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IHC Update: New and Adoption of Not So New Markers

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Disclosures

None

Objectives

Familiarize pathologists with and review antibodies recently introduced into clinical practice.

Adoption of selected established markers.

Illustrate optimal immunoreactivity patterns and pitfalls

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Outline

IDH1/ ATRX

BAP1

LEF1

PhoxB2

Adipophilin

SatB2/CADH-17

INSM1

NKX2.2

TLE1

PRAME

Clones indicated are most widely used and/or used in the Sonora-Quest IHC Lab

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IDH1 R132H

IDH1/2 mutated in the majority of diffuse astrocytomas, WHO grades 1-3, oligodendrogliomas and secondary GBM.

Also mutated in chondroid neoplasms.

R132H is the most common IDH mutation and the one the available mutation specific antibody recognizes; cytoplasmic immunoreactivity indicates mutation.

A negative result does not exclude the possibility of an alternate IDH mutation; sequencing may be required.

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ATRX

Normally expressed in all nucleated cells.

Mutation usually leads to loss of protein expression.

ATRX is mutated in most diffuse astrocytomas and in secondary GBM and retained in oligodendroglioma

Paired testing of all gliomas is now standard of practice.

ATRX clones: BSB-108 or D-5

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IDH1 RH132/ ATRX

Current Approach @Mayo		ATRX	
		LOSS of expression (i.e. **POS**)	**Retained** expression (i.e. **NEG**)
IDH1 R132H	**POS**	**IDH-mutant Astro** ? Grade (II/III/ IV)	**IDH-mutant glioma** ?Oligo <u>1p/19q Testing</u> • Codel = Oligo • Not = Astro
	NEG	**?? Another *IDH* mutation** ⇨ <u>*IDH1/ IDH2* Seq.</u> POS: IDH-mut Astro Neg: IDH-wt Astro	**IF** Not GBM OR age <54 yrs ⇨<u>*IDH* Seq</u> **IF** GBM <u>54+</u> ⇨<u>STOP</u> Likely IDH-wt (>99%)

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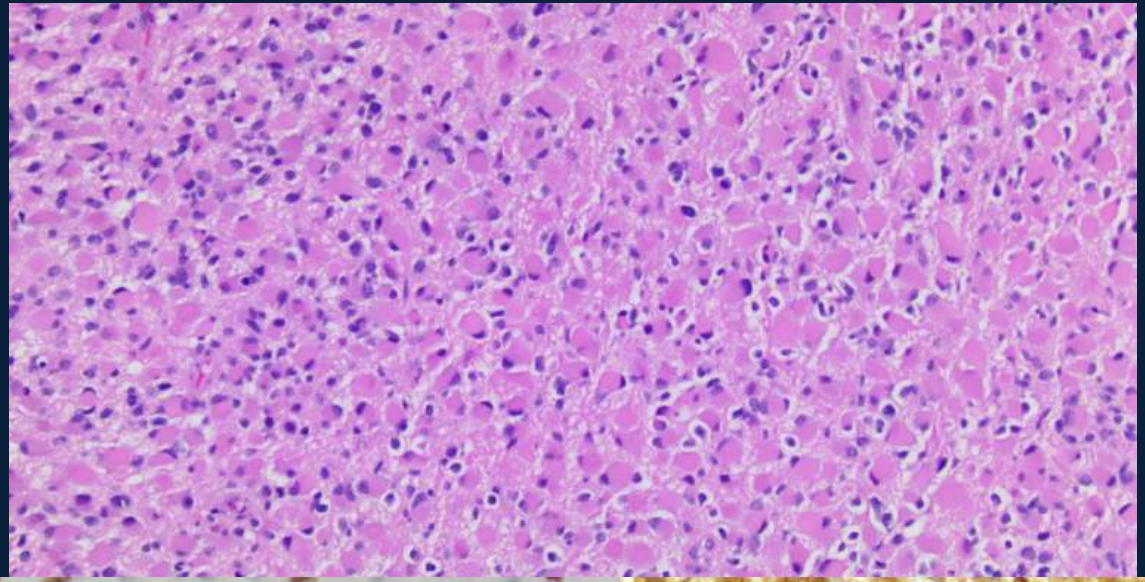
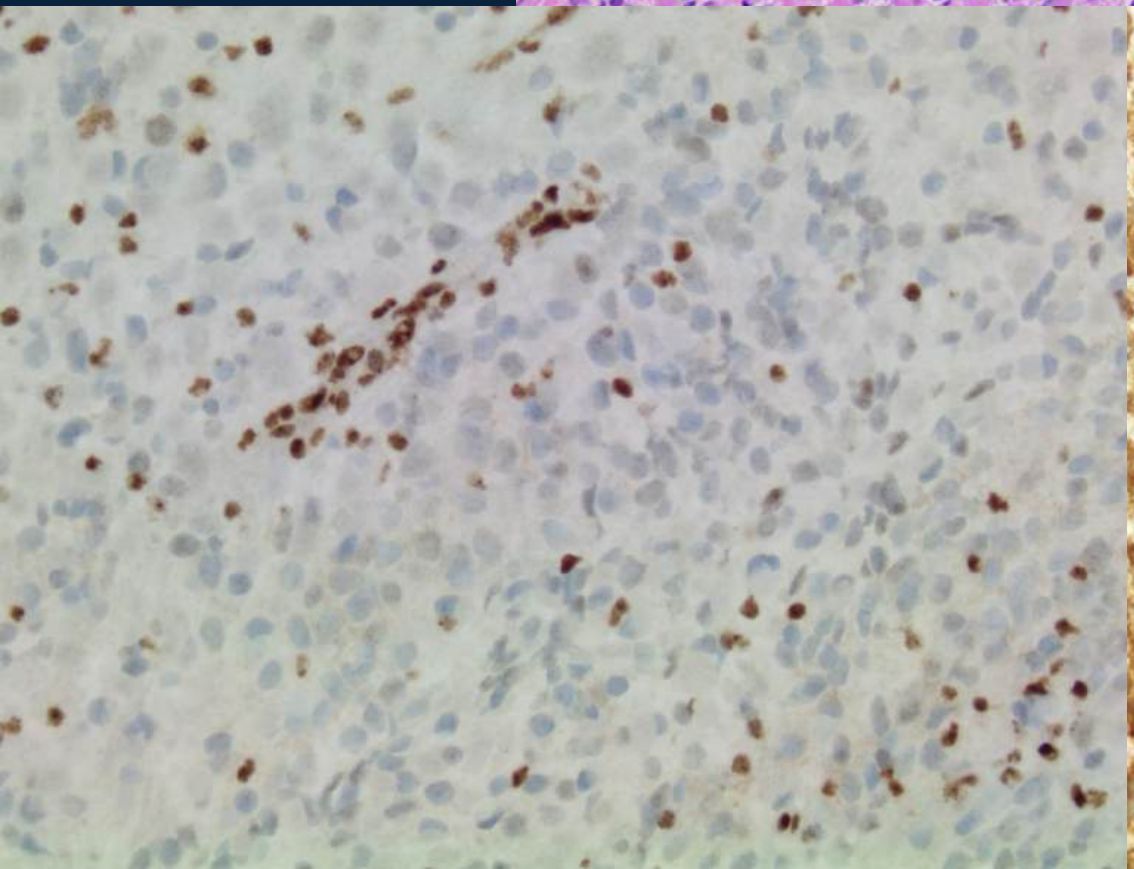
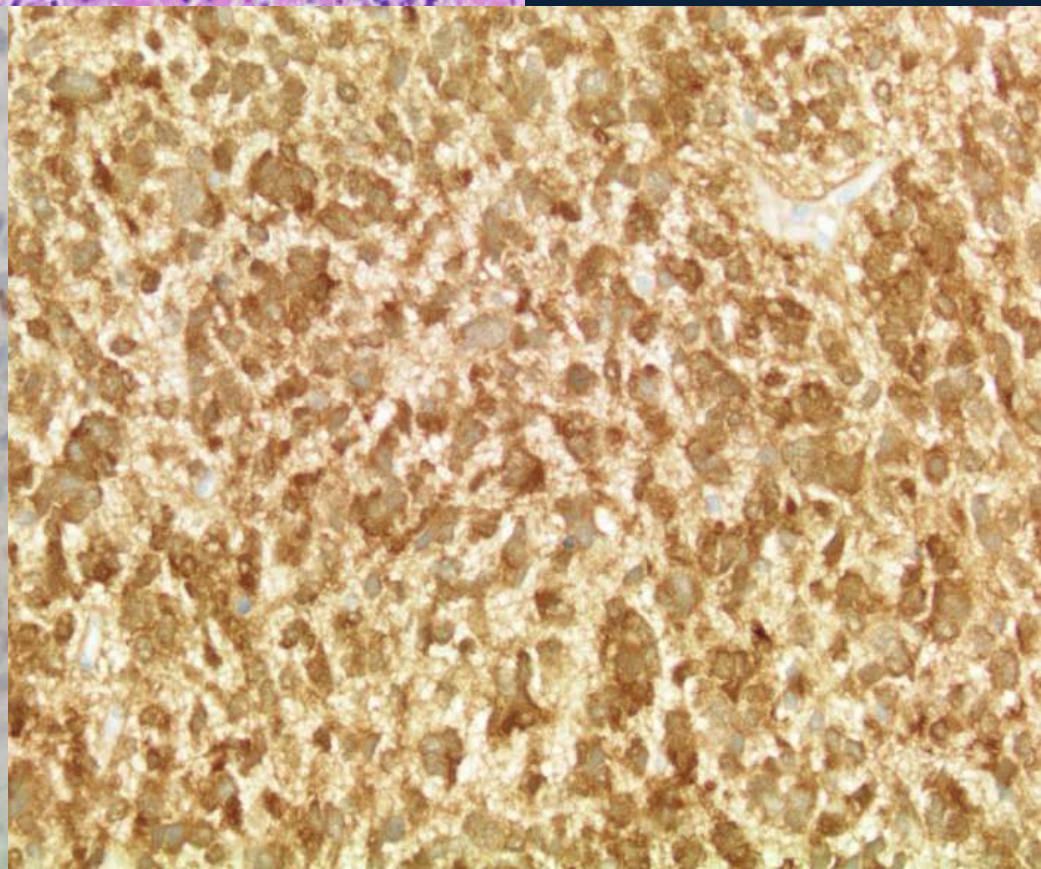
Diffuse astrocytoma



Clone:
BSB-108
ATRX loss

Clone MRQ-67
IDH1-RH132
mutant





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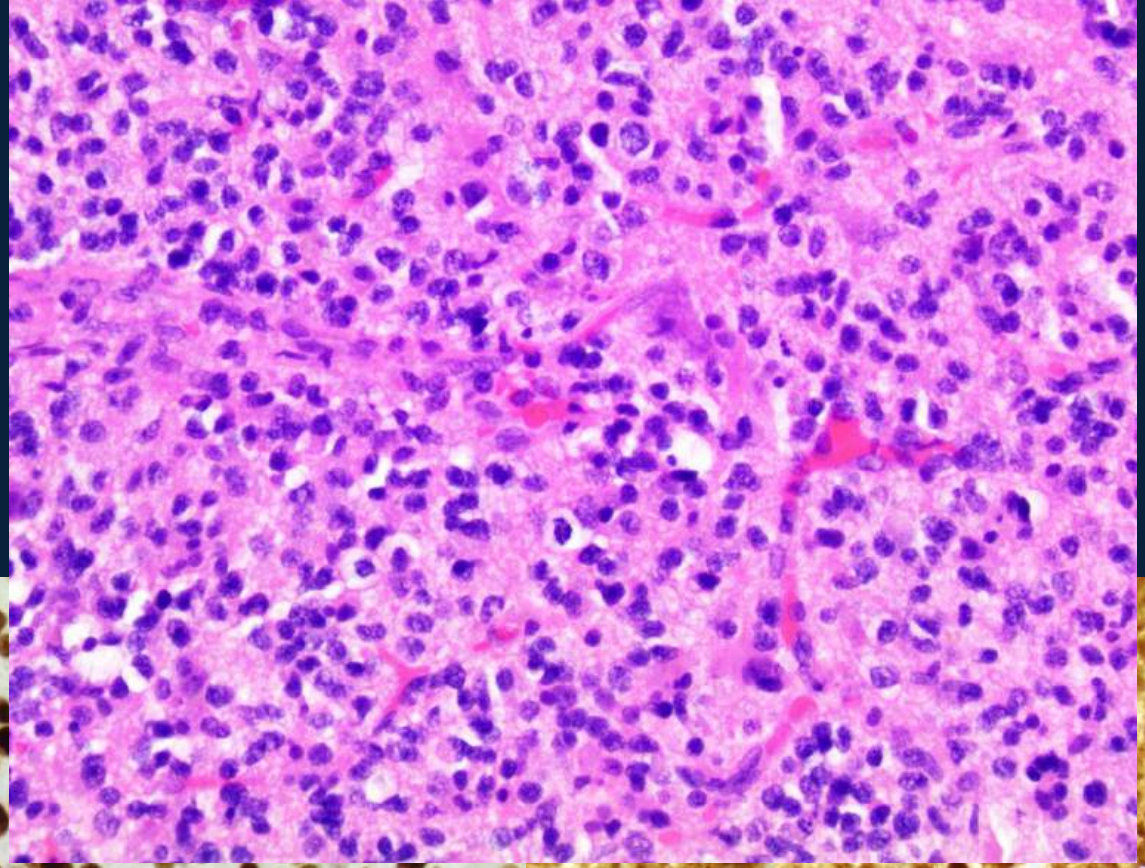
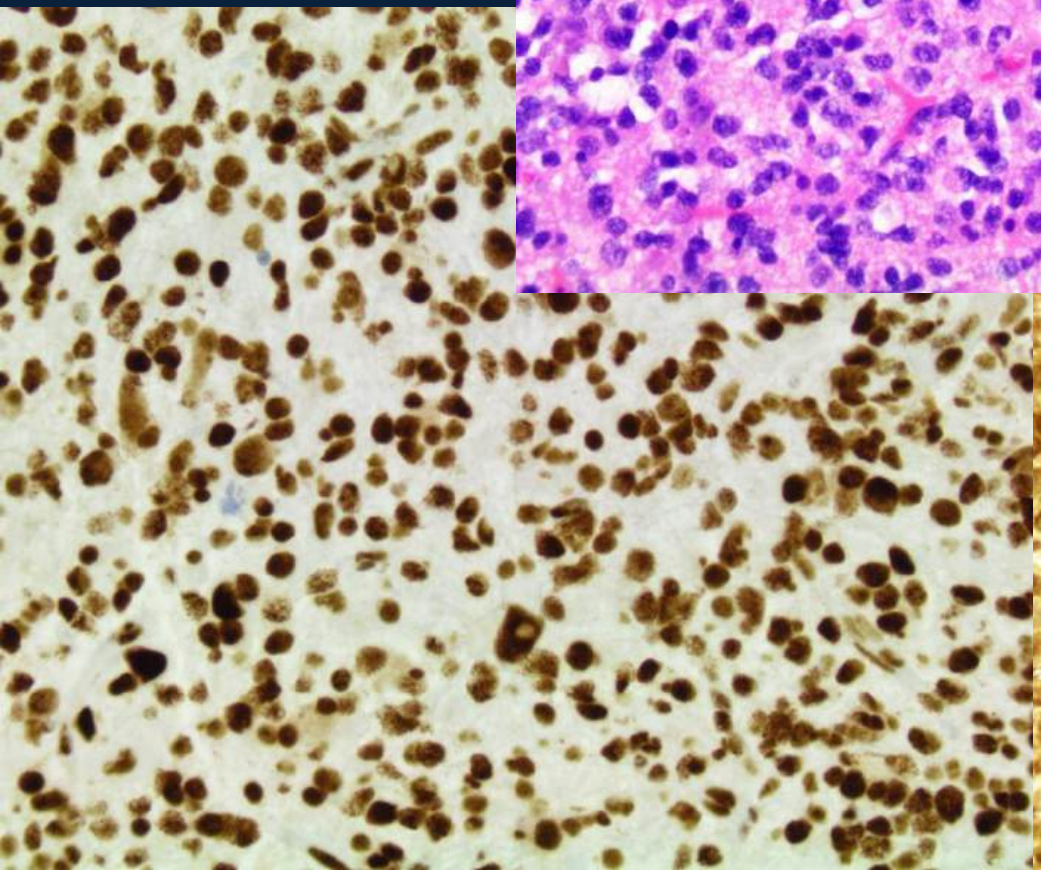
1p, 19q FISH
Testing
indicated

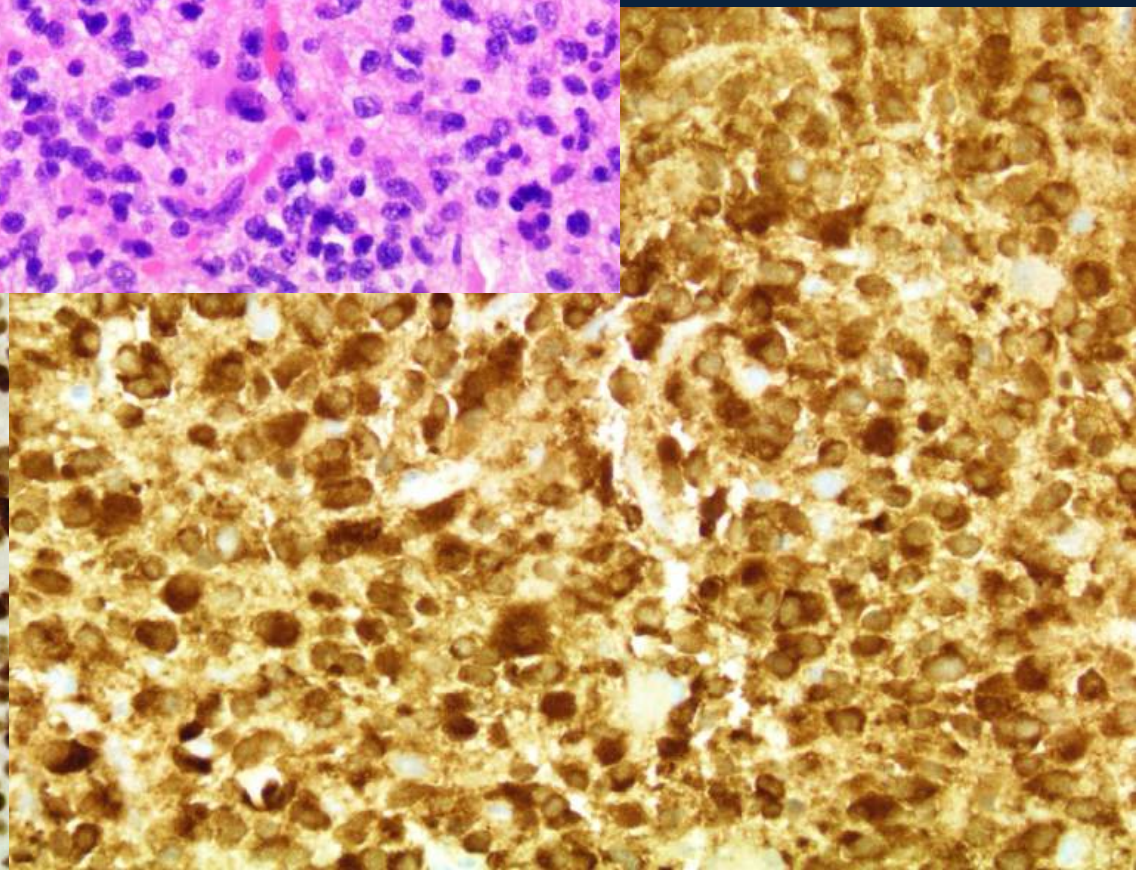
ATRX intact



Diffuse
Glioma
Likely oligo

IDH1-RH132
mutant





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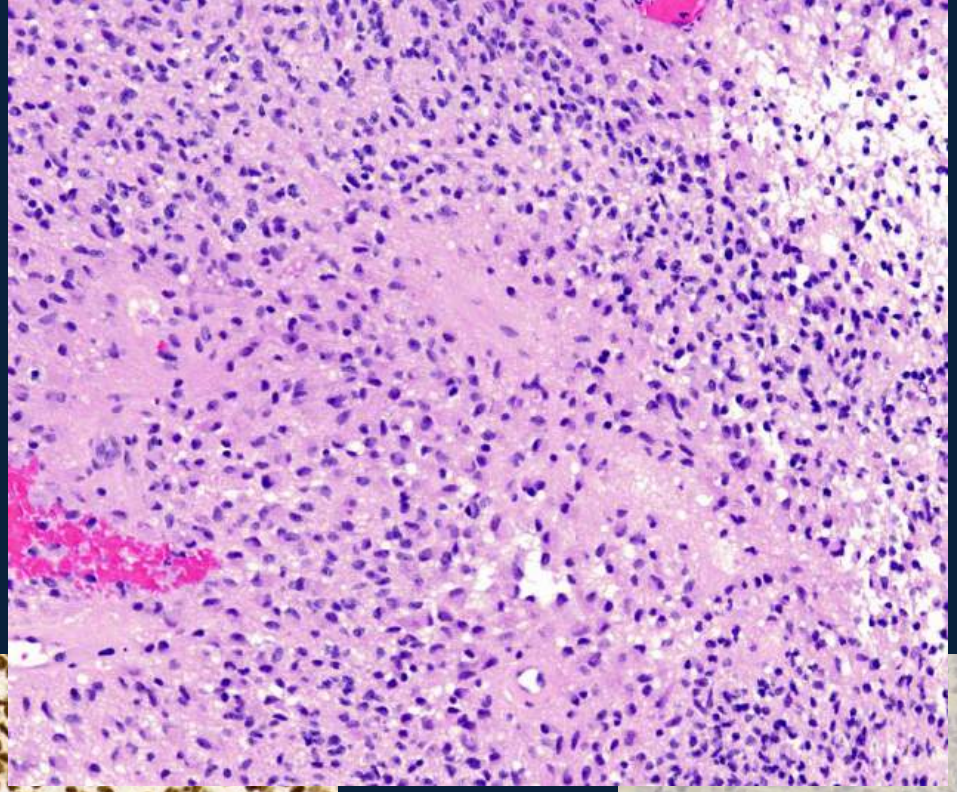
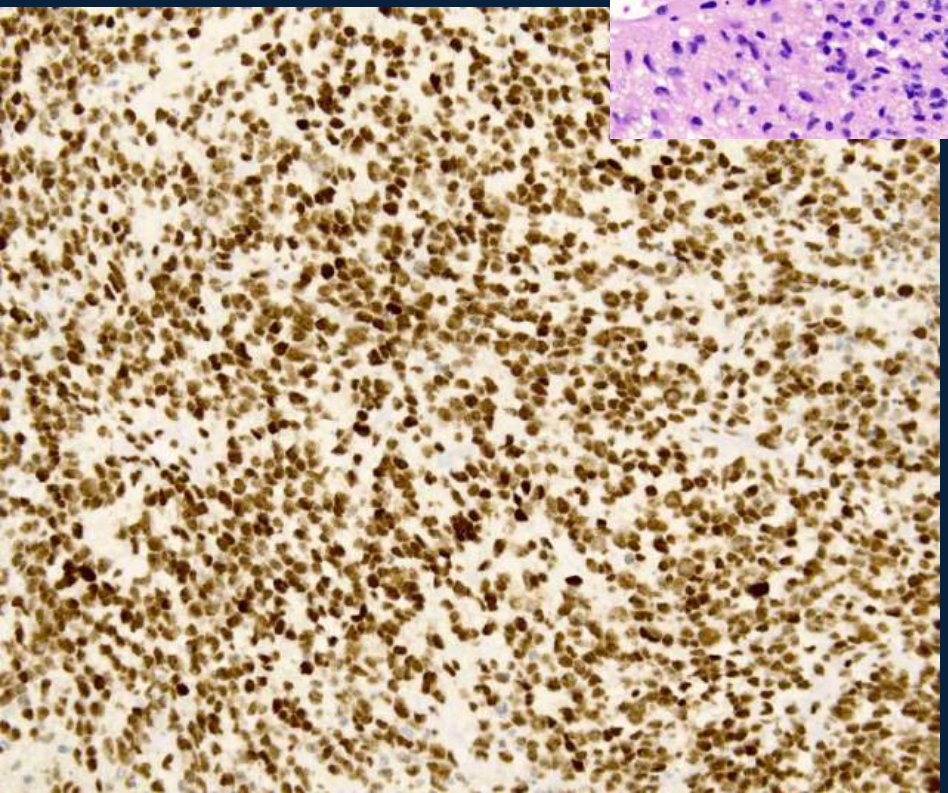
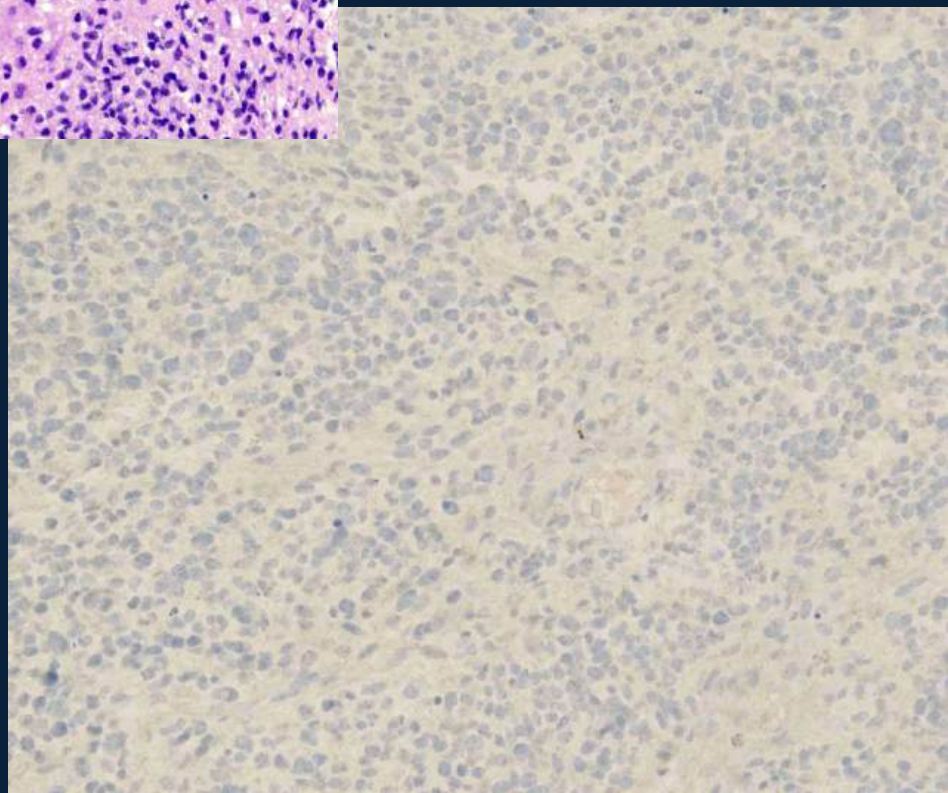
Primary
GMB



ATRX intact



IDH1-RH132
Wild type



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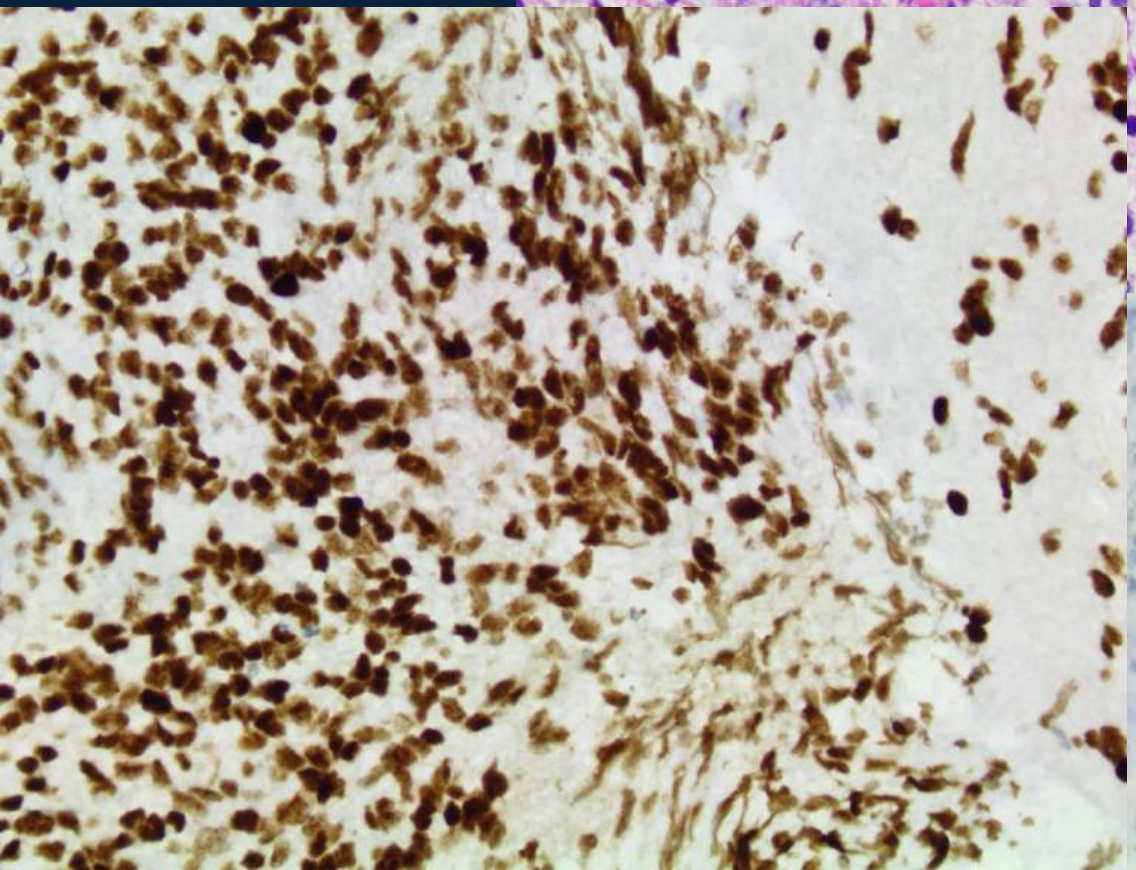
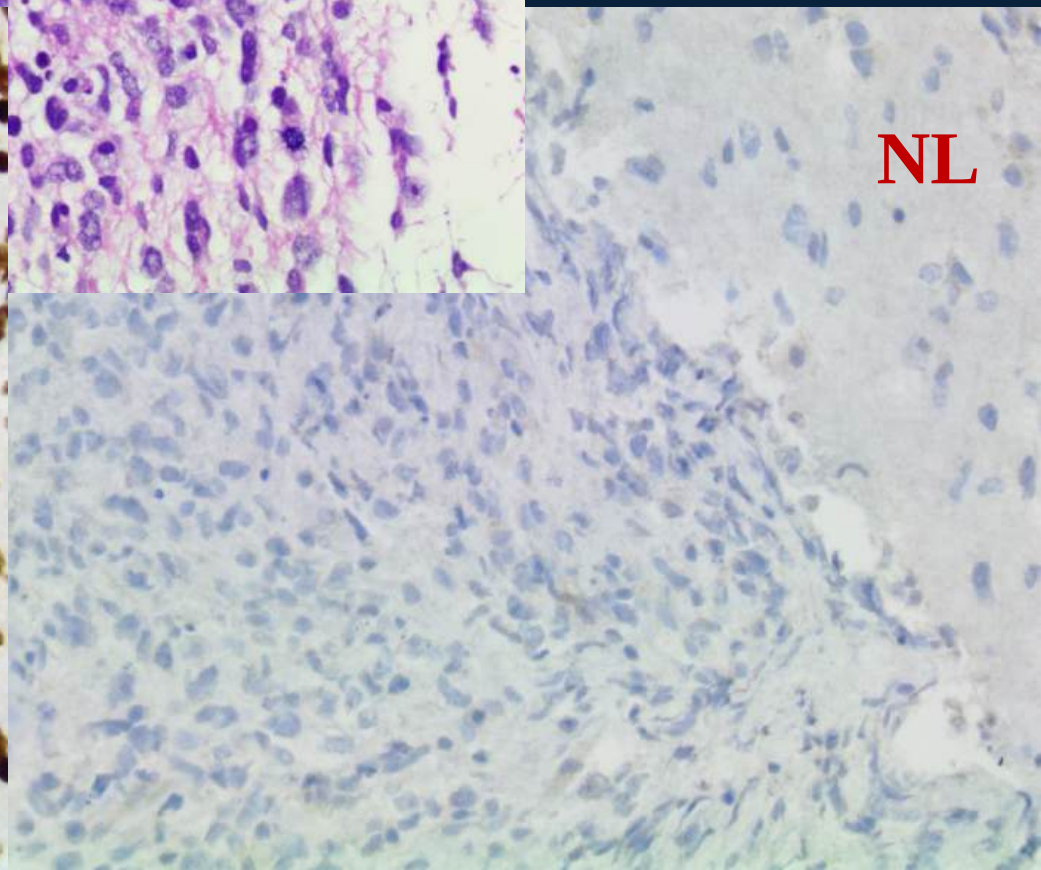
Use internal controls

Primary GMB

ATRX intact

IDH1-RH132 Wild type





NL

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IDH1/ ATRX references

Jinquan C, et al. Detection of ATRX and IDH1-R132H immunohistochemistry in the progression of 211 paired gliomas. Oncotarget. 2016;7(13): 16384-95.

Leeper HE, et al. IDH mutation, 1p19q codeletion and ATRX loss in WHO grade II gliomas. Oncotarget. 2015;6(30): 30295-30305.

Ikemura M, et al. Utility of ATRX immunohistochemistry in diagnosis of adult diffuse gliomas. Histopathology. 2016 (69): 260-67.

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SatB2

Nuclear transcription factor expressed in lower GI mucosa.

Osteoblasts and subset of neuronal cells in the CNS; weak to moderate expression in lining cells of testicular tubules and epididymis.

Preferentially expressed in colorectal and appendiceal adenocarcinomas, much less so in upper GI tract and pancreatico-biliary adenoca, as compared to CDX2.

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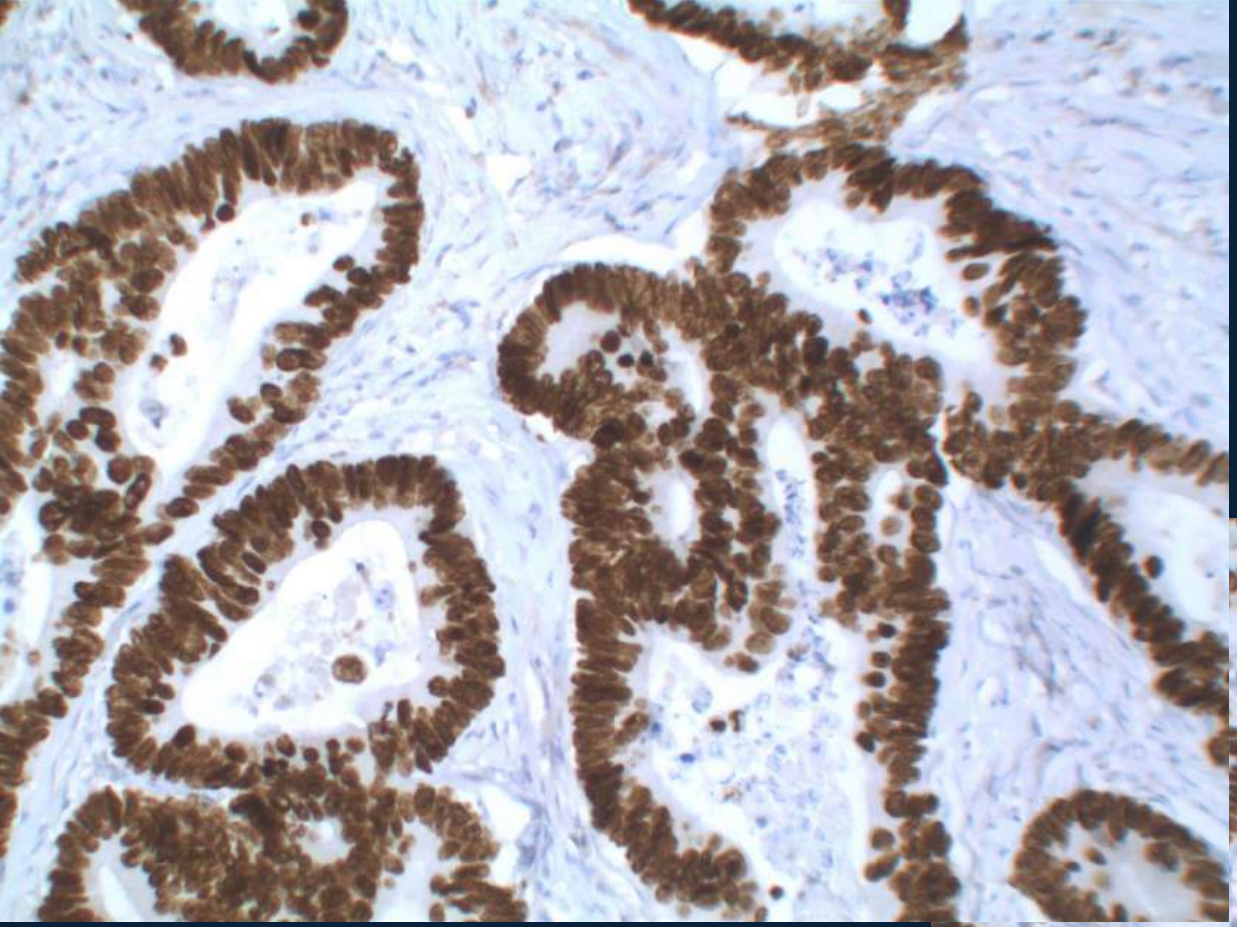
SatB2

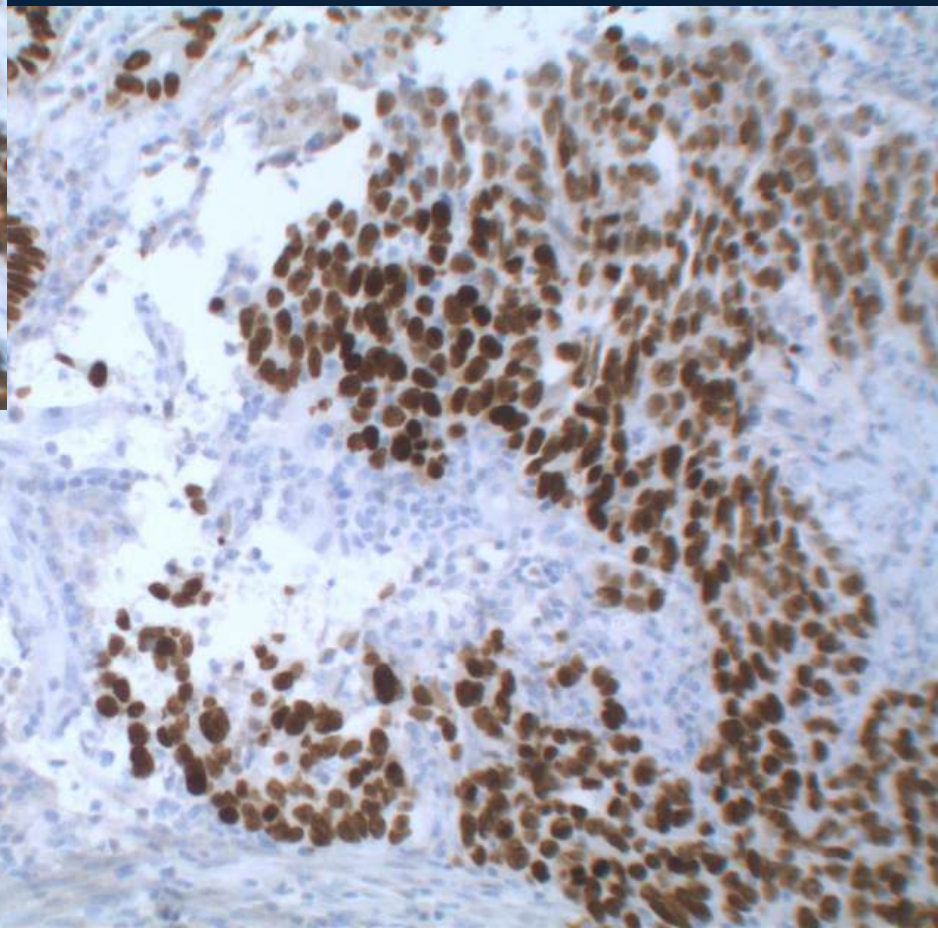
Coupled with CK20, identifies 97% of CRC/ medullary ca.

Coupled with CDX2, at least 90% specific for CRC, when > 50% of cell expression at moderate or strong intensity.

Loss of expression in IBD associated dysplasia and carcinoma.



SatB2 CRCa
Rabbit Monoclonal
EP281



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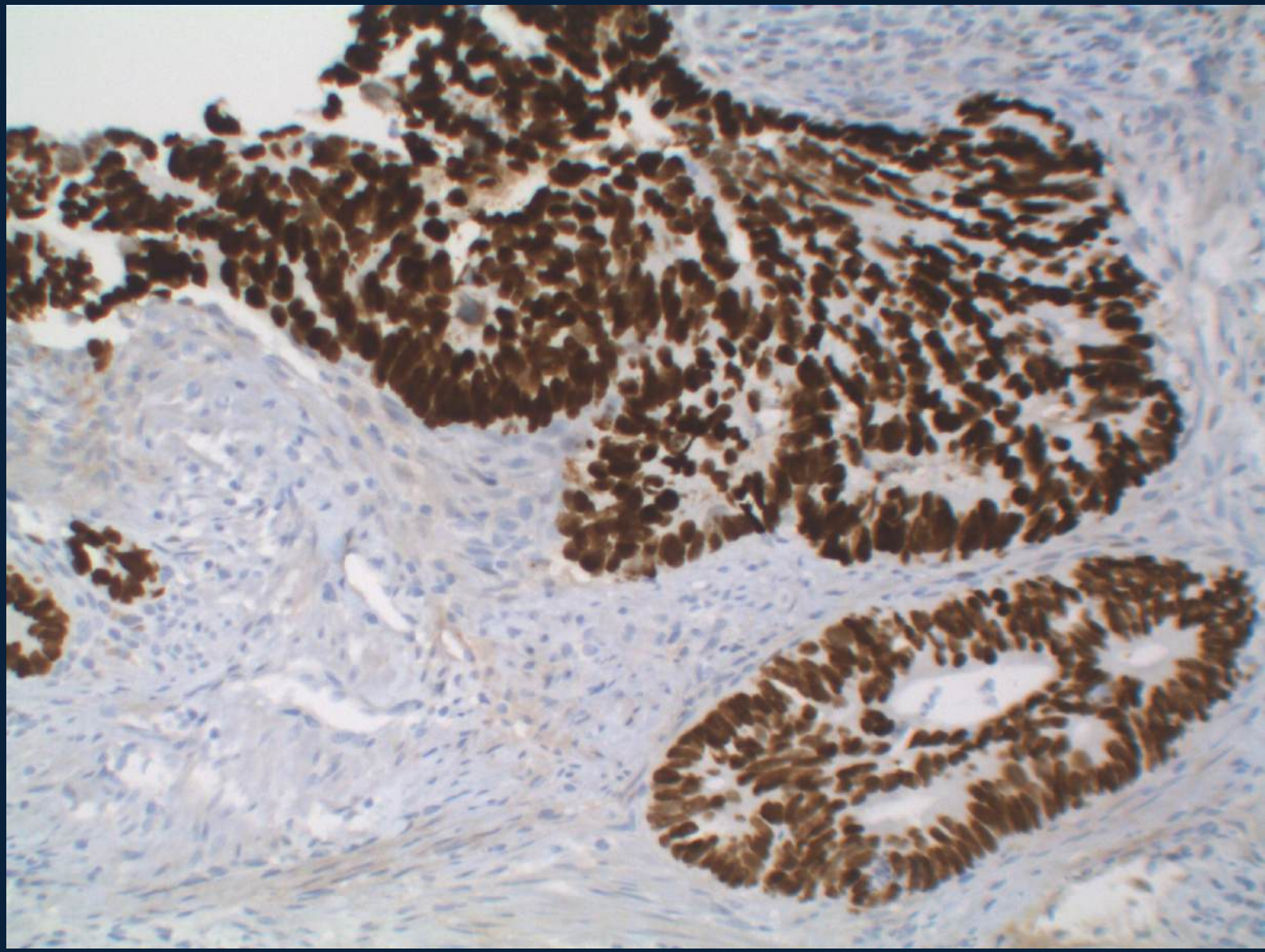
SatB2
CRCa



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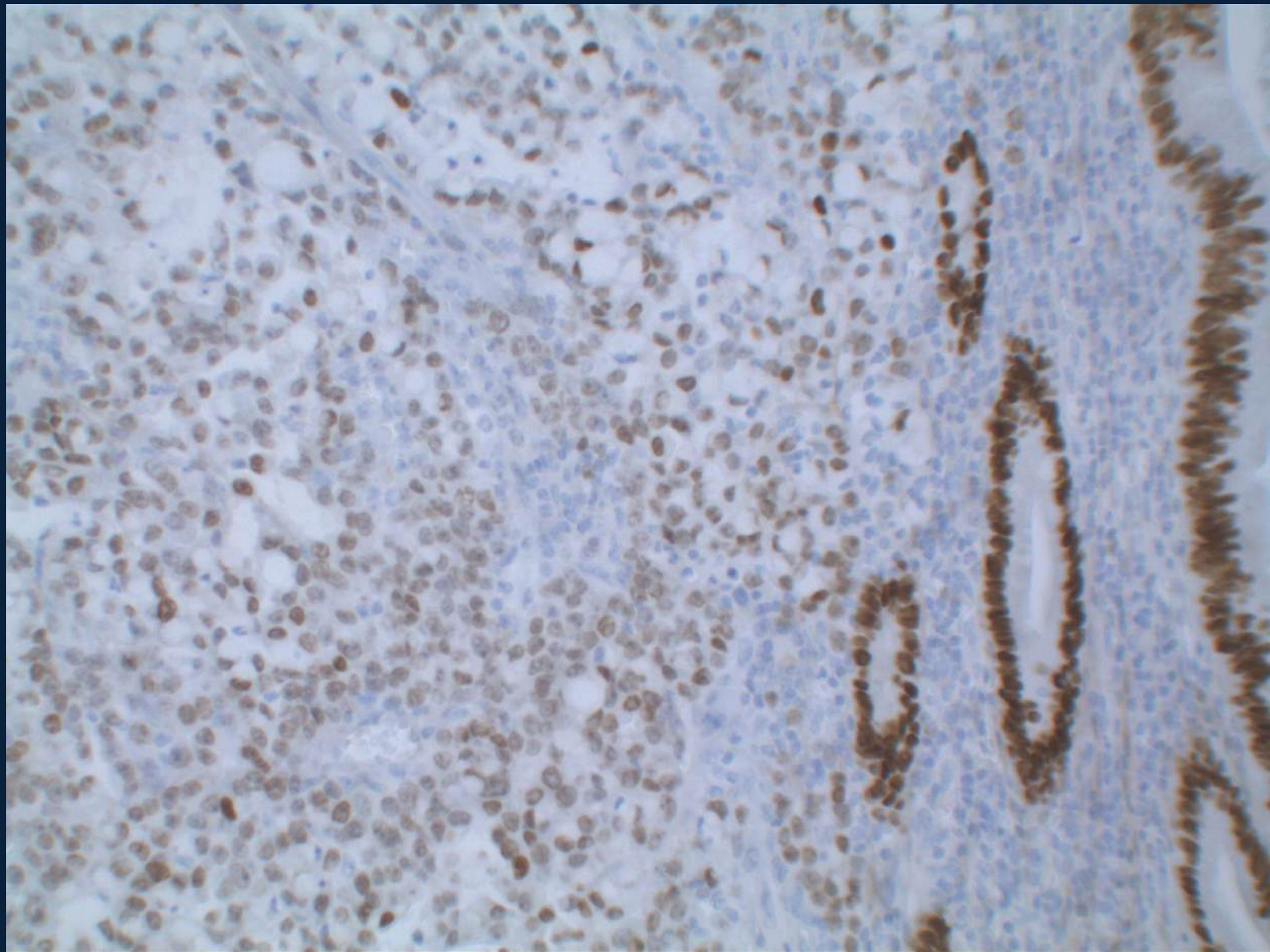
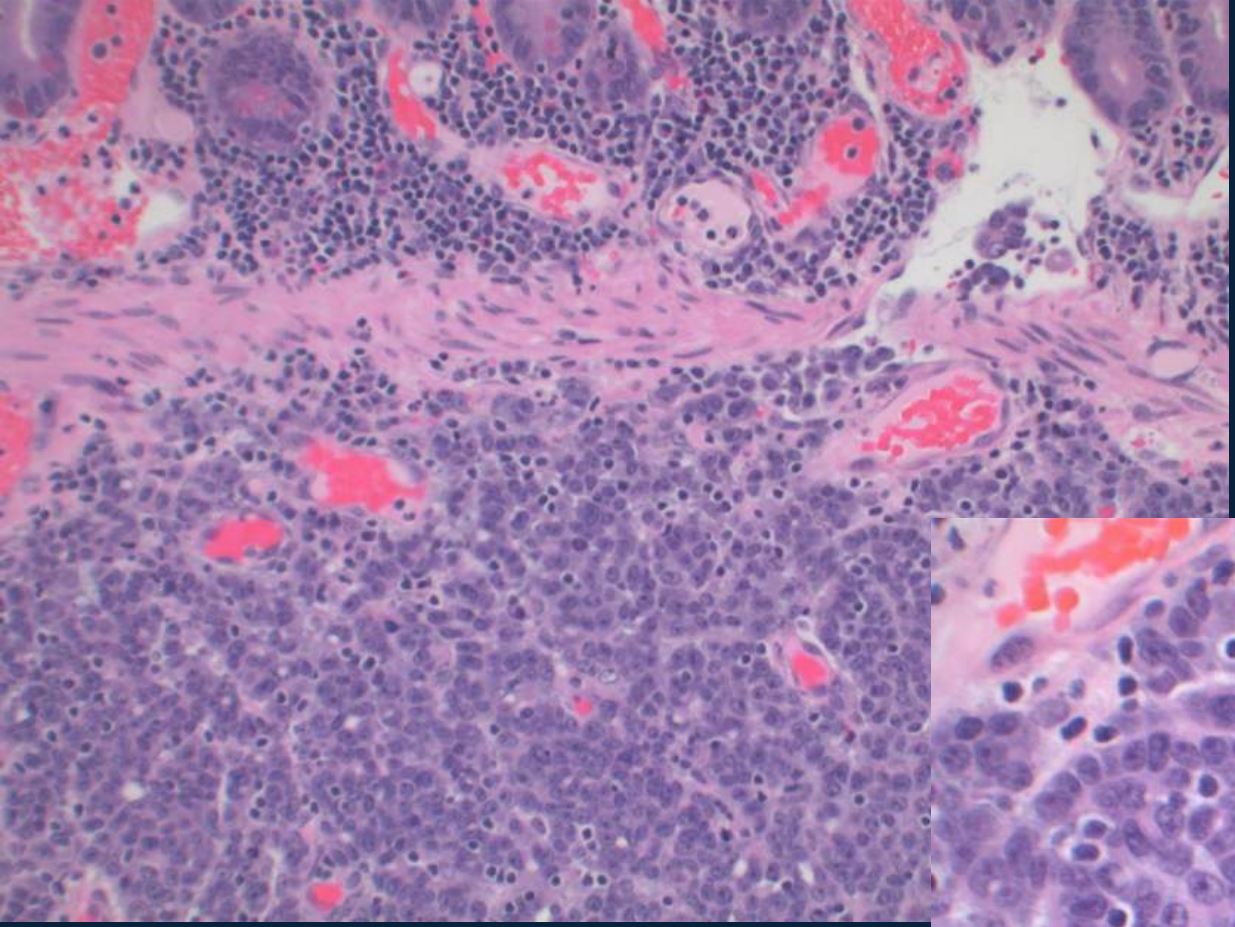
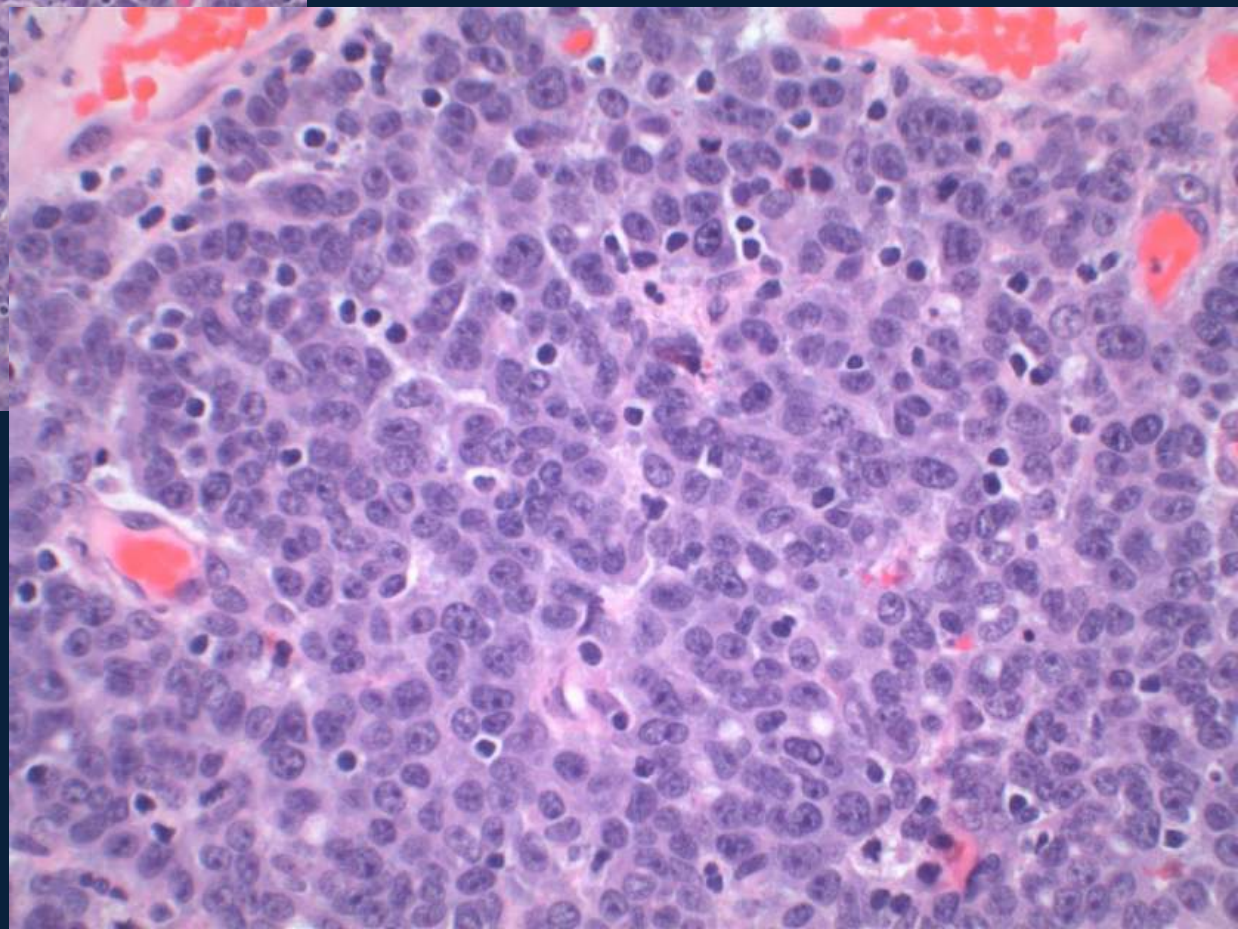
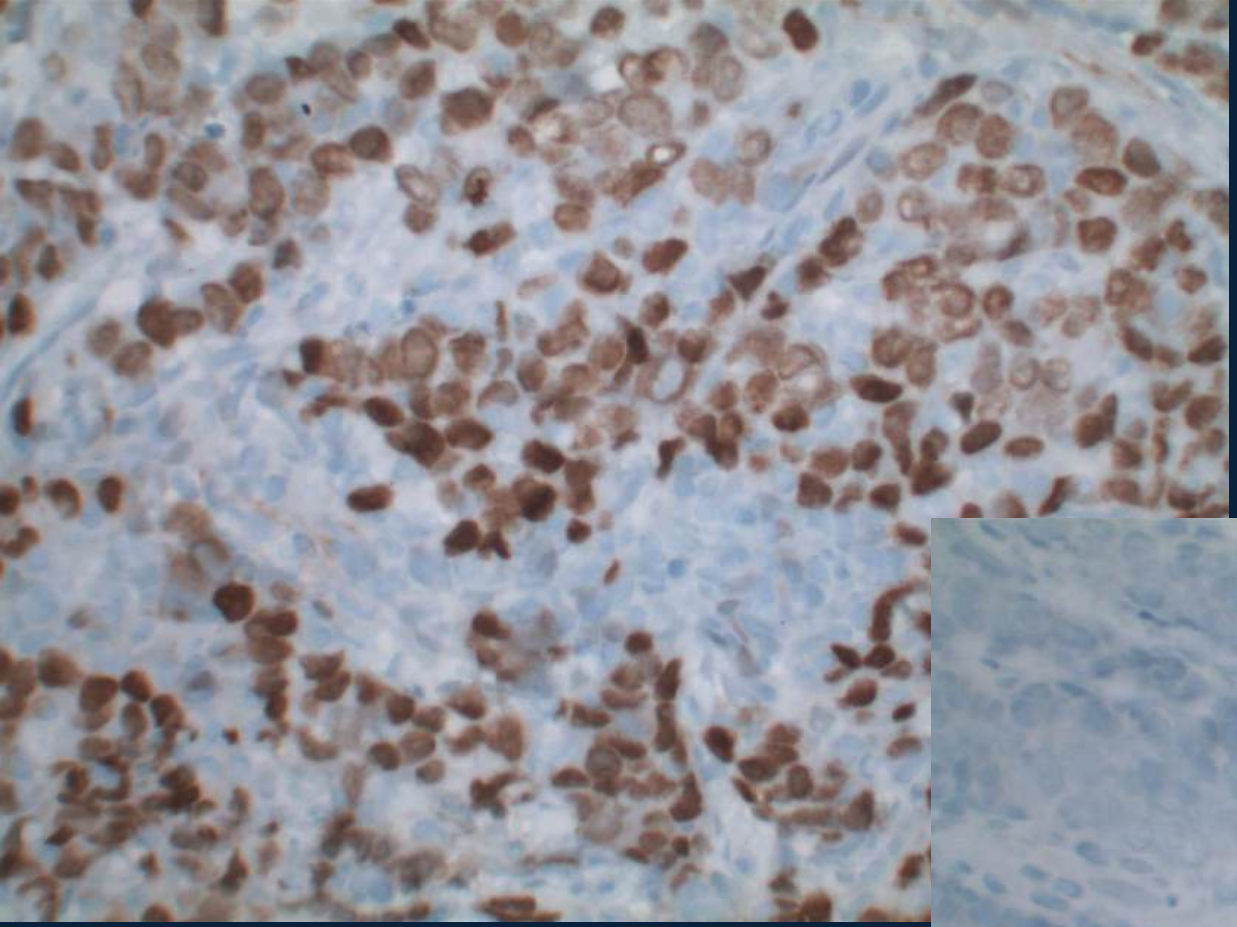
SatB2
Weak pos
CRCa





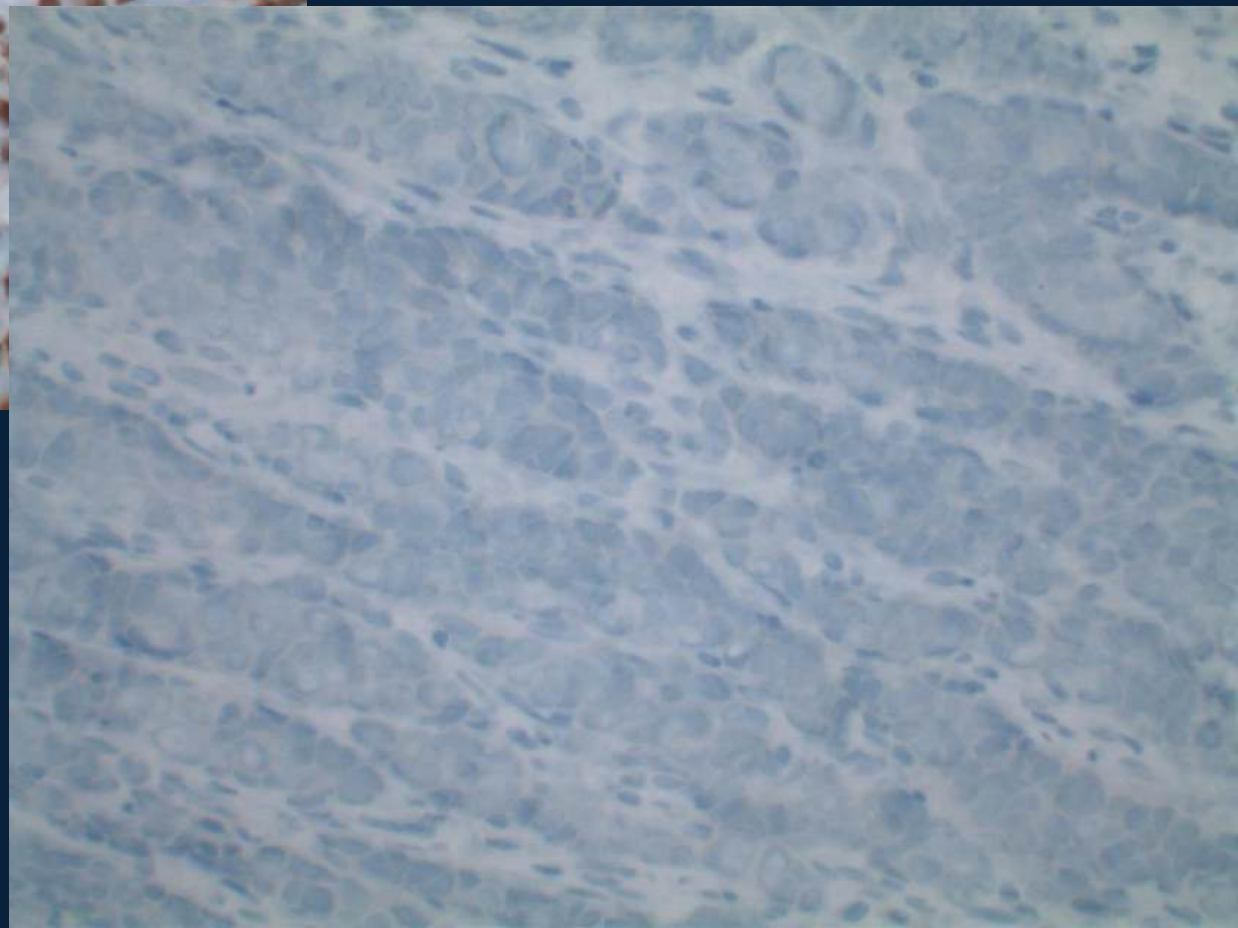


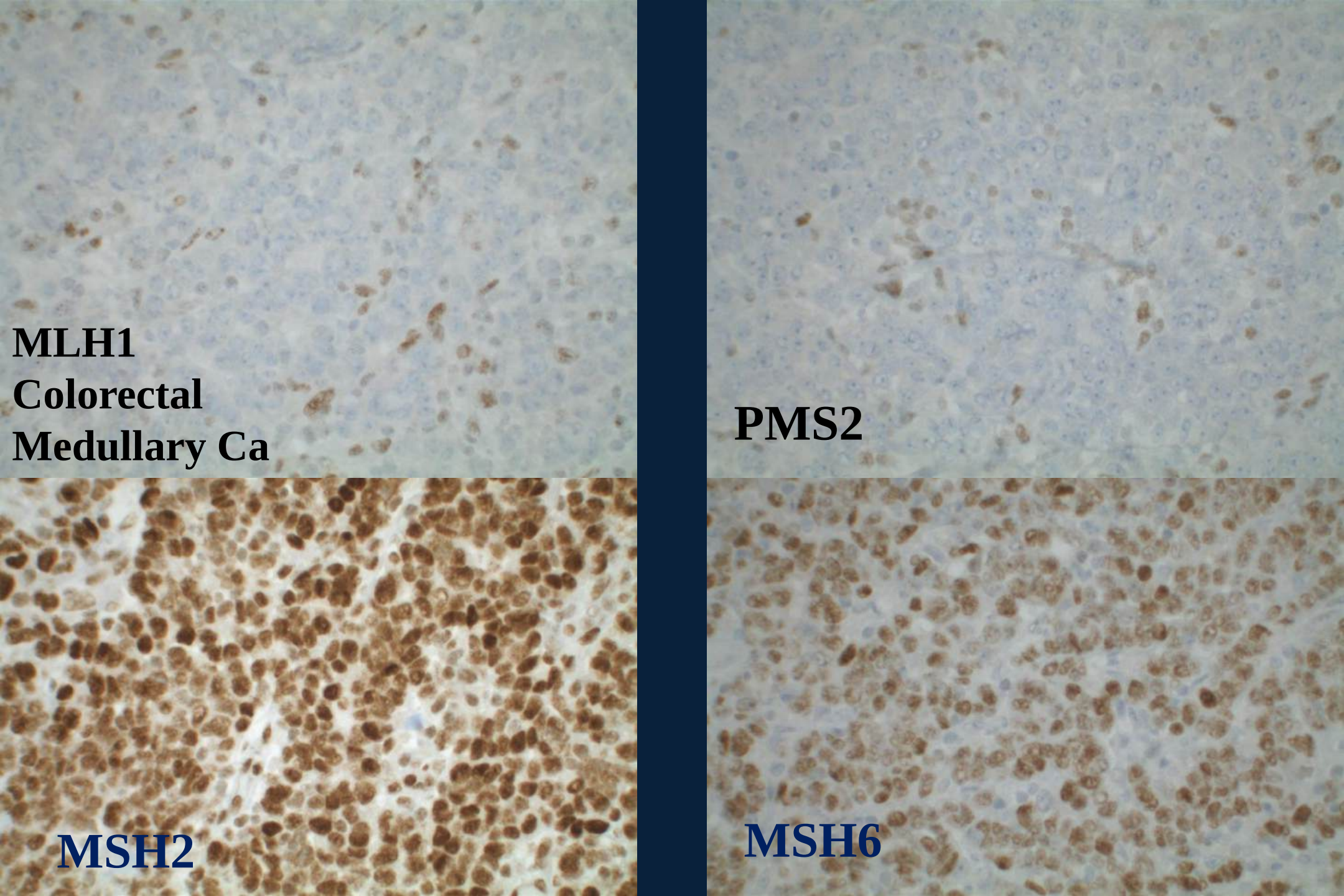
Colorectal
Medullary ca (2)

