SLOVENSKÁ DIVÍZIA MEDZINÁRODNEJ AKADÉMIE PATOLÓGIE
SLOVENSKÁ SPOLOČNOSŤ PATOLÓGOV SLS
a
ÚSTAV PATOLOGICKEJ ANATÓMIE JLF UK A UNM

Vás srdečne pozývajú na

XXX.

Martinský bioptický seminár SD-IAP

Martin, 14.- 15.11.2024

Prípad SD IAP č. 853

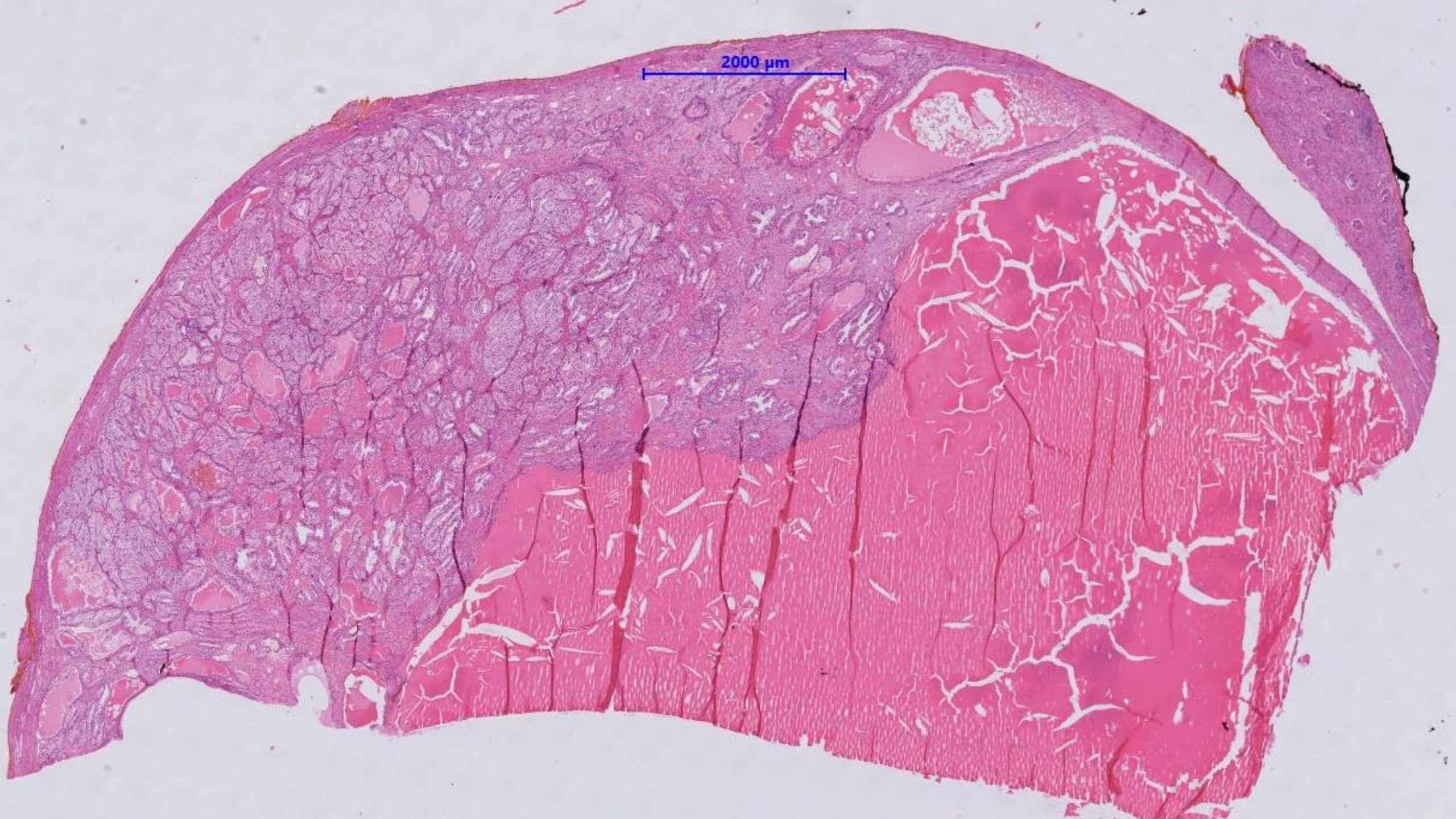
Kristýna Pivovarčíková

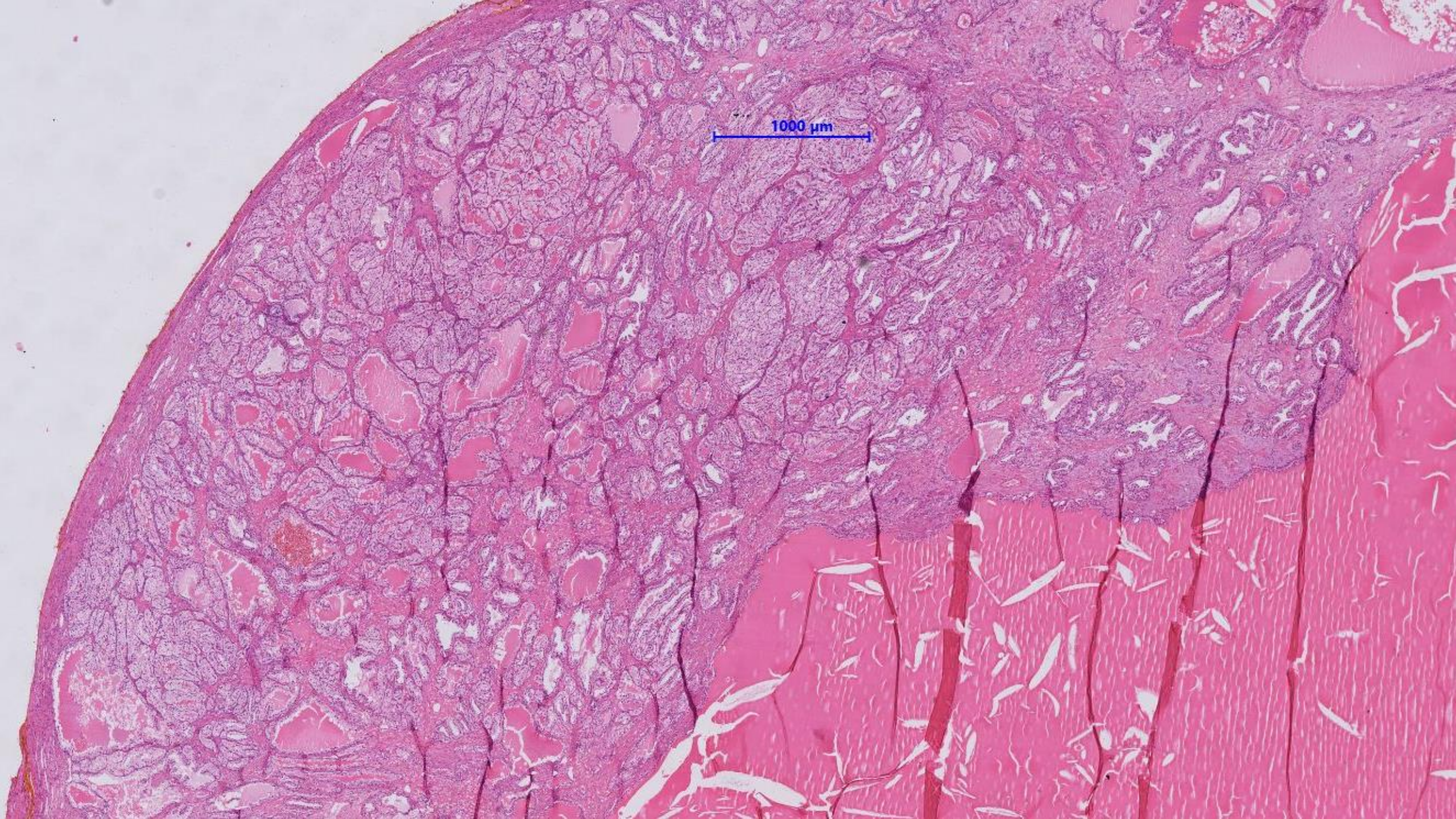
pivovarcikovak@fnplzen.cz

M143255/24

(konzultace Havířov – MUDr. Mahdalová)

- Muž, 51 let
- Parciální resekce souhrnných rozměrů 4 x 3,5 x 2,8 cm
- Na řezu zastižen cysticky utvářený tumor s dutinkami o maximálním rozměru od 3 do 25 mm, které vyplněné žlutavou gelatinózní hmotou


