IHC WORKUP OF KIDNEY TUMORS: WHAT'S THE POINT IN GETTING ALL WORKED UP?

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I HAVE NO DISCLOSURES

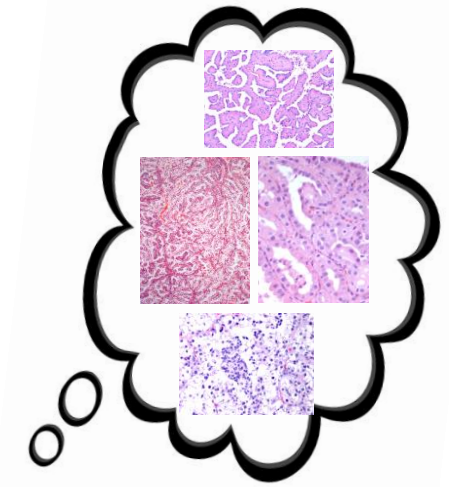
OBJECTIVES

- Distinguish renal tumors with favorable prognosis from tumor with aggressive behavior
- Review key morphologic and IHC features to recognize distinct entities
- Develop an algorithm based on morphologic features to reduce renal tumor-induced anxiety

OBJECTIVES

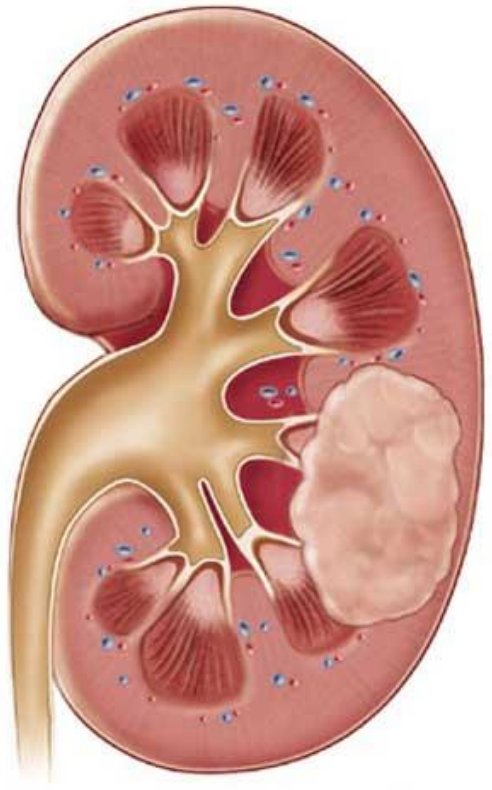
DO NOT PANIC!

KEEP CALM



TUMORS OF THE KIDNEY

- 2% of all cancer globally
- 2% of cancer deaths
- 5-year relative survival rates (2009-2015)
  - Localized 93%
  - Regional 70%
  - Distant 12%
  - All stage combined 75%
- Increase incidence since 1990s:
  - 7th most common cancer in men
  - 10th most common cancer in women
- 60% incidental (and increasing)



2-5% associated with **inherited syndromes**

Hereditary Renal Tumors

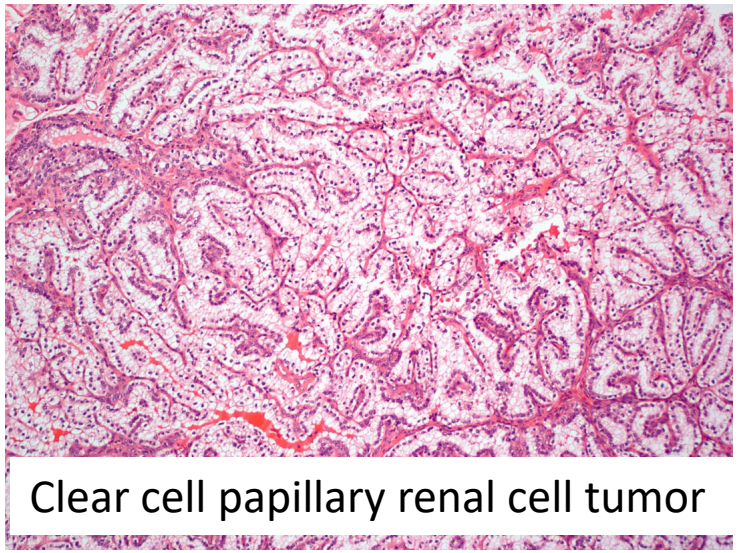
Syndrome	Clinical Manifestations	Gene (Chr.) - Protein	Histologic Features
von Hippel-Lindau **(VHL)** syndrome	Clear cell RCC, pheo, pancreatic endocrine tumors, CNS and retinal hemangioblastomas	*VHL* (3p25) - VHL protein	Clear cell RCC
Hereditary leiomyomatosis and RCC **(HLRCC)**	RCC, Leiomyomas of skin and uterus	*FH* (1q42.1) – Fumarate hydratase	Variable architectural patterns, prominent nucleoli with perinucleolar halo
Birt-Hogg-Dubé syndrome **(BHD)**	Renal tumors, fibrofolliculomas, pulmonary cysts	*BHD/FLCN* (17p11.2) – Folliculin (FLCN)	HOCT, oncocytoma, chromophobe RCC
Tuberous sclerosis complex **(TSC)**	Multiple renal AML, RCCs, Cardiac rhabdomyomas, Hamartomas, Neurologic disorders/seizures	*TSC1* (9q34) - Hamartin *TSC2* (16p13.3) - Tuberin	AML, renal cysts, RCC ~to clear cell, TCEB1-mutated RCC, chromophobe RCC, oncocytoma, or unclassified
Succinate dehydrogenase **(SDH)-**associated pheo/ paraganglioma syndrome	Bilateral and extraadrenal pheo/paraganglioma, RCC and other malignancies	*SDHB* (1p36.1-p35) – SDH subunit B	Cytoplasmic inclusions containing pale eosinophilic to clear material
Hereditary papillary RCC	Type I papillary RCC	*MET* (7q31) - MET	Type I papillary RCC

Adapted from Peng & Chen. Surgical Pathology Clinics 2018

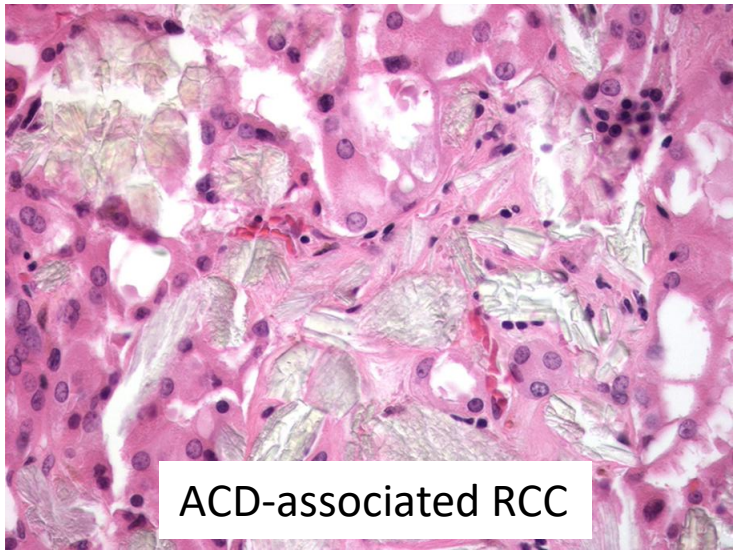
Renal Tumors – WHO 2022

Renal cell tumours

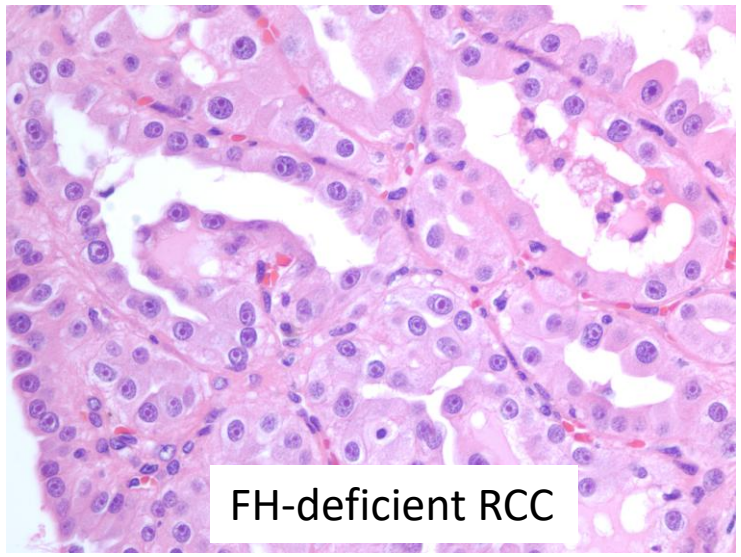
- 3.1.0.1: Renal cell tumours: Introduction
- 3.1.1: Clear cell renal tumours
  - 3.1.1.1: Clear cell renal cell carcinoma
  - 3.1.1.2: Multilocular cystic renal neoplasm of low malignant potential
- 3.1.2: Papillary renal tumours
  - 3.1.2.1: Renal papillary adenoma
  - 3.1.2.2: Papillary renal cell carcinoma
- 3.1.4: Oncocytic and chromophobe renal tumours
  - 3.1.4.1: Oncocytoma of the kidney
  - 3.1.4.2: Chromophobe renal cell carcinoma
  - 3.1.4.3: Other oncocytic tumours of the kidney
- 3.1.5: Collecting duct tumours
  - 3.1.5.1: Collecting duct carcinoma
- 3.1.6: Other renal tumours
  - 3.1.3.1: Clear cell papillary renal cell tumour
  - 3.1.2.3: Mucinous tubular and spindle cell carcinoma
  - 3.1.6.1: Tubulocystic renal cell carcinoma
  - 3.1.6.2: Acquired cystic disease-associated renal cell carcinoma
  - 3.1.6.3: Eosinophilic solid and cystic renal cell carcinoma
  - 3.1.6.4: Renal cell carcinoma NOS
- 3.1.7: Molecularly defined renal carcinomas
  - 3.1.7.1: TFE3-rearranged renal cell carcinomas
  - 3.1.7.2: TFEB-rearranged renal cell carcinomas
  - 3.1.7.3: ELOC (formerly TCEB1)-mutated renal cell carcinoma
  - 3.1.7.4: Fumarate hydratase-deficient renal cell carcinoma
  - 3.1.7.5: Succinate dehydrogenase-deficient renal cell carcinoma
  - 3.1.7.6: ALK-rearranged renal cell carcinomas
  - 3.1.5.2: SMARCB1-deficient renal medullary carcinoma



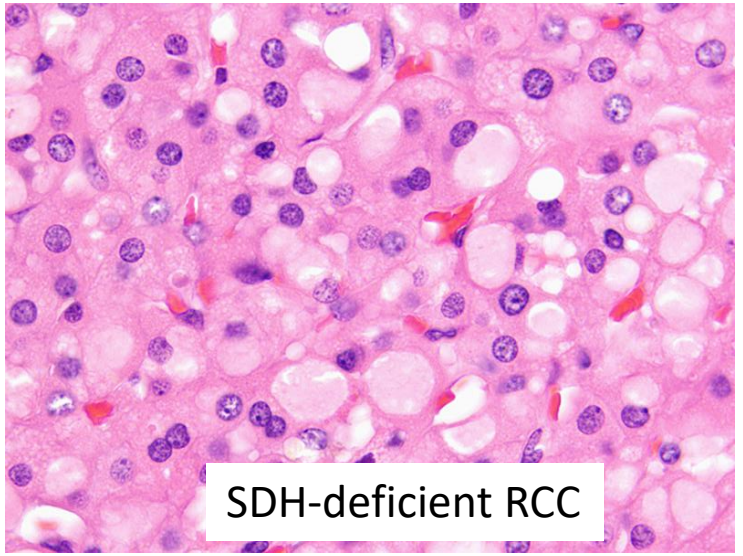
Clear cell papillary renal cell tumor



ACD-associated RCC



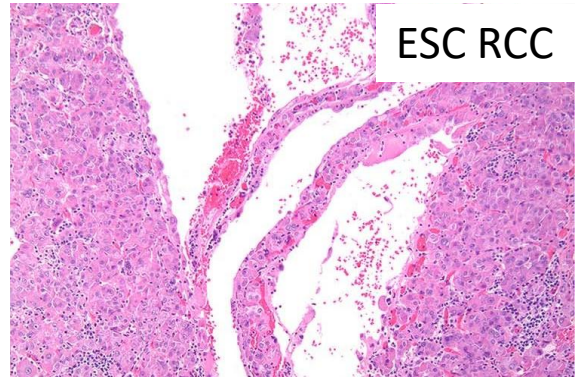
FH-deficient RCC

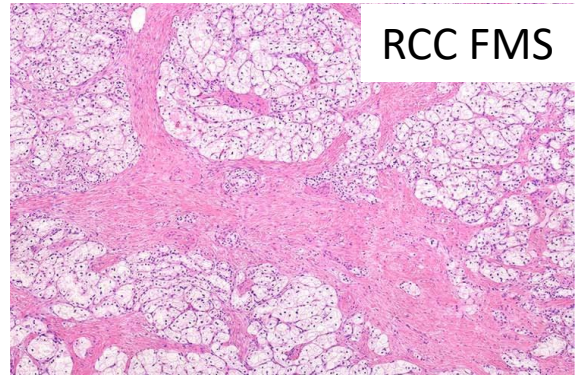


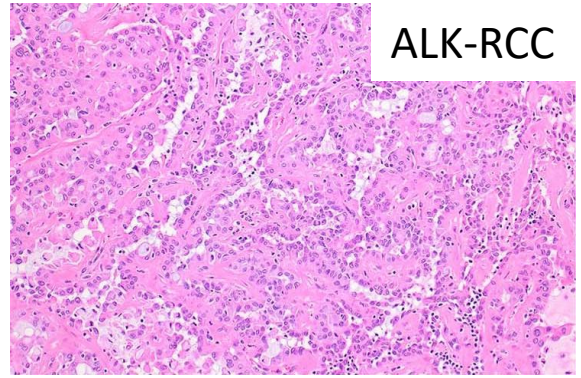
SDH-deficient RCC

Renal Tumors – Novel Entities

Type	Clinical features	Morphology	IHC	Molecular features	Prognosis	2016 WHO/Status
Eosinophilic solid and cystic RCC (ESC RCC)	Mostly females, ≤10% in TSC patients	Solid and cystic, voluminous eosinophilic cells, cytoplasmic coarse granularity	**CK20+,** CK7−, CD117−, vimentin+, **cathepsin K+**	Somatic bi-allelic loss or mutations of *TSC1* and *TSC2*	Good, rare cases aggressive (5–10%)	No
RCC with fibromyomatous stroma (RCC FMS)	No specific clinical features; ≤10% in TSC patients	Fibromyomatous stroma and clear cell areas with elongated, branching tubules, focal papillary morphology	**CK7+** CAIX+ CD10+ vimentin+	*TSC1/MTOR* mutations, some with *ELOC1* (*TCEB1*) mutations and monosomy 8, no *VHL* mutations	Usually favorable	Yes /Emerging/ provisional entity
Anaplastic lymphoma kinase rearrangement-associated RCC (ALK-RCC)	Adults (younger middle age or older), pediatric with sickle cell trait, medullary location	Variable admixed patterns, often mucinous/myxoid background; papillary; Medullary CA-like morphology in children	**ALK+,** PAX8+, non-specific, rare cases TFE3+ in children (without translocation)	*ALK* rearrangement in all (various fusion partners)	**Adverse** (metastasis, death) in about 25%	Yes/emerging /provisional entity

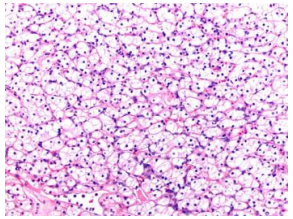
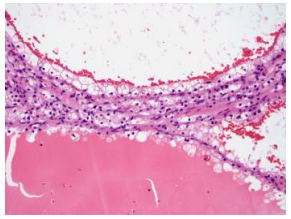
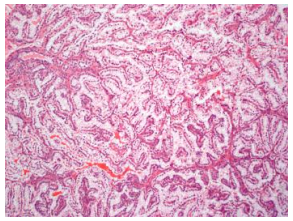
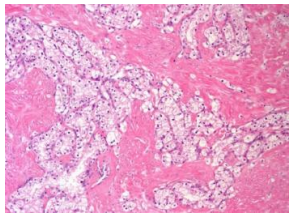
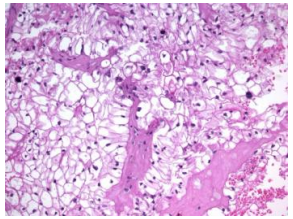






Trpkov et al. Mod Path 2021, GUPS

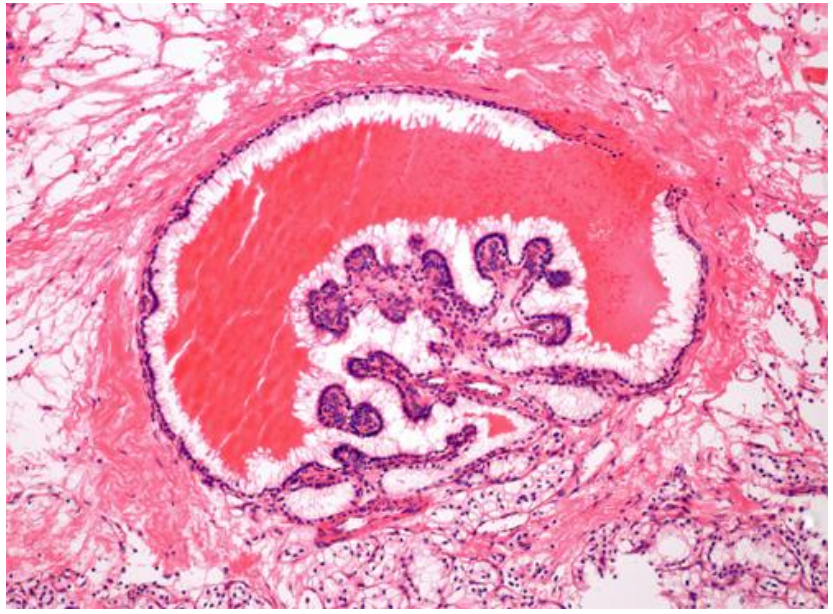
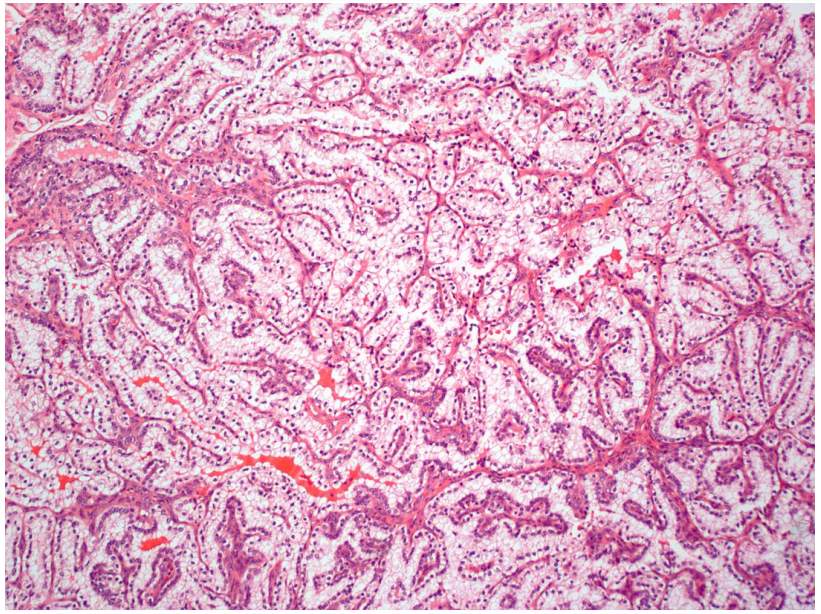
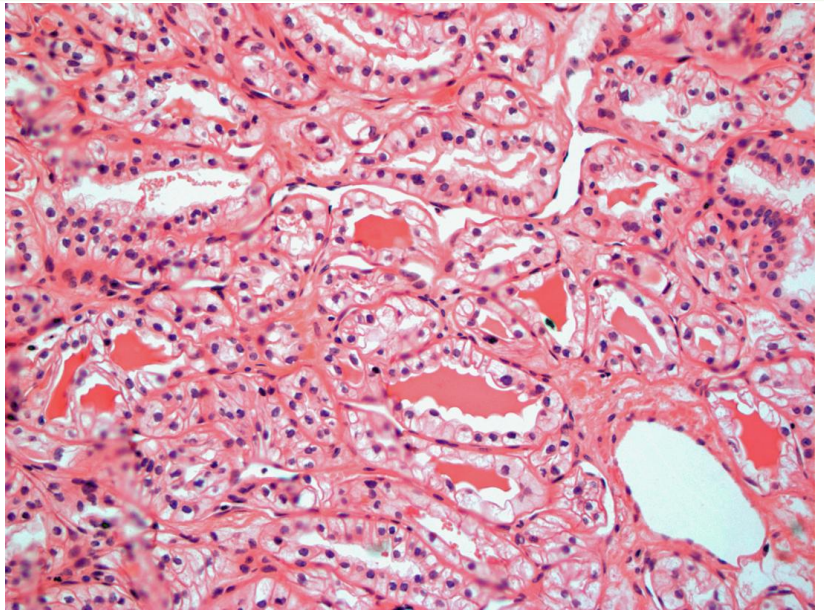
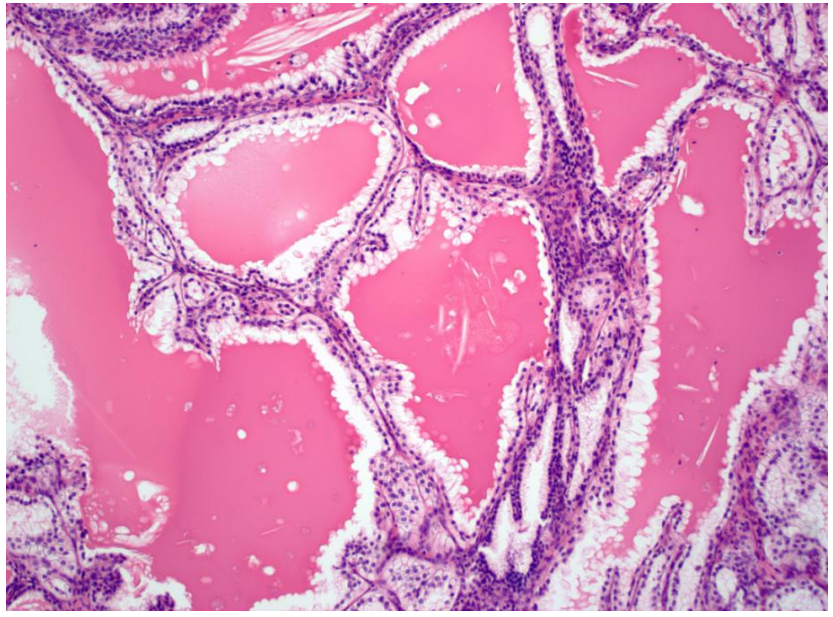
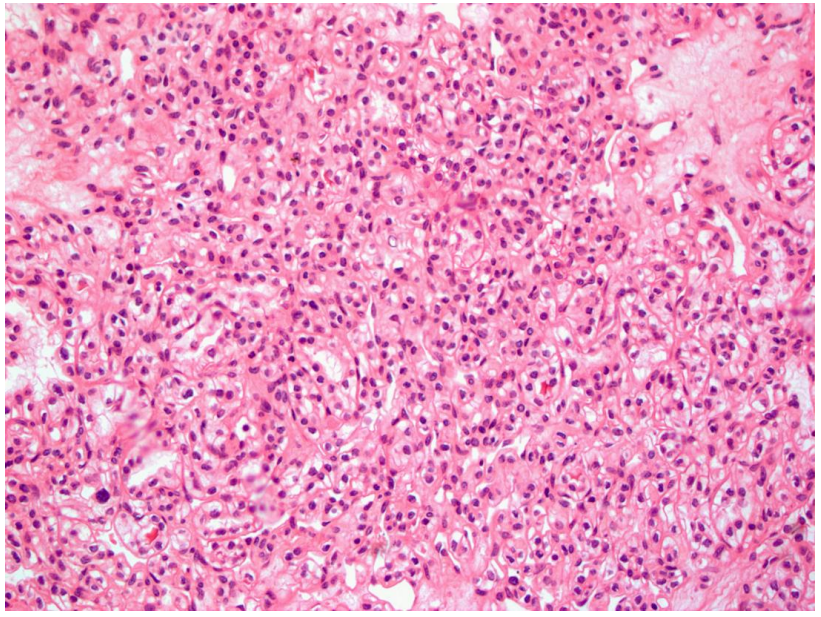
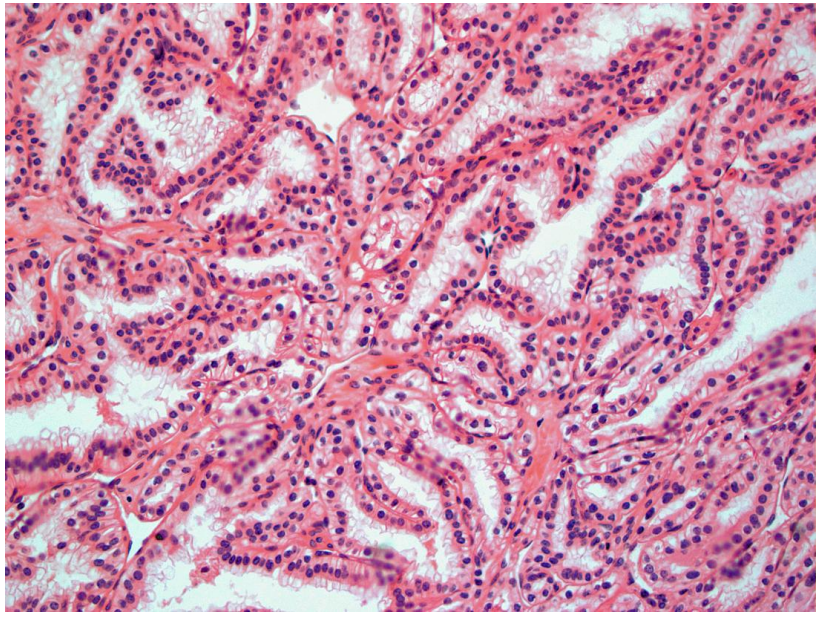
RENAL TUMOR WITH CLEAR CELLS

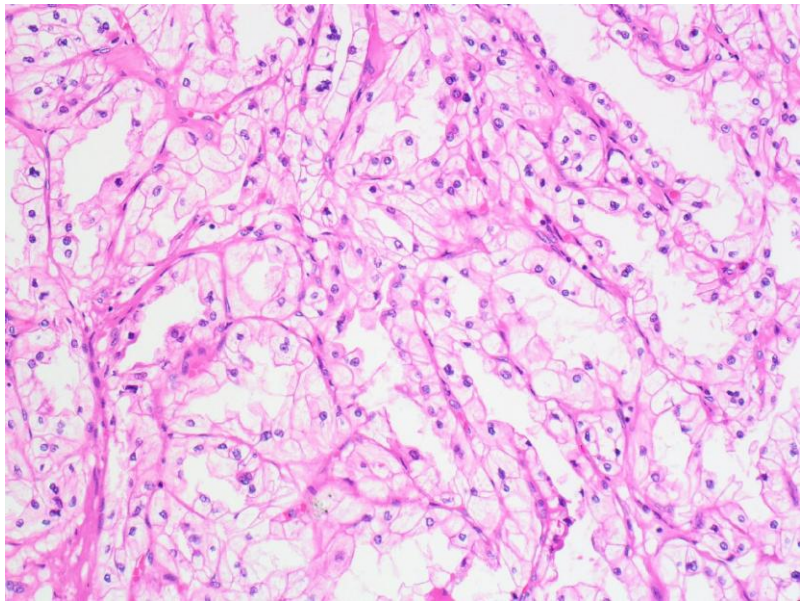
Tumor type	Clinical features	Morphology	IHC	Molecular features	Prognosis
Clear cell RCC (CCRCC)	~70% of renal tumors - 10% multifocal - 3% bilateral	Solid/acinar growth with delicate sinusoidal vascular pattern	**CAIX+, CK7–**/+ CD117– vimentin+ AMACR-/+	*VHL* mutations (>80%) or hypermethylation (8%) *PBRM1, SETD2, KDM5C, BAP1 mutations*	Depends on grade/stage
Multilocular cystic renal neoplasm of low malignant potential (MCRN-LMP)	- Male predom. - Rare variant of CCRCC	Cysts with thin fibrous septa lined by 1 or few layers of clear cells	**CAIX+** CK7+/-	*VHL* gene alterations similar to CCRCC 3p deletion by FISH in 74%	Excellent prognosis
Clear cell papillary renal cell tumor*	- Sporadic or in ACKD 4th most common renal tumor	Tubulopapillary architecture with compressed tubules lined by clear cells	**CK7+, CAIX+ (cup-like)** AMACR- CD10-; GATA3+	No LOH of 3p; no VHL mutations/methylation No chr. 7/17 trisomy	Favorable prognosis
RCC with fibromyomatous stroma	- Sporadic or in TSC patients (≤10%)	Fibromyomatous stroma, branching tubules with clear cells, focal papillary	**CK7+, CAIX+ CD10+** vimentin+	*TSC1/MTOR* mutations, some with *ELOC1* (*TCEB1*) mutations, monosomy 8, no *VHL* mutations	Usually favorable
TFE3-rearranged RCC*	Peak age: 20-29	Papillae lined by clear cells; broad spectrum	Cathepsin K+/- MelanA/HMB+/-	Translocations involving *TFE3* on chr. Xp11.2	Aggressive 47%
TFEB-rearranged RCC*	Peak age: 30-39 Female predom.	Usually biphasic morphology	**Cathepsin K+ MelanA/HMB+**	*Alpha-TFEB* gene fusion (MALAT1-TFEB)	Aggressive 17%

