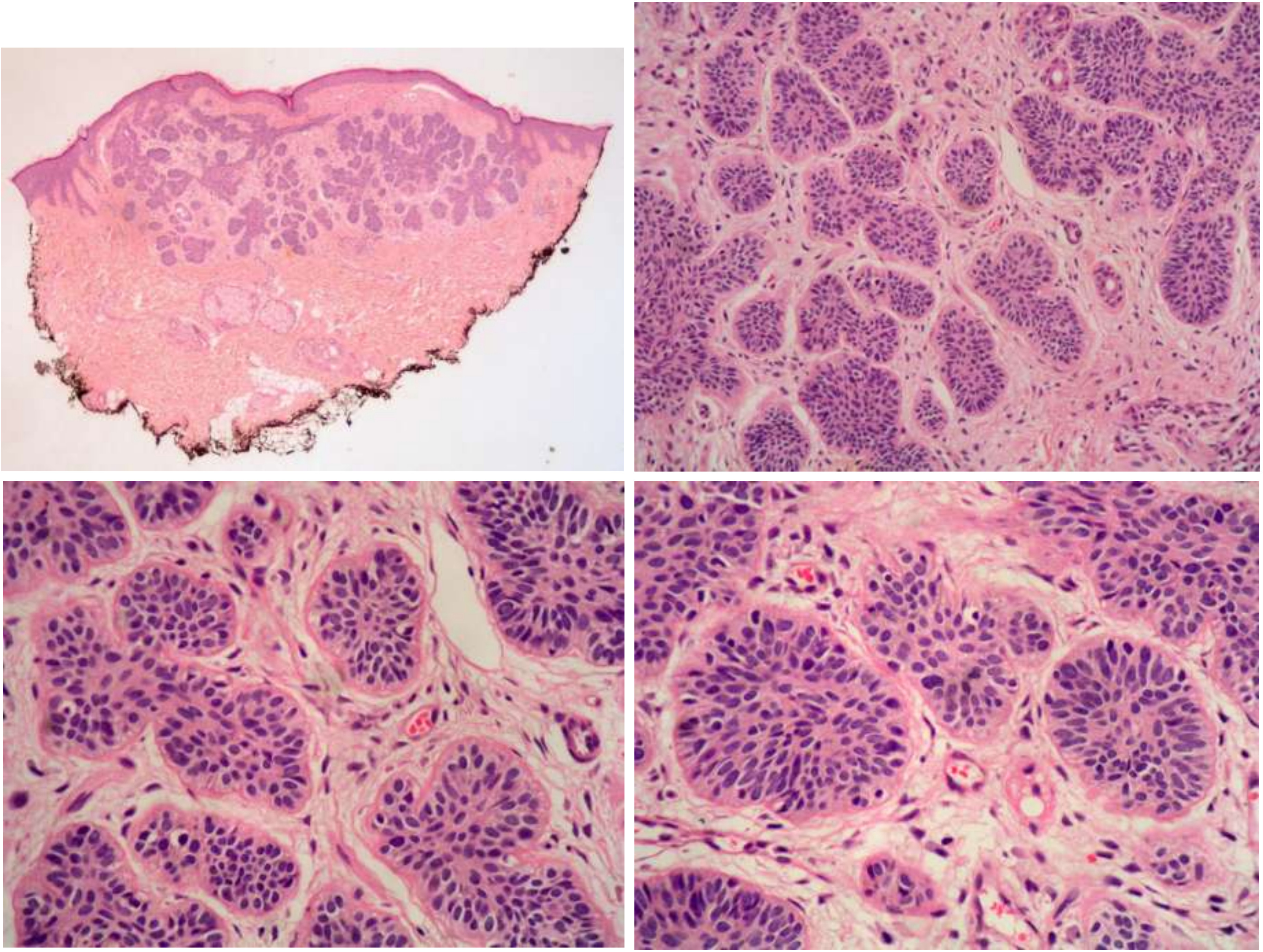
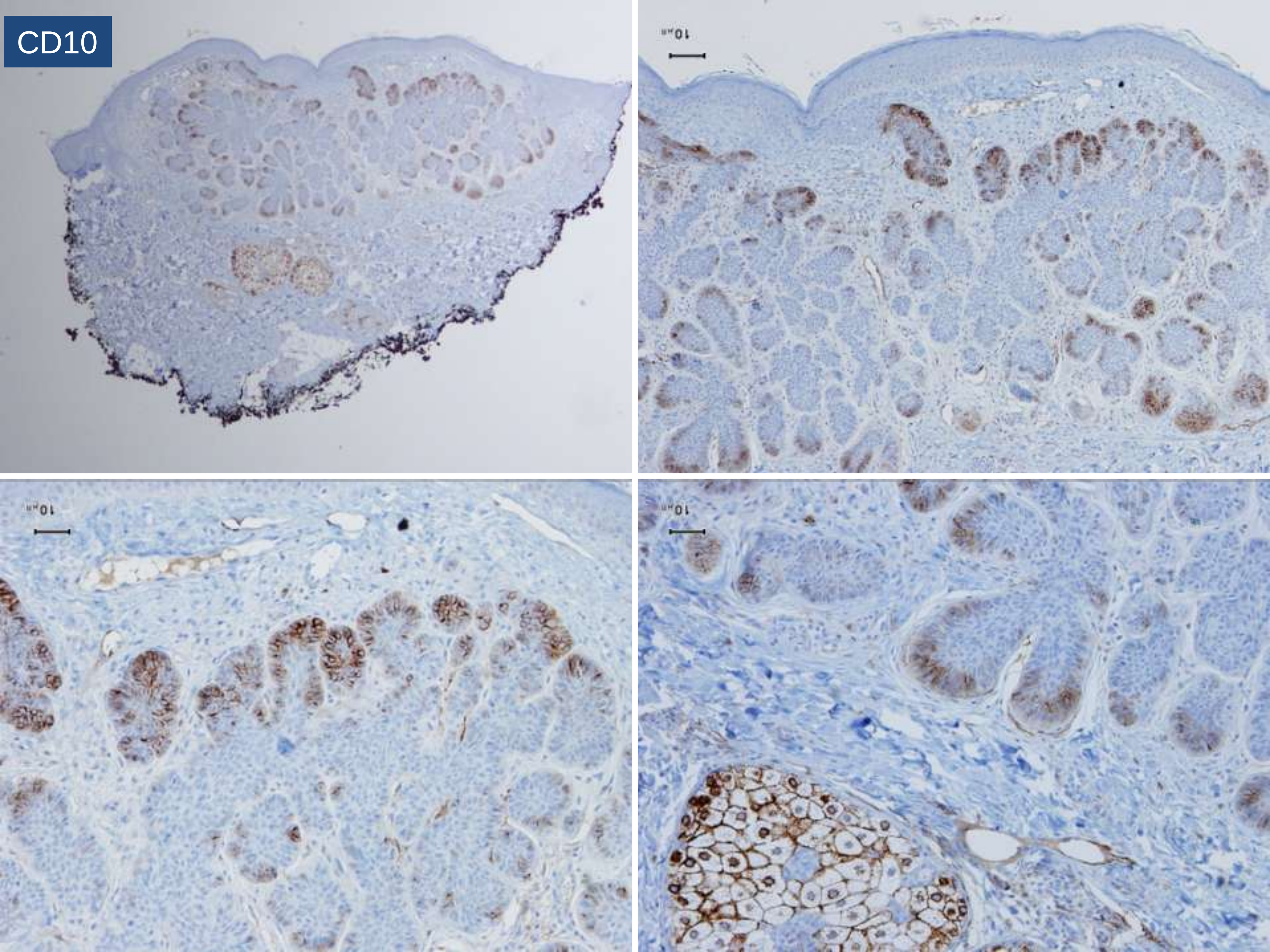


Table 1 Patterns of staining with Bcl-2 and CD10 antibodies

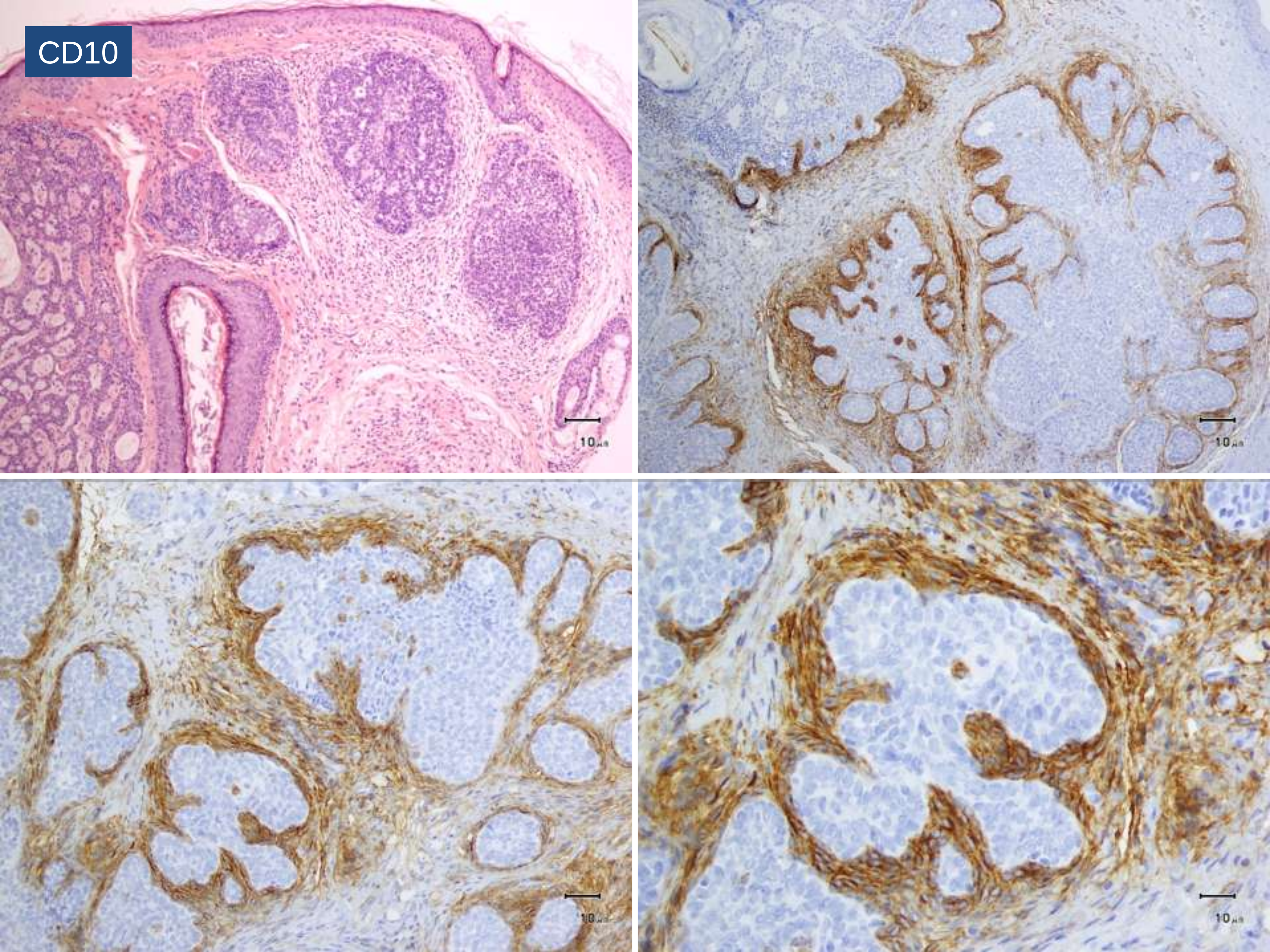
Diagnosis	Bcl-2 Epithelial cells	CD10 Epithelial cells	Stroma
Trichoblastoma	±/–	–	+
Basal cell carcinoma (BCC)	+	+	–
BCC with follicular differentiation	±	+	+

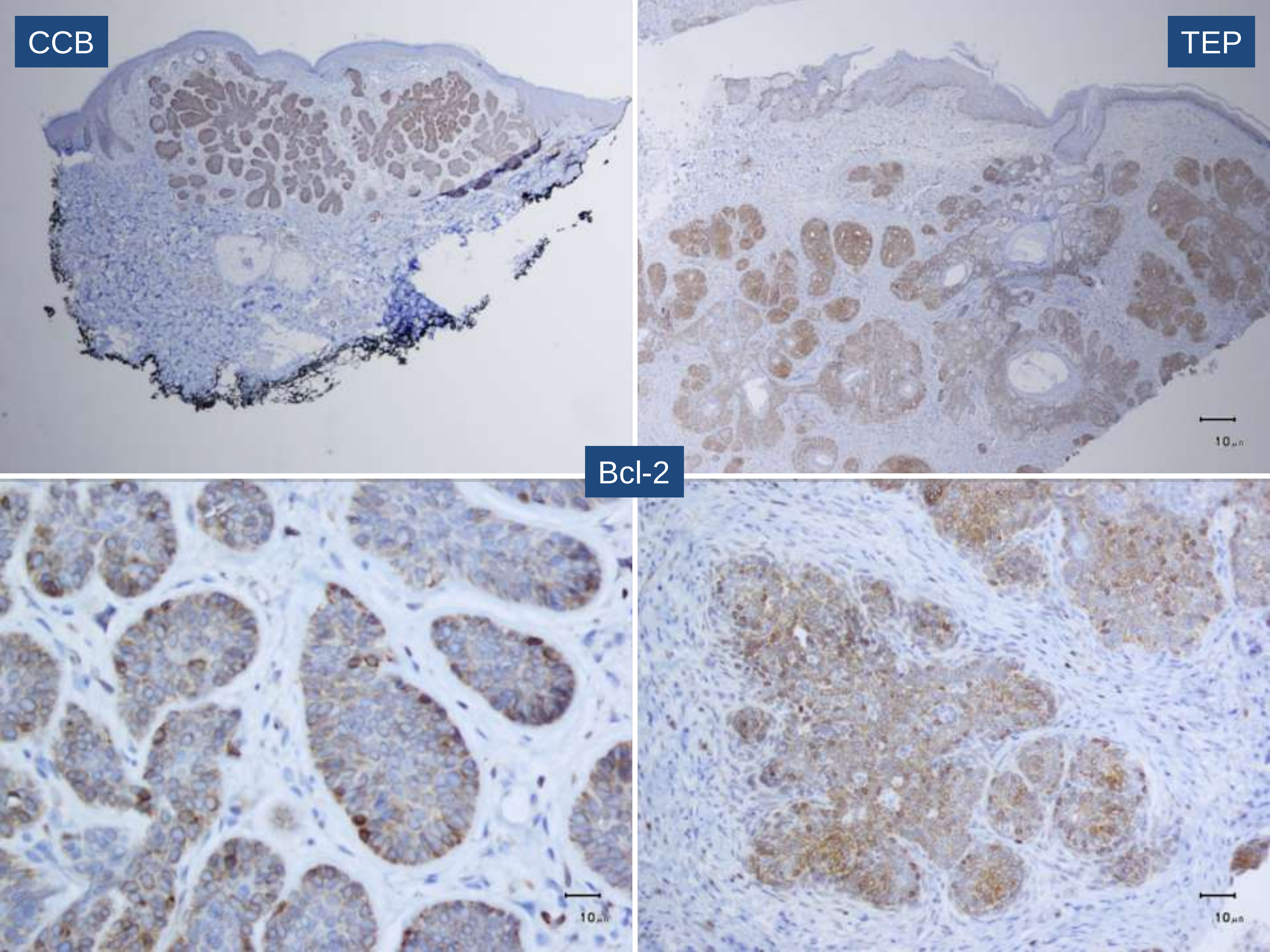
+, diffusely positive; –, negative; ±, areas of positive and negative expression.