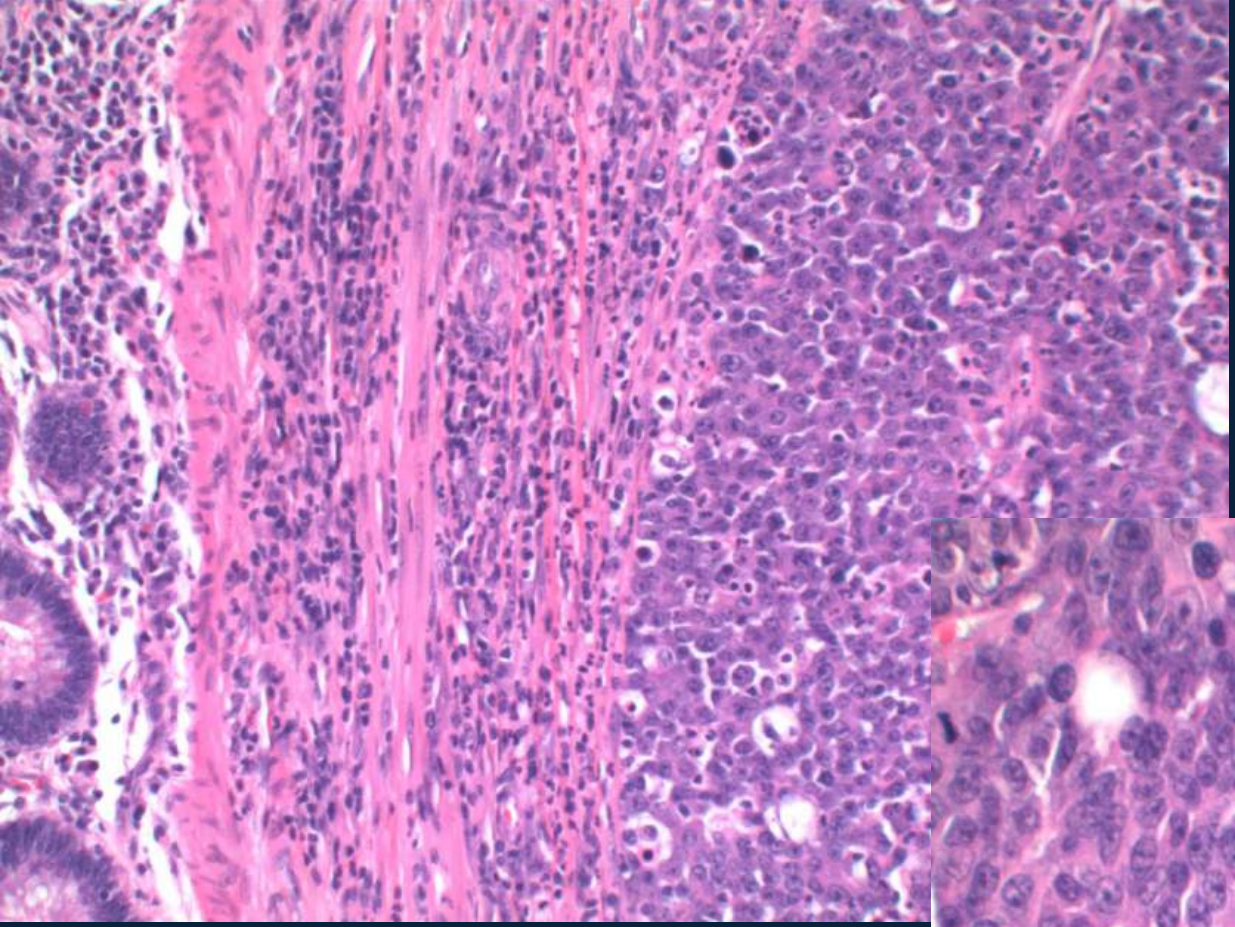


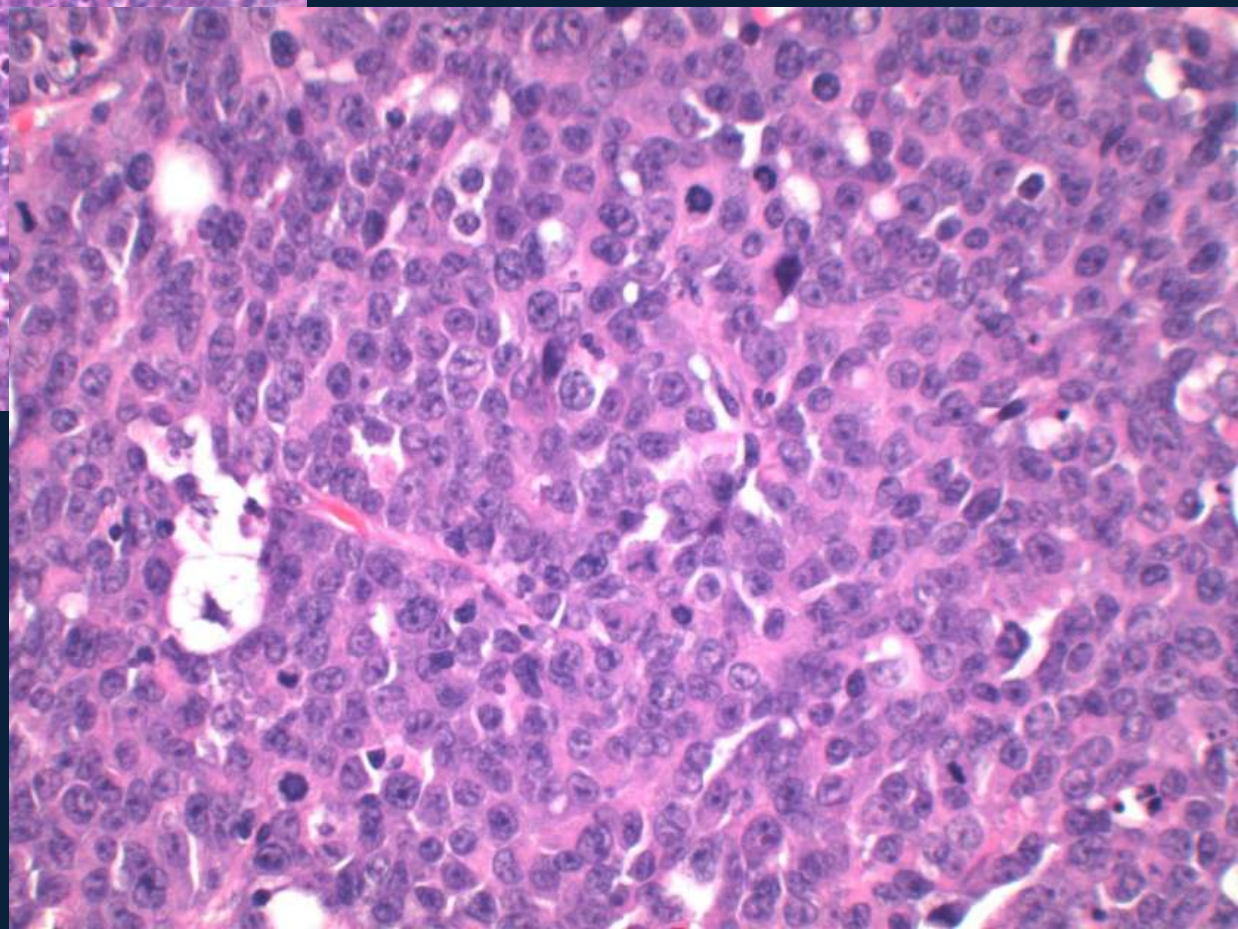
SatB2
Colorectal
Medullary ca

CK20
Colorectal
Medullary ca

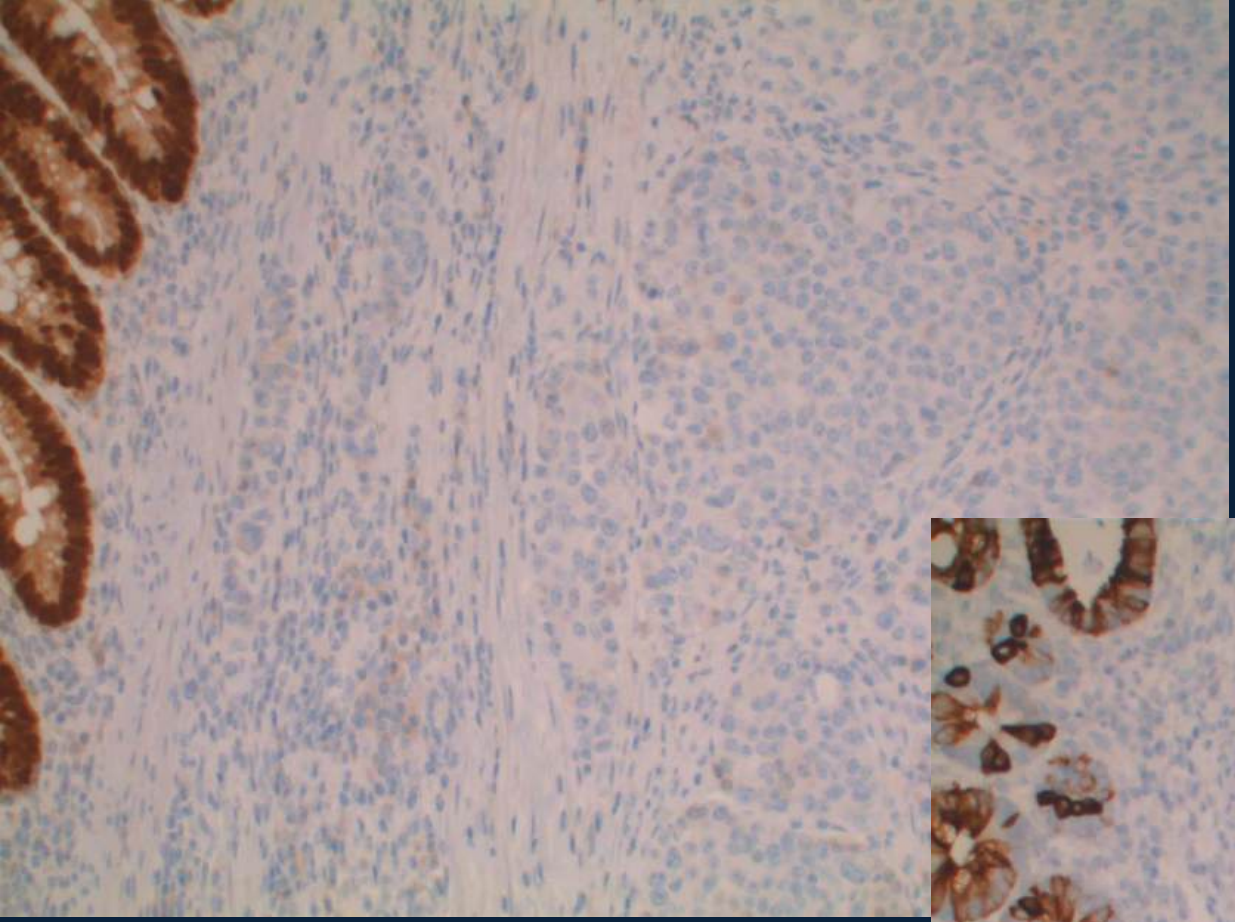



MLH1
Colorectal
Medullary Ca
PMS2
MSH2
MSH6



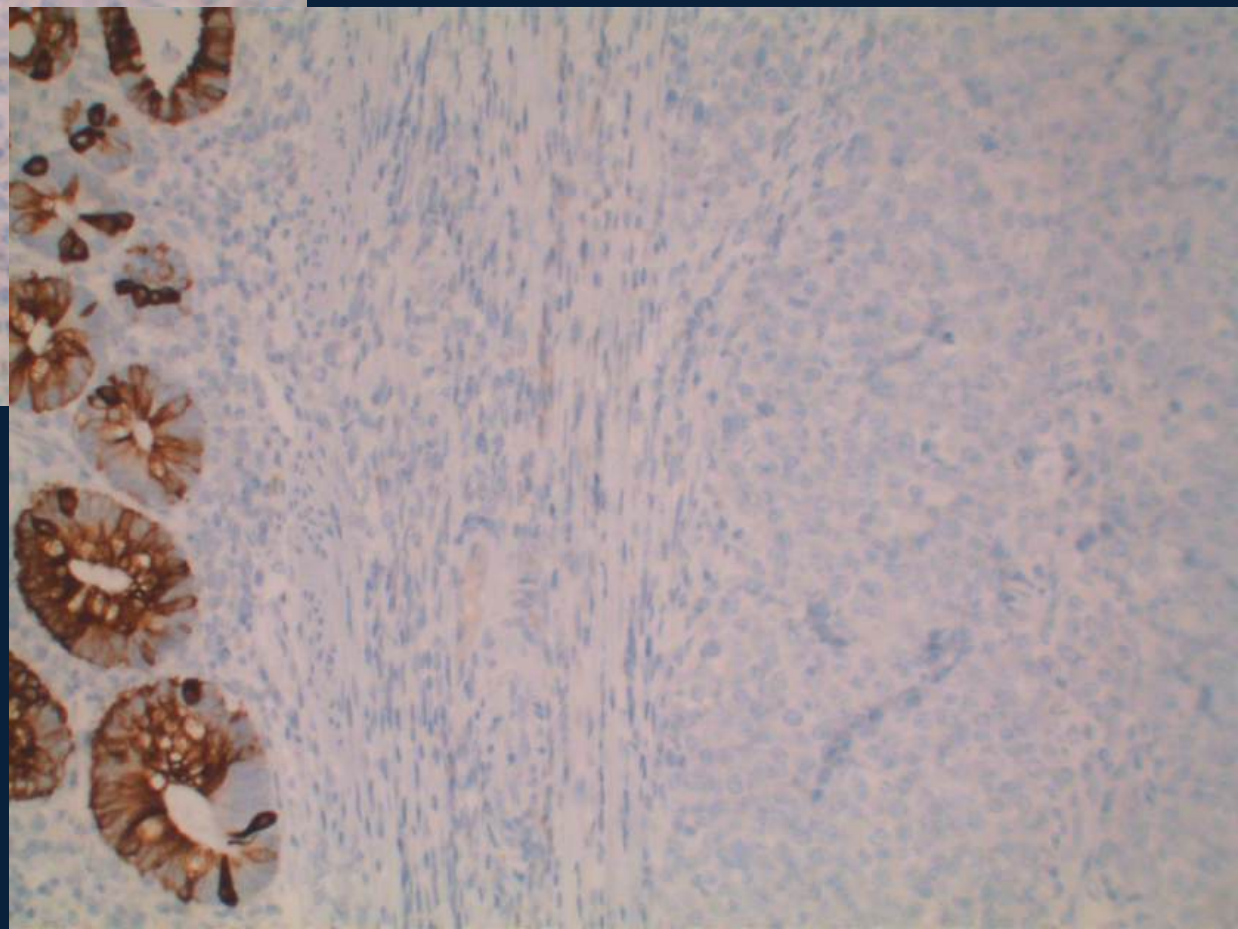


Colorectal
Medullary ca (3)



CDX2
Colorectal
Medullary ca

CK20
Colorectal
Medullary ca



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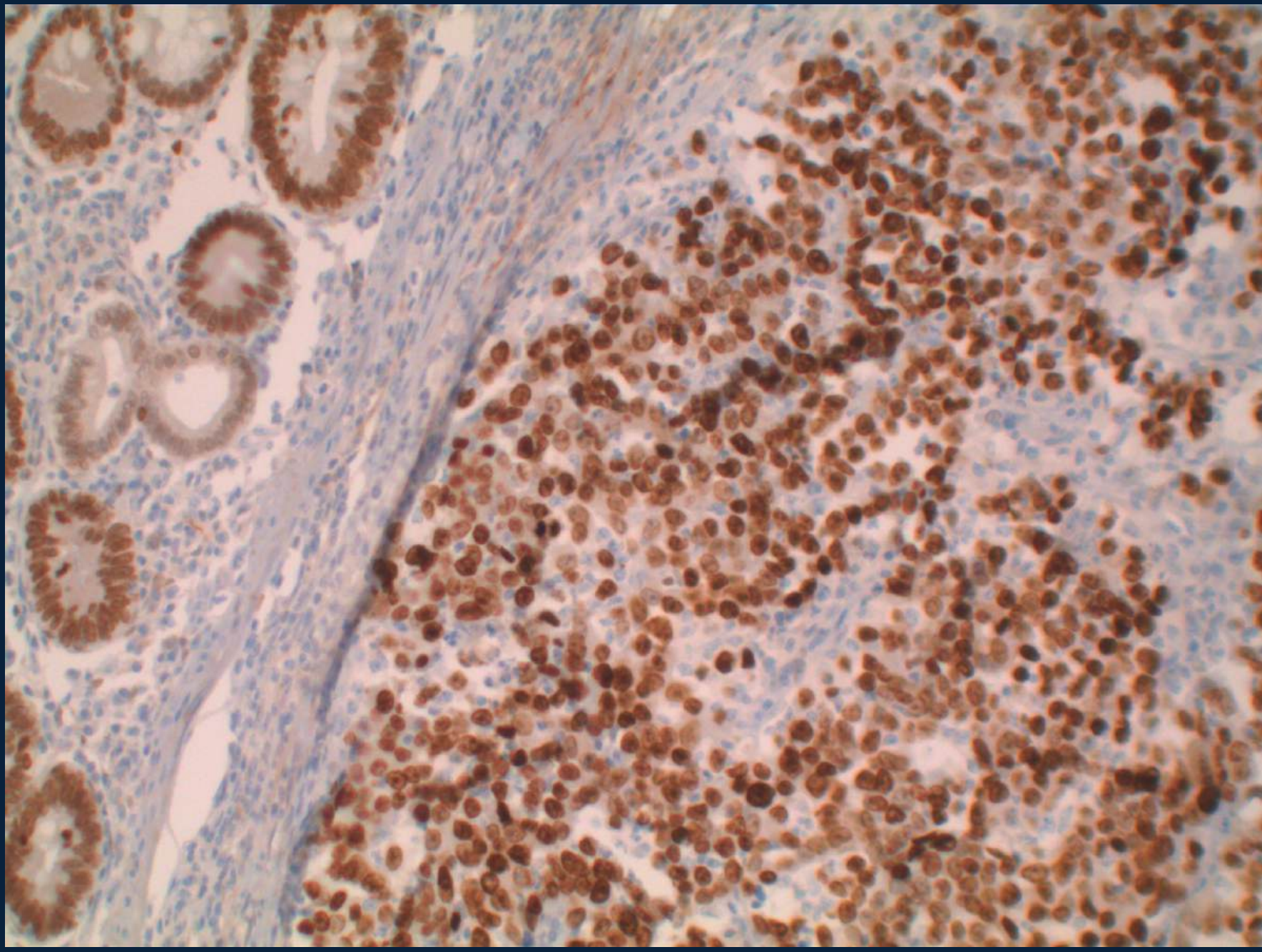
SatB2 Colorectal Medullary Ca



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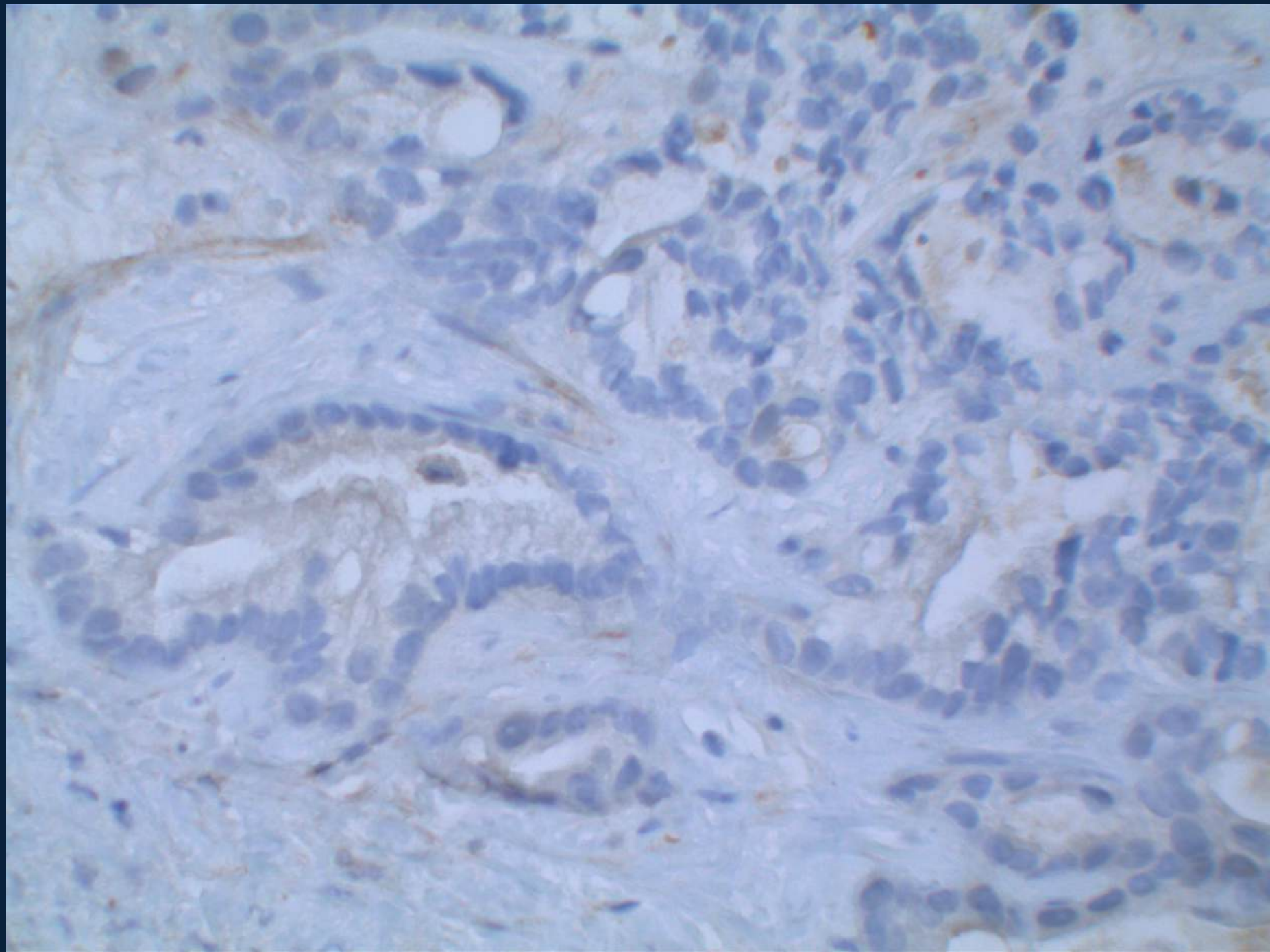
SatB2
Pancreas
Ductal ca



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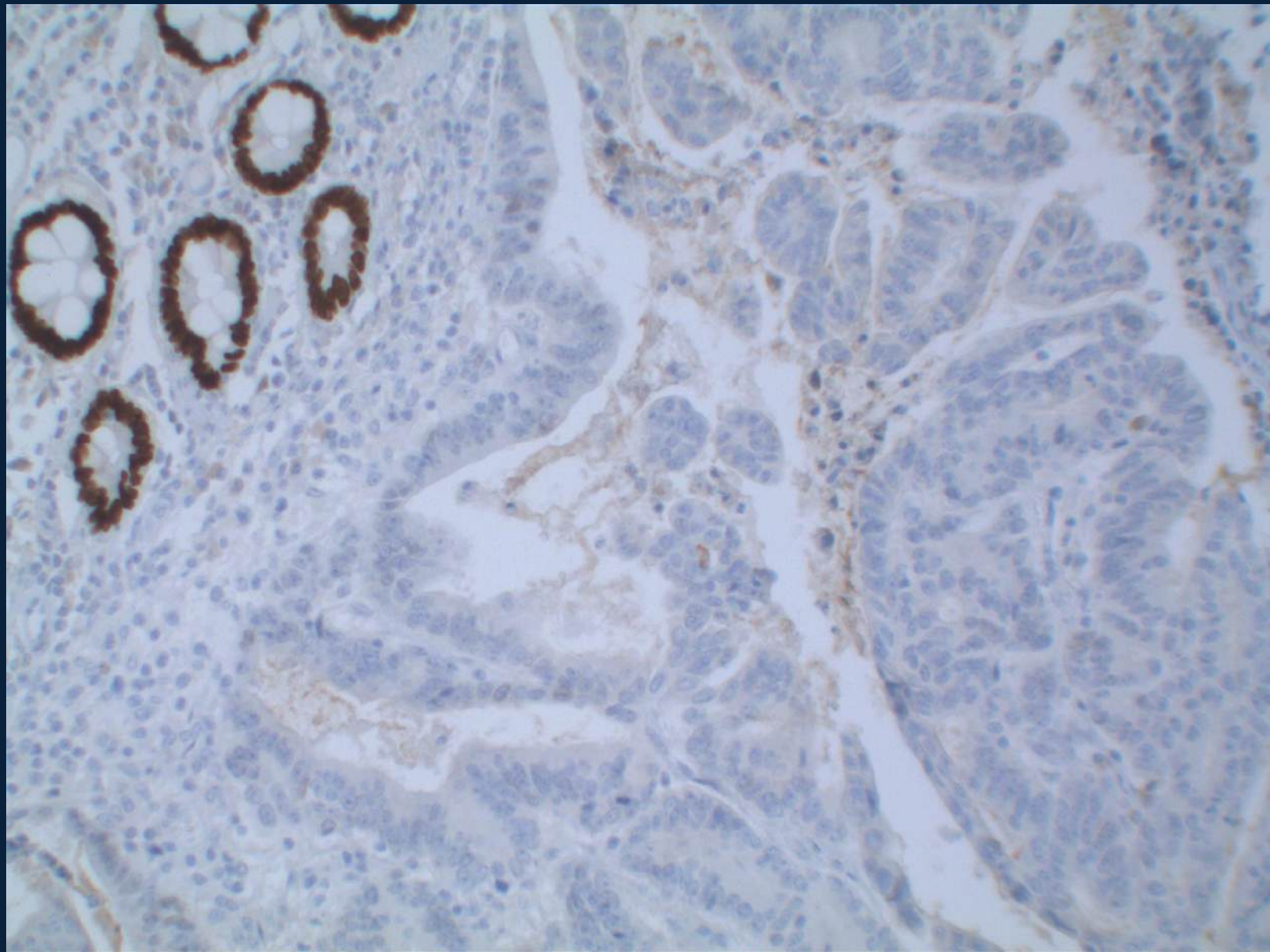
SatB2
Met
serous
ca ovary



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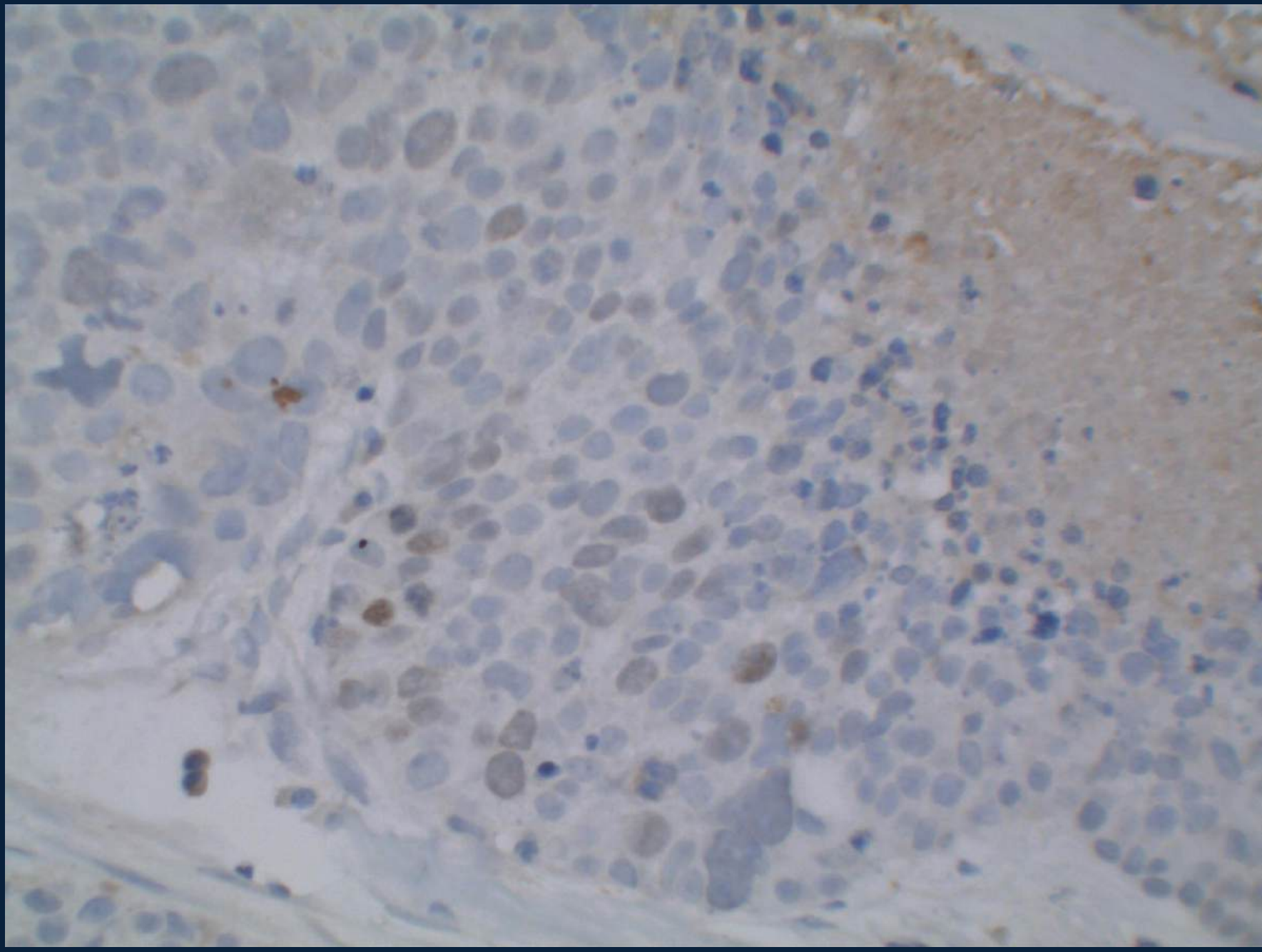
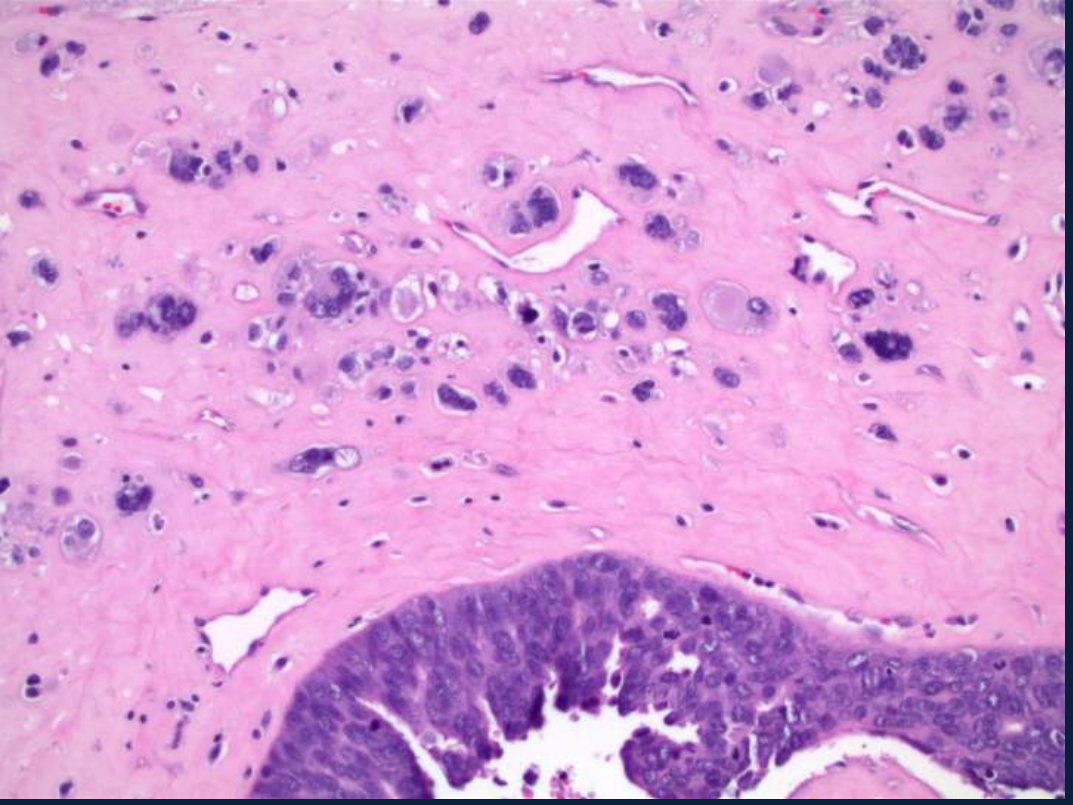
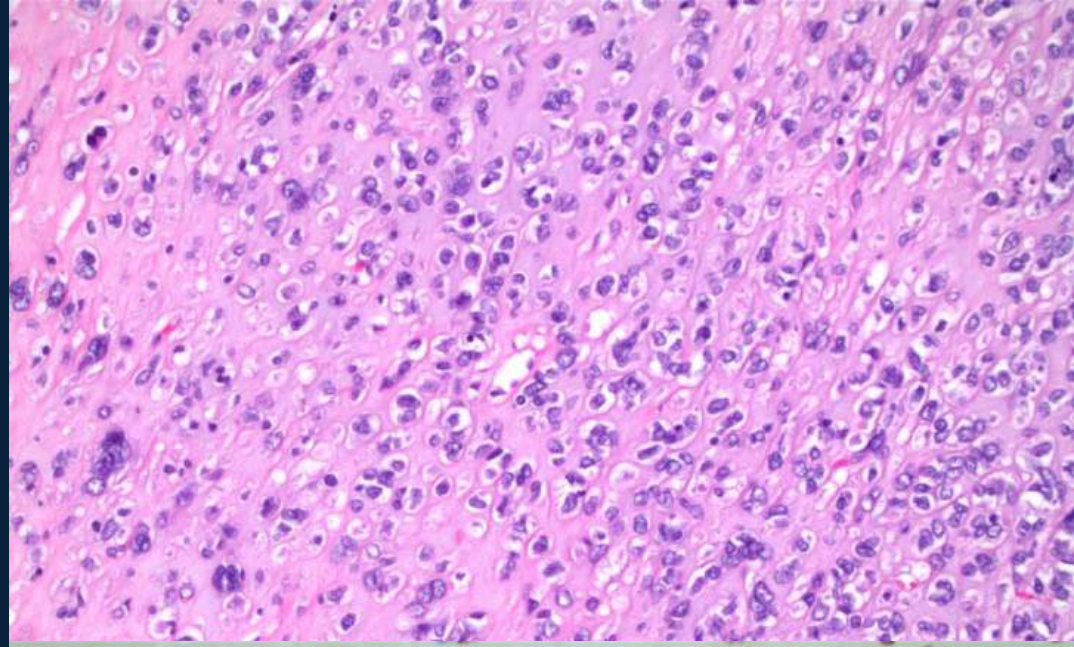
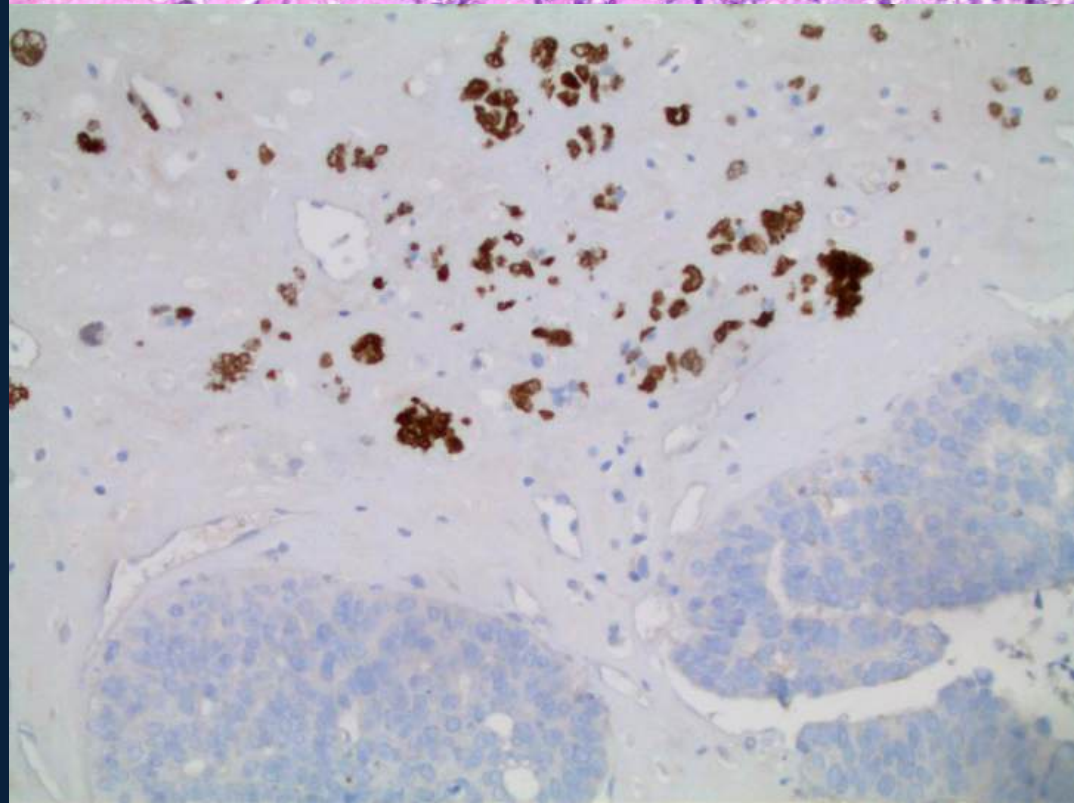
SatB2
SCCA









SatB2
osteosarcoma
Ovarian
carcinosarcoma

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SatB2: References

Magnusson K, et al. SATB2 in Combination With Cytokeratin 20 Identifies Over 95% of all Colorectal Carcinomas. Am J Surg Pathol 2011;35:937–948)

Brettfeld SM, et al. SATB2 Versus CDX2. A Battle Royale for Diagnostic Supremacy in Mucinous Tumors. Arch Pathol Lab Med. 2019;143:1119–1125.

Ma C, et al. Loss of SATB2 Expression is a Biomarker of Inflammatory Bowel Disease–associated Colorectal Dysplasia and Adenocarcinoma. Am J Surg Pathol 2019.

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Cadherin-17

CDH17 (Li-cadherin) is a member of the cadherin superfamily, a transmembrane glycoprotein.

Mediates cell adhesion and is an intestinal peptide transporter.

Preferentially expressed in epithelium of GI tract and pancreatic ducts.

Among adenocarcinomas, expressed at high levels in lower GI, esophageal and NE neoplasms.

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Cadherin-17

CDH17 Expression in 270 GI and Pancreatic Adenocarcinomas

Diagnosis	Neg.	1+	2+	3+	4+	#+/Tot (%)
Esophagus	10	3	15	2	0	20/30 (67)
Stomach	15	2	3	0	0	5/20 (25)
Colon	2	0	7	8	108	123/125 (98)
Pancreas	78	9	4	3	1	17/95 (18)

Infrequently expressed in other carcinomas (30% of endocervical and 13% of pulmonary). Arch Pathol Lab Med. 2014;138:1015–1026.

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Cadherin-17

CDH17 Expression in colorectal medullary carcinomas

CDH17	16/18 (87%)	75% ≥3+
SatB2	16/18 (87%)	75% ≥3+
CDX2	12/18 (67%)	42% ≥3+
CK20	5/18 (42%)	0% ≥3+

12/18 also expressed calretinin (akin to triple negative breast cancers)

Arch Pathol Lab Med. 2014;138:1015–1026.

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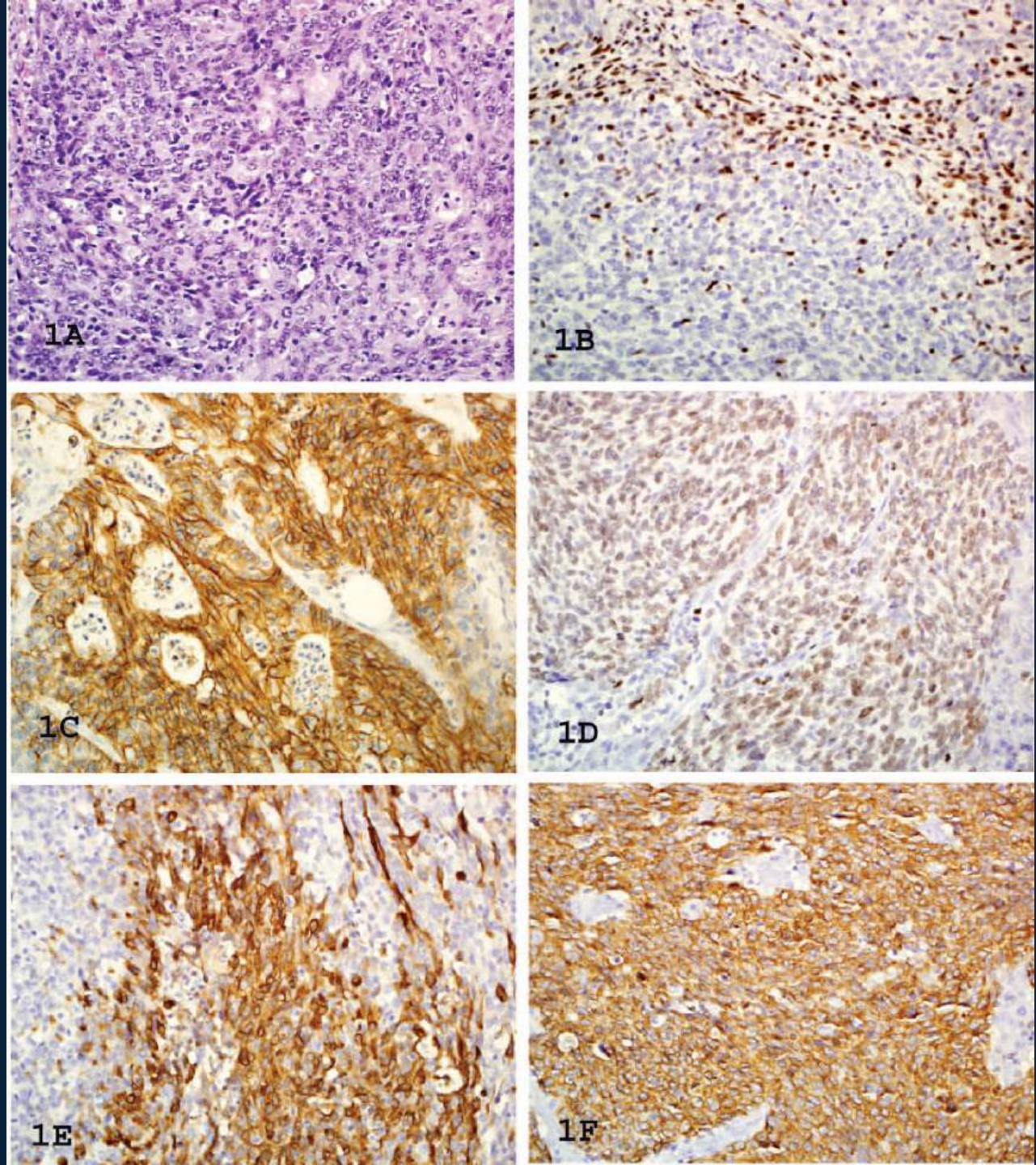
medullary carcinoma (case 16). Hematoxylin-eosin stain (A); loss of expression of MLH1 (B); positive for cadherin-17 (C), SATB-2 (D), TFF3 (E), MUC4 (F)

Arch Pathol Lab Med. 2014;138:1015–1026.



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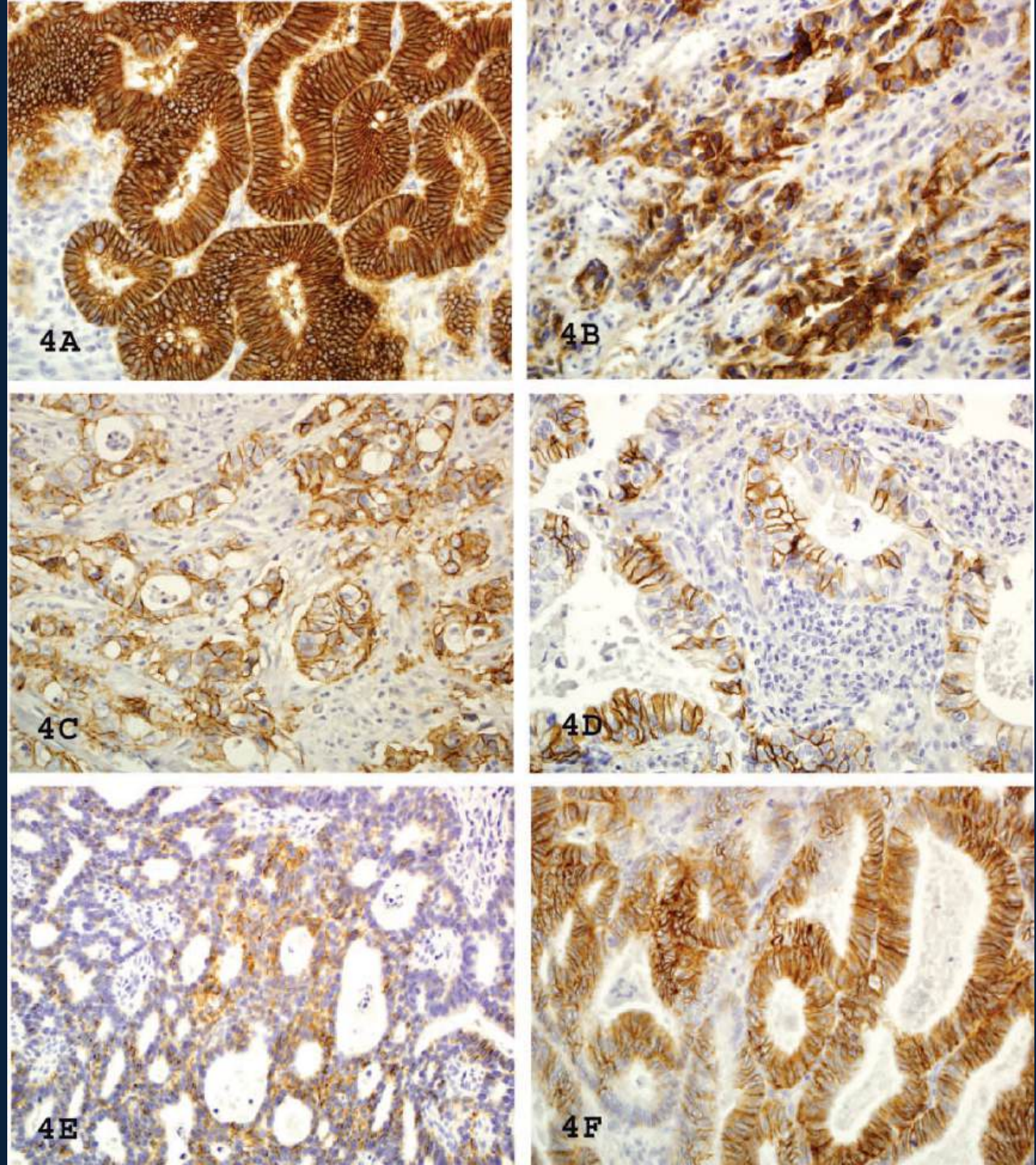
Cadherin-17 membranous staining of adenocarcinoma of the colon (A), esophagus (B), pancreas (C), lung (D), endocervix (E), and endometrium (F).

Arch Pathol Lab Med. 2014;138:1015–1026.



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BAP1

Tumor suppressor, BRCA-associated protein 1 (BAP1), located at 3p21.

Functions to inhibit cell proliferation and promote apoptosis of DNA damaged cells.

Expressed in most normal cells

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BAP1

Germline mutations in BAP1 have been associated with increased risk for malignant mesothelioma, melanoma, meningioma, RCC, lung adenoca, cutaneous SCC, BCC

BAP1 mutations have been demonstrated in non-hereditary mesotheliomas.

BAP1 IHC: prognostic value in uveal melanoma and renal cell carcinoma.

Loss of nuclear expression is abnormal; must have positive internal control cells for reliable evaluation.

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BAP1 IHC

TMA study: 0/49 benign mesothelial proliferations lost BAP-1.

0/37 benign proliferations lost BAP-1 or were positive for homozygous p16 deletion (FISH)

7/26 (27%) mesotheliomas lost BAP-1 by IHC

14/24 (58%) mesotheliomas lost BAP-1 or showed p16 deletion

Fluid Study: 15 paired mesotheliomas: 10/15 (67%) lost BAP1 in tissue and fluid CB.

12/15 biopsies (80%) and 8/11 fluids (73%) showed p16 deletion.

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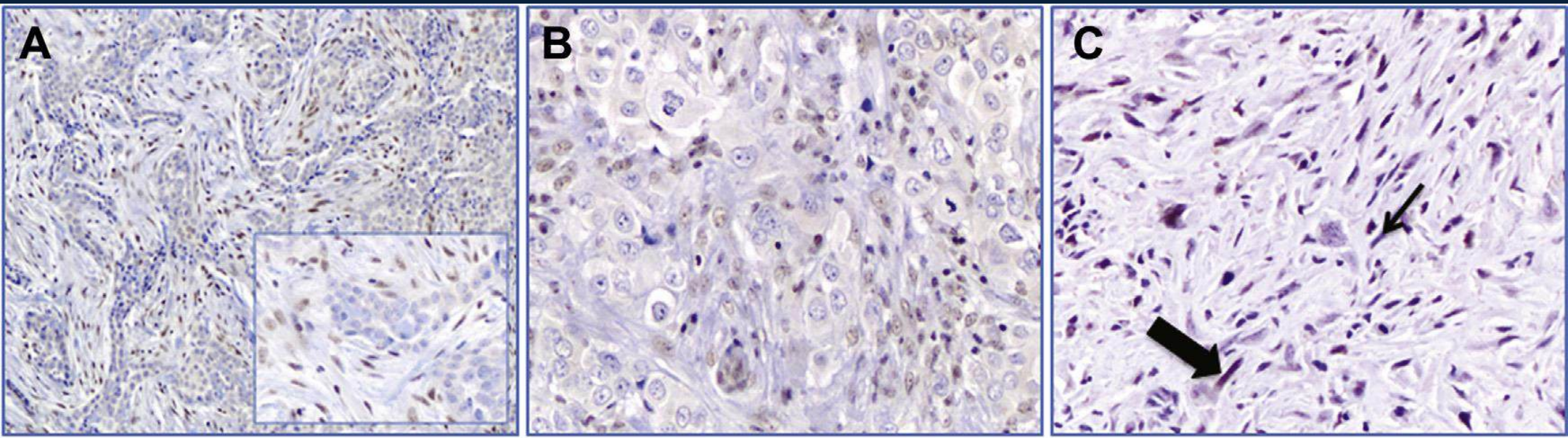
BAP1 IHC

Righi L, et al. (2016) studied 143 malignant pleural mesotheliomas.

67% lost nuclear expression; strong correlation with mutation.

Higher in epithelial vs sarcomatoid (22% lost in latter)

Biphasic tumors may show loss in epithelial component only.



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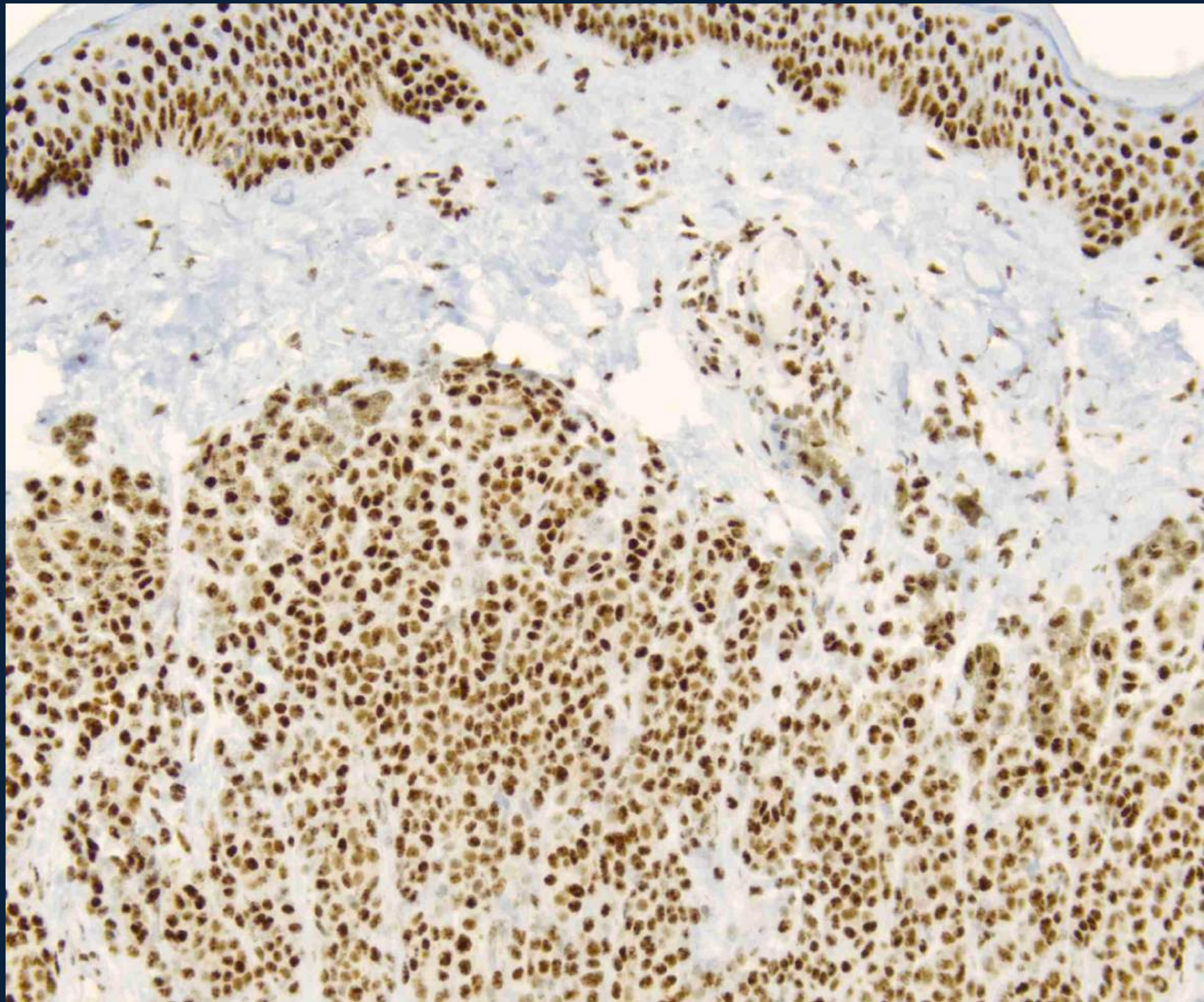
BAP1 Nevus Intact

Clone BSB-109



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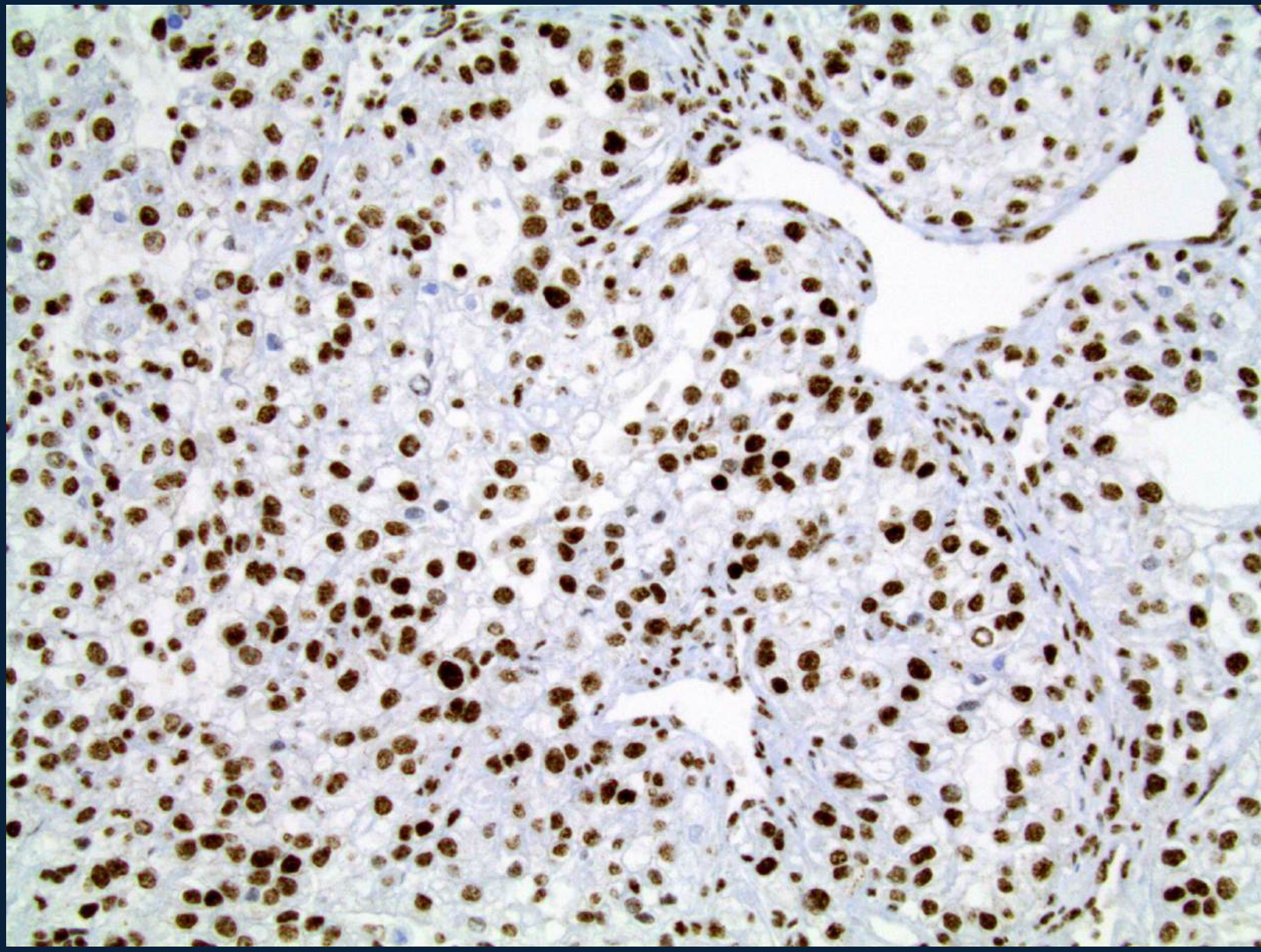
BAP1
RCC
intact



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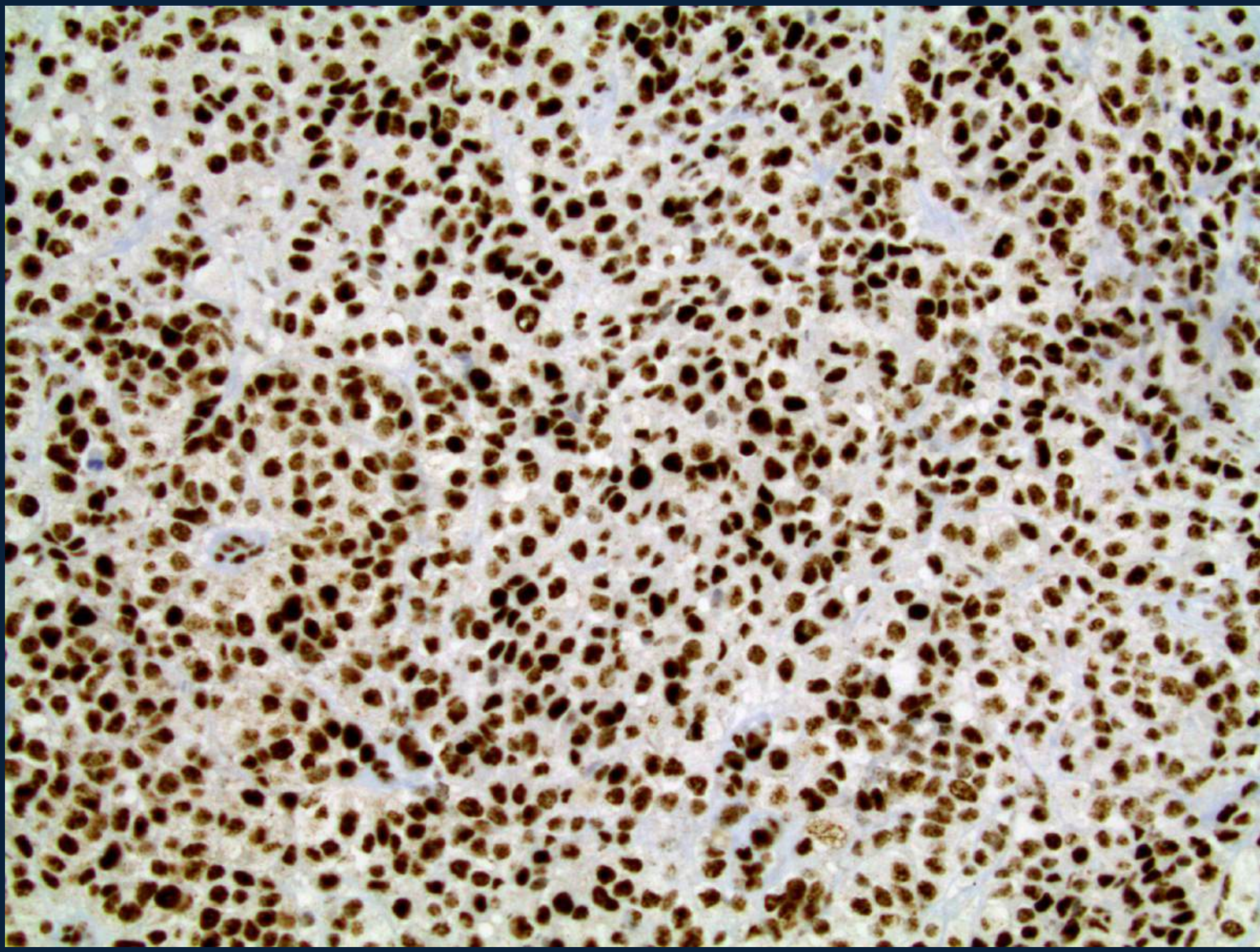
Metastatic Melanoma Intact/ retained



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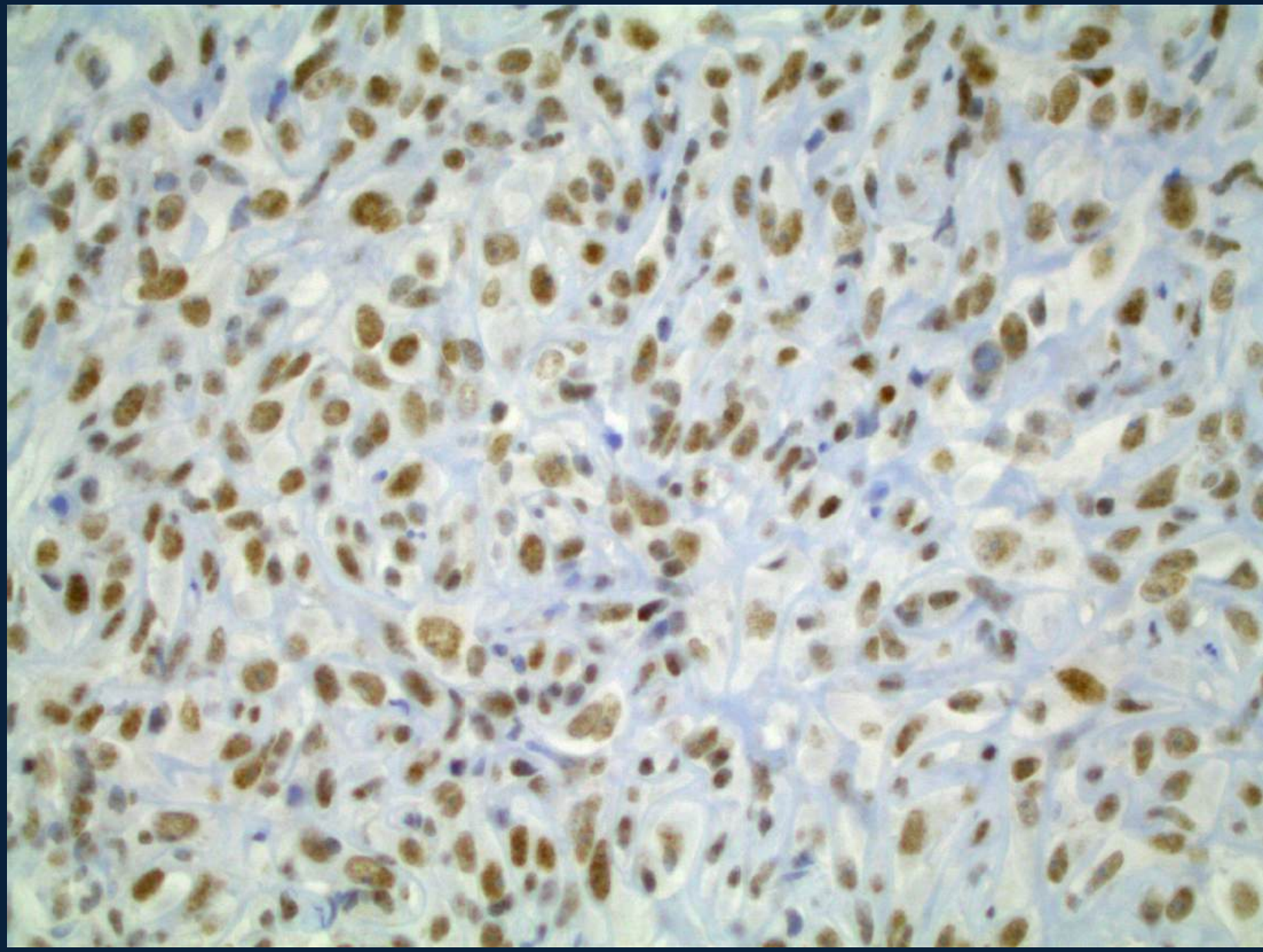
BAP1 mesothelioma retained