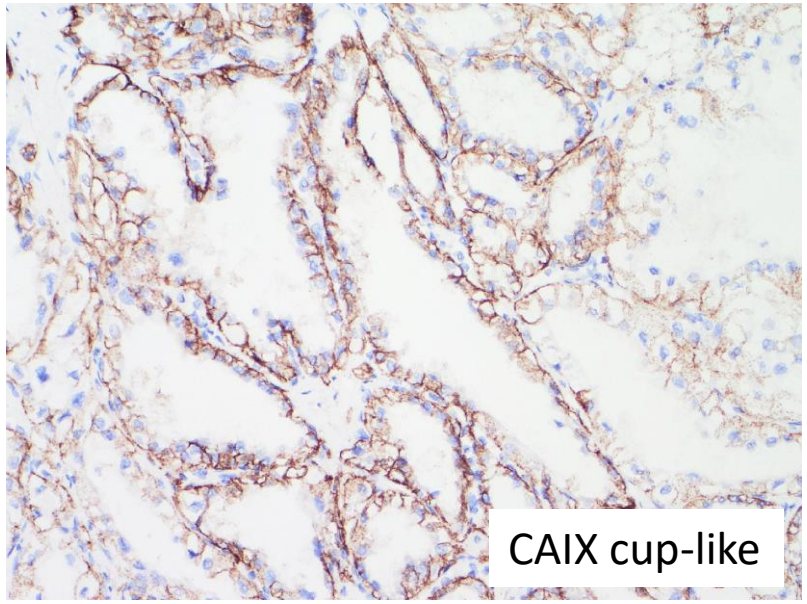
*papillary features

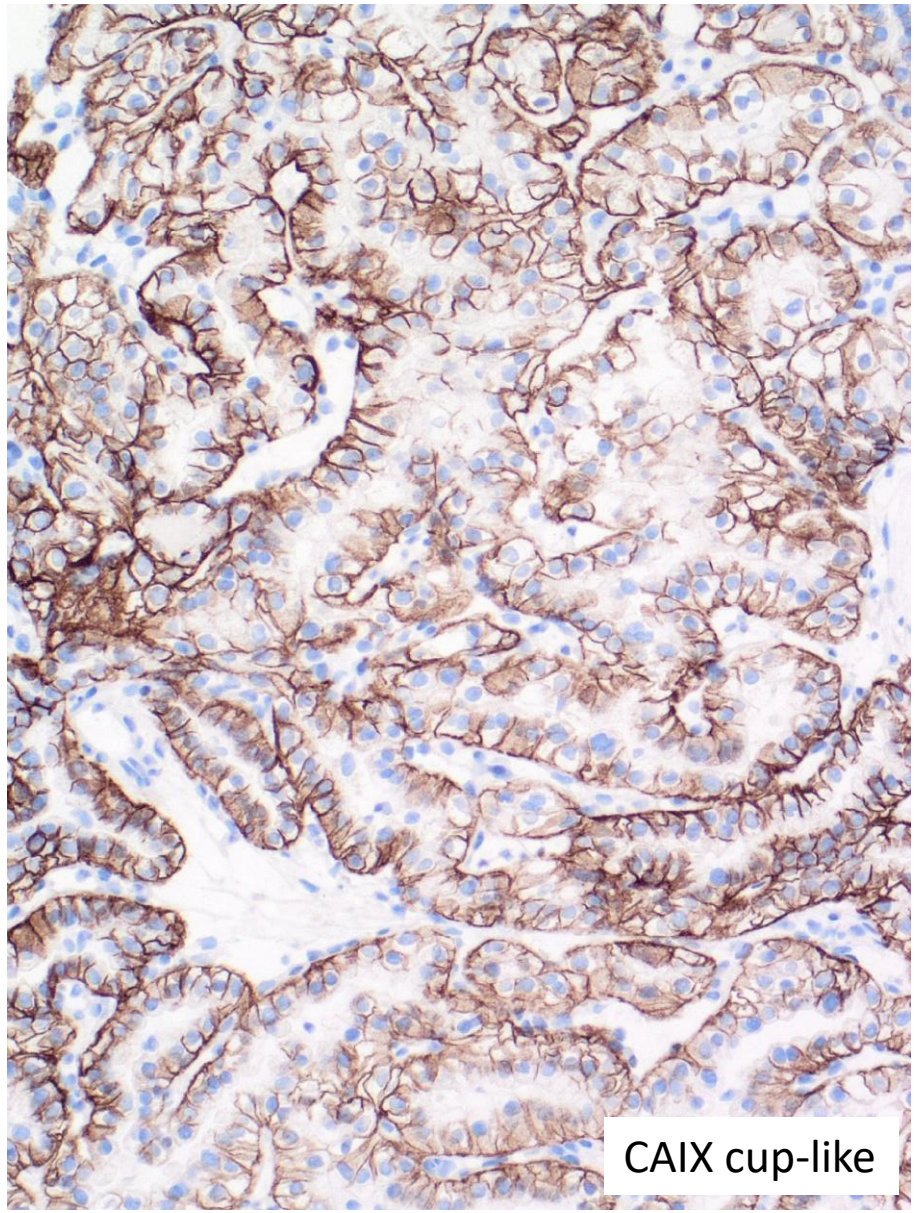
CLEAR CELL PAPILLARY RENAL CELL TUMOR

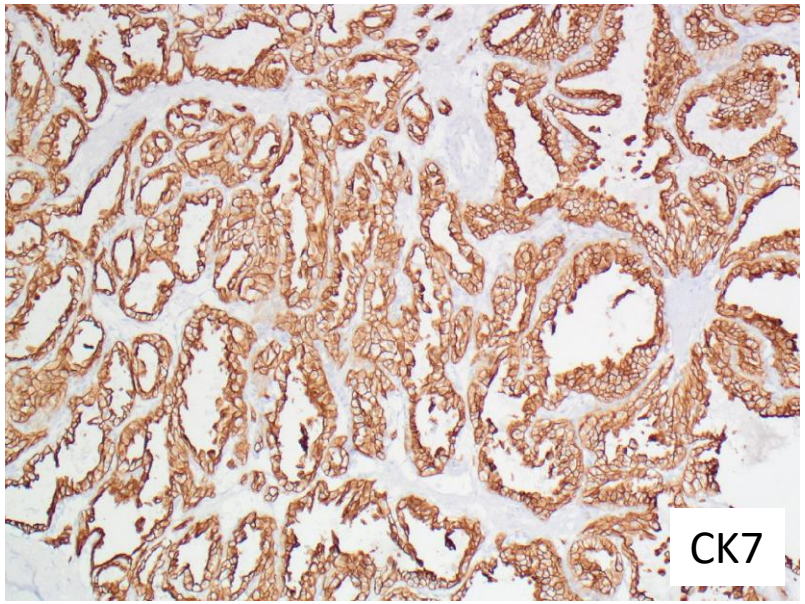







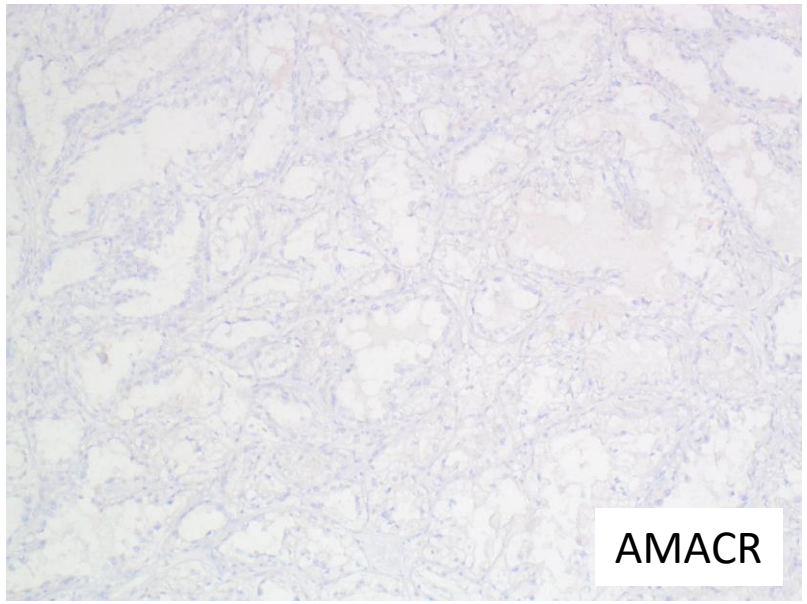
CLEAR CELL PAPILLARY RENAL CELL TUMOR



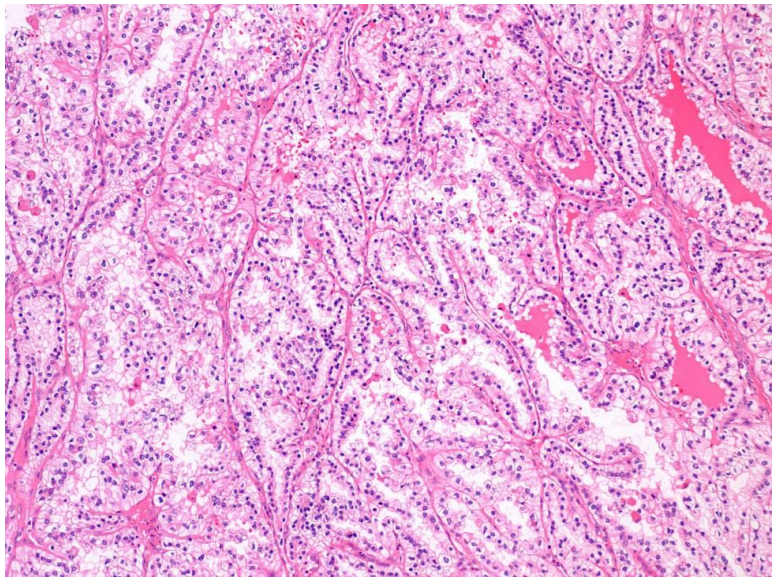


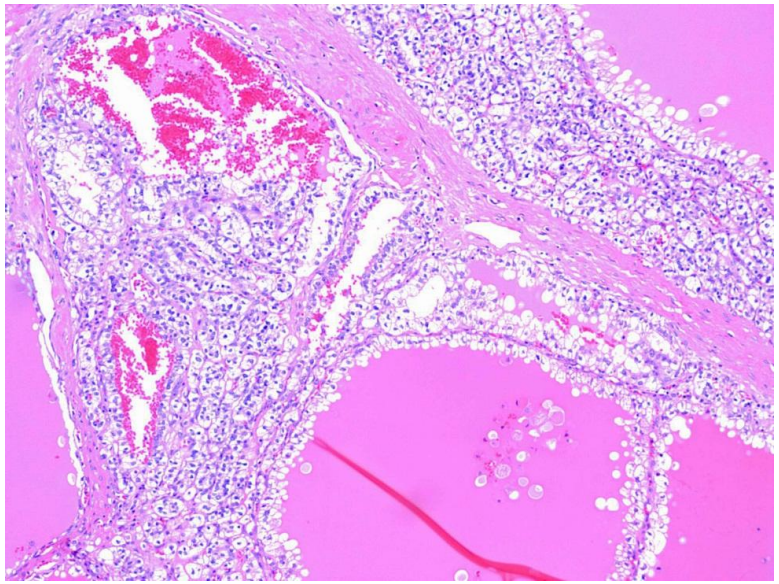


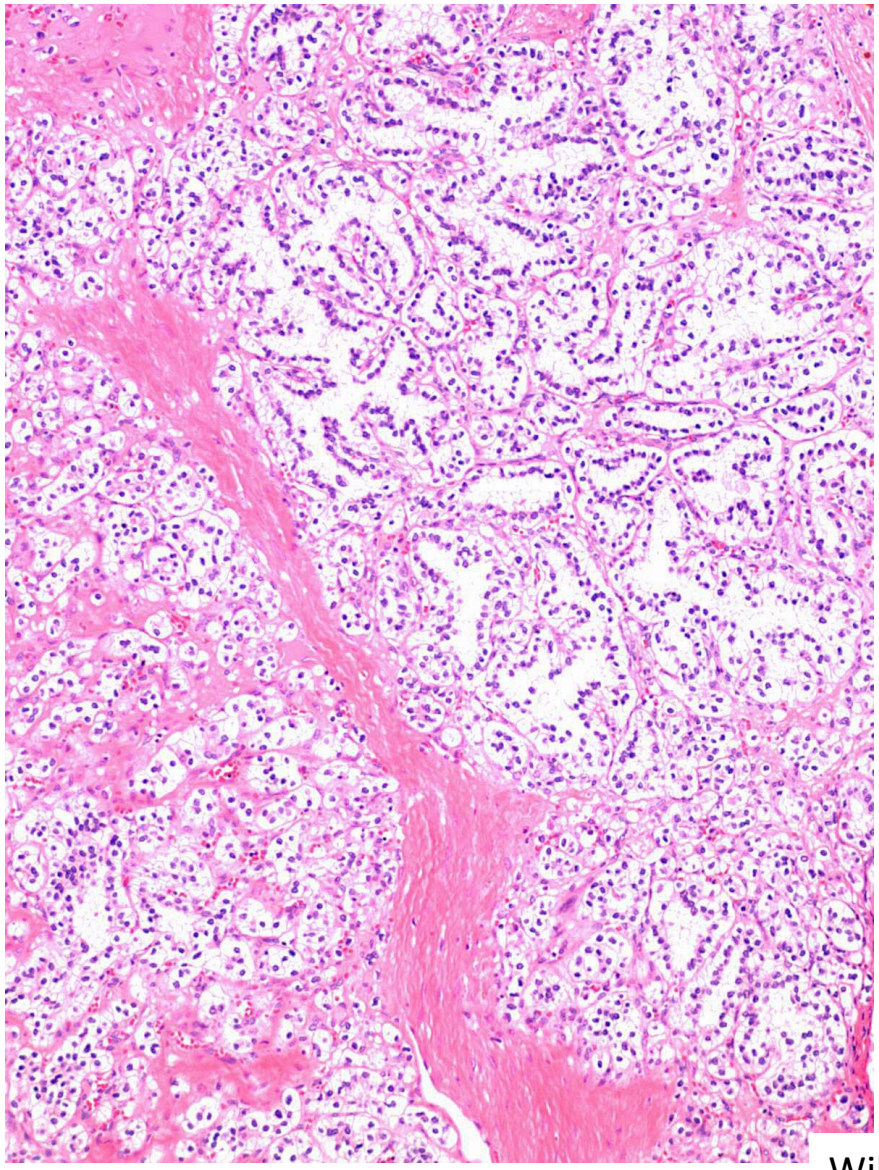


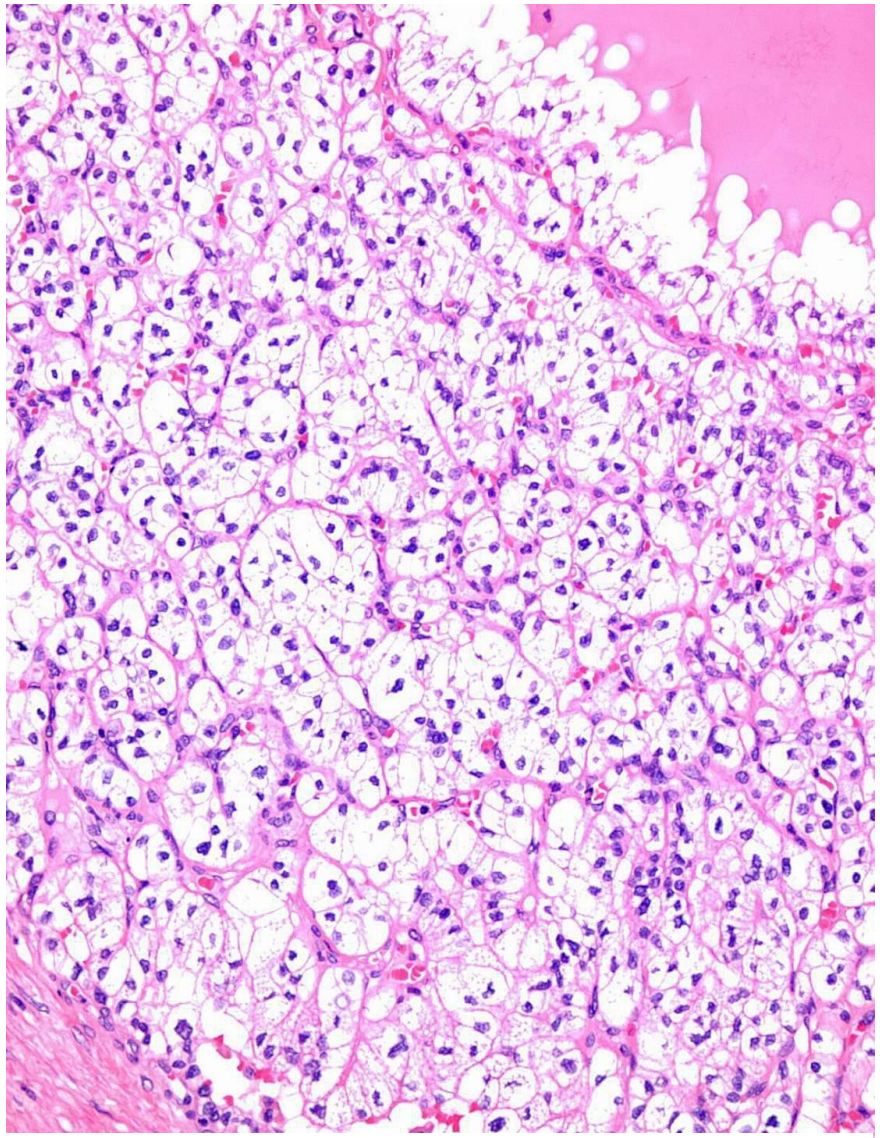


CCRCC WITH FEATURES MIMICKING CLEAR CELL PAPILLARY RENAL CELL TUMOR



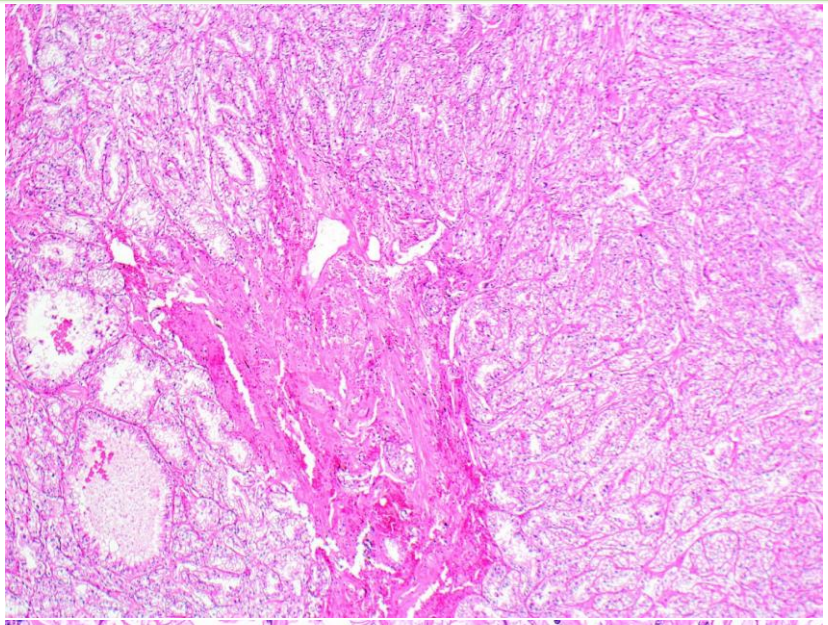


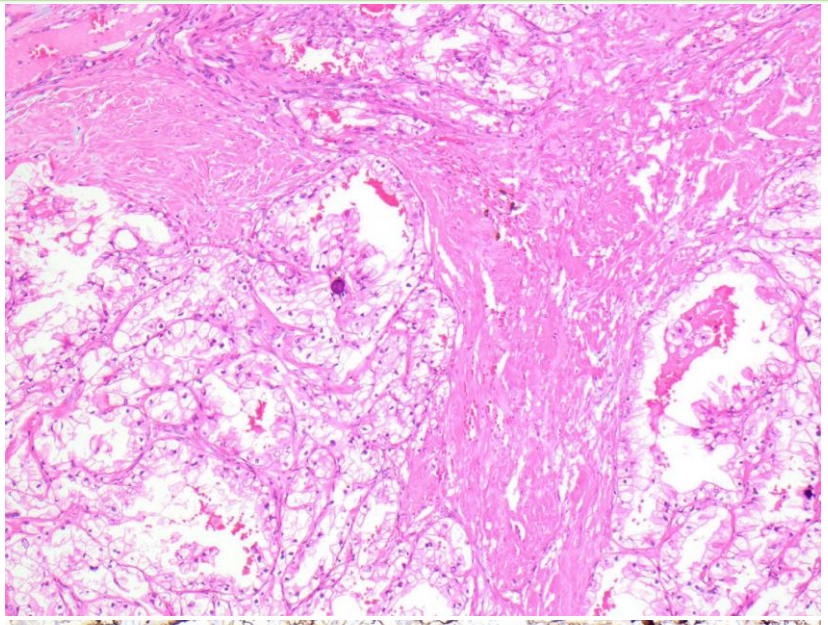


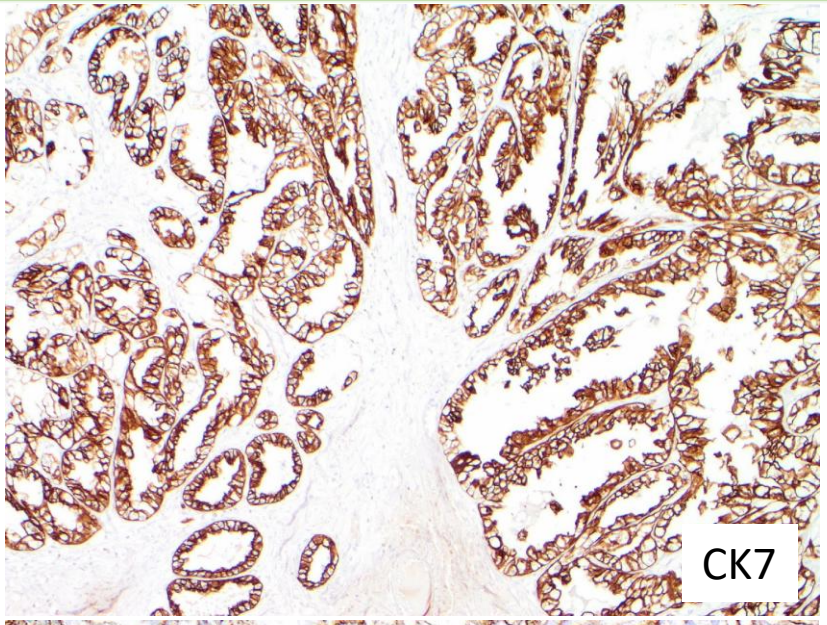


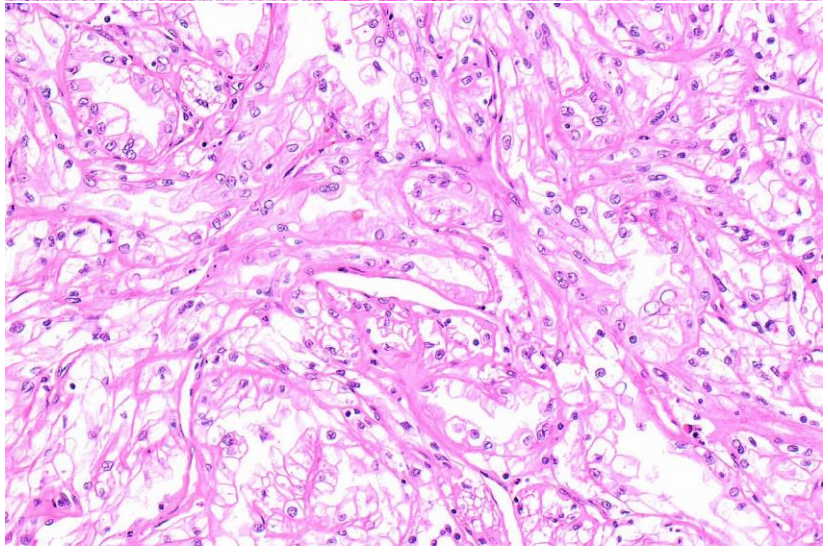
Williamson et al. AJSP 2015; Dhakal et al. AJSP 2016

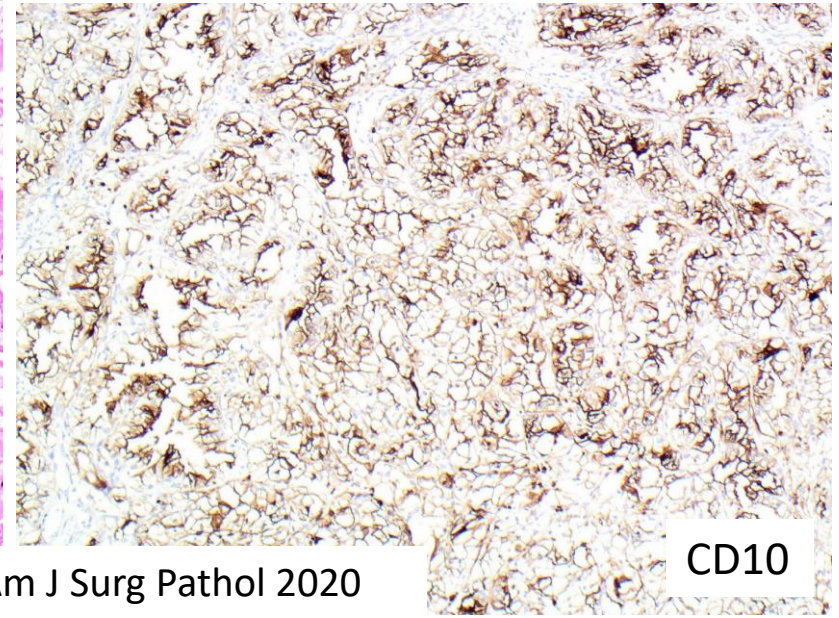
RCC WITH PROMINENT FIBROMUSCULAR SEPTATIONS AND CK7 POSITIVITY – ELOC MUTATED RCC

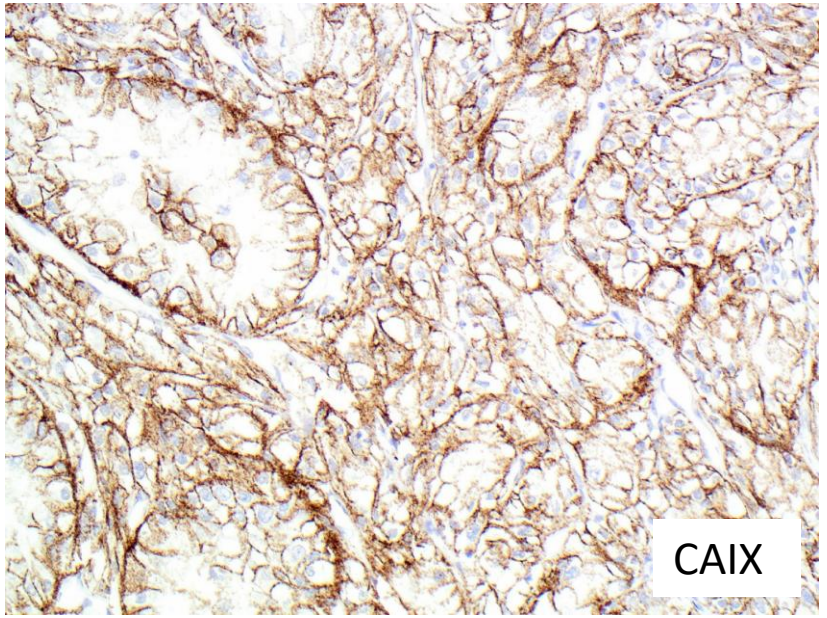






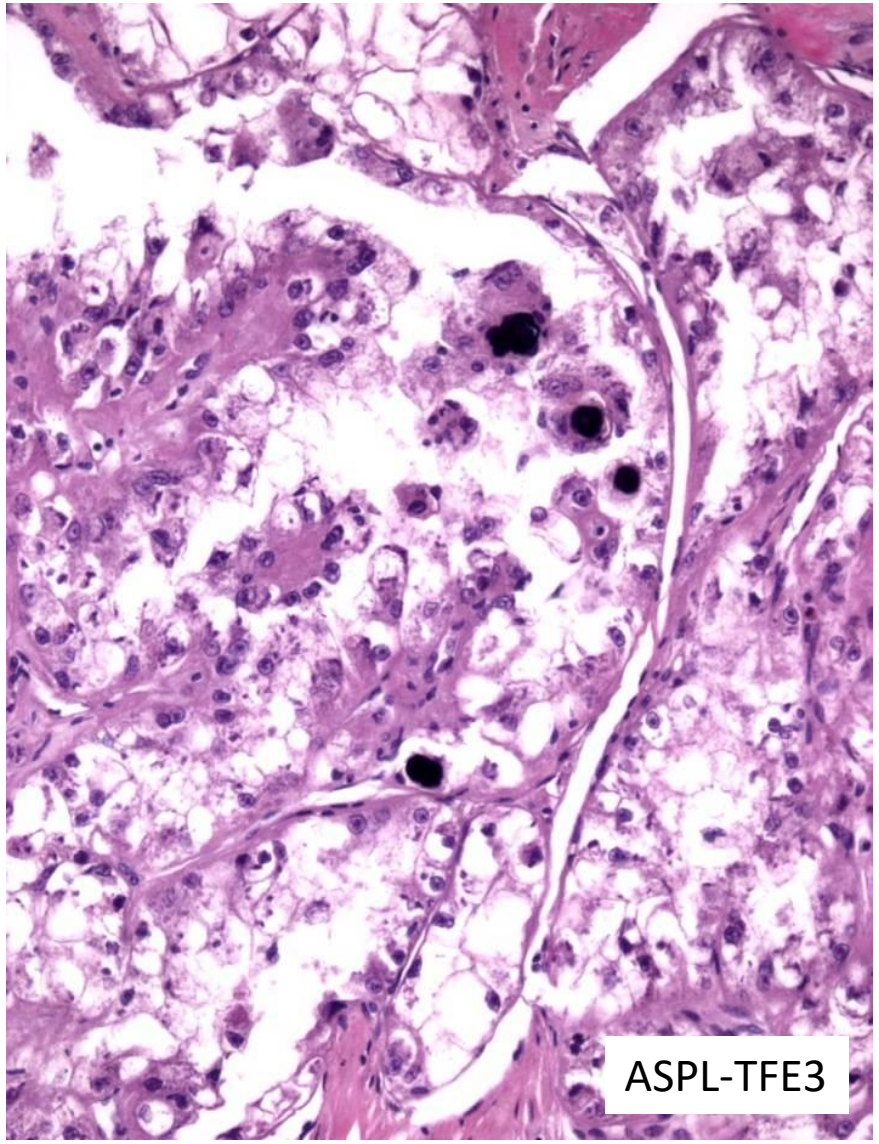


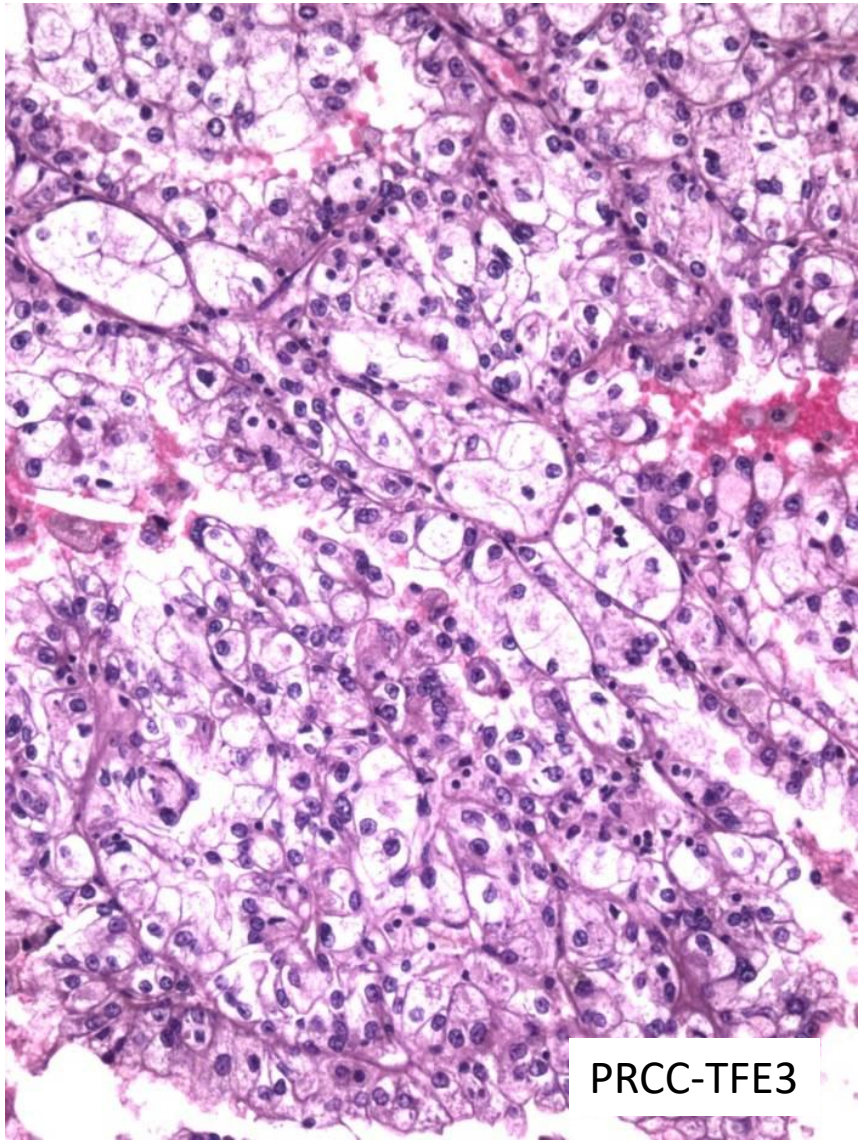


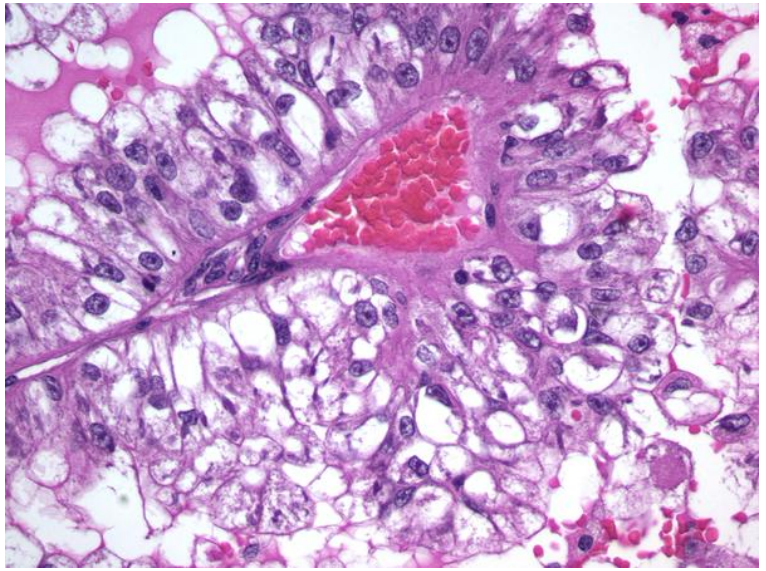


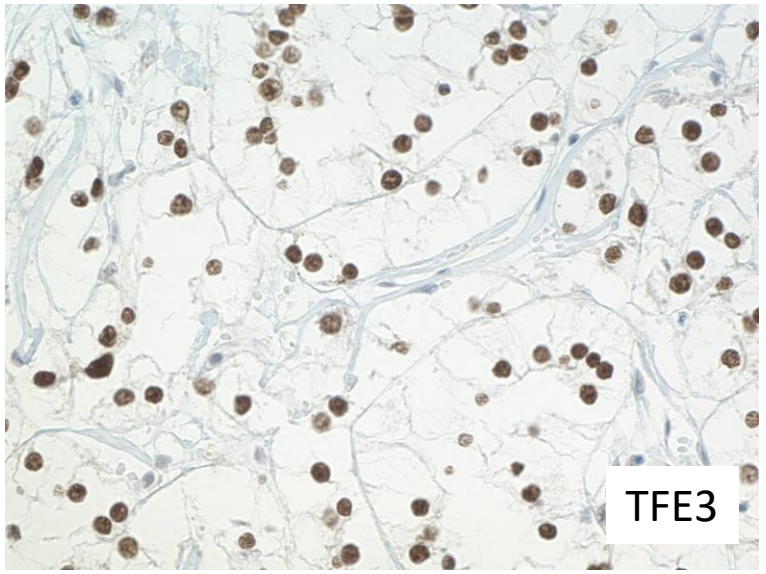
Trpkov & Hes. Histopathology 2019; Shah et al. Am J Surg Pathol 2020

XP11 TRANSLOCATION RENAL CELL CARCINOMA (*TFE3*)

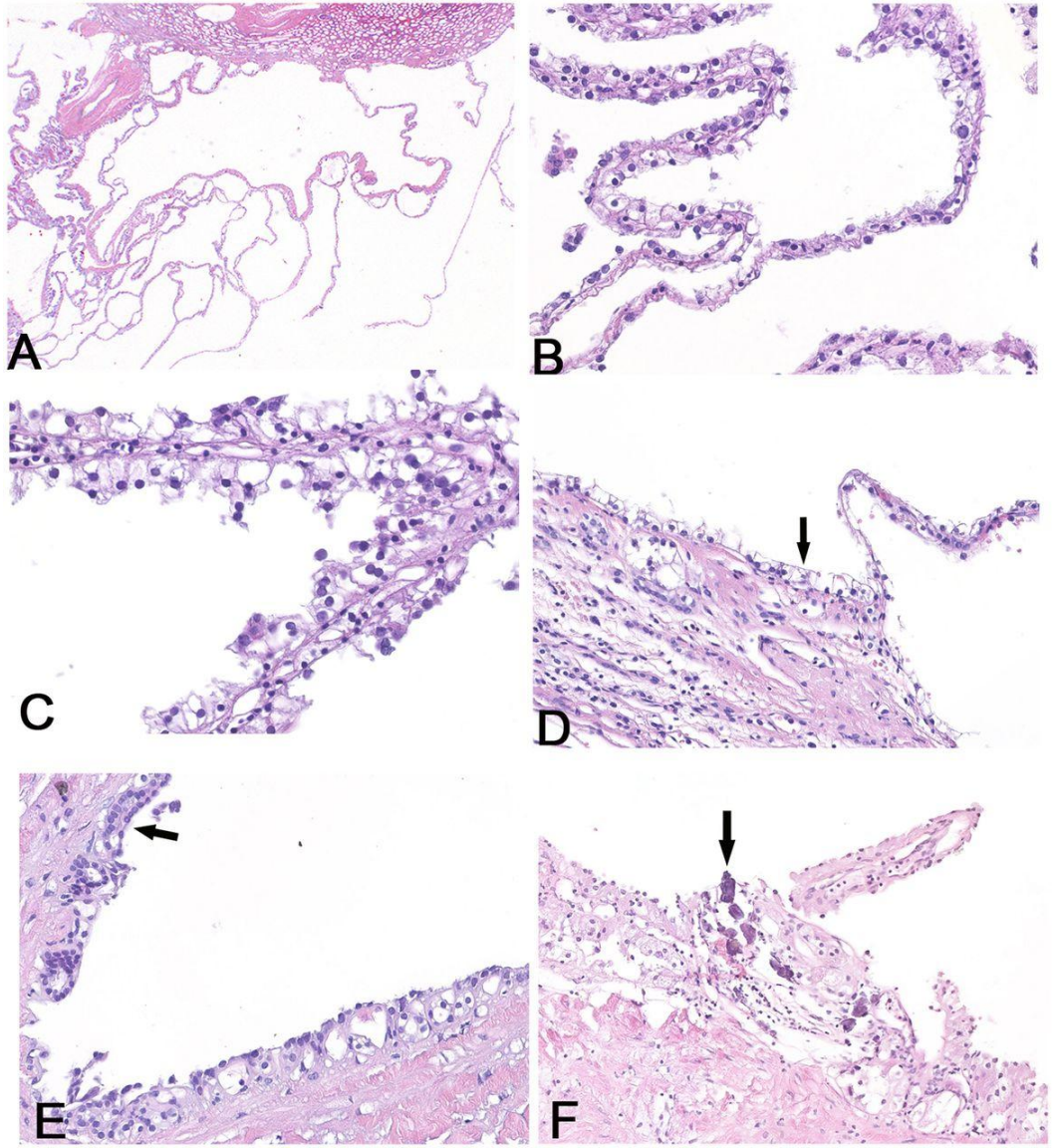








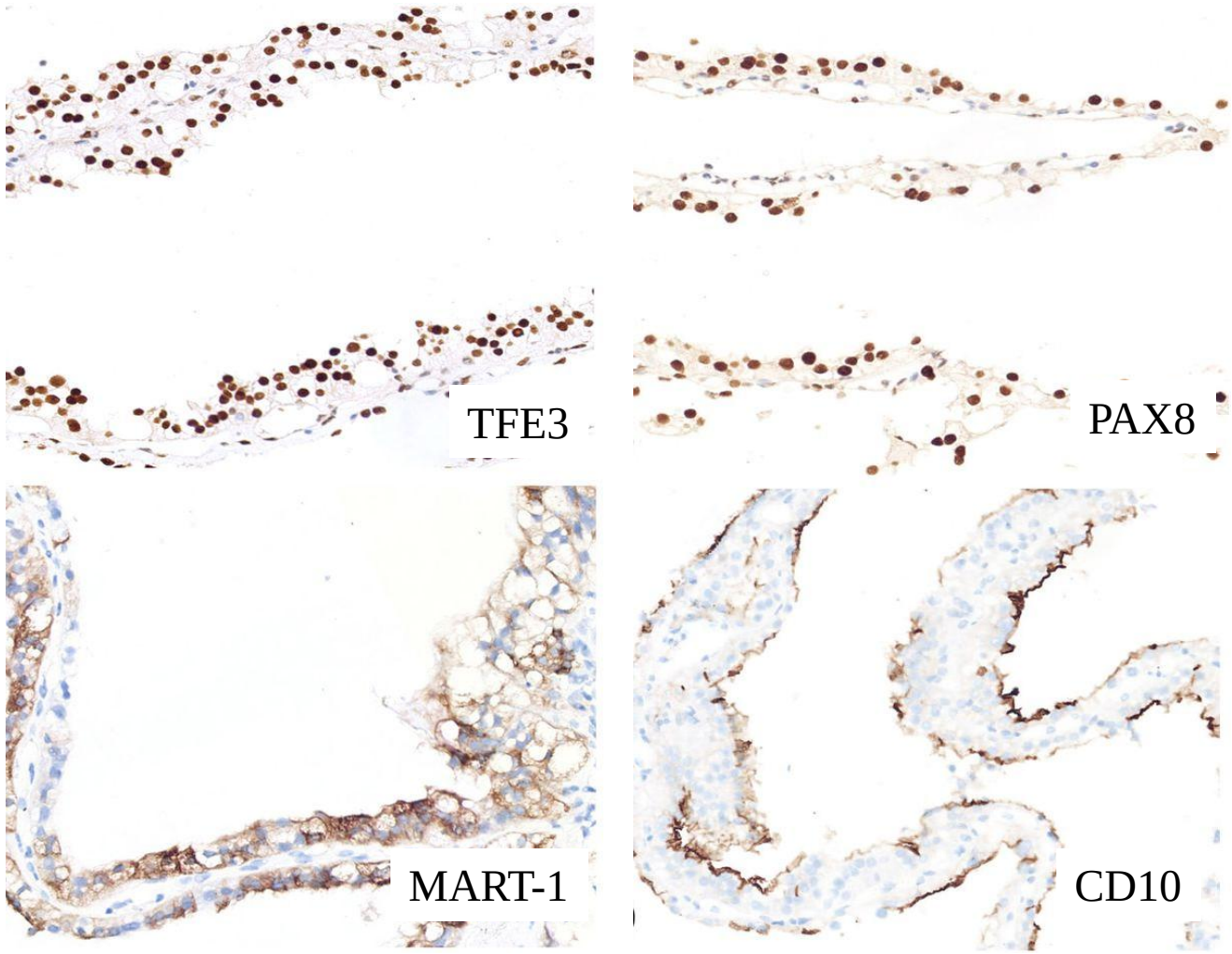
Xp11 tRCC with morphological features mimicking MCRN-LMP

