

XXX. Martinský bioptický seminár SD-IAP

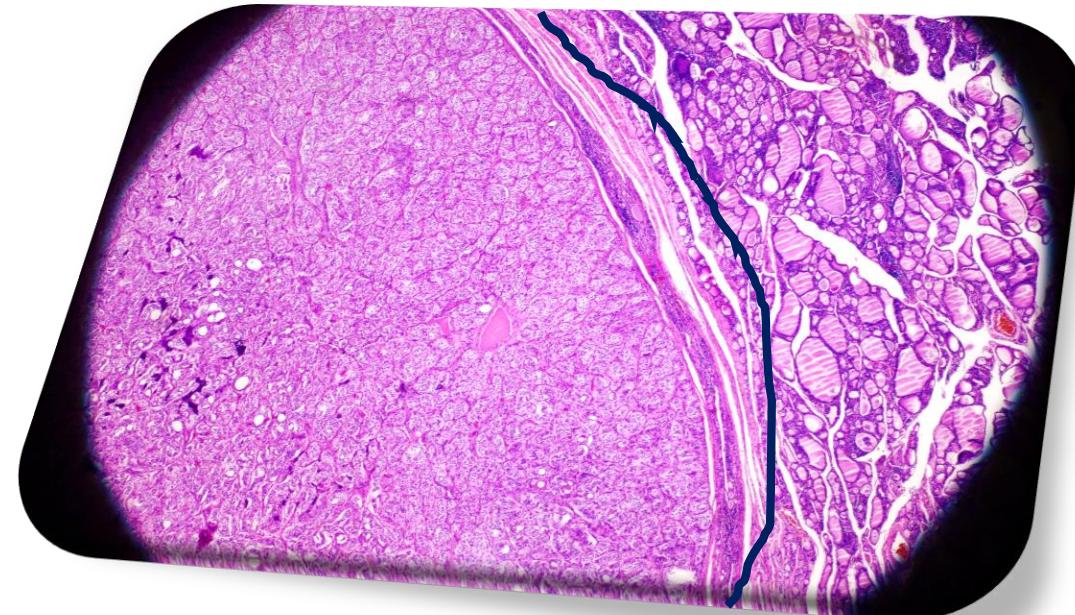
**14.-15. november 2024 Martin
hotel VICTORIA**

**Prípad SD-IAP č. 861
prezentuje P. Bohuš
Ústav patológie UNLP a LF UPJŠ Košice**

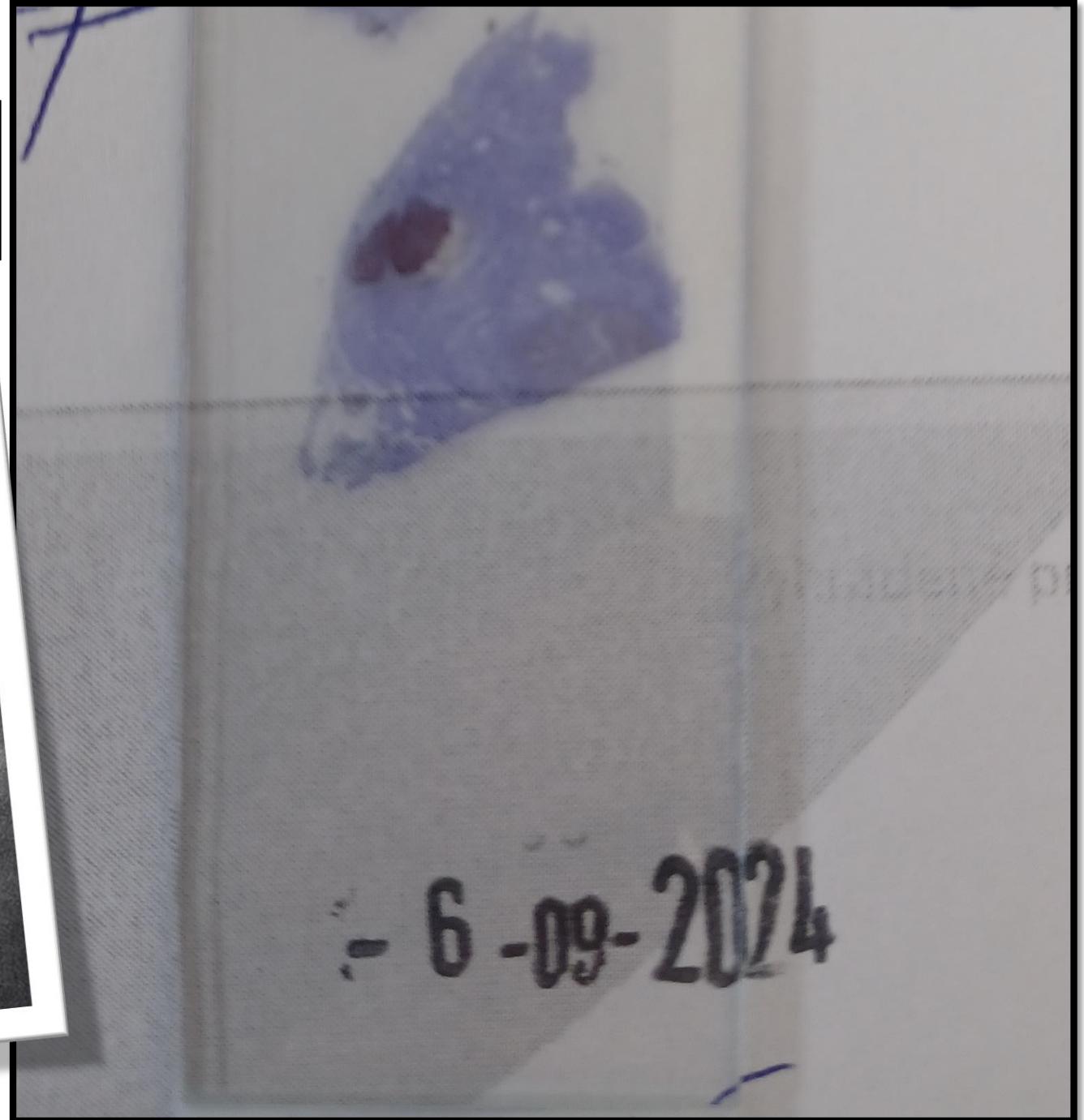
53-ročná pacientka

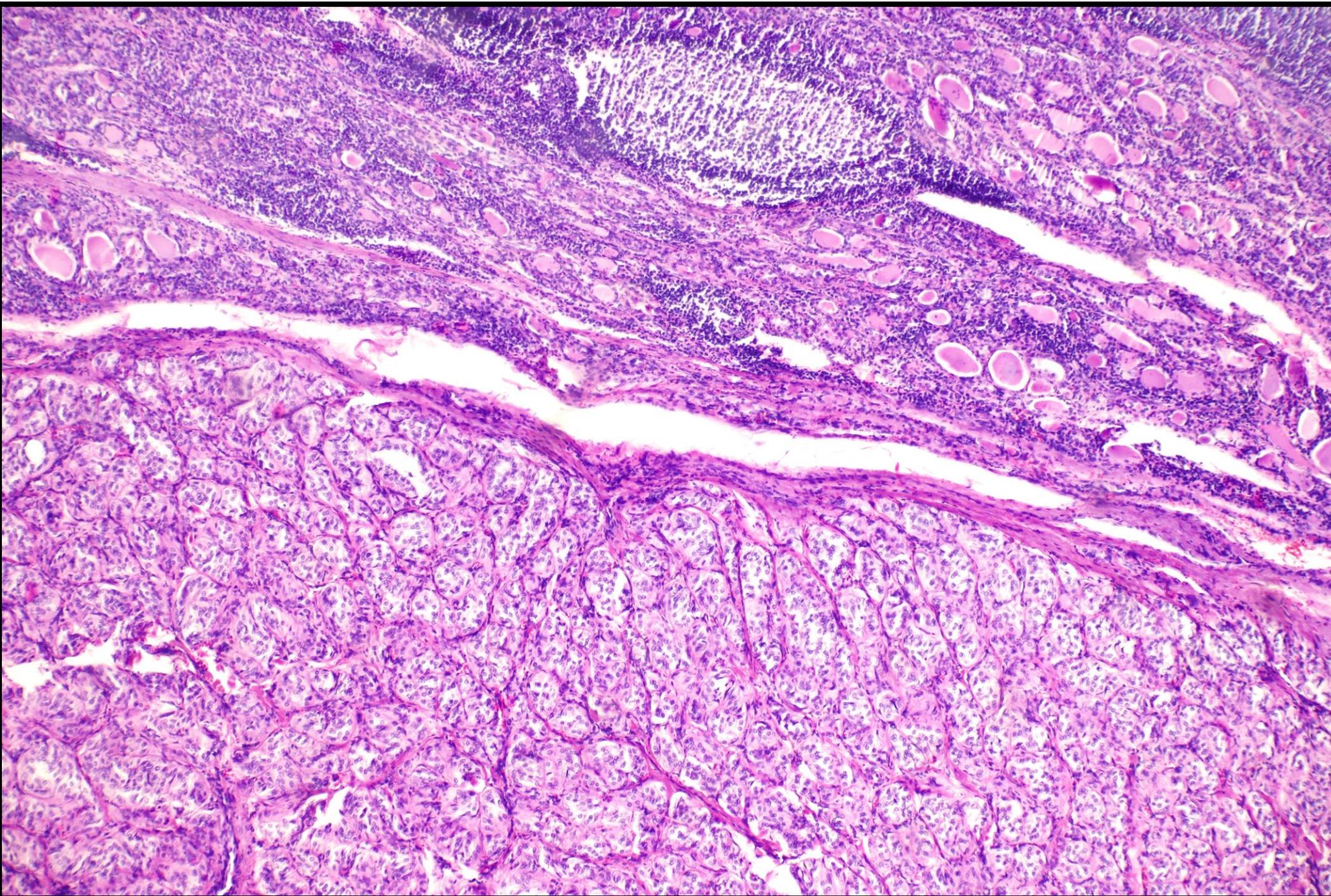
klin. dg: netoxická viacuzlová struma

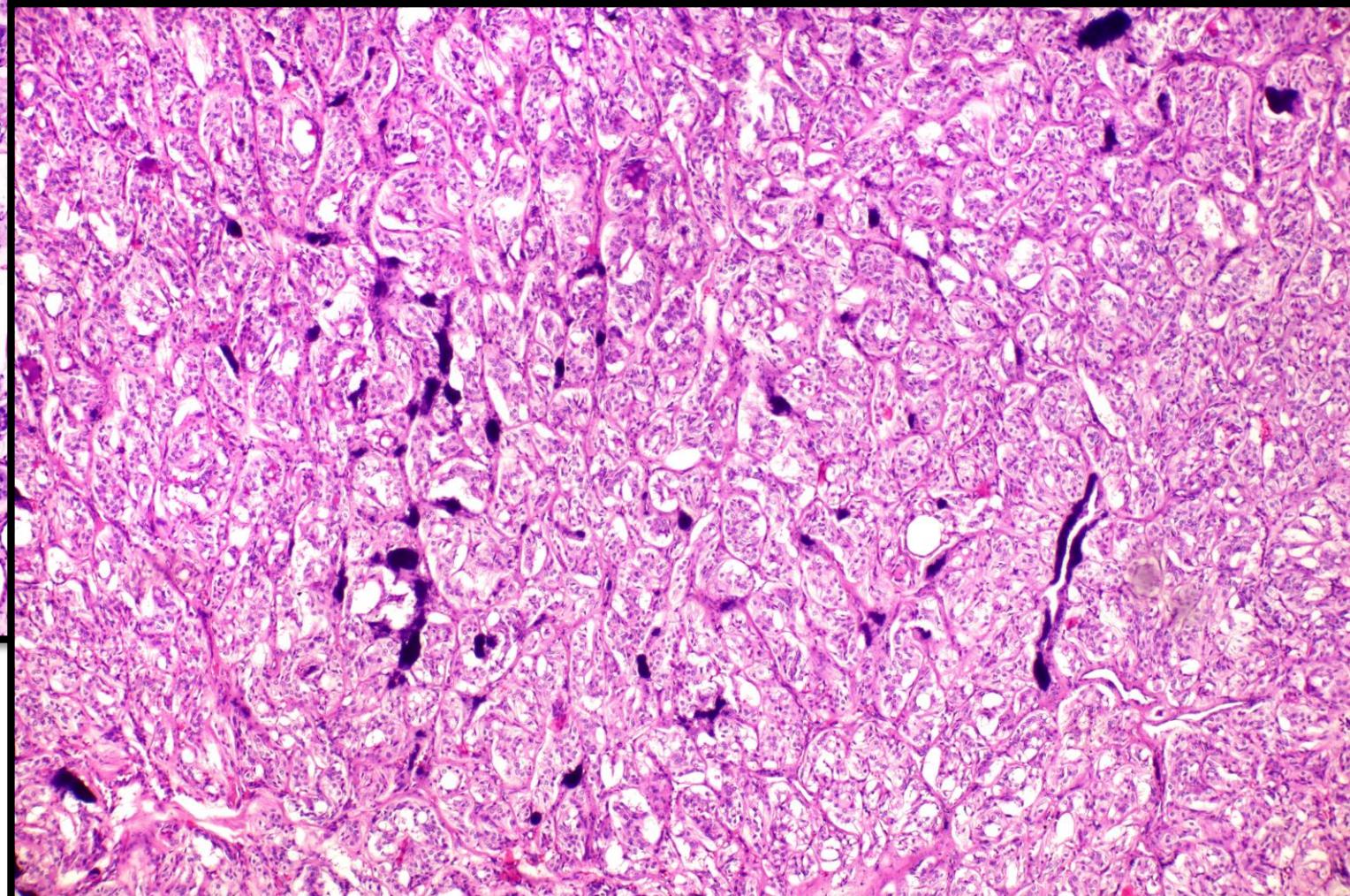
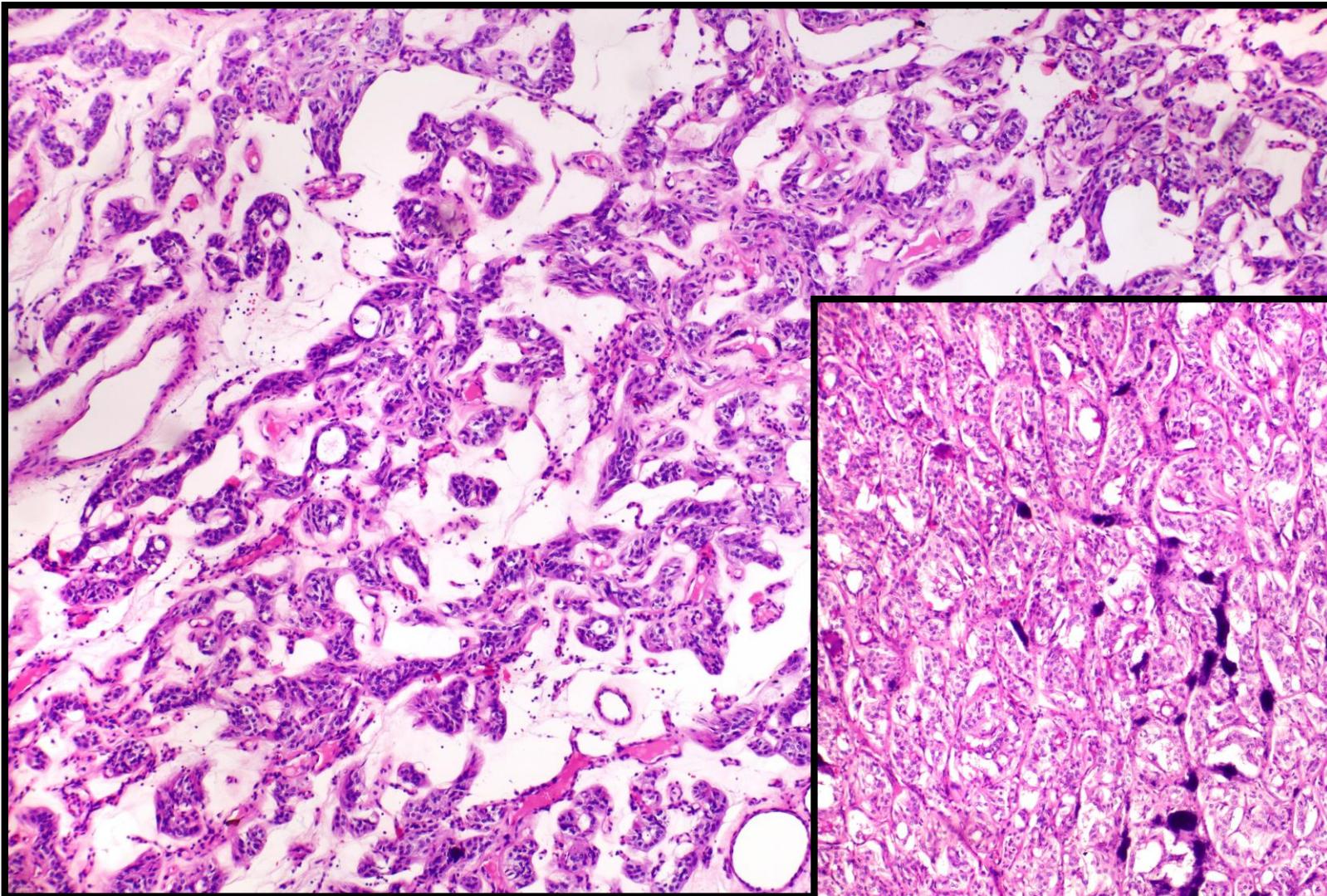
- Ľavý lalok thyreoidey veľkosti 60x35x30 mm
- Uzlovito zmenený
- **Centrálne ostro ohraničený uzol** veľkosti cca 50x35x30 mm