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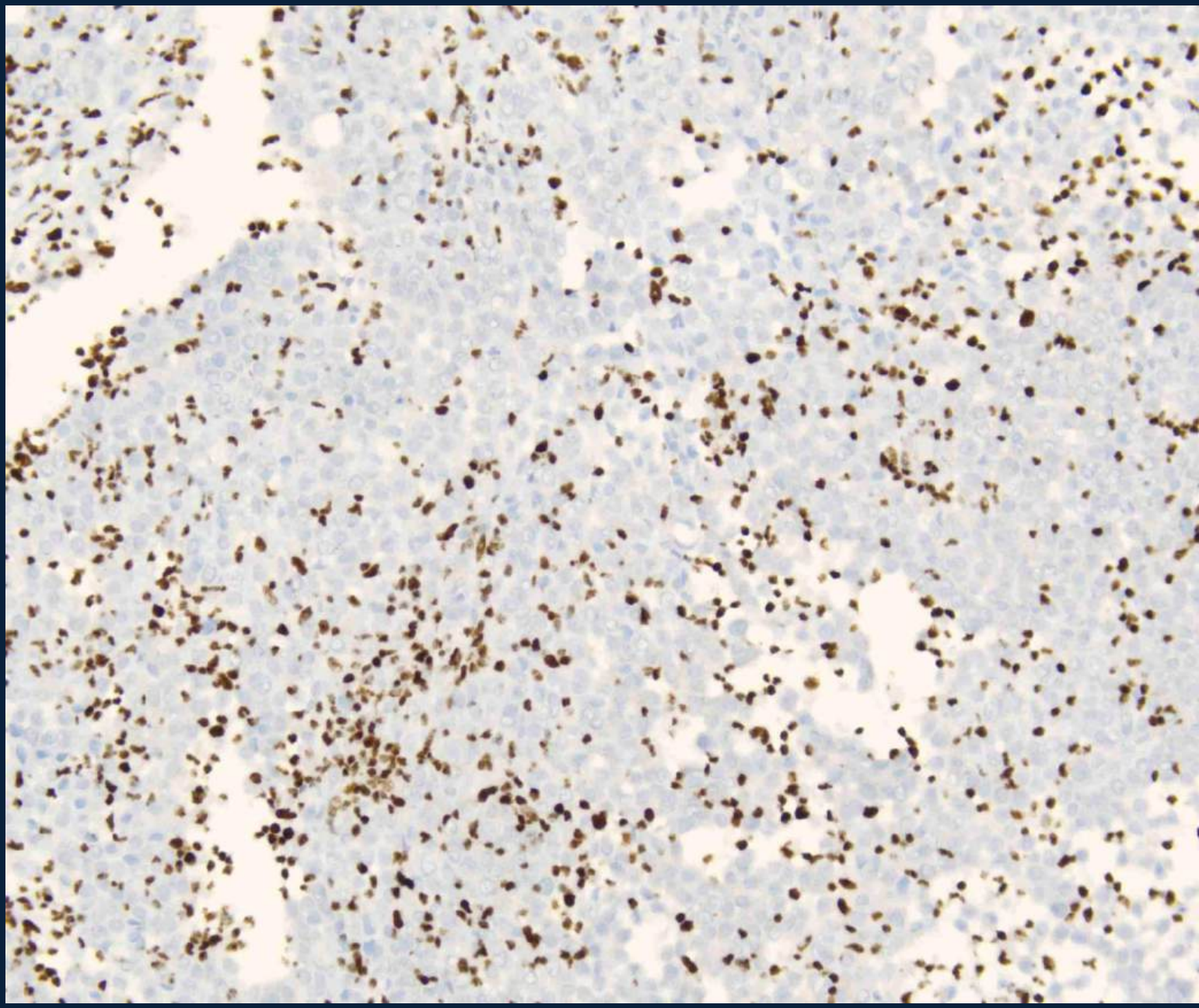
BAP1
Mesothelioma
Lost- biopsy
Note positive int.
Control cells



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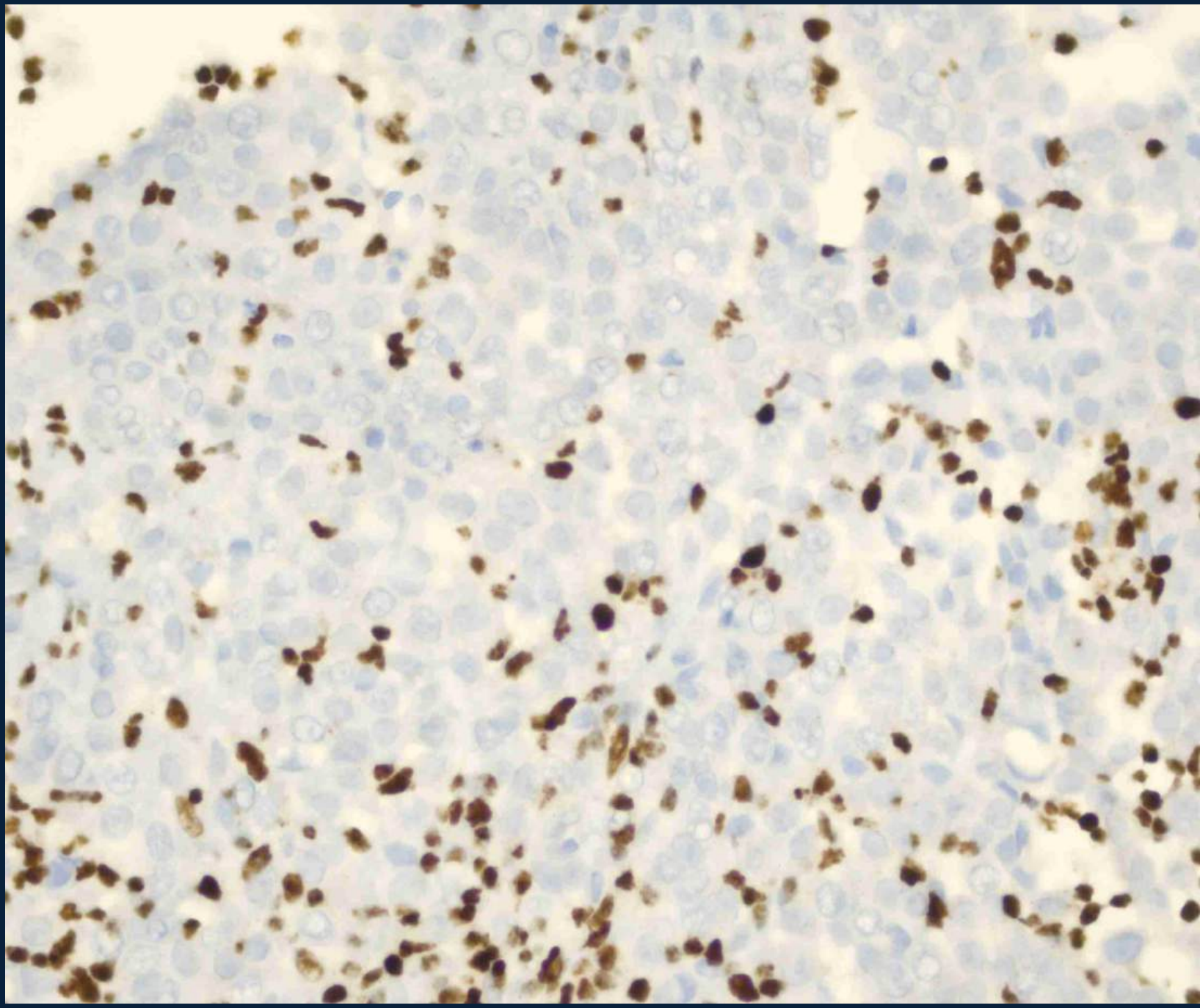
BAP1 Mesothelioma Lost- biopsy Sme case



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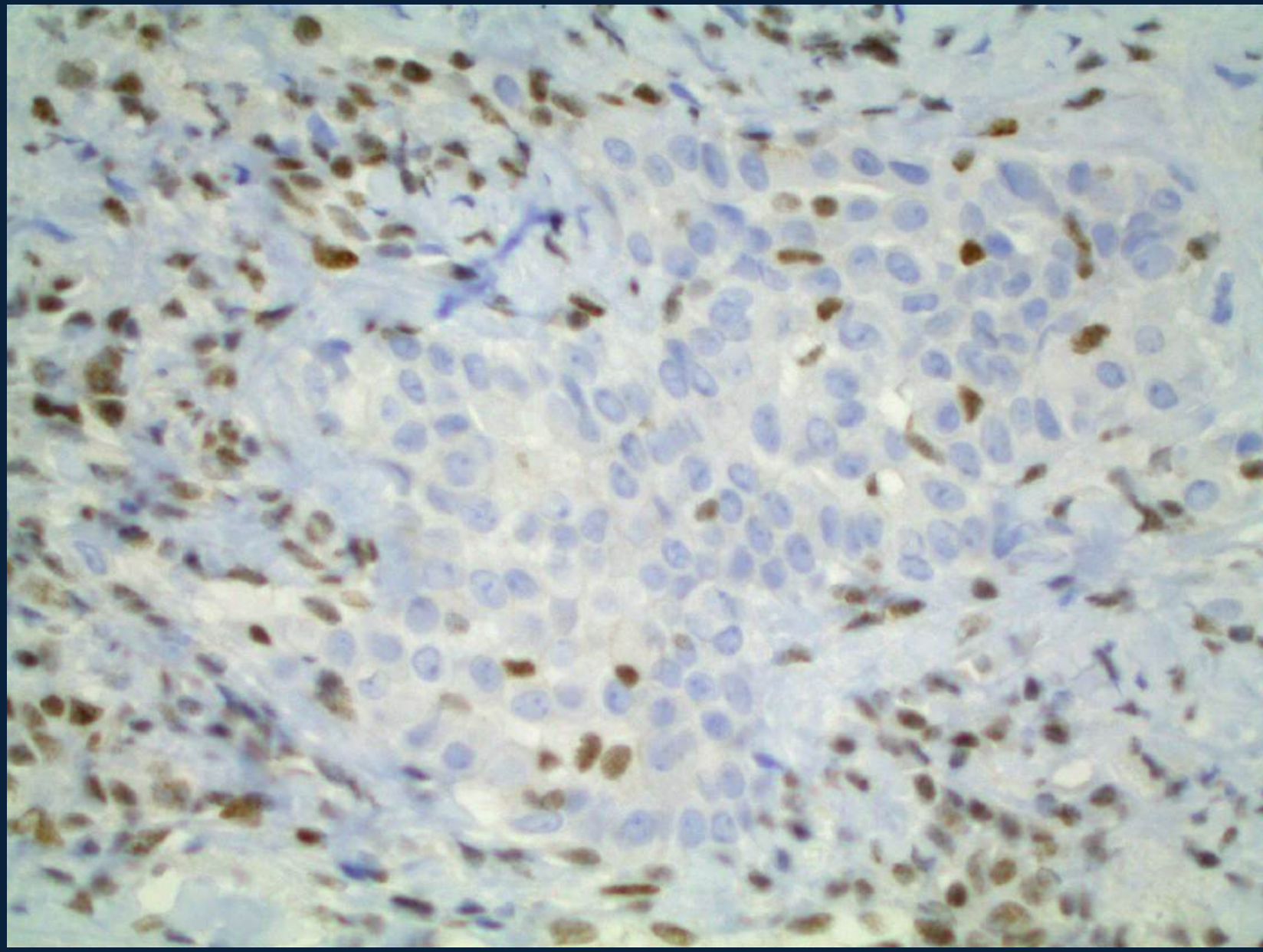
BAP1 Mesothelioma Lost- biopsy



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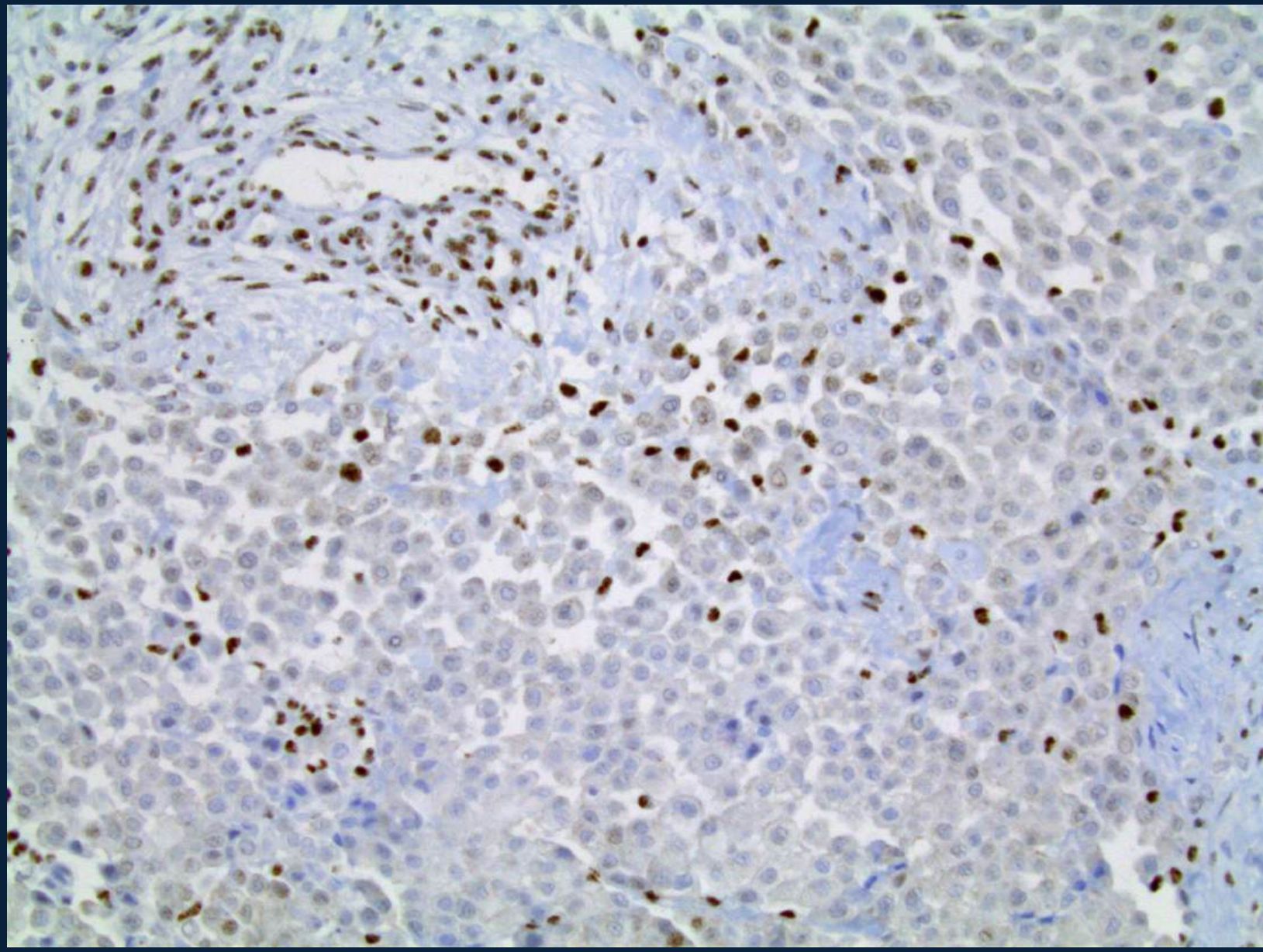
BAP1 Mesothelioma Lost- biopsy



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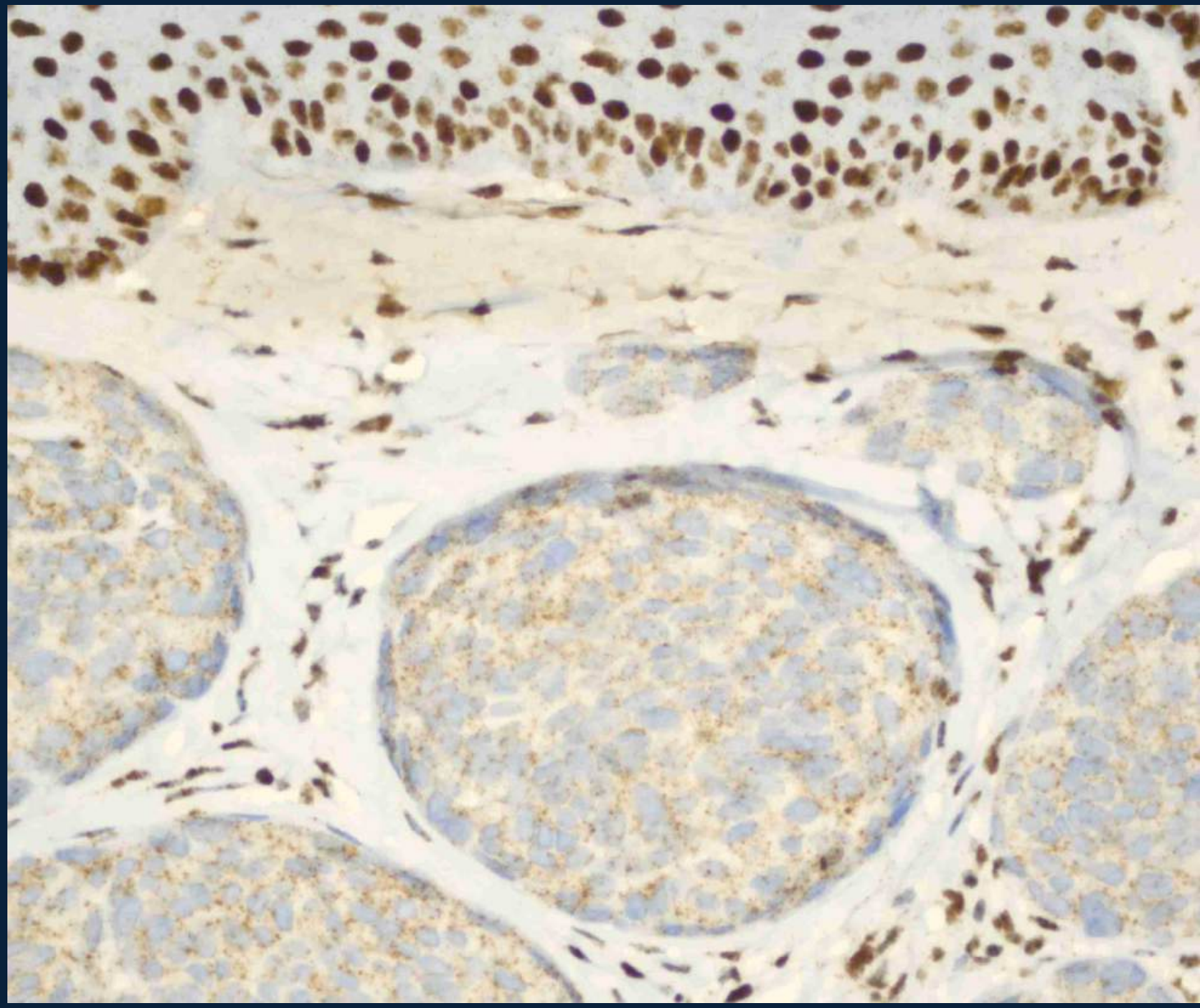
BAP1
Spitz nevus
Lost (clue to
Possible germline
in pts with multiple
Spitz nevi)



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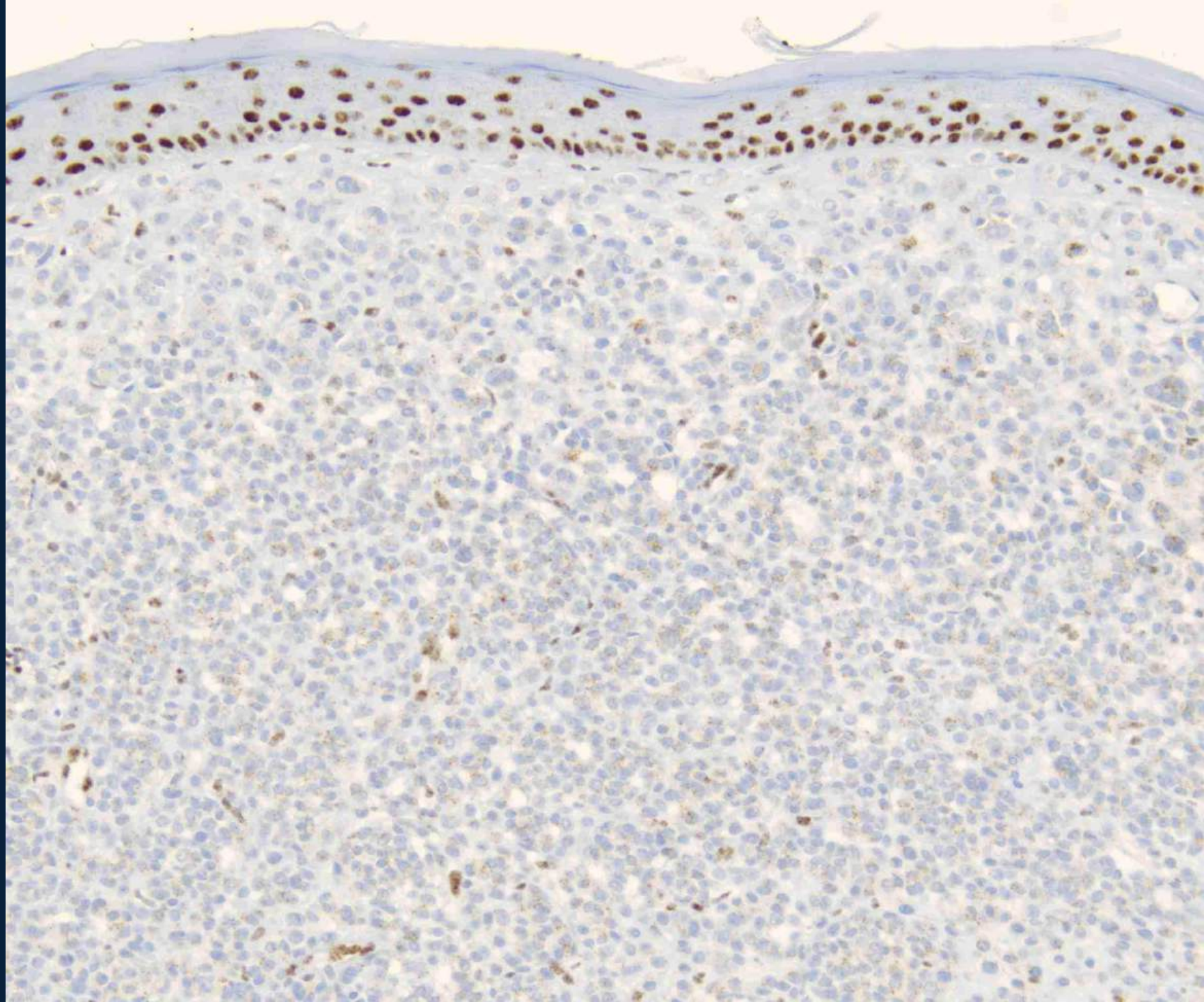
BAP1
Spitz
nevus
Lost



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BAP1: References

Hwang HC, et al. Utility of BAP1 Immunohistochemistry and p16 (CDKN2A) FISH in the Diagnosis of Malignant Mesothelioma in Effusion Cytology Specimens. Am J Surg Pathol. 2016;40:120–126.

Sheffield BS, Hwang HC et al. BAP1 Immunohistochemistry and p16 FISH to Separate Benign From Malignant Mesothelial Proliferations. Am J Surg Pathol. 2015;39:977–982)

Righi L, et al. BRCA1-Associated Protein 1 (BAP1) Immunohistochemical Expression as a Diagnostic Tool in Malignant Pleural Mesothelioma Classification: A Large Retrospective Study. Journal of Thoracic Oncology. Vol. 2016; 11 (11): 2006-2017

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INSM1

Insulinoma-associated protein, first isolated from pancreatic insulin producing tumors.

A zinc finger transcription factor expressed in NE cells, regulating synthesis of synaptophysin and chromogranin- pineal, pituitary, lung, skin, GI tract, pancreatic islets, adrenal medulla, thyroid C-cells, but not parathyroid.

Rosenbaum et al. assayed normal and neoplastic tissues by IHC in 2015.

Found in nearly all NE neoplasms except parathyroid tumors.

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Rosenbaum, JN. et al. A Novel Immunohistochemical and Molecular Marker for Neuroendocrine and Neuroepithelial Neoplasms. Am J Clin Pathol 2015;144:579-591

Table 1
INSM1 Is a Sensitive Immunohistochemical M and Neuroepithelial Neoplasms[a]

Neoplasm	Proportio No./Total
Neuroepithelial and NE neoplasms	
Carcinoid (lung)	6/6
Esthesioneuroblastoma	1/1
GI-NEN (GI carcinoid)	40[b]/42
Large cell NE carcinoma	2/2
Medullary thyroid carcinoma	2/3
Medulloblastoma	2/2
Merkel cell carcinoma	6/6
EMPSGC	1/1
NE carcinoma of breast	1/1
Neuroblastoma	3[b]/4
Pan-NEN	19[b]/21
Paraganglioma	9/9
Parathyroid adenoma	0/4
Parathyroid carcinoma	0/2
Pheochromocytoma	7/7
Pituitary adenoma	4/6
Pituitary carcinoma	3/3
PNET	1[c]/2
Retinoblastoma	2/2
Small cell carcinoma (lung)	3/3
Teratoma, immature	2[c]/2
Total	114/129
Non-NE neoplasms	
Adrenal cortical neoplasms	0/3
Breast adenocarcinoma	1/4
Colonic adenocarcinoma	0/2
Lung adenocarcinoma	0/2
Melanoma	0/4
Pancreatic carcinoma	0/3
Prostate adenocarcinoma	0/2
Thyroid carcinoma	0/4
Total	1/24
Neoplasms with NE differentiation recognized on H&E	
Colonic adenocarcinoma	1/1
Endometrioid carcinoma	1[c]/2
Prostate adenocarcinoma	2/2
Total	4/5

Table 2
Normal Adult Tissues Lacking Expression of INSM1 by Immunohistochemistry[a]

Tissue/Cell Type	No. of Slides Reviewed
Adnexa of skin	7
Adrenal cortex	7
Bone	6
Breast ductal epithelium	6
Brunner's glands	4
Cardiac muscle	1
Cartilage	5
Cerebellum	1
Cerebral cortex	2
Dermis	6
Endocardium	1
Endometrial glands	2
Endometrial stroma	2
Epithelium, unspecified	5
Exocrine pancreas	14
Glomeruli	2
Hair follicles	7
Liver	2
Lymphoid tissue	66
Olfactory epithelium	3
Optic nerve	2
Ovarian stroma	3
Pancreatic ductal epithelium	13
Parathyroid	3
Pleura	5
Pneumocytes	10
Prostate parenchyma	4
Renal tubular epithelium	2
Retina	2
Sclera	2
Seminiferous tubules	1
Serosa	2
Skeletal muscle	10
Squamous epithelium	9
Sustentacular cells	8
Thyroid	5
Urothelium	2

[a] Expression of INSM1 was evaluated on nonneoplastic tissue immunohistochemistry stain in the course of evaluating nec slides. INSM1 could not be detected in any of the listed tiss Blood vessels, smooth muscle, fibroconnective tissue, nerv consistently negative for INSM1 expression.

Rosenbaum, JN. et al. Am J Clin Pathol 2015;144:579-591

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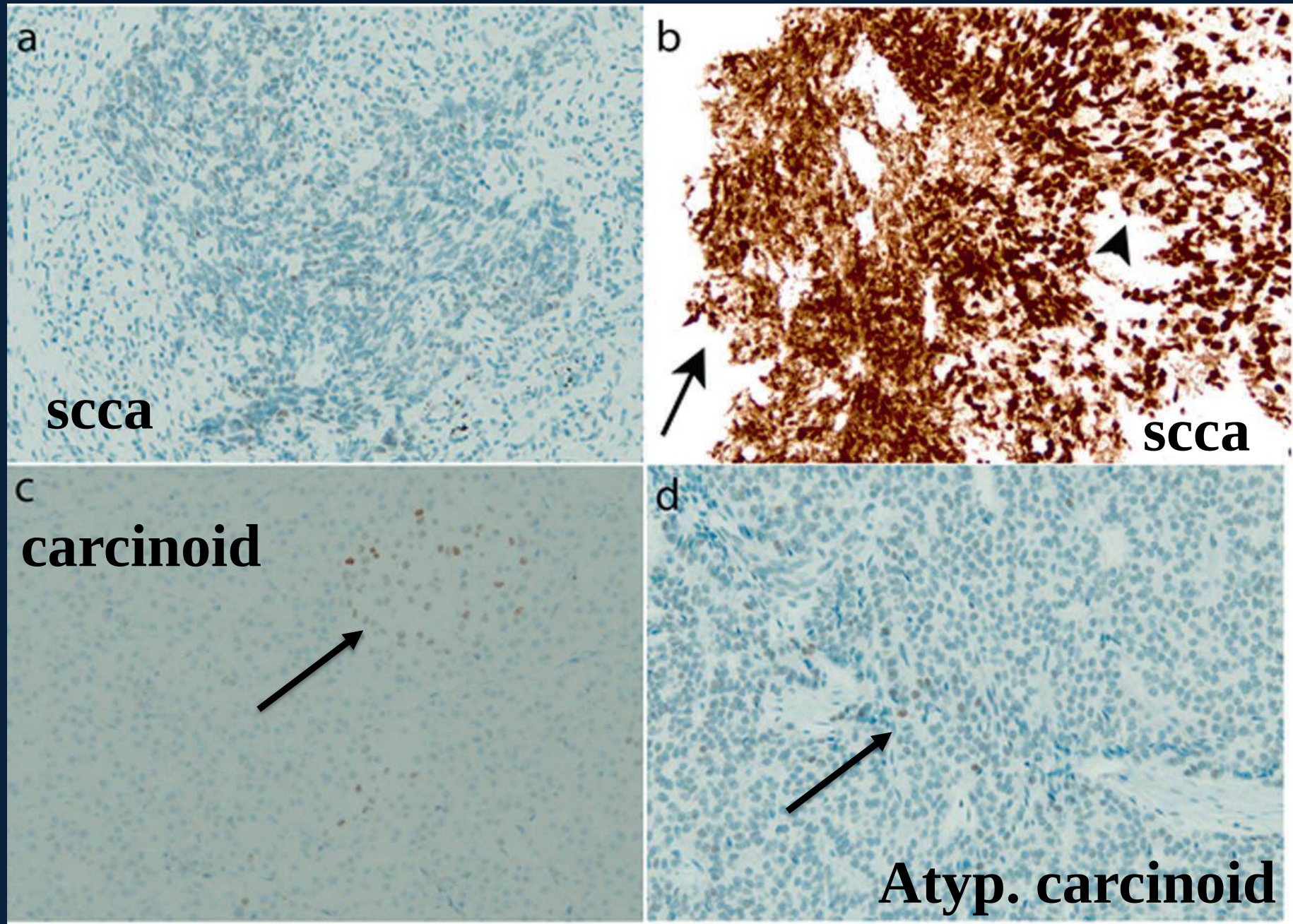
INSM1

Mukhopadhyay S, et al. Modern Pathology; July, 2018



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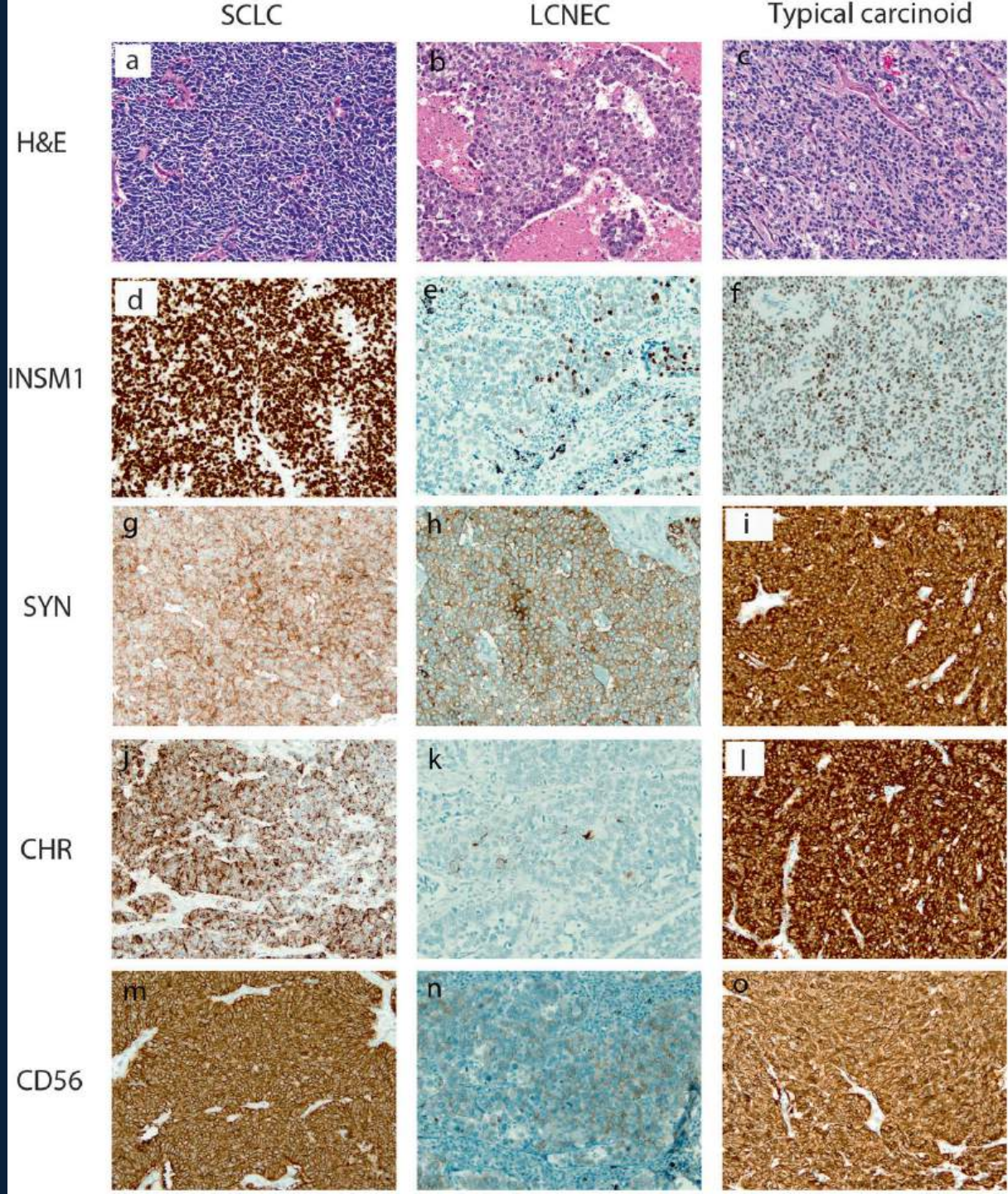
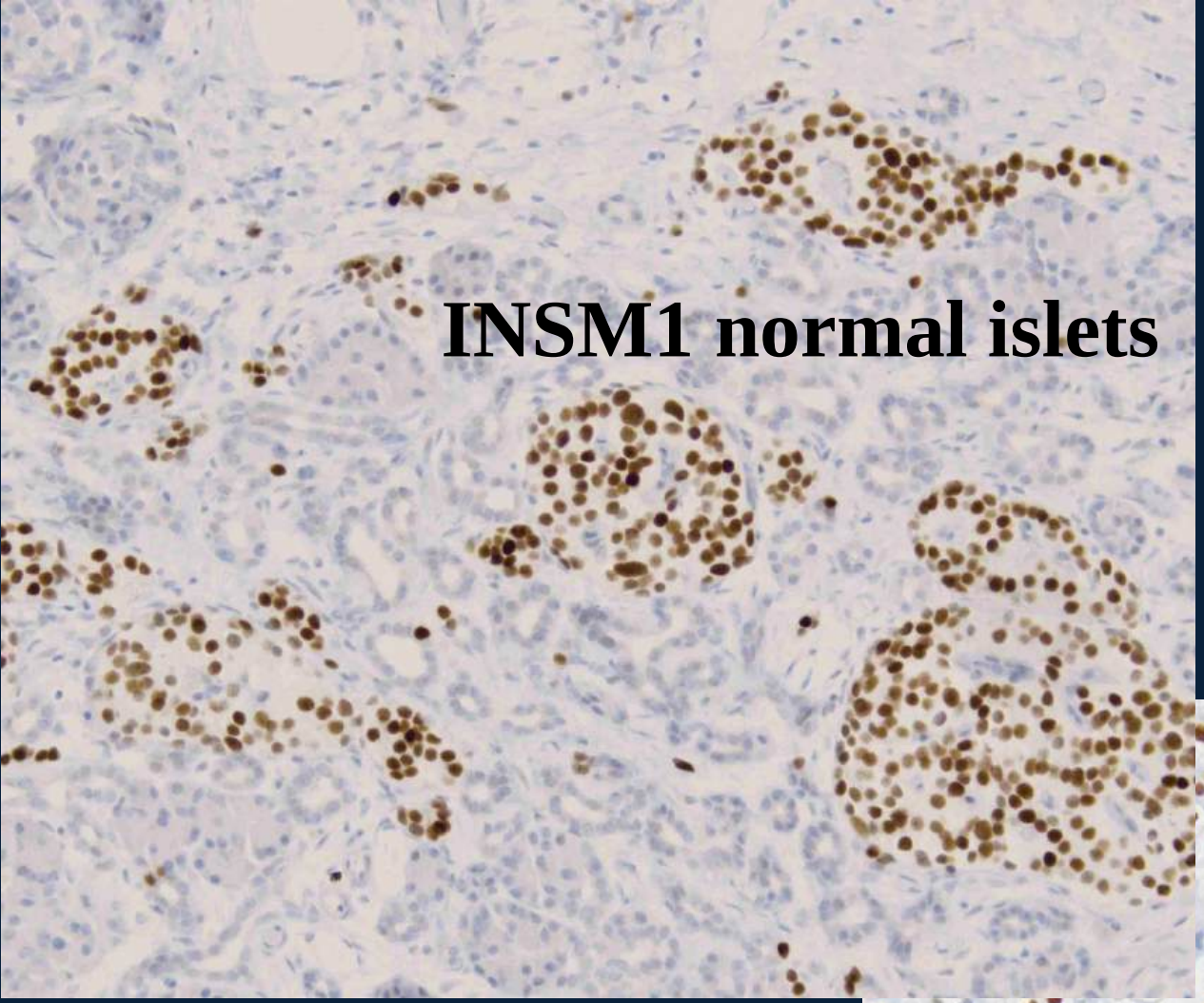
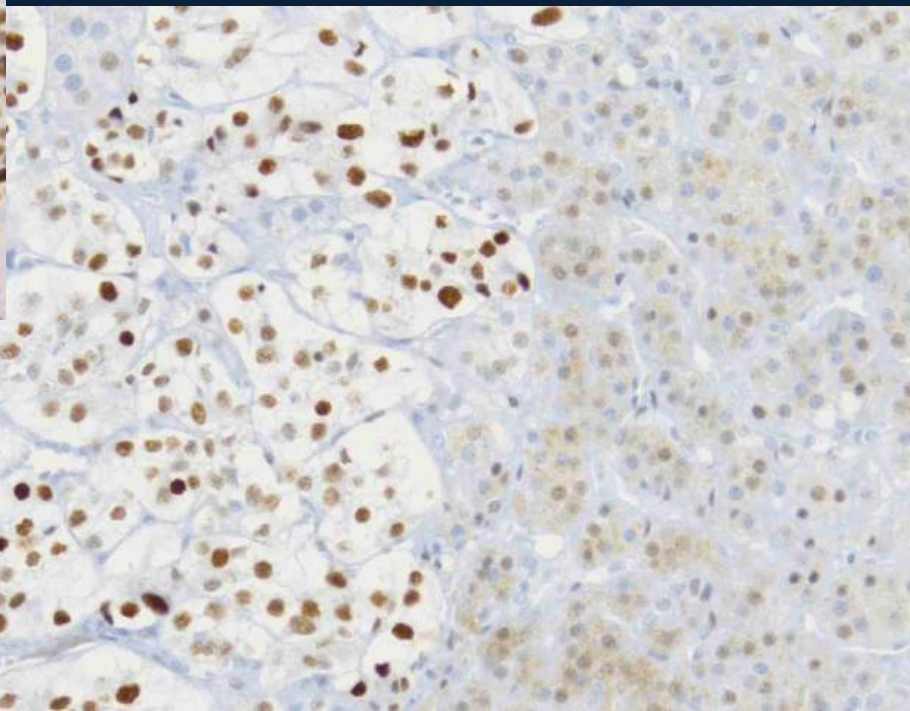
INSM1

Mukhopadhyay S, et al.
Modern Pathology; July, 2018

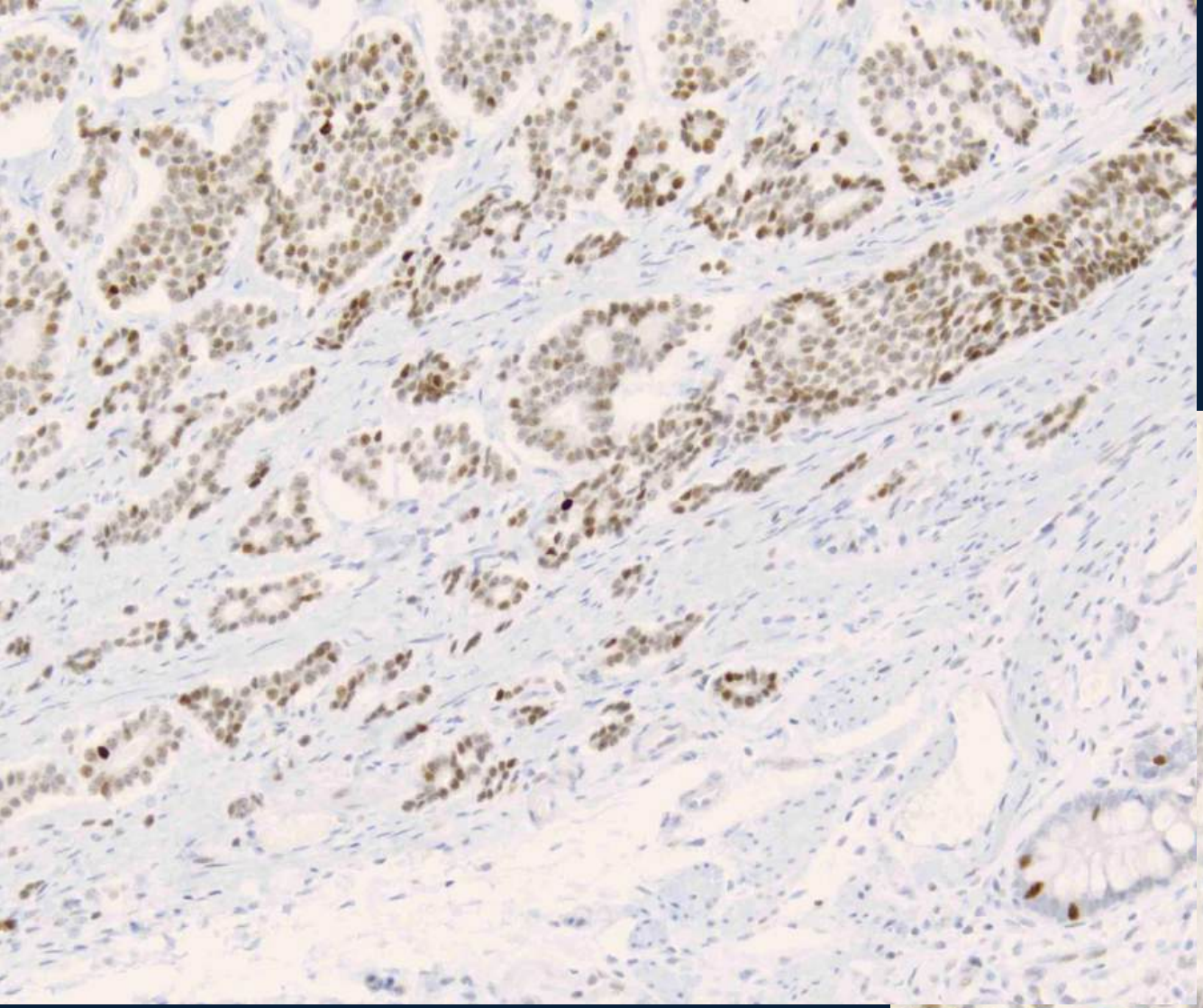


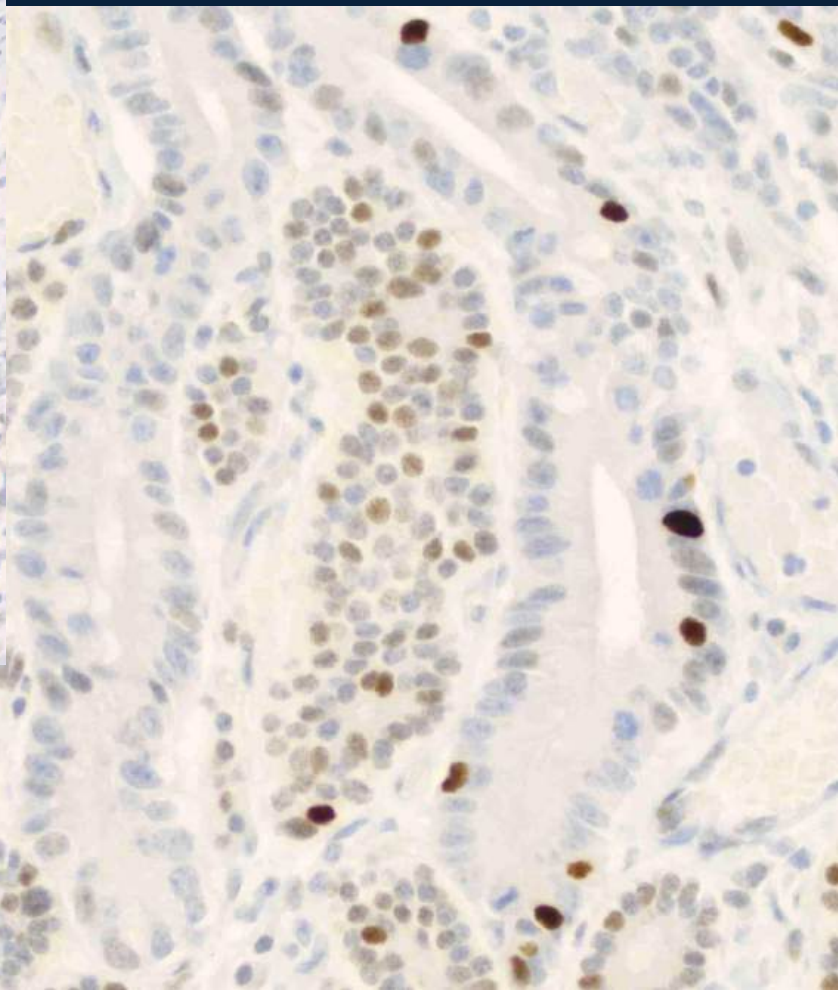


Medulla Cortex

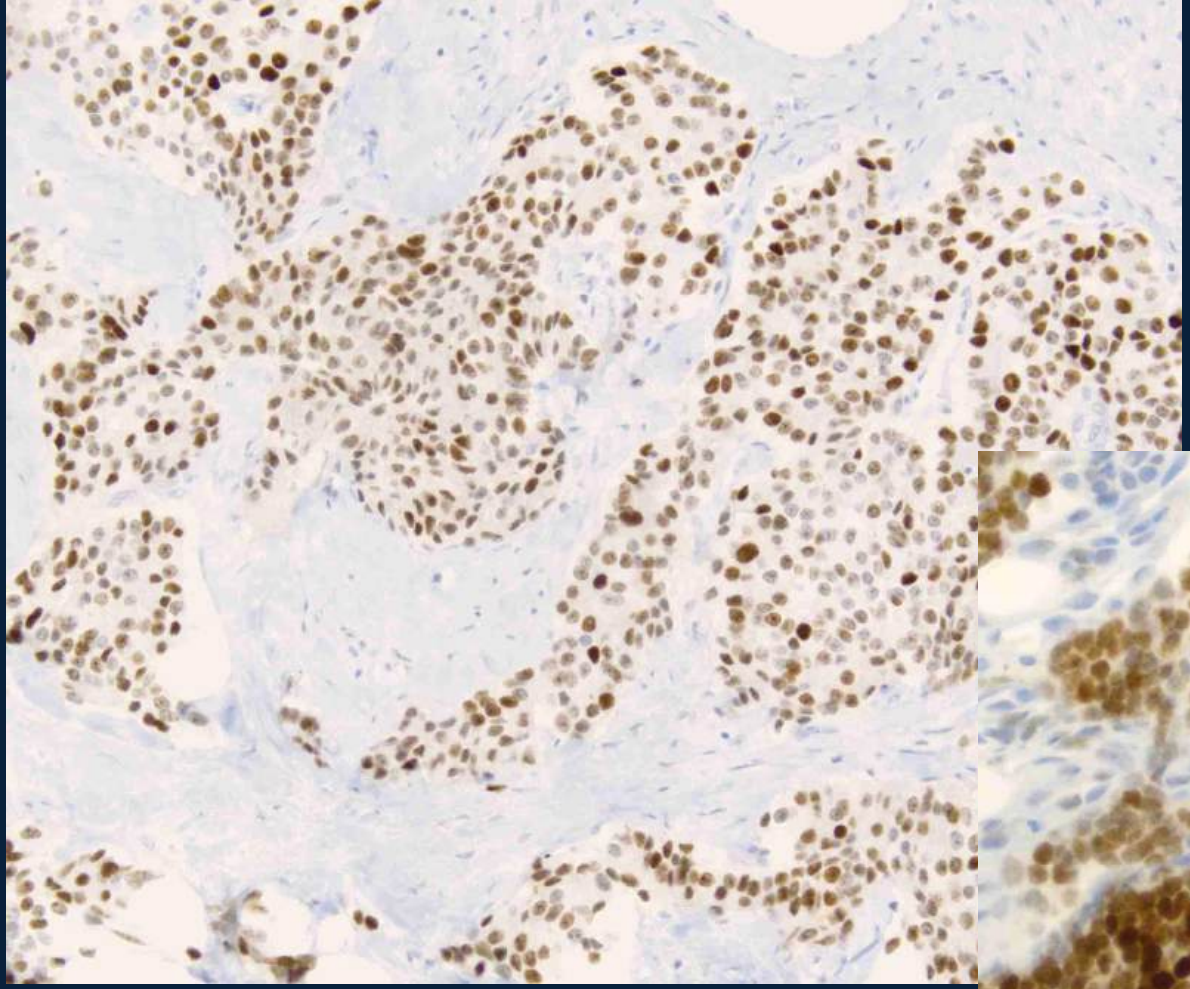


INSM1 normal adrenal
Clone A8

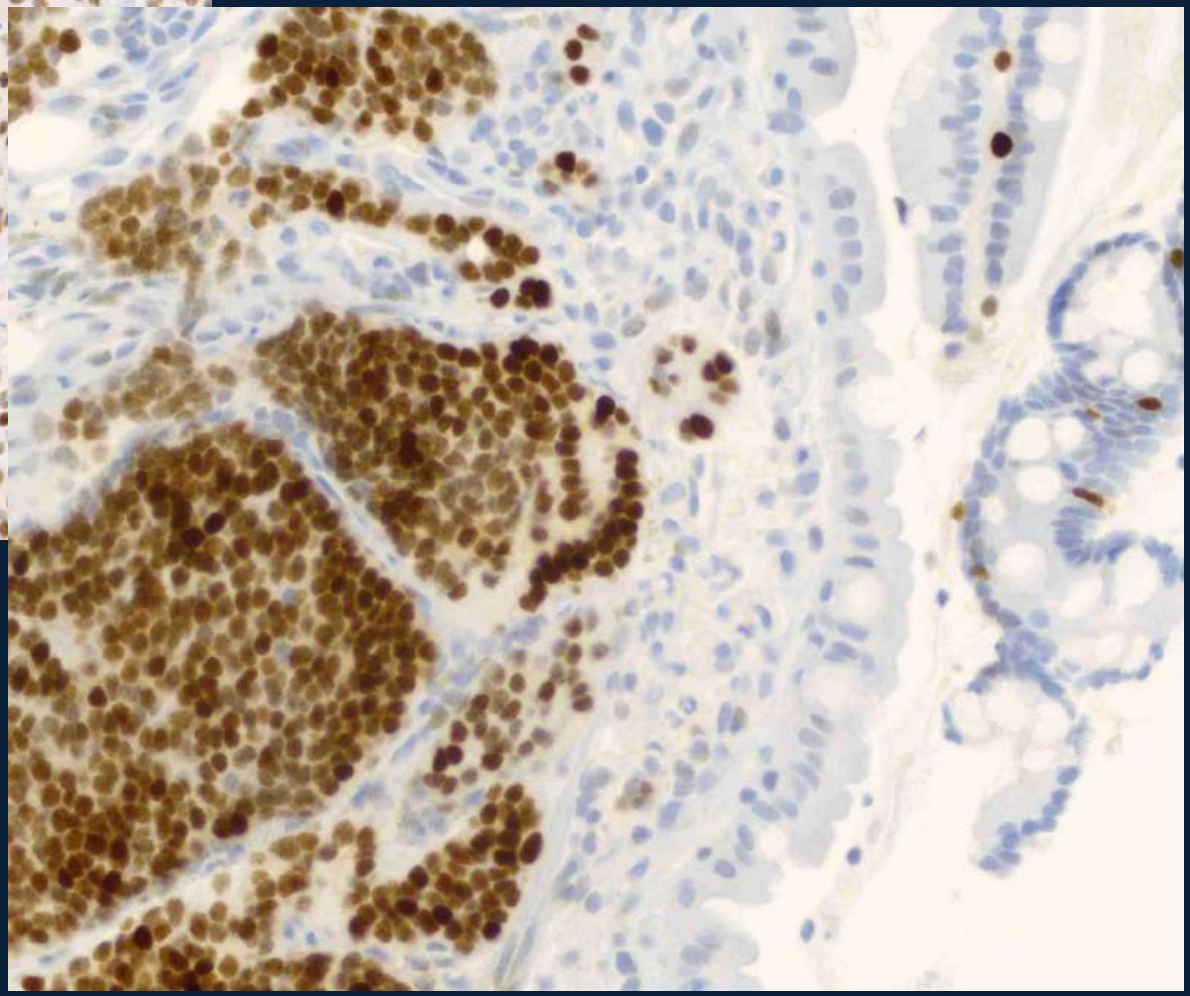




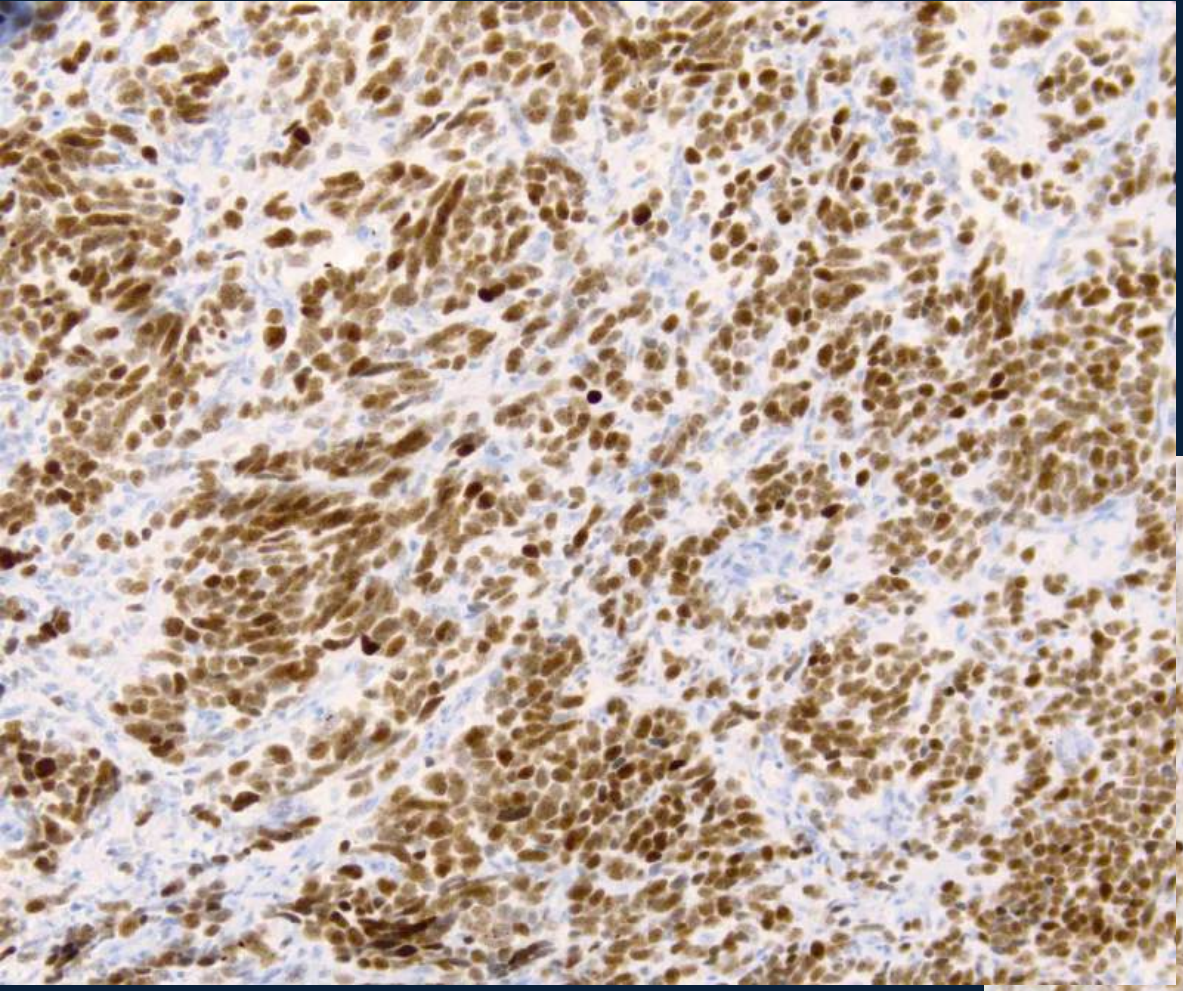
INSM1- Grade 1 NET
Small bowel



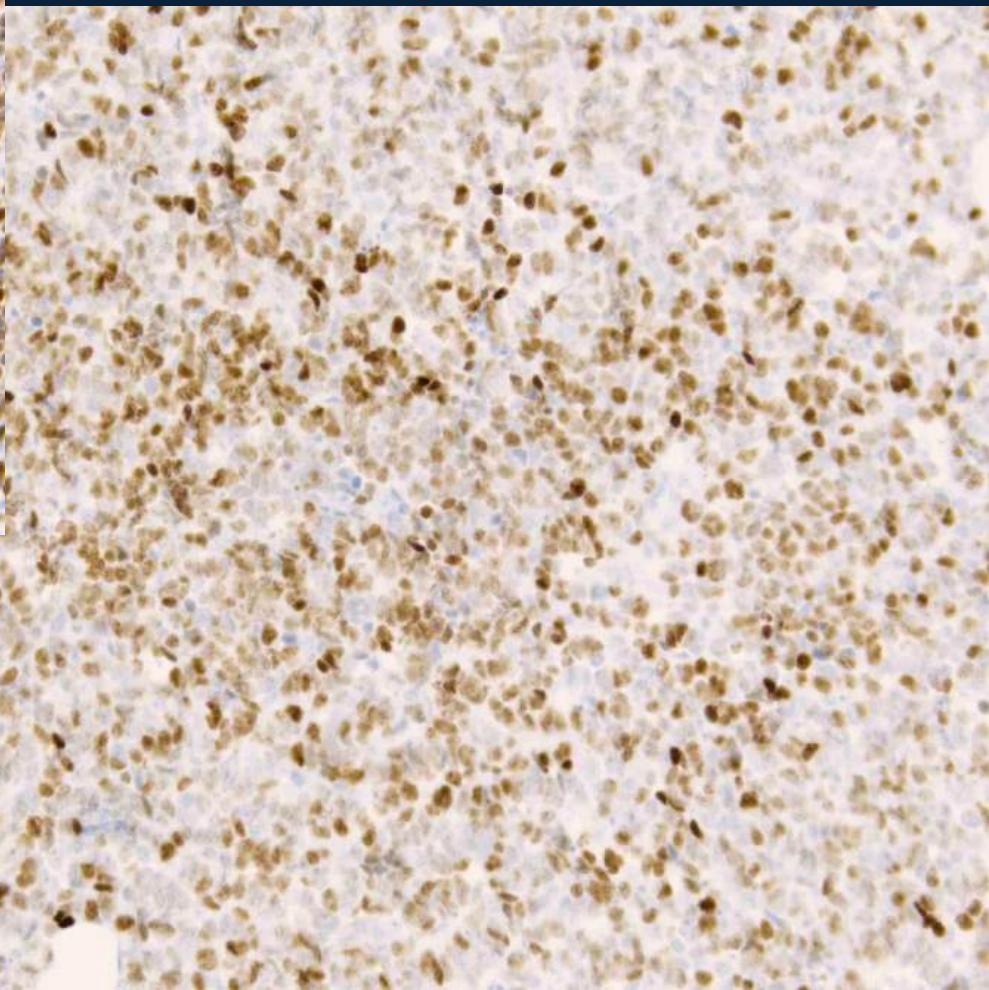
INSM1- Grade 2 NET pancreas



INSM1- Grade 1 NET duodenum



INSM1- grade 2 NET lung; atypical carcinoid



INSM1- LCNEC lung

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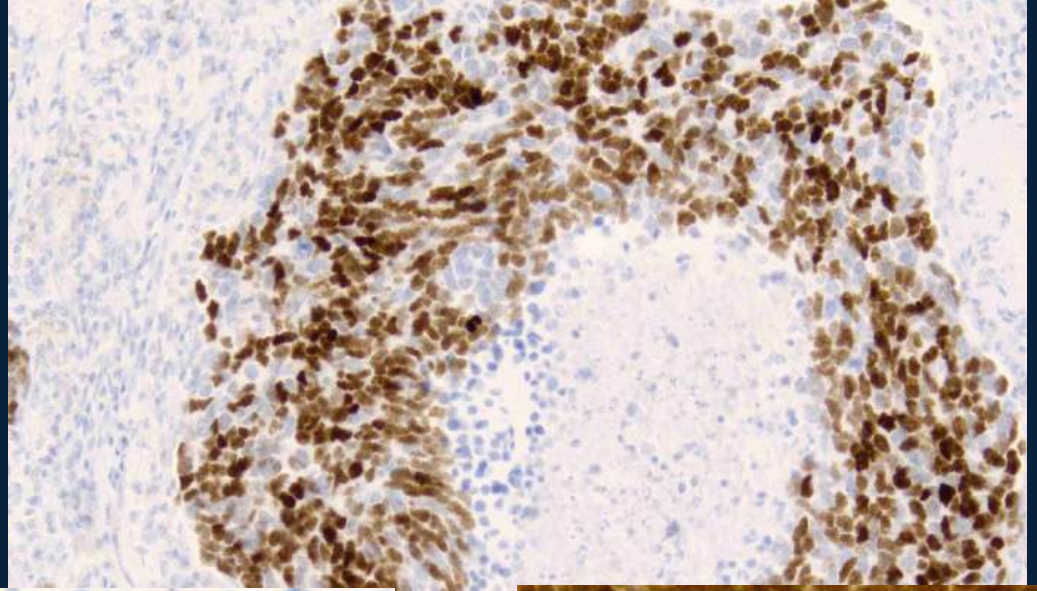
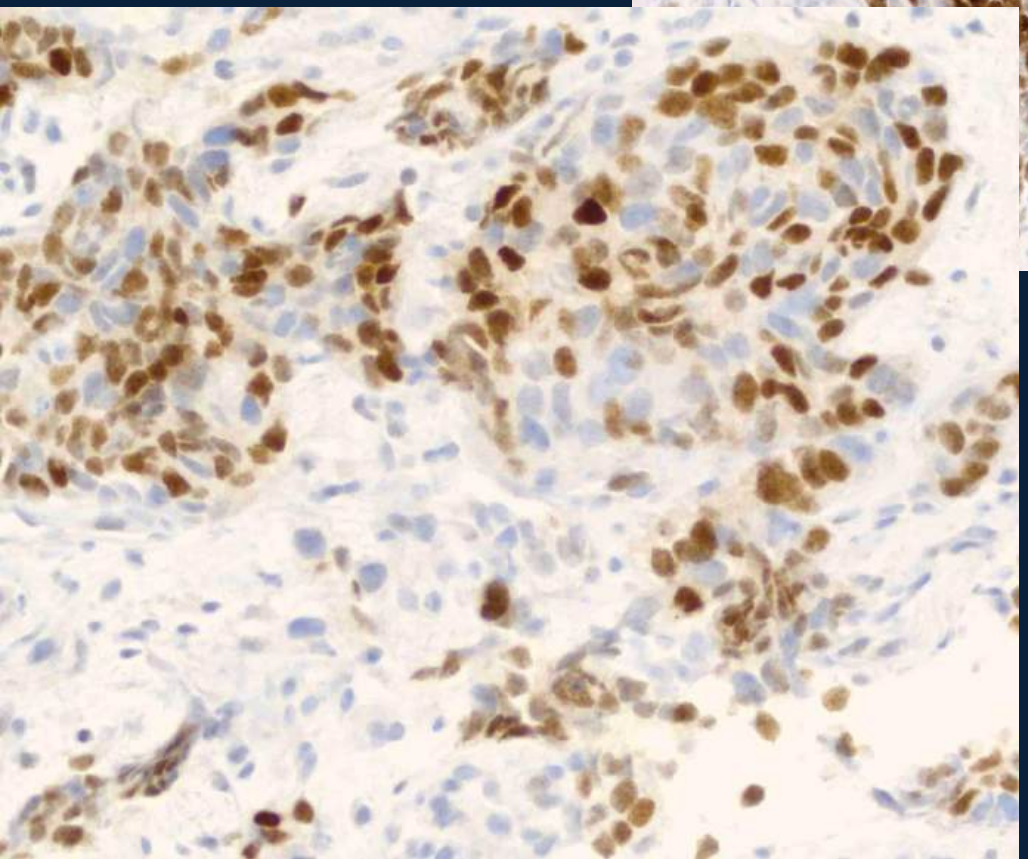
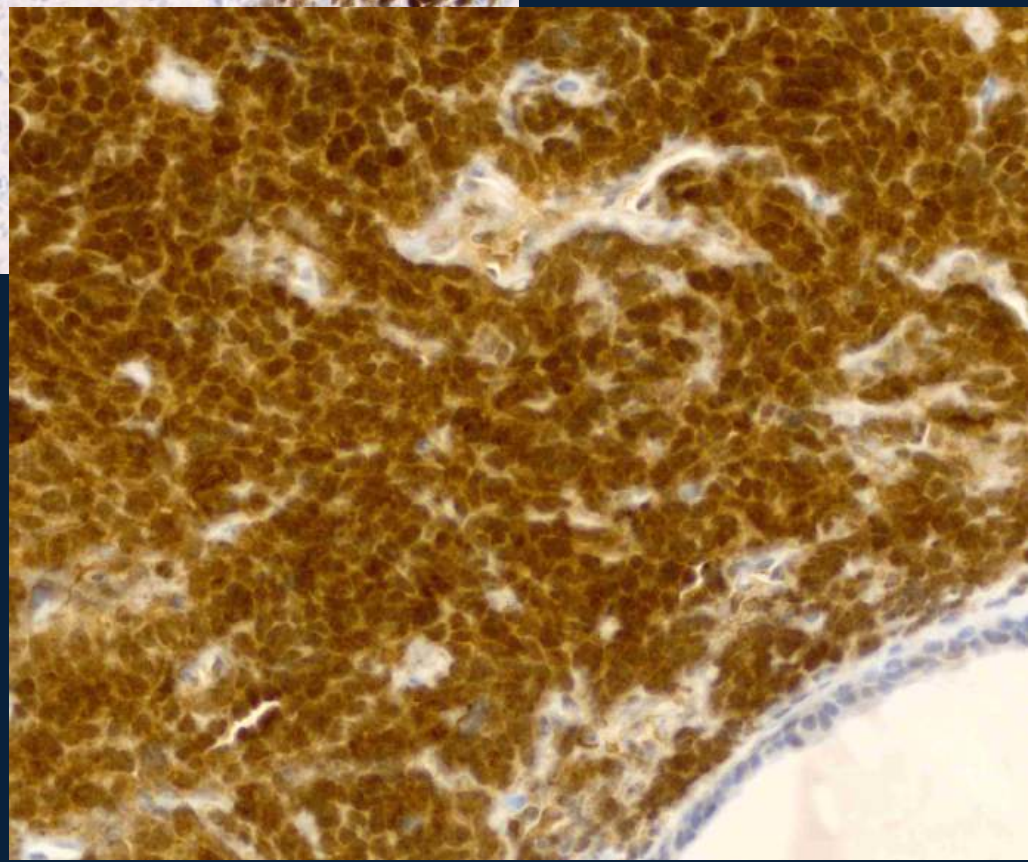
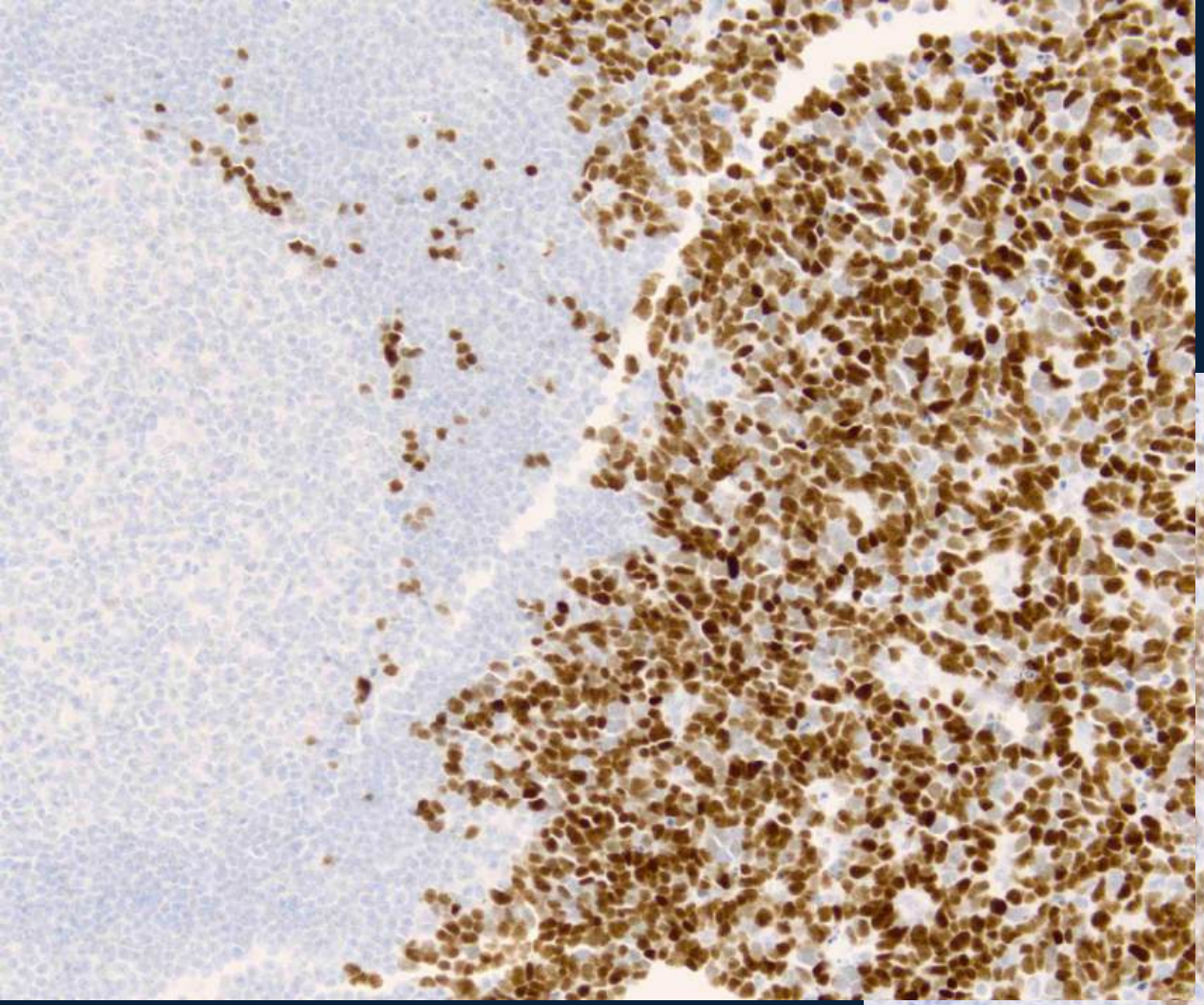
INSM1- small cell ca lung

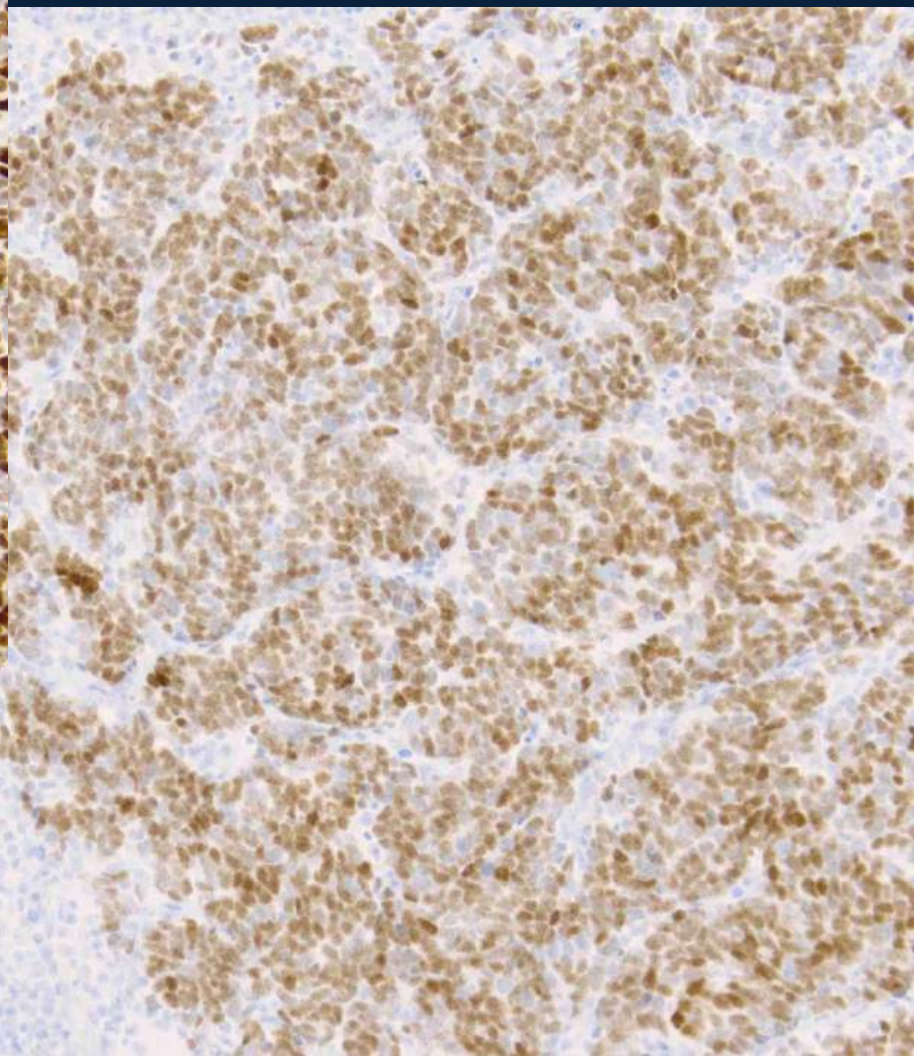


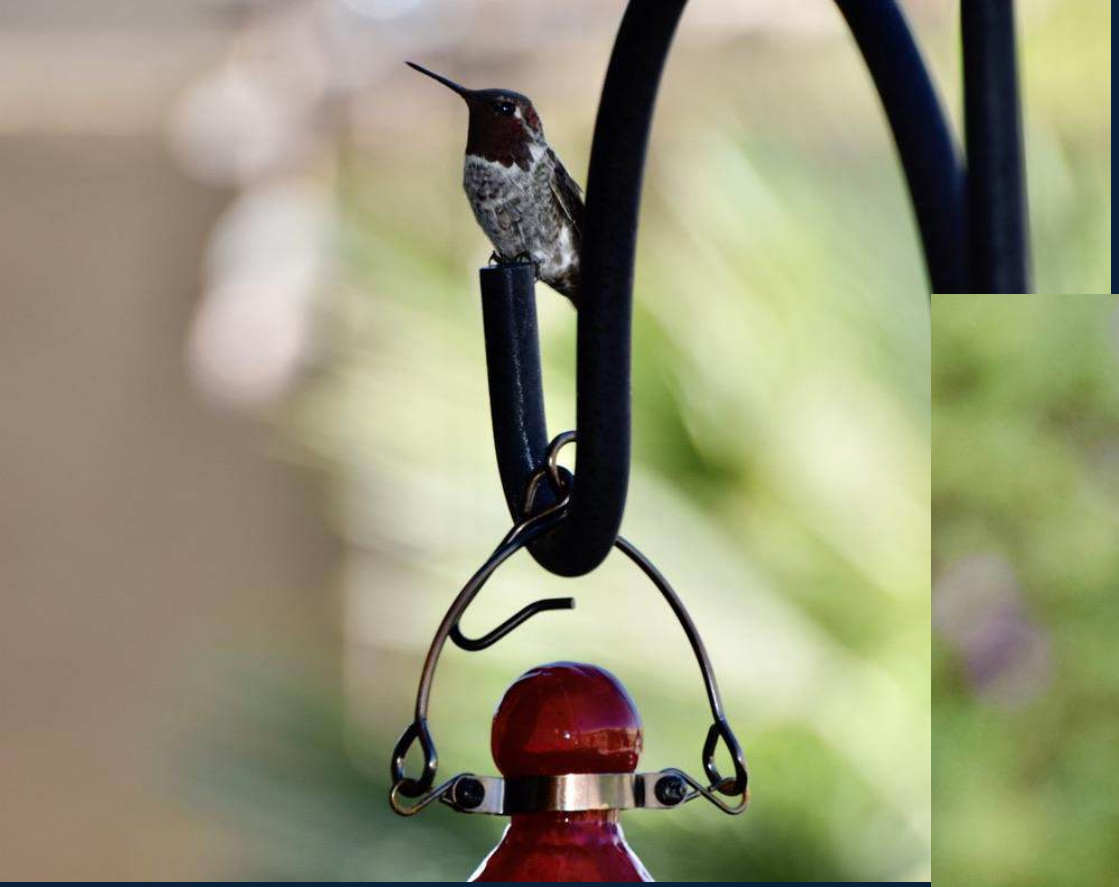




INSM1- Merkel cell ca







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LEF1: Lymphoid enhancer-binding factor 1

Expressed on T cells and pro-B cells but not mature B-cells

Aberrantly expressed in the neoplastic B-cells in majority of CLL/SLL (95-100%).