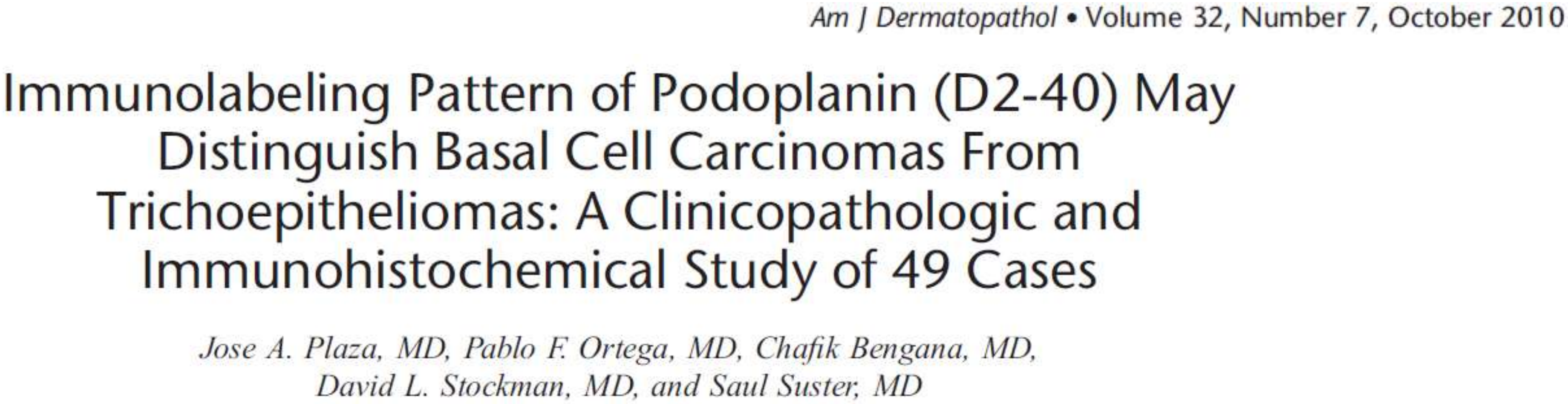



CD10
10µm
10µm
10µm

CD10


10 μm
10 μm
10 μm
10 μm

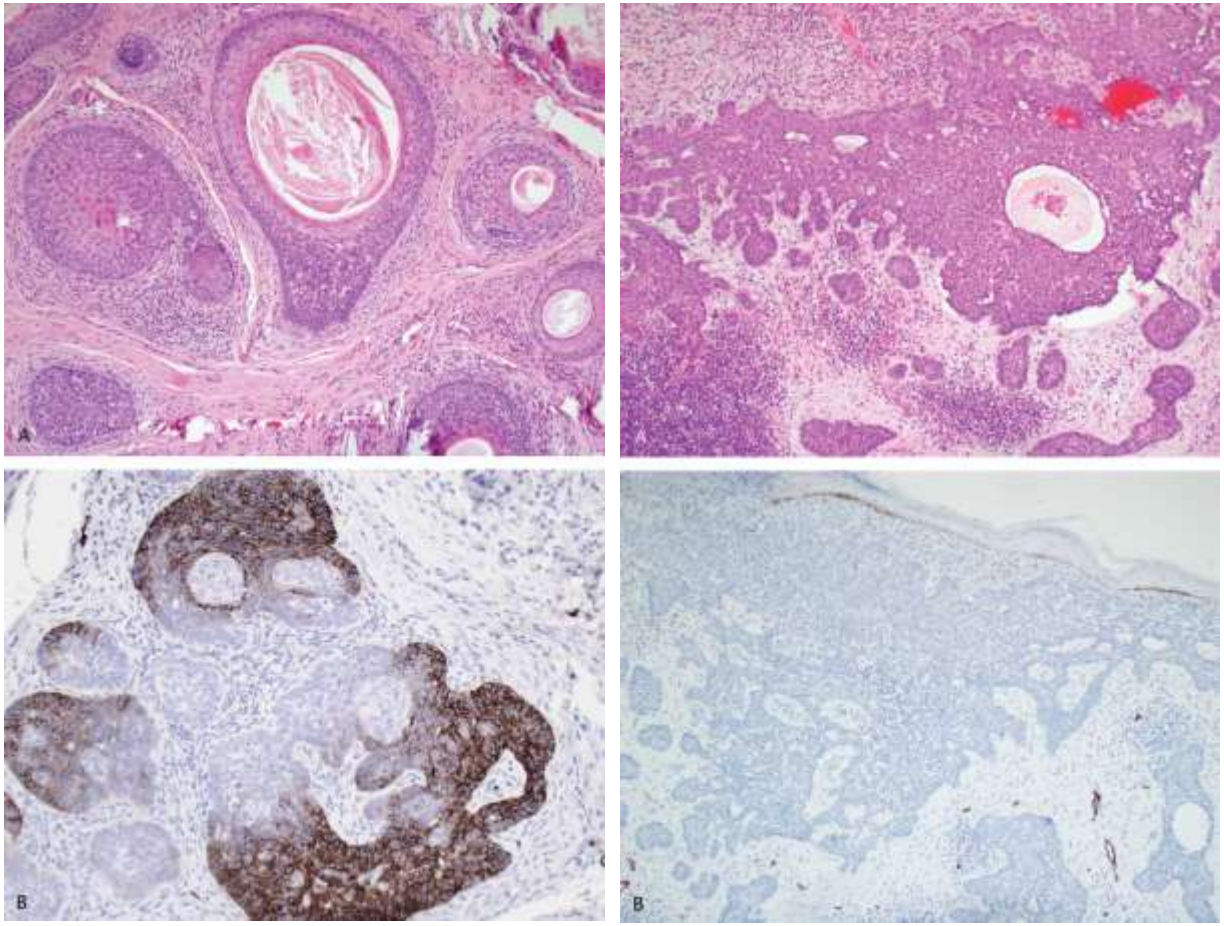

CCB
TEP
Bcl-2
10 µm
10 µm
10 µm



Am J Dermatopathol • Volume 32, Number 7, October 2010

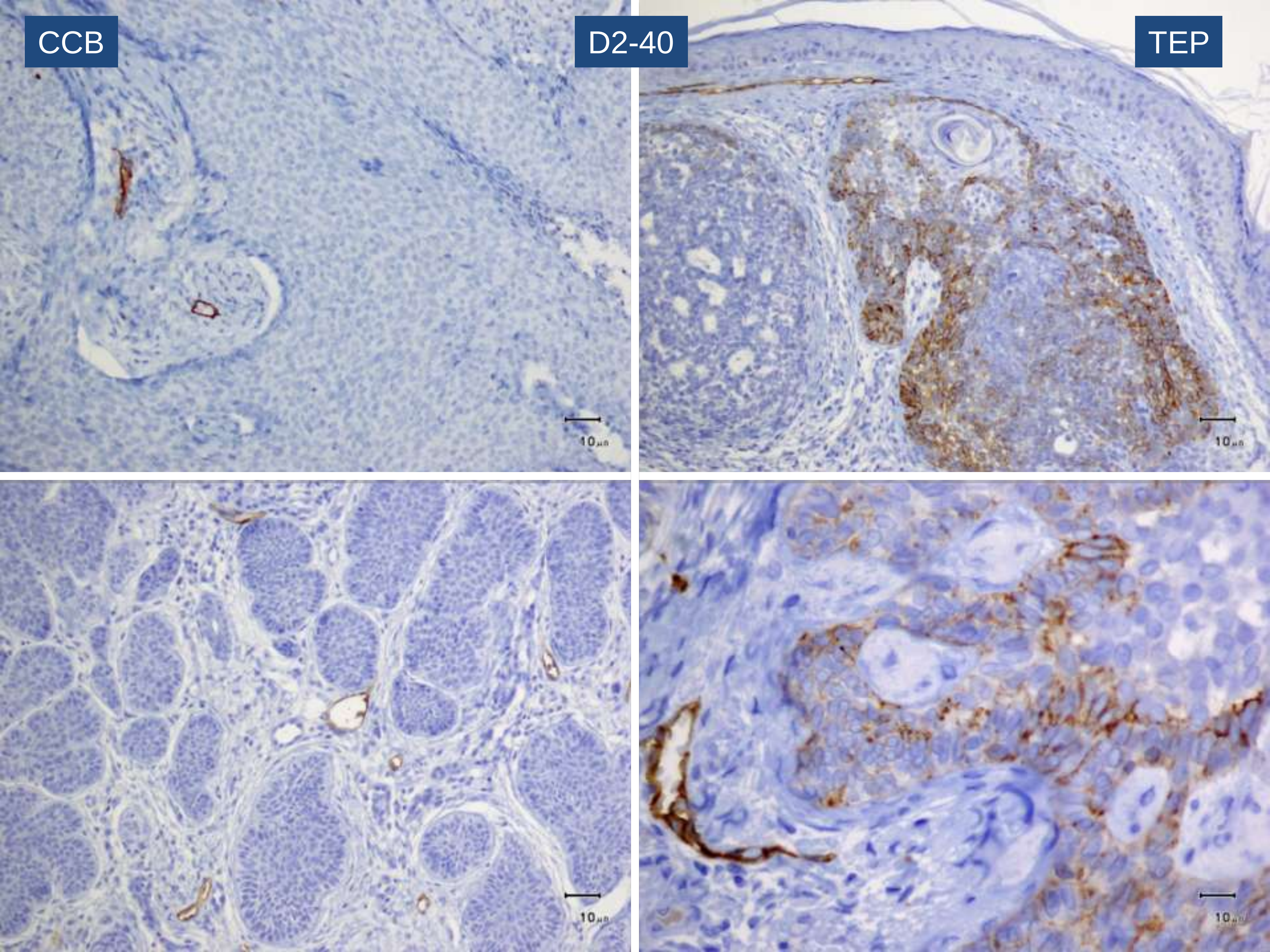
Immunolabeling Pattern of Podoplanin (D2-40) May Distinguish Basal Cell Carcinomas From Trichoepitheliomas: A Clinicopathologic and Immunohistochemical Study of 49 Cases

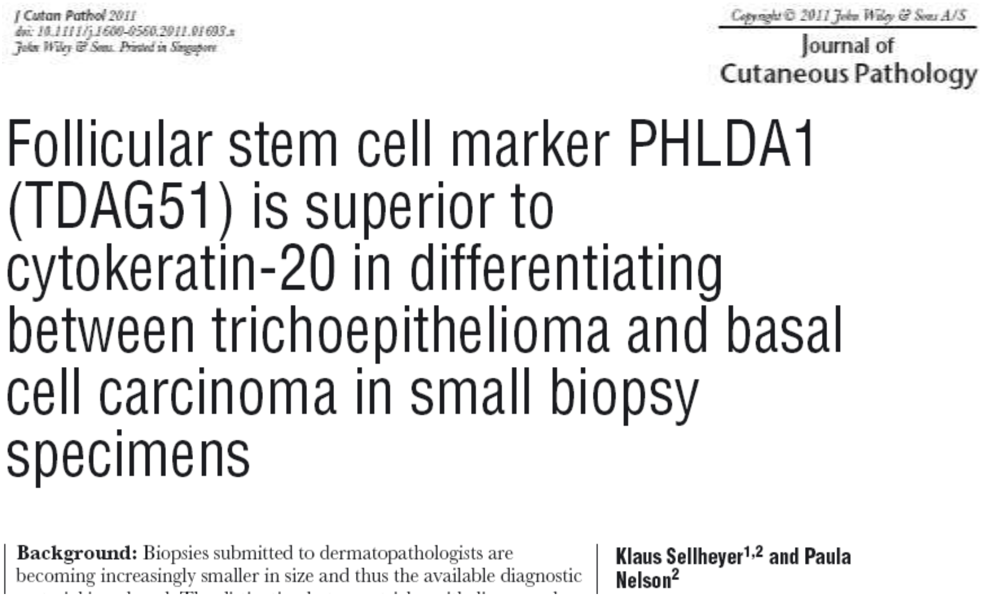
Jose A. Plaza, MD, Pablo F. Ortega, MD, Chafik Bengana, MD,
David L. Stockman, MD, and Saul Suster, MD



TEP 21/22 + (95,5%)
11 difusa
10 focal

CCB 6/27 + (22,2%)
2 difusa
4 focal
(periferia)


CCB
D2-40
TEP
10 µm
10 µm
10 µm
10 µm



J Cutan Pathol 2011
doi: 10.1111/j.1600-0560.2011.01693.x
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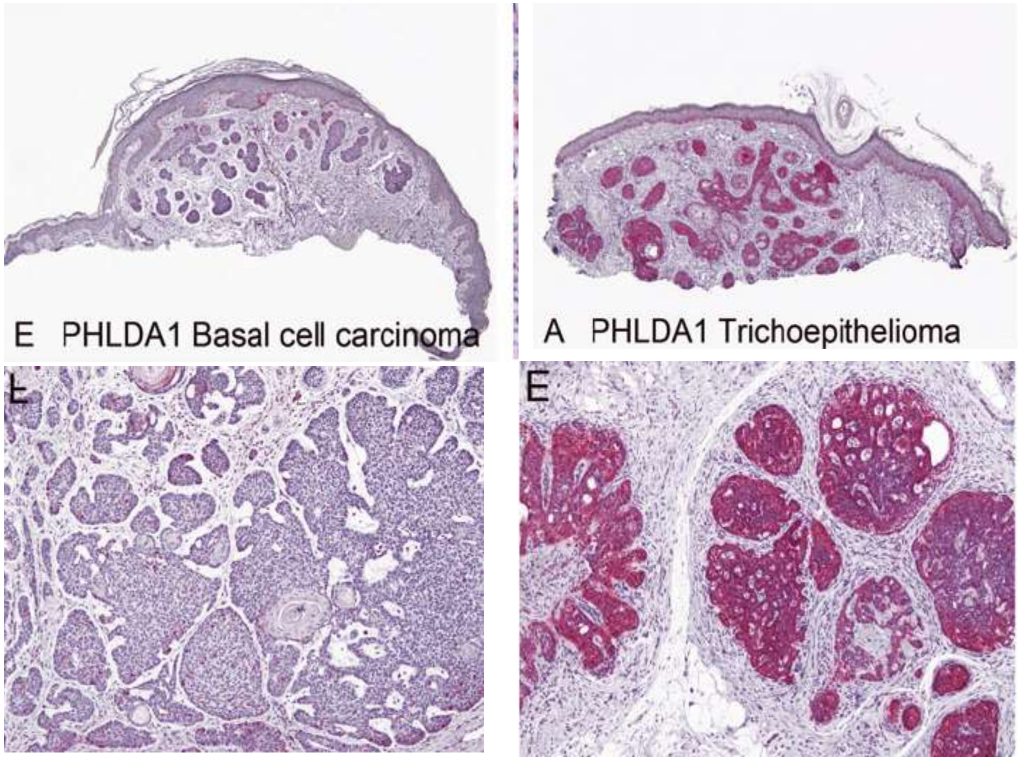
Journal of
Cutaneous Pathology

Follicular stem cell marker PHLDA1 (TDAG51) is superior to cytokeratin-20 in differentiating between trichoepithelioma and basal cell carcinoma in small biopsy specimens

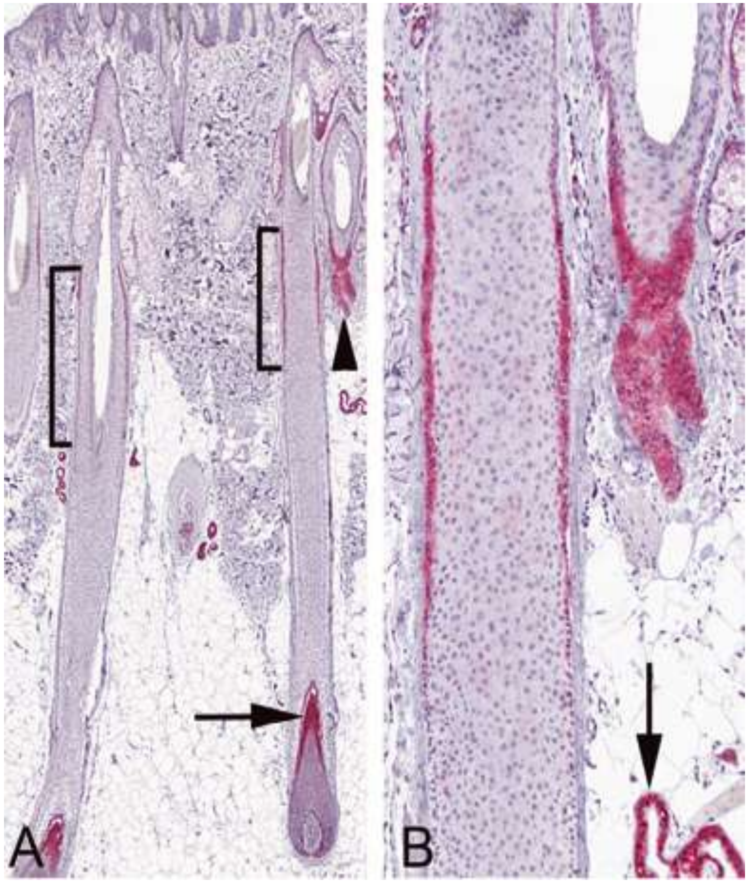
Background: Biopsies submitted to dermatopathologists are becoming increasingly smaller in size and thus the available diagnostic

Klaus Sellheyer[1,2] and Paula Nelson[2]



E PHLDA1 Basal cell carcinoma

A PHLDA1 Trichoepithelioma



PHLDA1: regulación de la apoptosis

TEP +: control de la apoptosis
CCB -: pérdida del control

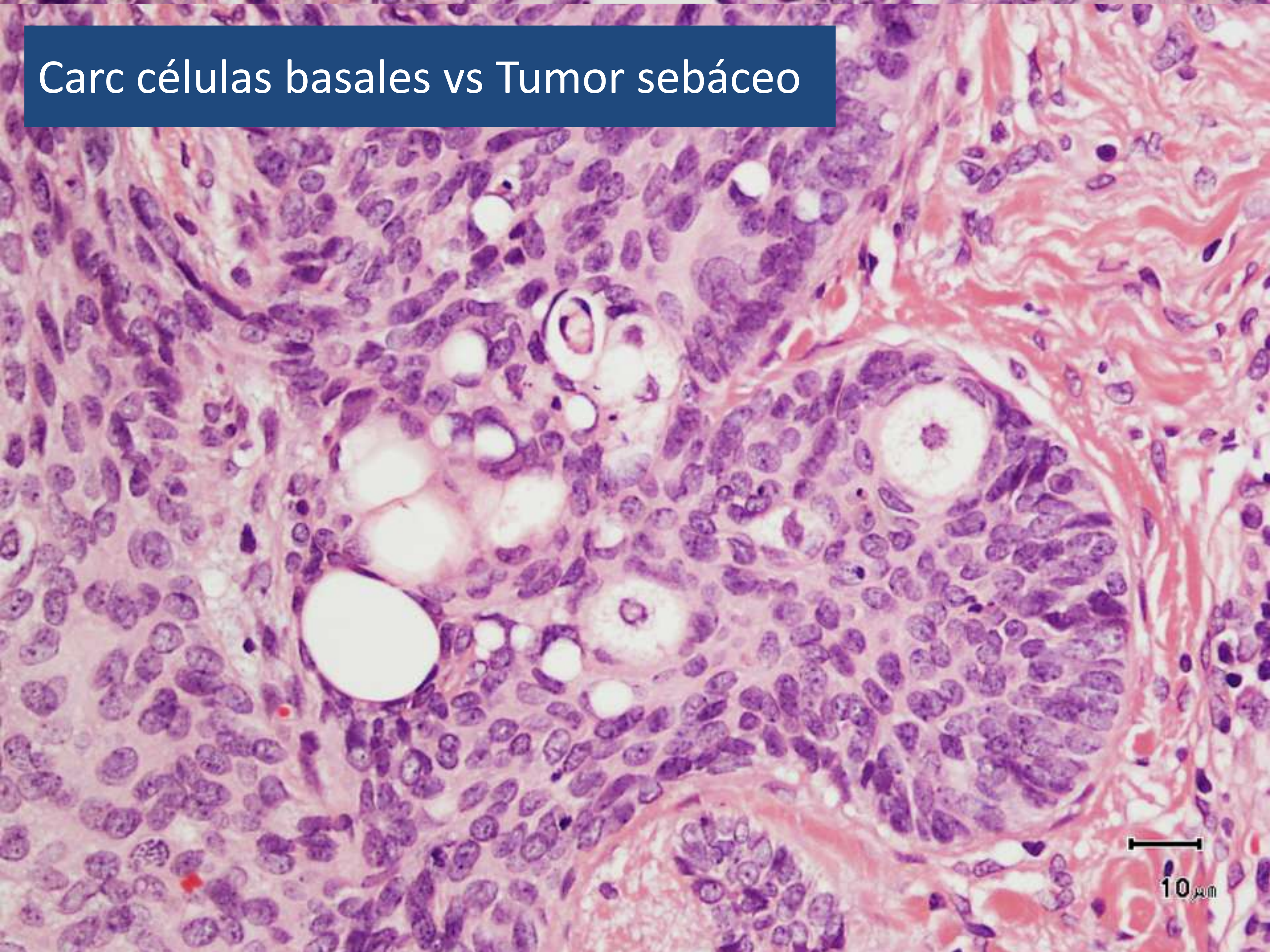
Carc células basales vs Tricoblastoma

- Ambas son neoplasias de origen folicular
  - No sirven las citoqueratinas

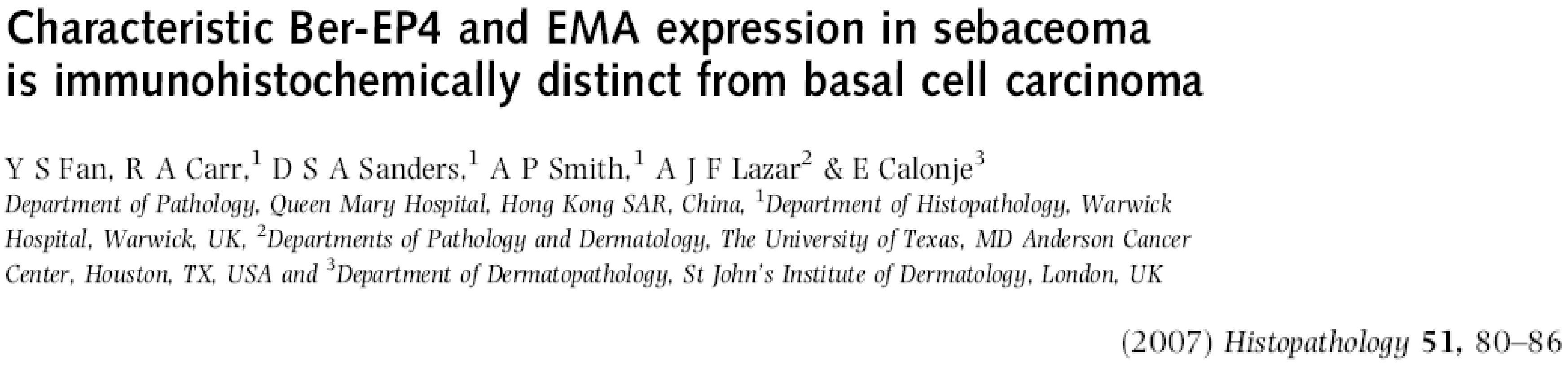
Marcadores IHQ

- CD10 → CCB epitelio
  TB estroma
- D2-40 ?
- PHLDA1 → CCB negativo
  TB positivo