2000 µm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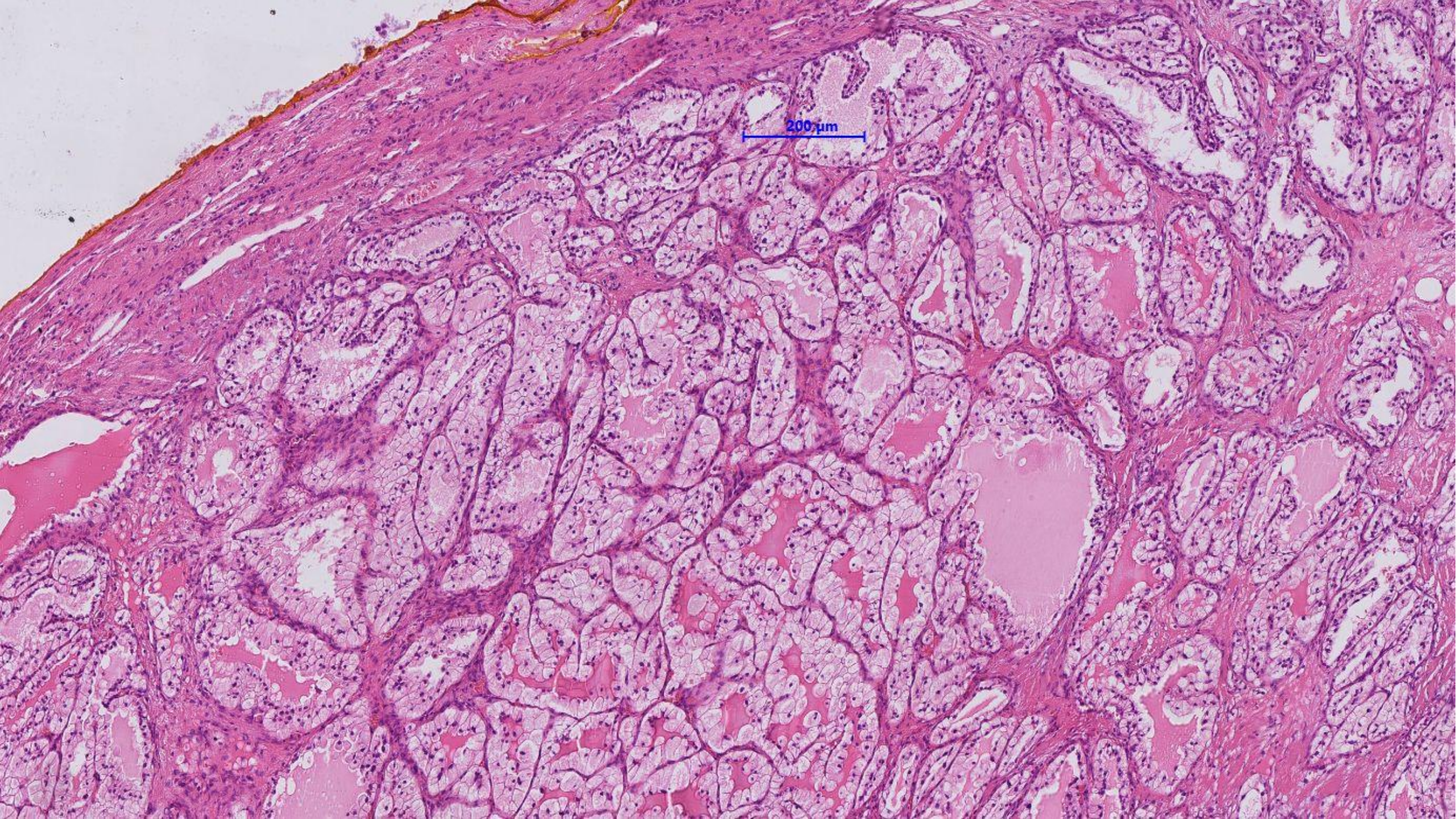
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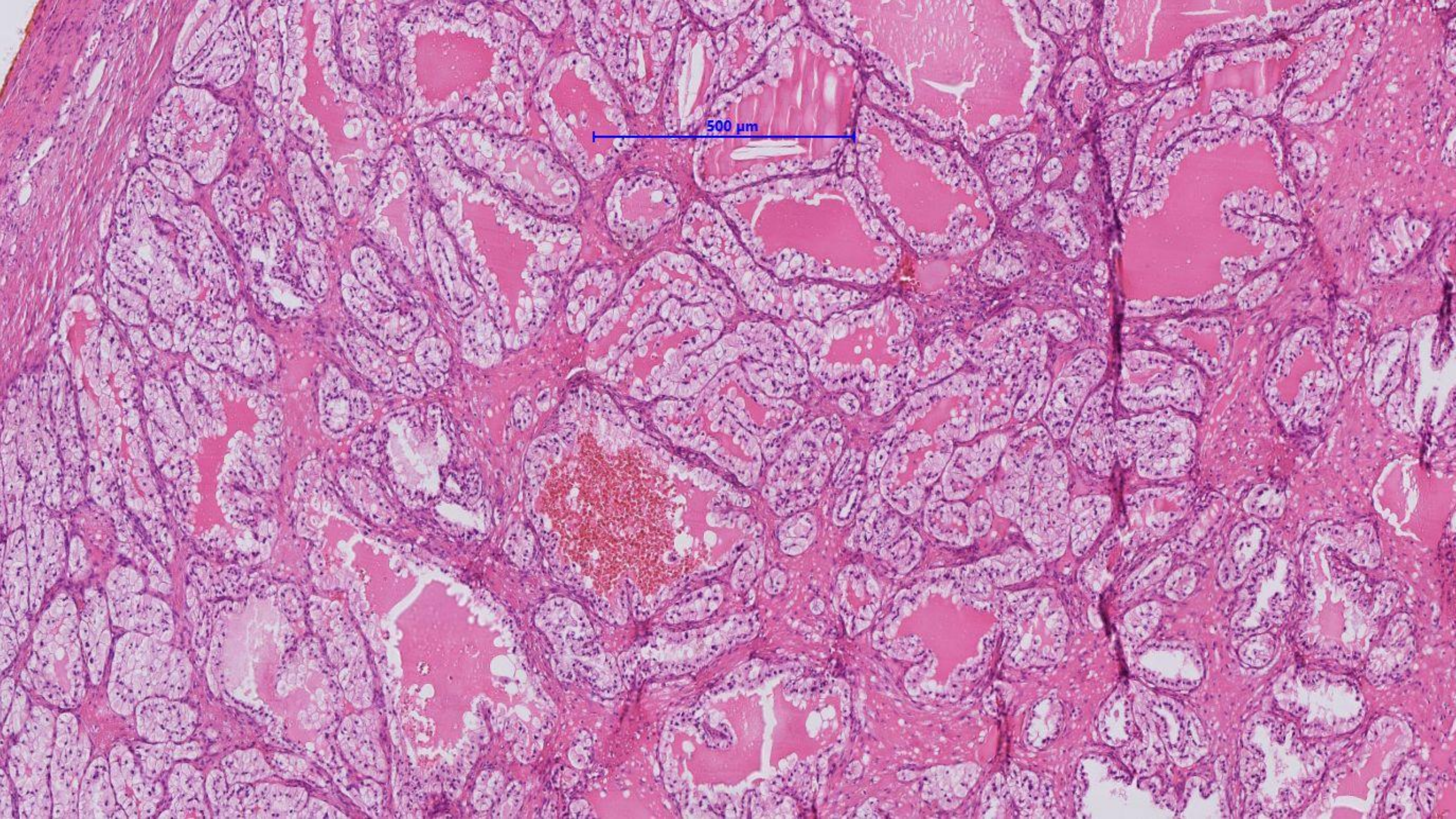
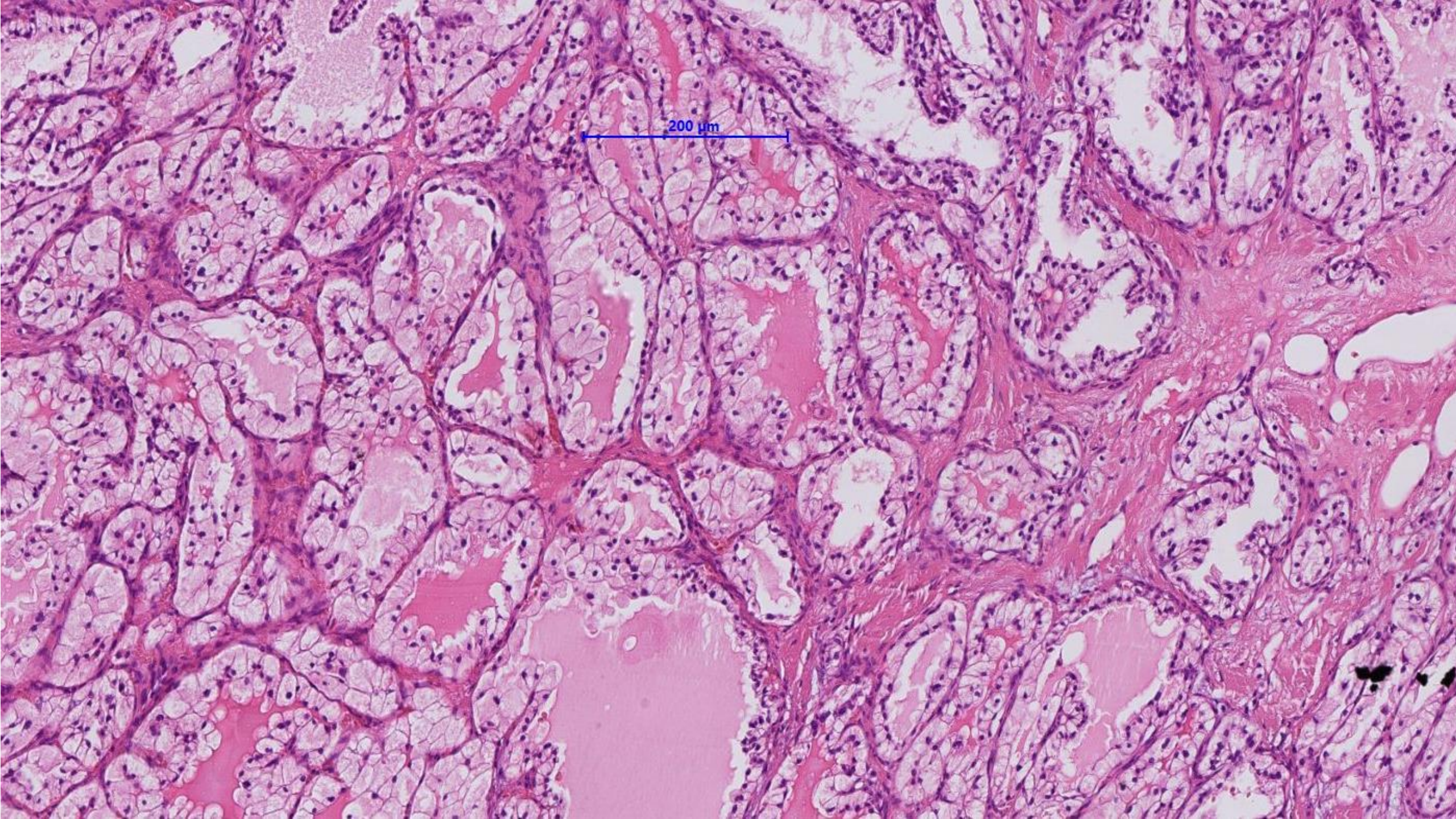