Nearly all cells should be positive; nuclear labeling only; must correlate with HE, results of other markers as % reactive T-cells vary

Not expressed in vast majority of other small lymphocytic neoplasms, mantle cell or marginal zone lymphoma, follicular lymphoma.

Expressed in subset of AML, ALL's, a subset of DLBCL and many solid malignancies.

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LEF1

Bevan T, Peterson L, et al. Nuclear overexpression of lymphoid-enhancer-binding factor 1 identifies chronic lymphocytic leukemia/small lymphocytic lymphoma in small B-cell lymphomas. Mod Pathol. 2011 Nov;24(11):1433-43.

290 lymphoid tumors analyzed:

92/92 (100%) SLL/ CLL cases positive, including 2 CD5 negative tumors. Virtually all neoplastic cells were immunoreactive.

All 53 mantle cell, 31 LG follicular and 31 MZ (3 CD5 +) lymphomas were negative.

In 12 grade 3 follicular lymphomas: 5-15% of tumor cells positive

DLBCL: 27/71 (38%) were LEF1 positive

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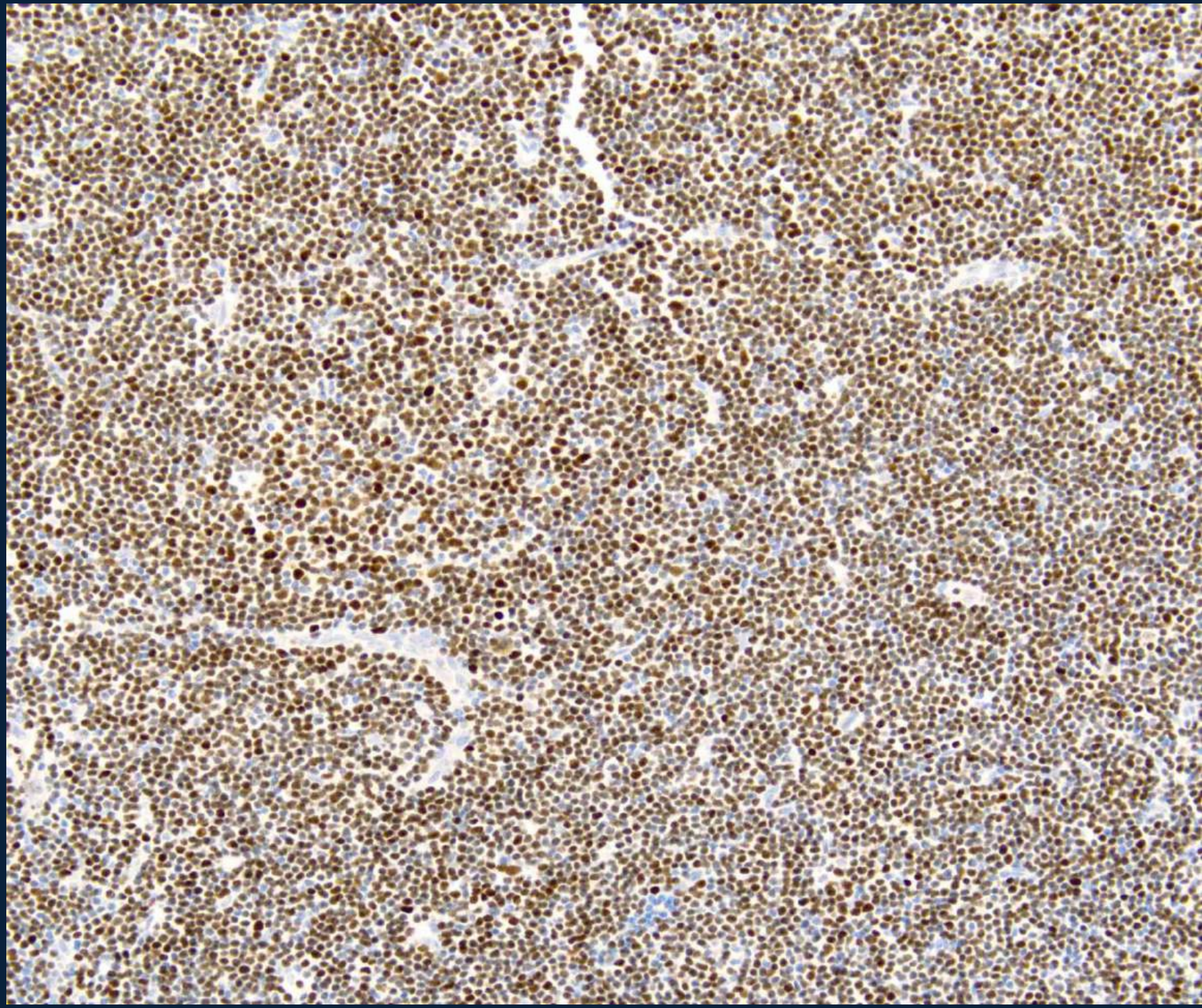
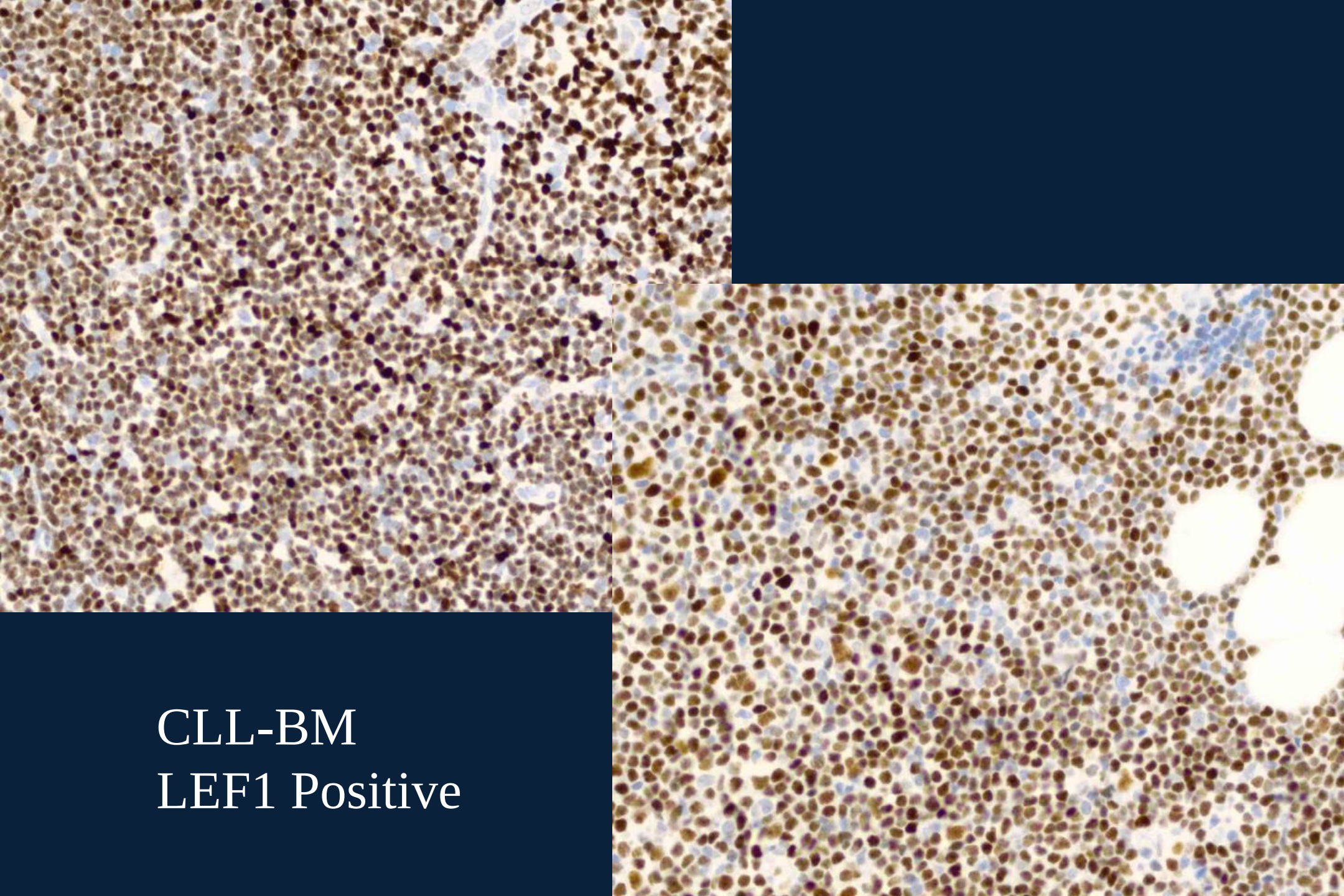
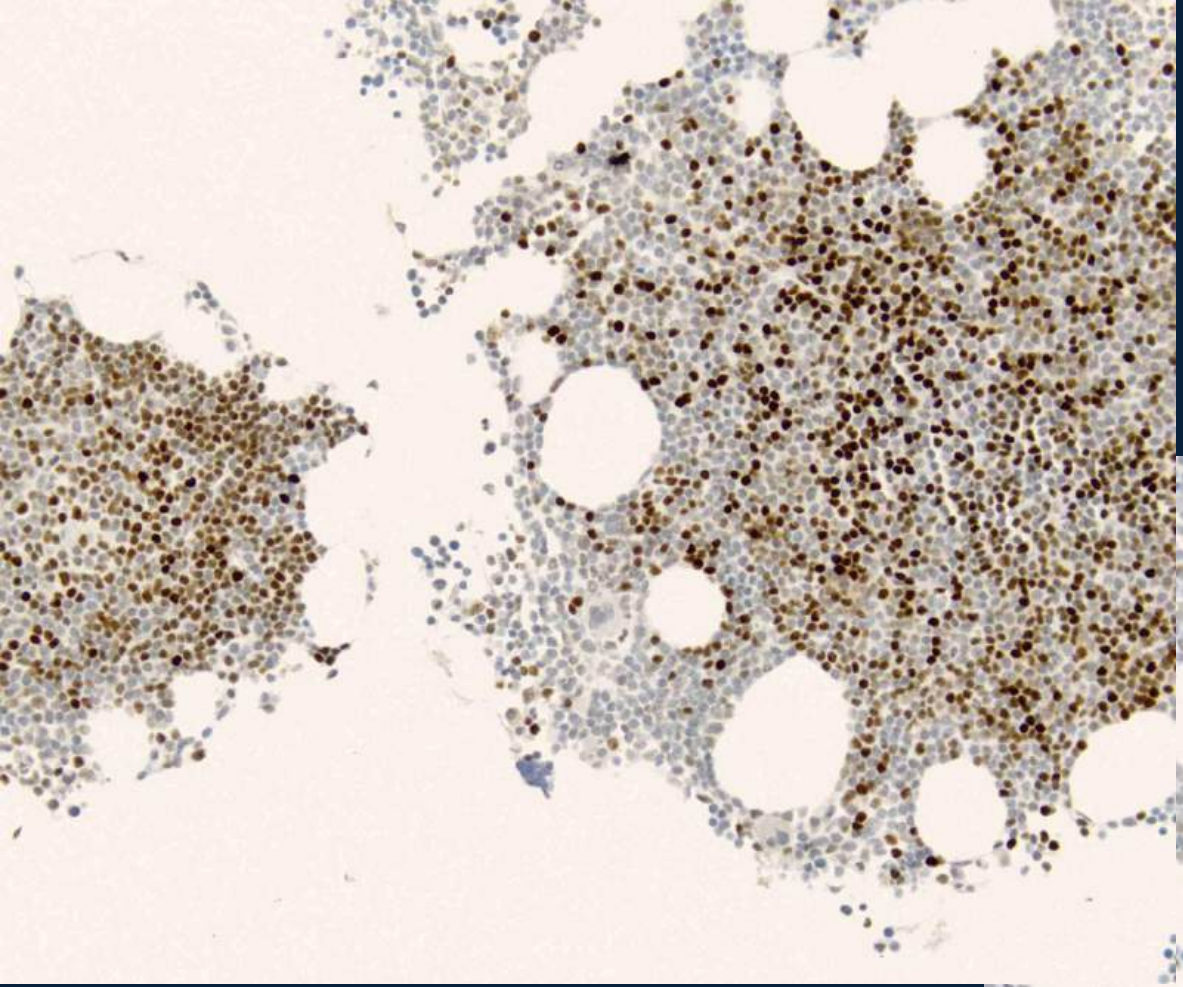
CLL-LEF1 lymph node bx RM clone EP310

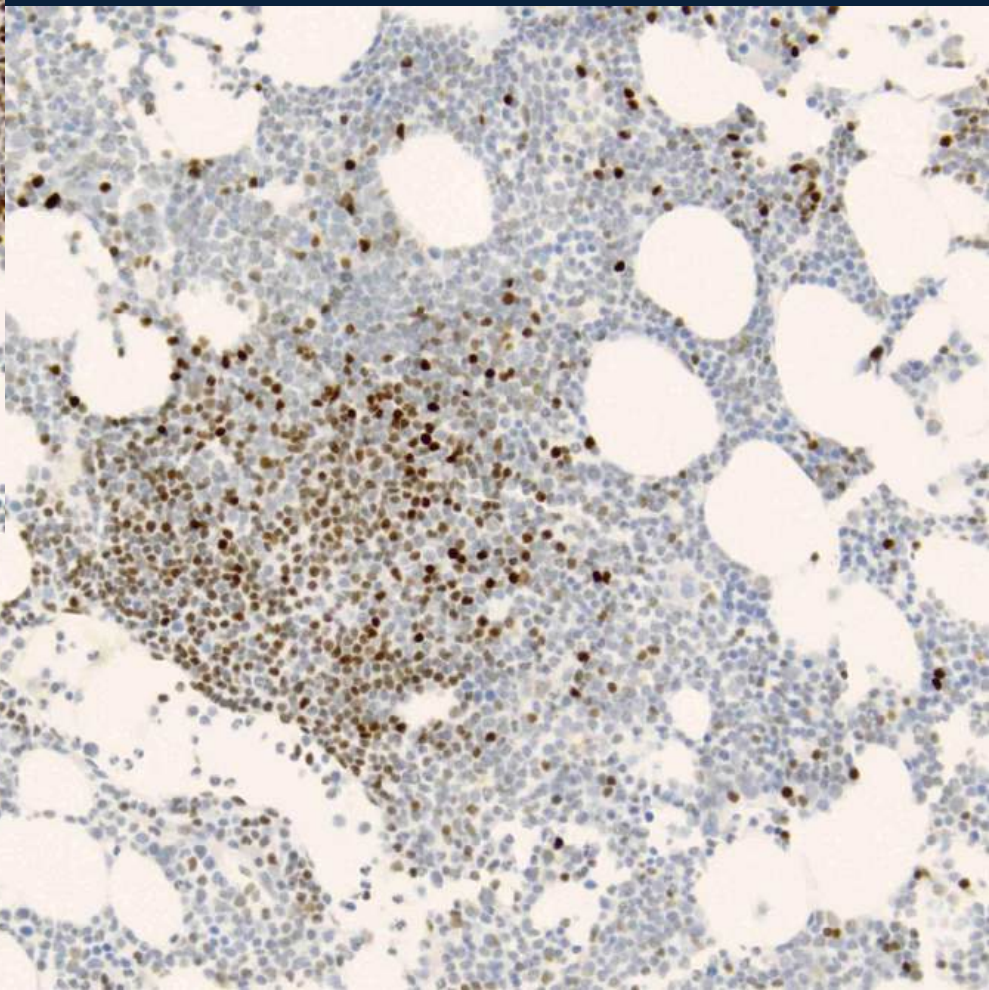




CLL-BM
LEF1 Positive



BM Bx



BM Clot

CLL-LEF1
Positive

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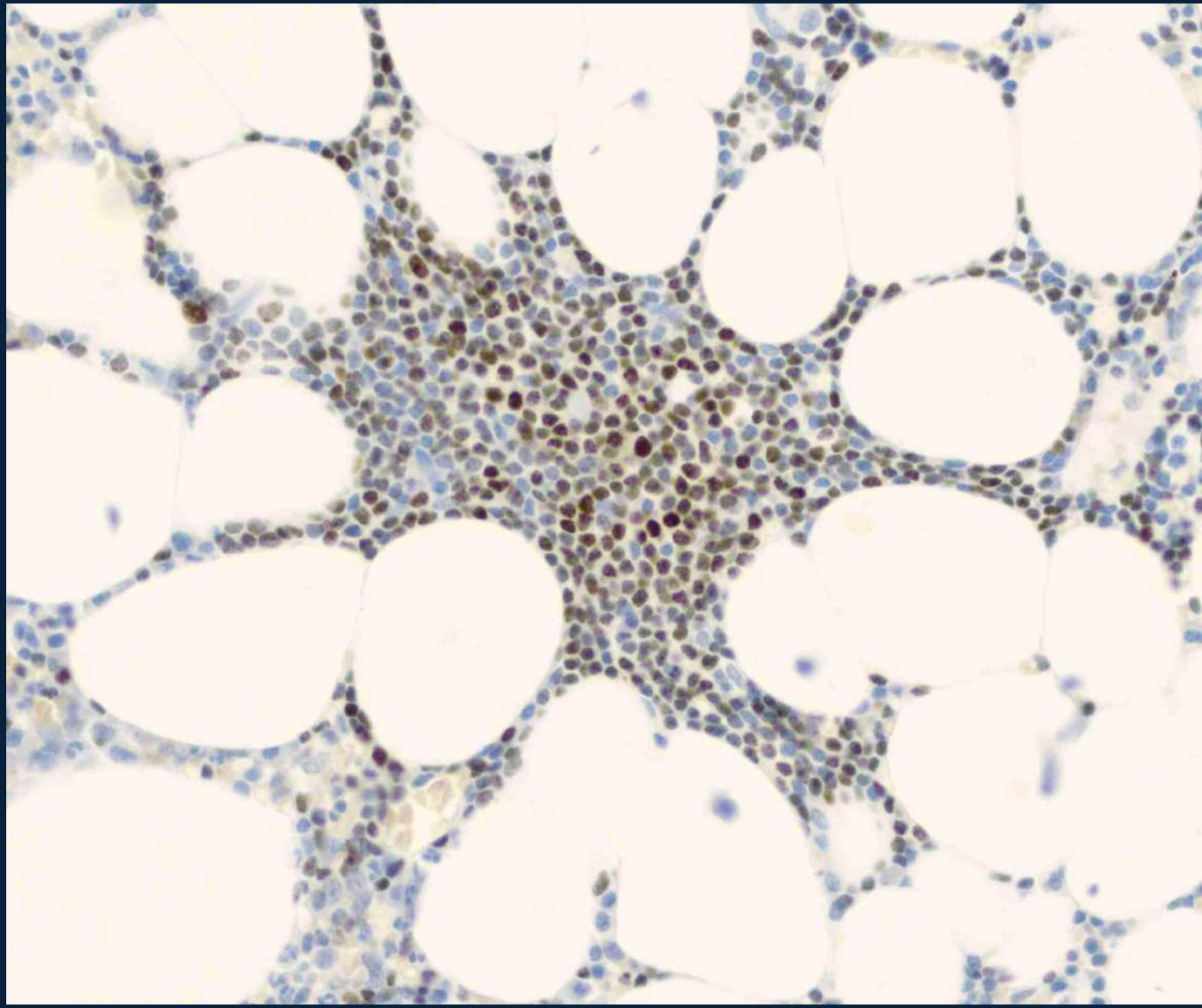
CLL Bone marrow LEF1 positive



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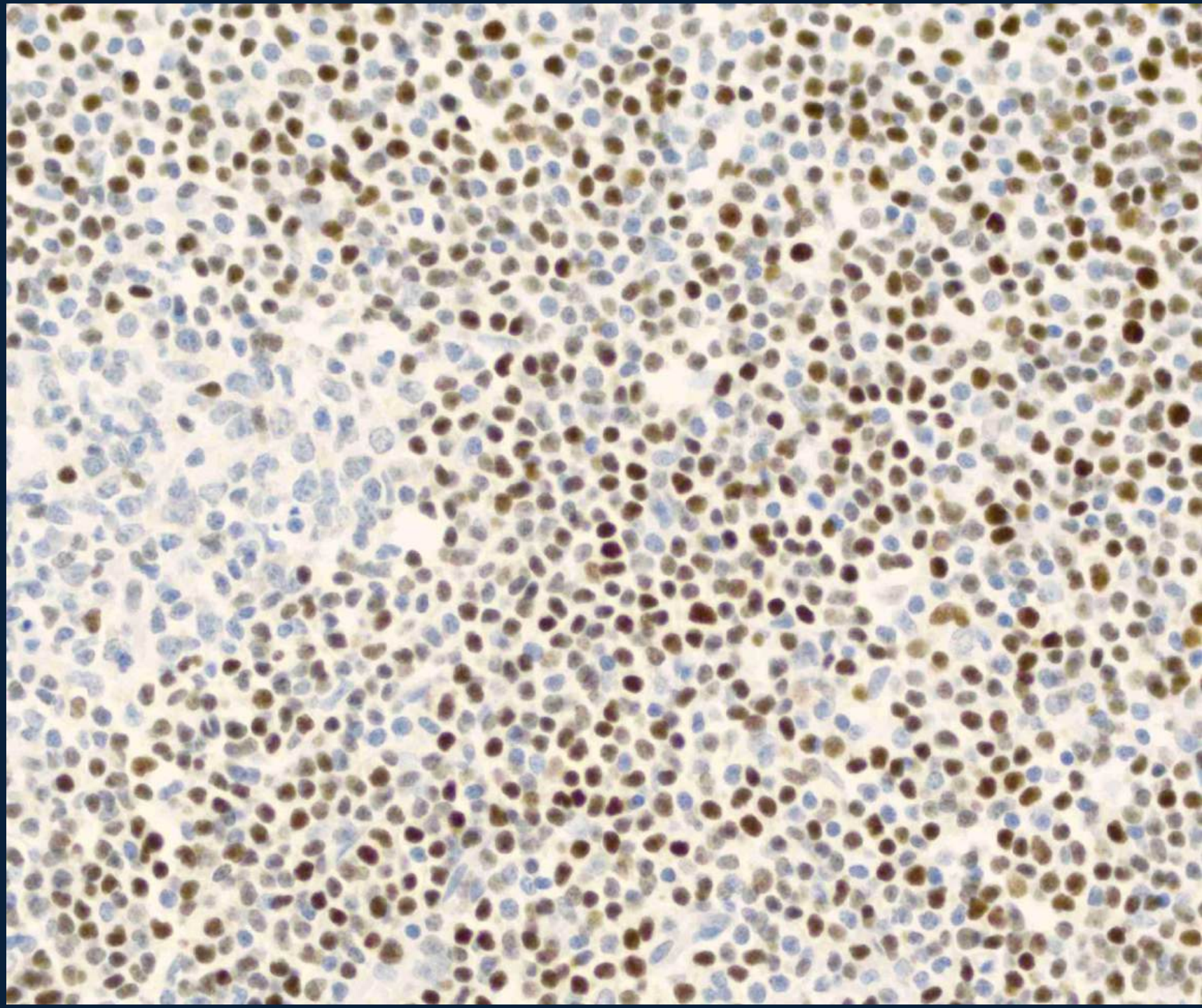
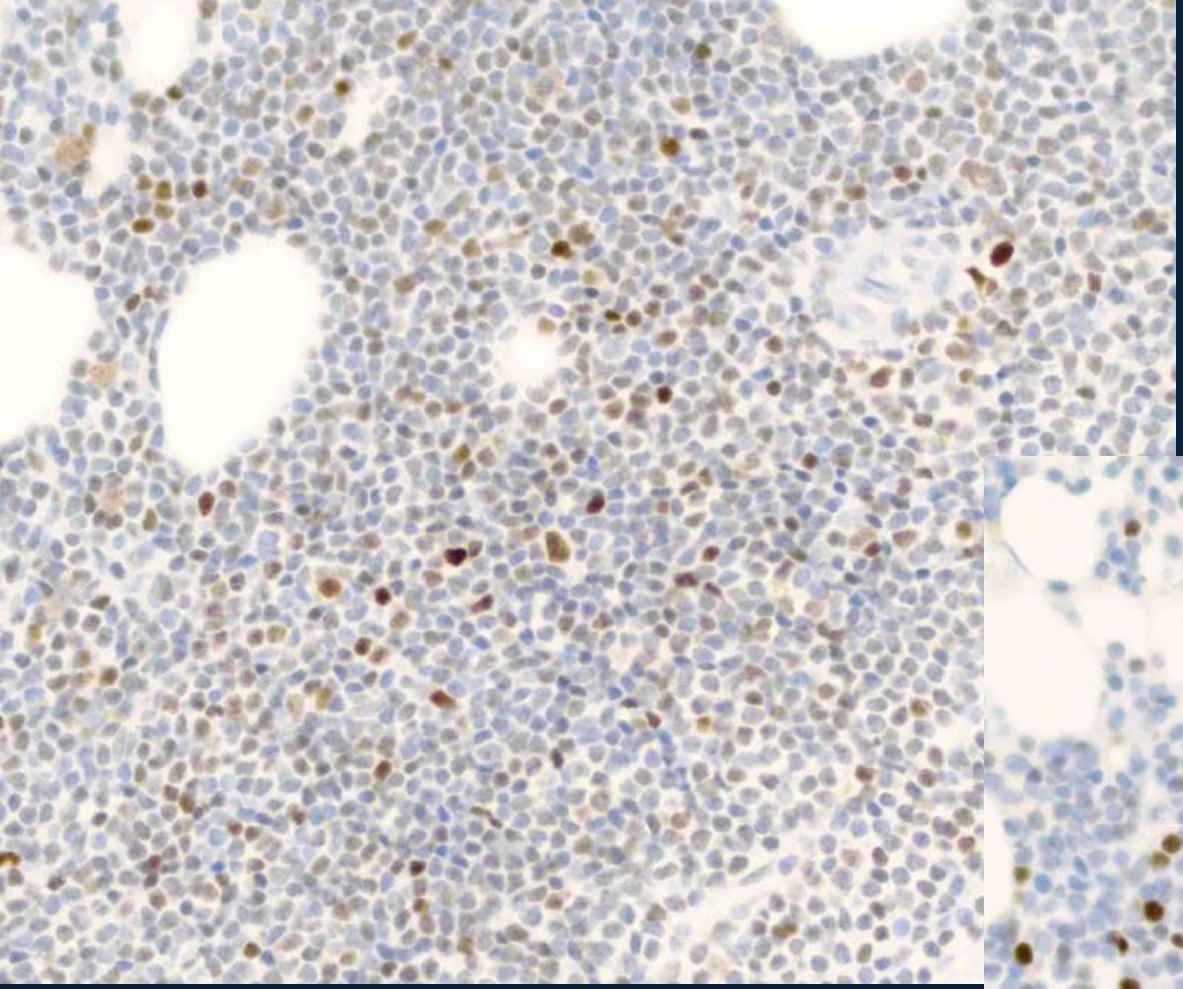
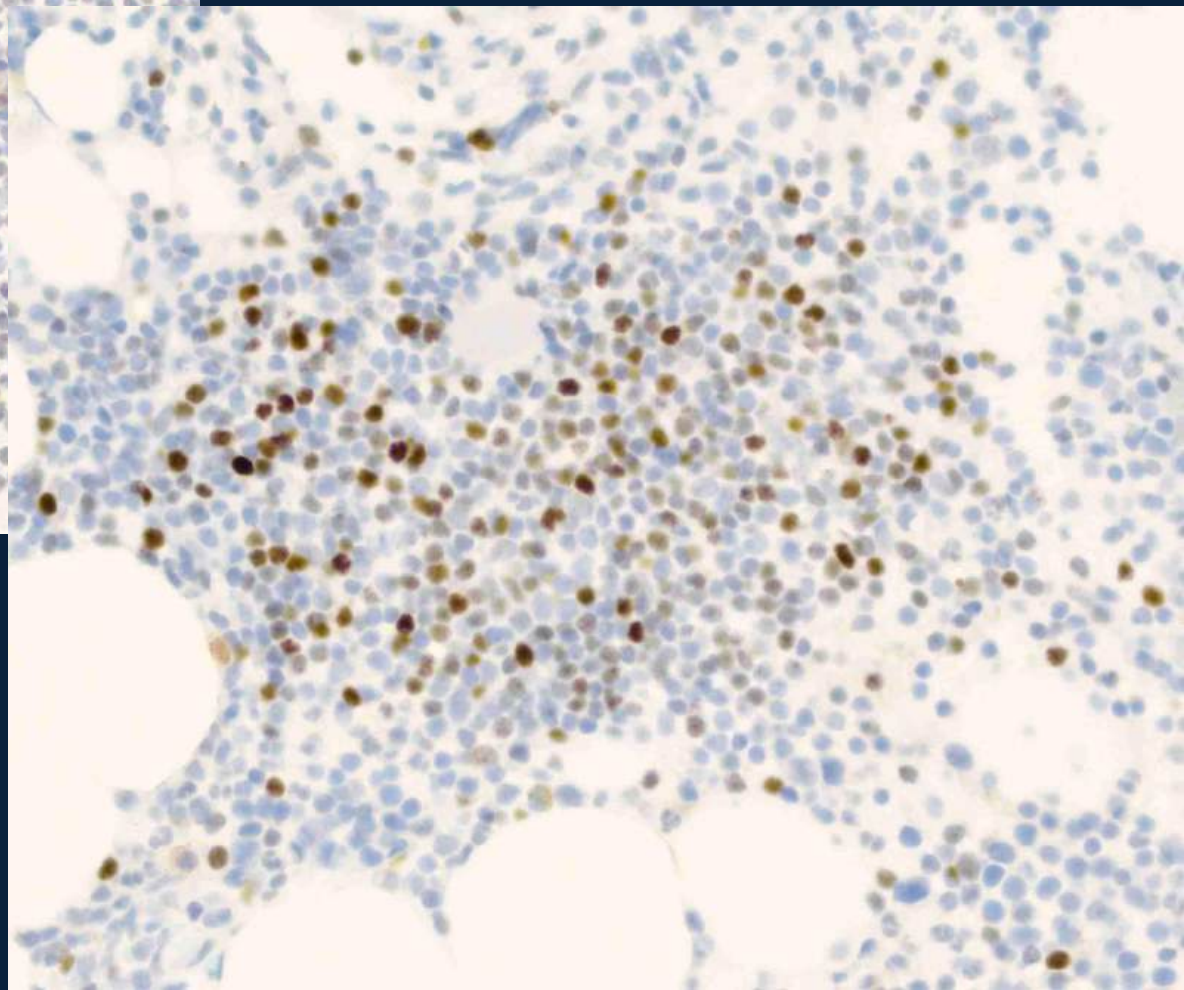
CLL-SLL Core bx LEF1 Pos







CLL-BM

LEF1 weak positive

Compare with CD3/CD5

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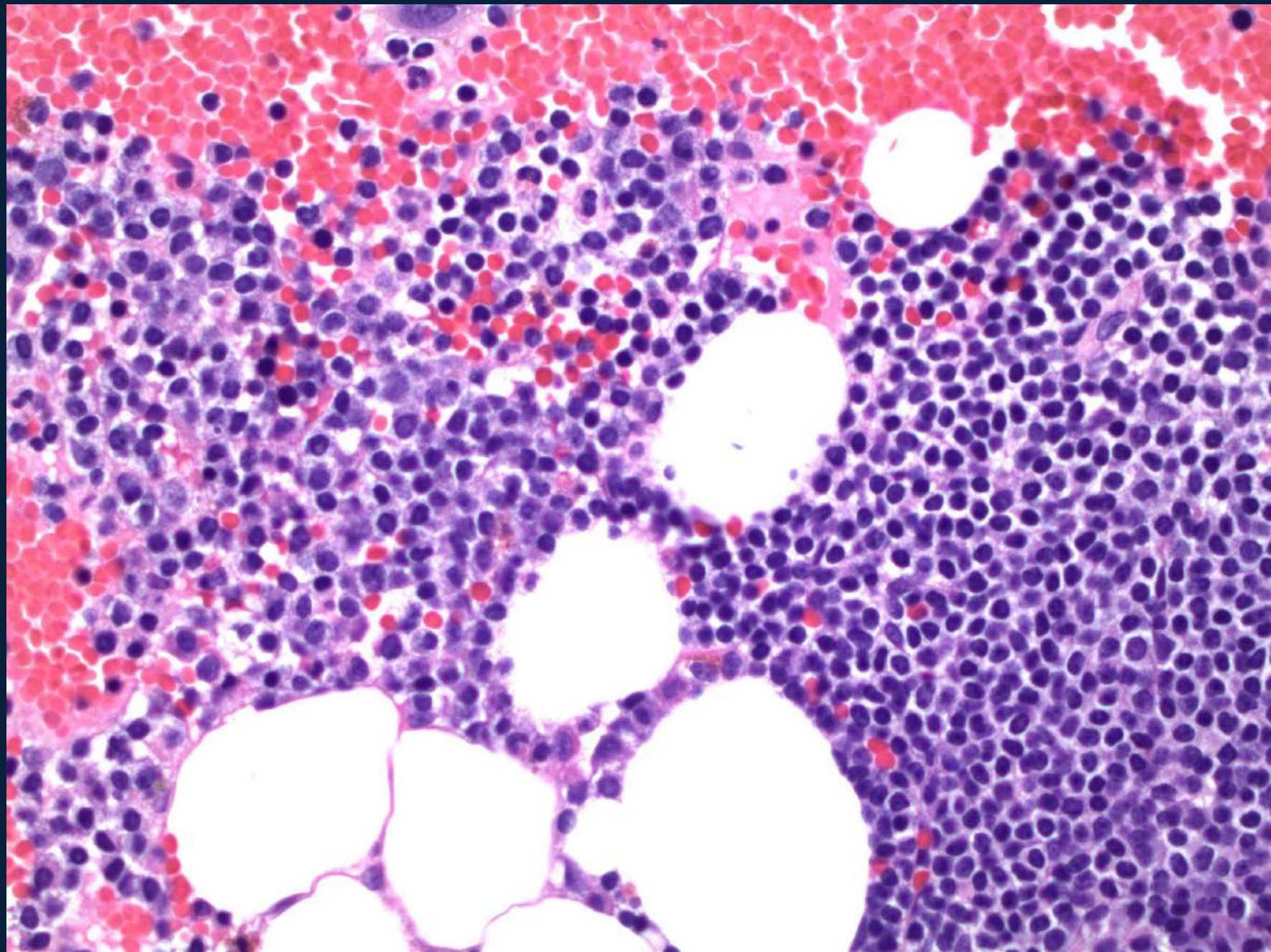
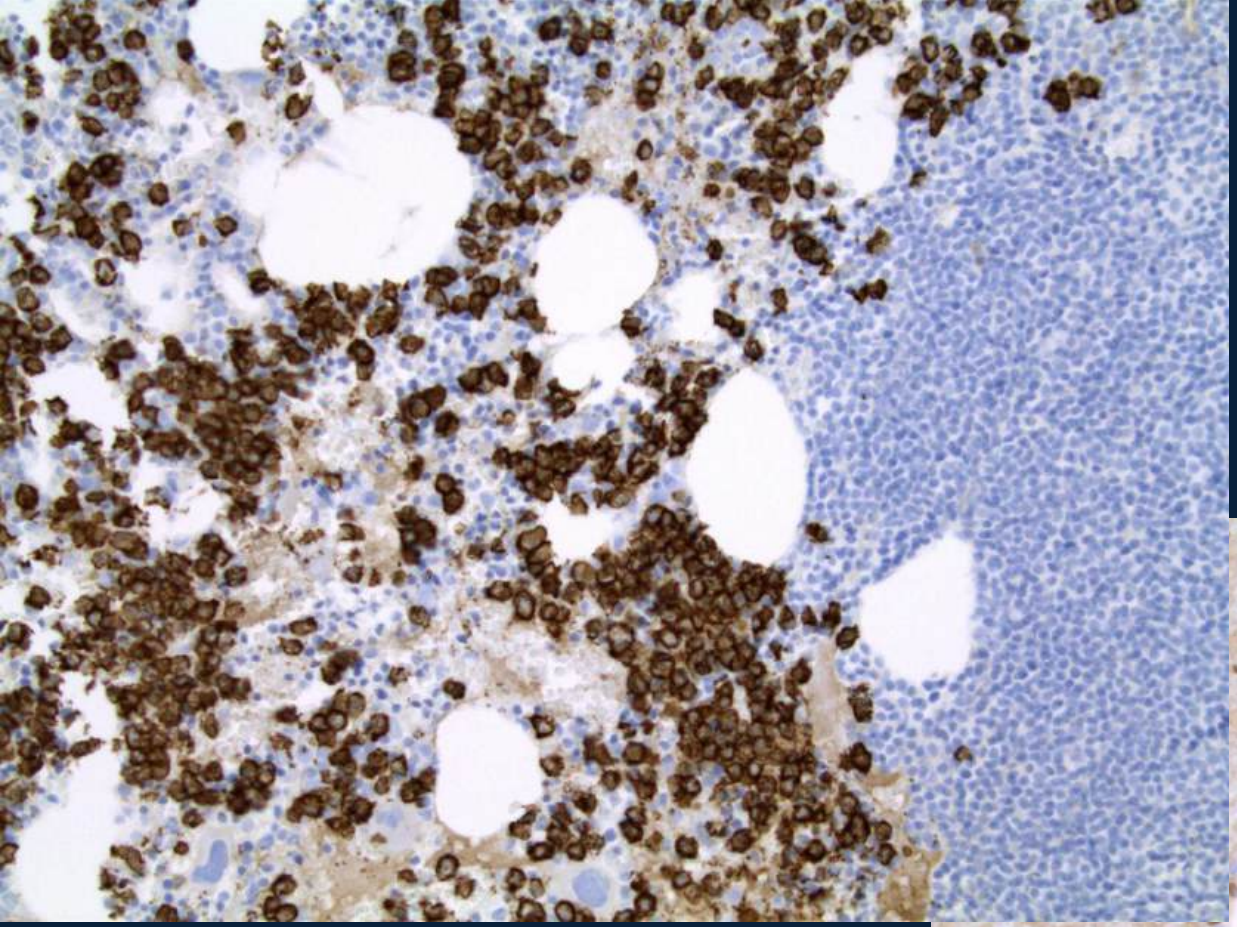
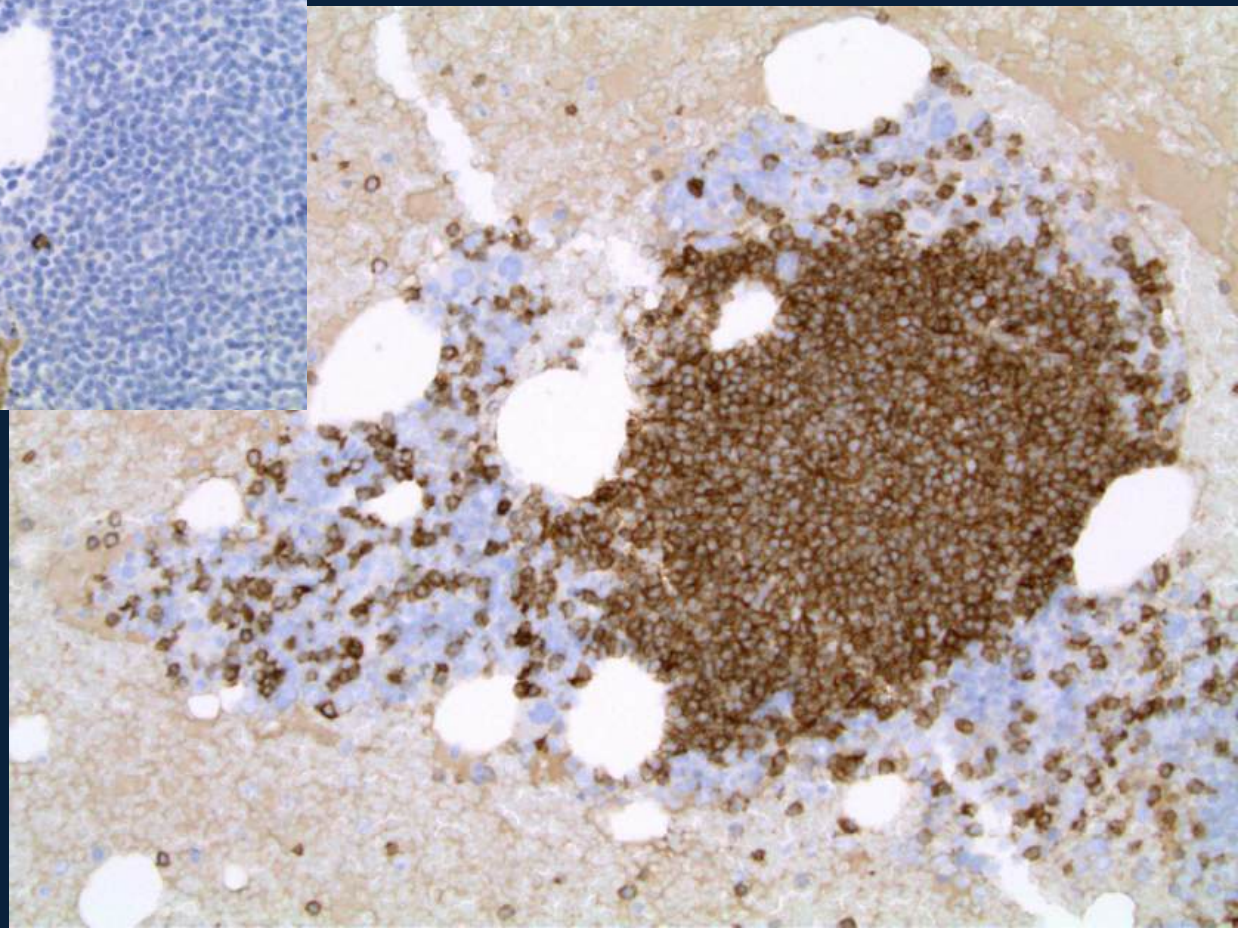
CLL-myeloma