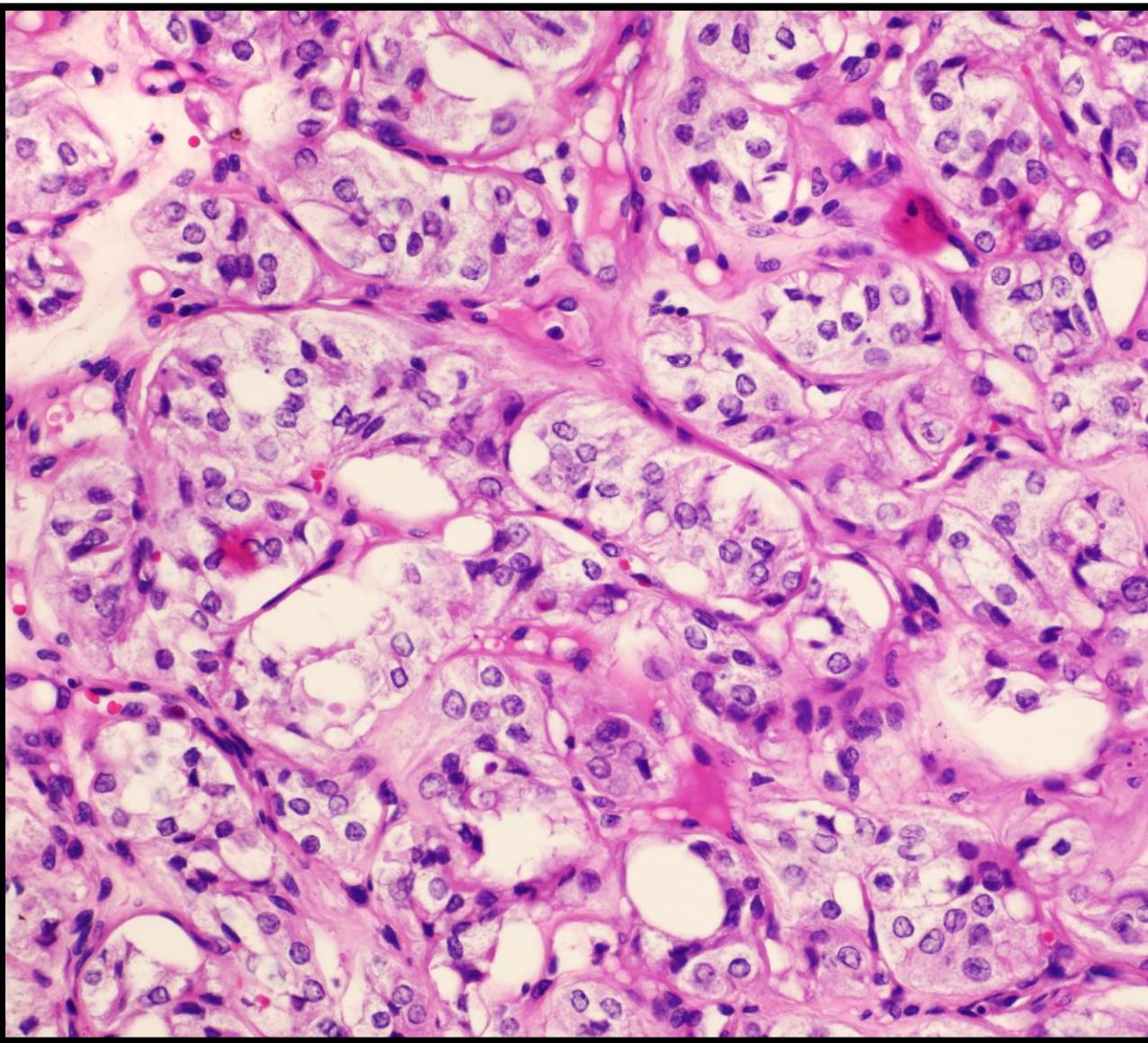
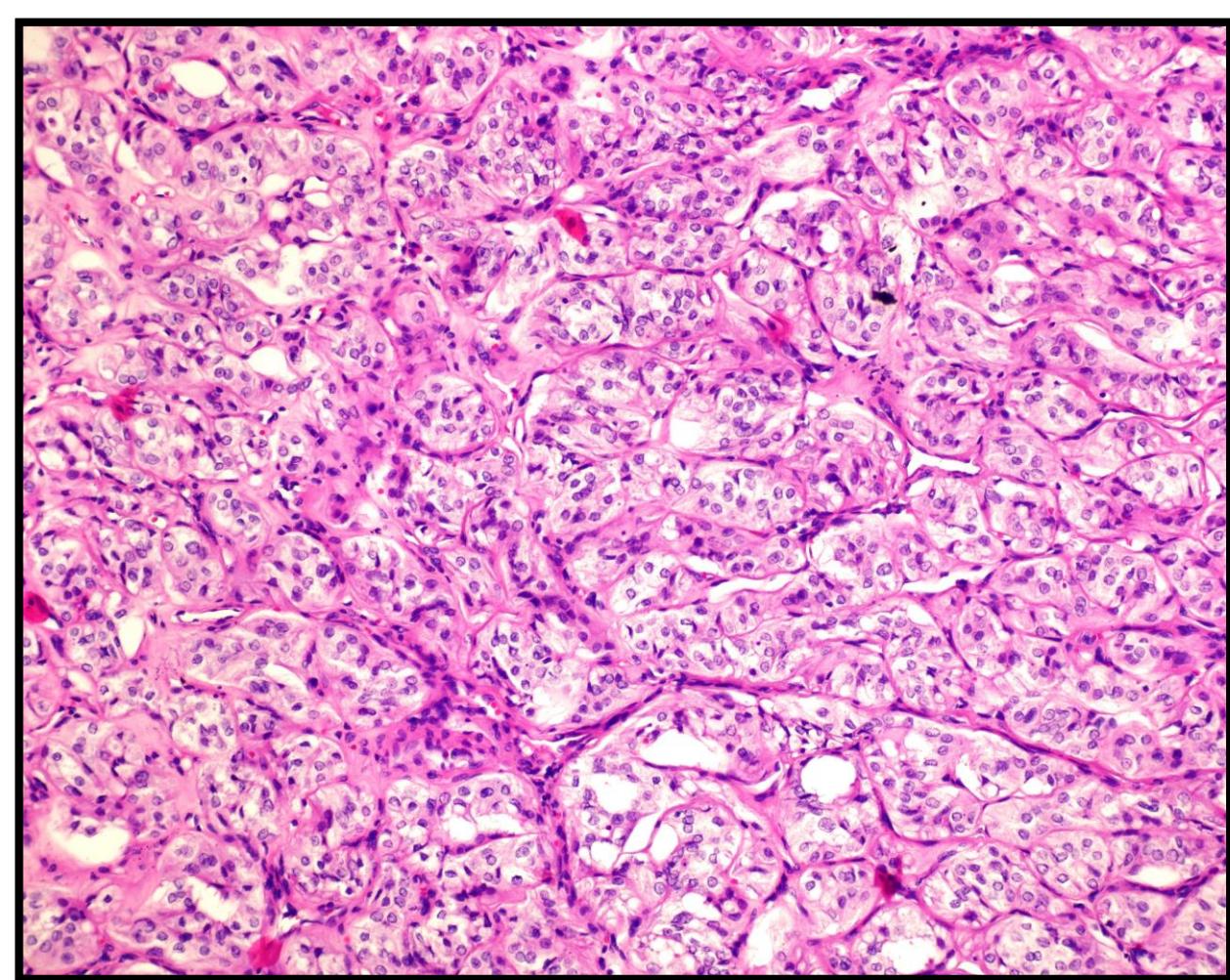


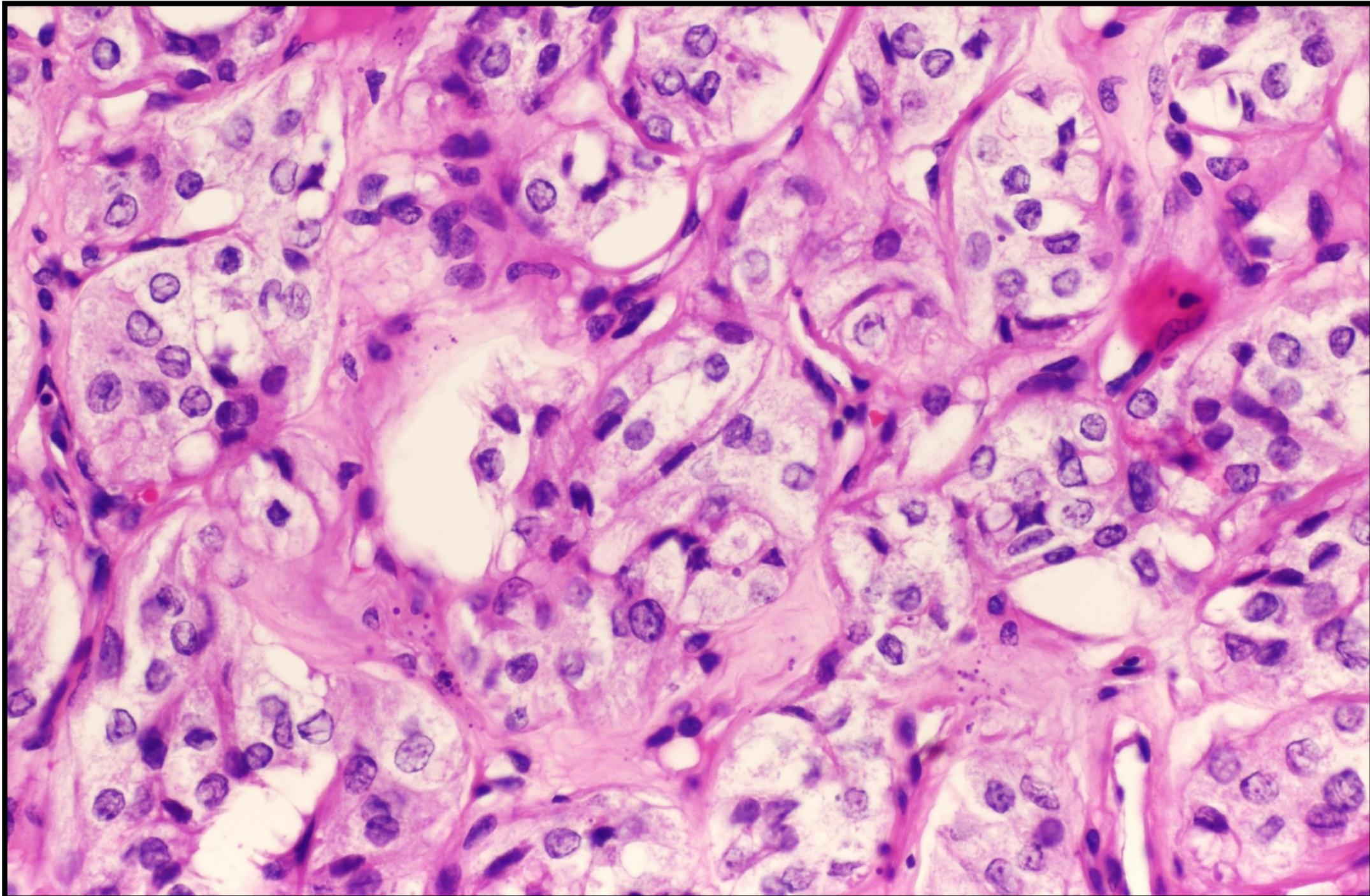
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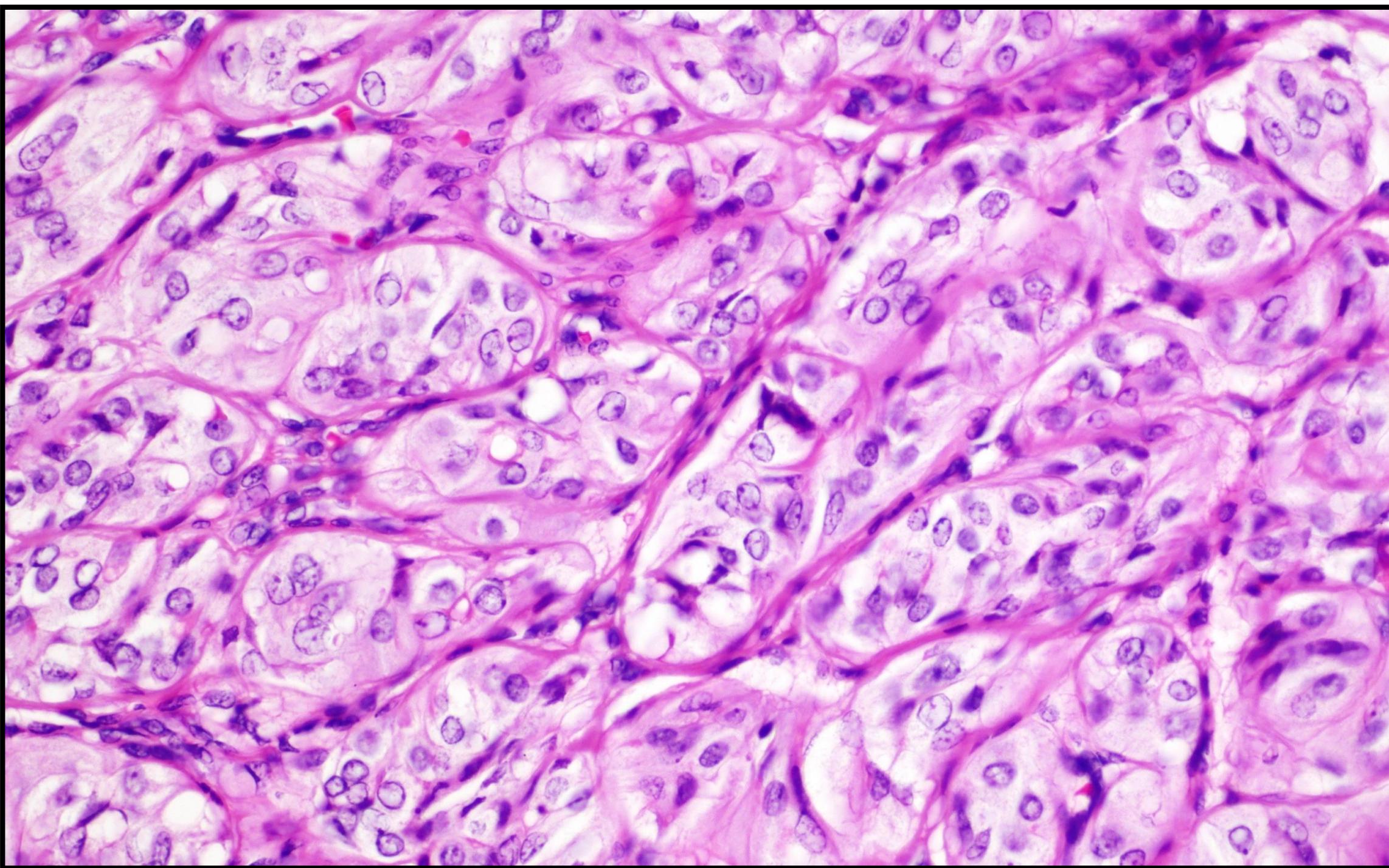