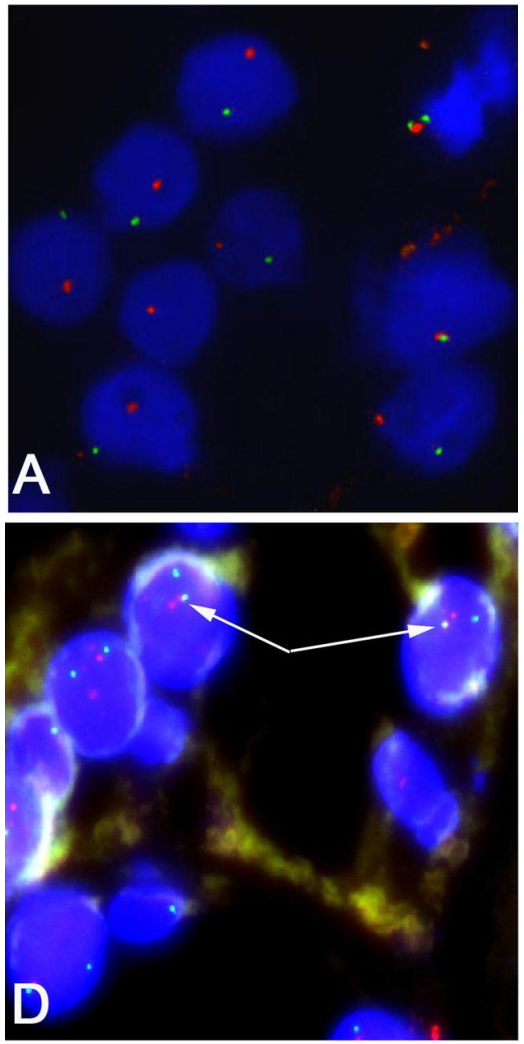


- Well circumscribed multilocular cystic mass
- Septa lined by a single layer of clear cells with low-grade nuclei
- **Psammoma bodies** detected in 4/6 cases
- *TFE3* FISH confirmed Xp11 translocation RCC
- Sequencing analysis confirmed *MED15-TFE3* fusion in all cases

Song et al. J Clin Pathol 2020

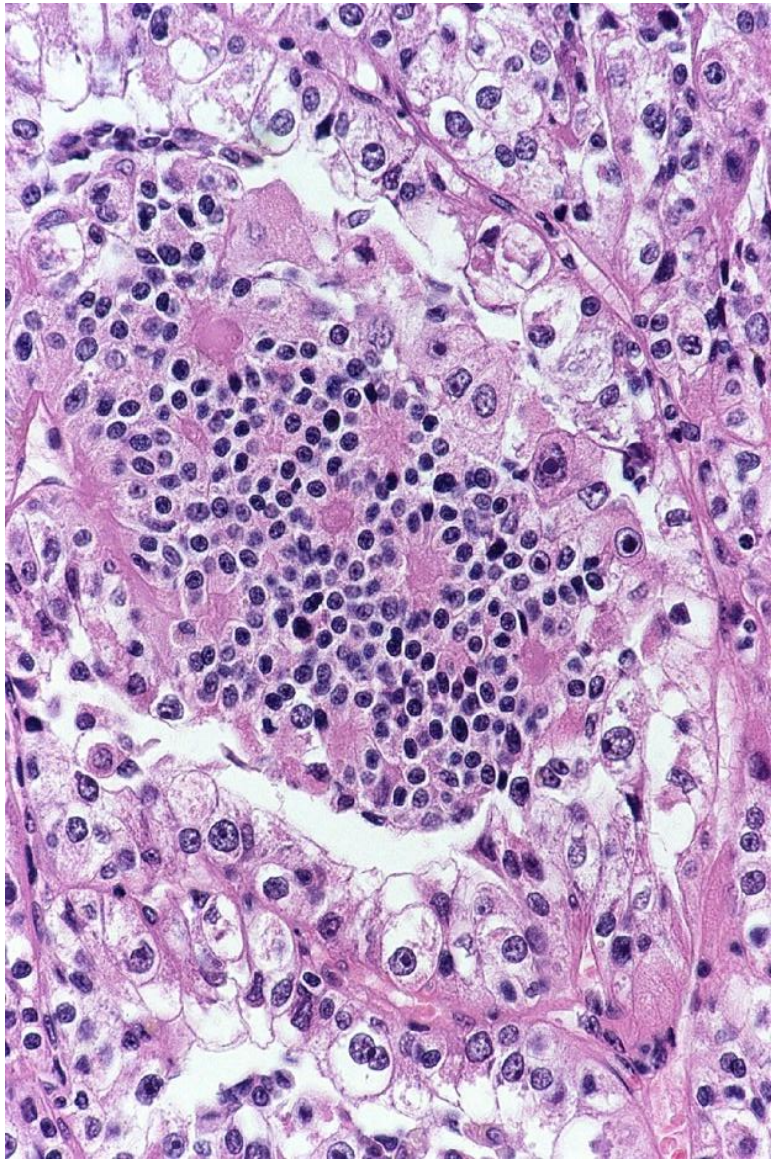
Xp11 tRCC with morphological features mimicking MCRN-LMP

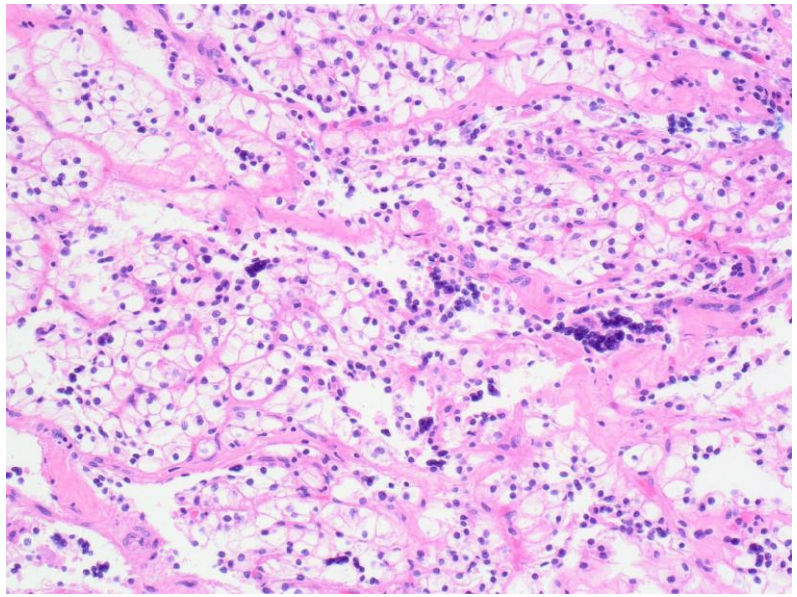


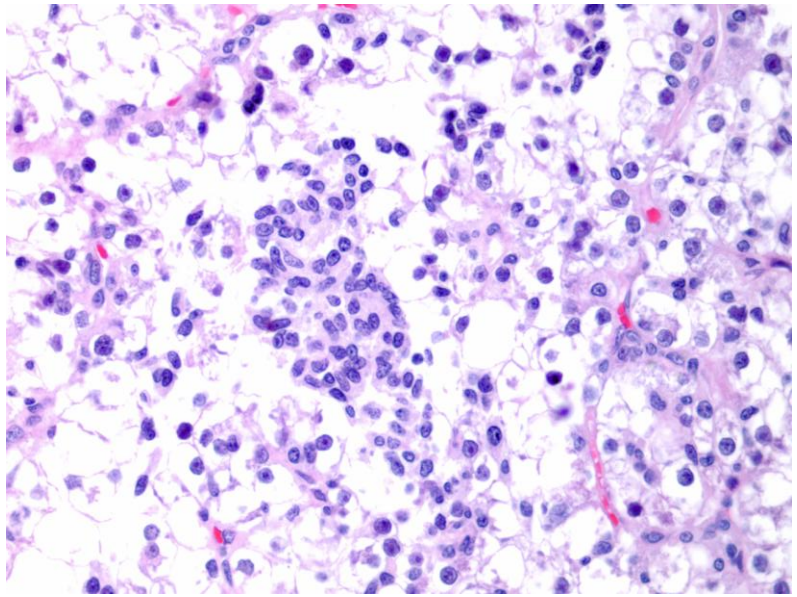


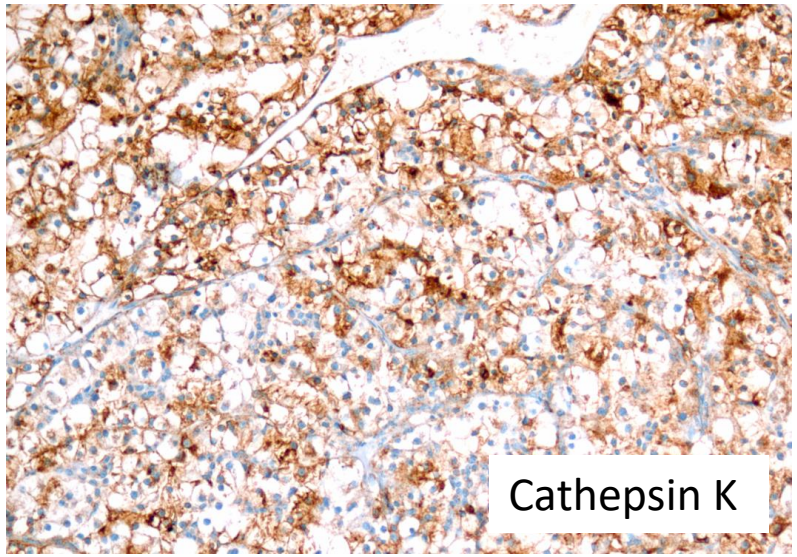
Song et al. J Clin Pathol 2020

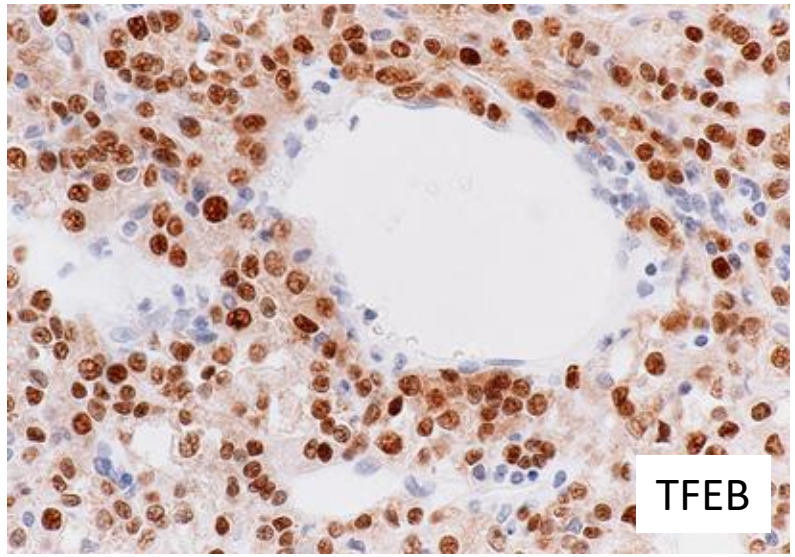
T(6;11)(P21;Q12) RENAL CELL CARCINOMA (*TFEB*)









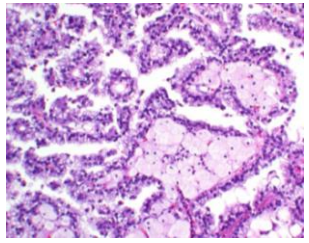


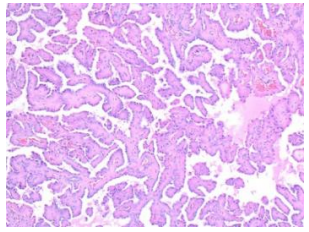
RENAL TUMOR WITH CLEAR CELLS

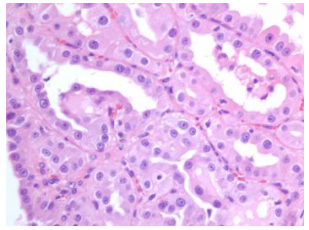
Tumor type	CK7	CAIX	AMACR	CD10	TFE3	TFEB	GATA3	CD117	HMB45/Melan A	Cathepsin K
Clear cell papillary renal cell tumor	+	+ cup-like	-	-	-	-	+			
MCRN-LMP	-/+	+			-	-				
RCC with fibromyomatous stroma	+	+		+	-	-				
Clear cell RCC	-/+ focal	+	-	+	-	-	-	-	-	-
TFE3 RCC*	-		+	+	+	-			+	+/-
TFEB RCC*	-				-	+			+	+

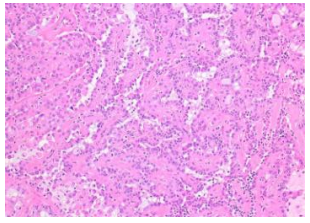
* rearrangements by FISH or NGS

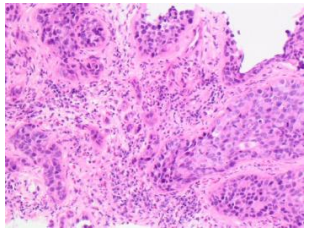
RENAL TUMOR WITH PAPILLARY ARCHITECTURE









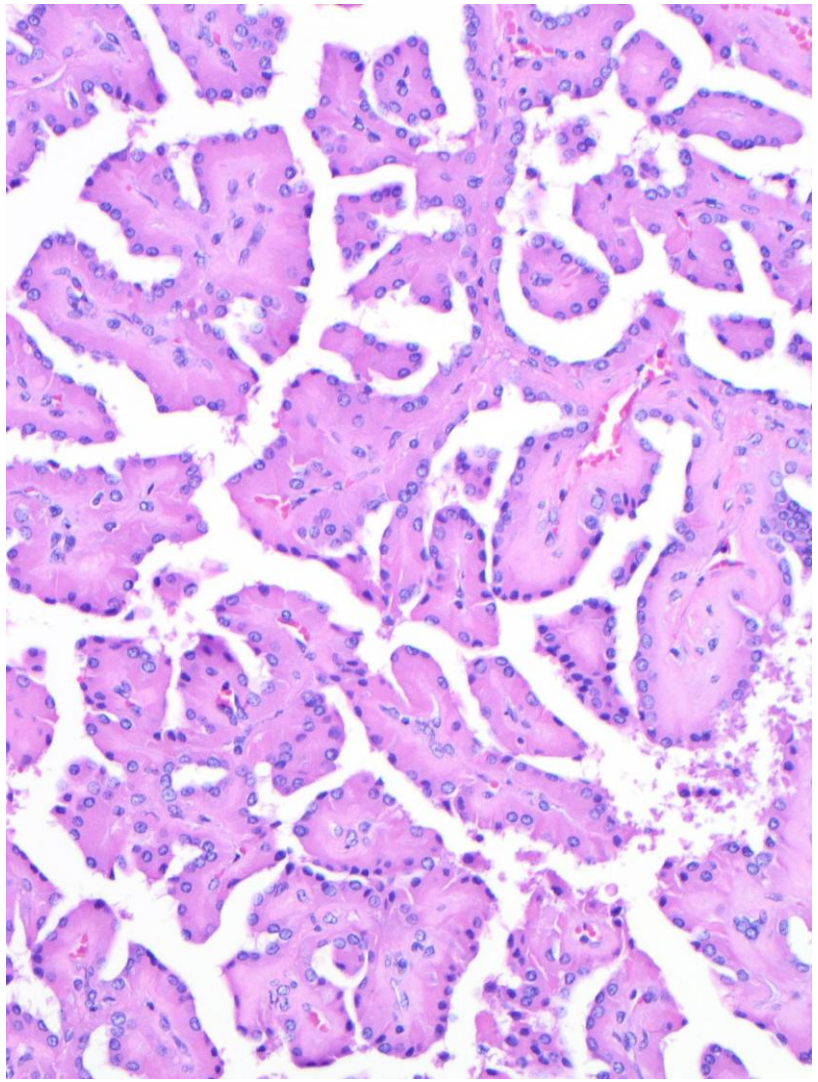


Tumor type	Clinical features	Morphology	IHC	Molecular features	Prognosis
Papillary renal cell carcinoma (PRCC) (type 1)	~15% of renal tumors; 30-49% multifocal 10% bilateral Most sporadic	Papillae lined by single layer of small cells with scant, pale cytoplasm, low grade nuclei; foamy macrophages; psammoma bodies	**CK7+ AMACR+** CAIX-	Gain of chr. 7 ± chr.17 Loss of Y chr. Germline mutations of MET (7q31)	Favorable prognosis
Oncocytic papillary RCC	Sporadic and in patients with ESRD, ACKD	Papillary/tubulopapillary, hyalinized cores, single layer of eosinophilic cells with low grade nuclei, reverse polarity	CK7+ AMACR+ CD10+/- **GATA3+**	Frequent KRAS mutations	Favorable prognosis
FH-deficient RCC (HLRCC)	Cutaneous and uterine smooth muscle tumors; unilateral renal tumors	Papillary/tubulopapillary, solid architecture; enlarged nuclei with prominent eosinophilic nucleolus; abundant eosinophilic cytoplasm	**FH-2SC+** CK7-, CAIX-	Germline mutation of *FH* (1q42.3-1q43), encoding fumarate hydratase	Aggressive behavior
ALK-RCC	Adults (younger middle age or older), pediatric with sickle cell trait, medullary location	Variable admixed patterns, often mucinous/myxoid background; medullary CA-like morphology in children; papillary	**ALK+, INI1+** TFE3+ rare in children - no translocation	*ALK* rearrangement (various fusion partners)	Adverse (metastasis, death) in about 25%
Upper tract urothelial carcinoma (UTUC)	Positive urine cytology; prior or concurrent history of UC elsewhere in the urinary tract	Papillary, solid architecture; enlarged nuclei; infiltrates renal parenchyma, between tubules	**CK7+, GATA3+ P63+ PAX8-/+**	Chr. amplification and losses; *p53* mutations; Lynch syndrome	Aggressive behavior

ONCOCYTIC PAPILLARY RCC, LOW-GRADE (PAPILLARY RENAL NEOPLASM WITH REVERSE POLARITY)

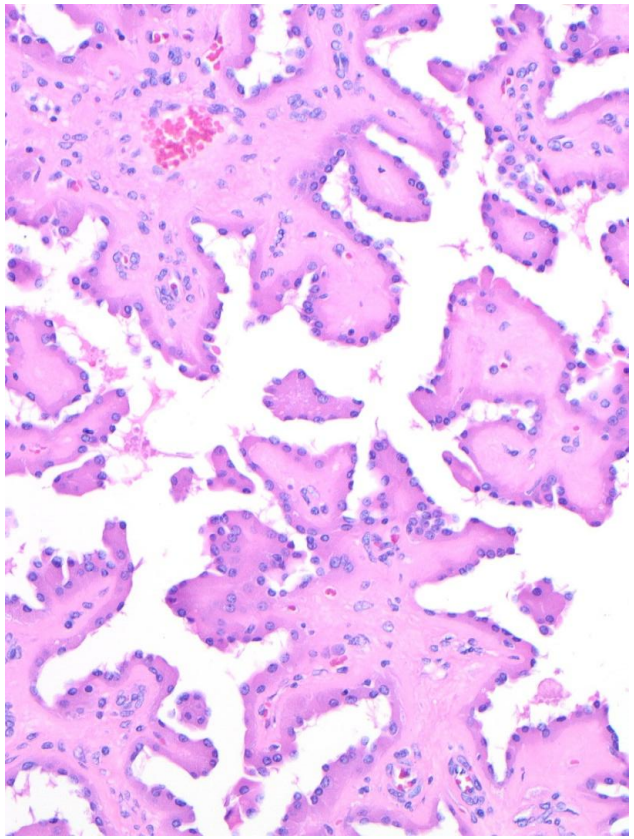
- Papillary/tubulopapillary architecture
- Hyalinized/edematous cores
- Single layer of eosinophilic cells with low grade nuclei (ISUP grade 1-2)
- Inverted nuclear pattern
- CK7, AMACR, GATA3 +; CD10 +/-
- KRAS missense mutation

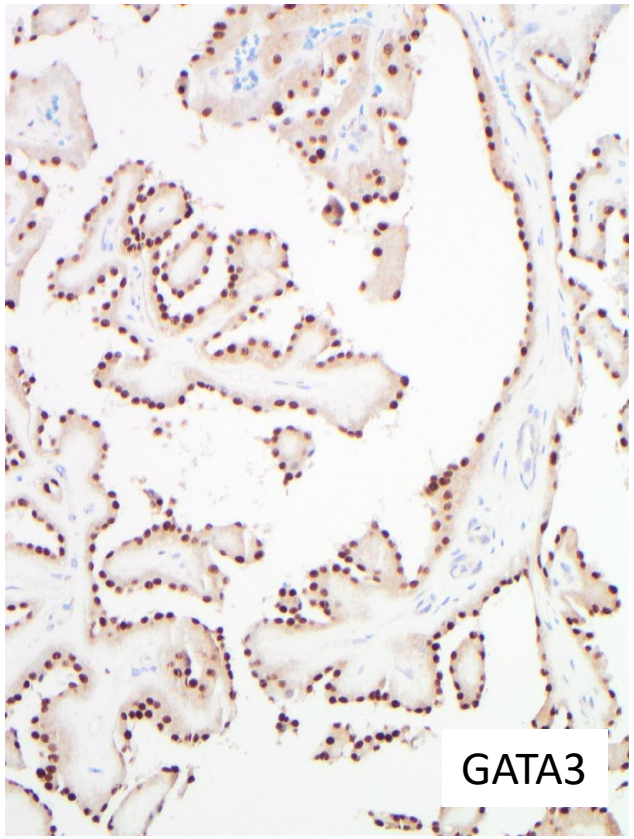
- No mitosis
- No necrosis
- No intracellular hemosiderin
- No foamy macrophages
- No psammoma bodies

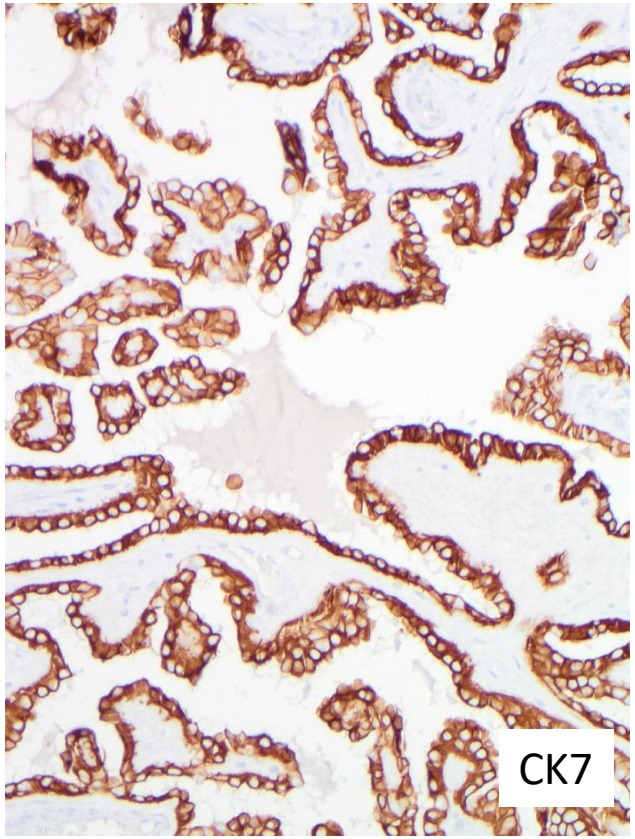


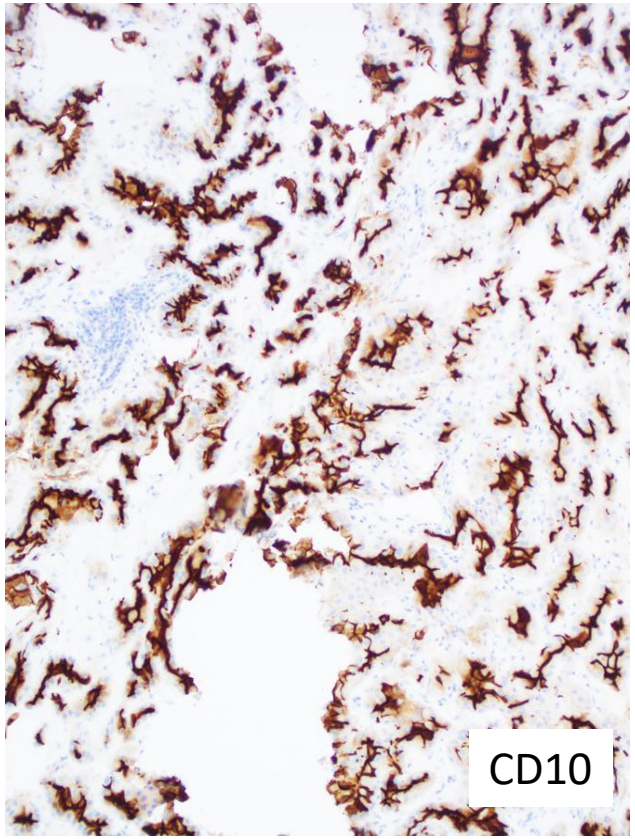
Kunju et al. Hum Pathol 2008; Park et al. Pathol Int 2009; Hes et al. Pathology 2013; Al-Obaidy et al. AJSP 2019, Chang et al. Histopathology 2021

ONCOCYTIC PAPILLARY RCC, LOW-GRADE (PAPILLARY RENAL NEOPLASM WITH REVERSE POLARITY)



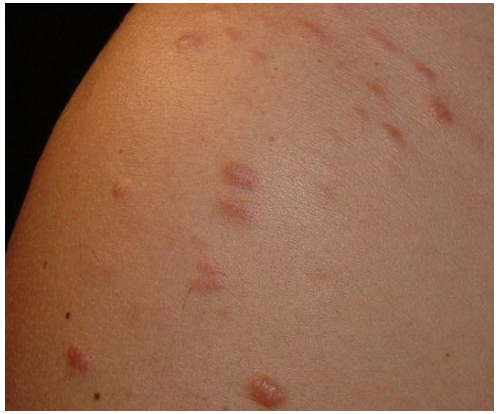






HEREDITARY LEIOMYOMATOSIS AND RENAL CELL CARCINOMA SYNDROME-ASSOCIATED RCC (HLRCC)

- Autosomal dominant
- Germline mutation of FH gene (1q42.3-1q43)

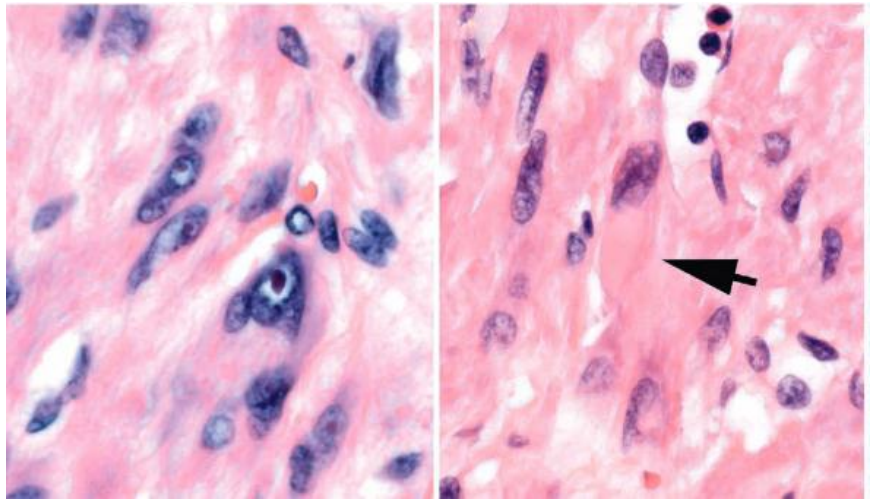


<u>Features definitional for HLRCC</u>:

- Multiple biopsy-proven cutaneous piloleiomyomas

or

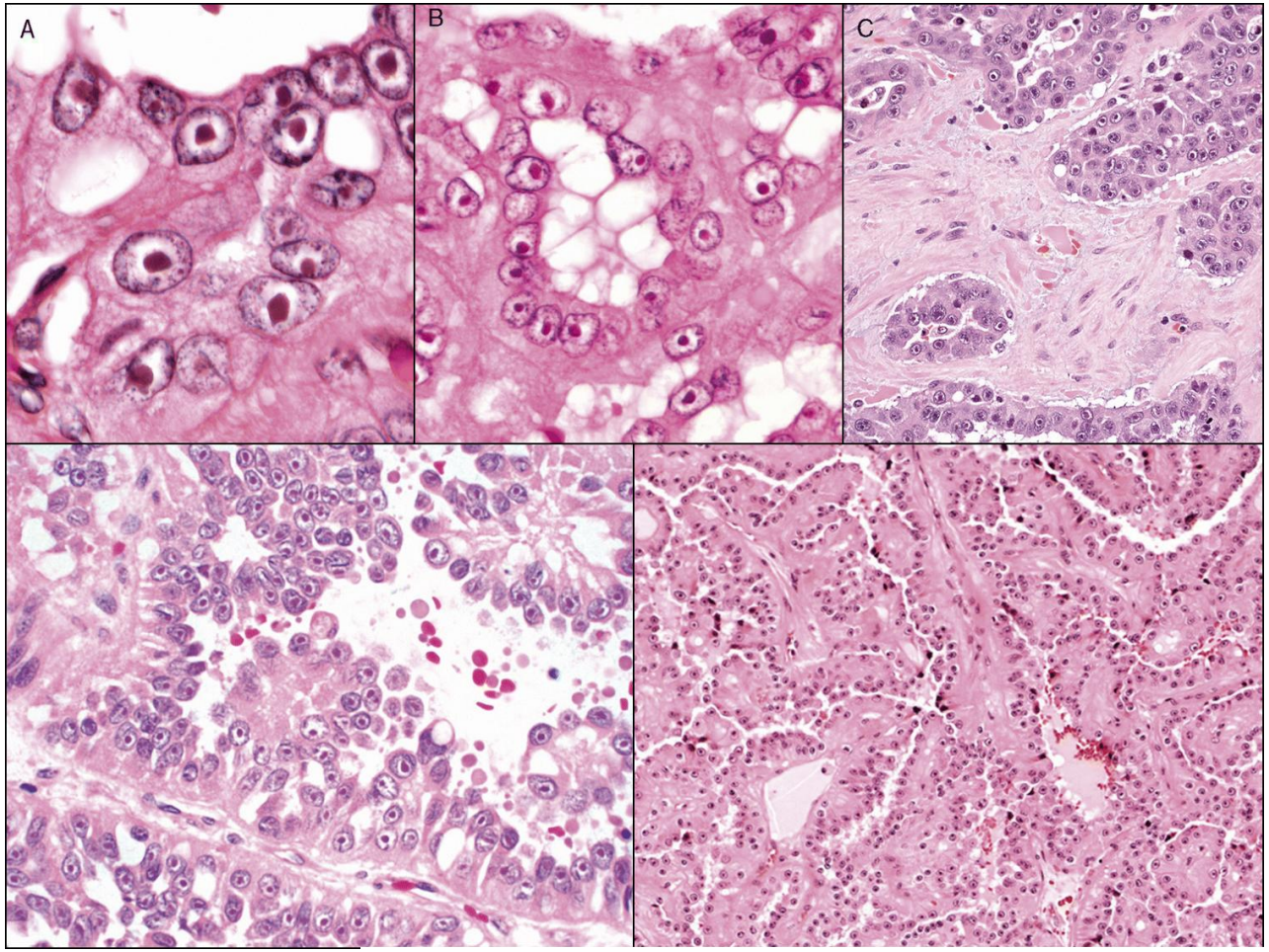
- Two of the following minor criteria:
  - Surgical treatment for symptomatic uterine leiomyomas before age 40
  - RCC with papillary features before age 40
  - 1st degree family member who meets these criteria