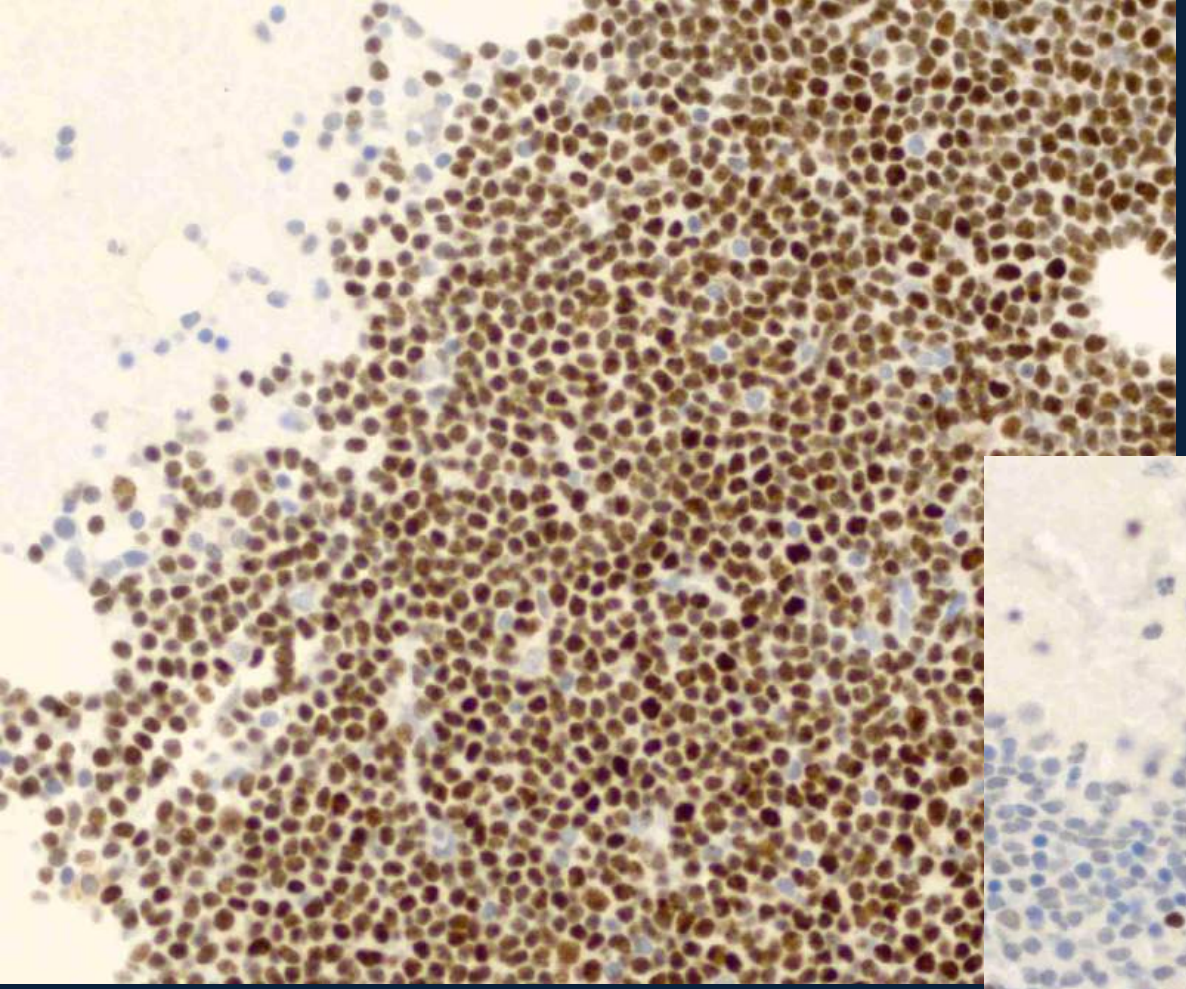


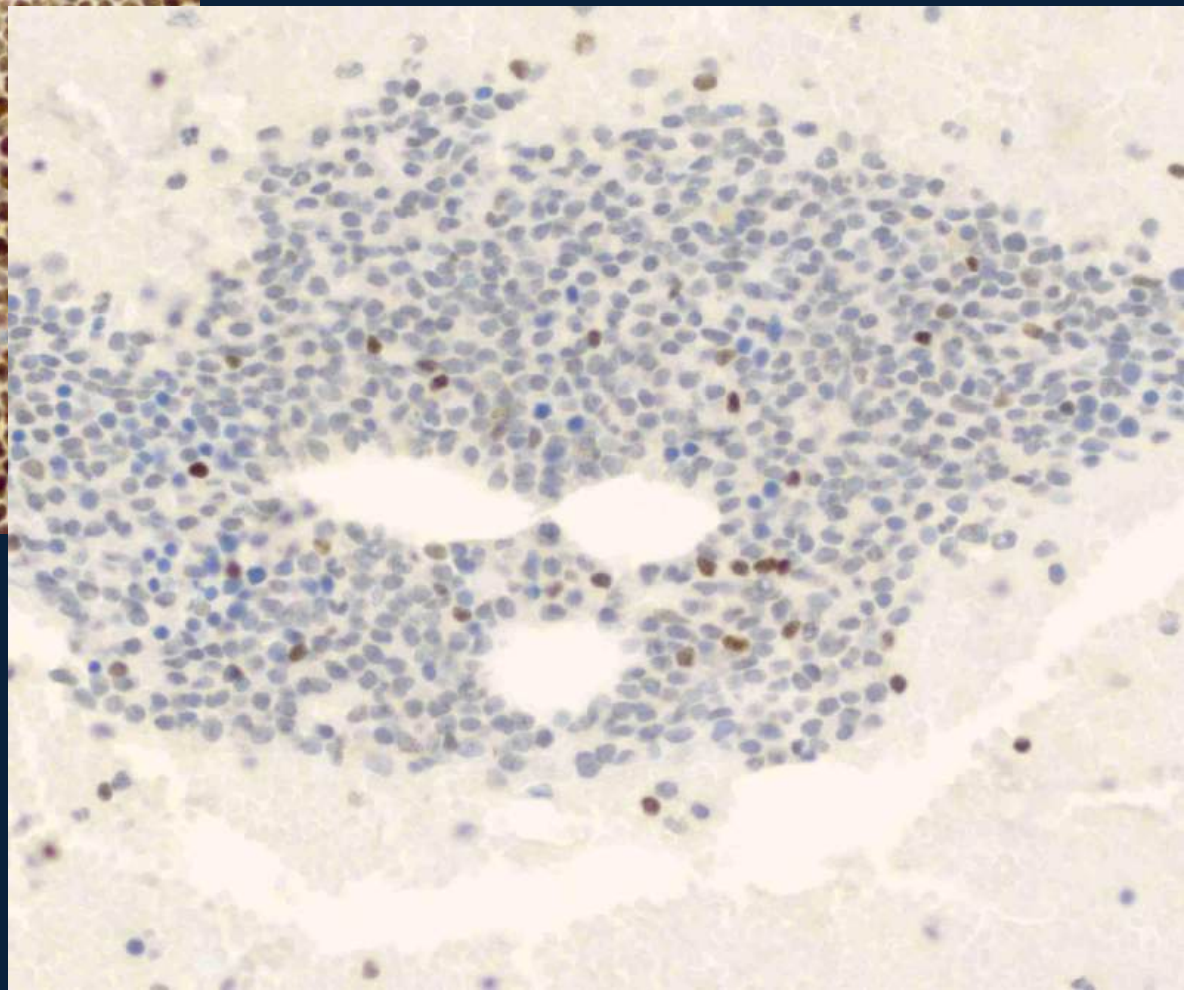


CLL
Concomitant myeloma
CD138

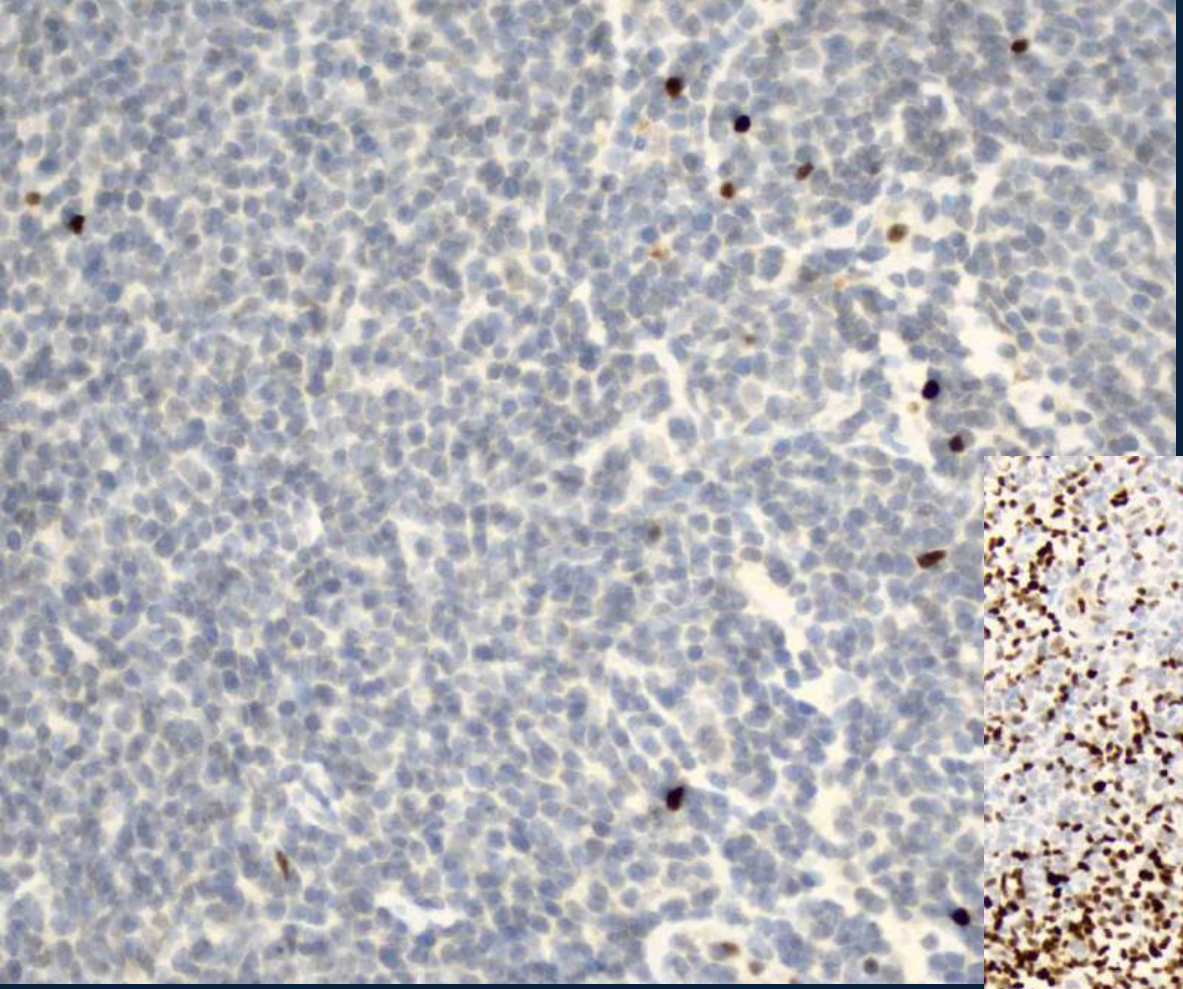
CLL
Concomitant myeloma
CD5

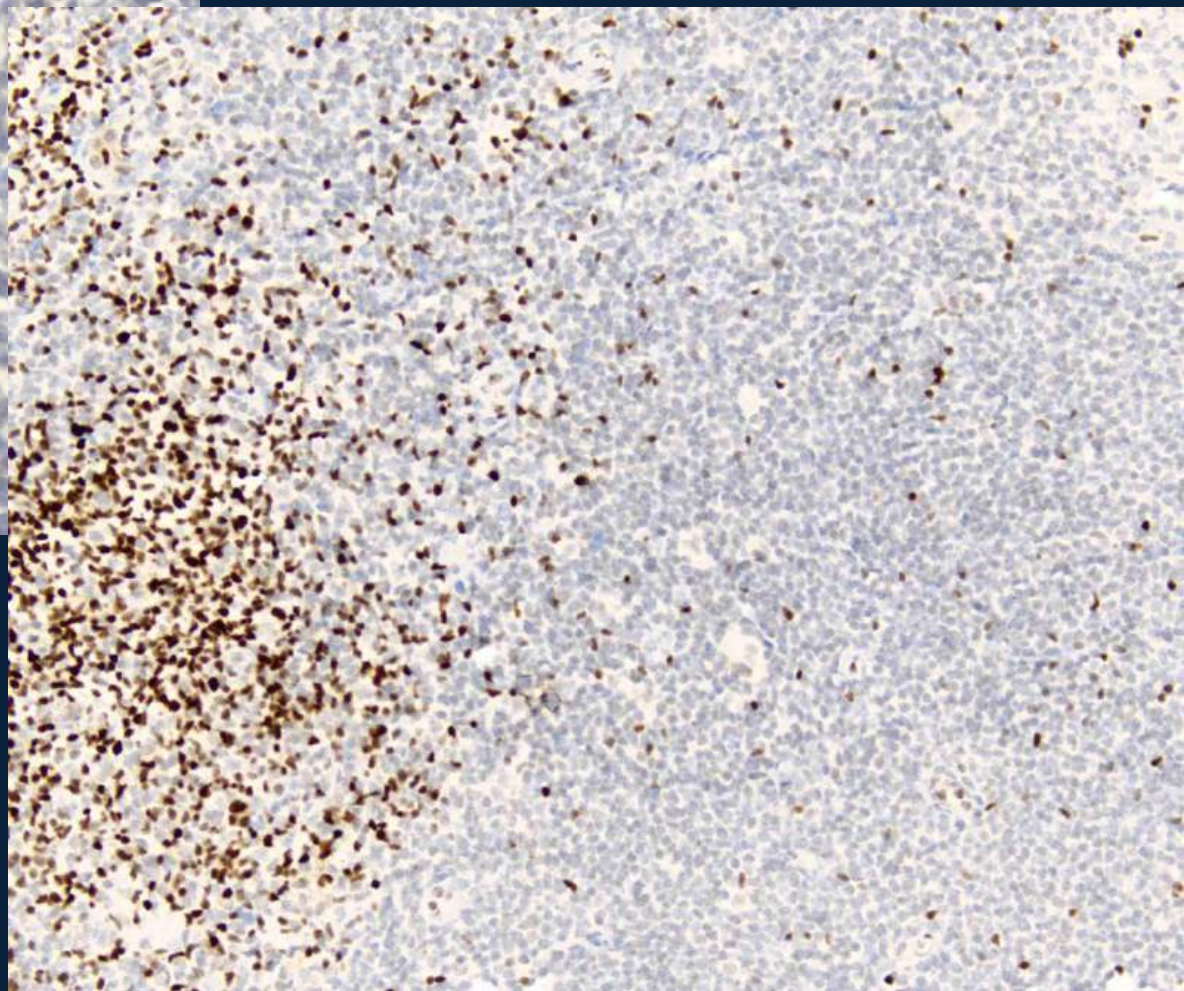






CLL-LEF1 +
Concomitant myeloma negative





Mantle cell lymphoma
LEF1 negative

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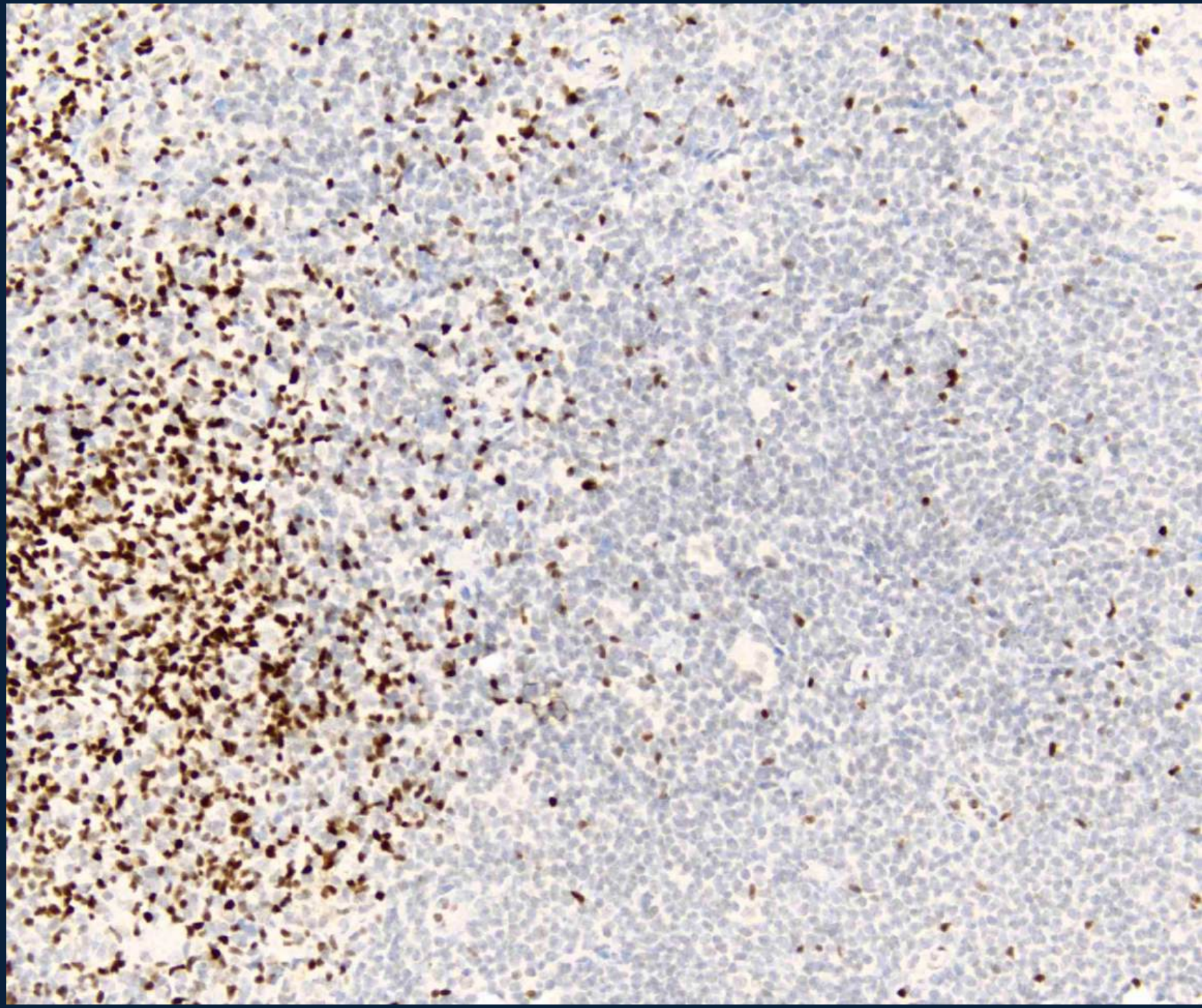
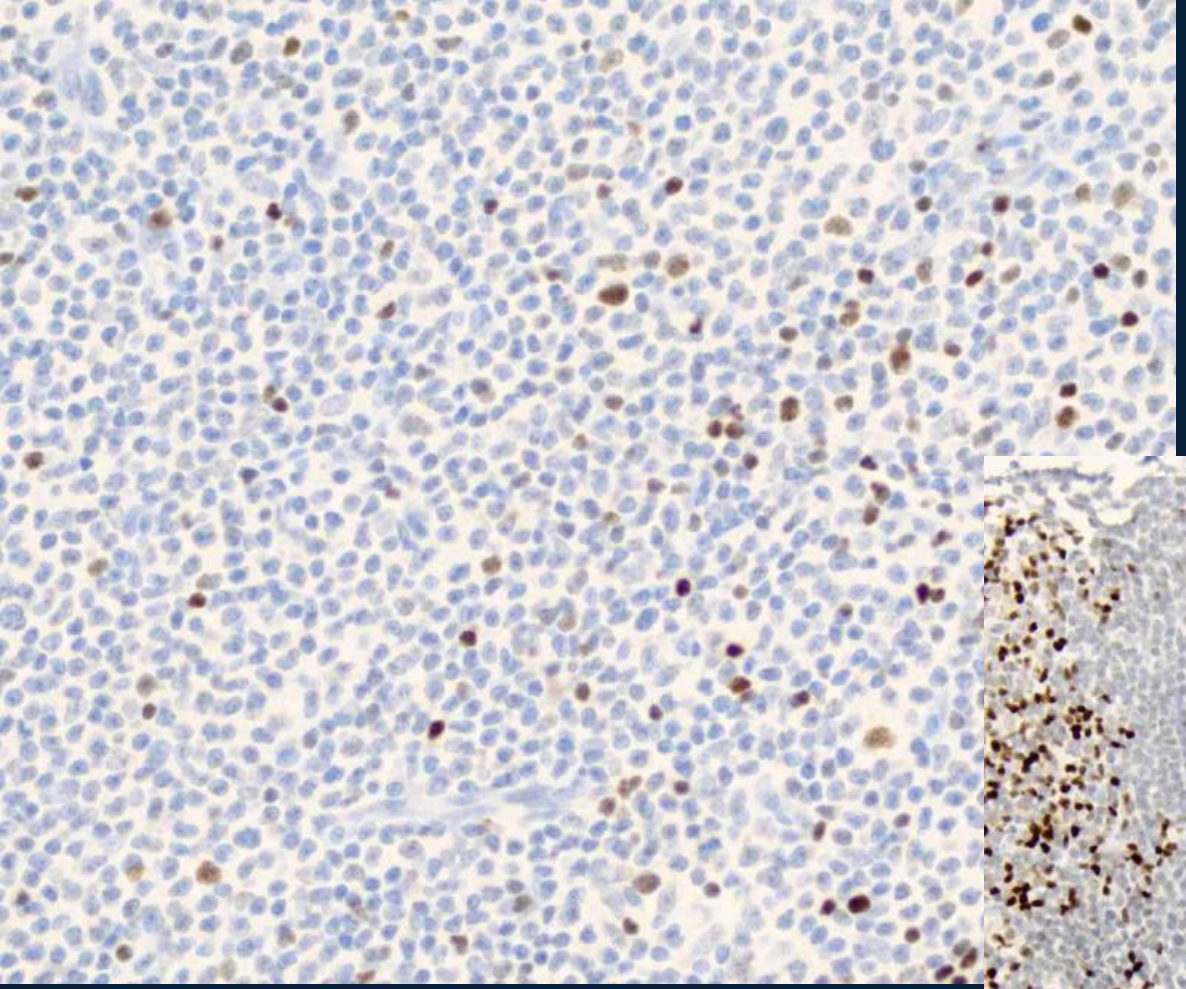
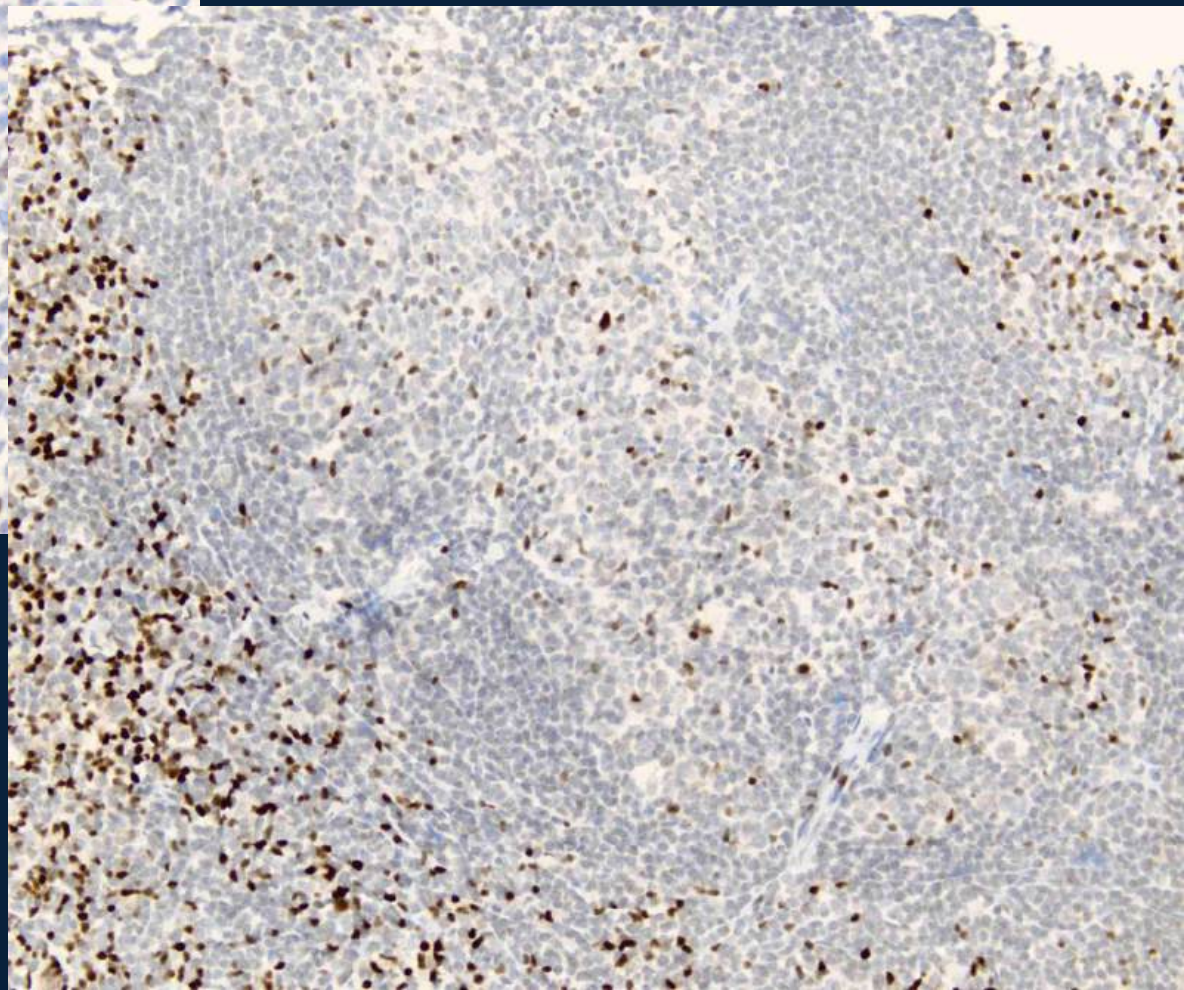
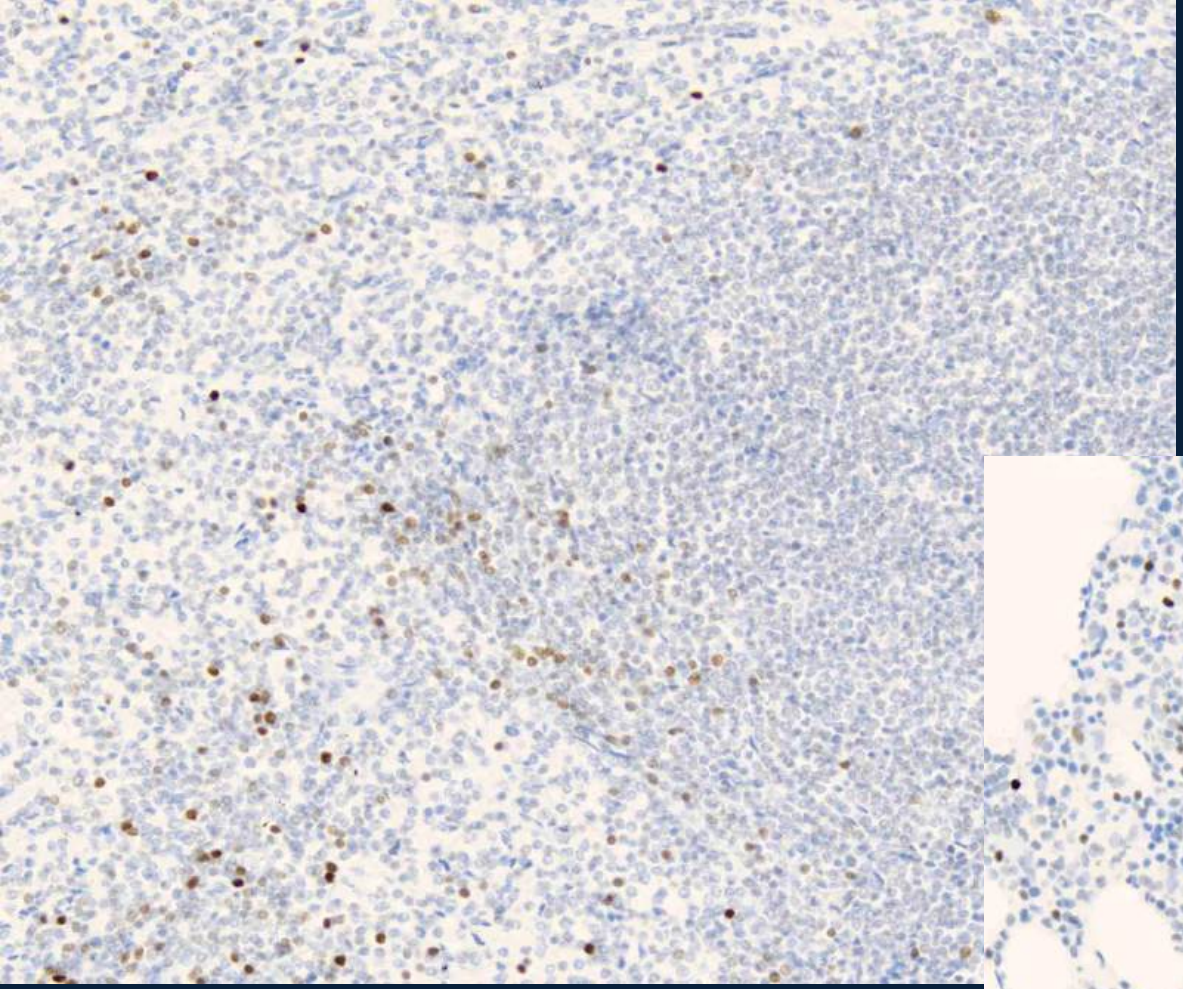
Mantle cell lymphoma LEF1 negative

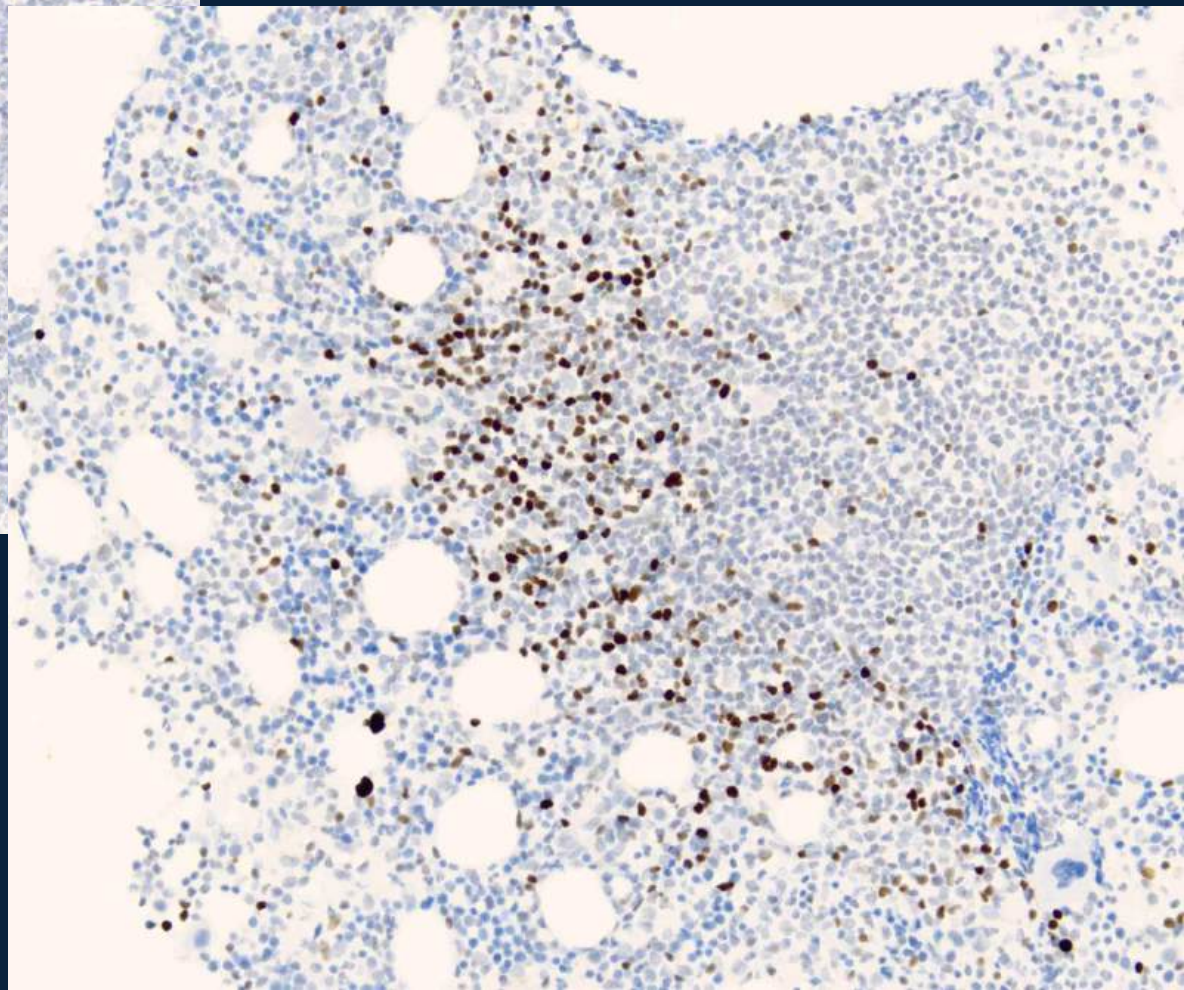




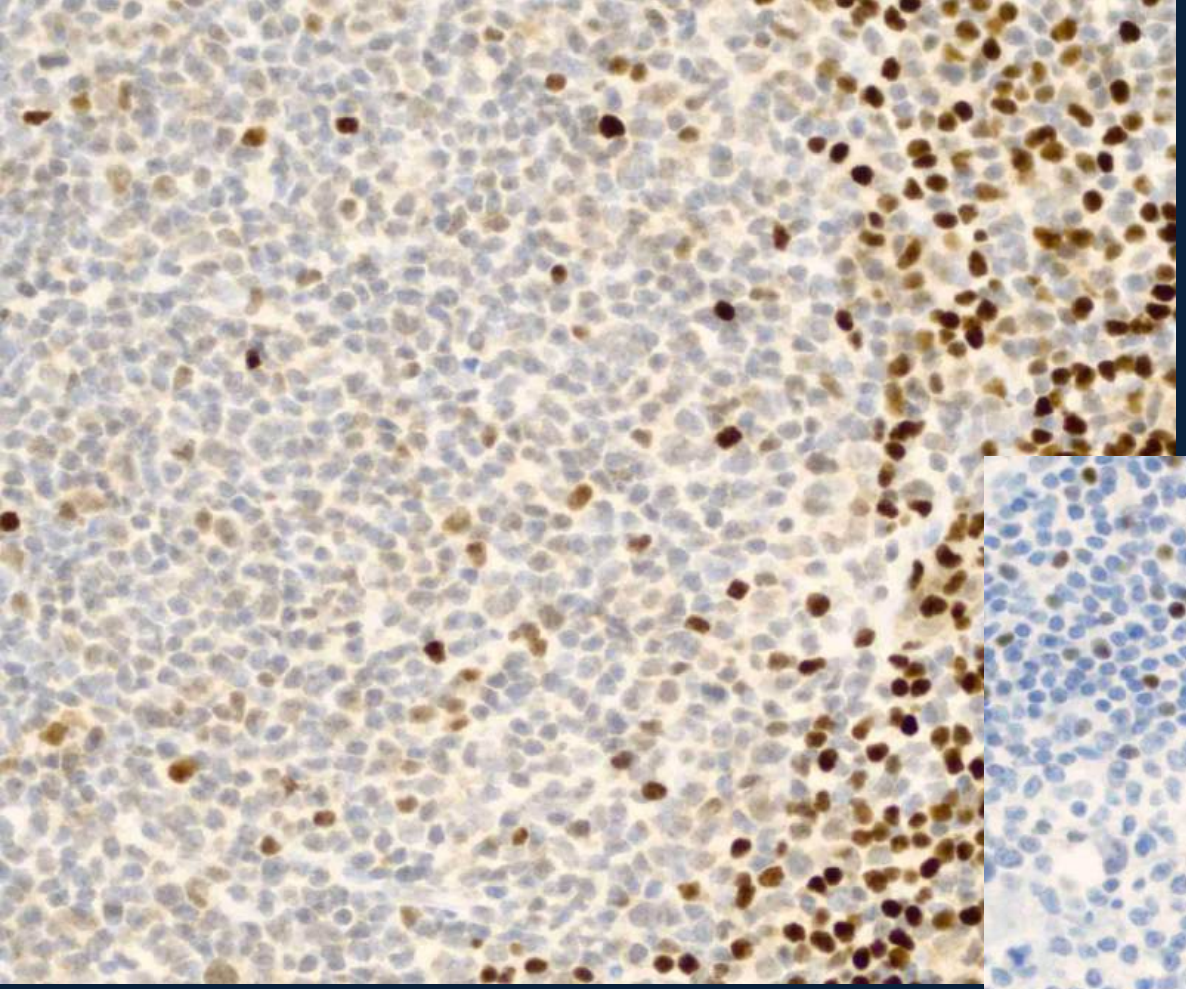


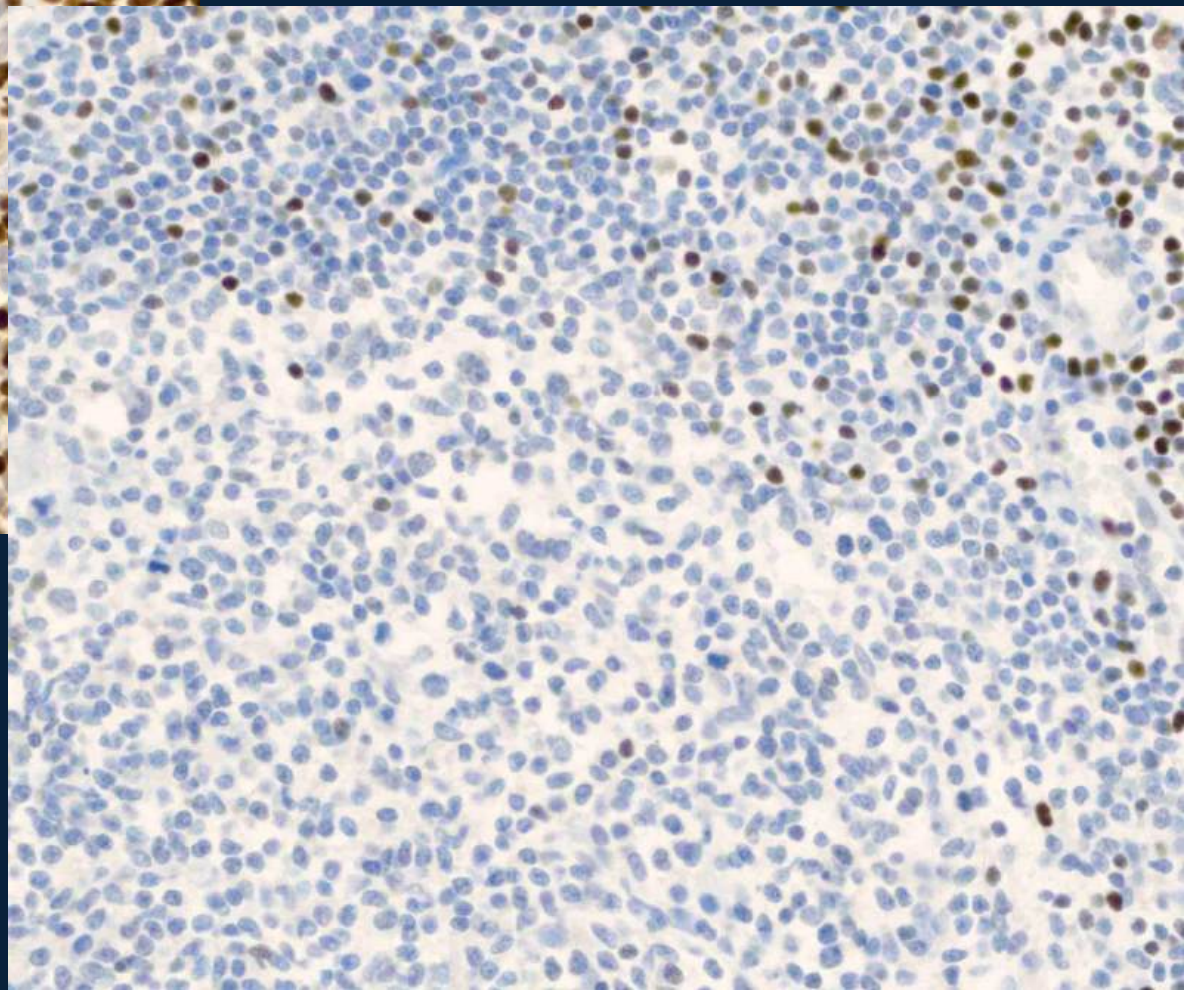
Marginal zone lymph
LEF1negative





Marginal zone lymph
LEF1negative





Follicular lymph
LEF1negative

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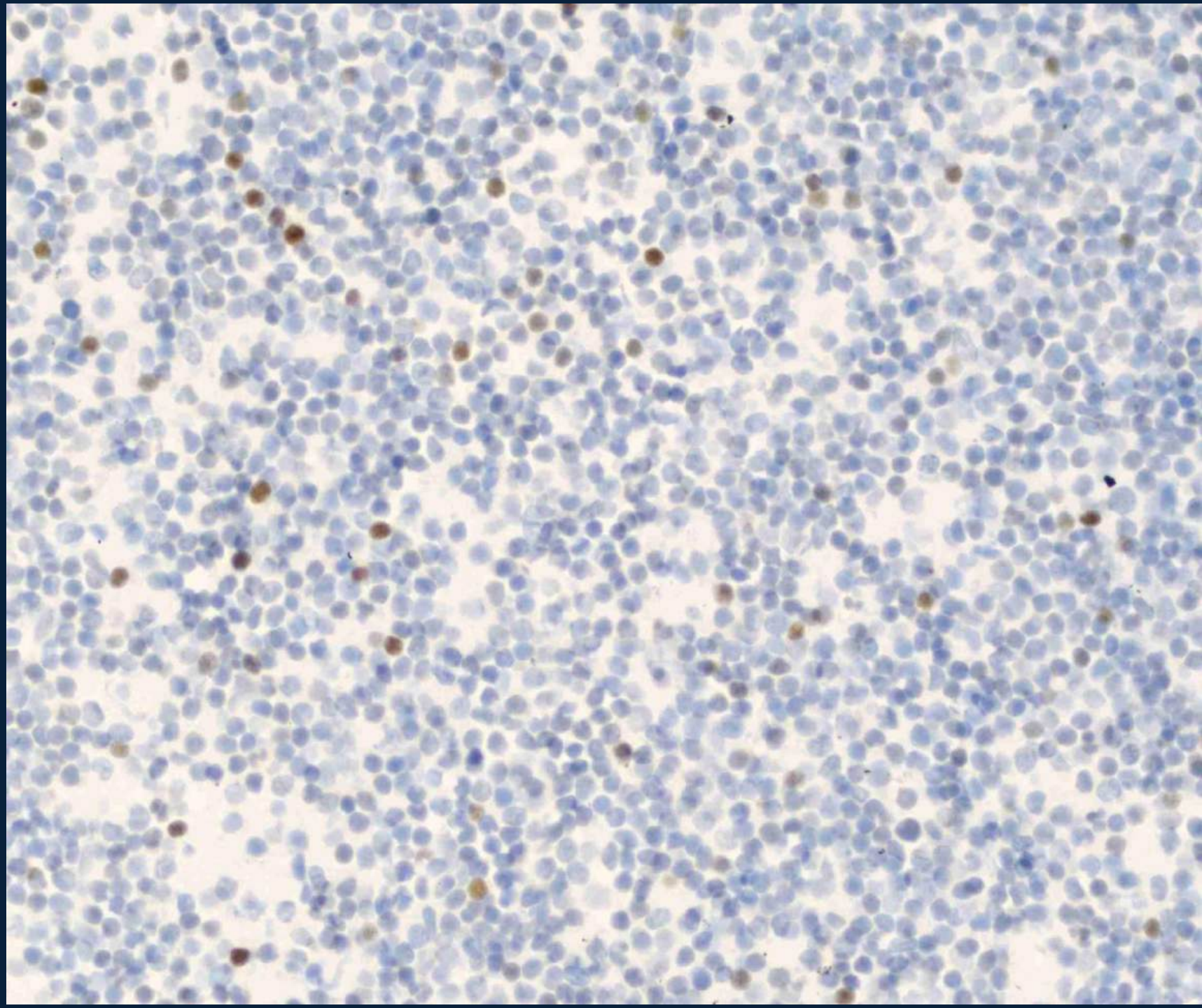
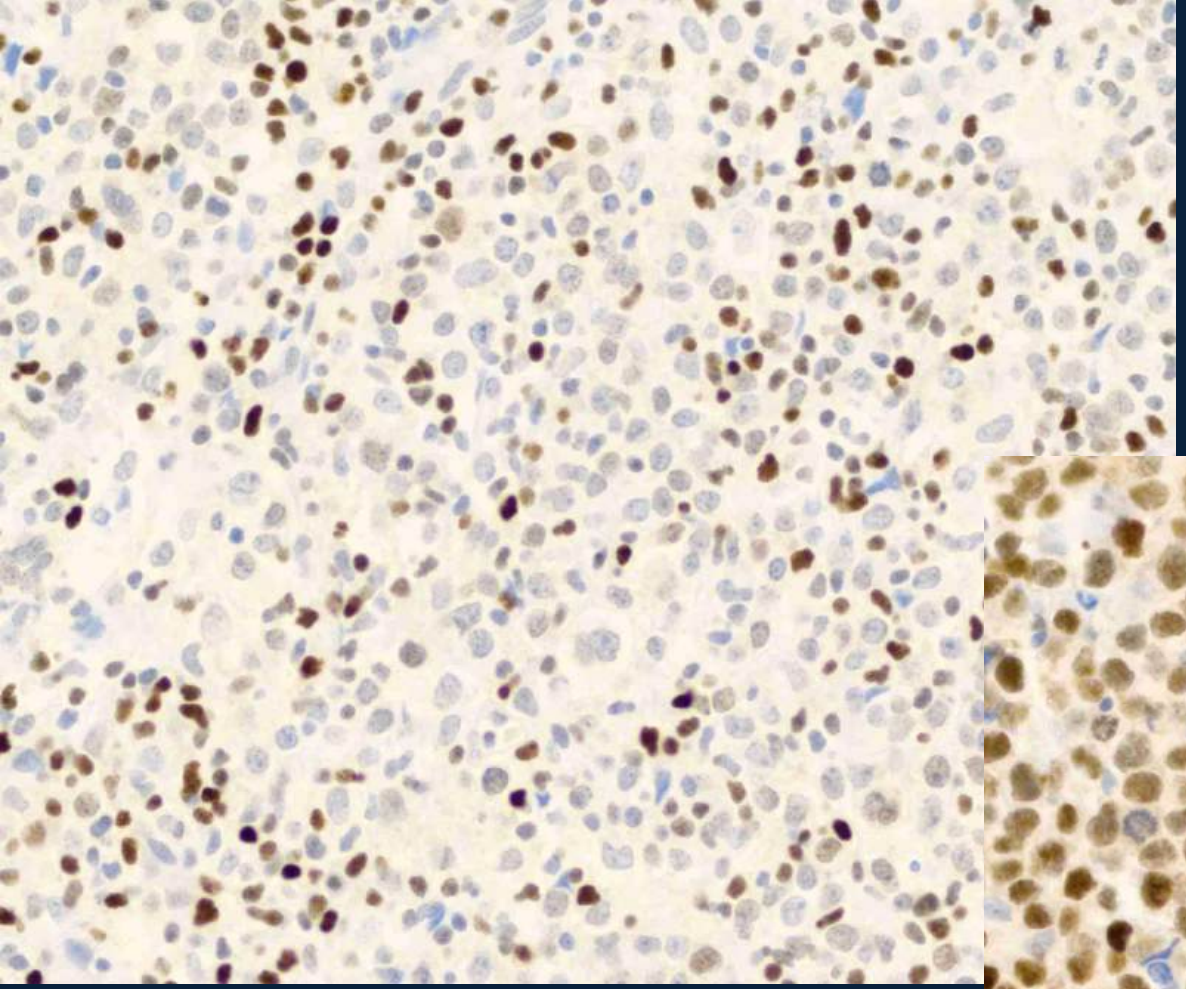
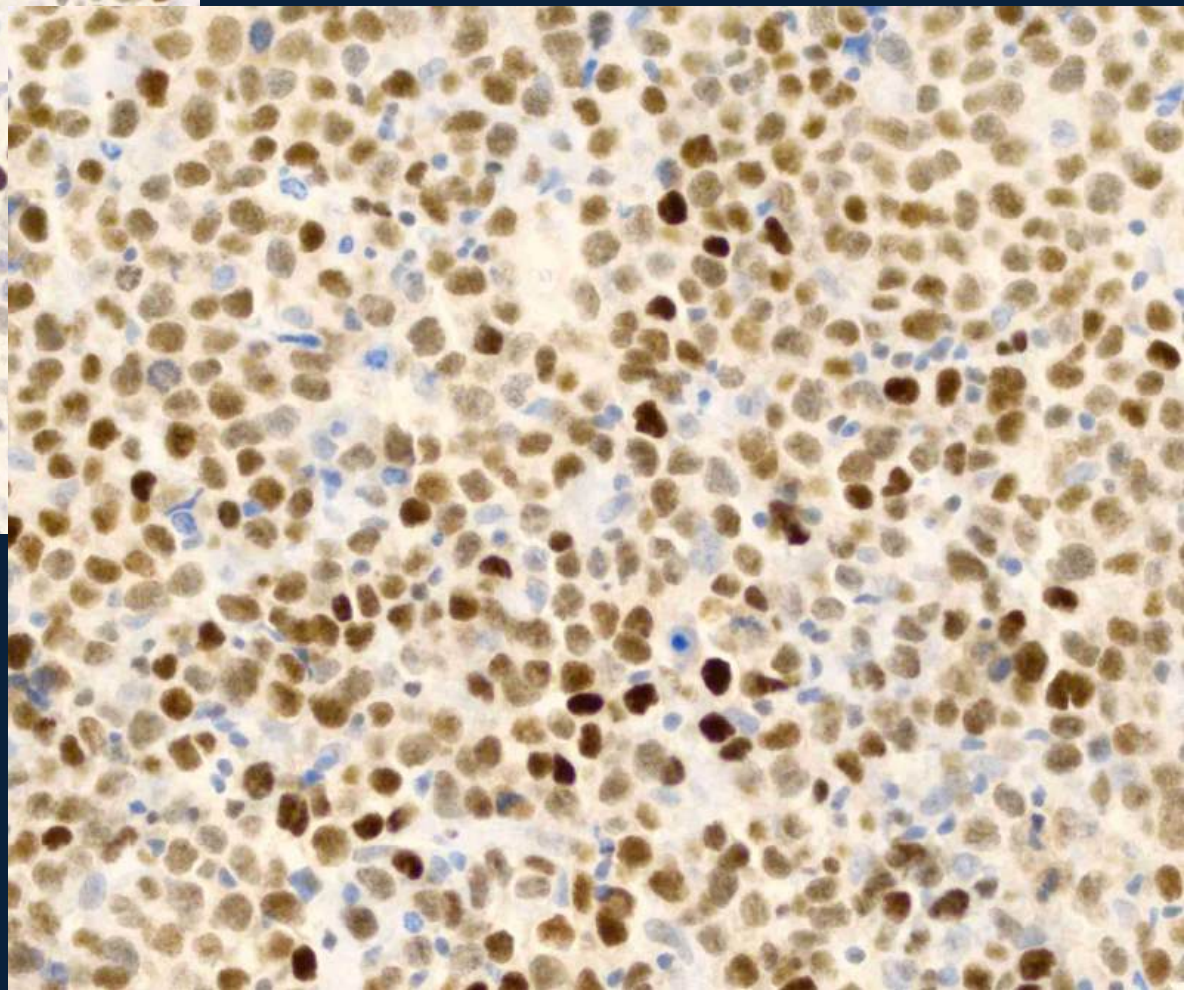
Follicular Lymphoma FNA LEF negative

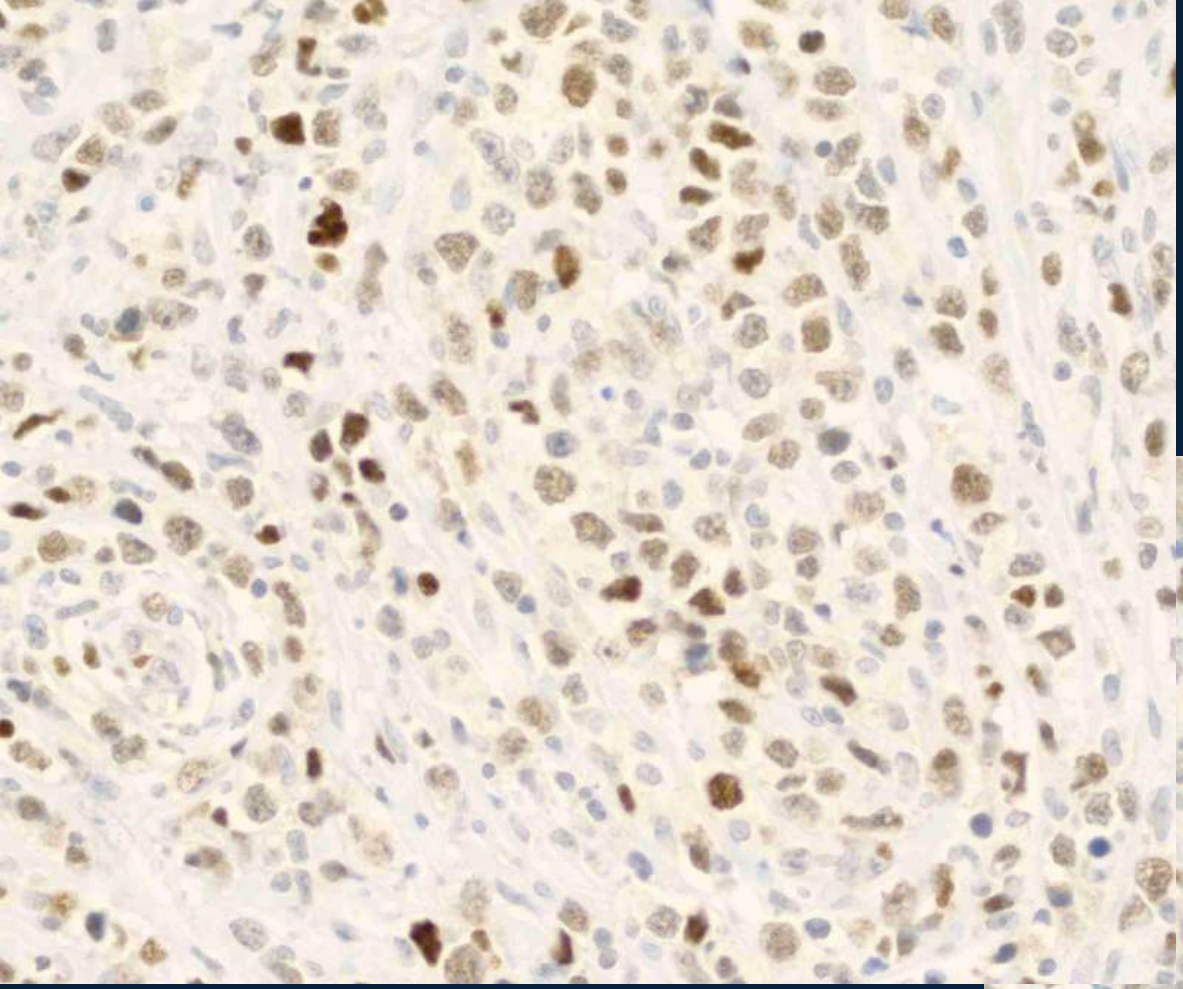


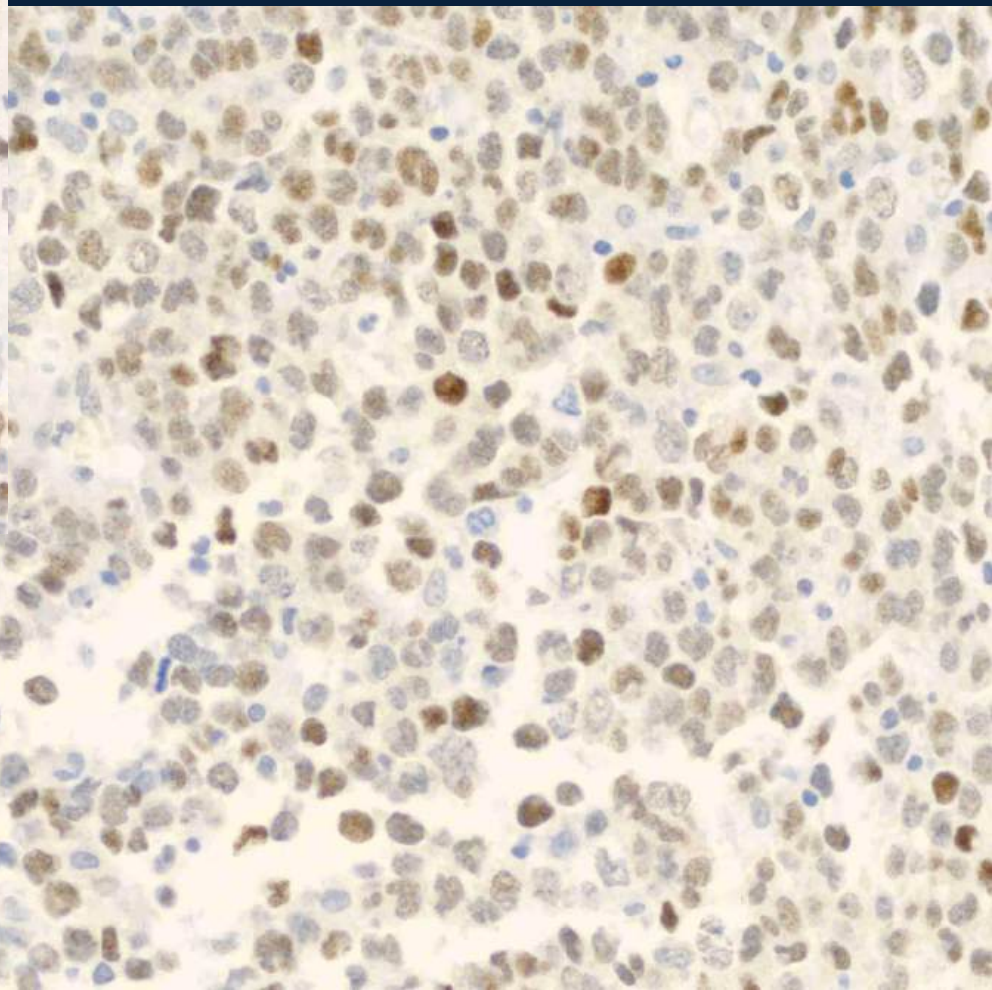


LEF1
DLBCL
negative

LEF1
DLBCL
CD5 +
positive







LEF1
DLBCL
Weak pos

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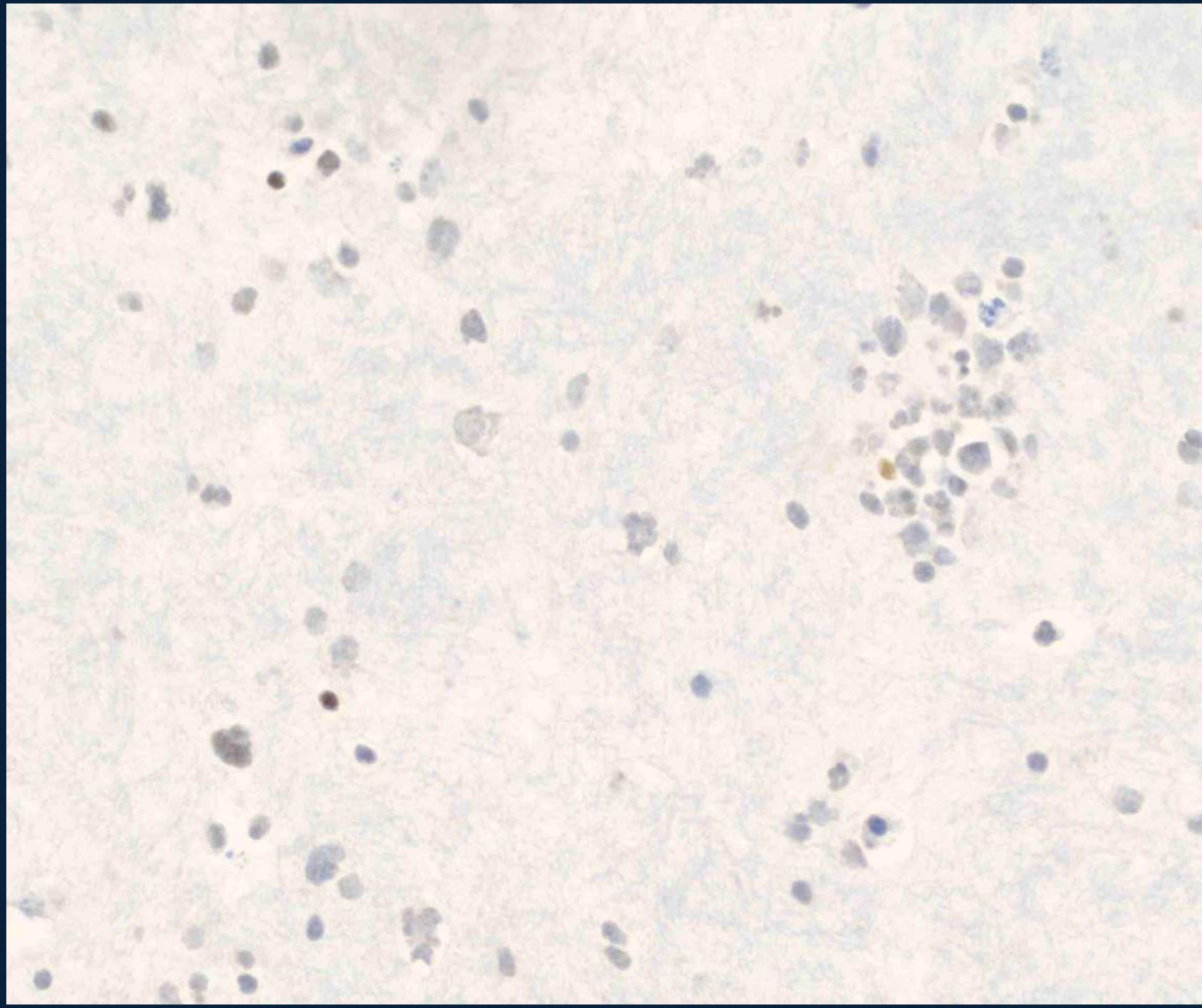
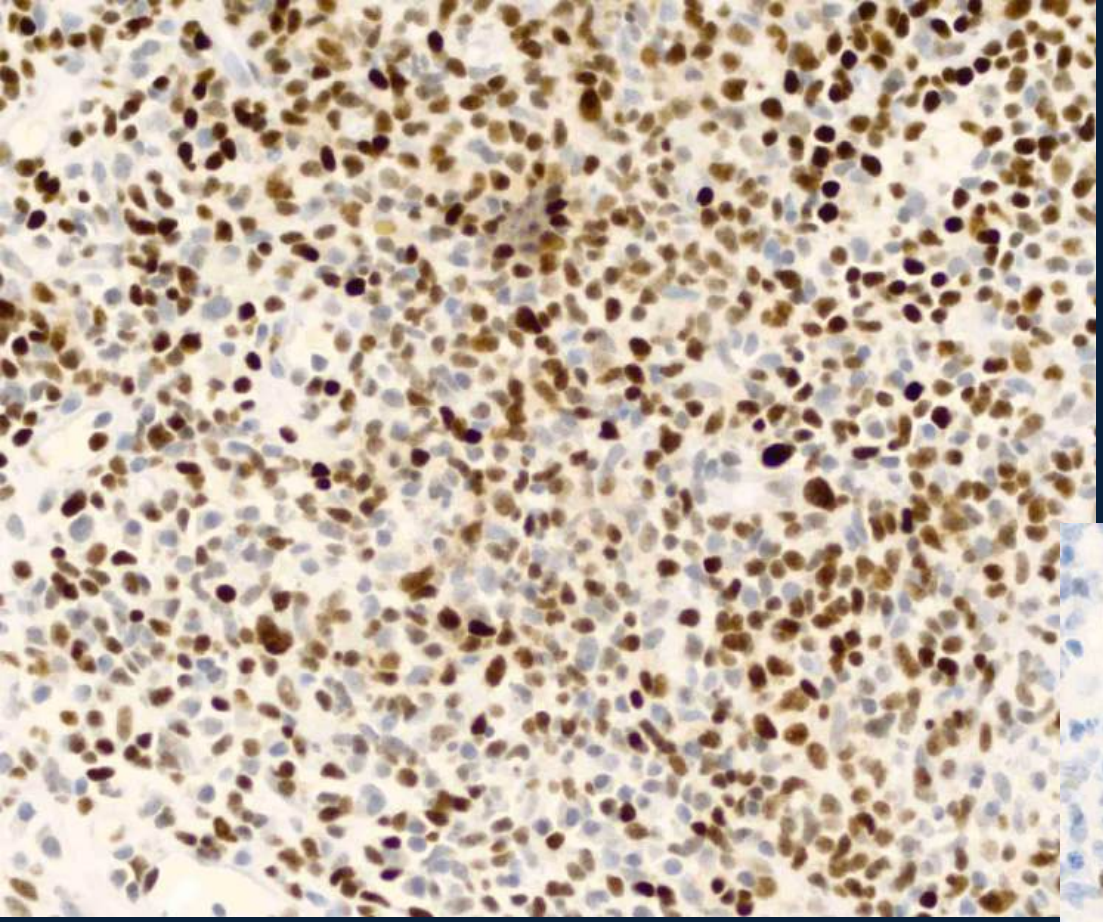
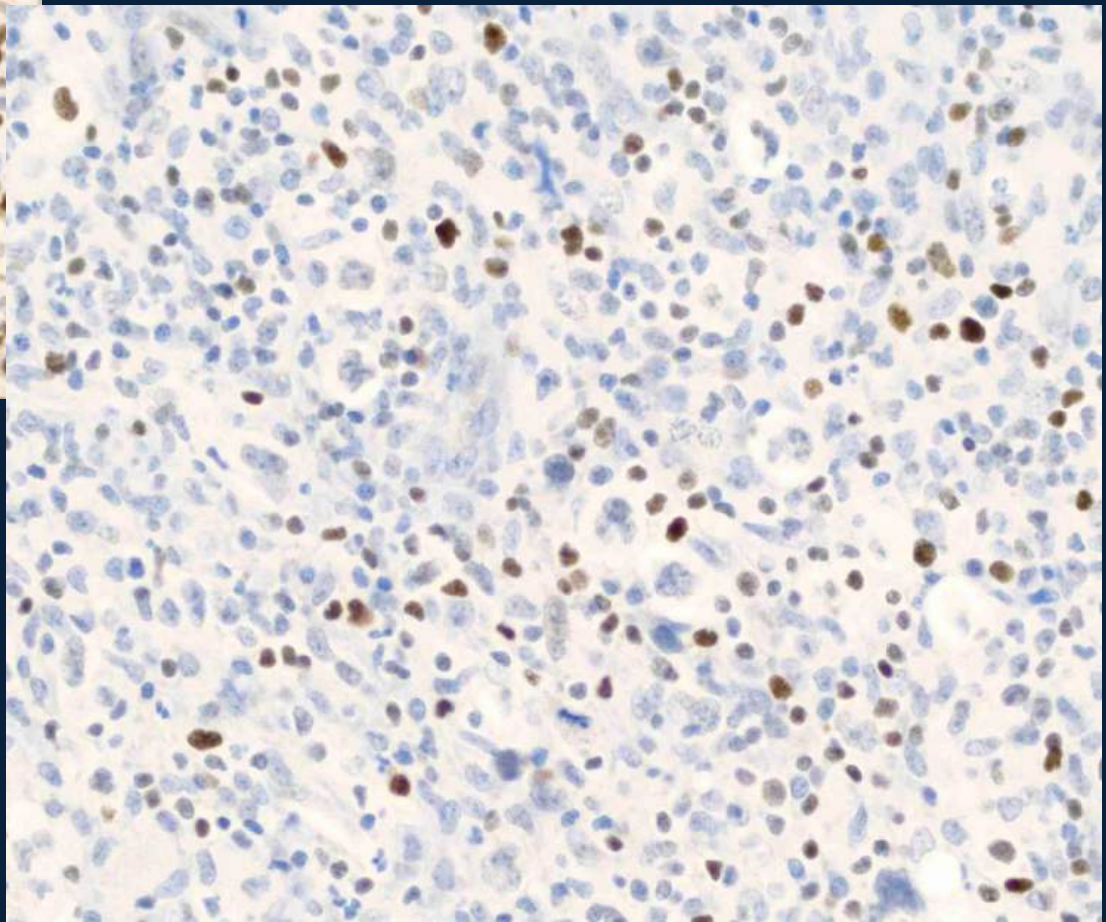
LEF1 DLBCL effusion negative





LEF1
Classical
Hodgkin
positive

LEF1
classical
Hodgkin
negative



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LEF1

Additional references:

O'malley DP, Lee JP and Bellizzi AM. Expression of LEF1 in mantle cell lymphoma. Ann Diagn Pathol. 2017 Feb;26:57-59.

2/23 mantle cell lymphomas expressed LEF1 (4-12% in literature)

Amador-Ortiz C, Goolsby CL, et al. Flow Cytometric Analysis of Lymphoid Enhancer-Binding Factor 1 in Diagnosis of Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma. Am J Clin Pathol 2015;143:214-222.

25/25 CLL positive by flow; 34 other low grade lymphomas neg.

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NKX2.2

- NKX2.2 is a nuclear protein with considerable usefulness in supporting a diagnosis of Ewing sarcoma with greater specificity than CD99. Coupled with Phox2b, synaptophysin, CD45, Pax-5, desmin and myogenin- a sensitive and specific small round blue cell panel

- The vast majority of Ewing sarcoma cases express NKX2.2 (a nuclear transcription factor). NKX2.2 will label up to 30% of pulmonary small cell carcinomas, olfactory neuroblastomas, mesenchymal chondroblastomas and very rarely conventional neuroblastoma and rare desmoplastic small round cell tumor cases (the latter reported in 1/12 cases, in 25-50% of cells).

- As with other transcription factor markers, strong nuclear labeling in over 50% of cells is most sensitive and specific.

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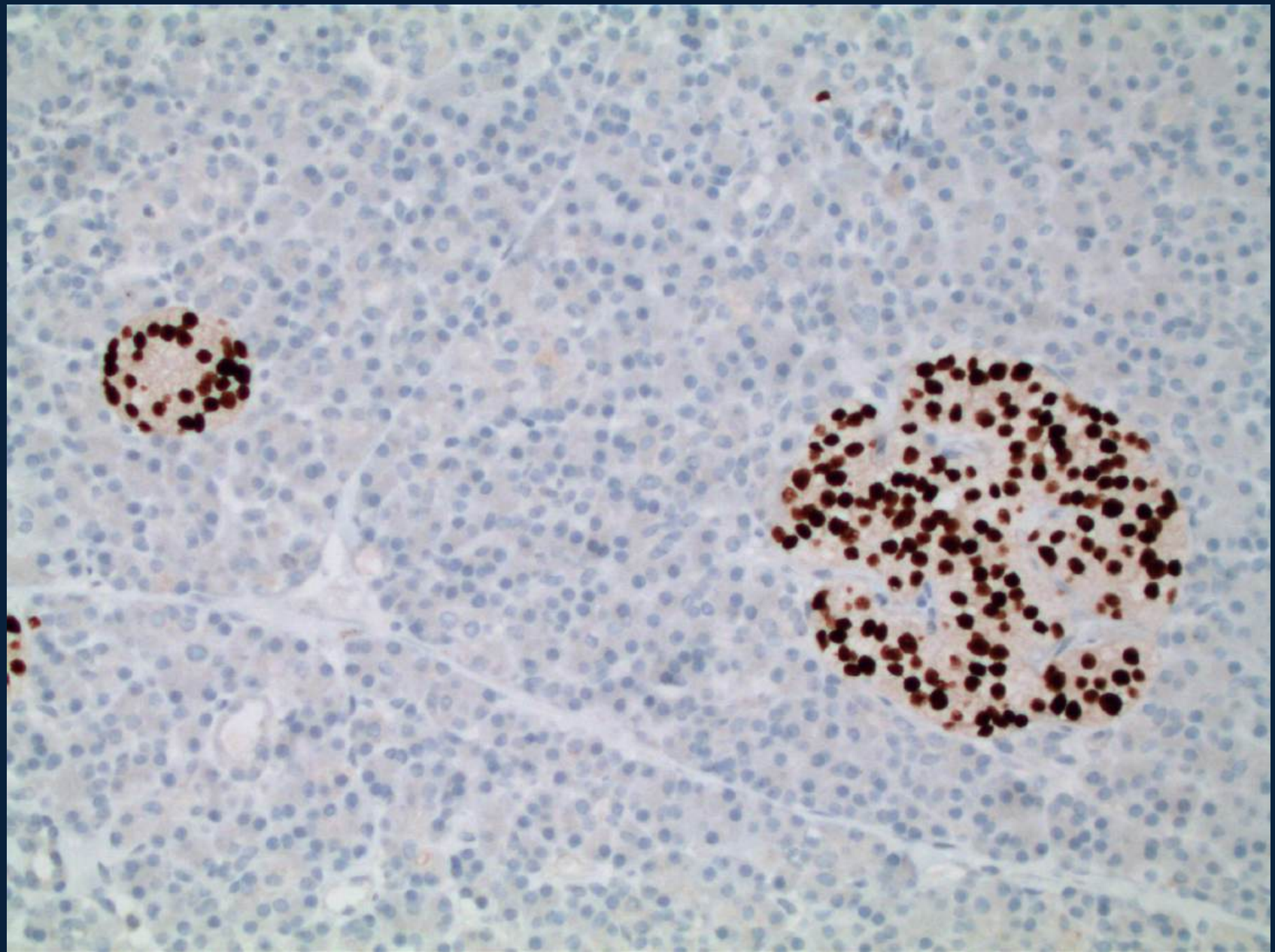
NKX2.2 Islet cell control- Rabbit Mono EP336



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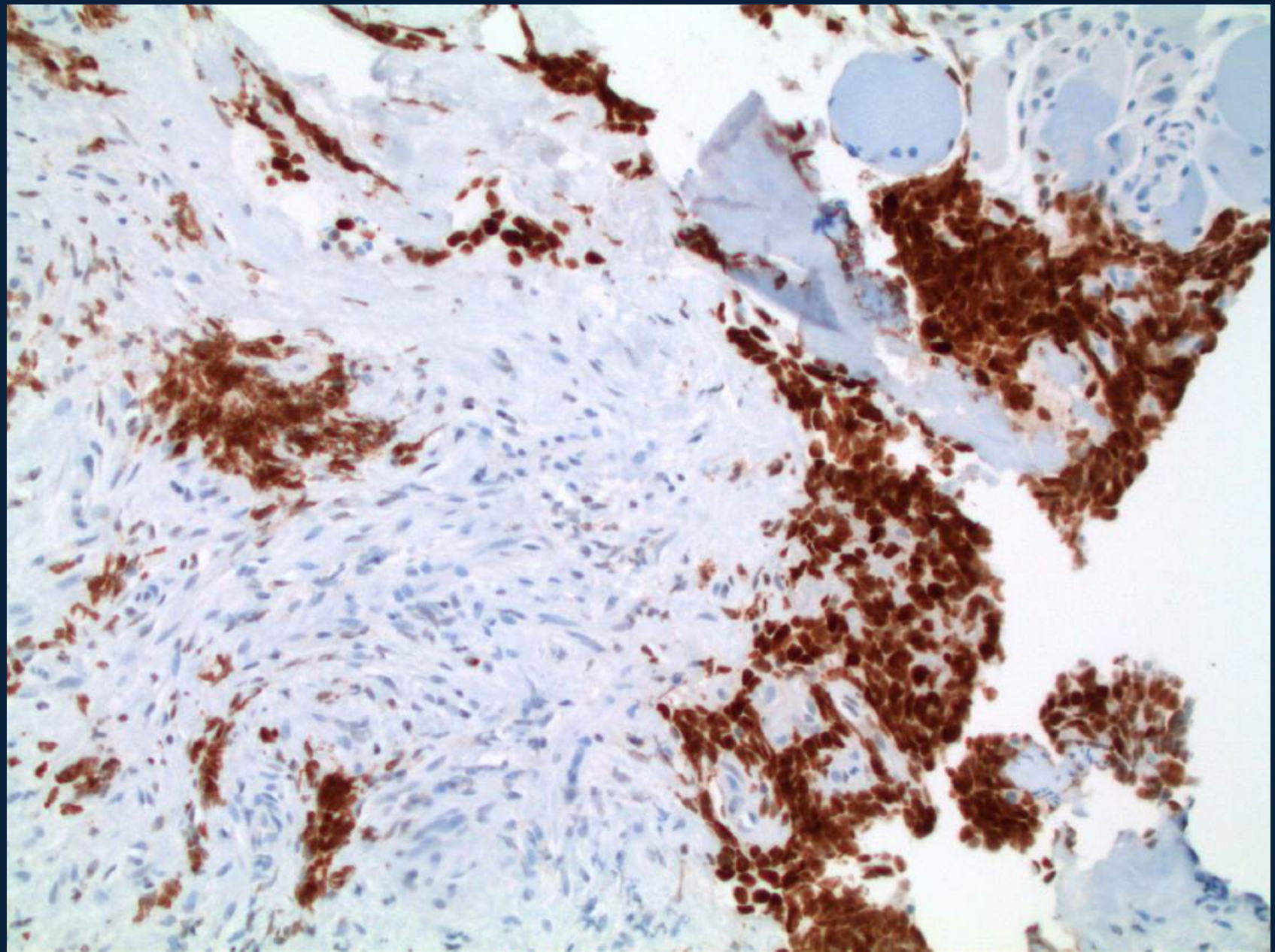
NKX2.2: Ewing Sarcoma



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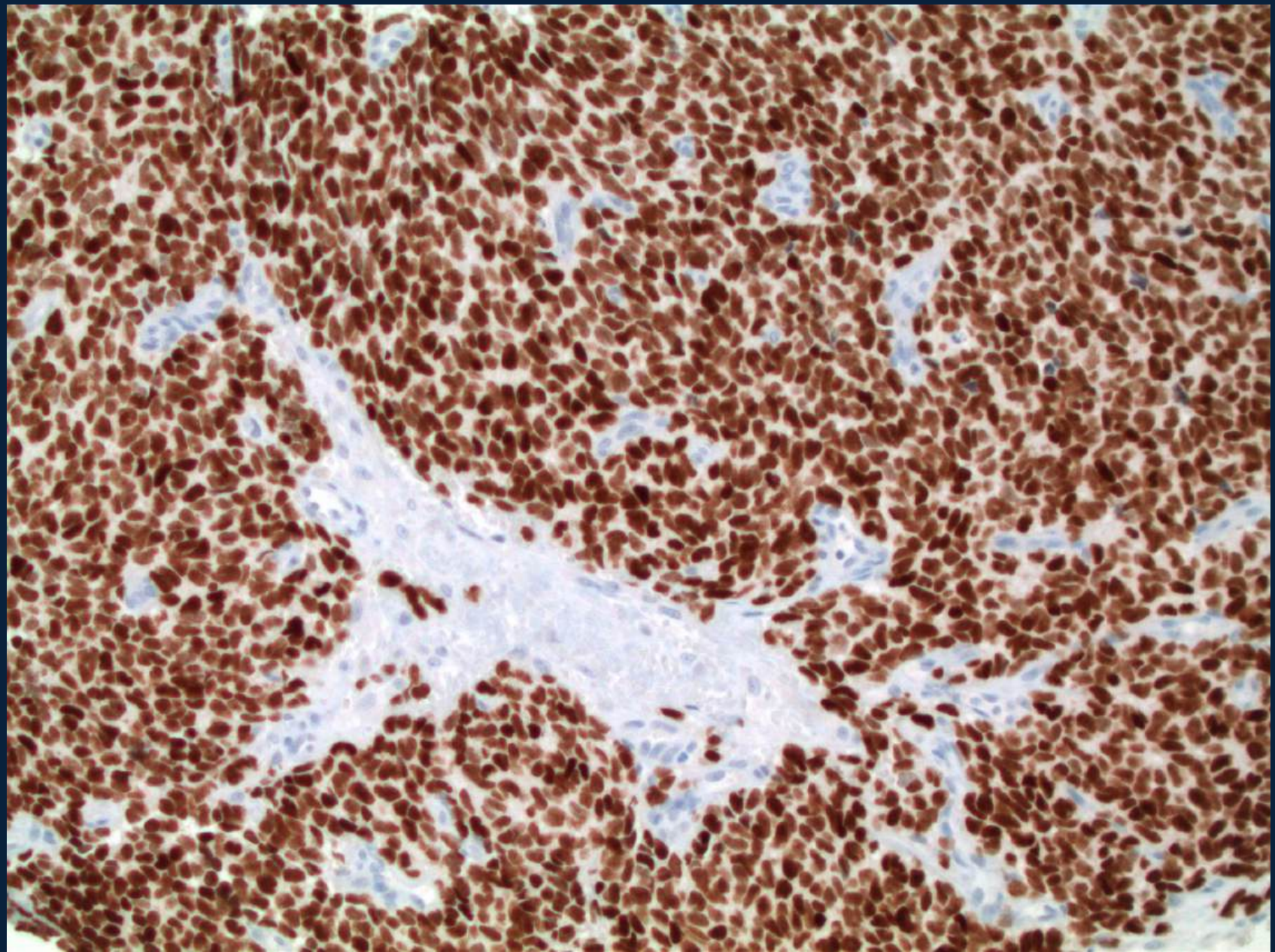
NKX2.2: Ewing Sarcoma