Carc células basales vs Tumor sebáceo



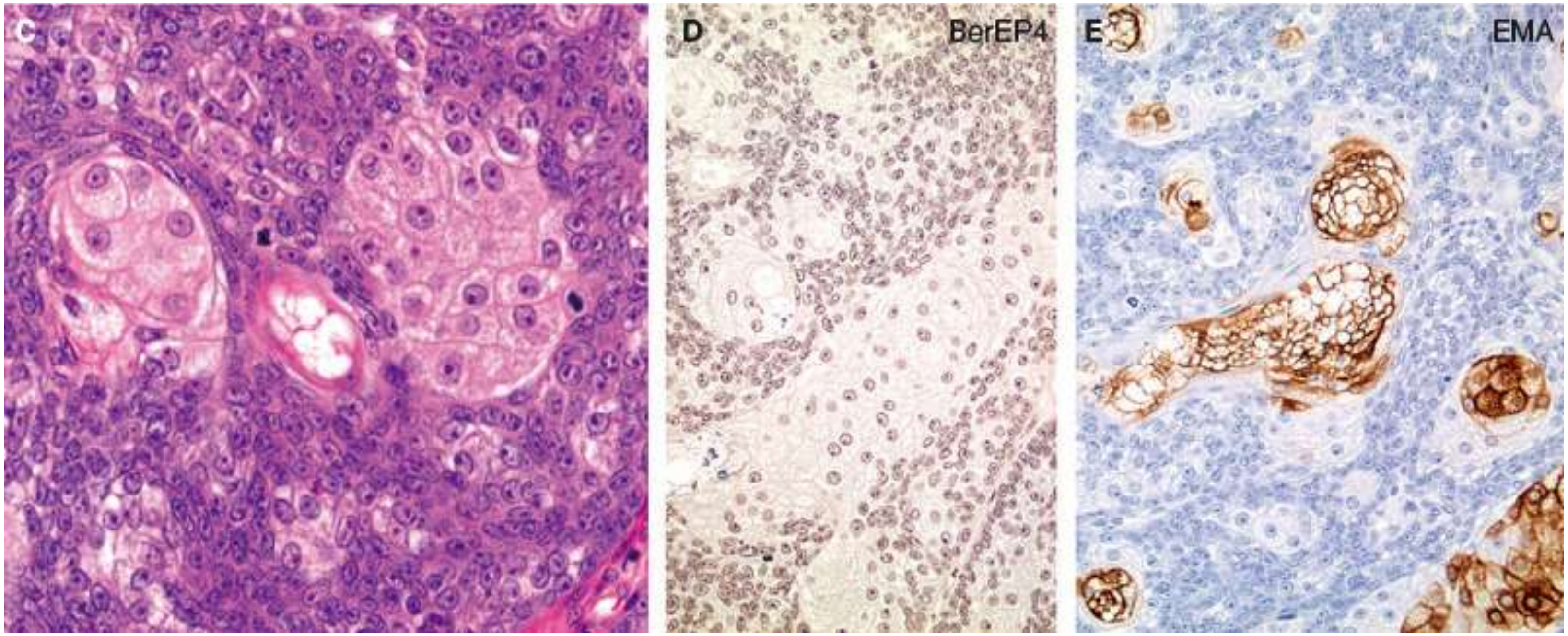
Carc células basales vs Tumor sebáceo

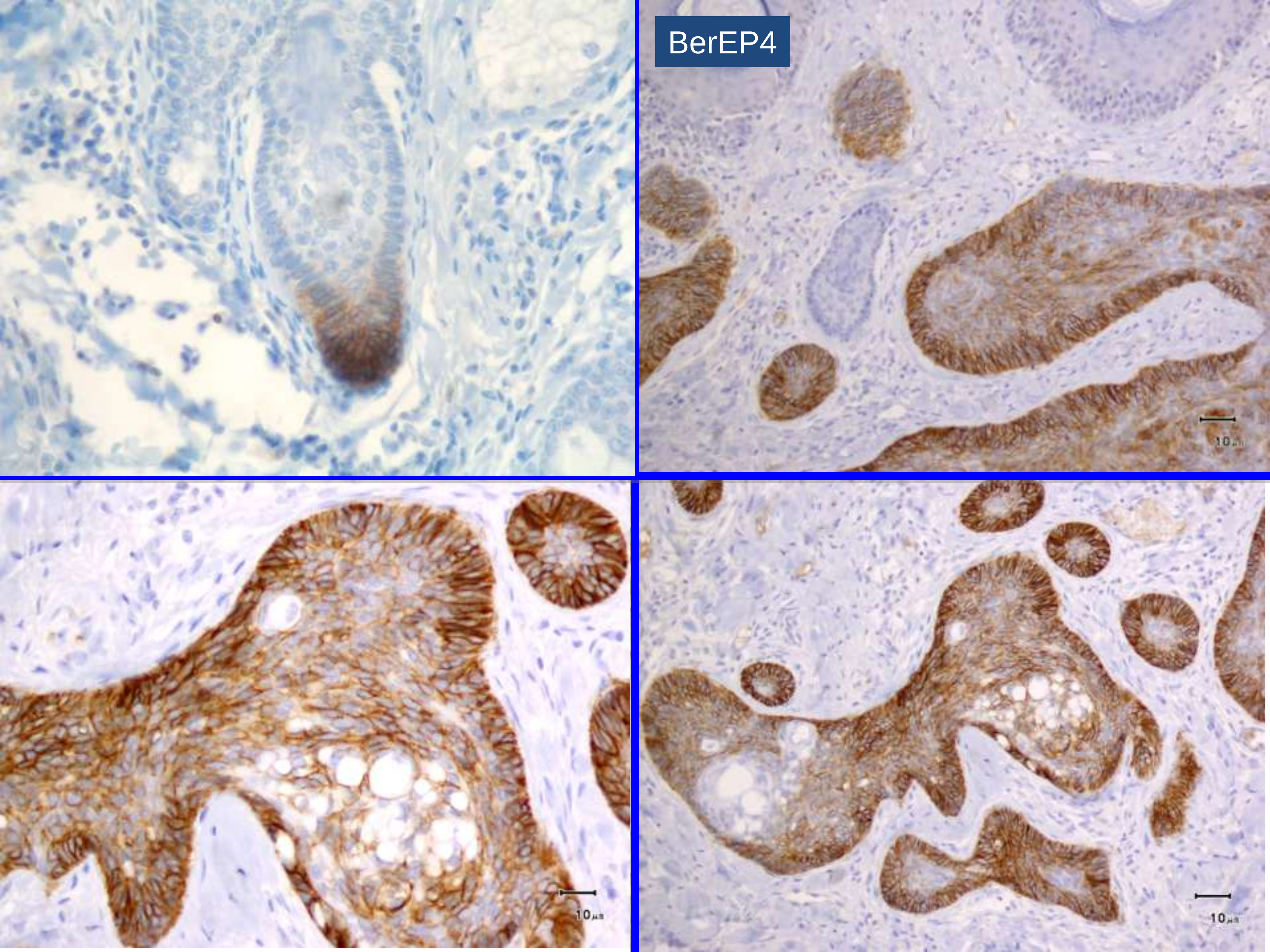


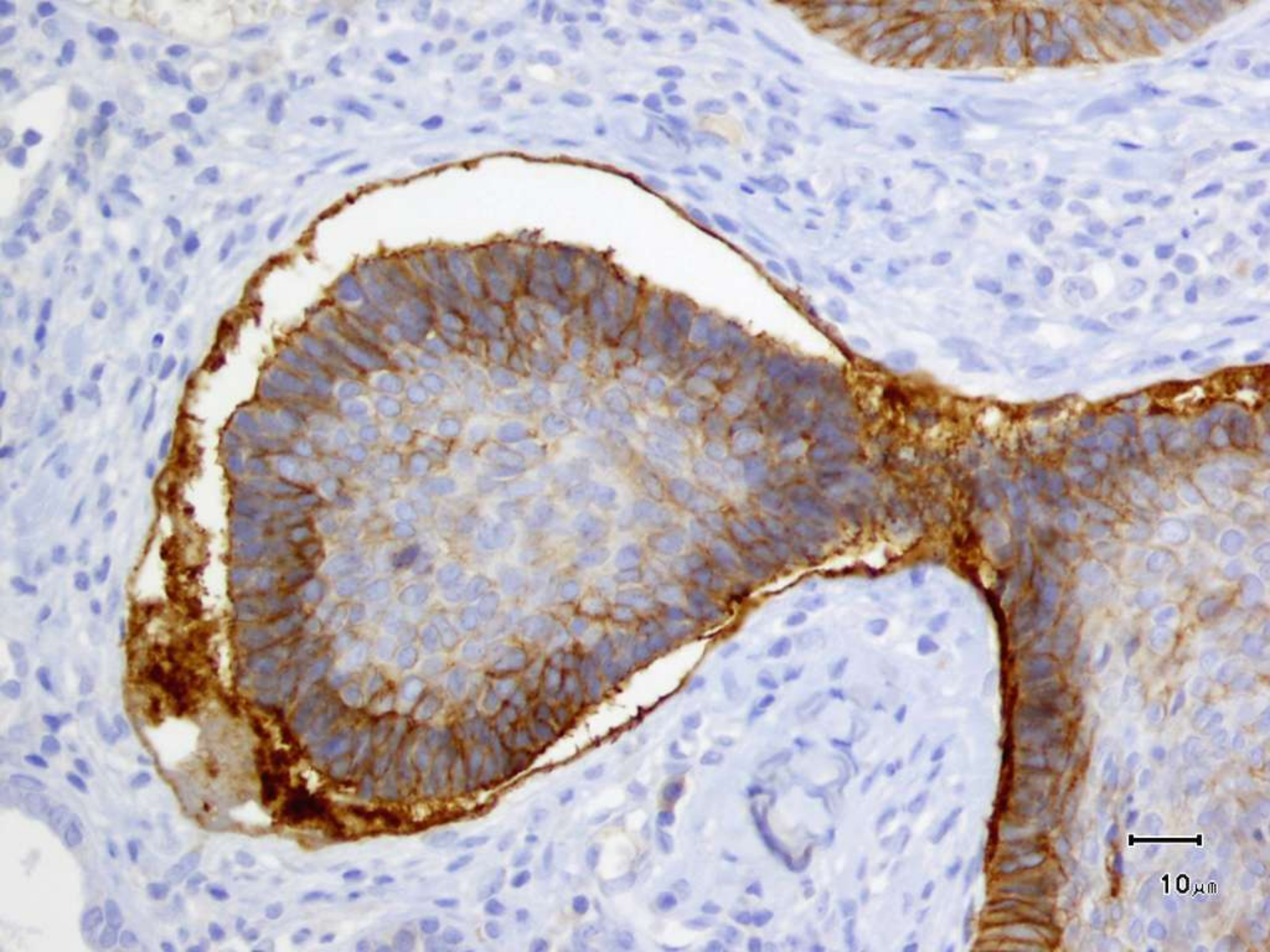
Characteristic Ber-EP4 and EMA expression in sebaceoma is immunohistochemically distinct from basal cell carcinoma

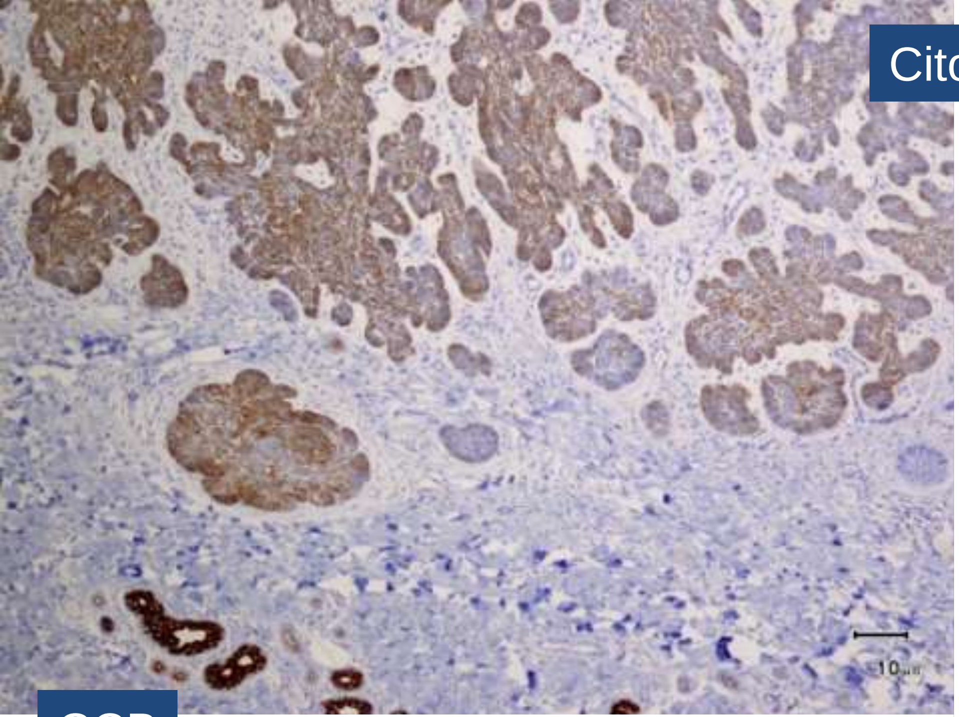
Y S Fan, R A Carr,[1] D S A Sanders,[1] A P Smith,[1] A J F Lazar[2] & E Calonje[3]
Department of Pathology, Queen Mary Hospital, Hong Kong SAR, China, [1]Department of Histopathology, Warwick Hospital, Warwick, UK, [2]Departments of Pathology and Dermatology, The University of Texas, MD Anderson Cancer Center, Houston, TX, USA and [3]Department of Dermatopathology, St John's Institute of Dermatology, London, UK

