Southbay October 2023

Disclosures
October 2, 2023

Dr. Brooke Howitt has disclosed a financial relationship as a consultant for Tempus. The planners have determined that this relationship is not relevant to the clinical diagnostic case being presented. The remaining activity planners and faculty listed below have no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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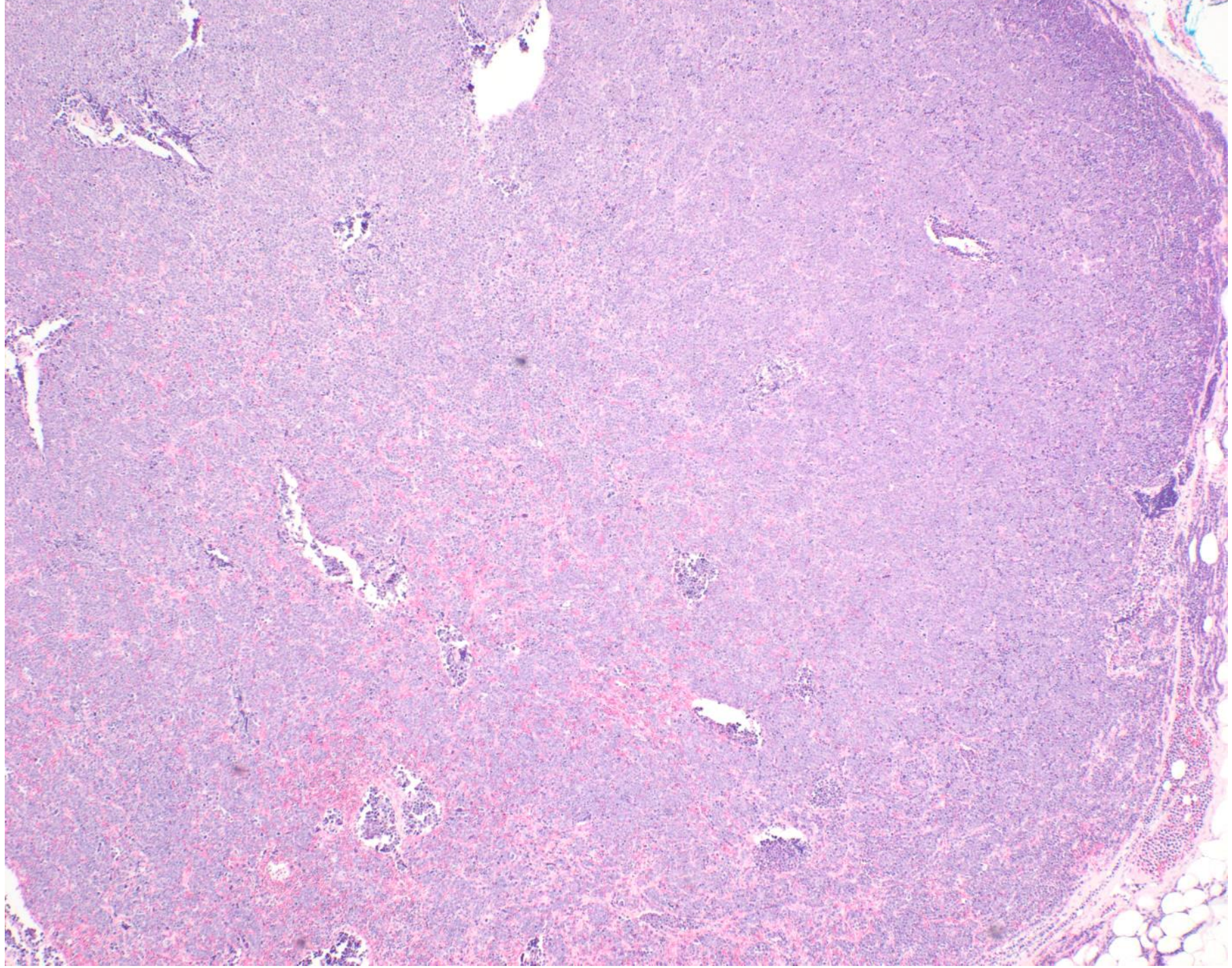
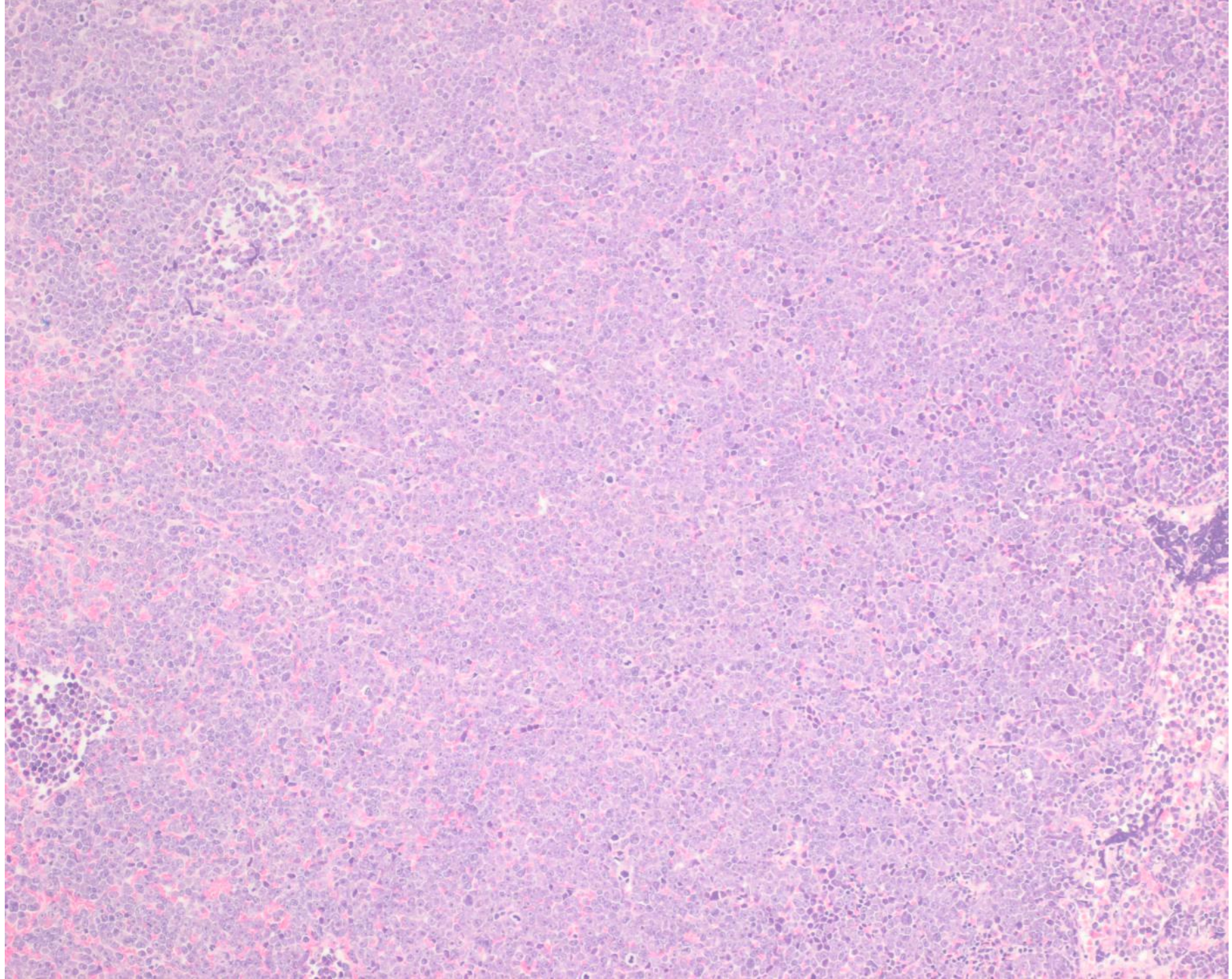
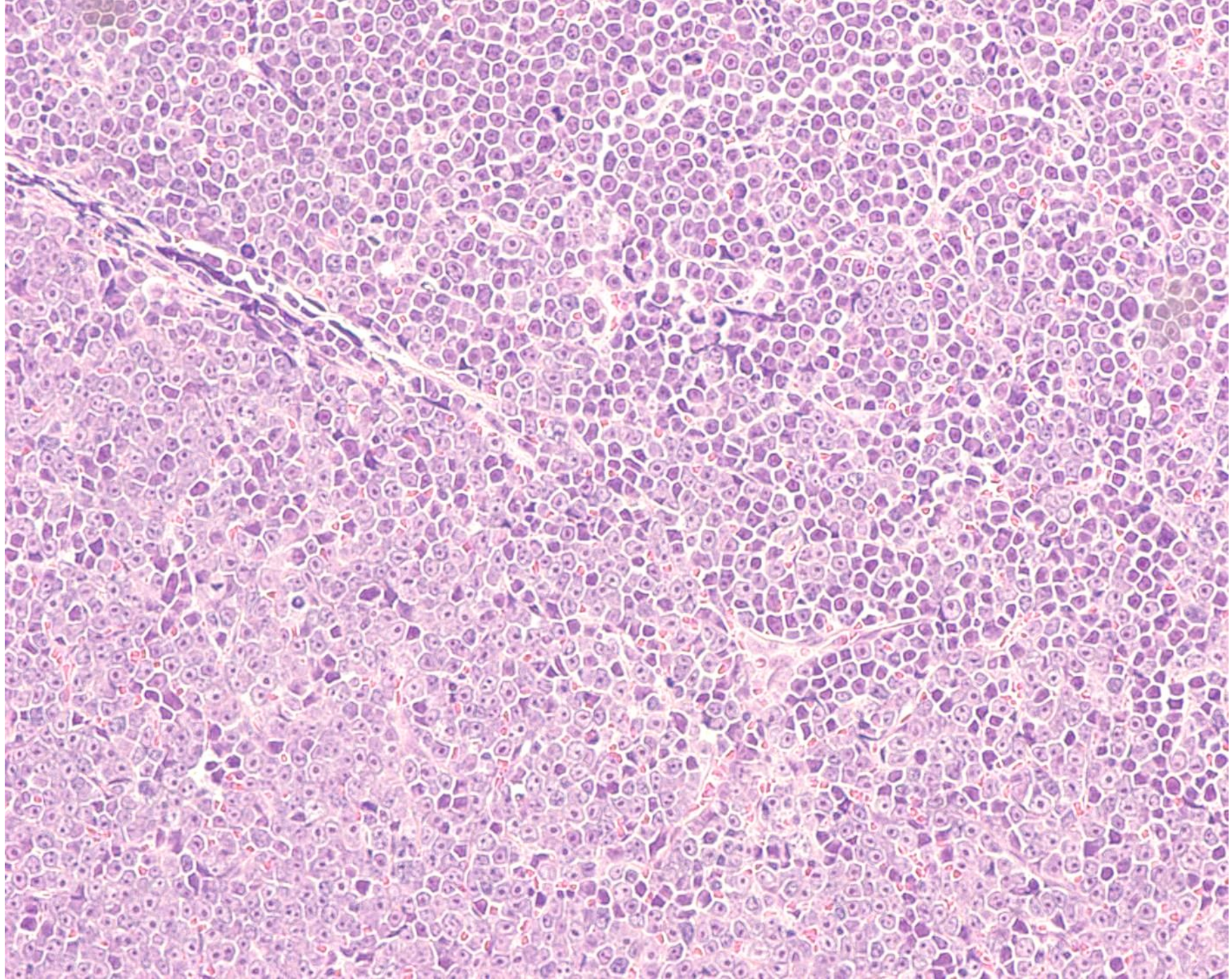
23-1001

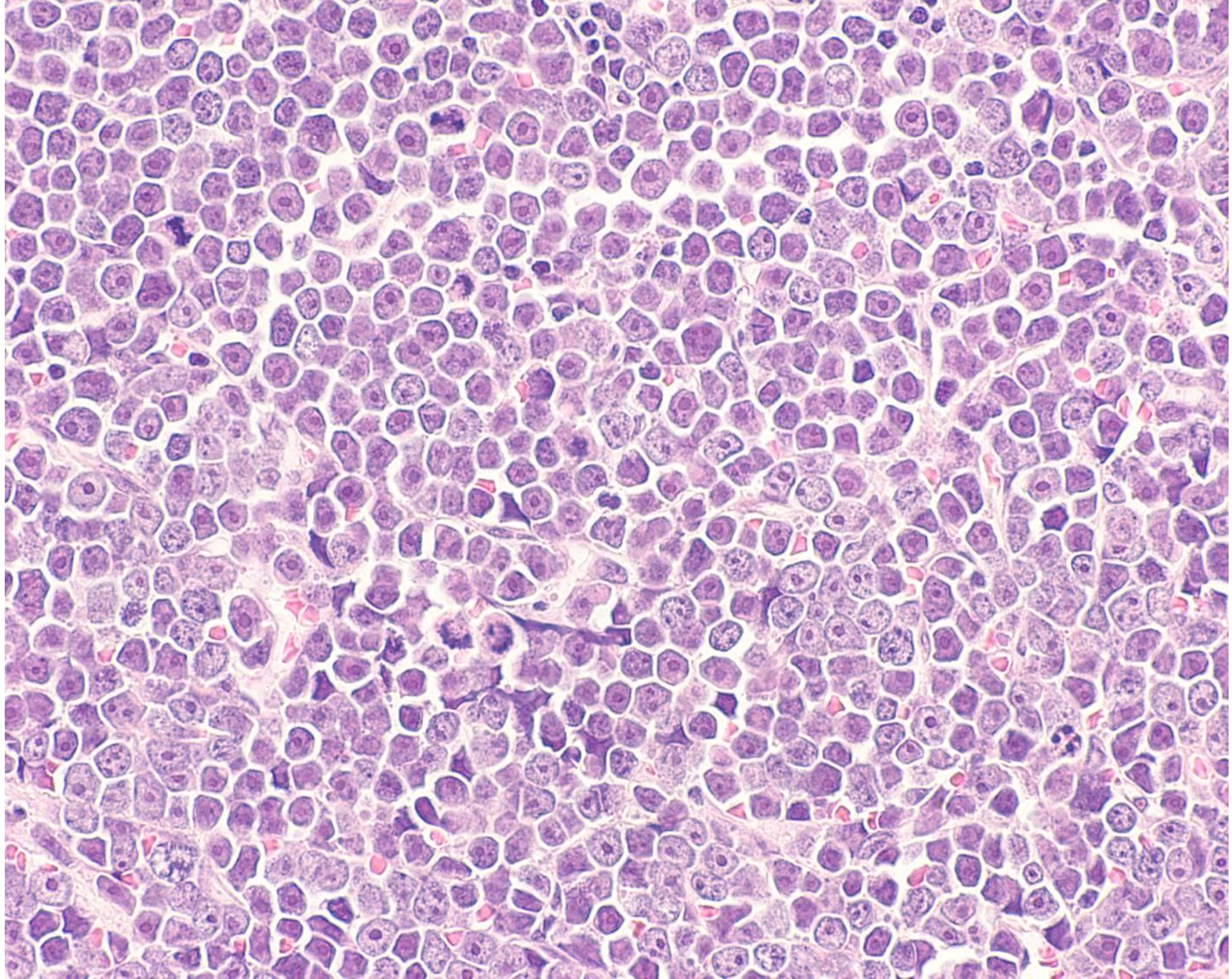
Andrew Xiao and Malary Mani; SFVA

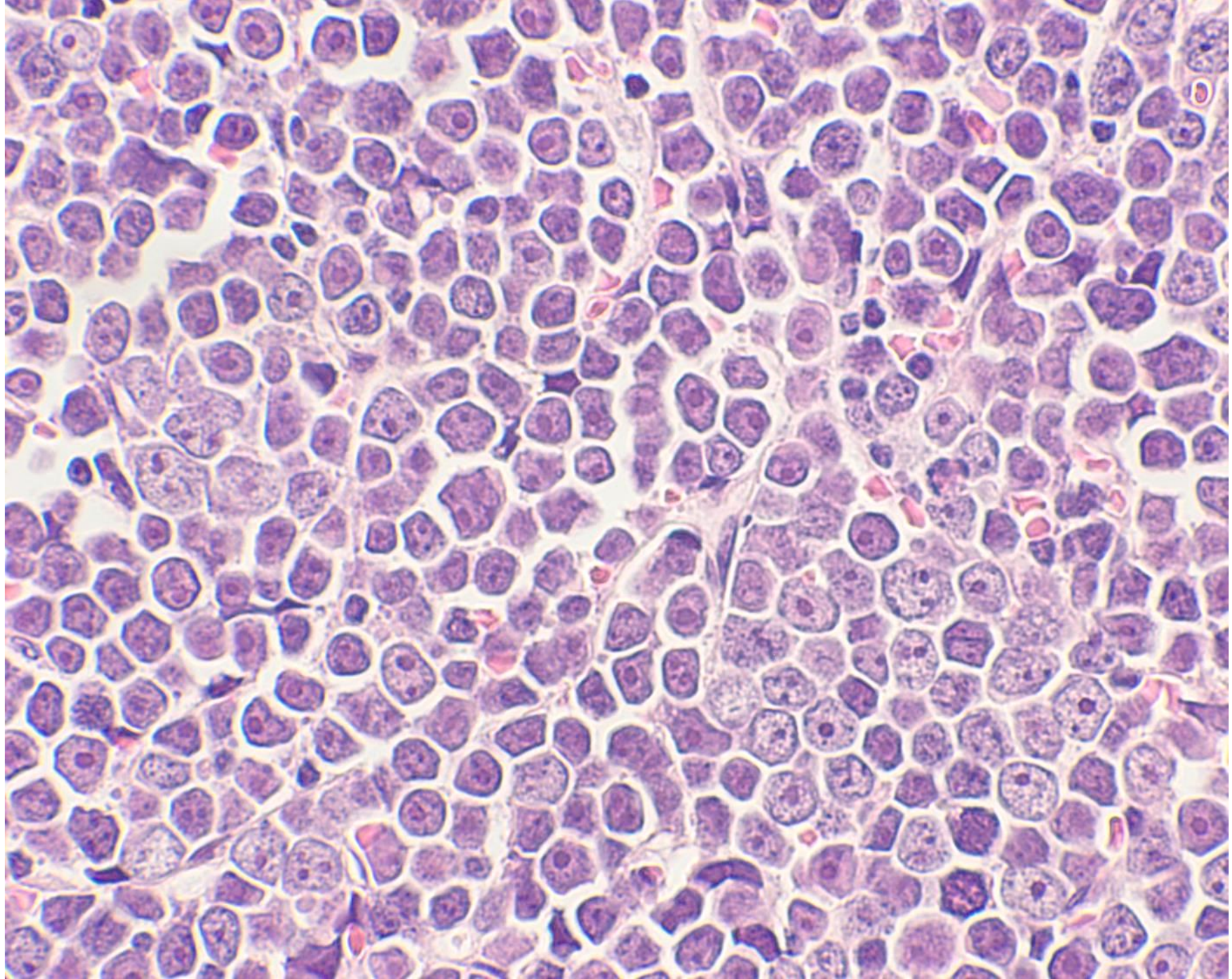
72-year-old male with retroperitoneal mass & enlarged supraclavicular lymph nodes. He undergoes lymph node excision.

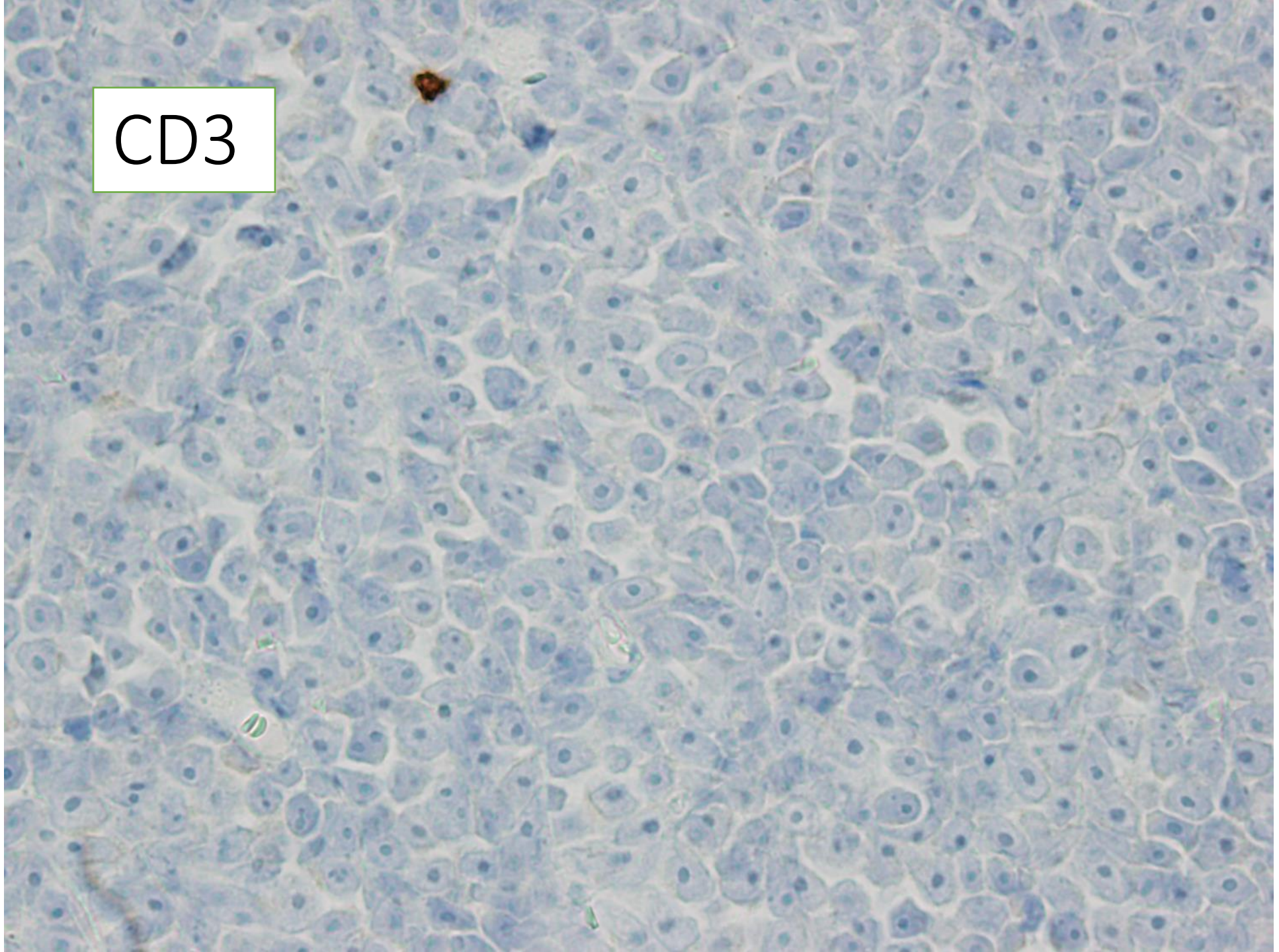


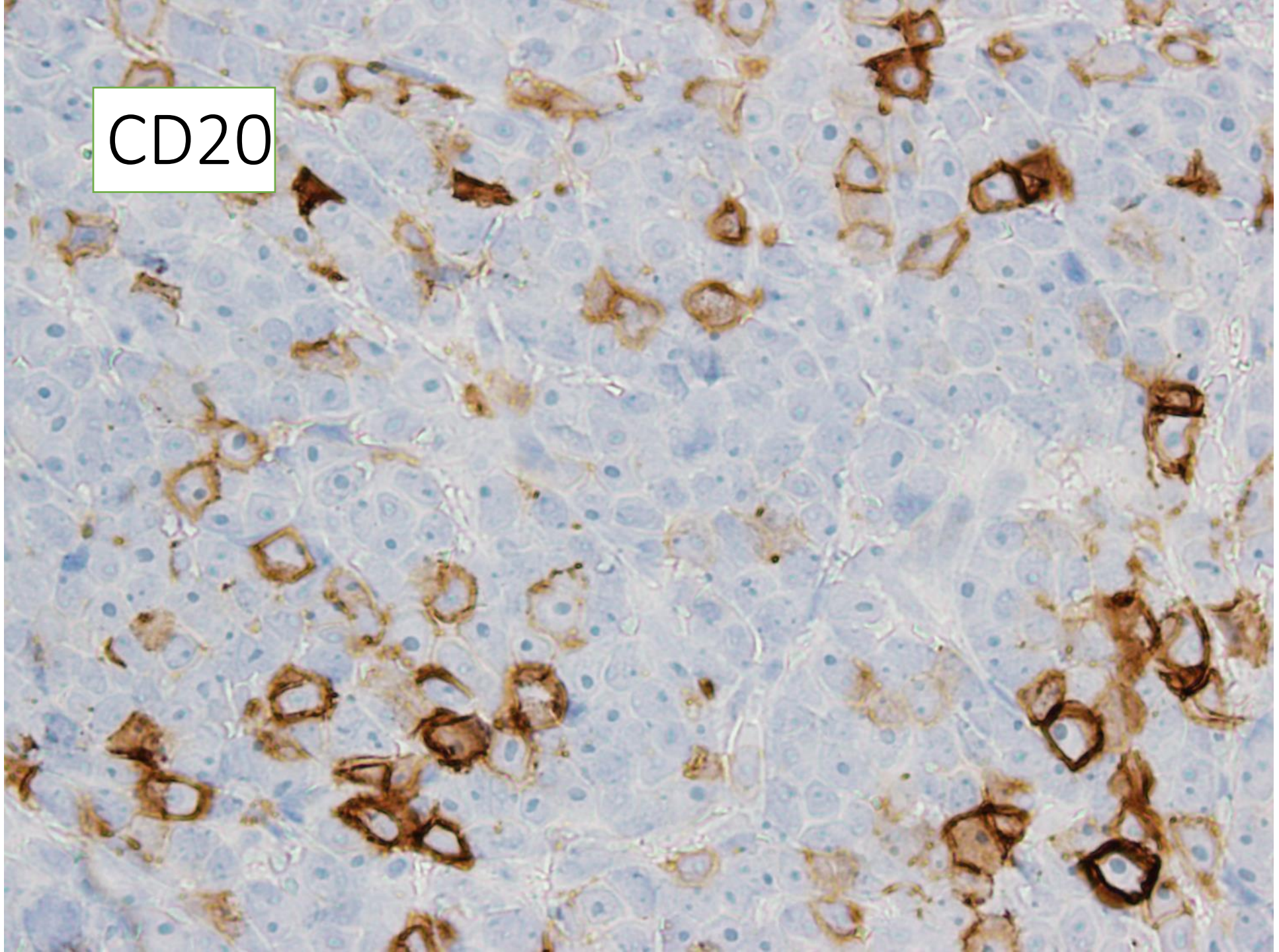









CD3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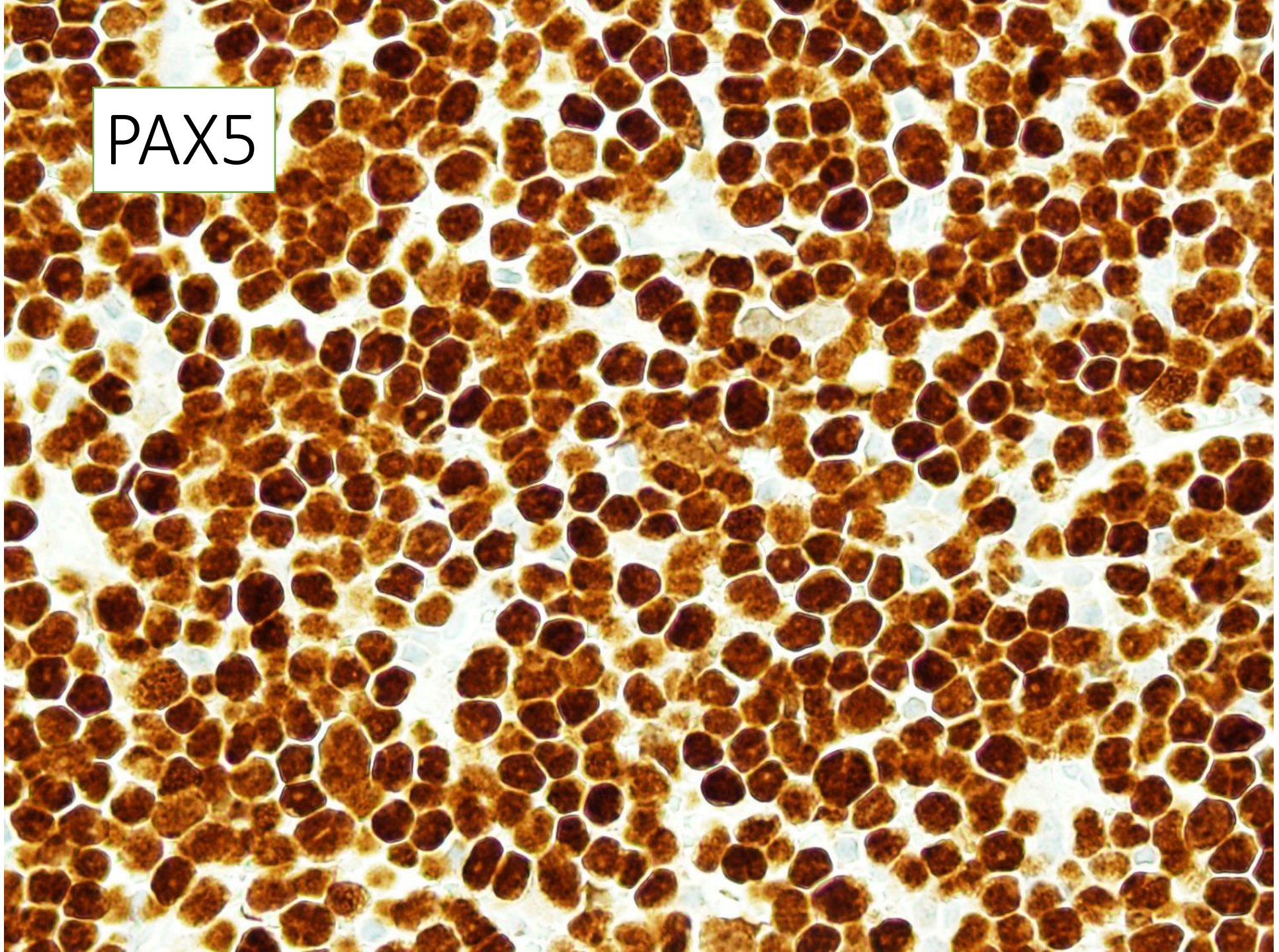
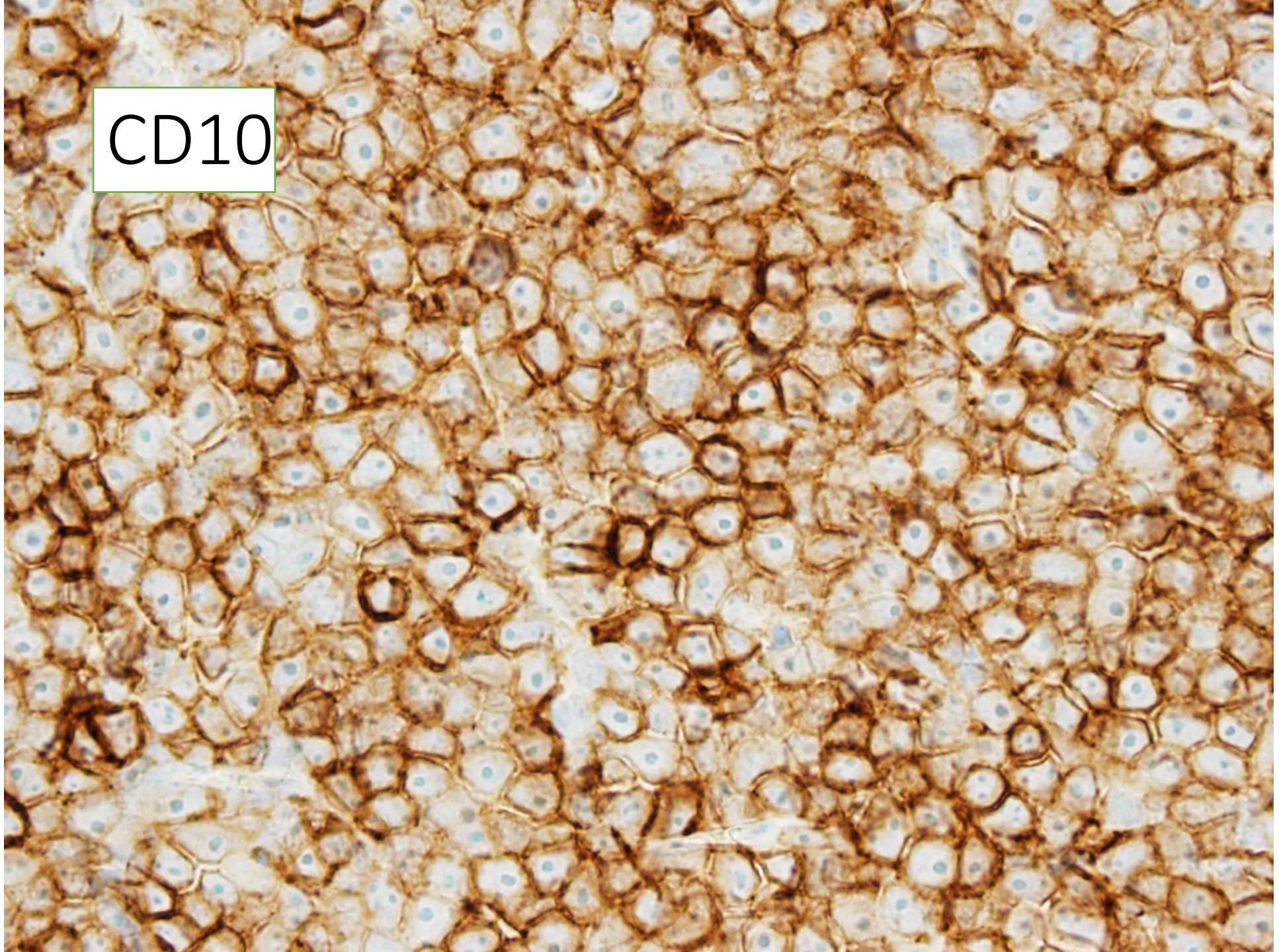
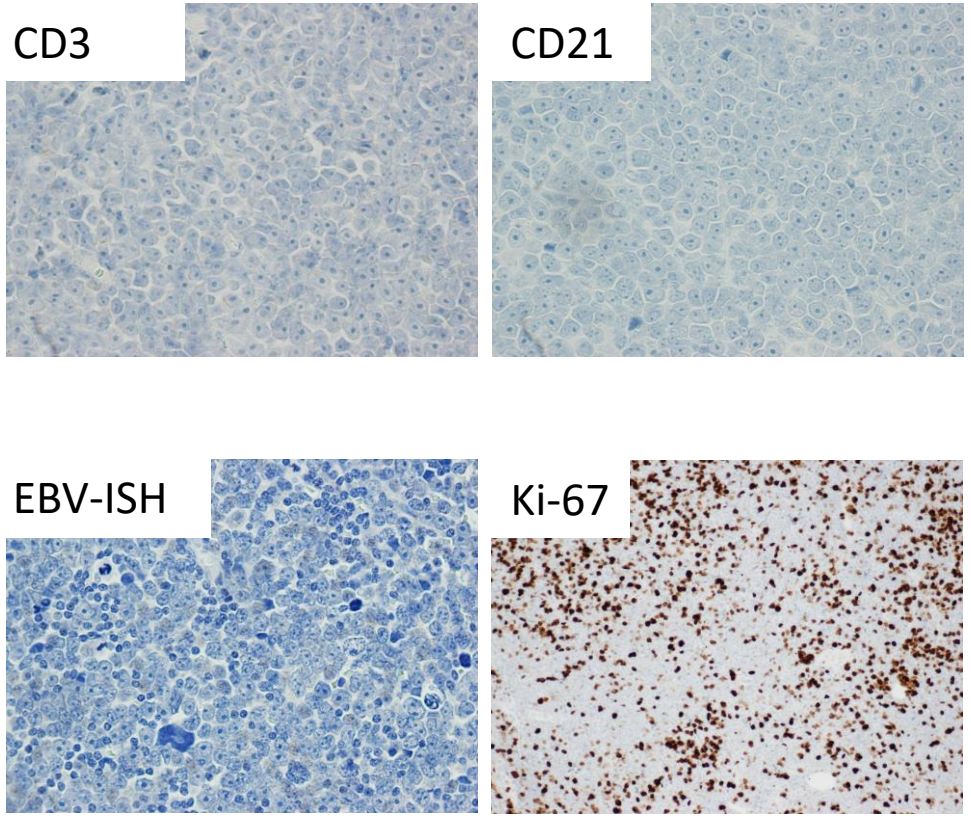

PAX5


CD10

DIAGNOSIS?

IHC Results

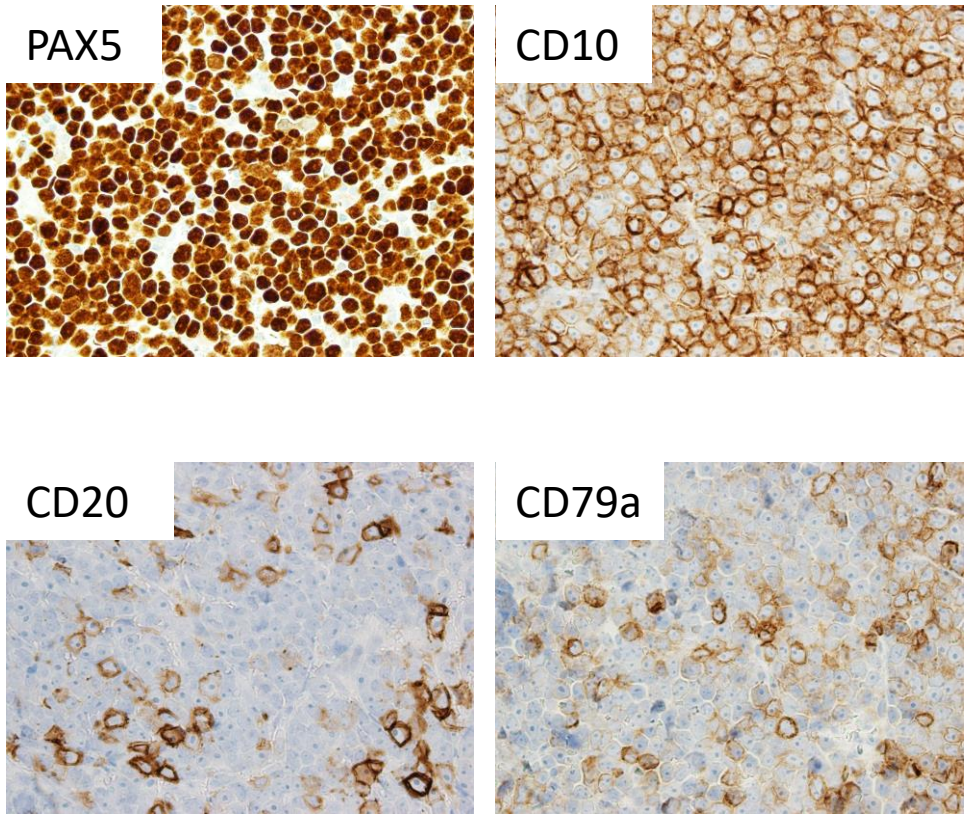
- Negative:
  - CD3
  - CD5
  - CD21
  - CD23
  - CD30
  - Cyclin D1
  - EBV-ISH
- Ki-67: overall 60% (high)
- p53 overexpressed



IHC Results

Positive:

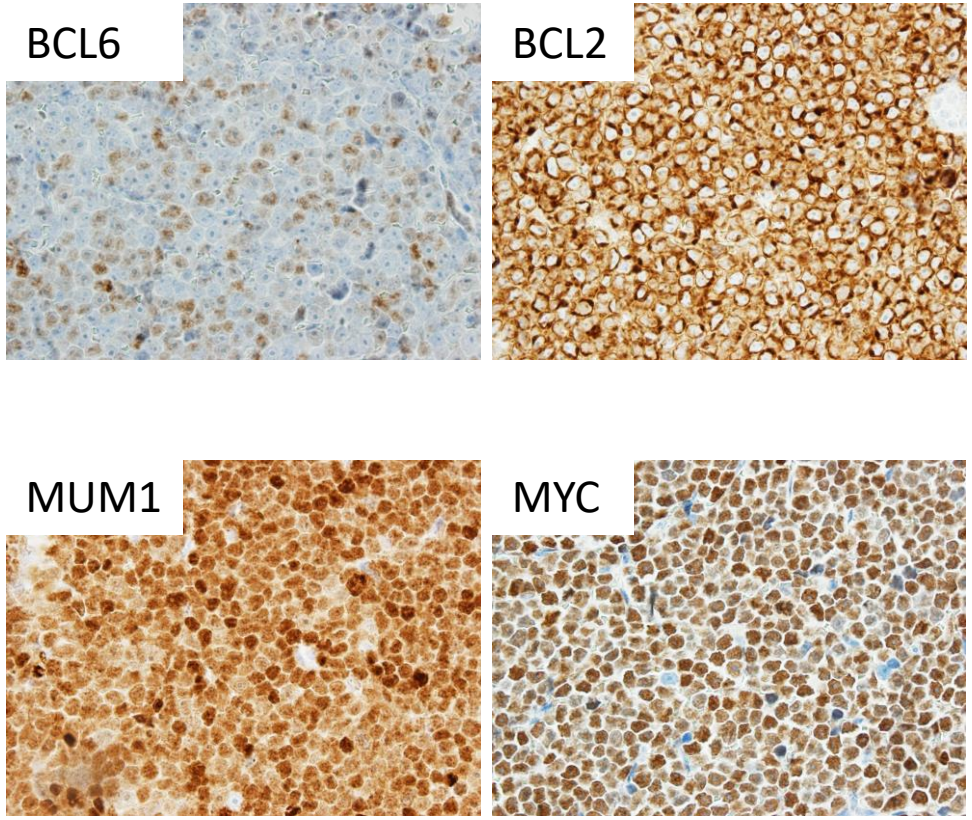
- PAX5
- CD20 (partial positive)
- CD79a (patchy weak)
- CD10 (strong diffuse)



IHC Results

Positive:

- BCL6 (subset weak)
- MUM1 (strong diffuse)
- BCL2 (strong and diffuse)
- MYC (strong diffuse)



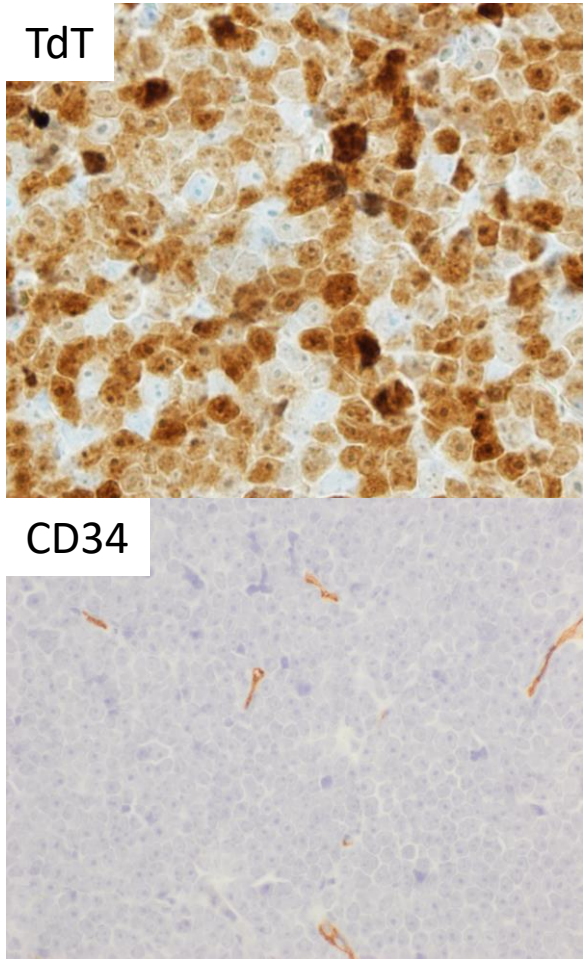
IHC Results

Positive:

- TdT (diffuse)

Negative:

- CD34



Differential Diagnosis

- Large B-cell lymphomas
- B-lymphoblastic leukemias/lymphomas
- Burkitt lymphoma

Flow Cytometry Results

- Interpretation: Abnormal CD10+ large B-cell population with surface kappa light chain restriction (80% of analyzed cells)
  - There is an abnormal dim CD45+ large B-cell population that is positive for CD19, CD10, surface kappa, CD38, and TdT, and partial positive for CD20 and CD22 (20%).
  - They are negative for MPO, cCD3, and CD79a.

FISH Results

- MYC and IGH::BCL2 gene rearrangement (double hit lymphoma)
- Copy gain of BCL6 gene, negative for rearrangement

Diagnosis

- Final Diagnosis: MYC/BCL2 rearranged high grade B-cell lymphoma with TdT expression

- WHO classification diagnostic pitfall:
  B lymphoblastic leukemia/lymphoma (BALL)

WHO Classification Diagnostic Pitfall

- Issues supporting different classification:
  - Lack other features of immaturity (e.g. CD34)
  - Mature B-cell neoplasm features (e.g. positive expression of surface Ig light chain)
  - Aggressive clinical course (median survival 5 months)
  - Molecularly closely related to mature B-cell lymphomas
    - Recurrent gene mutations/alterations in chromatin modifiers (TNFRSF14, CREBBP, ARID1A, KMT2D, EZH2)
    - BLC2 rearrangement

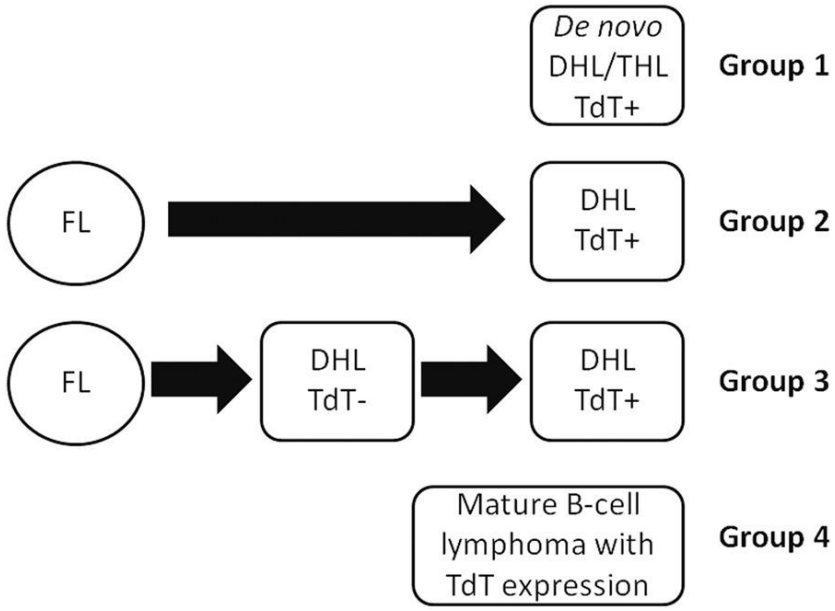
- Hamdan H, Luu L, Opsahl M, et al. Genomic profile of $TdT^{positive}$ MYC/BCL2 rearranged high-grade B-cell lymphoma supporting its diagnosis as mature aggressive lymphoma. *Cytometry B Clin Cytom*. 2022;102(6):448-450. doi:10.1002/cyto.b.22092
- Bhavsar S, Liu YC, Gibson SE, Moore EM, Swerdlow SH. Mutational Landscape of TdT+ Large B-cell Lymphomas Supports Their Distinction From B-lymphoblastic Neoplasms: A Multiparameter Study of a Rare and Aggressive Entity. *Am J Surg Pathol*. 2022;46(1):71-82. doi:10.1097/PAS.0000000000001750

Documented Developments

~2% of DLBCL / HGBL - MYC / BCL2 have been reported to contain TdT-positive B-cells

1. De novo HG B-cell lymphoma with double/triple hit genetics and TdT expression

2. FL followed by TdT-positive aggressive B-cell lymphoma

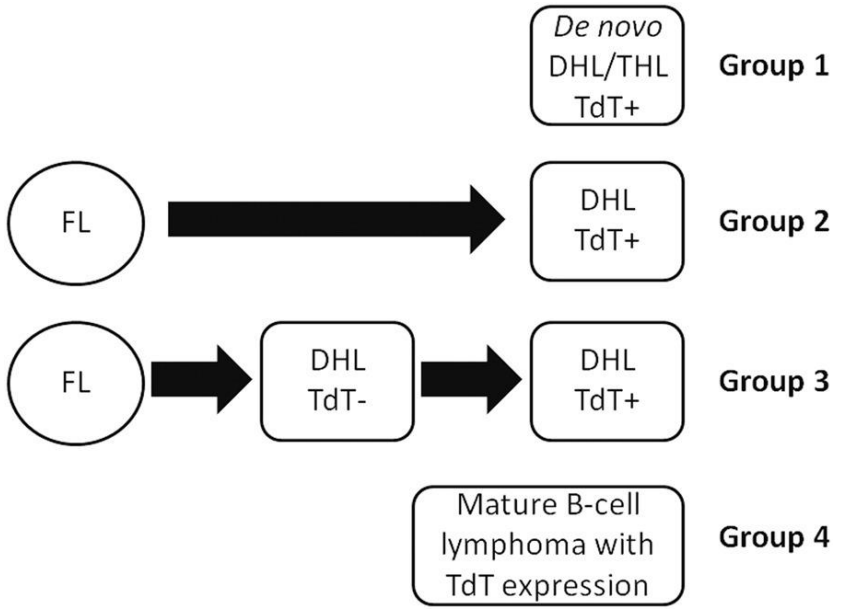


1. Tooze R, Rosenwald A, Leoncini L, Macon WR. Diffuse large B-cell lymphoma / high grade B-cell lymphoma with MYC and BCL2 rearrangements. World Health Organization. Accessed September 18, 2023. https://tumourclassification.iarc.who.int/chaptercontent/63/161.
2. Ok CY, Medeiros LJ, Thakral B, et al. High-grade B-cell lymphomas with TdT expression: a diagnostic and classification dilemma. *Mod Pathol*. 2019;32(1):48-58. doi:10.1038/s41379-018-0112-9

Documented Developments

3. FL followed by TdT-negative aggressive B-cell lymphoma followed by relapse and acquired TdT expression

4. Mature B-cell lymphomas that acquire TdT expression at relapse



Ok CY, Medeiros LJ, Thakral B, et al. High-grade B-cell lymphomas with TdT expression: a diagnostic and classification dilemma. *Mod Pathol*. 2019;32(1):48-58. doi:10.1038/s41379-018-0112-9

Take Home Points

- Multiparameter approach, including phenotypic and genomic studies
- Recognize TdT-positive high-grade B-cell lymphoma as a distinct group of aggressive mature B-cell lymphomas

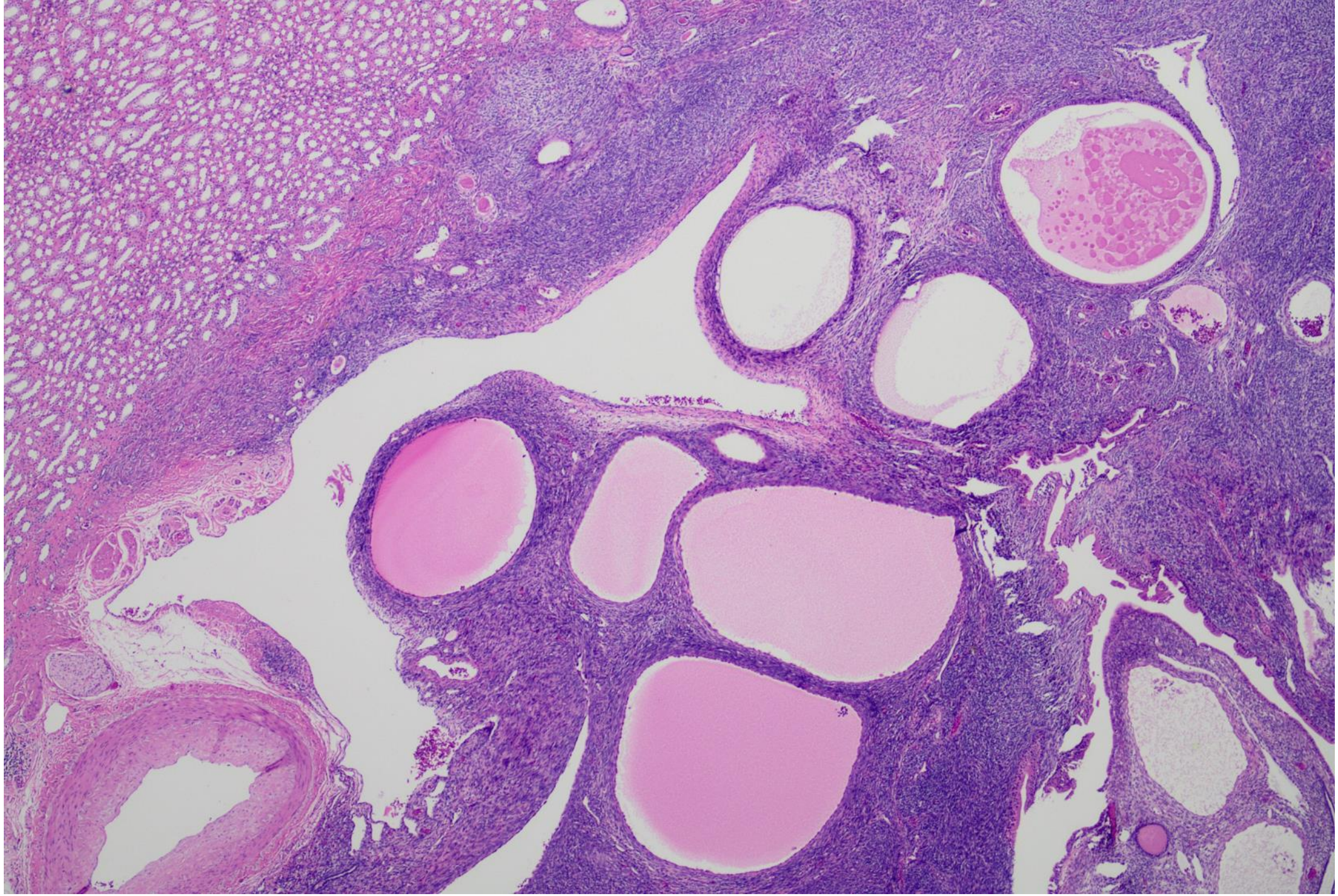
Questions?

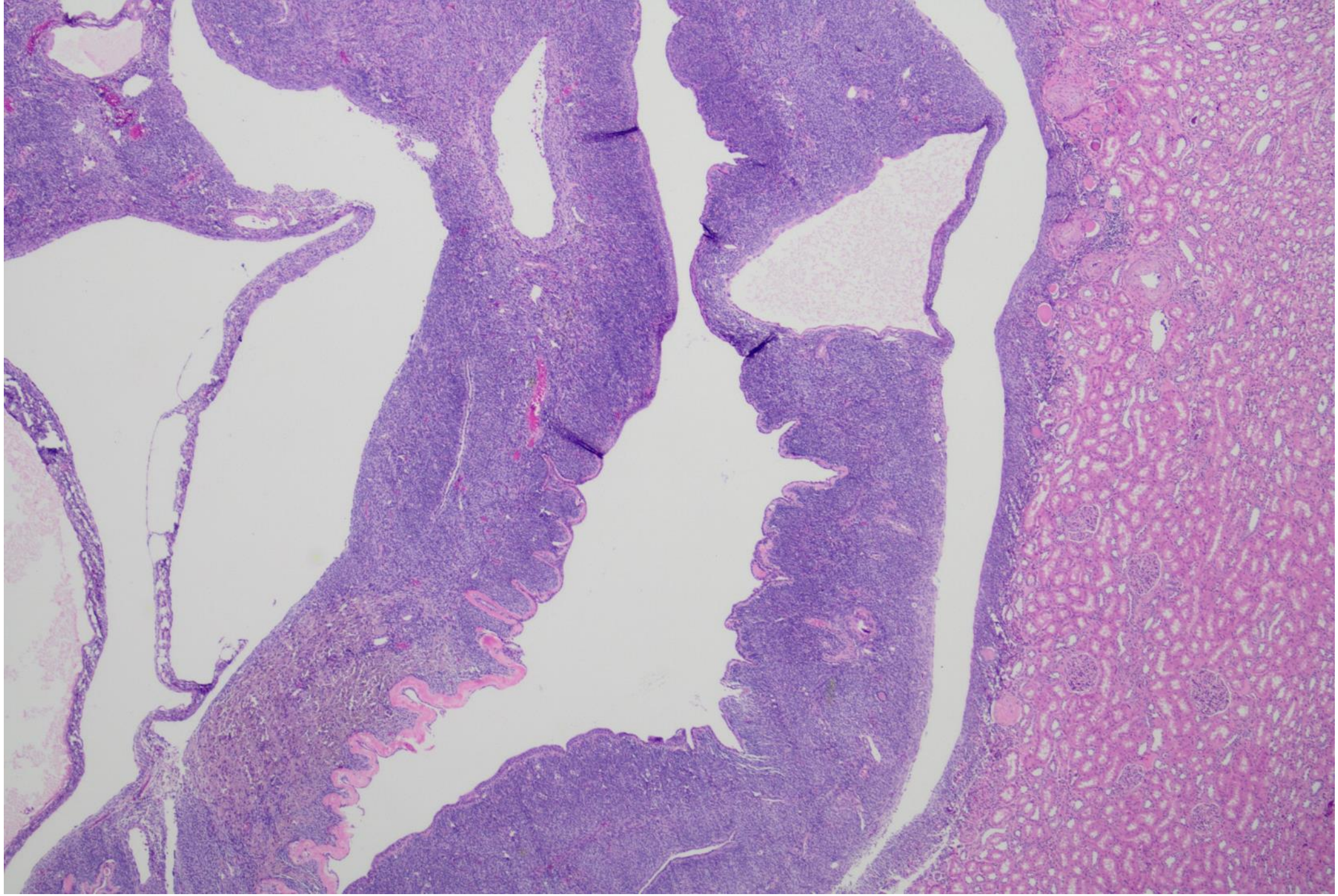
- Thank you Dr. Malary Mani!