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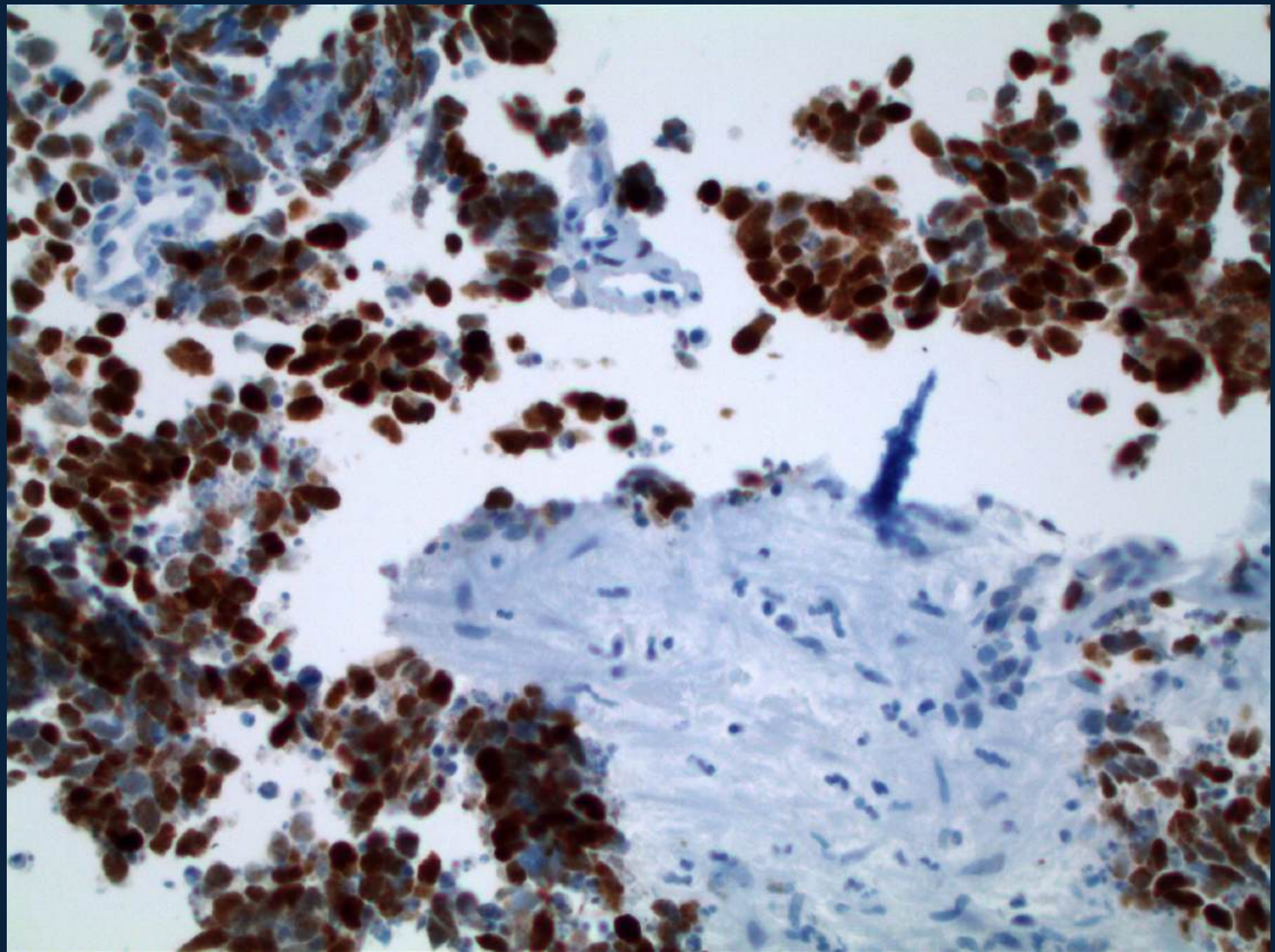
NKX2.2 Pulmonary small cell ca



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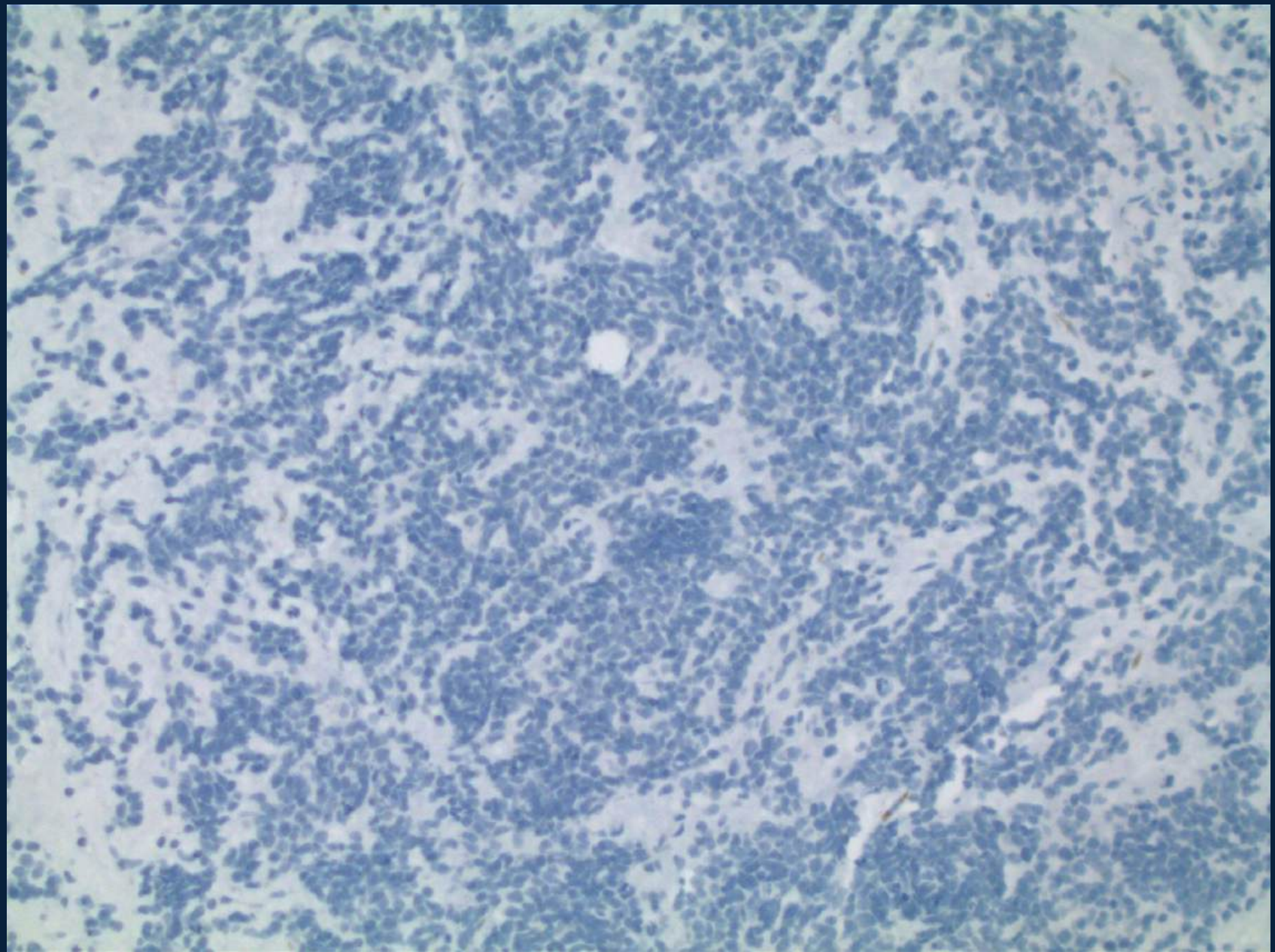
NKX2.2 Neuroblastoma



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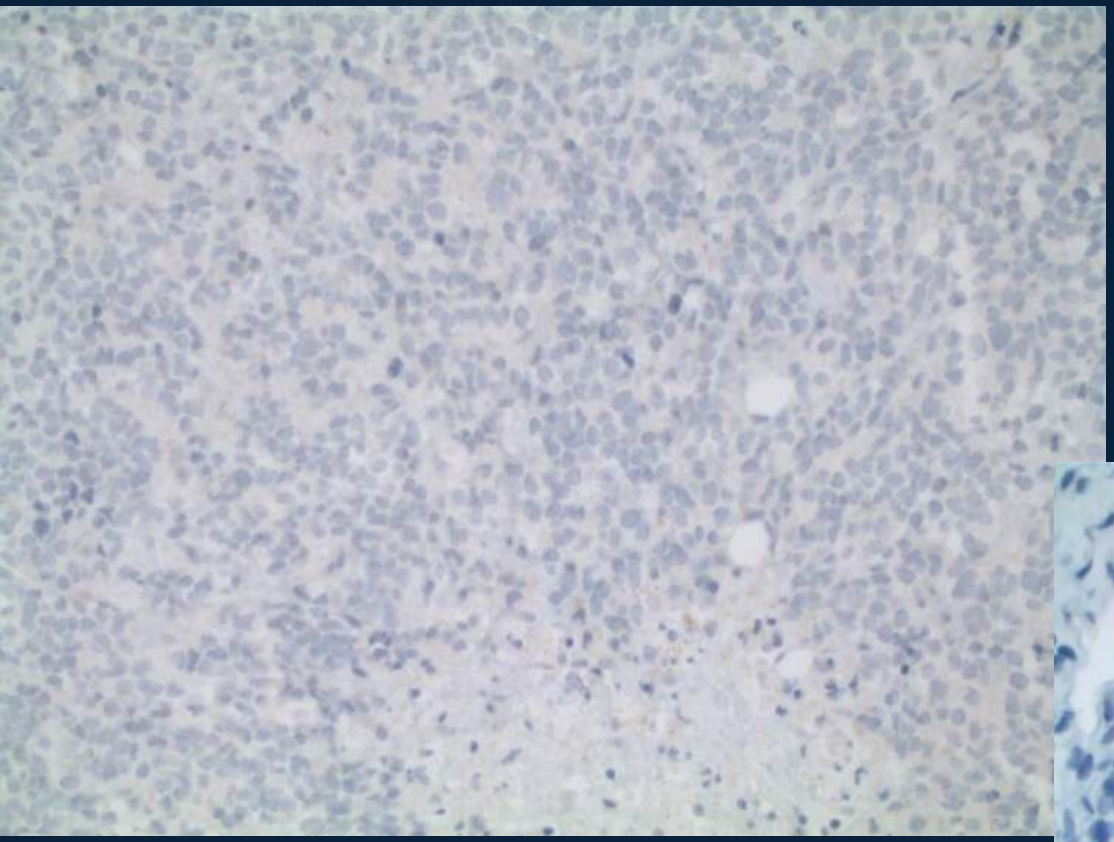
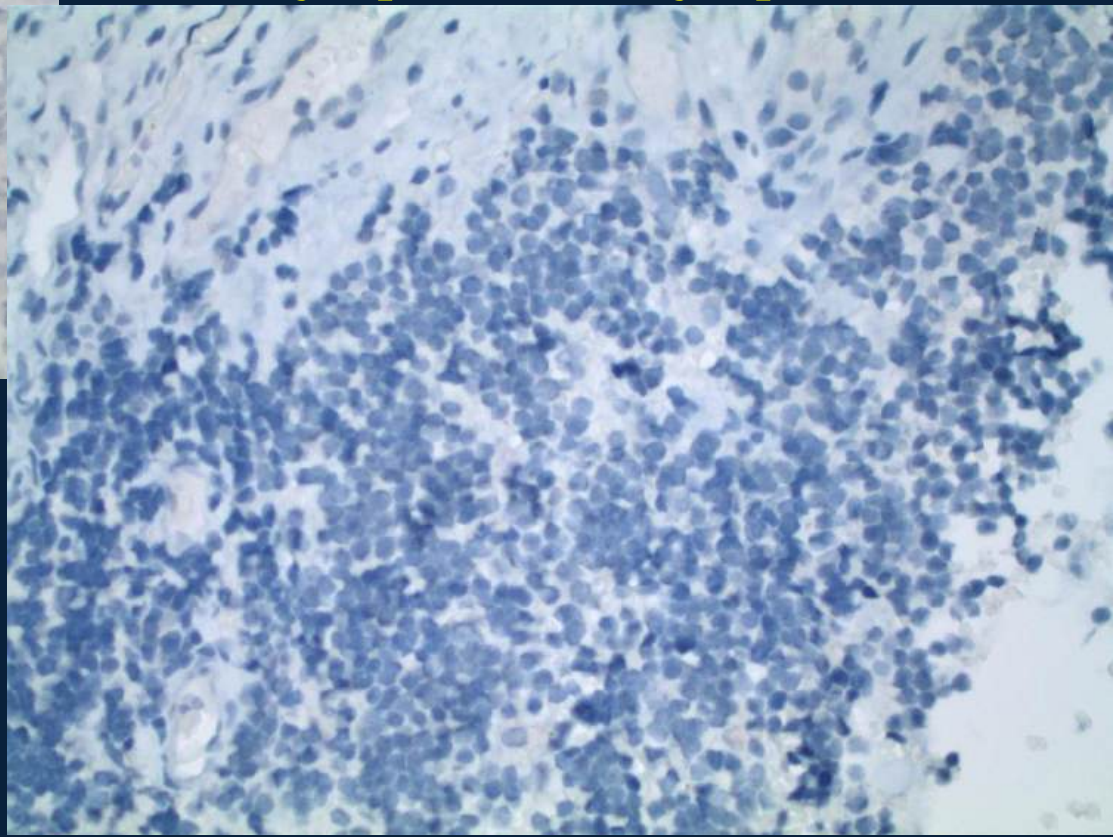
NKX2.2 negative



Desmoplastic small round cell tumor

Lymphoblastic lymphoma



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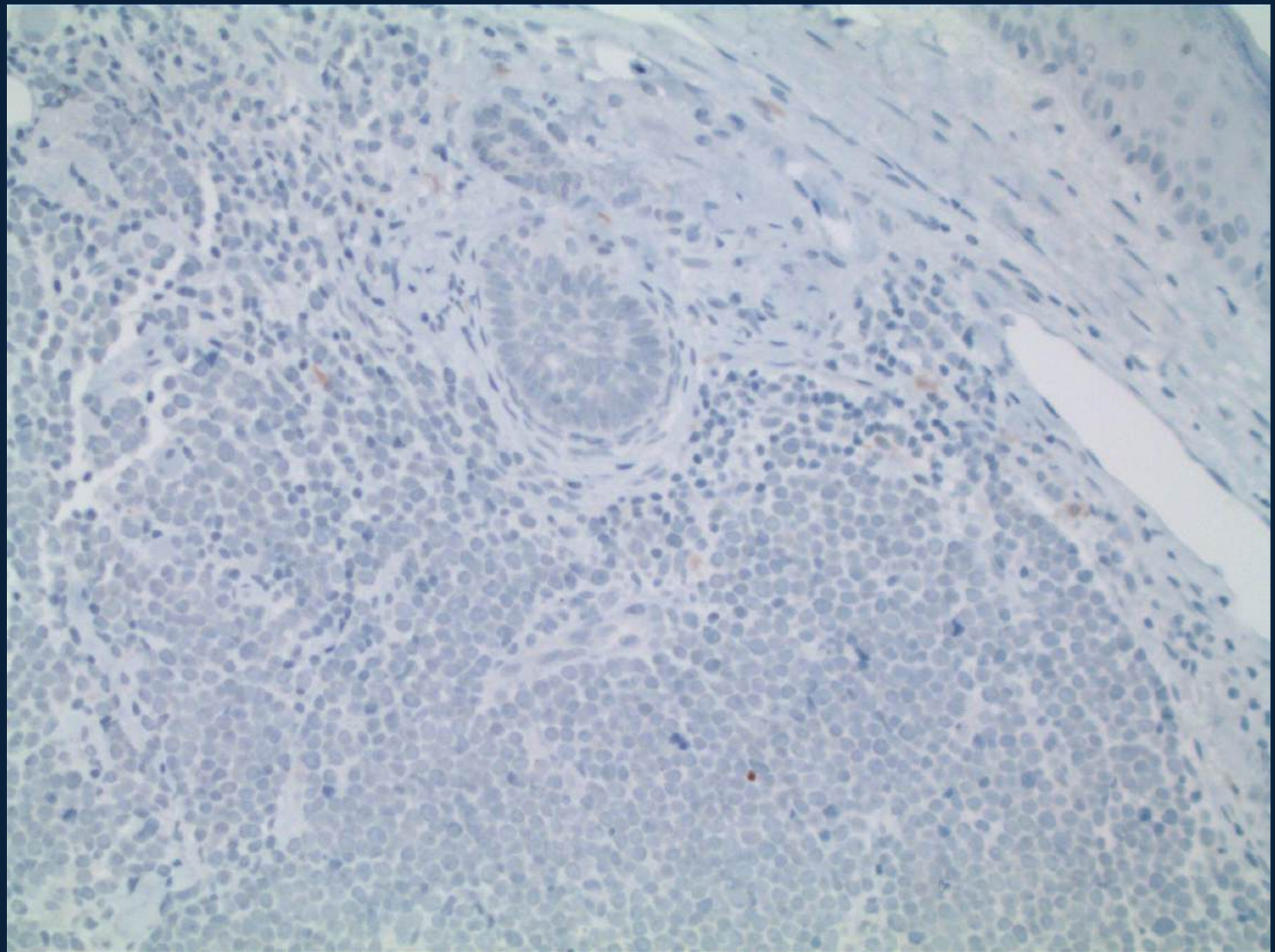
NKX2.2 negative: Merkel cell tumor



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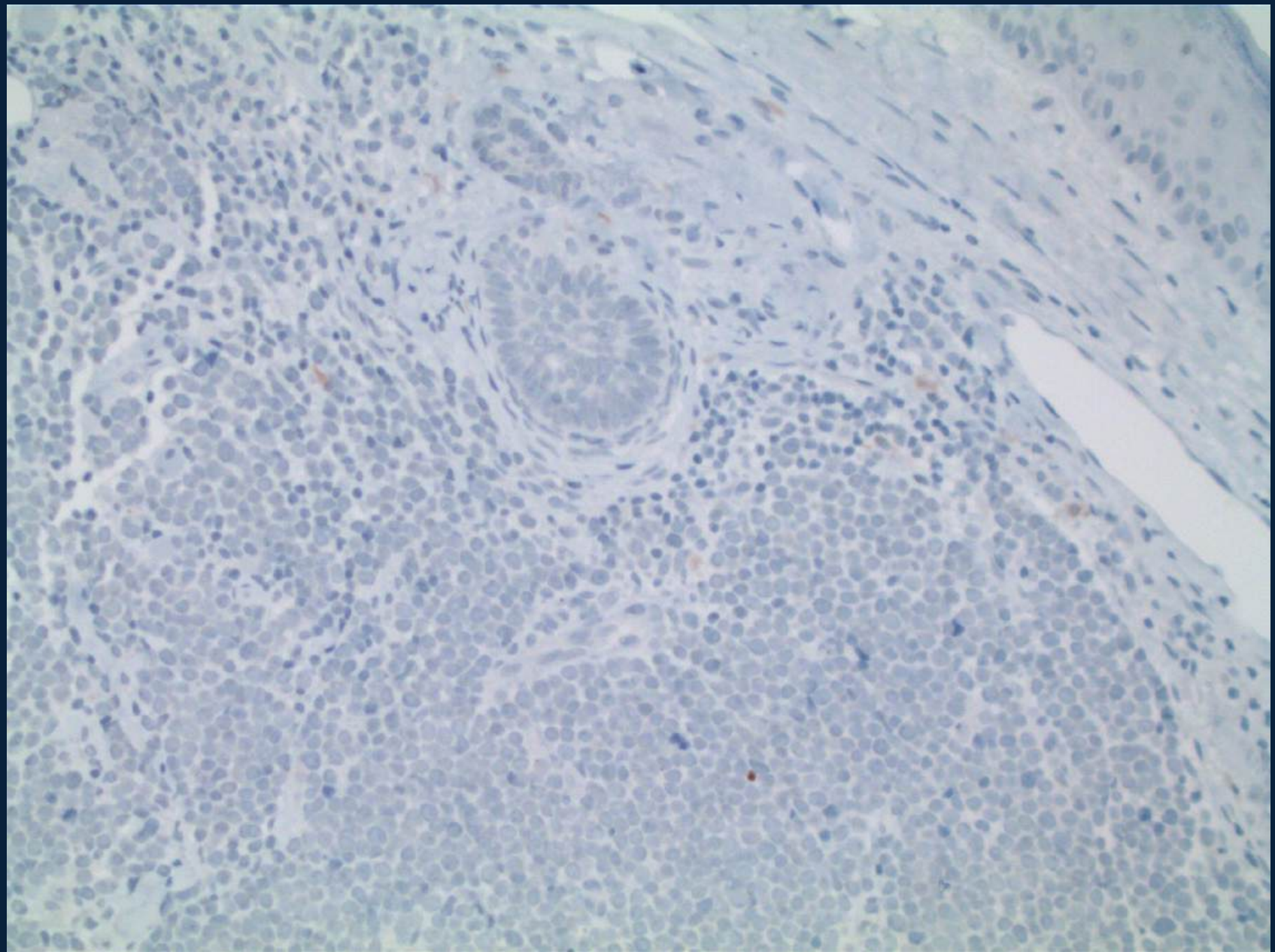
NKX2.2 negative: Merkel cell tumor



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NKX2.2: References

Yoshida A, et al. NKX2.2 is a Useful Immunohistochemical Marker for Ewing Sarcoma. Am J Surg Pathol 2012;36:993–999.

Hung YP, Fletcher CDM and Hornick JL. Evaluation of NKX2-2 expression in round cell sarcomas and other tumors with EWSR1 rearrangement: imperfect specificity for Ewing sarcoma. ModernPathology(2016) 29, 370–380.

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Phox2b

- Phox2b is expressed in neuroblastoma with great specificity amongst small round cell malignancies. It is a nuclear transcription factor responsible for autonomic nervous system development.

- It will also label ganglioneuroblastoma, ganglioneuroma and up to 50% of paragangliomas (potentially useful in a panel with GATA3, S-100 and neuroendocrine markers).

- Rare cases of Merkel cell, Wilms and CIC-rearranged sarcomas may label a minor population of cells.

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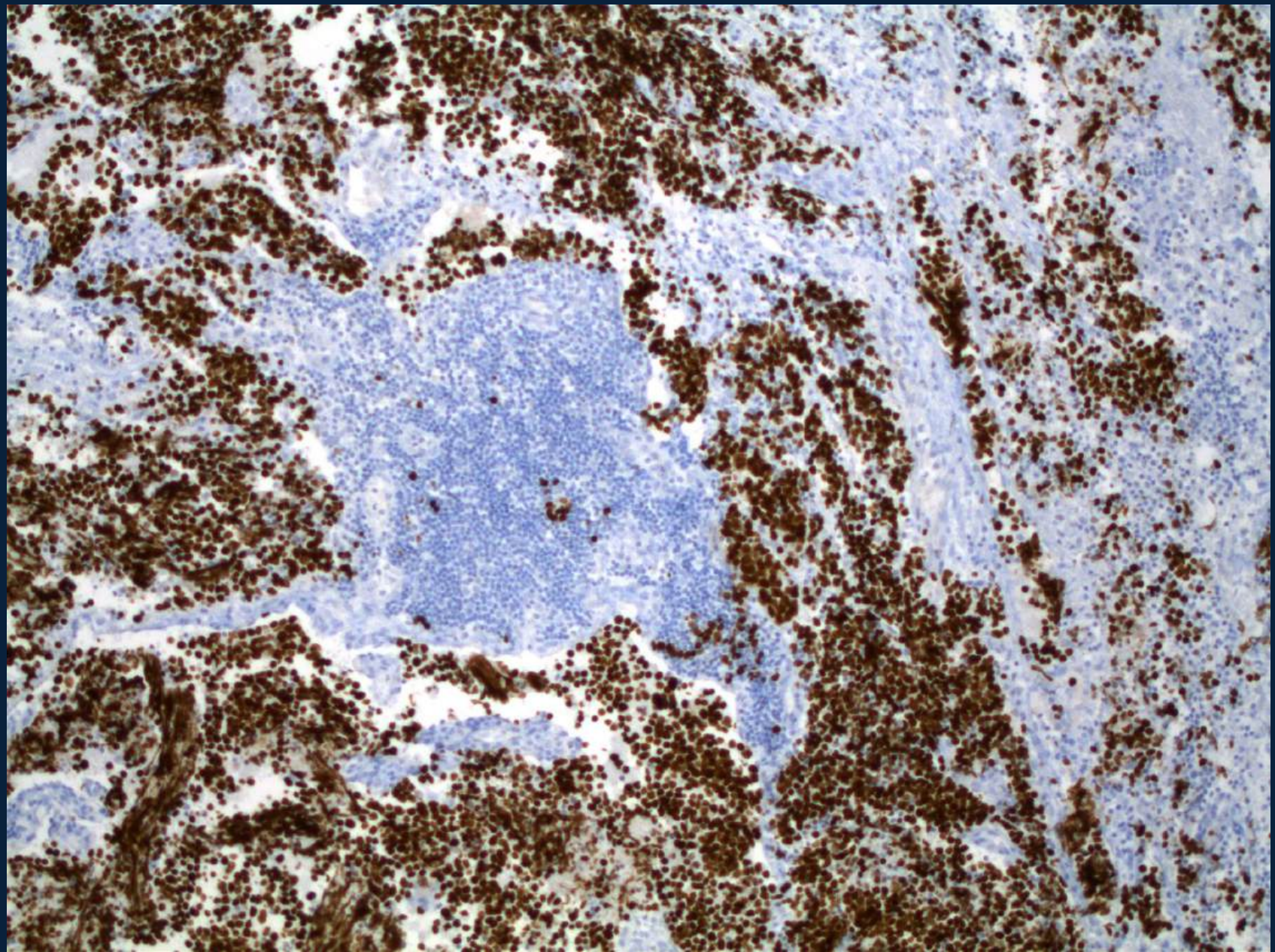
Phox2b: Neuroblastoma; rabbit mono: clone EP312



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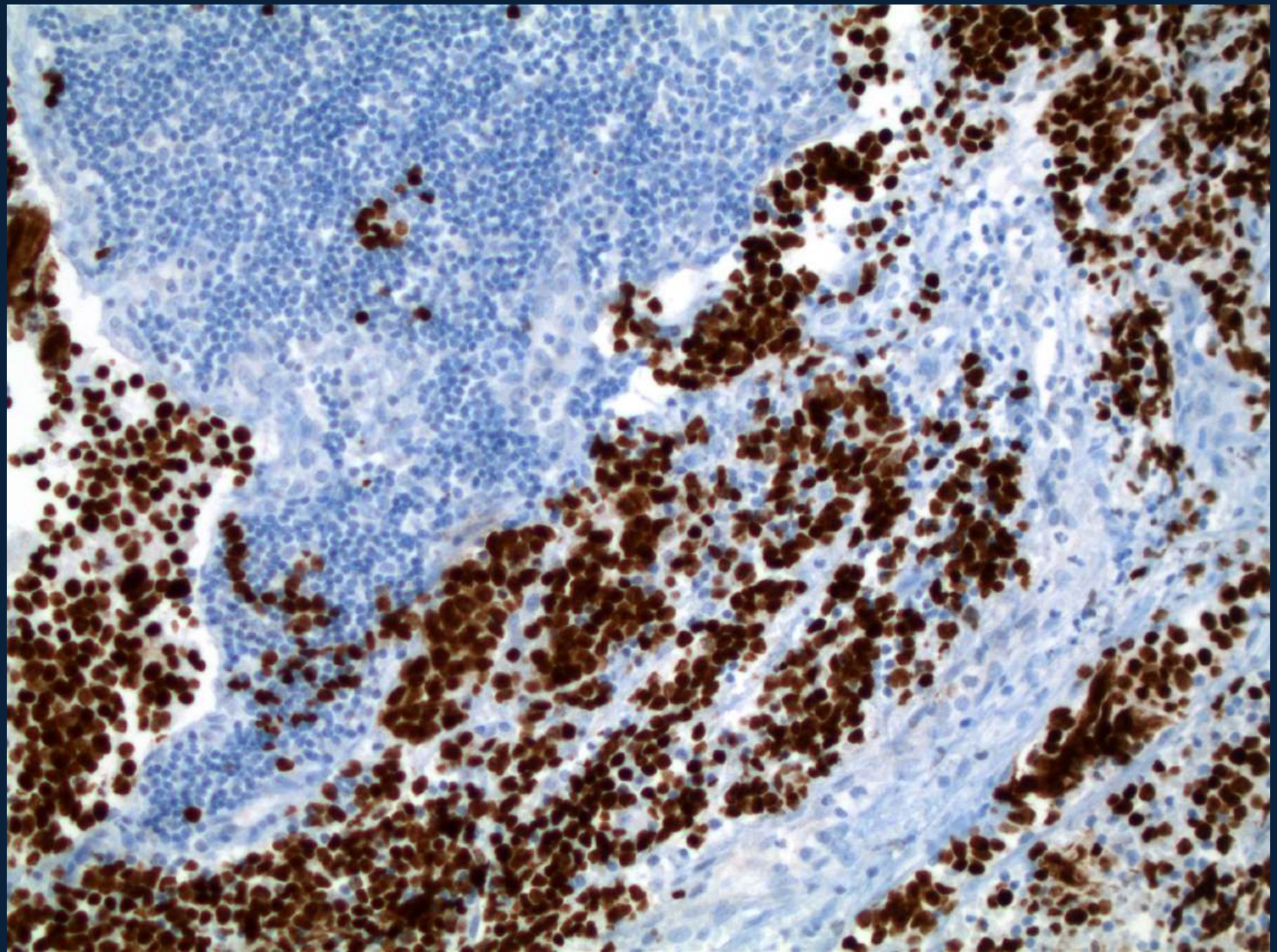
Phox2b: Neuroblastoma



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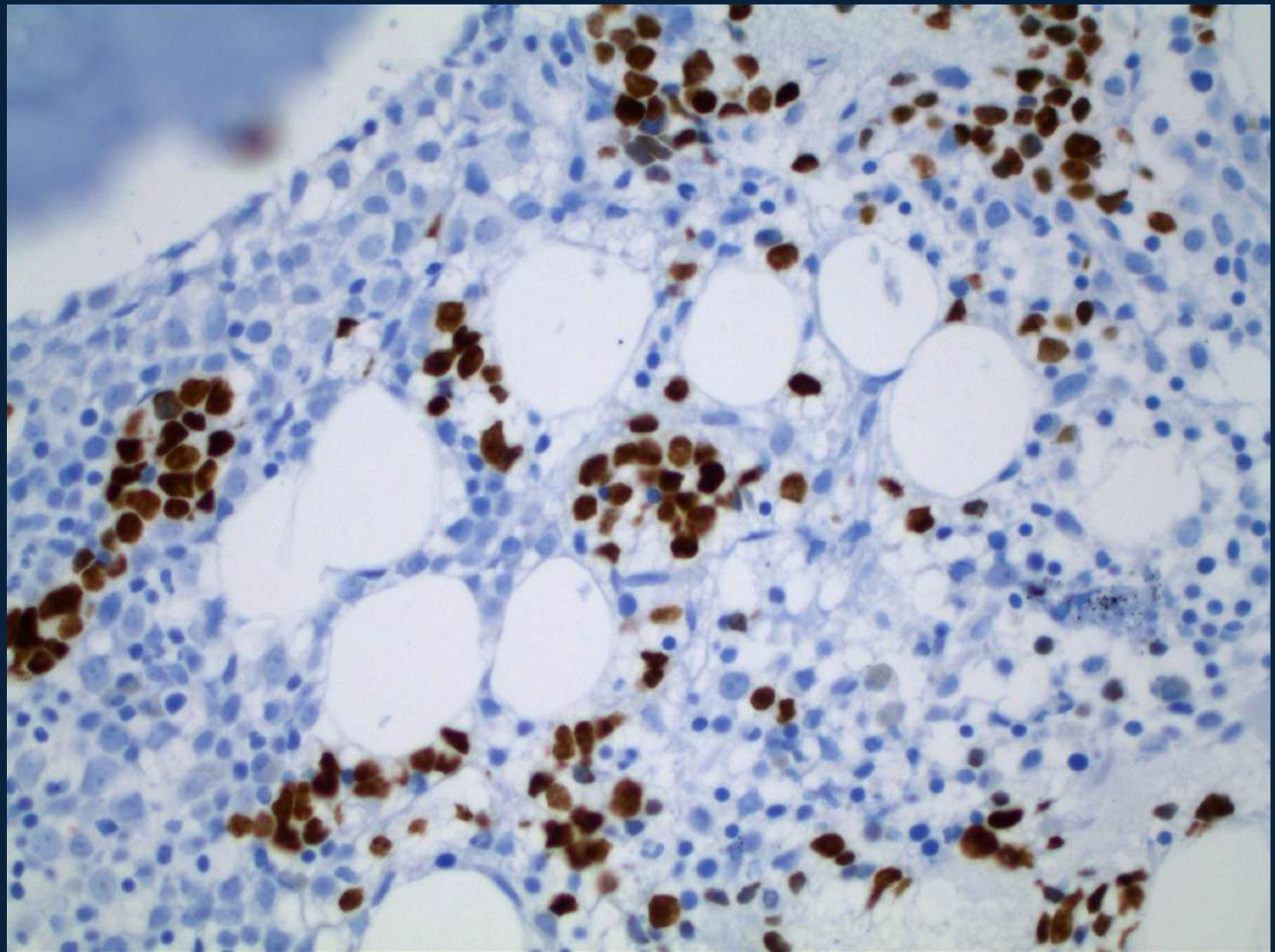
Phox2b: Neuroblastoma- met to BM



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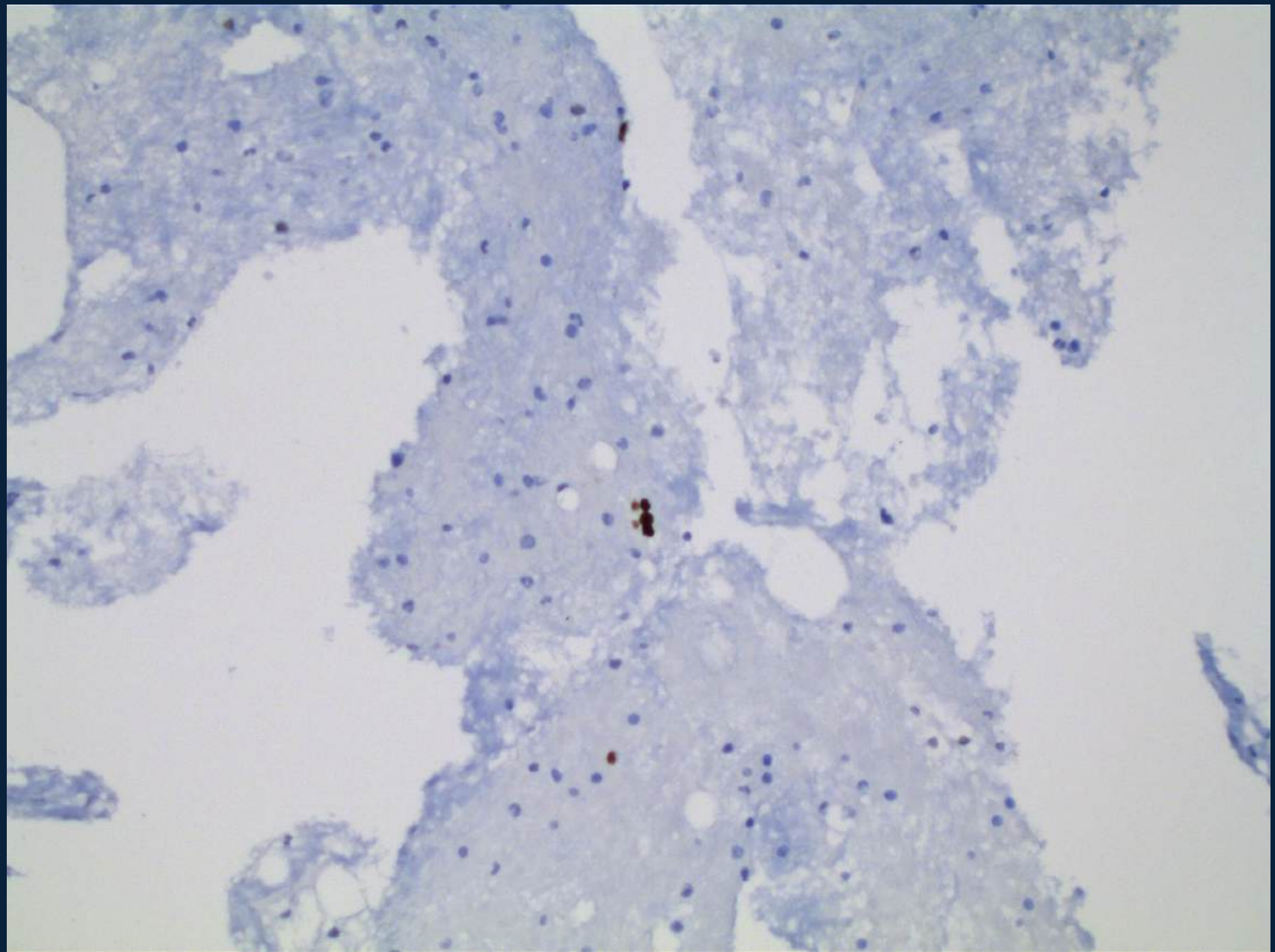
Phox2b: Neuroblastoma- rare cells- BM clot



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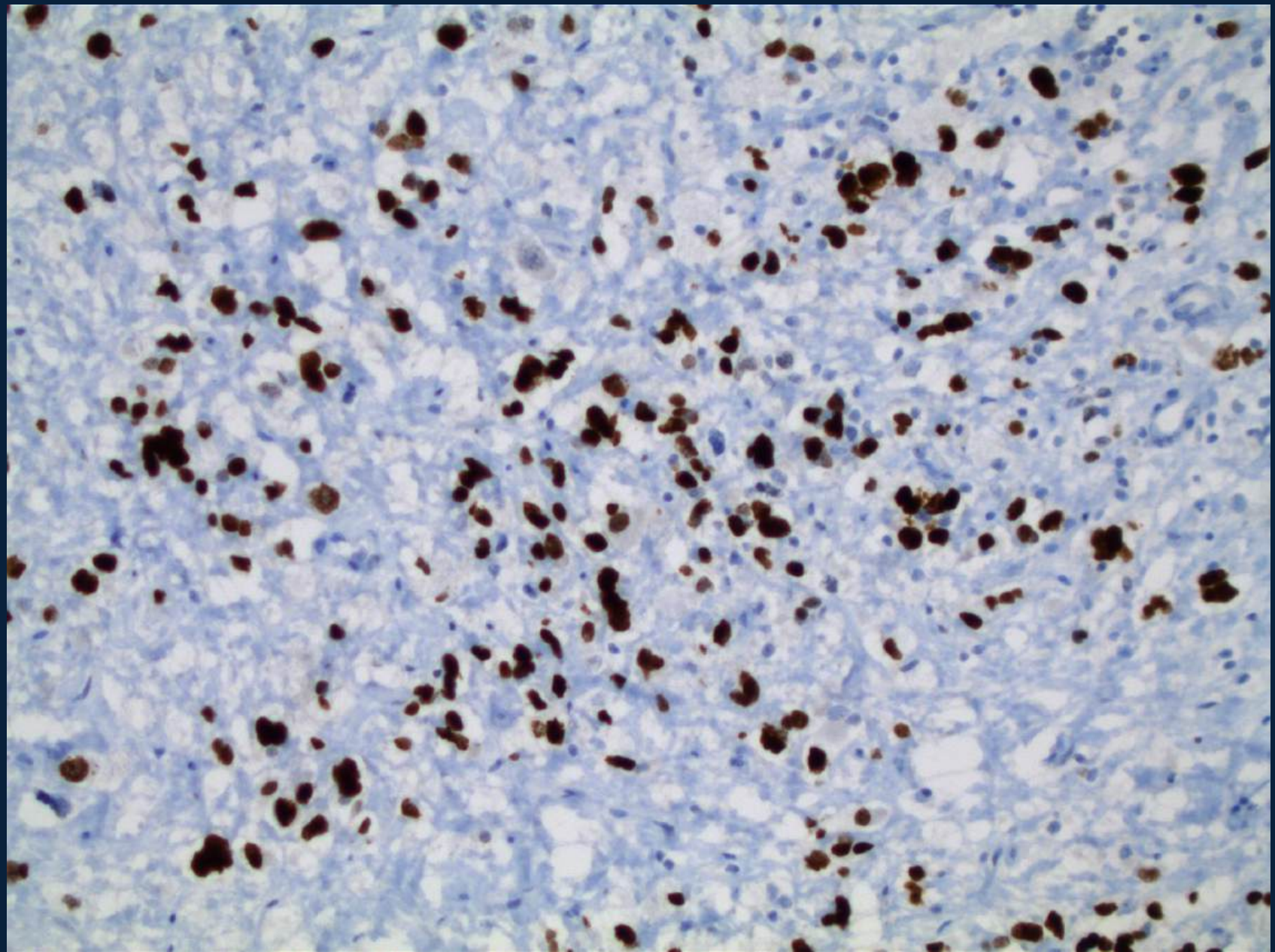
Phox2b: treated Neuroblastoma



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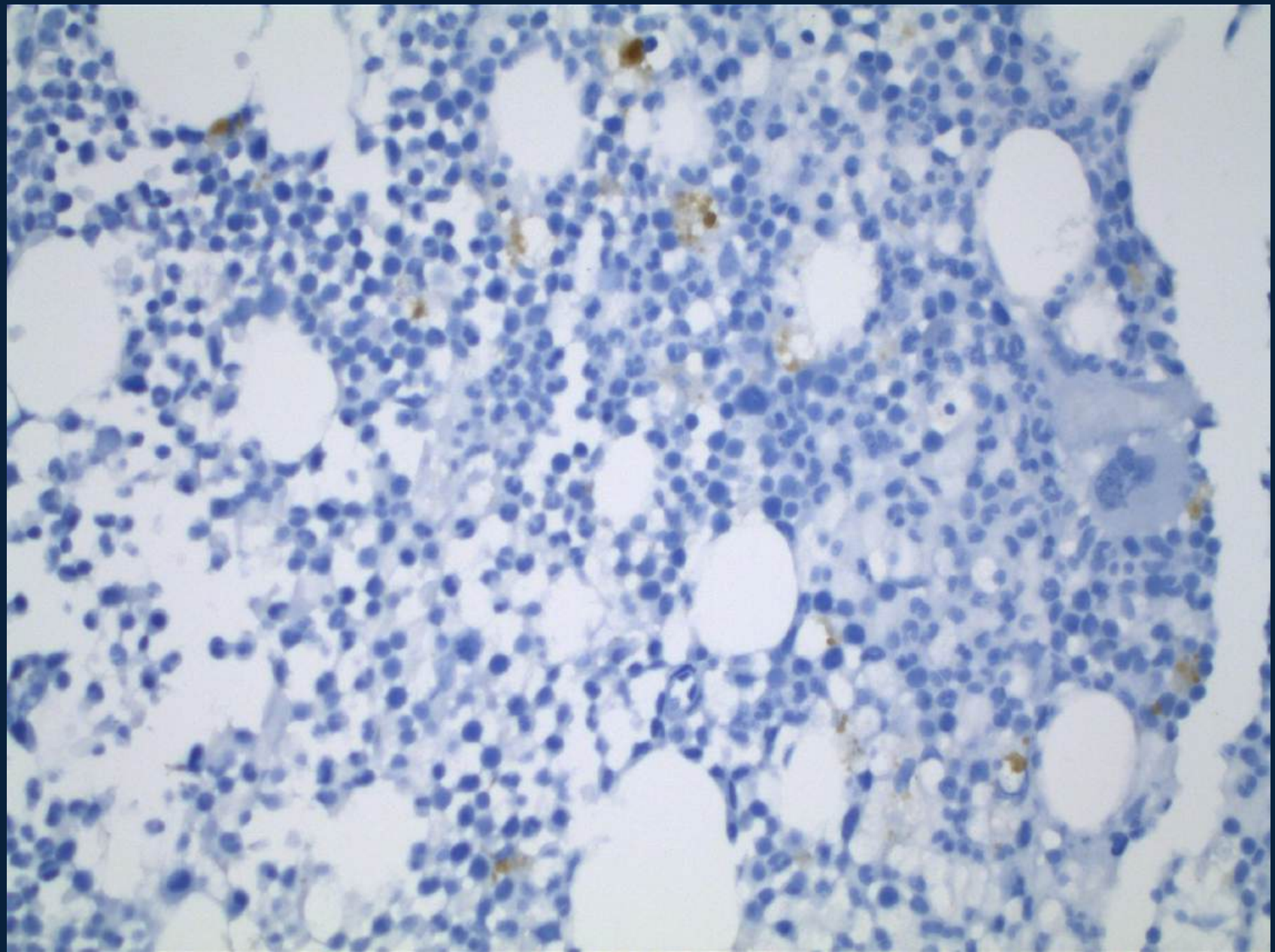
Phox2b: negative BM



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Phox2B: Reference

Hung YP, et al. PHOX2B reliably distinguishes neuroblastoma among small round blue cell tumours. Histopathology. 2017,71,786–794.

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TLE1: Transducin-Like Enhancer of Split 1

TLE1 is a transcription regulator of Wnt signaling.

TLE1 is involved in lateral inhibition, segmentation, eye development, sex determination, neuronal development and hematopoeisis.

Normally expressed in basal keratinocytes, adipocytes, perineural cells, endothelial cells and mesothelial cells

Found to be overexpressed in synovial sarcomas (SS) by GEP

82-97% of SS immunoreactive, usually in majority of or all tumor cells with strong intensity.

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TLE1: Transducin-Like Enhancer of Split 1

Also expressed in nerve sheath tumors (MPNST 15-18%) and 8% of SFT. Occasionally in other sarcomas. Usually weak or focal, non-homogeneous in these tumors.

Greater specificity reported with monoclonal than polyclonal antibodies.

Lin G and Doyle LA. An Update on the Application of Newly Described Immunohistochemical Markers in Soft Tissue Pathology. Arch Pathol Lab Med. 2015;139:106–121;

Rooper LM, et al. The Utility of NKX2.2 and TLE1 Immunohistochemistry in the Differentiation of Ewing Sarcoma and Synovial Sarcoma. Appl Immunohistochem Mol Morphol 2019;27:174–179.

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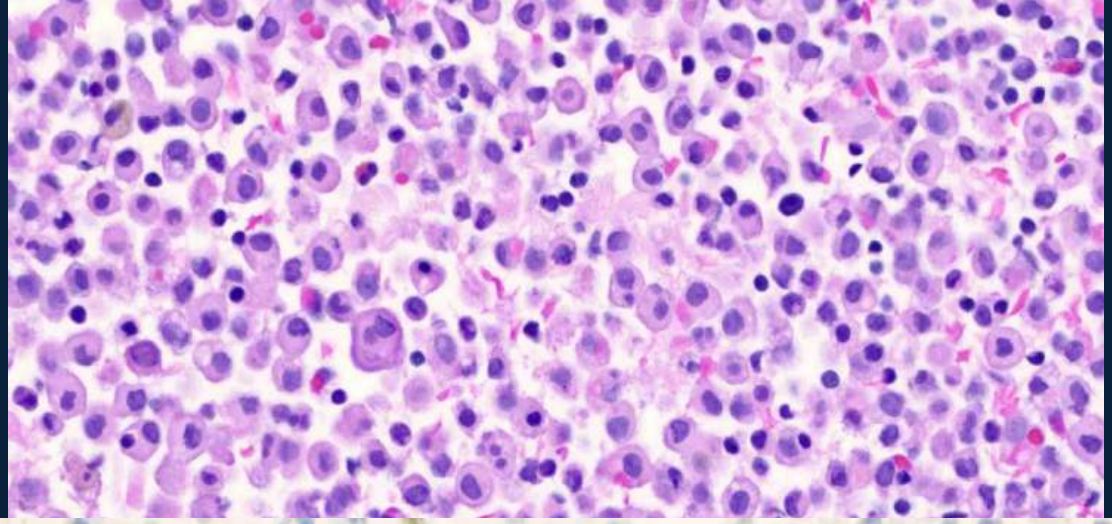
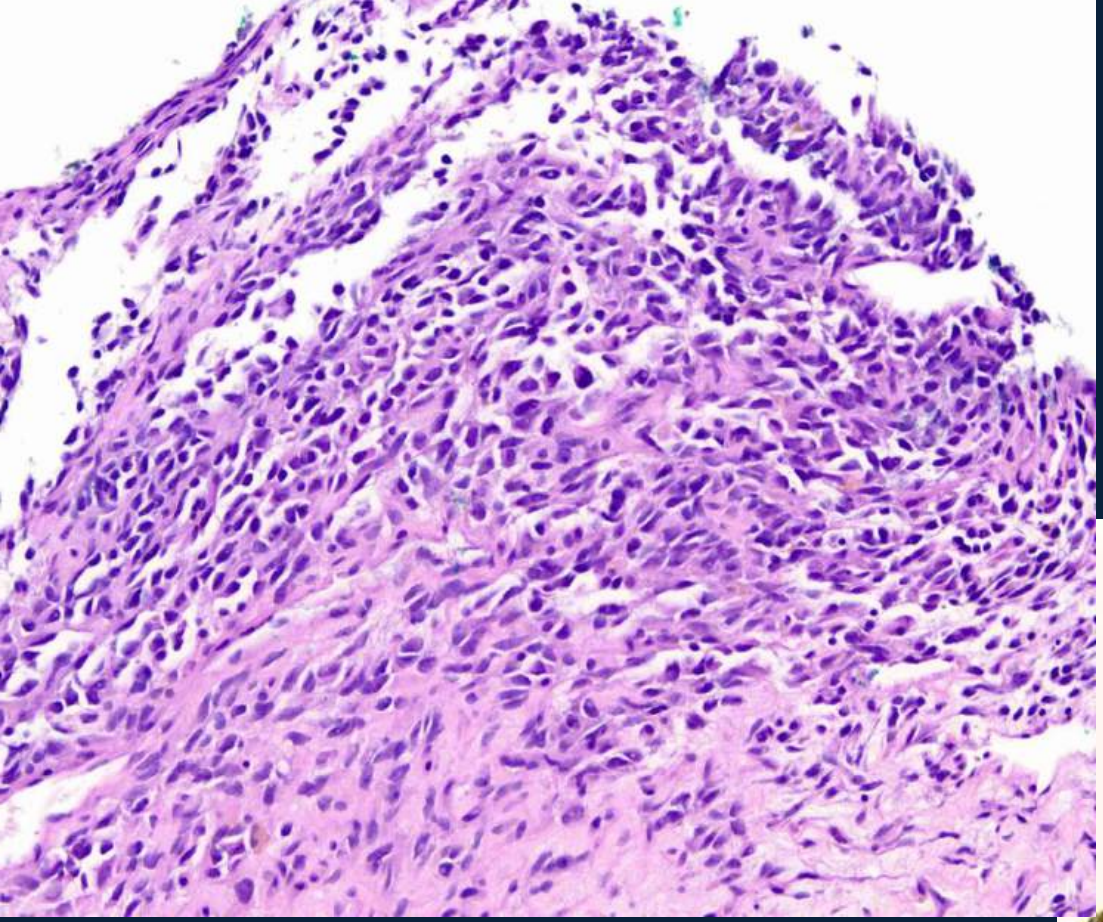
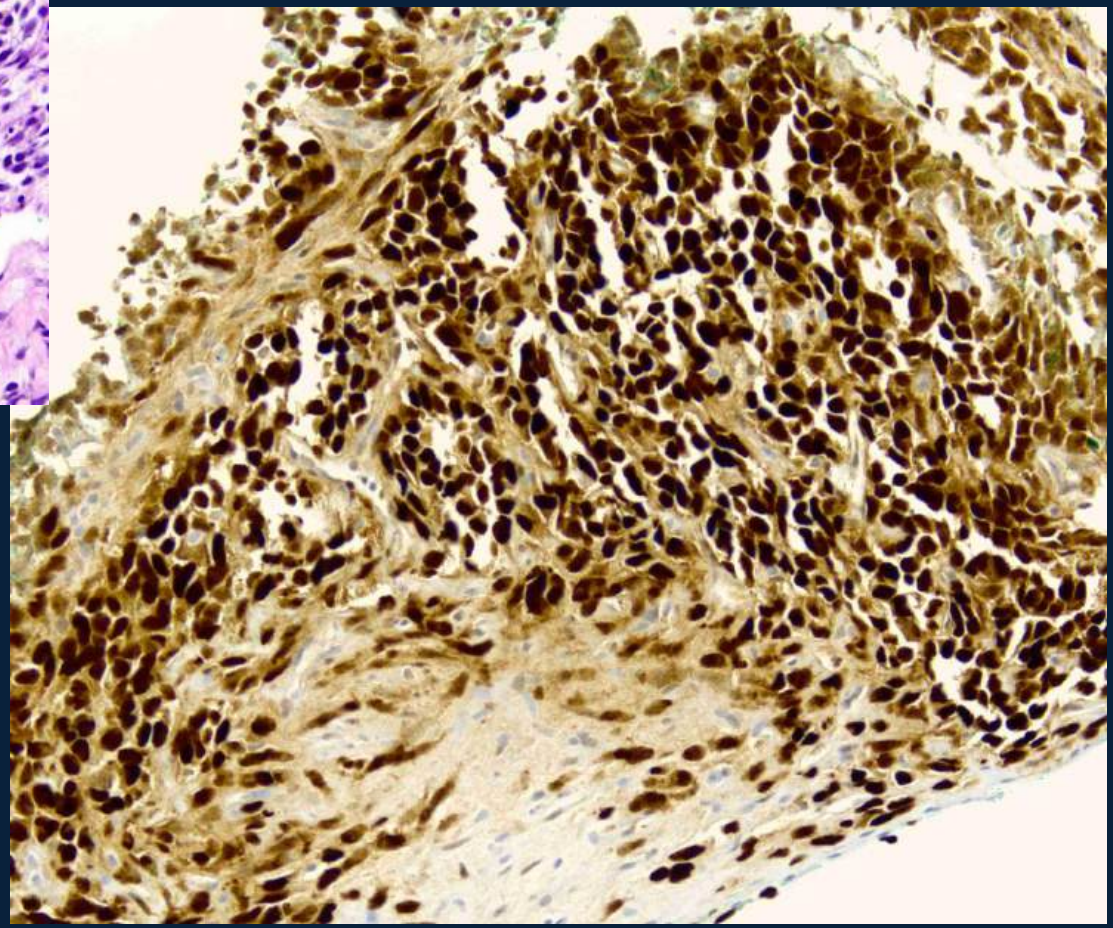


TLE1 Clone 1F5
Mesothelial cells



TLE1
Synovial sarcoma biopsy



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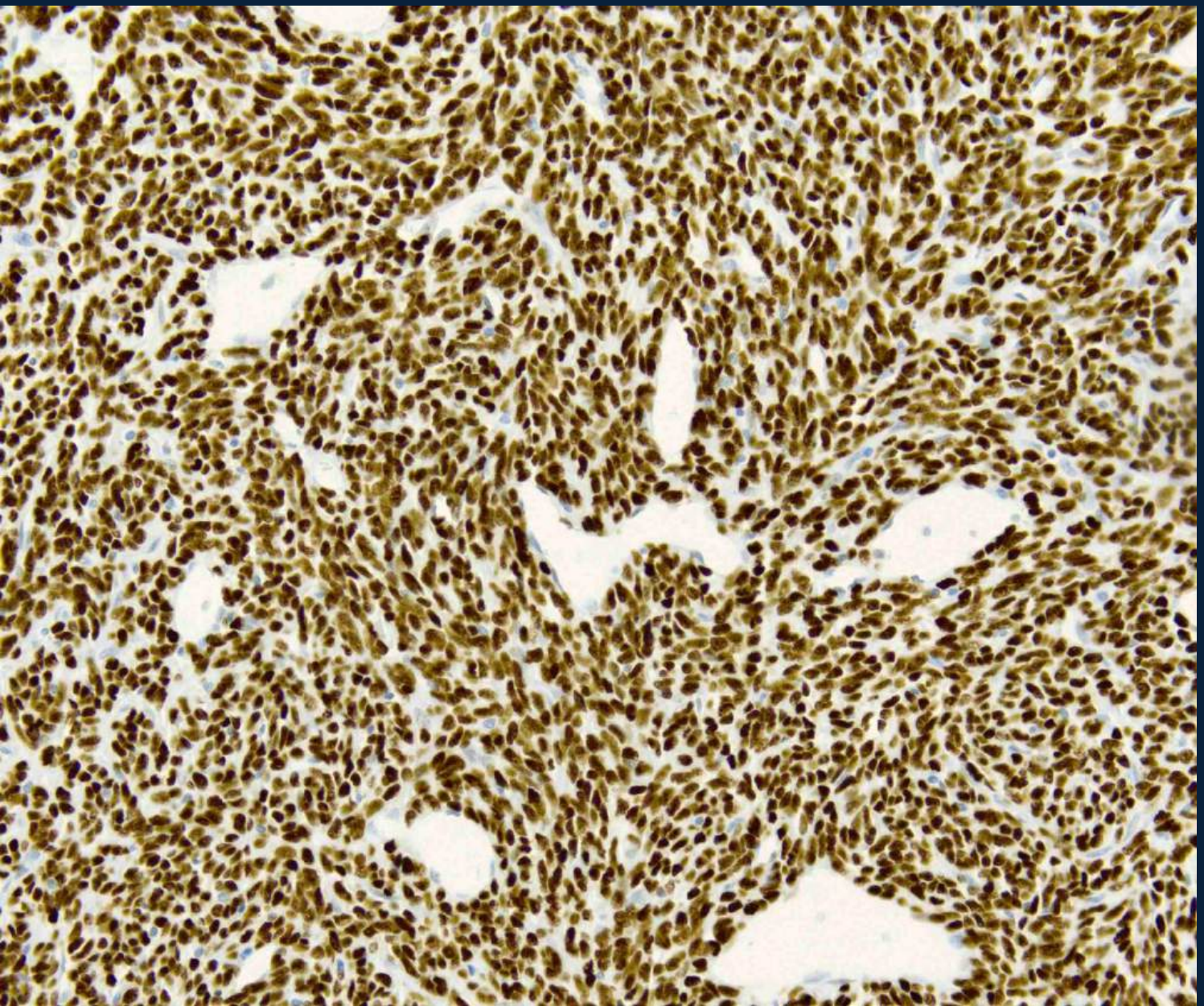

TLE1
Synovial sarcoma

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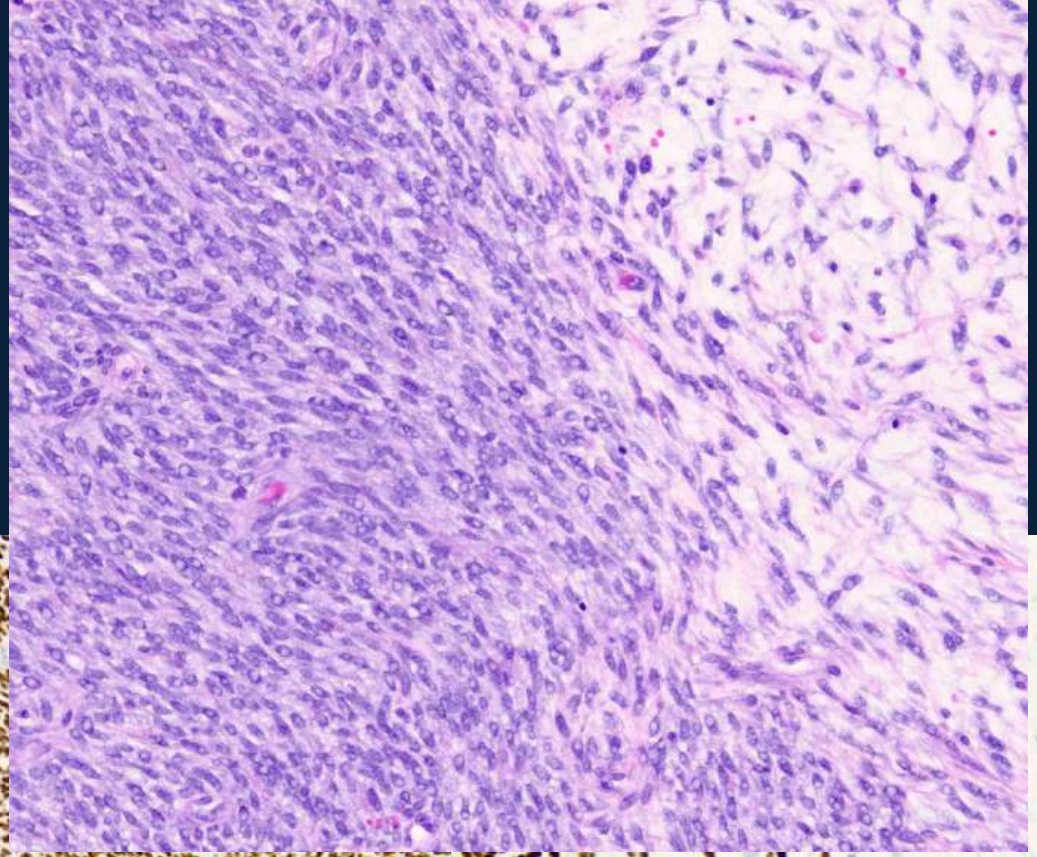
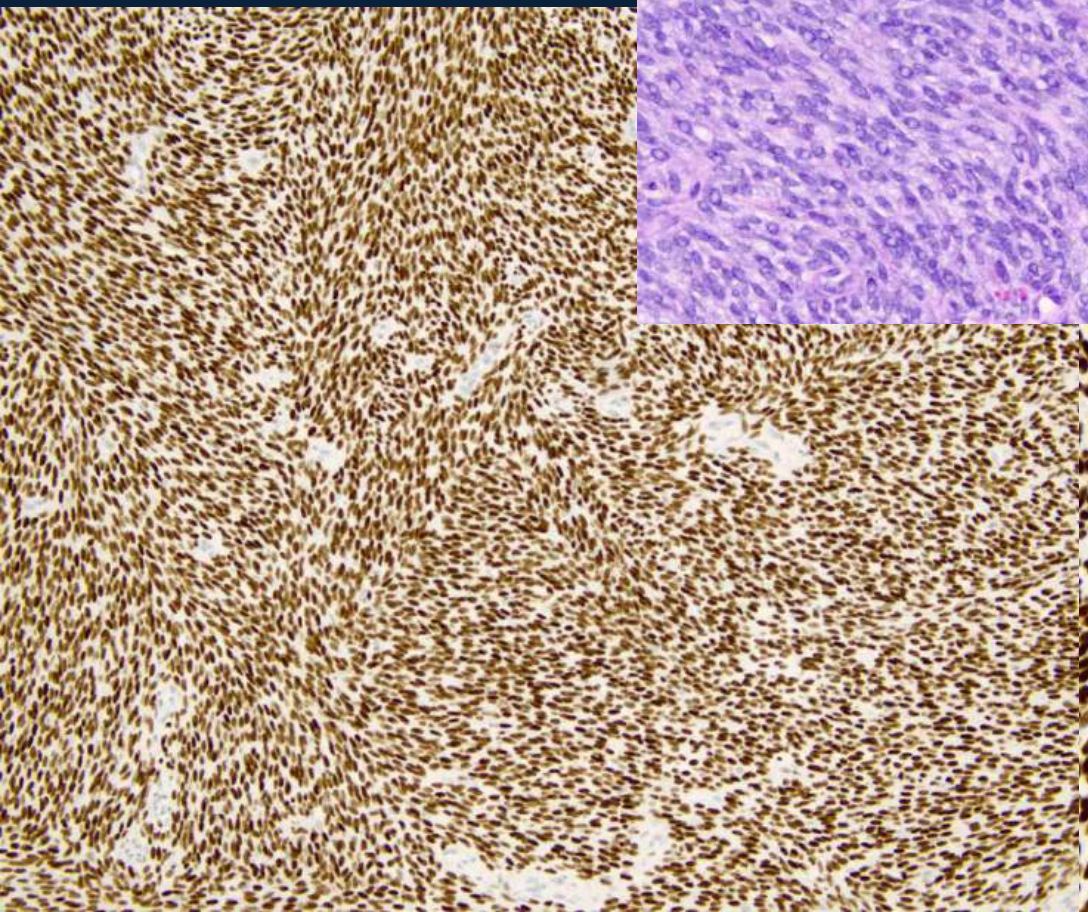
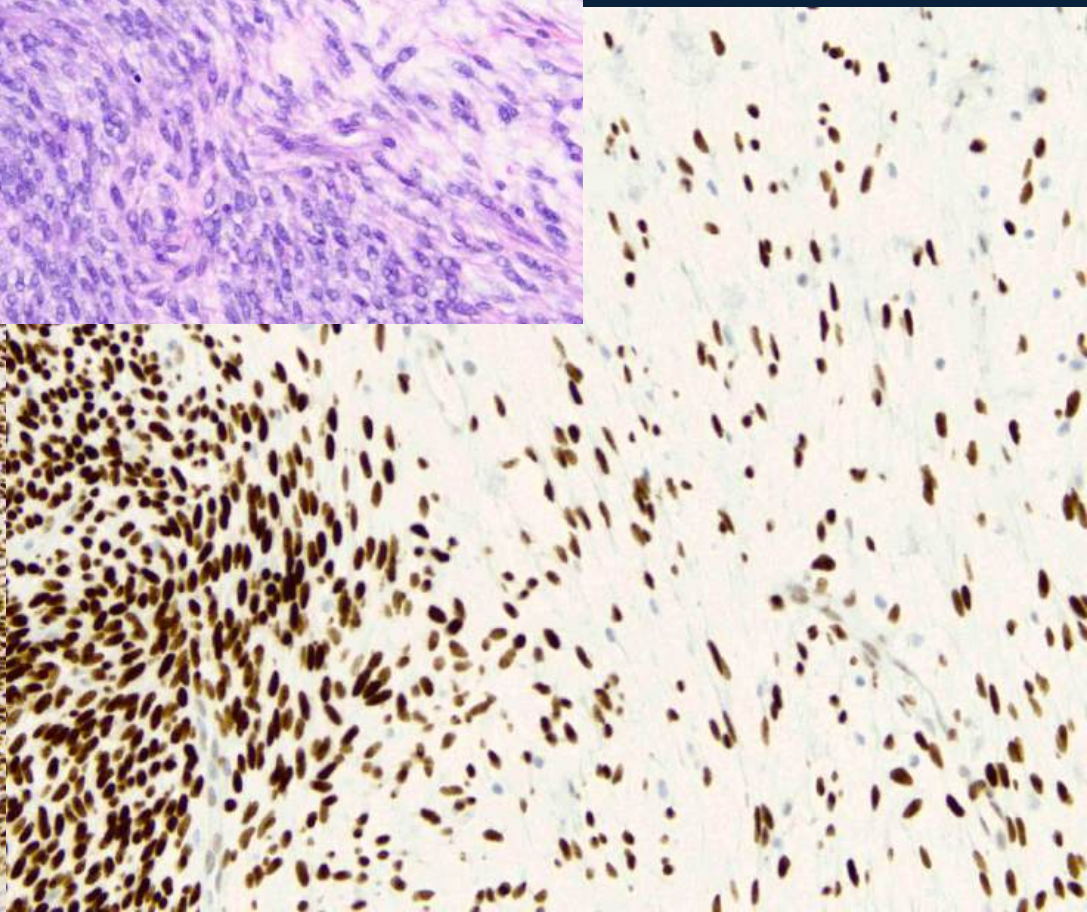
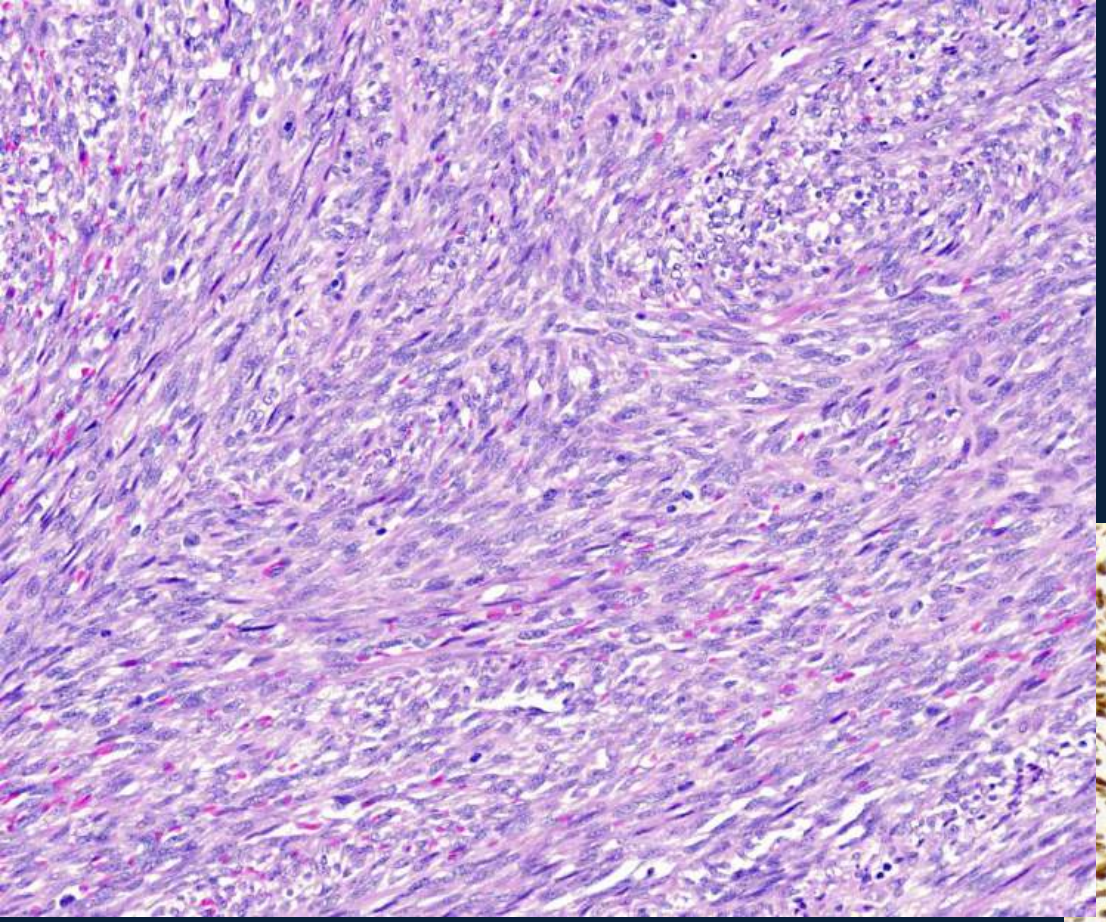
TLE1
Synovial sarcoma