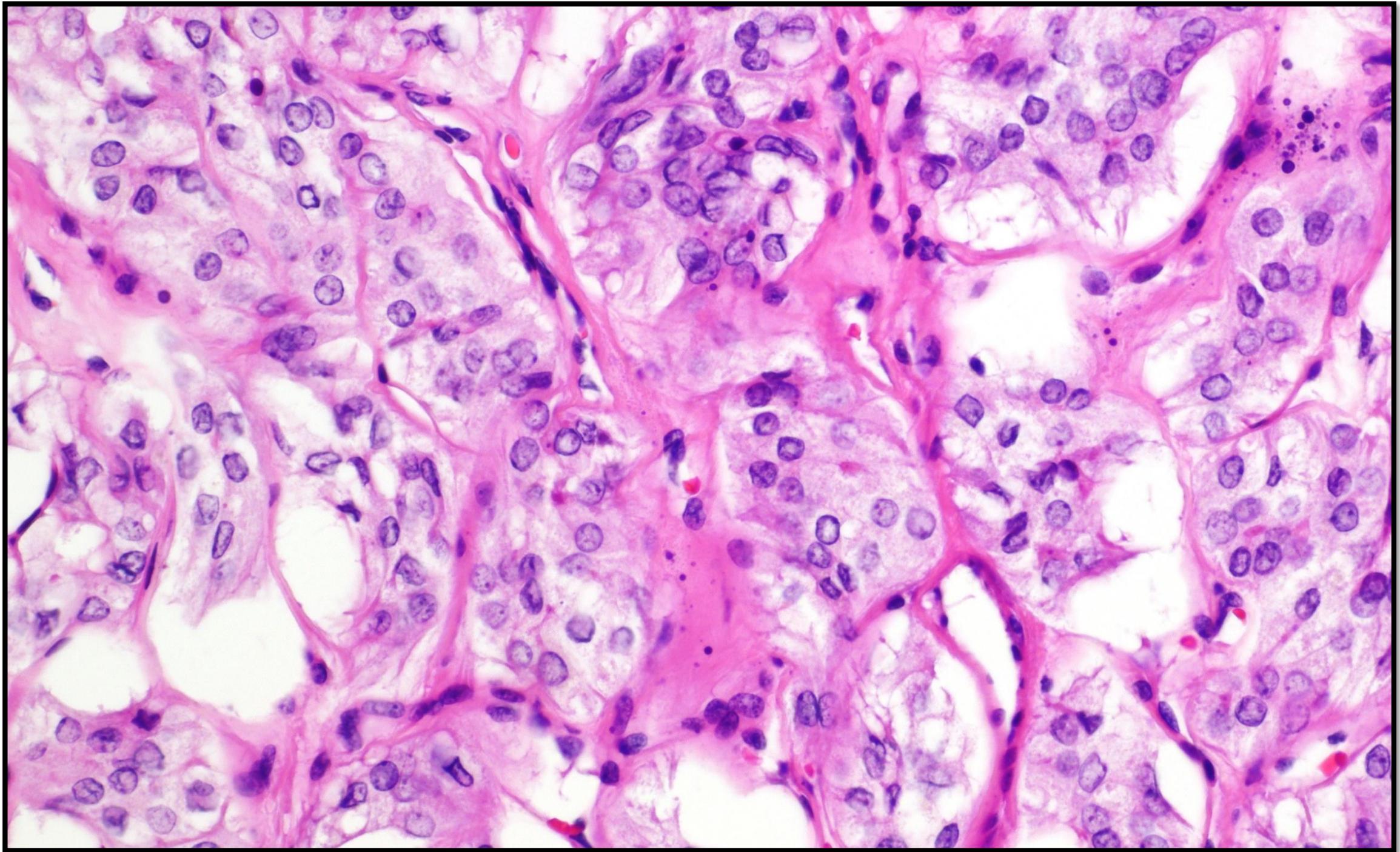




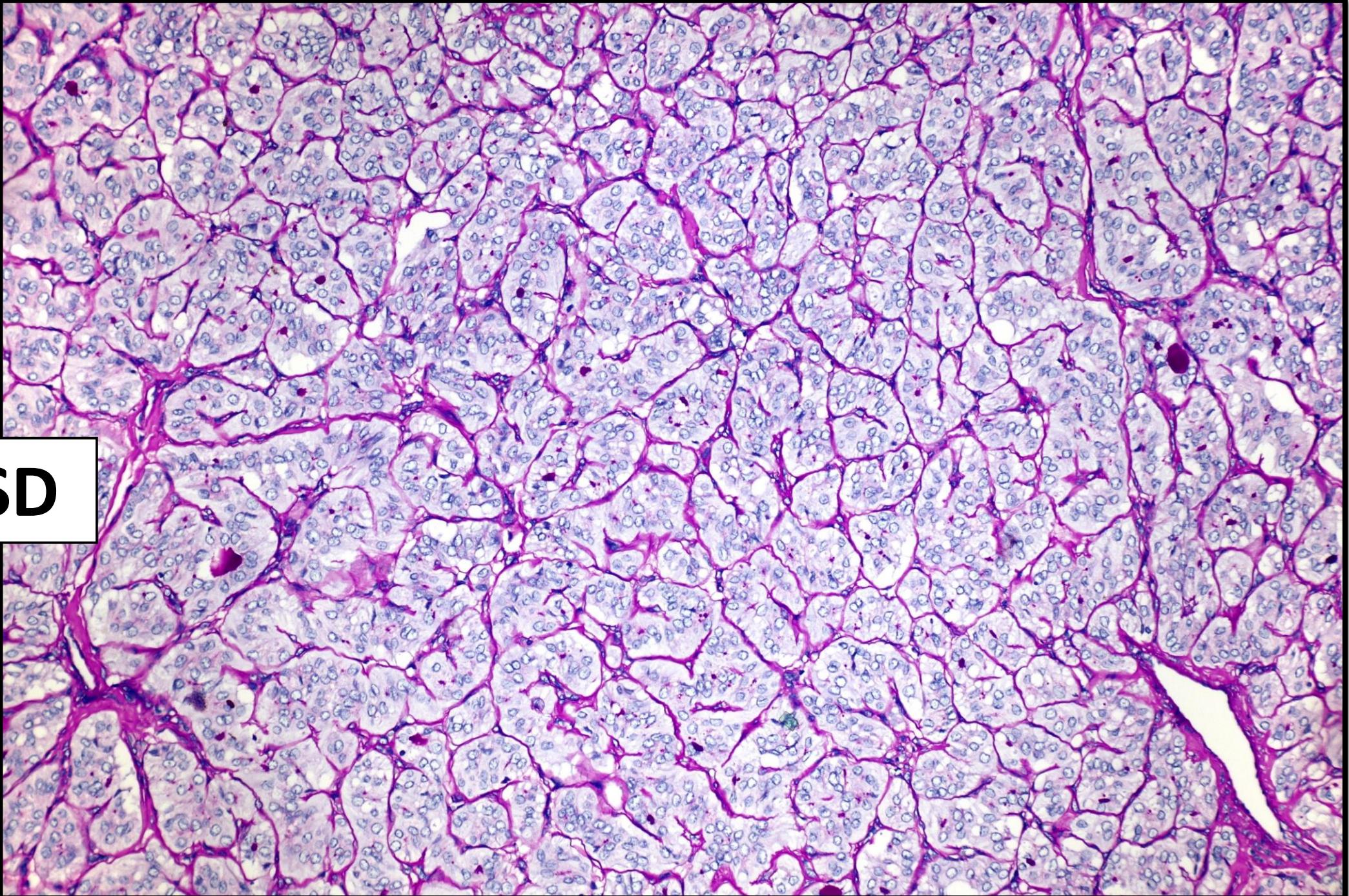




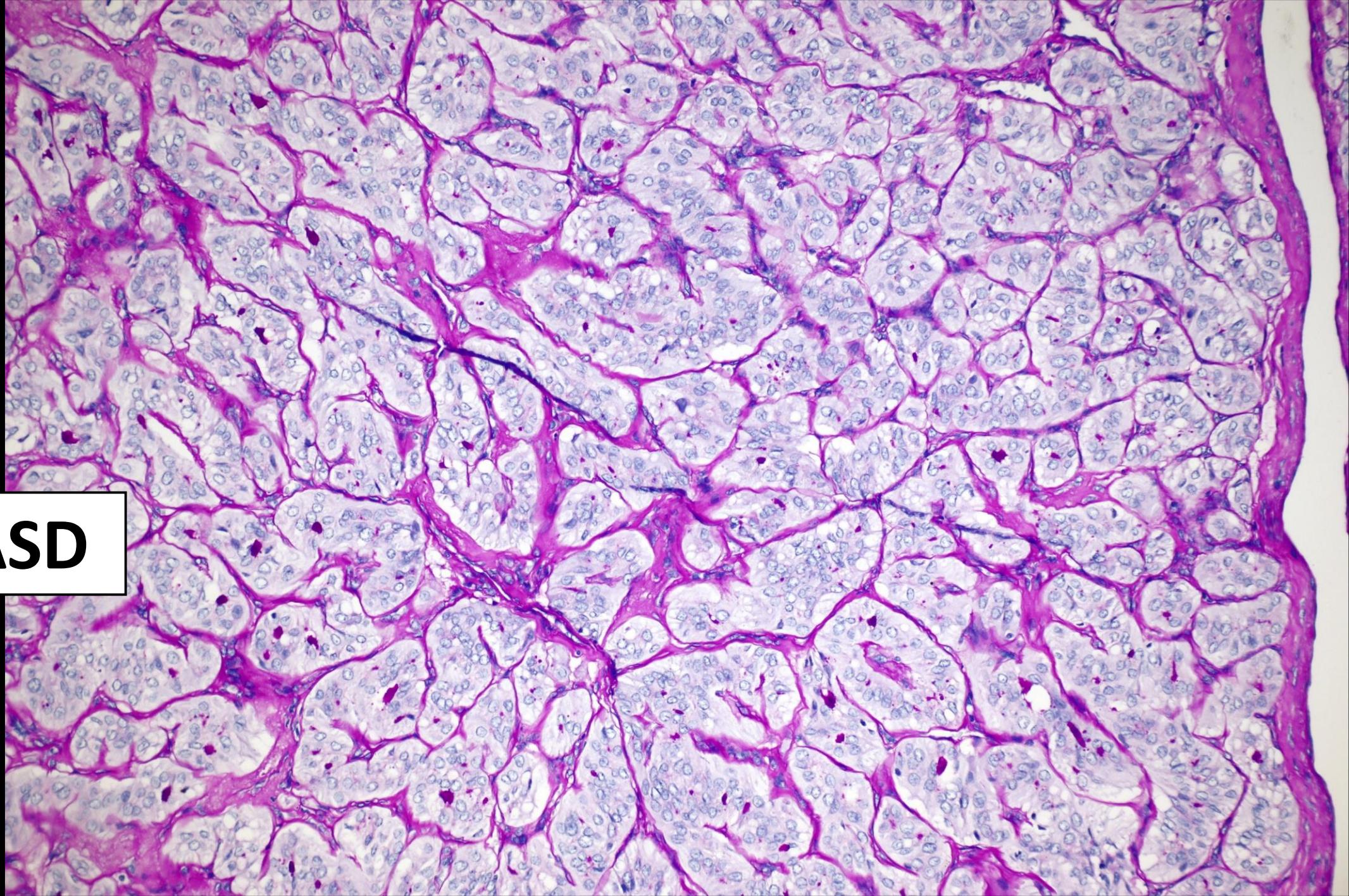


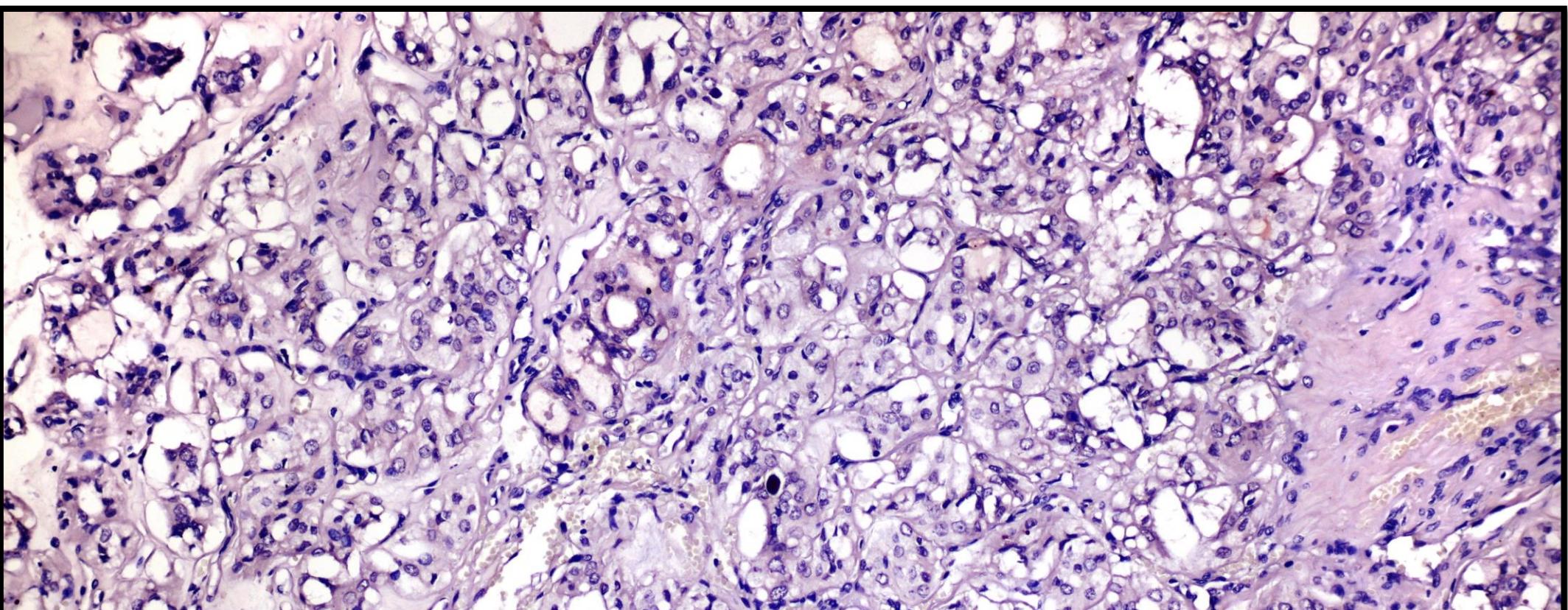


PASD

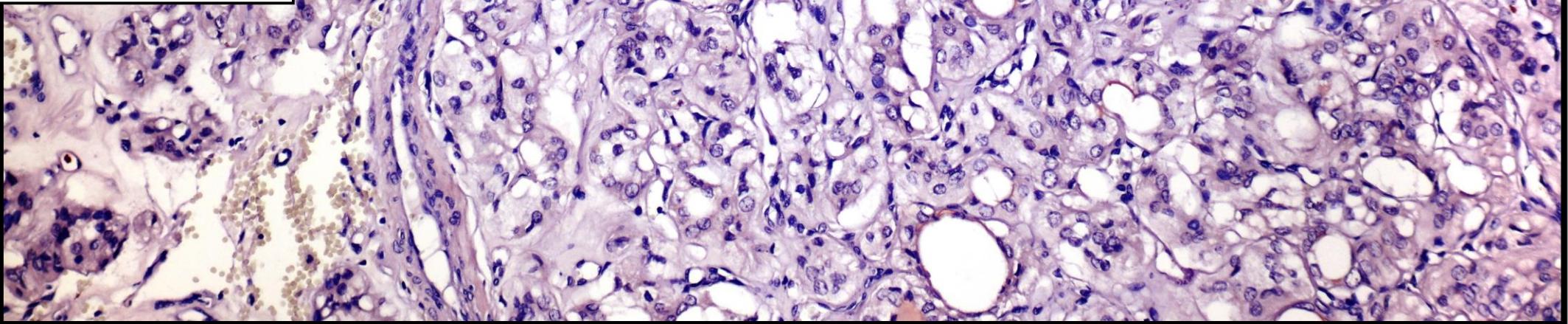


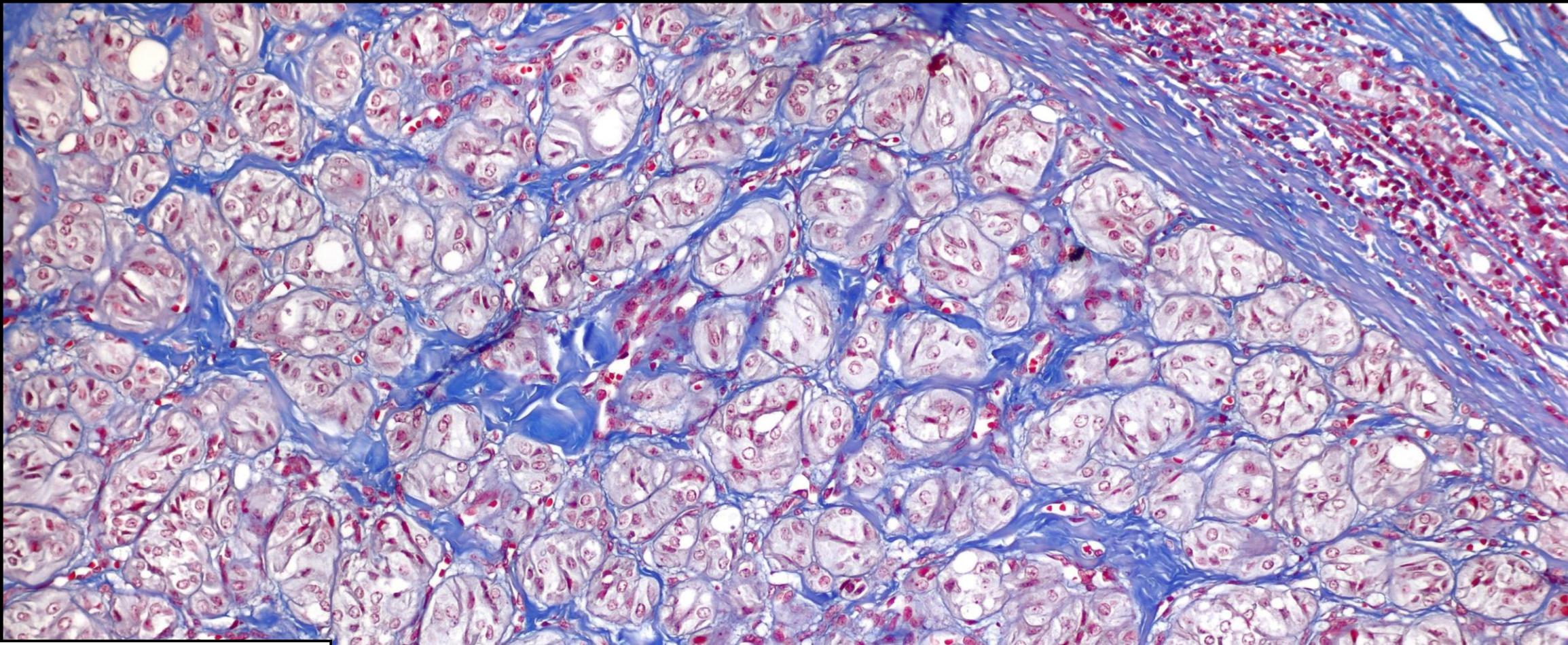