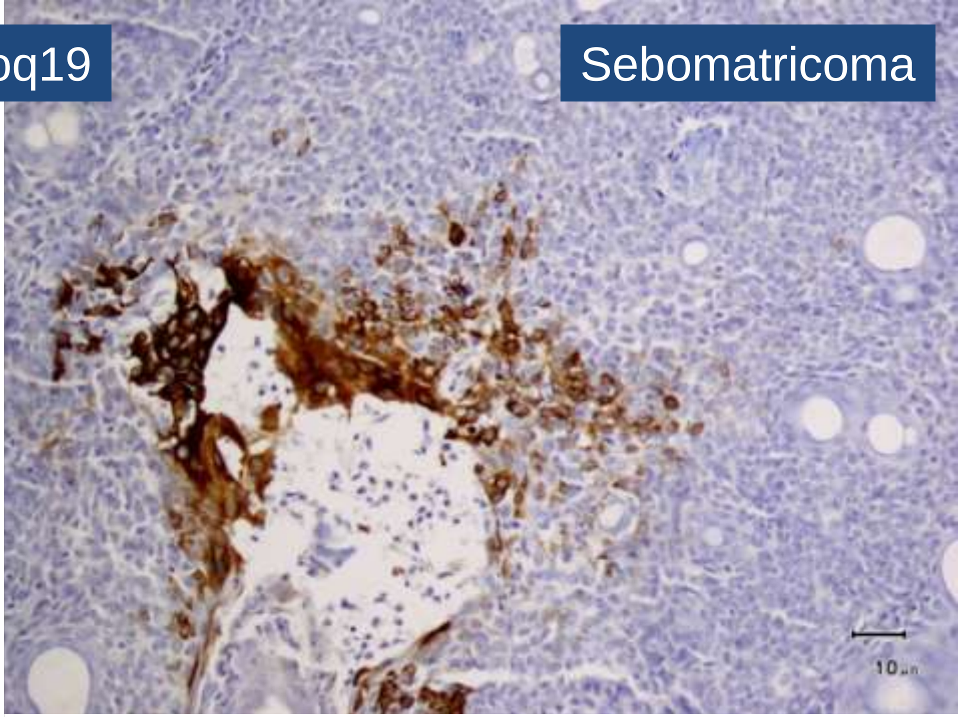
(2007) *Histopathology* **51**, 80–86

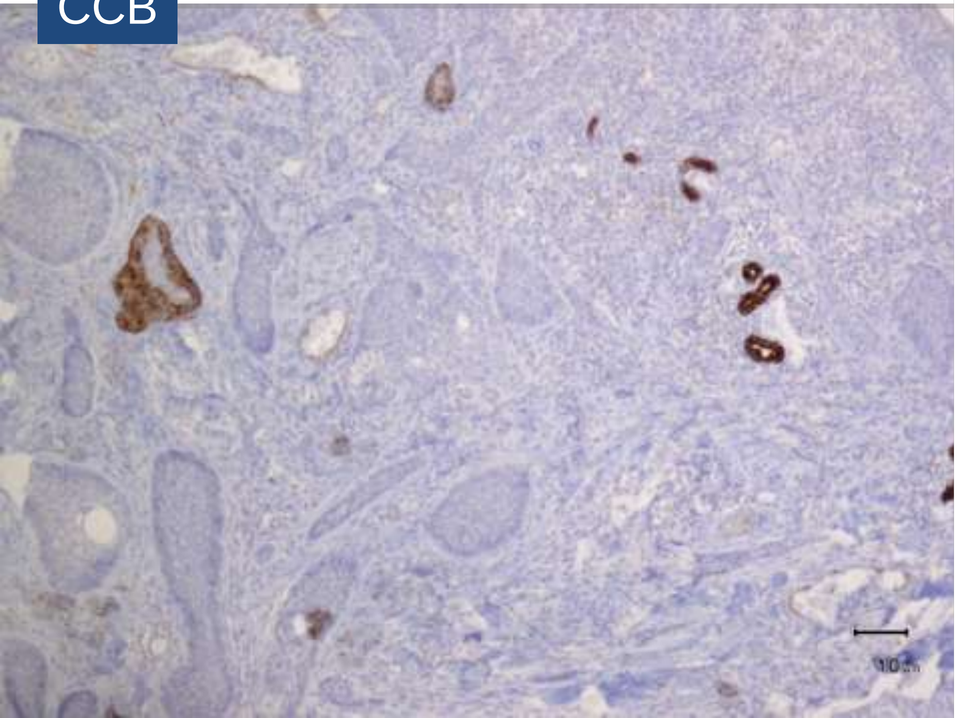


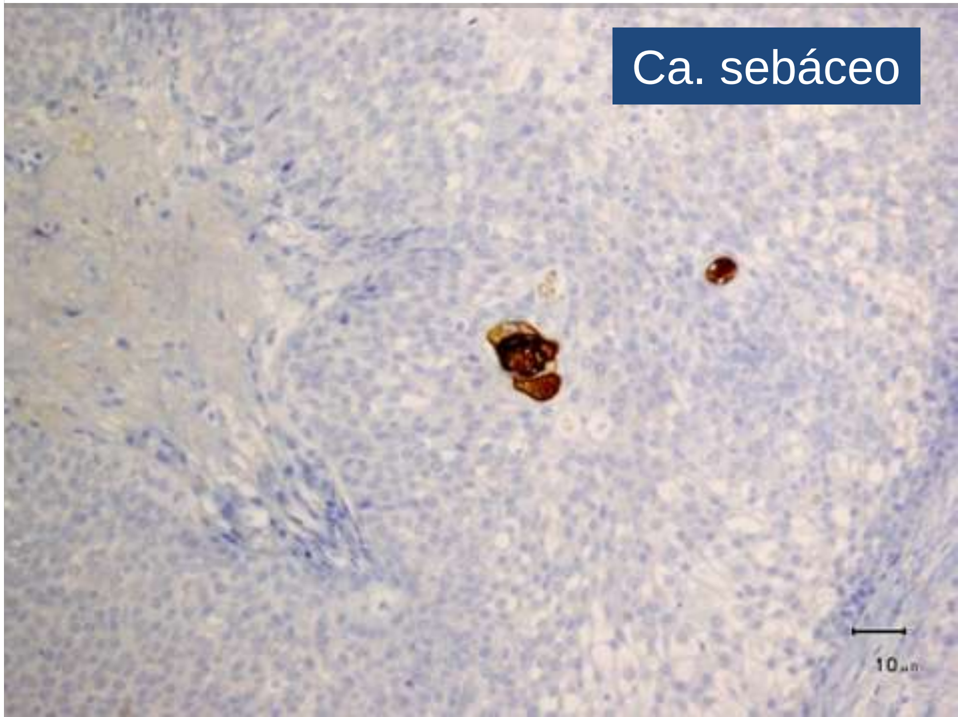

BerEP4
10 µm
10 µm
10 µm

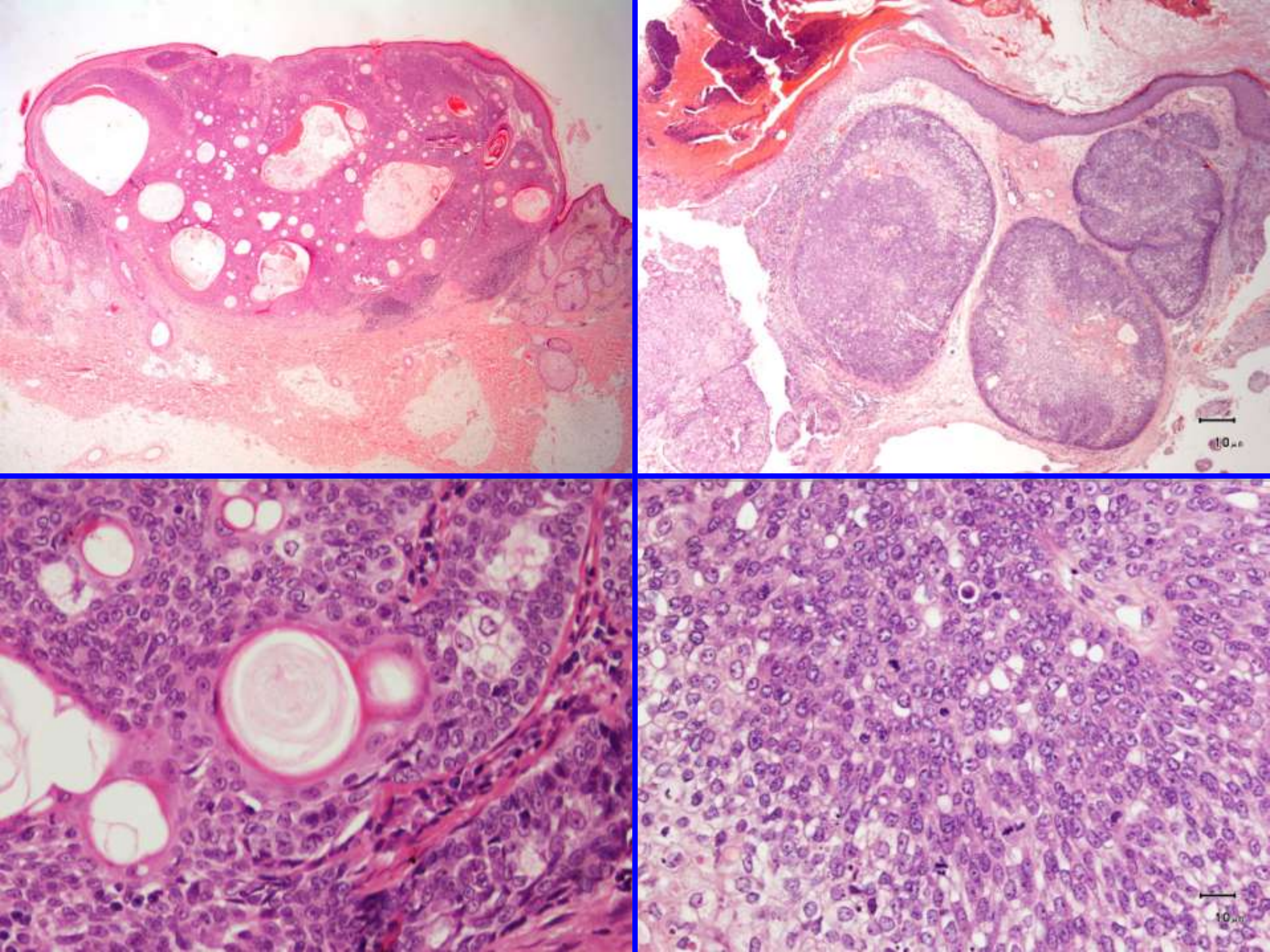

10㎛


Citoq19
10 µm

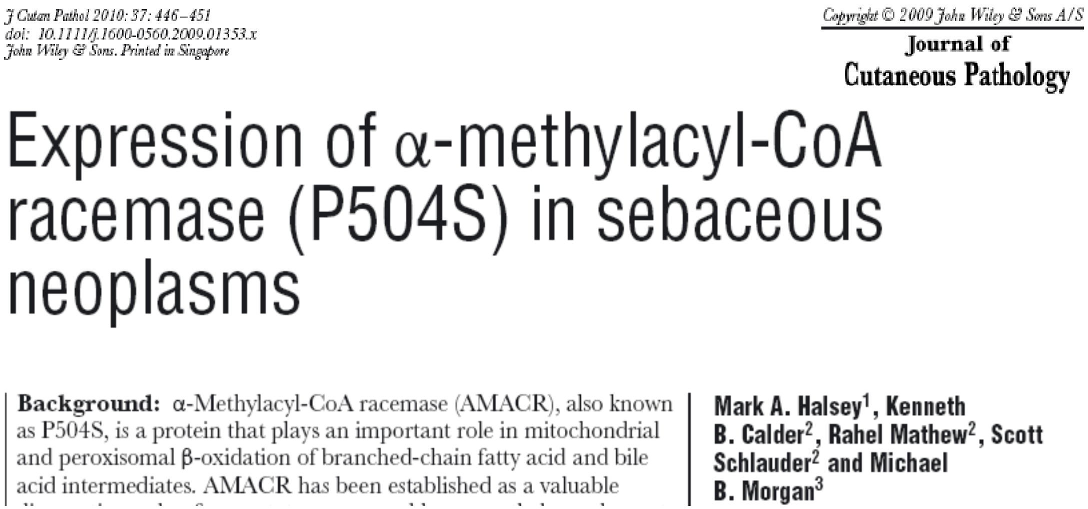

Sebomatricoma
10 µm


CCB
10 µm


Ca. sebáceo
10 µm


10 μm
10 μm

Tumor sebáceo benigno vs maligno



J Cutan Pathol 2010: 37: 446–451
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Journal of
Cutaneous Pathology

Expression of α-methylacyl-CoA racemase (P504S) in sebaceous neoplasms

Background: α-Methylacyl-CoA racemase (AMACR), also known as P504S, is a protein that plays an important role in mitochondrial and peroxisomal β-oxidation of branched-chain fatty acid and bile acid intermediates. AMACR has been established as a valuable

Mark A. Halsey[1], Kenneth B. Calder[2], Rahel Mathew[2], Scott Schlauder[2] and Michael B. Morgan[3]

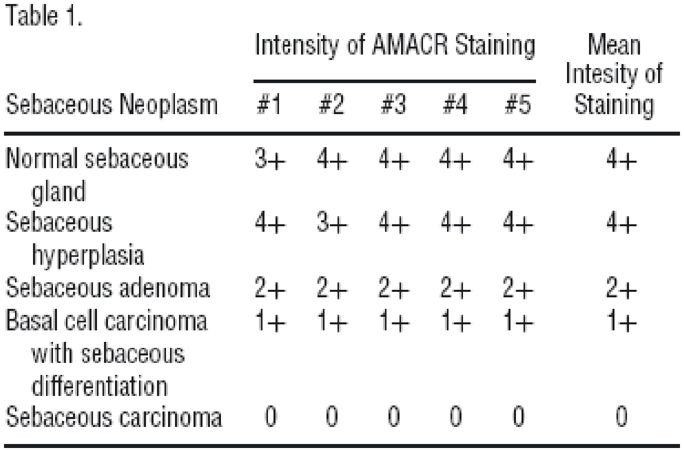
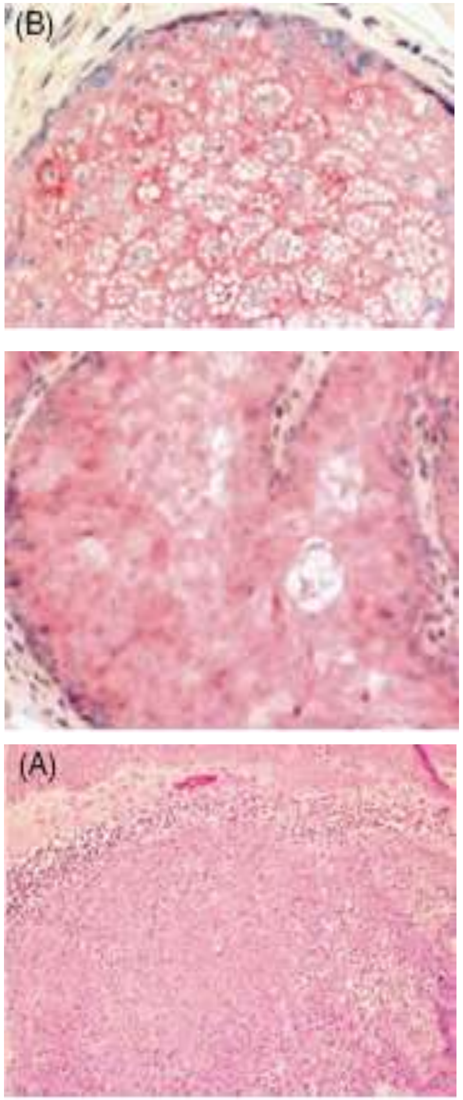
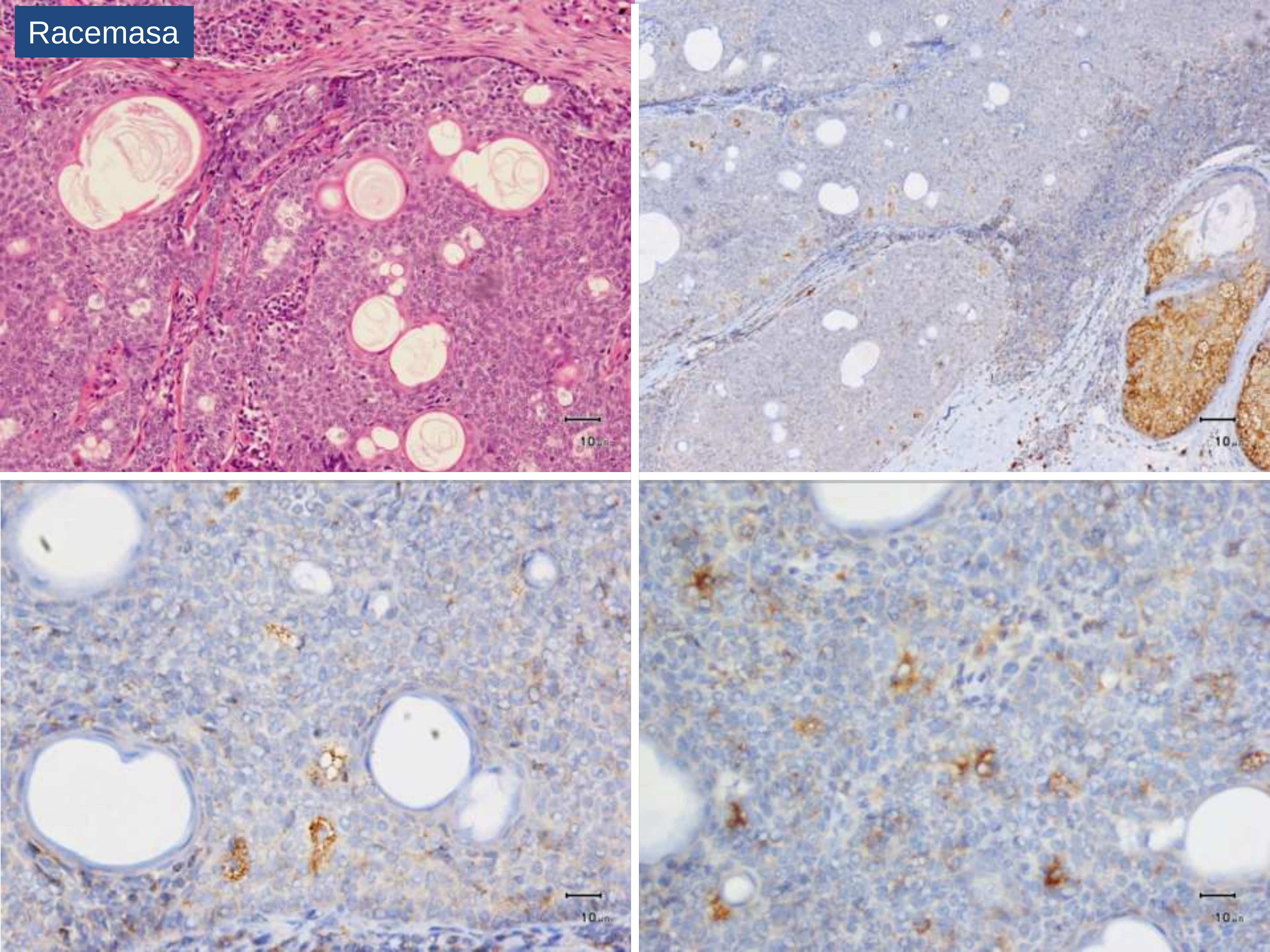


Table 1.

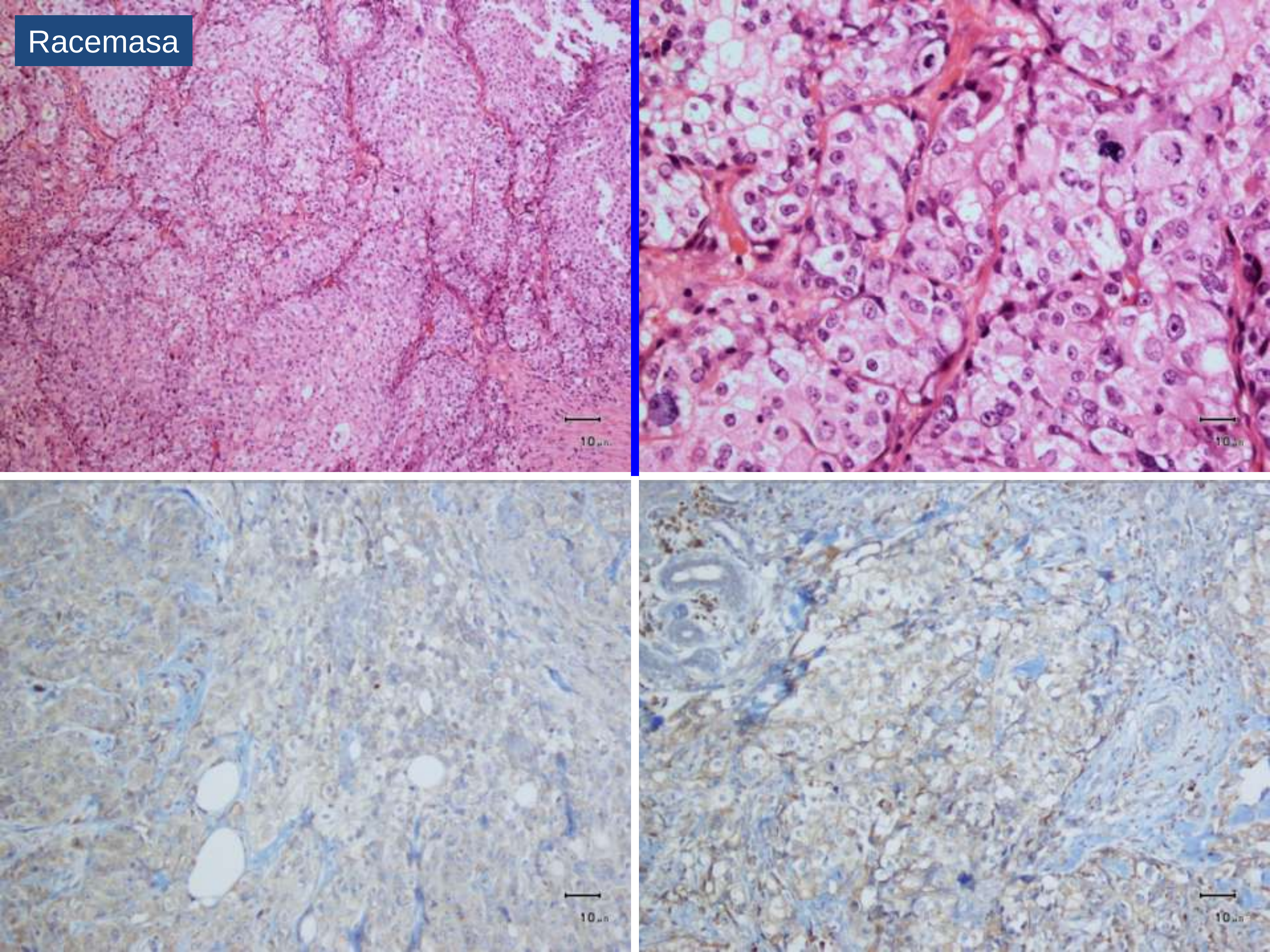
Sebaceous Neoplasm	Intensity of AMACR Staining #1	#2	#3	#4	#5	Mean Intesity of Staining
Normal sebaceous gland	3+	4+	4+	4+	4+	4+
Sebaceous hyperplasia	4+	3+	4+	4+	4+	4+
Sebaceous adenoma	2+	2+	2+	2+	2+	2+
Basal cell carcinoma with sebaceous differentiation	1+	1+	1+	1+	1+	1+
Sebaceous carcinoma	0	0	0	0	0	0