500 µm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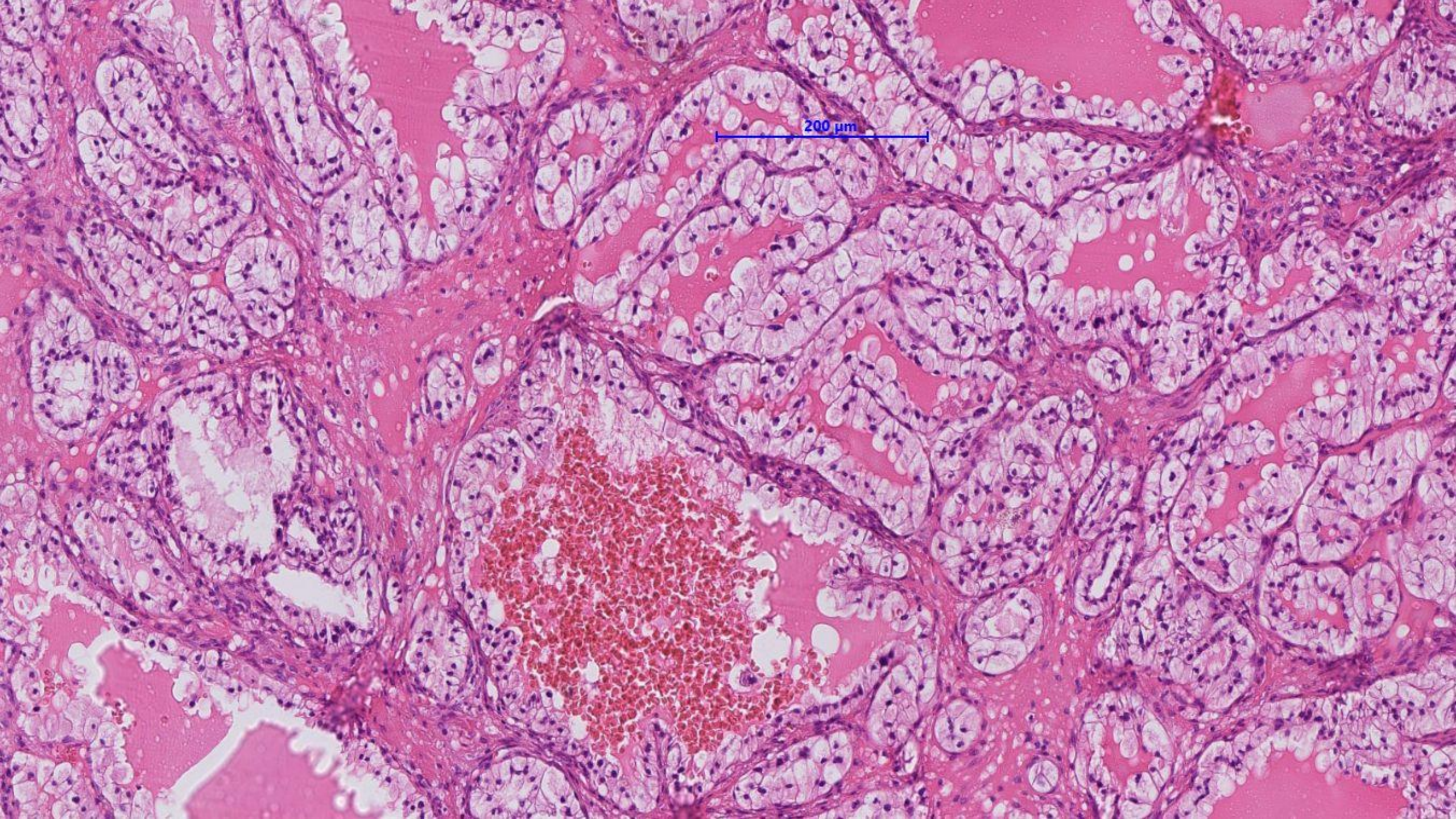
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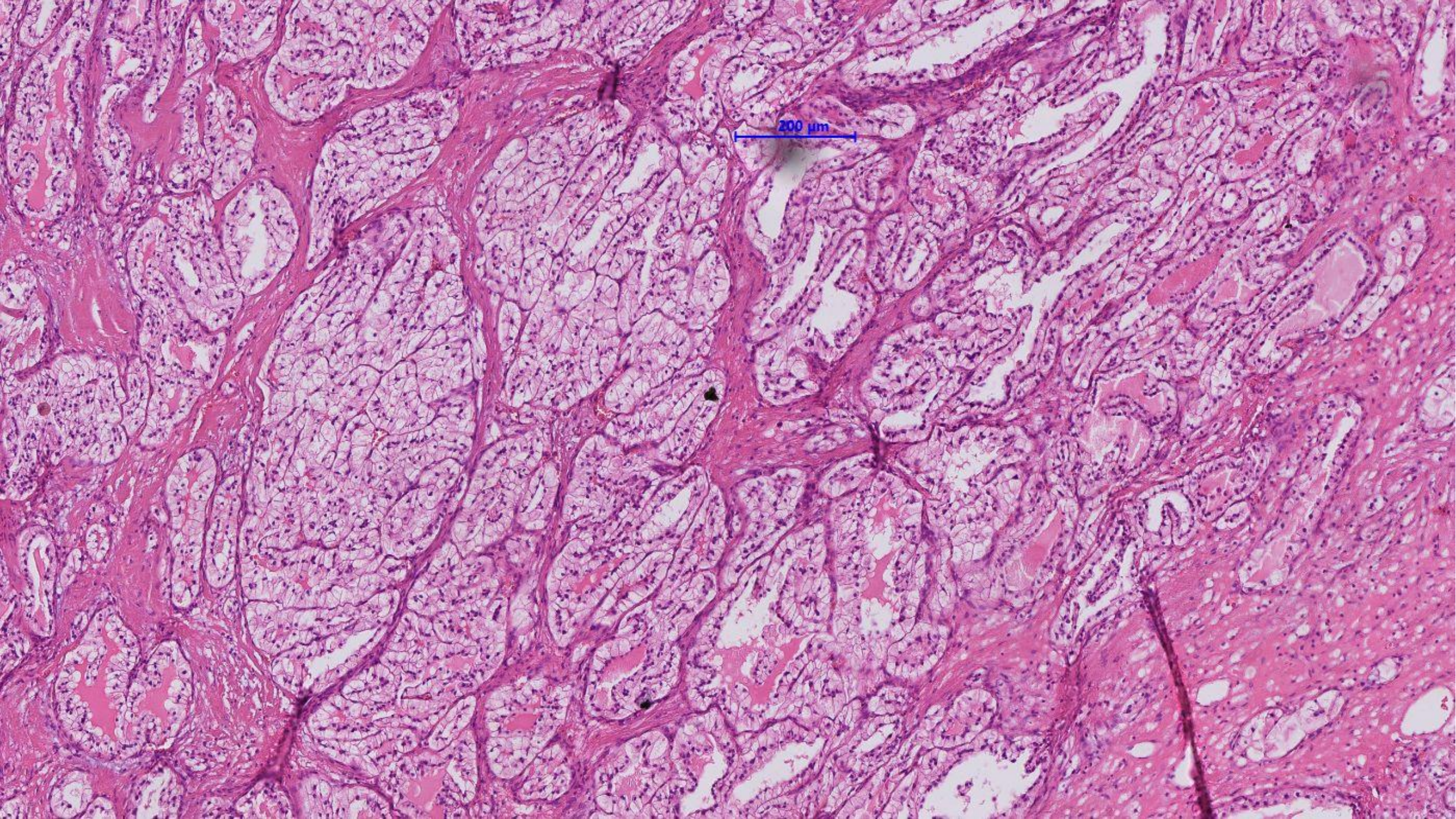
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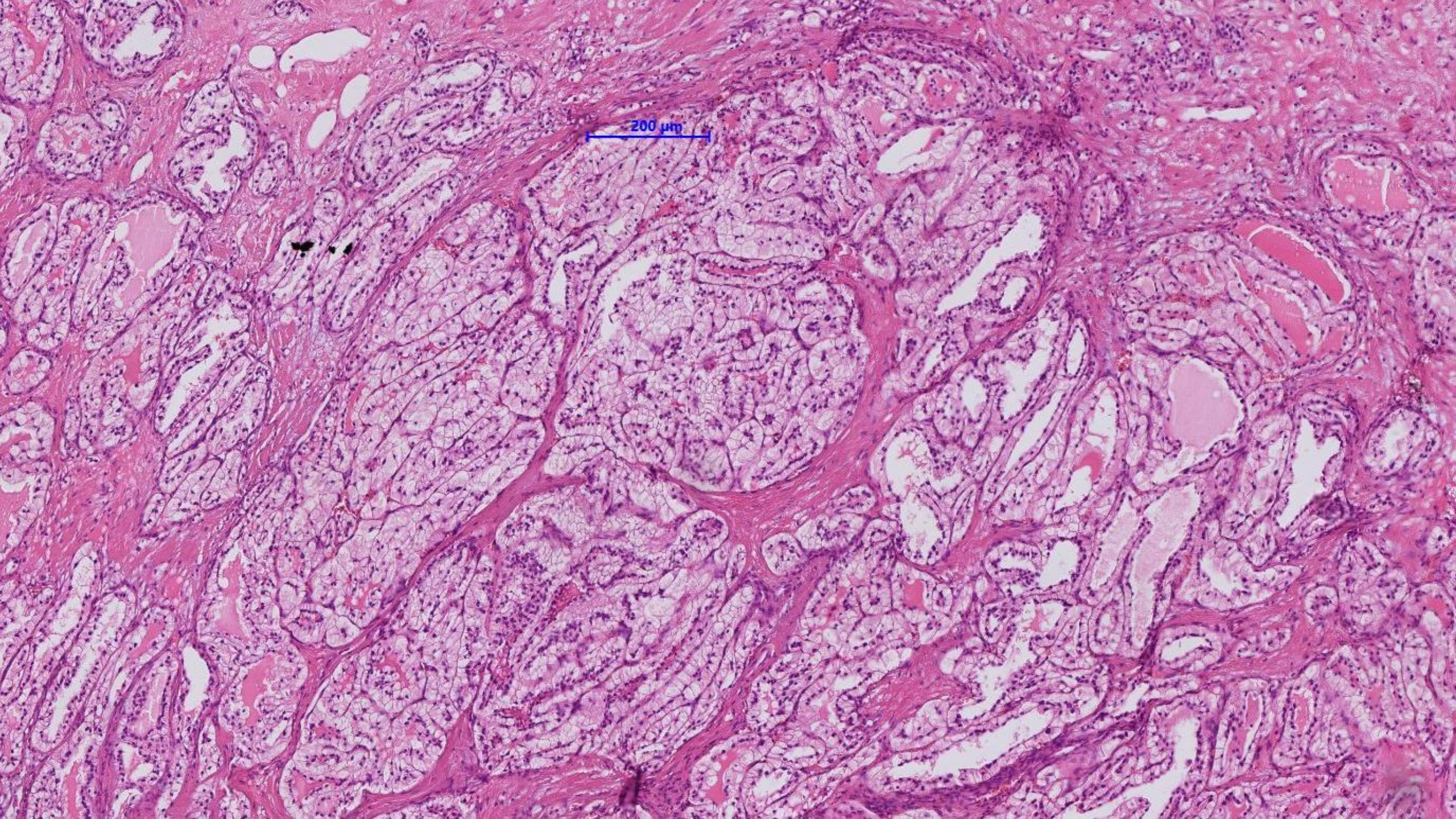
200 µm