PASD



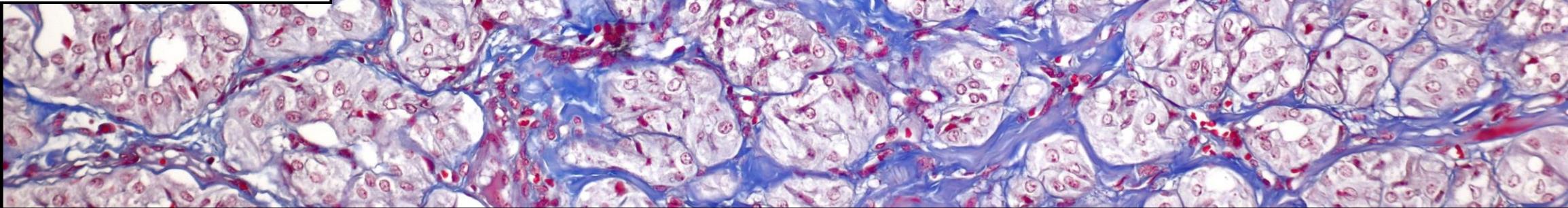


Congo Red



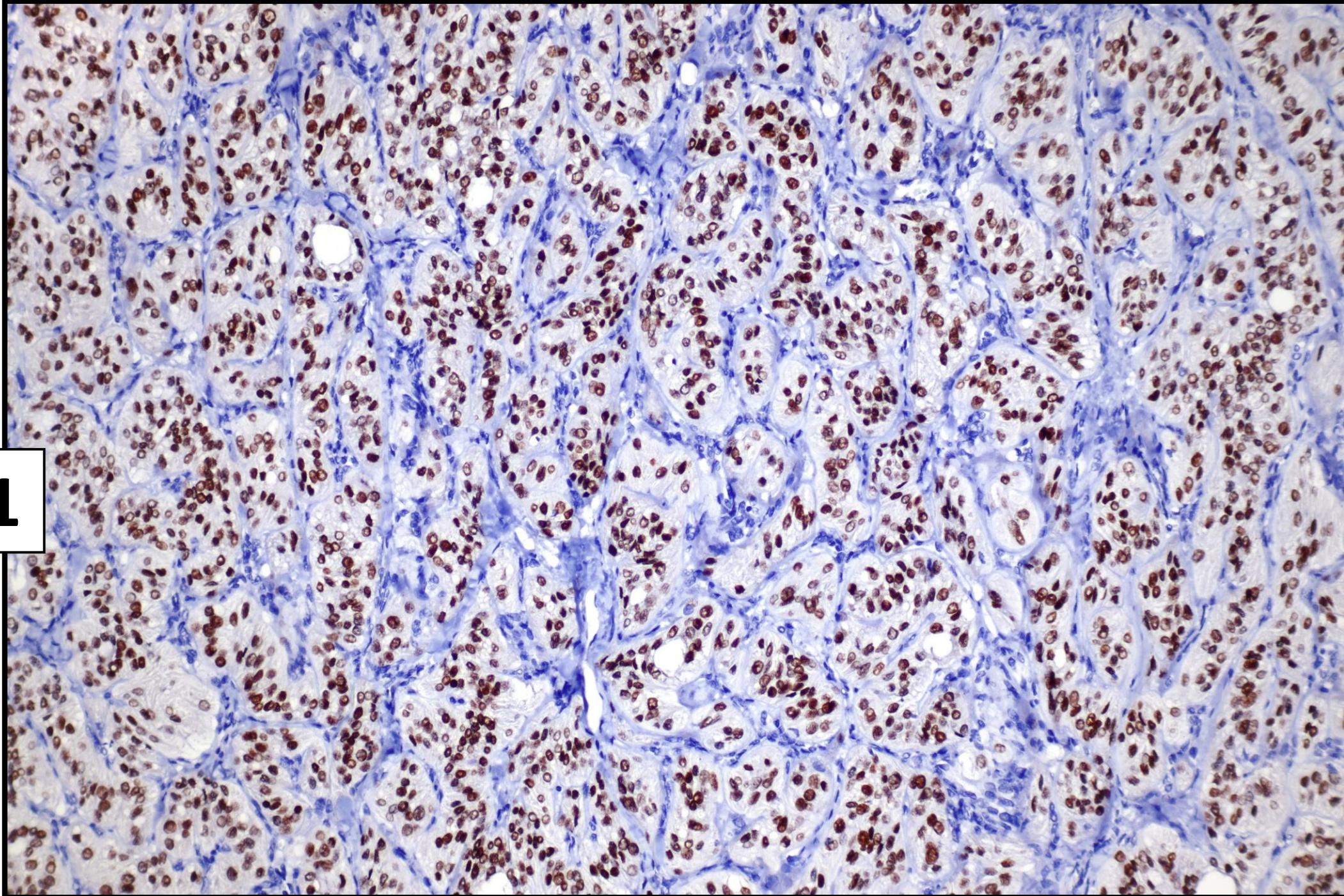


Trichrome

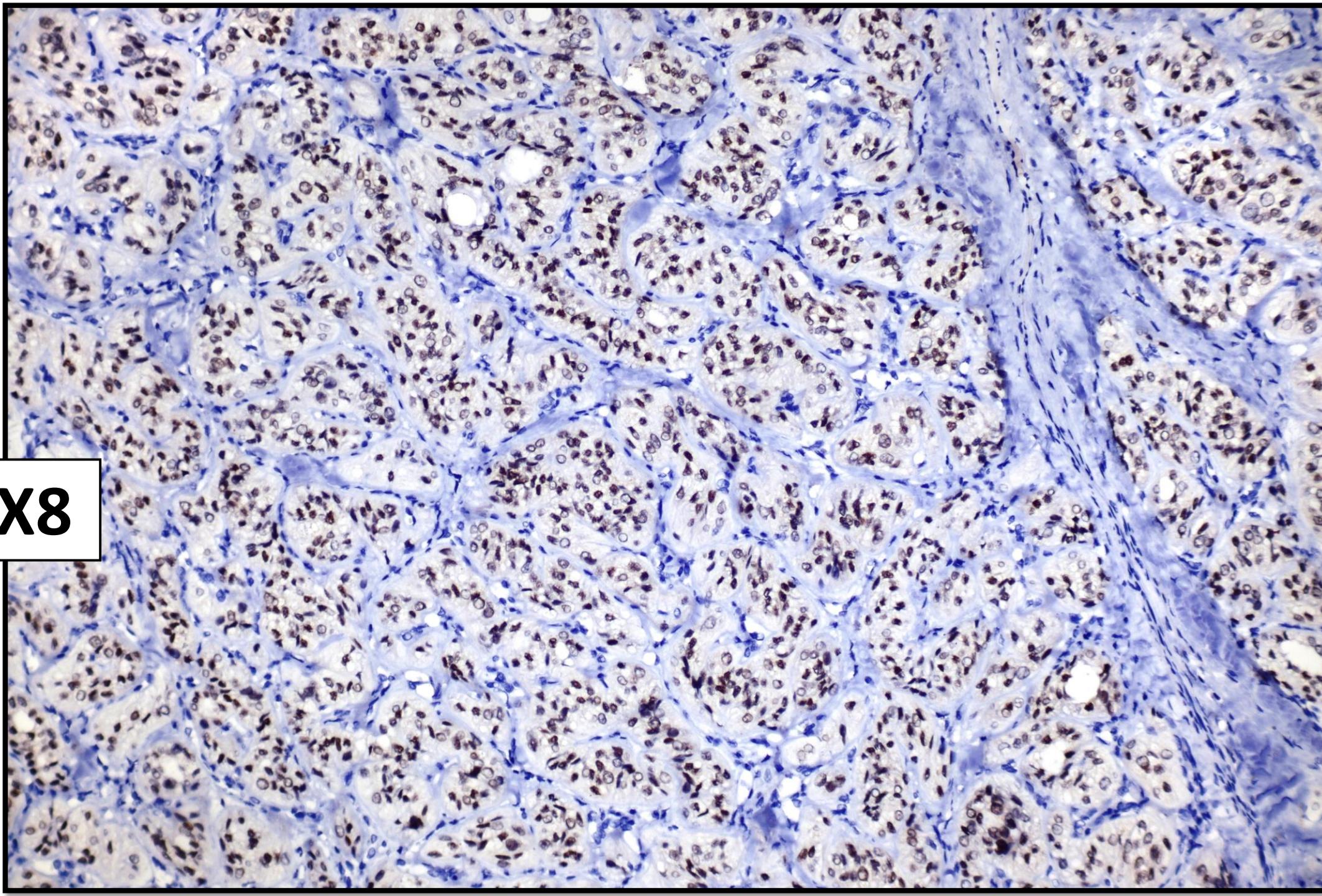


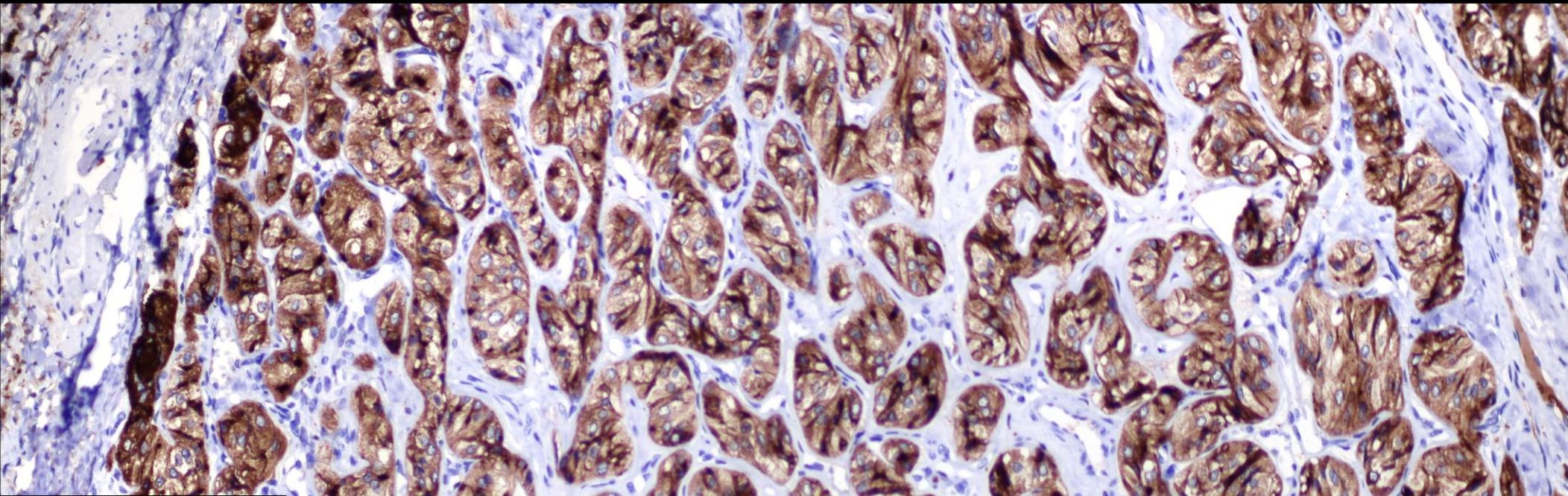
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TTF1