Howitt et al. *Diagnostic Gynecologic and Obstetric Pathology*, 2018

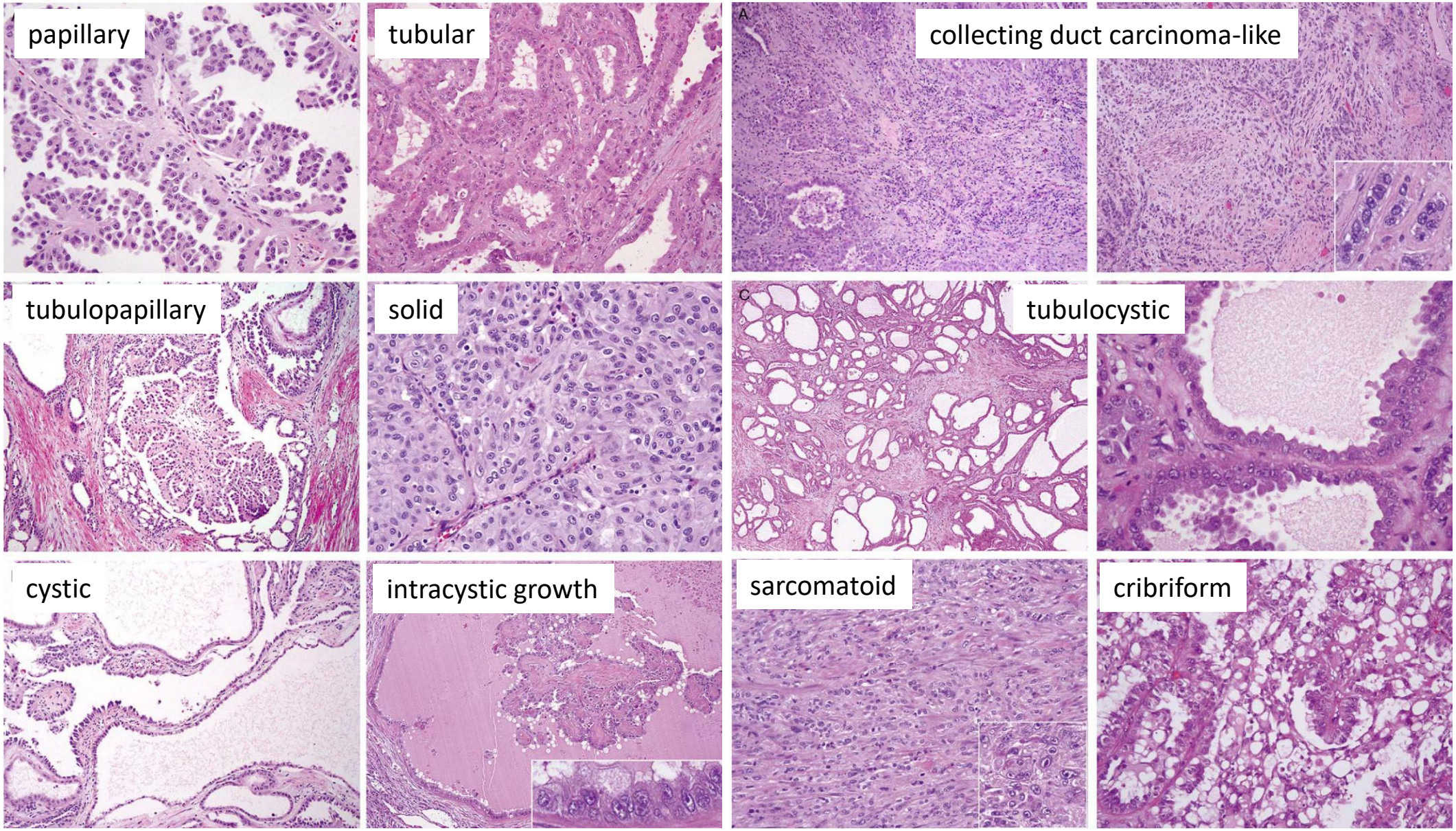
HLRCC

- **Unilateral renal tumors**:
  - Papillary/tubulopapillary/solid architecture
  - Eosinophilic cytoplasm
  - Enlarged nuclei with margination of chromatin
  - Prominent eosinophilic nucleolus surrounded by clear halo
- High stage at presentation, poor clinical outcome



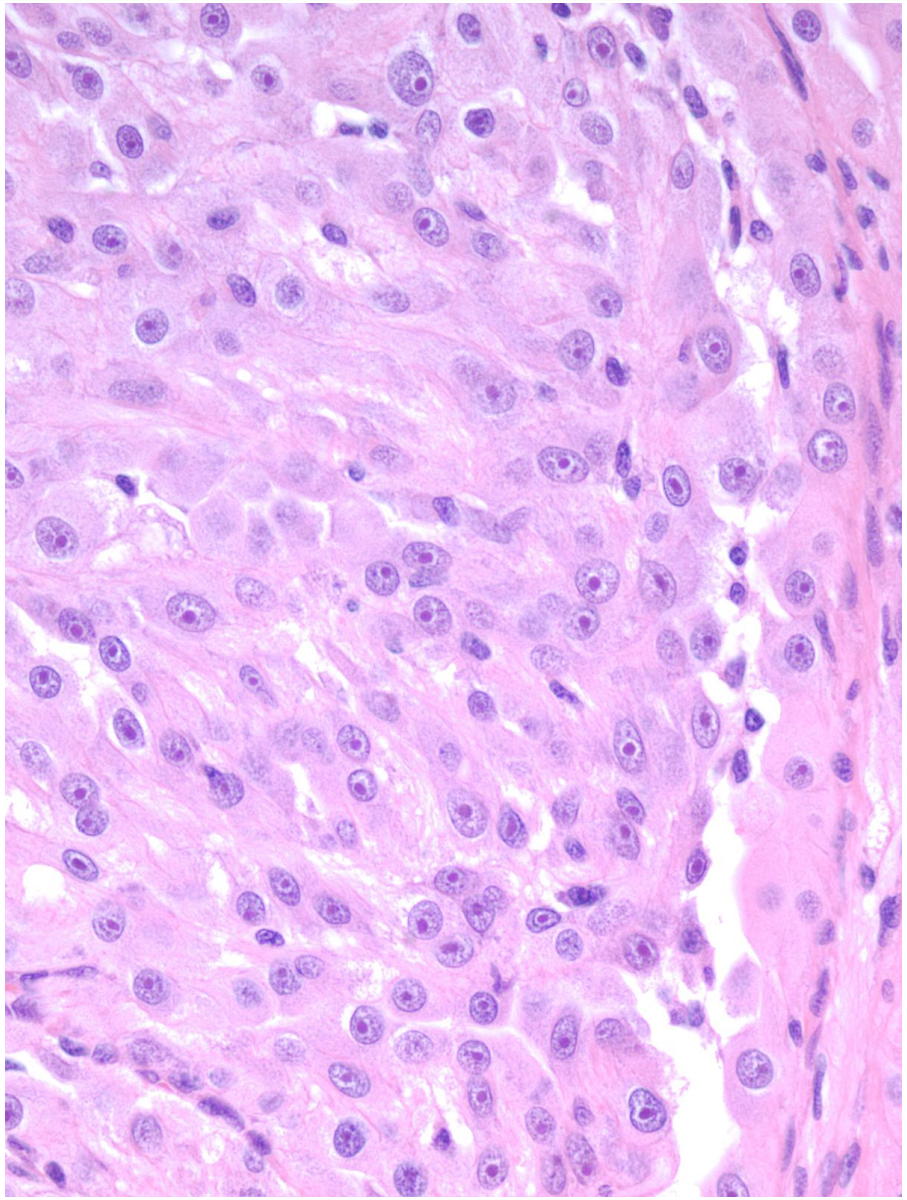
Merino et al. AJSP 2007

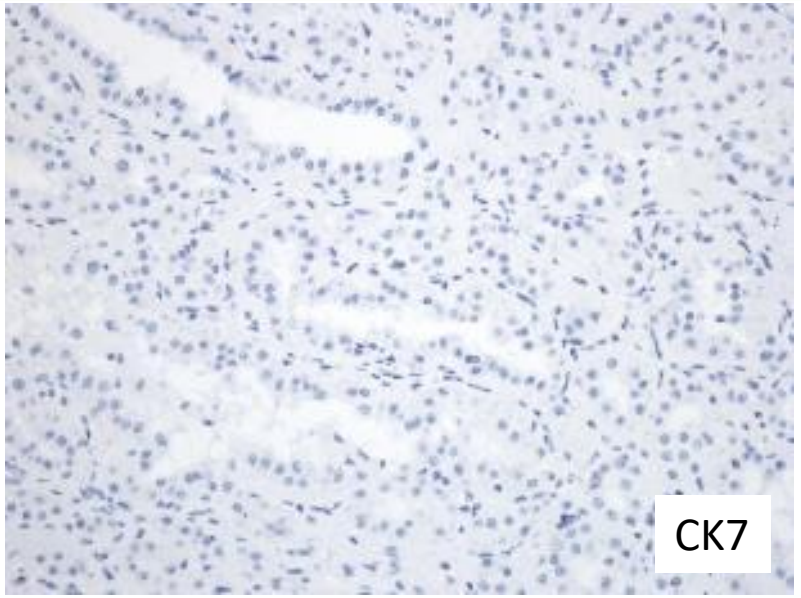
FH-deficient RCC

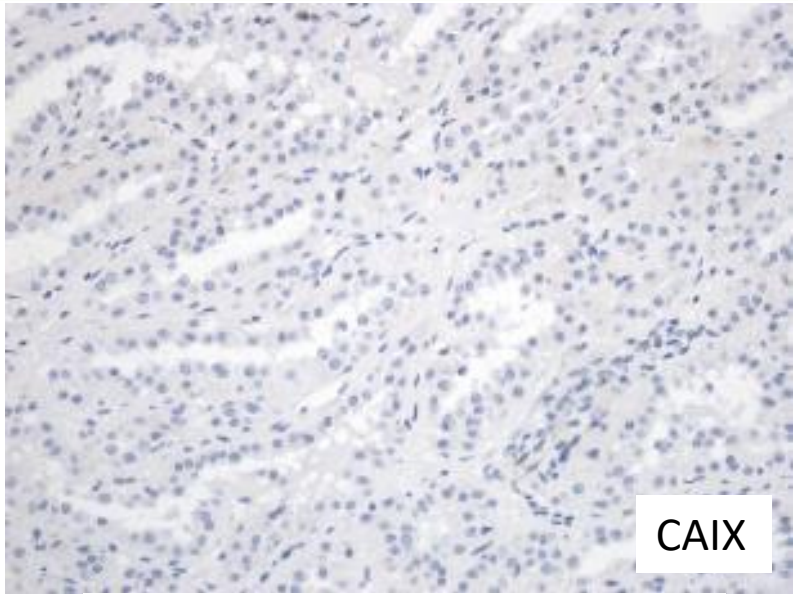


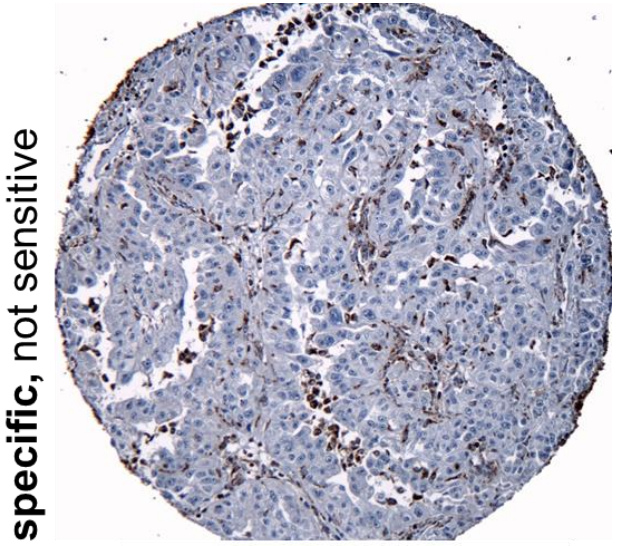
Chen YB et al. Am J Surg Pathol 2014

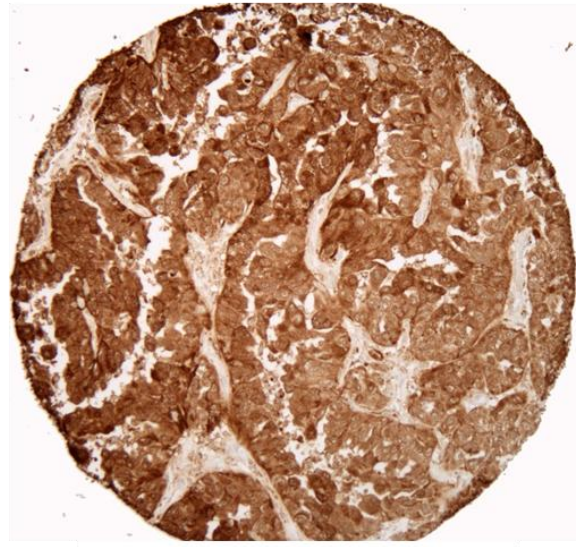
FH-DEFICIENT RENAL CELL CARCINOMA



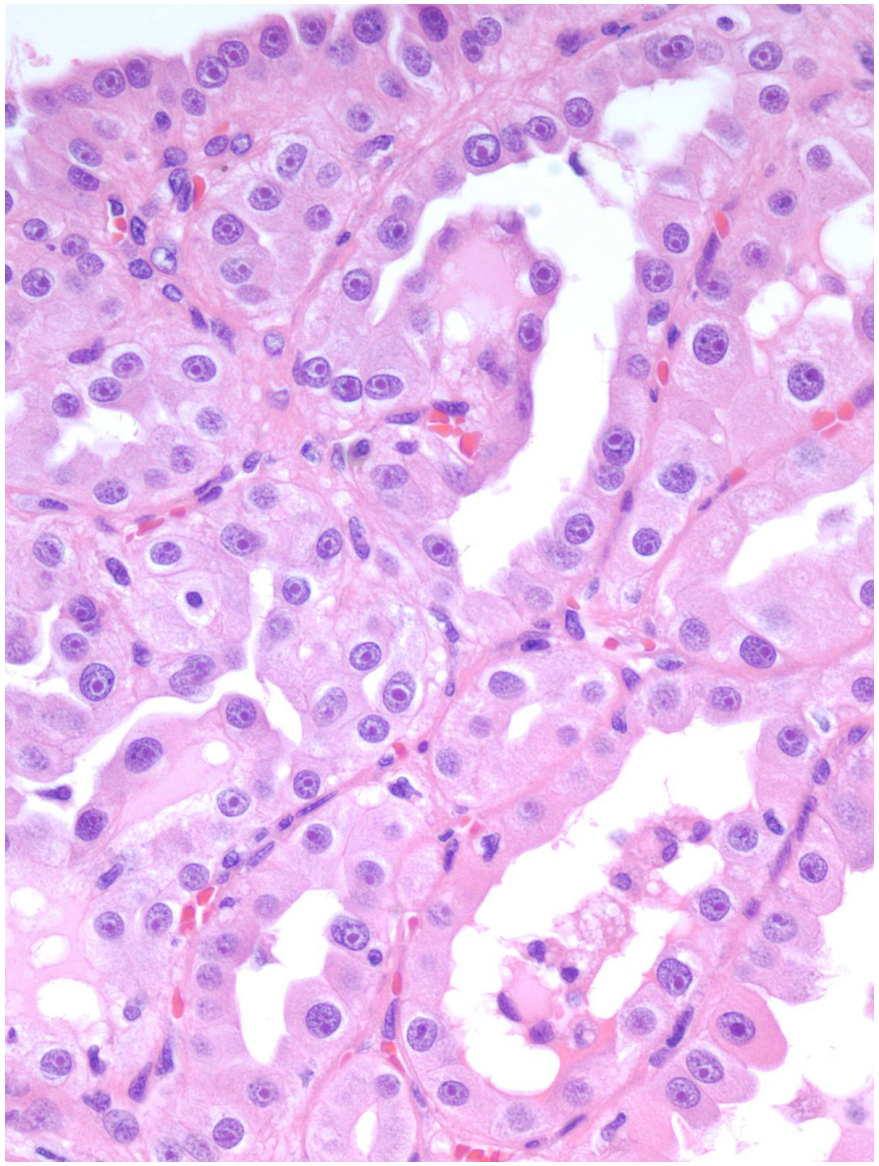


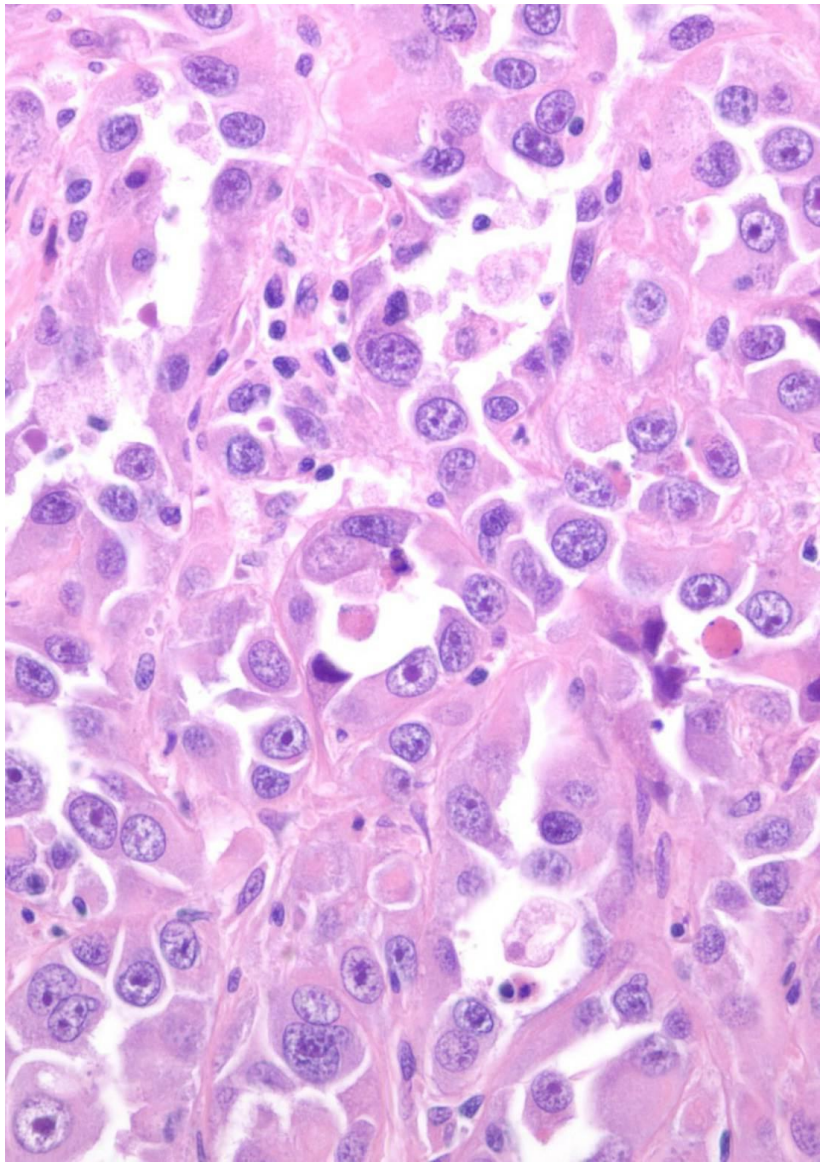


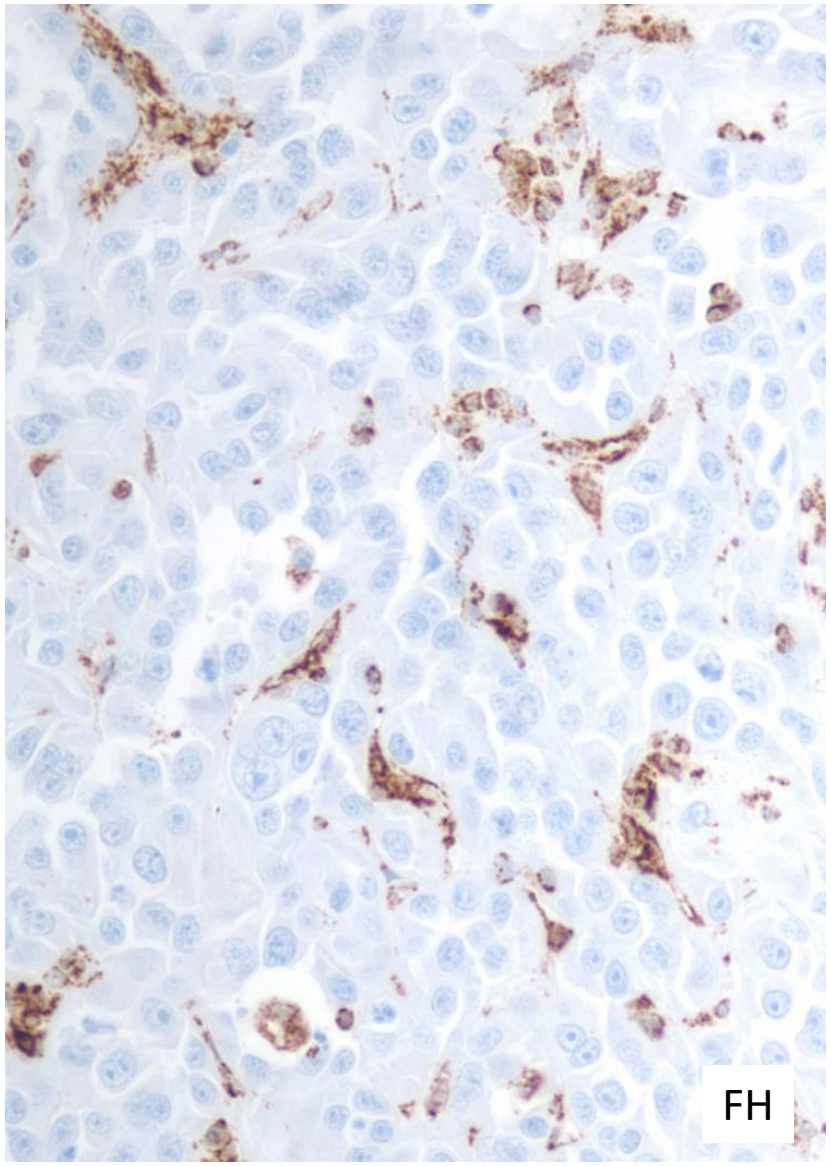




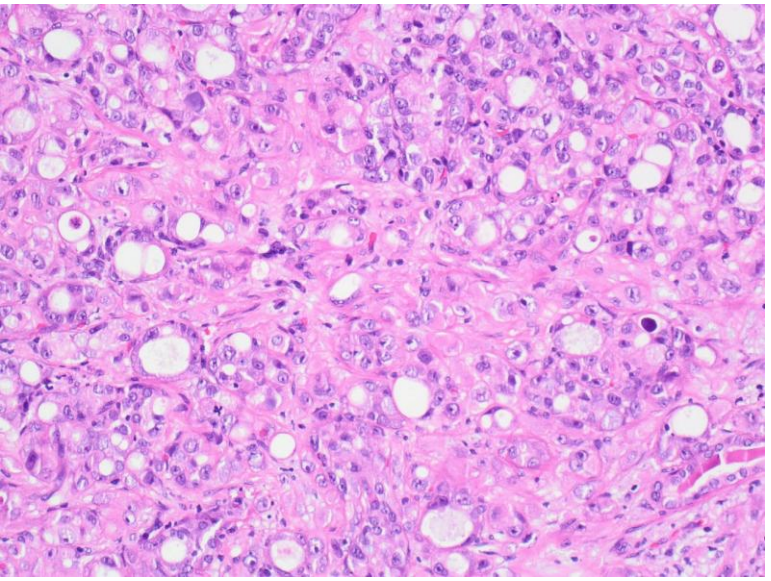
FH-DEFICIENT RENAL CELL CARCINOMA

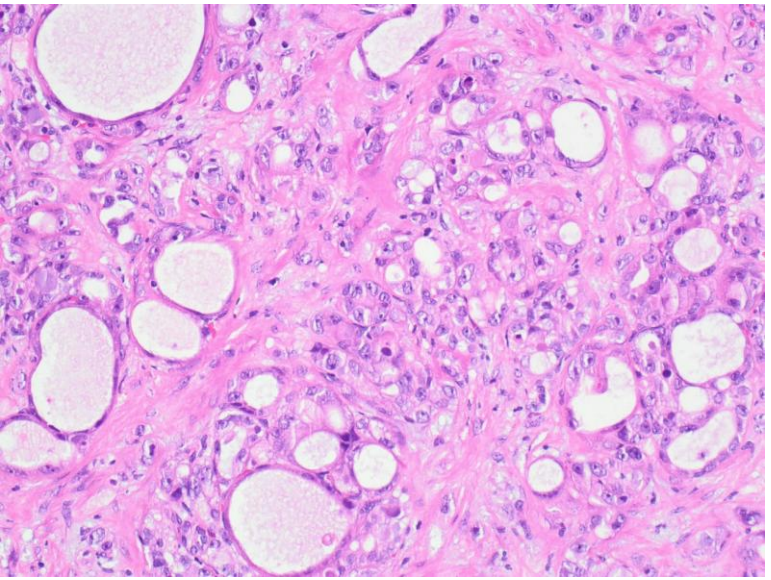


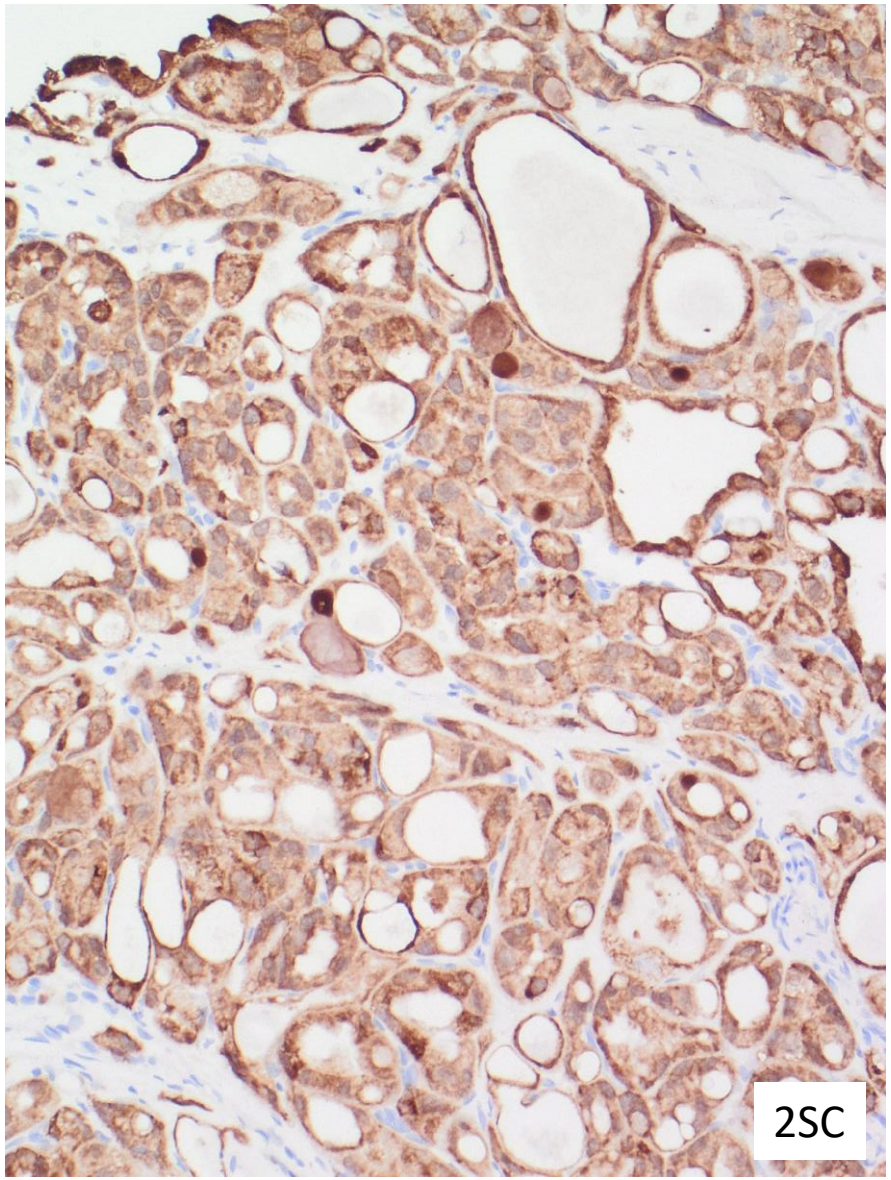


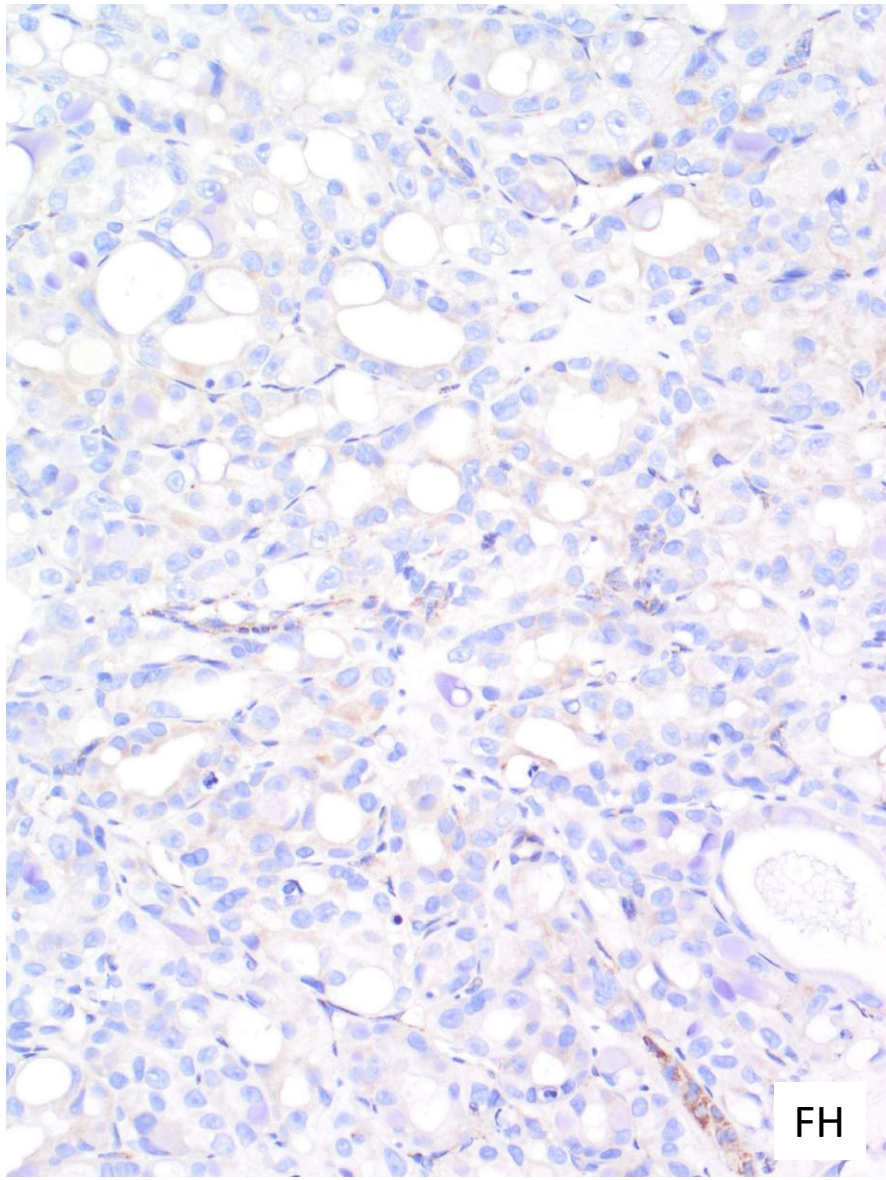


FH-DEFICIENT RENAL CELL CARCINOMA



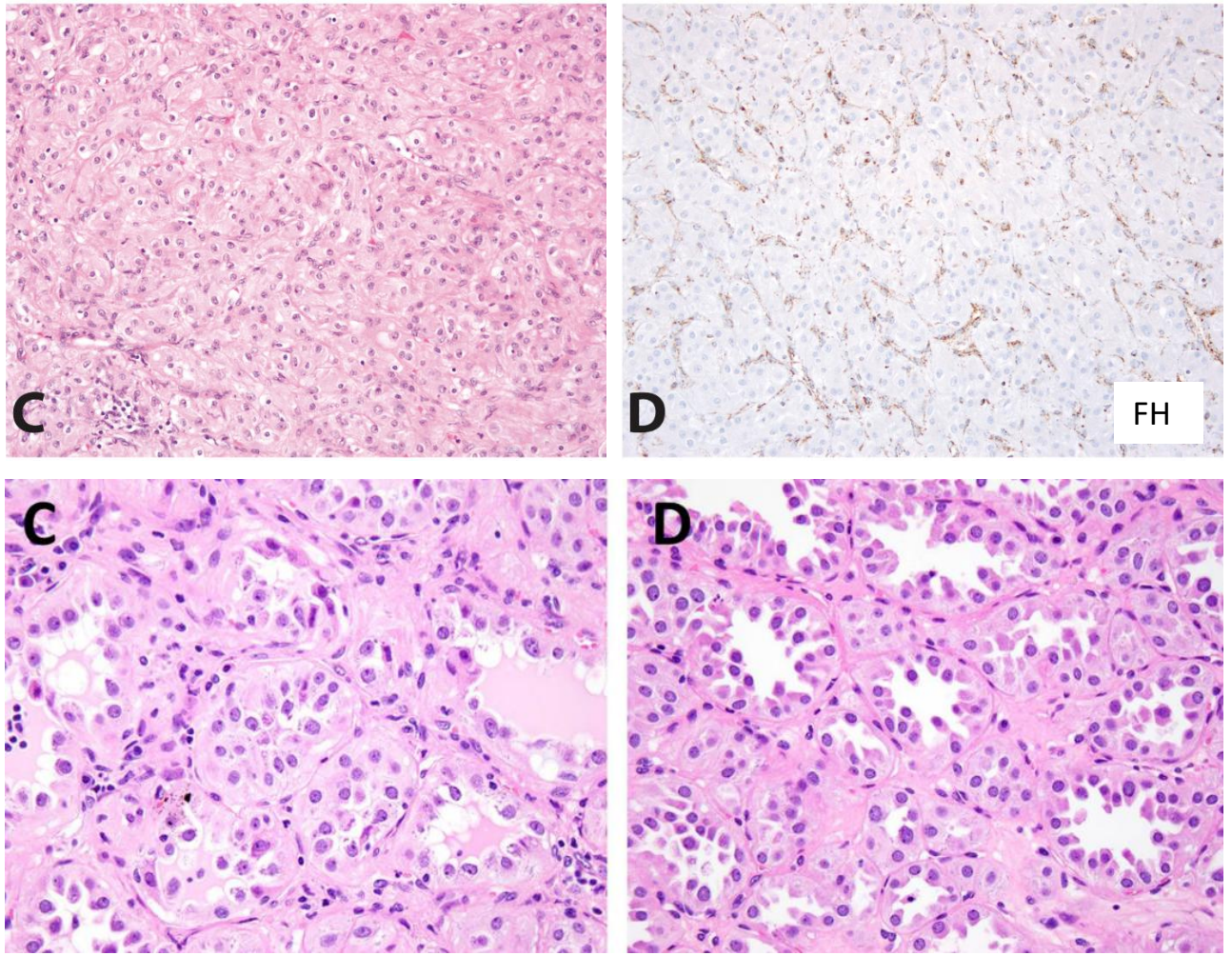






LOW-GRADE FH-DEFICIENT RENAL CELL CARCINOMA

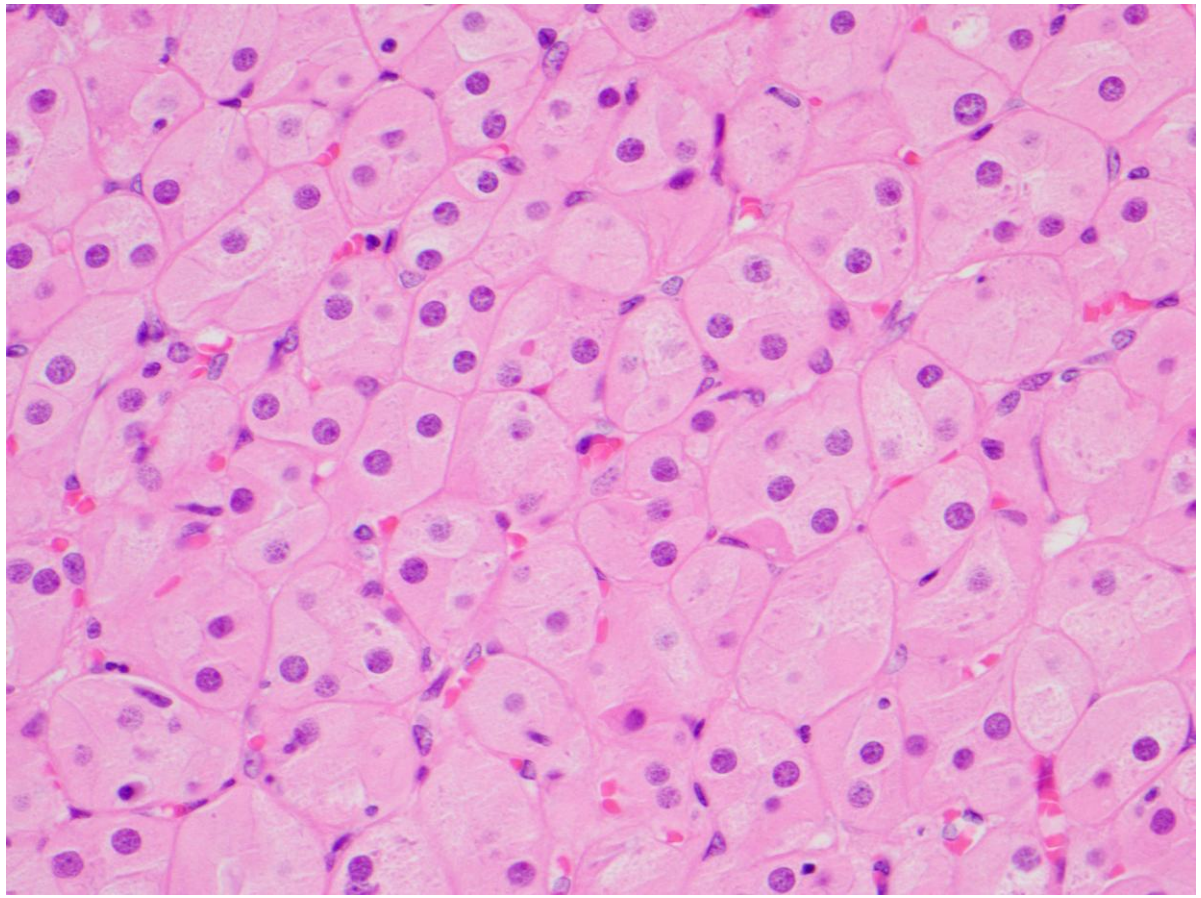
- FH-deficient RCC with low-grade oncocytic morphology
- Solid, nested/tubular architecture; uniform polygonal cells; vacuolated eosinophilic cytoplasm, scattered inclusions, fine chromatin, small nucleoli
- Differential diagnosis: SDH-deficient, ESC, LOT, EVT
- SDHB+, CK20-, CK7-
- FH-, 2SC+