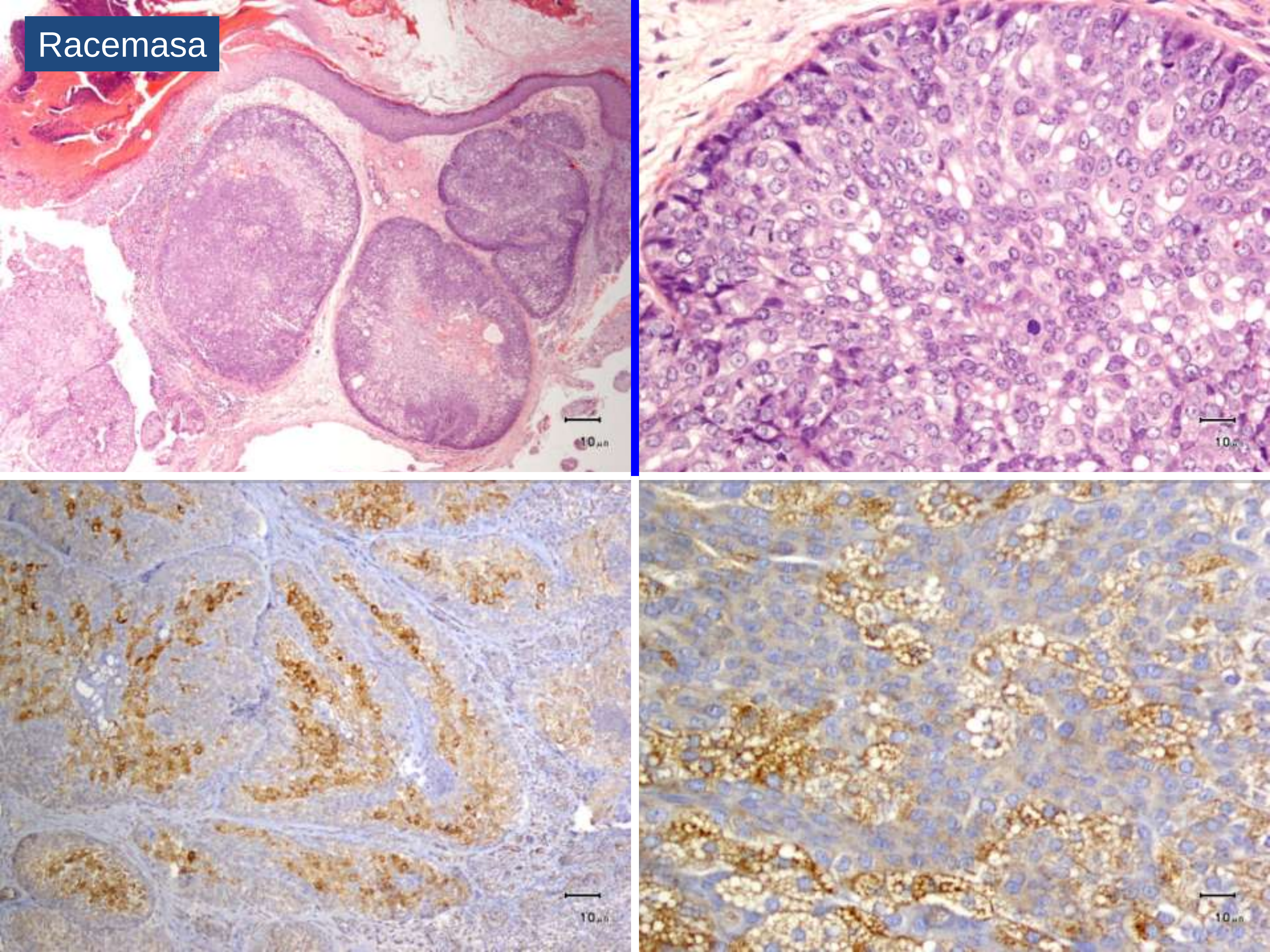
Racemasa

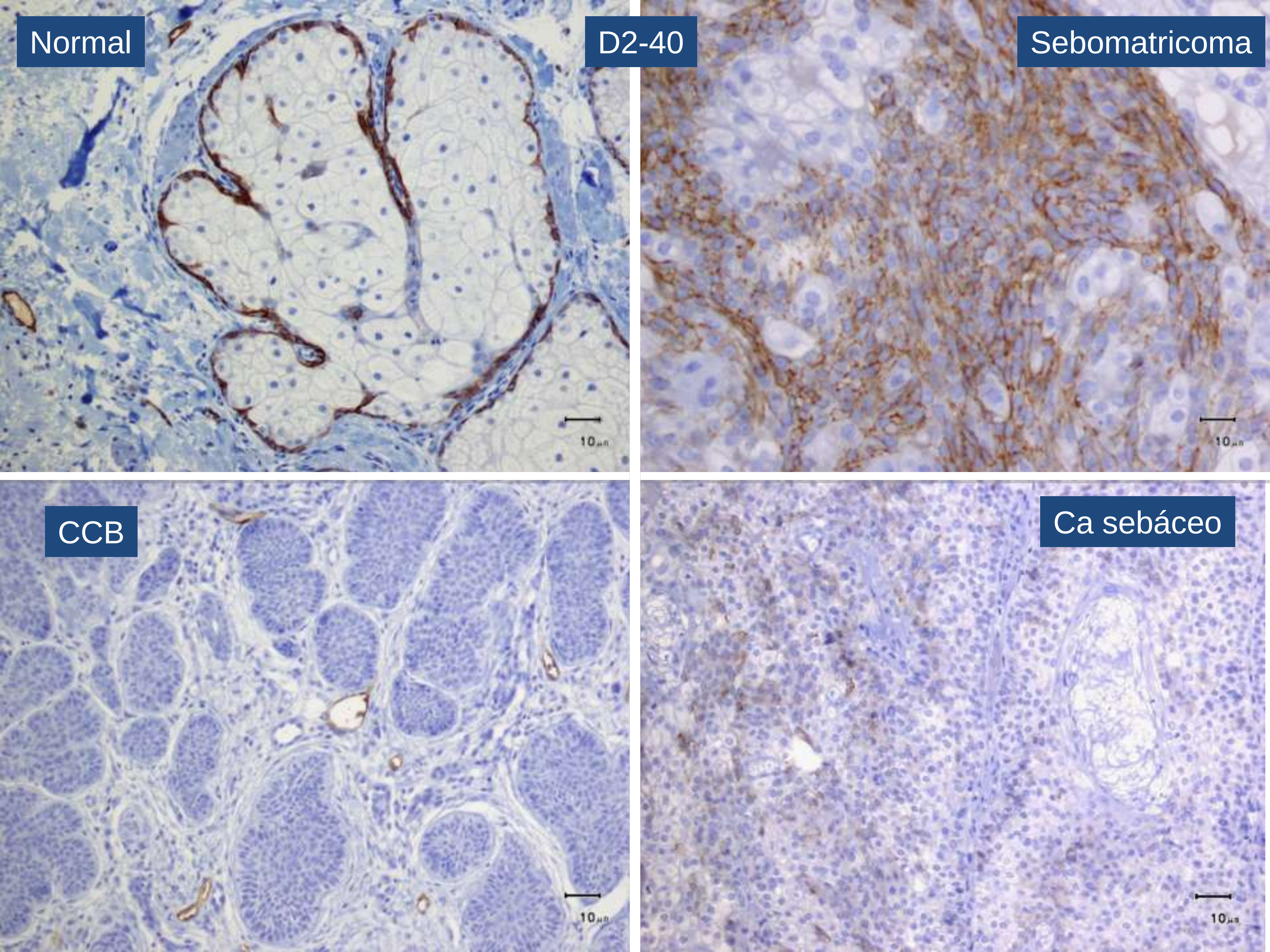

10 μm
10 μm
10 μm
10 μm

Racemasa


10 µm
10 µm
10 µm
10 µm

Racemasa

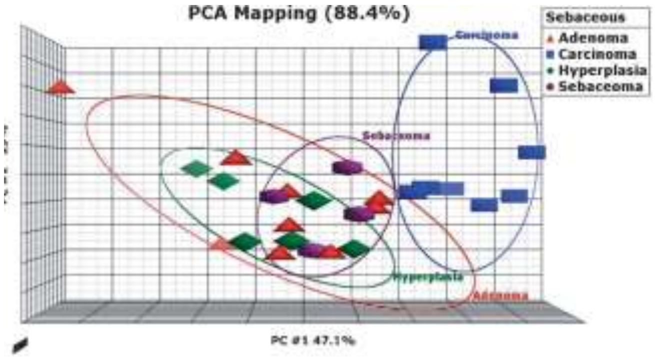

10 μm
10 μm
10 μm
10 μm


Normal
D2-40
Sebomatricoma
10μm
10μm
CCB
Ca sebáceo
10μm
10μm

Distinction of Benign Sebaceous Proliferations From Sebaceous Carcinomas by Immunohistochemistry

Erik S. Cabral, BA, Aaron Auerbach, MD,† J. Keith Killian, MD, PhD,‡ Terry L. Barrett, MD,§ and David S. Cassarino, MD, PhD**

Am J Dermatopathol 2006;28:465–471



Ki67, p53, Bcl2, p21

Immunohistochemical Expression of Survivin in Cutaneous Sebaceous Lesions

Kenneth B. Calder, MD, Farah K. Khalil, MD,*† Scott Schlauder, MD,* H. D. Cualing, MD,*† and Michael B. Morgan, MD*‡*

Am J Dermatopathol 2008;30:545–548

Carc células basales vs Tumor sebáceo

Marcadores IHQ

- BerEP4 → CCB +
TS -
- Citoq 19 → CCB +/-
TS + focal

TS benigno - maligno

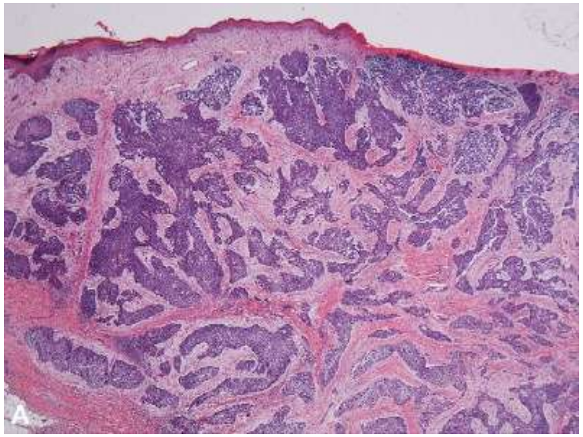
- D2-40
- Racemasa
- Histología
Proliferación y apoptosis

Carcinoma basoescamoso (metatípico)

Basaloid squamous cell carcinoma of the skin

Alan S. Boyd, MD,[a,b] Thomas S. Stasko, MD,[a] and Yi-Wei Tang, MD, PhD[a,b]
Nashville, Tennessee

J Am Acad Dermatol 2011;64:144-51



J Cutan Pathol 2011: 38: 354–356
doi: 10.1111/j.1600-0560.2010.01627.x
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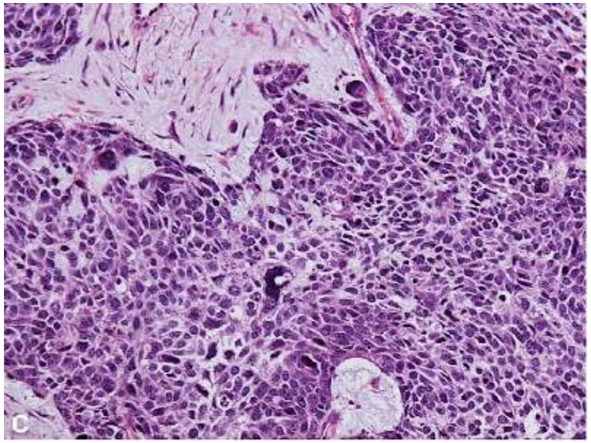
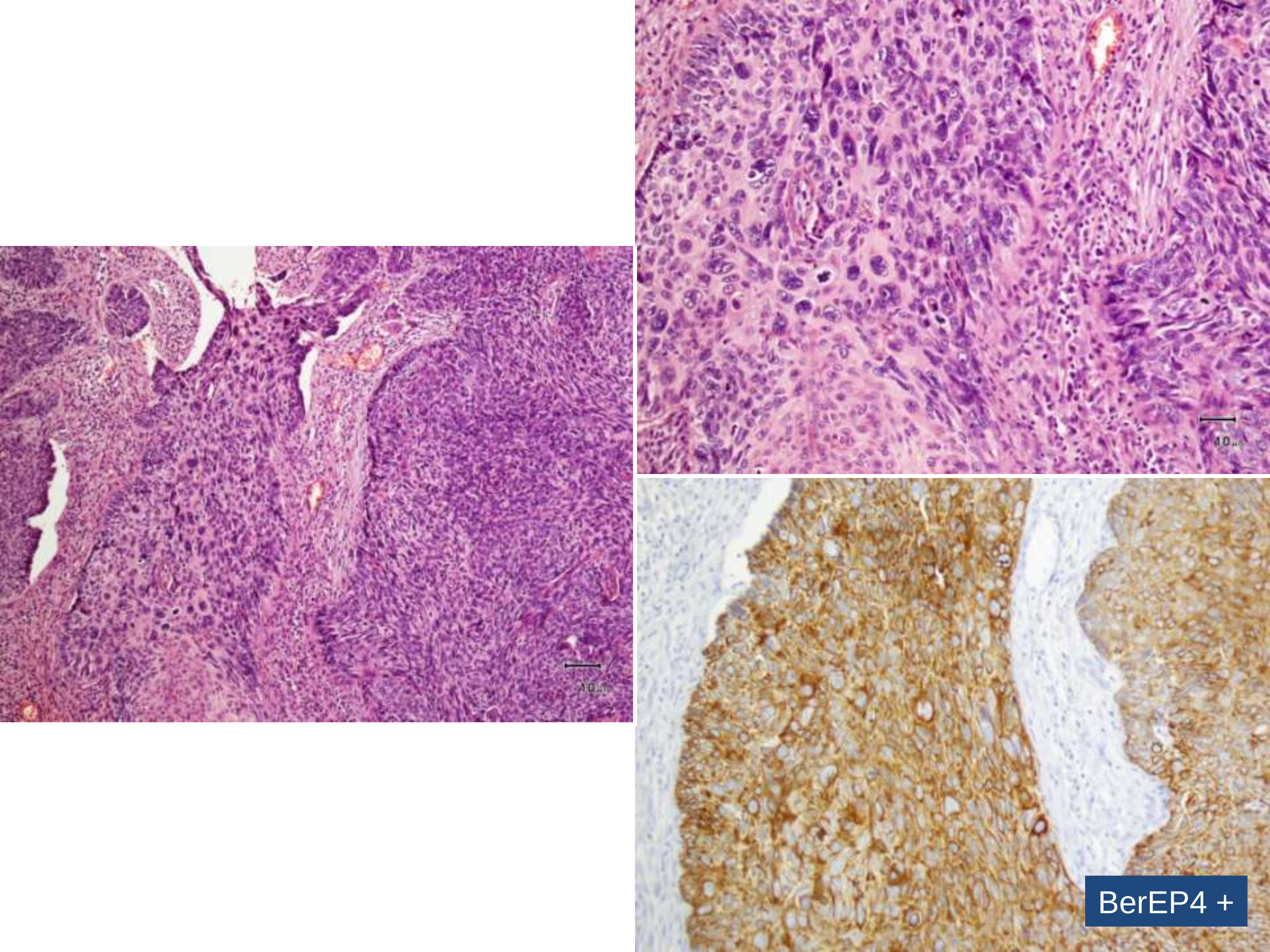
Basaloid squamous cell carcinoma with 'monster' cells: a mimic of pleomorphic basal cell carcinoma

Pleomorphic giant or 'monster' cells represent a well-recognized yet uncommon finding associated with basal cell carcinoma (BCC), usually of nodular type. We present a case of basaloid squamous cell

Clare L. Defty[1], Joseph Segen[2], Jonathan J. Carter[1], Imtiaz Ahmed[1] and Richard A Carr[2]

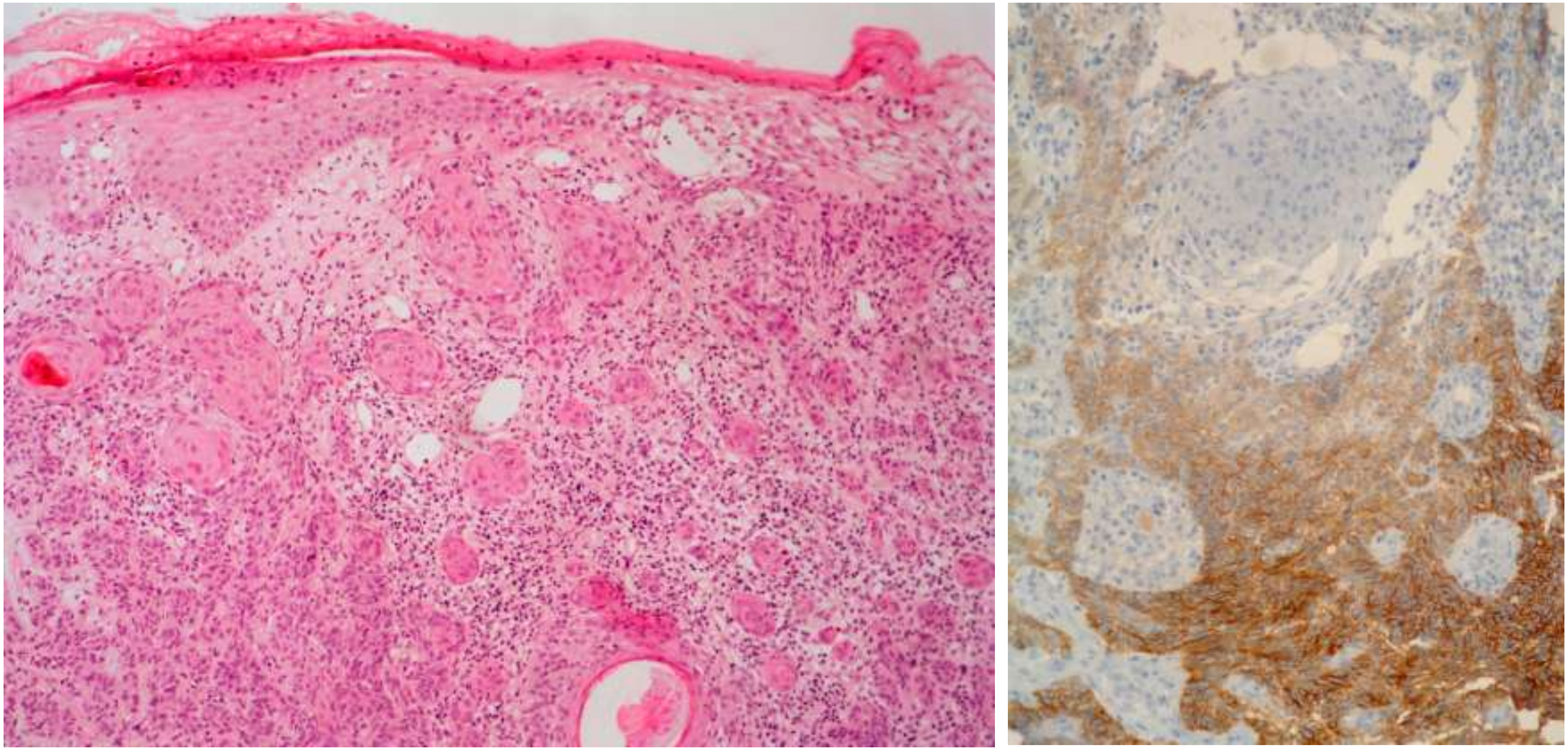



10 µm
10 µm
BerEP4 +

J Cutan Pathol 2009: 36: 1074–1076
doi: 10.1111/j.1600-0560.2008.01223.x
John Wiley & Sons. Printed in Singapore

Caveats in BerEP4 staining to differentiate basal and squamous cell carcinoma

Limin Yu[1], Anjela Galan[2,3] and Jennifer M. McNiff[2,3]

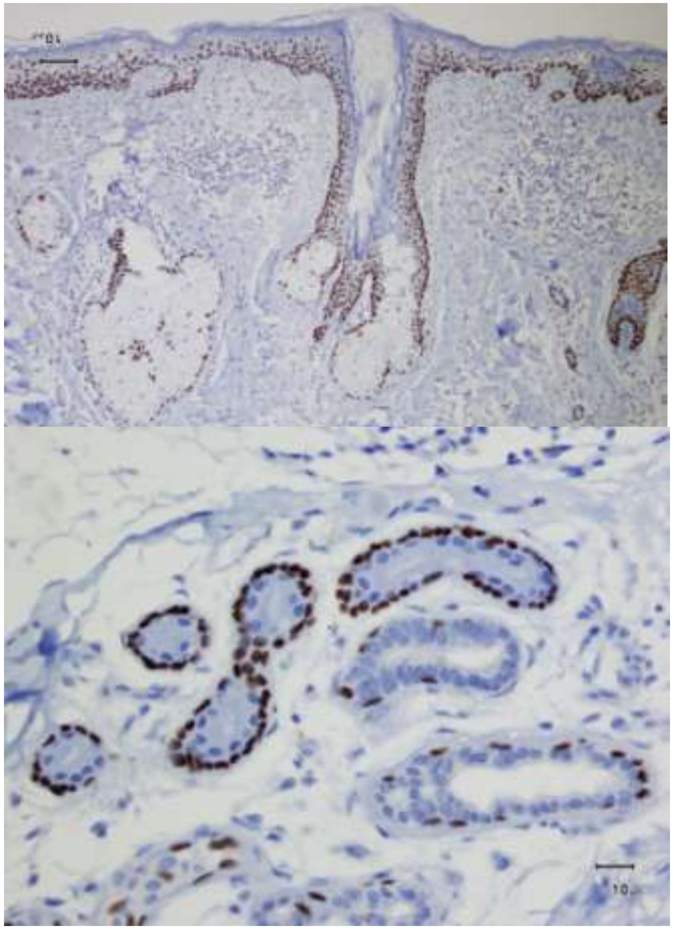


Carc células basales infiltrante vs Tumores esclerosantes

Am J Dermatopathol • Volume 32, Number 3, May 2010

p63 Immunohistochemistry Is a Useful Adjunct in Distinguishing Sclerosing Cutaneous Tumors