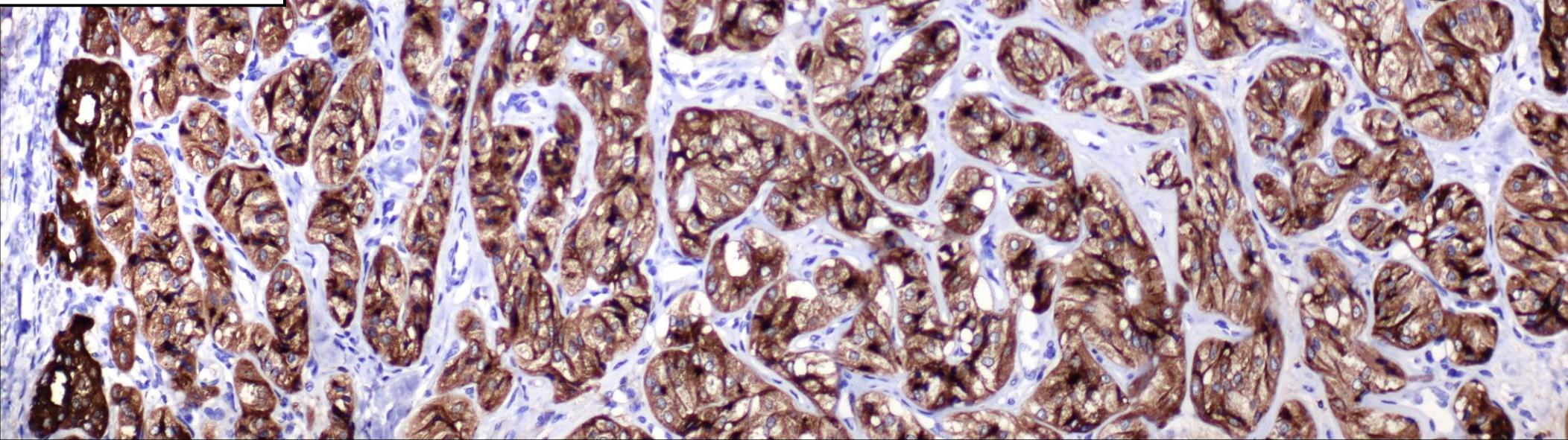


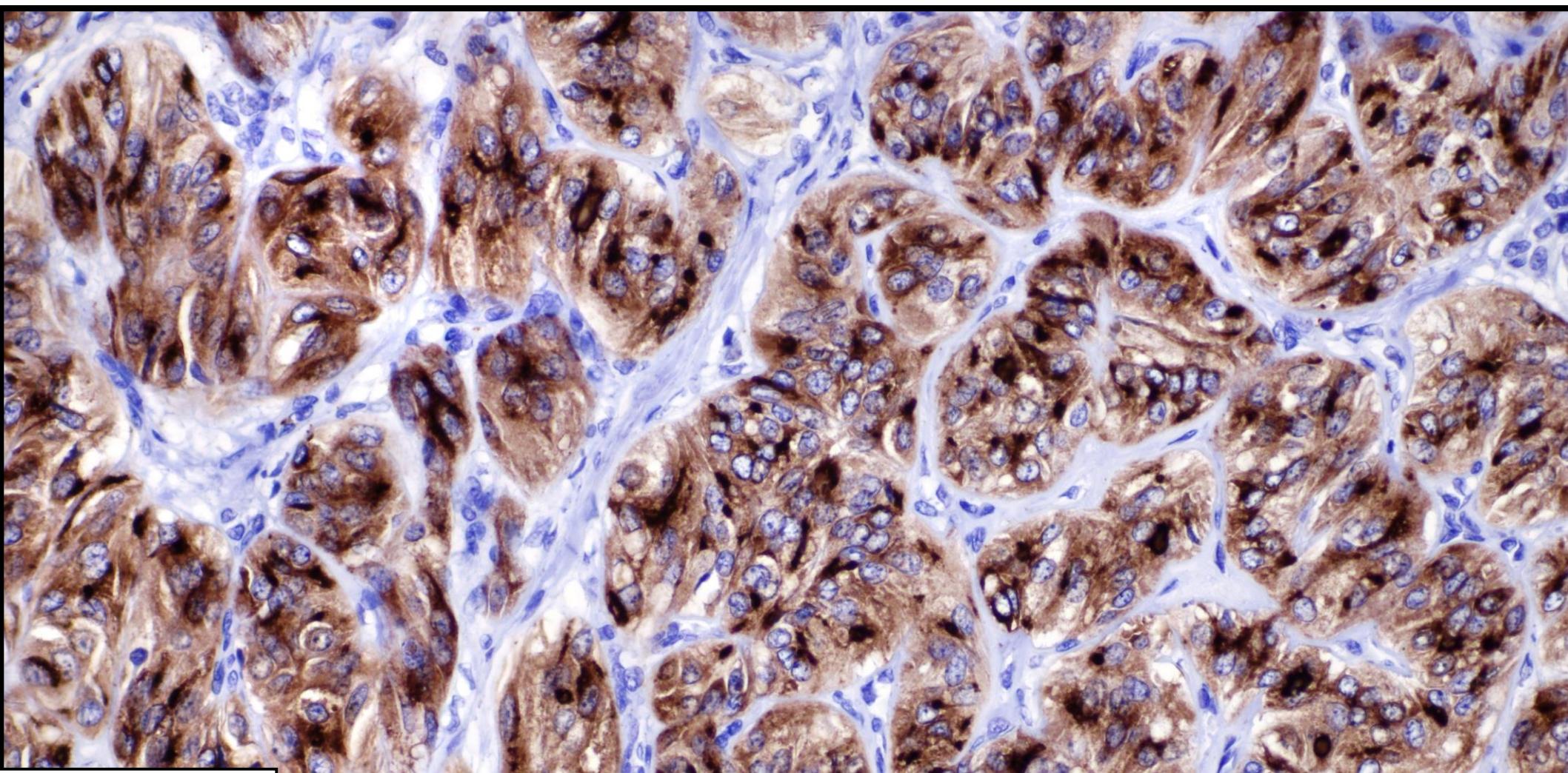
PAX8



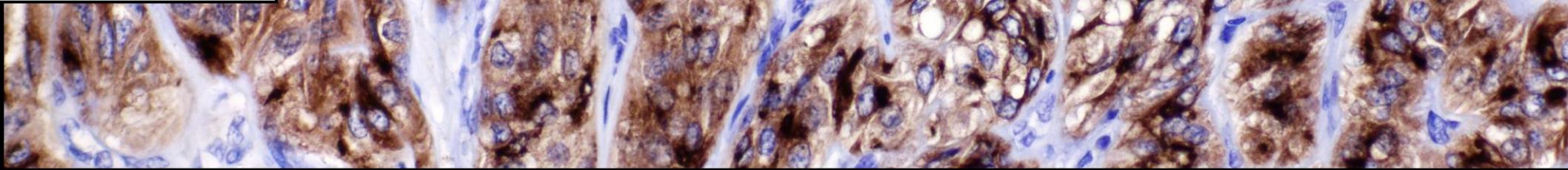


Thyroglobulin

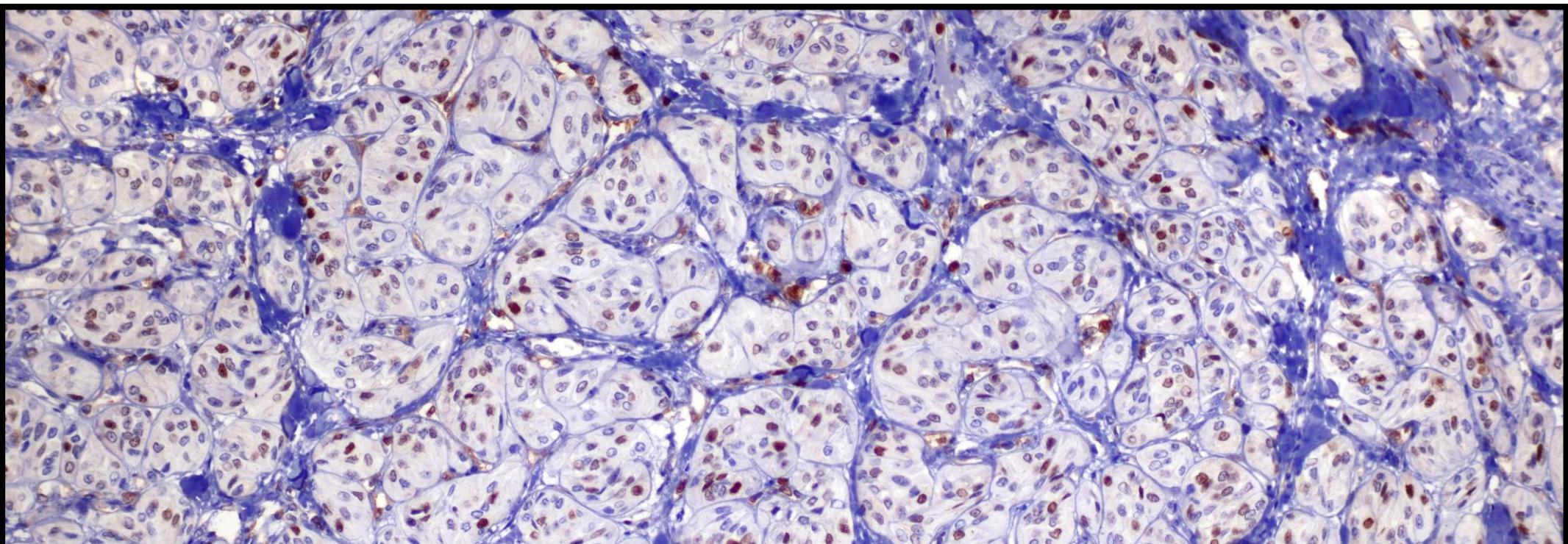
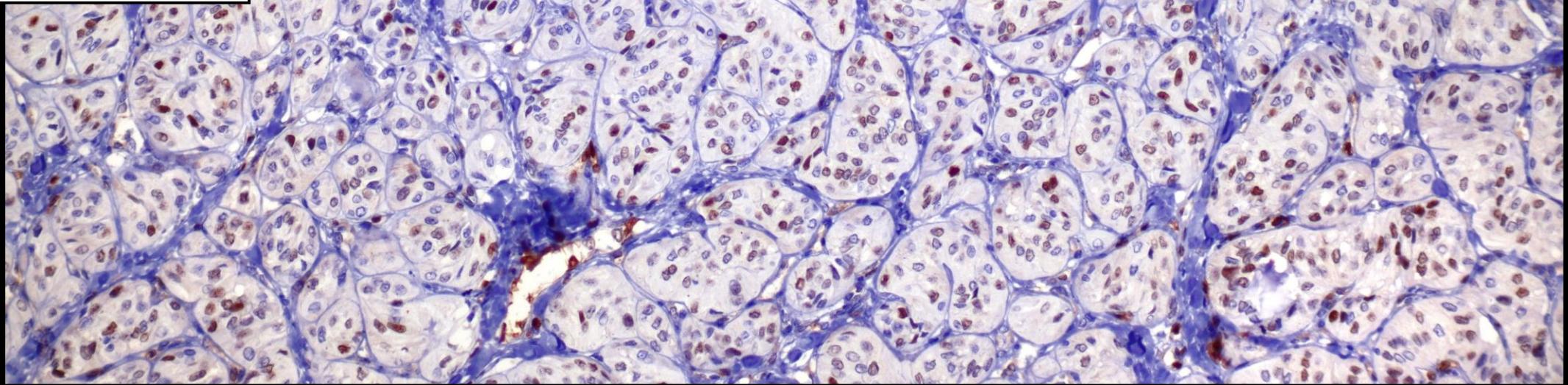