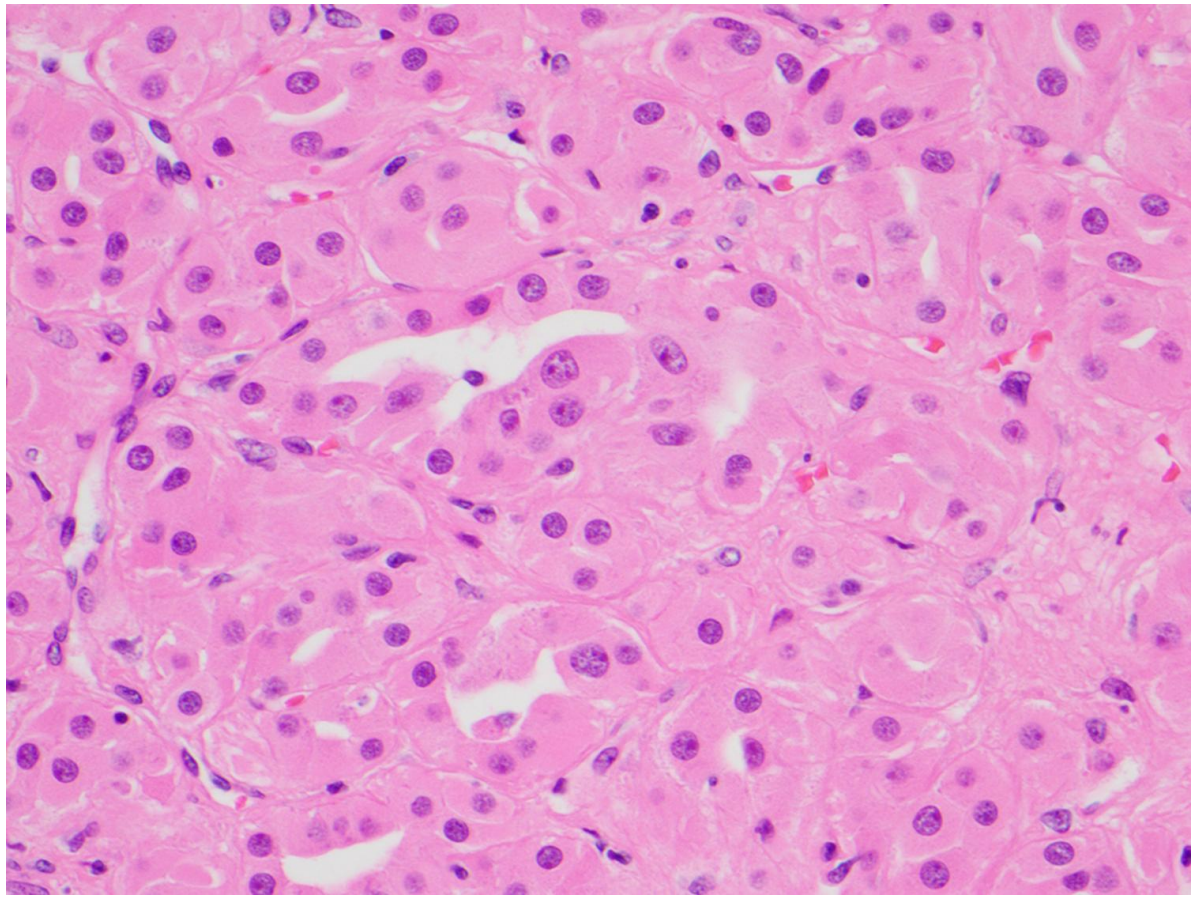


Smith et al. Histopathol 2017; Wyvekens et al. Int J Surg Pathol 2022; Hamza et al. Adv Anat Pathol 2021

LOW-GRADE FH-DEFICIENT RENAL CELL CARCINOMA

14 y/o female with renal lesion, subsequently known to have HLRCC

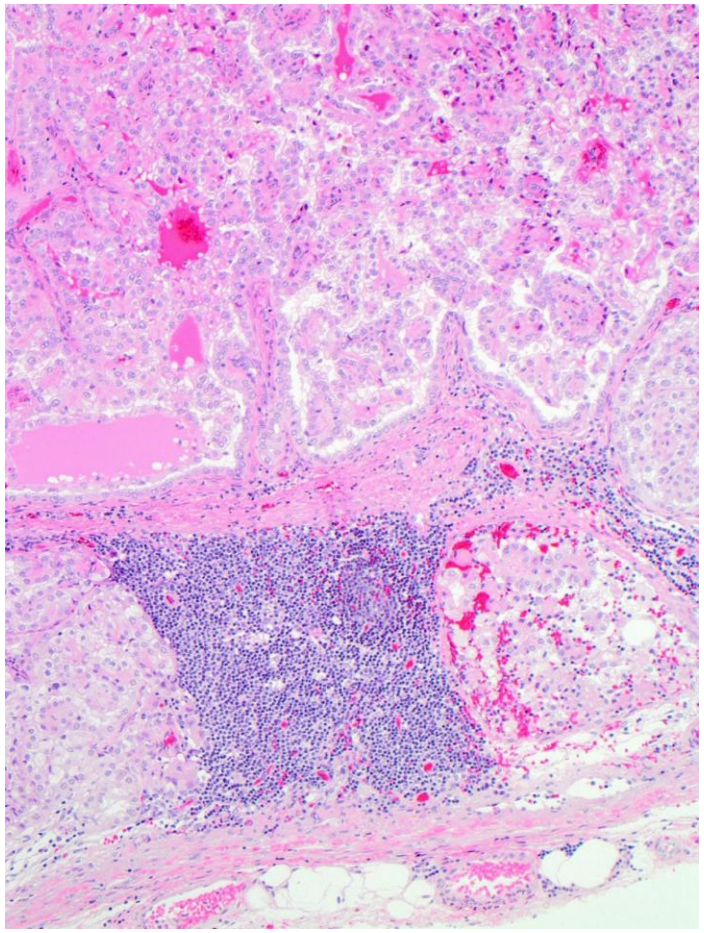
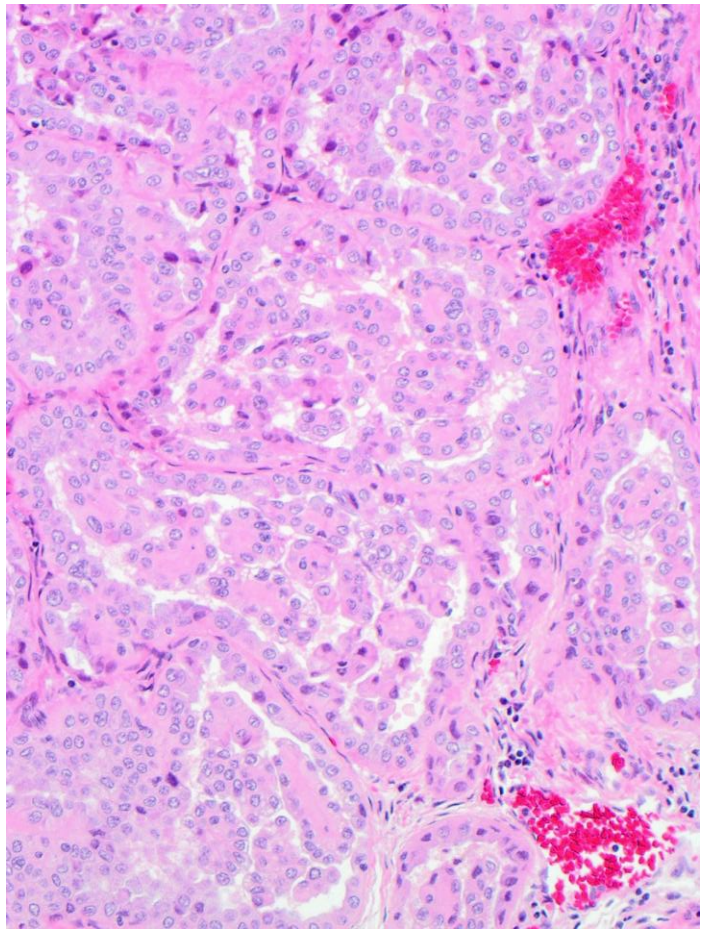
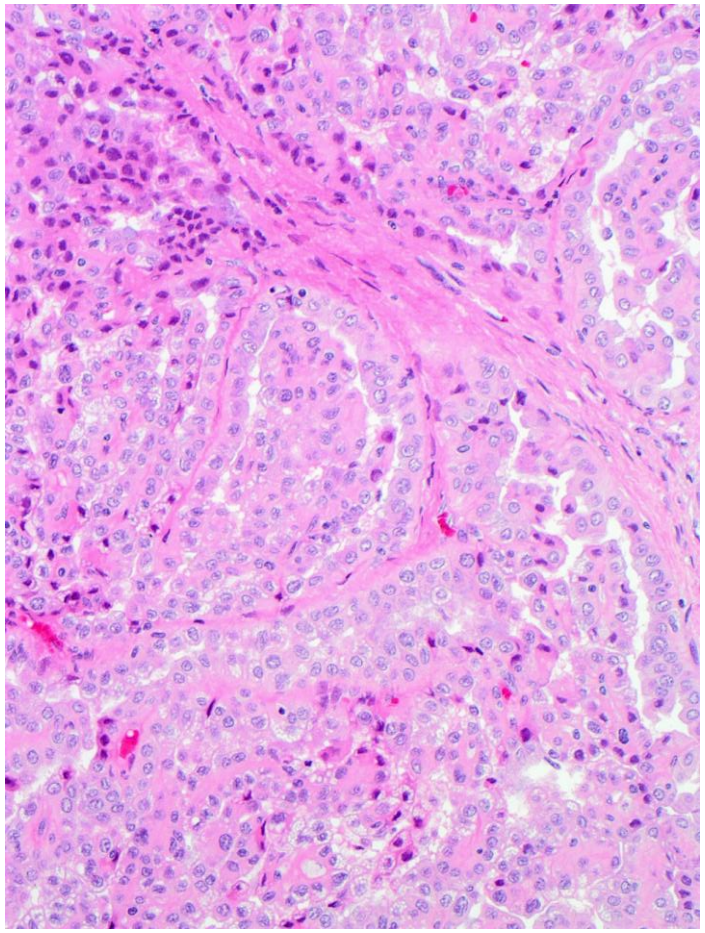




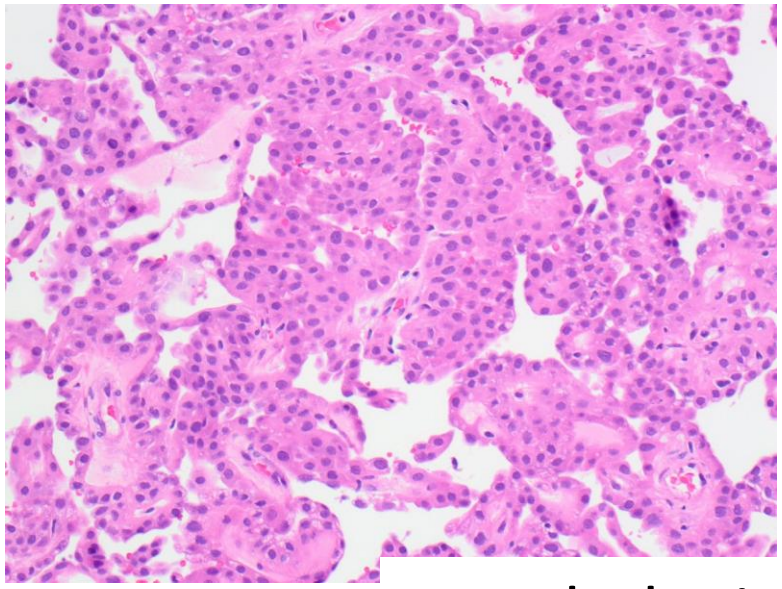
Have a low-threshold for ordering **SDHB, FH** and **2SC** IHC stains in pink renal tumors!

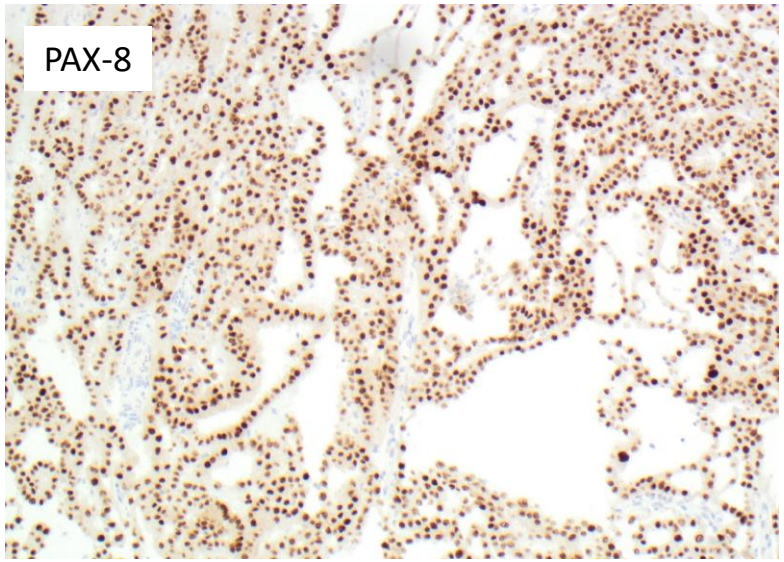
RENAL CELL CARCINOMA WITH PAPILLARY & SARCOMATOID FEATURES

- 40 y/o female
  - H/O “papillary RCC with sarcomatoid features (4.5 cm)” in 2015 (TFE3-)
  - PET positive nodes in 2017

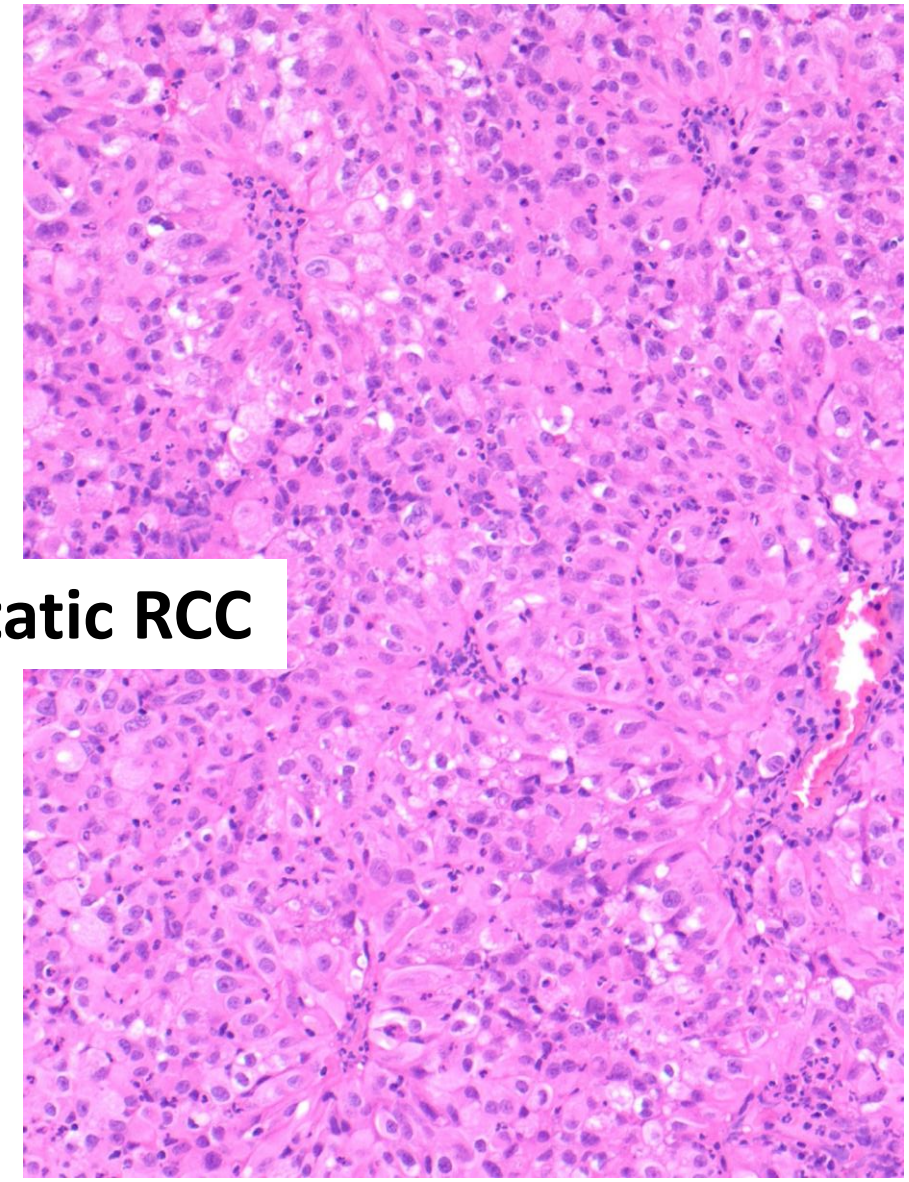




2020: Lung lesion

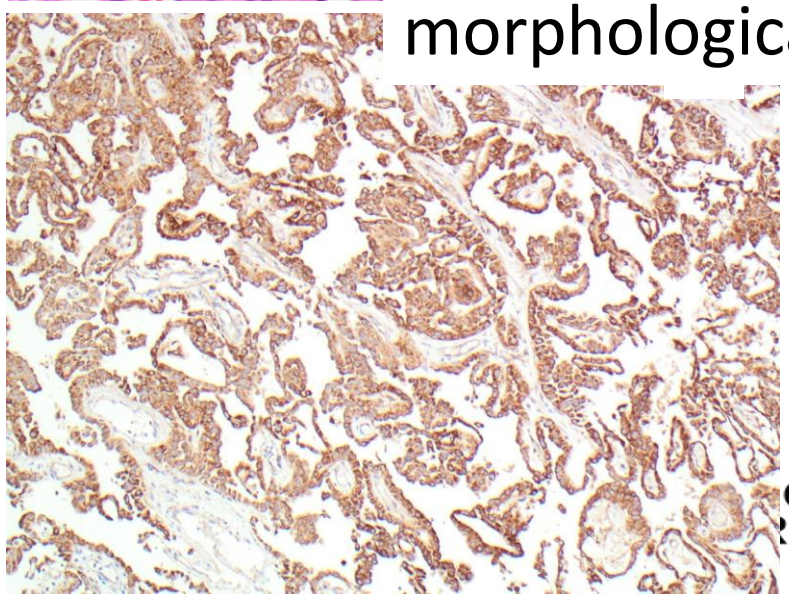


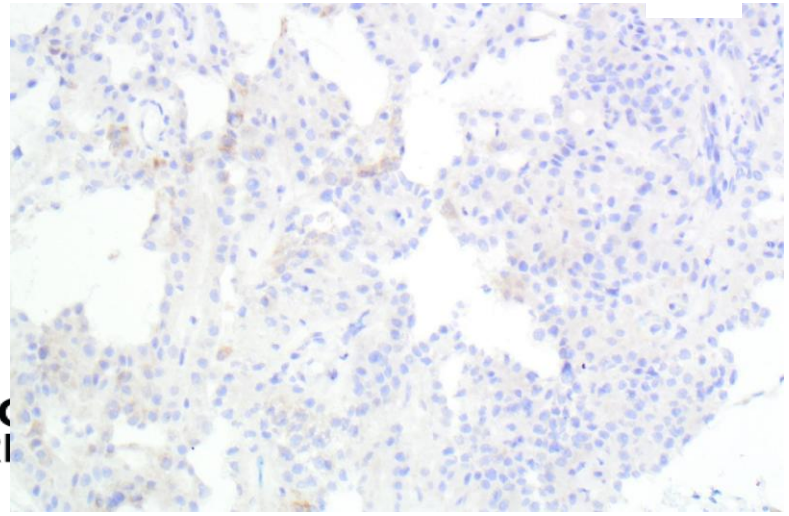


Brain lesion

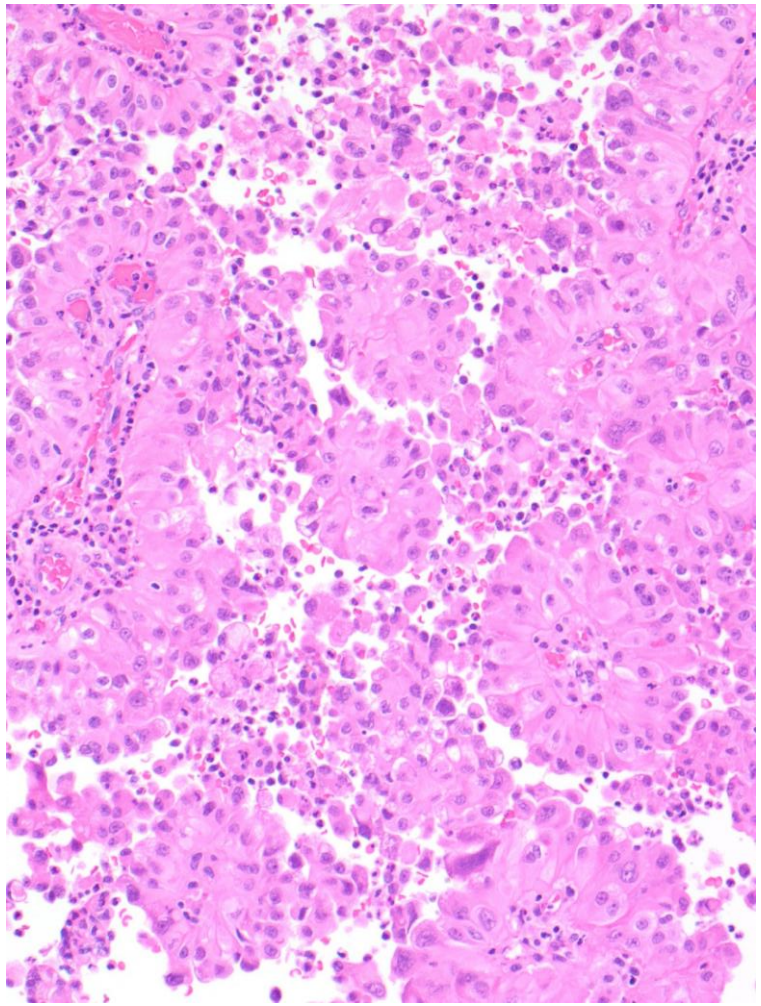


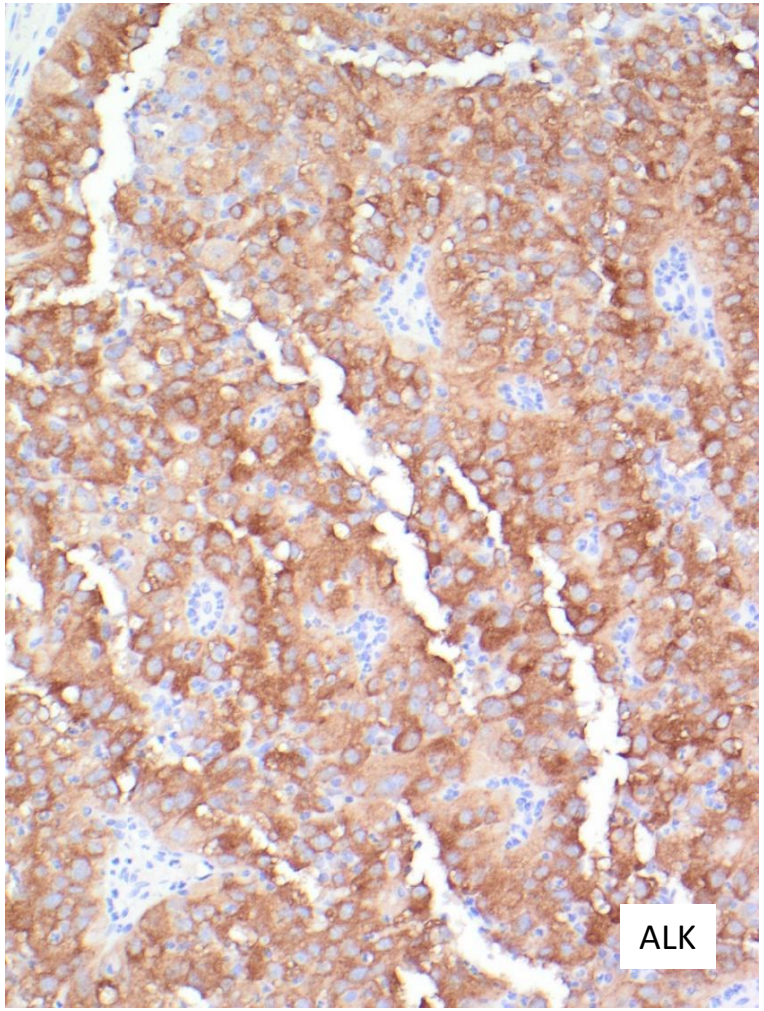
morphologically consistent with **Metastatic RCC**



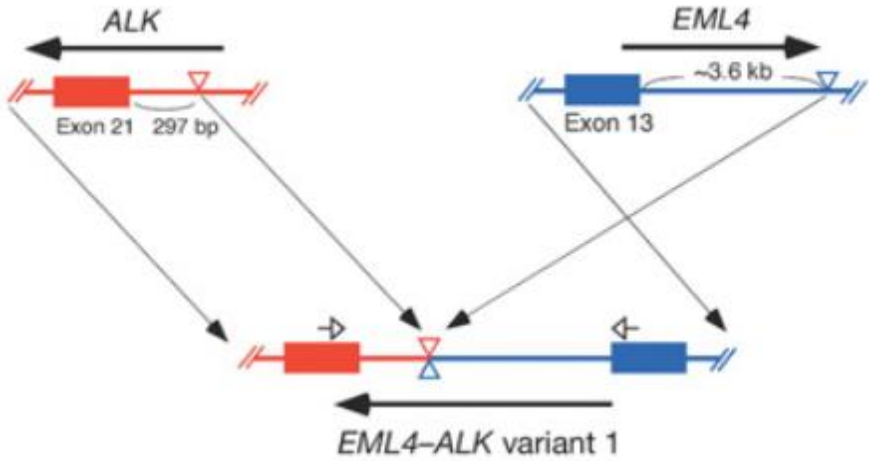


ANAPLASTIC LYMPHOMA KINASE REARRANGED RCC (ALK-RCC)





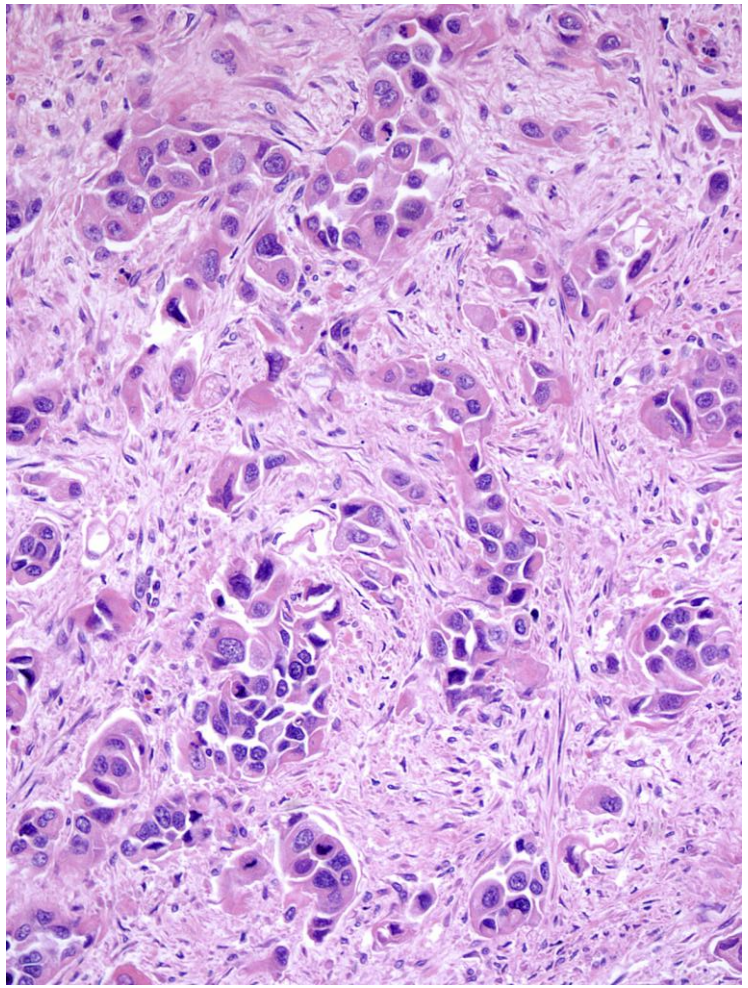
NGS: **EML4-ALK fusion**

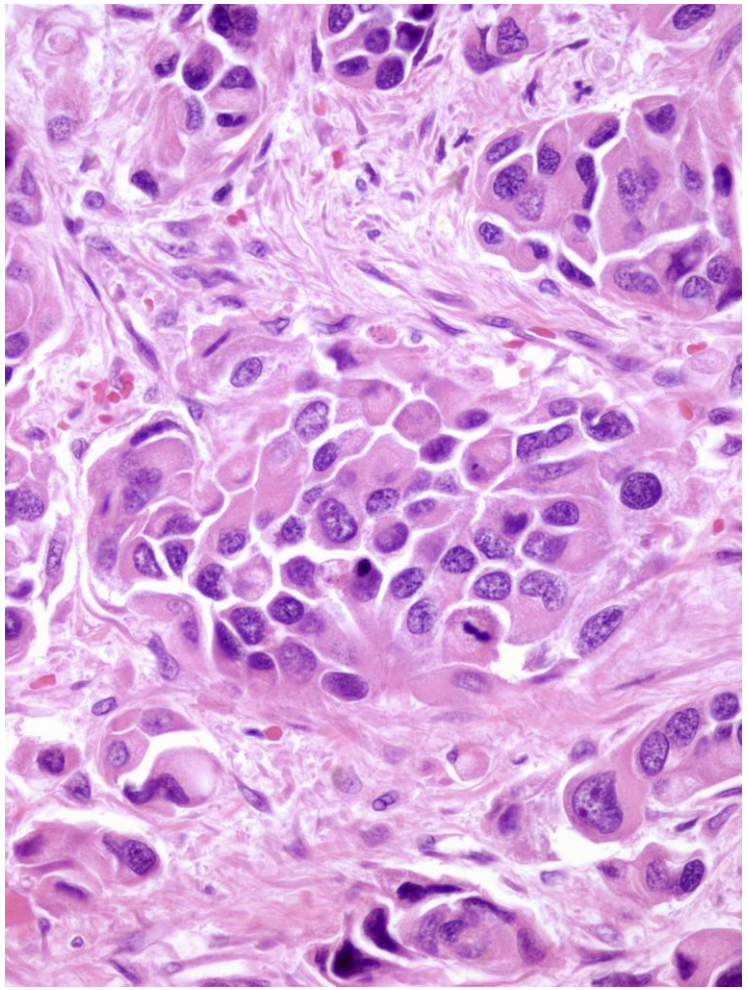


- Patient has been treated with ALK TKI
- She died few weeks later

HIGH-GRADE UPPER TRACT UROTHELIAL CARCINOMA

- May present as infiltrative mass with ambiguous histology
- Extensive involvement of renal parenchyma can resemble primary RCC
- Desmoplastic response and glandular differentiation can be seen
- Gross and microscopic examination for in situ component does not always yield results





CK7+, GATA3+, P63+

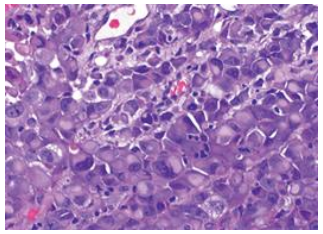
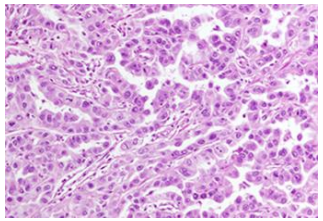
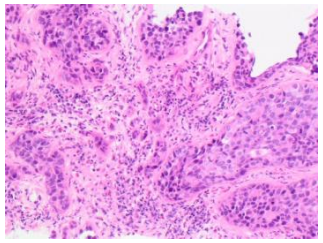
PAX8 -/+

RENAL TUMOR WITH PAPILLARY ARCHITECTURE

Tumor type	CK7	CAIX	AMACR	TFE3	TFEB	GATA3	FH	2SC	ALK*	HMB45/Melan A	Cathepsin K
Papillary RCC (type 1)	+	-	+	-	-		+	-	-		
Oncocytic papillary RCC	+	-	+	-	-	+	+	-	-		
FH-deficient RCC	-	-		-	-	-	**-**	**+**	**-**		
ALK-RCC				-/+	-		+	-	+	-	-
UTUC	+	+/-	+/-	-	-	+	+	-	-	-	-
TFE3 RCC	-			+	-	-	+	-	-	+/-	+/-
TFEB RCC				-	+	-	+	-	-	+	+

***D5F3 is the most sensitive clone**

MEDULLARY BASED TUMORS

	Tumor type	Clinical features	Morphology	IHC	Molecular features	Prognosis
	**SMARCB1 (INI1)-deficient renal medullary carcinoma**	Patients with sickle cell trait; hematuria, flank pain, male predominance, African ancestry	Infiltrating cords, nests, microcysts, sheets, and tubules; cribriform, adenoid cystic carcinoma-like appearance; myxoid desmoplastic reaction	**SMARCB1 (INI1)- PAX8+, OCT3/4+ CK7+/- HMWCK+/-**	Inactivating genomic alterations in SMARCB1/INI1	Highly aggressive
	**Collecting duct carcinoma**	Male predominance High stage @ presentation	Tubular or tubulopapillary pattern with angulated glands; desmoplastic stromal reaction	PAX8+ HMWCK+/- CK7+/- AMACR-	Inconsistent and variable results	Aggressive behavior
	**Upper tract urothelial carcinoma (UTUC)**	Positive urine cytology; prior or concurrent history of UC elsewhere in the urinary tract	Papillary, solid architecture; enlarged nuclei; infiltrates renal parenchyma, between tubules	**CK7+, GATA3+ P63+ PAX8-/+ INI1+/-**	Chr. amplification and losses; *p53* mutations; Lynch syndrome	Aggressive behavior

Include **Melanoma, Metastatic carcinoma, Lymphoma** in your differential diagnosis!