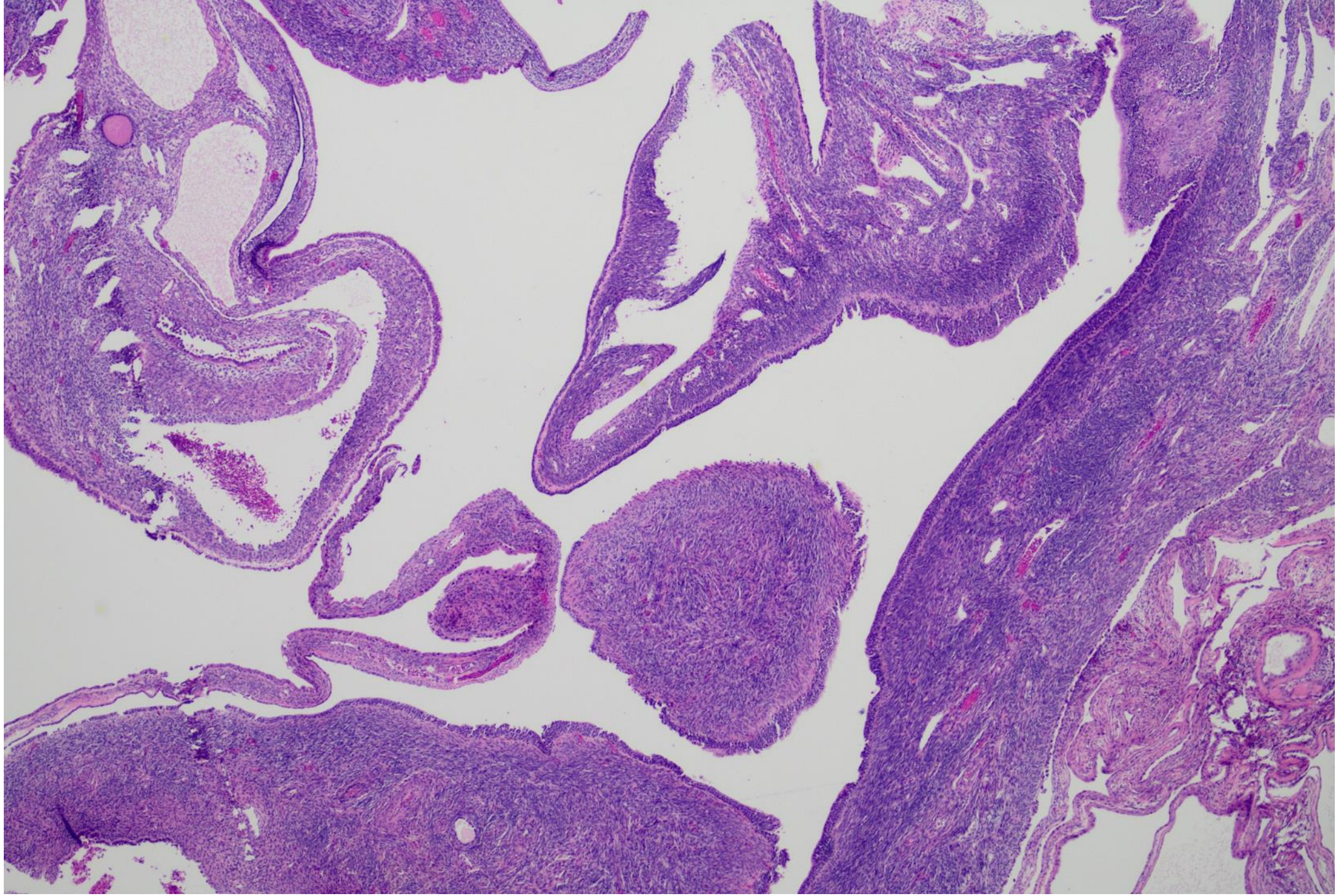
23-1002

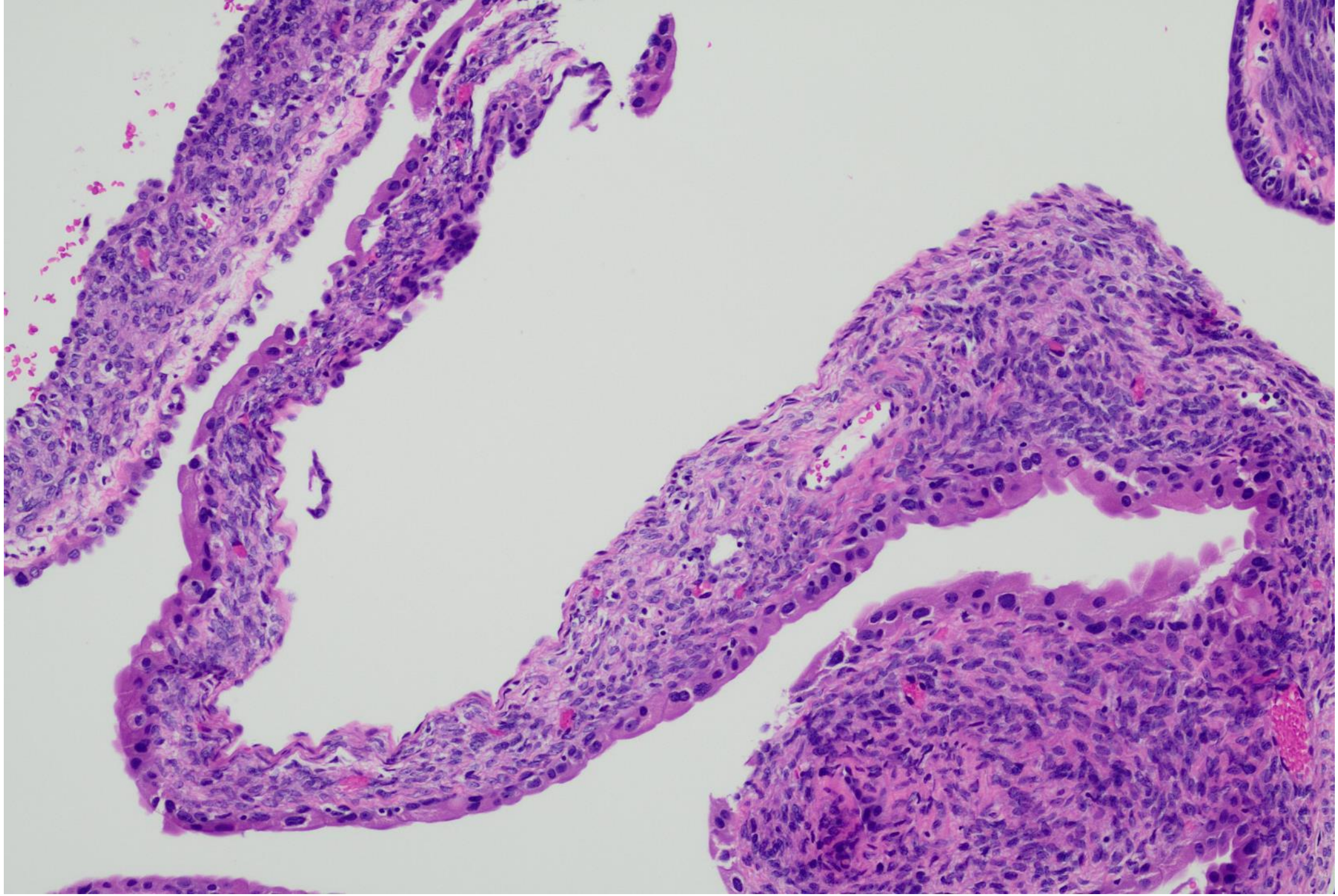
Armen Khararjian; Walnut Creek Kaiser Permanente

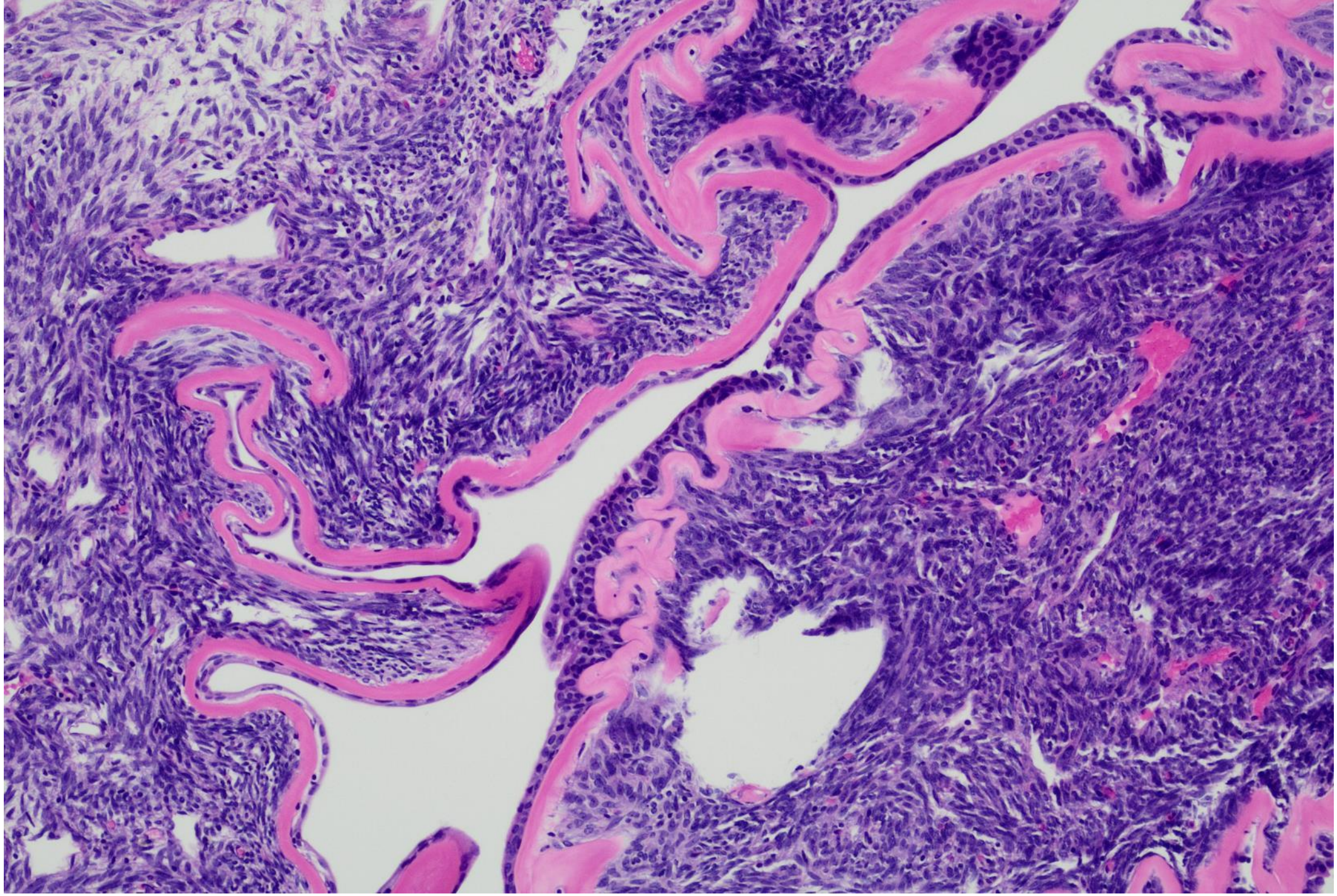
Middle aged woman with a 6 cm renal mass

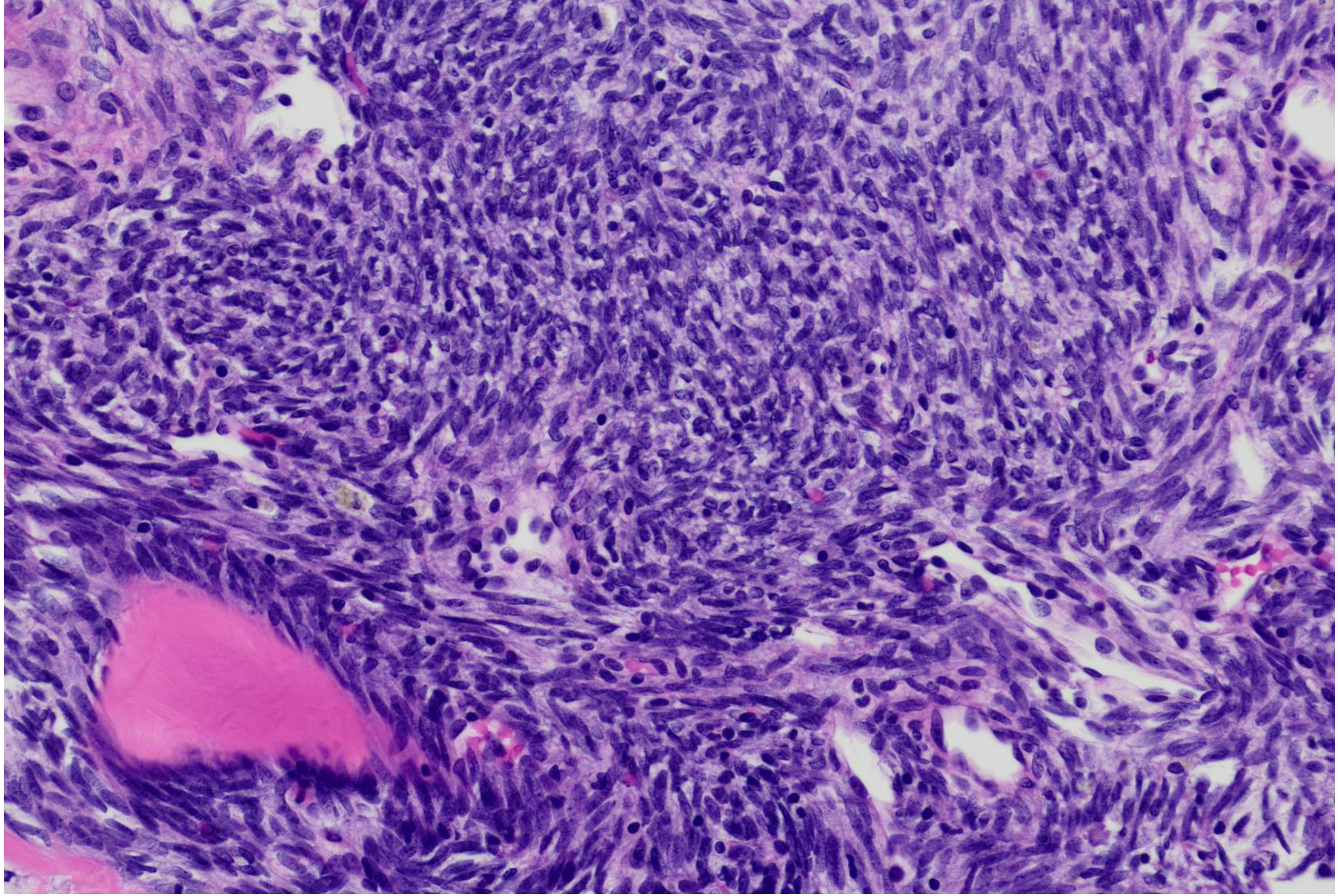


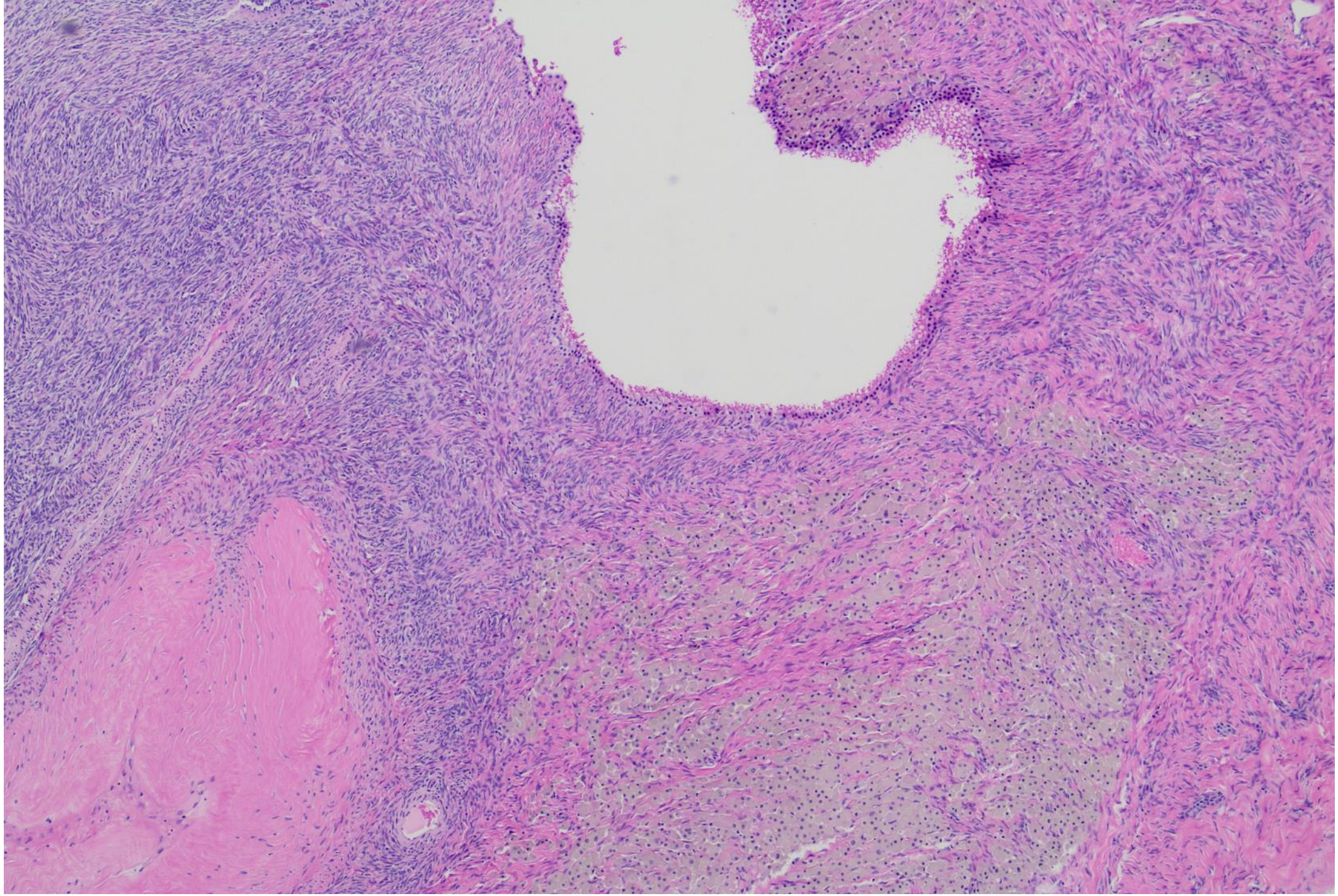


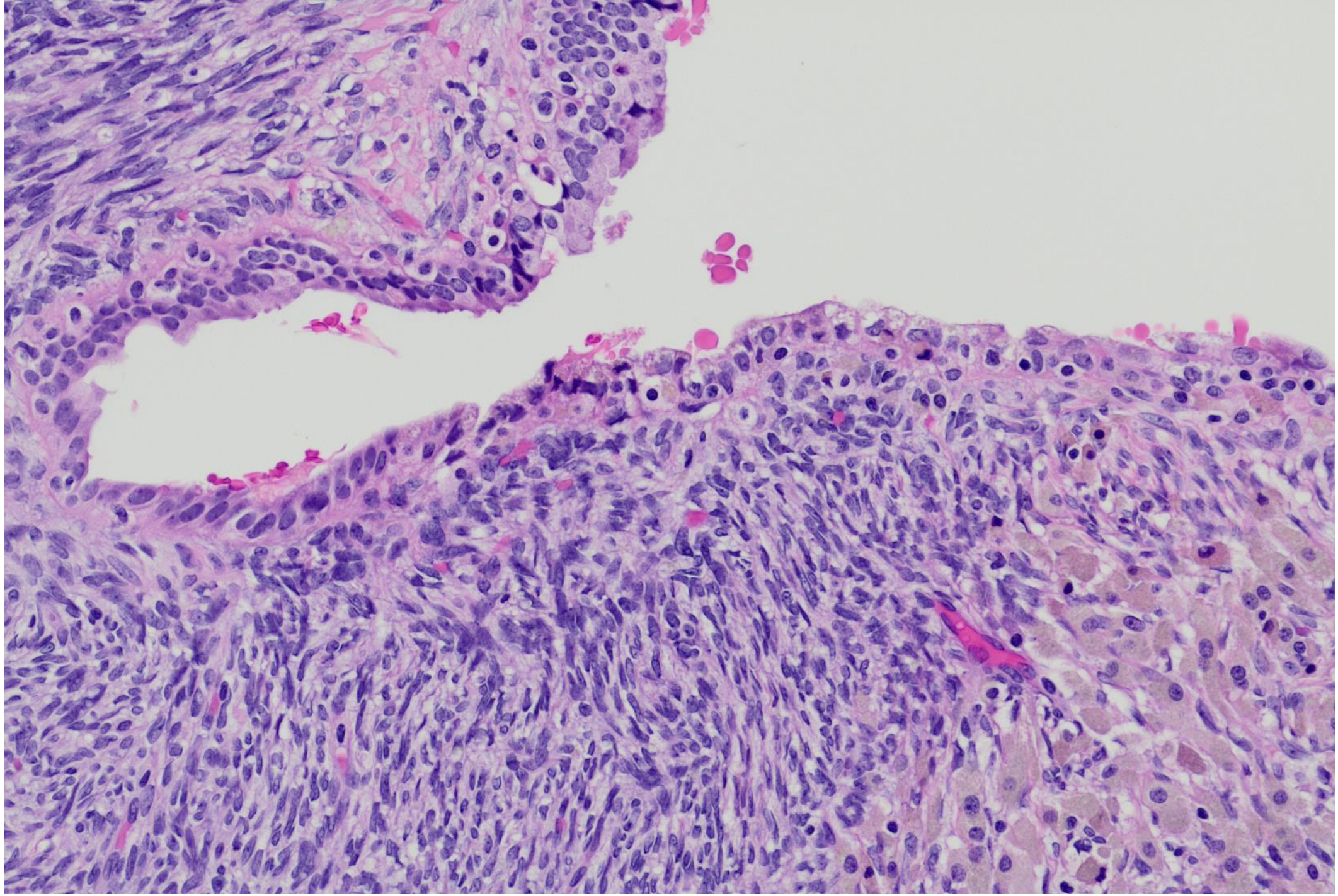


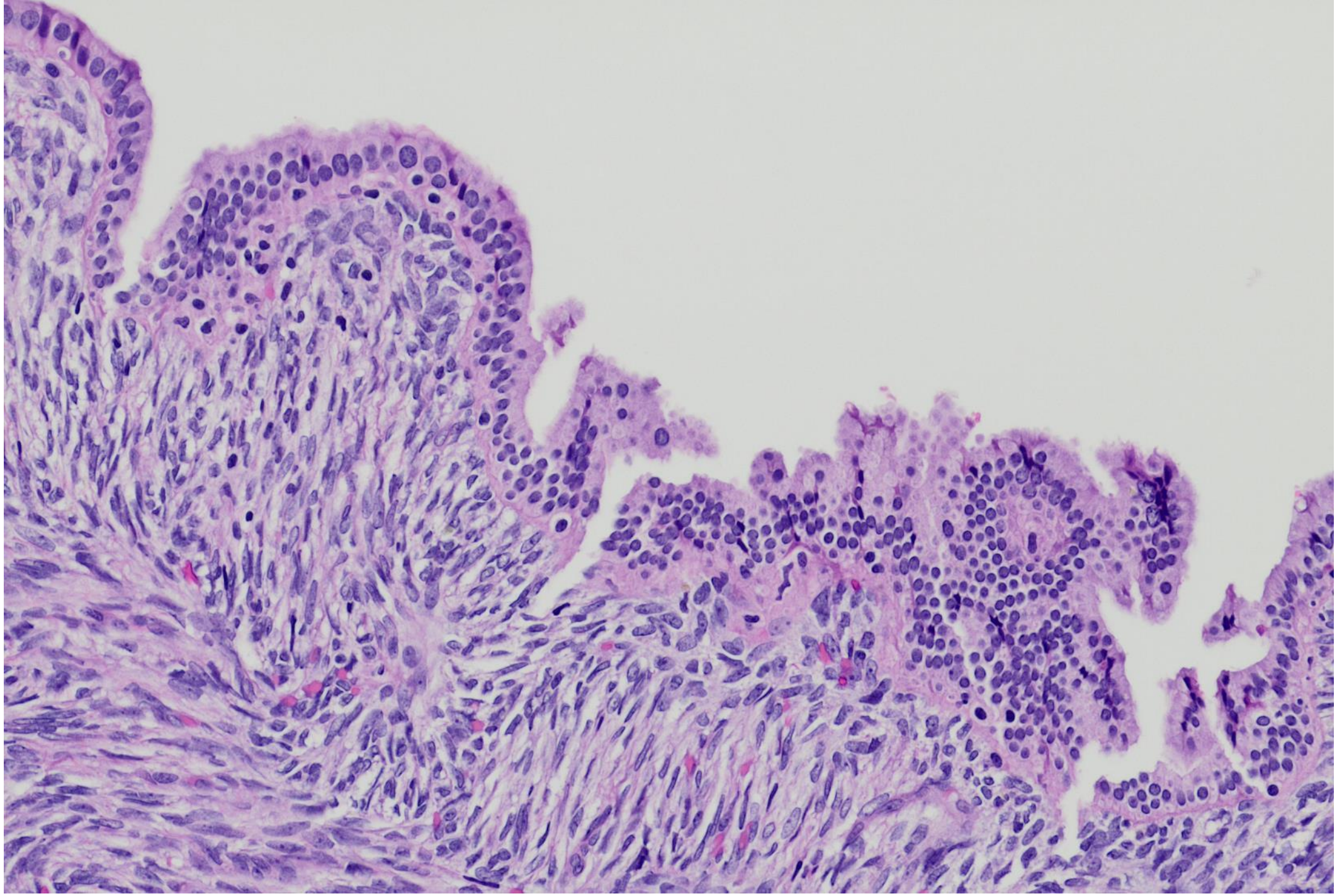












DIAGNOSIS?

Mixed Epithelial and Stromal Tumor

- Uncommon tumor composed of variable cystic and solid components
- Most common in perimenopausal women
  - Often have a history of long term hormonal treatment
- Solitary and well circumscribed
- Stroma and epithelium have a variety of features/elements
- Part of “MEST family” with adult cystic nephroma at opposite end of spectrum

Histologic Features

- Epithelium
  - Cysts vary in size
  - Lined by a broad spectrum of epithelium (flat, cuboidal, columnar, hobnail, etc)
  - Combinations of different epithelial components is common
- Stroma
  - Ranges from pauci to hypercellular
  - Wide spectrum of morphology
  - Can show smooth muscle or ovarian type stroma
  - Condensation of spindle cells around epithelial components
  - Foamy histiocytes
  - Positive for SMA, desmin, ER, PR
- Minimal cytologic atypia
- Mitoses, hemorrhage, and necrosis not usually seen

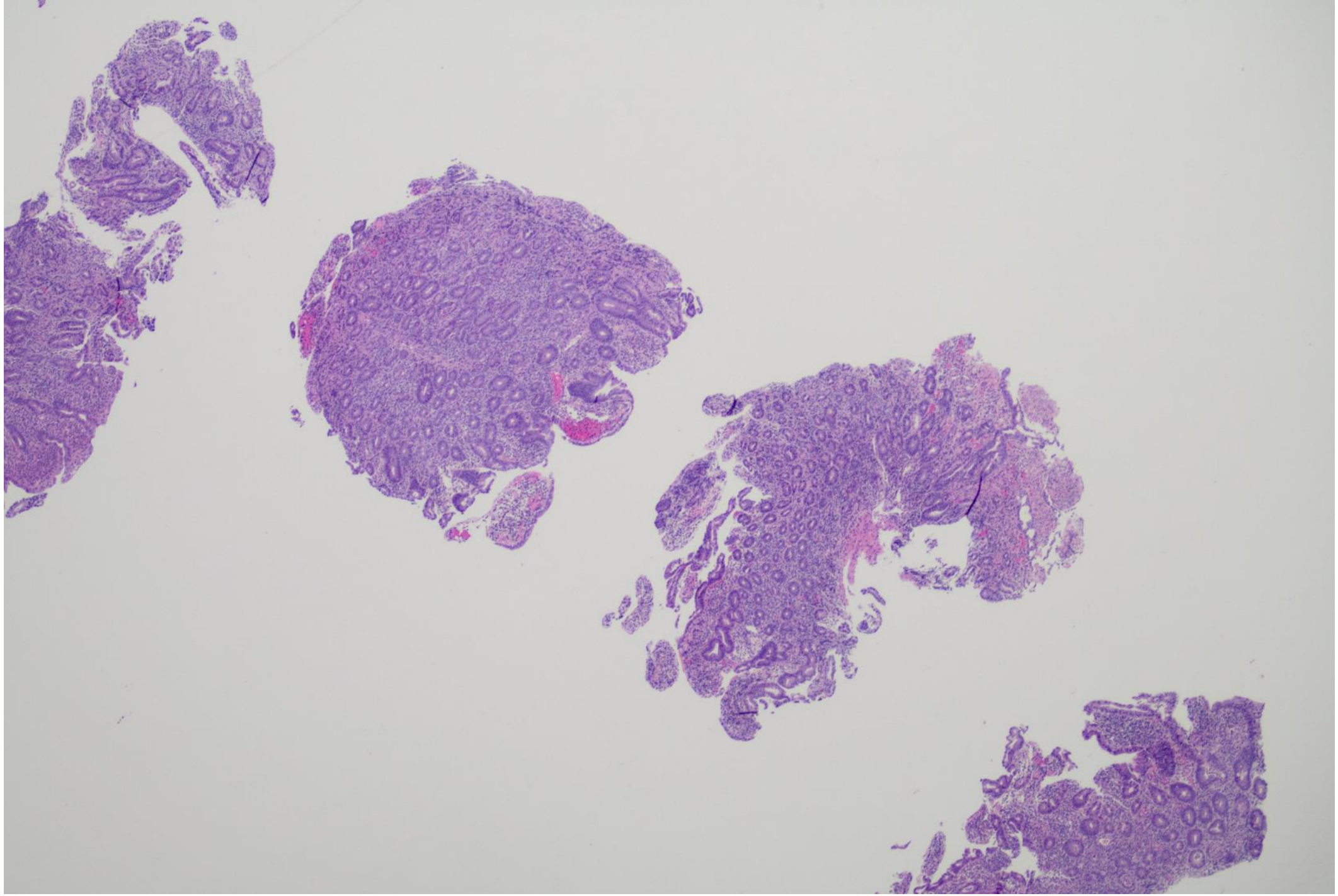
Clinical Course

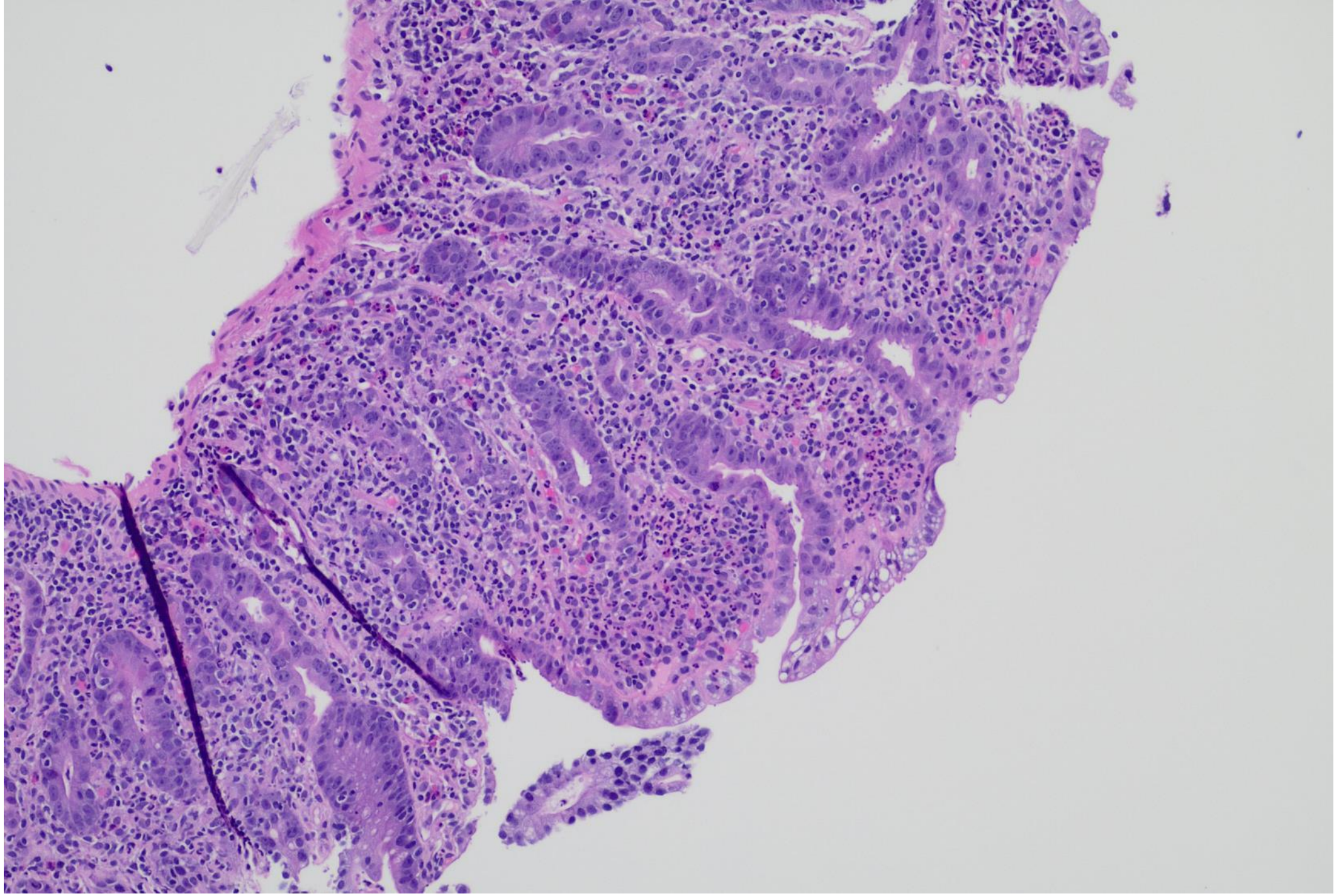
- Generally behave in a benign/indolent fashion but local recurrence, malignant transformation, and metastases have been reported

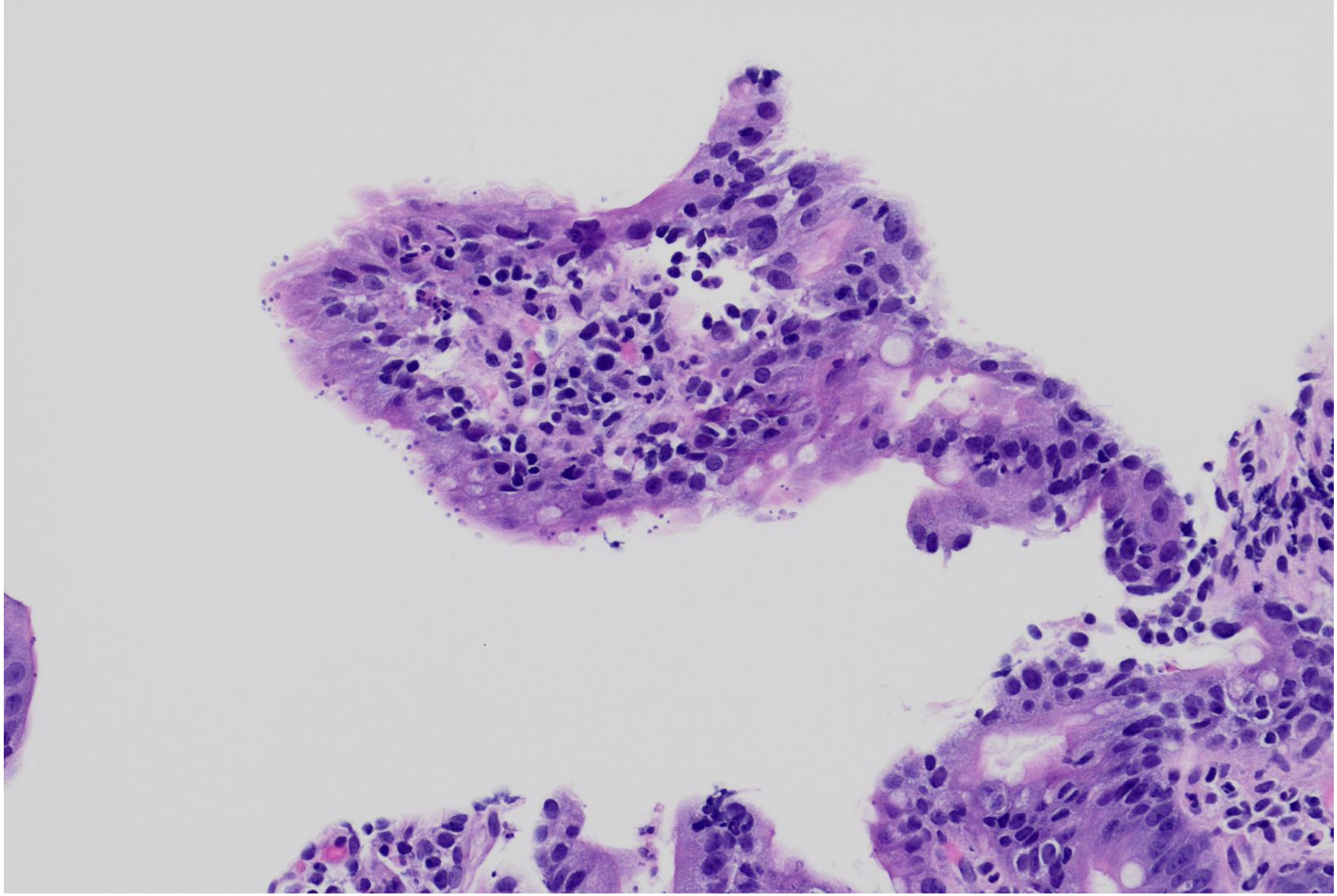
23-1003

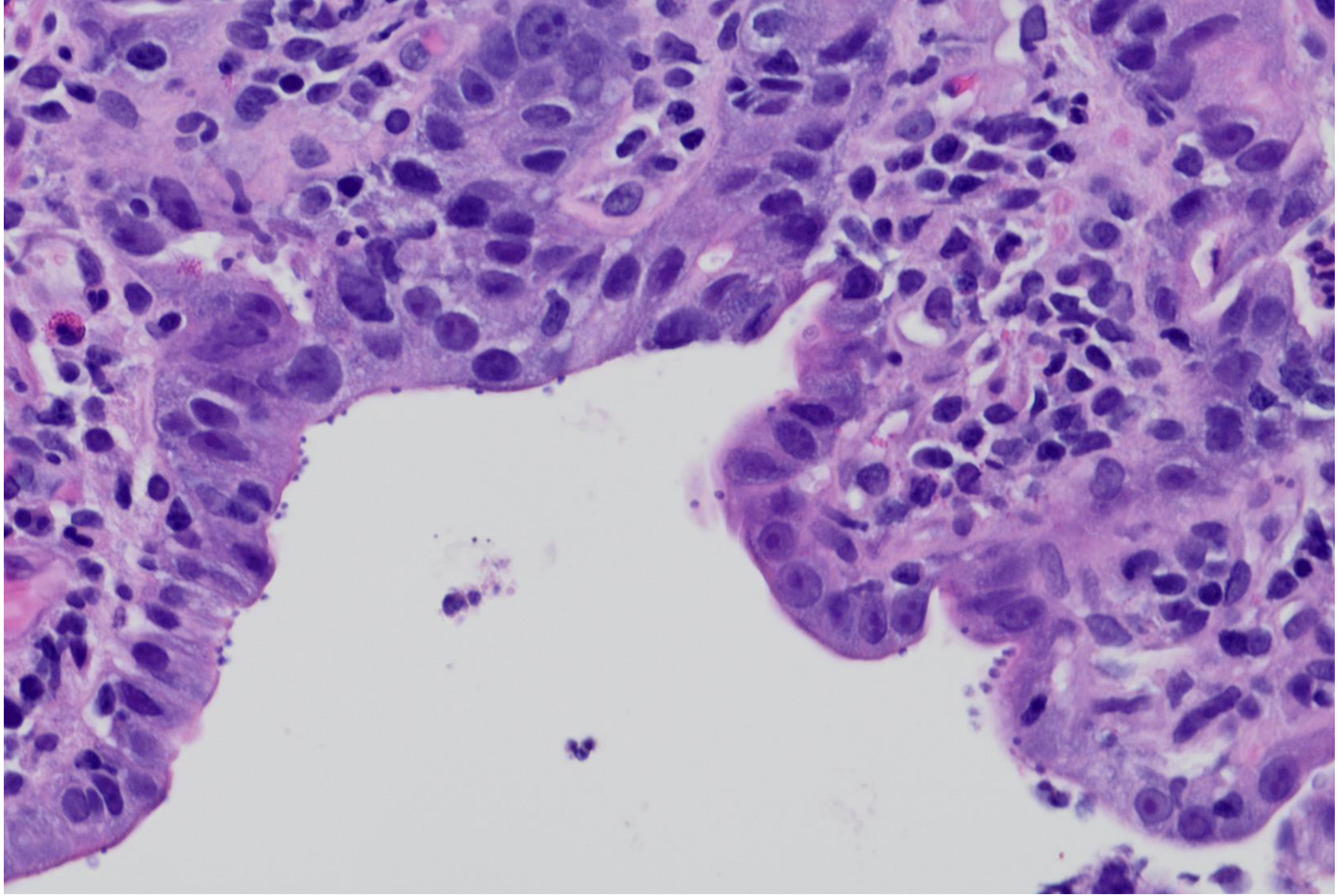
Armen Khararjian: Walnut Creek Kaiser Permanente

Young adult male with Evans Syndrome presented with N/V, abdominal pain, and diarrhea. Biopsy of duodenum is shown.









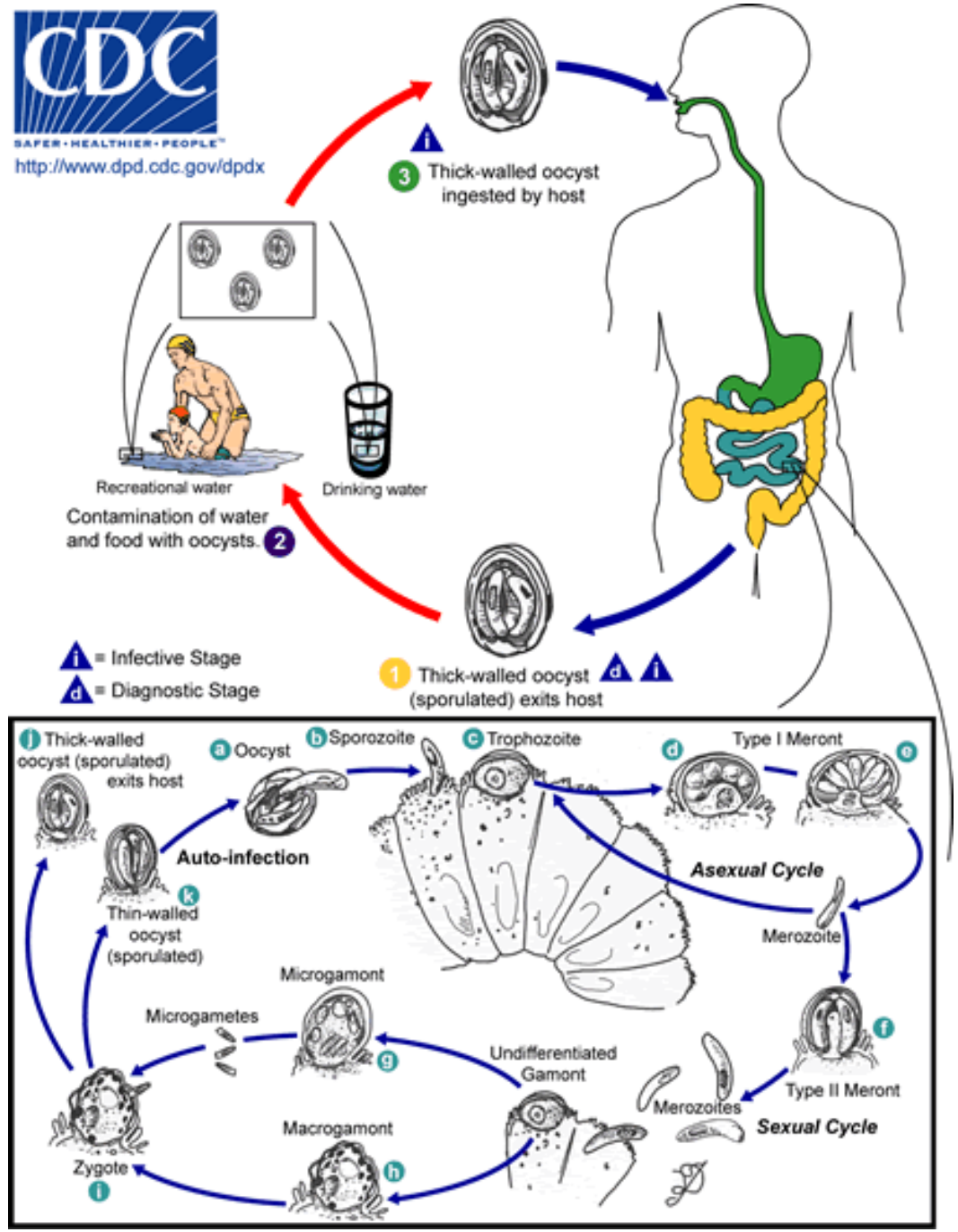
DIAGNOSIS?

Cryptosporidiosis

- Can affect both immunocompetent and immunocompromised individuals
  - Immunosuppressed folks get more severe, chronic, or fatal illness
- Small intestine is most common site affected
- Symptoms usually begin 2-10 days post infection
- Stool studies with direct fluorescent antibodies and/or immunoassays can help with diagnosis
  - Molecular methods also available
- Healthy individuals can recover without treatment

Histology

- Small (2-5 um), basophilic, round bodies seen along luminal border (“blue beads”)
- Background villous atrophy, crypt hyperplasia, cryptitis
- Giemsa, PAS, modified AFB, and silver stain can highlight
- Differential
  - Cyclospora: 8 um
  - Isospora: 20-30 um
  - Microsporidium: intracellular fungus, not modified acid fast

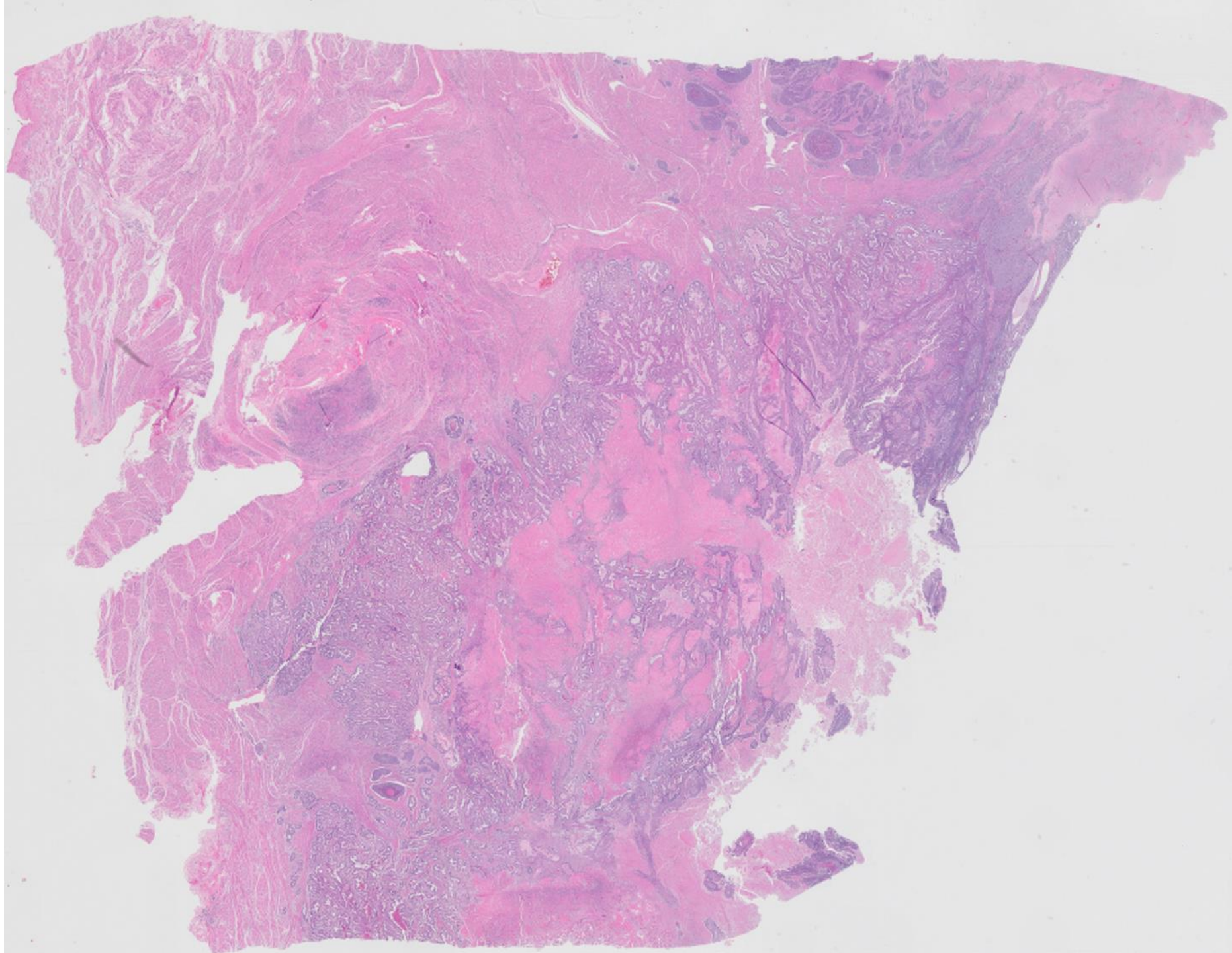

CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx
3 Thick-walled oocyst ingested by host
Recreational water
Drinking water
Contamination of water and food with oocysts. 2
i = Infective Stage
d = Diagnostic Stage
1 Thick-walled oocyst (sporulated) exits host
j Thick-walled oocyst (sporulated) exits host
a Oocyst
b Sporozoite
c Trophozoite
d Type I Meront
e
Auto-infection
k Thin-walled oocyst (sporulated)
Asexual Cycle
Merozoite
Microgamont
Microgametes
g
Undifferentiated Gamont
f
Type II Meront
Merozoites
Sexual Cycle
Macrogamont
h
Zygote
i

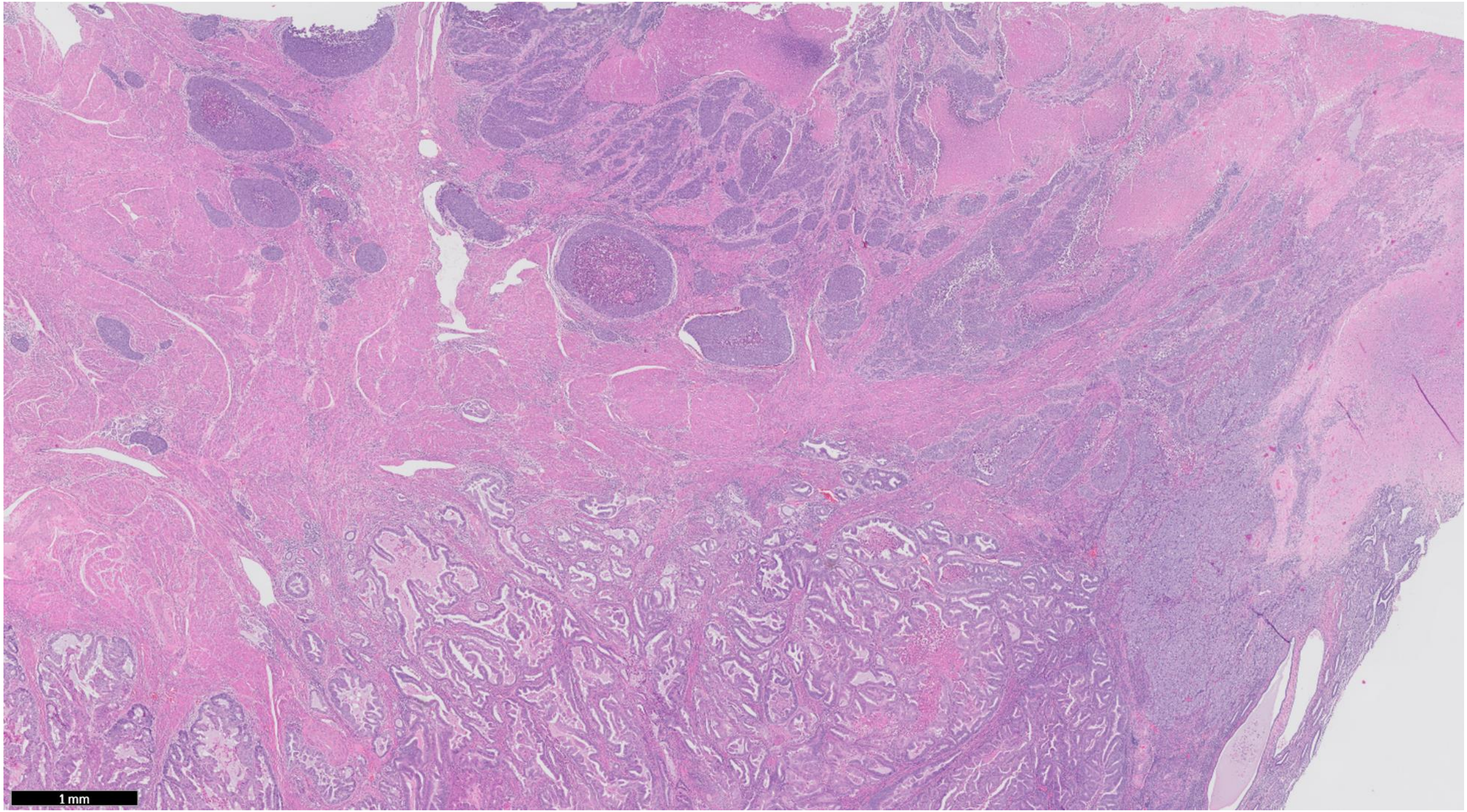
23-1004

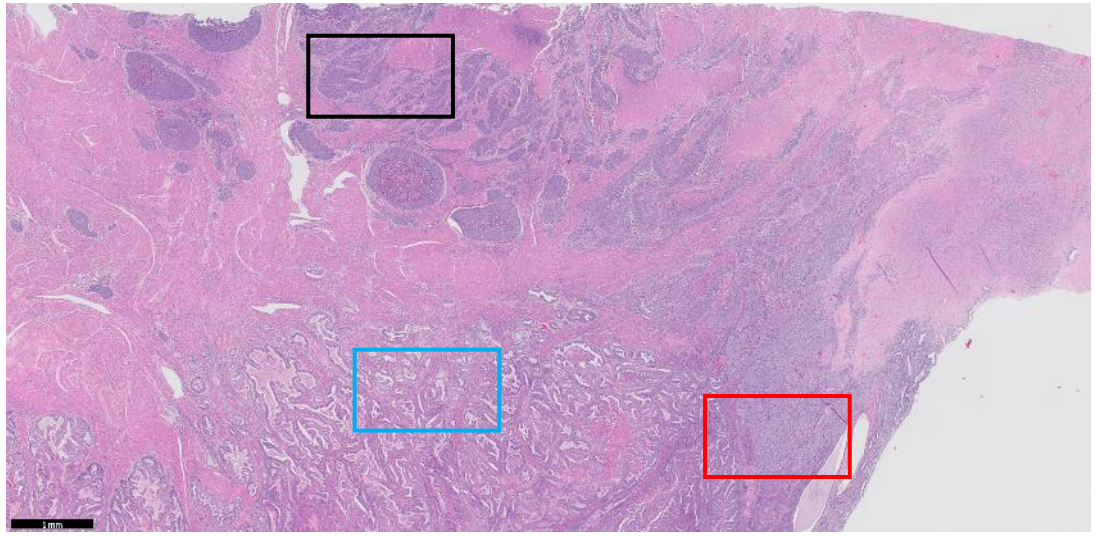
Austin McHenry/Brooke Howitt; Stanford

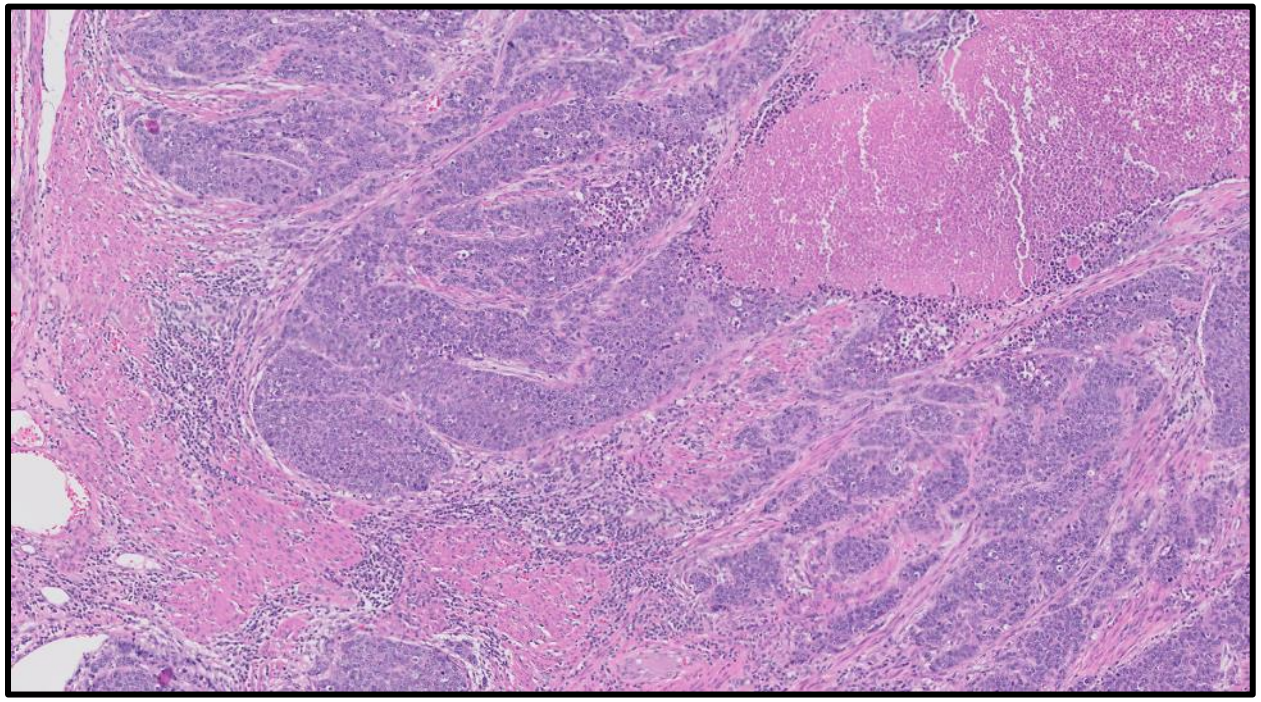
62F w/ abdominal pain, urinary retention/UTI, constipation. CT Ab/Pel: 11.8 cm peripherally enhancing, centrally hypoattenuating/necrotic appearing mass within pelvis, posteriorly displacing/indistinguishable from the proximal-mid rectum; CA125 51, CEA 3.9, CA19-9 43.