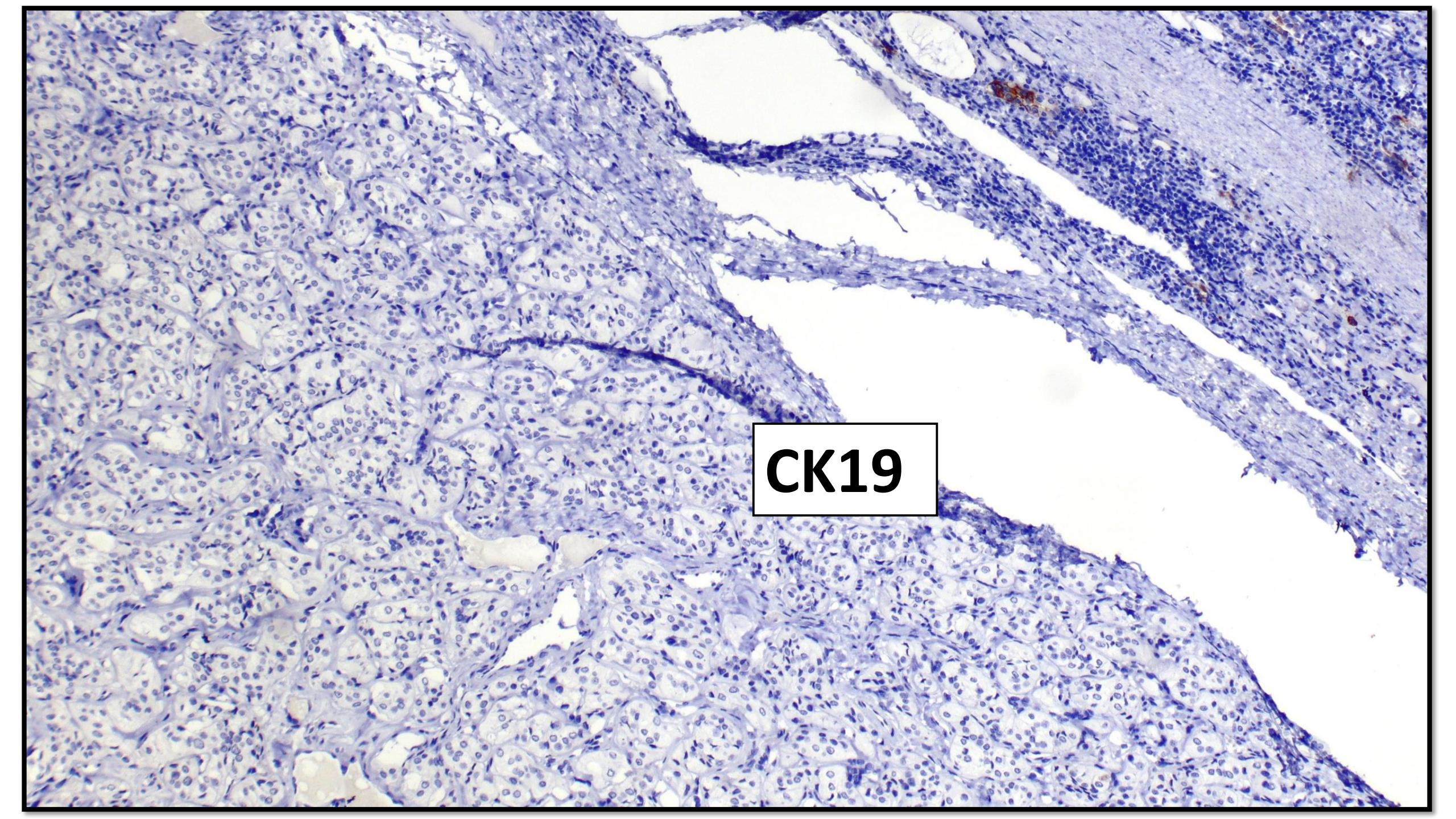


Thyroglobulin

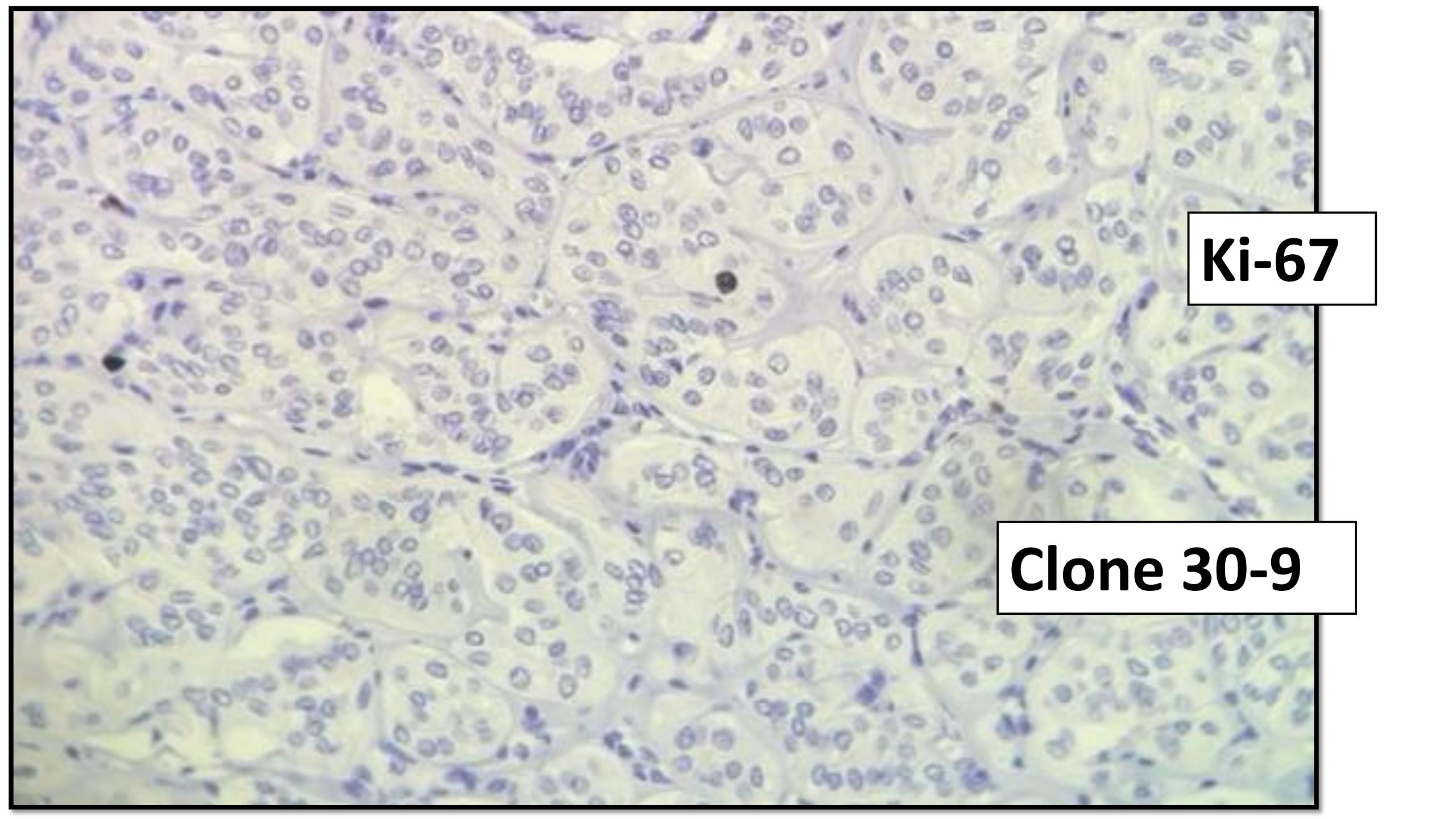


Cyclin D1





CK19



Ki-67

Clone 30-9

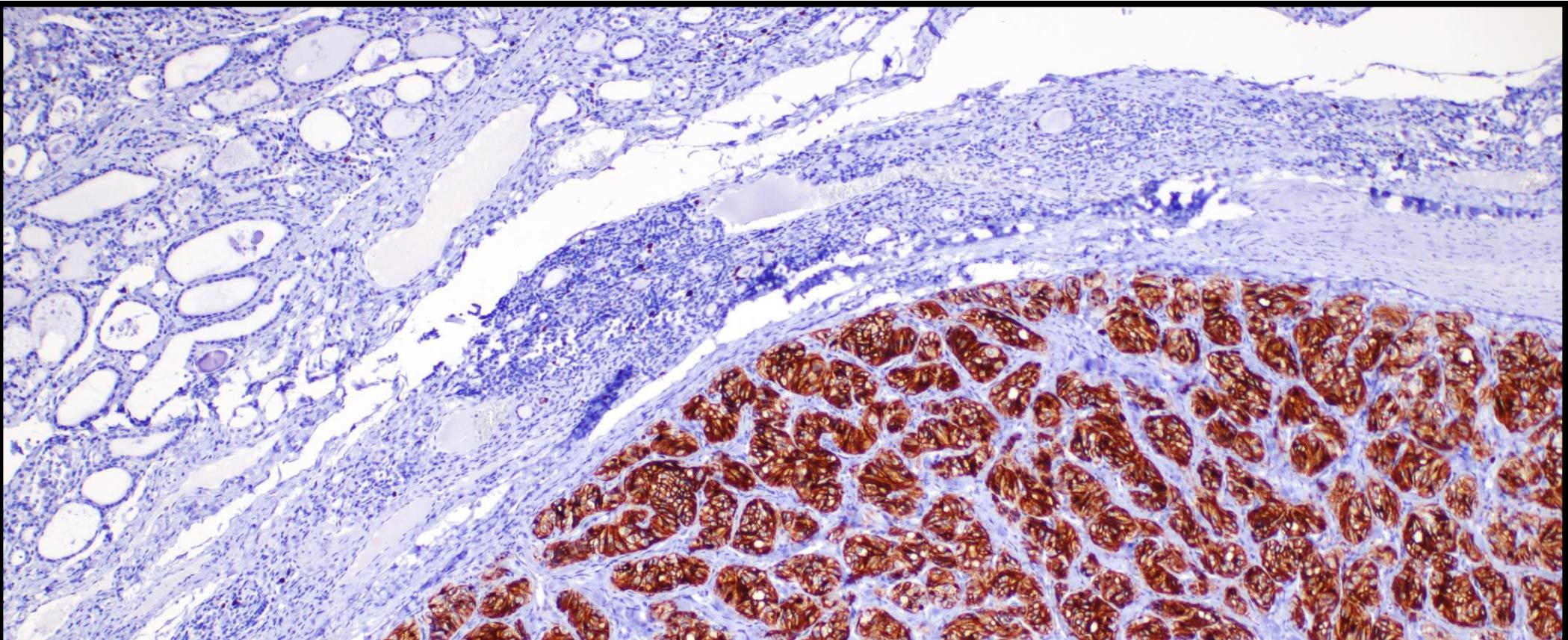
110545 7 2

llon M181-

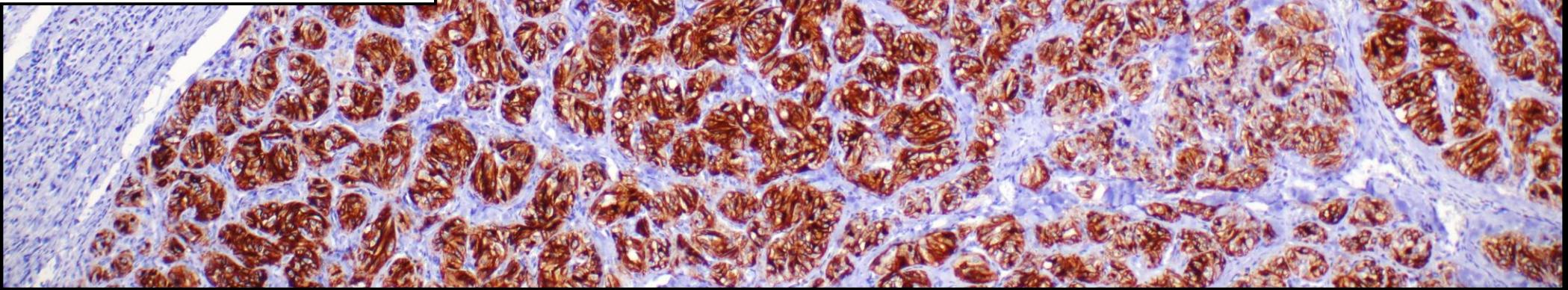


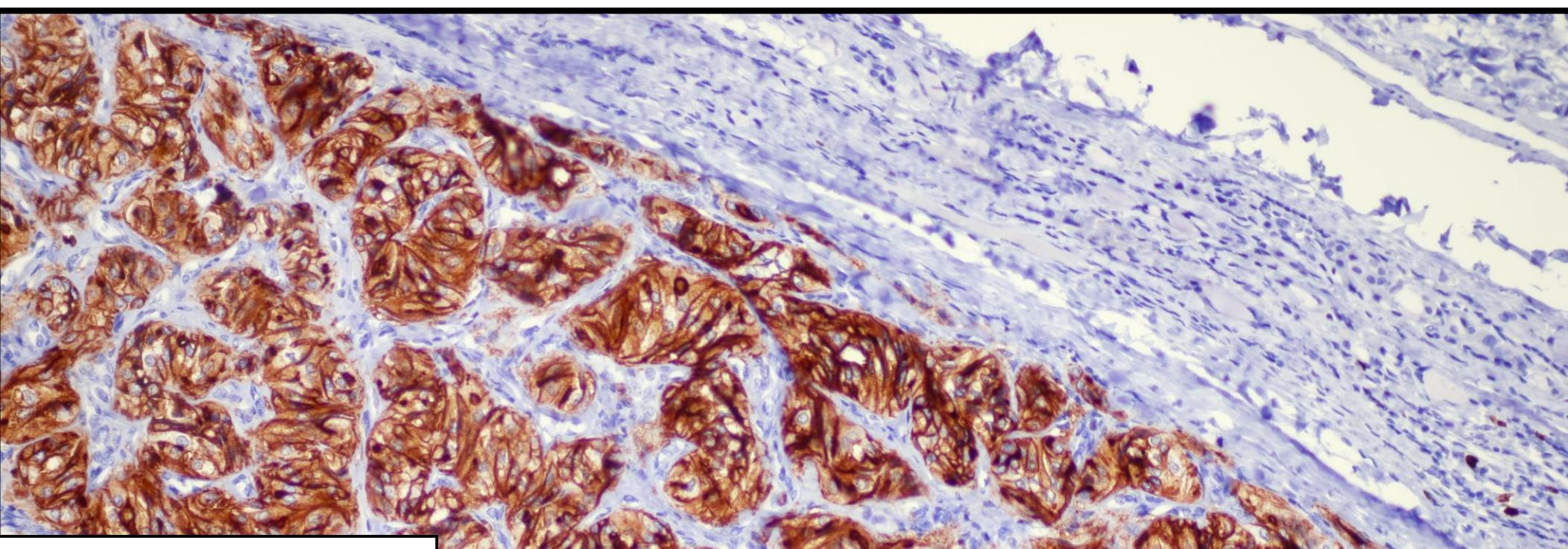
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- 6 -09-2024

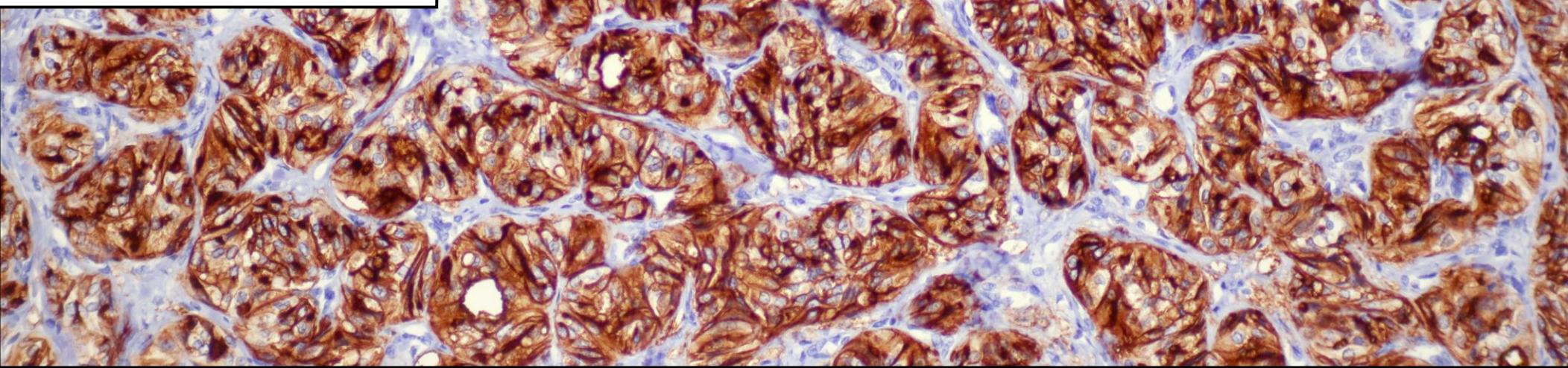


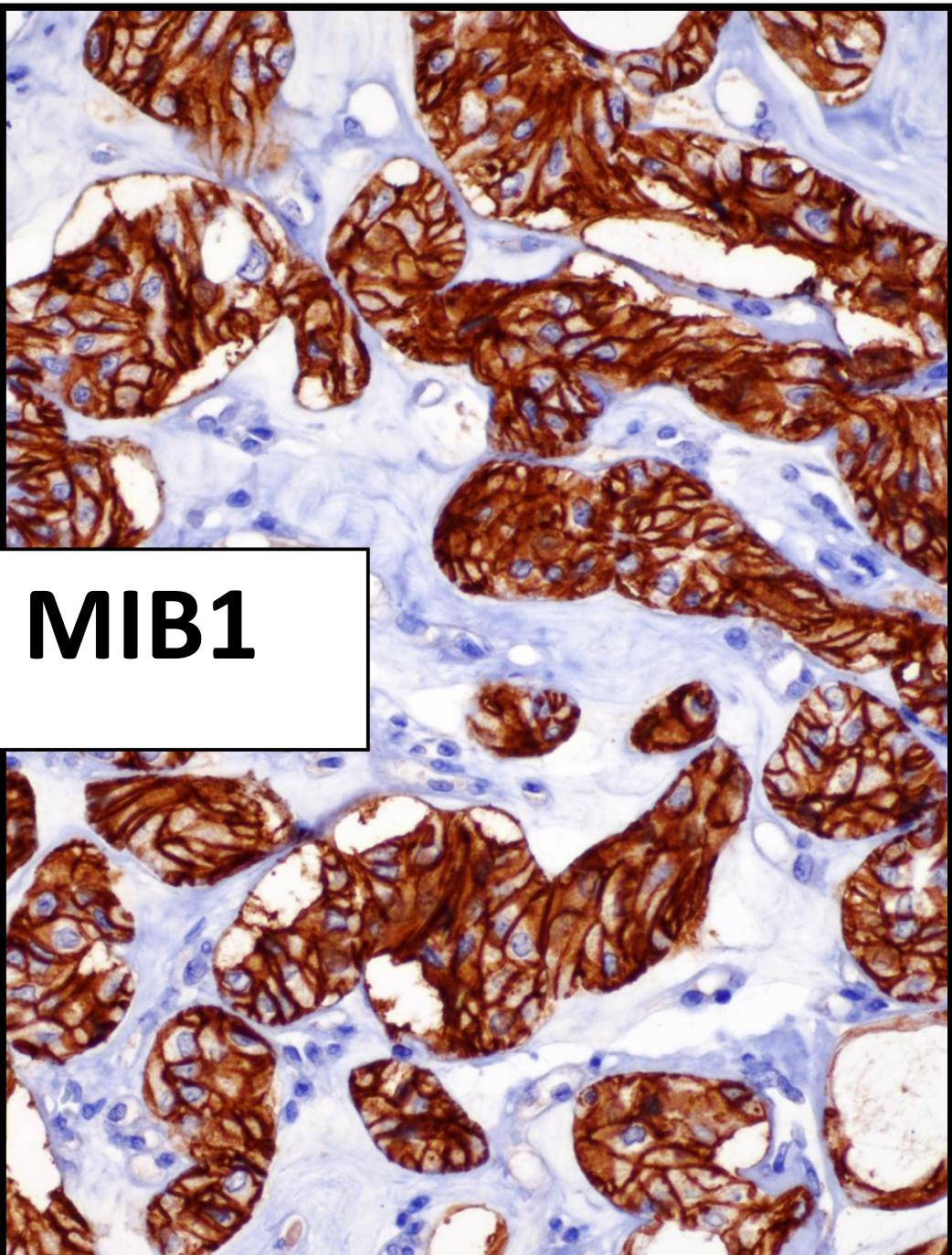
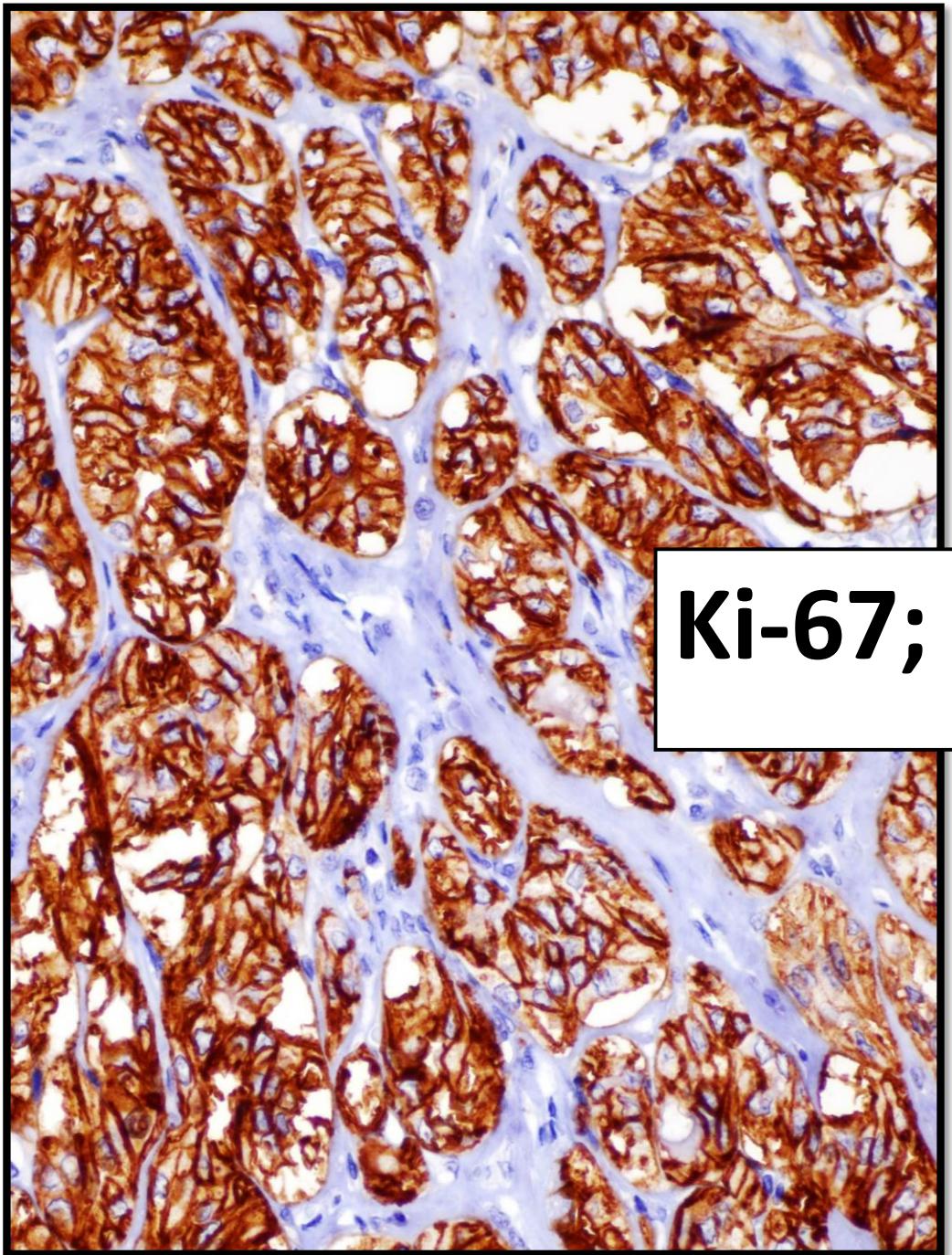
Ki-67; clone MIB1



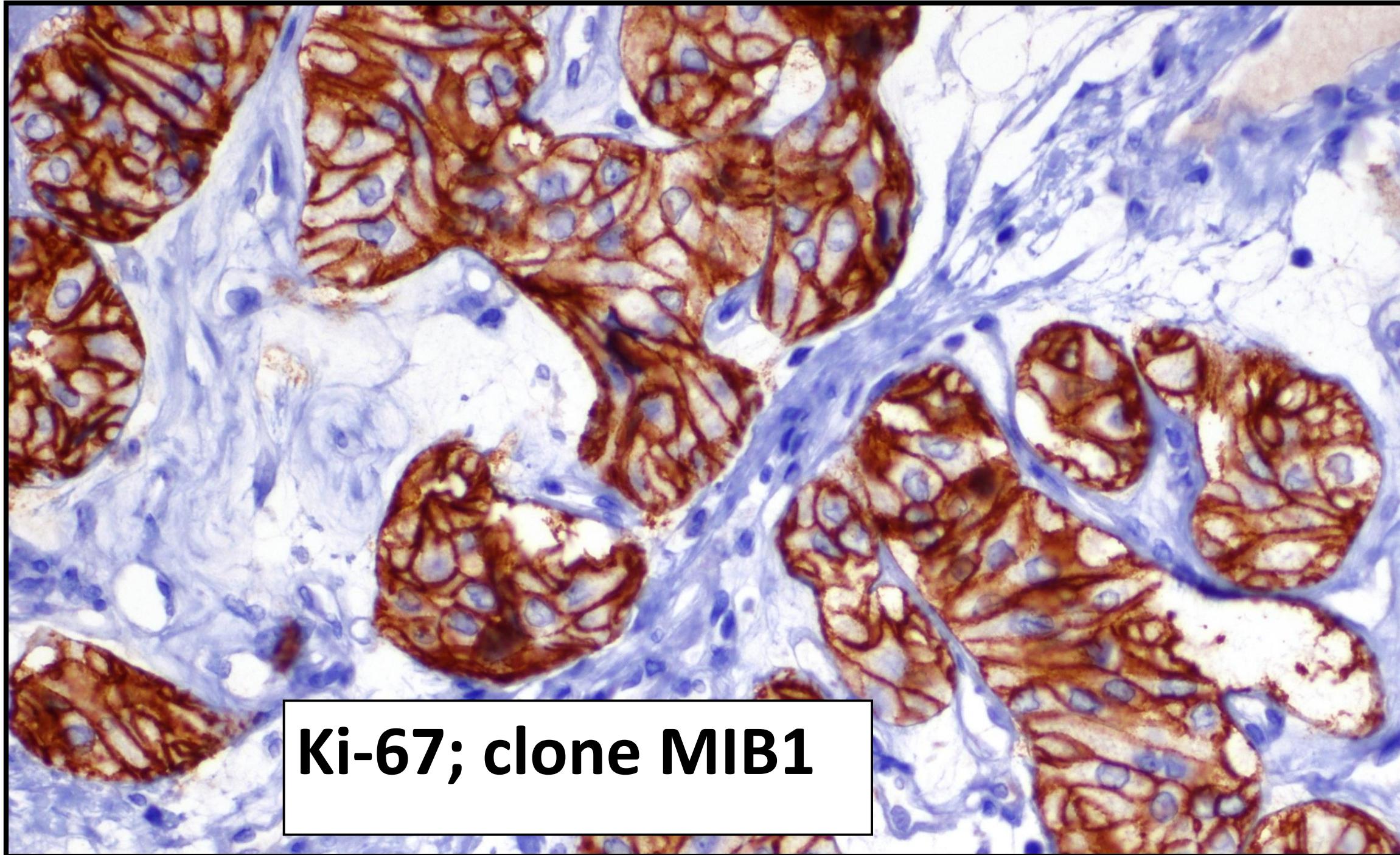


Ki-67; clone MIB1





Ki-67; clone MIB1



Ki-67; clone MIB1

IHC

POSITIVE	NEGATIVE
<ul style="list-style-type: none">• TTF1• PAX8• Thyroglobulin• Ki-67 (clone MIB-1) – memb.• CD56 • Bcl2• Cyclin D1	<ul style="list-style-type: none">• CK19• Chromogranin A

?