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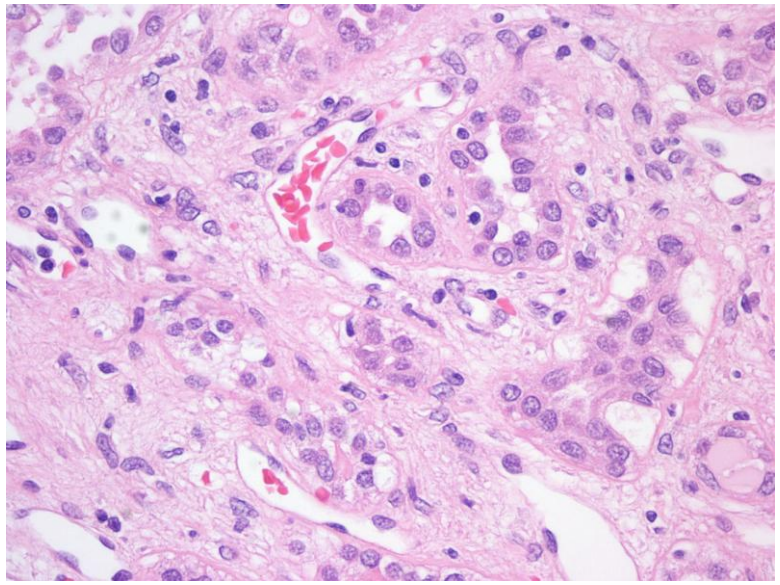
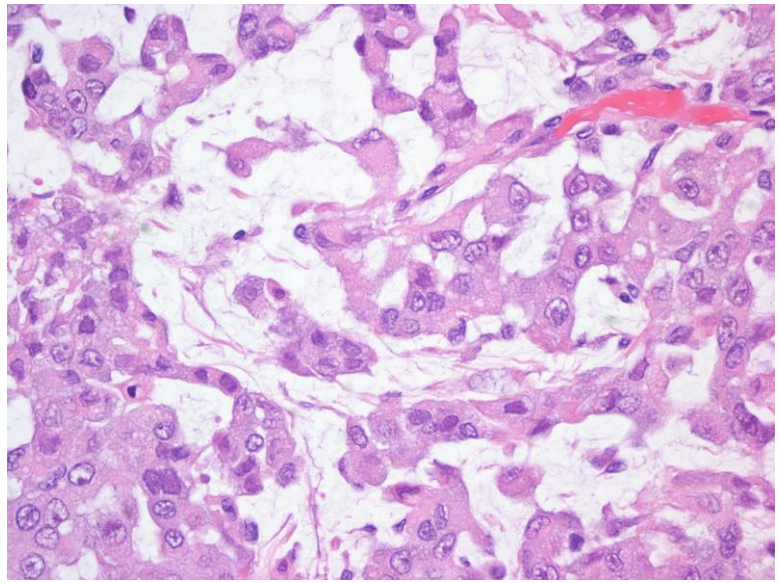
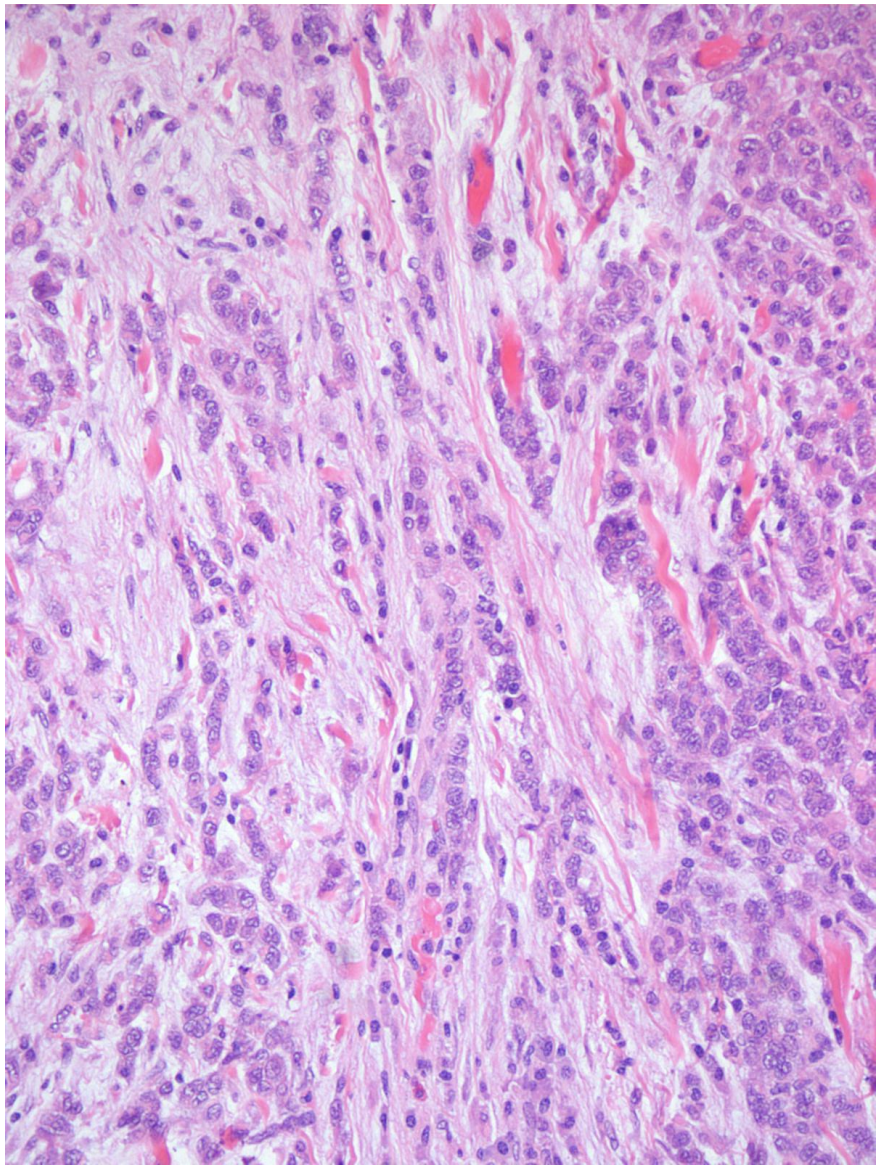
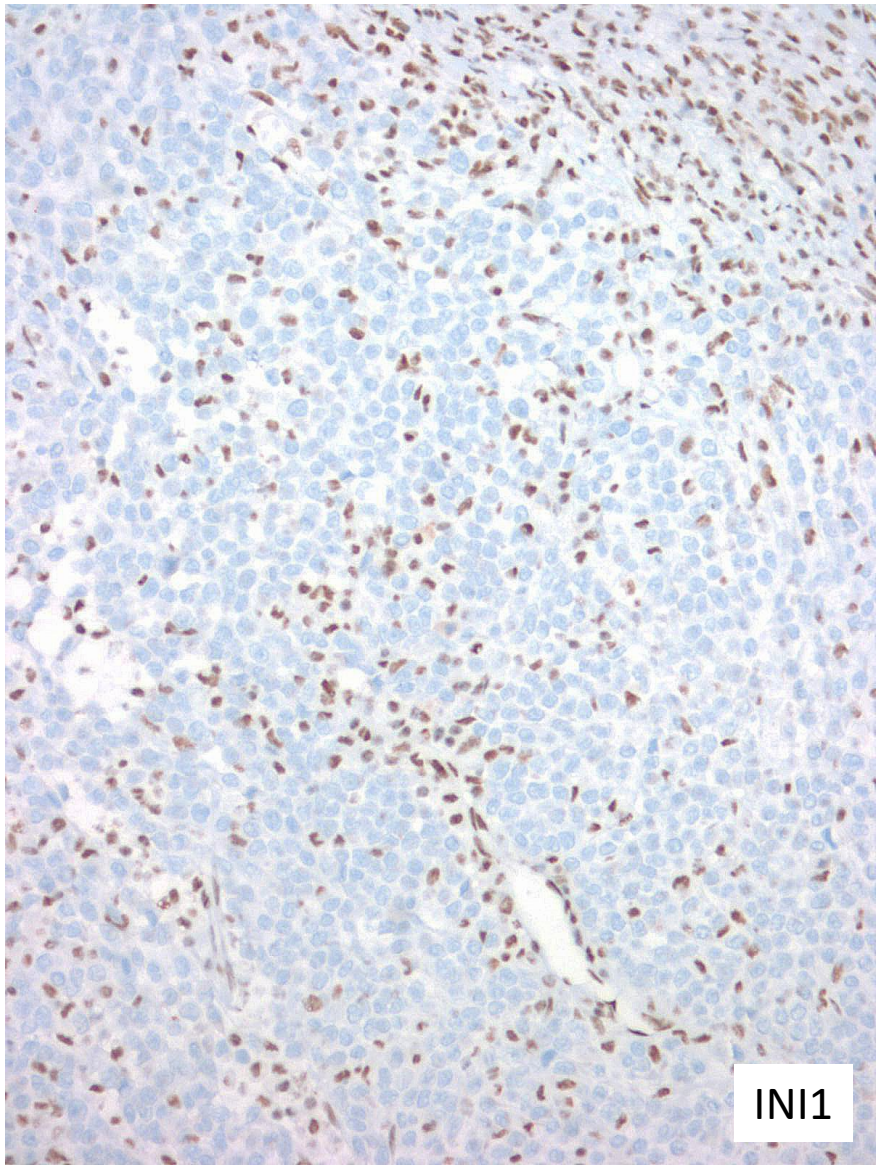
SMARCB1/INI1 DEFICIENT RENAL MEDULLARY CARCINOMA

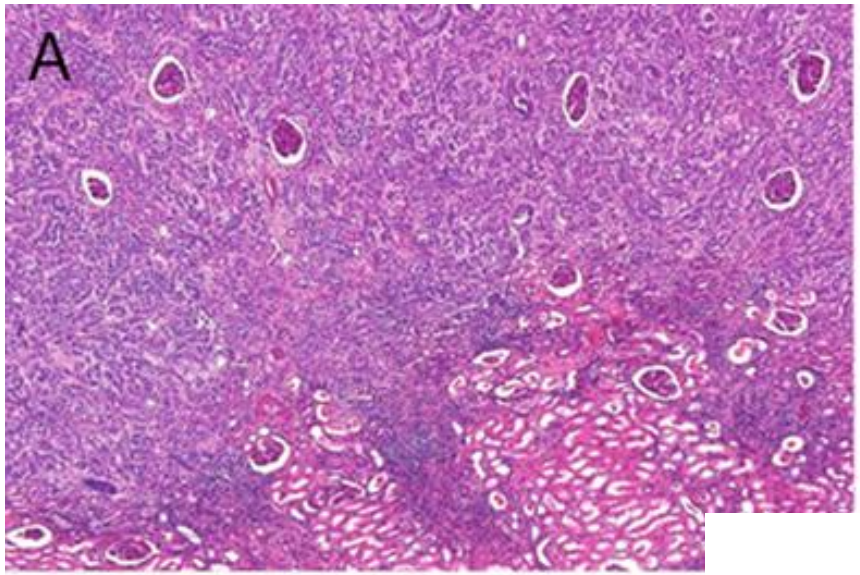


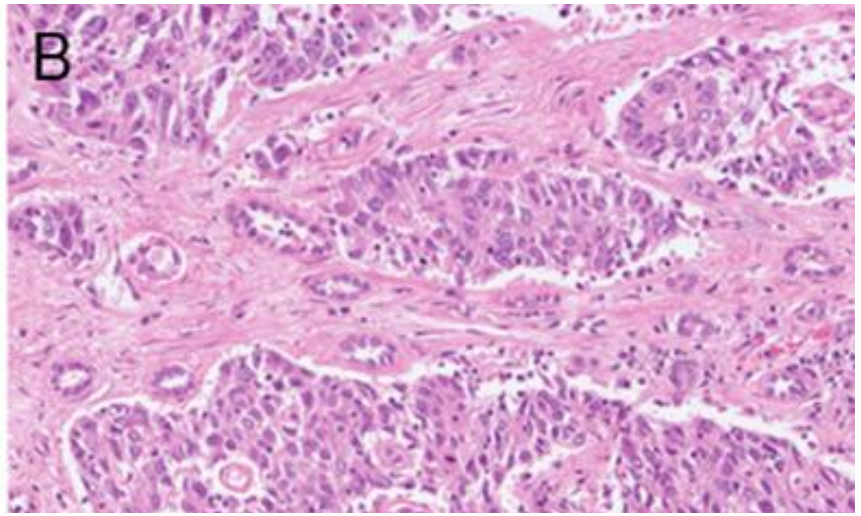


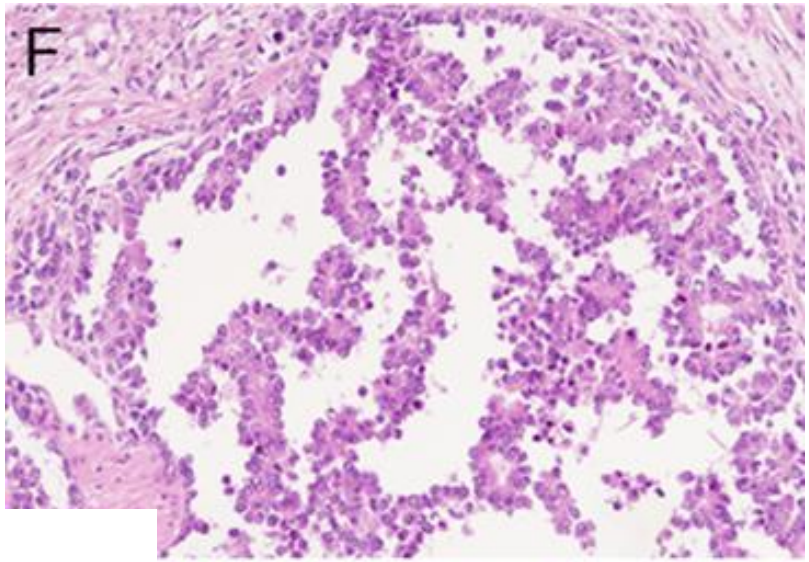




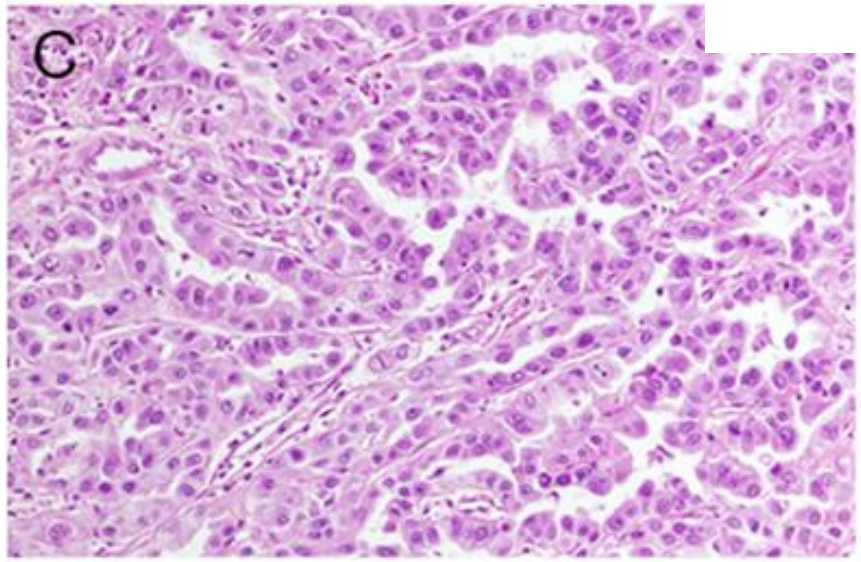
COLLECTING DUCT CARCINOMA

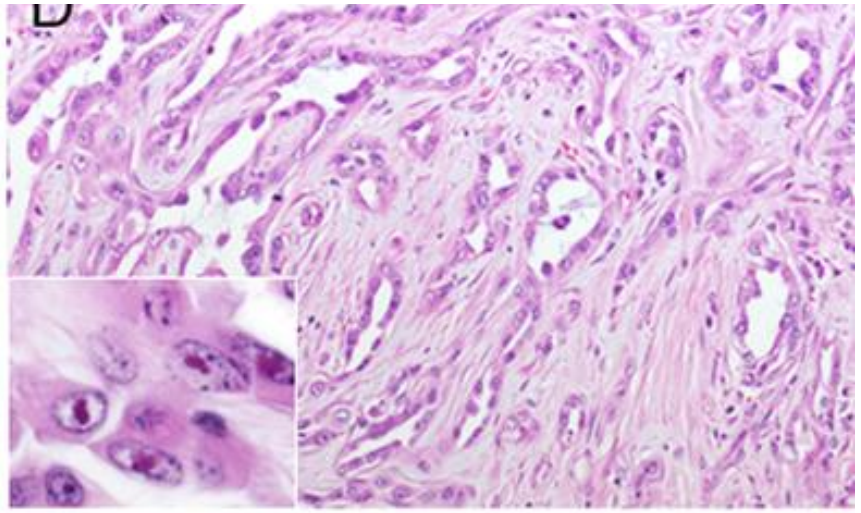


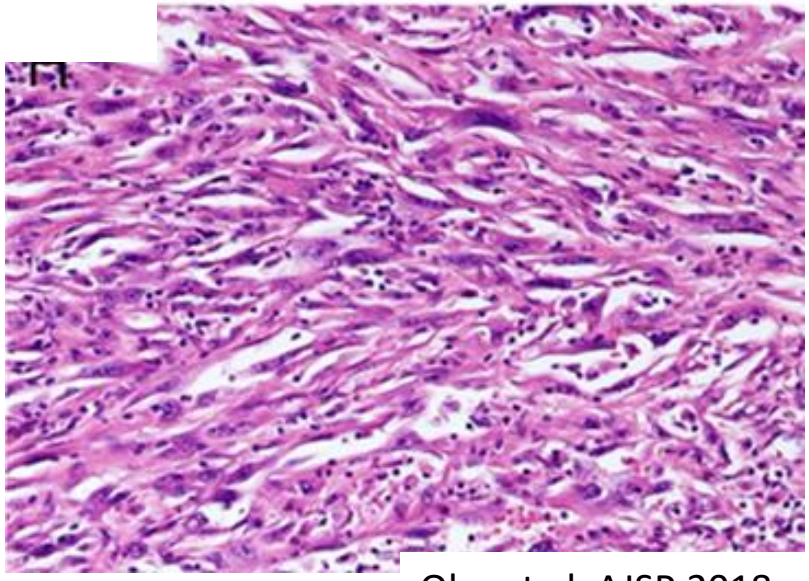




Diagnosis of exclusion!!!







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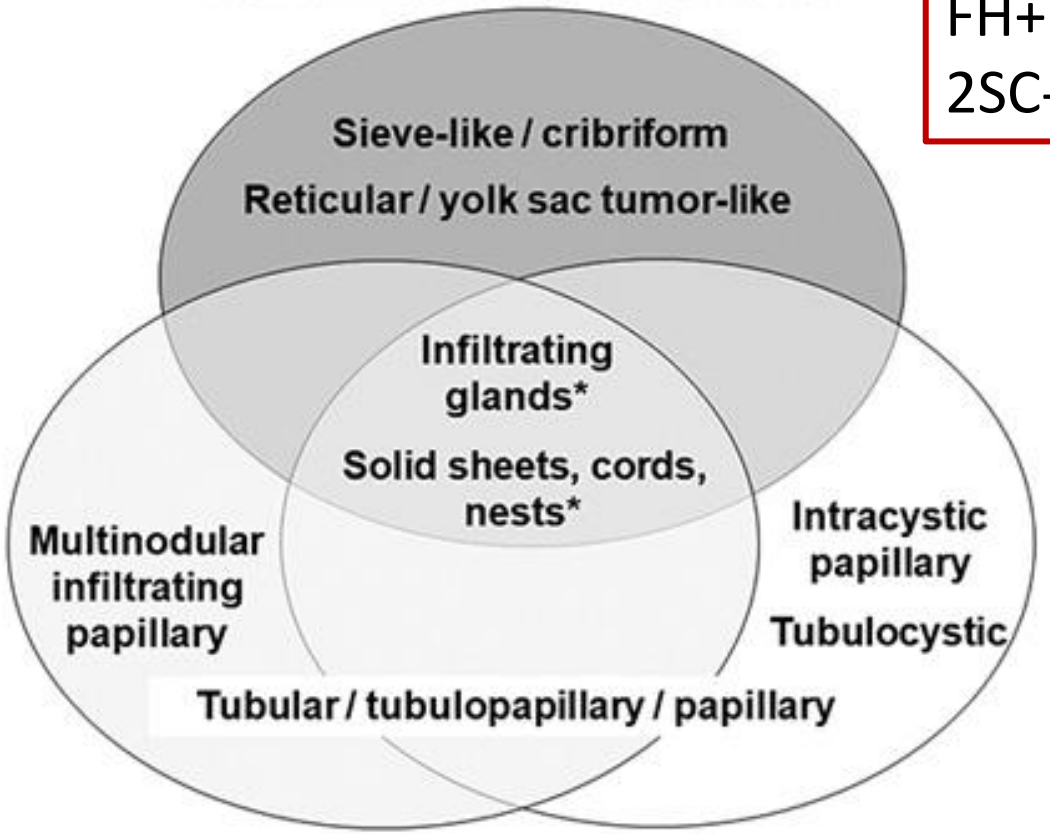
COMPARISON OF MORPHOLOGIC PATTERNS

INI1-
FH+
2SC-



CK7+/-
FH+
2SC-
INI1+

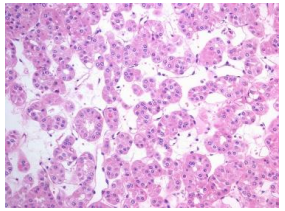
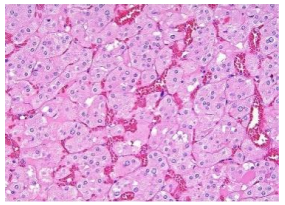
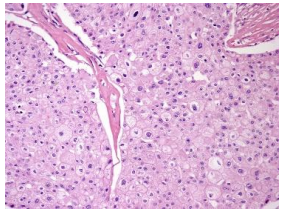
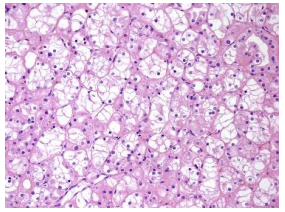
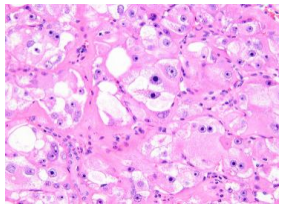
FH-
2SC+
INI1+

Ohe et al. AJSP 2018

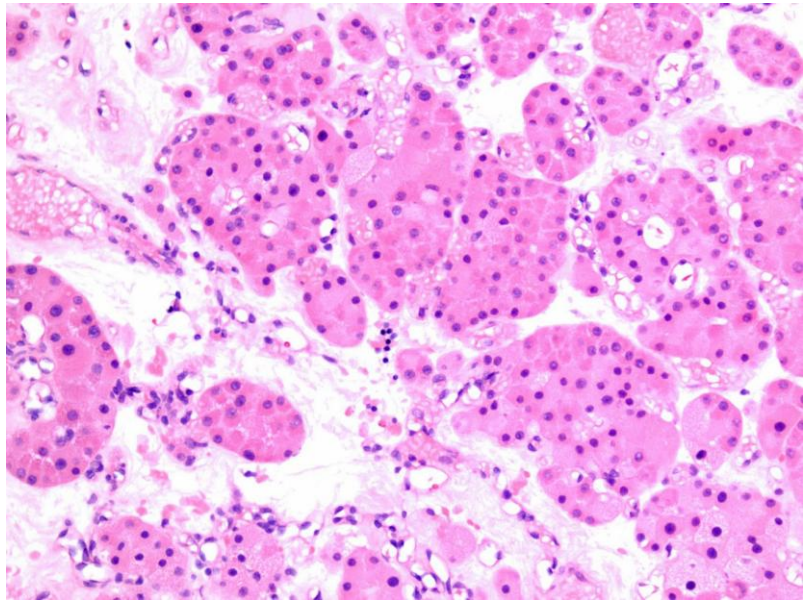
MEDULLARY BASED RENAL TUMORS WITH

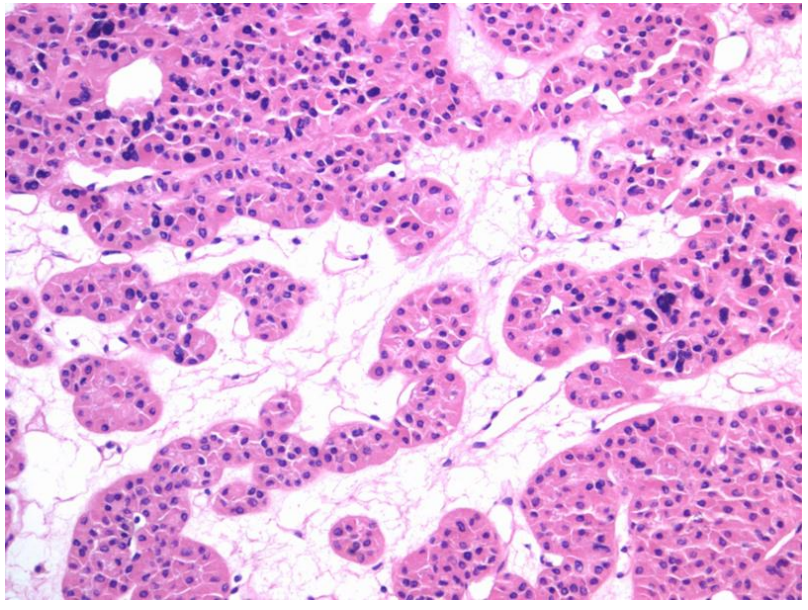
Tumor type	CK7	CAIX	AMACR	GATA3	FH	2SC	ALK	SMARCB1/INI1	OCT3/4	PAX8
FH-deficient RCC	-	-		-	-	+	-	+	-	+
SMARCB1 (INI1)-deficient renal medullary carcinoma	+/-	+/-			+	-	-	-	+	+
Collecting duct carcinoma	+/-	-	-	-	+	-	-	+	-	+
ALK-RCC					+	-	+	+	-	
UTUC	+			+	+	-	-	+	-	-/+

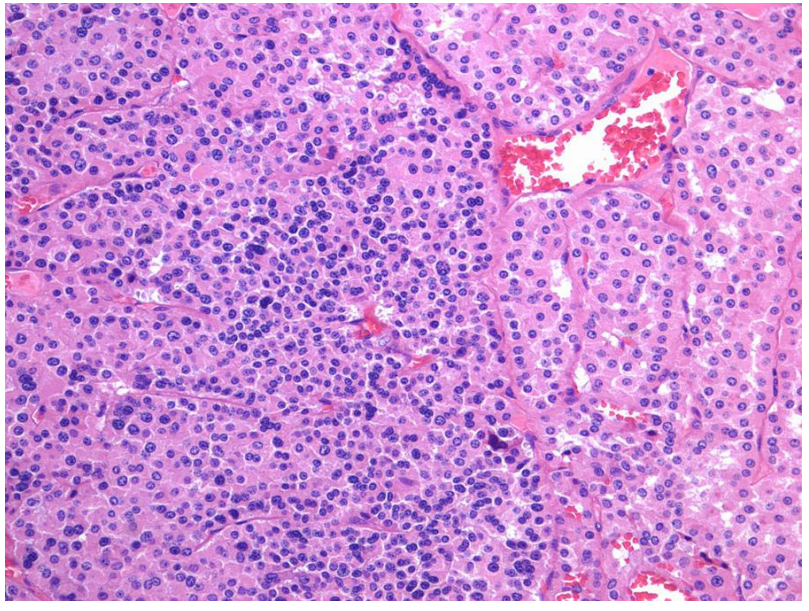
RENAL TUMORS WITH EOSINOPHILIC CYTOPLASM

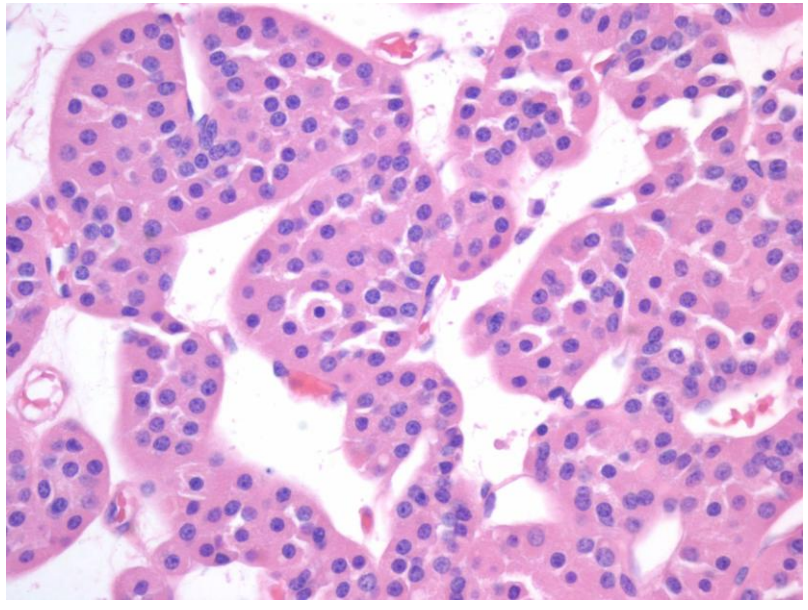
	Tumor type	Clinical features	Morphology	IHC	Molecular features	Prognosis
	**Oncocytoma**	~5% of renal neoplasms	Nests/tubules lined by cells with granular cytoplasm; myxoid/hyalinized stroma; round, regular nuclei with visible central nucleoli	**CK7-/+ (focal)** **CD117+** Vimentin-	Diploid karyotype; loss of chr. 1 & Y	Indolent behavior
	**Low-grade oncocytic tumor (LOT)**	Emerging entity	Solid and compact nests, edematous stroma, loosely arranged cells with bland round to oval nuclei, focal perinuclear halos	**CK7+** CD117- **GATA3+**	Deletions at 19p13.3, 1p36.33, 19q13.11	Indolent behavior
	**Chromophobe RCC (ChRCC)**	~10% of RCC	Abundant cytoplasm with prominent cell borders; perinuclear halos/clearing irregular, wrinkled nuclear membrane ('raisinoid')	**CK7+** **CD117+** Vimentin- GATA3-/+	Extensive chromosomal loss involving Y, 1, 2, 6, 10, 13, 17, 21	Variable behavior
	**Hybrid oncocytic tumor**	Sporadic, in renal oncocytosis, or Birt-Hogg-Dube syndrome	Cells displaying cytologic features of ChRCC and oncocytoma	CD117+ CK7-/+ Cathepsin K+/-	Intermediate between ChRCC and oncocytoma	Indolent behavior
	**Eosinophilic vacuolated tumor (EVT)**	Sporadic; rare cases reported in TSC patients	Solid growth of cells with pink cytoplasm, intracytoplasmic vacuoles and prominent nucleoli	**CK7-/+** **CD117+,** CD10+ **Cathepsin K+**	Mutations in *TSC1*, or *TSC2*, or *mTOR*	Indolent behavior