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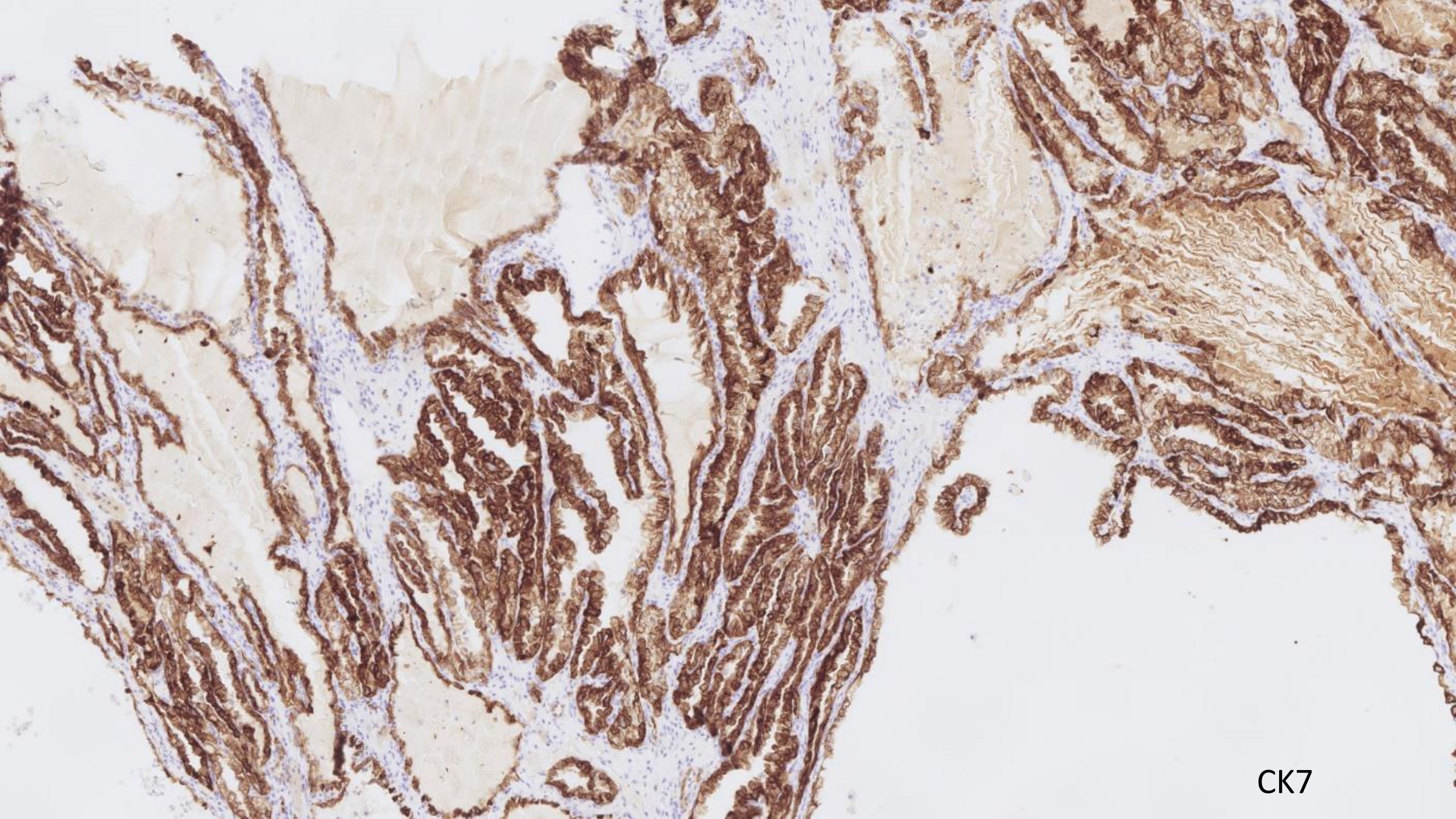
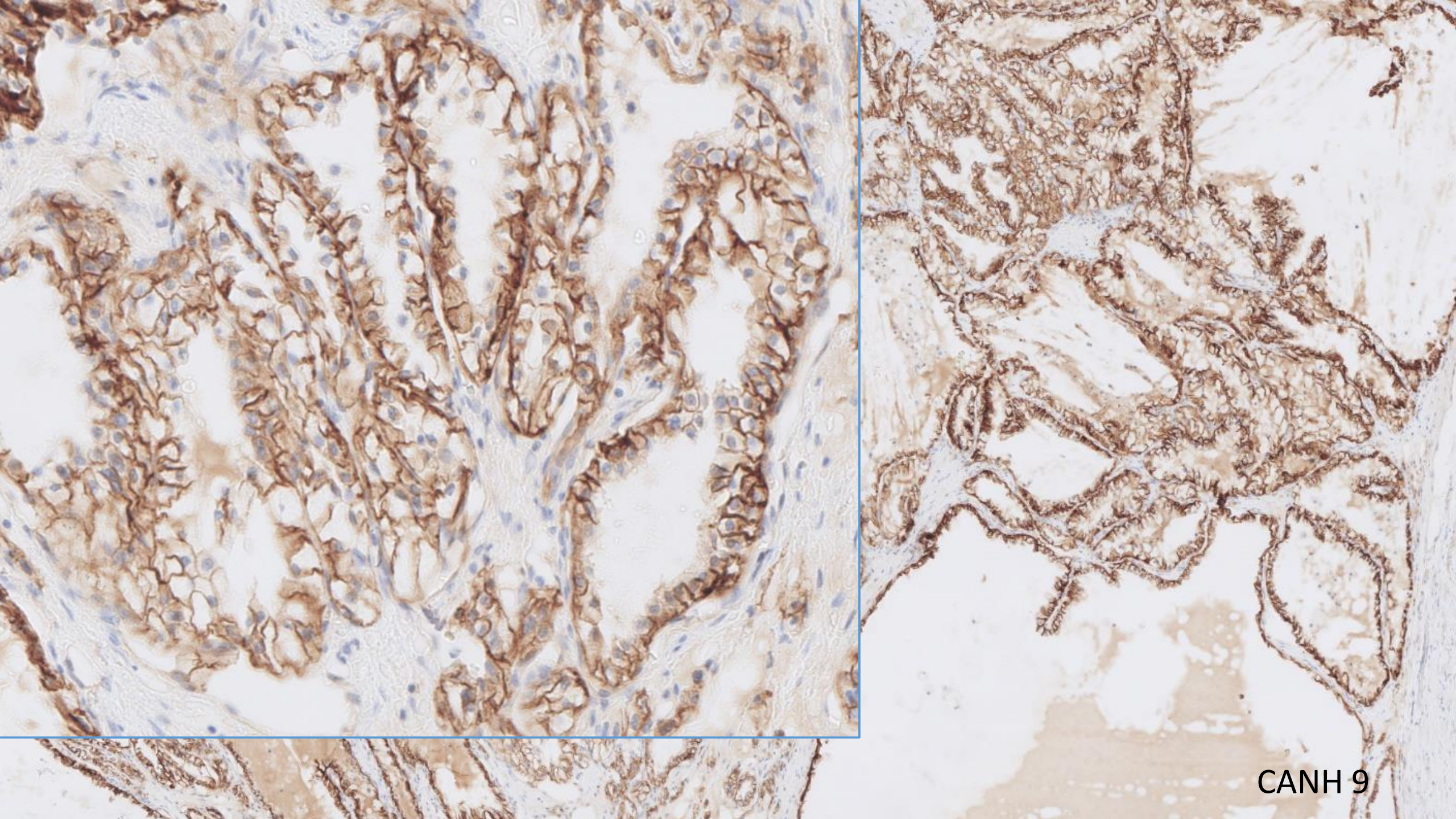
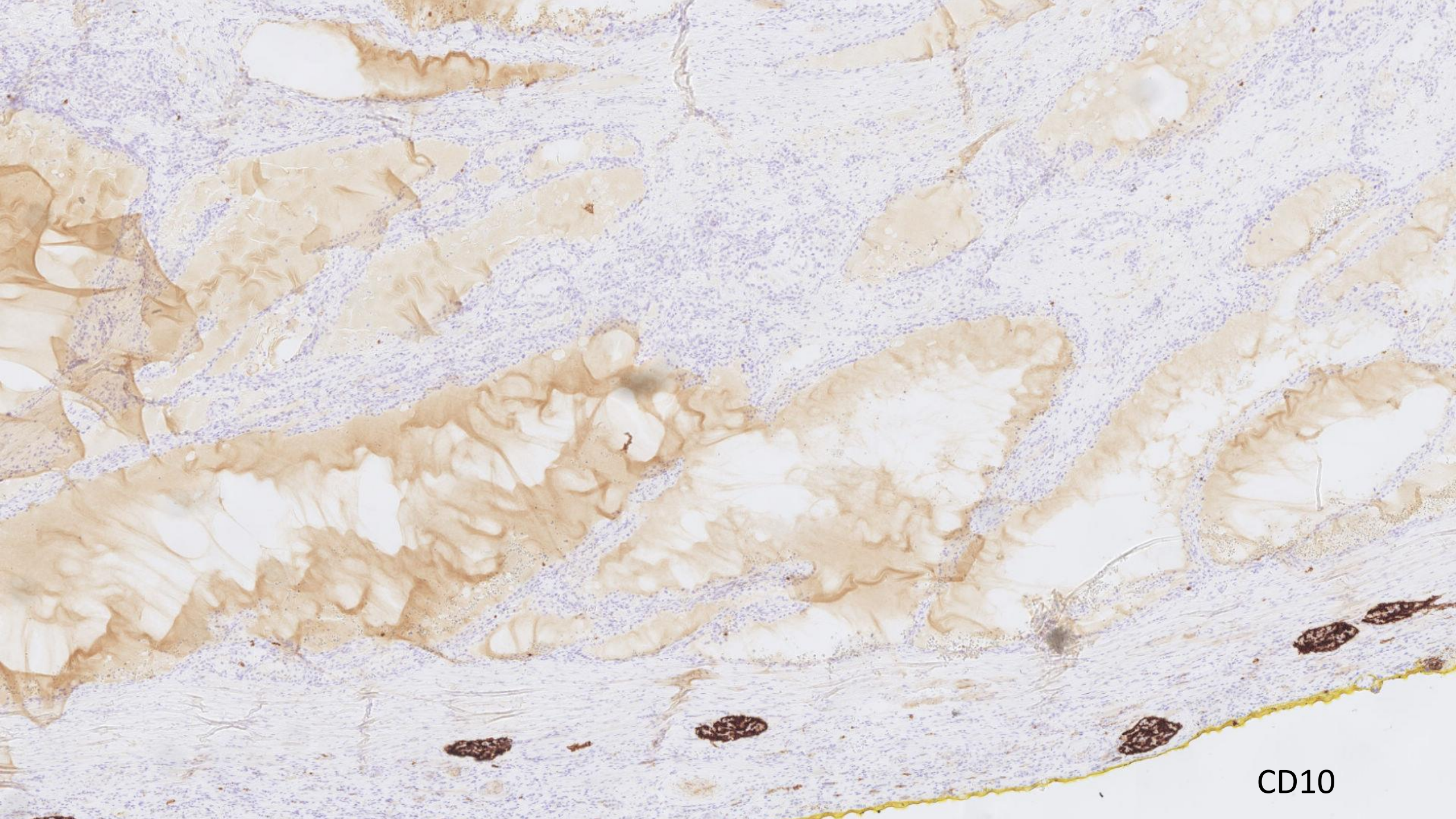
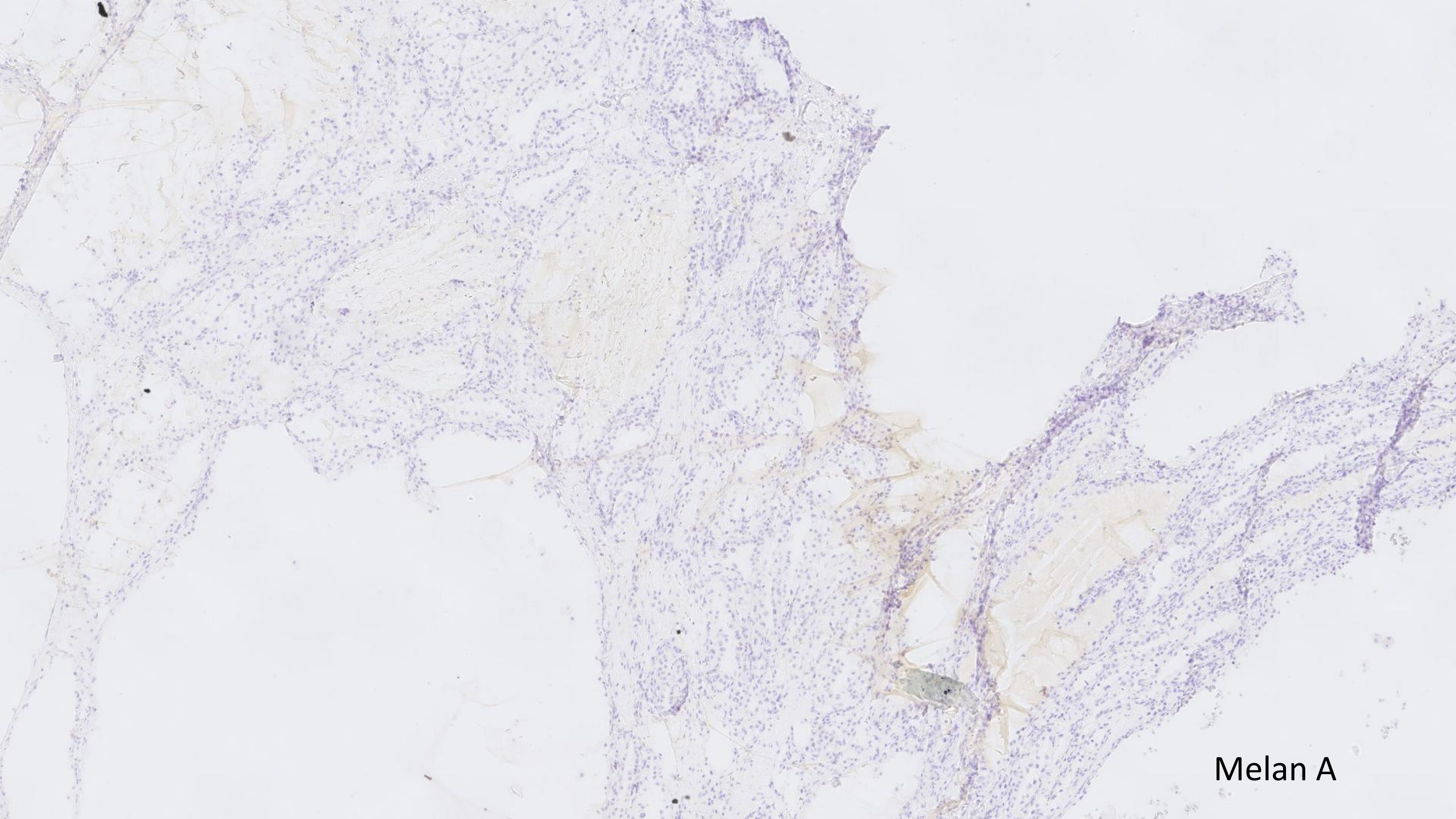
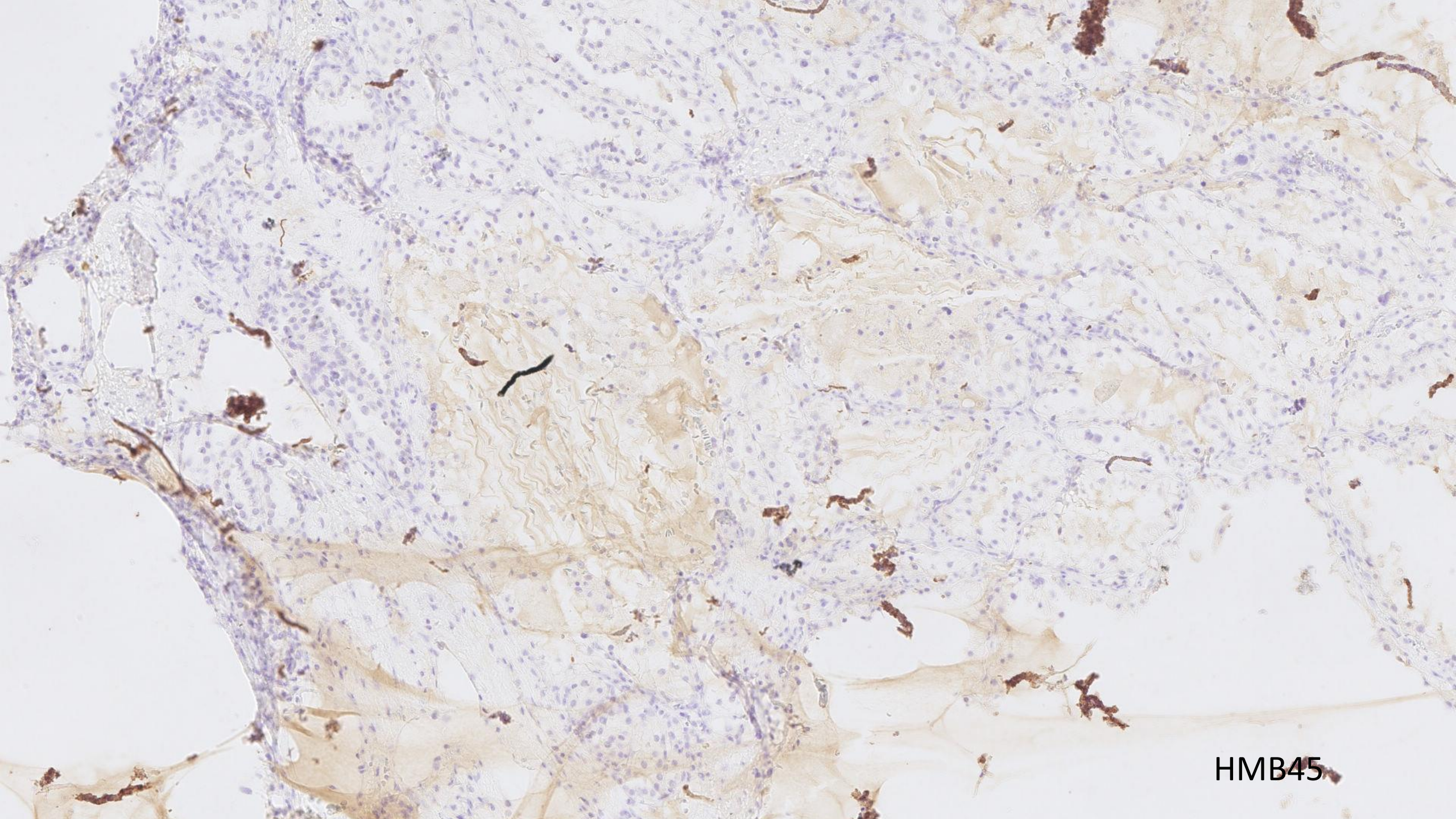