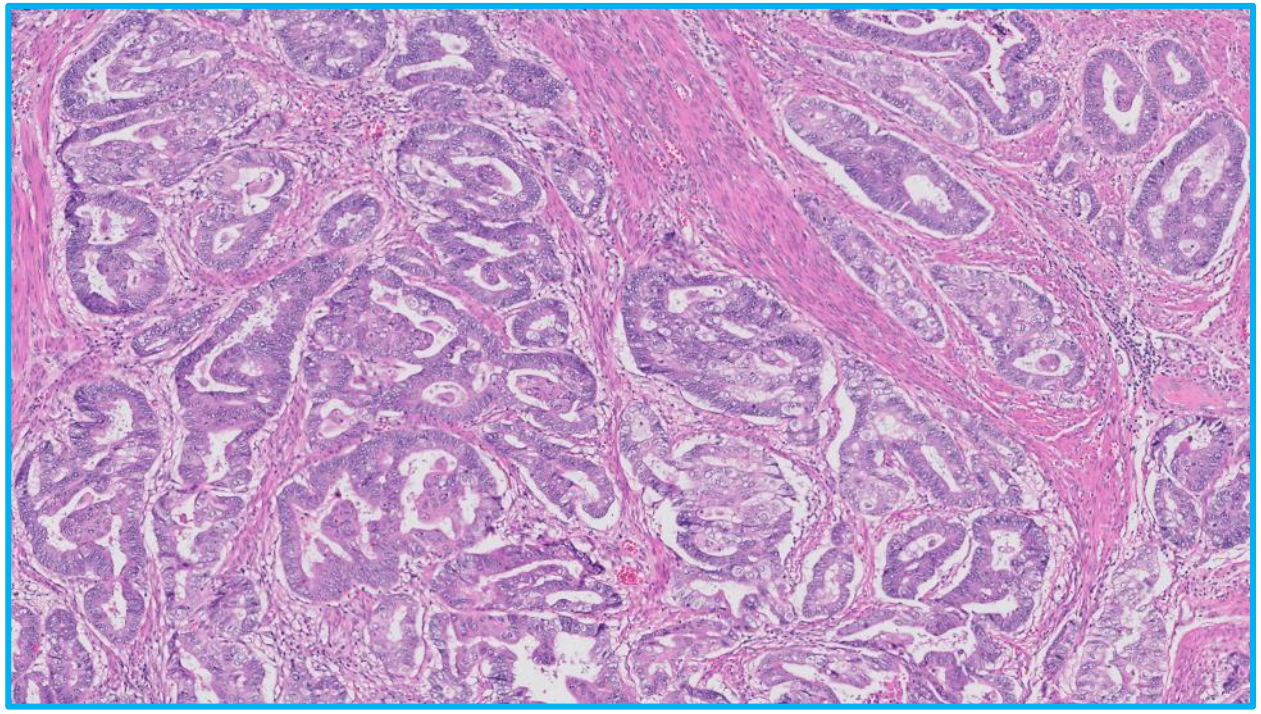
Endomyometrium

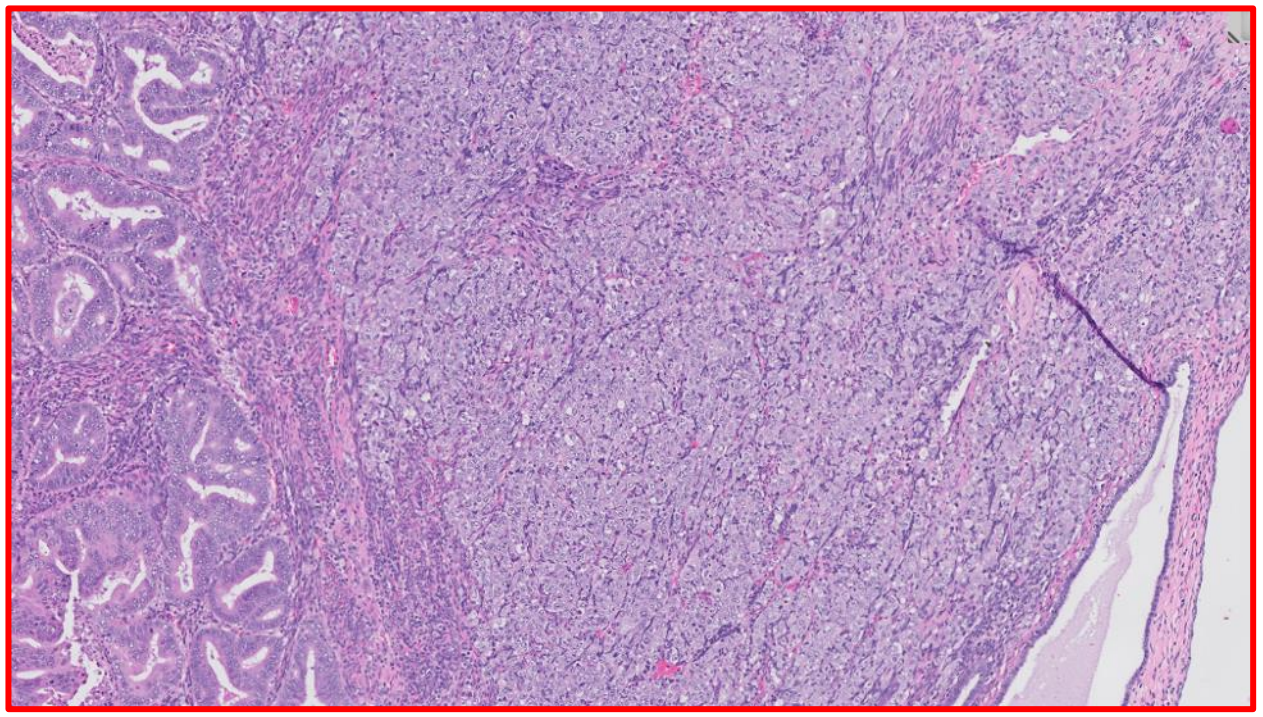


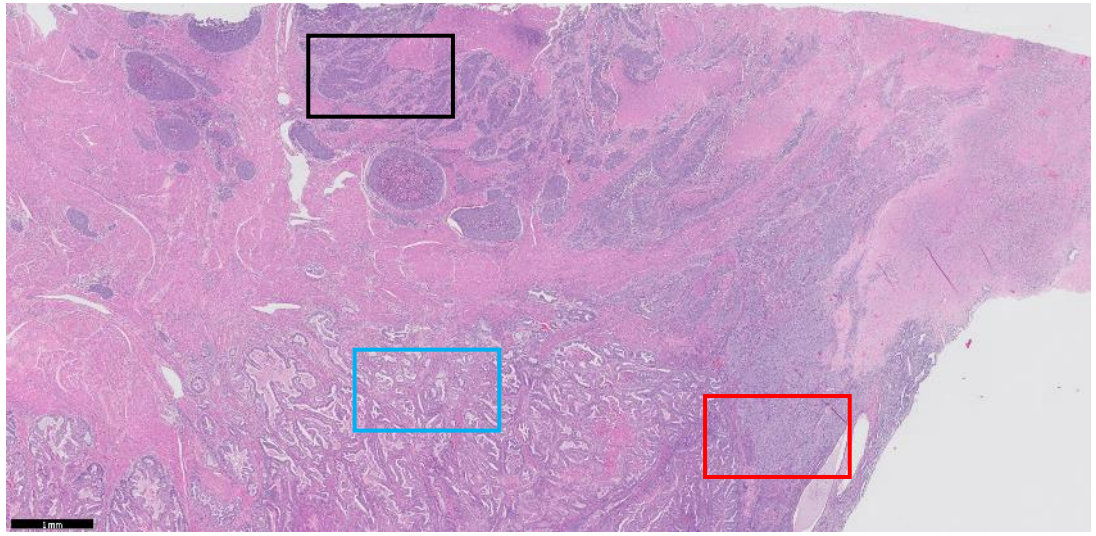

1 mm


5mm





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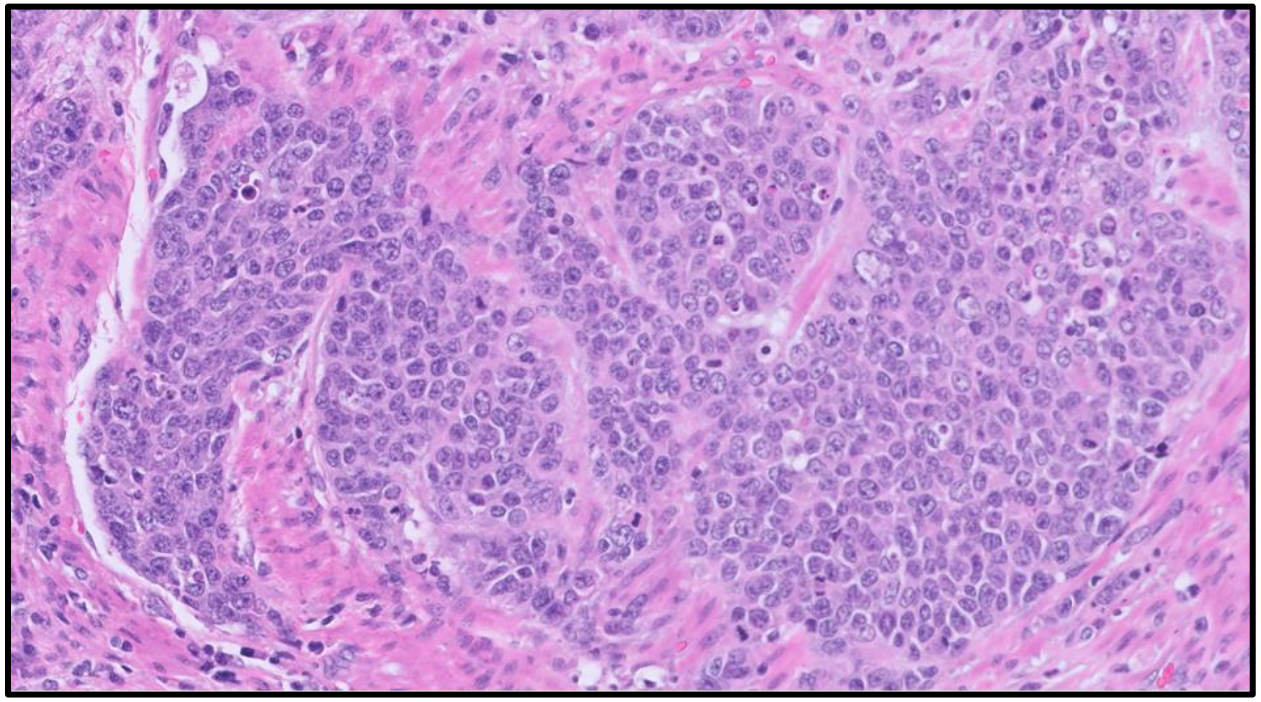
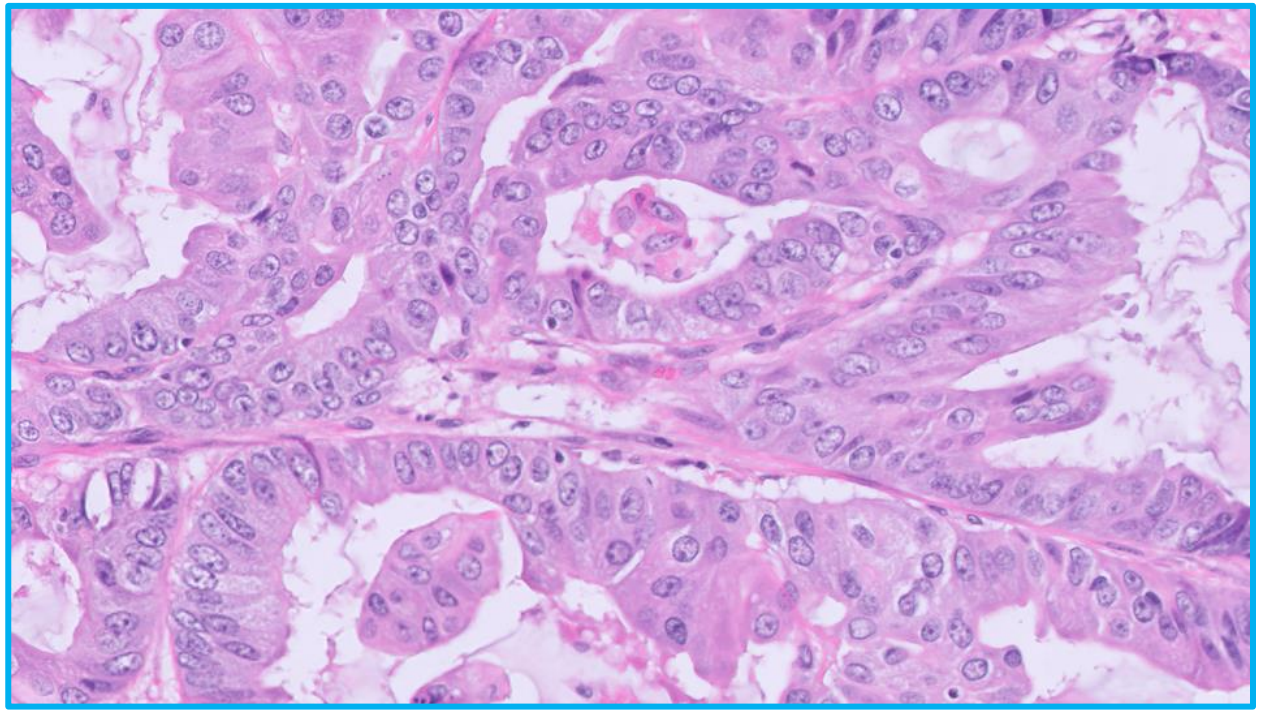
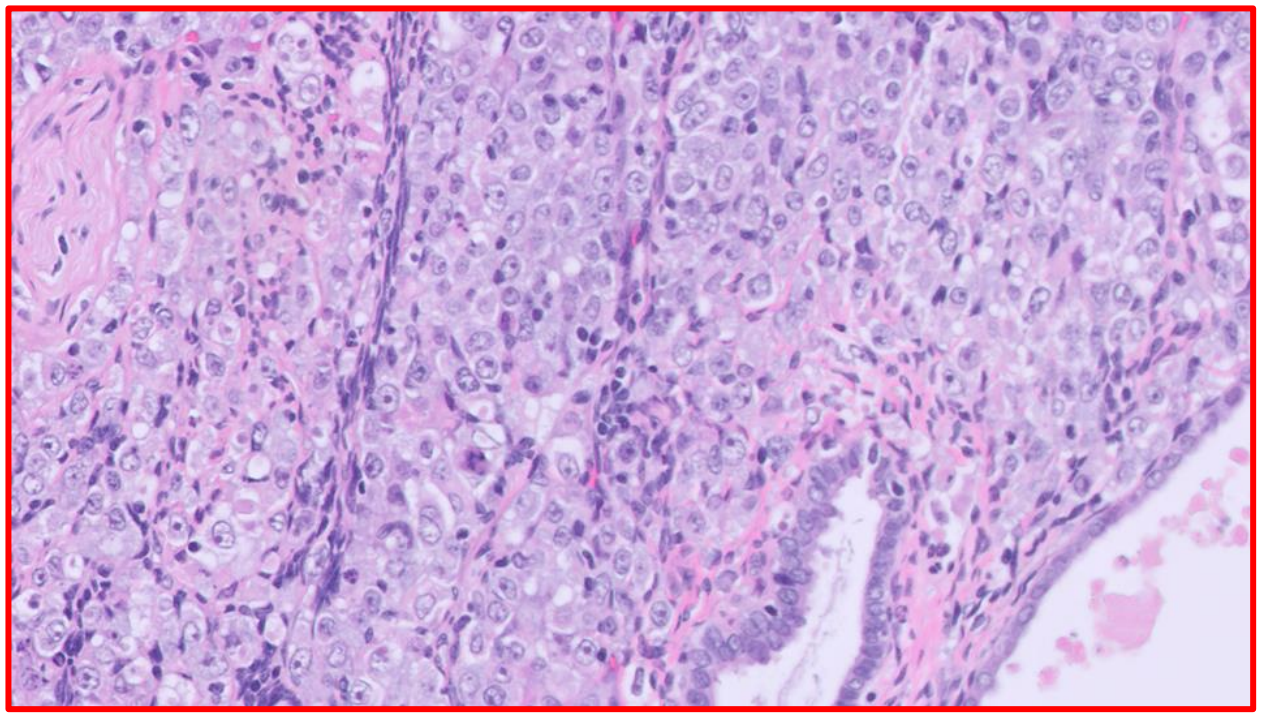
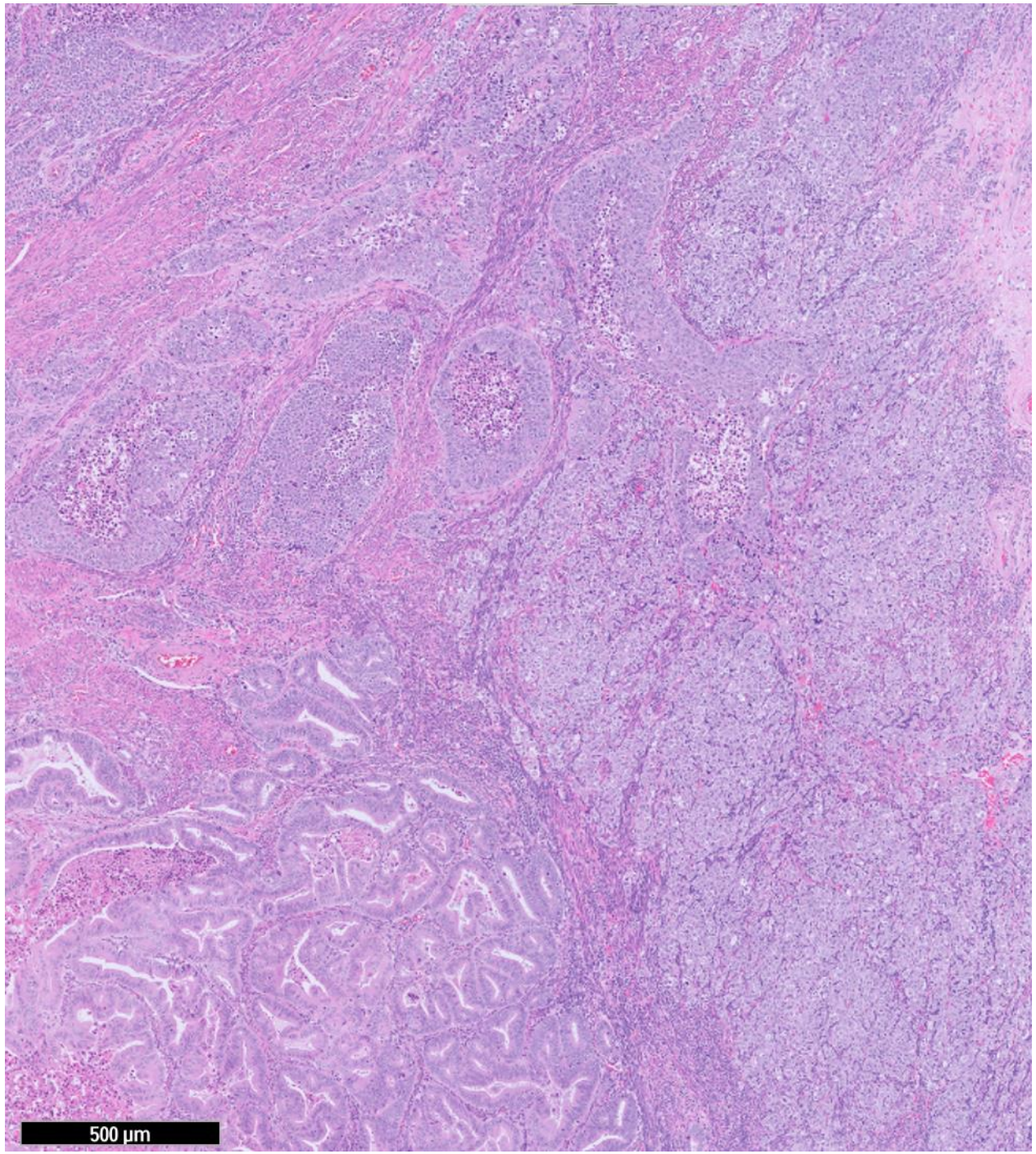
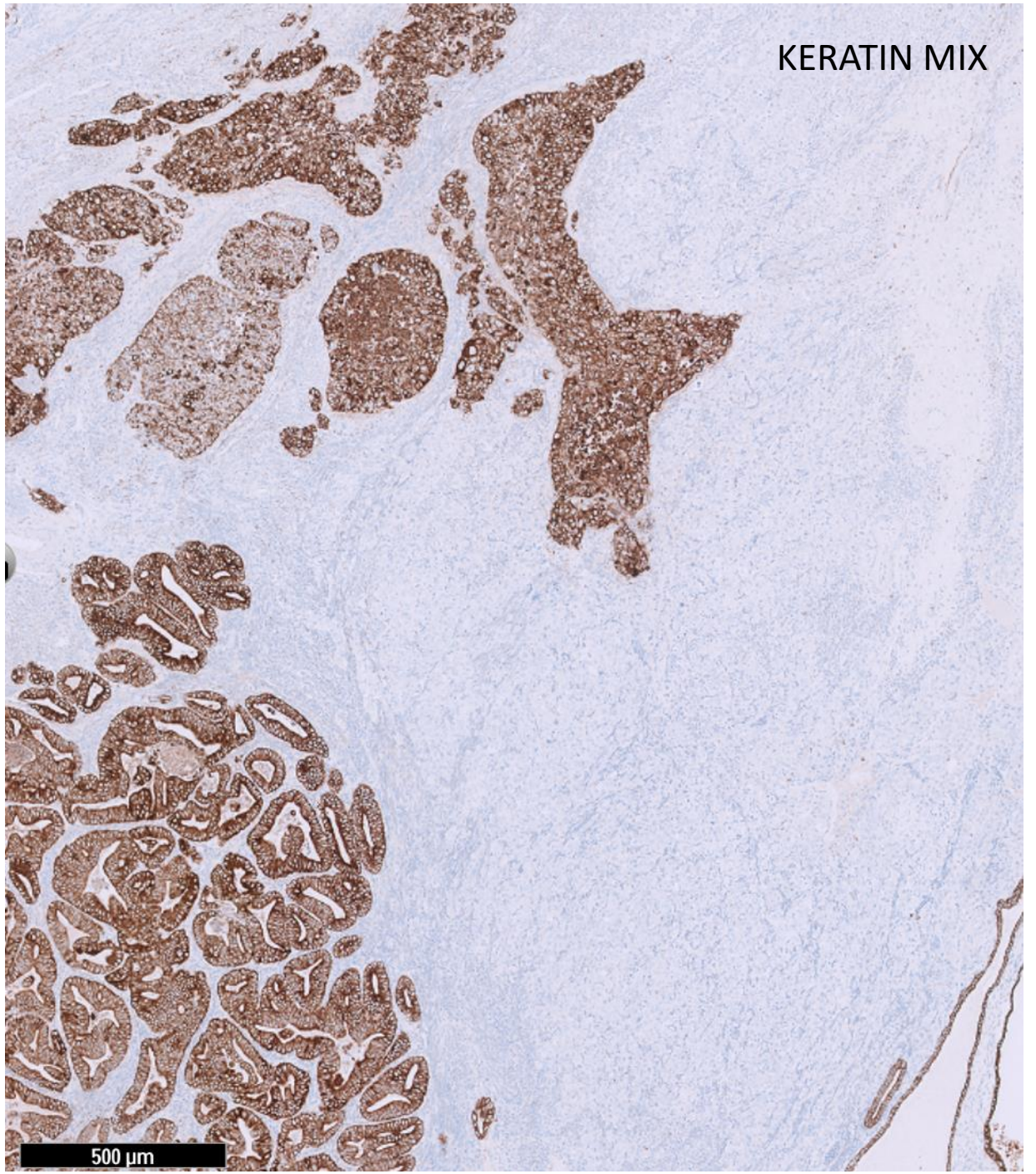
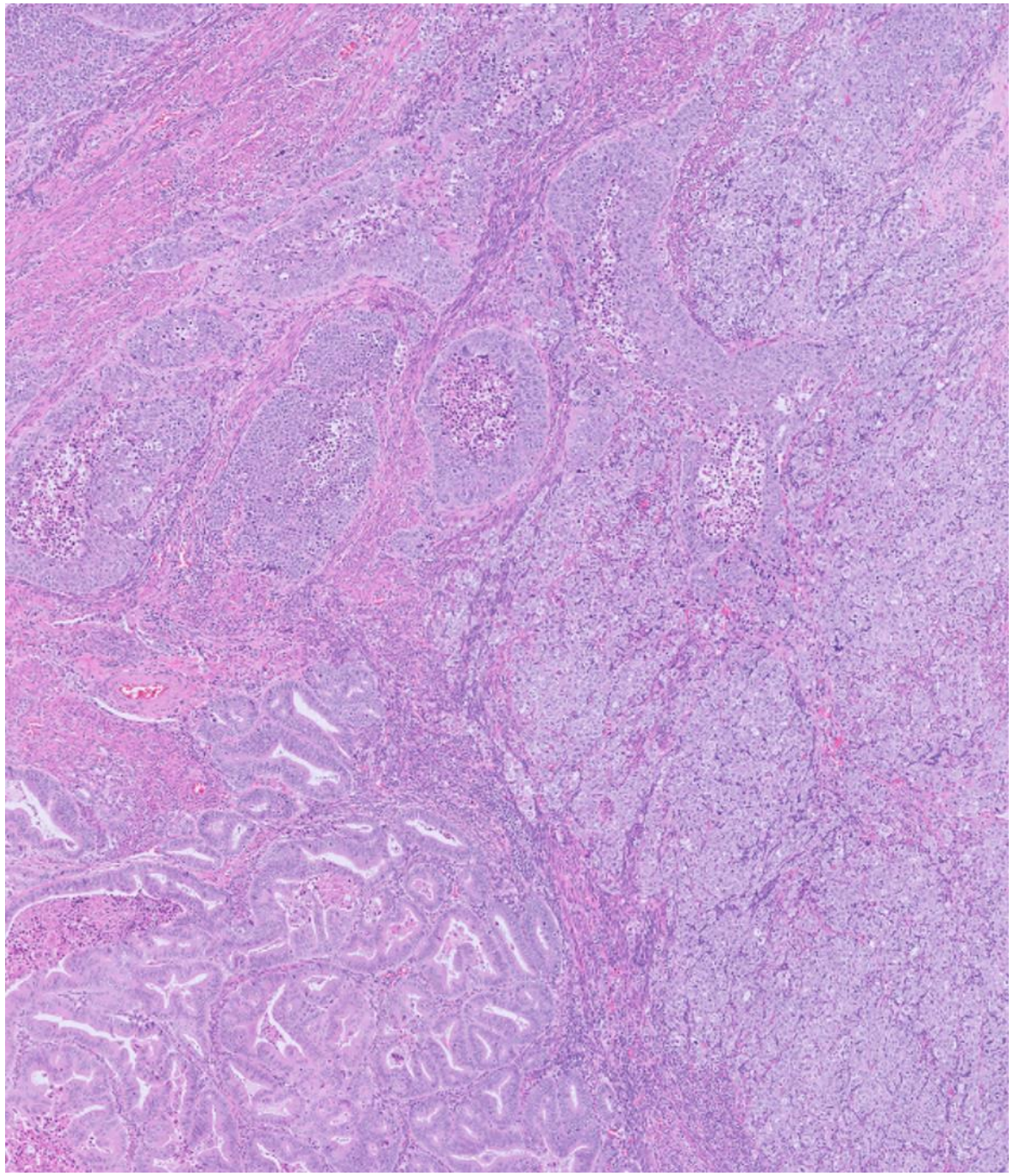


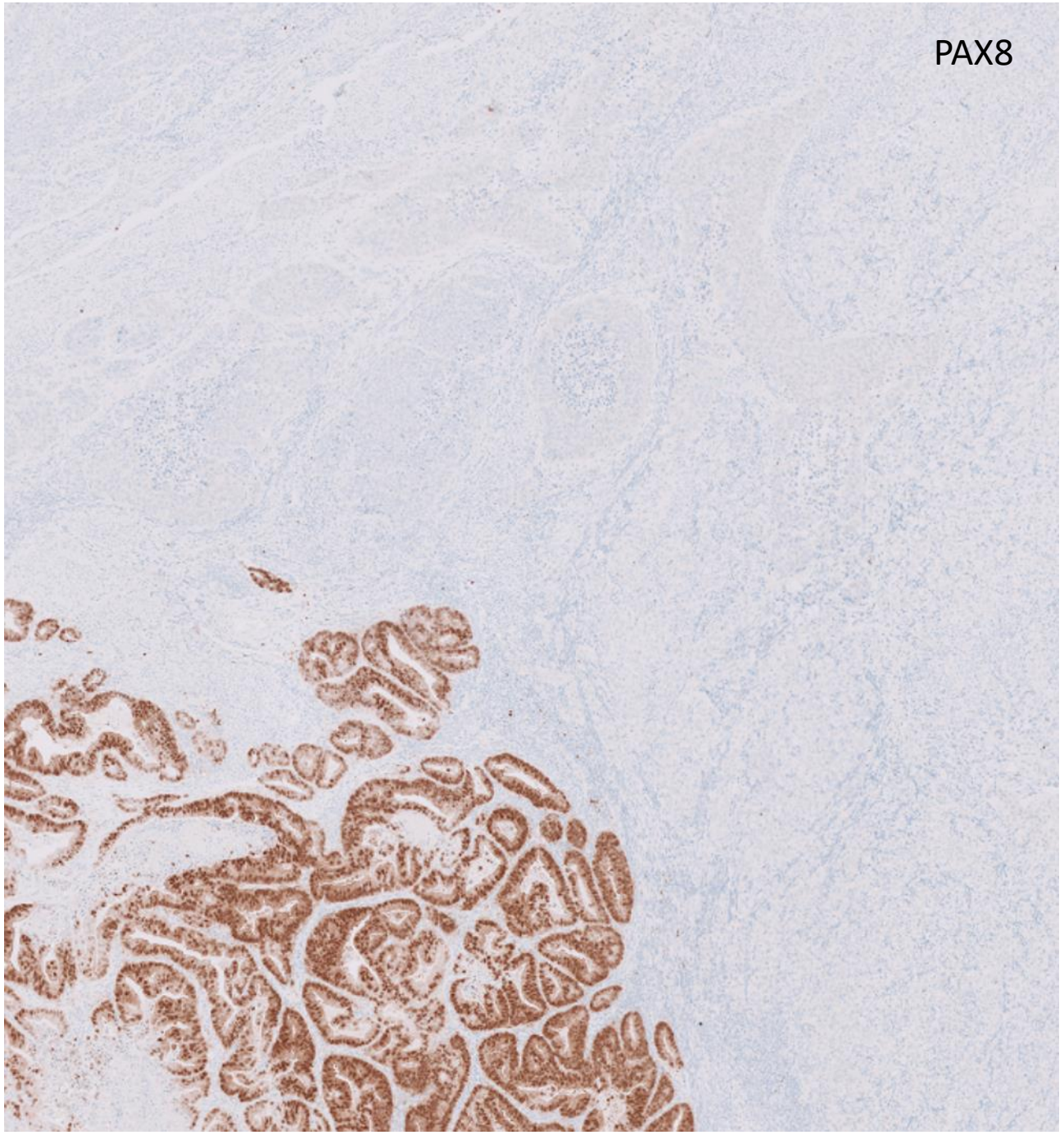


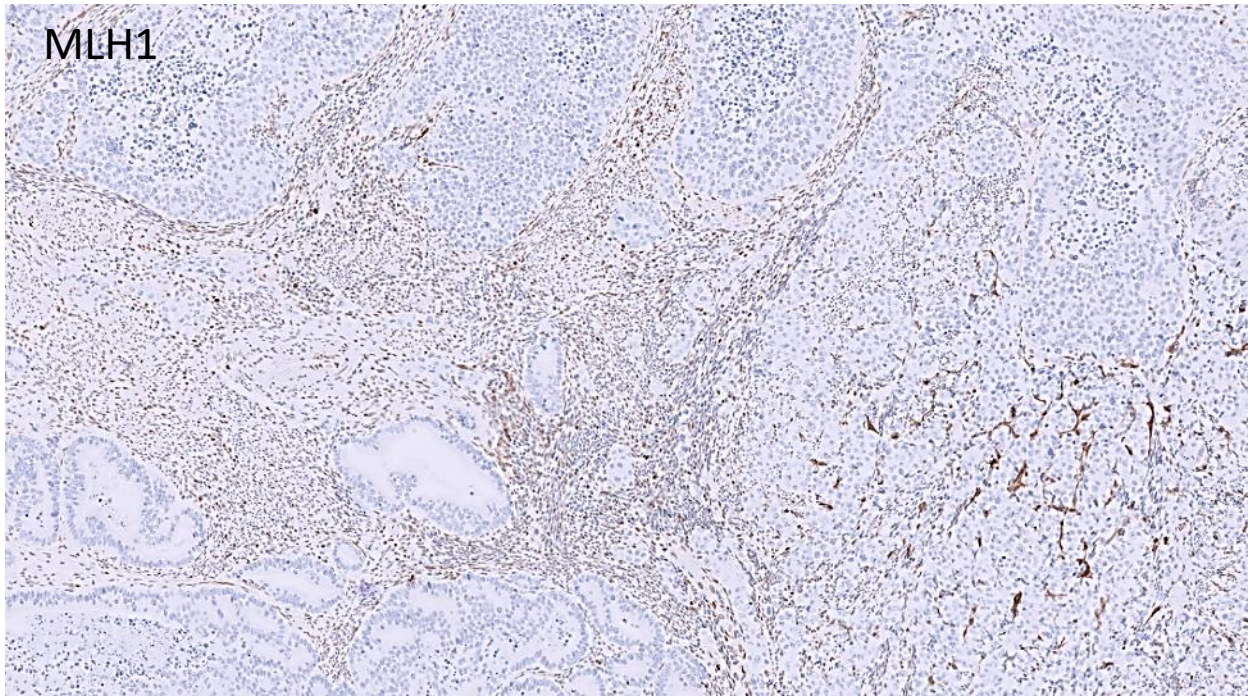



500 µm


KERATIN MIX
500 µm




PAX8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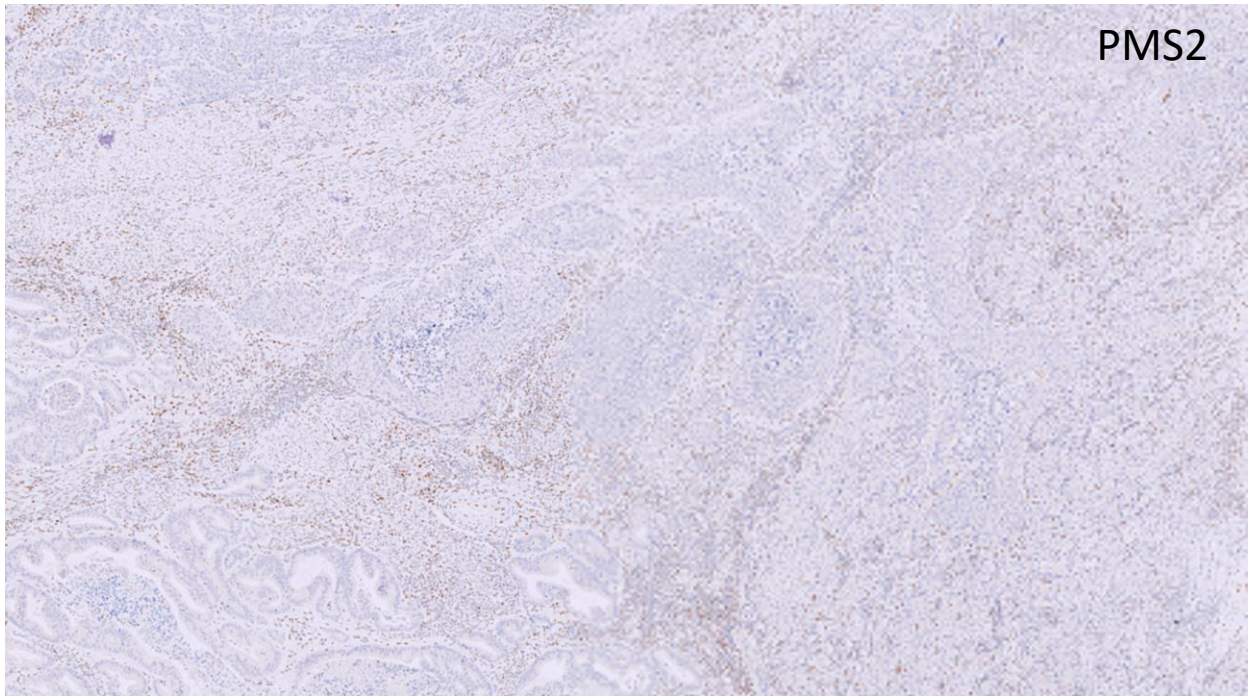
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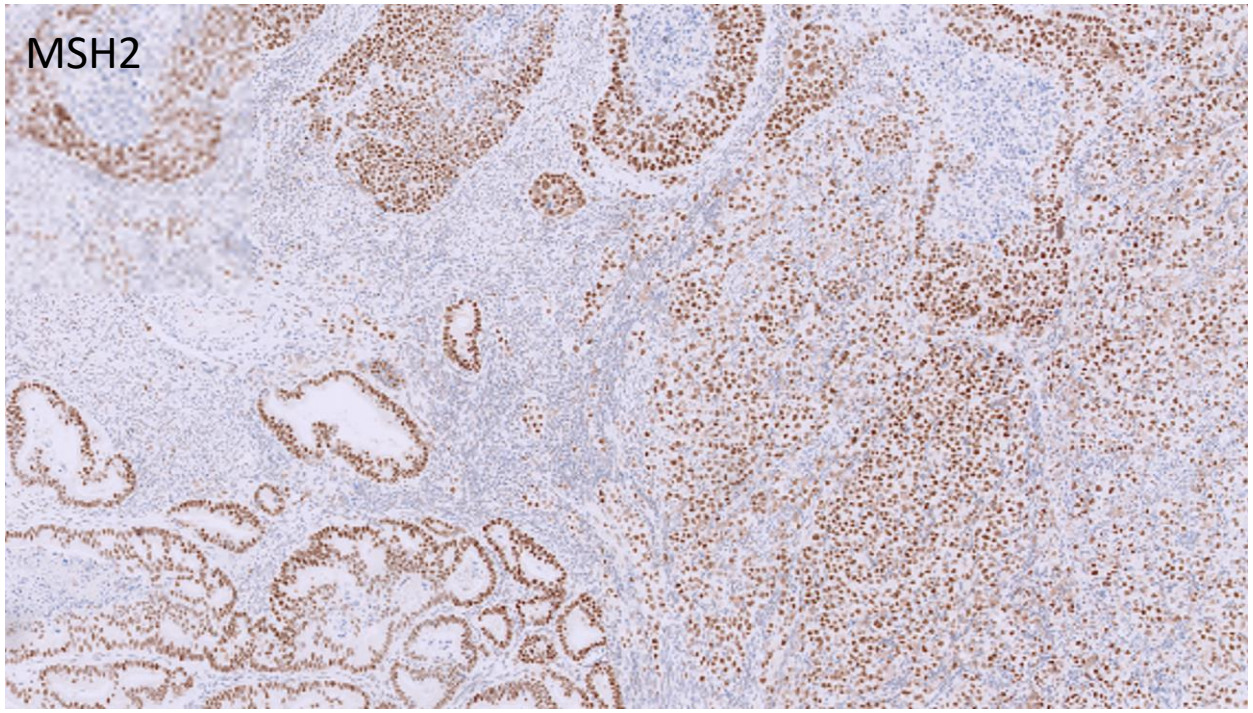
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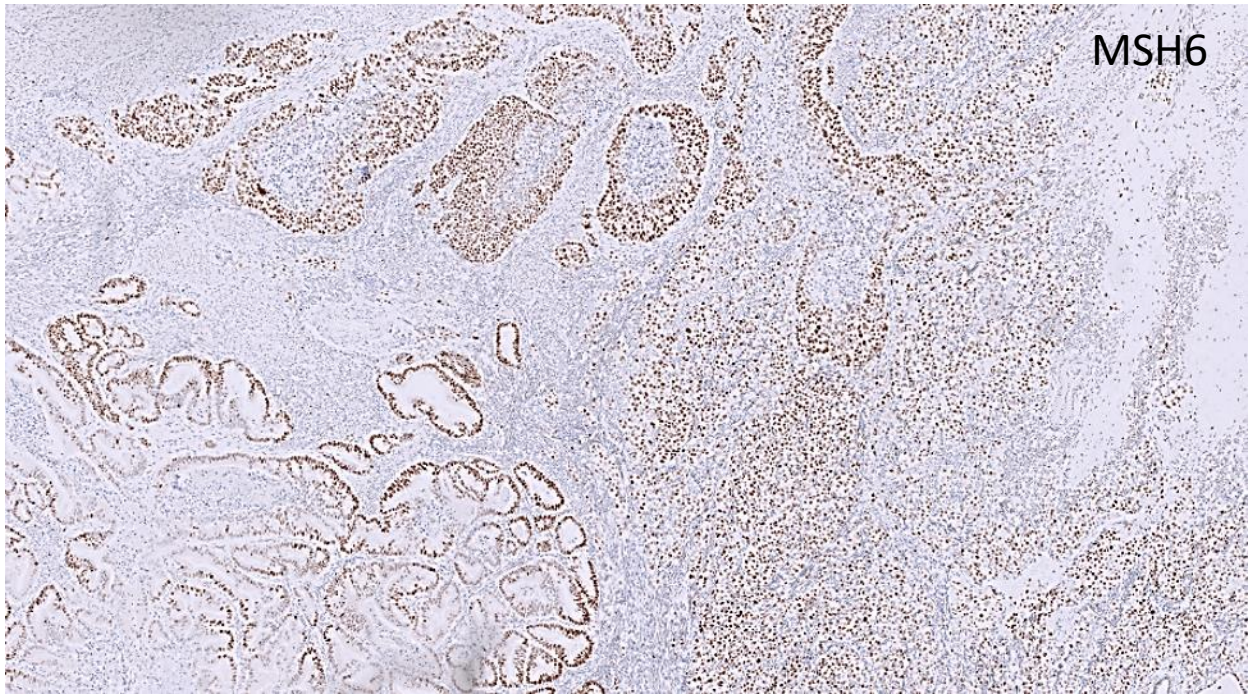
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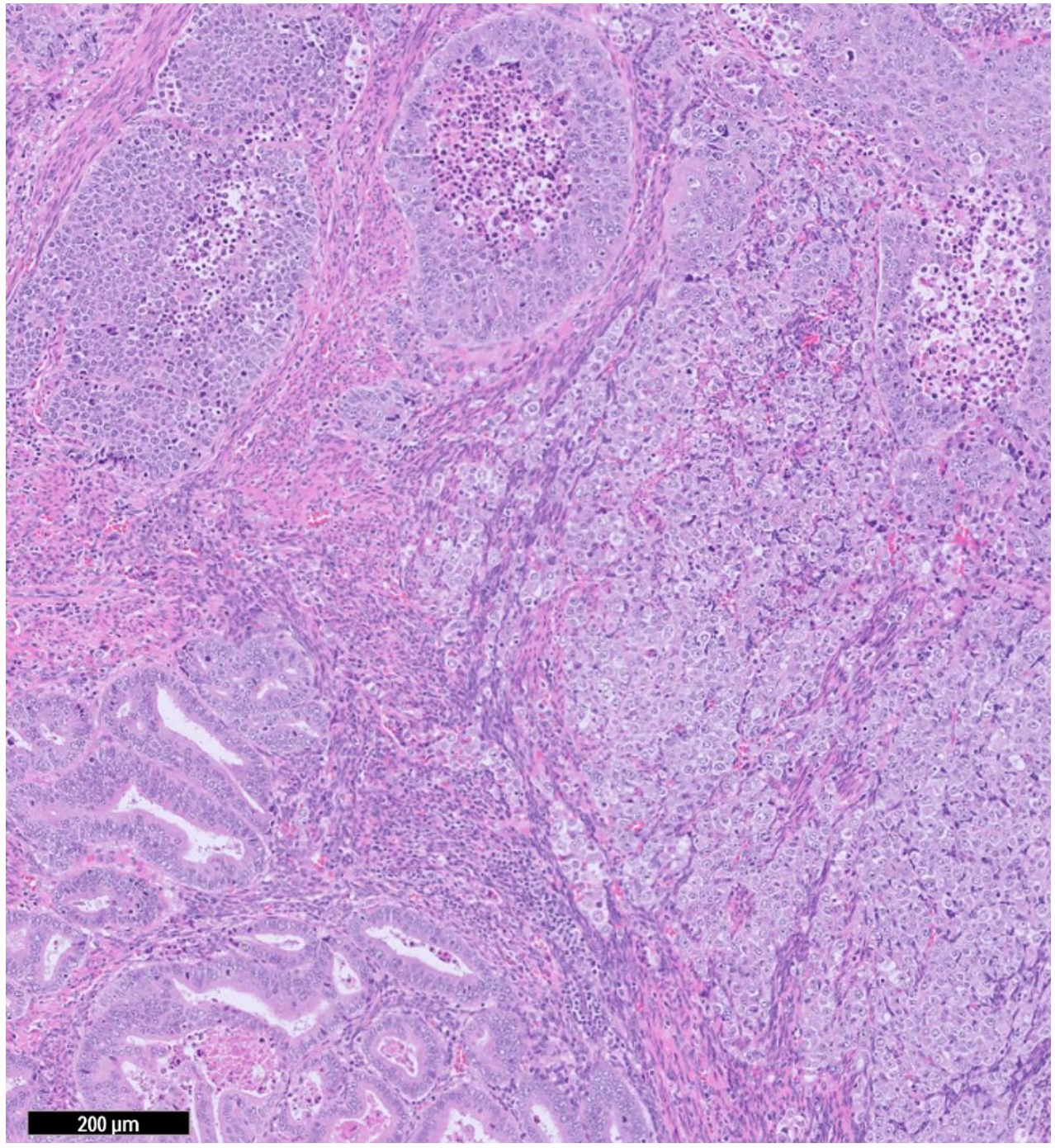
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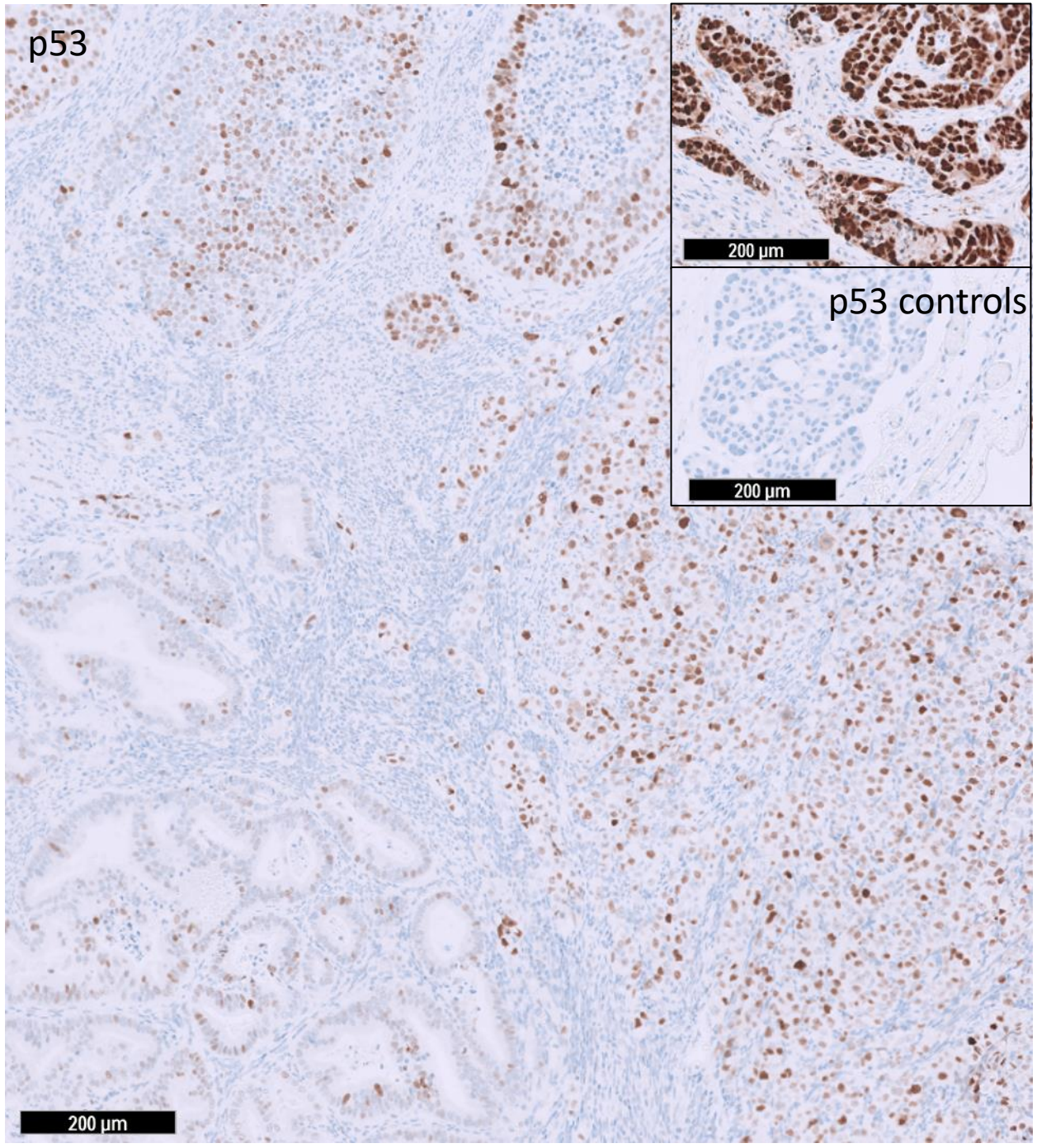
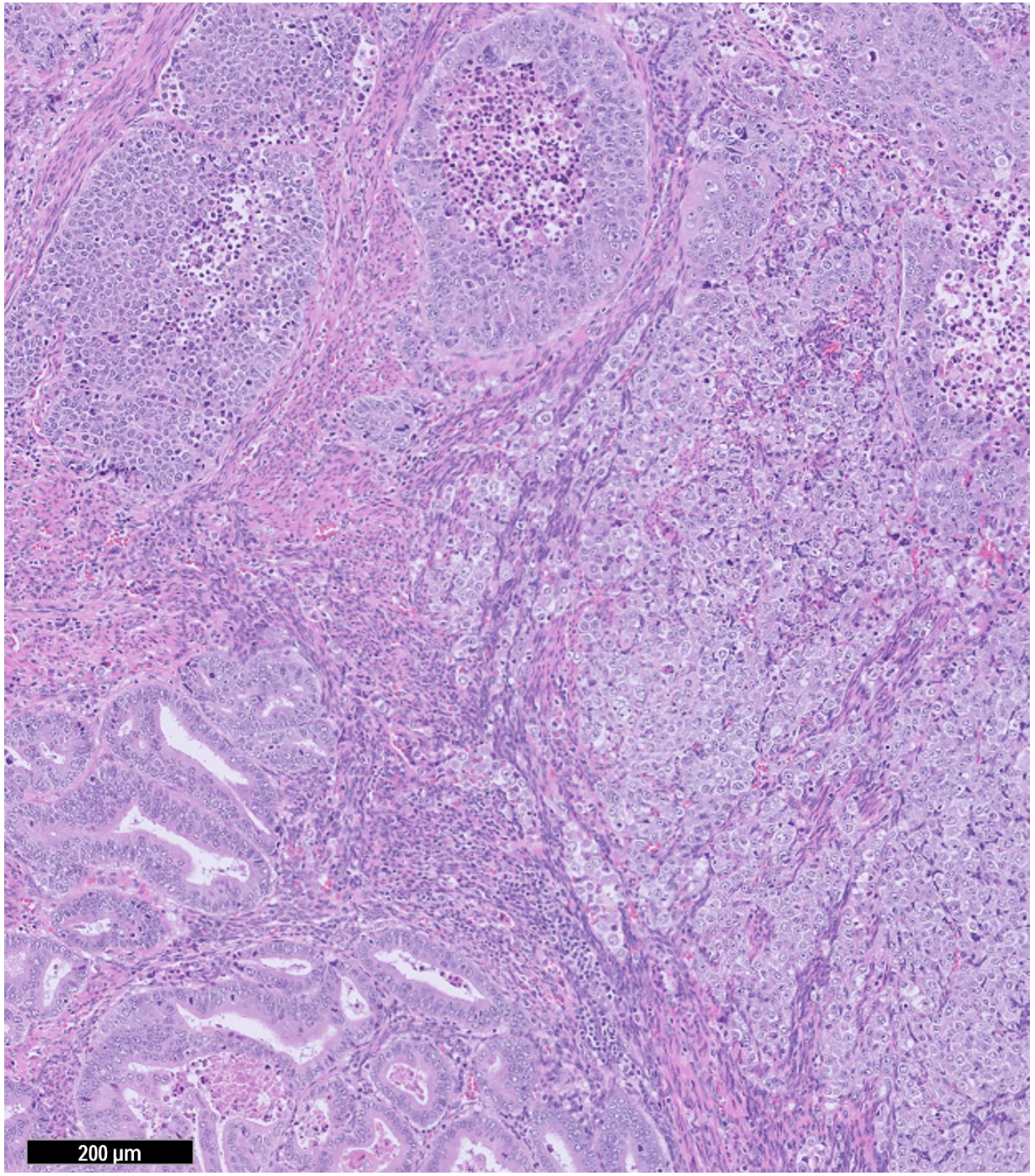

p53
200 µm
p53 controls
200 µm
200 µm

DIAGNOSIS?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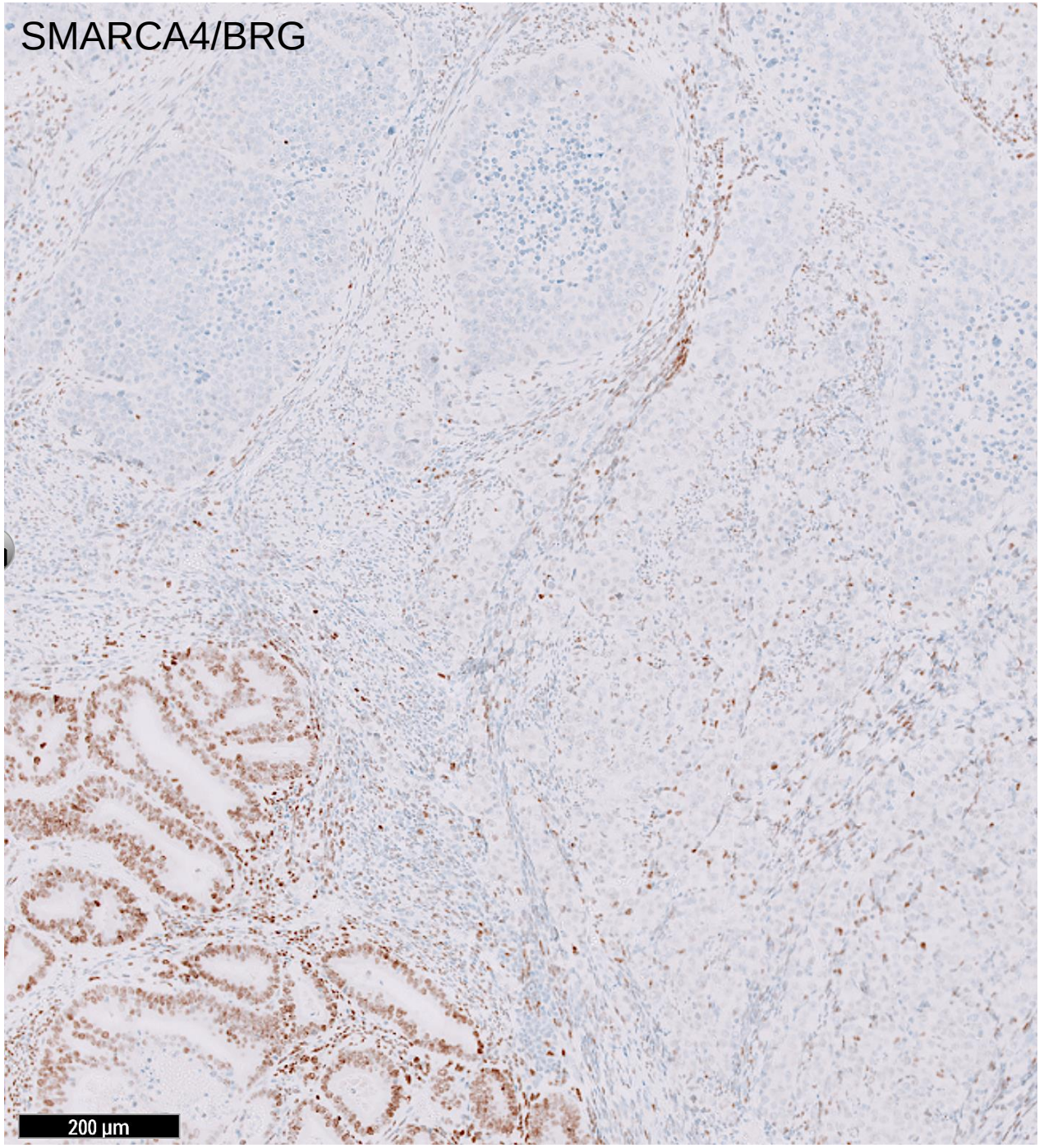
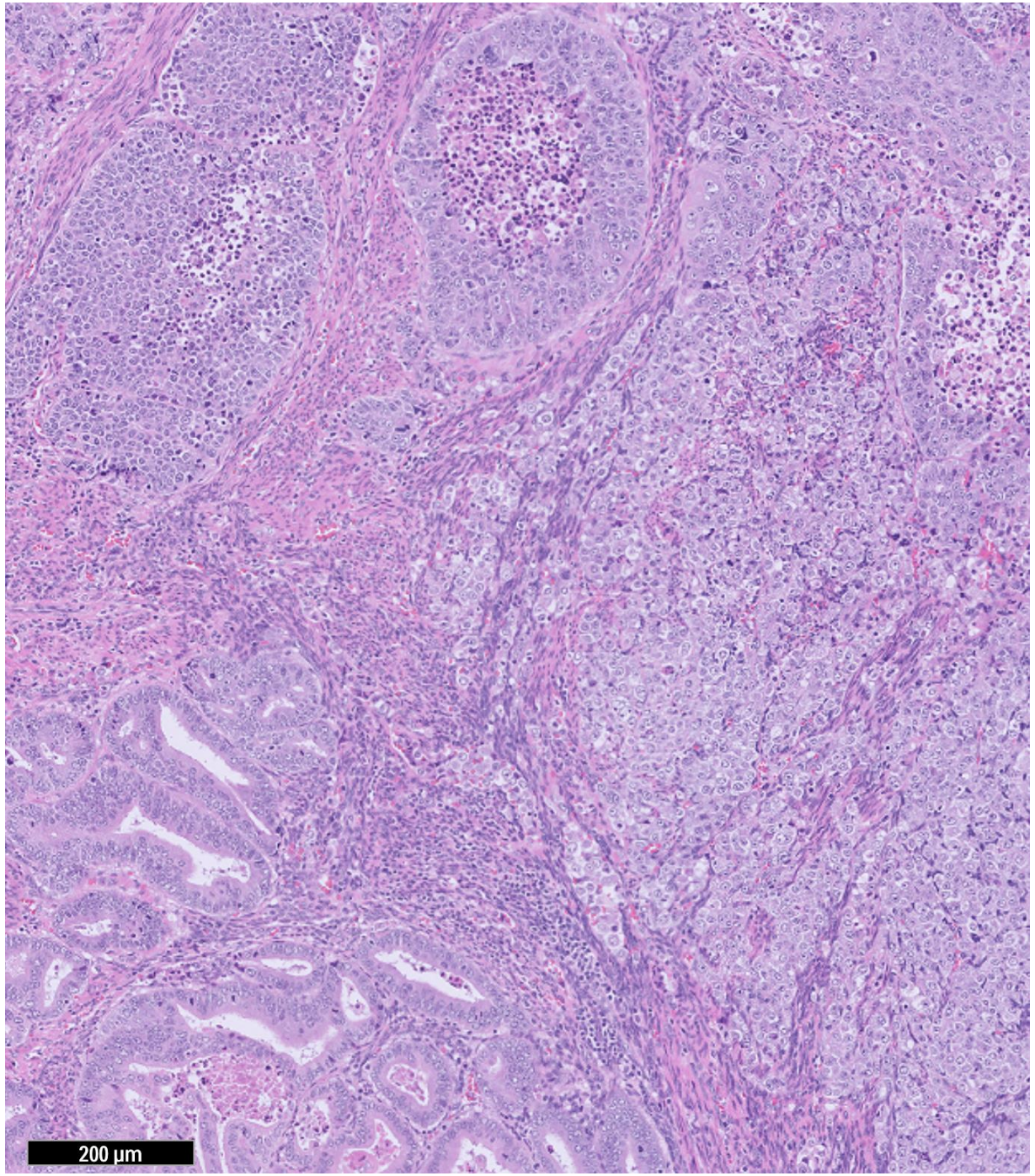