HYALINIZING TRABECULAR TUMOUR

M-8336/1

- Lobectomia glandulae thyreoideae lateris dextri:
- HYALINIZING TRABECULAR TUMOUR (M-8336/1)
- *vzácny tumor derivovaný z folikulárnych buniek (v naprostej väčšine prípadov benígne biologické správanie)*
- *imunohistochemicky TTF1+, thyroglobulin+, PAX8+, CD56+, CK19-, membránózne farbenie Ki-67*
- *v okolí nevýrazná lymfocytová tyreoidítida*
- *bez iných podstatnejších histologických zmien*

Hyalinähnliche collagene Kugeln als Produkte epithelialer Zellen in malignen Strumen

Published: December 1905

Volume 182, pages 374–406, (1905) [Cite this article](#)



[Virchows Archiv für pathologische
Anatomie und Physiologie und für](#)

Rahel Zipkin

•Pathologischen Institut der Universität Bern, Berr, Schwliz

1905

Hyalinizing Trabecular Adenoma of the Thyroid Gland

Carney, J Aidan M.D., Ph.D., F.R.C.P.I.; Ryan, John M.B., B.Ch., F.R.C.S.I.; Goellner, John R. M.D.

[Author Information](#)

The American Journal of Surgical Pathology 11(8):p 583-591, August 1987.

BUY



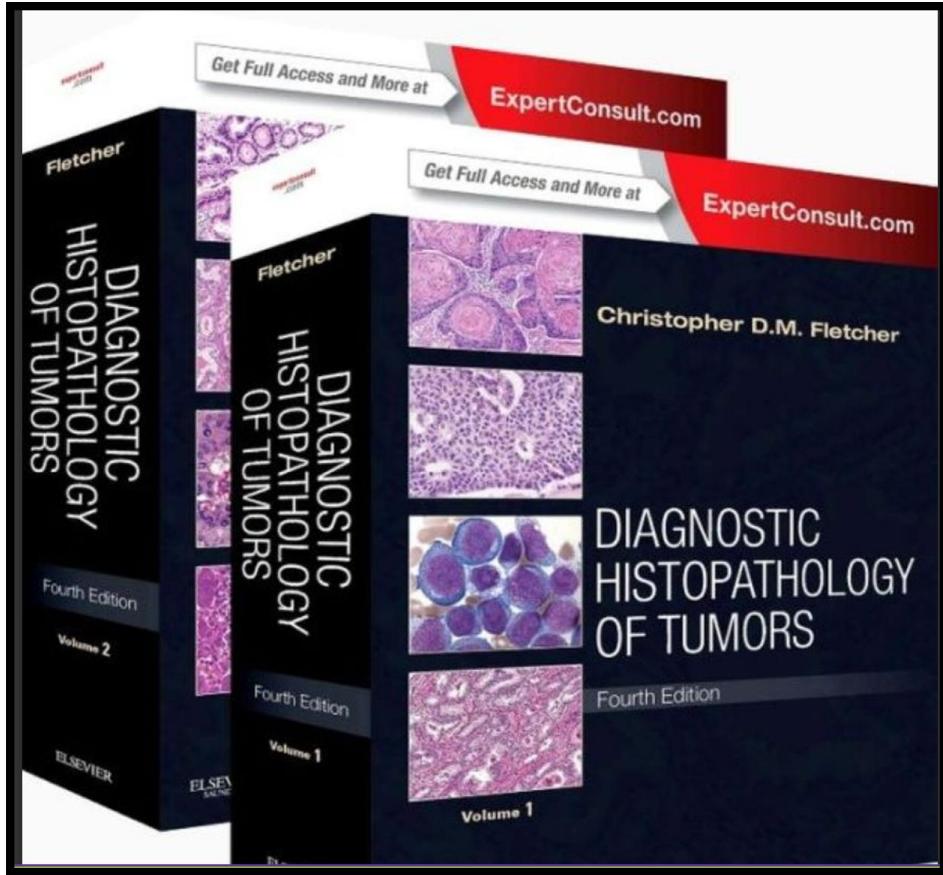
Carney

Department of Pathology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

1987

cases, adenoma (two cases), paraganglioma (one case), and indeterminate (three cases). None of the tumors recurred or metastasized (mean follow-up, 10 years). Grossly, the neoplasms measured

- 1904 - **Rahel Zipkin** – 1.členka/žena Nemeckej Spol. Patológov
- „*became the first female member of the German Pathological Society [Deutsche Pathologische Gesellschaft (DPG), today known as the Deutsche Gesellschaft für Pathologie (DGP)].*“
- **J. Aiden Carney** was also impressed by her research:
- ‘who, a century previously, had provided a meticulous description of the type of hyalin-producing thyroid tumour that I thought my colleagues and I had introduced in 1987’.

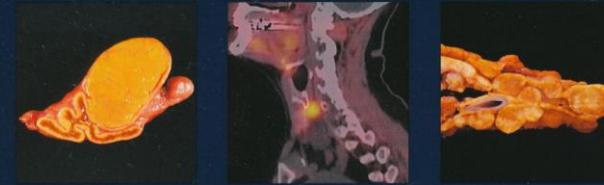


Christopher D. M. Fletcher (13 March 1958 - 28 July 2024)
In Memoriam

Déjà vu

WHO Classification of Tumours of Endocrine Organs

Edited by Ricardo V. Lloyd, Robert Y. Osamura, Günter Klöppel, Juan Rosai



WHO Classification of Tumours of Endocrine Organs

Edited by

Ricardo V. Lloyd
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Günter Klöppel
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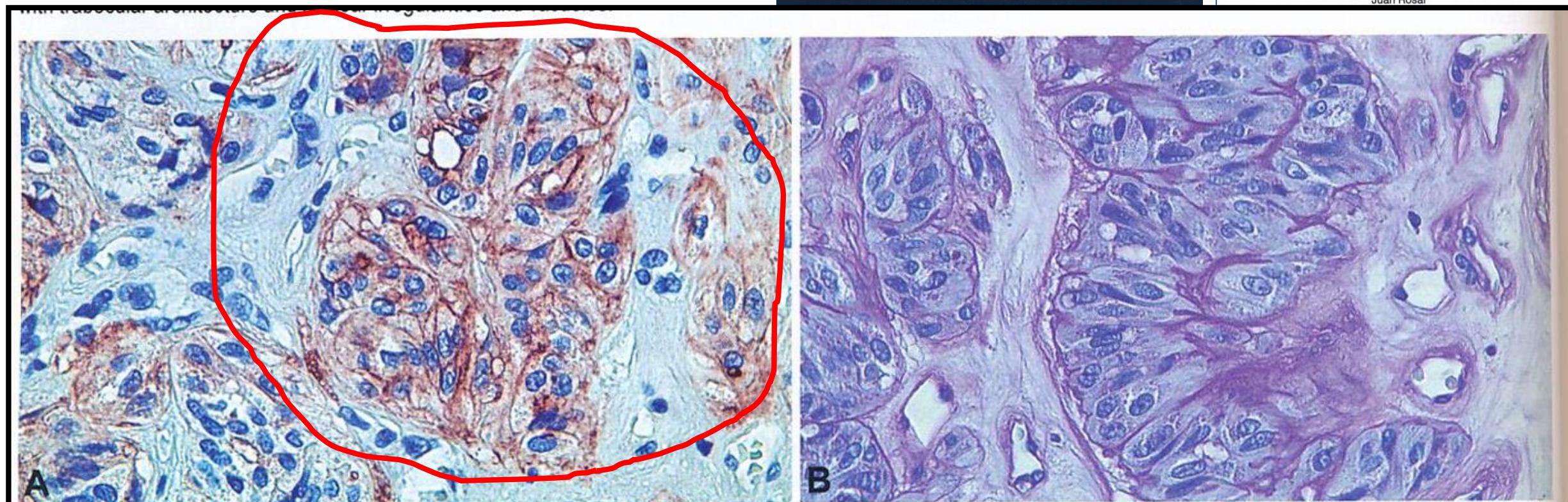
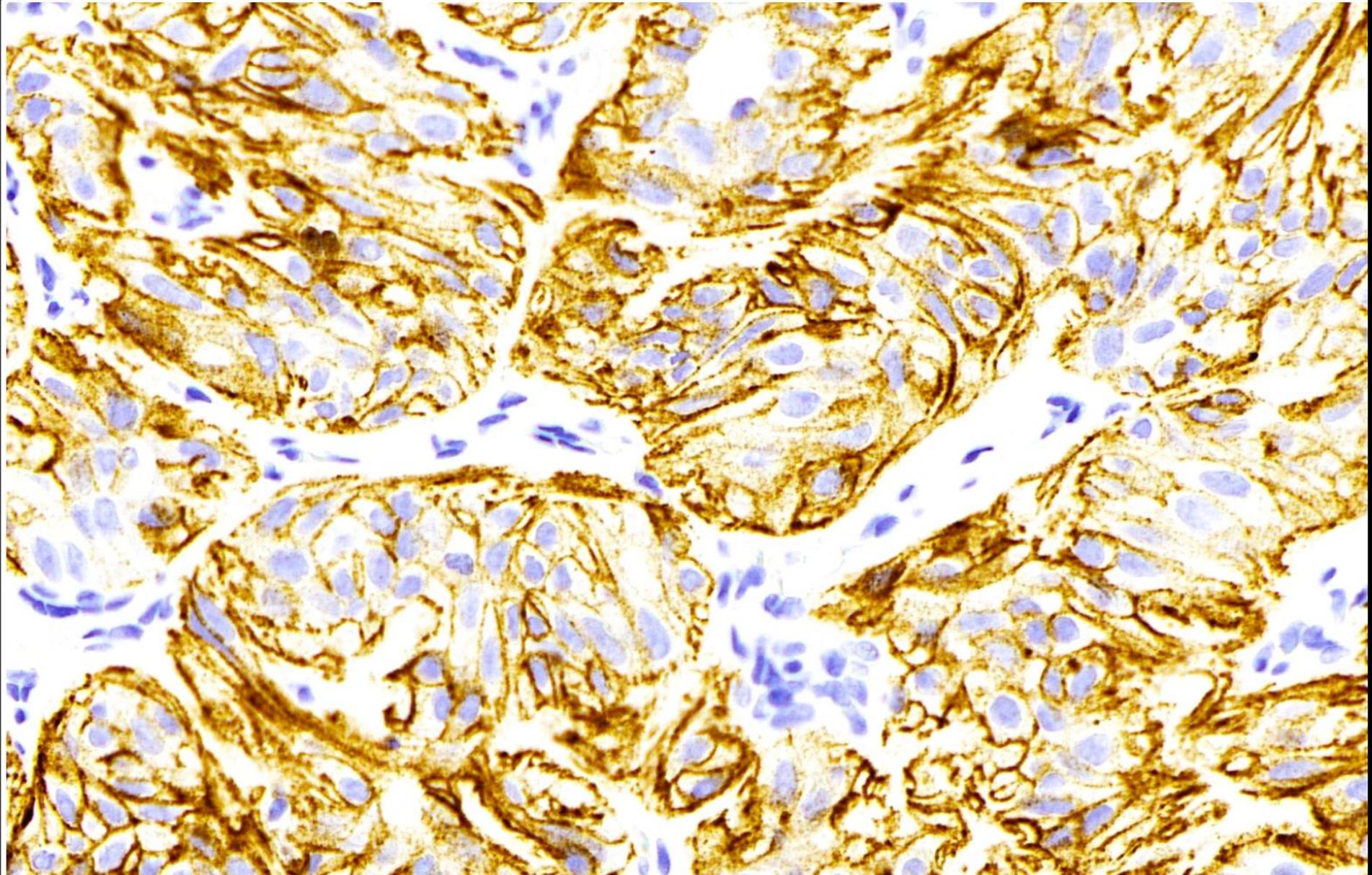


Fig. 2.15 Hyalinizing trabecular tumour. **A** Ki-67 immunostaining using the MIB1 monoclonal antibody shows strong, distinctive cell membrane reactivity. **B** Intratrabecular hyaline material that gives a positive periodic acid–Schiff (PAS) reaction is present in association with tumour cells.

• Stromal calcifications are frequent.



Membrane staining with Ki67 (MIB1 antibody).
Contributed by Virginia A. Livolsi, M.D.

HTT – definícia WHO 2017

- Novotvar derivovaný z folikulárnych bb
- Tvorený veľkými trabelulami elongovaných, alebo polygonálnych bb
- Zmiešaný s variabilným množstvom intratrabekulárneho a intertrabekulárneho hyalínneho materiálu

HTT - klinika

- Ž>M
- 50 rokov (21-79)
- 1 popísaný malígy nyprípad (28-r M, 3cm, kapsulárna penetrácia)
- Vpravo>vľavo (mierna predilekcia)
- USG ako follicular adenoma / follicular variant PTC (solídny, oválny/okrúhly, ohraničený, hypoechogénny)
- Scintigrafia: studený uzol
- Veľkosť 0,5 – 7,5cm (polovica <3cm)

HTT - mikroskopia

- Ohraničený, bez kapsulárnej / vaskulárnej invázie
- Široké trabekuly (zriedkavejšie malé hniezda) – lobulárny/Zellballen vzhľad
- Bb veľké, stredné (11% prímes malých bb), polygonálne, elongované
- Cytoplazma eozinofílná, jemne granulárna, miestami svetlá
- Niekedy perinukleárne „yellow bodies“ (?)
- Jadrá vezikulárne a okrúhle, zárezy, vakuoly, irregularity
- V trabelulách hyalínny amorfny materiál (Congo Red negat, PASD pozit) – basal membrane-like
- 43% - kalcium v trabekulách (laminated, aj psammomatoid)

HTT - IHC

- TTF1 + a thyroglobulin+ / calcitonin-
- CK19, HBME1, galectin3 – parciálne pozit (0-50%)
- Hyalínny materiál collagen IV pozit
- Membránová expresia Ki-67 – clone MIB-1 (pri izbovej teplote)

HTT - cytológia

- Často
- Zárezy
- Pseudoinkúzie
- Nepravidelné hranice
- V Bethesda system často kategória IV – VI
- Dg kľúč: hyalínovitá amyloid-like materiál, málo kohezívne skupiny bb šíriace sa z hyalínovitého centra, objemná cytoplazma, absencia papíl a kalcifikátov

HTT – genetický profil

- Rearanže RET/PTC1 v ½ prípadov HTT – pôvodne sugestívne pre asociáciu s PTC
- Absencia RAS a BRAF mutácií

A red rectangular box with a black border, tilted diagonally upwards from the bottom-left. The text "WHO 2017" is written in white, bold, sans-serif font inside the box.

HTT – prognostické a prediktívne faktory

- WHO – 119 prípadov
- 1x plúcna MTS ..(?)
- Zriedka (?) MTS do LU

GL/S Rearrangements in Thyroid Nodules: A Key to Preoperative Diagnosis of Hyalinizing Trabecular Tumor

Marina N. Nikiforova, MD  ; Yuri E. Nikiforov, MD, PhD  ; and N. Paul Ohori, MD 

Hyalinizing trabecular tumor (HTT) is a rare thyroid neoplasm with peculiar morphologic features that overlap with those of papillary thyroid carcinoma (PTC). Specifically, the presence of enlarged oval nuclei, nuclear grooves, and intranuclear pseudooinclusions makes precise cytopathologic diagnosis challenging. If the cytopathologic diagnosis is suspicious for malignancy (Bethesda V) or is malignant (Bethesda VI), a total thyroidectomy, which would be considered an overtreatment, may follow. The recent discovery of the strong association between *GL/S* fusions and HTT sheds light on its pathogenesis and offers a pathway for its presurgical identification. Although the number of cases analyzed is limited, the recent landmark study shows that *GL/S* fusions are highly specific for HTT and that lobectomy is the likely appropriate surgical treatment, because these neoplasms, which lack invasion, are benign. For overall success, cytopathologic recognition of the subtle features is important to avoid false-positive diagnoses and directing potential HTT cases toward indeterminate cytopathologic diagnoses, which would trigger further molecular testing. Additional studies are needed to determine whether a malignant counterpart of *GL/S* fusion-positive HTT exists and if more conservative approaches may be taken. *Cancer Cytopathol* 2019;127:560-566. © 2019 American Cancer Society.

KEY WORDS: fusion; *GL/S3*; hyalinizing trabecular tumor (HTT); next-generation sequencing; *PAX-GL/S3*.