Claudia I. Vidal, MD, PhD, Matthew Goldberg, BA,* David E. Burstein, MD,†‡*
*Henry J. Emanuel, BDS, and Patrick O. Emanuel, MD**

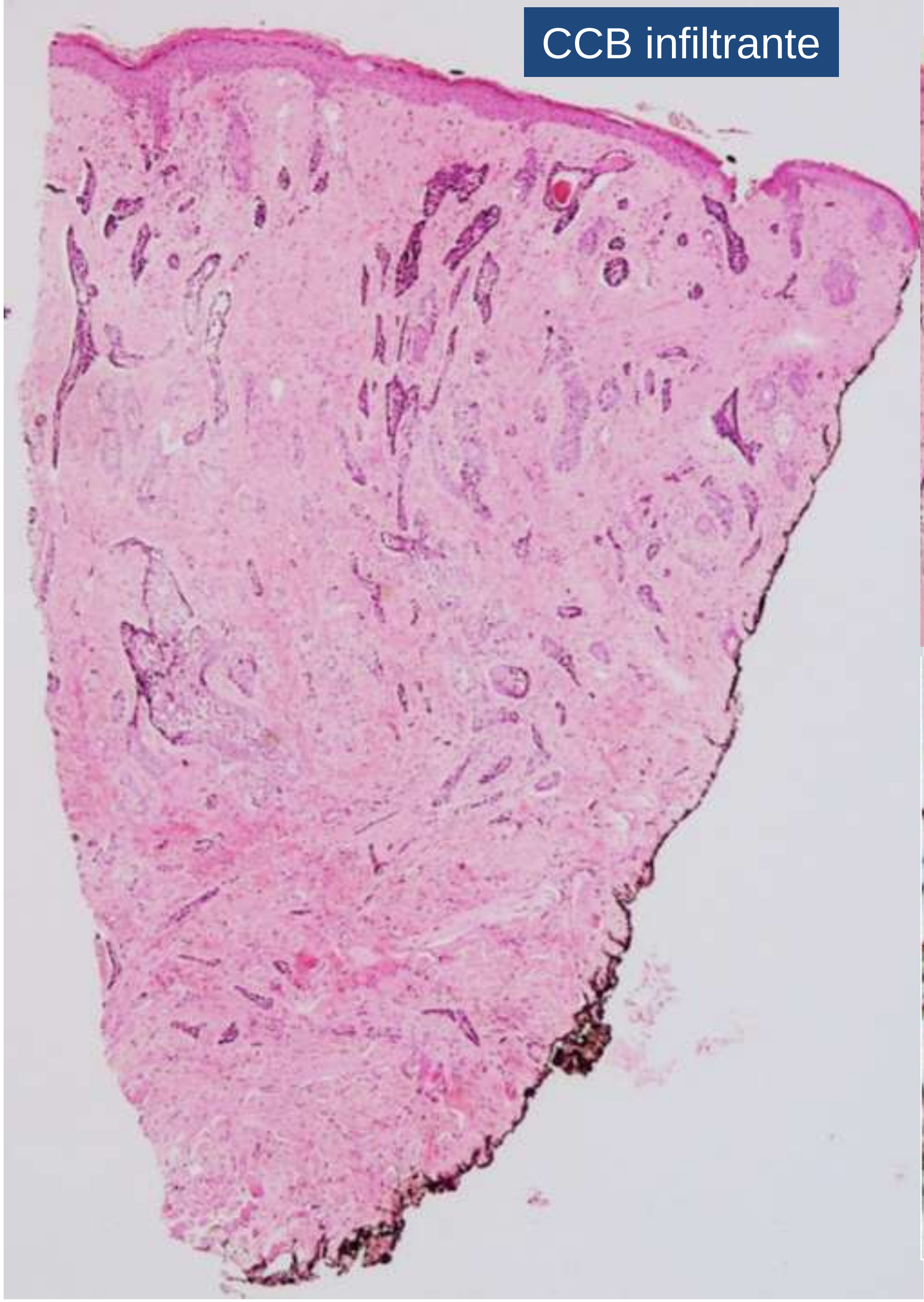


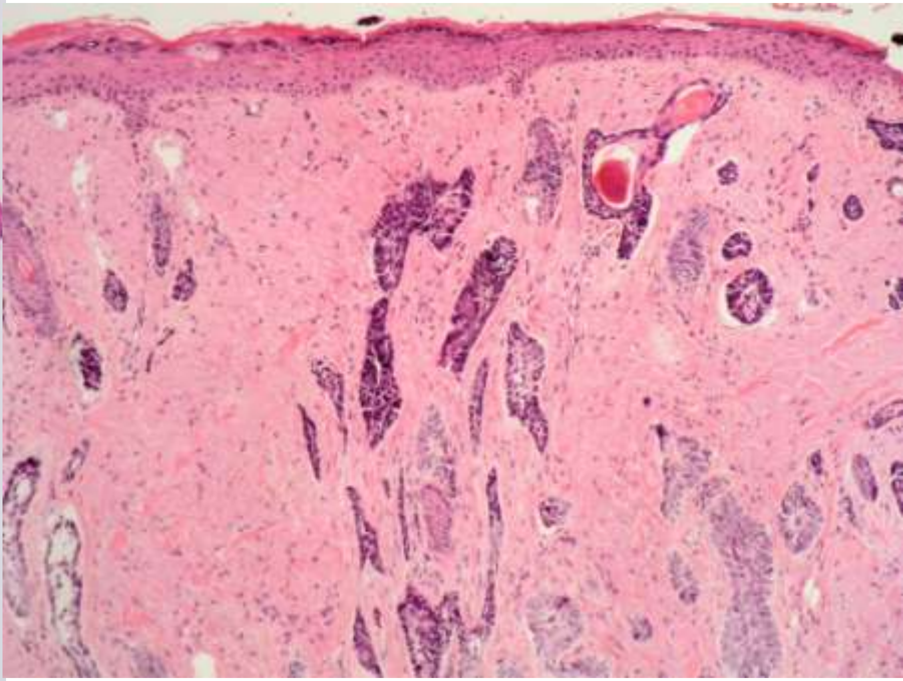
- Carcinoma anexial microquístico
- Tricoepitelioma desmoplásico

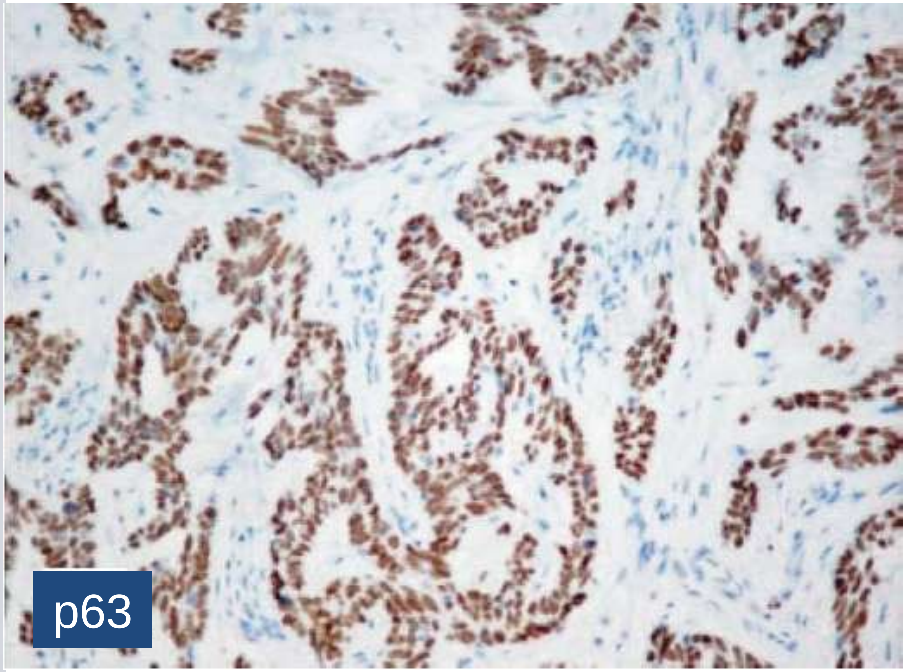
- Carcinoma cél. escamosas desmoplásico

- Metástasis cutáneas

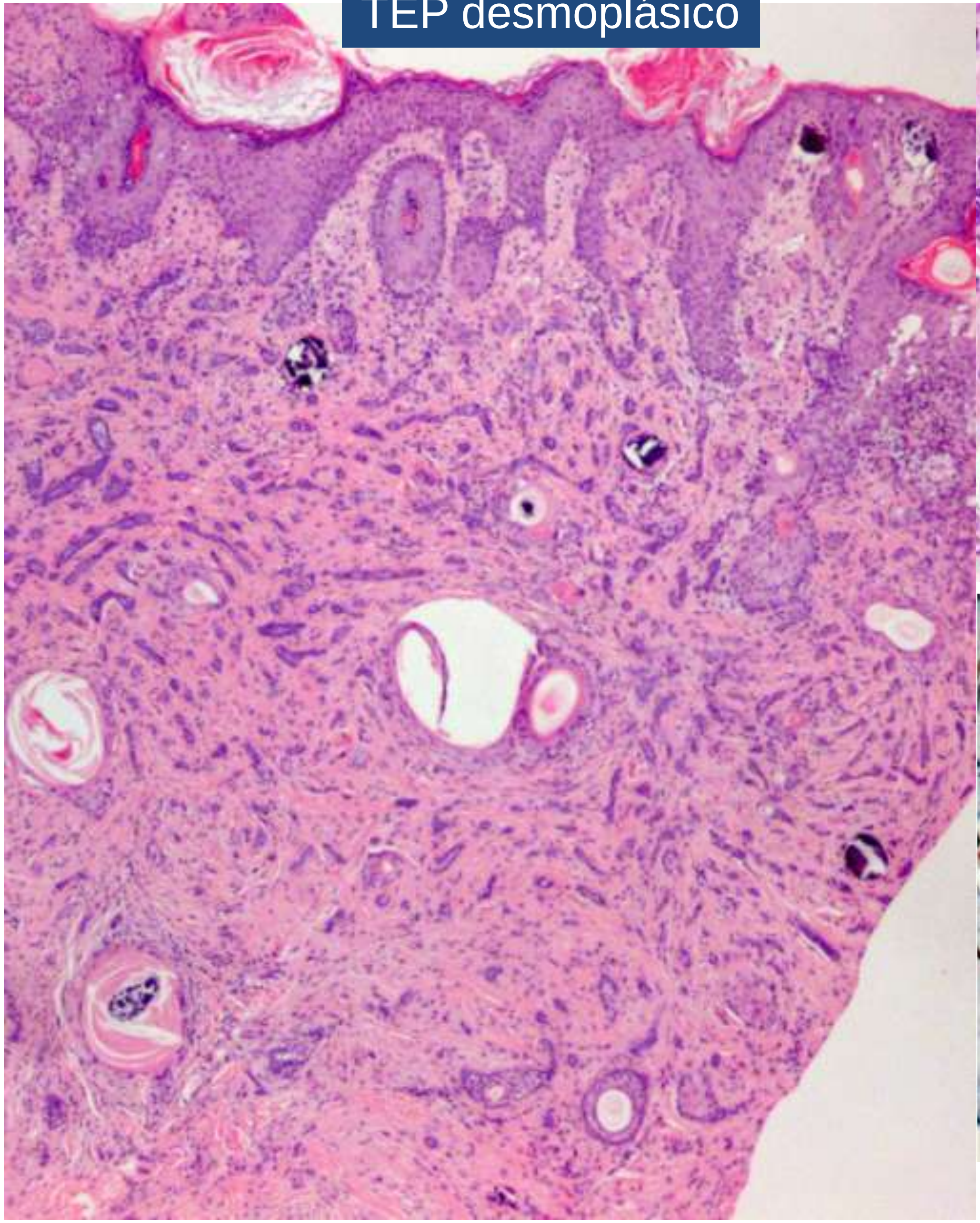
CCB infiltrante

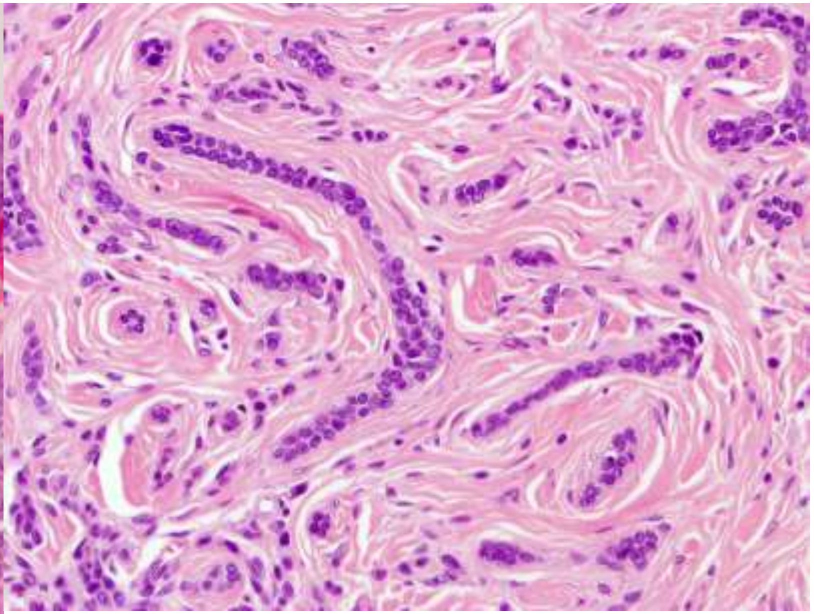


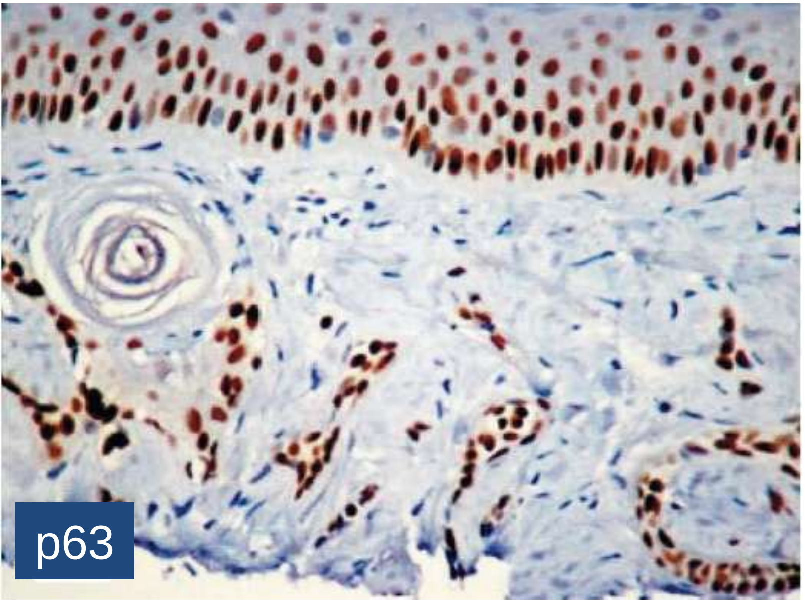


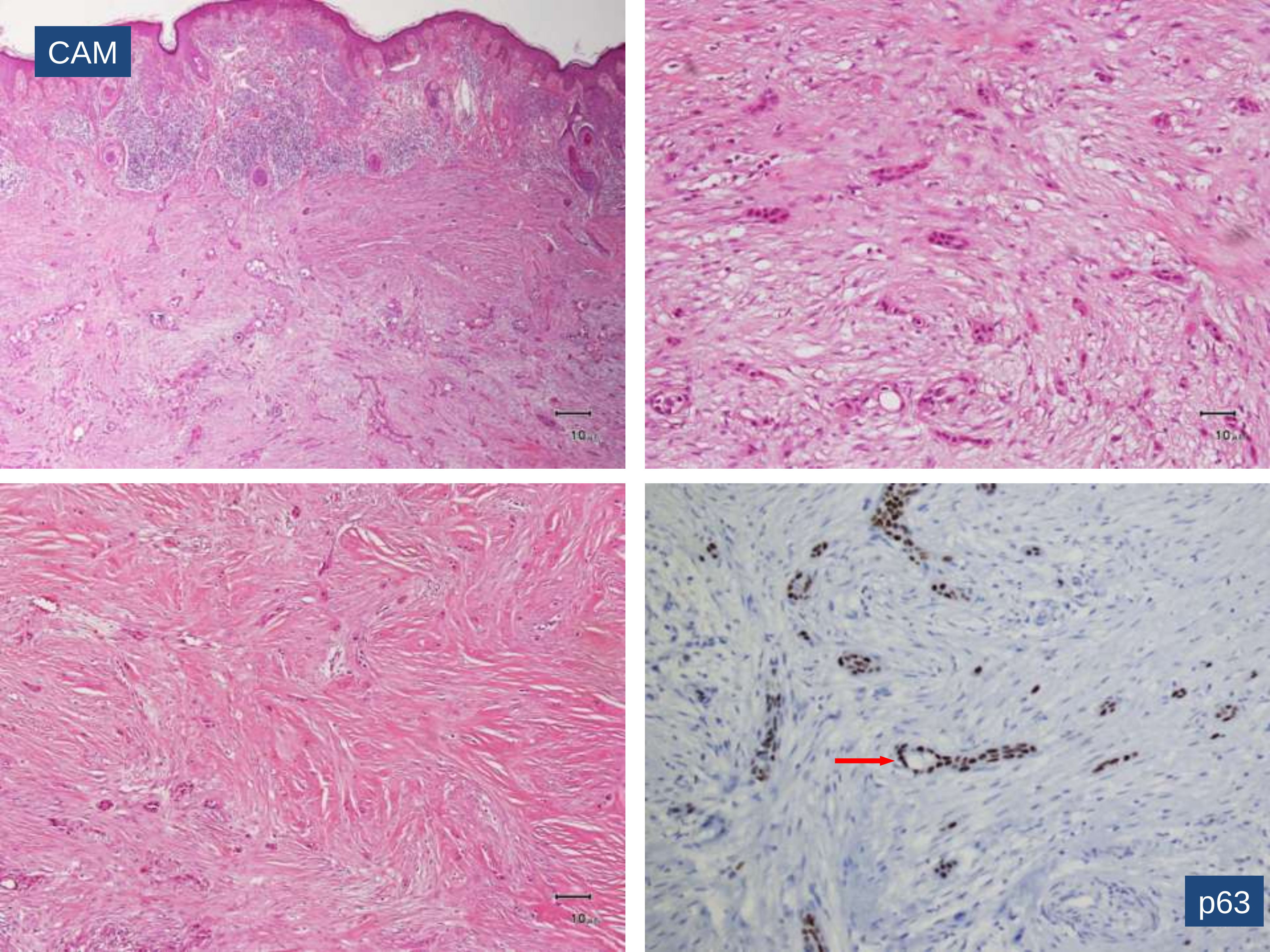


TEP desmoplásico







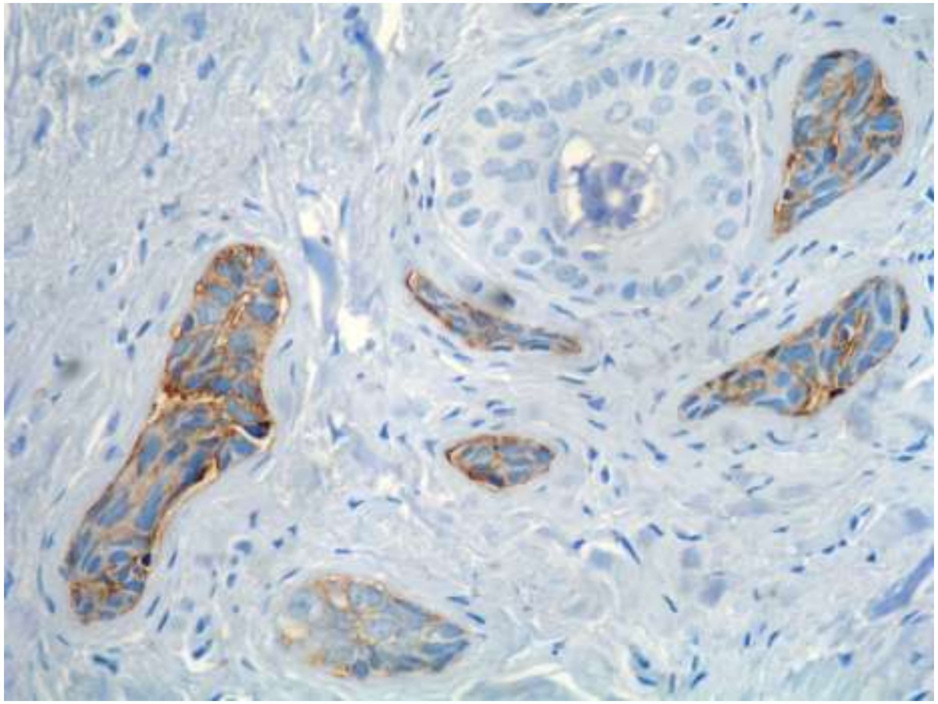

CAM
p63

Modern Pathology (2008) 21, 178–185

Microcystic adnexal carcinoma: an immunohistochemical reappraisal

Mai P Hoang[1], Karen A Dresser[1], Payal Kapur[2], Whitney A High[3] and Meera Mahalingam[1]