SMARCA4/BRG
200 µm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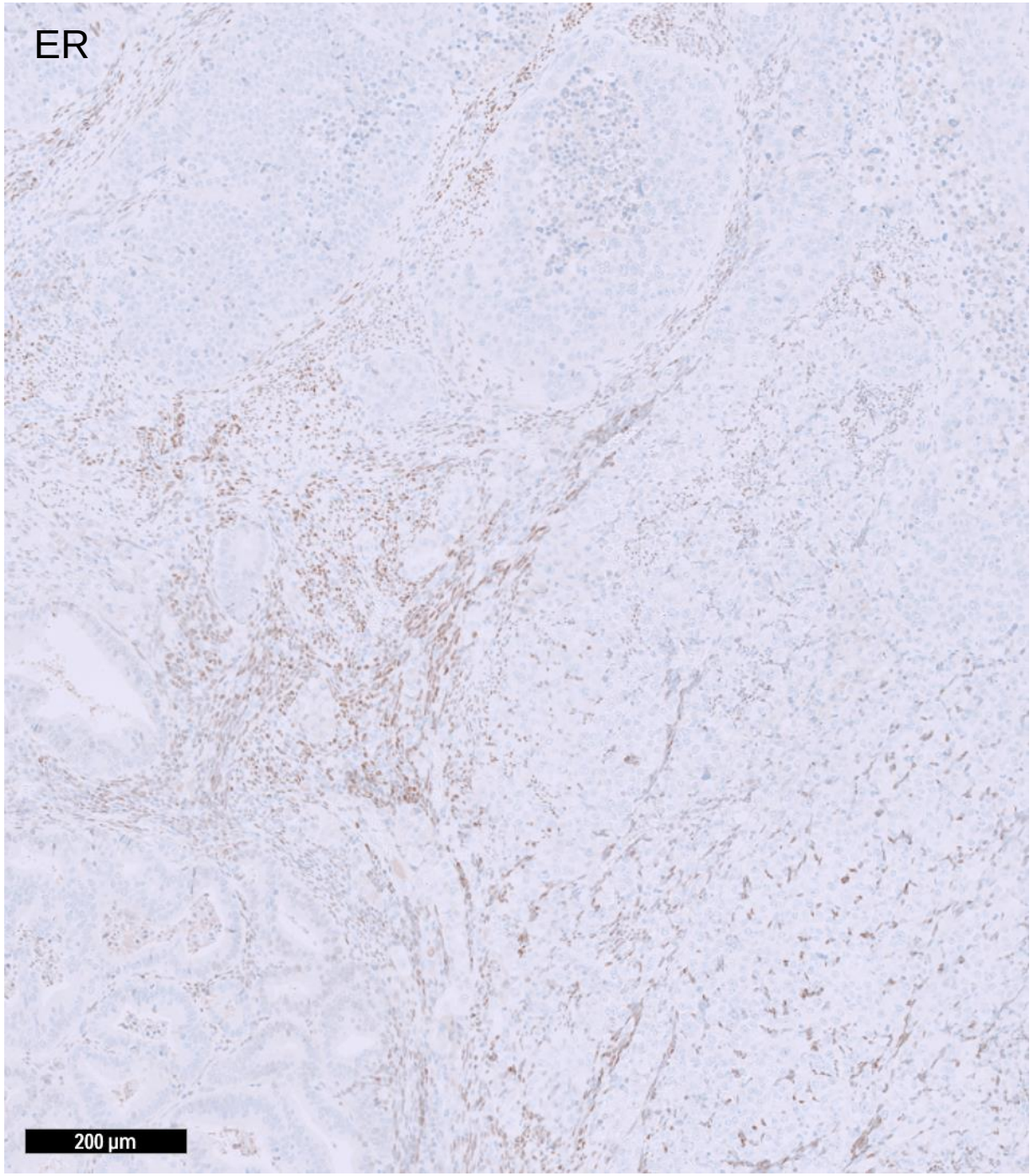
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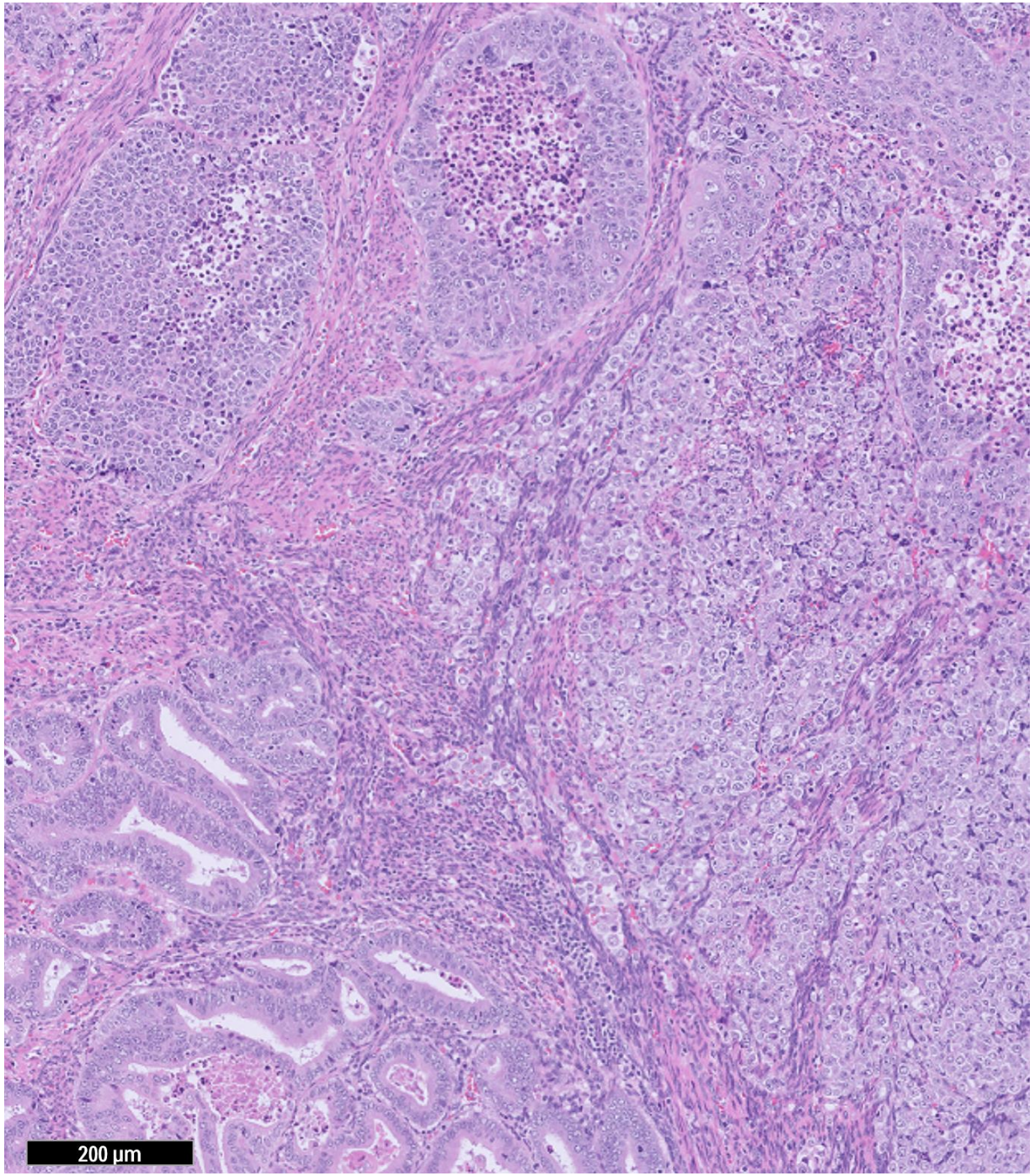
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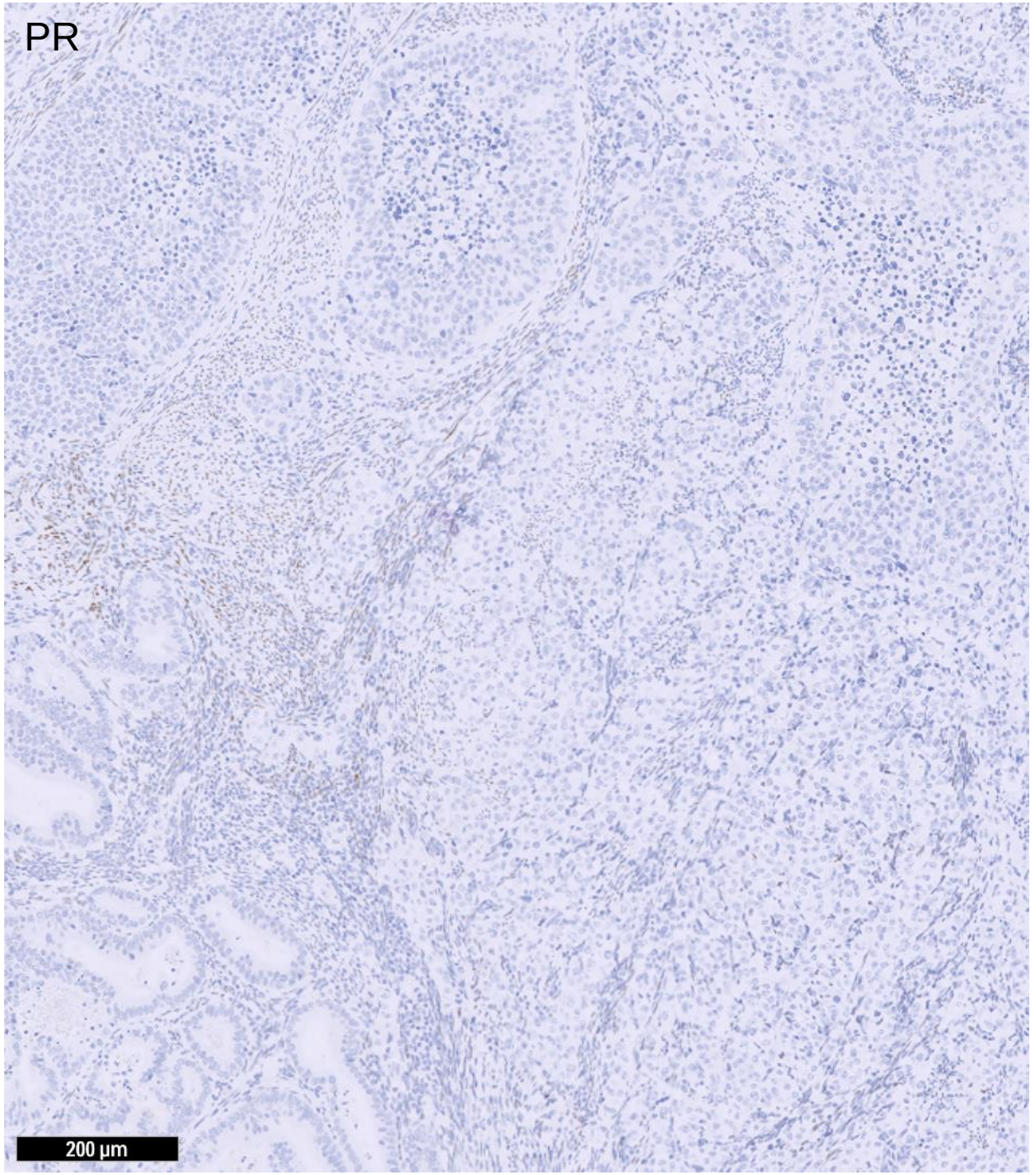
PR
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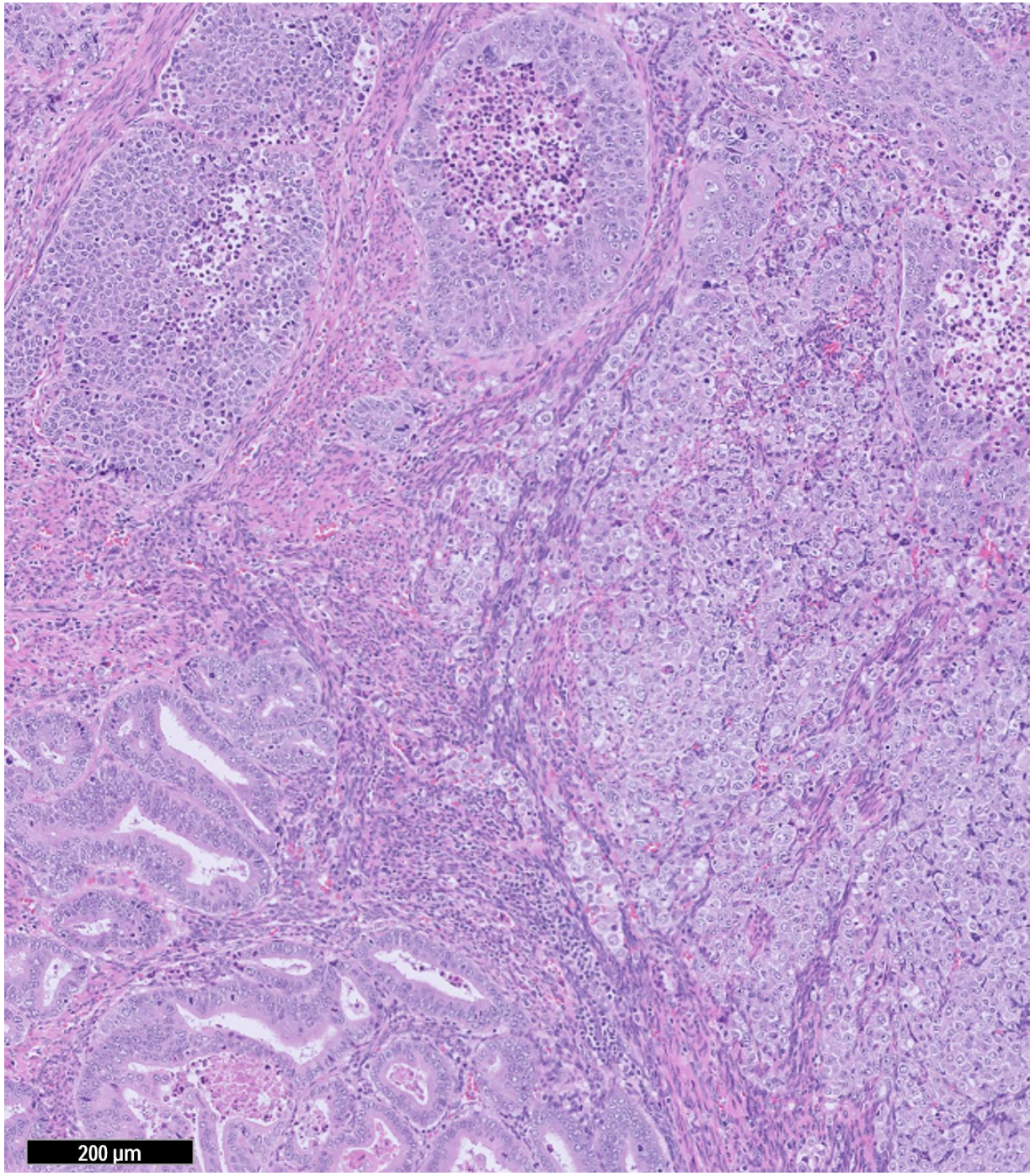
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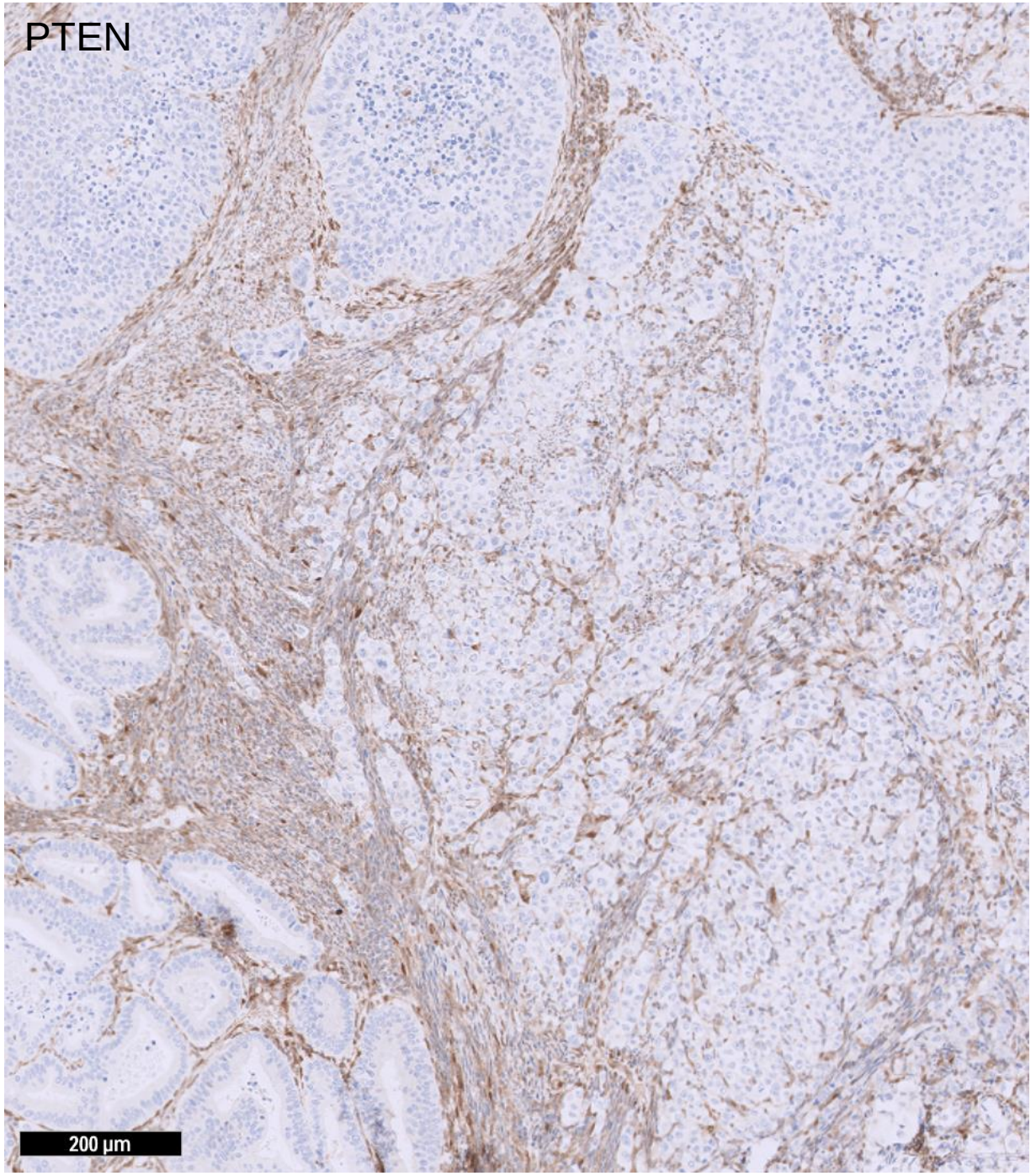
PTEN
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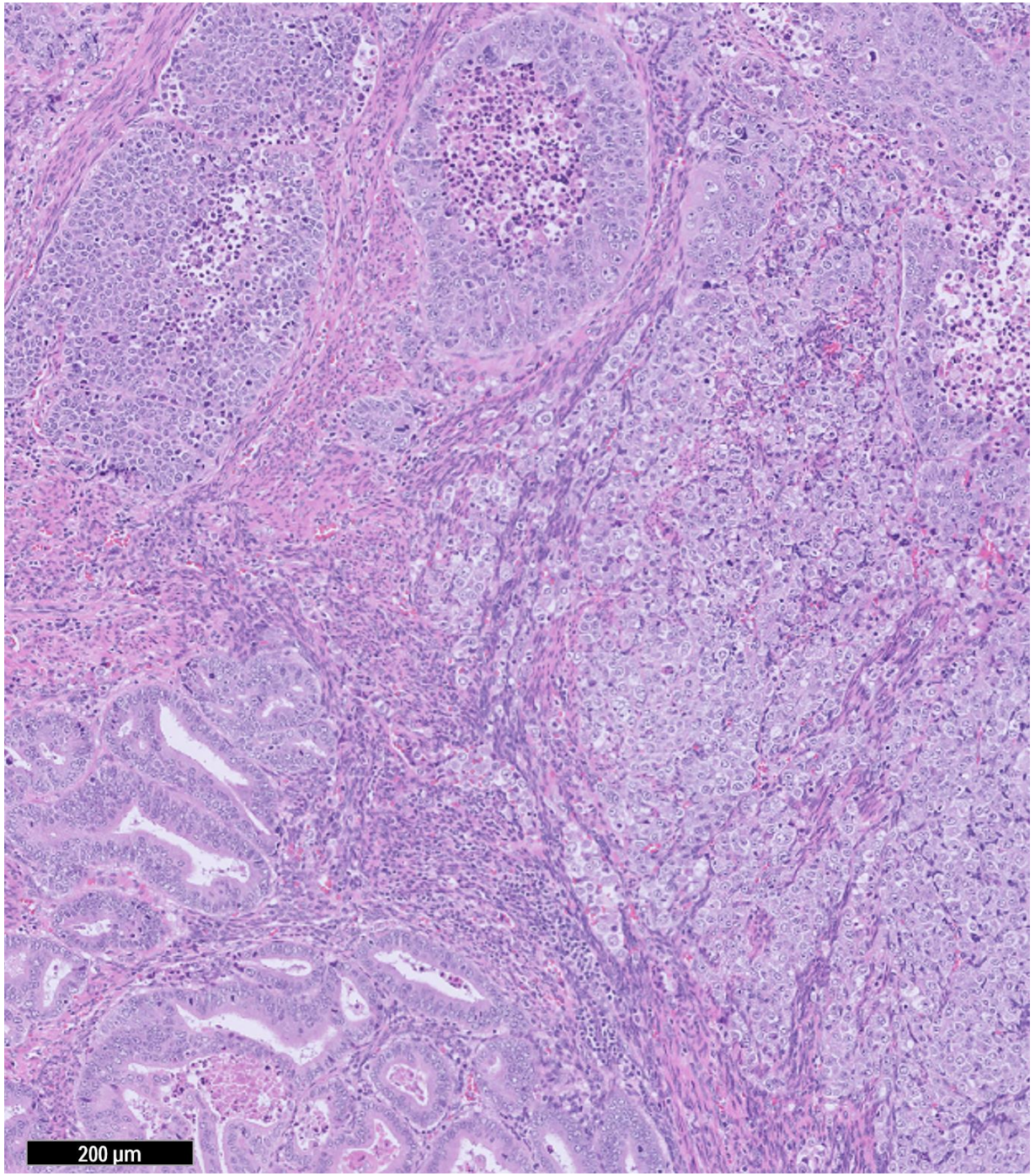
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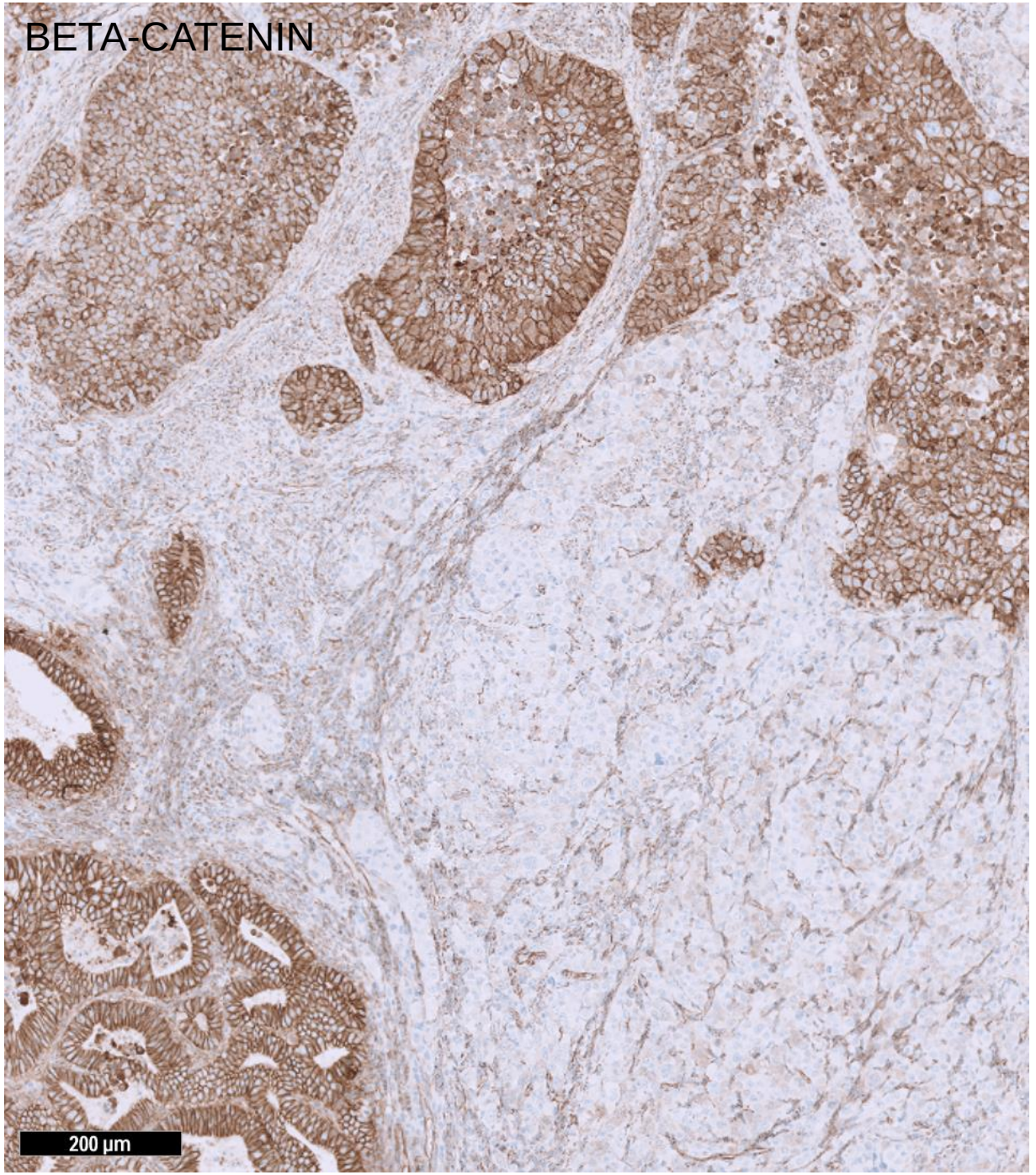
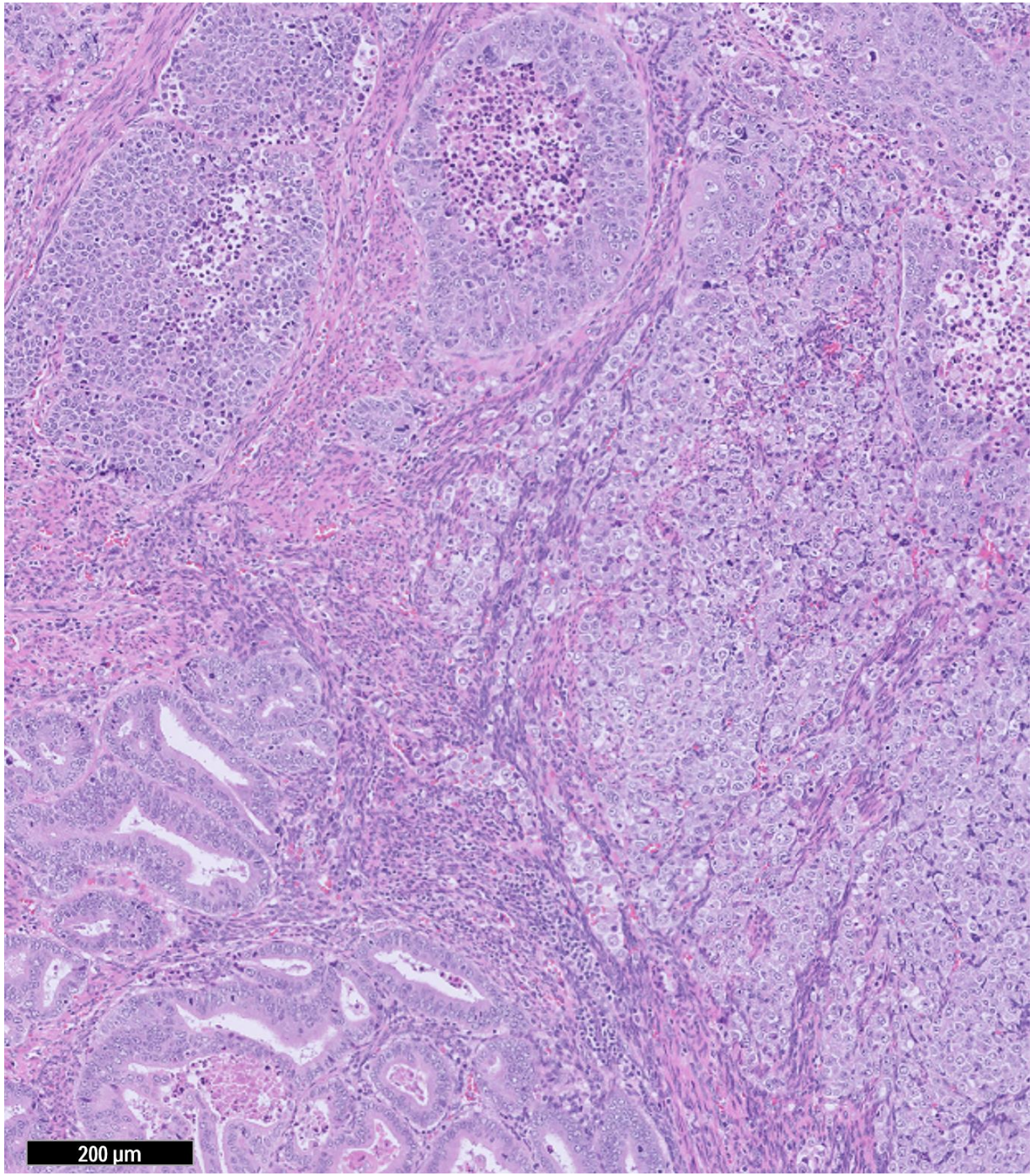
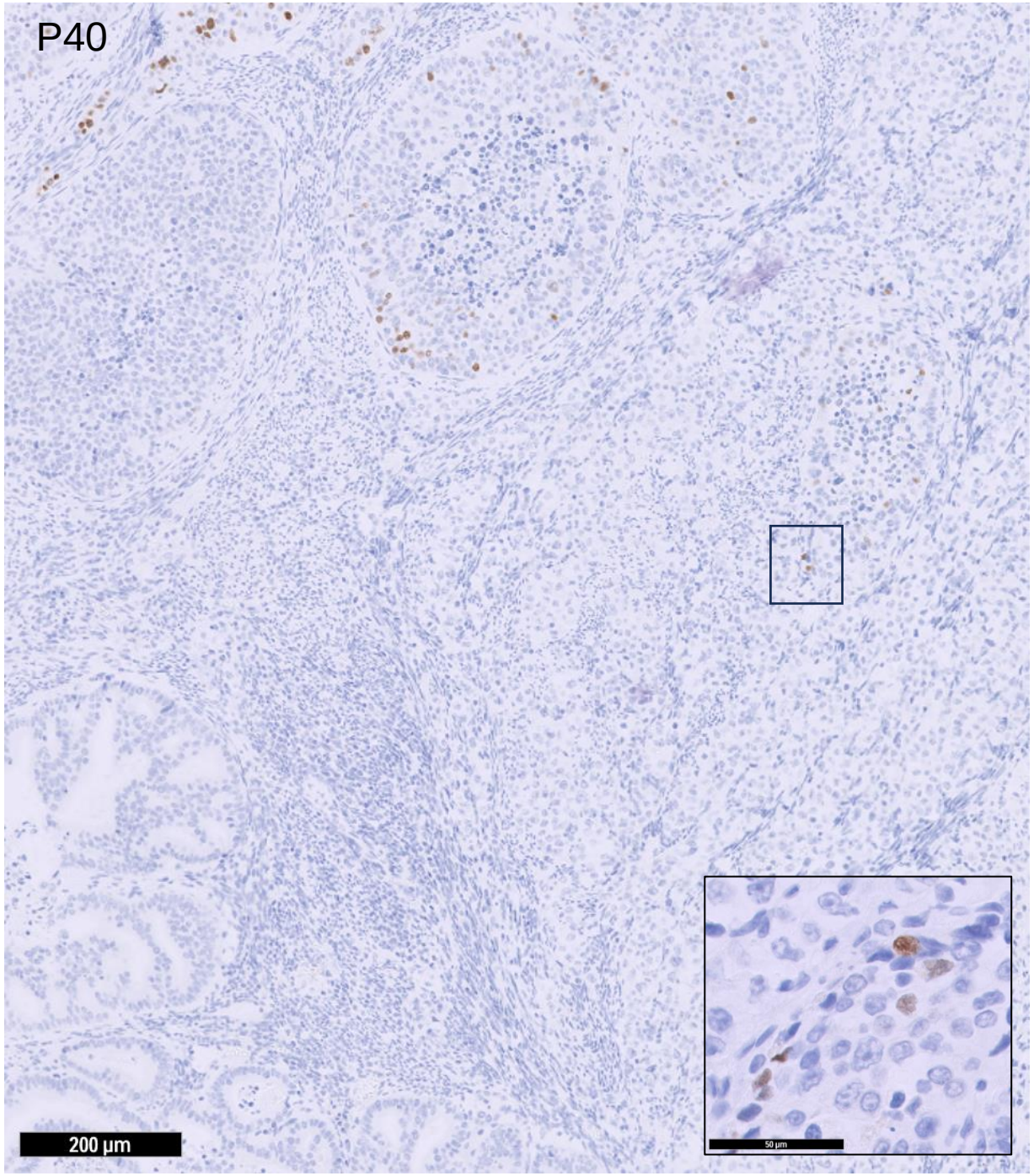
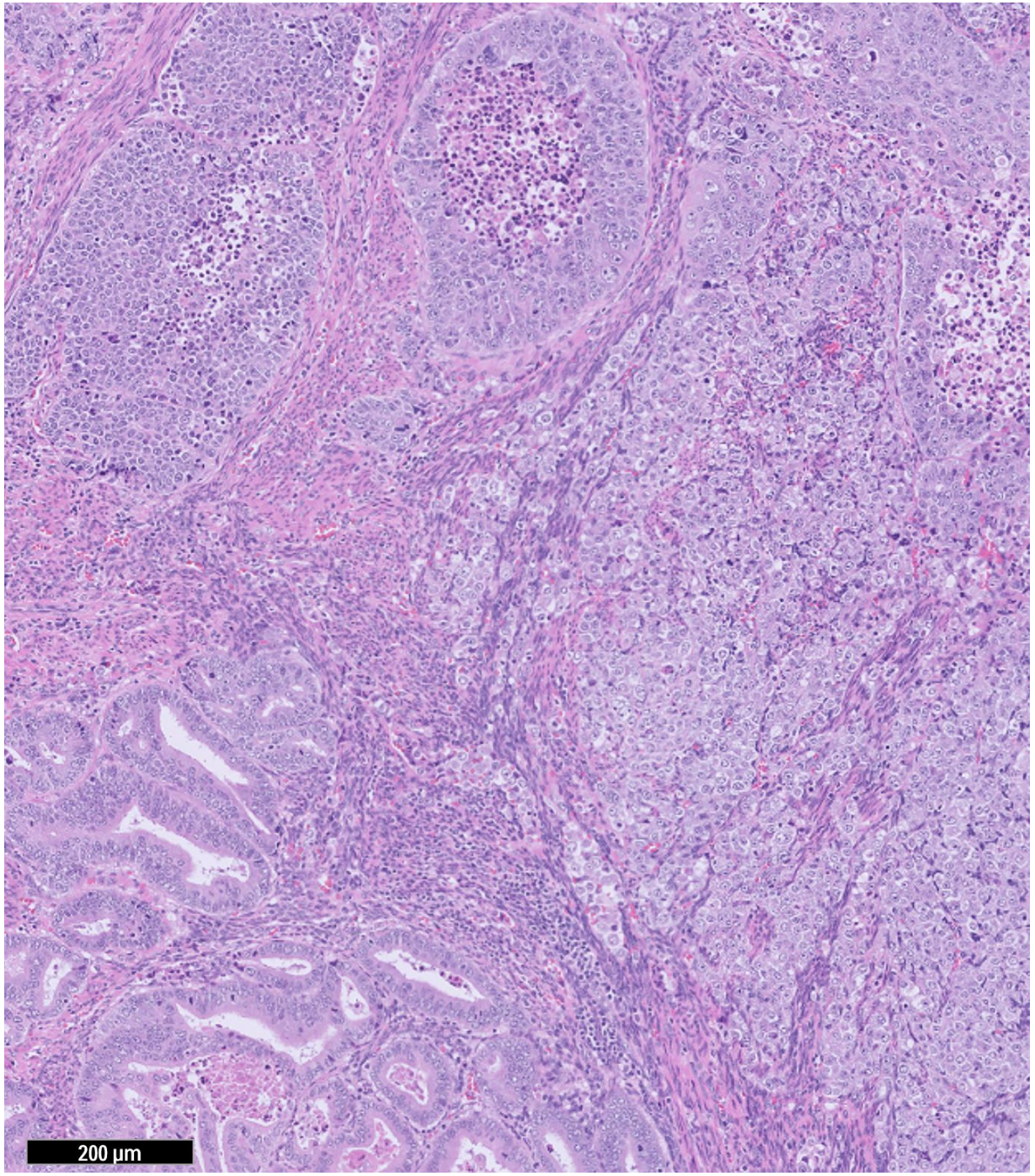
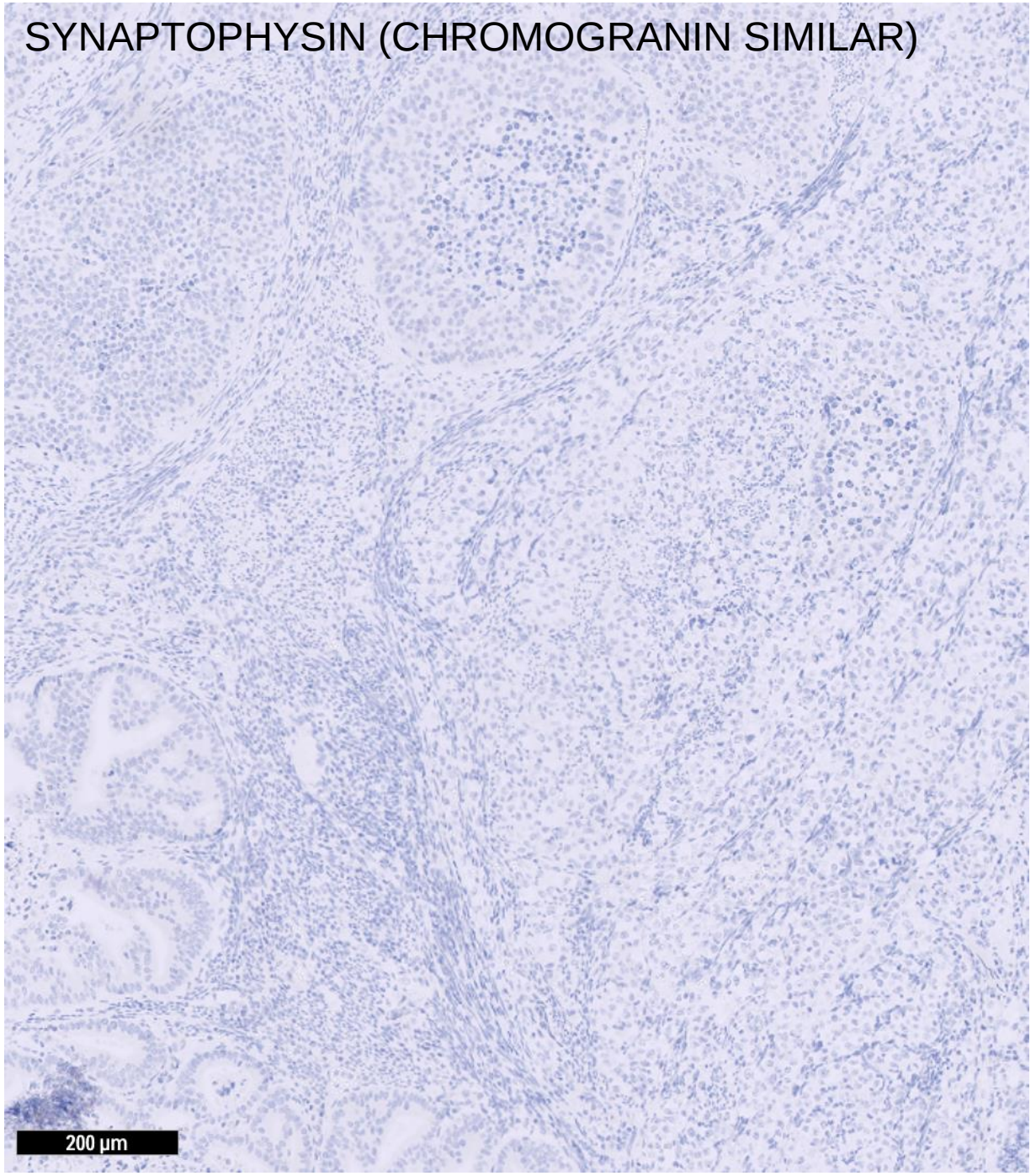

BETA-CATENIN
200 µm

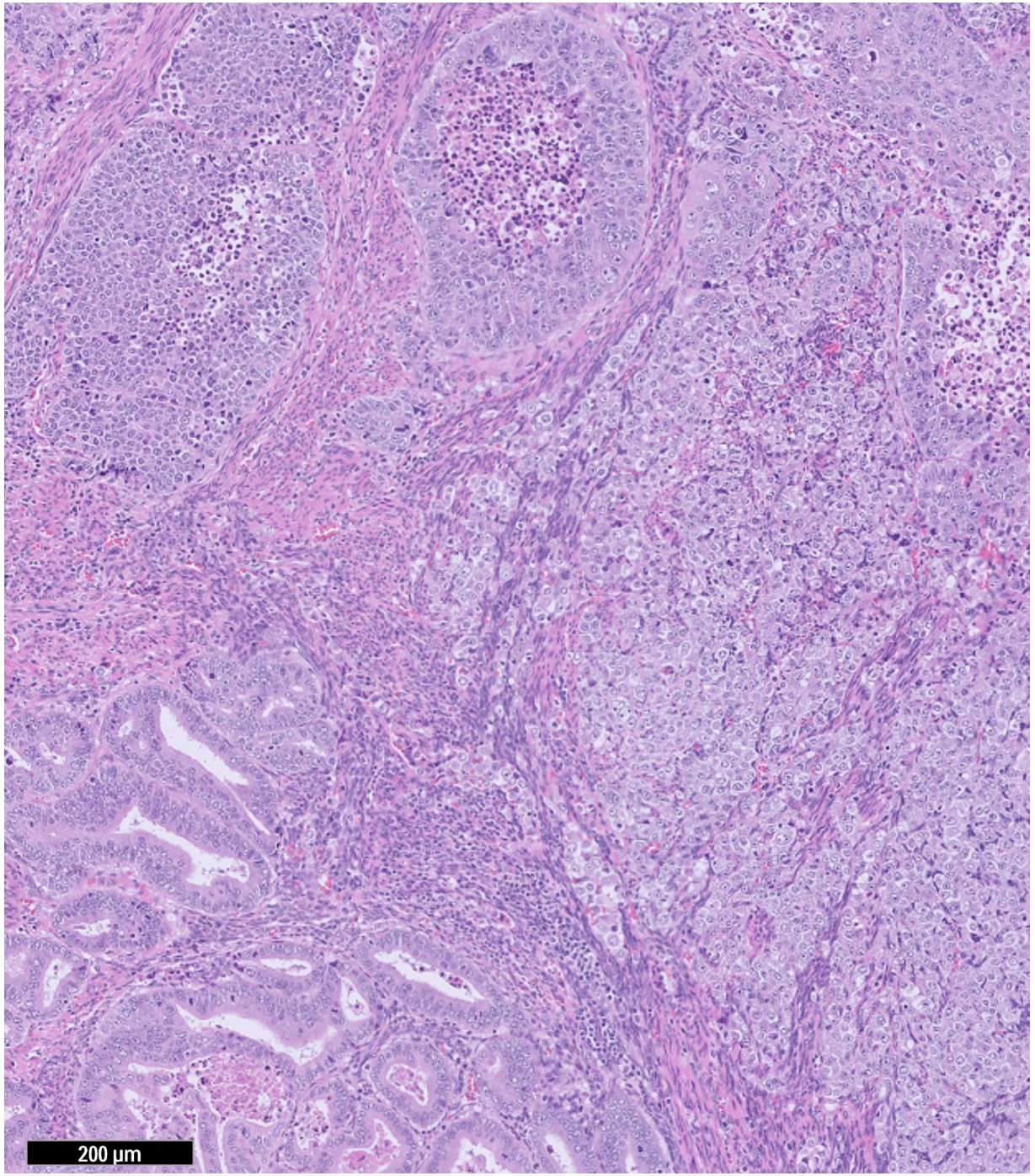

200 µm


P40
200 µm
50 µm



SYNAPTOPHYSIN (CHROMOGRANIN SIMILAR)

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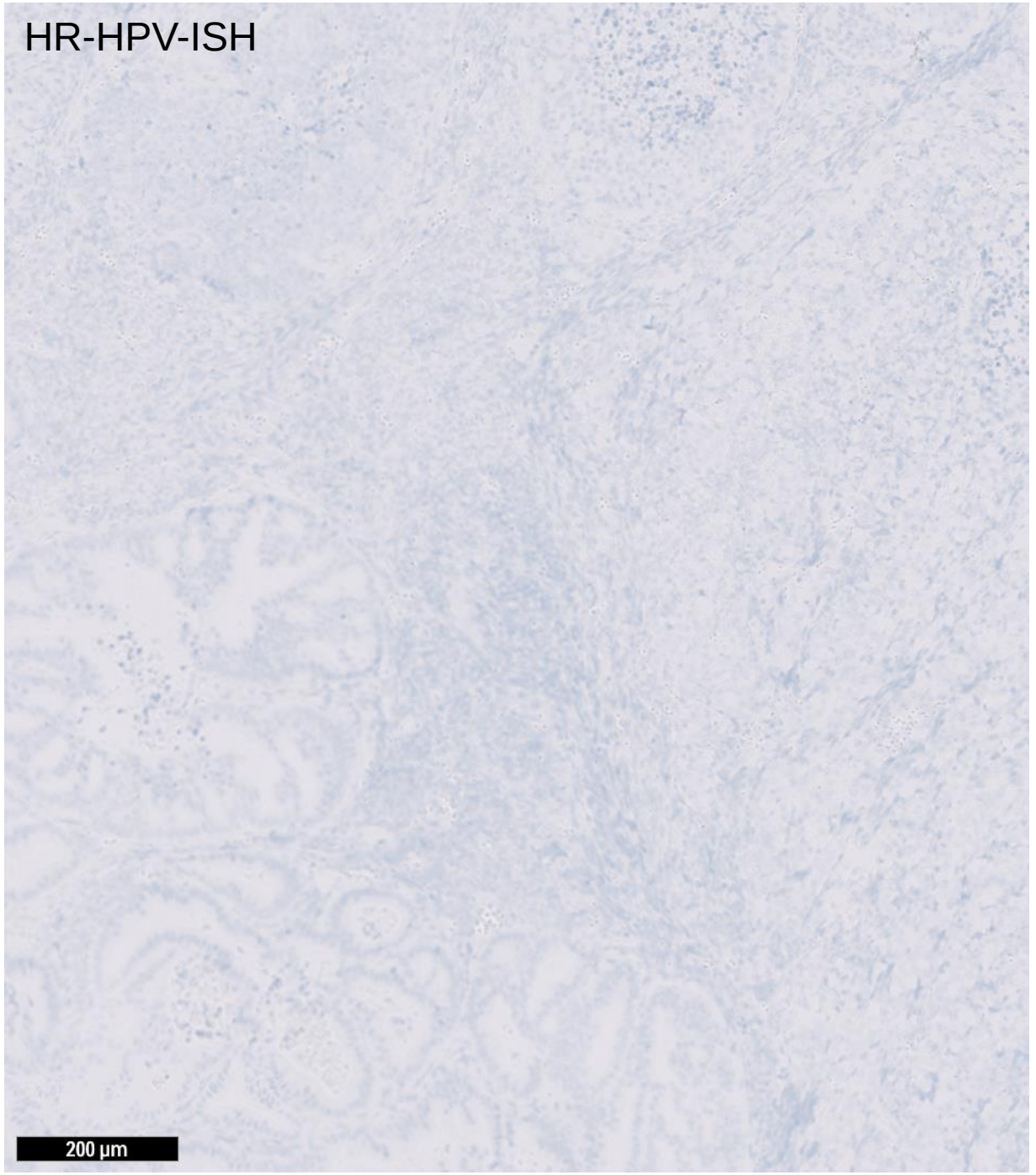

HR-HPV-ISH
200 µm

DEDIFFERENTIATED ENDOMETRIAL CARCINOMA

DEFINITION:
- Dedifferentiated Carcinoma (DC): undifferentiated + differentiated carcinoma (typically endometrioid)
    - Undifferentiated Carcinoma (UC): epithelial neoplasm with no overt cell lineage differentiation

CLINICAL:
- Median Age 55 yo (30–80 yo)
- 2% of Endometrial Cancer
- Highly Aggressive (regardless of UC%) but POLE-mutation associated with favorable prognosis

PATHOGENESIS:
- UC clonally related differentiated component
- ½ to 2/3 MMR-D/MSI-H associated (possible in copy-number–low, POLE-mutated, TP53-mutated)
- PTEN, PIK3CA, and/or PIK3R1 in > ½.
- SWI/SNF complex mutations in 2/3 DC, ½ UC (SMARCA4/BRG1, SMARCB1/INI1, ARID1A/B in UC component)

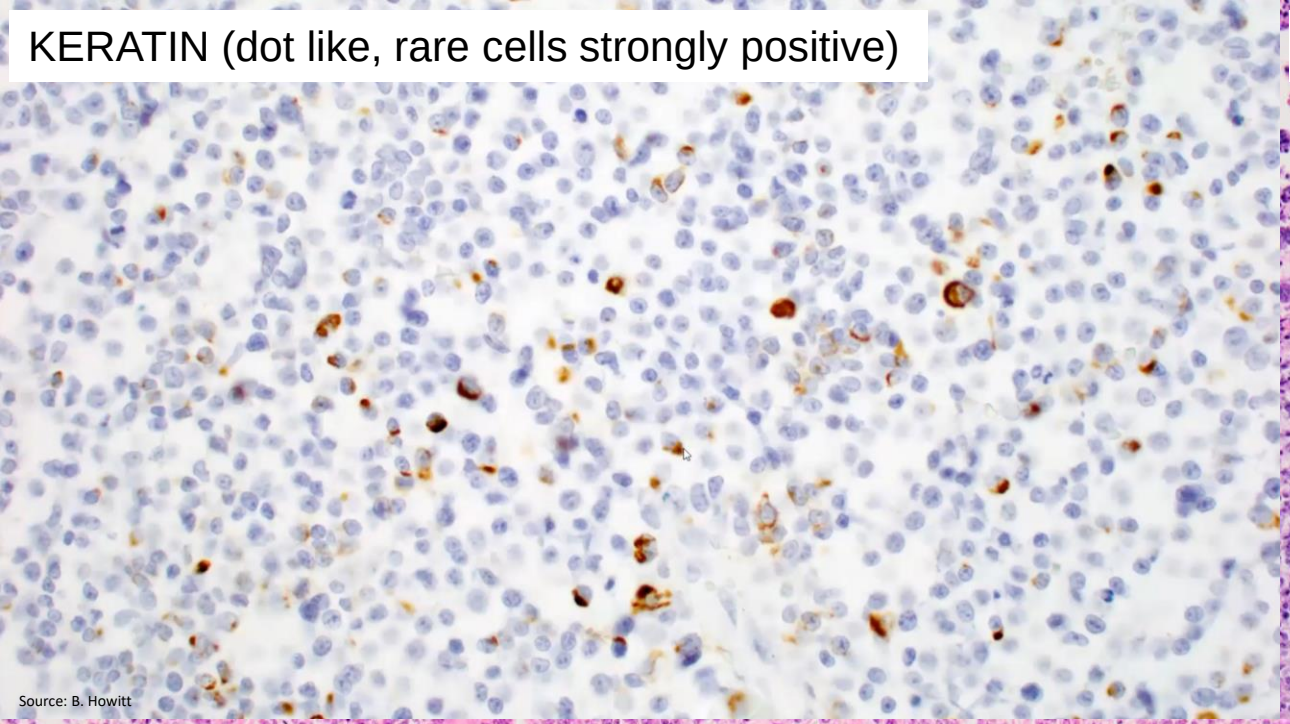
DDX:
- FIGO Grade 3 EC, Solid Serous Carcinoma
- High-Grade Neuroendocrine Carcinoma
- Sarcoma, Carcinosarcoma, Hematolymphoid

MORPHOLOGY:
- Monomorphic, small-intermediate, discohesive
- Sheets (no nests, trabeculae, glands)
- Occasionally rhabdoid; stroma unapparent or myxoid
- Chromatin usually condensed, >30 mitoses/10 HPF
- TILs often numerous, geographical necrosis frequent
- Differentiated carcinoma: mostly FIGO grade 1-2 endometrioid carcinoma (rare FIGO grade 3 endometrioid, serous carcinoma reported)
- Components vary in proportion, abrupt or admixed

IHC: (UC)
- Epithelial differentiation: rare; very focal but intense/often perinuclear dot-like EMA/Keratin. Diffuse strong Pancytokeratin should NOT be present. Claudin4 helpful.
- Often Lost: PAX8, ER, PR, E-cadherin (50%)
- SMARCA4(BRG1)/SMARCB1(INI1): loss in 33%
- p53: often mutant in SMARCA4/B1-intact tumors
- MMR: 50-66% MMR-D/MSI-H
- Chromogranin/Synaptophysin: positive in < 10% of cells
- CD34: negative

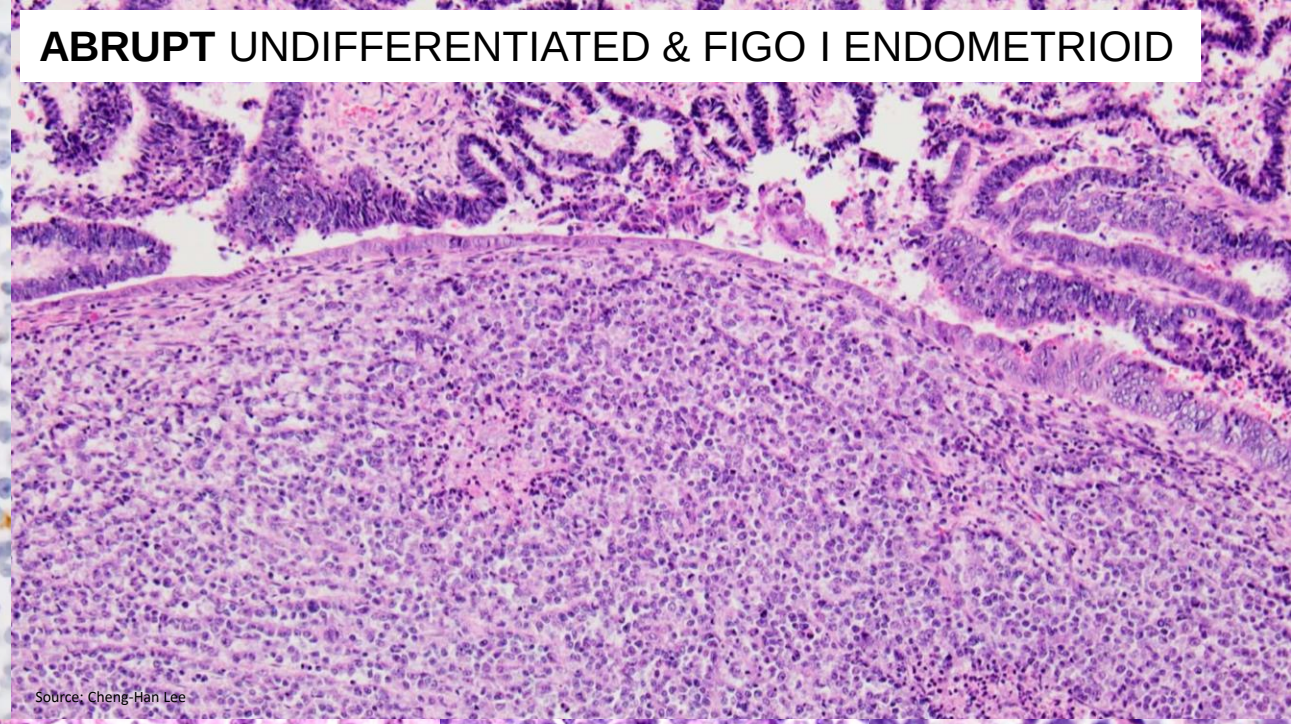
Palacios J, Ramalingam P, Cheng-Han L, et al. Undifferentiated and dedifferentiated carcinomas of the uterine corpus. In: WHO Classification of Tumours Editorial Board. Female genital tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2020 [cited 2023 09 28]. (WHO classification of tumours series, 5th ed.; vol. 4). Available from: https://tumourclassification.iarc.who.int/chapters/34.

KERATIN (dot like, rare cells strongly positive)

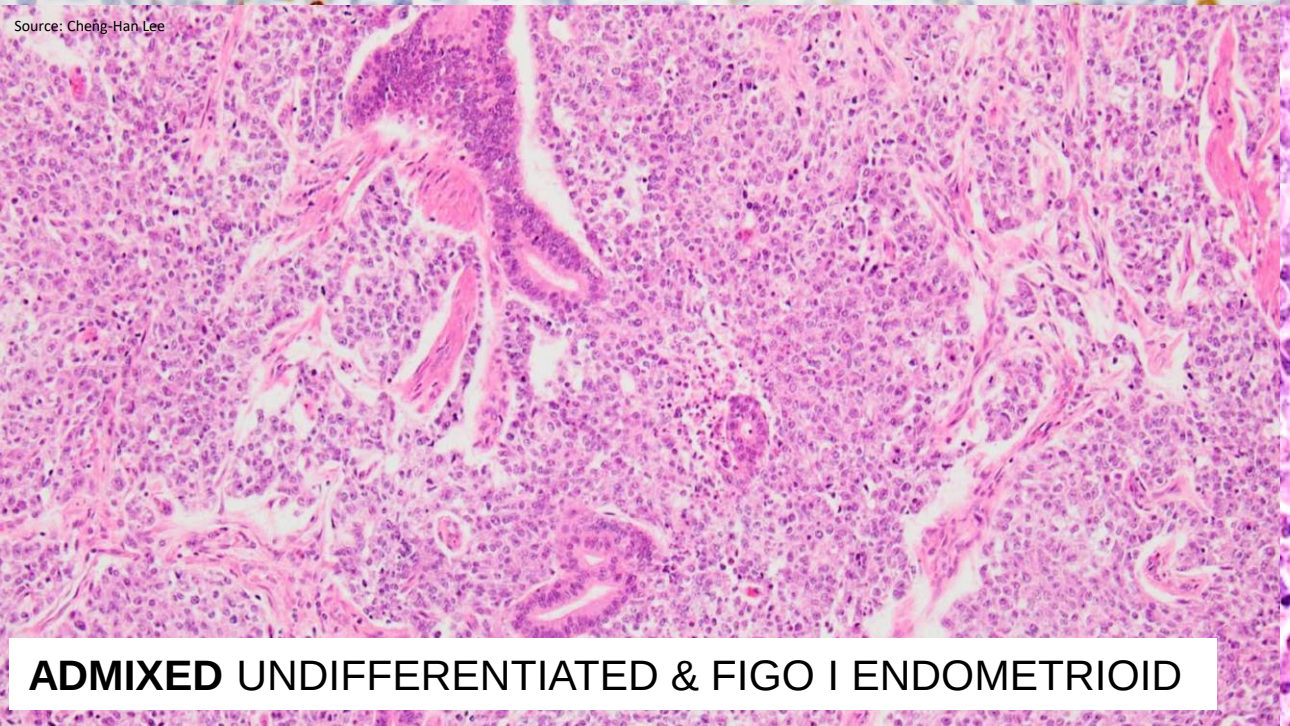


Source: B. Howitt

ABRUPT UNDIFFERENTIATED & FIGO I ENDOMETRIOID

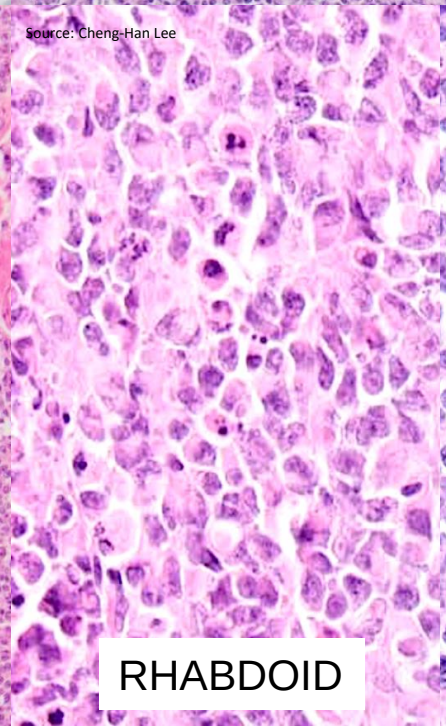


Source: Cheng-Han Lee



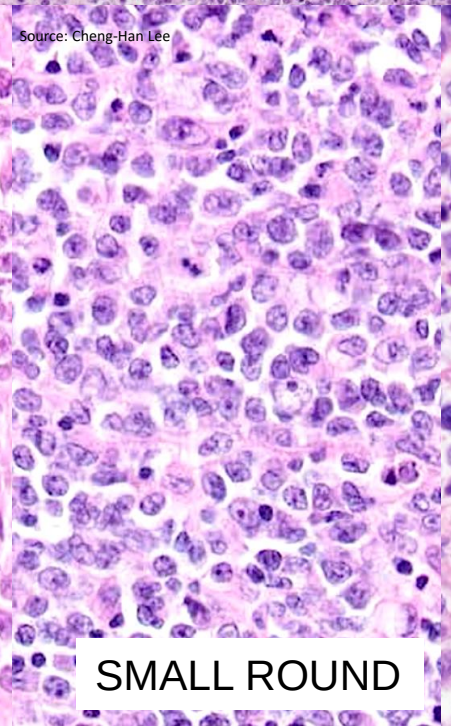
Source: Cheng-Han Lee

ADMIXED UNDIFFERENTIATED & FIGO I ENDOMETRIOID



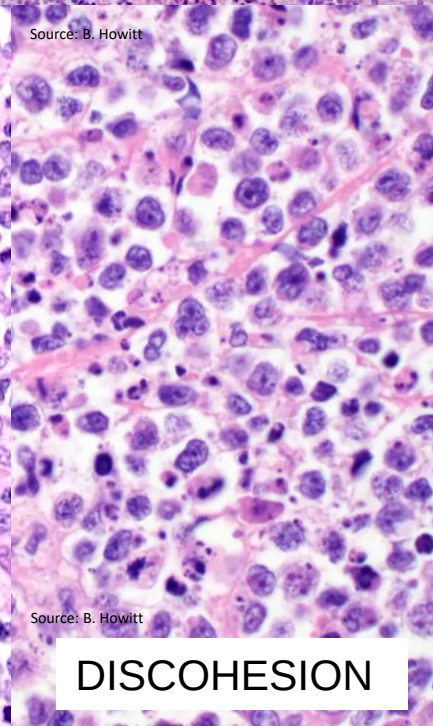
Source: Cheng-Han Lee

RHABDOID



Source: Cheng-Han Lee

SMALL ROUND



Source: B. Howitt

Source: B. Howitt

DISCOHESION

SMARCA4/BRG1

- SMARCA4: a member of the SWI/SNF chromatin remodeling complex

- Undifferentiated carcinomas of many sites have loss of SMARCA4 or SMARCB1; typically have many additional genetic abnormalities
  - Thoracic SMARCA4-deficient undifferentiated tumour:
    - 44% show additional mutations in *KRAS*, *STK11*, and/or *KEAP1*. Multiple, mostly non-recurrent copy-number alterations are present across the tumour genome. *TP53* inactivation is common.
  - Undifferentiated Endometrial Carcinoma:
    - 50-66% MMR-D/MSI-H associated, (some copy-number–low, POLE-mutated, TP53-mutated); many have *PTEN, PIK3CA*, and/or *PIK3R1* mutations.
  - Gastric Undifferentiated Carcinoma:
    - Origin via dedifferentiation

- SWI/SNF-Deficient Sarcomas: younger age, even more aggressive, fewer genetic abnormalities compared with carcinomas (*SMARCA4* sole driver mutation; few other somatic protein-coding mutations); Microsatellite stable; thought to be Claudin-4 negative.
  - Small Cell Carcinoma of the Ovary Hypercalcemic Type
  - SMARCA4 Deficient Undifferentiated Uterine Sarcoma
  - Atypical Teratoid/Rhabdoid Tumors

Palacios J, Ramalingam P, Cheng-Han L, et al. Undifferentiated and dedifferentiated carcinomas of the uterine corpus. In: WHO Classification of Tumours Editorial Board. Female genital tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2020 [cited 2023 09 28]. (WHO classification of tumours series, 5th ed.; vol. 4). Available from: https://tumourclassification.iarc.who.int/chapters/34.

DEDIFFERENTIATED ENDOMETRIAL CARCINOMA
Take home points

- Diagnostic Criteria (WHO 2020):
  - Essential: undifferentiated histology and immunophenotype (for the undifferentiated carcinoma/component).
  - Desirable: genetic analysis or IHC showing inactivating mutations or loss of expression of SMARCA4 (BRG1), SMARCB1 (INI1), or both ARID1A and ARID1B.

- Undifferentiated Histology:
  - Discohesive, no nests/glands/trabeculae, loss of PAX8/ER, reduced keratin, <10% reactivity for NE markers

- Importance of recognition:
  - Worse prognosis most of the time
  - 25% of pts < 40 years old
  - Ddx considerations have different clinical management and/or prognosis

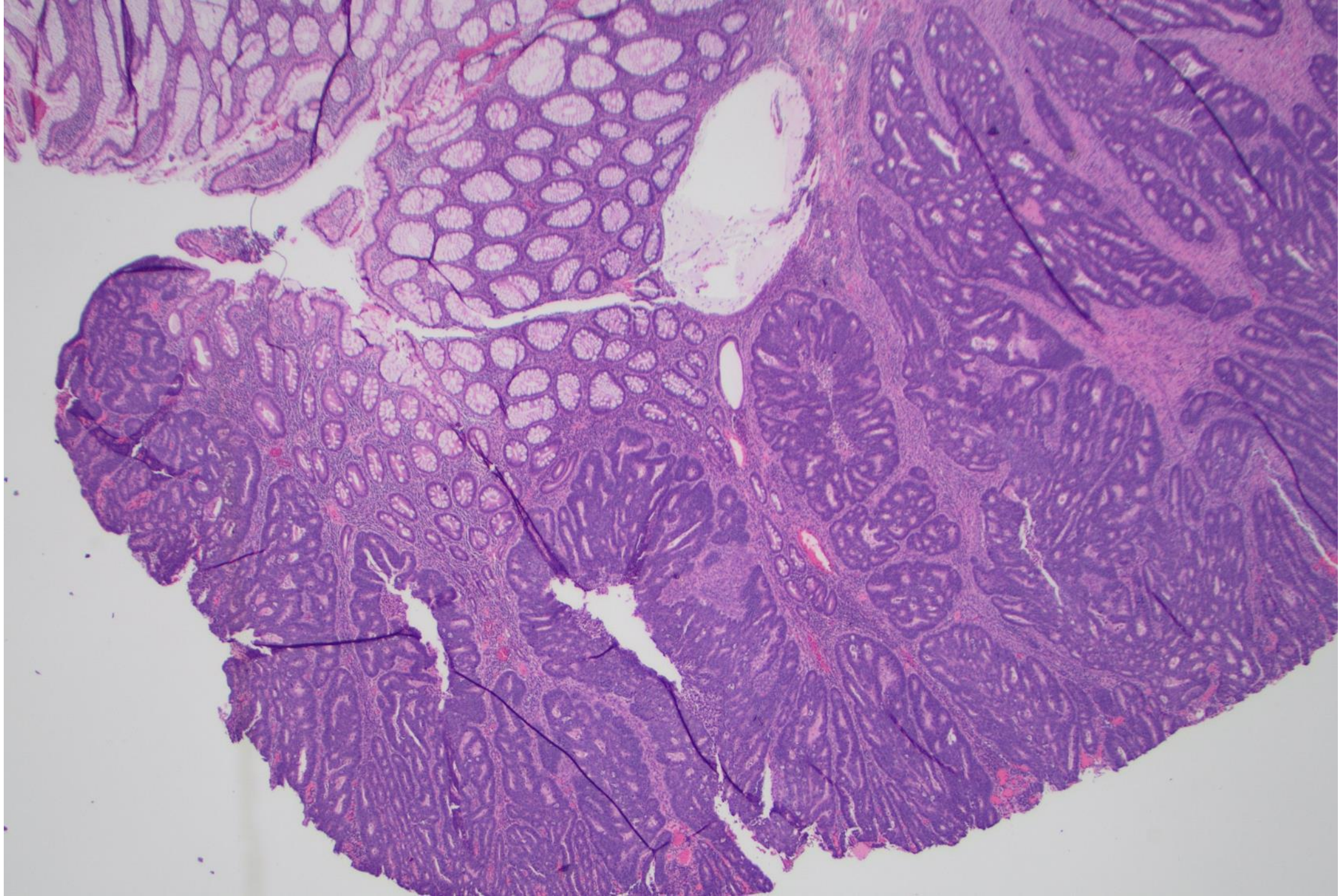
END

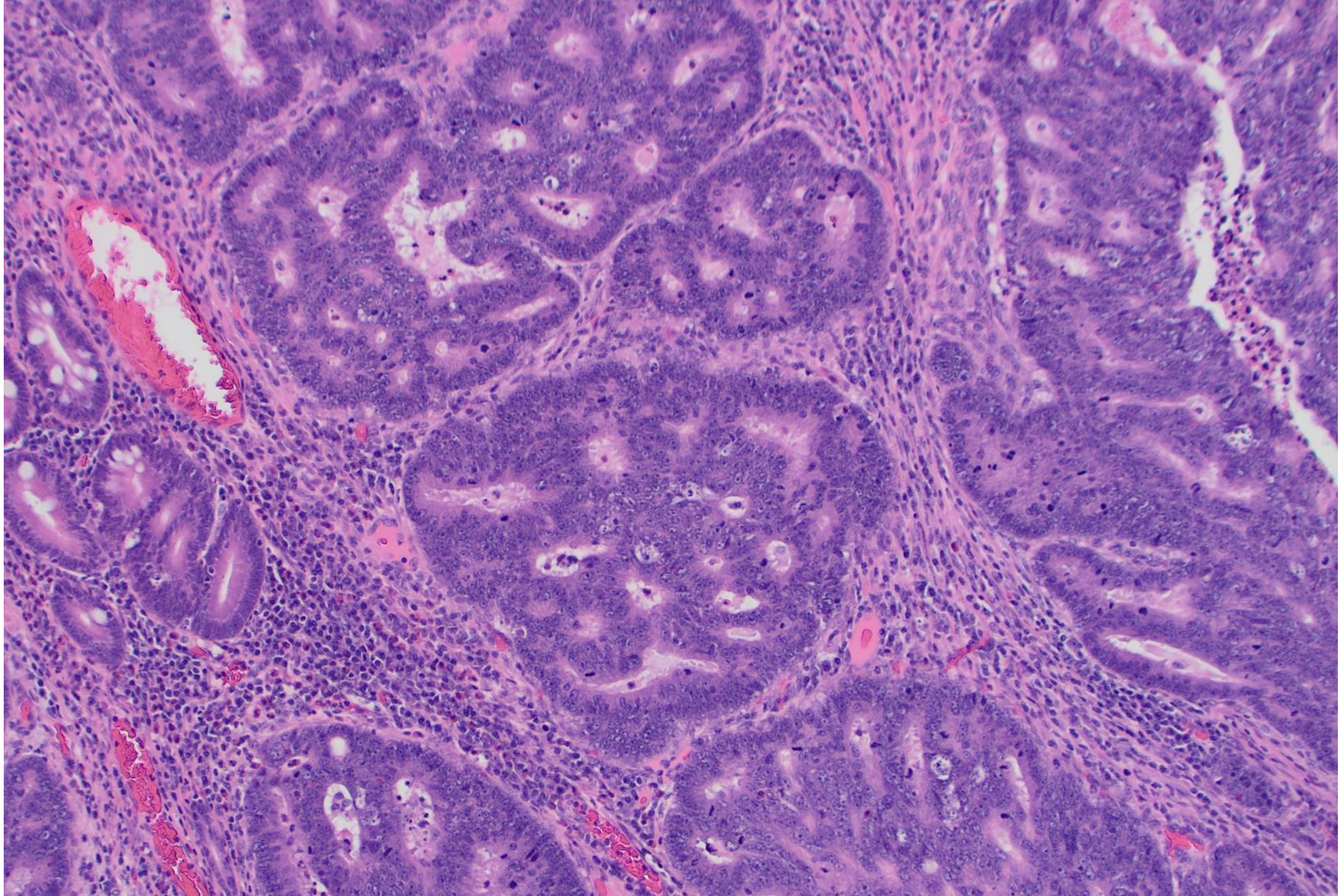
23-1006

Gregory Rumore; Kaiser Permanente

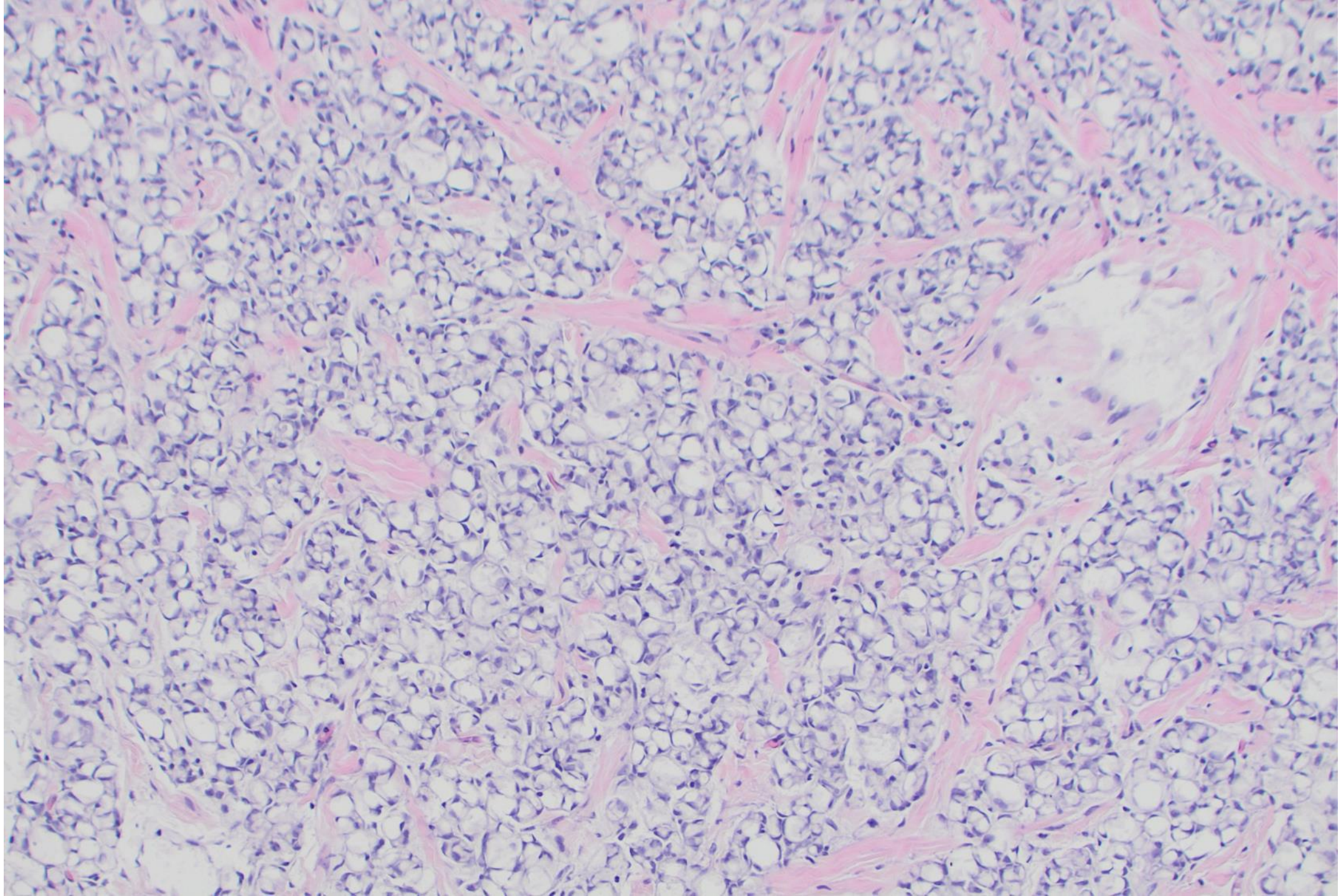
Late 50’s female with rectal CA. Omental nodules discovered during surgery.