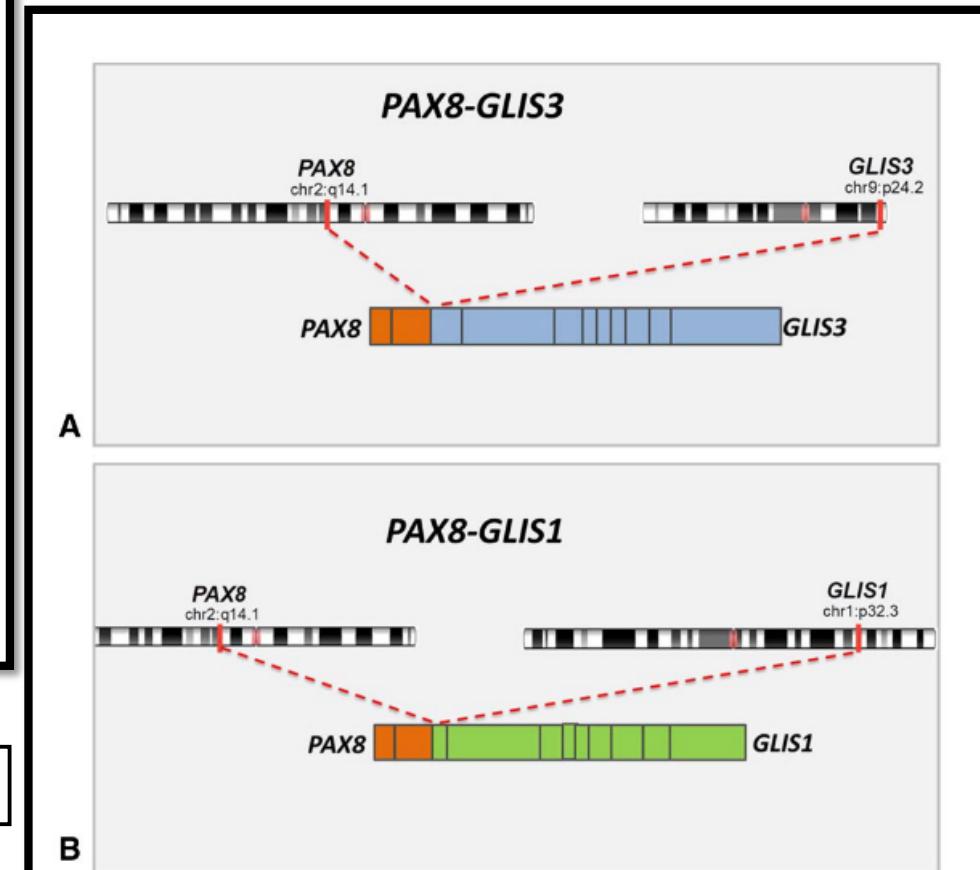


Figure 1. The structure of *PAX8-GLIS3* and *PAX8-GLIS1* fusions are identified in samples of hyalinizing trabecular tumors. (A, B) These are schematic representation of the *PAX8*, *GLIS3*, and *GLIS1* genes and the *PAX8-GLIS3* and *PAX8-GLIS1* fusion transcripts.

- **GLIS FUSION IS A GENETIC HALLMARK OF HTT**

- **GLIS-rearranged HTT** carried *no other genetic alterations*, including BRAF andRAS point mutations, RET/PTC, or other gene fusions characteristic of PTC and all of its variants
- **none of the 220 PTCs** tested by Nikiforova et al and **none of the 484 PTCs** in theTCGA study²⁰ *were positive for PAX8-GLIS3 fusion*
- sharply different genetic profiles between HTT and PTC, arguing strongly against biological similarity between these 2 tumor types
- reclassify HTT as “GLIS-rearranged hyalinizing trabecular adenoma.”

PathologyOutlines.com 2023

Remembering Professor Virginia LiVolsi, MD (1943-2024)

March 11, 2024



Virginia A. LiVolsi, MD

1943 - 2024



and Laboratory Medicine, has passed away. Dr. LiVolsi was a unique and dearly beloved colleague, friend and mentor.

- **Essential features**
- Trabecular architecture
- Yellow bodies
- MIB1 membrane staining of tumor cells
- *GLIS* translocation is unique to this thyroid tumor
- ICD-O: **8336/0** - hyalinizing trabecular adenoma

Ki-67 a jeho klony

- MIB-1
- SP6
- MM1
- 30-9
- 8D5
- 1297A

The screenshot shows a journal article page from the website of Modern Pathology. The header features the journal's name in large, bold, black letters. Below the header is a navigation bar with two dropdown menus: "Explore content" and "About the journal". A green horizontal bar separates the header from the main content area. In the main area, the URL "nature > modern pathology > articles > article" is displayed above the article title. The title itself is prominently displayed in large, bold, black text. Below the title, the authors' names are listed in blue, underlined text. The entire screenshot is enclosed in a thick black border.

MODERN PATHOLOGY

Explore content ▾ About the journal ▾

nature > modern pathology > articles > article

Article | Published: 03 February 2021

A new tool for technical standardization of the Ki67 immunohistochemical assay

Thazin Nwe Aung, Balazs Acs, Jonathan Warrell, Yalai Bai, Patricia Gaule, Sandra Martinez-Morilla, Ioannis Vathiotis, Saba Shafi, Myrto Moutafi, Mark Gerstein, Benjamin Freiberg, Regan Fulton & David L. Rimm

Membránová expresia MIB-1 ako diagnostický znak LTT

- Hirokawa , 2000

ORIGINAL ARTICLES

Cell Membrane and Cytoplasmic Staining for MIB-1 in Hyalinizing Trabecular Adenoma of the Thyroid Gland

Hirokawa, Mitsuyoshi M.D., Ph.D.; Carney, J. Aidan M.D., Ph.D.

[Author Information](#) 

The American Journal of Surgical Pathology 24(4):p 575-578, April 2000.

BUY

Abstract

The monoclonal MIB-1 antibody reacts with the nuclei of cells in the late G1, S, G2, and M phases of the cell cycle. Previously, we found two cases of hyalinizing trabecular adenoma that showed cell membrane and cytoplasmic immunopositivity for the antibody. The purpose of this investigation was to confirm this exceptional reactive pattern of MIB-1 in hyalinizing trabecular adenoma. For the study, we collected 13 additional hyalinizing trabecular adenomas and stained a total of 15 tumors using MIB-1 antibody. Ten cases of papillary thyroid carcinoma were studied similarly. All hyalinizing trabecular adenomas showed strong positivity for the antibody in 90% or more of the tumor cells, localized especially to the cell membrane and also to the cytoplasm. There was no cell membrane

2018

Membránová expresia Ki-67

> Endocr J. 2018 Feb 26;65(2):239-244. doi: 10.1507/endocrj.EJ17-0413. Epub 2017 Dec 2.

Re-evaluation of MIB-1 immunostaining for diagnosing hyalinizing trabecular tumour of the thyroid: semi-automated techniques with manual antigen retrieval are more accurate than fully automated techniques

Nami Takada ¹, Mitsuyoshi Hirokawa ², Chiho Ohbayashi ³, Takeshi Nishikawa ³, Tomoo Itoh ⁴, Naoko Imagawa ⁴, Tetsunari Oyama ⁵, Tadashi Handa ⁵, Tadashi Hasegawa ⁶, Shintaro Sugita ⁶, Akiko Murata ⁷, Akira Miyauchi ⁸

Revitalizáciu antigénu robiť manuálne

HTT uchovať ako externú pozitívnu kontrolu

2024

| RESEARCH ARTICLE OPEN ACCESS

Comparison of MIB-1-Specific Membrane Staining in Hyalinising Trabecular Tumor Using Mainstream Automated Immunohistochemical Staining Platforms

Bo Hong¹  | Yanfei Xu² | Yufei Xiao³ | Xiaoyan Yu¹

¹Department of Pathology, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, People's Republic of China

²Department of Pathology, Quzhou Second People's Hospital, Quzhou, Zhejiang, People's Republic of China | ³Department of Clinical Laboratory, The Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, People's Republic of China

Correspondence: Bo Hong (hongbo_sahzu@zju.edu.cn)

Received: 11 June 2024 | **Revised:** 19 September 2024 | **Accepted:** 23 September 2024

3.3 | Comparison of the Diagnostic Value of Various Automated Staining Platforms Under Different Conditions

None of the automated staining methods produced false positives, whereas certain instances of false negatives were detected (Figure 2). The receiver operating characteristic (ROC)

diagnostic criterion. Clinically, the presence of mKi-67 staining can assist in confirming HTT when combined with other histopathological features [8].

Considering that automated immunohistochemical platforms not only save the required workforce but also provide a standardized staining process [22], an increasing number of laboratories have stopped utilizing manual stainin

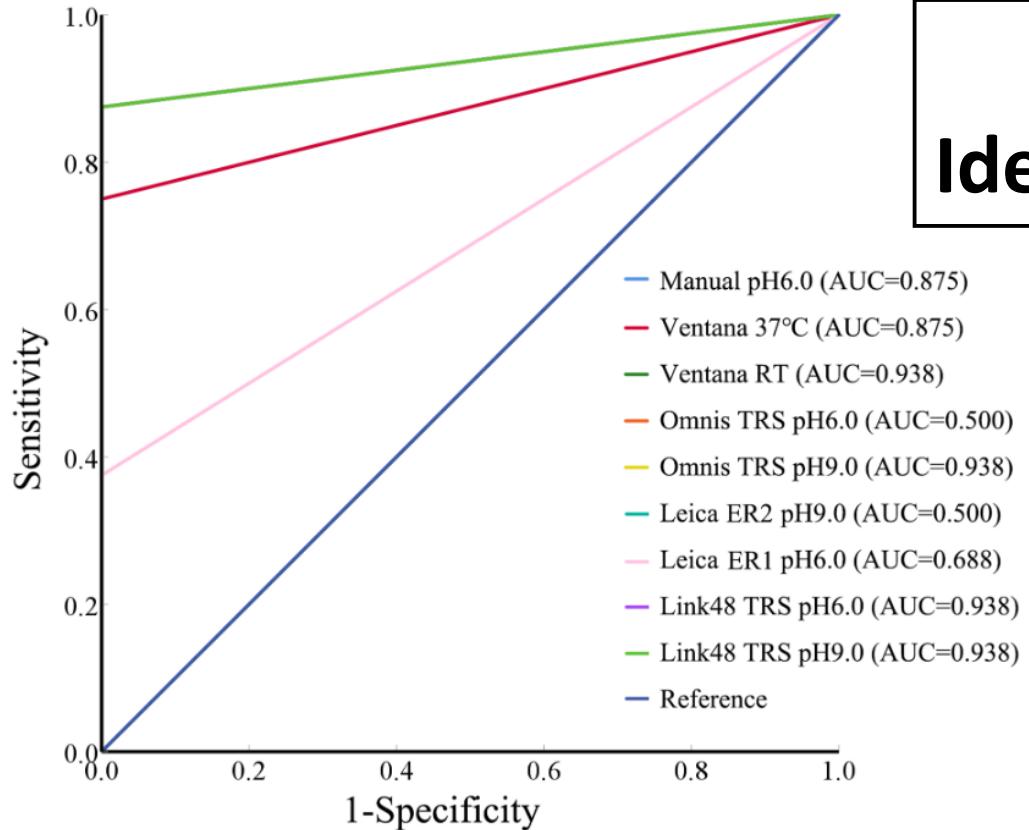


FIGURE 3 | Receiver Operating Characteristic (ROC) curves of the various immunohistochemical staining platforms.

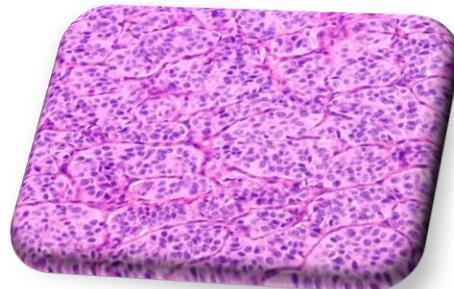
ZÁVER
Ide to aj cez immunostainery...

Iné tumory s popísanou membránovou expresiou MIB-1

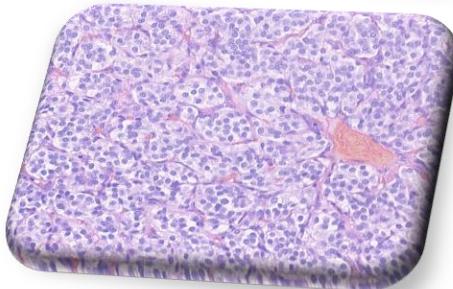
- karcinóm prsníka
- salivárny pleomorfný adenóm
- plúcny sclerozujúci haemangióm
- renálny onkocytóm
- sarkomatoidný pleurálny mezotelióm
- **Bez klinickej signifikancie a/alebo reproducibility**

Diferenciálna diagnostika

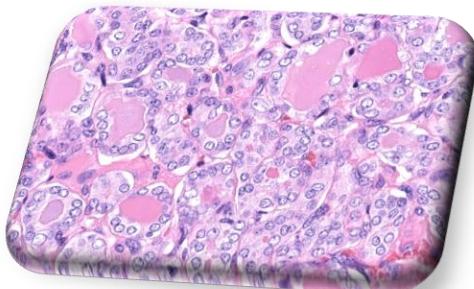
- Medullary thyroid CA



- Paraganglioma



- Papillary thyroid CA



TTF1
PAX8
TGB
AE1/AE3
CK19
CD56
Chromogranin
Synaptophysin
mCEA
Calcitonin
GATA3
S100
Ki-67 clone MIB-1

ZÁVER

HTT/HTA

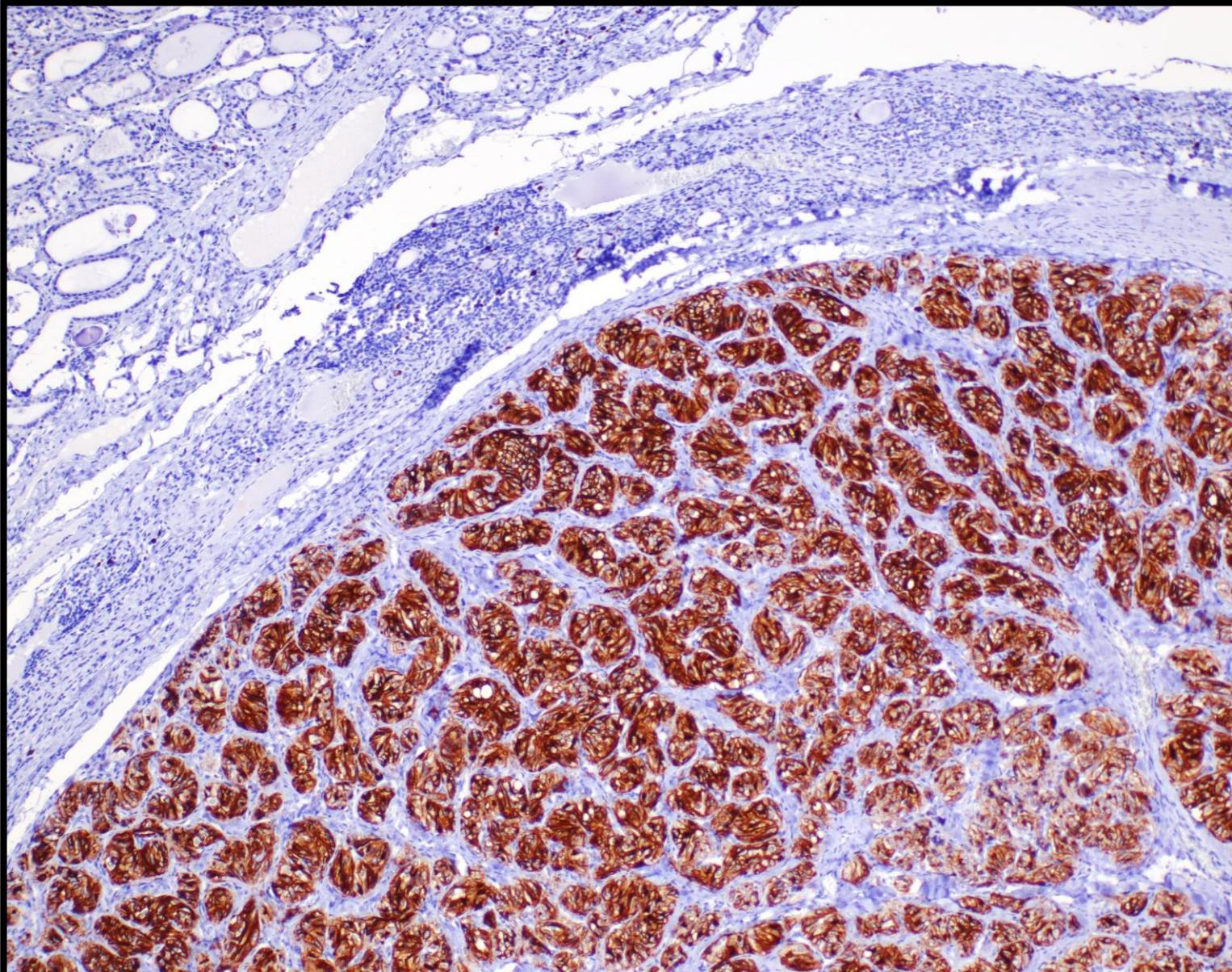
Vzácny tumor

Benígy tumor

Dobre definovaný tumor

Raz uvidíte

Navždy si zapamätáte



ĎAKUJEM ZA POZORNOSŤ