	BerEP4	CQ15
CAM	+ (38%)	+ (92%)
TEPd	+ (57%)	+ (100%)
CCBm	+ (100%)	-



Neoplasia esclerosante BerEP4 negativa NO es un CCBm

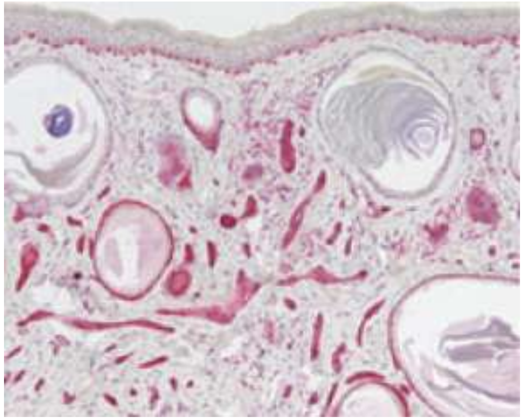
British Association of Dermatologists 2011 **164,** pp141–147

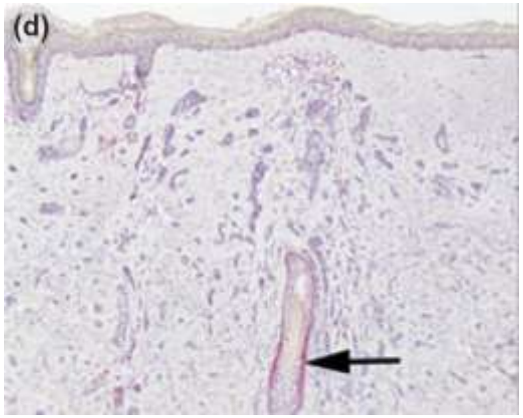
DERMATOPATHOLOGY

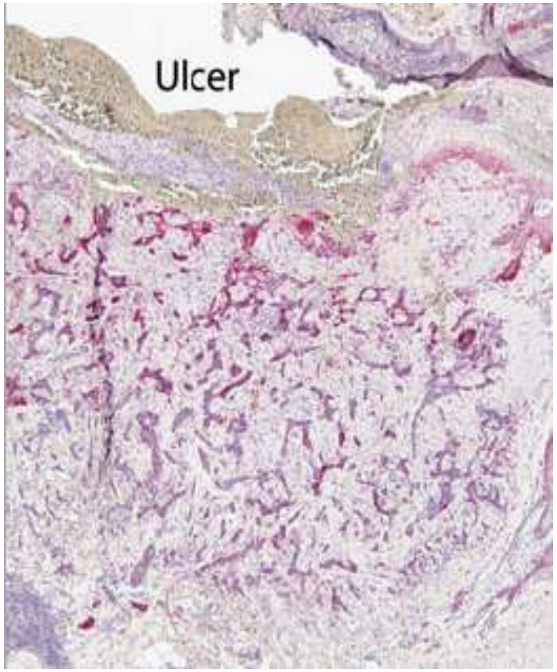
BJD
British Journal of Dermatology

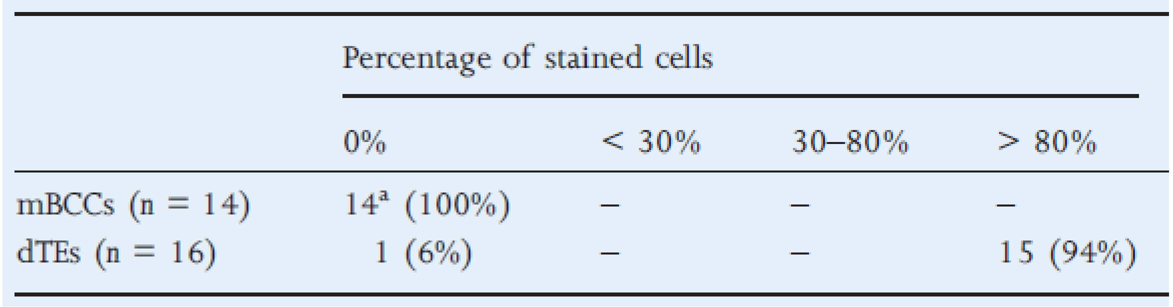
PHLDA1 (TDAG51) is a follicular stem cell marker and differentiates between morphoeic basal cell carcinoma and desmoplastic trichoepithelioma

K. Sellheyer*† and D. Krahl‡

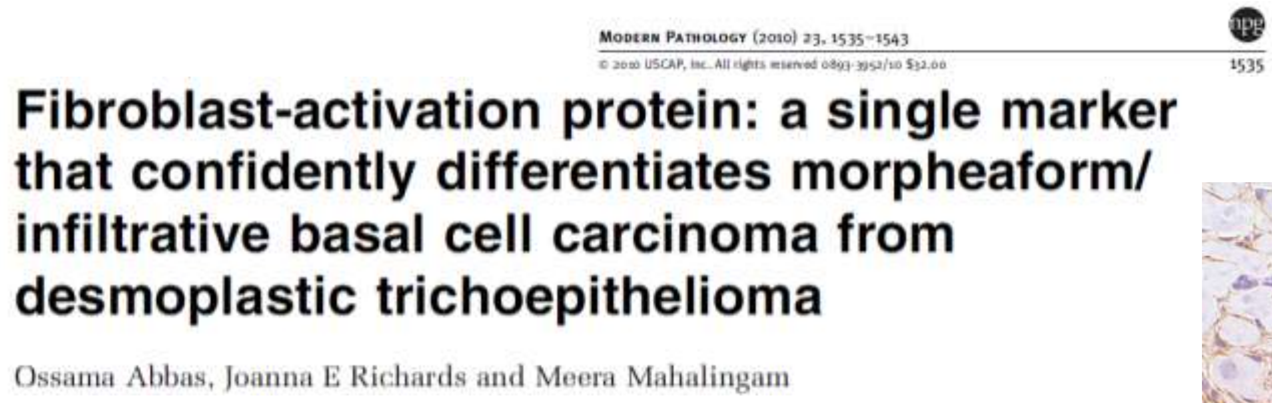








	Percentage of stained cells			
	0%	< 30%	30–80%	> 80%
mBCCs (n = 14)	14^{a} (100%)	–	–	–
dTEs (n = 16)	1 (6%)	–	–	15 (94%)



MODERN PATHOLOGY (2010) 23, 1535–1543
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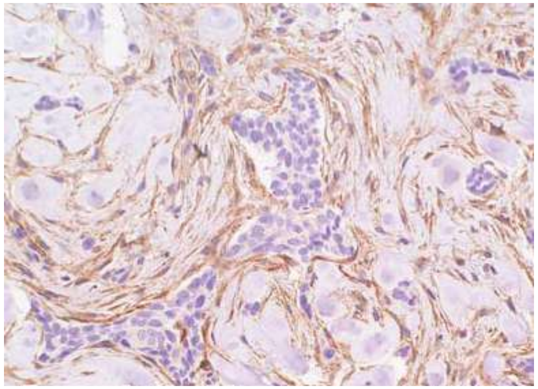
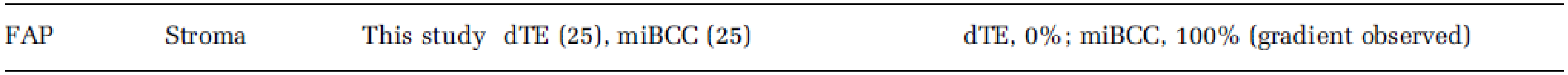
1535

Fibroblast-activation protein: a single marker that confidently differentiates morpheaform/infiltrative basal cell carcinoma from desmoplastic trichoepithelioma

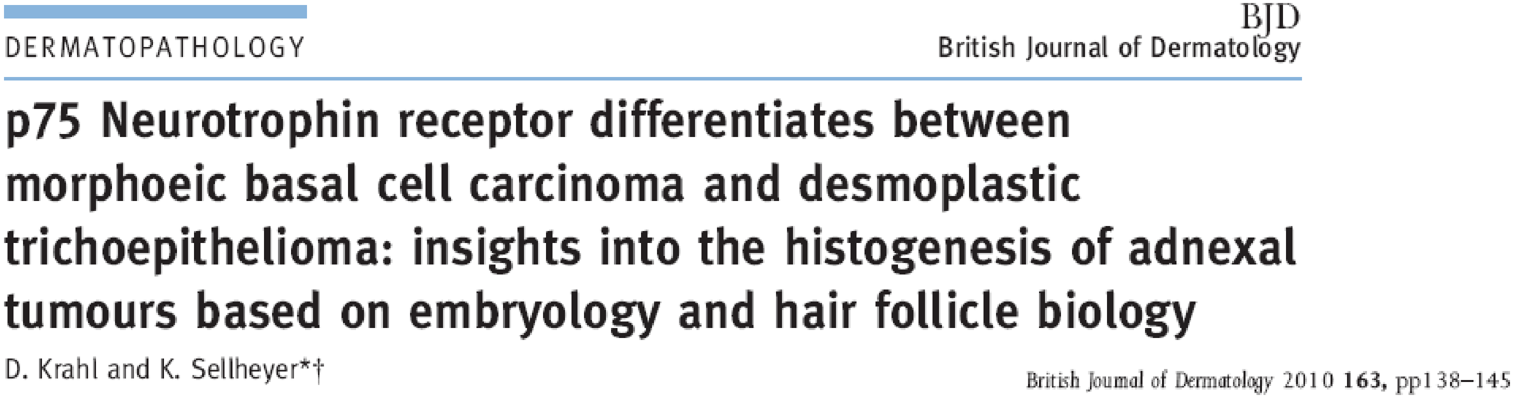
Ossama Abbas, Joanna E Richards and Meera Mahalingam



Marcador de fibroblastos reactivos



FAP	Stroma	This study	dTE (25), miBCC (25)	dTE, 0%; miBCC, 100% (gradient observed)



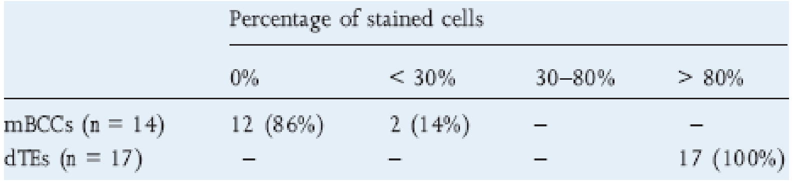
DERMATOPATHOLOGY

BJD
British Journal of Dermatology

p75 Neurotrophin receptor differentiates between morphoeic basal cell carcinoma and desmoplastic trichoepithelioma: insights into the histogenesis of adnexal tumours based on embryology and hair follicle biology

D. Krahl and K. Sellheyer*†

British Journal of Dermatology 2010 163, pp138–145



	Percentage of stained cells			
	0%	< 30%	30–80%	> 80%
mBCCs (n = 14)	12 (86%)	2 (14%)	–	–
dTEs (n = 17)	–	–	–	17 (100%)

P75 NTR: CD271
interviene en el ciclo del folículo piloso
¿Posible relación con células de Merkel?

Carc células basales infiltrante vs Tumores esclerosantes

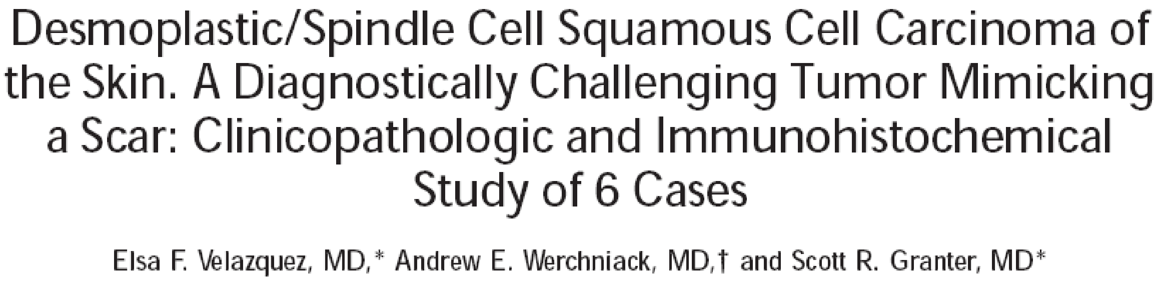
Marcadores IHQ

- p63 → CAM + gradiente periferia
- BerEP4 → Si es – no CCB

Nuevos anticuerpos

- PHLDA1
- P75 NTR
→ TEPd +
- PAF → CCBm +

Am J Dermatopathol 2010;32:333–339


Desmoplastic/Spindle Cell Squamous Cell Carcinoma of the Skin. A Diagnostically Challenging Tumor Mimicking a Scar: Clinicopathologic and Immunohistochemical Study of 6 Cases

Elsa F. Velazquez, MD,* Andrew E. Werchniack, MD,† and Scott R. Granter, MD*

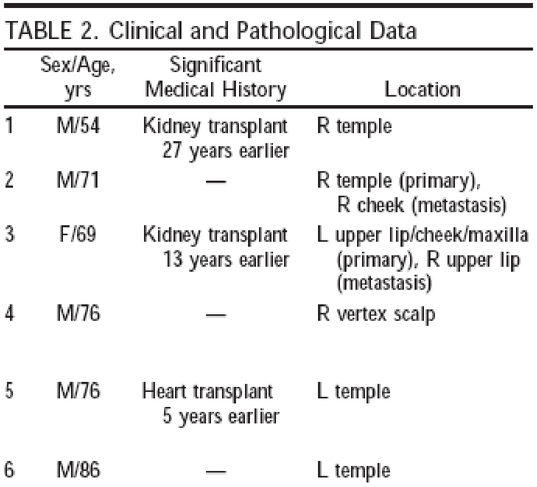
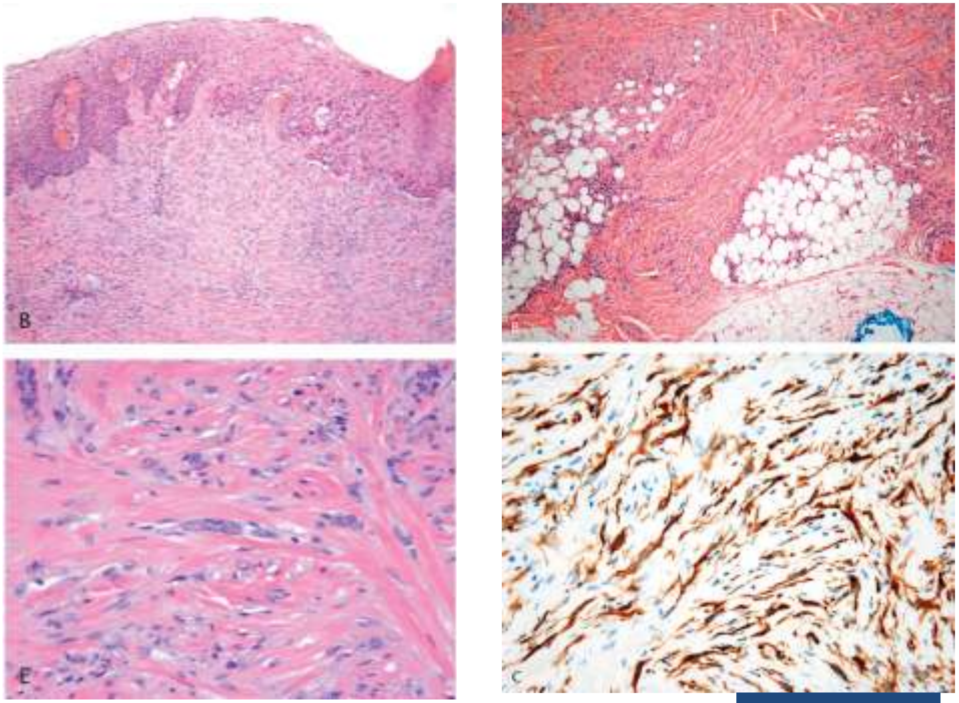
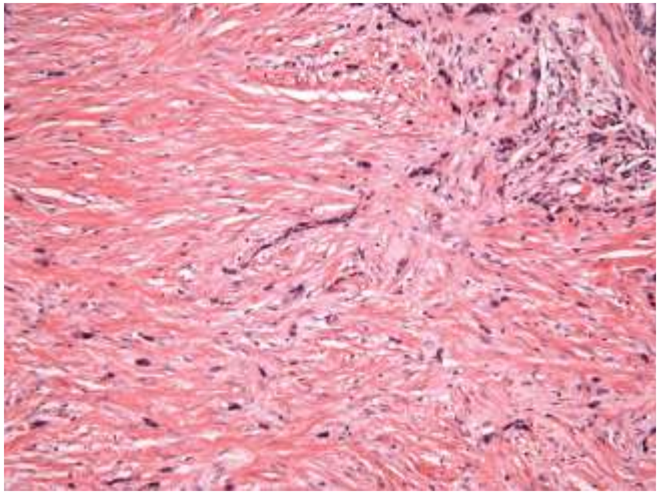