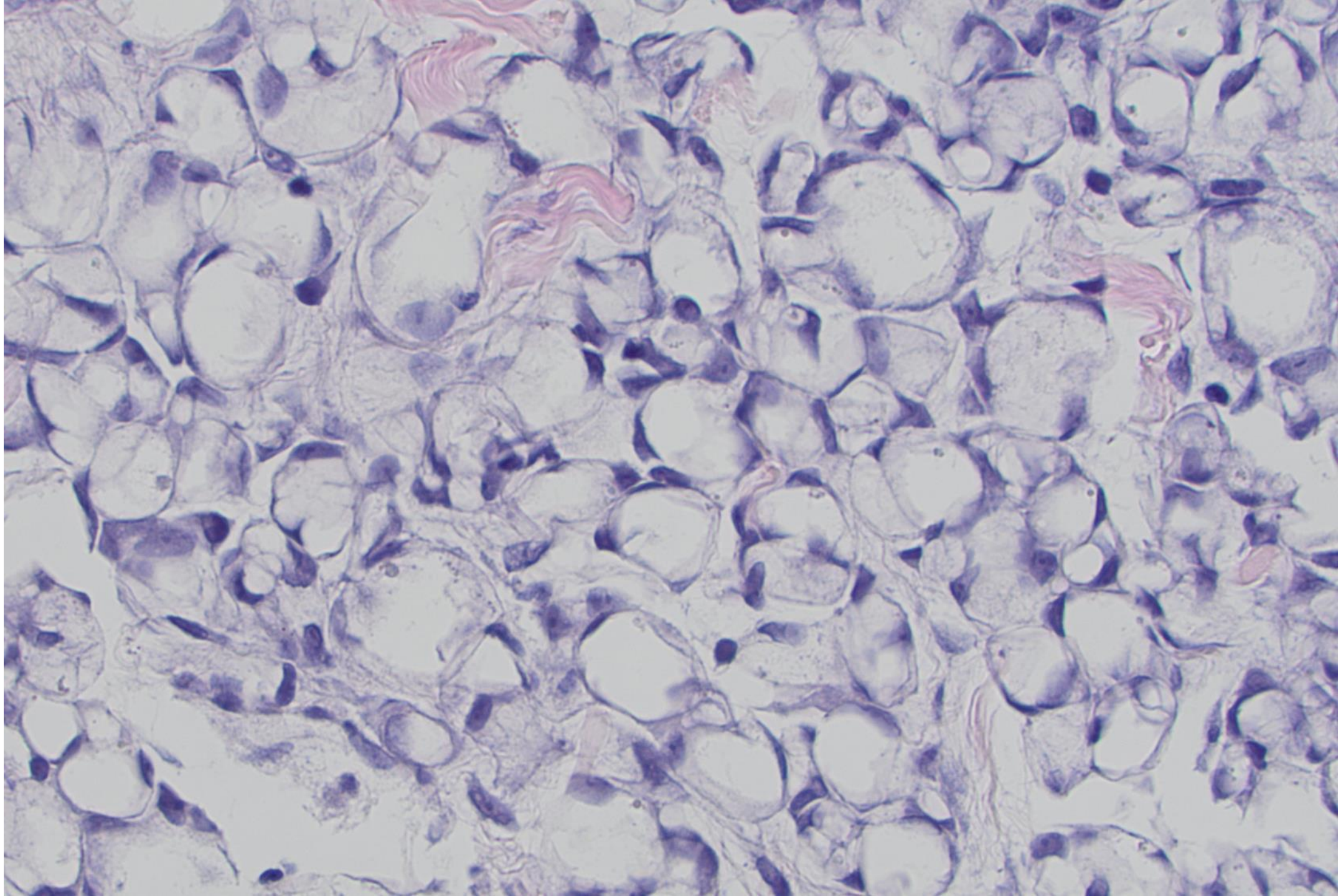
Rectum

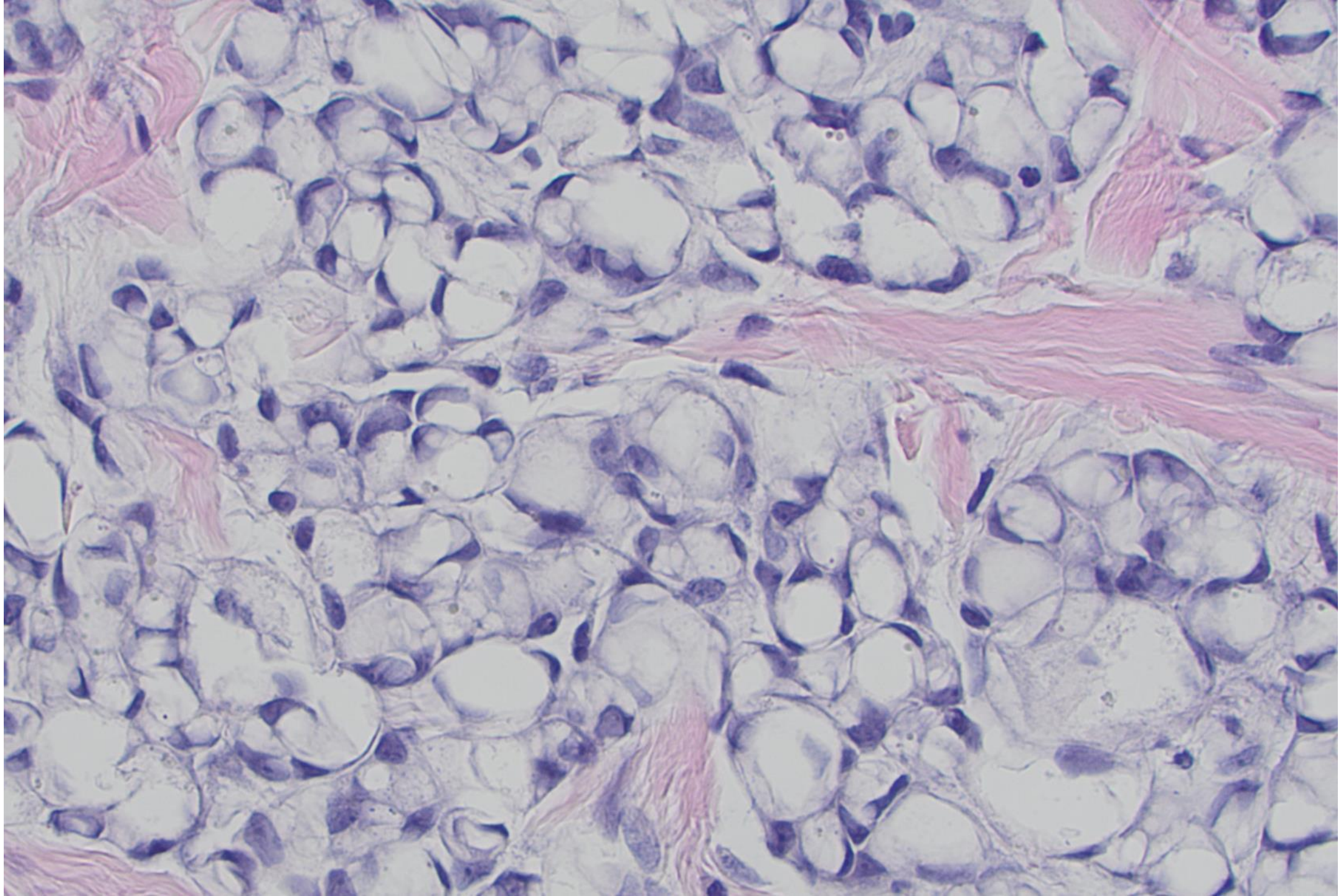


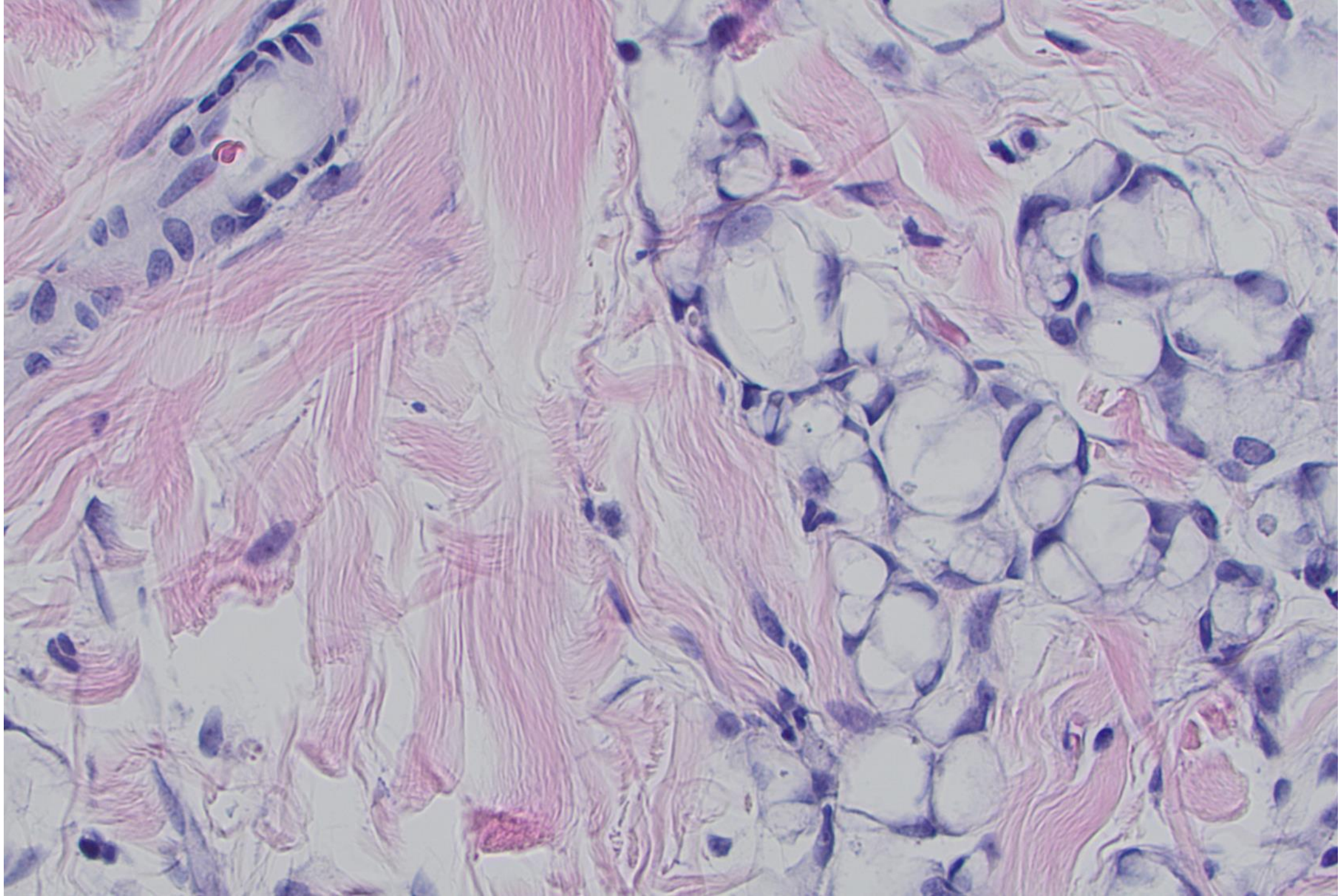


Omentum

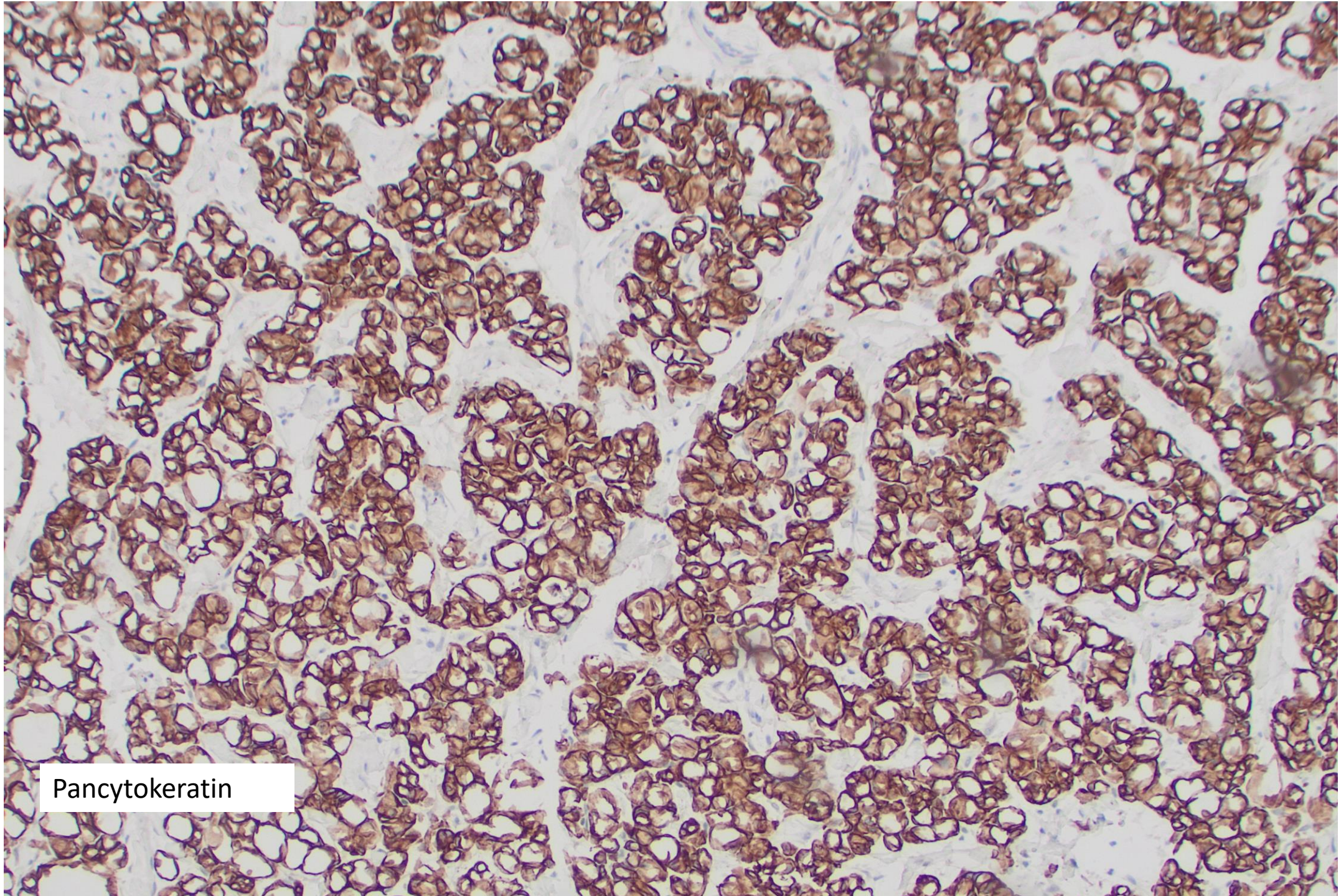


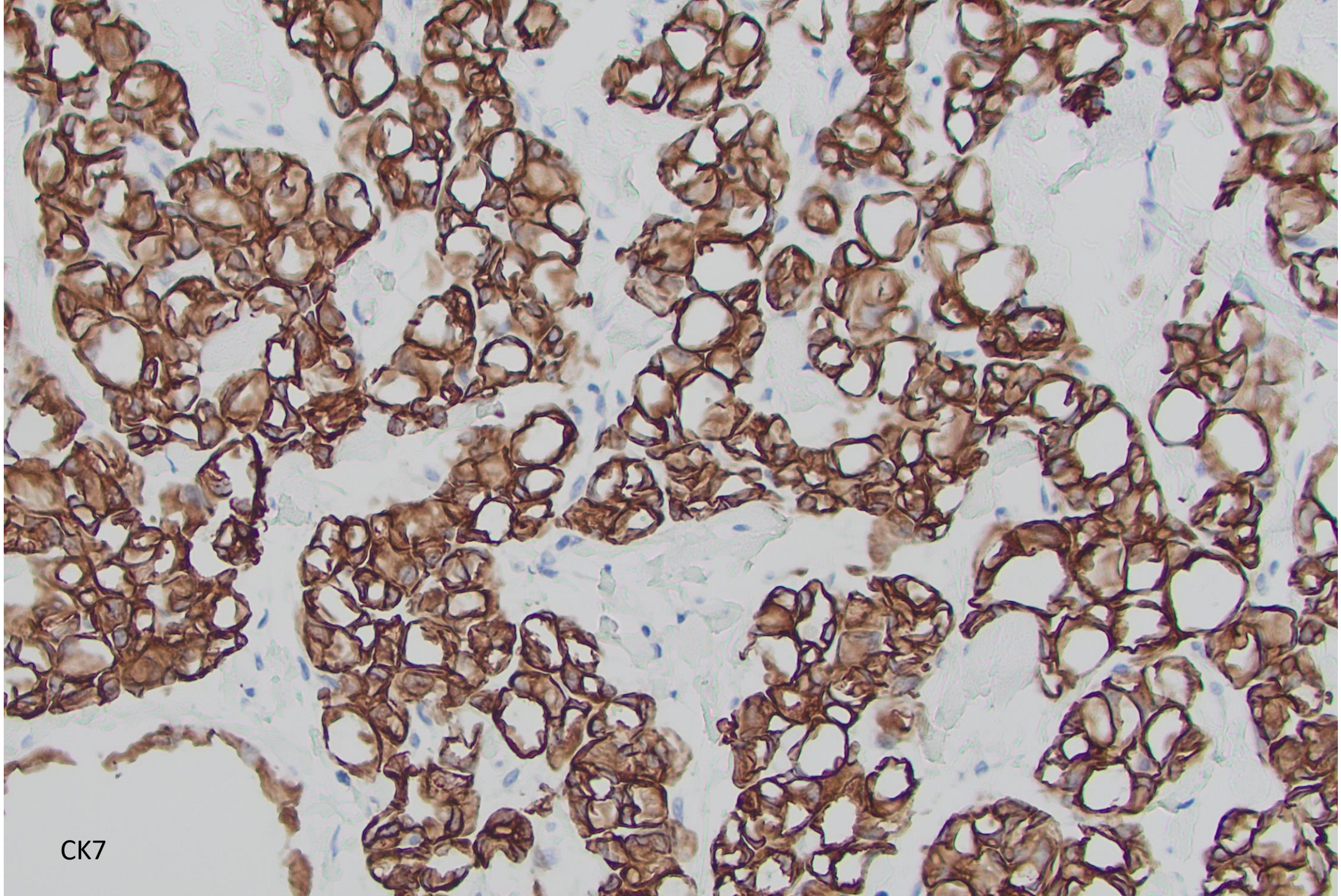


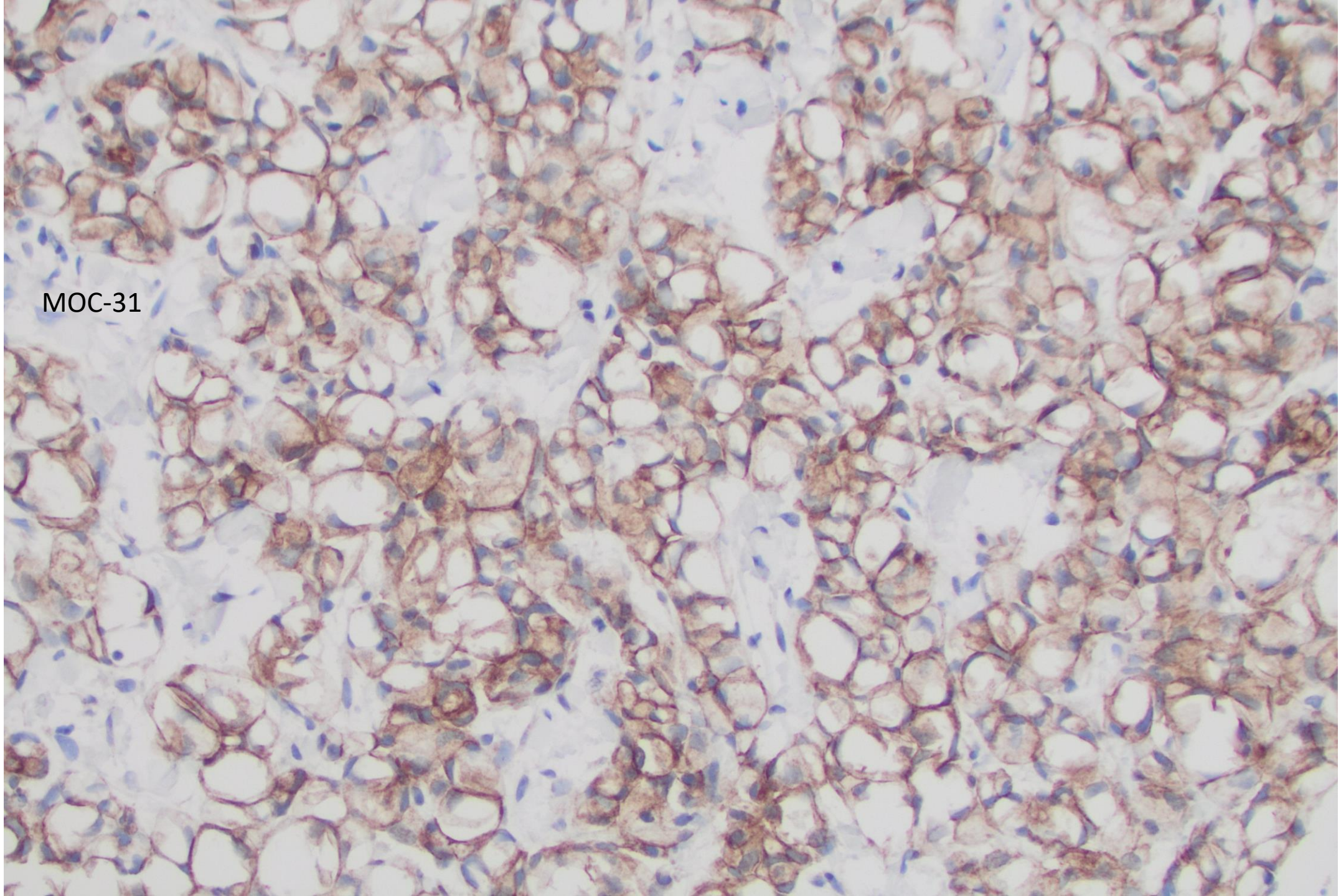




DIAGNOSIS?

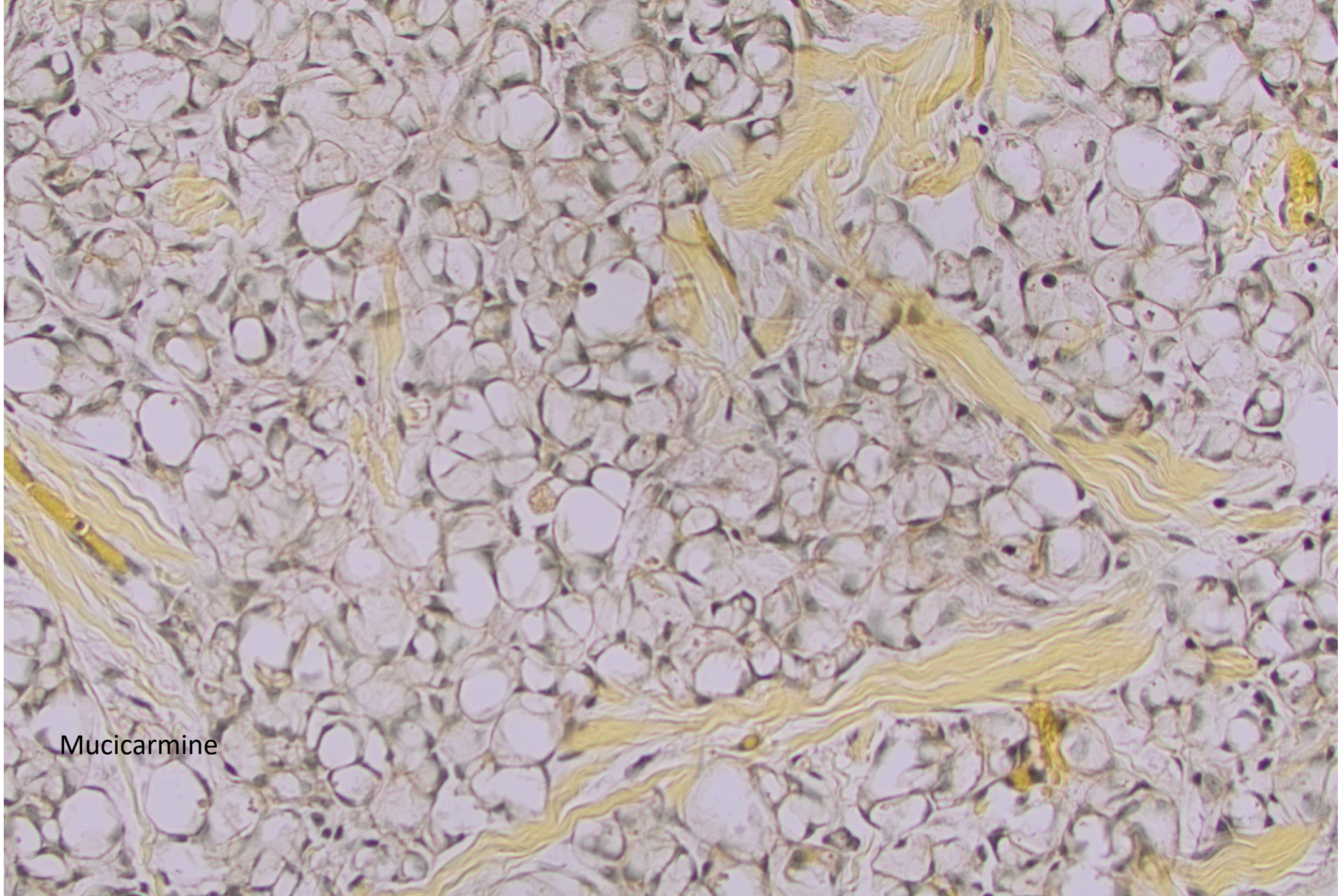

Pancytokeratin

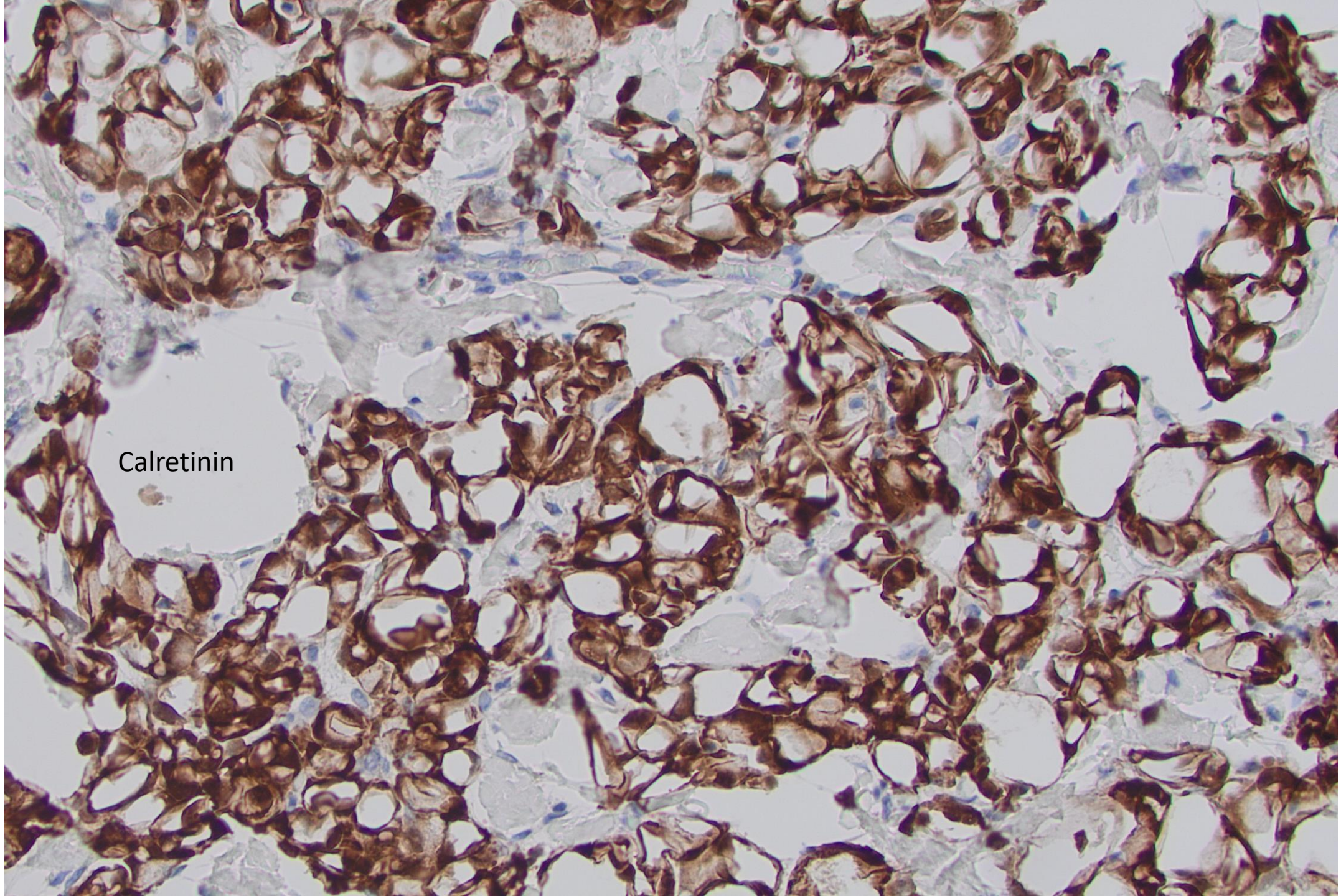

CK7

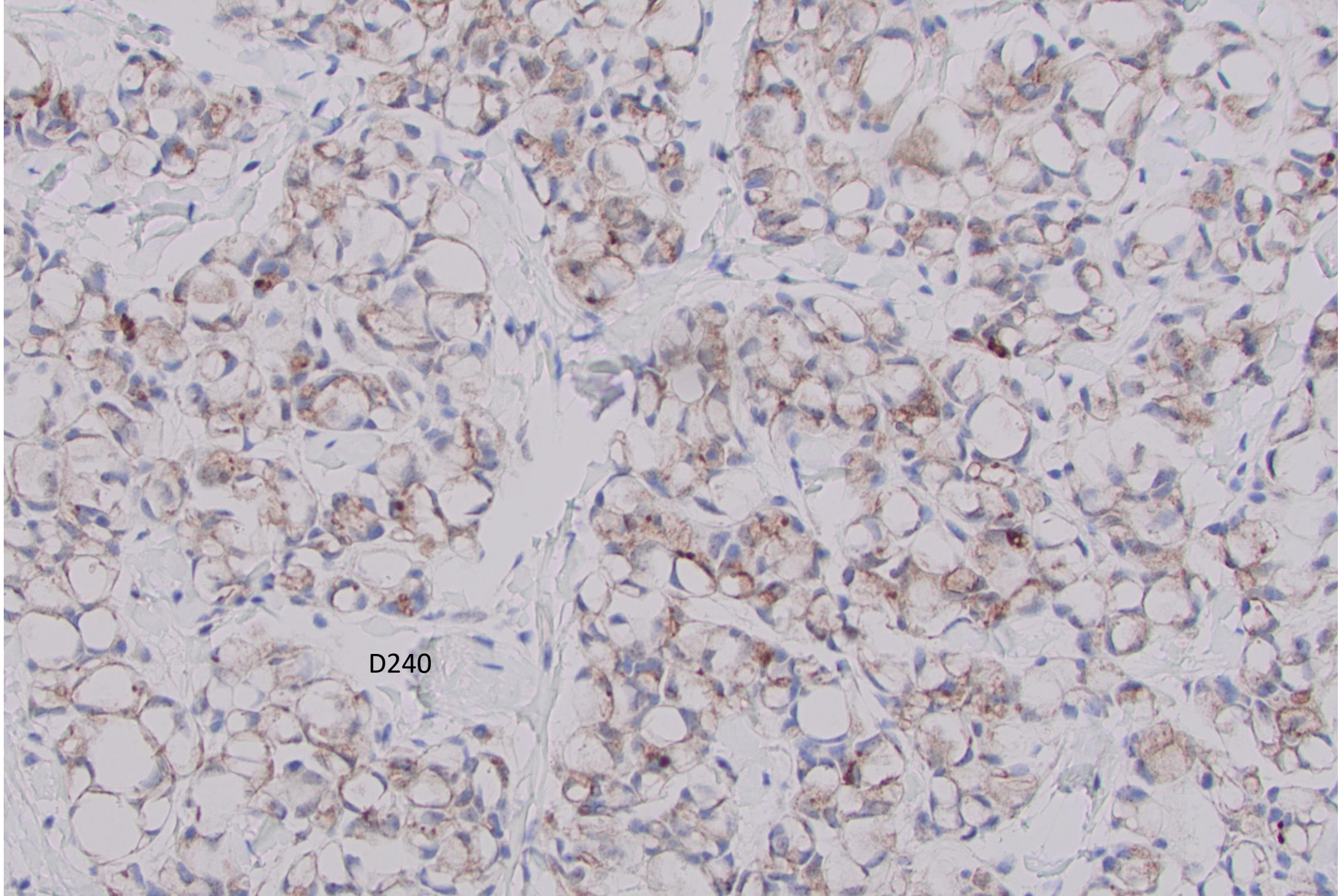

MOC-31

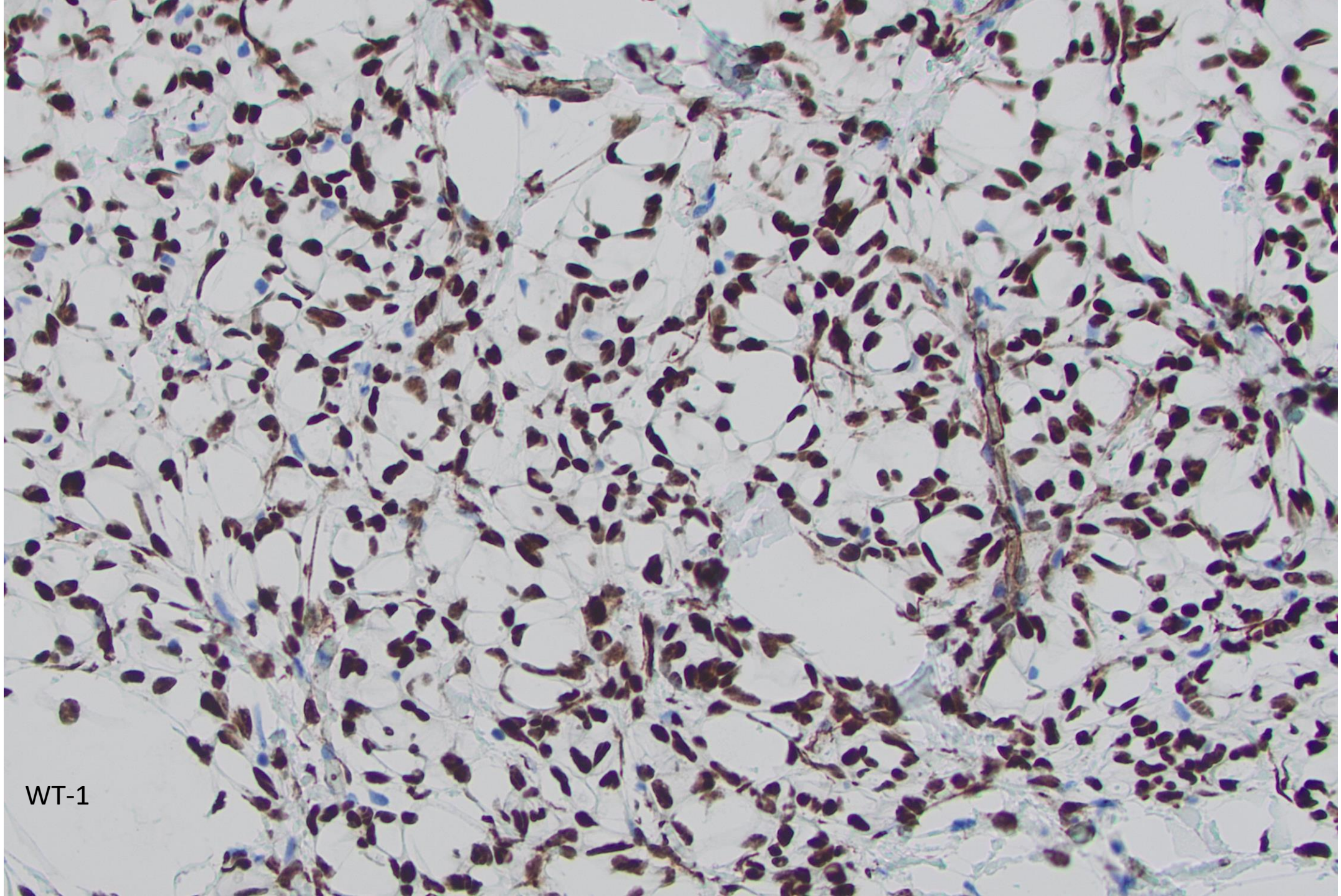
Negative IHC stains

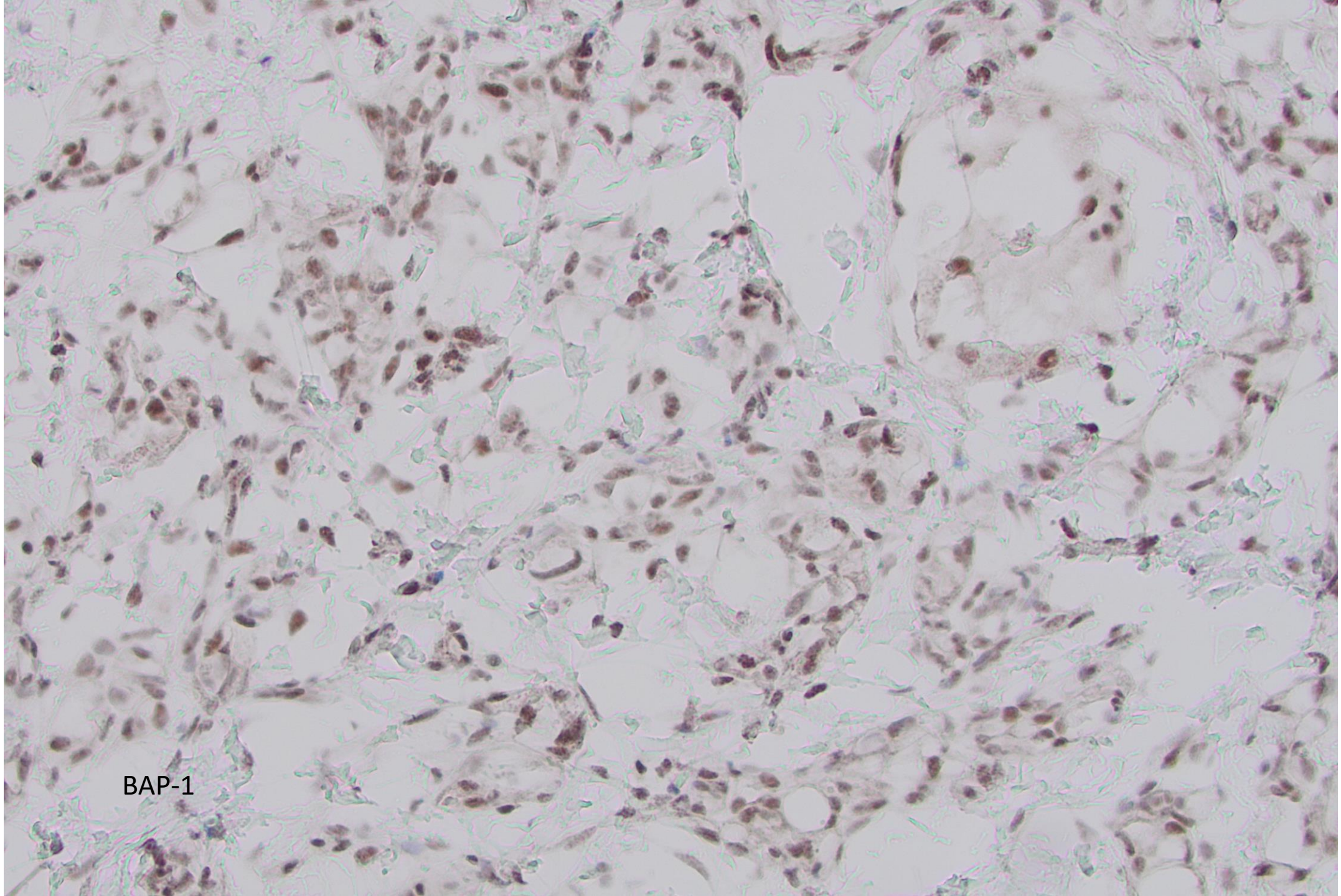
- CDX-2
- CK20
- Chromogranin
- Synaptophysin


Mucicarmine


Calretinin


D240


WT-1


BAP-1

Adenomatoid Tumor

- Benign Localized Tumors of Mesothelial Origin
- Usually present in genitourinary tract
- Rarely in extragenital sites-liver, mesentery, omentum
- Usually solitary, but occasionally multiple
- “Signet ring” morphology is relatively common
- Differential diagnosis-adenocarcinoma, mesothelioma
- Preservation of BAP-1 staining favors AT (some mesotheliomas do not show BAP-1 loss)

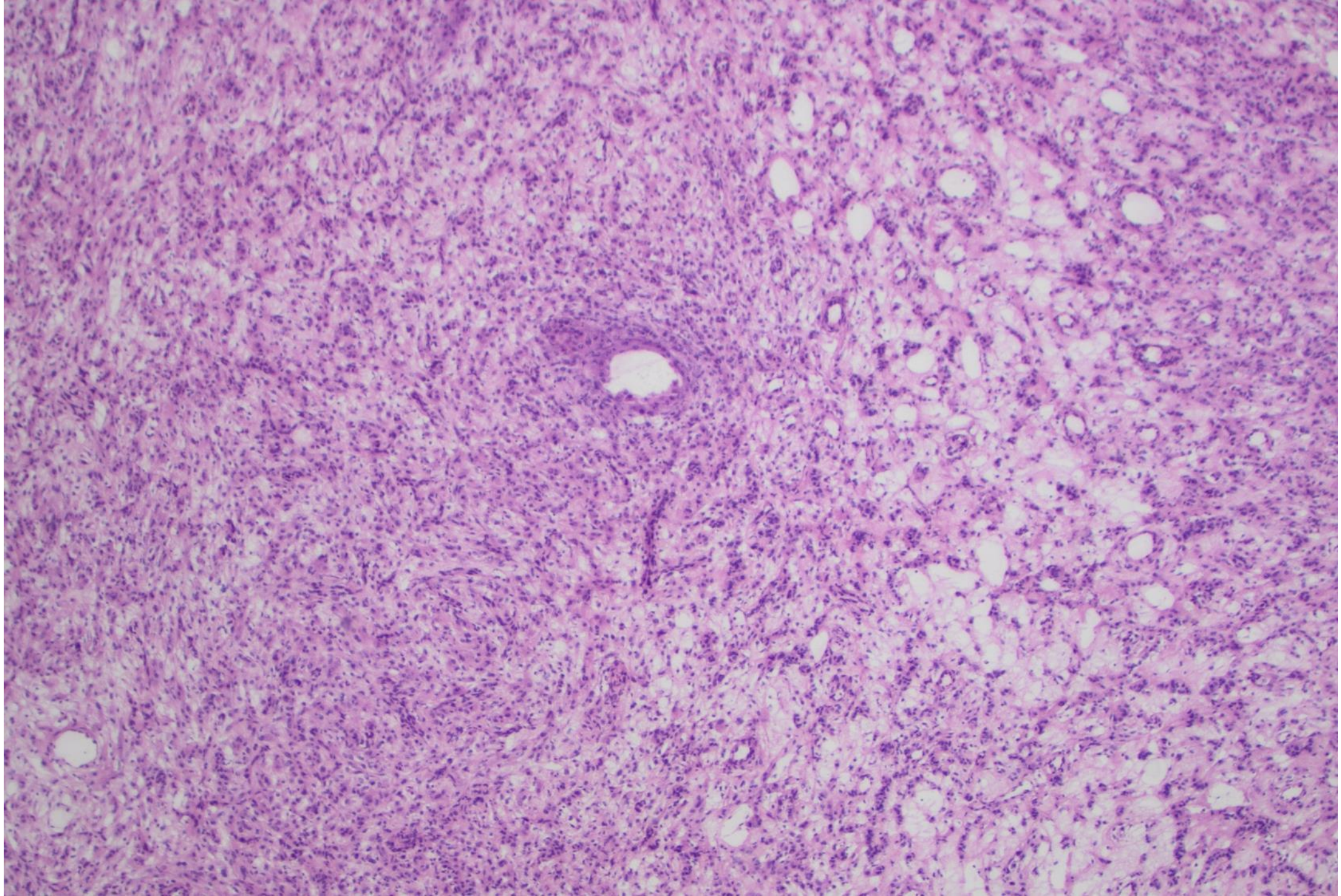
Reference

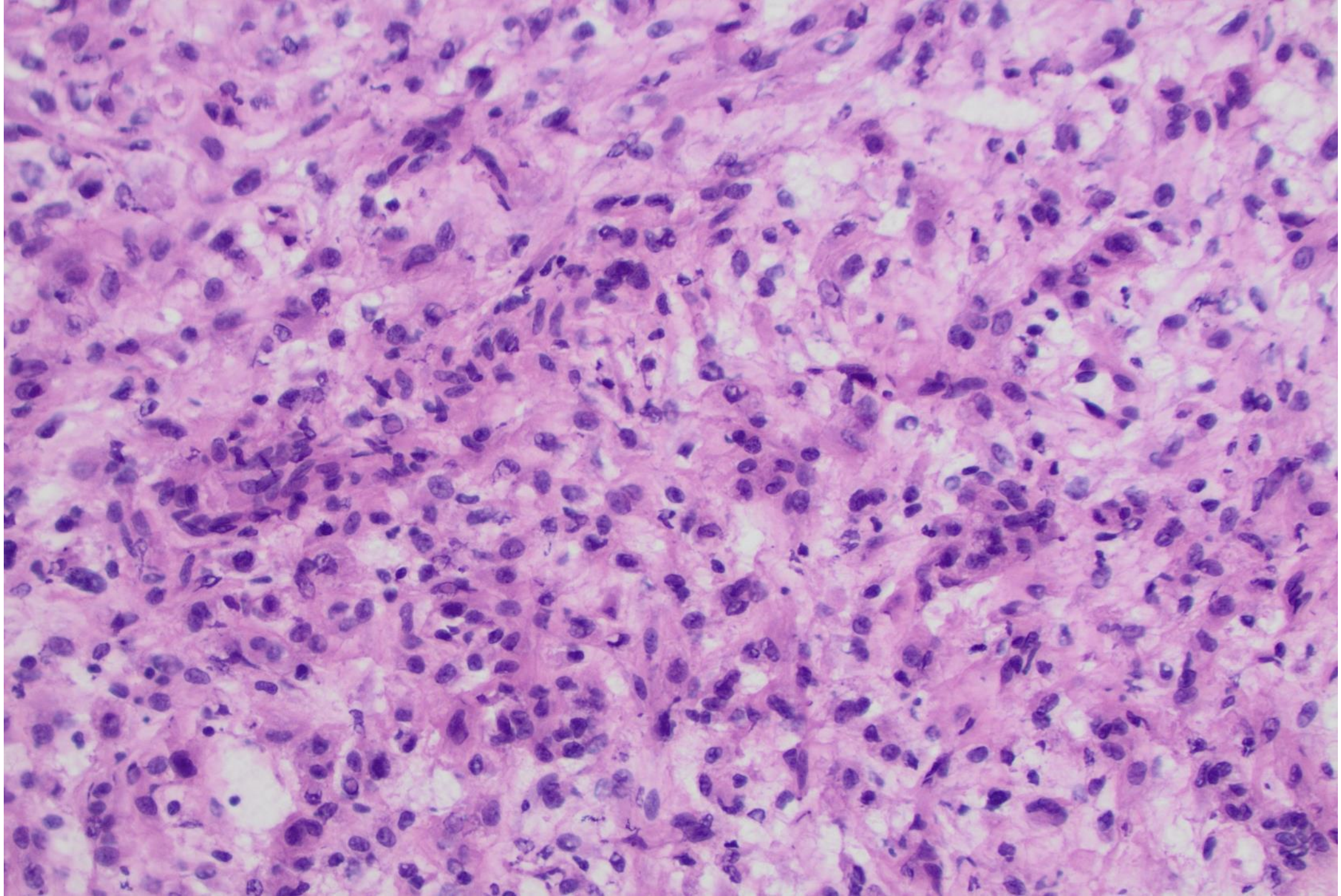
- Hissong E, Graham RP, Wen KW, Alpert L, Shi J, Lamps LW. Adenomatoid Tumors of the Gastrointestinal Tract-a case series and review of the literature. Histopathology. 2022 Jan; 80(2): 348-359

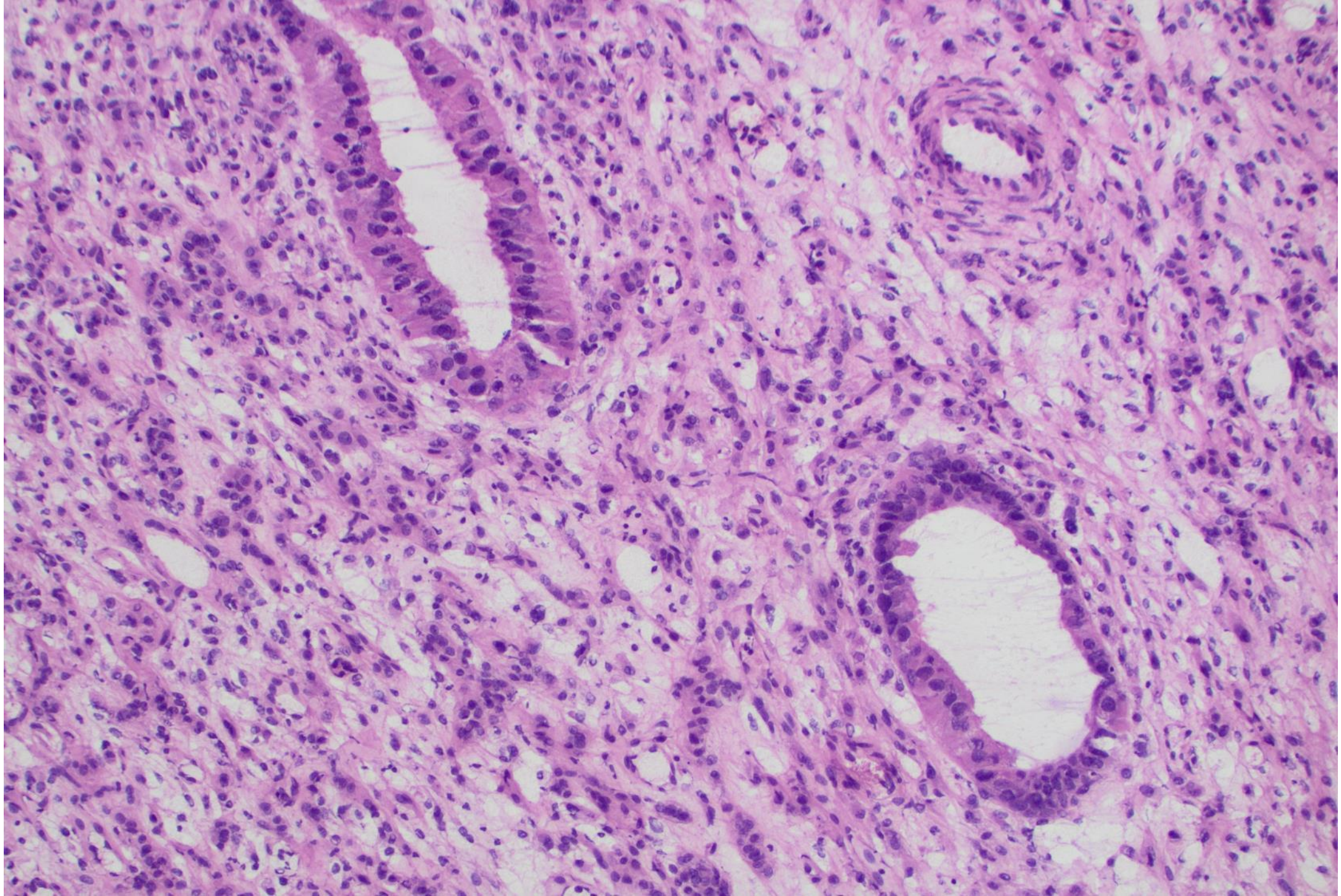
23-1007

Gregory Rumore; Kaiser Permanente

Early 40’s female with R Ovarian mass submitted for frozen section

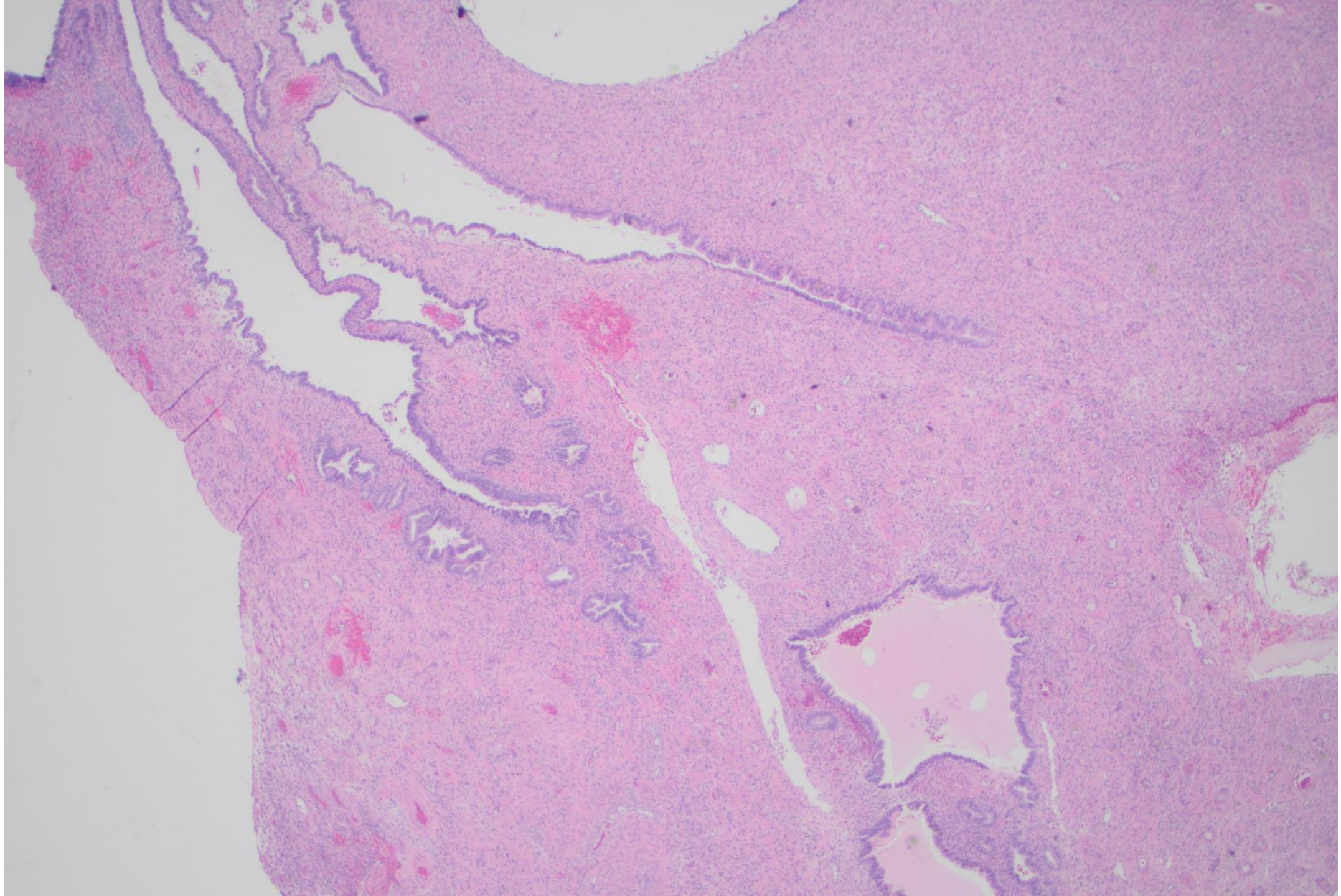


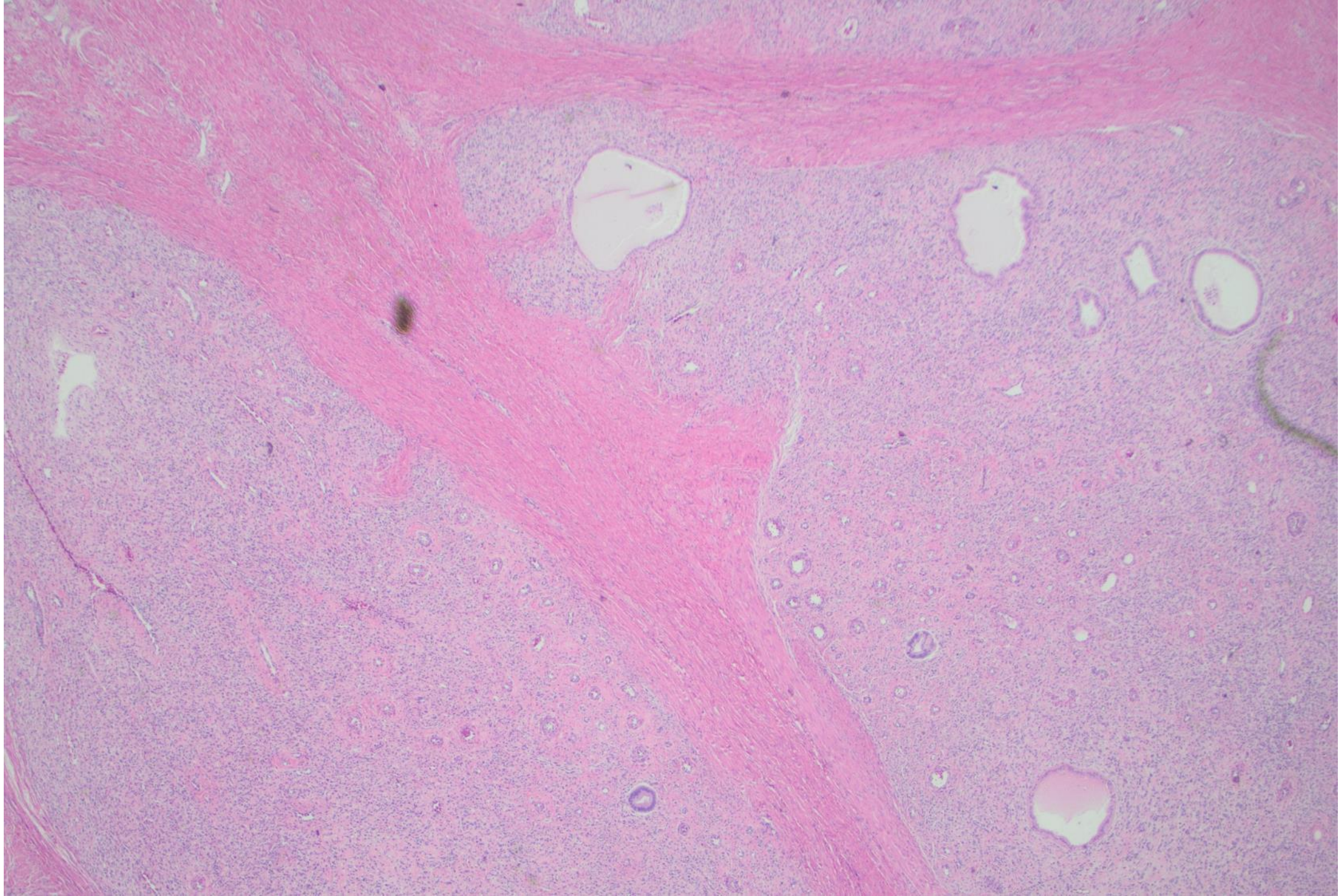


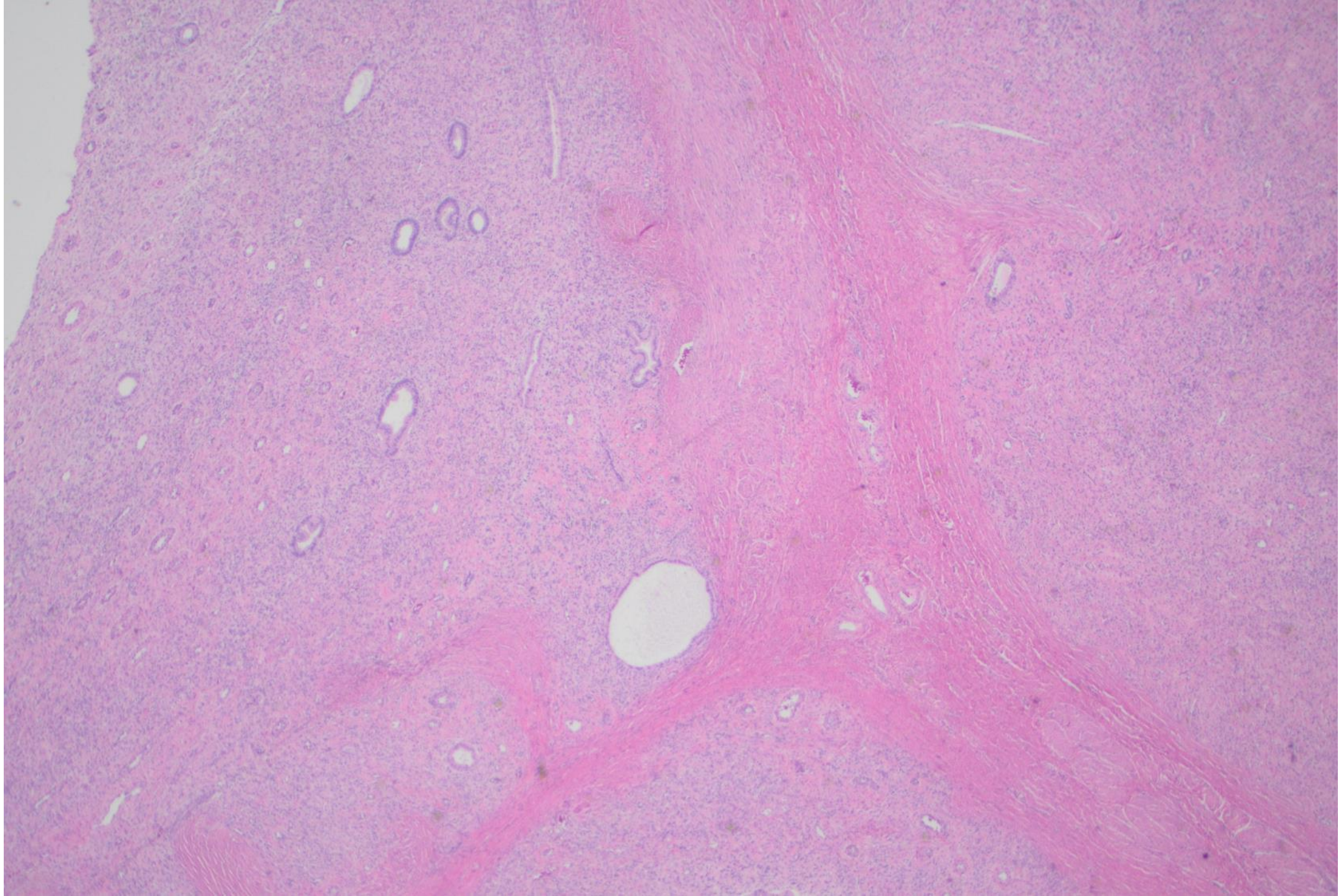


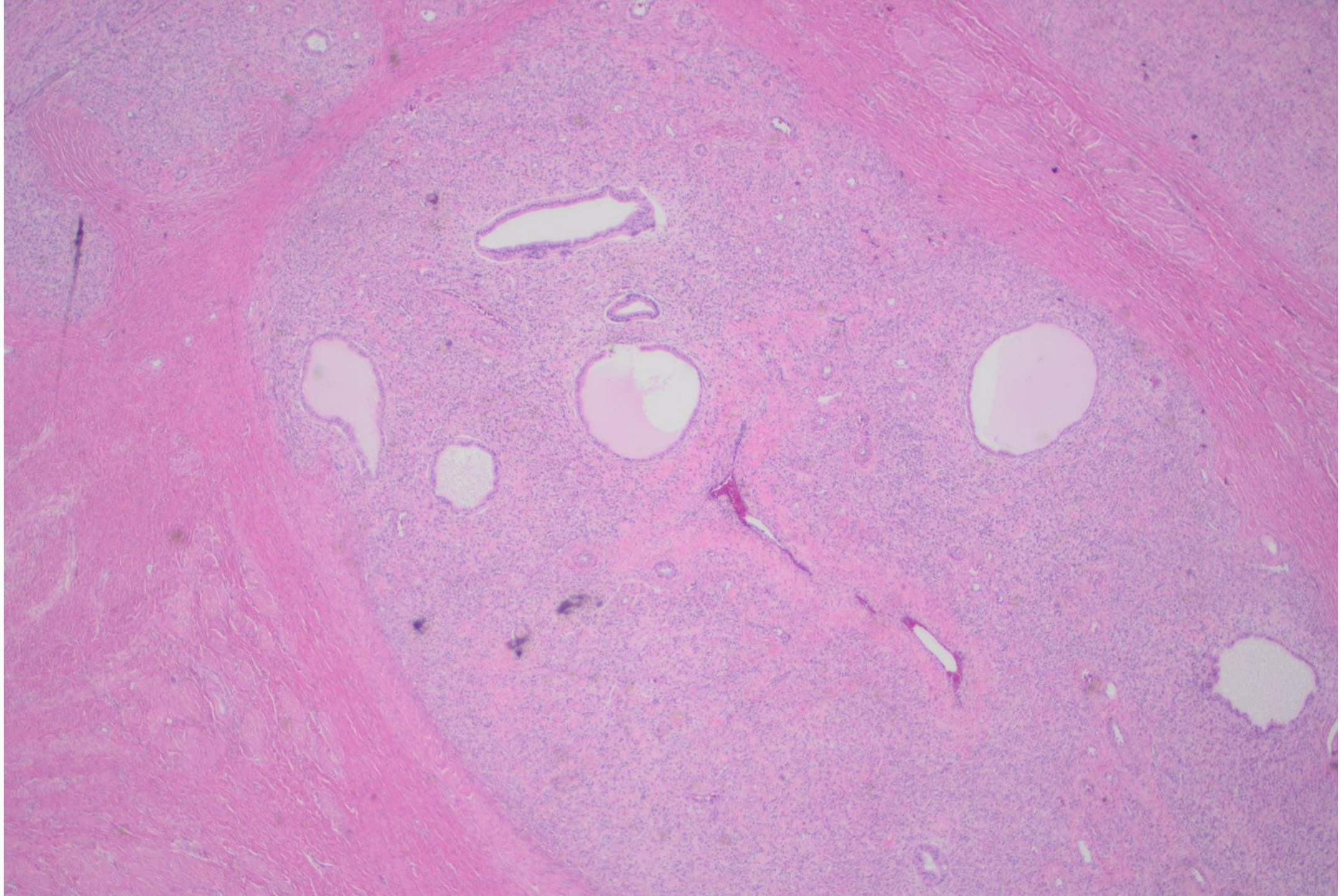
Diagnosis?