CK7



CANH 9


CD10


Melan A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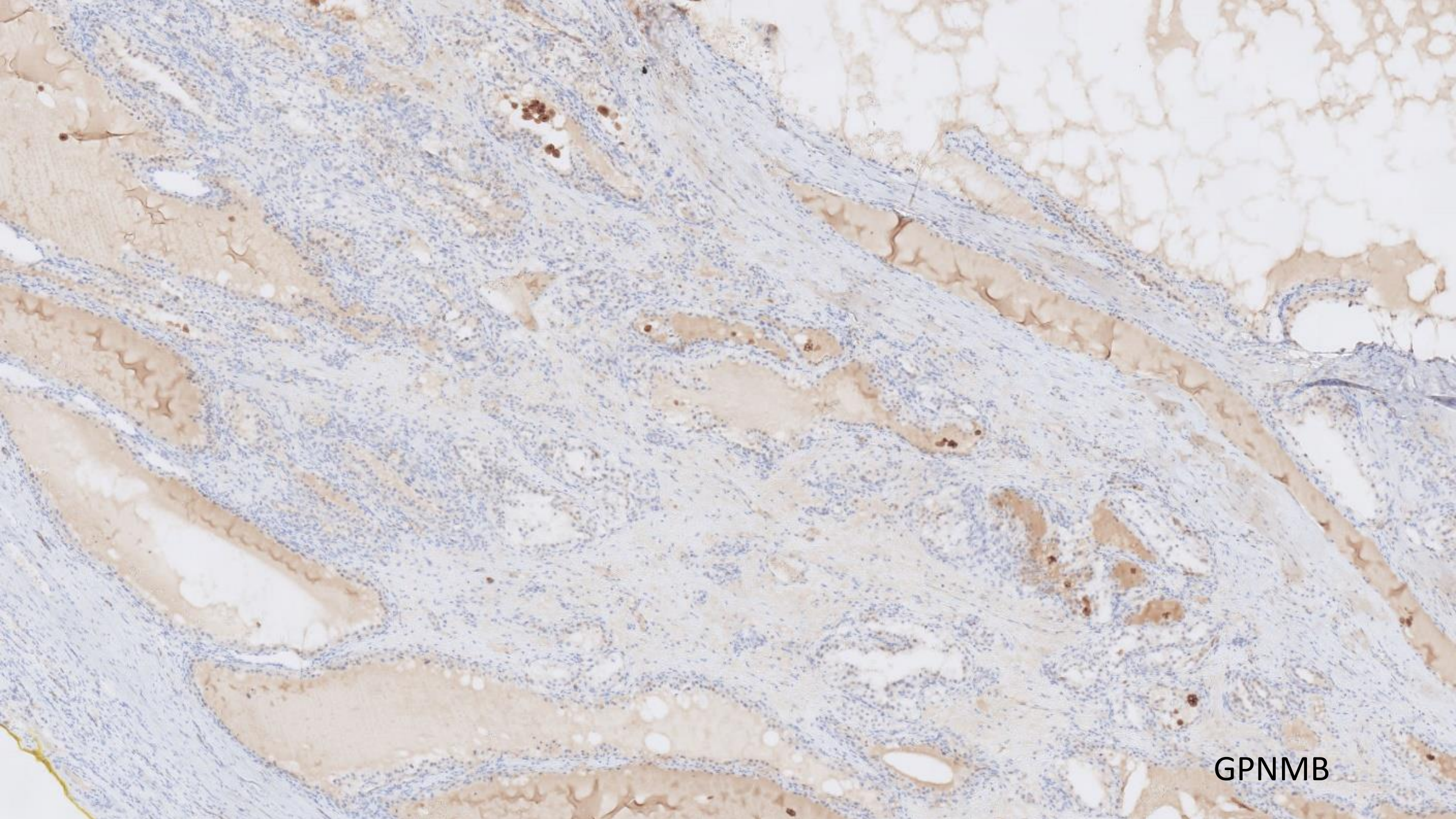
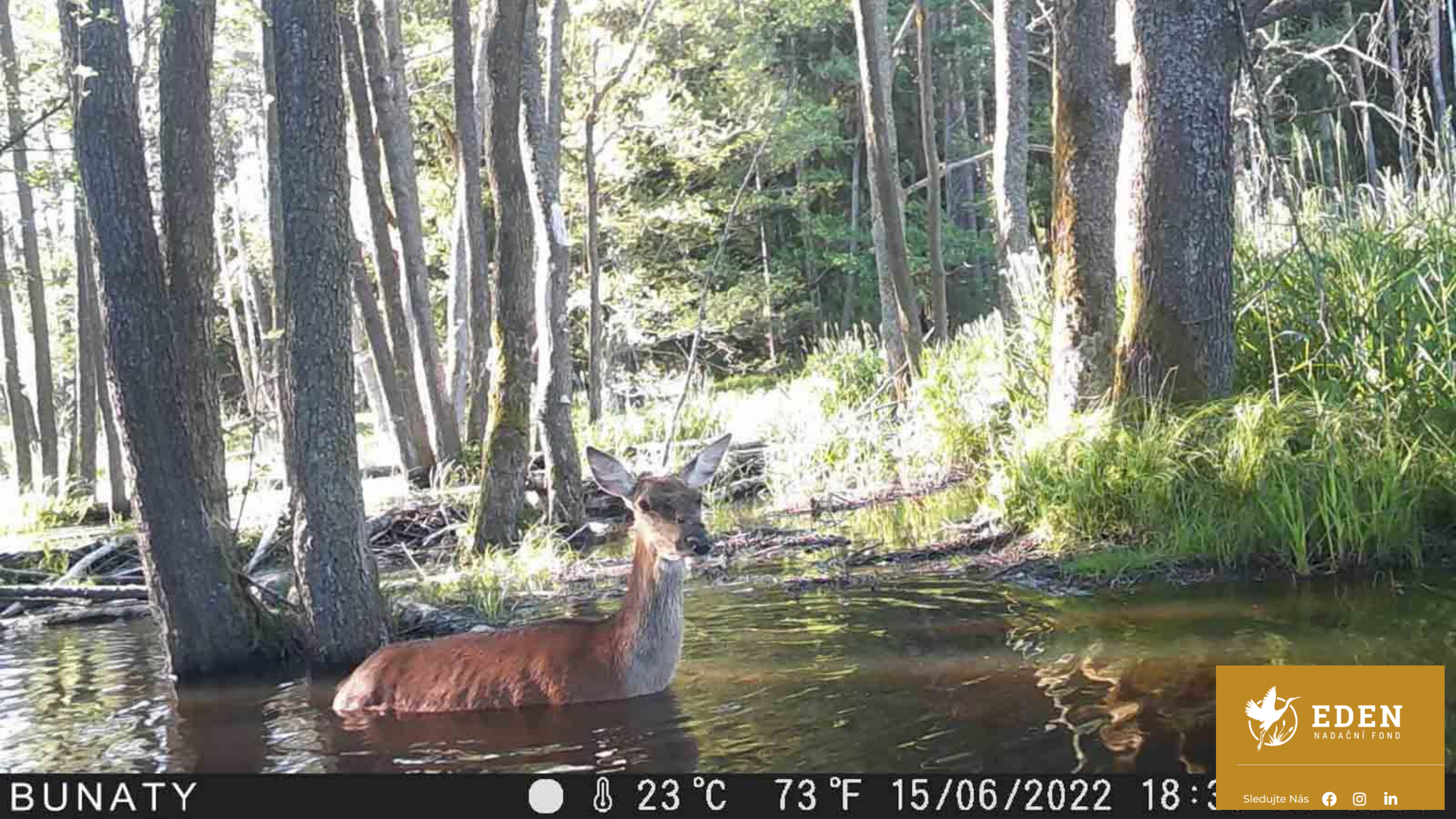

GPNMB


BUNATY
23 °C
73 °F
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18:3
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Genetické vyšetření

- MATERIÁL:
Primární vzorek: biopsie ledviny.
Vyšetřovaný vzorek: parafínový blok.
Izolace RNA byla provedena kitem Maxwell RSC RNA FFPE.
Izolace DNA byla provedena kitem Qiasymphony DSP DNA mini.

- **TruSight Oncology 500 Panel - DNA část**

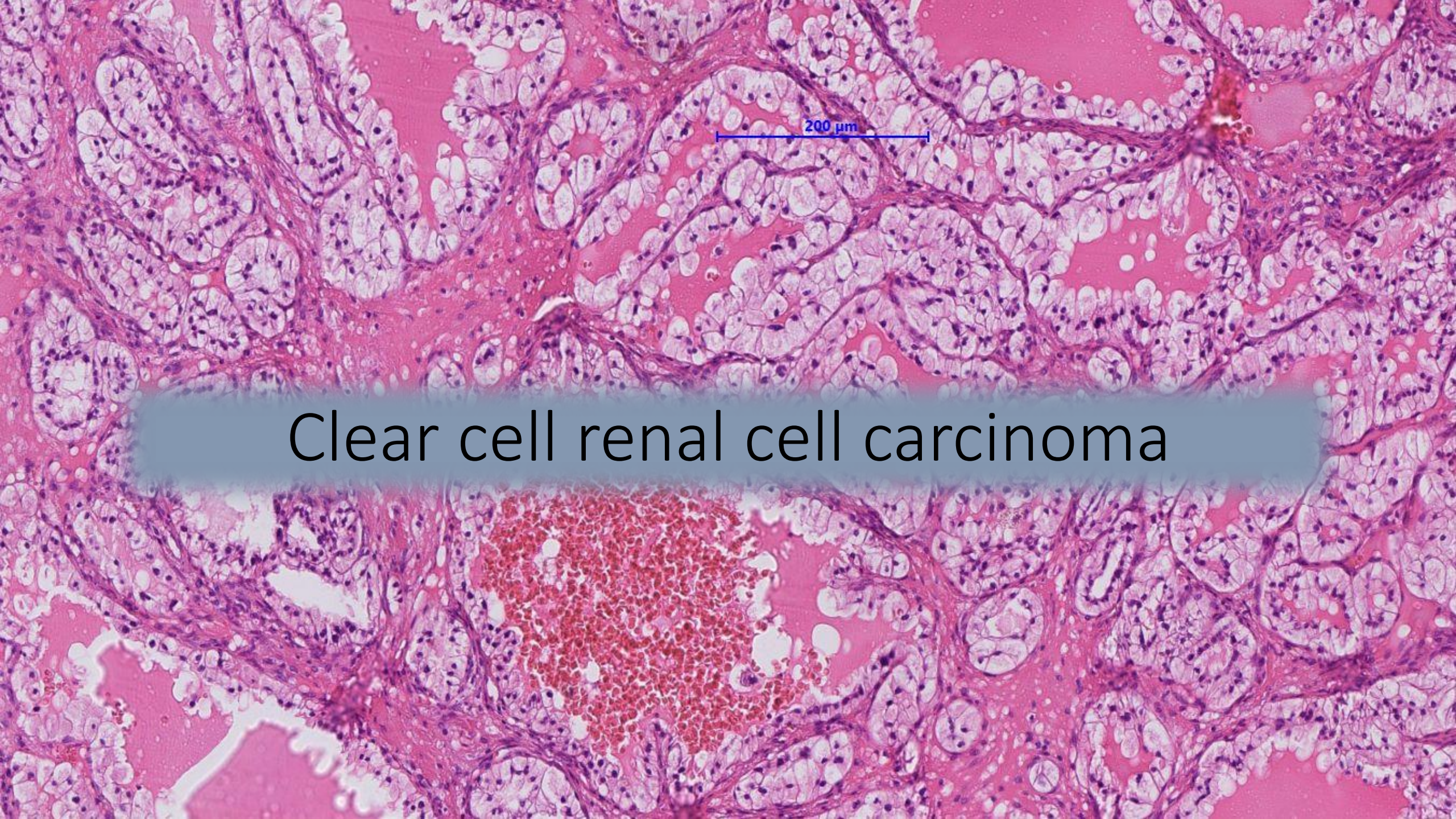
Detekce somatických mutací v klinicky relevantních oblastech 523 genů NGS kitem TruSight Oncology 500 (Illumina). Kit také umožňuje detekci amplifikace v 59 vybraných genech, mutační nálože (TMB) a mikrosatelitní nestability (MSI). Metoda akreditována dle SOP 22.* LOD: 5% (reportovány pouze patogenní/pravděpodobně patogenní varianty)