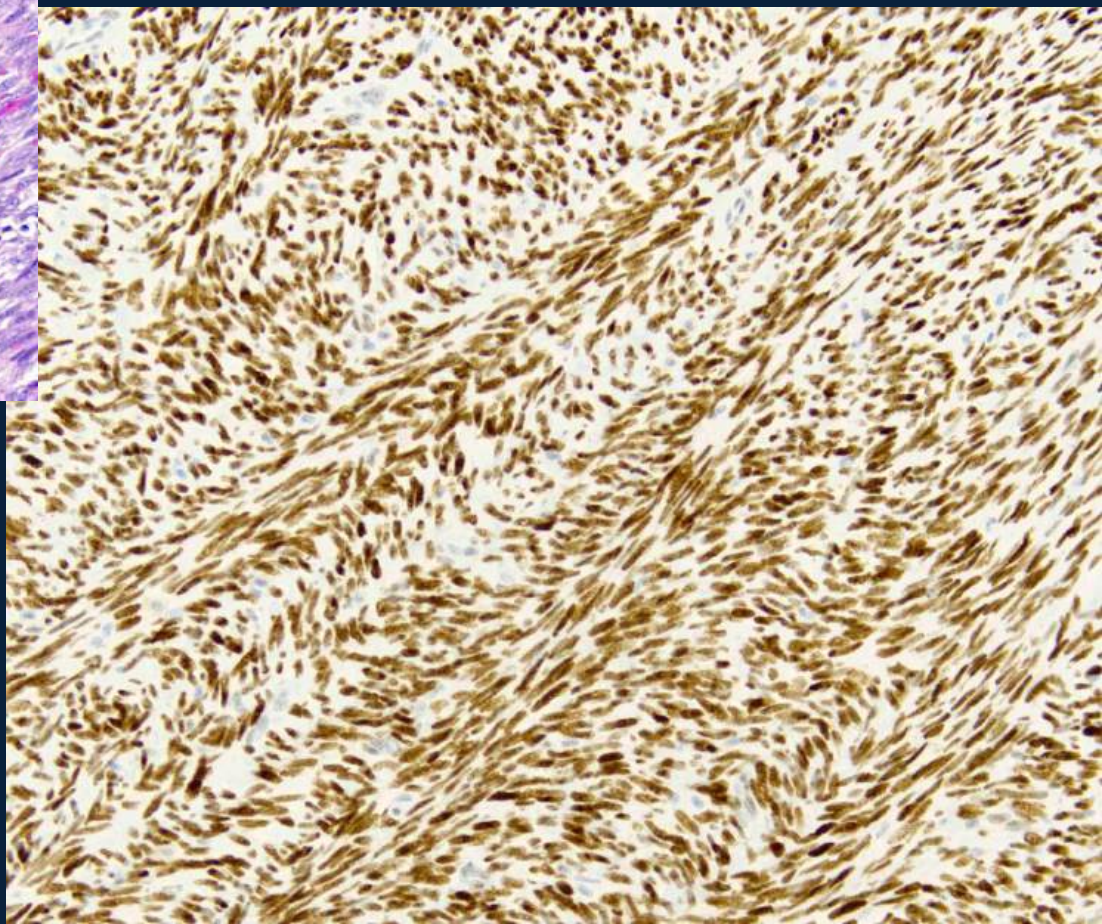




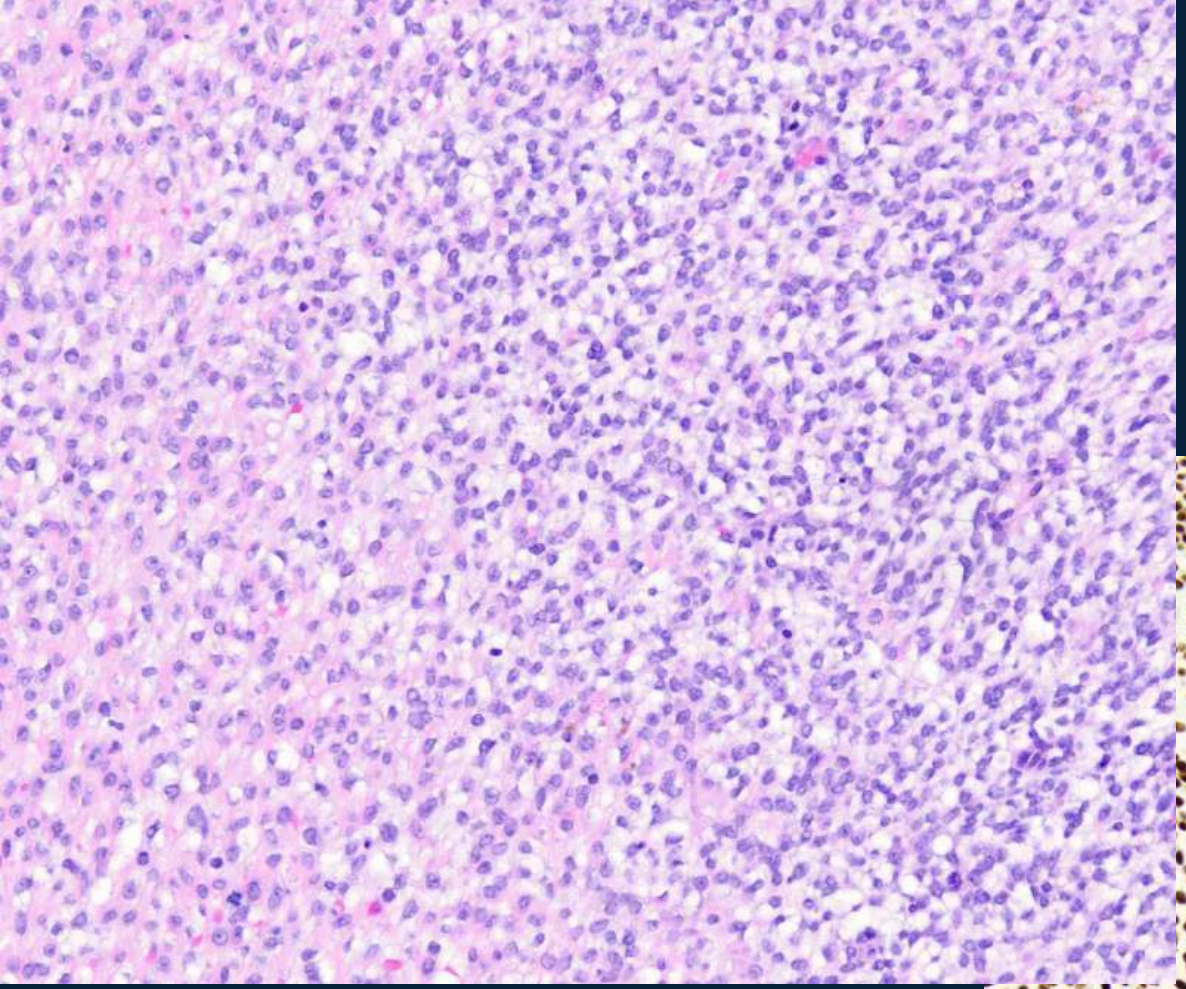


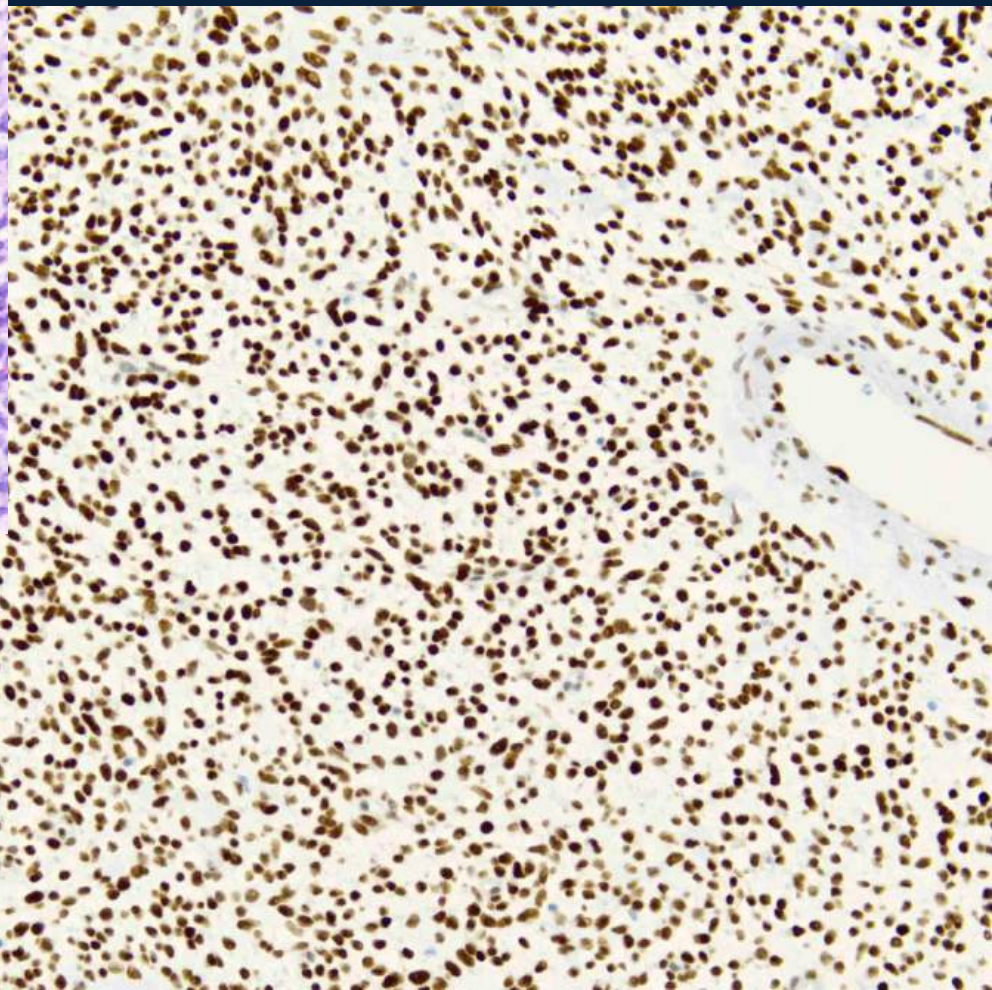


TLE1
Synovial sarcoma



TLE1 Synovial sarcoma





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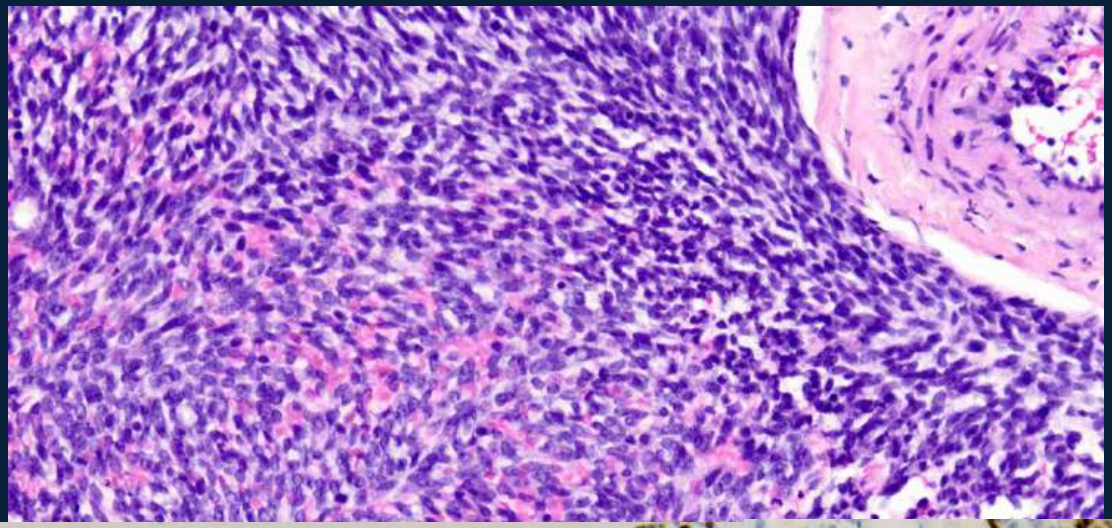
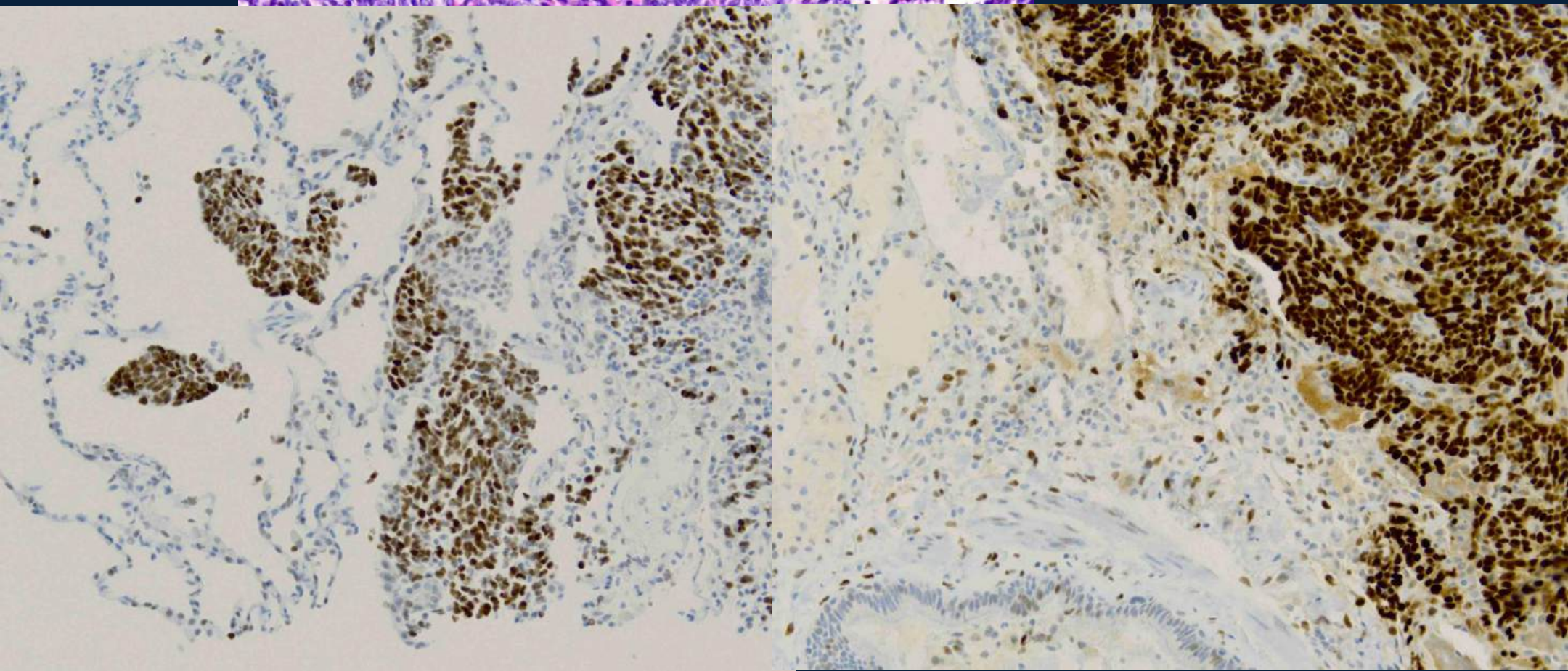
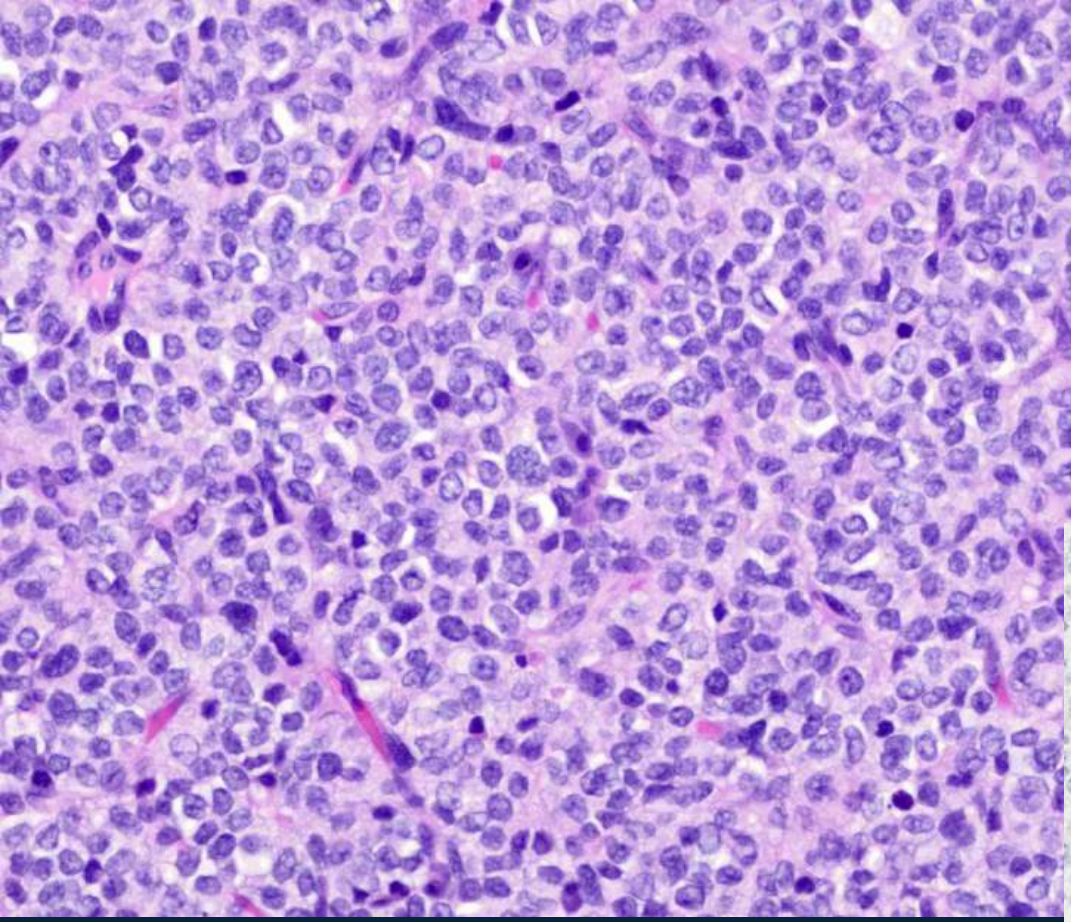
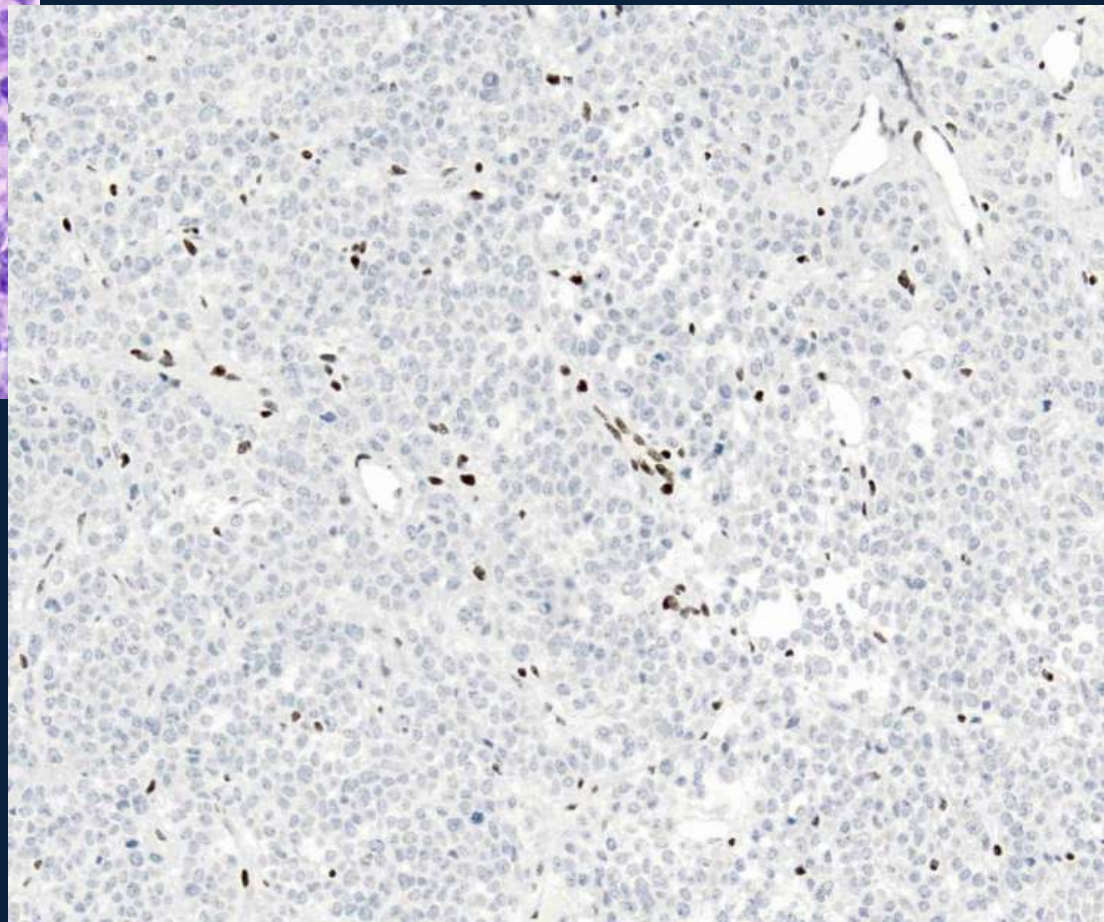


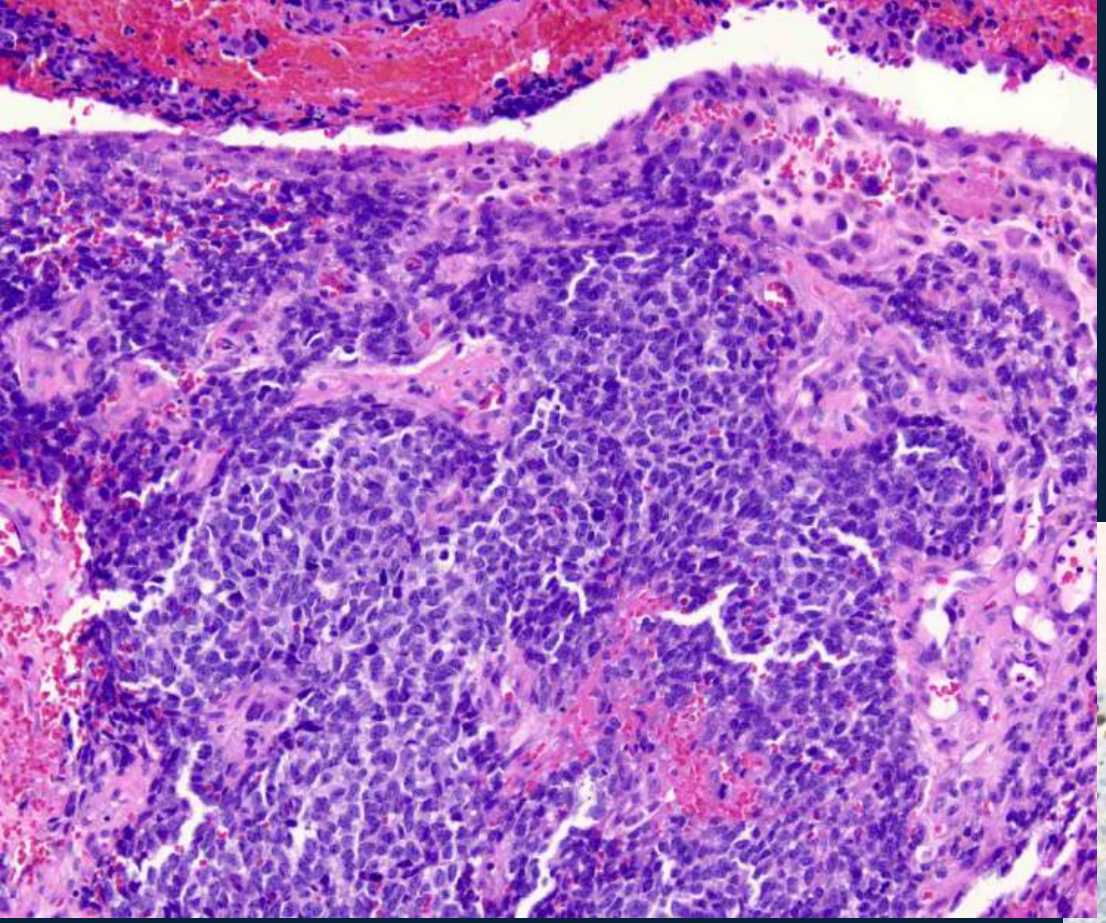
TLE1
metastatic synovial sarcoma to lung



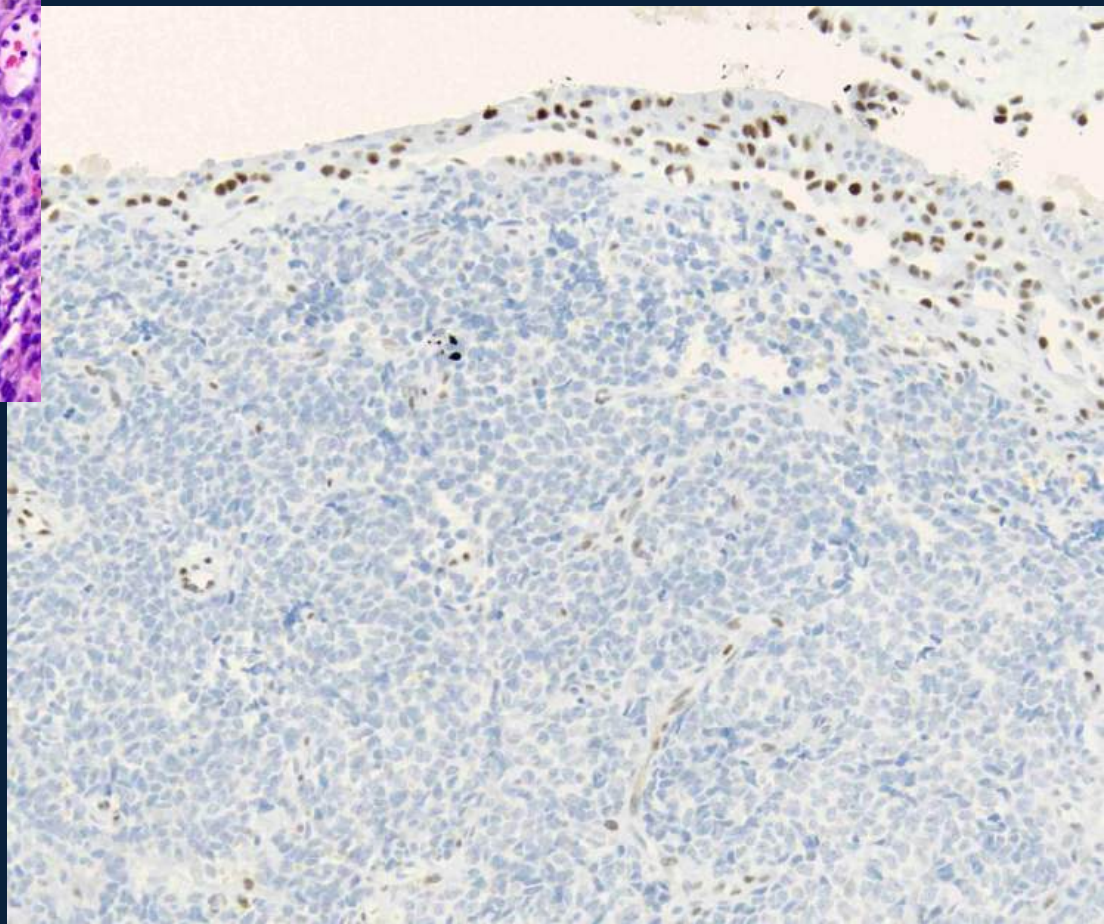


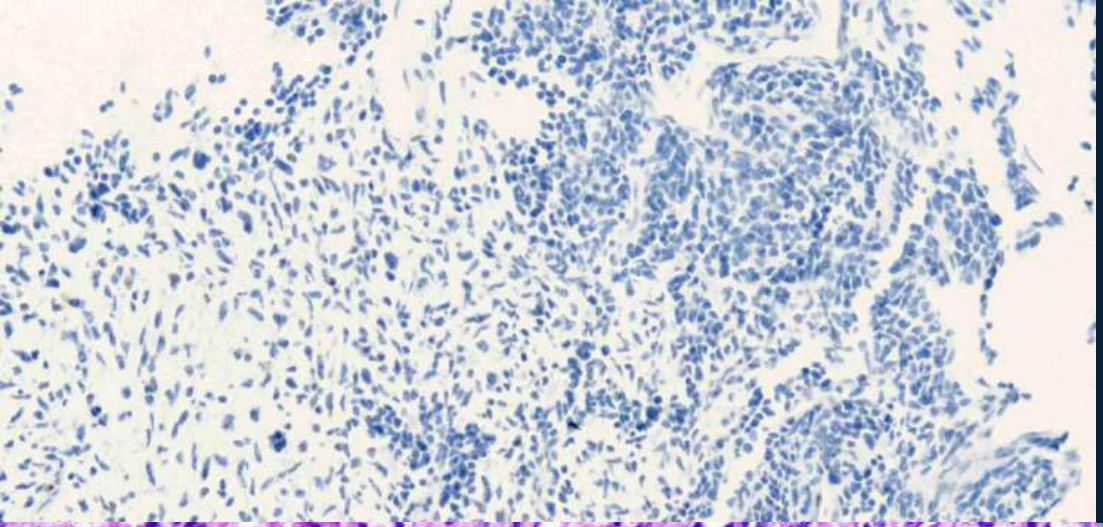
TLE1 neg
Ewing sarcoma





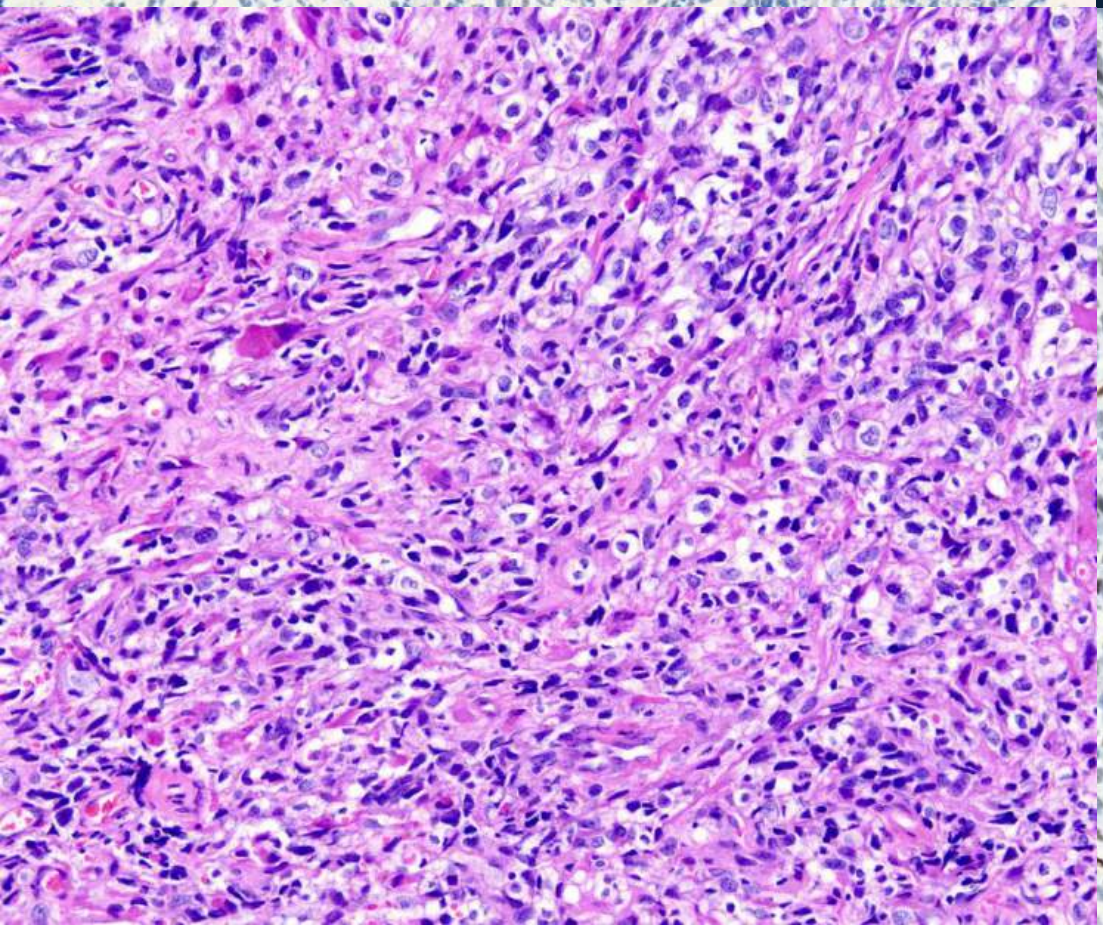
TLE1 neg
Ewing sarcoma met to lung mesothelial cells reactive

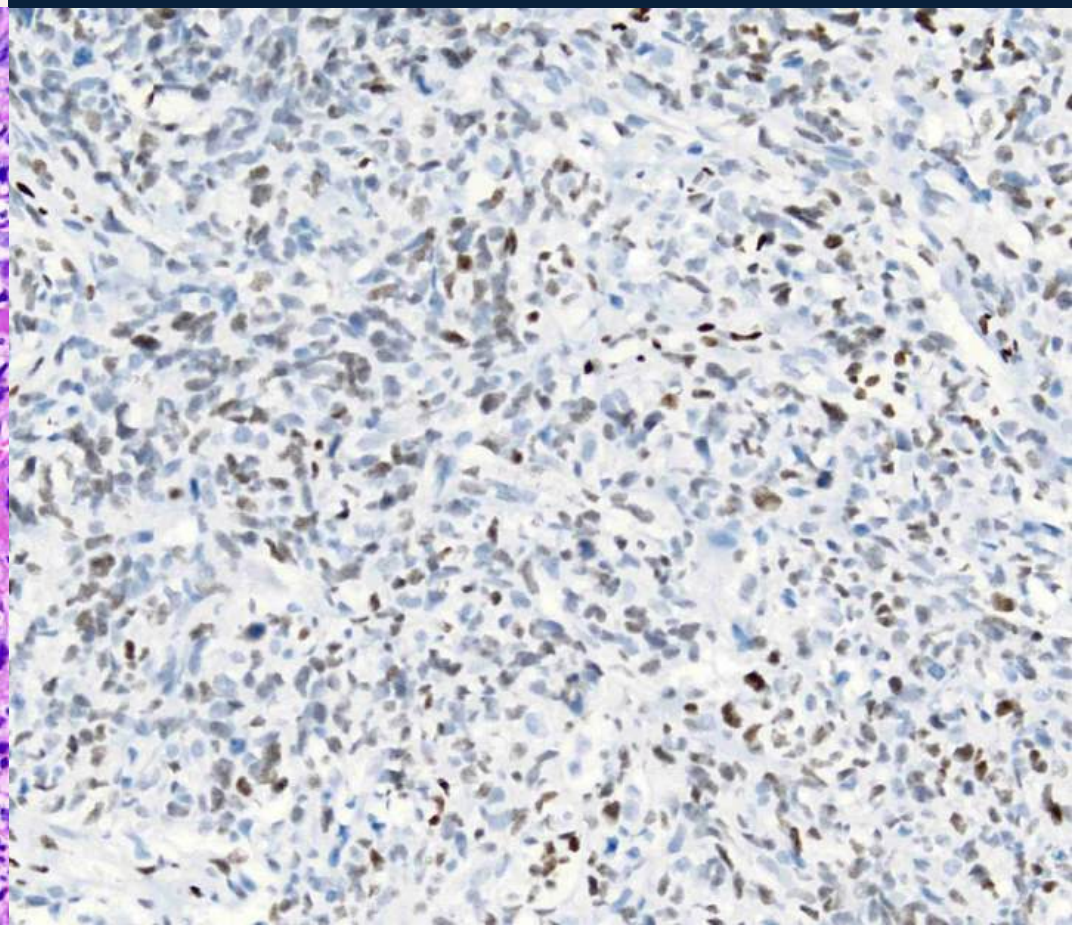


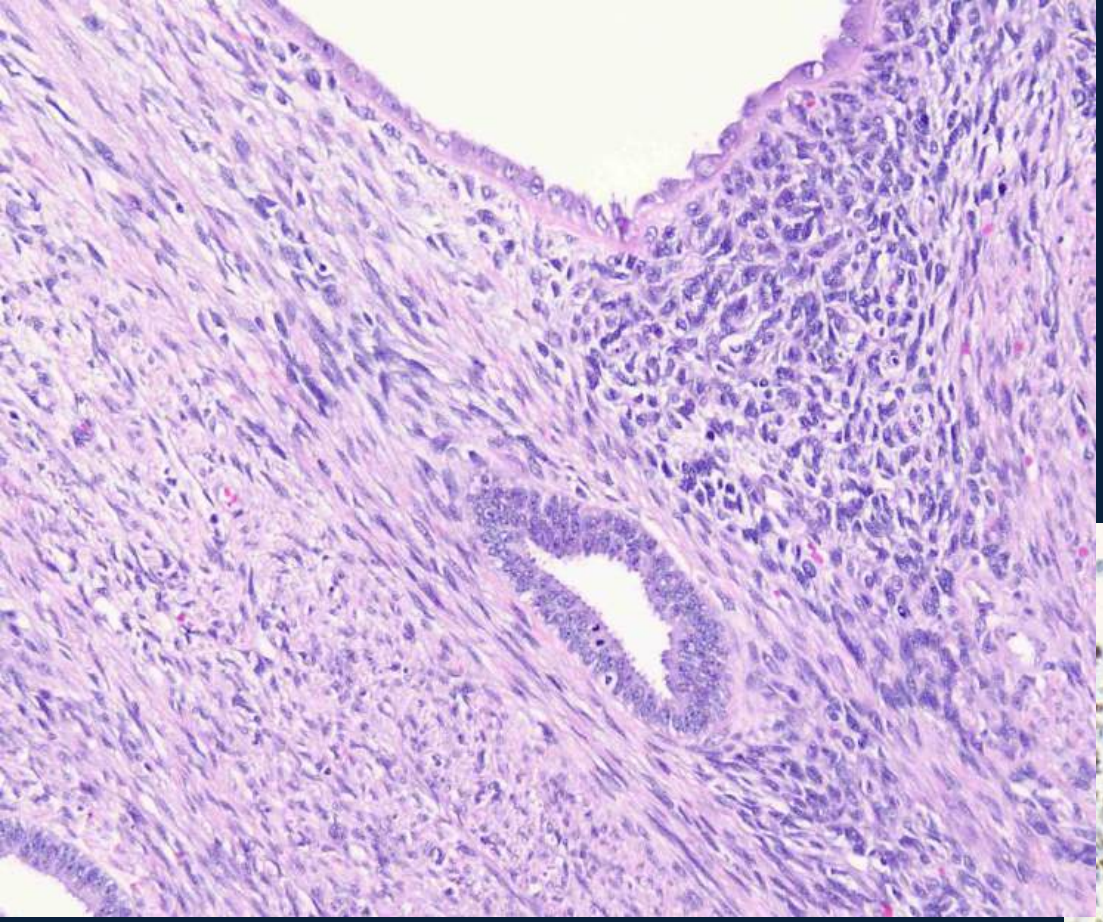


TLE1 neg. embryonal rhabdomyosarcoma

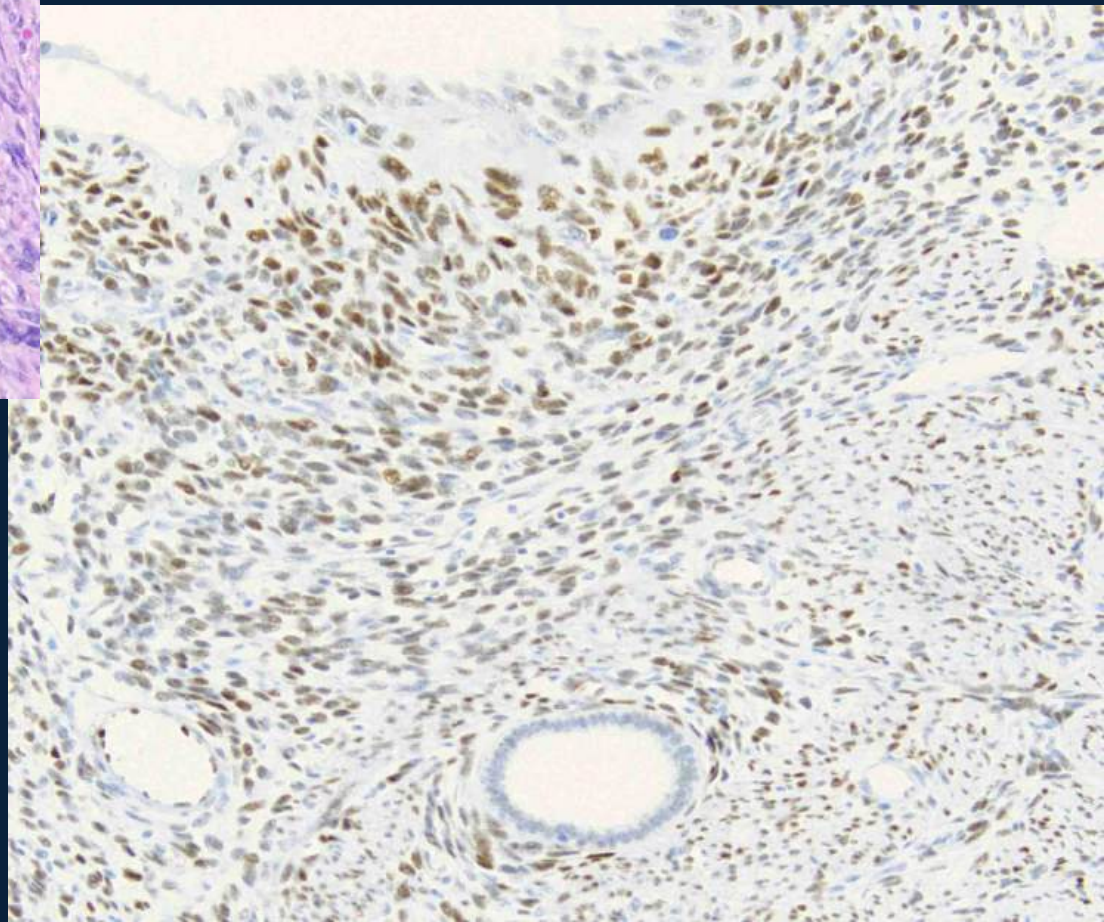
TLE1 weakly + emb. rhabdomyosarcoma

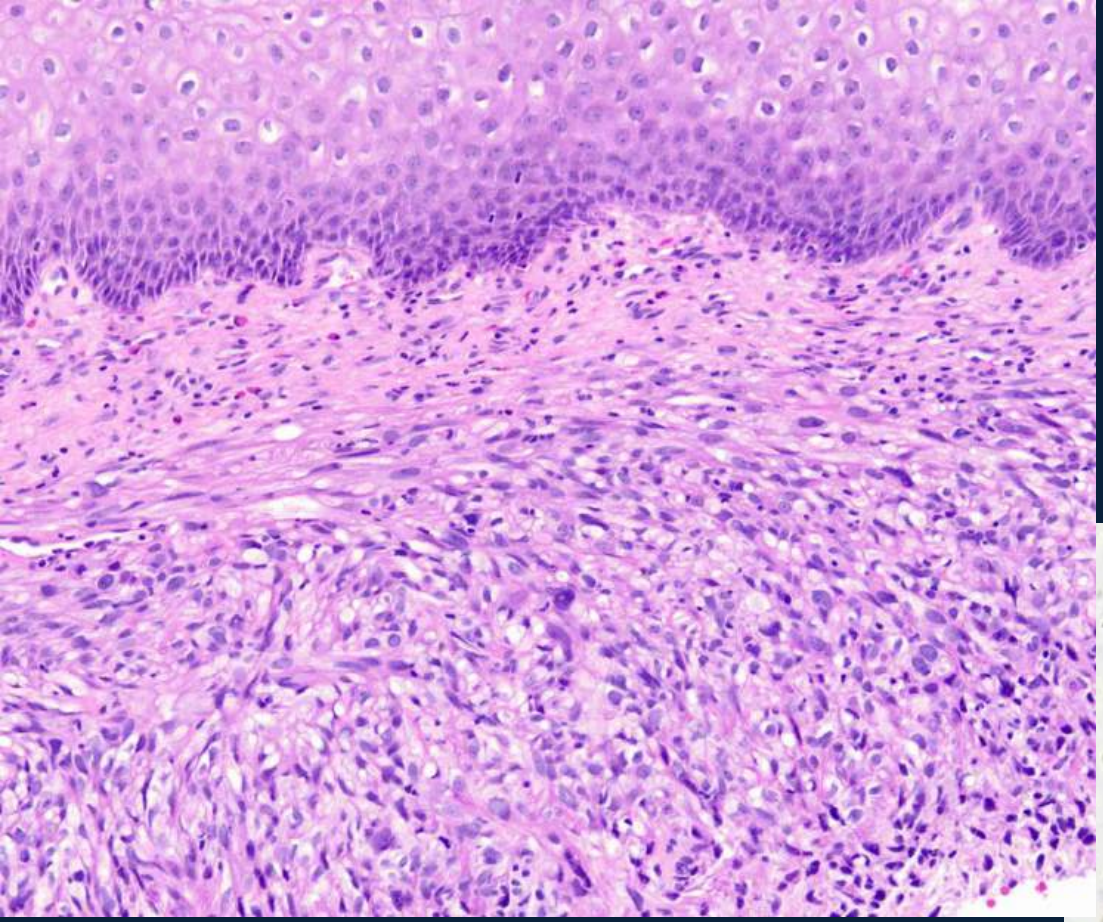




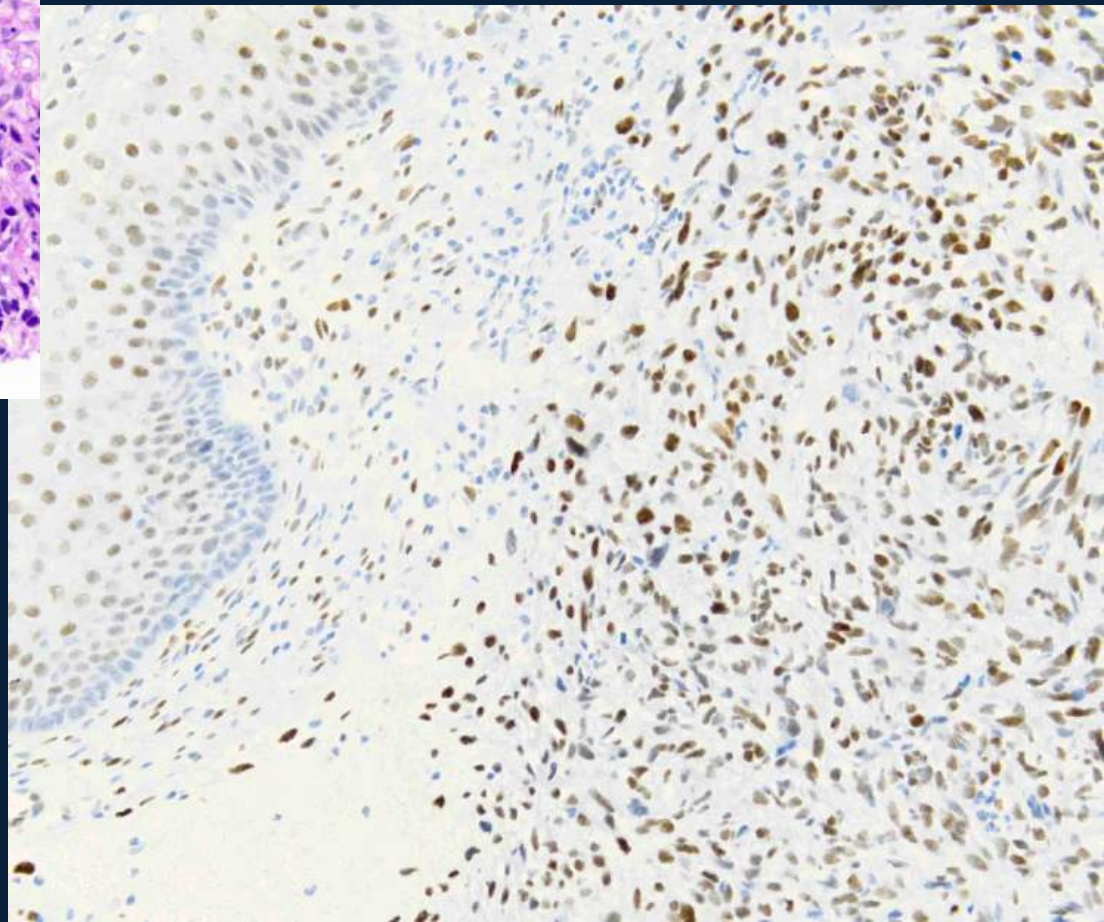


TLE1
MEST kidney





TLE1
vaginal sarcoma



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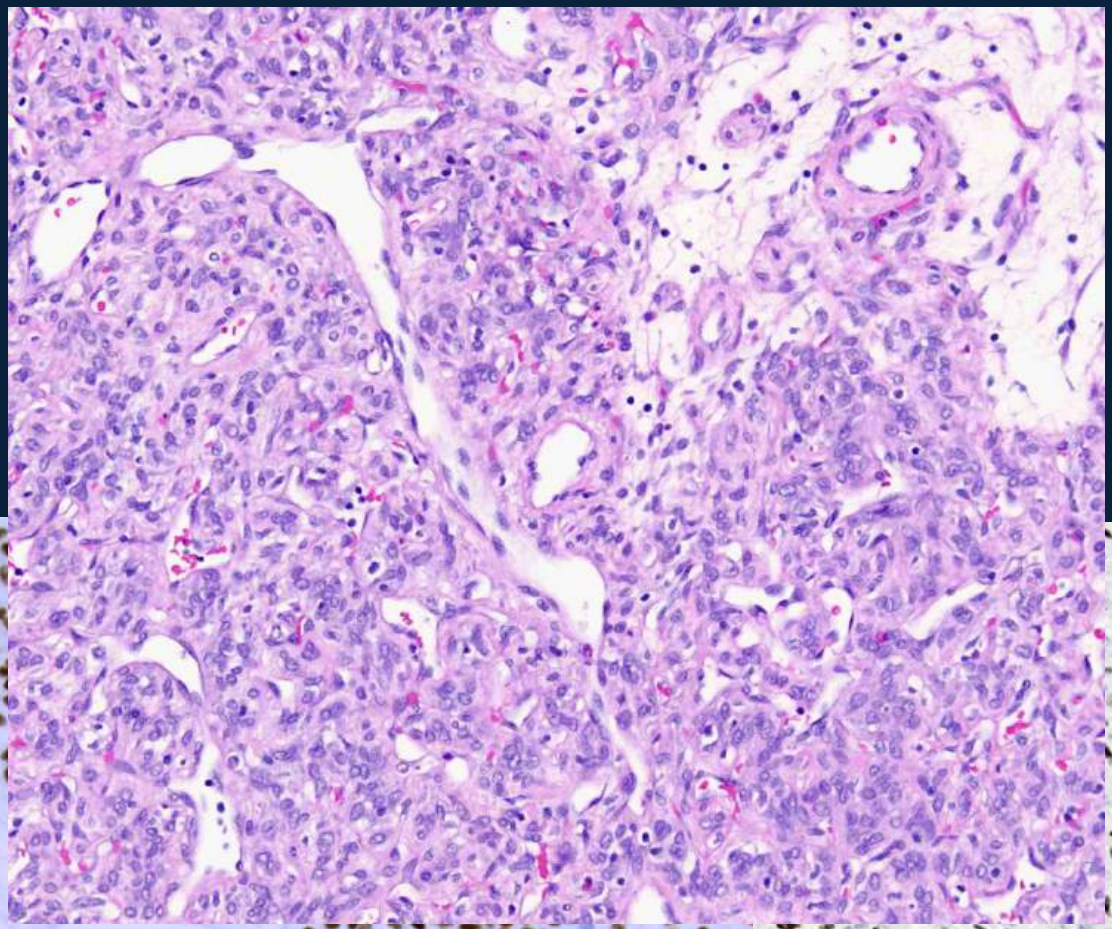
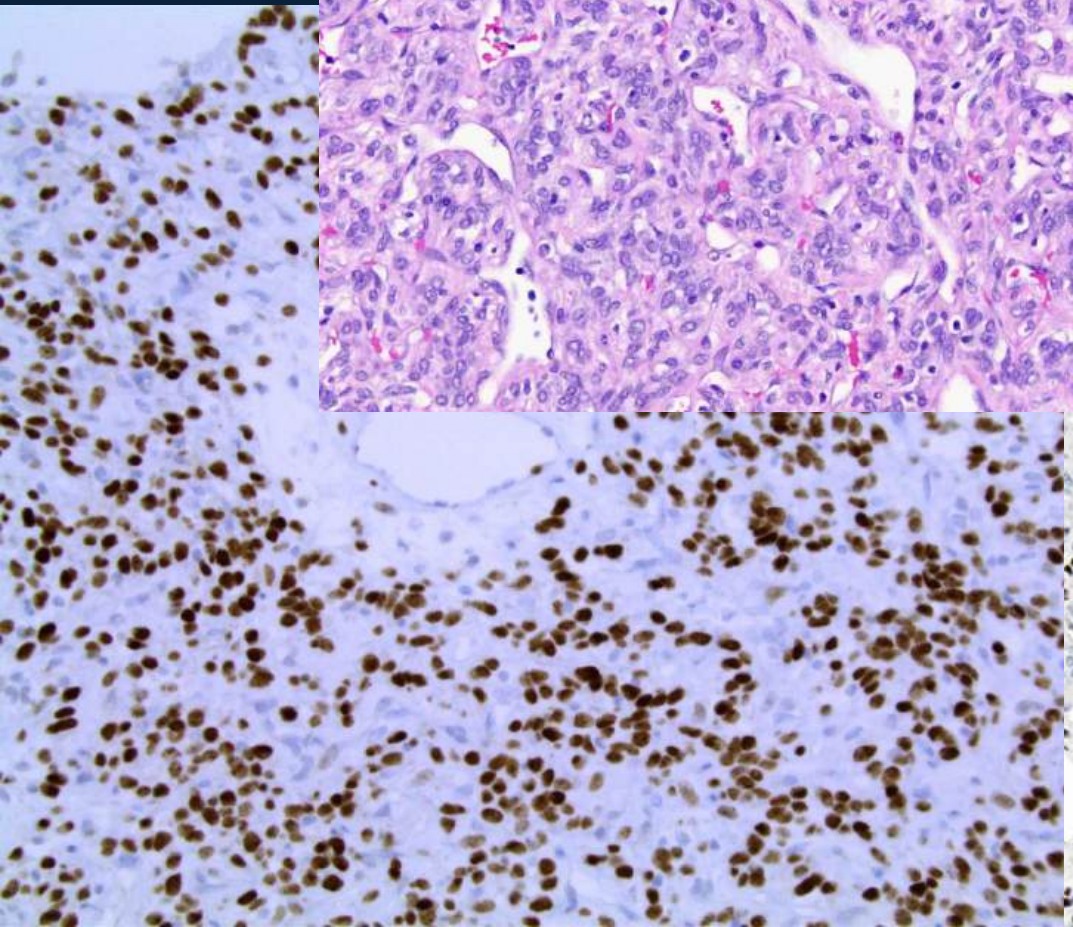
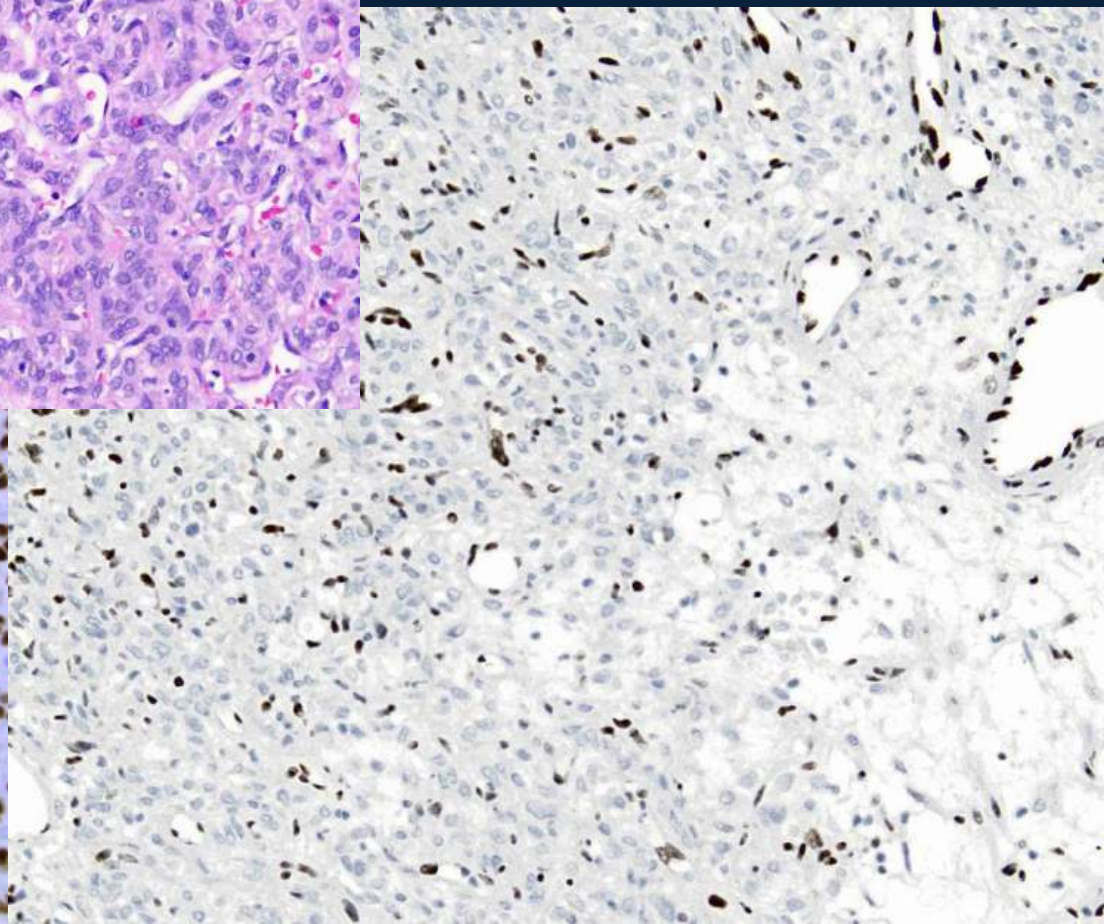
Solitary fibrous tumor



STAT6



TLE1



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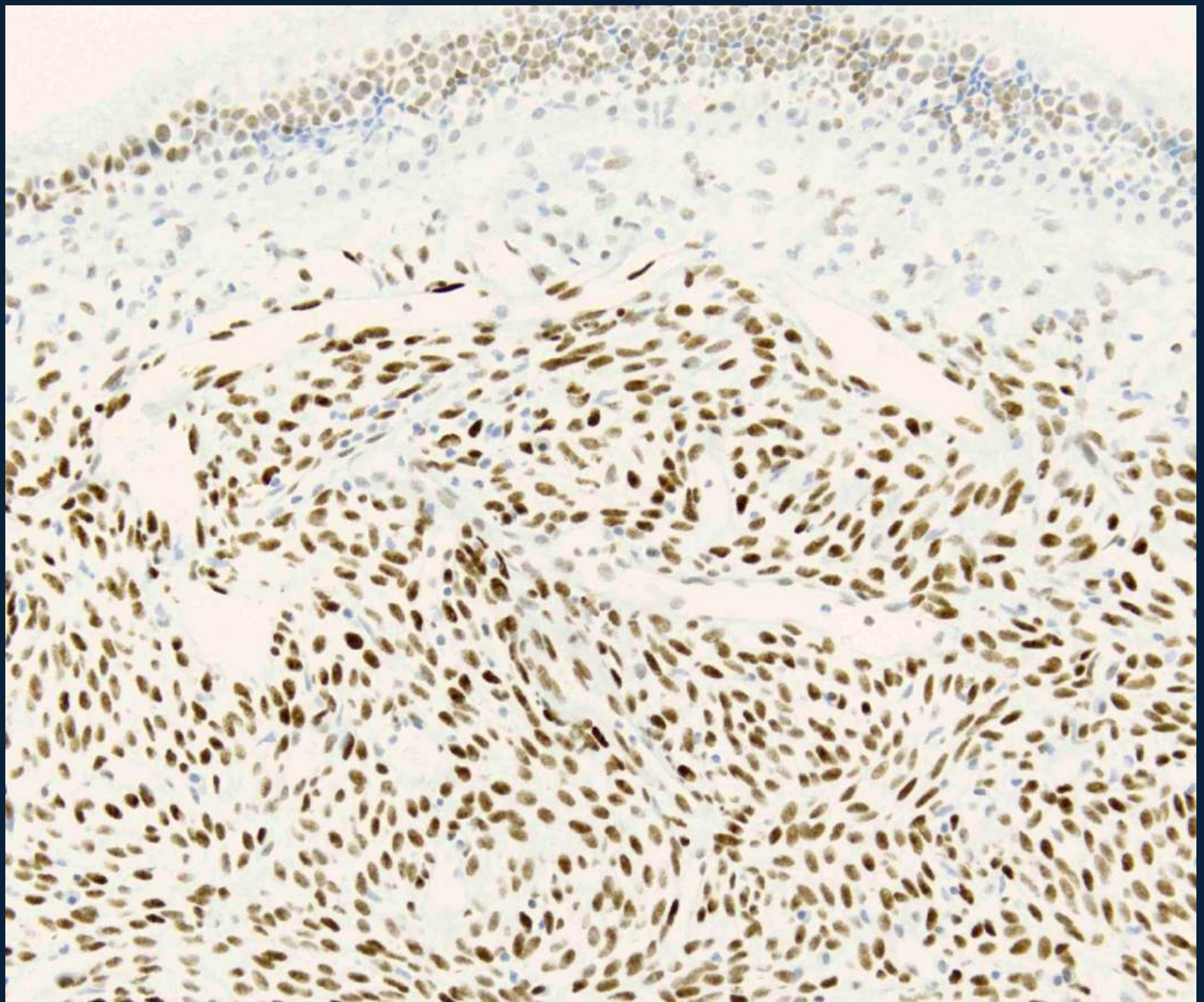
TLE1 nasal glomangiopericytoma



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Adipophilin

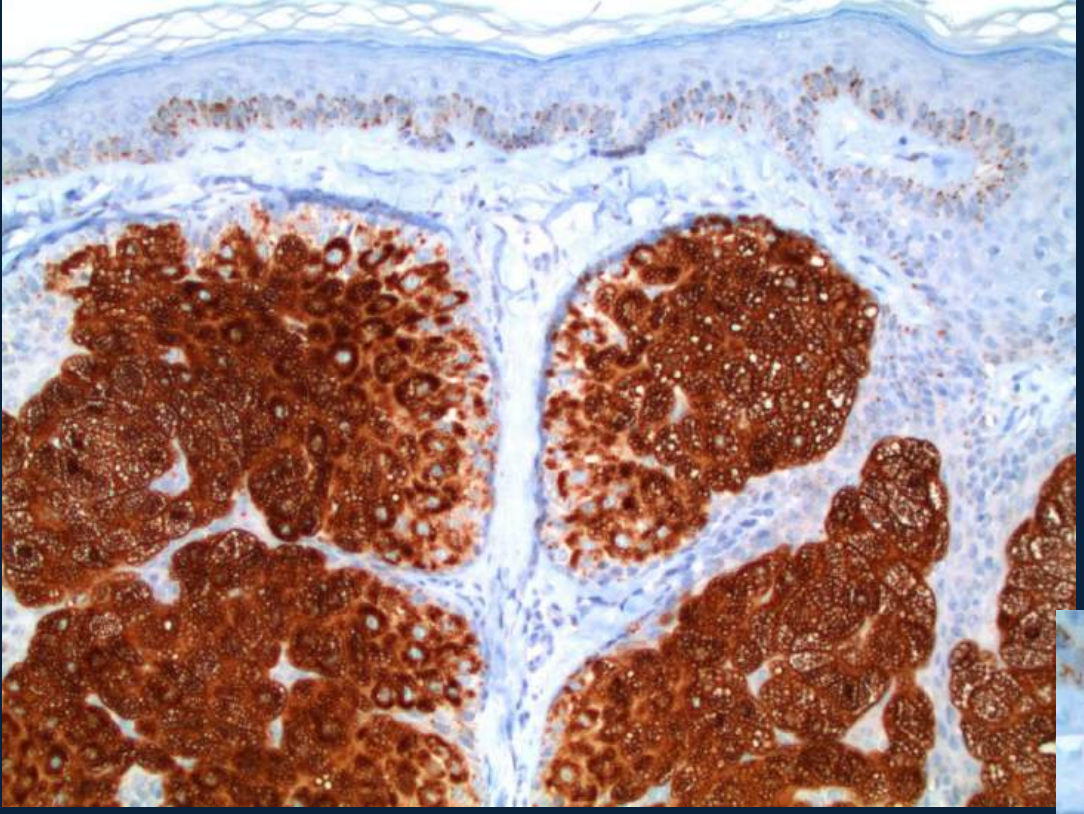
Adipophilin protein is localized to the lipid membrane (member of the PAT or perlipin family).