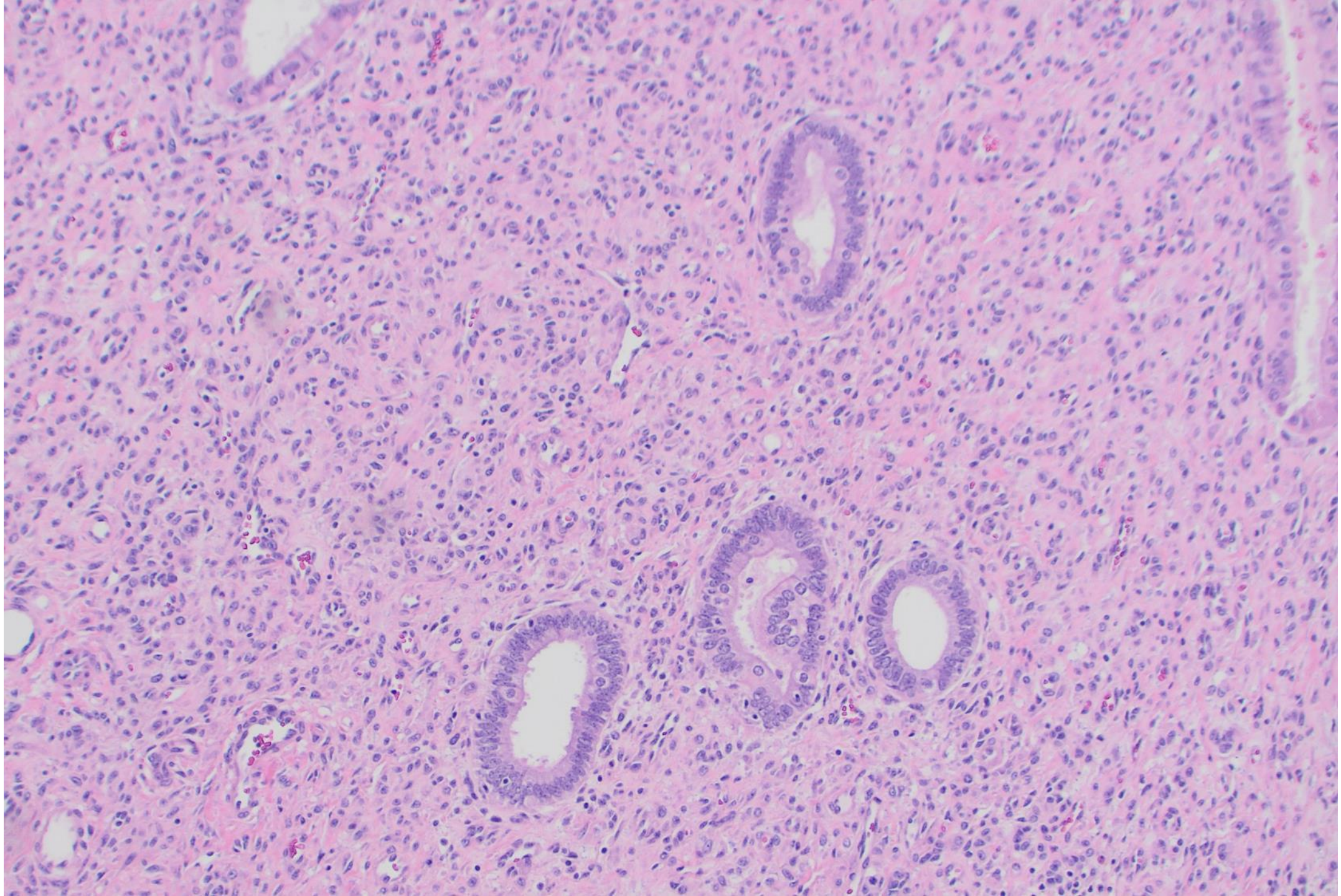
Uterus

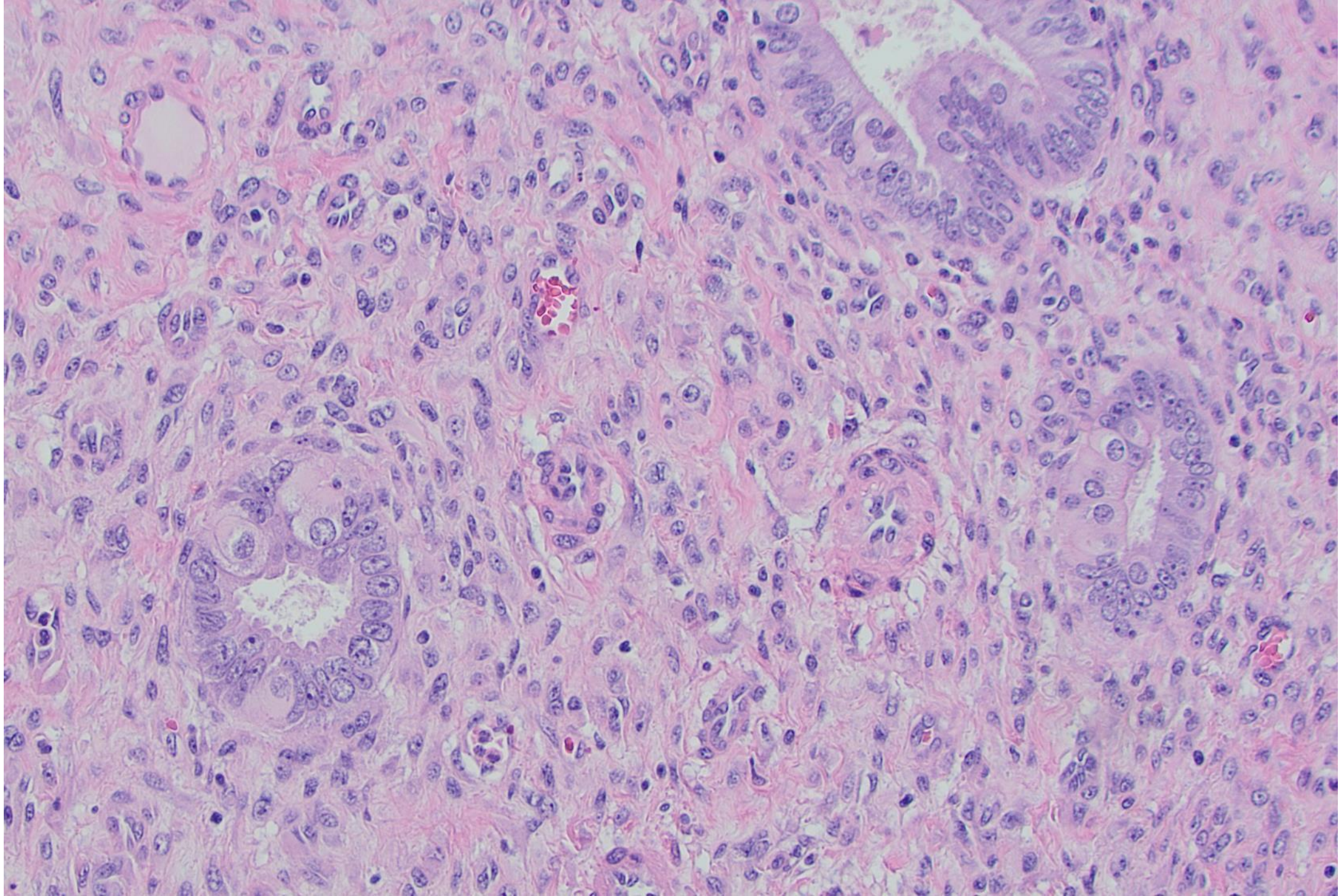


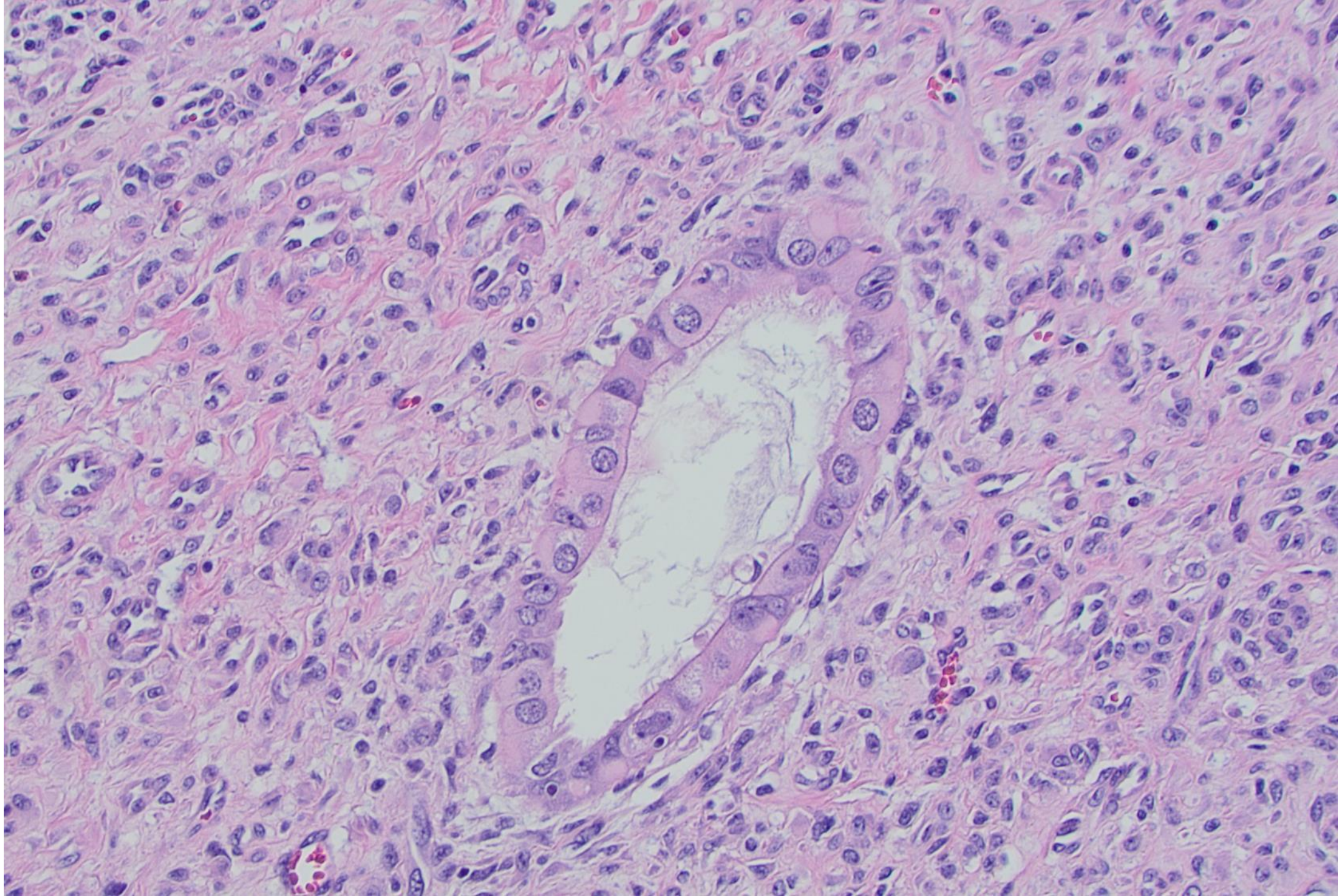




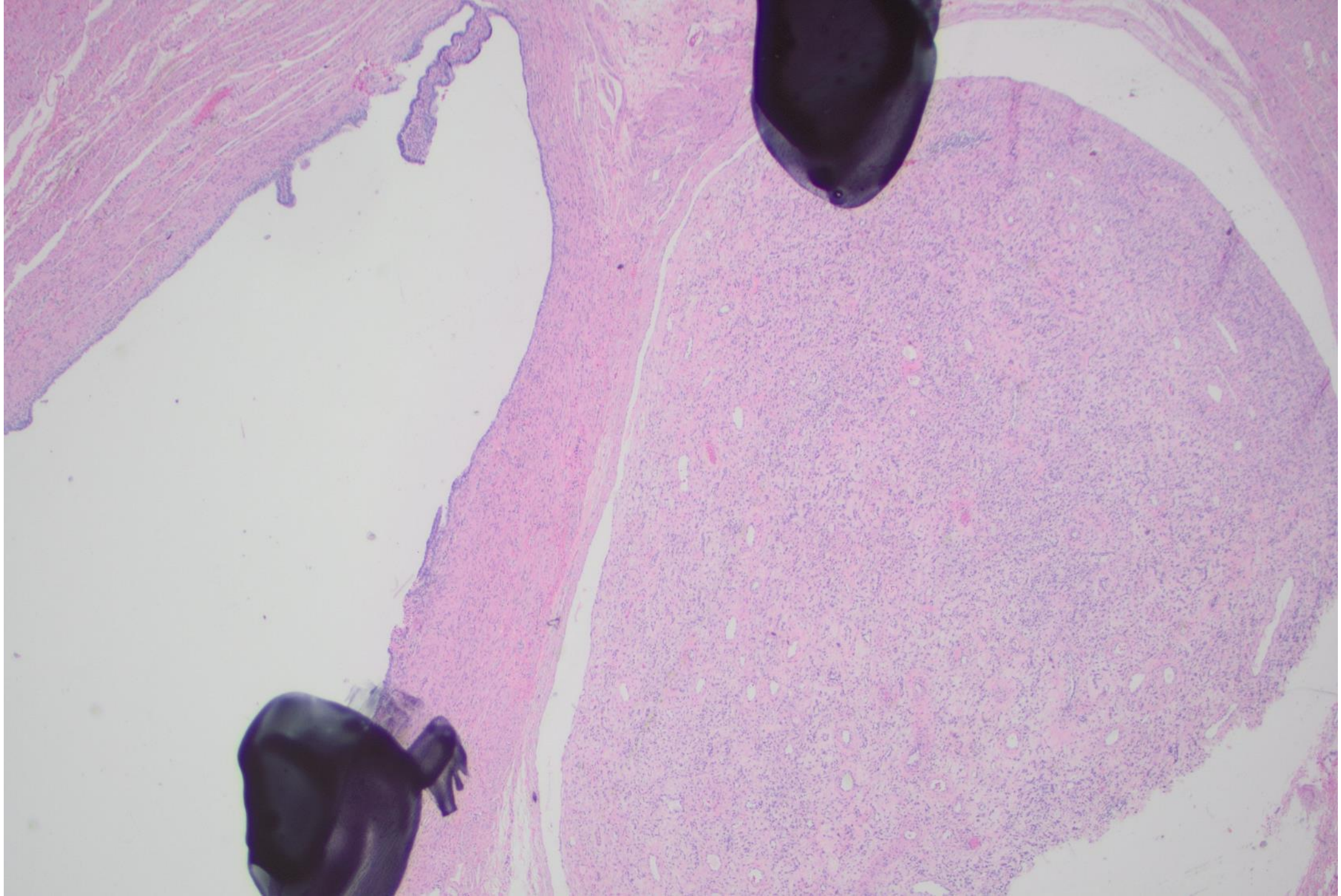


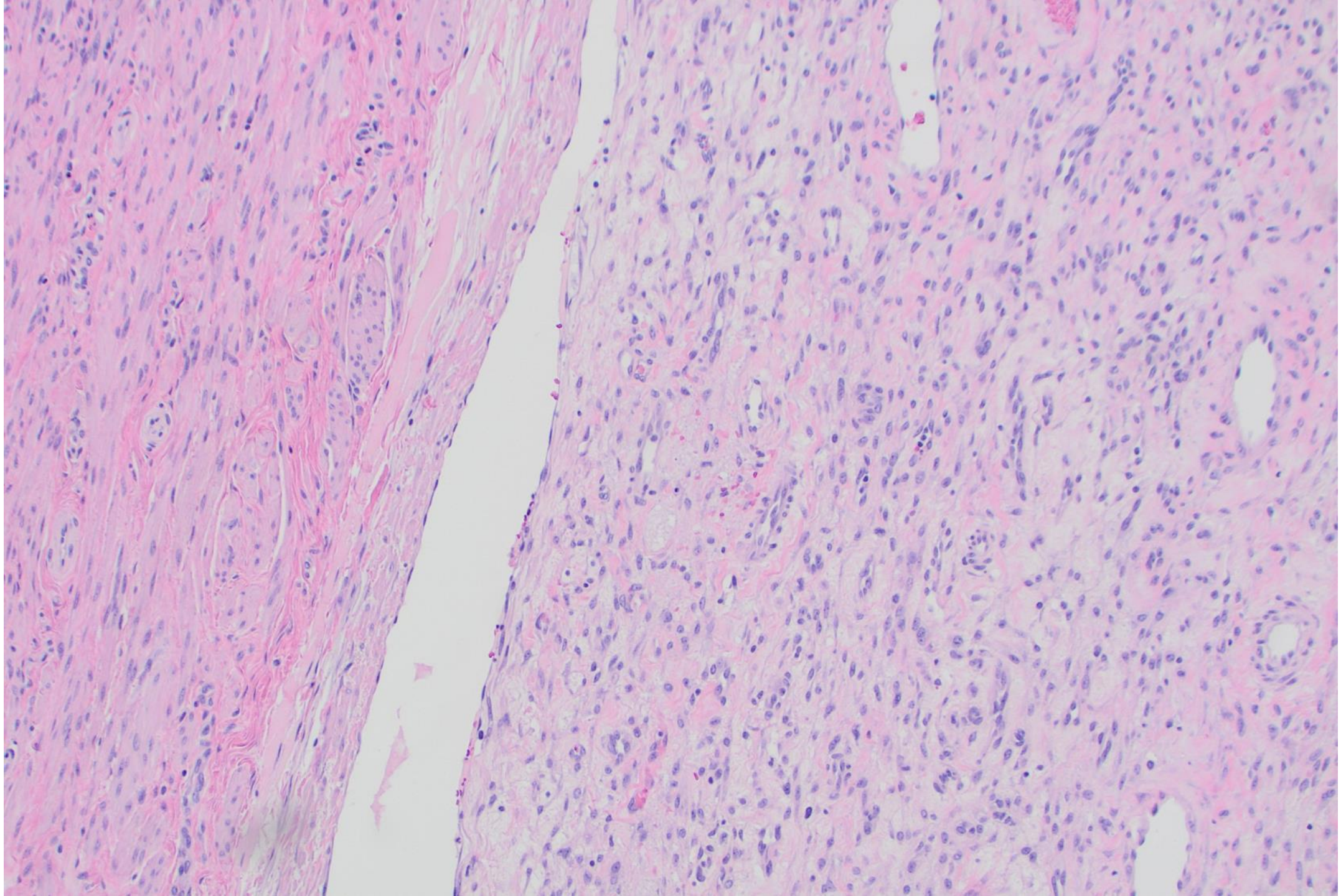




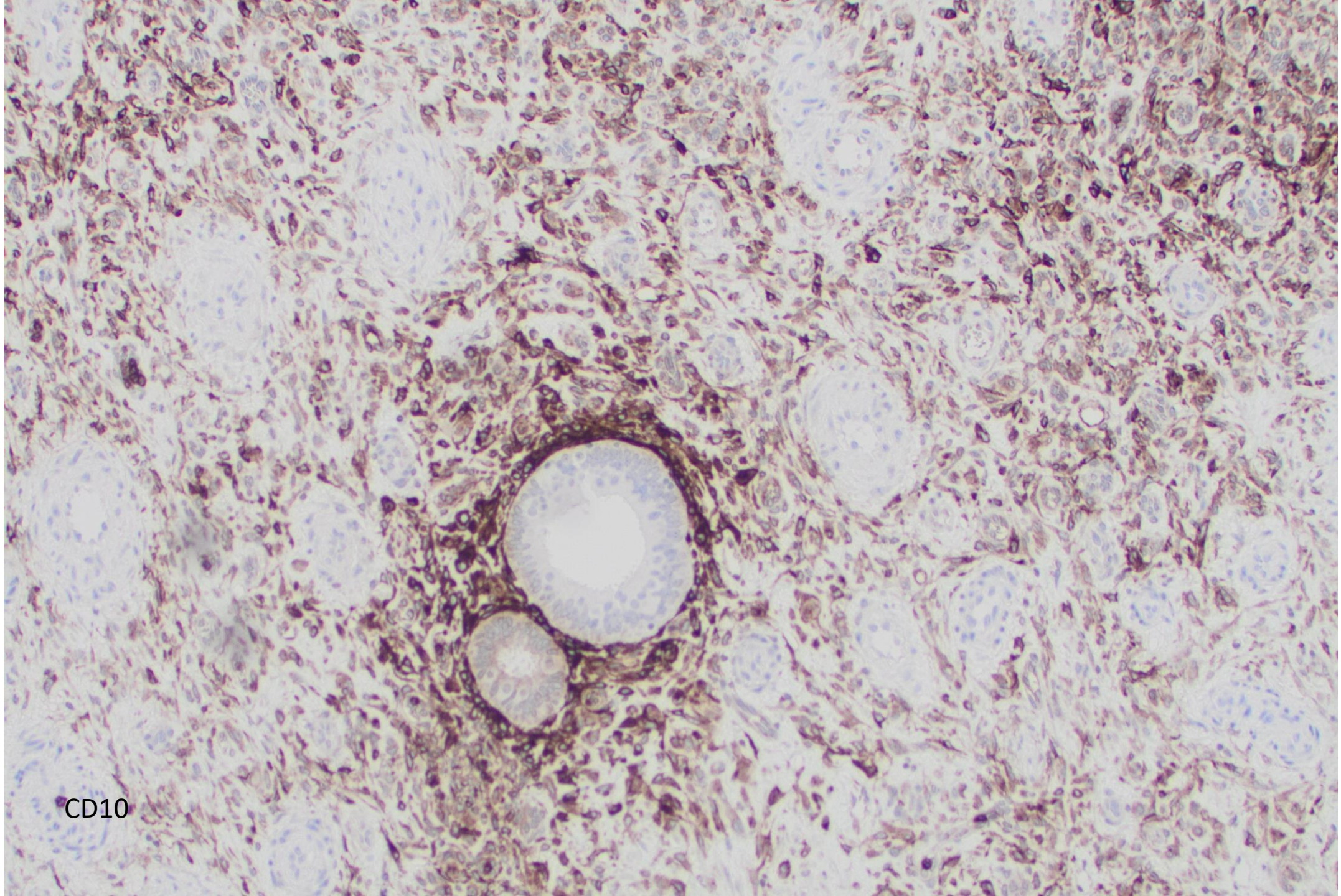


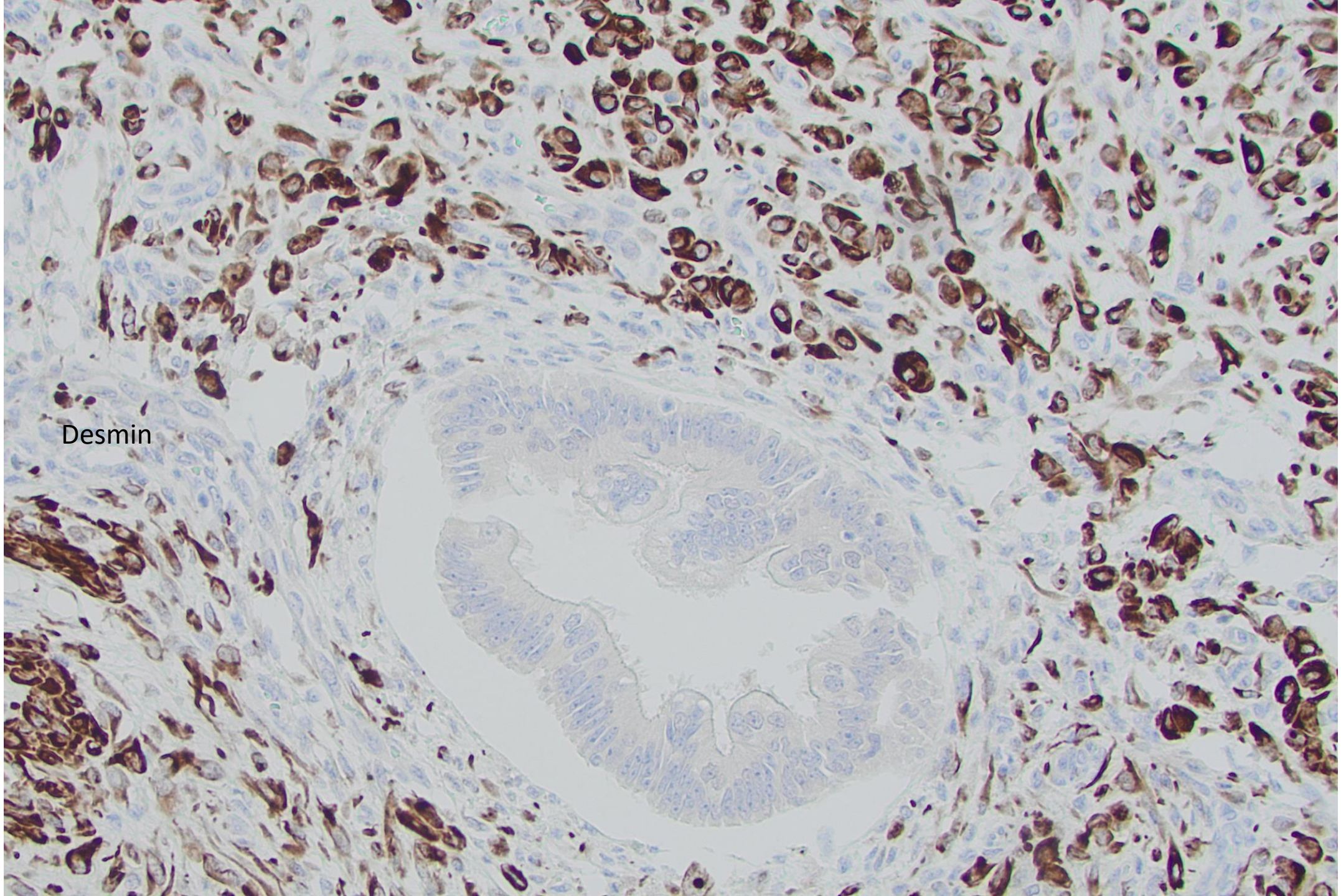
Left Fallopian tube

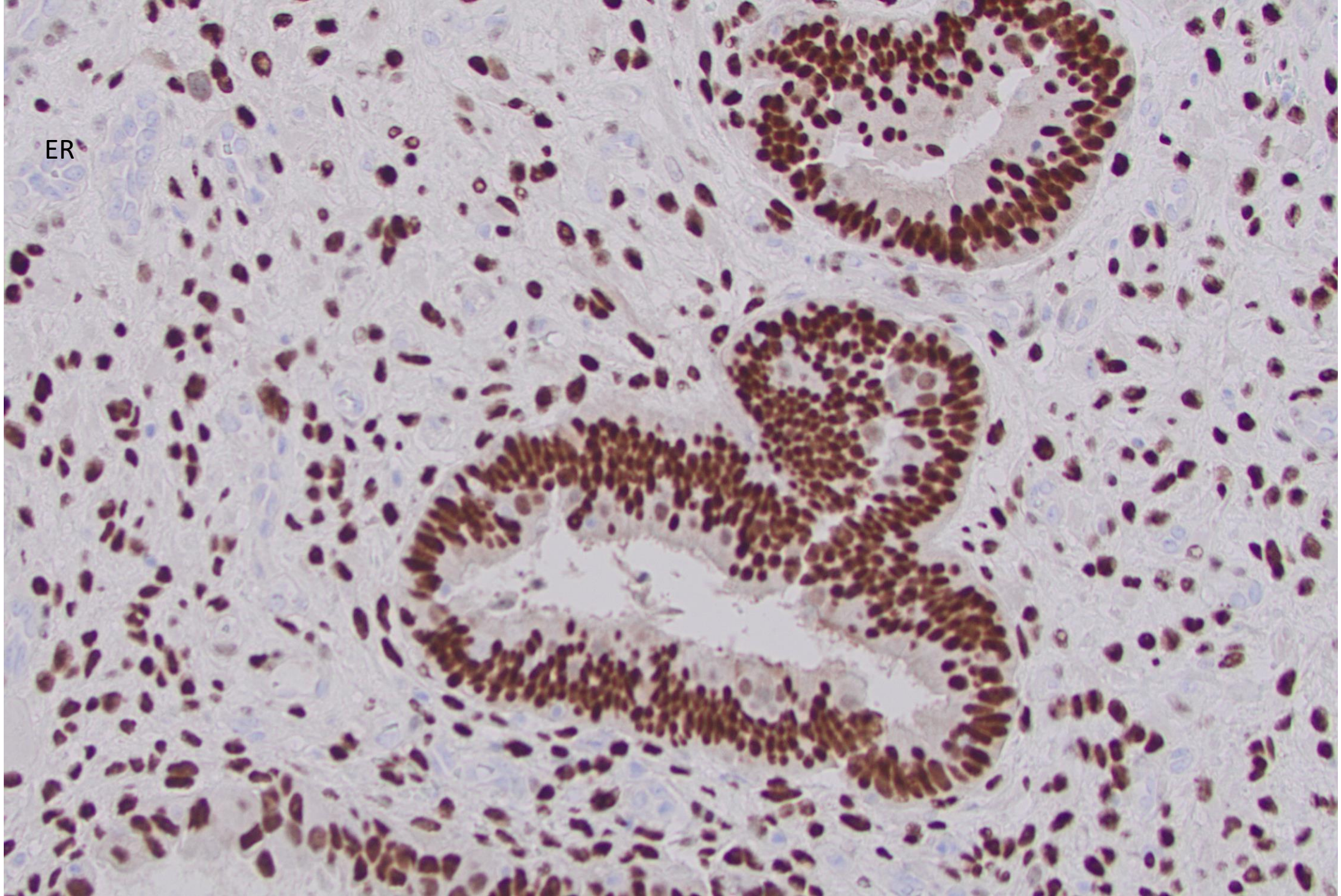




DIAGNOSIS?


CD10


Desmin


ER

Low grade endometrial stromal sarcoma with smooth muscle differentiation and glandular component

Differential diagnosis

- Mullerian adenosarcoma (+/- stromal overgrowth)
- Carcinosarcoma (MMMT)
- Endometriosis
- adenomyosis
- Atypical polypoid adenomyoma
- Intravenous adenomyosis

Adenosarcoma

- Polypoid mass filling endometrial cavity
- Phyllodes-like growth pattern
- Stromal condensation (periglandular cuffing)
- Deep myometrial invasion unusual unless stromal overgrowth, and then usually “destructive”
- Vascular invasion unusual

ESS with glandular differentiation

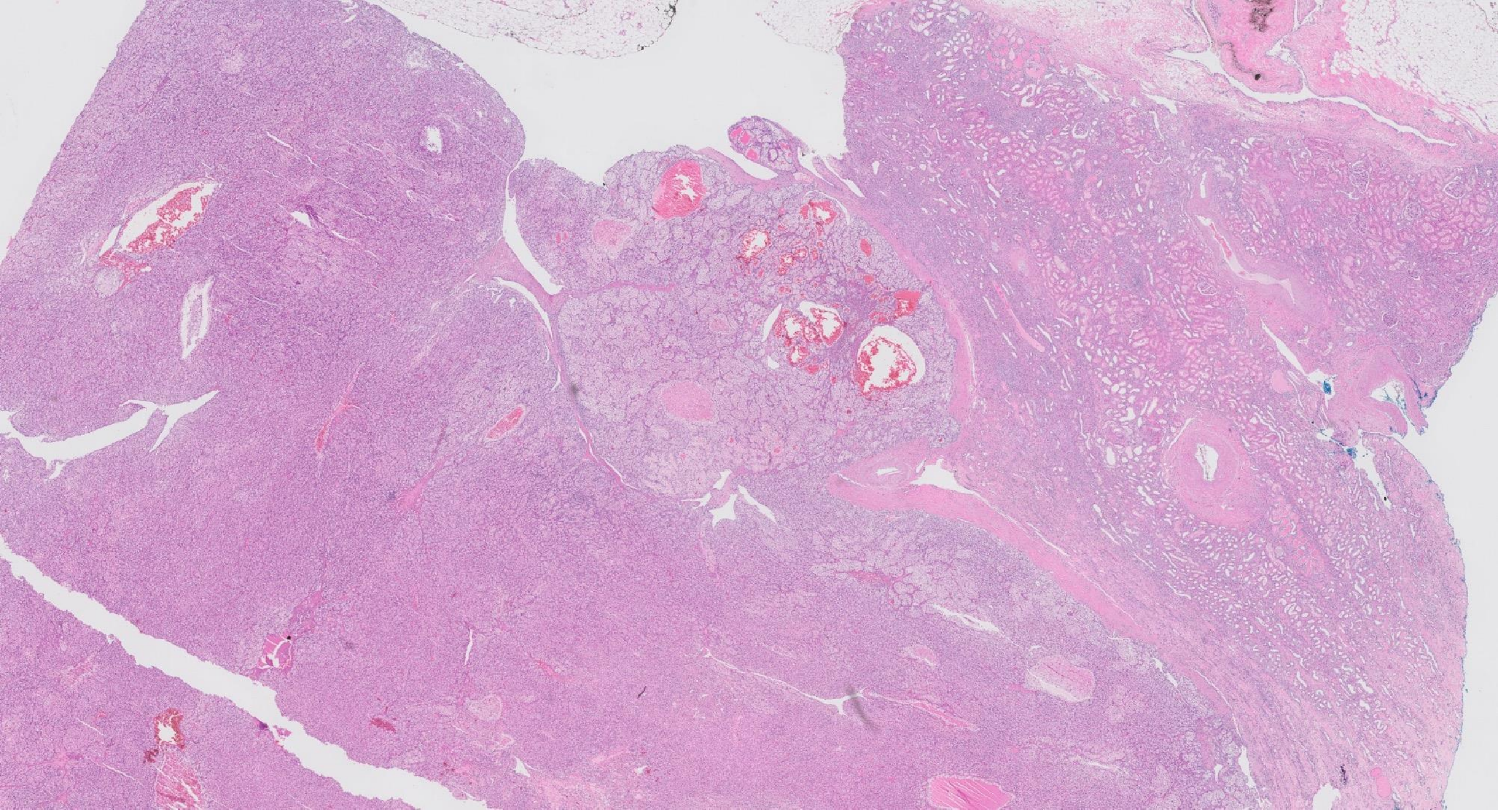
- Usually endometrioid-type glands, widely spaced, focal or diffuse
- Permeative (vs. destructive) growth pattern
- Lacks periglandular cuffing or phyllodes architecture
- More uniform appearance
- Intravascular growth

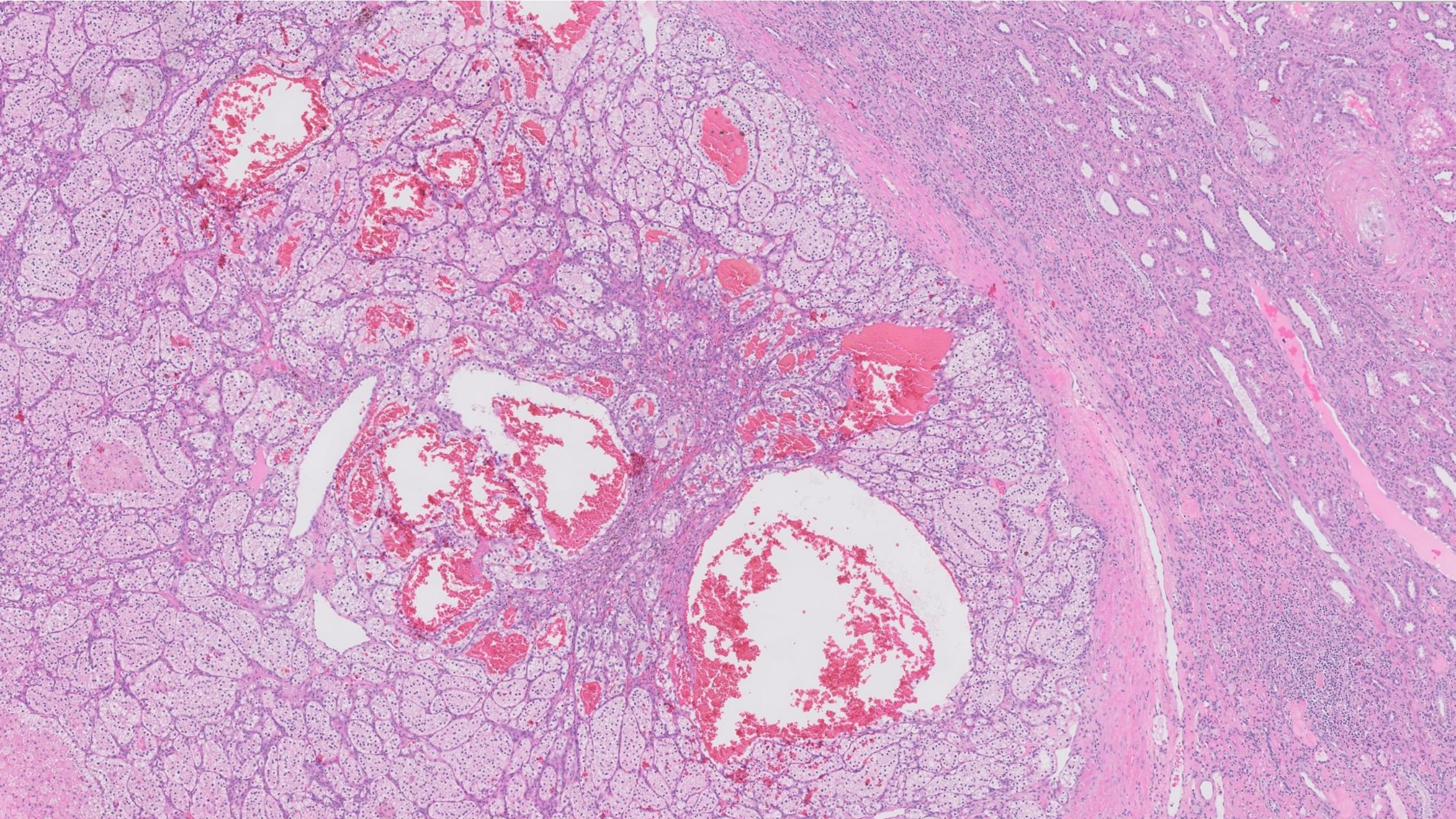
Not everything submitted as ovary is actually ovarian!

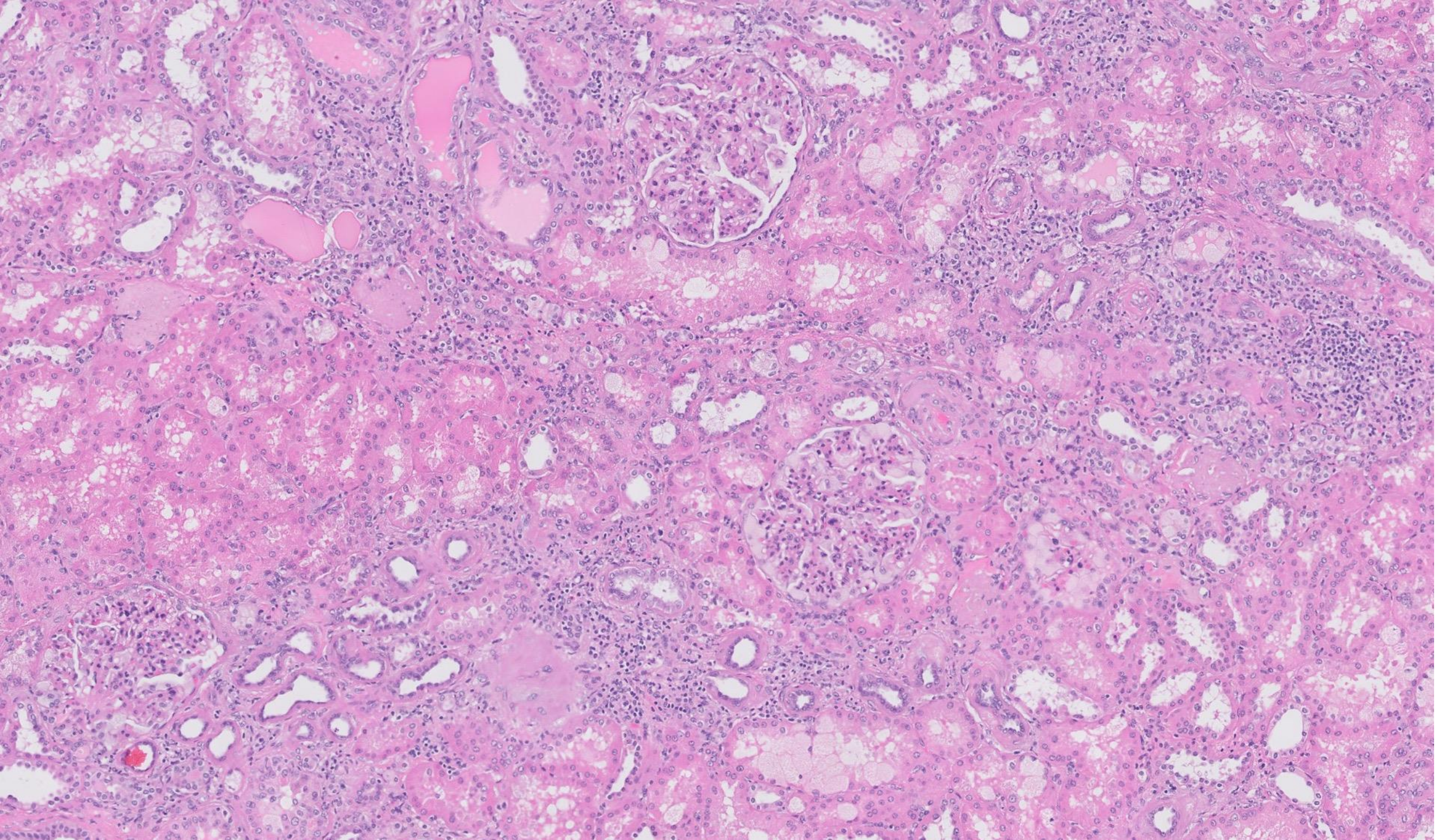
23-1008

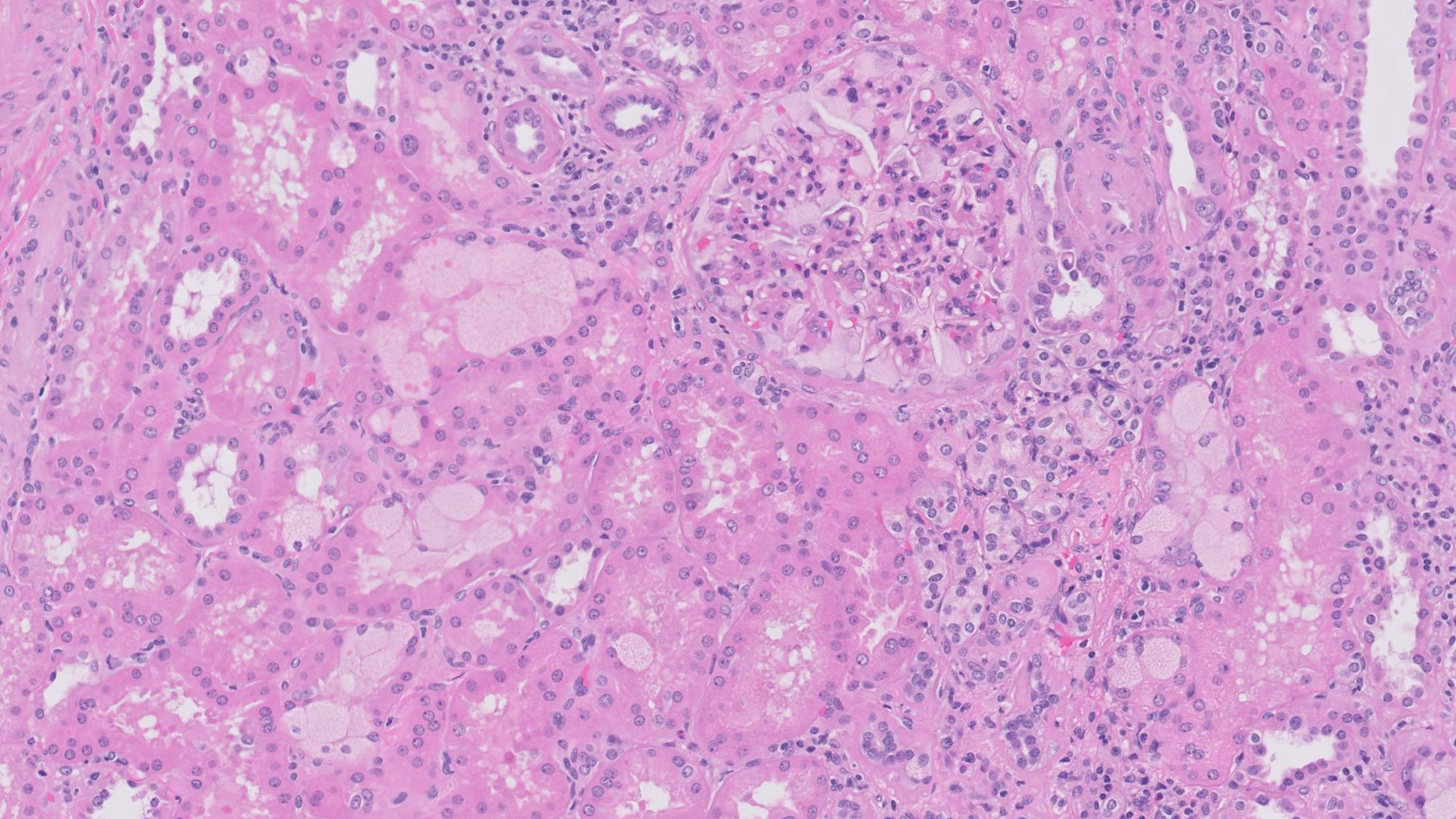
Megan Troxell/Adrian Lee Agostino; Stanford

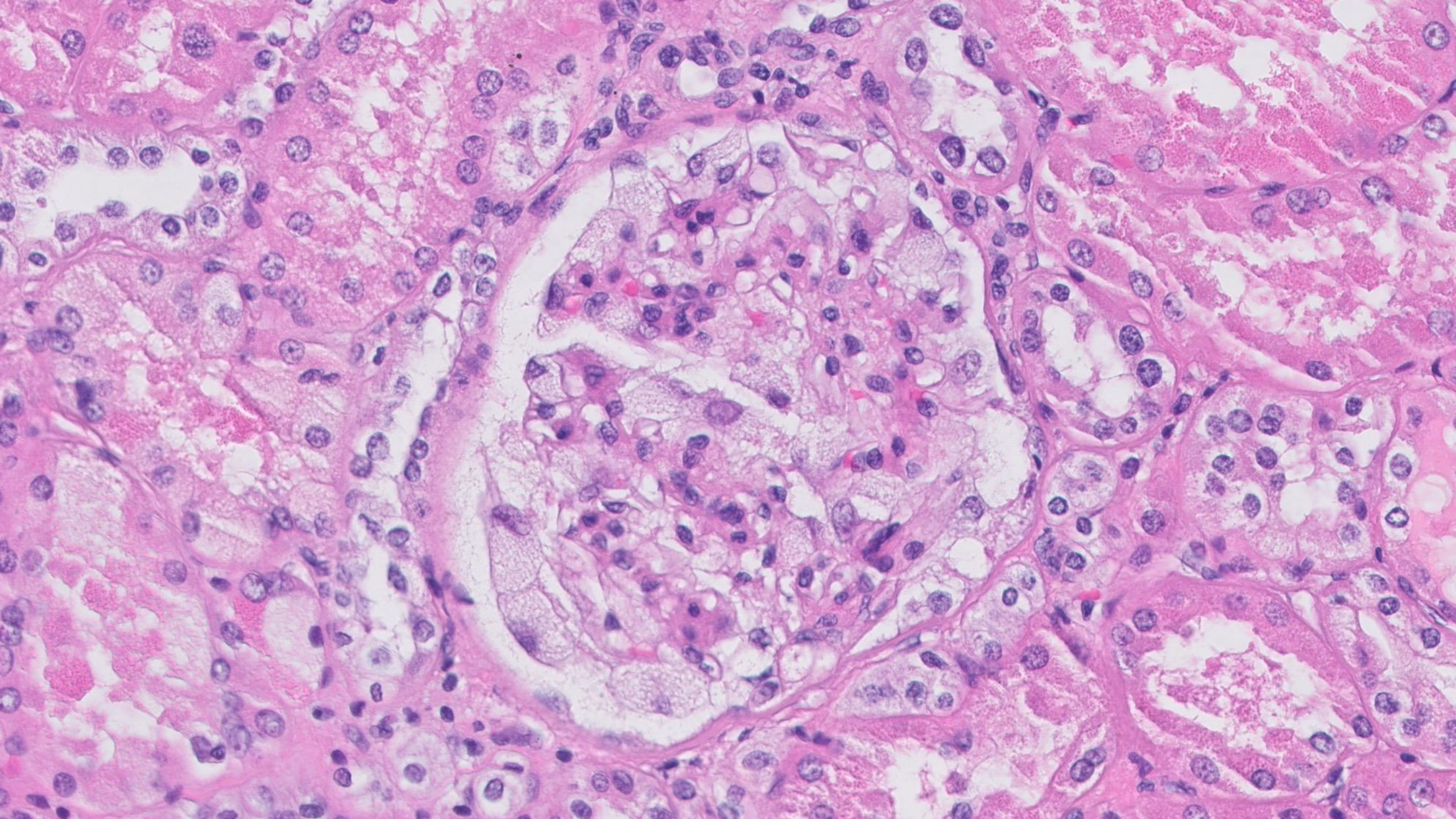
70+ year old woman with bilateral renal masses unilateral partial nephrectomy

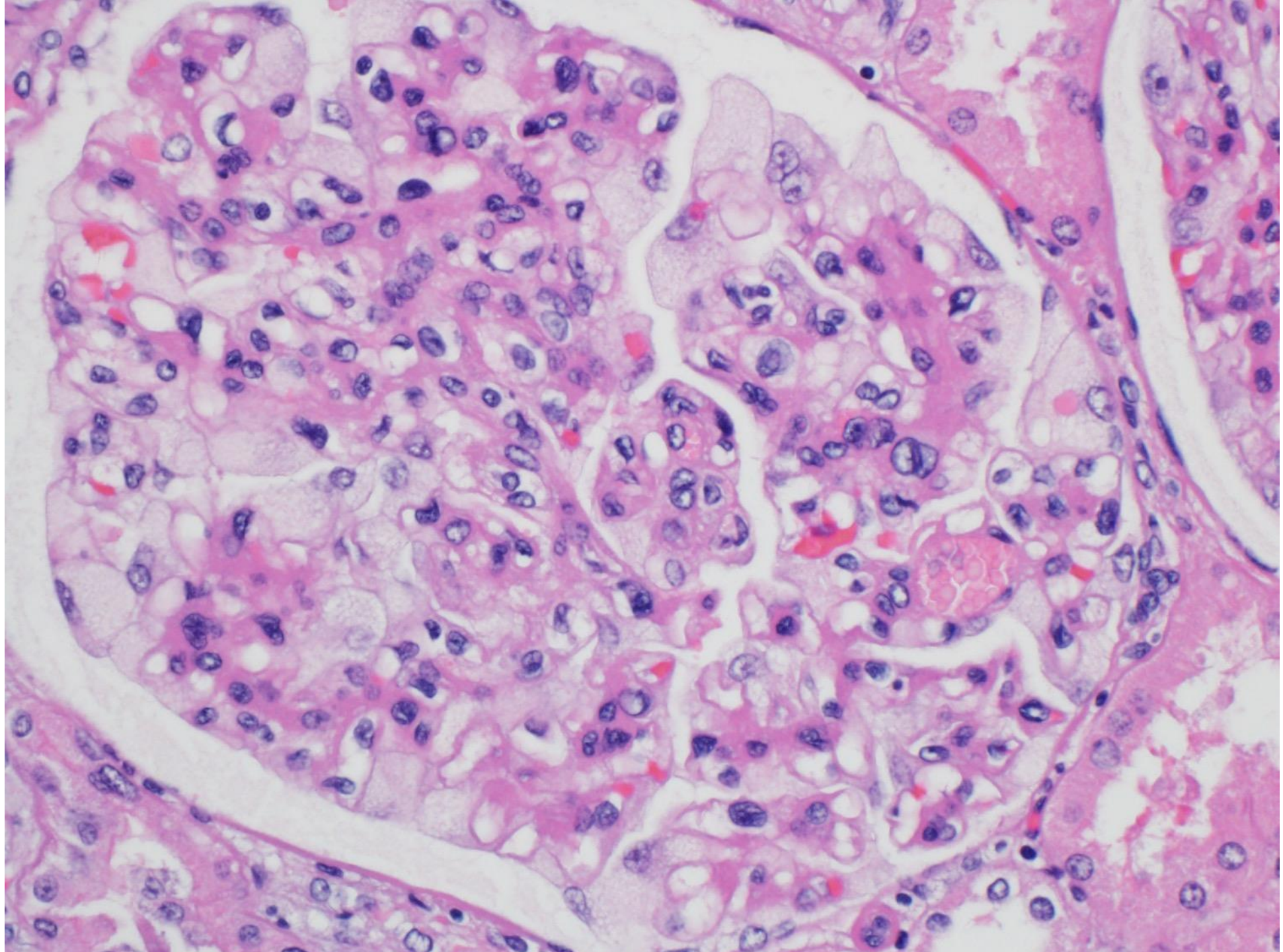


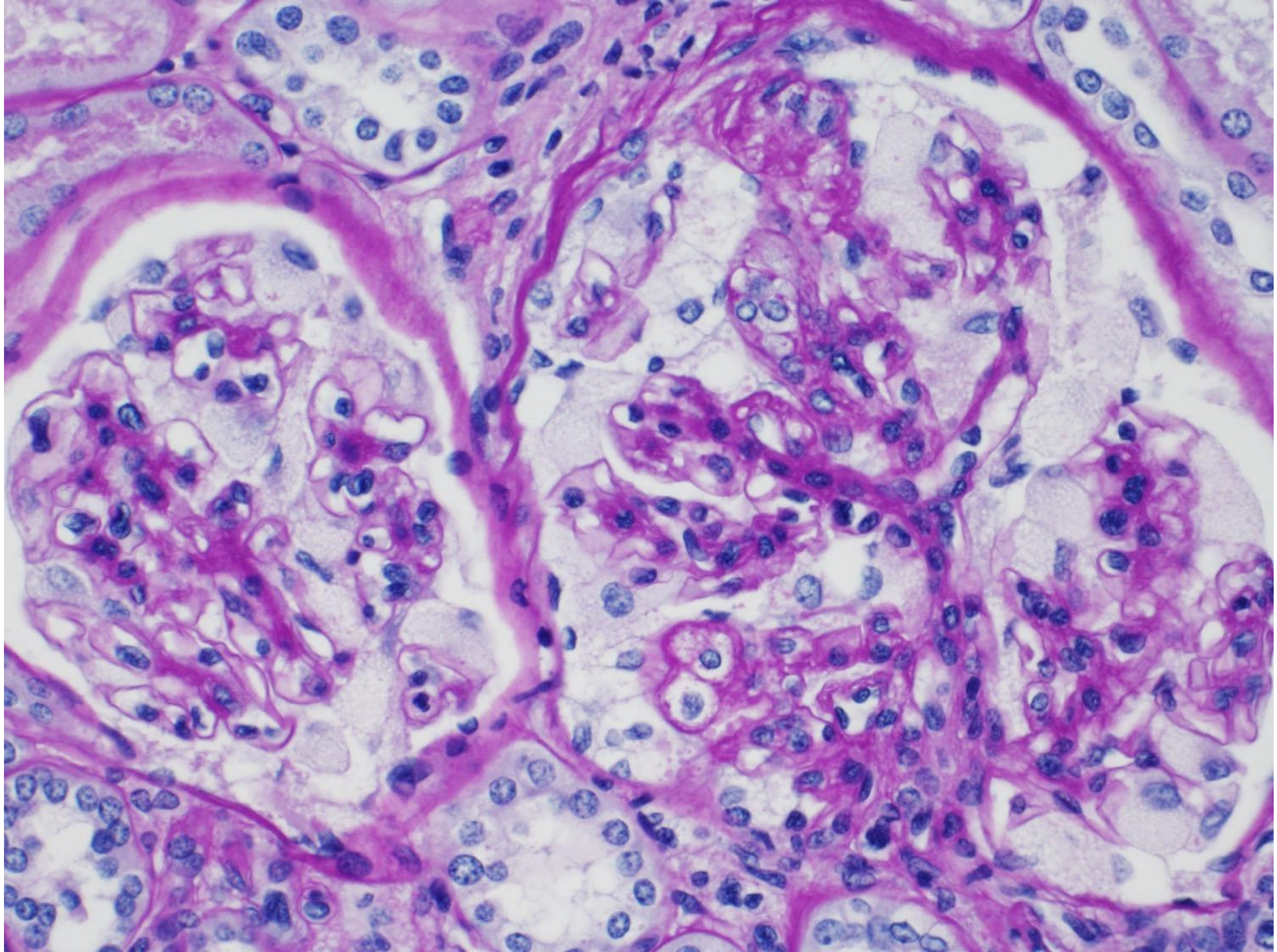


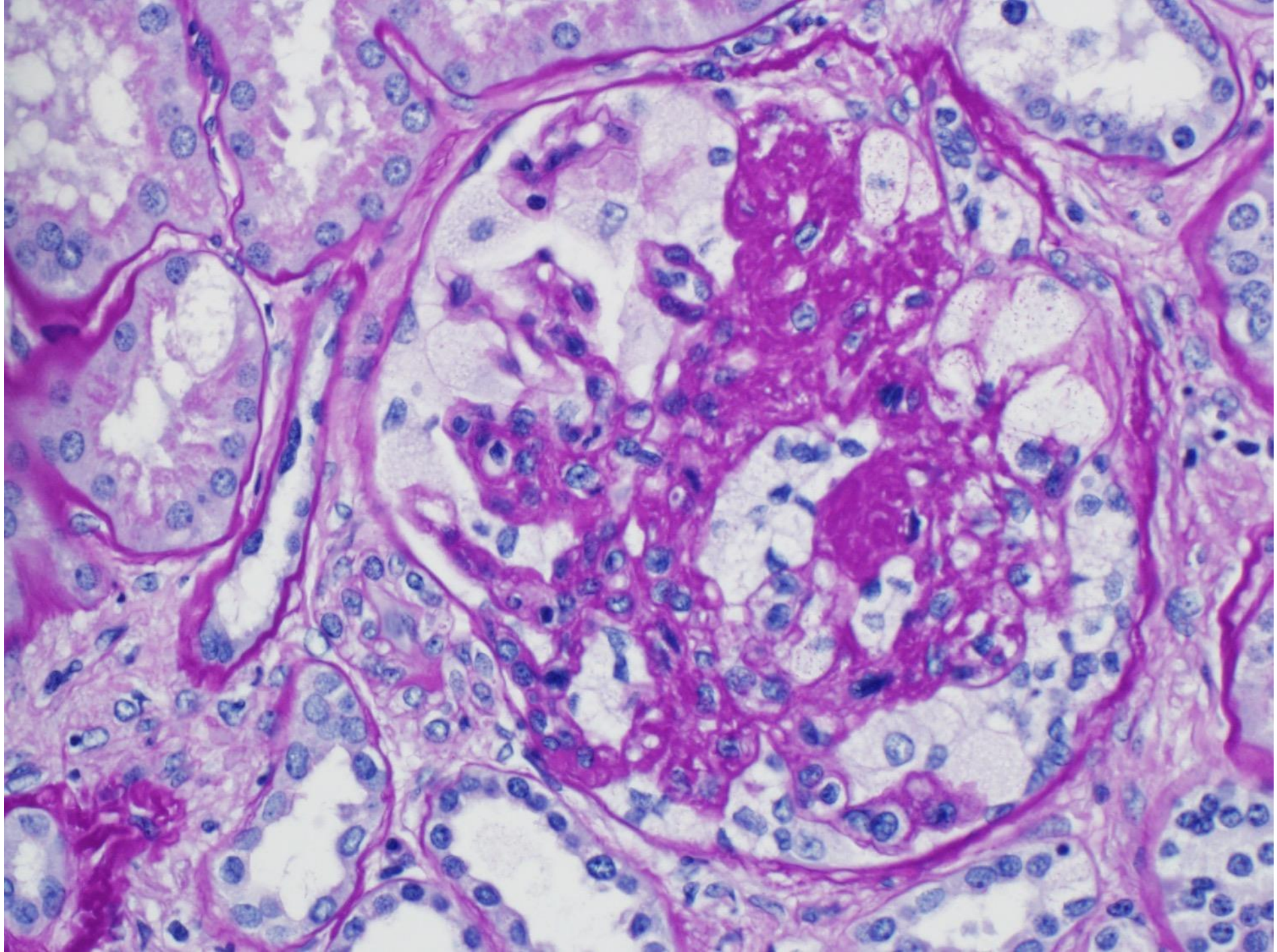


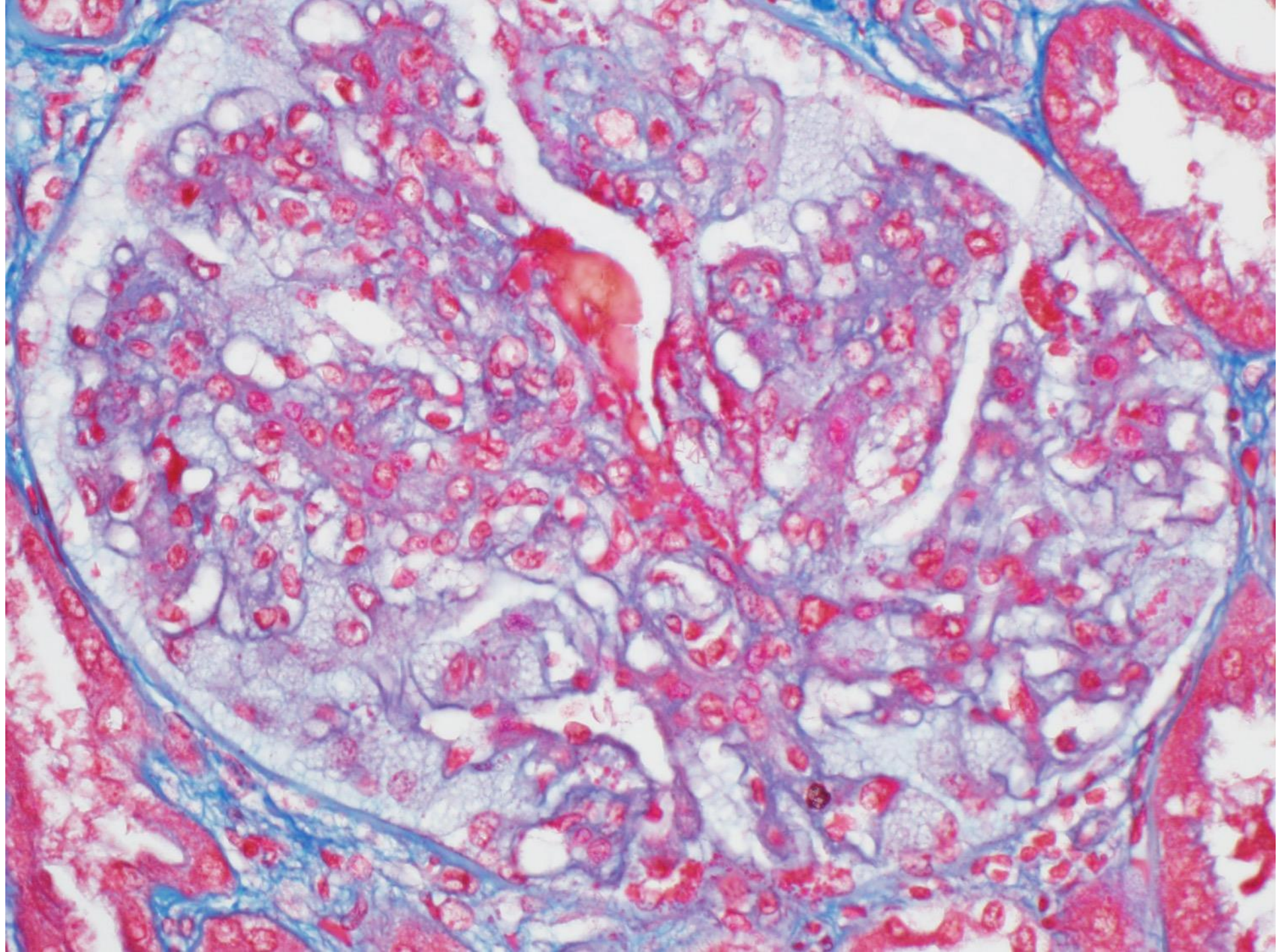












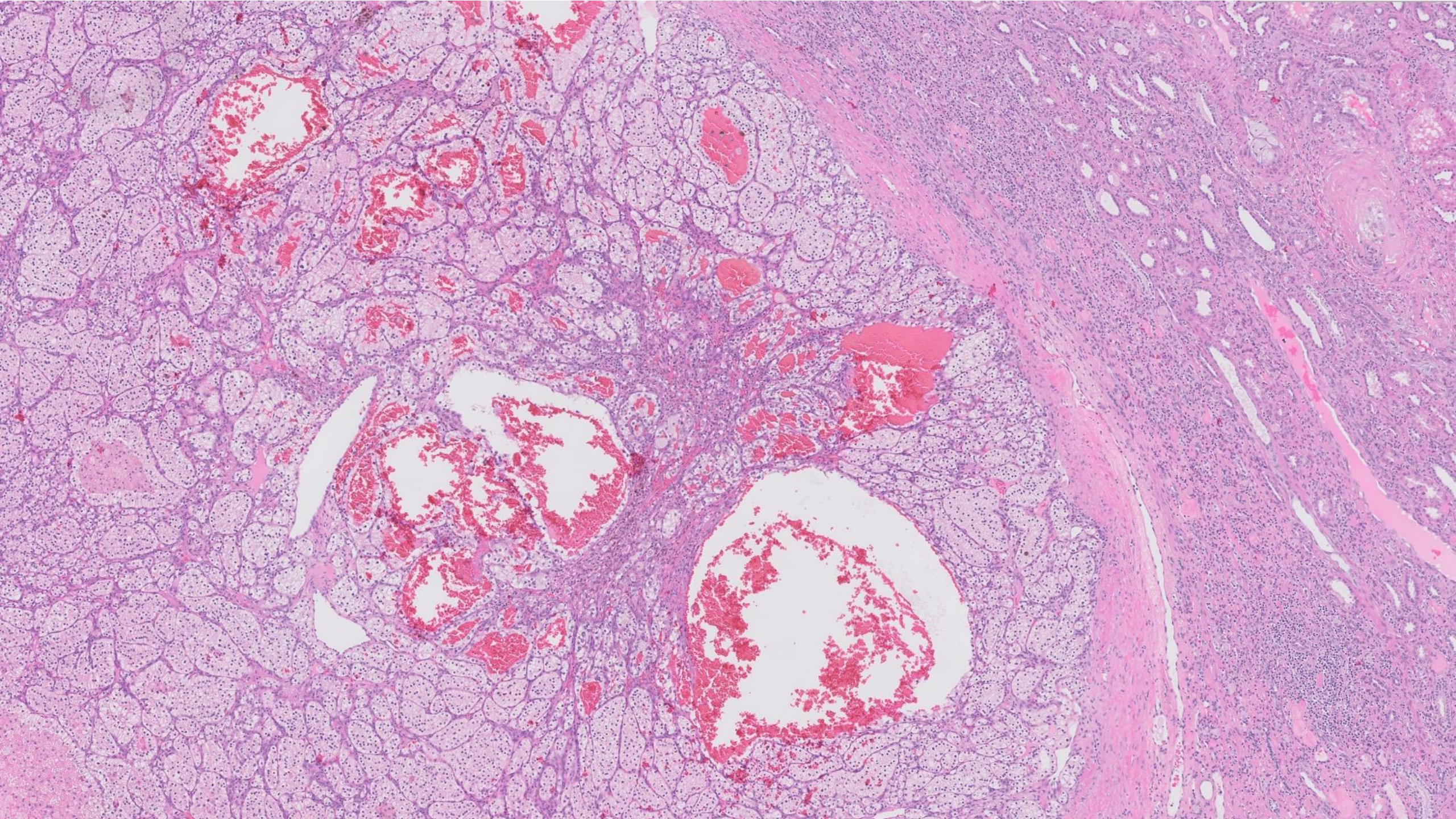
DIAGNOSIS?