Ve vyšetřovaném vzorku PROKAZUJEME klinicky významnou mutaci genu:
FLT4 c.952C>T, p.(Arg318Ter), (alias R318X), AF: 45% - susp. germinální, (NM_182925.5, NP_891555.2, chr5:180056292, hg19).

Prokazujeme NÍZKOU mutační nálož - (TMB: Low; 0 mut/Mb).
NEPROKAZUJEME mikrosatelitní nestabilitu (MSS; 0 % lokusů).
NEPROKAZUJEME klinicky významné amplifikace ve vyšetřovaných genech.

- **Metylační status genu VHL**

Na základě analýzy dat z metylačního čipu **PROKAZUJEME metylaci promotoru genu VHL**.



Clear cell renal cell carcinoma

Clear cell renal cell carcinoma (CCRCC)

- CANH IX +, CK7 – (většinou!), CD10 +
- Abnormality *VHL* (metylace, mutace), LOH3p
- *PBRM1* mutations are present in approximately 40% of ccRCC, whereas *BAP1* and *SETD2* are found to be mutated in approximately 10% of ccRCC

Histopathology

Histopathology 2019, **74**, 608–617. DOI: 10.1111/his.13791

Annals of Diagnostic Pathology 71 (2024) 152297

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ELSEVIER

Alpha-methyl CoA racemase (AMACR) reactivity across the spectrum of clear cell renal cell neoplasms

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AMACR
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Multilocular Cystic Renal Neoplasm of Low Malignant Potential

ABSTRACT

a-Methylacyl coenzyme A racemase (AMACR) is traditionally considered to be a marker of papillary renal cell carcinoma. However, AMACR expression can be seen in other renal tumors. The aim of this study was to investigate AMACR immunoreactivity within the spectrum of clear cell renal cell neoplasms.

Fifty-three clear cell renal epithelial tumors were used in assembling the following four cohorts: low grade (LG) clear cell renal cell carcinoma (CCRCC), high grade (HG) CCRCC, CCRCC with cystic changes, and multilocular cystic renal neoplasm of low malignant potential (MCRNLMP). Representative blocks were stained for AMACR, using two different clones (SP52 and OV-TL12/30).

There were at least some AMACR immunoreactivity in 77.8 % and 68.9 % of CCRCCs (using SP52 and OV-TL12/30 clone, respectively). Moderate to strong positivity, or positivity in more than one third of the tumor (even weak in intensity) was detected in 46.7 % of CCRCCs using SP52 and in 48.9 % of CCRCC using OV-TL12/30 clone. The highest AMACR reactivity was observed in HG CCRCC (60 % by SP52 and 66.7 % by OV-TL12/30). Strong and diffuse AMACR positivity was detected in 8.9 % of all CCRCCs. AMACR immunoreactivity in MCRNLMP was 37.5 % (SP52 clone) and 25 % (OV-TL12/30 clone).

Renal tumours with fibromyomatous stroma dif. dg.:

- challenges regarding this entity stem from the use of variable names used for such tumors in the literature, including:

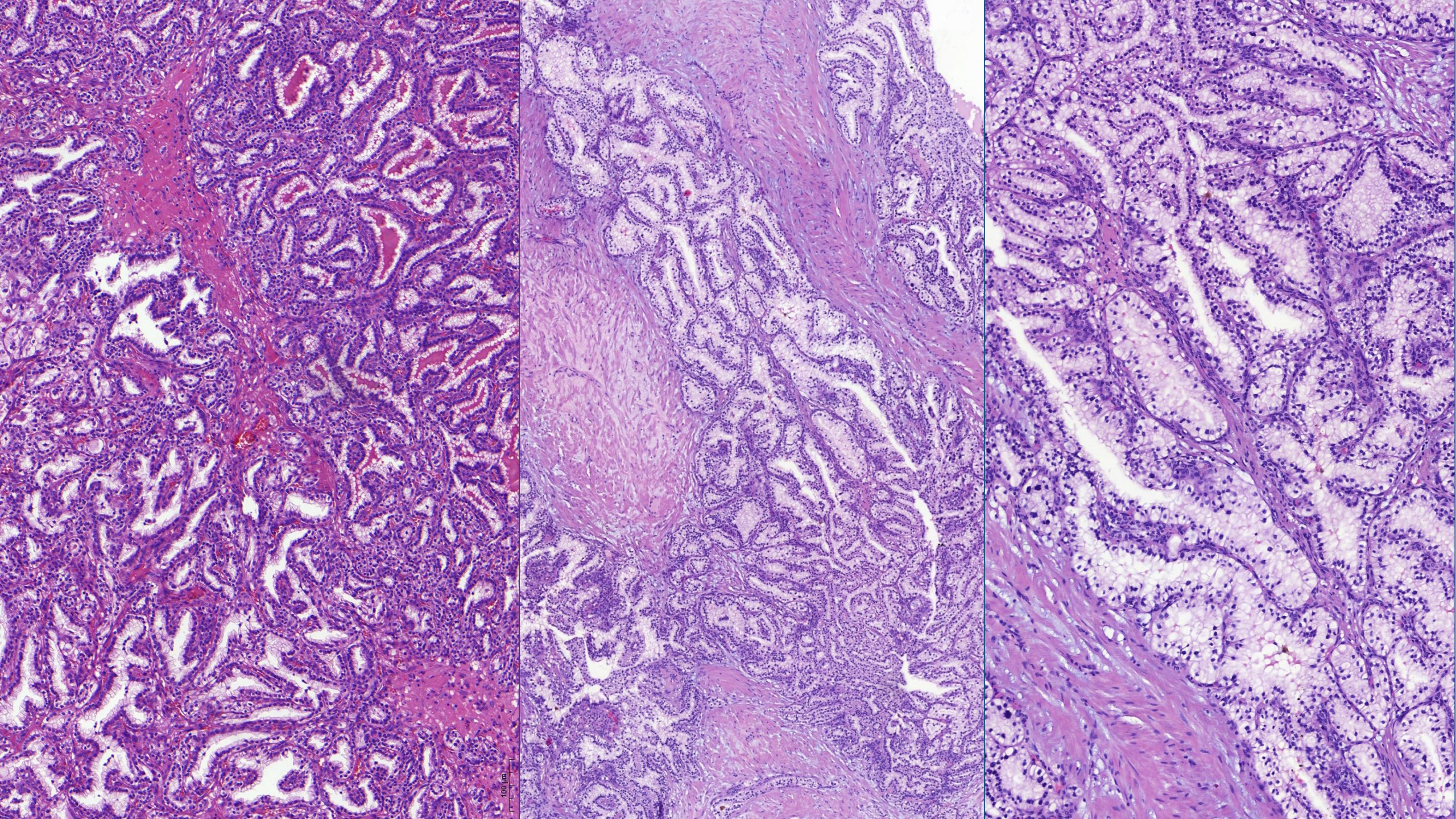
“mixed renal tumor with carcinomatous and fibroleiomyomatous components,” “RCC associated with prominent angioleiomyoma-like proliferation,” “clear cell renal cell carcinoma (CCRCC) with smooth muscle stroma,” “RCC with clear cells, smooth muscle stroma and negativity for 3p deletion,” “RCCLMS,” “RAT,” “TCEB1-mutated RCC,” and “unclassified RCC with tubulopapillary architecture, clear cell phenotype, and chromosome 8 monosomy

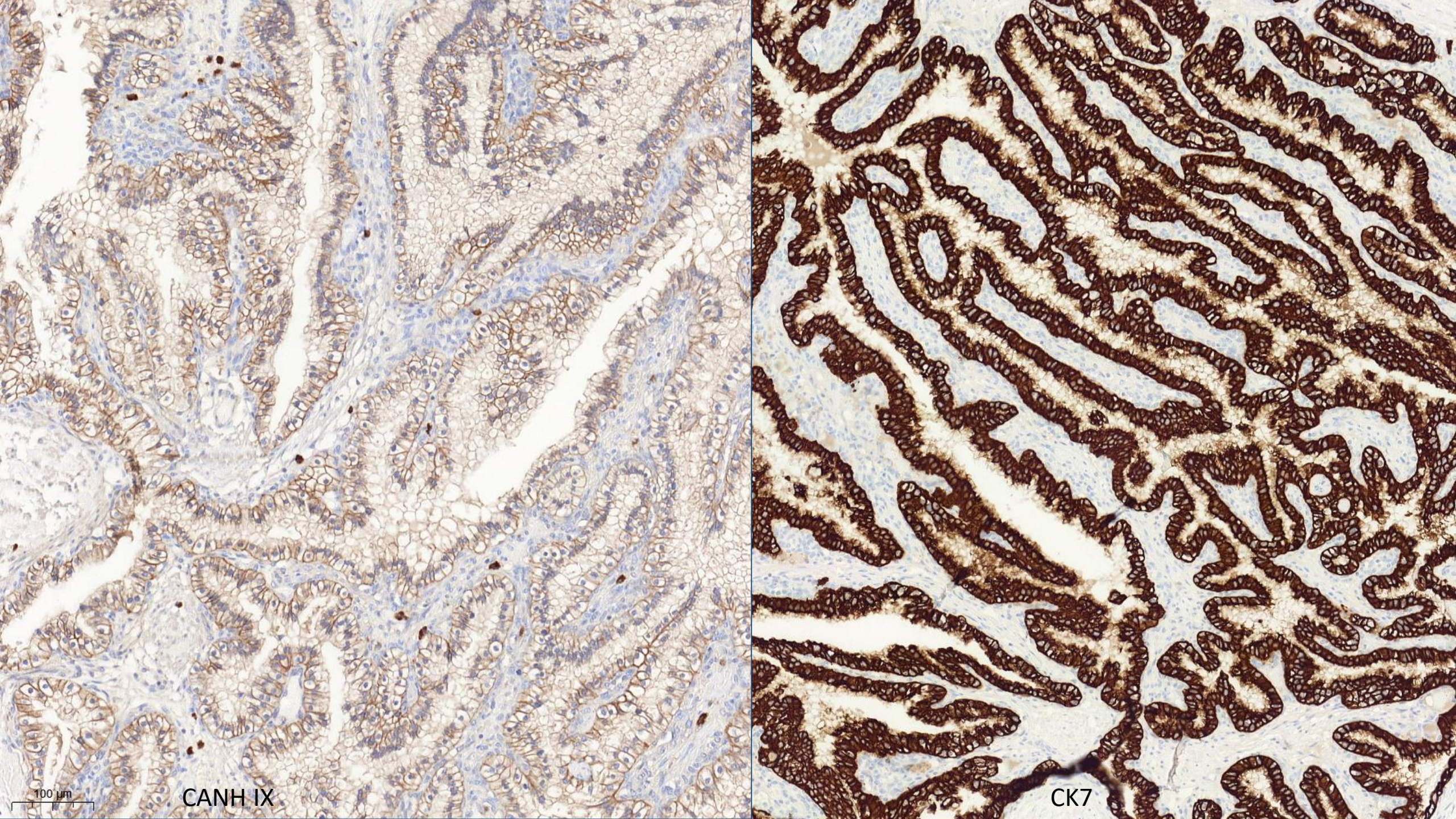
- *ELOC* (formerly *TCEB1*)-mutated renal cell carcinoma
- renal cell carcinoma with fibromyomatous stroma (RCCFMS)
- clear cell papillary renal cell tumour (CCPRCT)
- clear cell renal cell carcinoma (CCRCC)