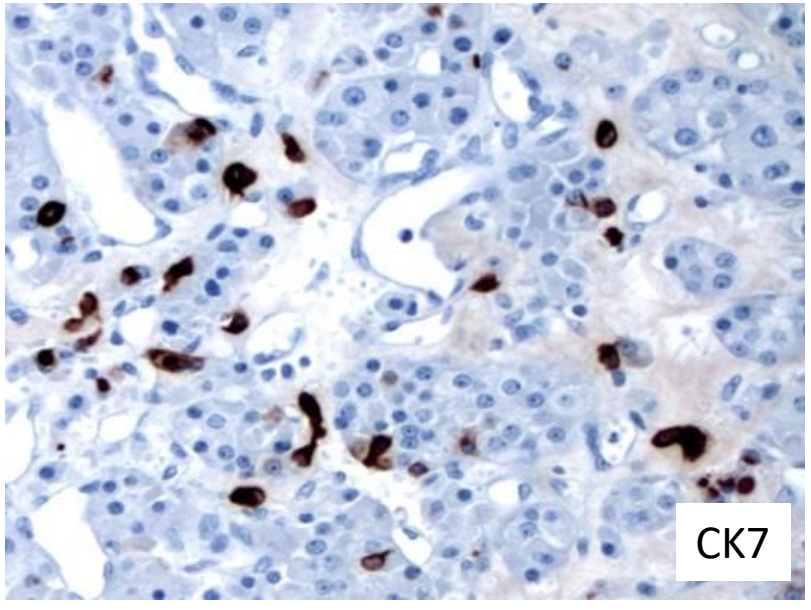
RENAL ONCOCYTOMA

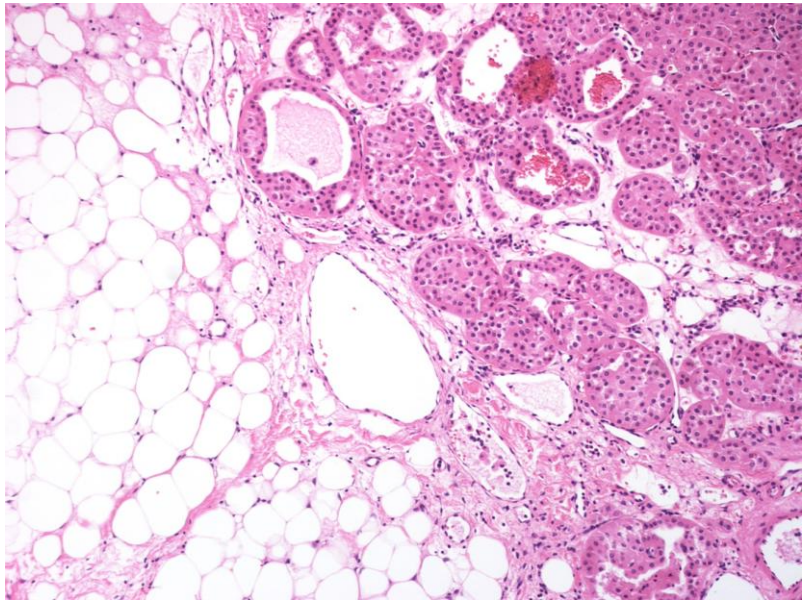




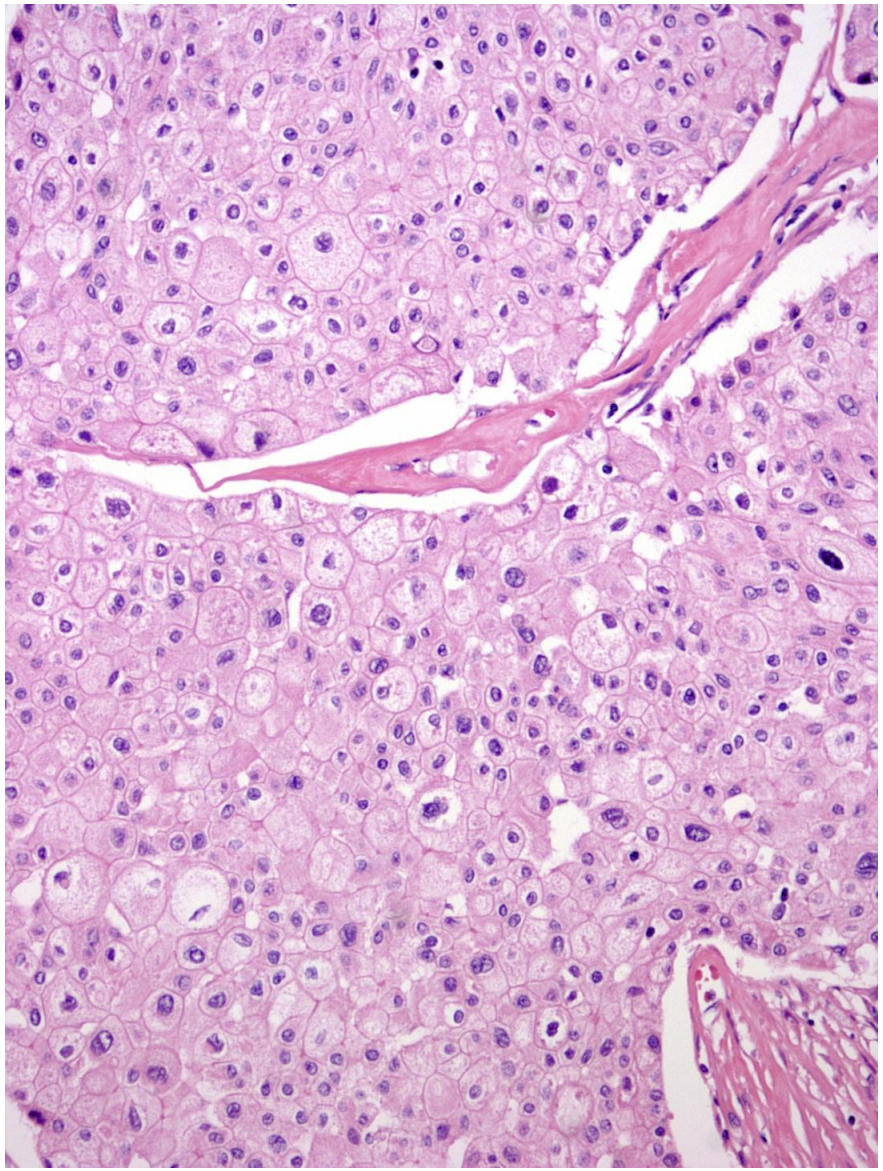


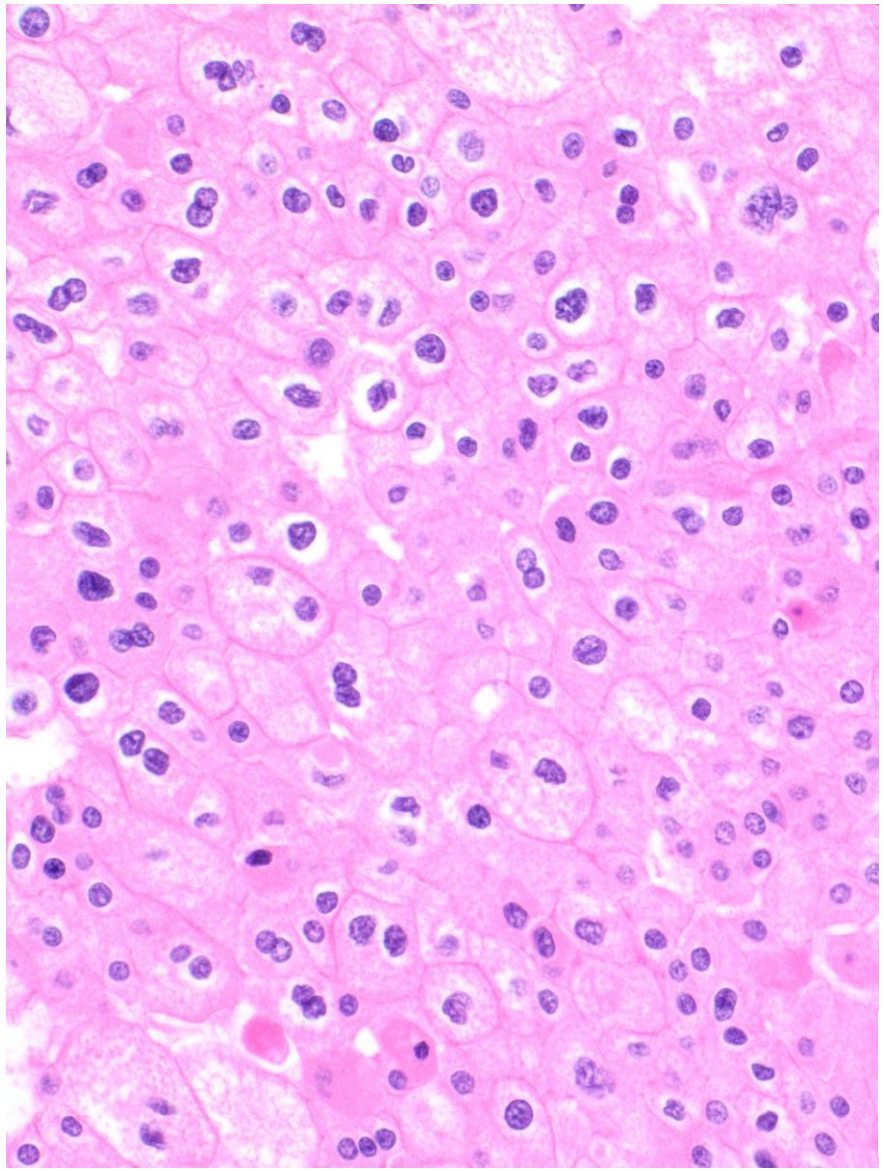


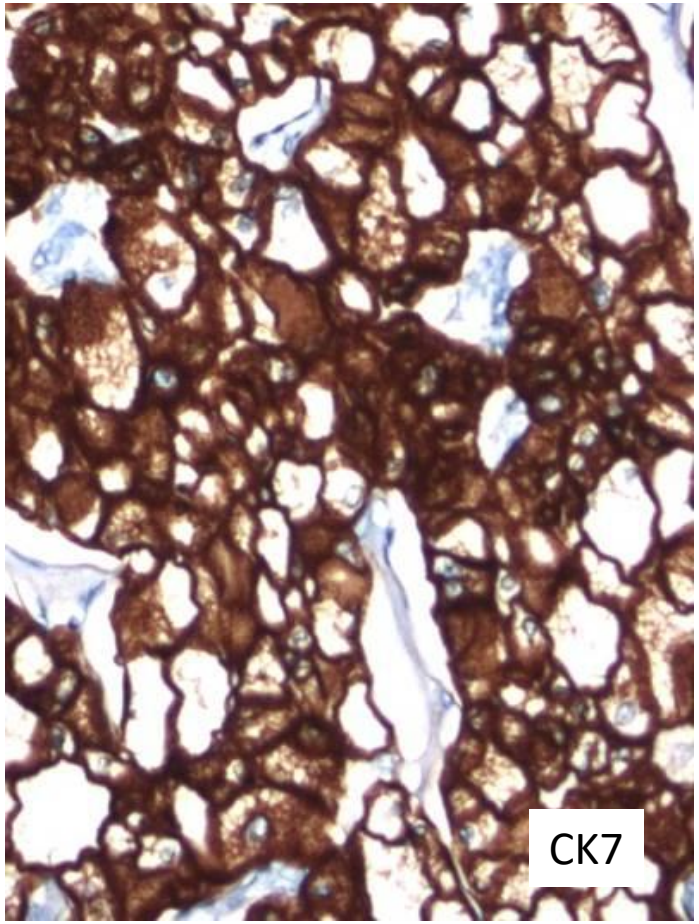




CHROMOPHOBE RENAL CELL CARCINOMA

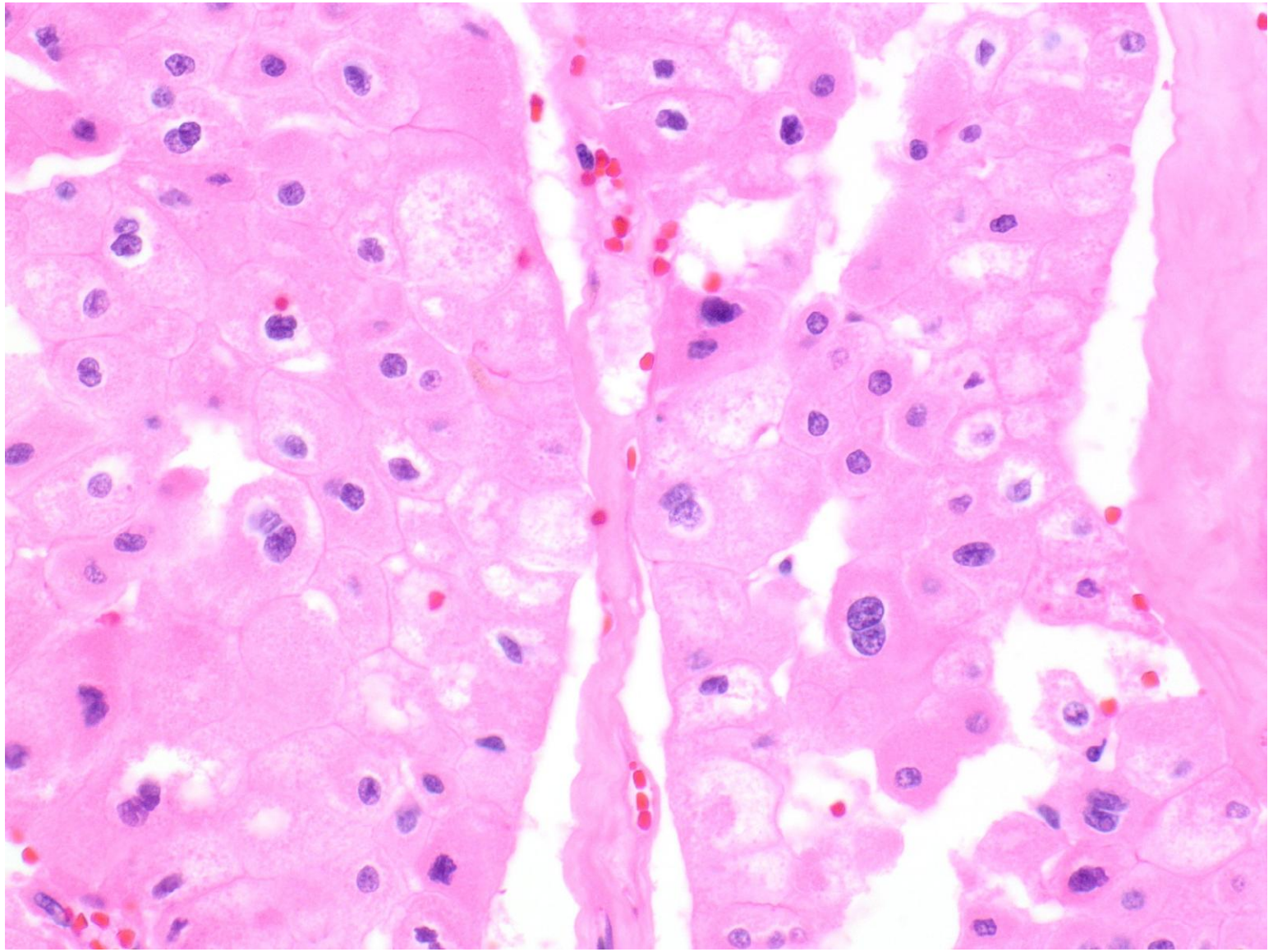






EOSINOPHILIC CHROMOPHOBE RENAL CELL CARCINOMA

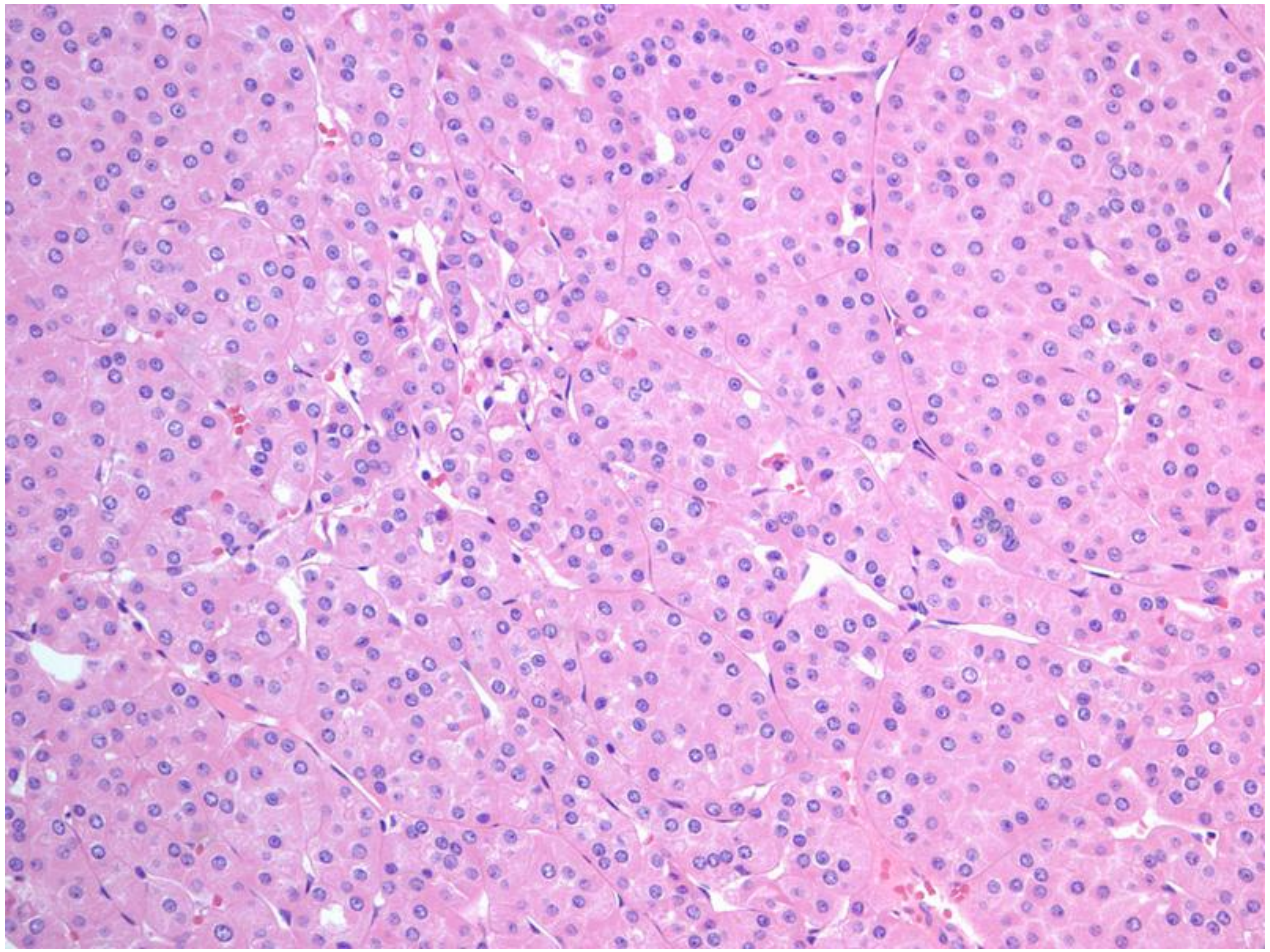
- Prominent, easily recognizable nuclear irregularities
- Diffuse eosinophilic appearance with absence of pale cells
- Lack of adverse features:
  - Necrosis
  - Sarcomatoid
  - Vascular invasion

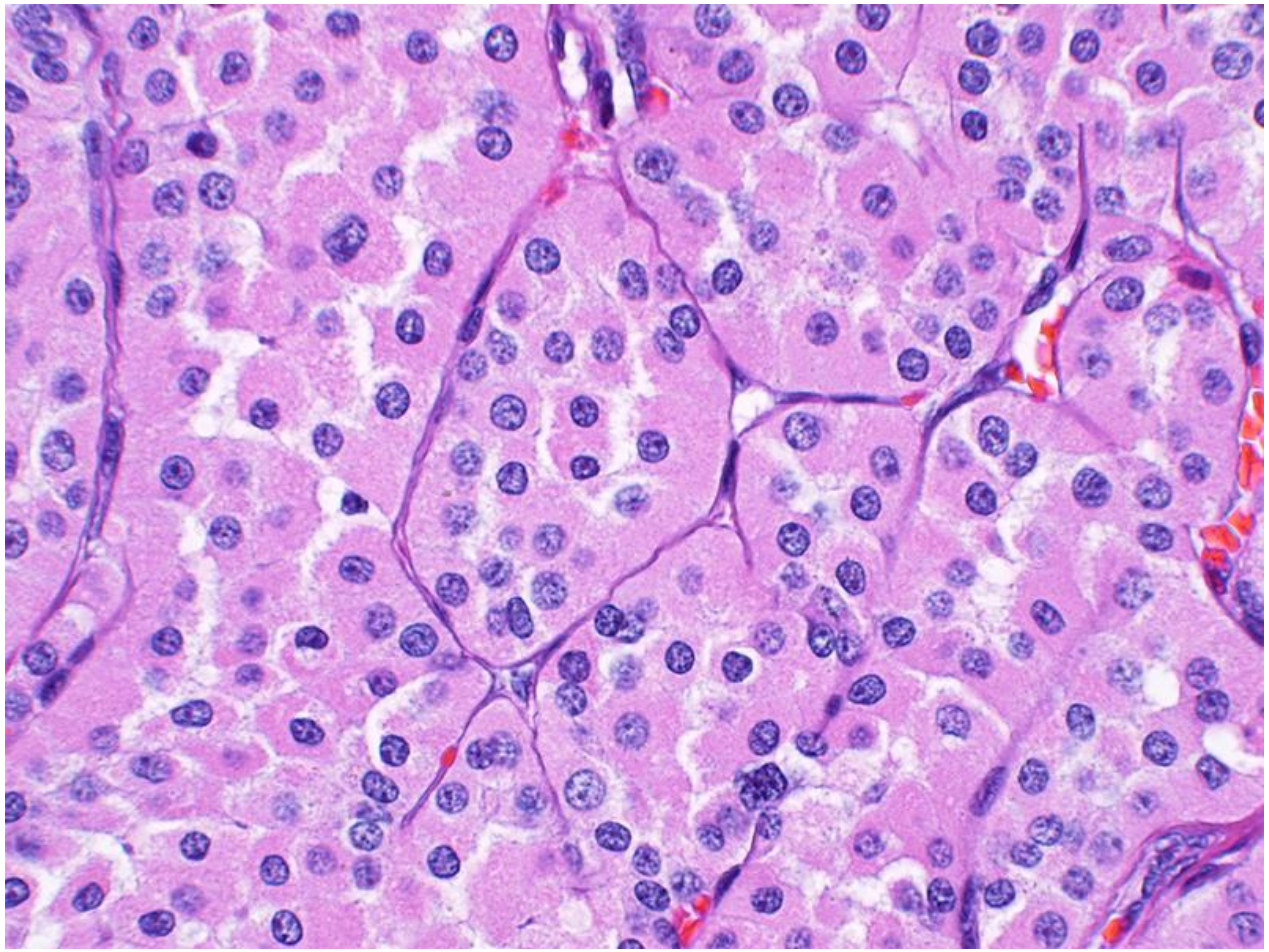


Hes & Trpkov. Mod Pathol 2022

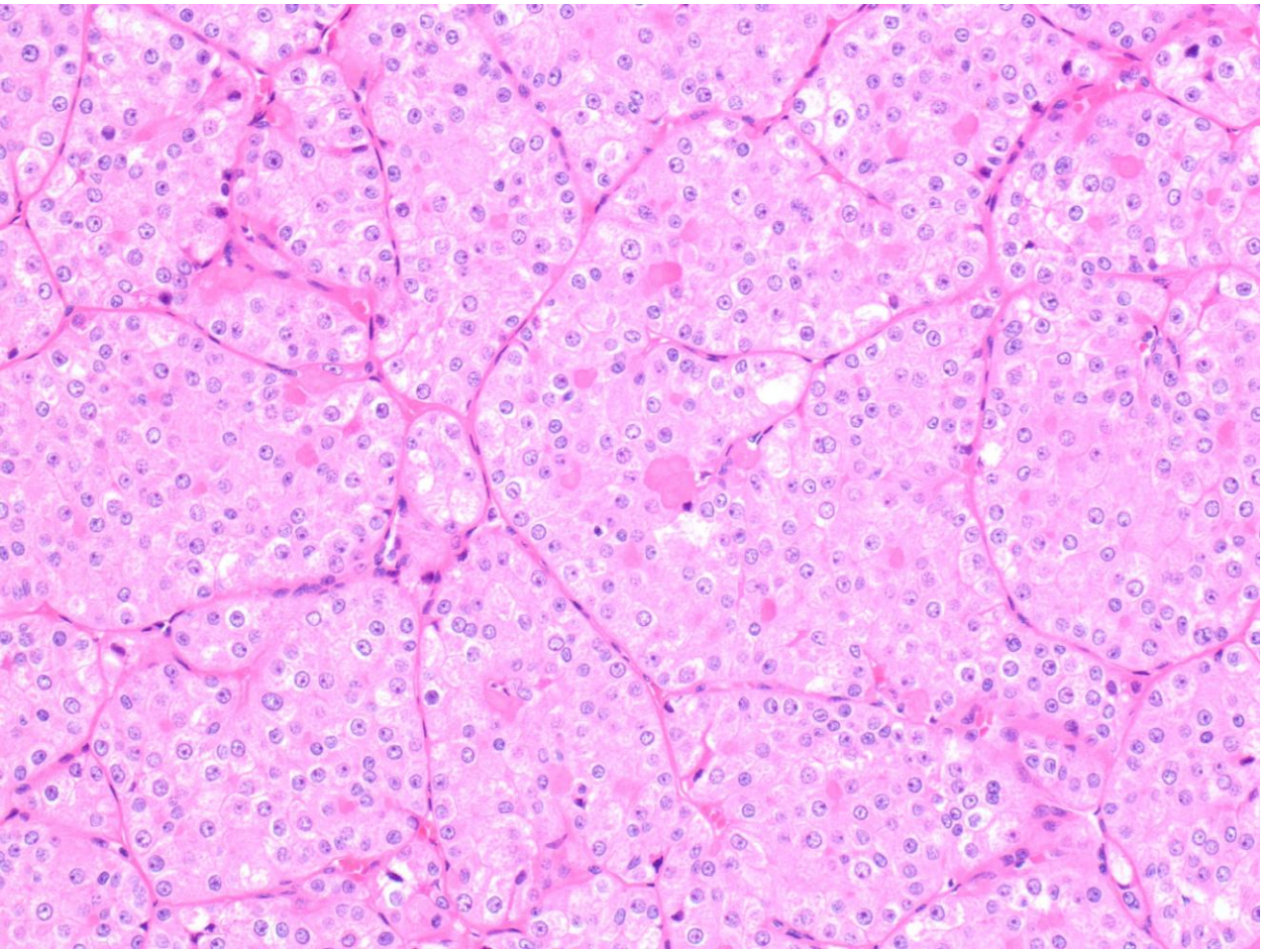
ONCOCYTIC RENAL NEOPLASMS OF LOW MALIGNANT POTENTIAL

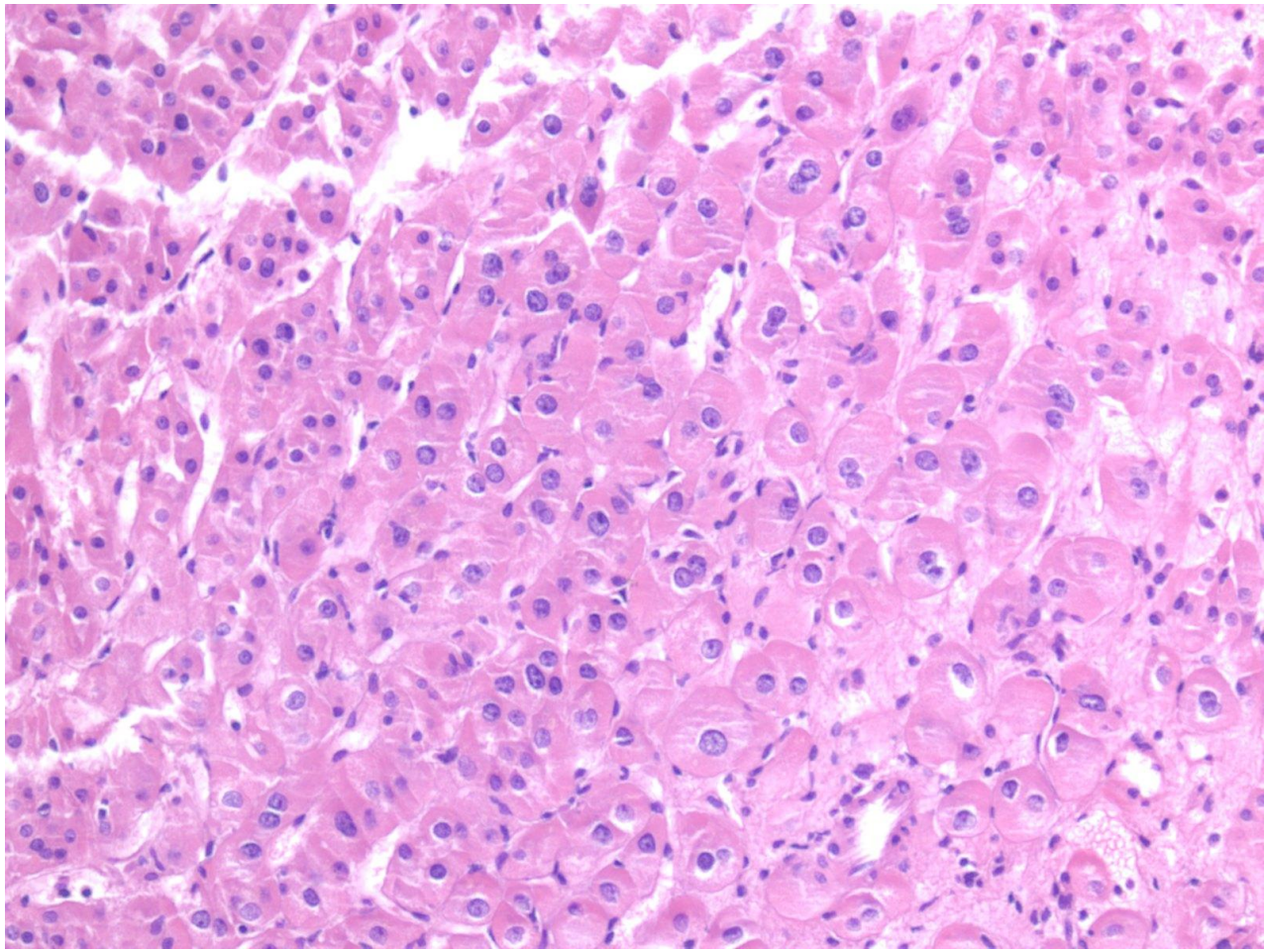
- Highly compact nested architecture, almost solid
- Variation in cell size or slight nuclear irregularity





ONCOCYTIC RENAL NEOPLASMS OF LOW MALIGNANT POTENTIAL

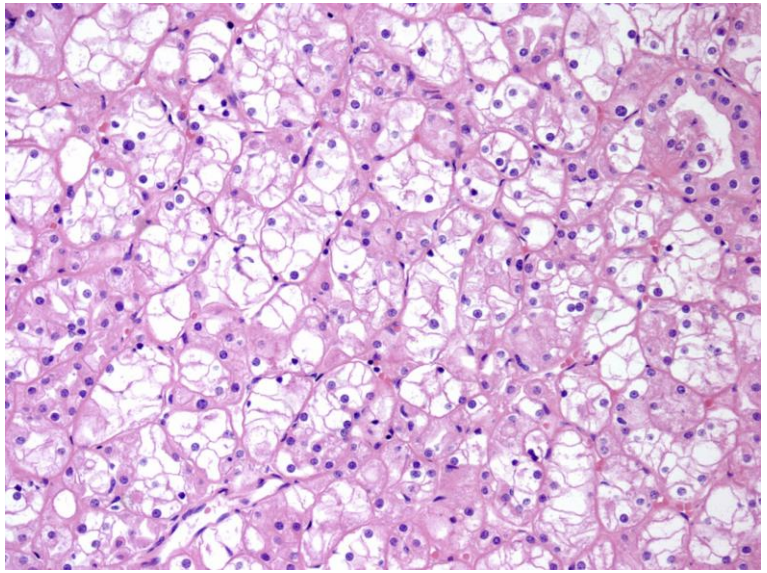


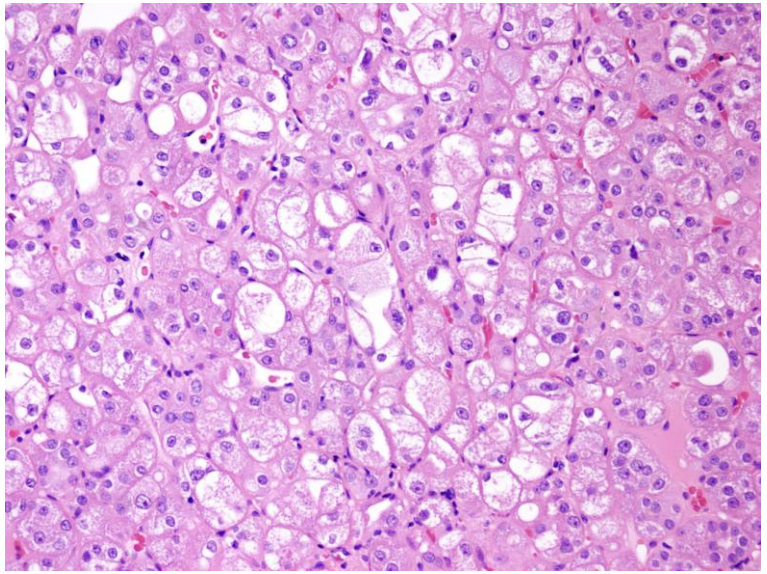


Category expressing uncertainty between oncocytoma & eosinophilic ChRCC

HYBRID ONCOCYTIC TUMORS

- Multiple and/or bilateral tumors
- Contain cells displaying cytologic features of ChRCC and oncocytoma
- Should be restricted to hereditary cases: **Birt-Hogg-Dube (BHD) syndrome** or renal oncocytosis
- Hybrid tumors may preclude a definitive diagnosis of oncocytoma on needle core biopsy
- CK patchy +; cathepsin K +





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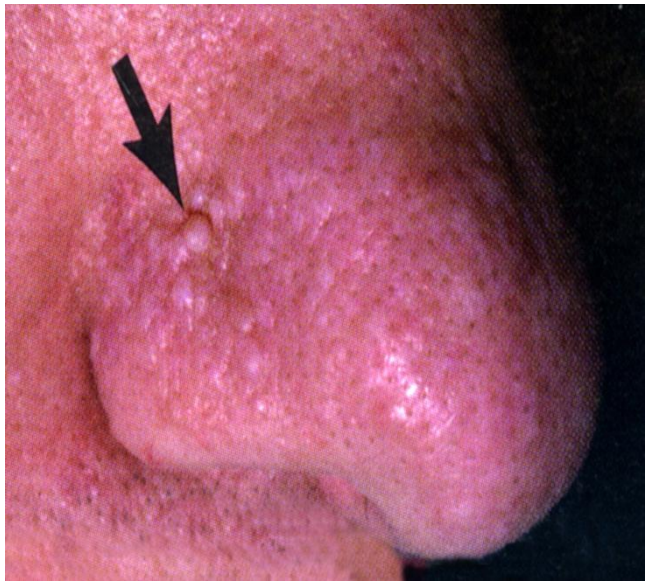
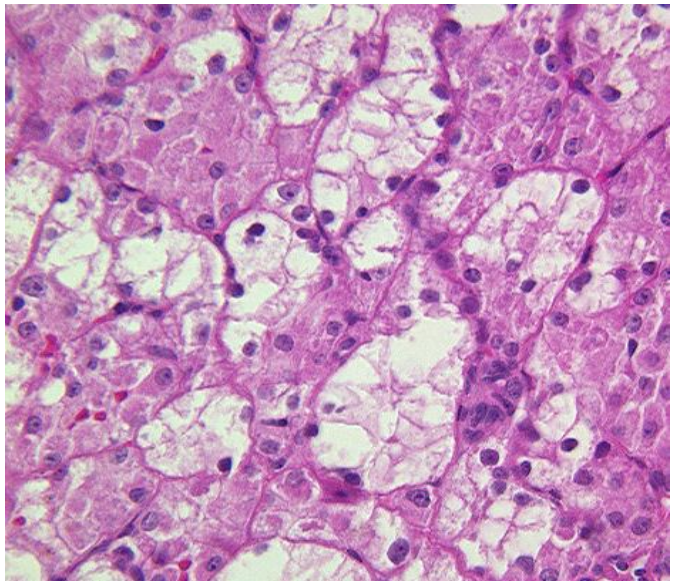
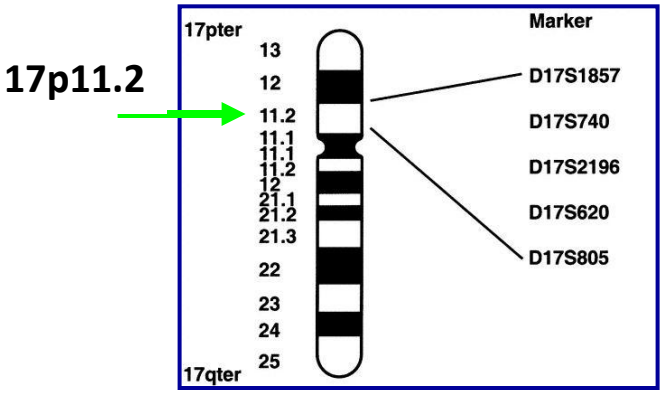
BIRT-HOGG-DUBE SYNDROME