South Bay Pathology Conference

October 2023,

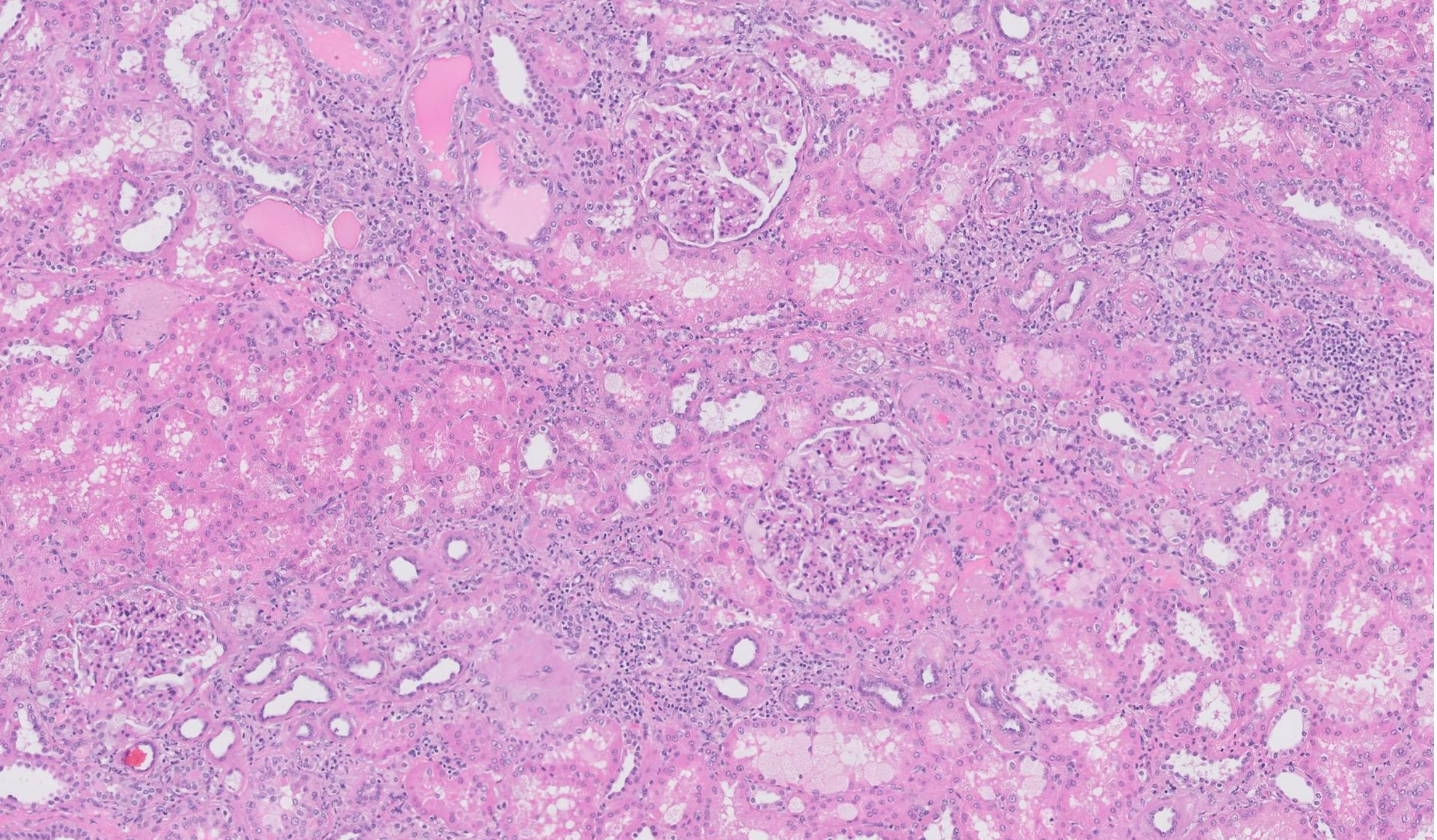
Adrian Agostino

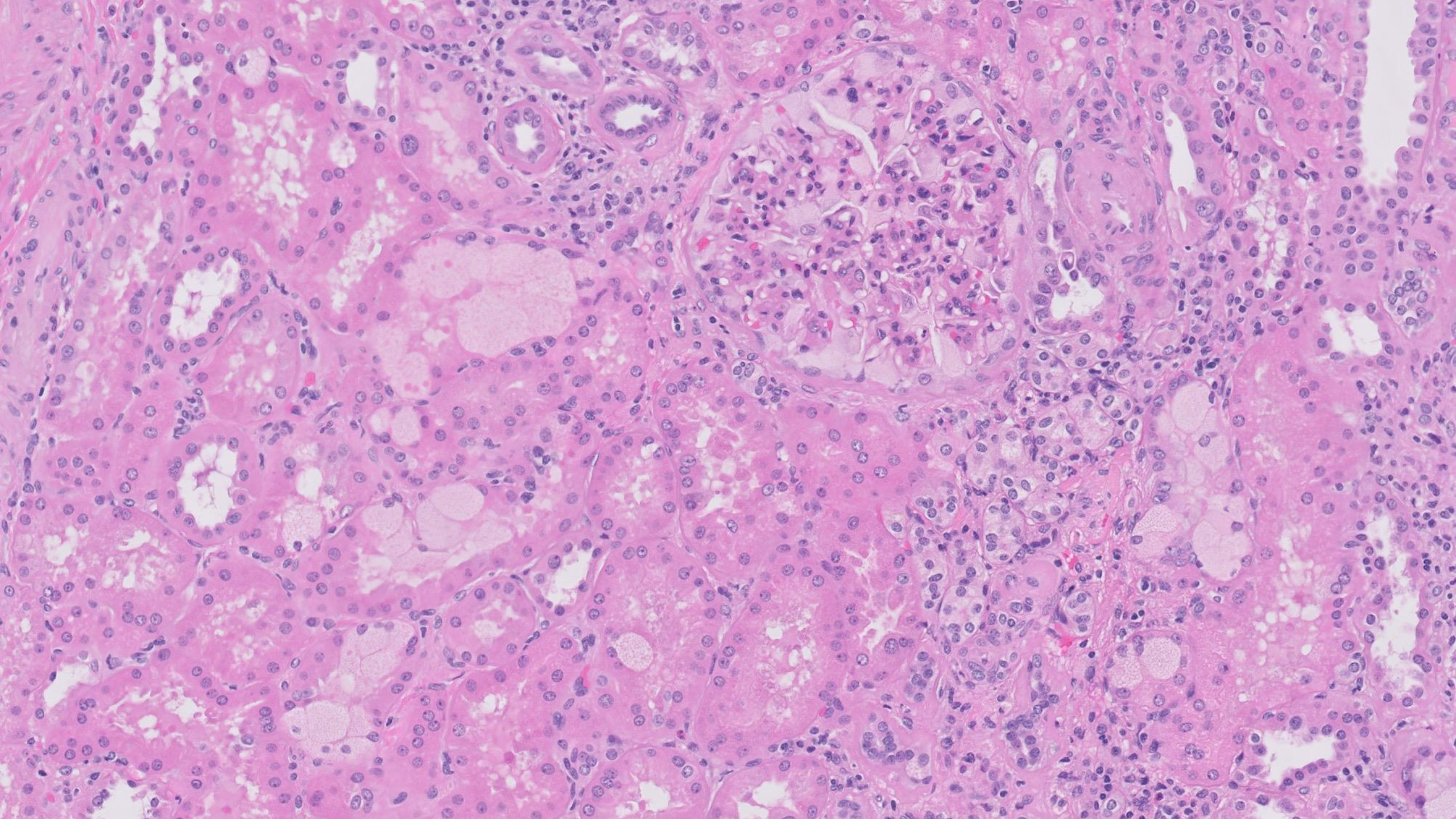
Renal Pathology Fellow

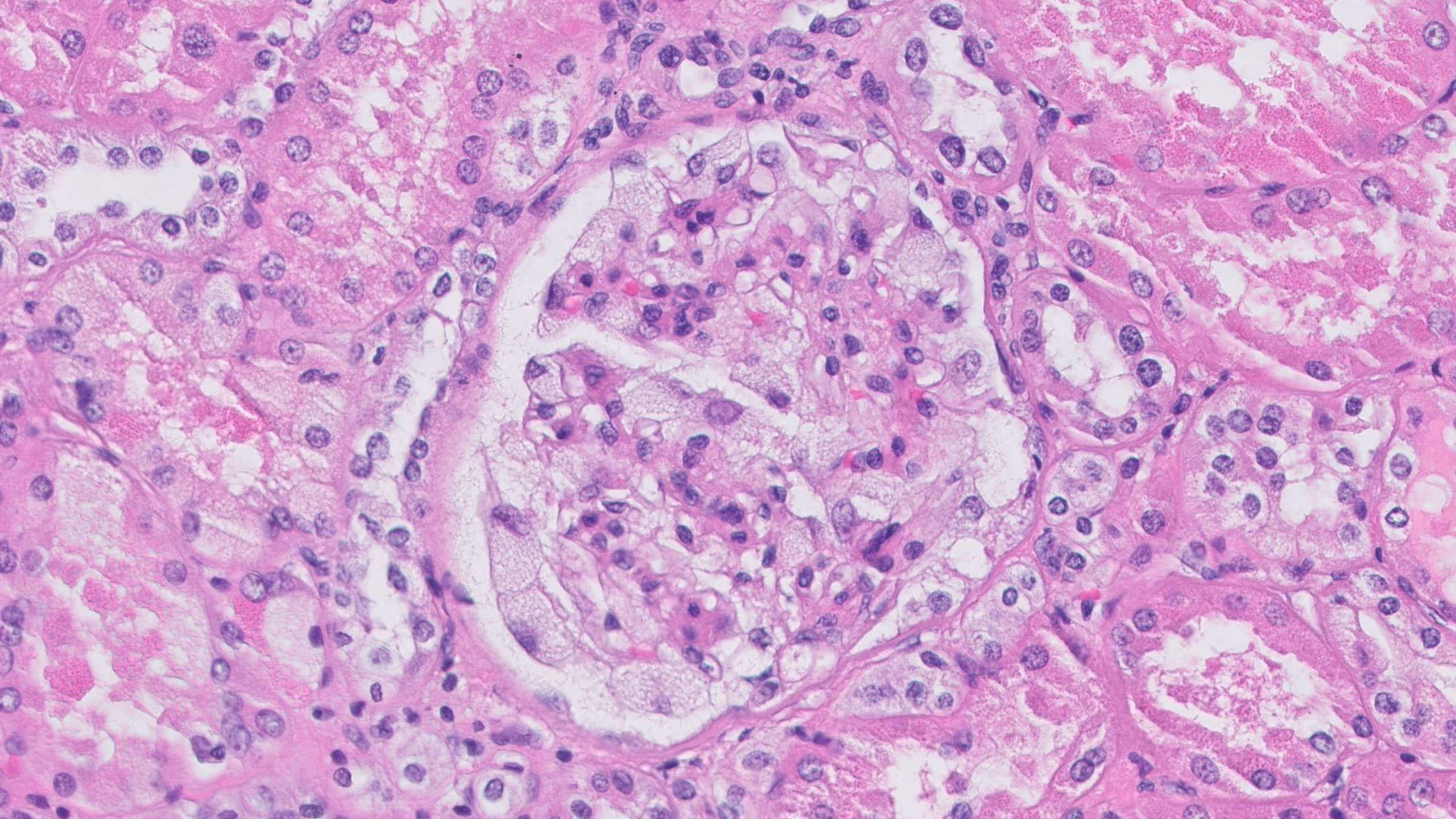


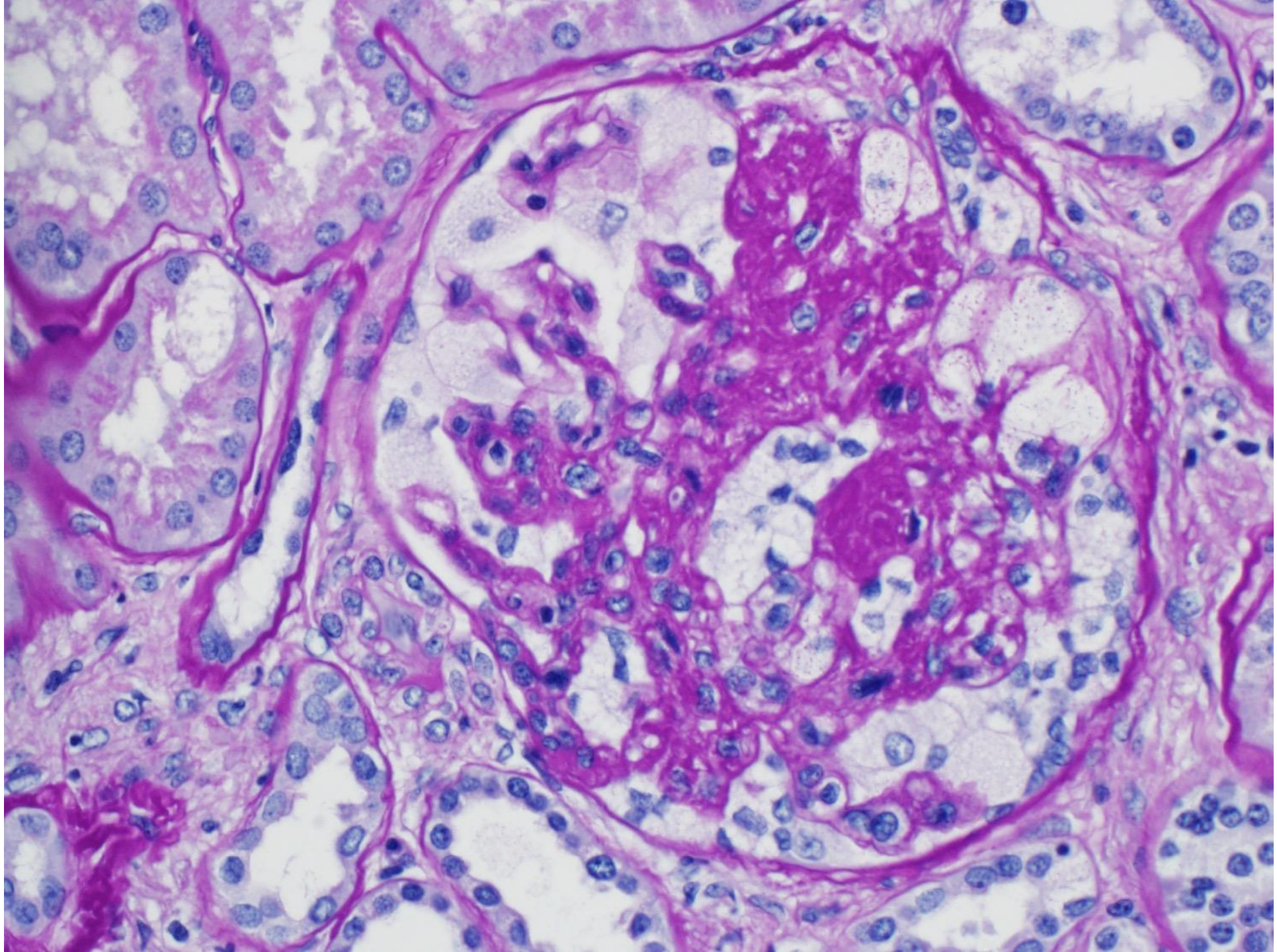
The rest of the story….

- 15 year history of IgG-k multiple myeloma
- Undergone targeted treatment and stem cell transplant
- Bilateral renal masses
  - Partial nephrectomy -> RCC
- Non-neoplastic kidney review

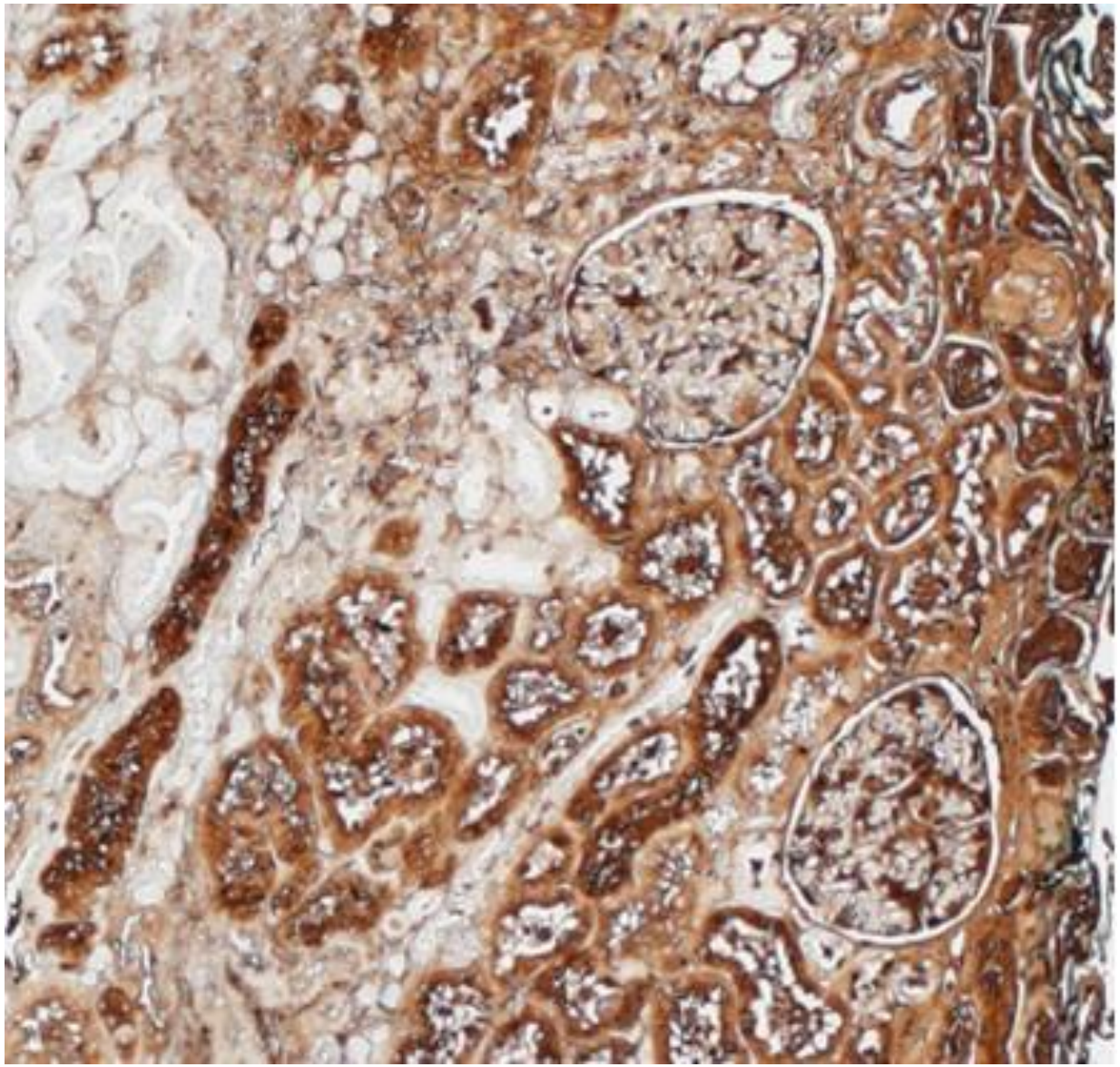




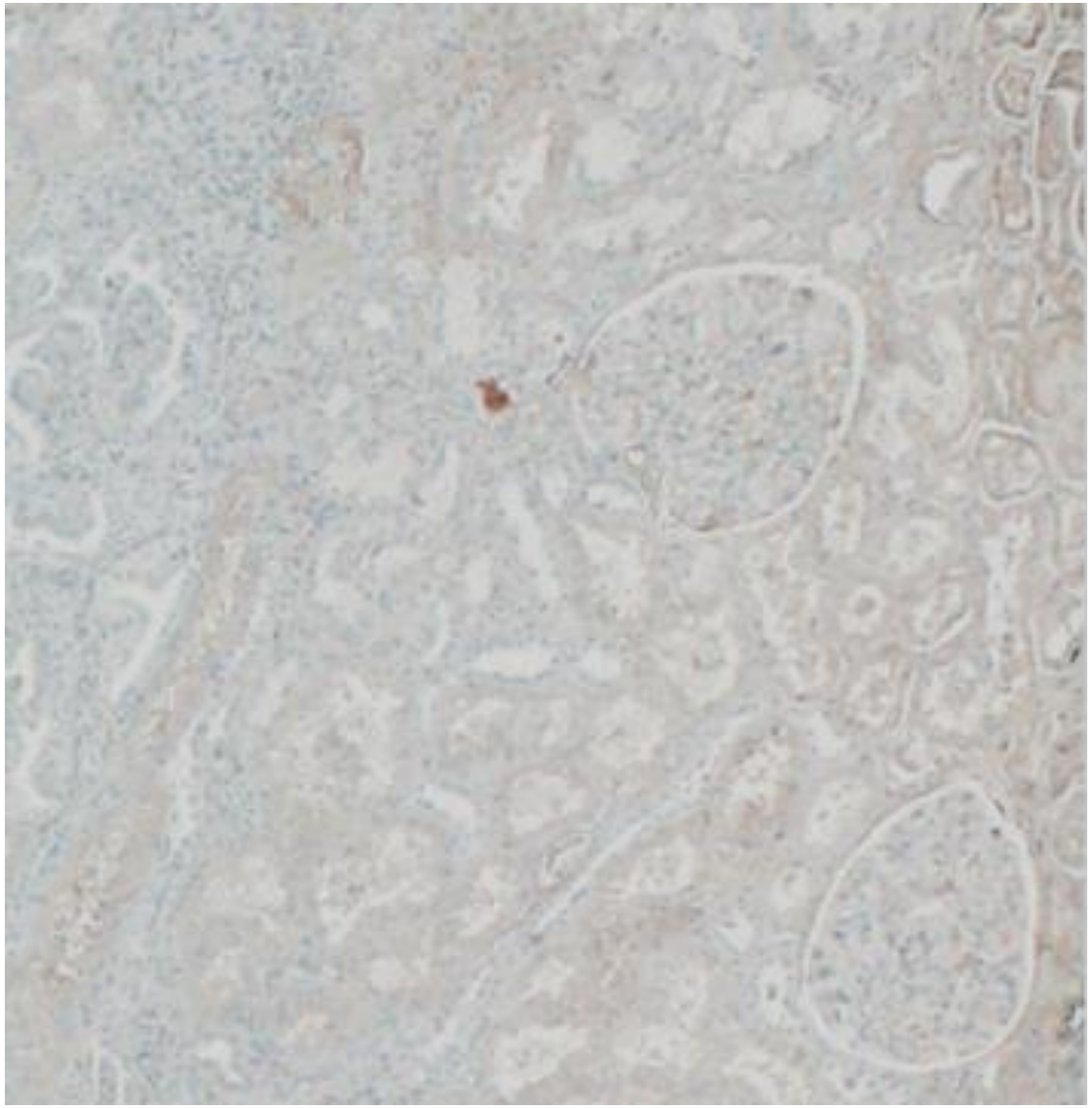




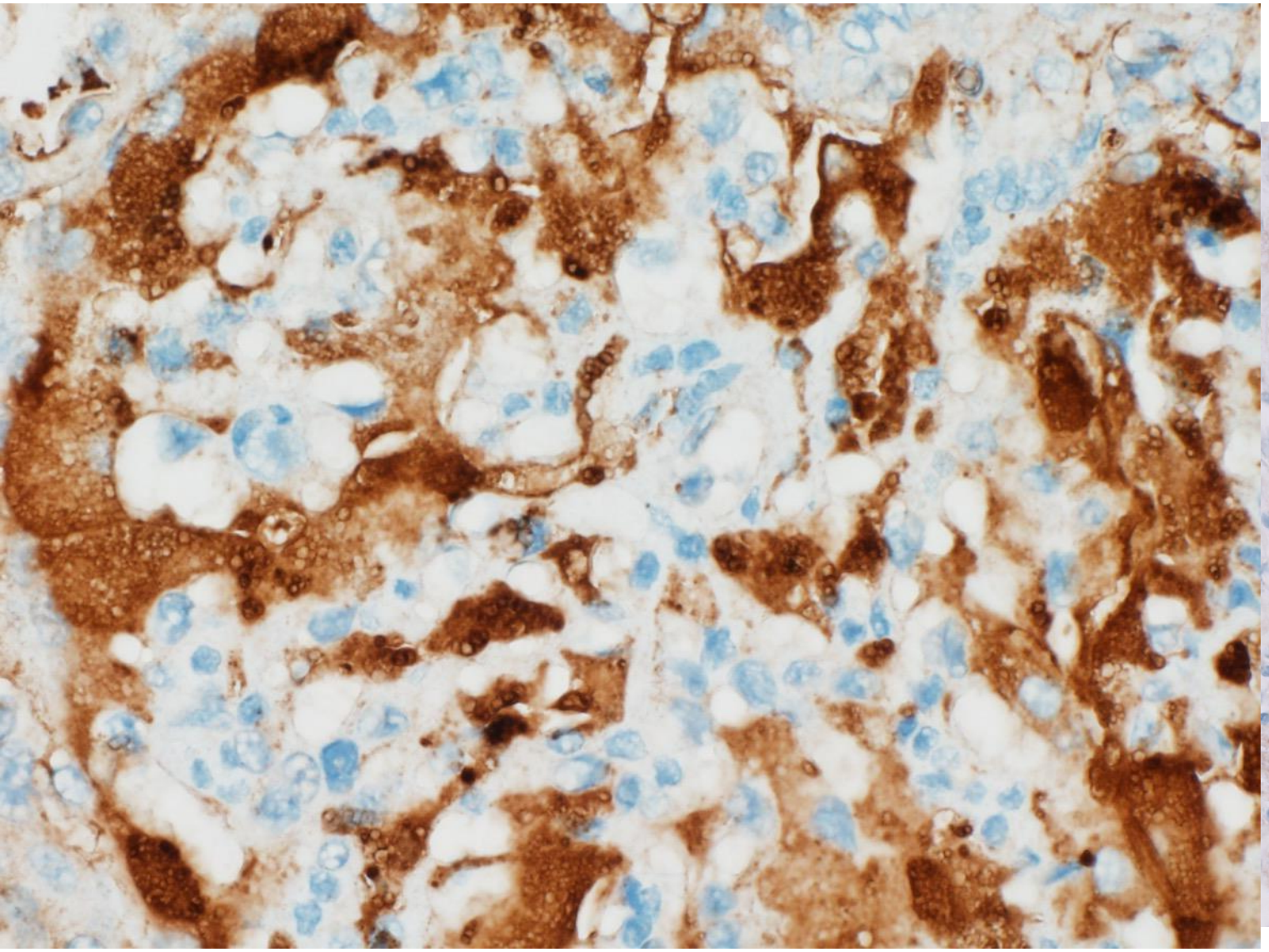
Kappa IHC



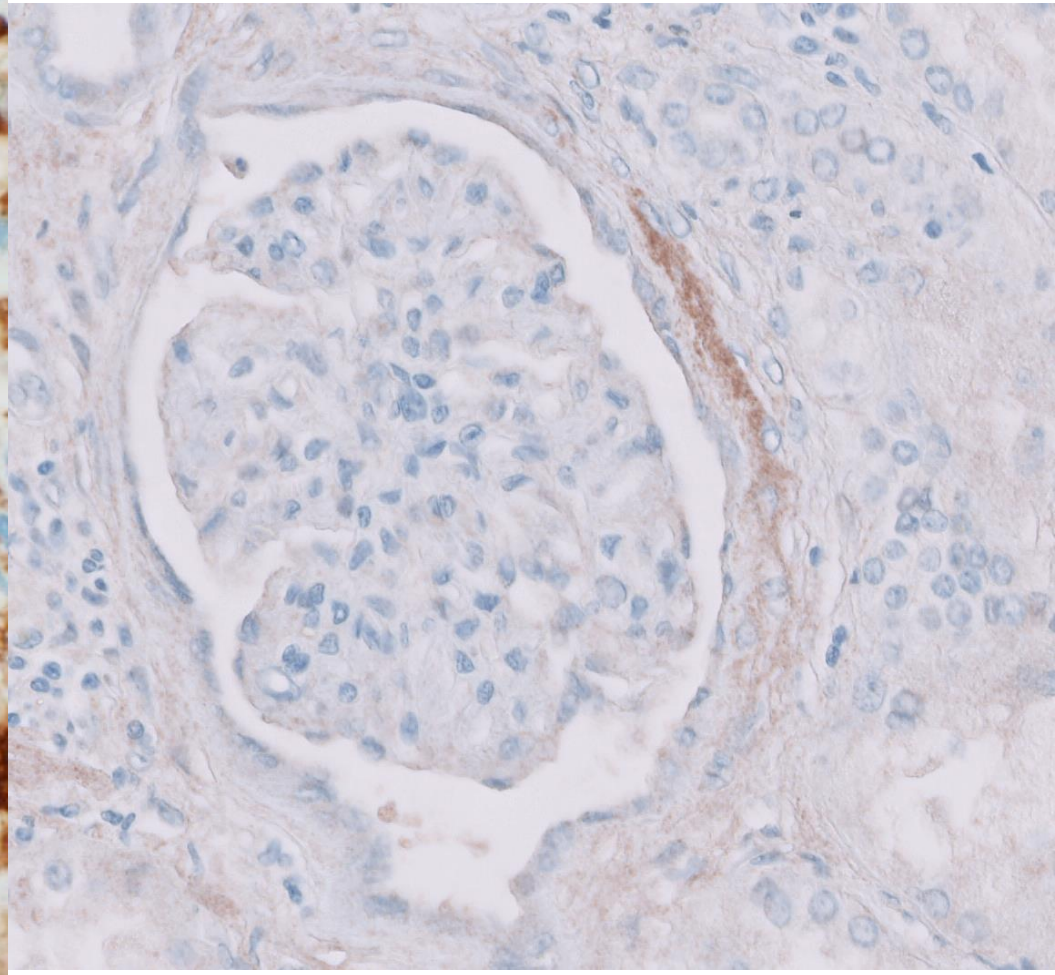
Lambda IHC

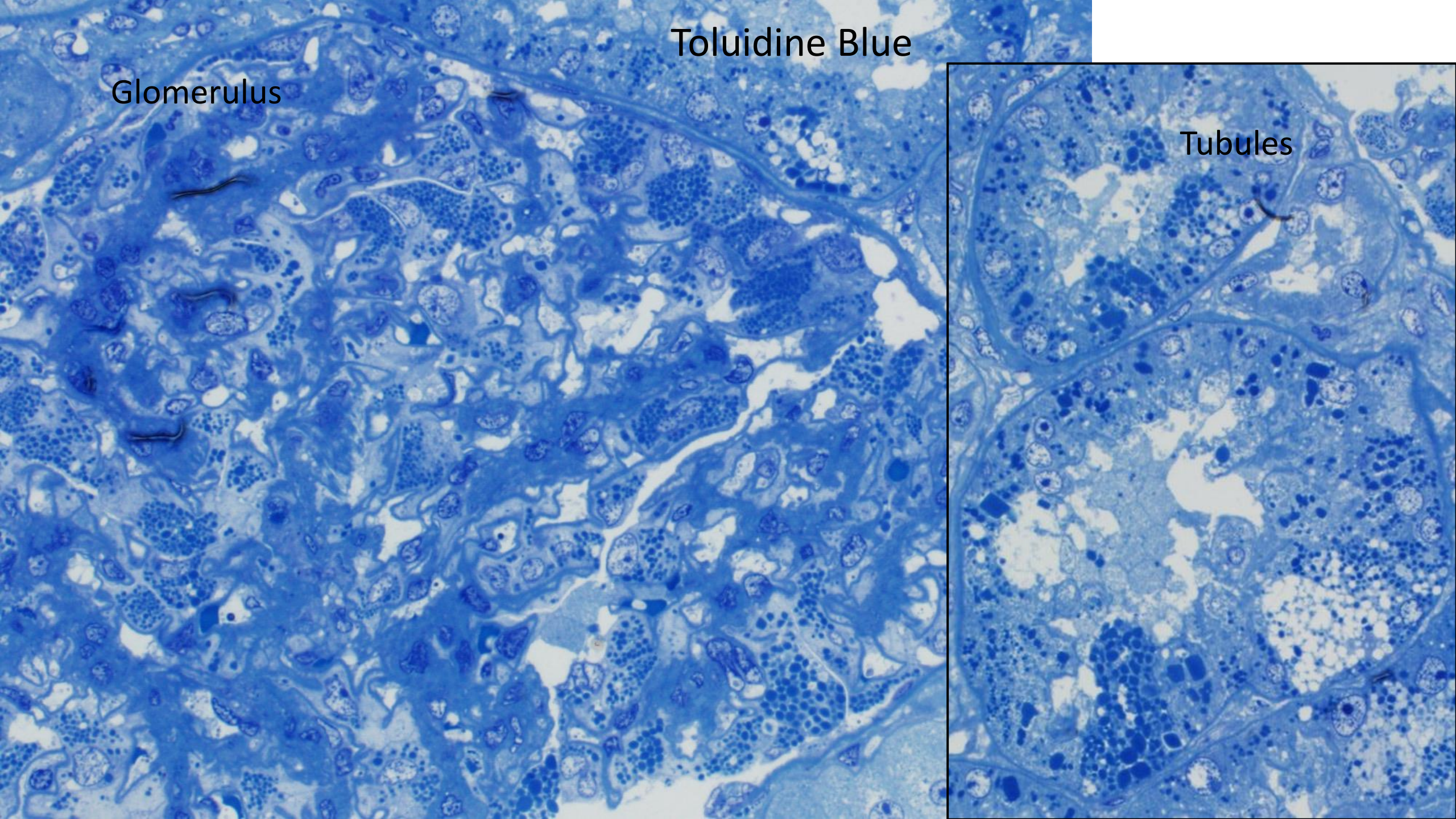


Kappa IHC

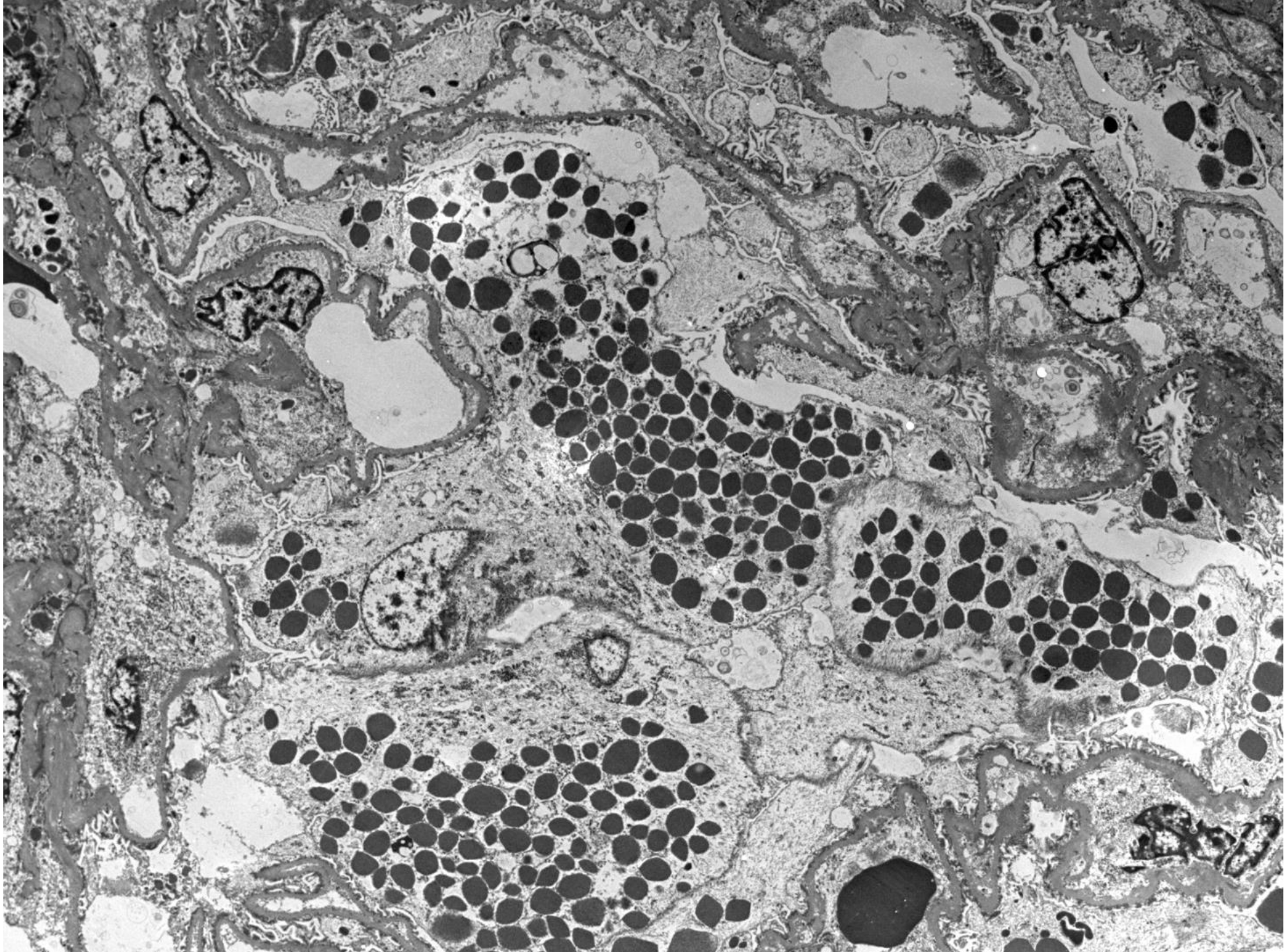


Lambda IHC

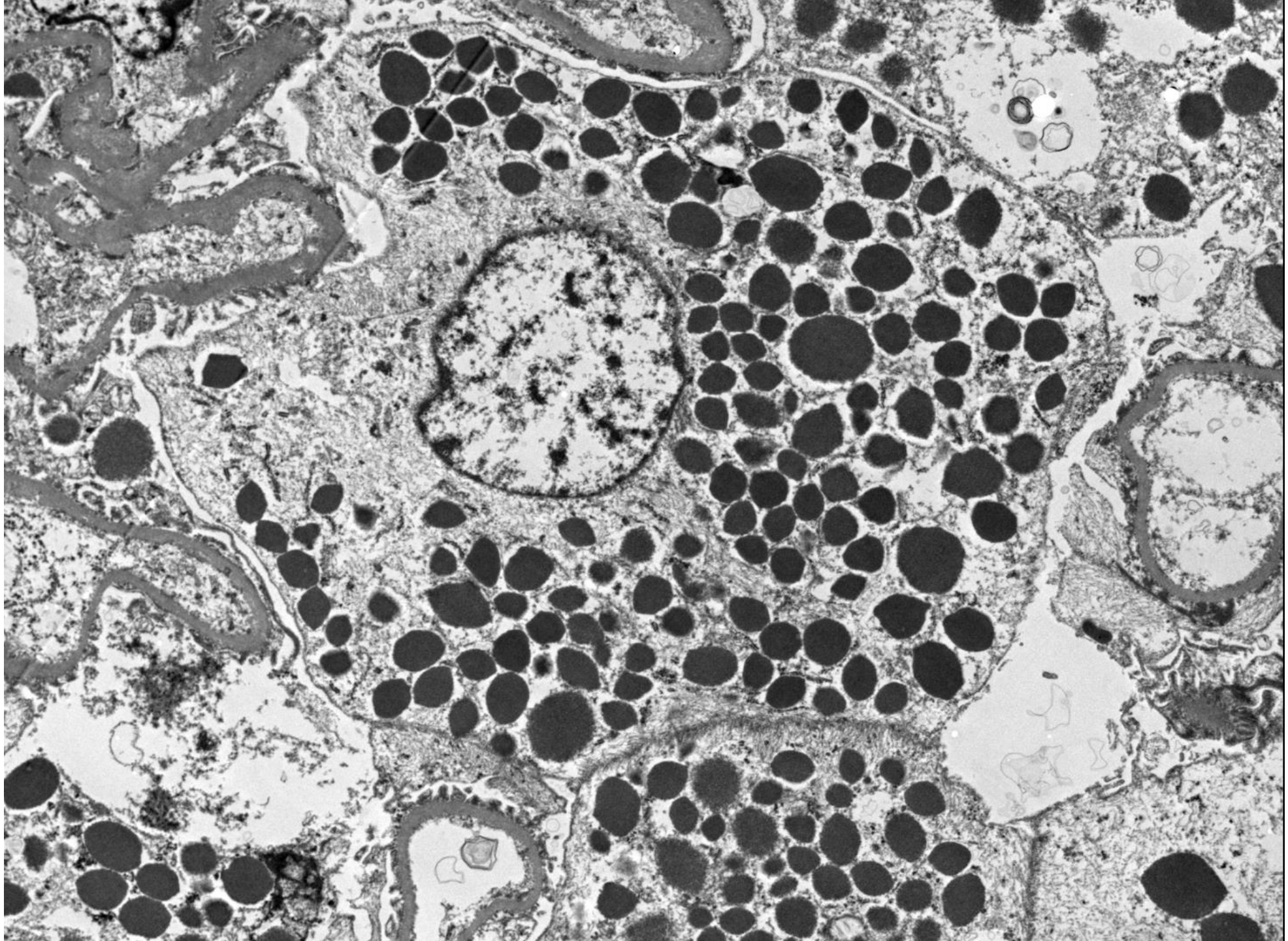



Toluidine Blue
Glomerulus
Tubules

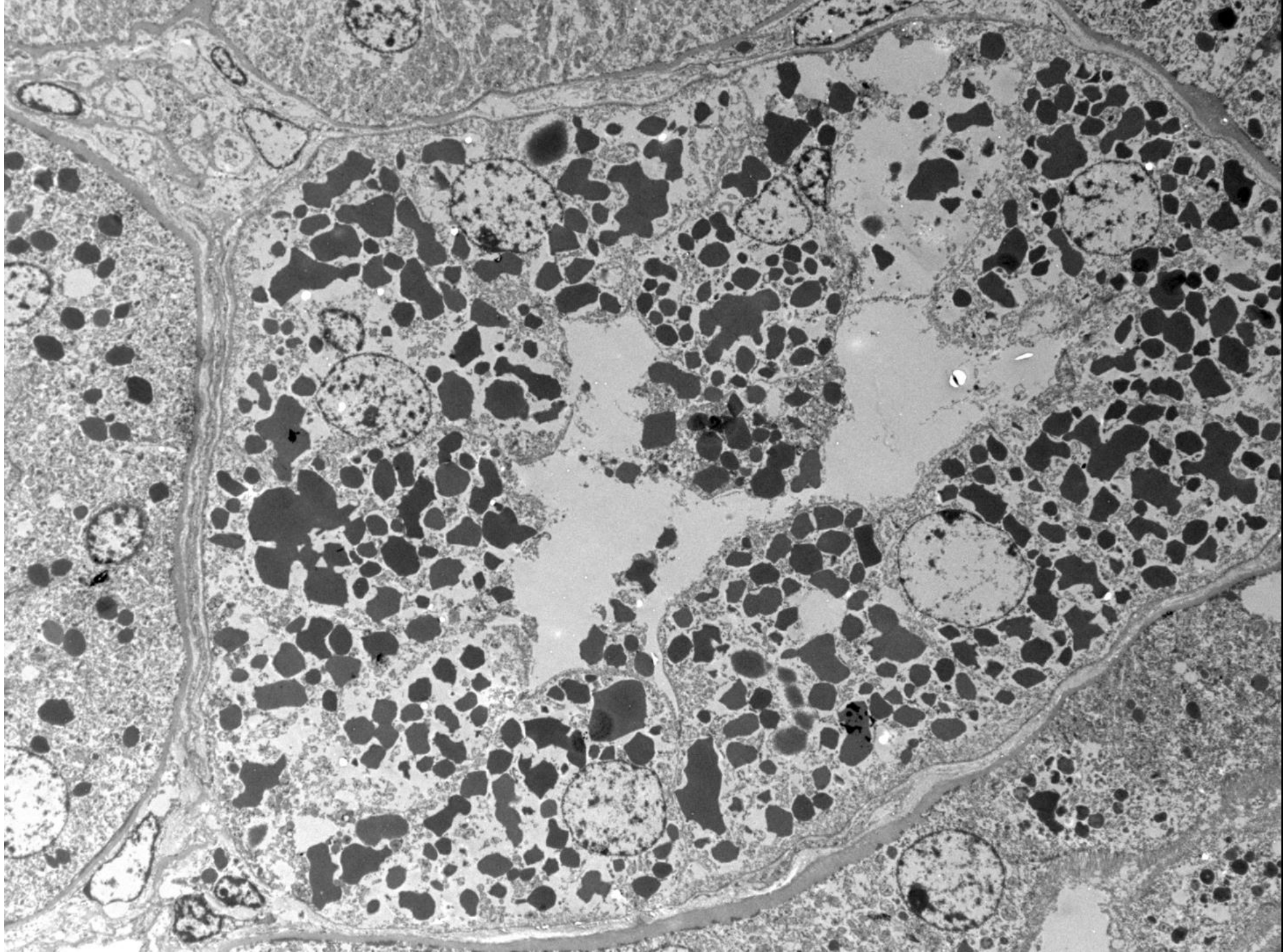
EM



EM



EM Tubule



Diagnosis:

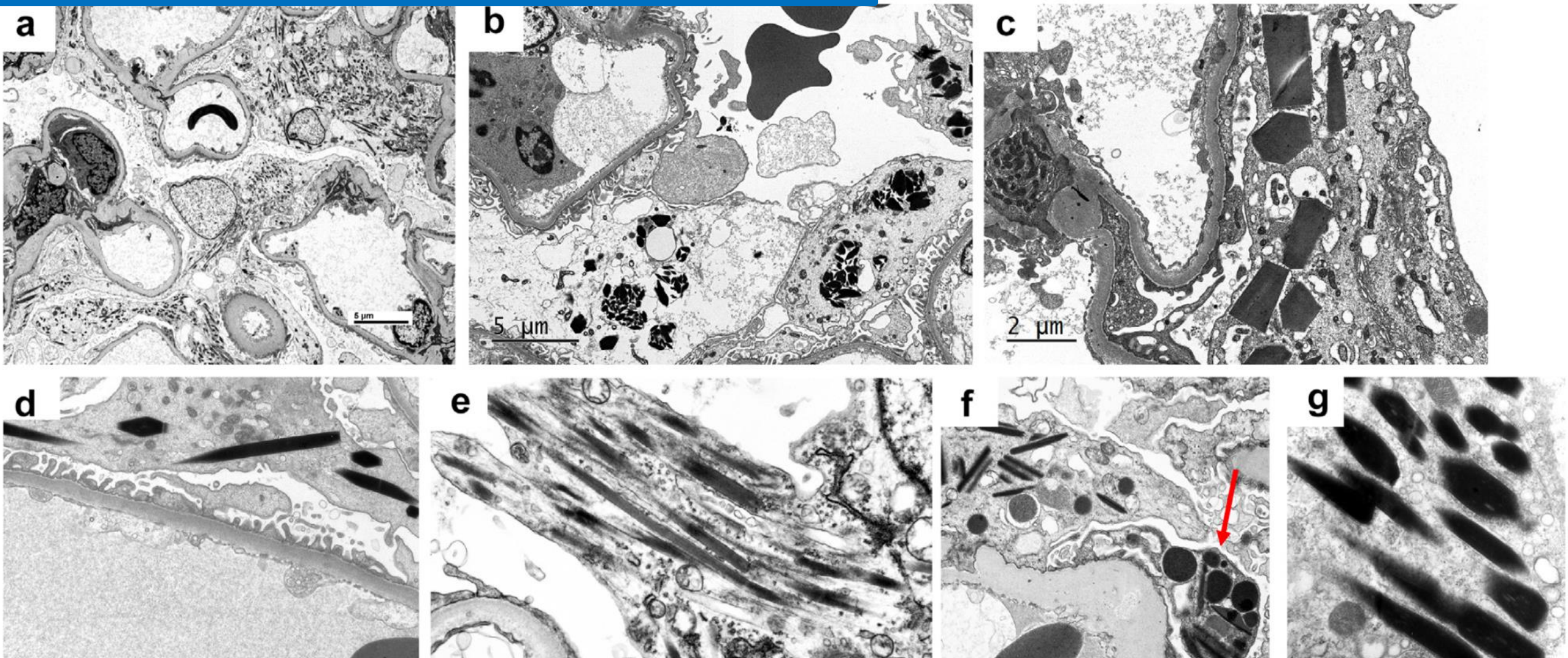
- Kappa - Light chain crystalline podocytopathy and tubulopathy

clinical investigation

Nasr et al. Kidney International (2023) 103, 616–626

Pathological characteristics of light chain crystalline podocytopathy

FSGS: direct podocyte injury, then dysfunction and depletion due to toxic light chain crystals

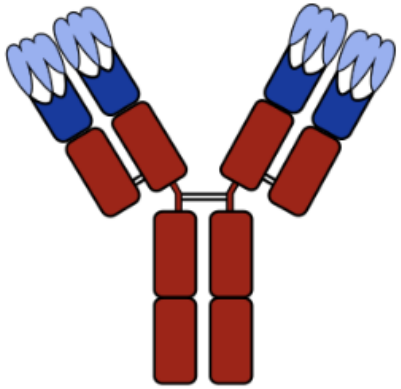


Additional information:

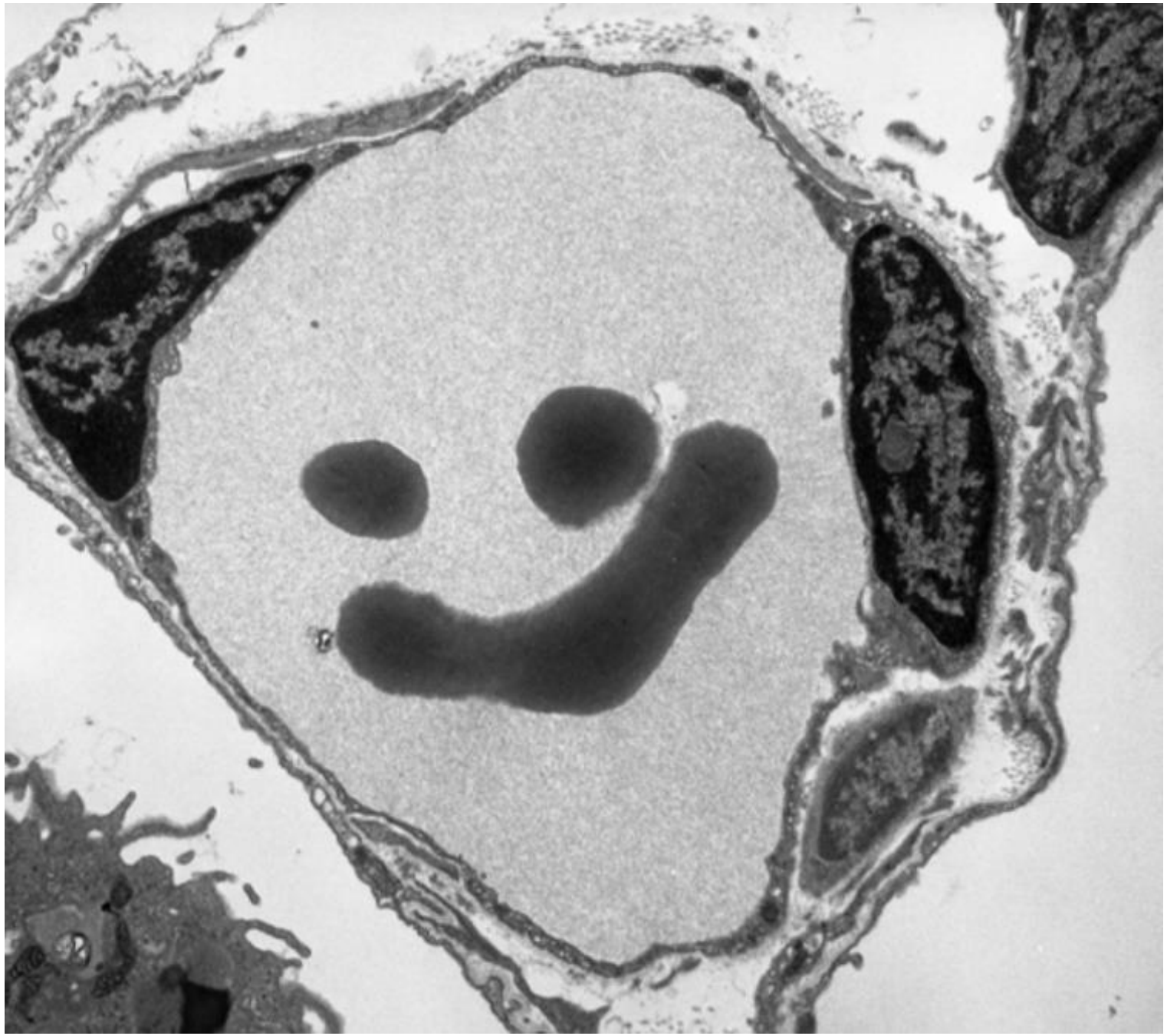
Nasr et al. Kidney International (2023) 103, 616–626

Parameter	Present series	Literature review
Age	56 (39–74)	53 (23–71)
Male/Female	17/8	15/8
Cases with FSGS Collapsing FSGS	15/25 (60%) 10/15 (67%)	17/23 (74%) 6/16 (38%)
Kappa vs Lambda	23/2	17/0
Detected by Standard IF Paraffin IF Paraffin IHC	2/25 (12%) 17/22 (77%) 5/6 (83%)	3/17 (18%) 4/7 (57%) 8/10 (80%)
Proximal tubulopathy	15/20 (80%)	14/18 (78%)

- MGUS 55% while multiple myeloma 45%
- Pathogenesis of LCCP remains unknown
- Propensity for crystallization due to resistance of LCs to lysosomal proteases because of somatic mutations in the CDR