Clear cell papillary renal cell tumour (CCPRCT)

- angiomyoadenomatous tumour (RAT)
- Indolentní renální neoplázie
- Kuboidální a nízce kolumnární neoplastické bb s low-grade morfologií (grade 1/2 WHO/ISUP) se světlou cytoplasmou a jádry nadzdviženými od BM luminárně (shark smile, piano keys)
- tubulární, papilární uspořádání, ale i malá hnízda a cysty (různá kombinace, může být kompletně cystický) a přítomnost různě vyjádřeného fibrózního/fibromyomatózního stromatu

- bez *VHL* abnormalit (mutace, hypermetylace, LOH3p), bez mutací v genech *TSC1*, *TSC2*, *MTOR*, or *ELOC* (*TCBE1*)
- Nebyla popsána žádná rekurentní alterace
- CK7 difúzně +, CAIX + („cup-like“), GATA3 +, PAX8 +, AMACR -, CD10 –




100 µm
CANH IX
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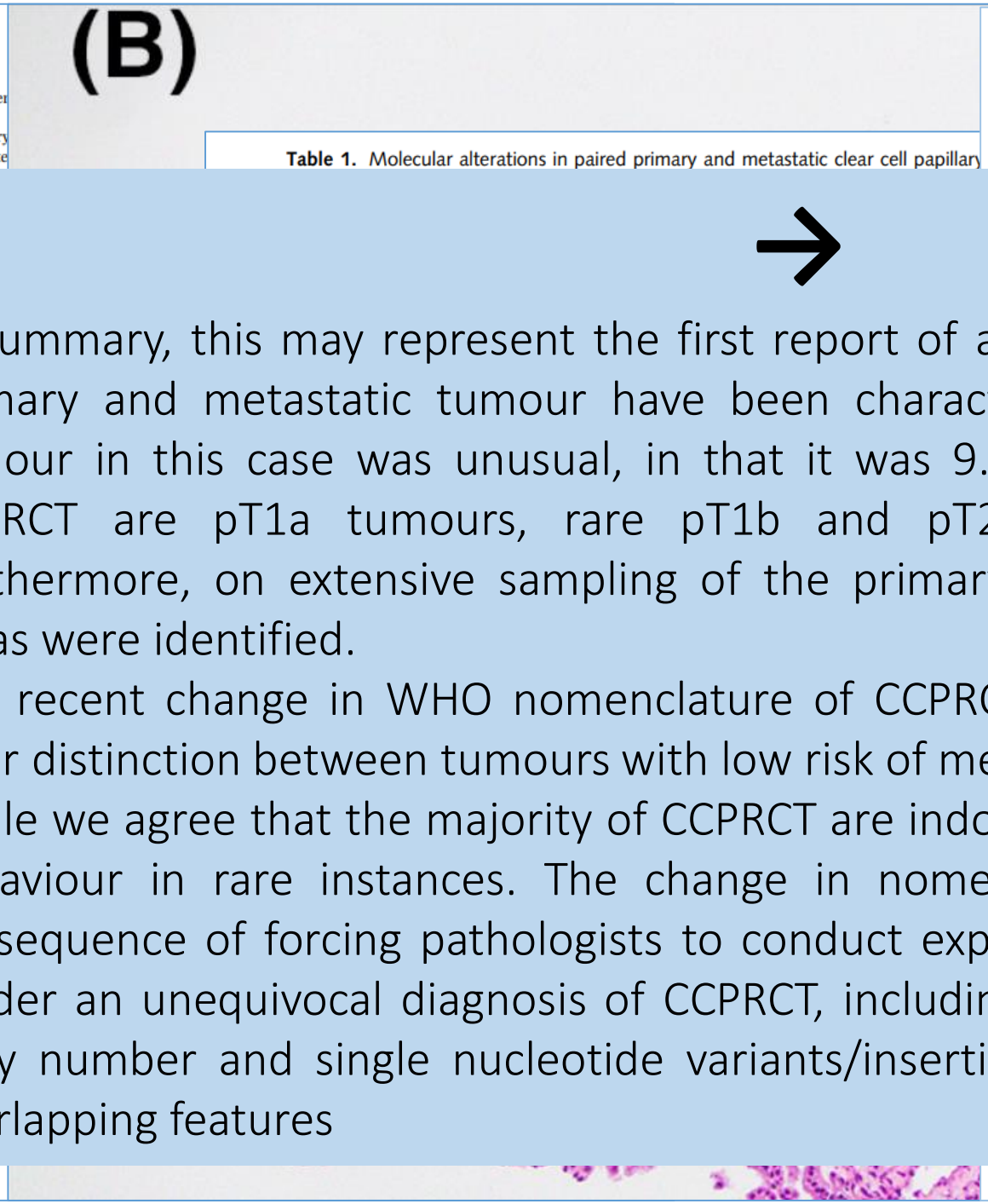

AMACR, while nephroge
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Histopathology, 84, 903–912.

Table 1. Molecular alterations in paired primary and metastatic clear cell papillary

908 *Correspondence*

The recent change in WHO nomenclature of CCPRCT from RCC to 'tumour' suggests a clear dis-

on clinical decision-making, in addition to variables such as tumour size, grade and pathological stage, extensive

report.

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a Dasari[2]
Sharma[3]
D Atwell[4]
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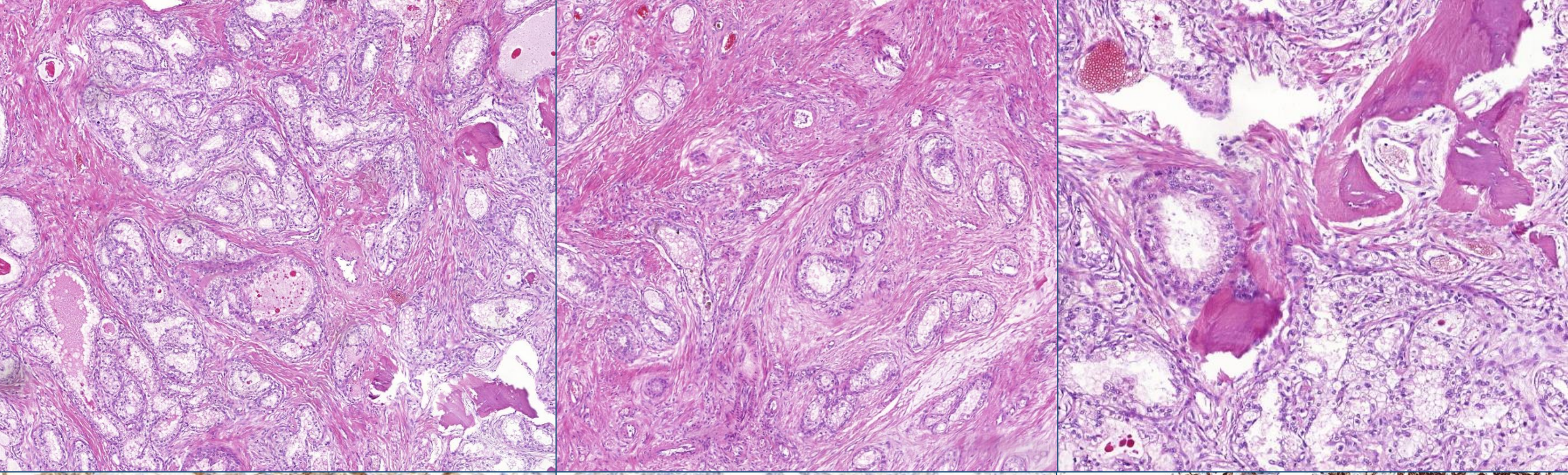
→

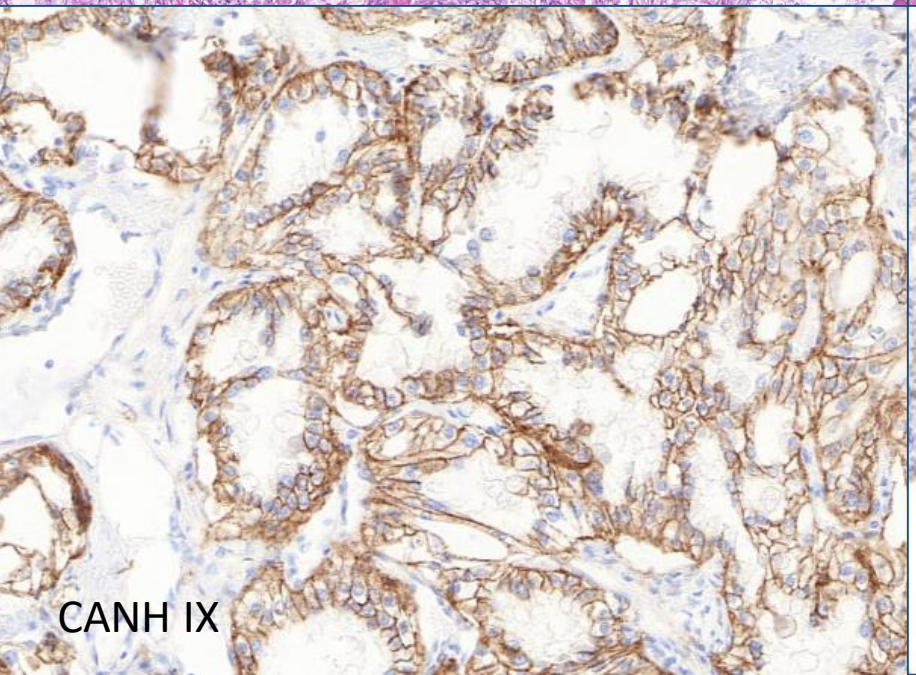
- In summary, this may represent the first report of a metastatic CCPRCT where both the primary and metastatic tumour have been characterised. The partially cystic primary tumour in this case was unusual, in that it was 9.4 cm in size. While the majority of CCPRCT are pT1a tumours, rare pT1b and pT2a tumours have been described. Furthermore, on extensive sampling of the primary tumour no unusual or high-grade areas were identified.
- The recent change in WHO nomenclature of CCPRCT from RCC to 'tumour' suggests a clear distinction between tumours with low risk of metastasis and benign tumours.
- While we agree that the majority of CCPRCT are indolent, our reports highlight metastatic behaviour in rare instances. The change in nomenclature may have the unintended consequence of forcing pathologists to conduct expensive ancillary diagnostic testing to render an unequivocal diagnosis of CCPRCT, including assessment of methylation status, copy number and single nucleotide variants/insertion deletion events in tumours with overlapping features

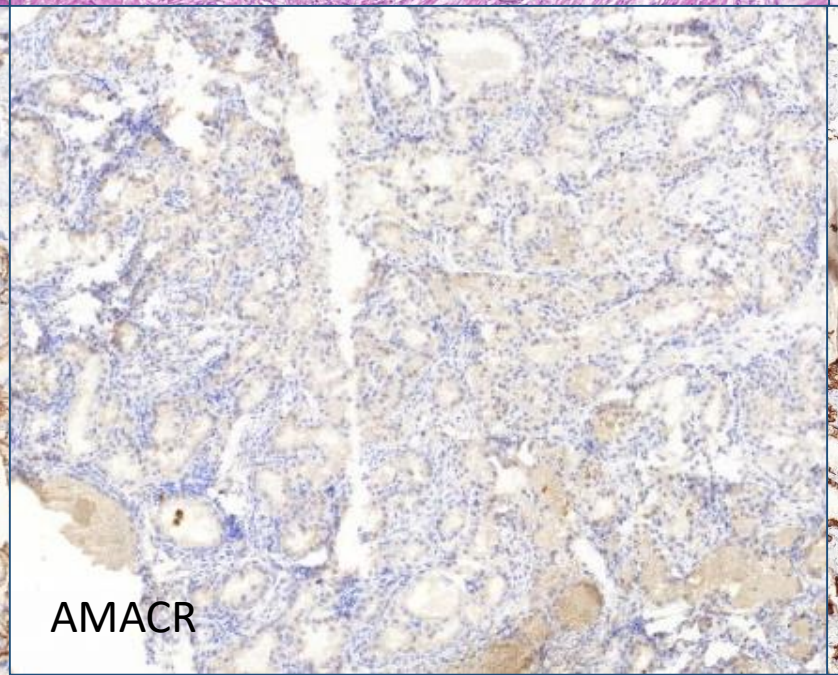
Renal cell carcinoma with fibro(leio)myomatous stroma (RCCFMS)