Expressed in sebaceous cells, lipoblasts, adrenal cortex, Sertoli and Leydig cells, lactating mammary acinar cells, steatotic hepatocytes but not mature fat.

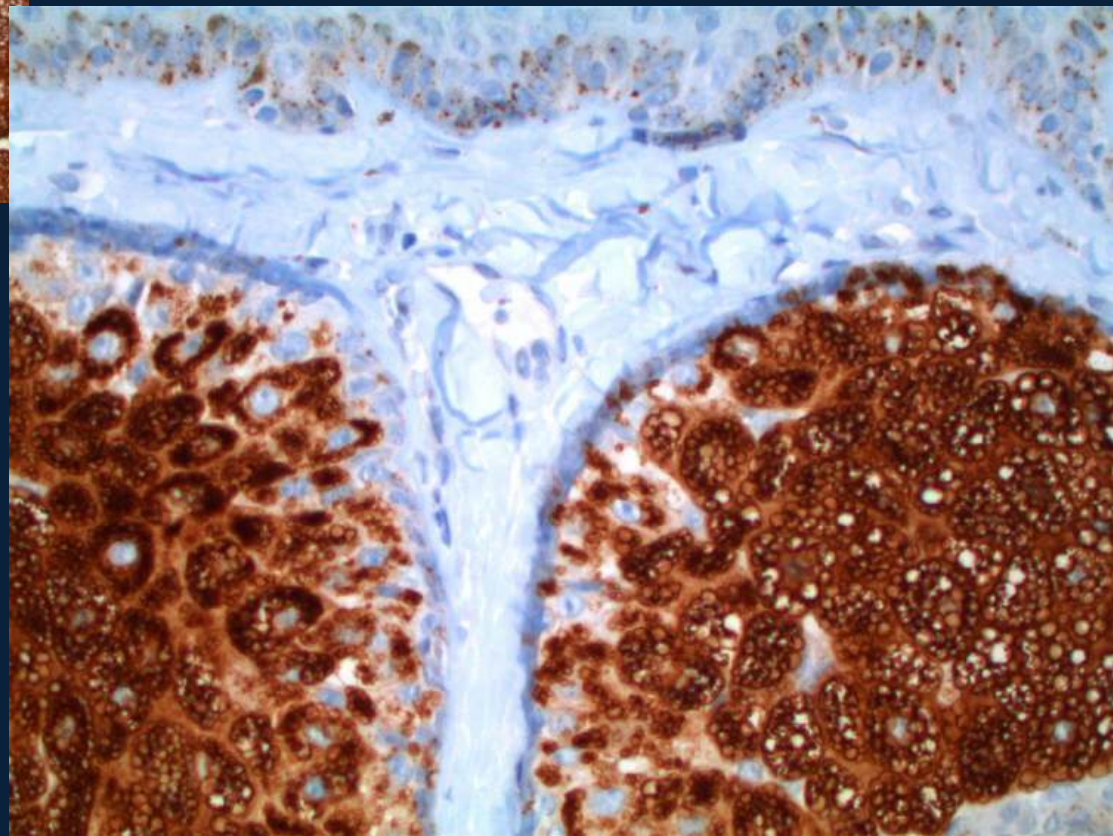
Useful in identifying sebaceous neoplasms and some liposarcomas. It will also label a subset of clear cell renal cell carcinomas.

The IHC labeling pattern should be a membranous vesicular one, outlining small vesicles to be specific.

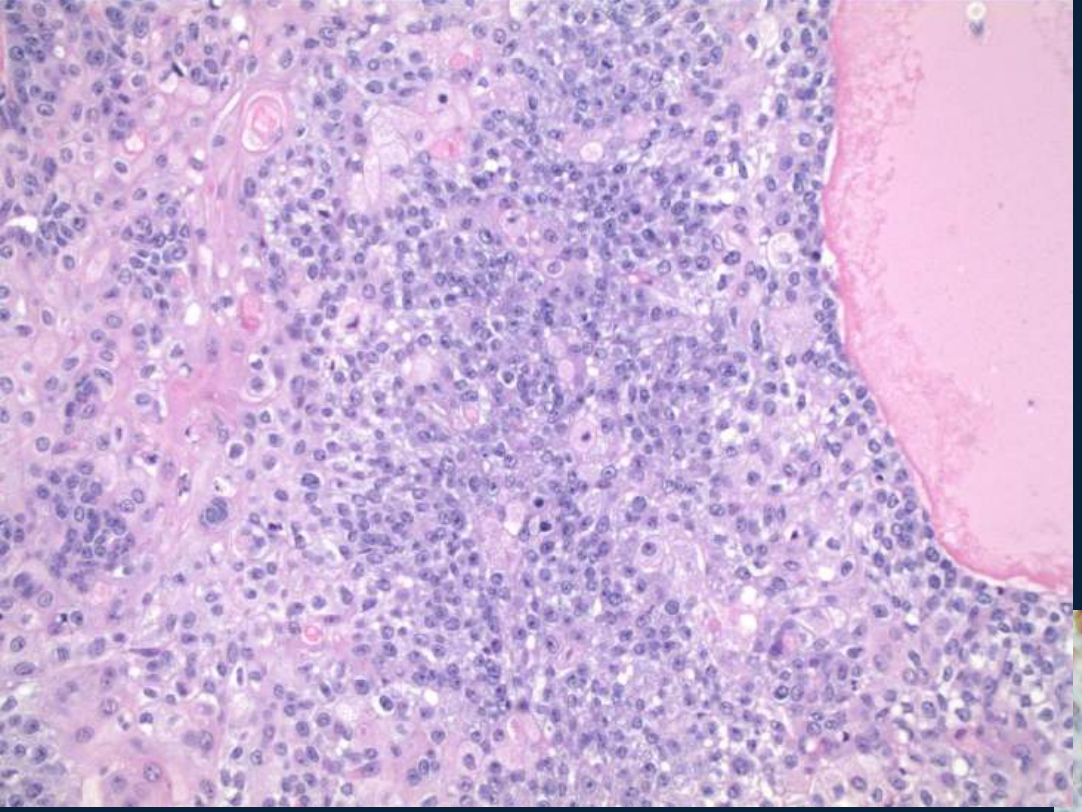
Granular staining without this pattern is not specific for sebaceous or lipogenic differentiation.

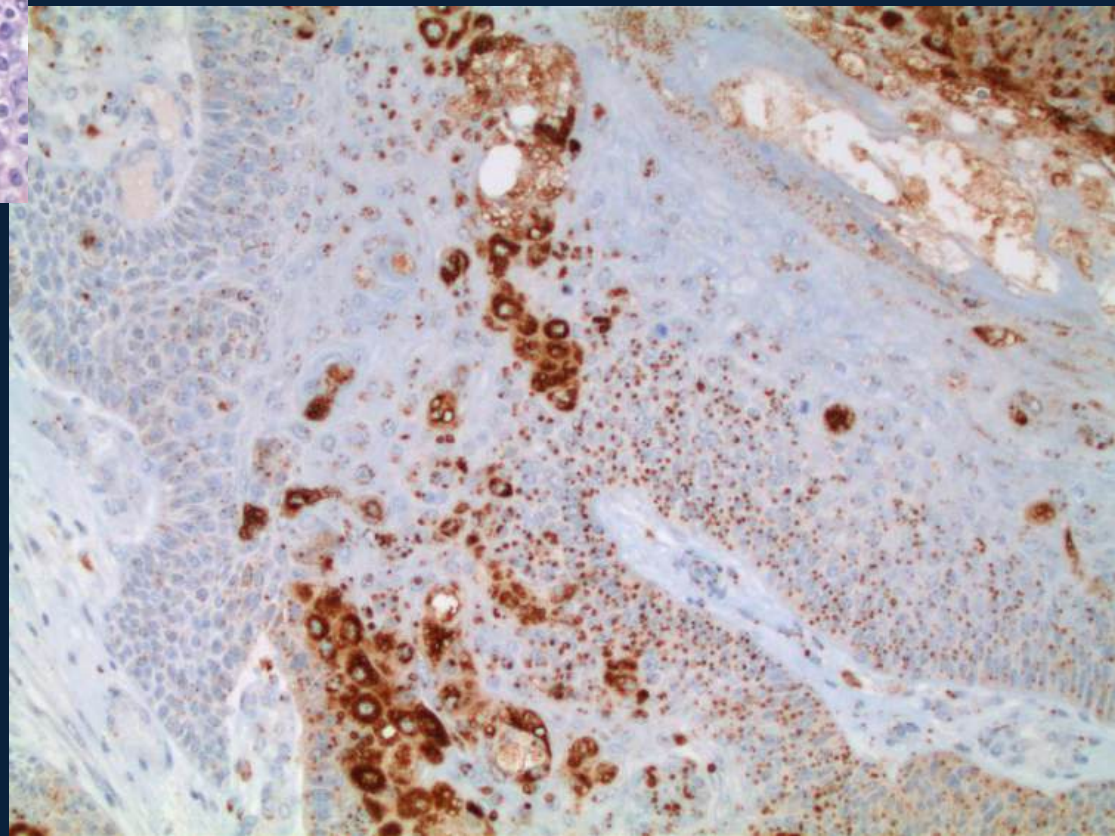


Rabbit polyclonal

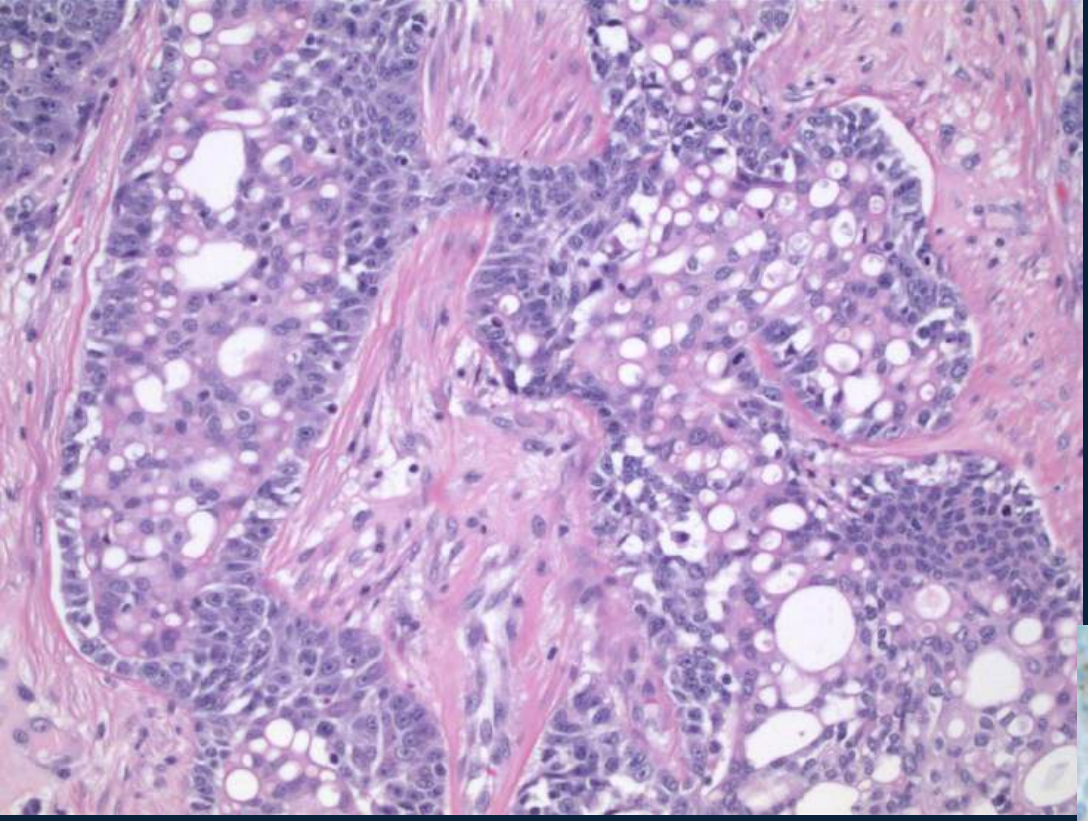


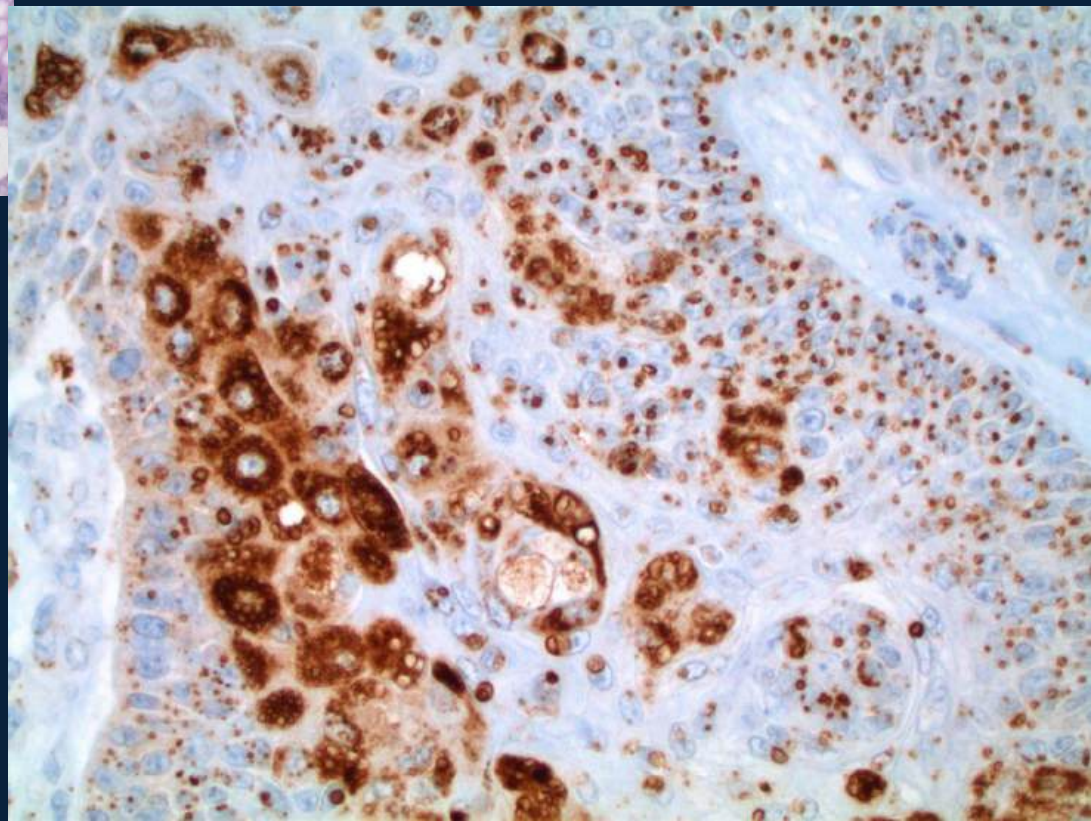
Adipophilin in benign sebaceous glands. Note the vesicular pattern.





Adipophilin
Sebaceous
Carcinoma.





Adipophilin
Sebaceous
Carcinoma.

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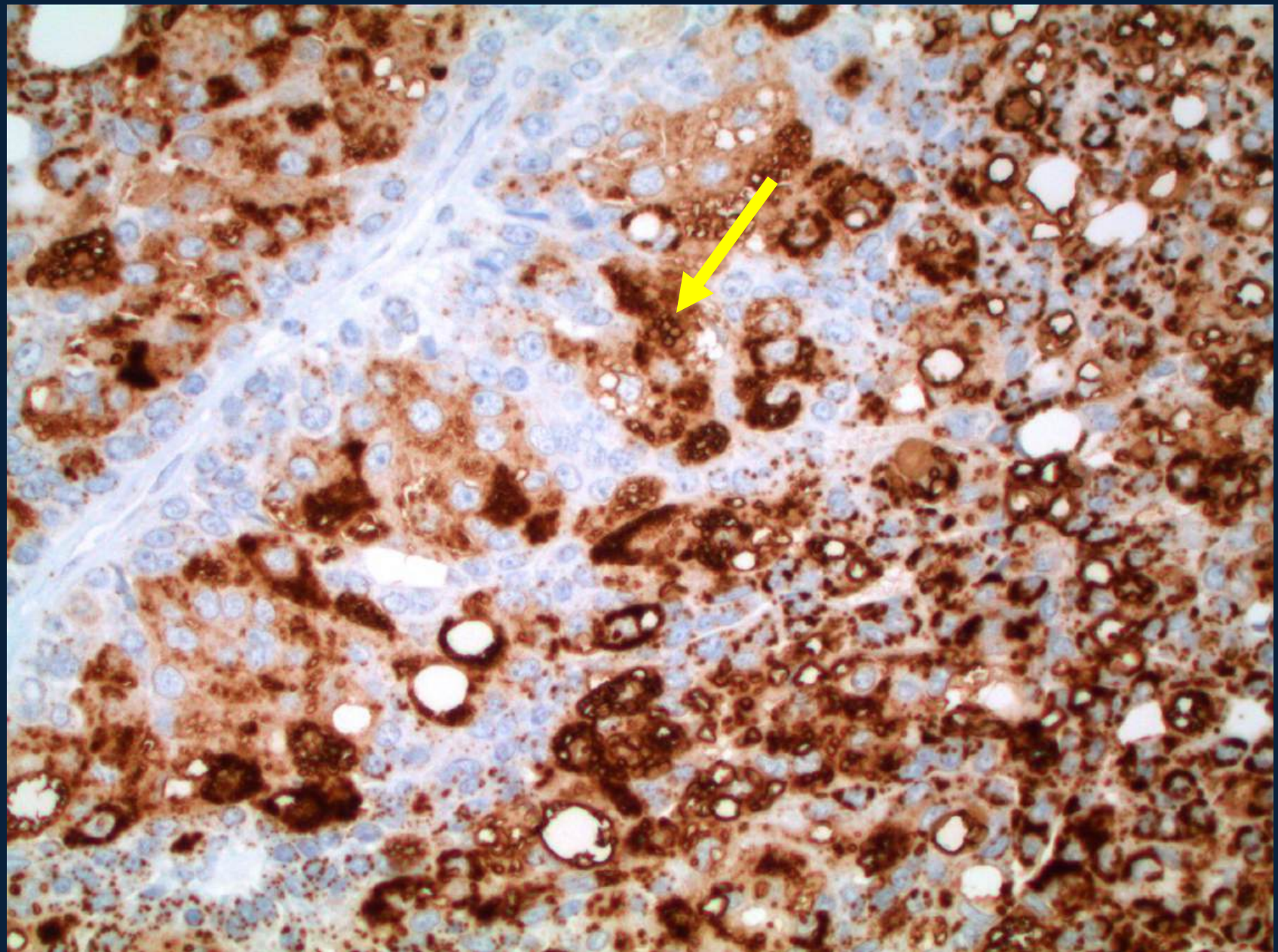
Sebaceous ca- adipophilin



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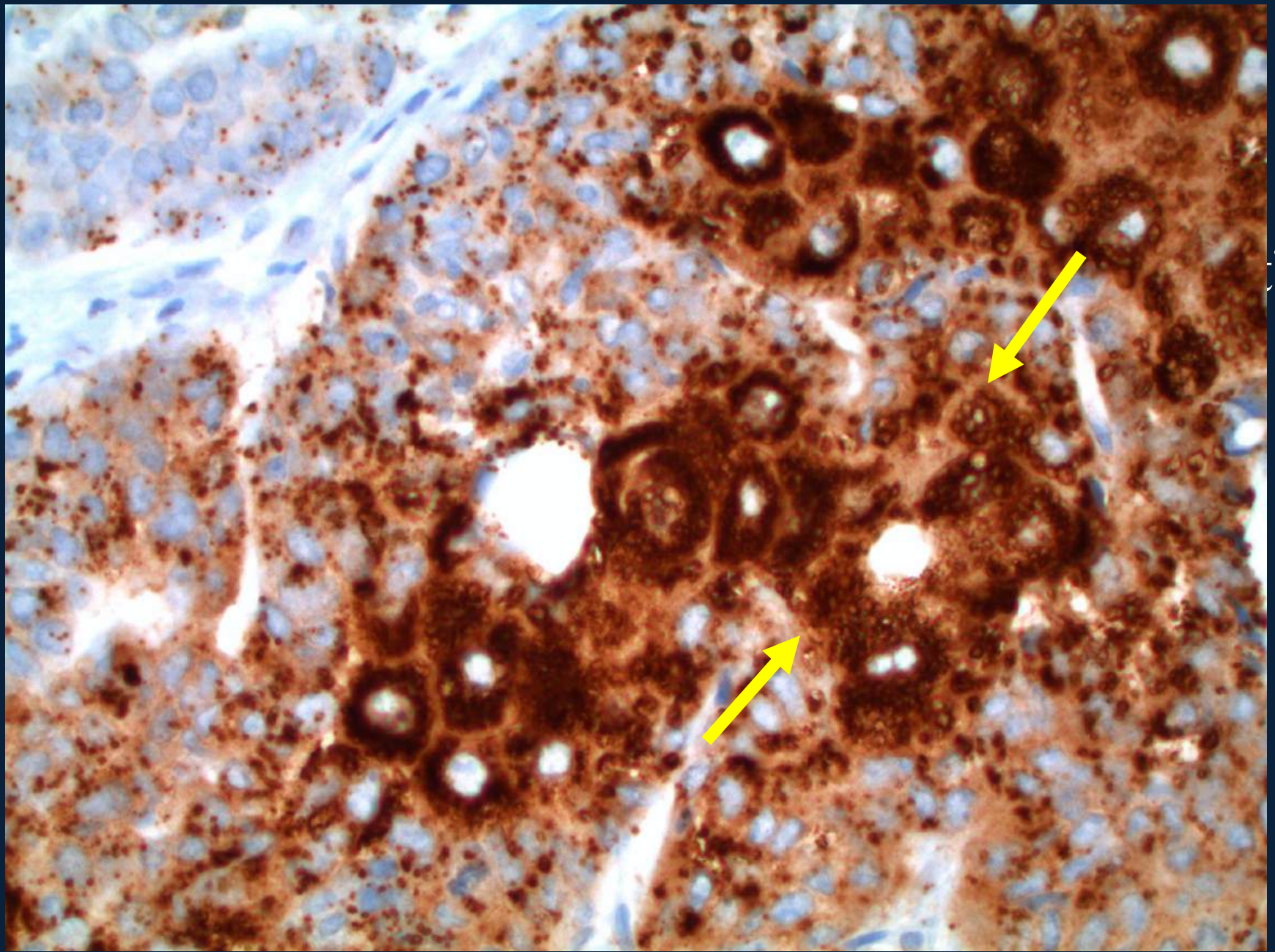
Sebaceous ca- adipophilin: membranous vesicular



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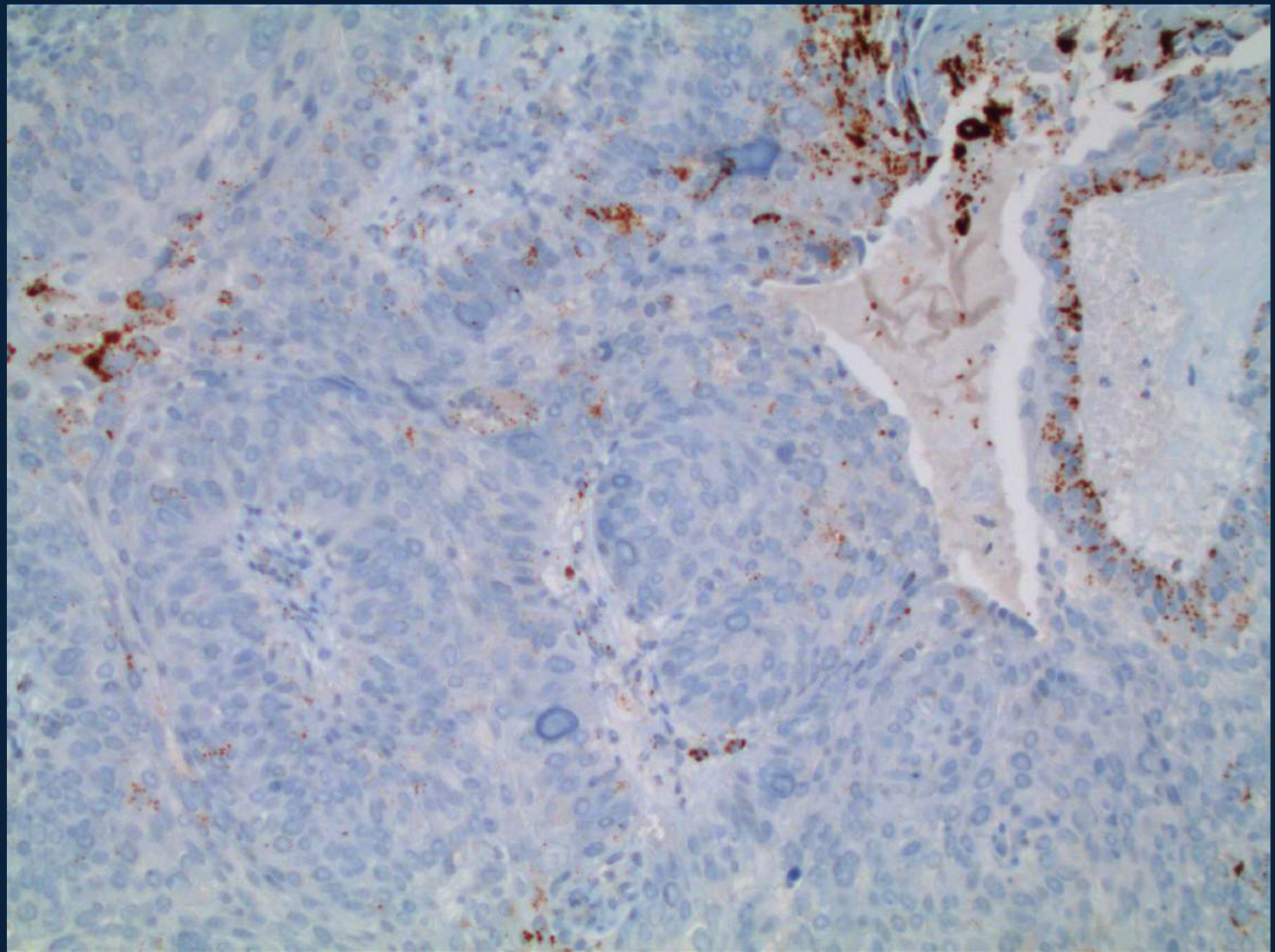
Adipophilin neg. adnexal tumor- NS granular



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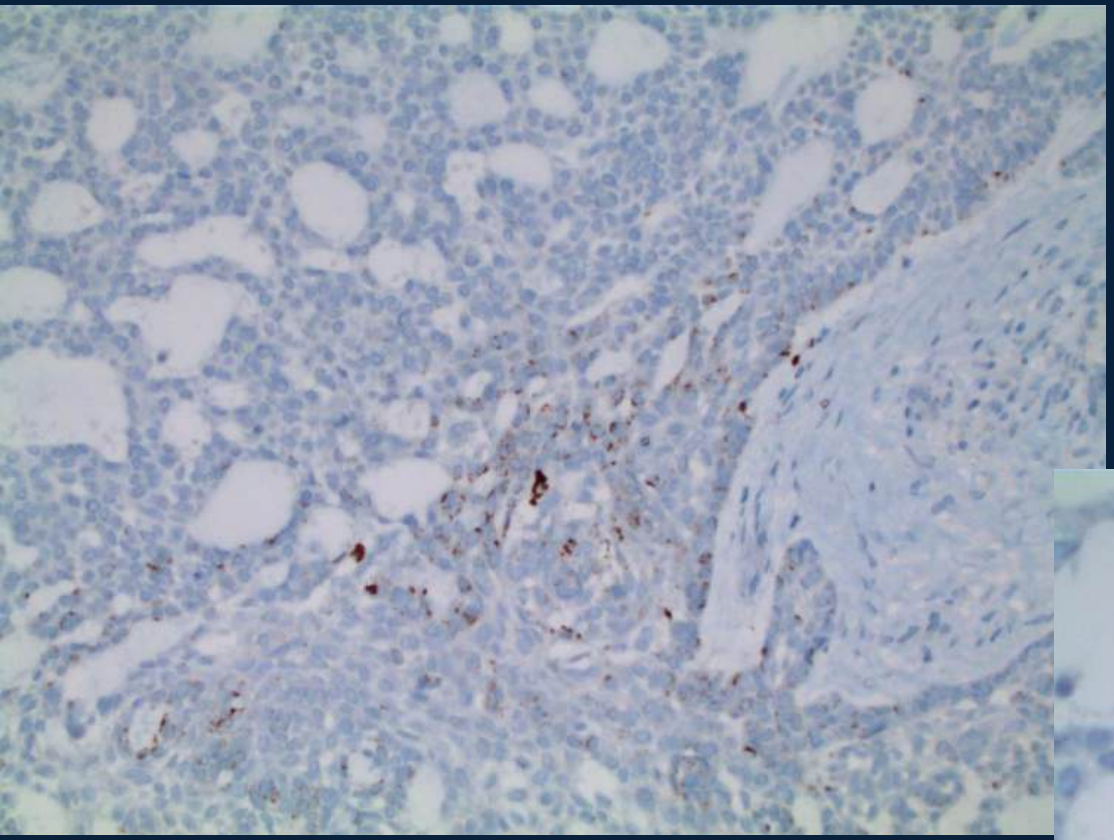
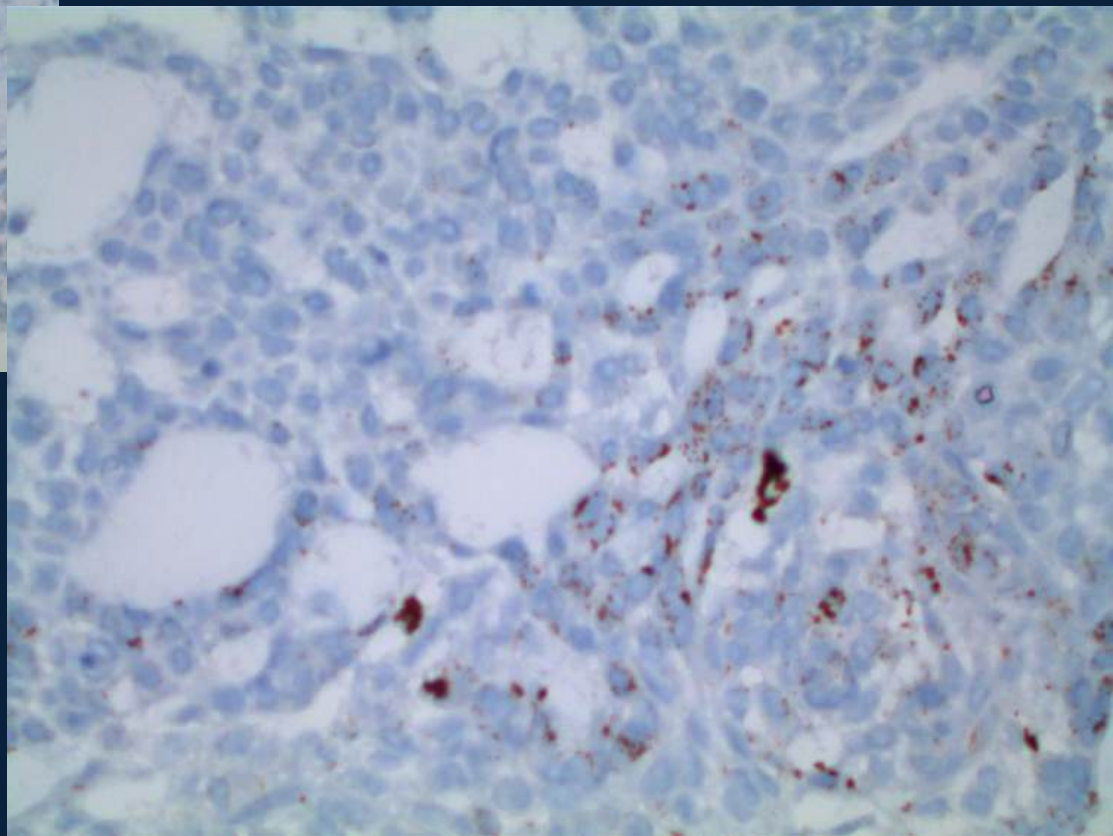
Adipophilin neg. BCC- NS granular





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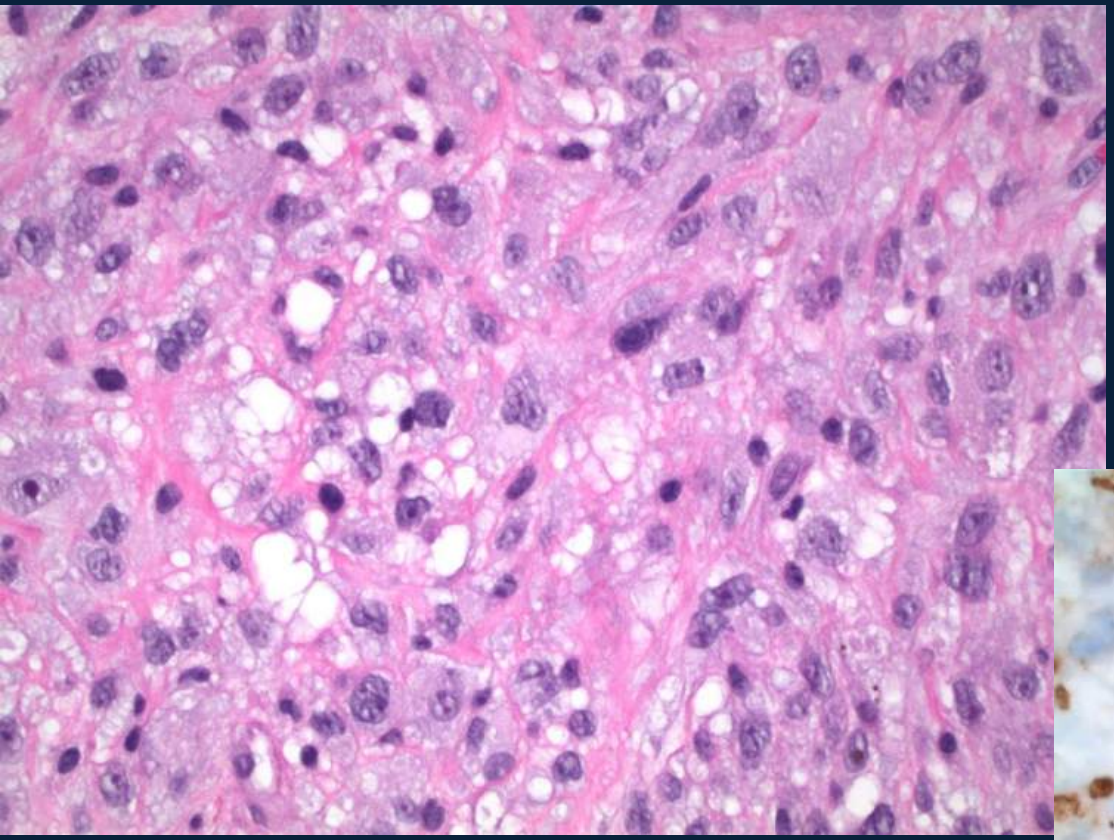
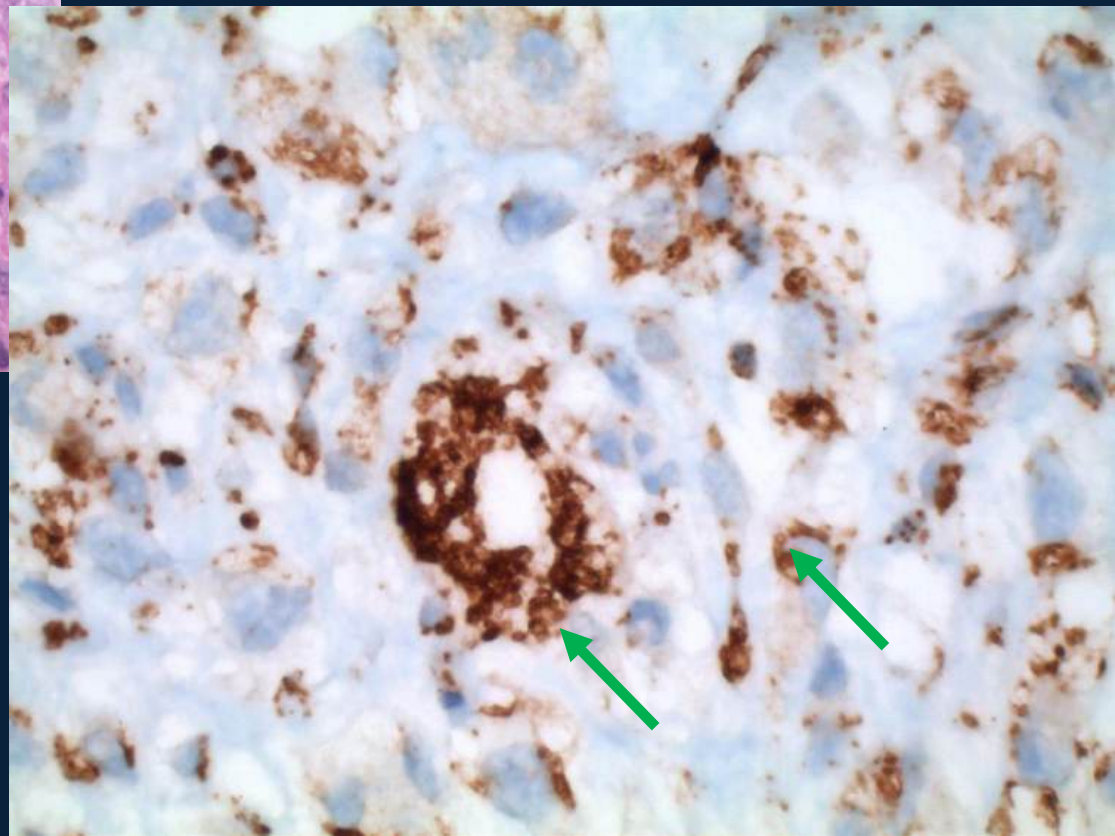
Adipophilin- De-diff. liposarcoma





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Adipophilin- References

Adipophilin expression in sebaceous tumors and other cutaneous lesions with clear cell histology: an immunohistochemical study of 117 cases. Ostler DA, et al. Modern Pathology (2010) 23, 567–573.

Tjarks BJ, et al. Evaluation and comparison of staining patterns of factor XIIIa (AC-1A1), adipophilin and GATA3 in sebaceous neoplasia. J Cutan Pathol. 2018;45:1–7.

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PRAME

PRAME (PReferentially expressed Antigen in MElanoma): melanoma-associated antigen that was isolated from a melanoma patient.

IHC for PRAME in 400 melanocytic tumors, including 155 primary and 100 metastatic melanomas, and 145 melanocytic nevi:

Diffuse nuclear + in 87% metastatic/ 83.2% primary melanomas

94.4% acral, 92.5% superficial spreading, 90% nodular melanomas, 88.6% lentigo maligna, and 35% desmoplastic melanomas.

Expressed in both situ and non-desmoplastic invasive melanoma components where present.

140 cutaneous melanocytic nevi, 86.4% were completely negative

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PRAME

PRAME expression correlated with genetic alterations present in melanoma by FISH and SNP arrays in a series of 110 ”diagnostically challenging melanocytic lesions.”

IHC + in a minor subpopulation of melanocytes, in 13.6% of nevi.

Rare isolated junctional melanocytes + in solar lentigines and benign non-lesional skin.

Expressed in cutaneous melanoma, ocular melanoma;

Expressed in seminoma, non-small cell lung cancer, breast carcinoma, renal cell carcinoma, ovarian carcinoma, leukemia, synovial sarcoma, and myxoid liposarcoma.

PRAME IHC can be used in the workup of atypical melanocytic lesions

PRAME: References

Reference: Lezcano C, Jungbluth AA, et al. PRAME Expression in Melanocytic Tumors. AJSP. 2018;42(11):1456-65.

Lezcano C, Jungbluth AA and Busam K. Comparison of Immunohistochemistry for PRAME With Cytogenetic Test Results in the Evaluation of Challenging Melanocytic Tumors. Am J Surg Pathol 2020;44:893–900.

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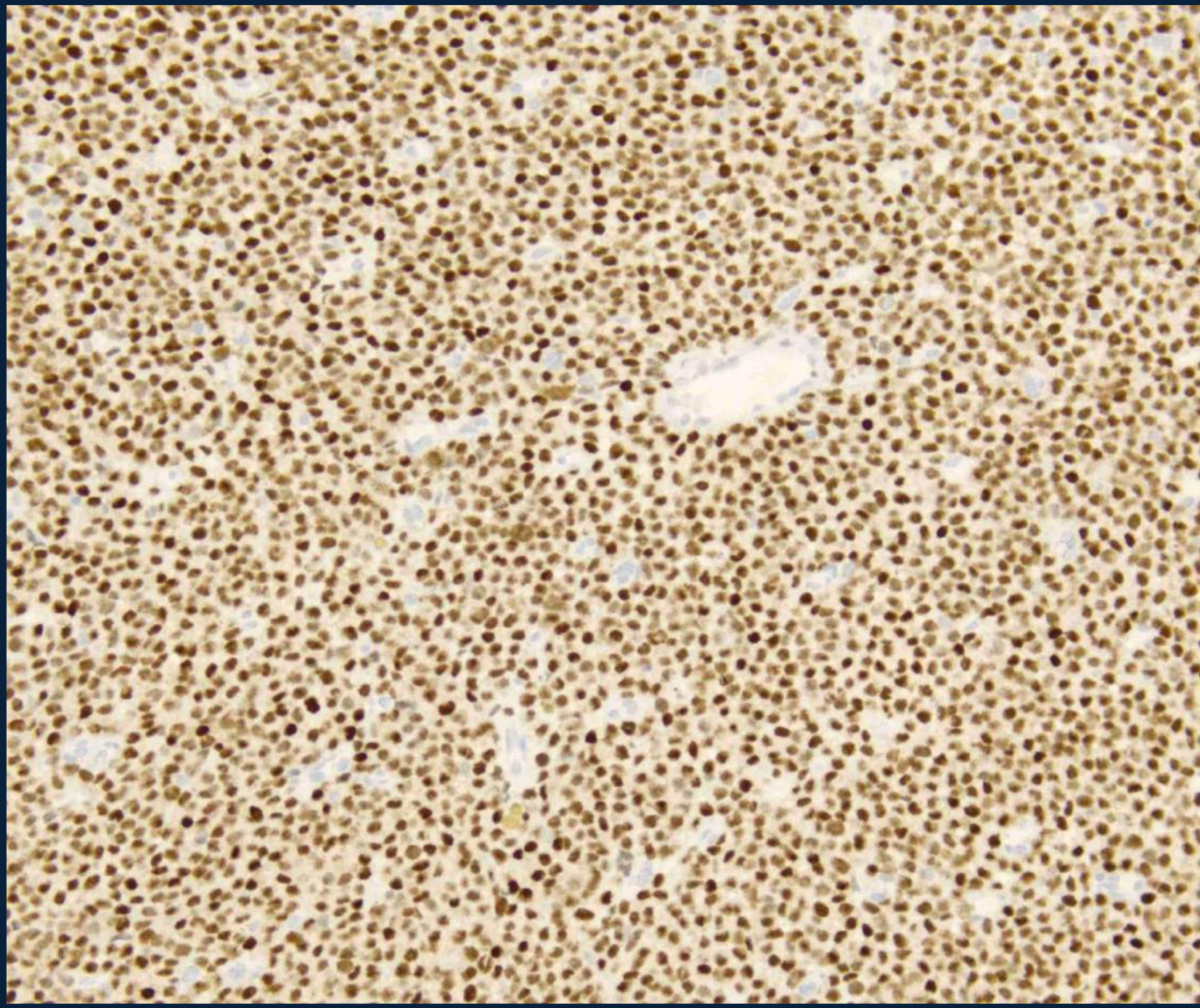
PRAME Metastatic Melanoma clone RBT-Prame



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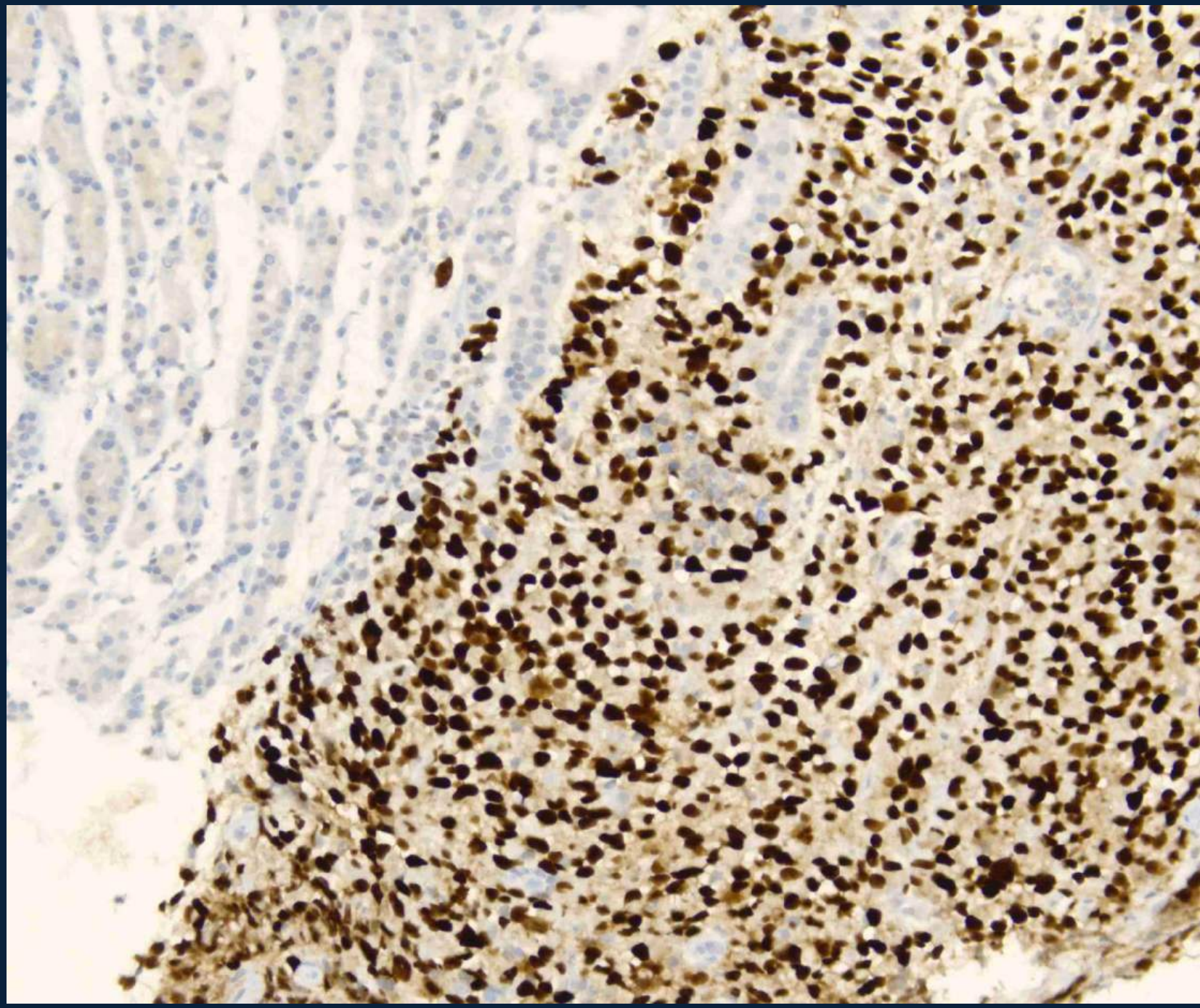
PRAME Metastatic melanoma



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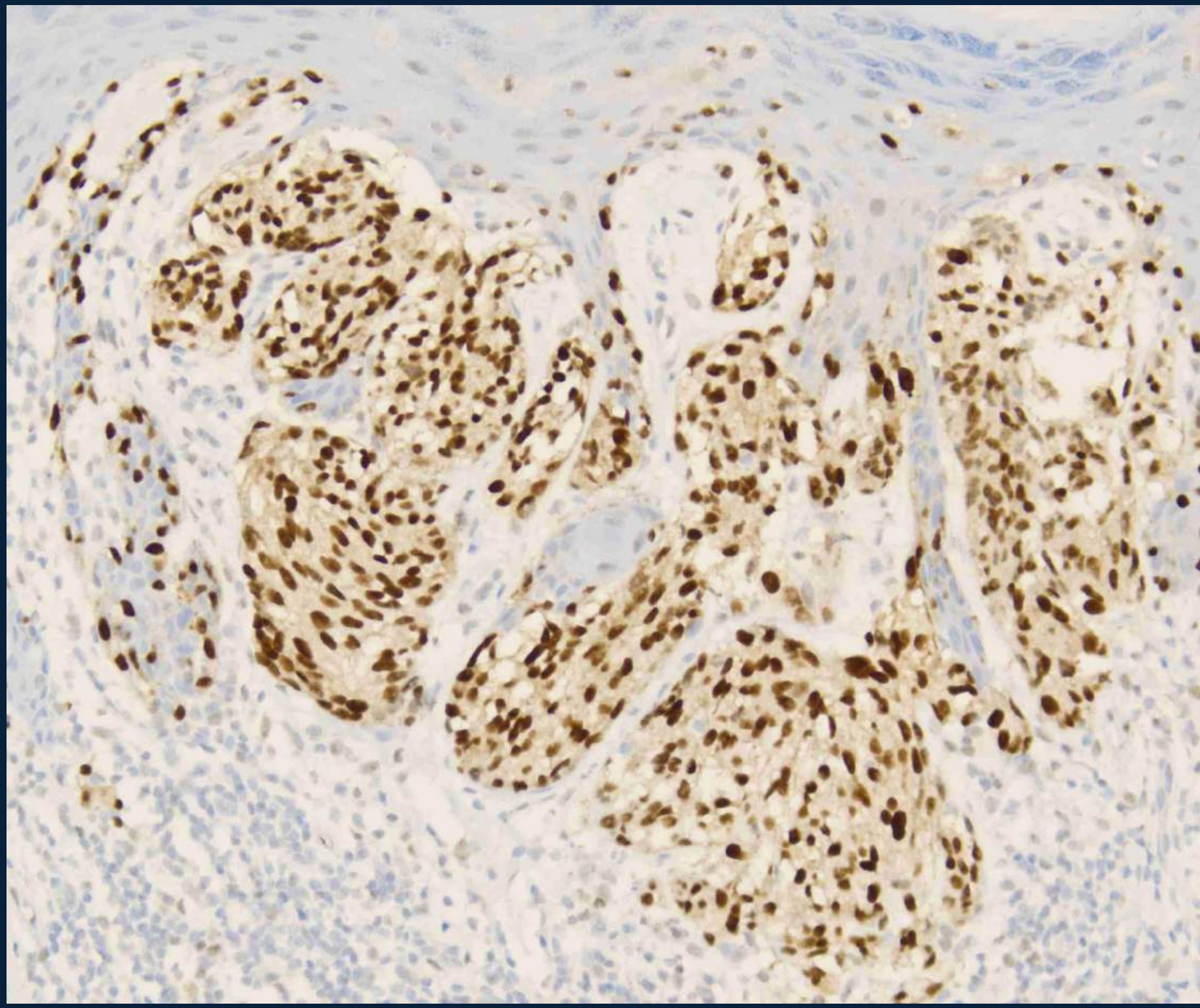
PRAME cutaneous melanoma



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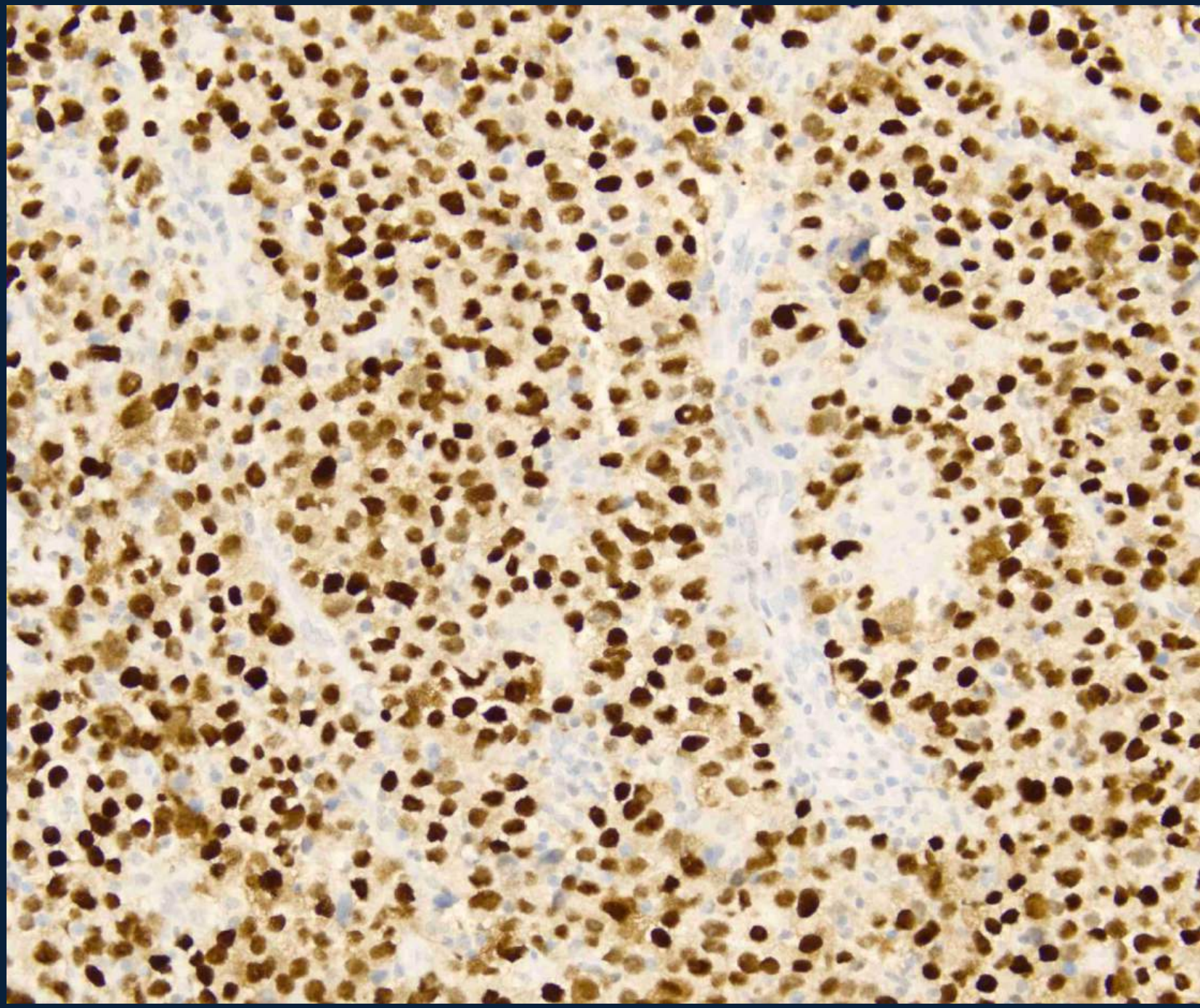
PRAME Seminoma positive



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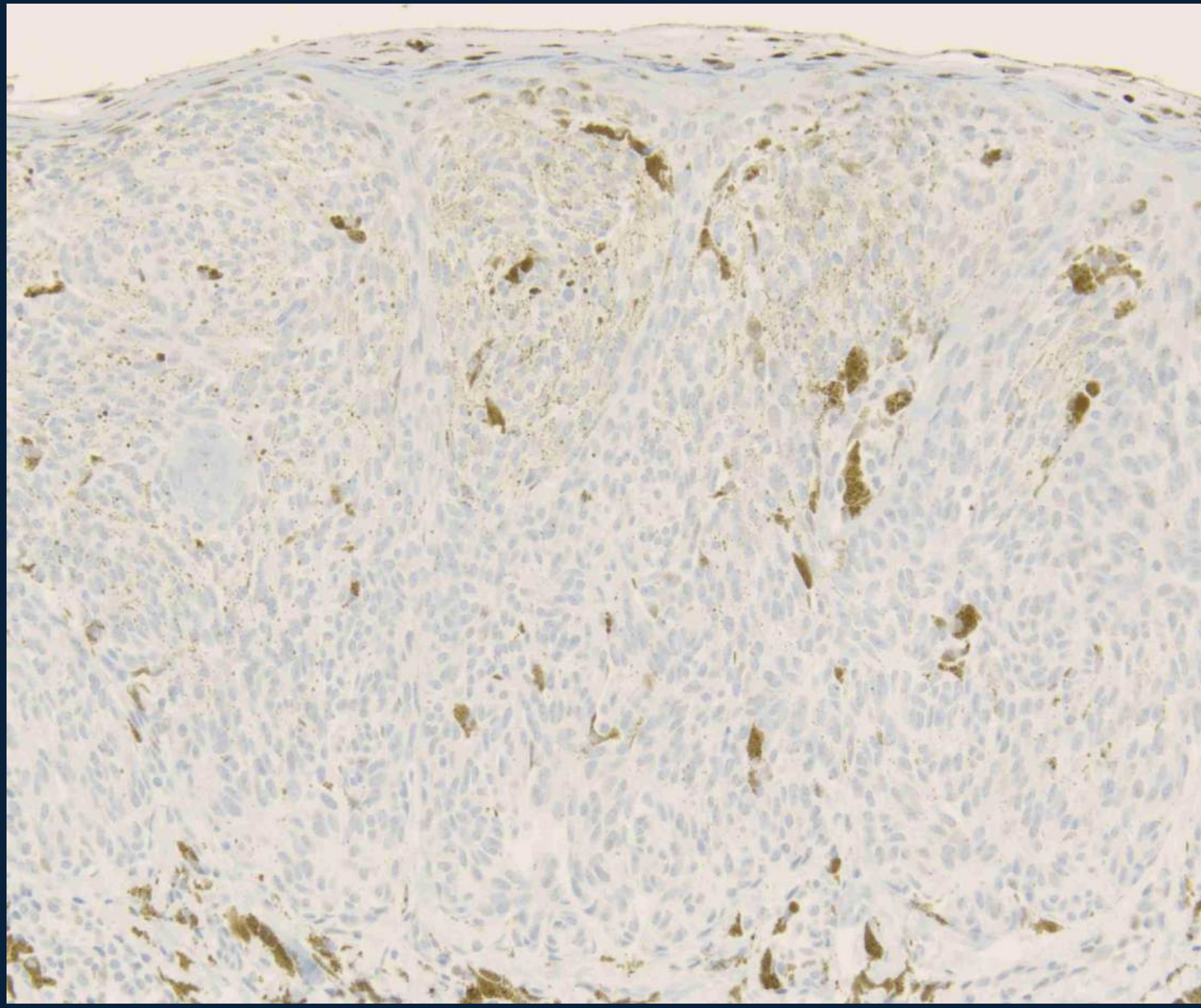
PRAME
Spitz
nevus
Negative



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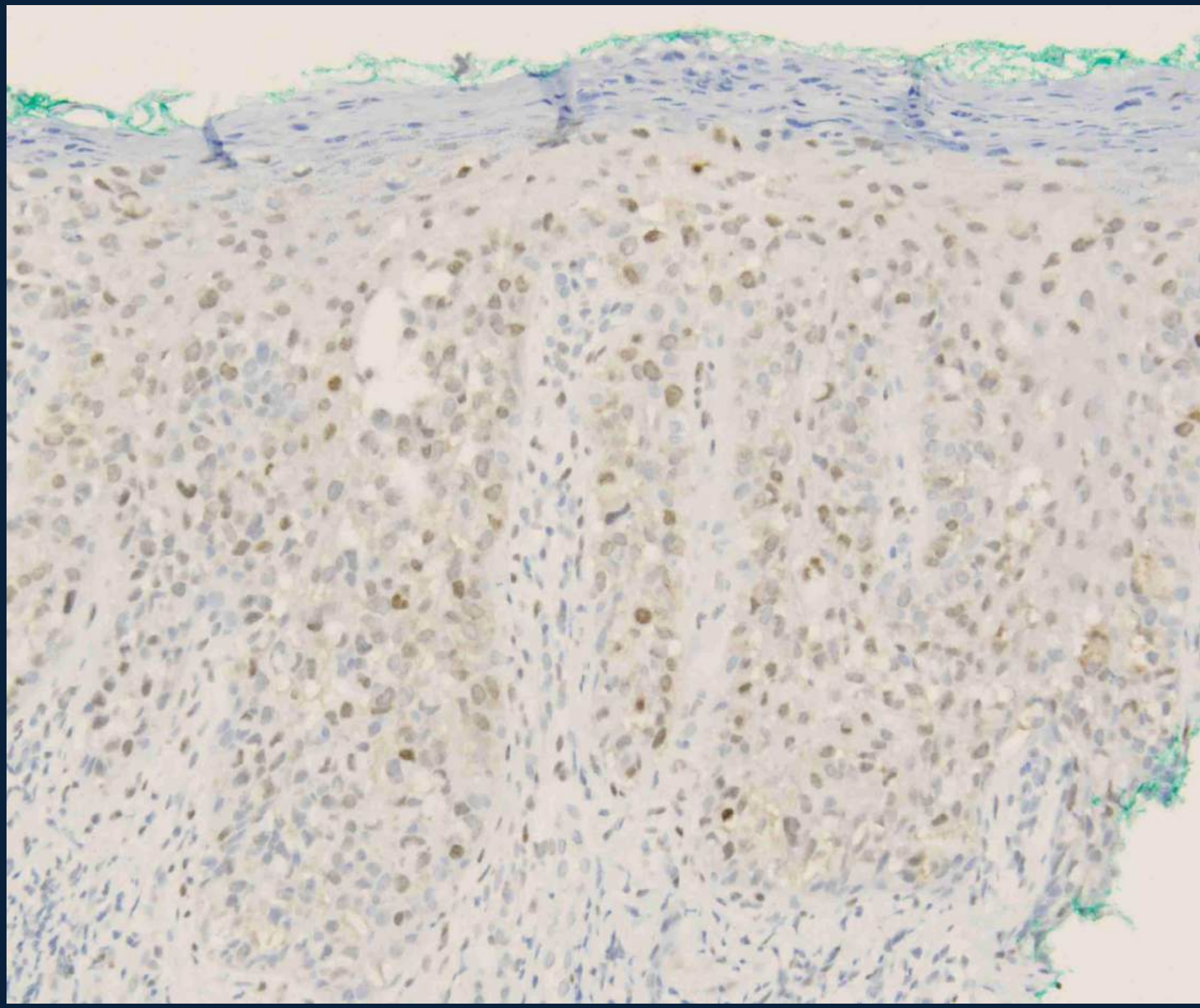
PRAME
Vulvar
Pagets
Weak +



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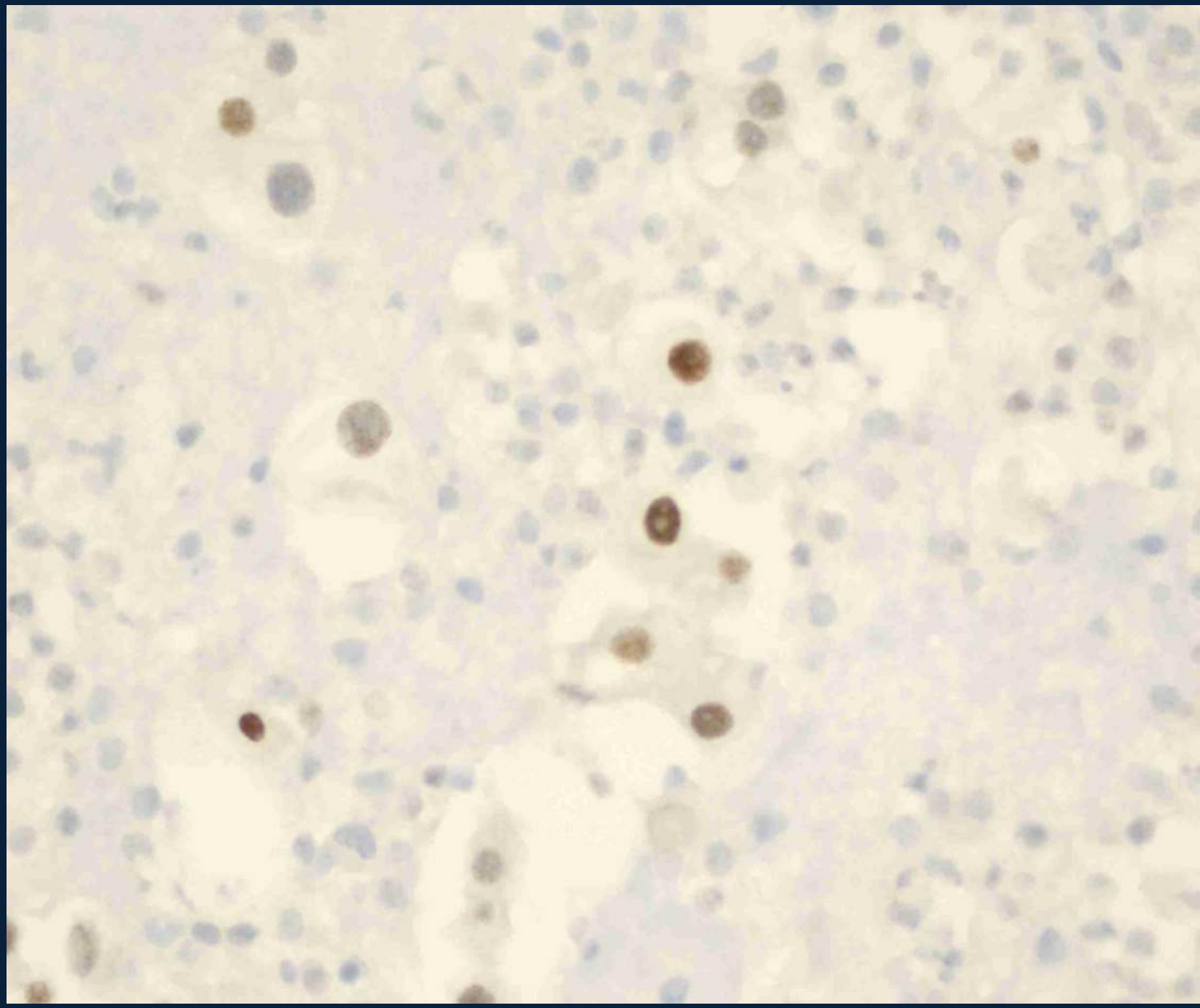
PRAME
Met ca
Fluid CB
Weak/focal positive



Acknowledgements

My colleagues in Pathology at BTMC/ BUMC/ PSA for sharing their cases.

Jacqui Ketterer: IHC Technical Supervisor and the IHC technical staff at our central lab, Sonora-Quest Laboratories, for their assistance and dedication to the performance of high quality results for our patients.


Honey Island Swamp Band. Jazz Fest 2019