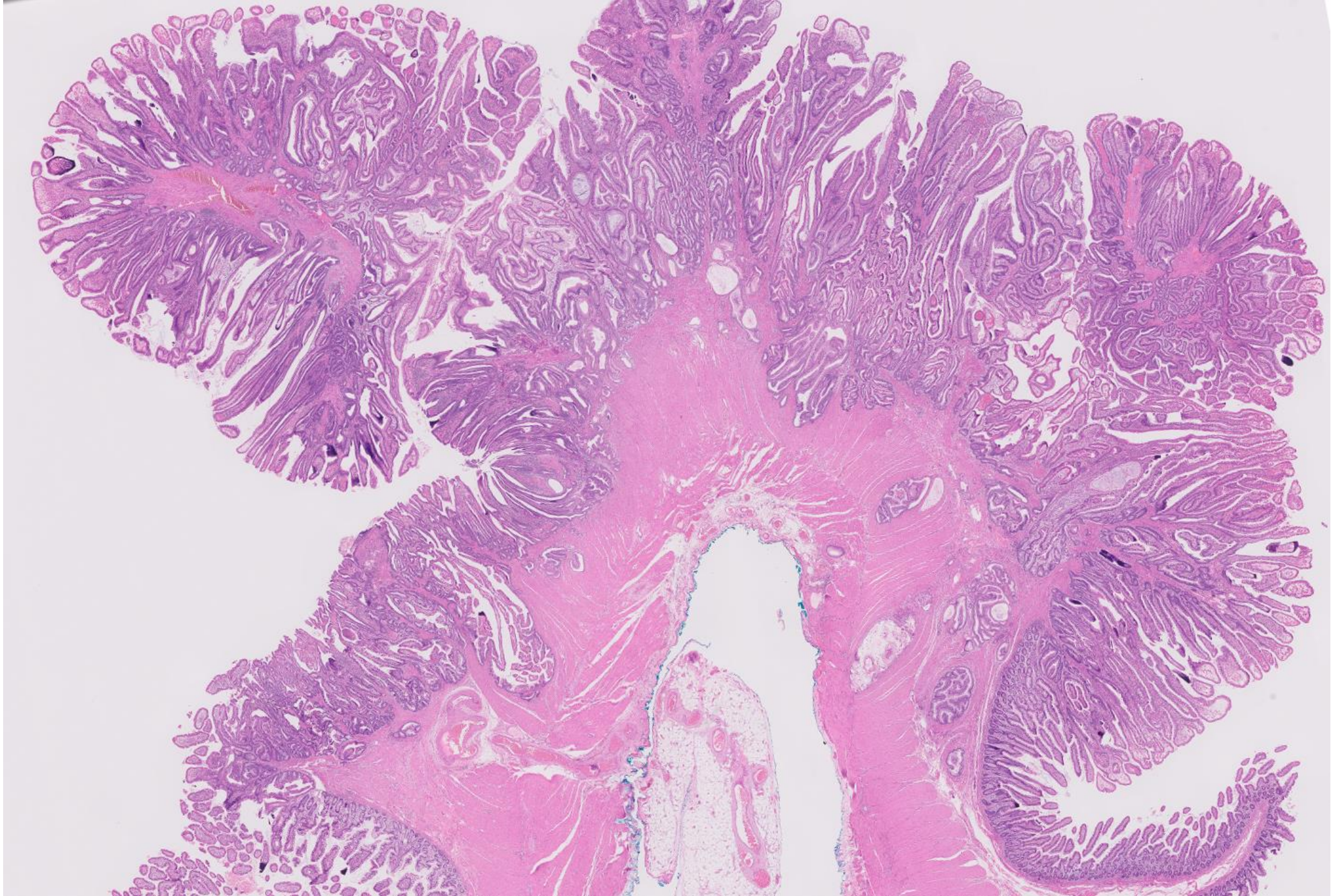
Thank You

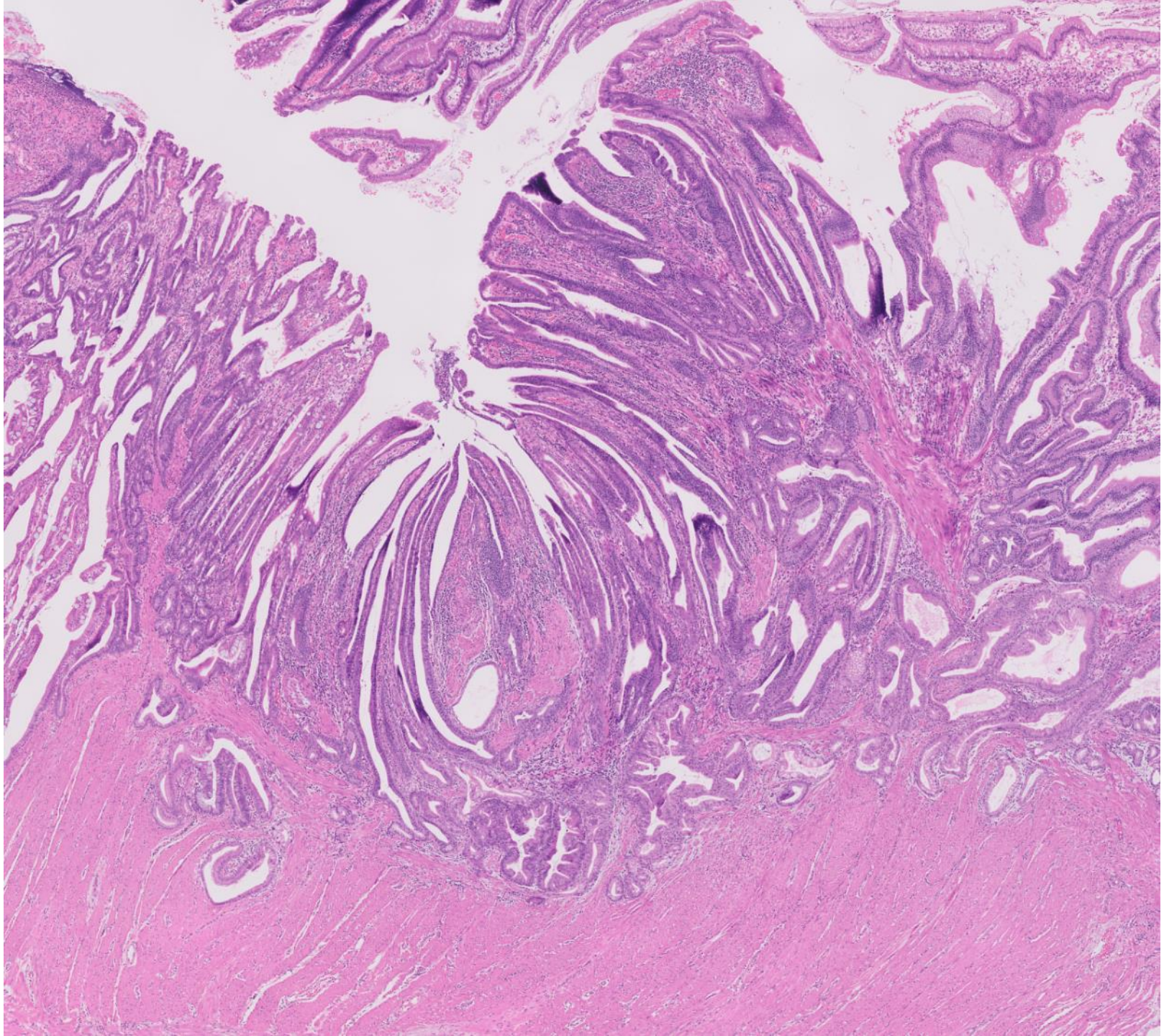


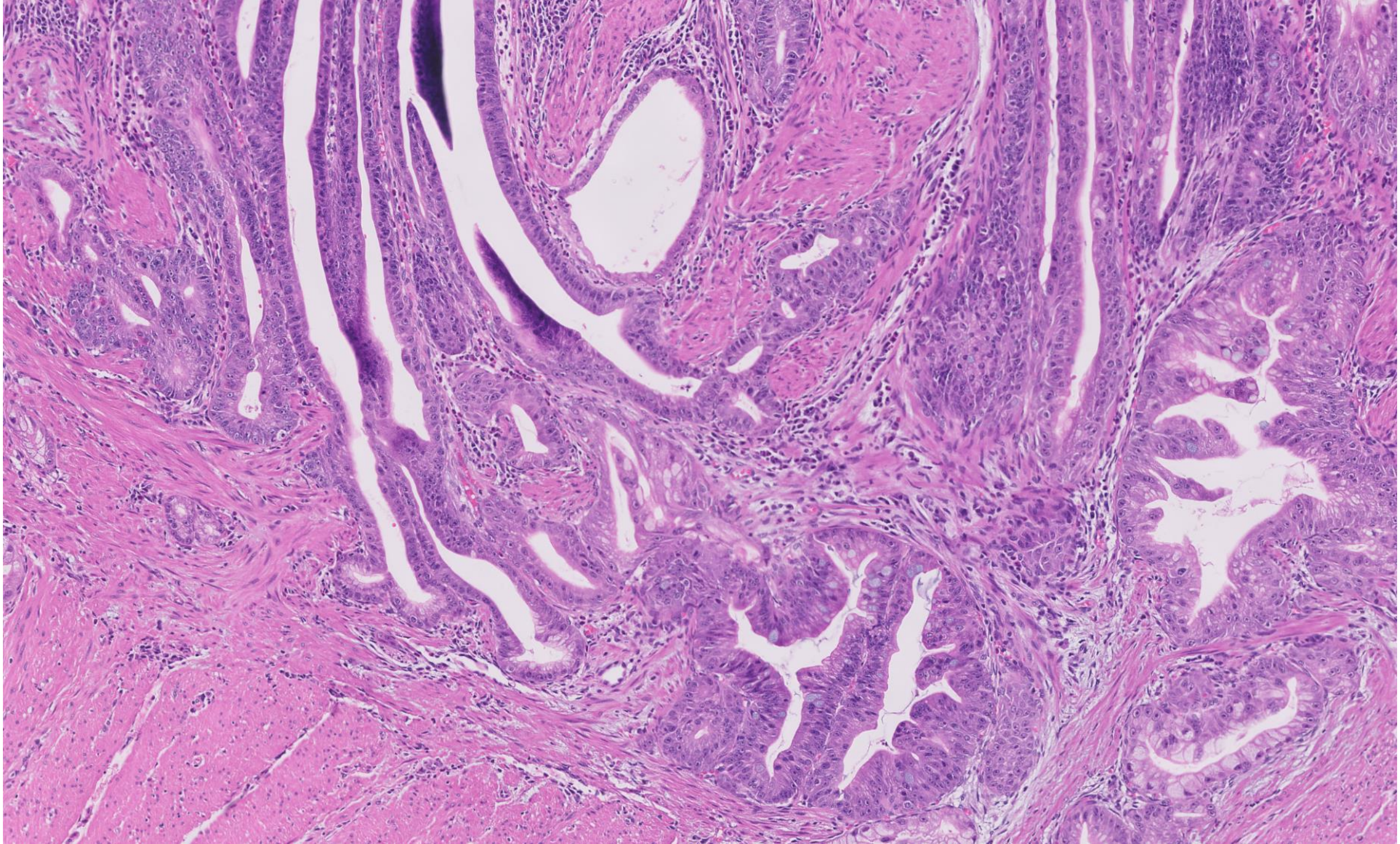
23-1005

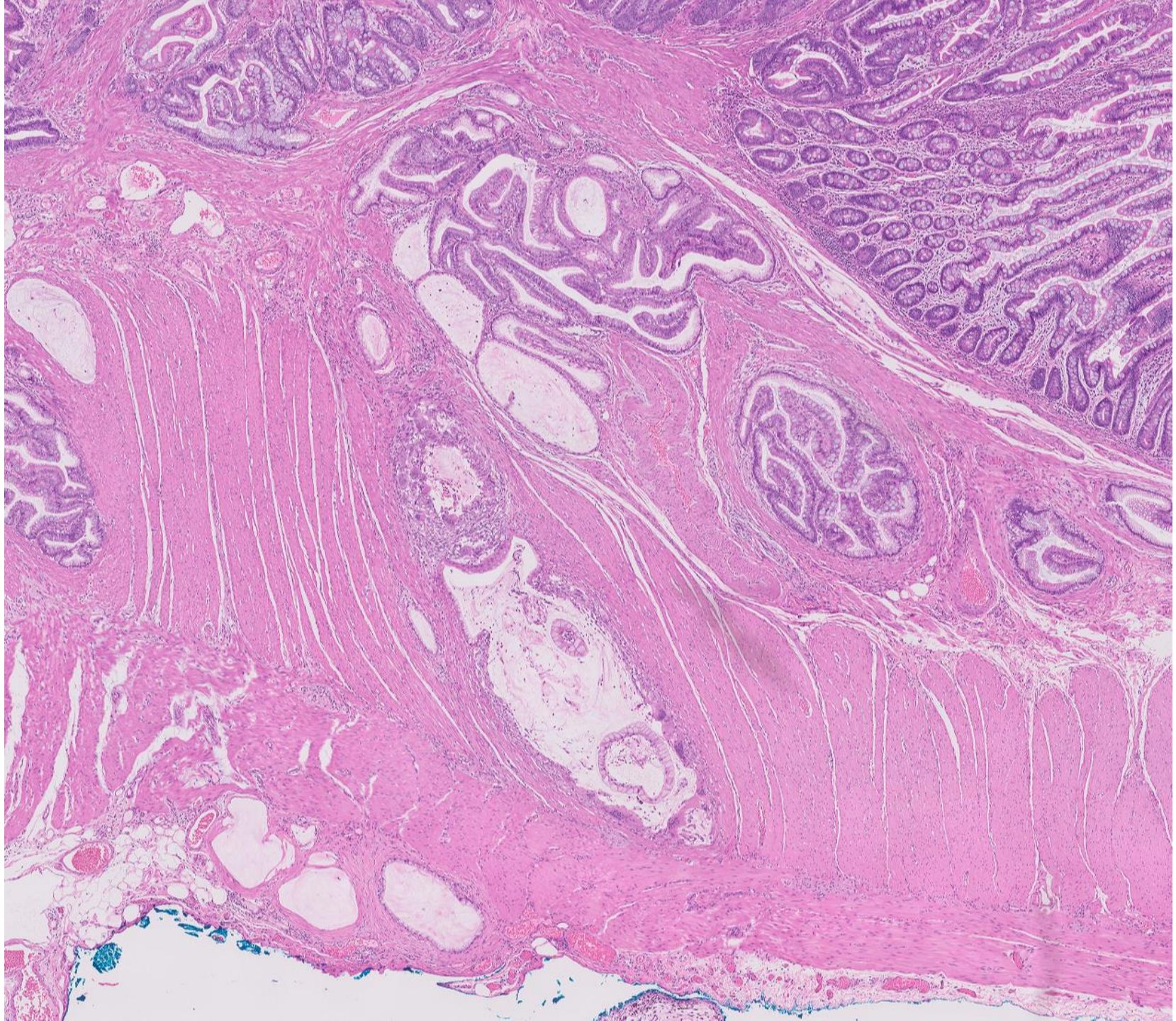
Cindy Wang and David Bingham; Stanford

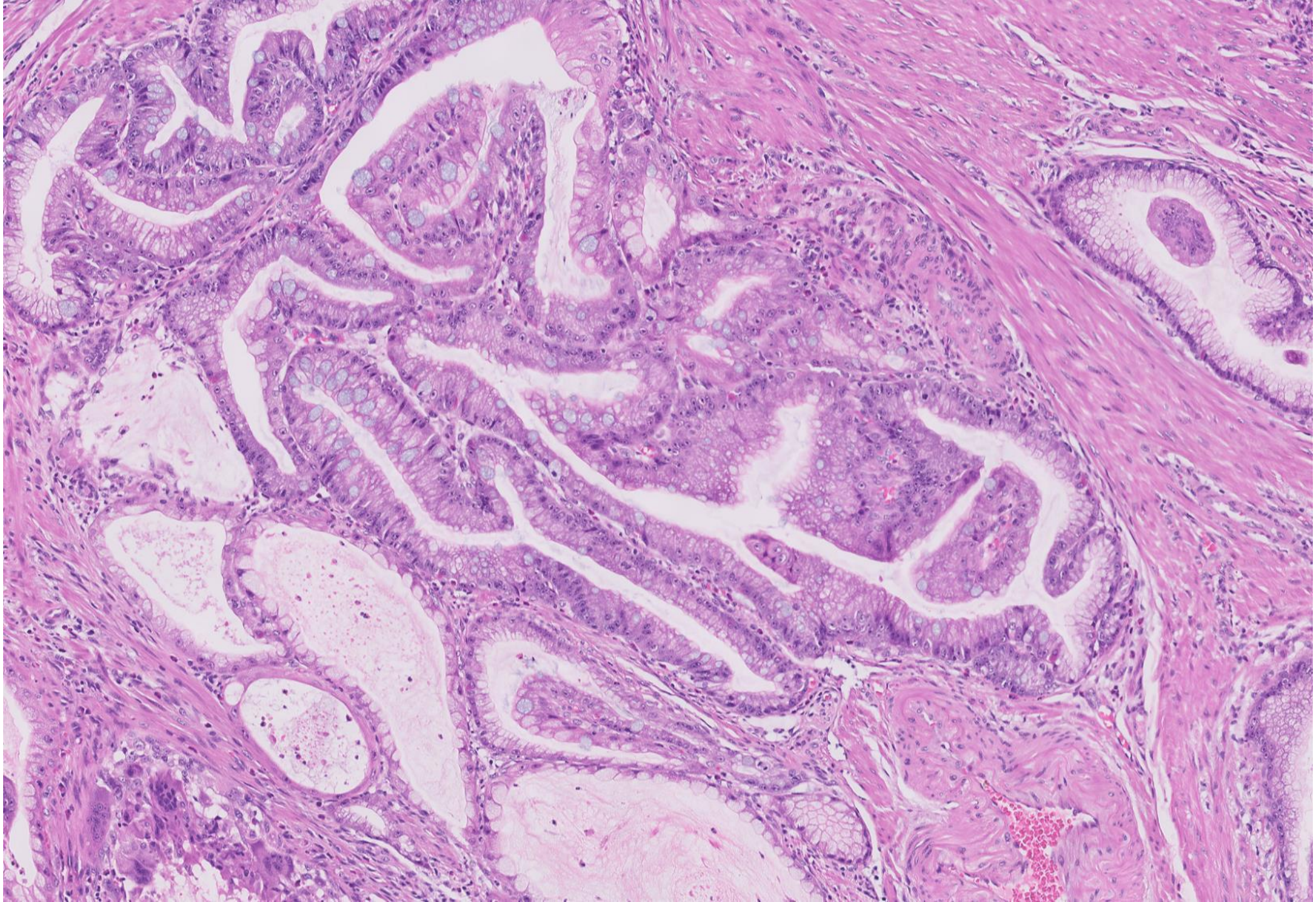
50 yo M with small bowel mass

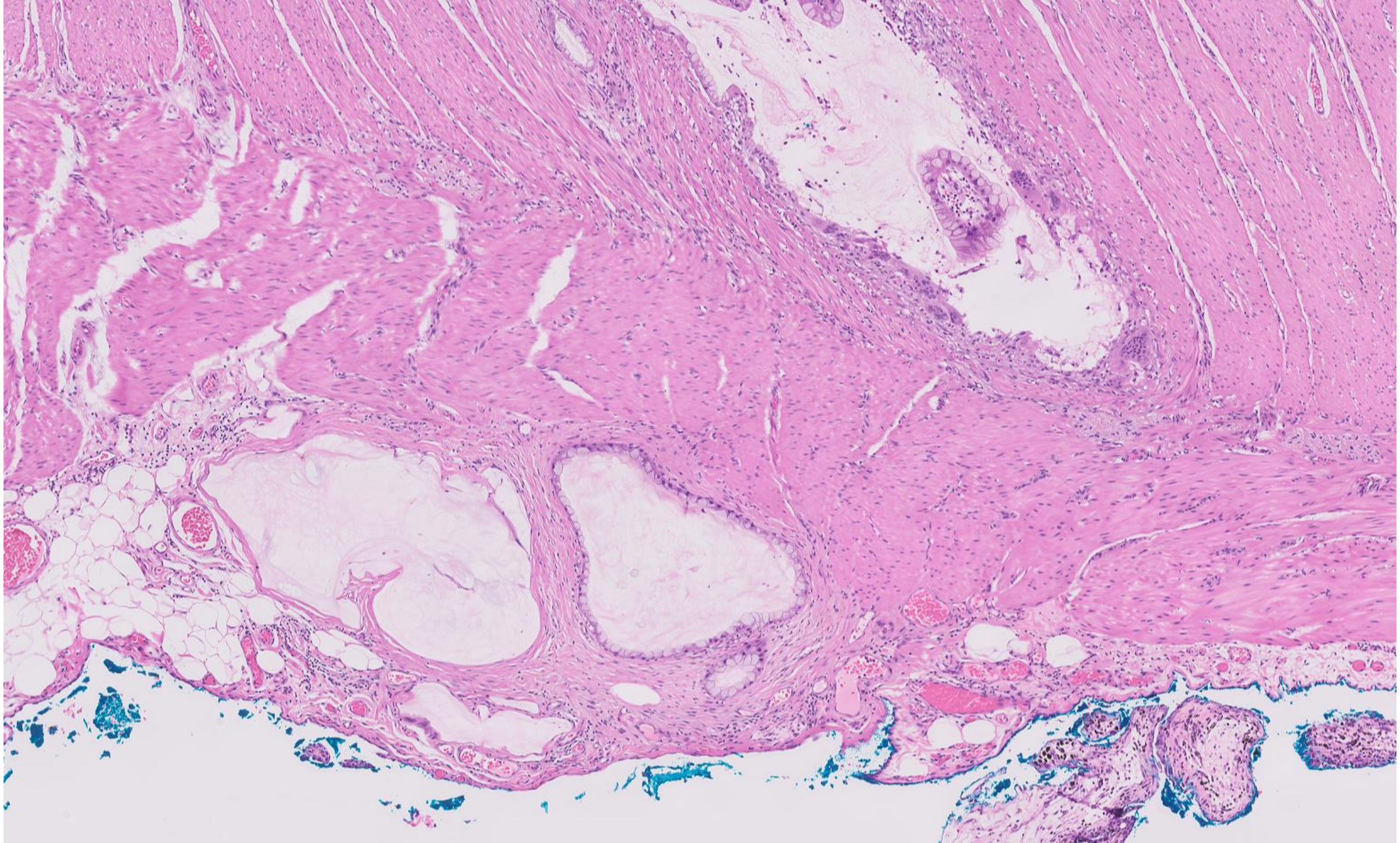










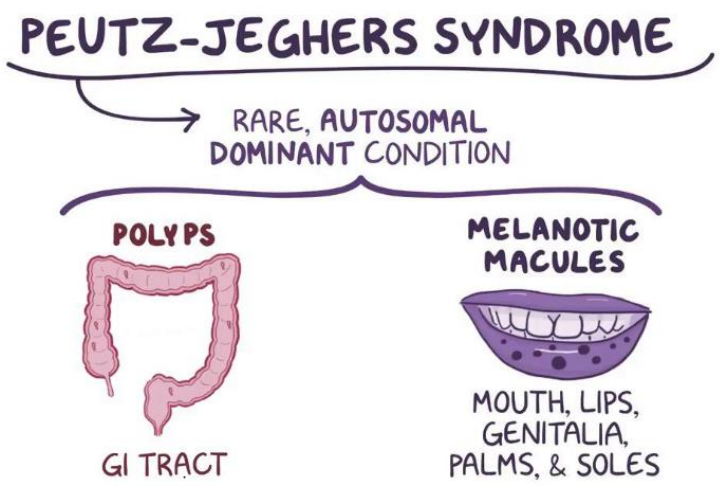


DIAGNOSIS?

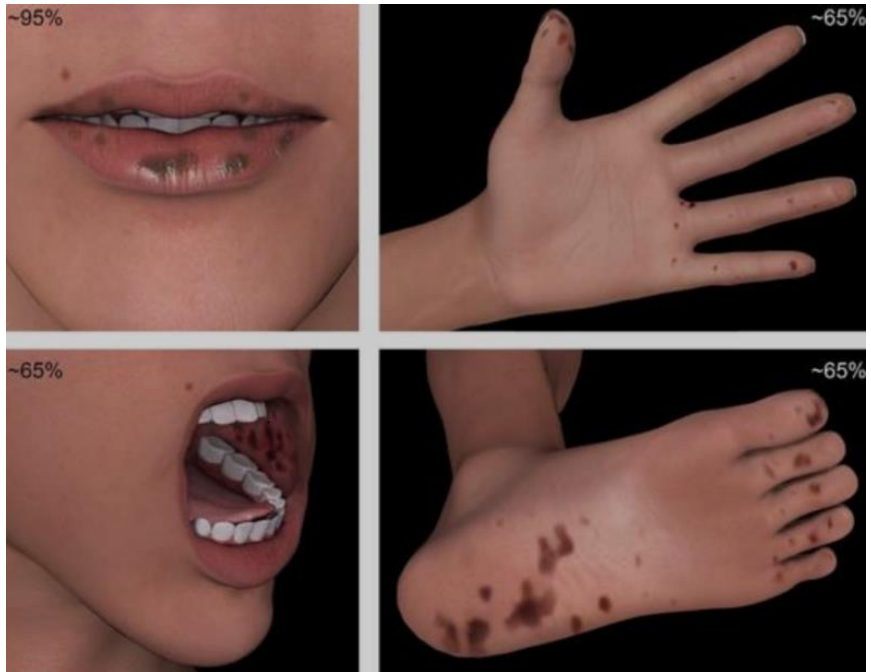
Diagnosis:

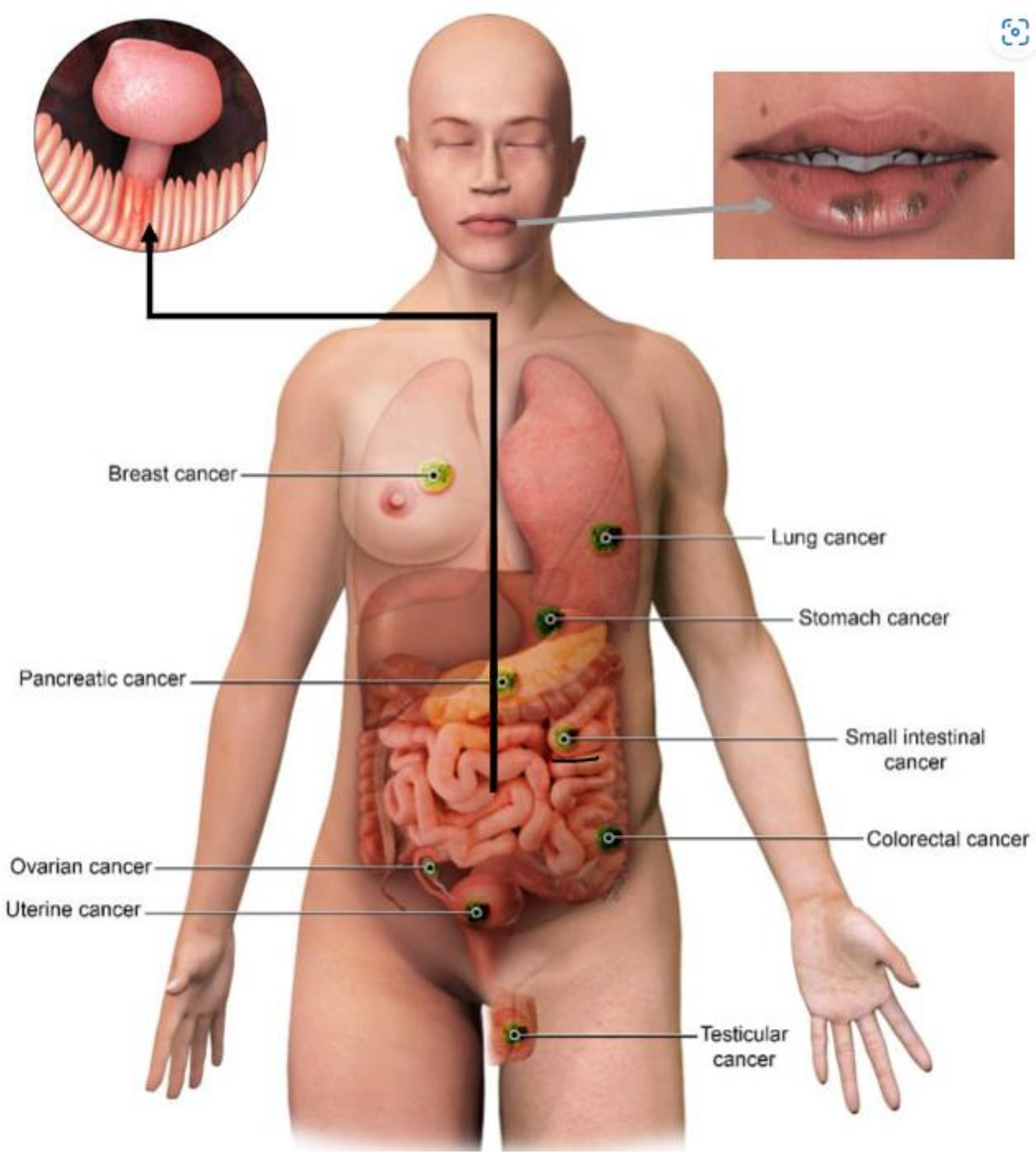
Intramucosal adenocarcinoma arising from a hamartomatous polyp with extensive epithelial misplacement

Patient with Peutz-Jeghers syndrome



1 in 25,000 to 300,000 births





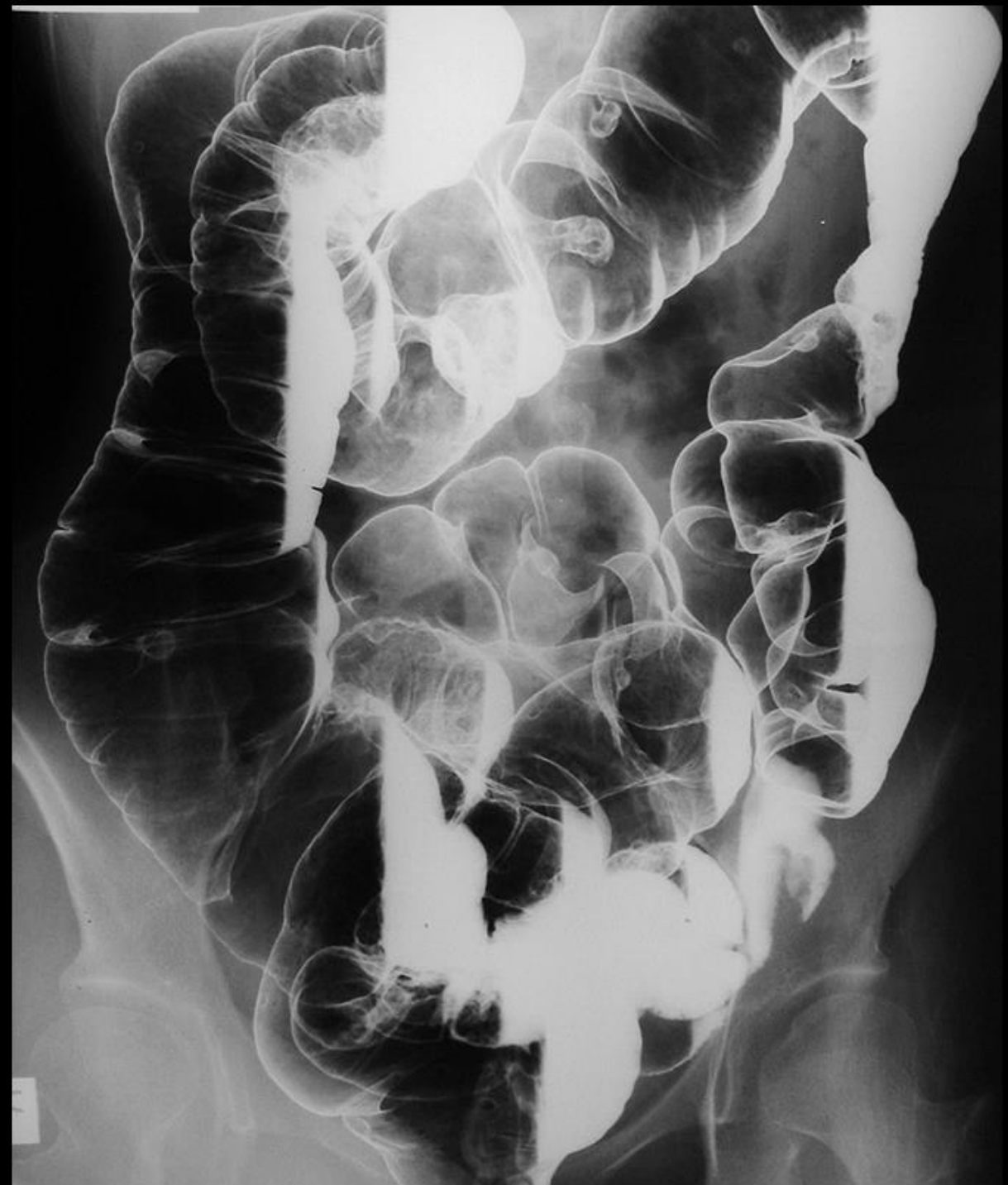
Peutz-Jeghers Syndrome

The main criteria for clinical diagnosis

- Family history
- Mucocutaneous lesions
- Hamartomatous polyps in the gastrointestinal tract

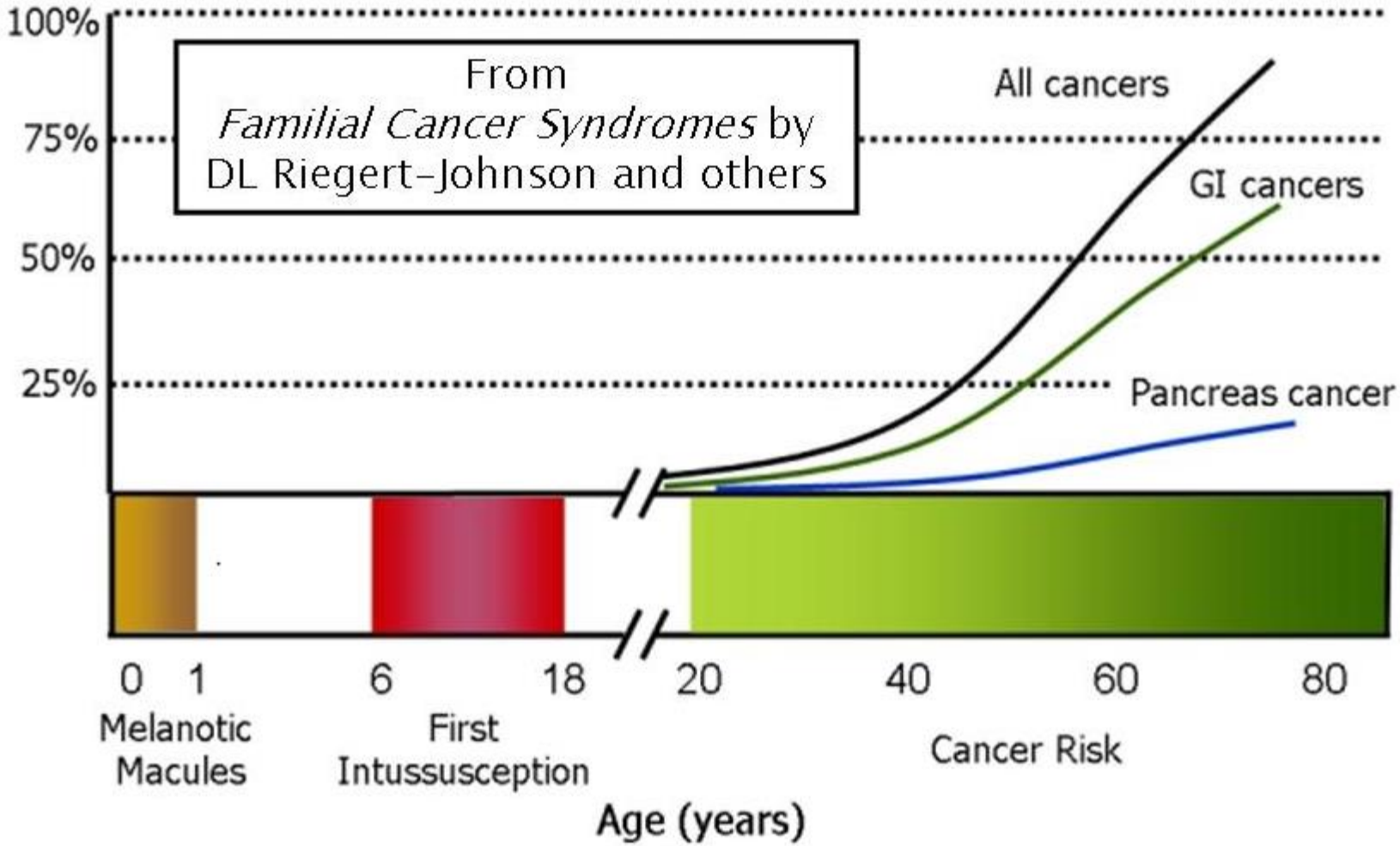
Having two of the three listed clinical criteria indicates a positive diagnosis

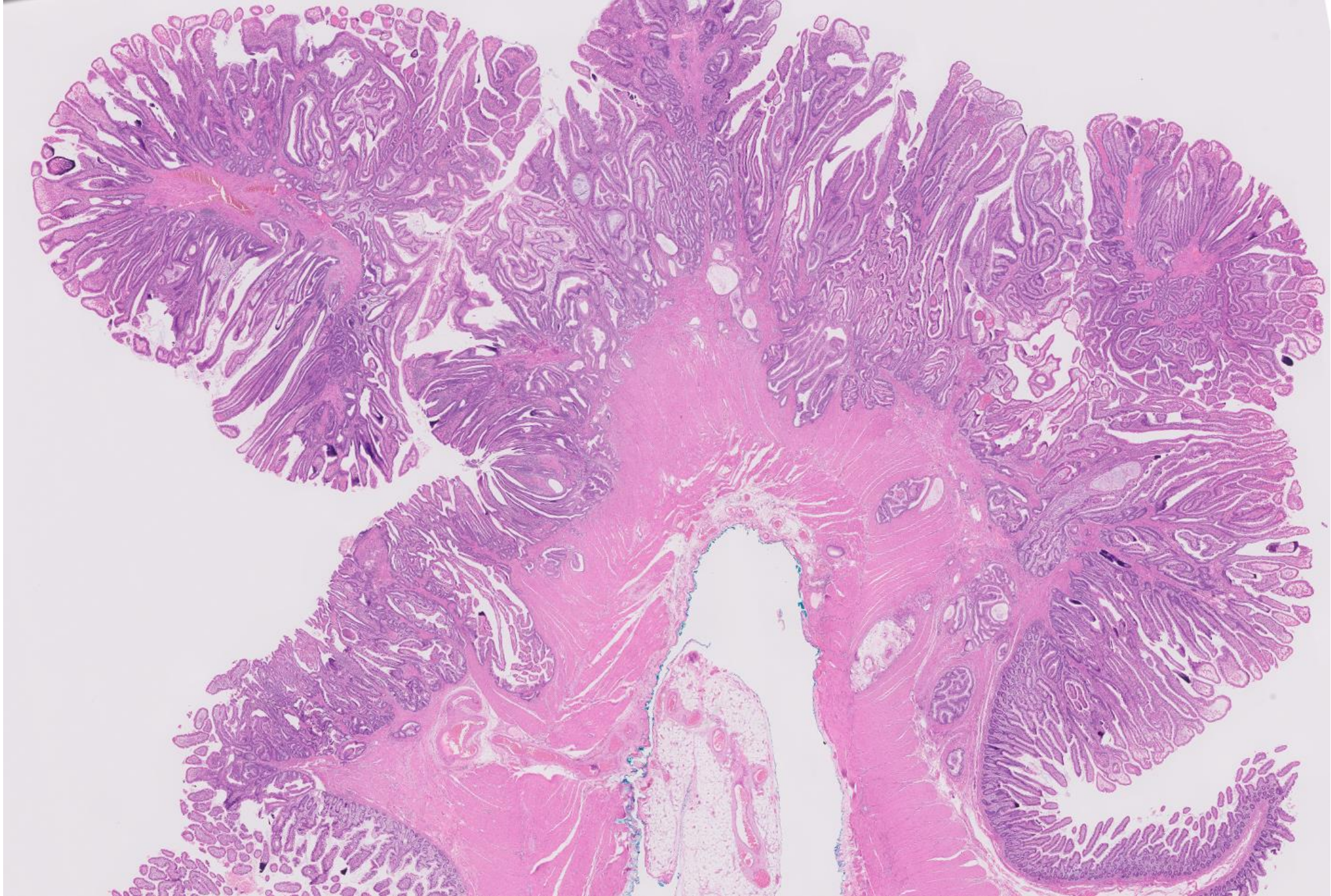
90–100% of patients with a clinical diagnosis of PJS have a mutation in the STK11/LKB1 gene (possible tumor suppressor gene, discovered 1998 on chromosome 19)

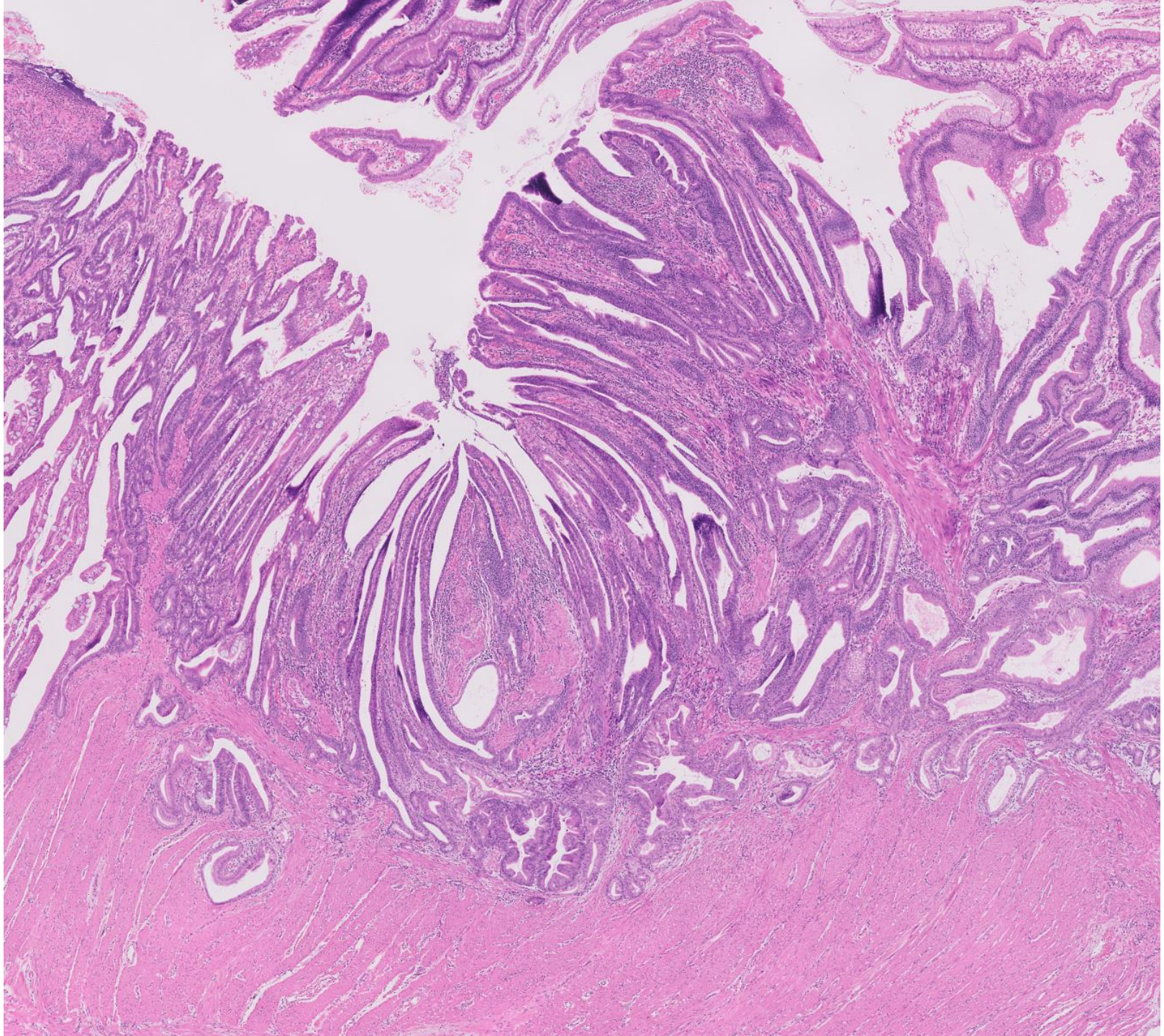


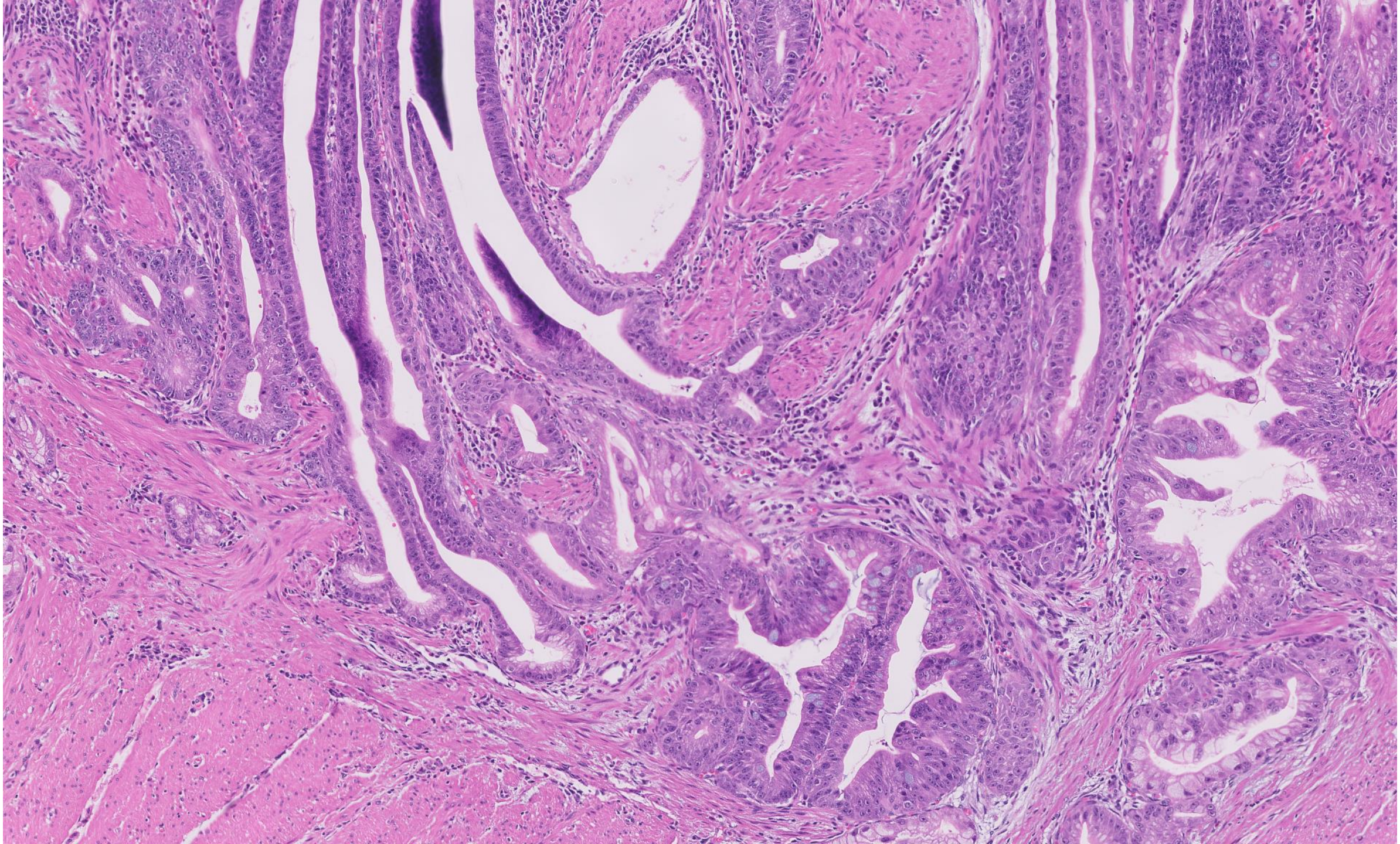
Natural History of Peutz-Jeghers Syndrome

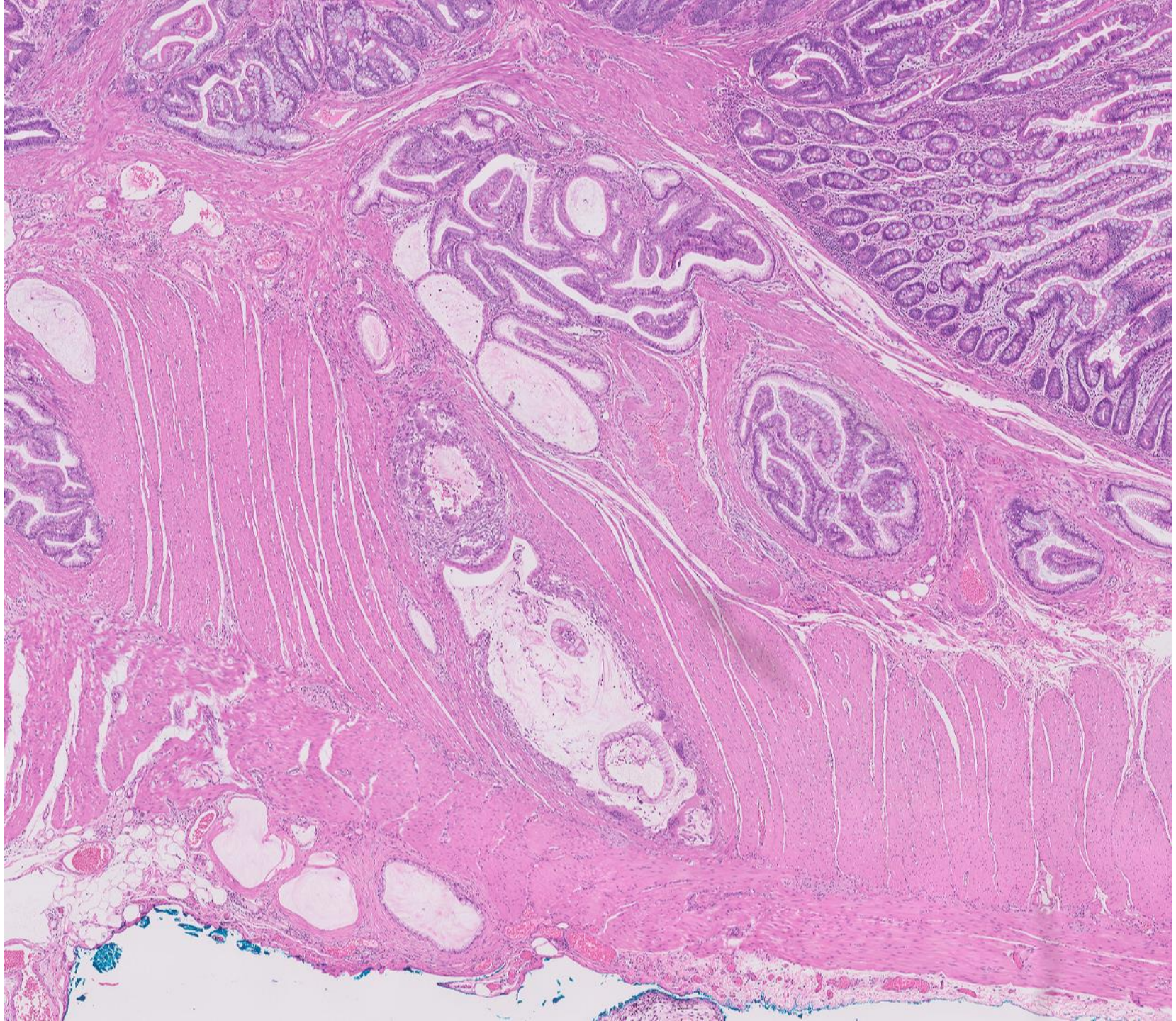
Cumulative Cancer Risk

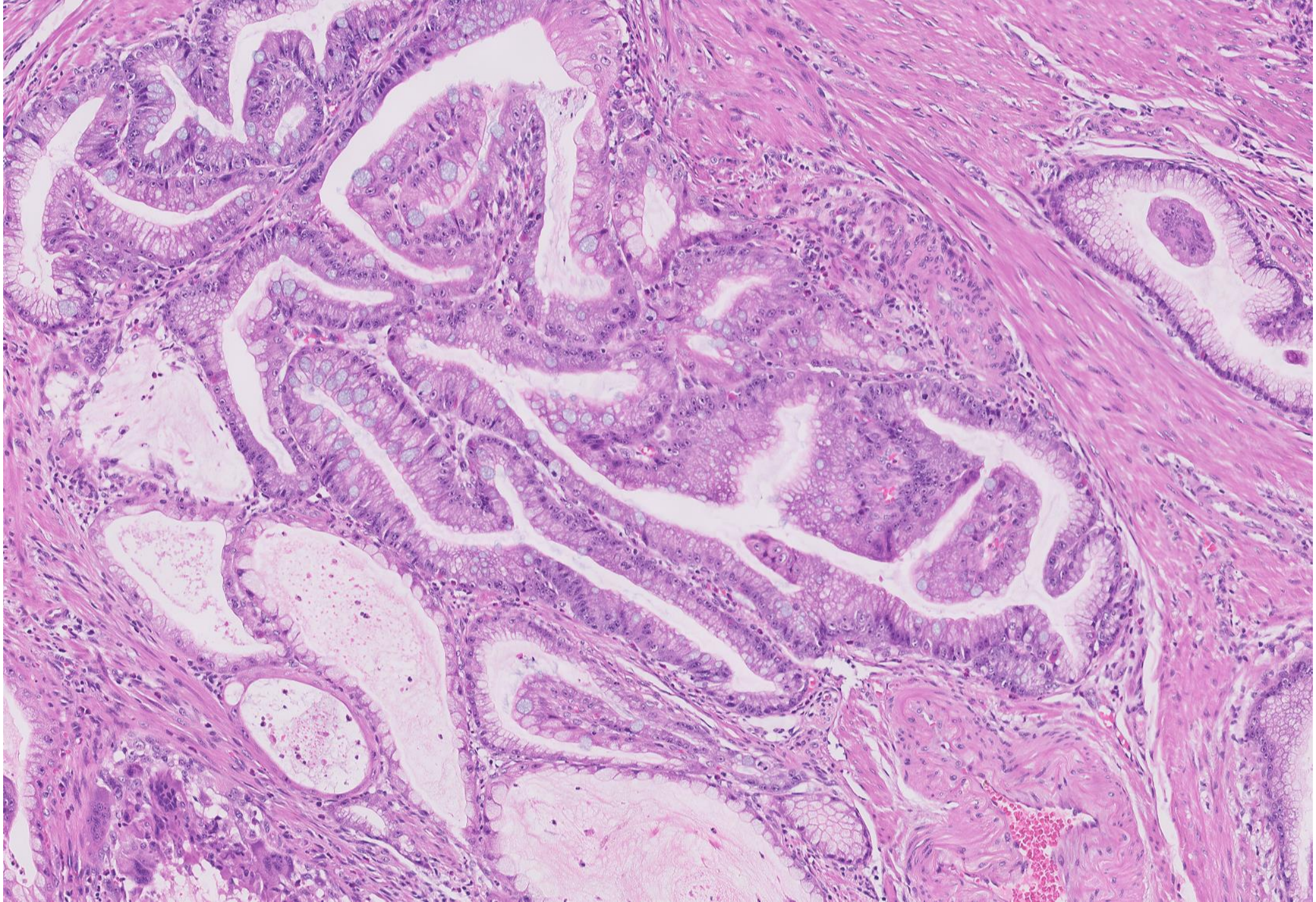


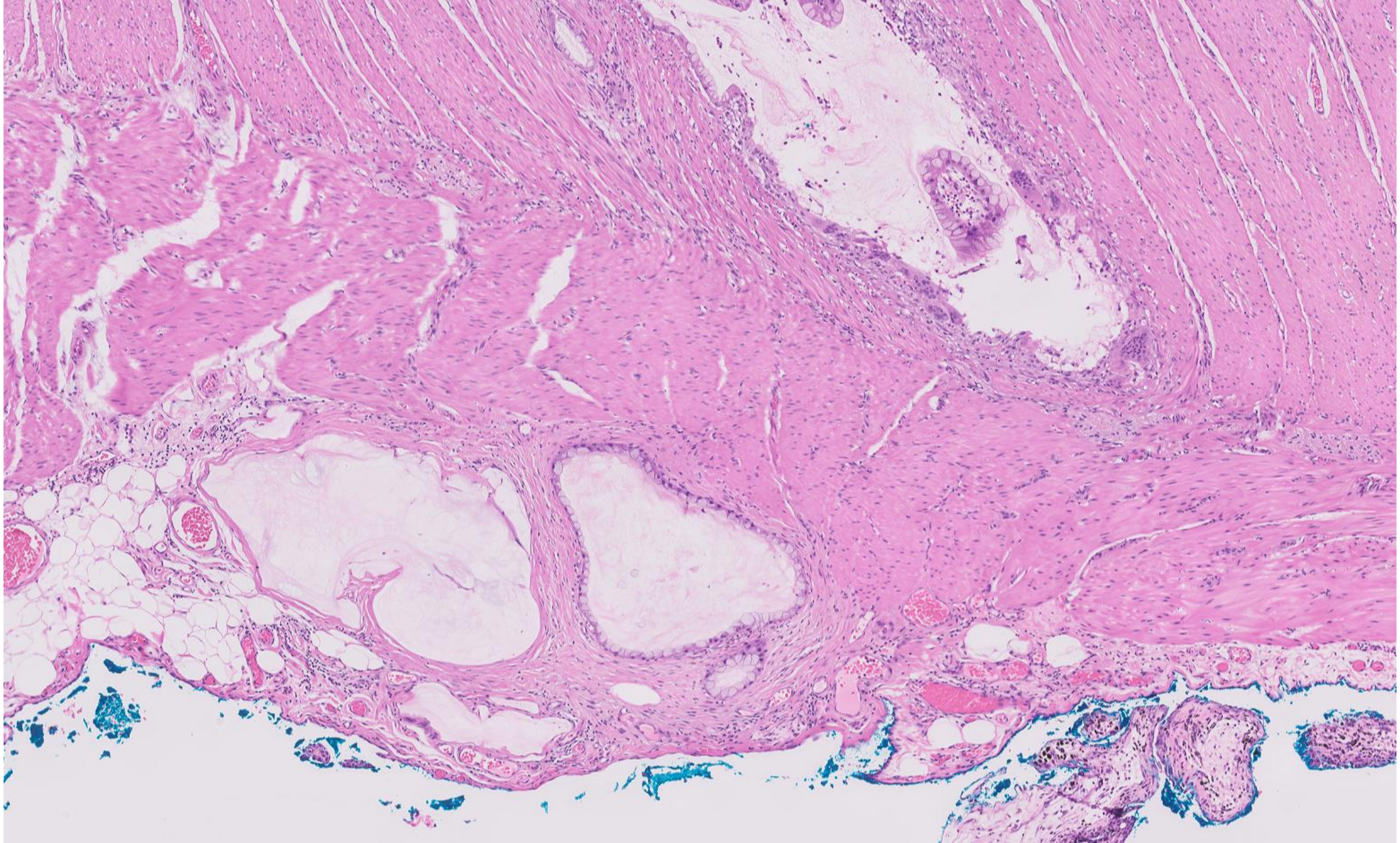


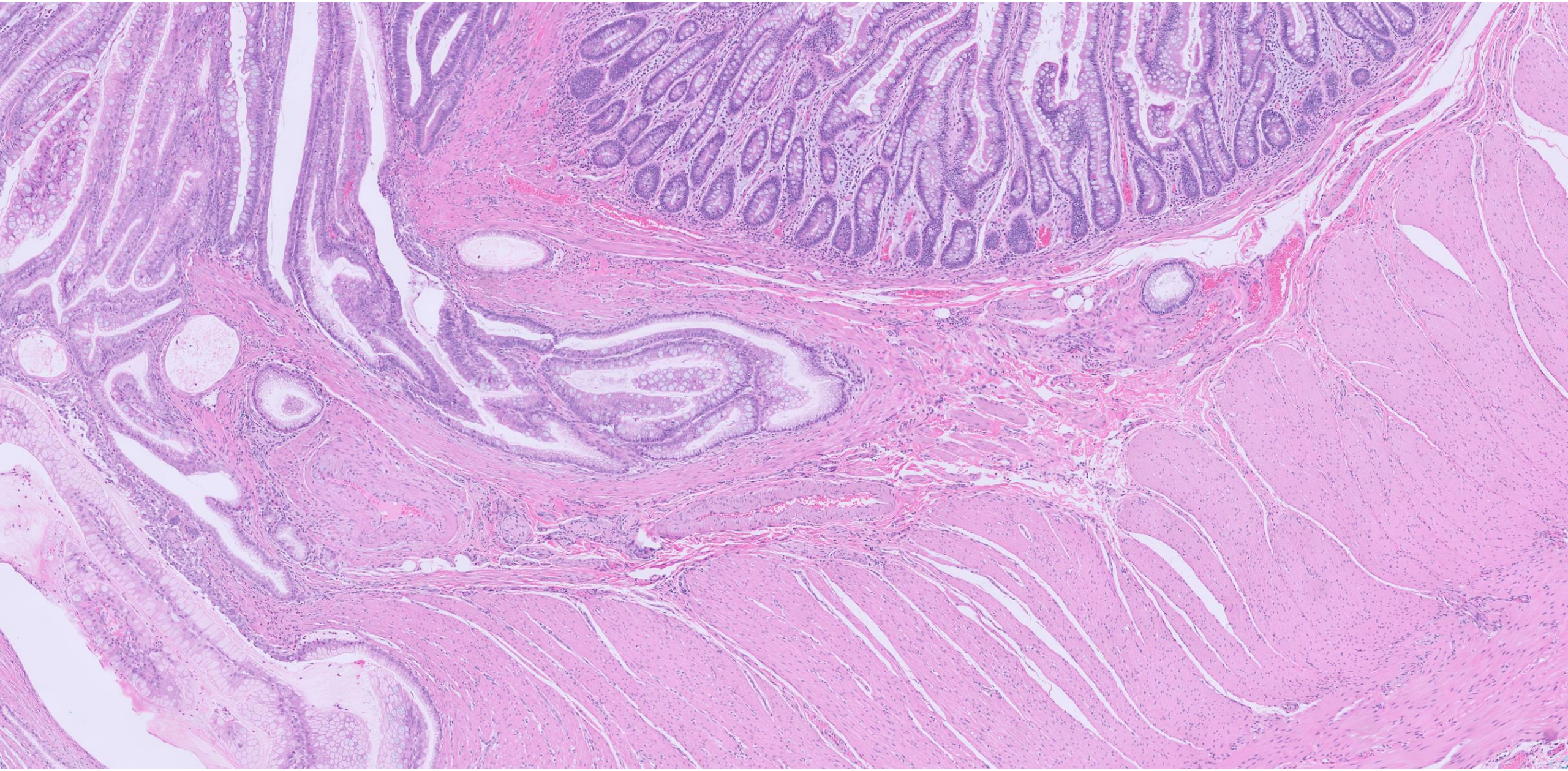


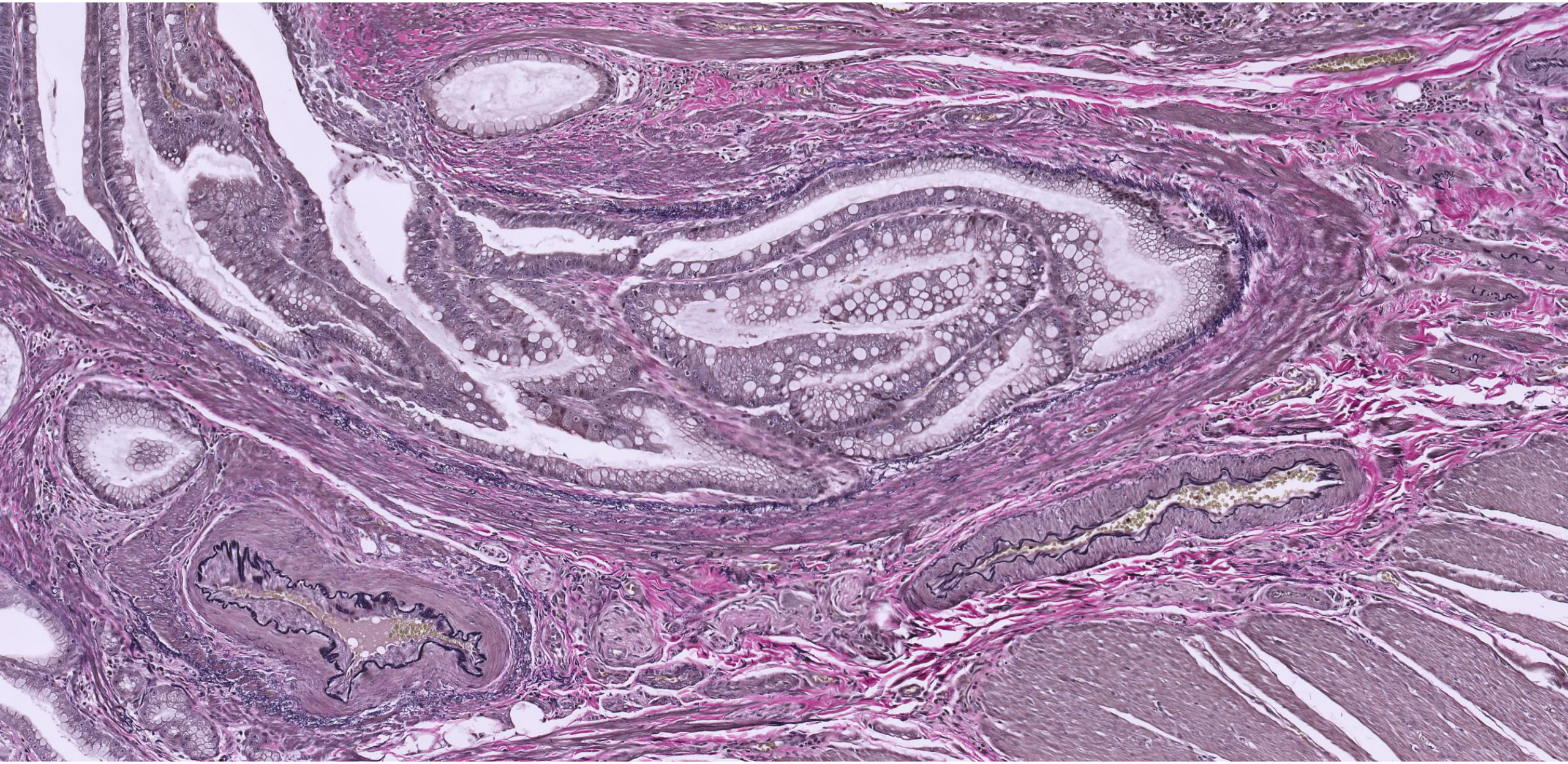












Pseudoinvasion in a PJ polyp- take home points

- Epithelial misplacement is diagnostic pitfall for over diagnosis as cancer
- Epithelial misplacement/pseudoinvasion can be seen in ~10% of PJ polyps
- While cancer is common in PJ patients, cancer or dysplasia only very rarely is present in PJ polyps (cancer develops in non-polypoid areas)
- Helpful histologic features to identify dysplastic epithelial misplacement from invasion:
- Deep glands showing with nondysplatic epithelium, presence of lamina propria and lack of desmoplastic response
- Most cases will be pseudoinvasion rather than invasion!

References:

Malignancy and overdiagnosis of malignancy in Peutz Jeghers polyposis.
Zurac S, Micu G, Bastian A, Grămadă E, Lavric L, Andrei R, Stăniceanu F, Voiosu R, Croitoru A.
Rom J Intern Med. 2008;46(2):179-84.

Peutz-Jeghers syndrome with pseudoinvasion of hamartomatous polyps and multiple epithelial neoplasms. Bolwell JS, James PD. Histopathology. 1979 Jan;3(1):39-50.

Epithelial misplacement in Peutz-Jeghers polyps: a diagnostic pitfall. Shepherd NA, Bussey HJ, Jass JR. The American journal of surgical pathology. 1987 Oct 1;11(10):743-9.

Misplacement of dysplastic epithelium in Peutz–Jeghers polyps: the ultimate diagnostic pitfall? Petersen VC, Sheehan AL, Bryan RL, Armstrong CP, Shepherd NA. The American journal of surgical pathology. 2000 Jan 1;24(1):34.

Vascular pseudoinvasion in a solitary Peutz-Jeghers polyp in the ileum. Okada H, Itagaki S, Enatsu K, Kiriu T, Ishizawa M. Pathology International. 2013 Mar;63(3):188-92.