TABLE 2. Clinical and Pathological Data

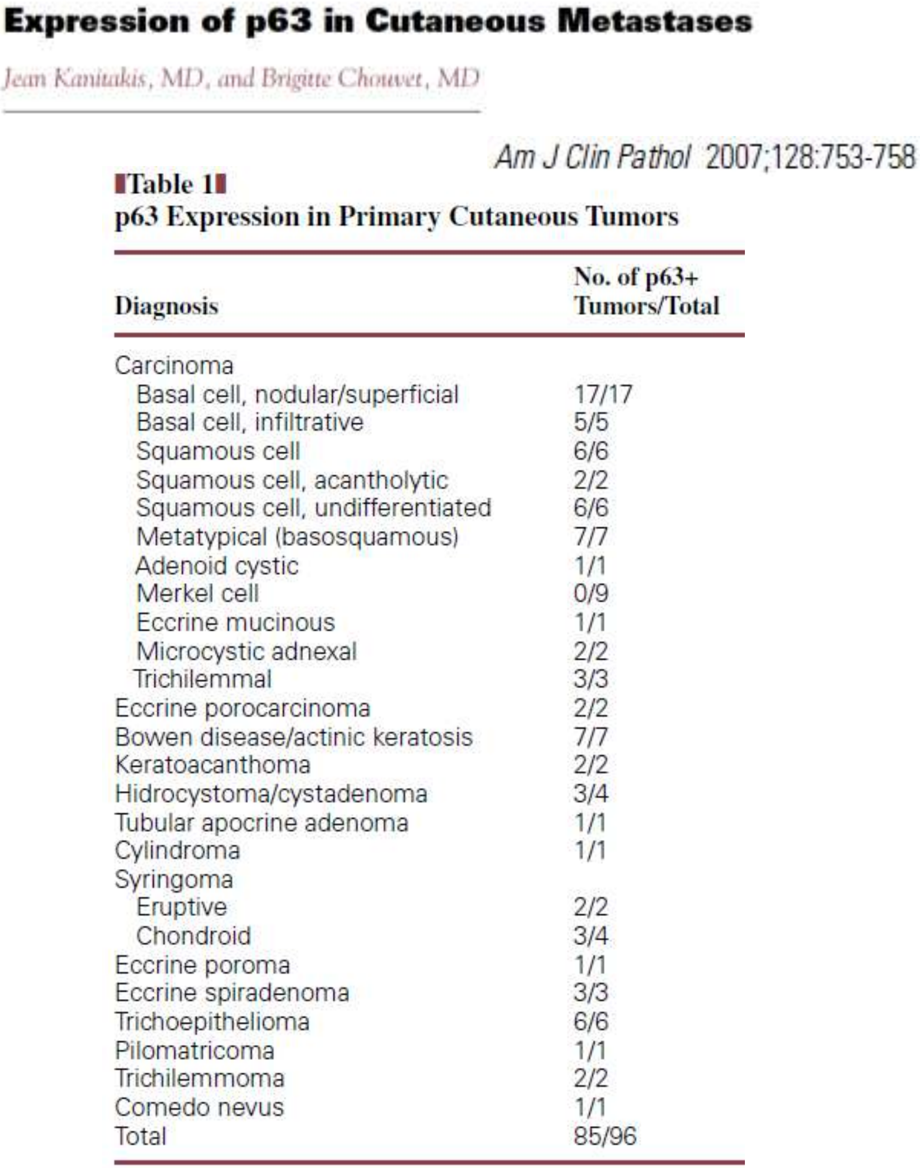
	Sex/Age, yrs	Significant Medical History	Location
1	M/54	Kidney transplant 27 years earlier	R temple
2	M/71	—	R temple (primary), R cheek (metastasis)
3	F/69	Kidney transplant 13 years earlier	L upper lip/cheek/maxilla (primary), R upper lip (metastasis)
4	M/76	—	R vertex scalp
5	M/76	Heart transplant 5 years earlier	L temple
6	M/86	—	L temple



34bE12



Tumor 1º vs Metástasis



Expression of p63 in Cutaneous Metastases

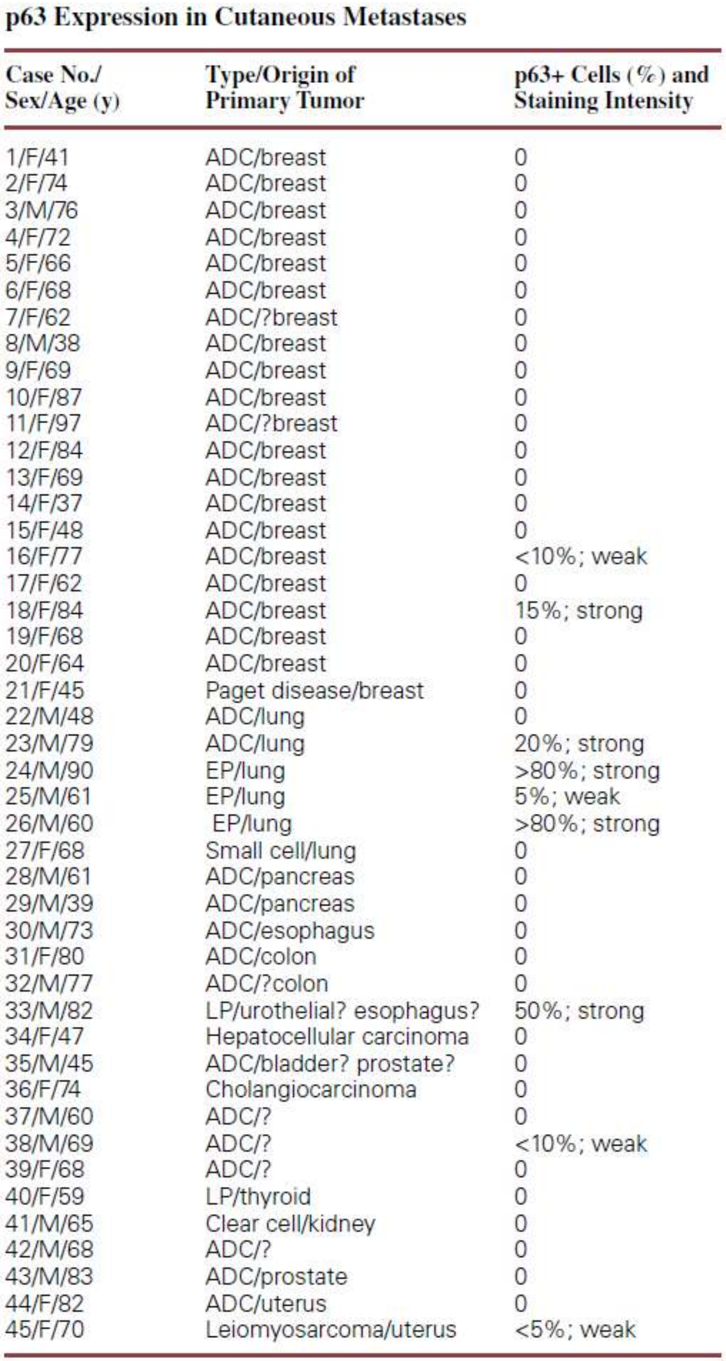
Jean Kanitakis, MD, and Brigitte Chouvet, MD

Am J Clin Pathol 2007;128:753-758

Table 1

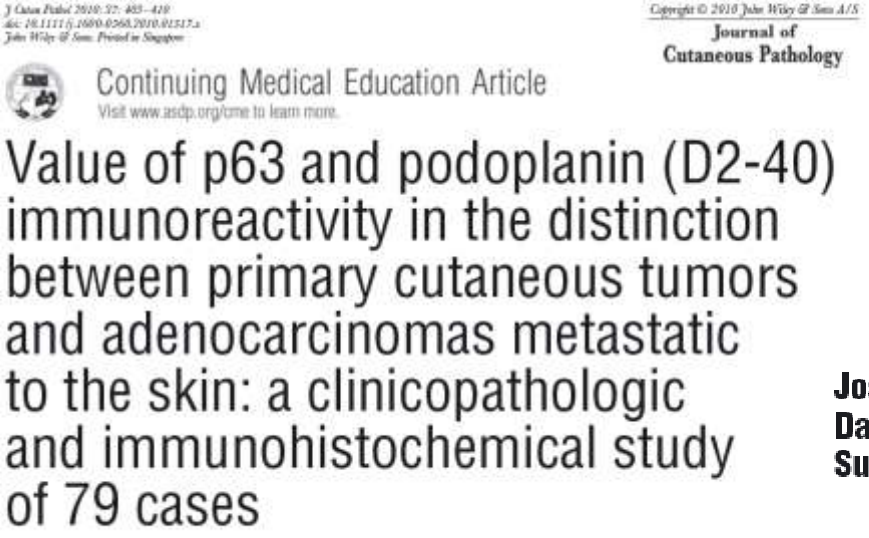
p63 Expression in Primary Cutaneous Tumors

Diagnosis	No. of p63+ Tumors/Total
Carcinoma	
Basal cell, nodular/superficial	17/17
Basal cell, infiltrative	5/5
Squamous cell	6/6
Squamous cell, acantholytic	2/2
Squamous cell, undifferentiated	6/6
Metatypical (basosquamous)	7/7
Adenoid cystic	1/1
Merkel cell	0/9
Eccrine mucinous	1/1
Microcystic adnexal	2/2
Trichilemmal	3/3
Eccrine porocarcinoma	2/2
Bowen disease/actinic keratosis	7/7
Keratoacanthoma	2/2
Hidrocystoma/cystadenoma	3/4
Tubular apocrine adenoma	1/1
Cylindroma	1/1
Syringoma	
Eruptive	2/2
Chondroid	3/4
Eccrine poroma	1/1
Eccrine spiradenoma	3/3
Trichoepithelioma	6/6
Pilomatricoma	1/1
Trichilemmoma	2/2
Comedo nevus	1/1
Total	85/96



p63 Expression in Cutaneous Metastases

Case No./ Sex/Age (y)	Type/Origin of Primary Tumor	p63+ Cells (%) and Staining Intensity
1/F/41	ADC/breast	0
2/F/74	ADC/breast	0
3/M/76	ADC/breast	0
4/F/72	ADC/breast	0
5/F/66	ADC/breast	0
6/F/68	ADC/breast	0
7/F/62	ADC/?breast	0
8/M/38	ADC/breast	0
9/F/69	ADC/breast	0
10/F/87	ADC/breast	0
11/F/97	ADC/?breast	0
12/F/84	ADC/breast	0
13/F/69	ADC/breast	0
14/F/37	ADC/breast	0
15/F/48	ADC/breast	0
16/F/77	ADC/breast	<10%; weak
17/F/62	ADC/breast	0
18/F/84	ADC/breast	15%; strong
19/F/68	ADC/breast	0
20/F/64	ADC/breast	0
21/F/45	Paget disease/breast	0
22/M/48	ADC/lung	0
23/M/79	ADC/lung	20%; strong
24/M/90	EP/lung	>80%; strong
25/M/61	EP/lung	5%; weak
26/M/60	EP/lung	>80%; strong
27/F/68	Small cell/lung	0
28/M/61	ADC/pancreas	0
29/M/39	ADC/pancreas	0
30/M/73	ADC/esophagus	0
31/F/80	ADC/colon	0
32/M/77	ADC/?colon	0
33/M/82	LP/urothelial? esophagus?	50%; strong
34/F/47	Hepatocellular carcinoma	0
35/M/45	ADC/bladder? prostate?	0
36/F/74	Cholangiocarcinoma	0
37/M/60	ADC/?	0
38/M/69	ADC/?	<10%; weak
39/F/68	ADC/?	0
40/F/59	LP/thyroid	0
41/M/65	Clear cell/kidney	0
42/M/68	ADC/?	0
43/M/83	ADC/prostate	0
44/F/82	ADC/uterus	0
45/F/70	Leiomyosarcoma/uterus	<5%; weak



J Cutan Pathol 2010: 37: 403–410
doi: 10.1111/j.1600-0560.2010.01517.x
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Journal of
Cutaneous Pathology

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Value of p63 and podoplanin (D2-40) immunoreactivity in the distinction between primary cutaneous tumors and adenocarcinomas metastatic to the skin: a clinicopathologic and immunohistochemical study of 79 cases

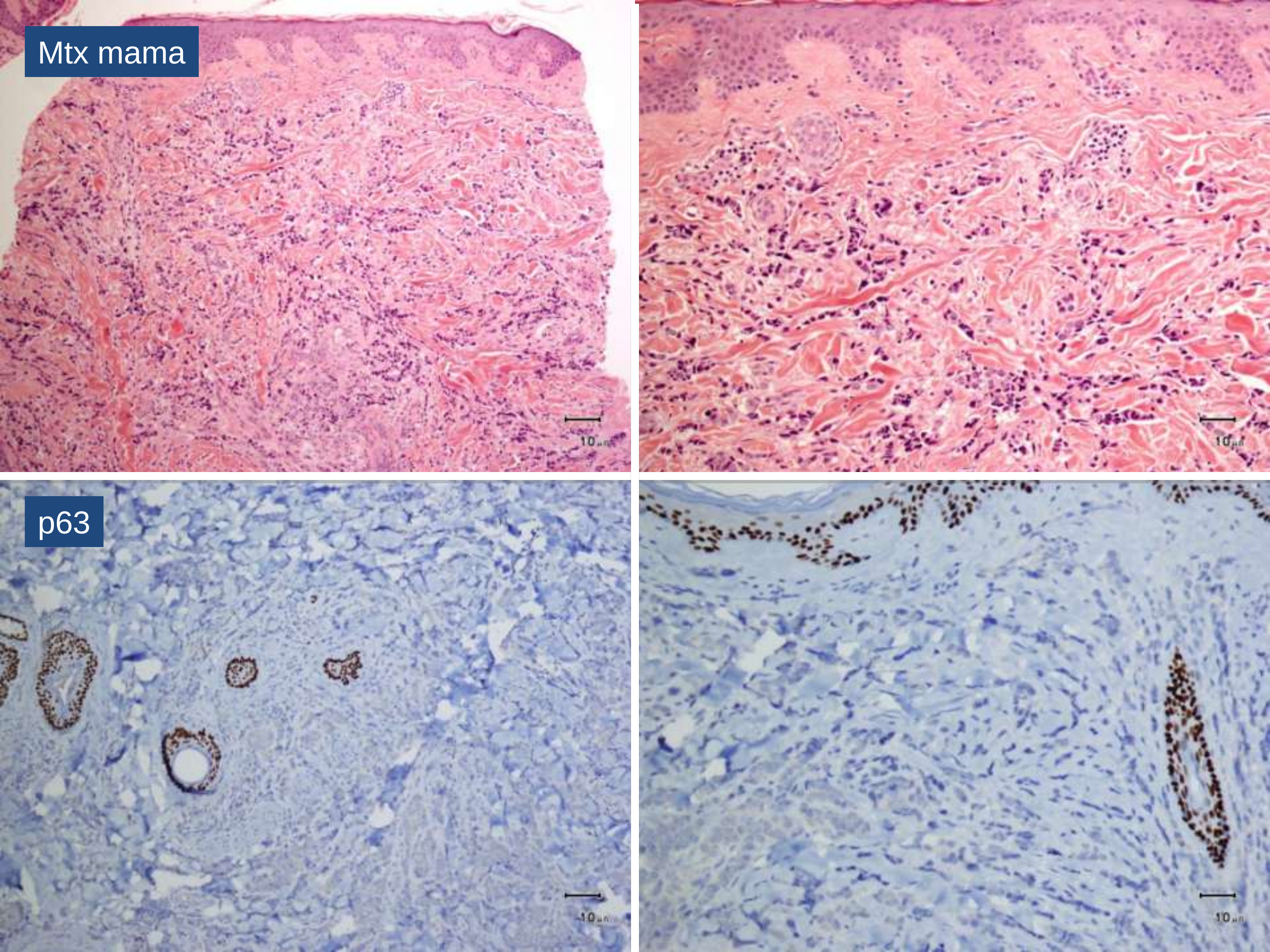
Jose A. Plaza, Pablo F. Ortega, David L. Stockman, and Saul Suster

Table 2. p63 expression in cutaneous metastatic carcinomas

Score	0
Breast	29
Endometrium	1
Esophagus	4
Gastric	3
Liver	1
Lung	2
Renal	2
Total	42

Table 4. Podoplanin expression in metastatic carcinomas to the skin

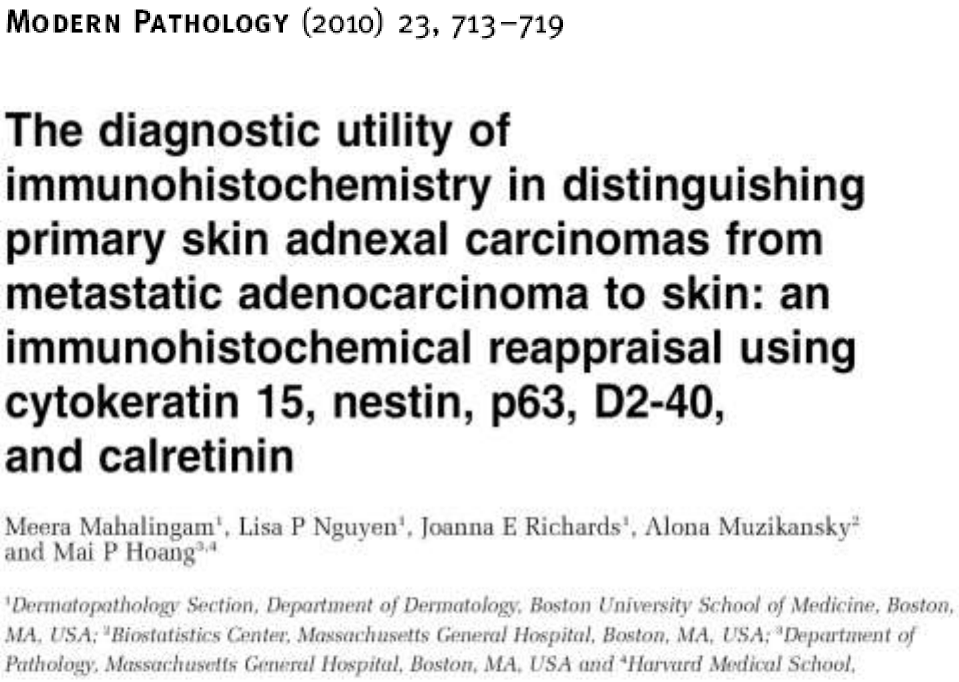
Score	Negative
Breast	29
Endometrium	1
Esophagus	4
Gastric	3
Liver	1
Lung	2
Renal	2
Total	42


Mtx mama
10 µm
10 µm
p63
10 µm
10 µm

Tumor 1º vs Metástasis

p63
D2-40 +
Citoq 15

TUMOR PRIMARIO



MODERN PATHOLOGY (2010) 23, 713–719

The diagnostic utility of immunohistochemistry in distinguishing primary skin adnexal carcinomas from metastatic adenocarcinoma to skin: an immunohistochemical reappraisal using cytokeratin 15, nestin, p63, D2-40, and calretinin

Meera Mahalingam[1], Lisa P Nguyen[1], Joanna E Richards[1], Alona Muzikansky[2] and Mai P Hoang[3,4]

[1]Dermatopathology Section, Department of Dermatology, Boston University School of Medicine, Boston, MA, USA; [2]Biostatistics Center, Massachusetts General Hospital, Boston, MA, USA; [3]Department of Pathology, Massachusetts General Hospital, Boston, MA, USA and [4]Harvard Medical School,

	Sensibilidad	Especificidad
D2-40 +	44%	96%
p63 +	91%	92%
Citoqueratina 15 +	40%	98%

Resumen: “Ideas claves”

- CCB vs TB
  - CD10 (+ epitelio en CCB; + estroma en TB)
  - No sirve Bcl-2
- Tum. Sebáceos
  - BerEP4 negativos
  - Citoq 19 puede ser útil
  - La IHQ no resuelve el dd benigno-maligno
    - D2-40 y racemasa pueden ayudar
- CCB metatípico
  - BerEP4 positivo

Resumen: “Ideas claves”

- Tumores esclerosantes
  - Si BerEP4 es negativa no es un CCB
  - CAM: p63 patrón distintivo
  - Nuevos marcadores:
    - PHLDA1 (TEP, TEPd)
    - P75 NTR (TEPd)
    - PAF (CCBm)

- Metástasis vs tumor 1º
  - P63, D2-40 y citoq 15 +: tumor 1º

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siempre de primera
Gracias Afición