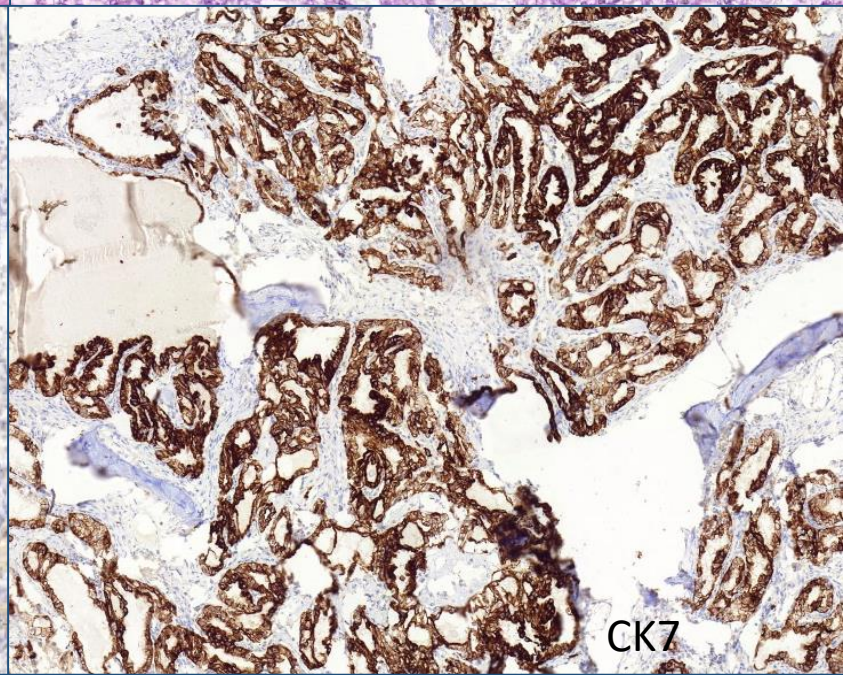
- Recent studies have demonstrated that RCCFMS indeed represents a distinct entity with subtle but distinguishable features that can be separated from other RCCs that exhibit clear cells, as well as tubulopapillary morphology and smooth muscle/fibromatous stroma
- Microscopically, the epithelial component forms tumor nodules composed of elongated and frequently branching tubules, lined by clear or mildly eosinophilic cells containing voluminous cytoplasm. Focal papillary morphology is also frequently present.
- Diffuse CK7 positivity is typical and is required for the diagnosis.
- Molecular analysis of these tumors demonstrated recurrent mutations involving the TSC/mTOR pathway.

- A subset of tumors with similar morphology has shown mutations involving *ELOC* (previously referred to as *TCEB1*) → **It is currently debated whether TSC/mTOR and ELOC mutated RCCFMS should be grouped together, based on their shared and overlapping morphology and common CK7 reactivity, despite the differing molecular alterations**




CANH IX

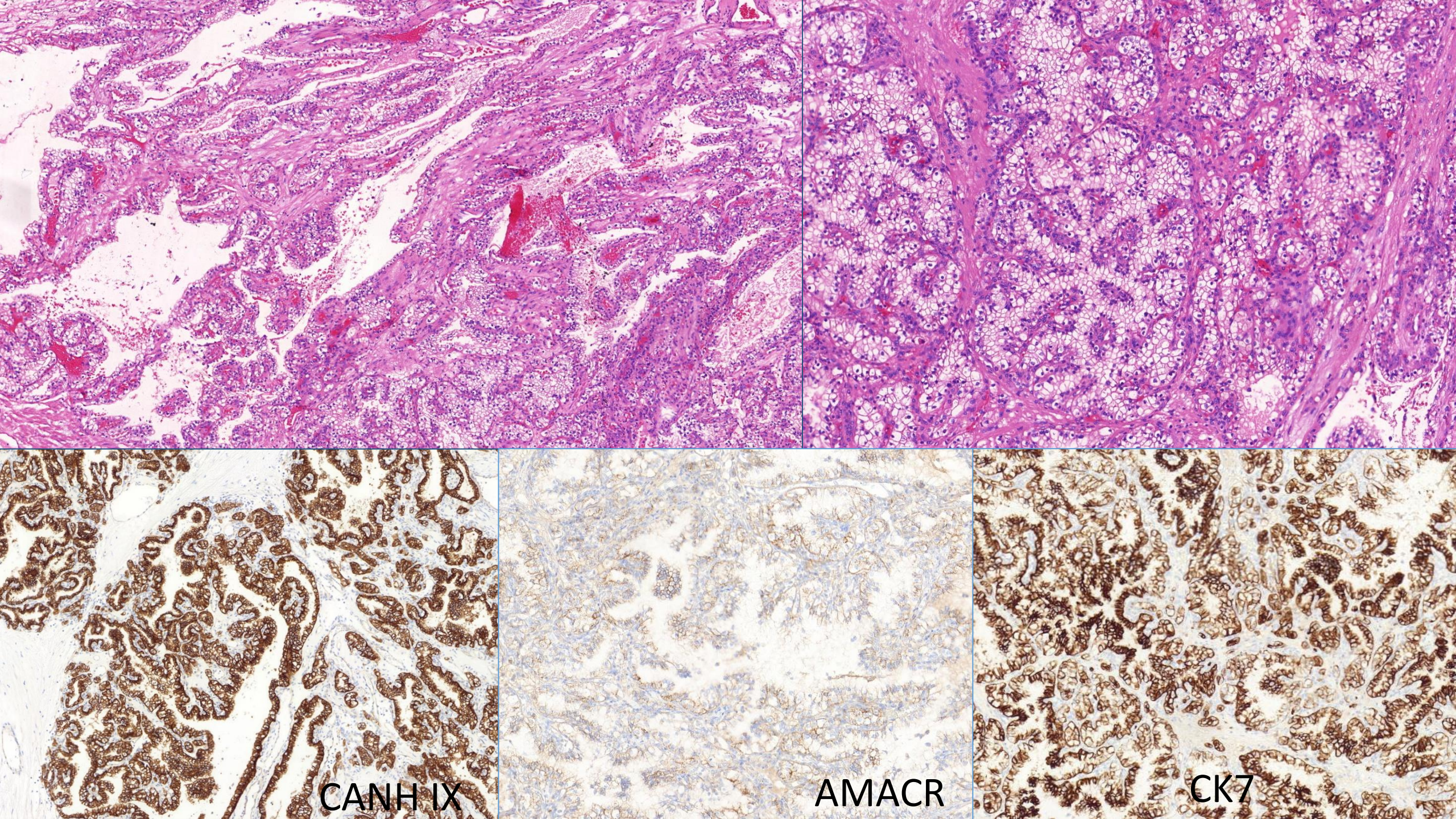

AMACR


CK7

ELOC (formerly *TCEB1*)-mutated renal cell carcinoma

- *ELOC*-mutated renal cell carcinomas (RCCs) are RCCs that harbour mutations in the *ELOC* (*TCEB1*) gene at 8q21.11
- neoplasms have a nodular appearance at low power, created by thick transecting fibromuscular bands. The architecture is that of branching infolding tubules and well-formed papillae.
- The neoplastic cells have voluminous clear cytoplasm and prominent cell borders.
- The neoplastic cells are consistently immunoreactive for CK7 (with labelling ranging from patchy to diffuse), CAIX (typically in a complete membranous fashion), and CD10.
- demonstration of *ELOC* mutation is required to definitively diagnose this neoplasm
- The majority of these neoplasms have an indolent course

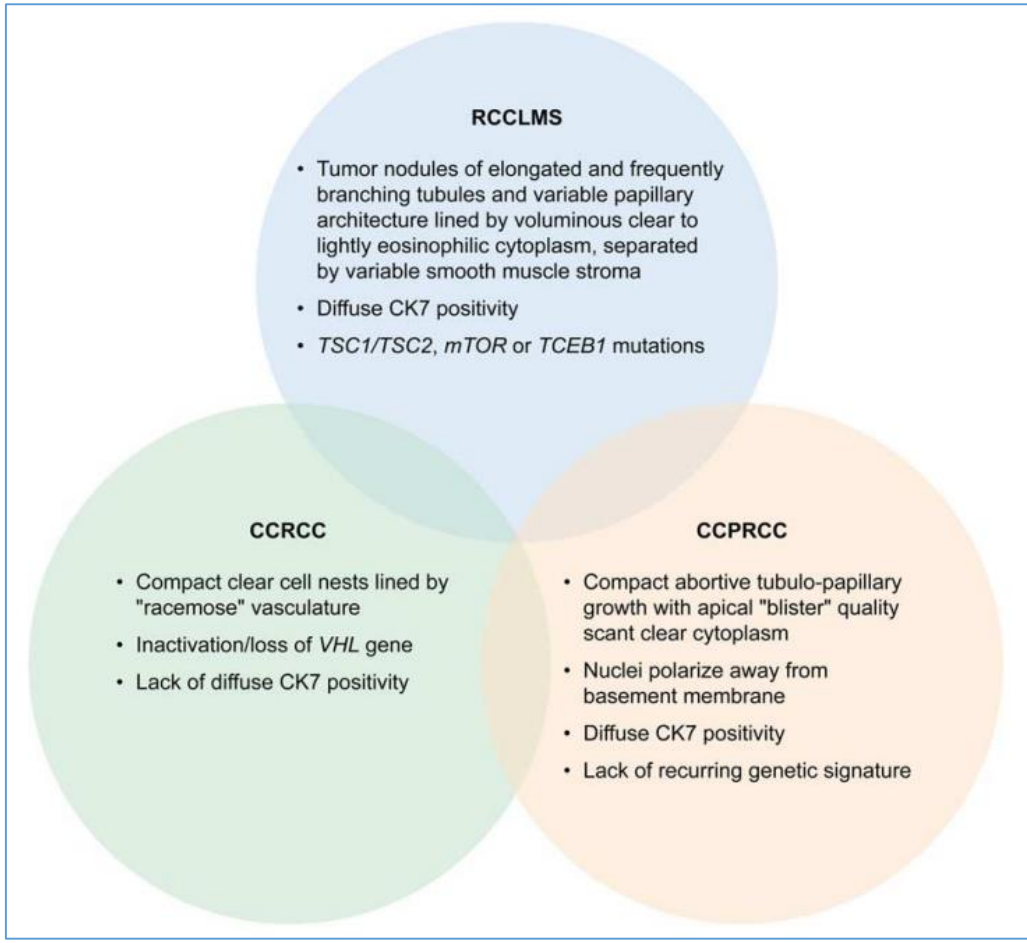
- **Essential and desirable diagnostic criteria (according to WHO 2022)**
  - *Essential:* demonstration of *ELOC* mutation is required to definitively diagnose this neoplasm.


CANH IX
AMACR
CK7

TaHoMe

- Leiomyomatózní stroma není absolutně specifické pro určitý subtyp RCC
- CCRCC má mnoho tváří, dokáže napodobovat různé renální tumory a různé renální tumory mohou napodobovat CCRCC
- Osud CCPRCT nejistý???

- Dg. CCRCC je důležitý atribut při rozhodování o léčbě…



Shah, R.B et al. “Renal Cell Carcinoma With Leiomyomatous Stroma” Harbor Somatic Mutations of TSC1, TSC2, MTOR, and/or ELOC (TCEB1): Clinicopathologic and Molecular Characterization of 18 Sporadic Tumors Supports a Distinct Entity. Am J Surg Pathol 2020;44:571–581

Děkuji za pozornost!

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