- Aut. Dom. genodermatosis:
  - small dome-shaped papules on face, neck, trunk (fibrofolliculomas)
  - higher risk of renal tumors, lung cysts, spontaneous pneumothorax
- Male predominance
- Mean of 5.3 renal tumors/patient
- Multiple (77%), bilateral (60%) tumors



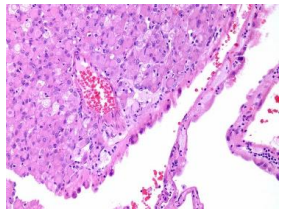
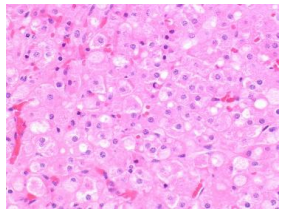
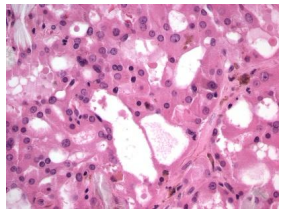
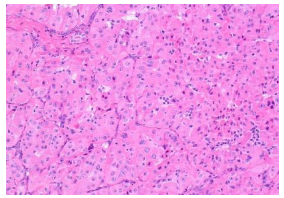
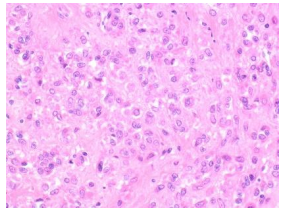




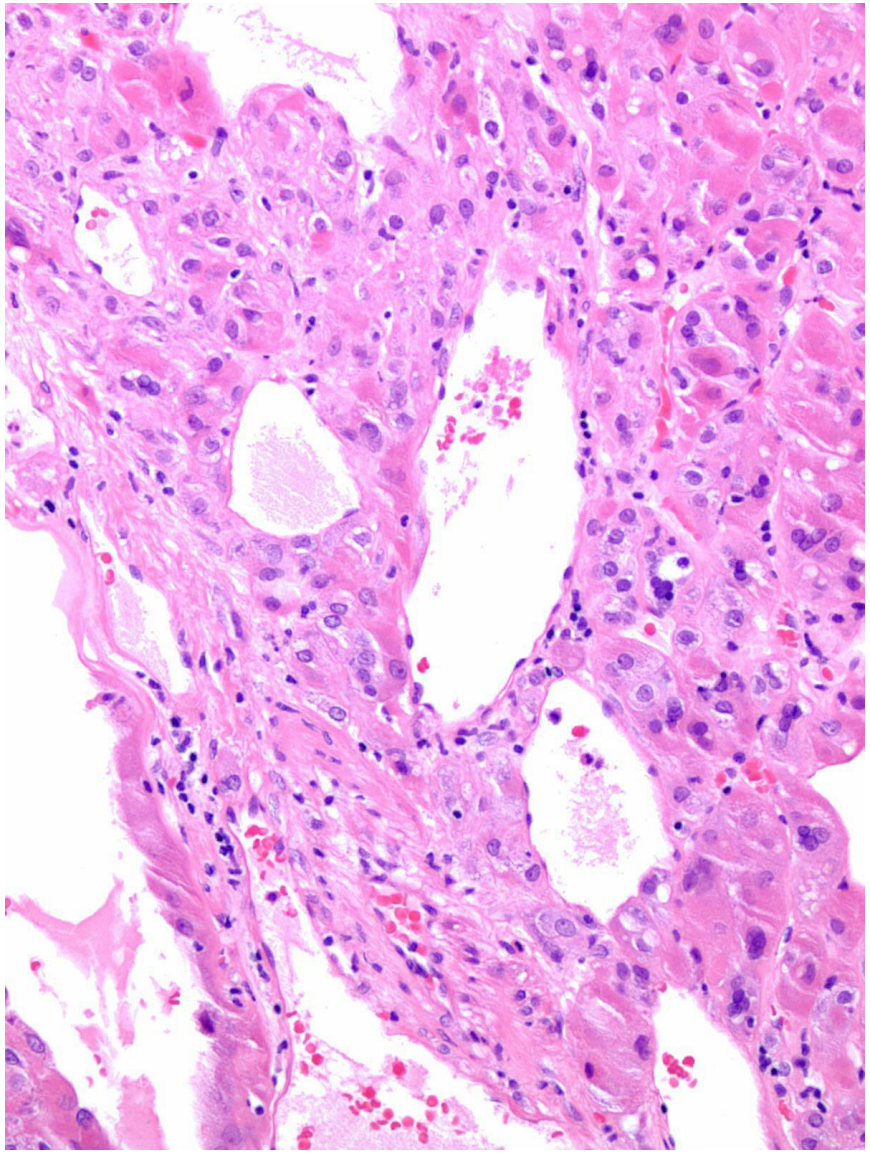
Hybrid tumors
Eos. ChRCC
Oncocytoma
Eos. Papillary
Clear cell RCC

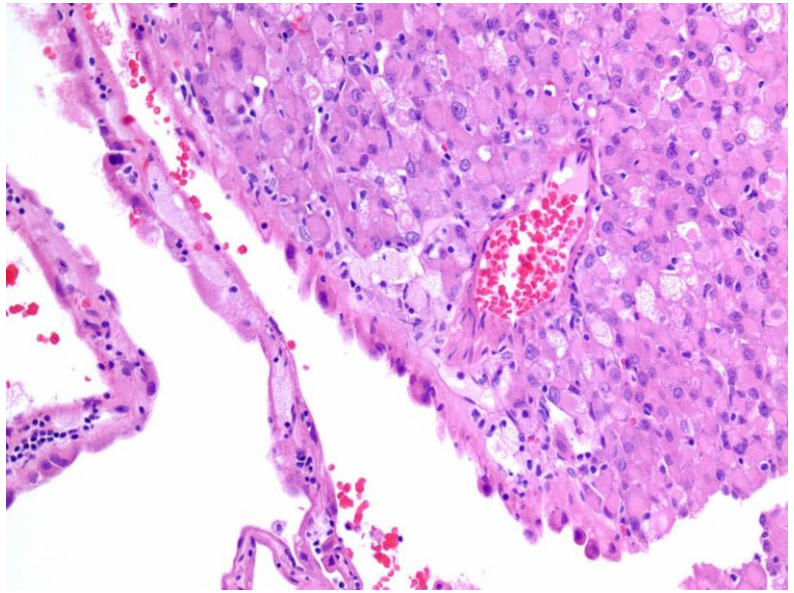
Pulmonary cysts

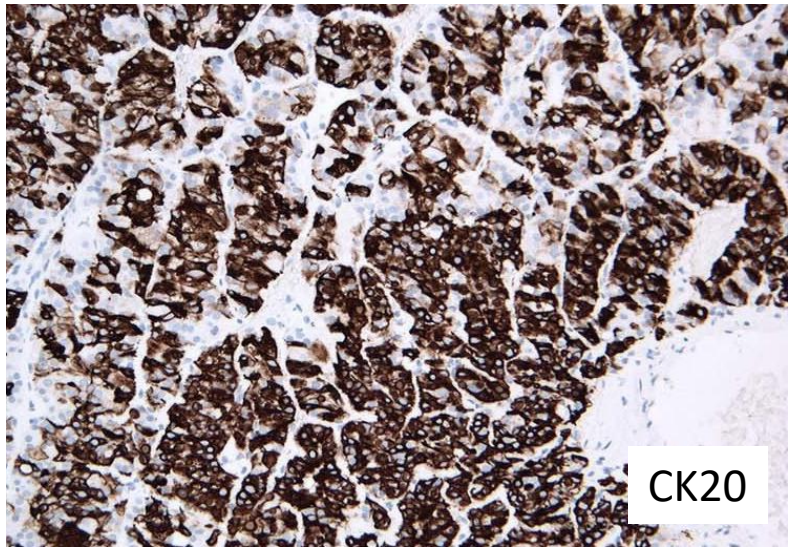
RENAL TUMORS WITH EOSINOPHILIC CYTOPLASM

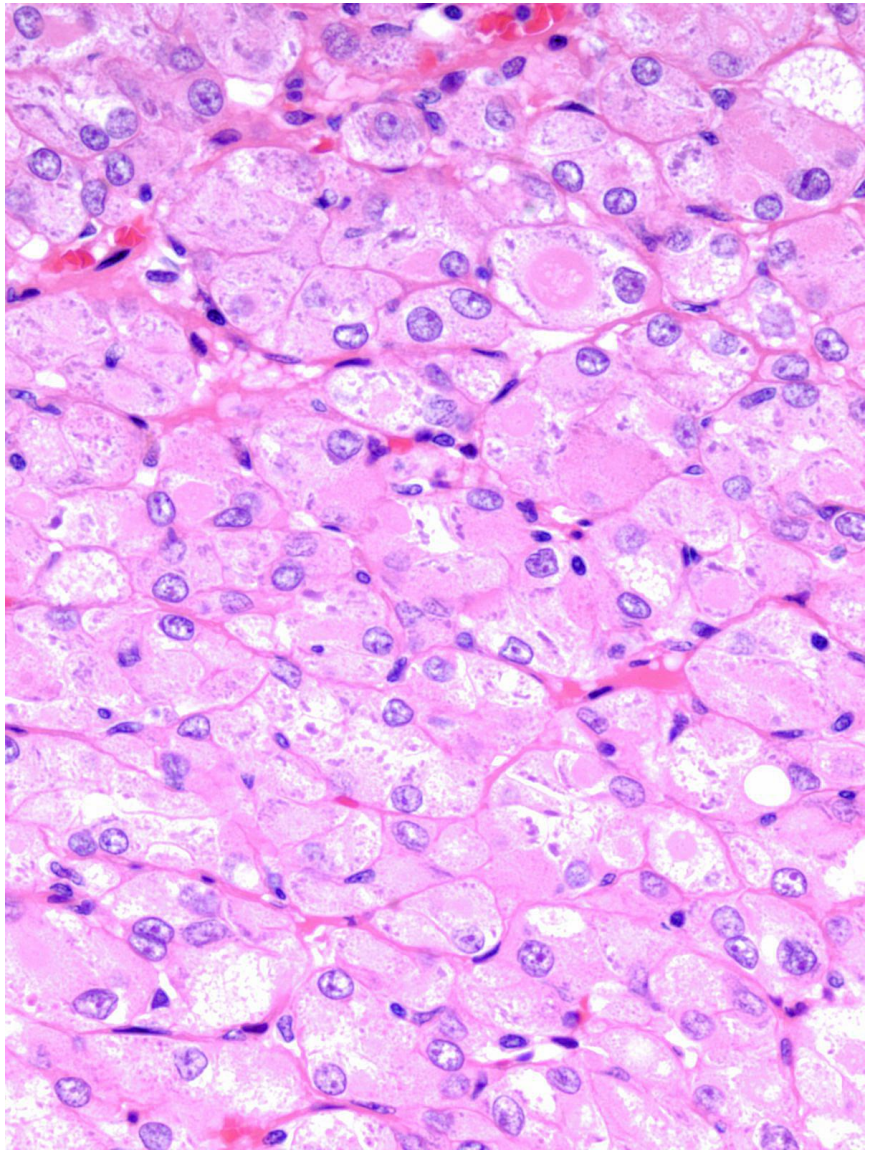
	Tumor type	Clinical features	Morphology	IHC	Molecular features	Prognosis
	**Eosinophilic solid & cystic RCC**	Mostly females, ≤10% in TSC patients	Solid and cystic, eosinophilic cytoplasmic; coarsely granular, basophilic cytoplasmic stippling	**CK20+/-** CK7-, CD117– **Cathepsin K+**	Somatic bi-allelic loss or mutations of *TSC1* and *TSC2*	Favorable; rare cases aggressive
	**SDH-deficient RCC**	~0.1% of all RCC Solid and cystic ~30% multifocal or bilateral	Uniform cytology, flocculent cytoplasm, intracytoplasmic vacuolations or inclusions, round-oval low-grade nuclei	**SDHB-** CD117- CK7-	Germline mutations of genes encoding SDH subunits	Variable behavior; 11% metastatic
	**Acquired cystic disease-associated RCC**	ACKD patients on long-term dialysis; often multiple & bilateral	Tubulocystic/papillary; microlumen formation, eosinophilic cells with large nuclei and prominent nucleoli; intratumoral oxalate crystals	**AMACR+ CD10+** CK7-, CAIX- CD117-	No essential alterations	Usually indolent; can be aggressive
	**TFEB amplified RCC**	Older patients	High-grade poorly differentiated RCC with frequent oncocytic and papillary features	**Melan A+/- Cathepsin K+** HMB45 +	Amplification of 6p21 locus harboring TFEB (TFEB overexpression)	Poor outcome
	**Epithelioid AML (EAML)**	~5% of all AML More common in TSC	80% epithelioid cells; lacks significant amount of intratumoral fat & malformed vessels; epithelioid morphology	**CK-**, HMB45+ Melan A+ Cathepsin K+ S100+, **PAX8-**	Mutations of TSC2 reported in sporadic EAMLs	Malignant behavior may occur

EOSINOPHILIC SOLID AND CYSTIC RENAL CELL CARCINOMA

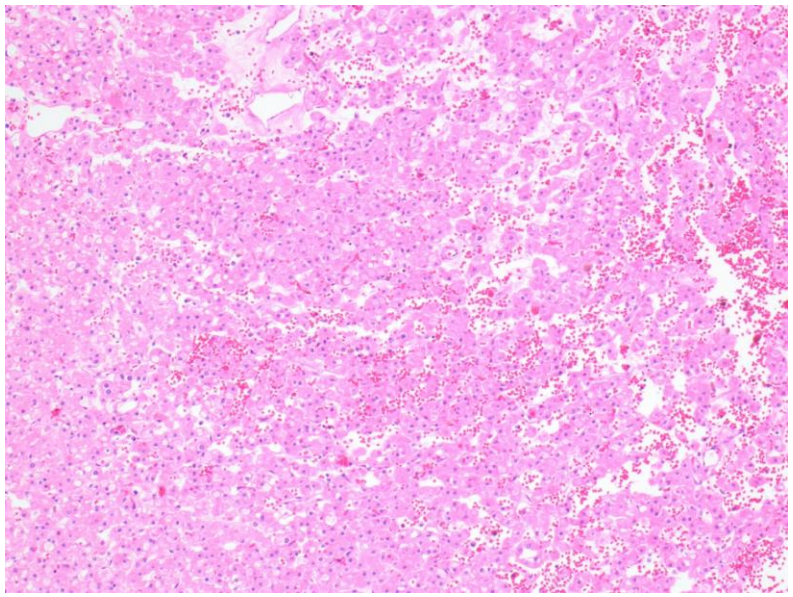


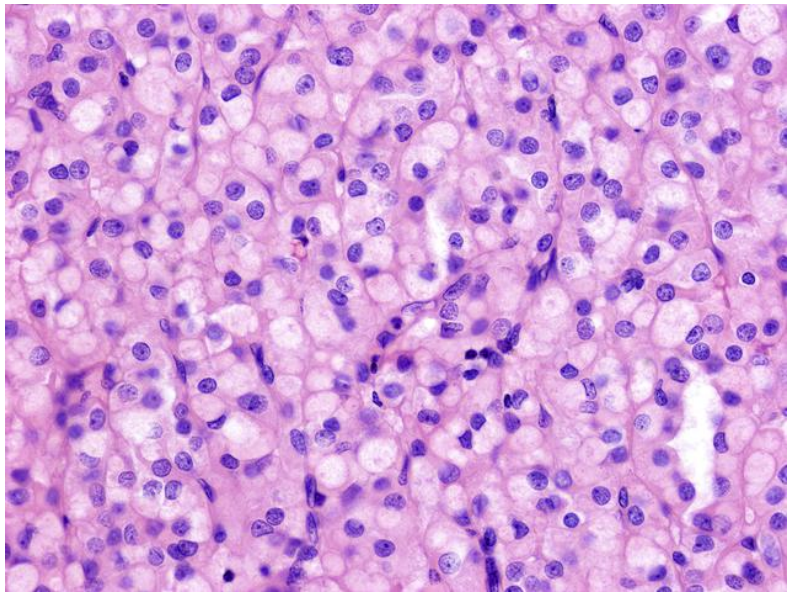


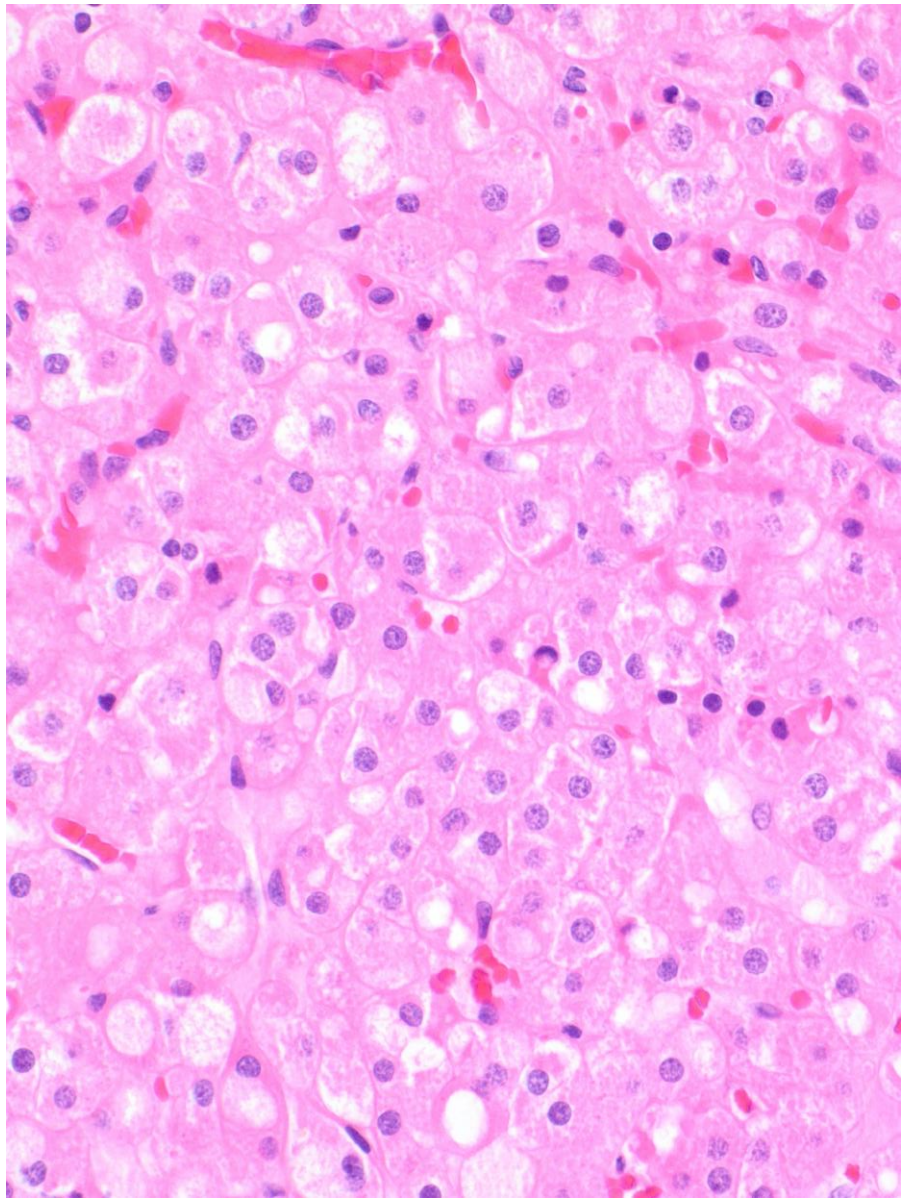


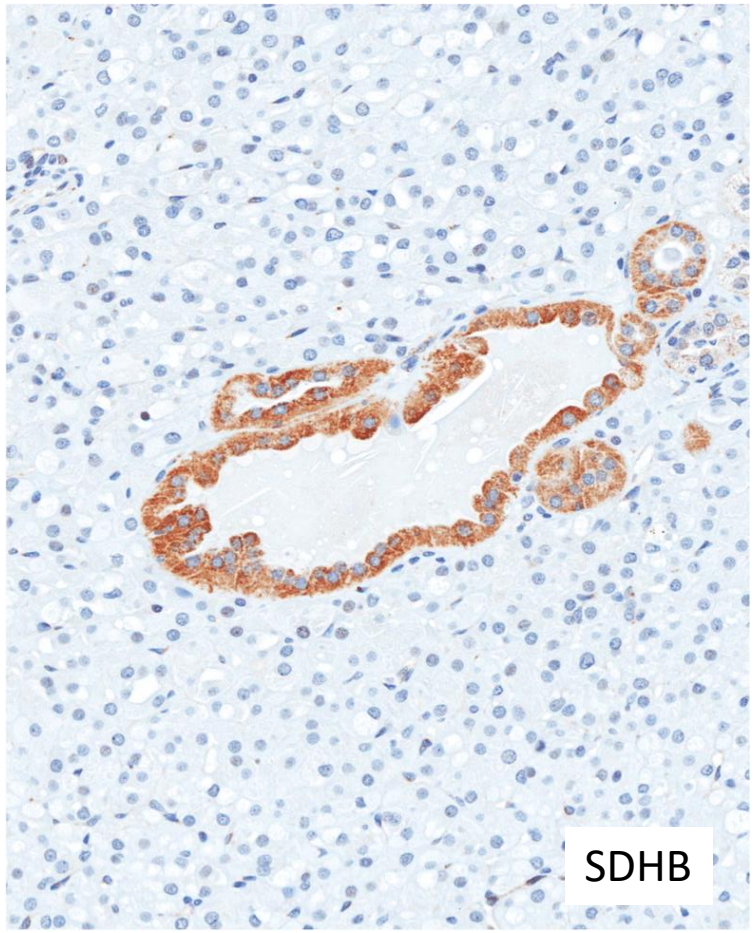


SDH-DEFICIENT RENAL CELL CARCINOMA

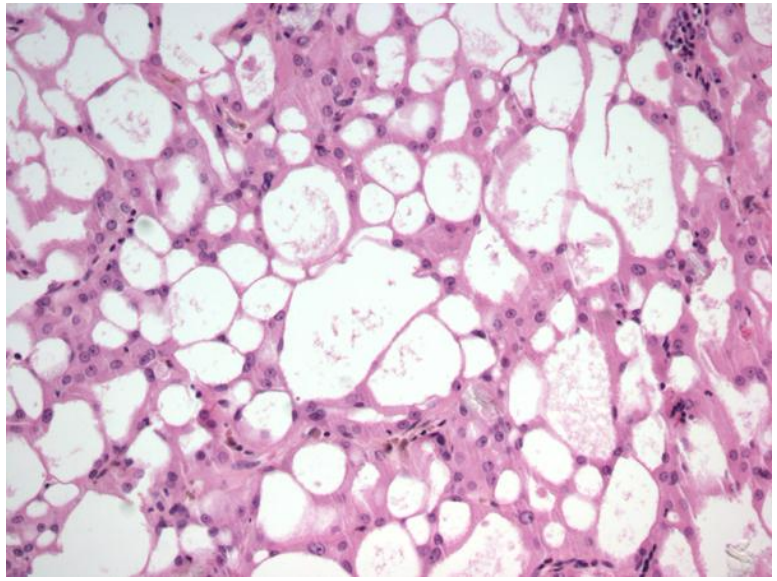


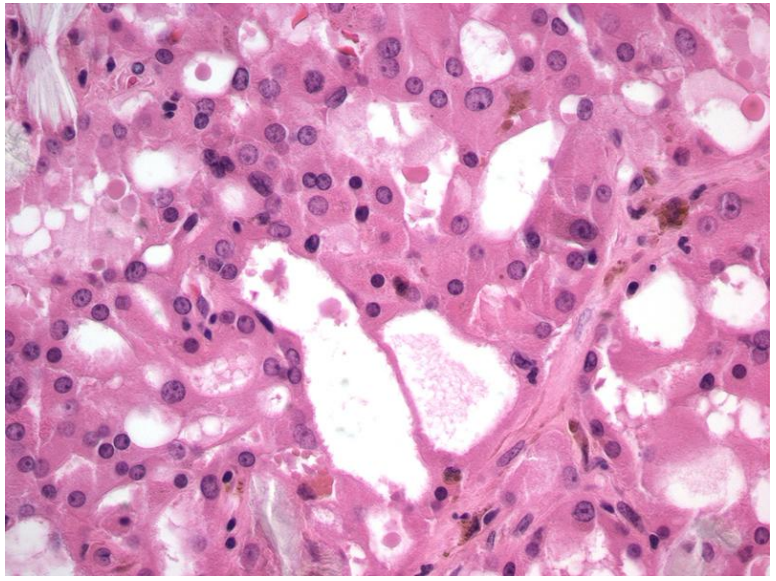


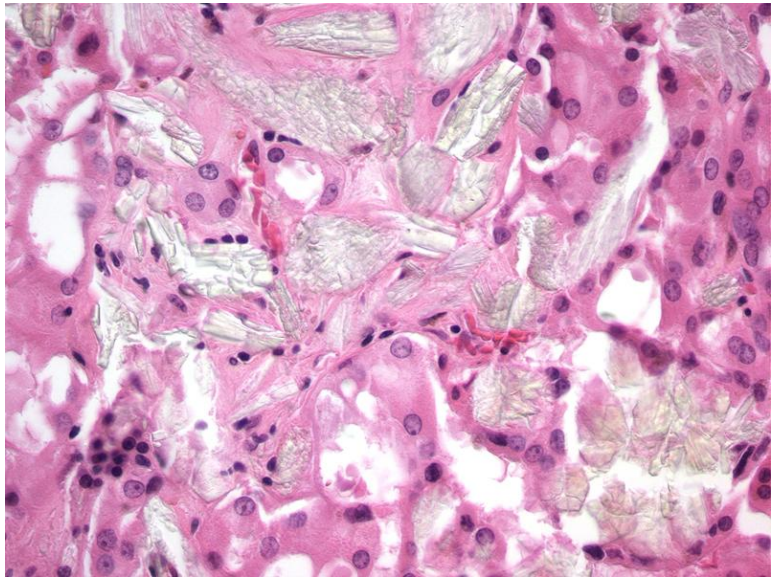


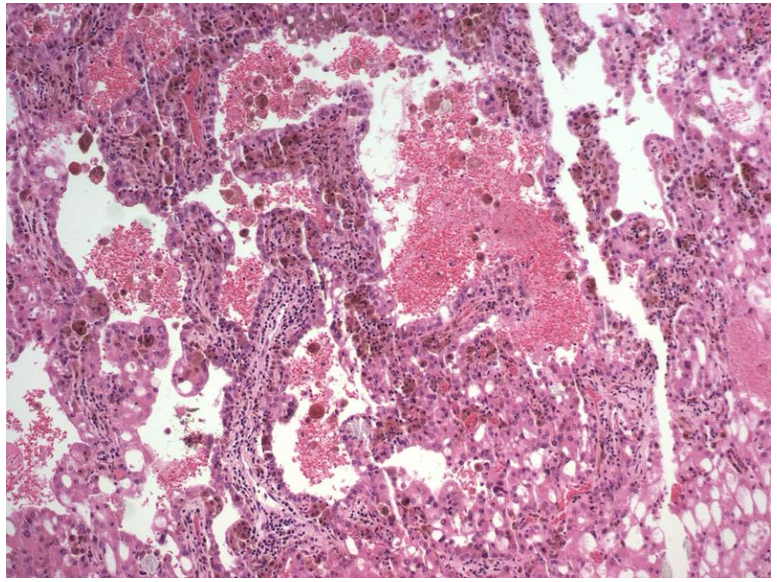


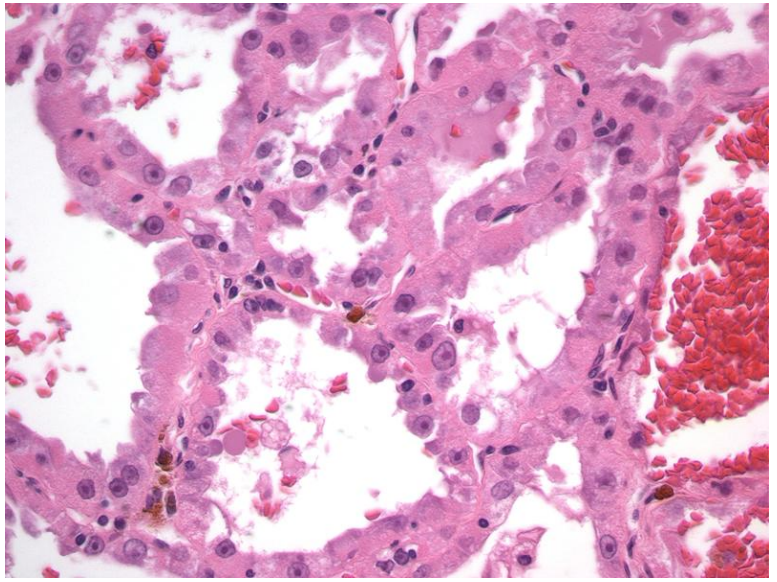
ACQUIRED CYSTIC DISEASE-ASSOCIATED RCC

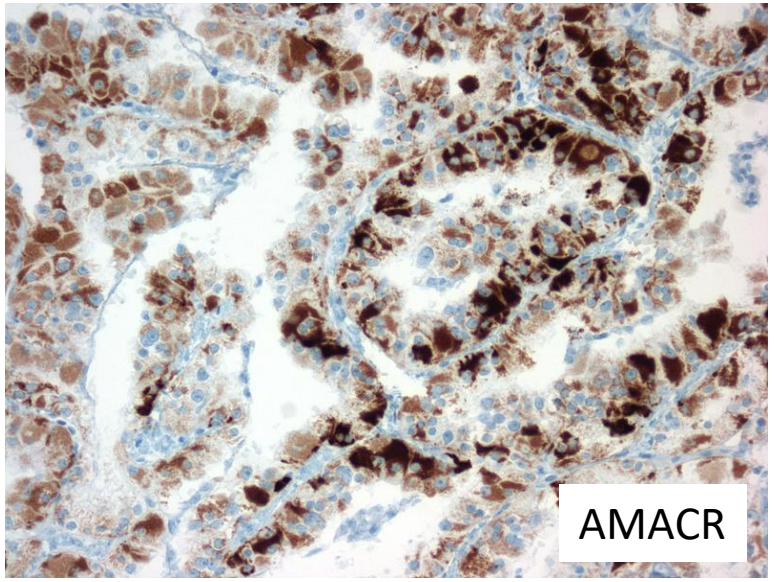




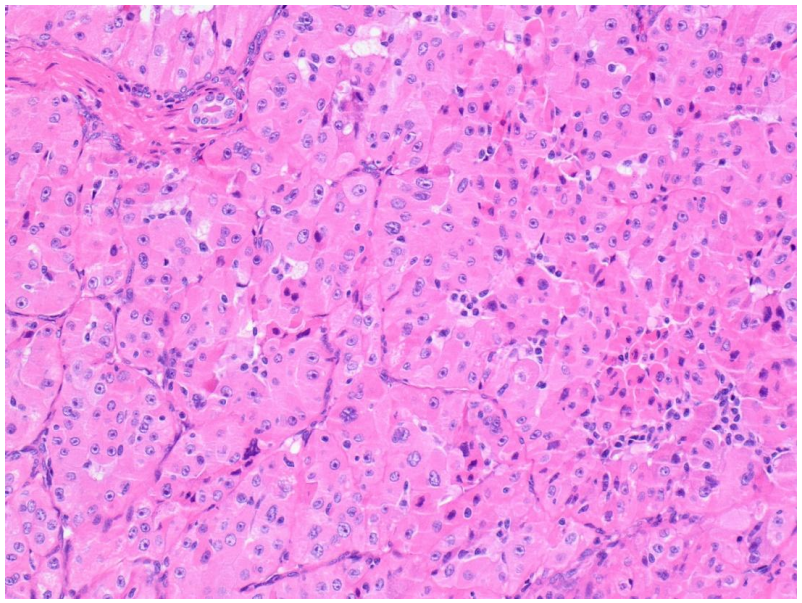


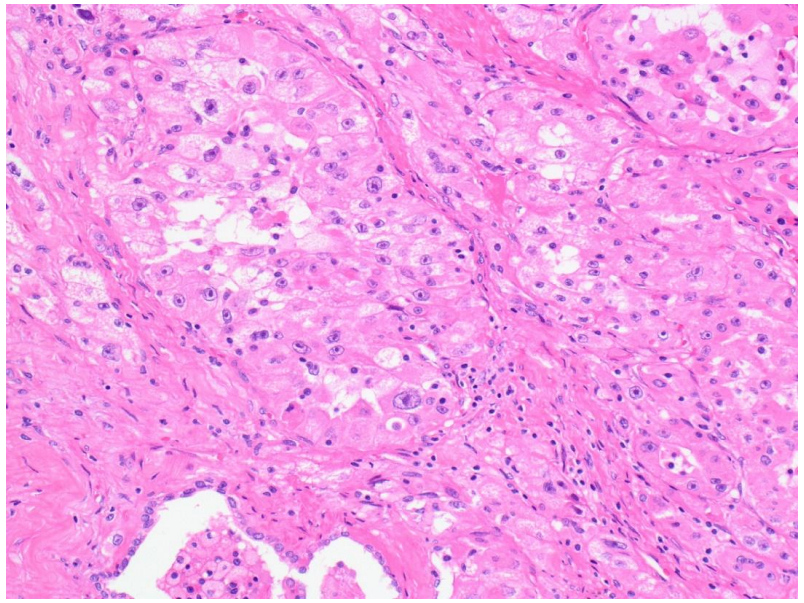


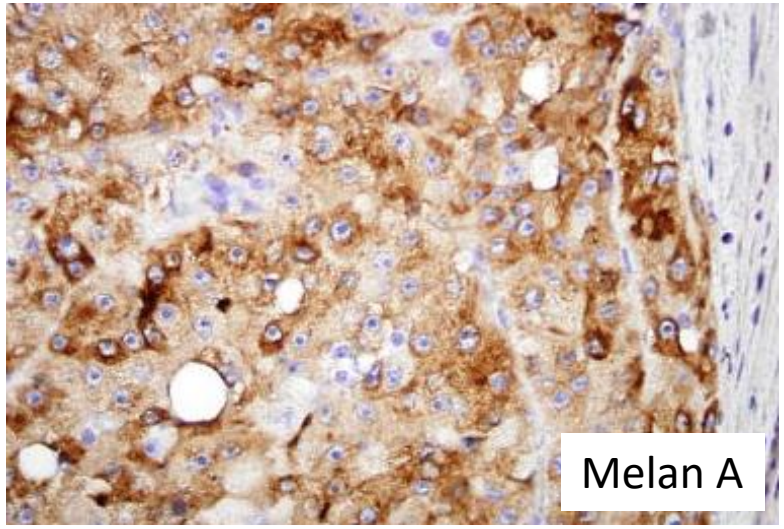


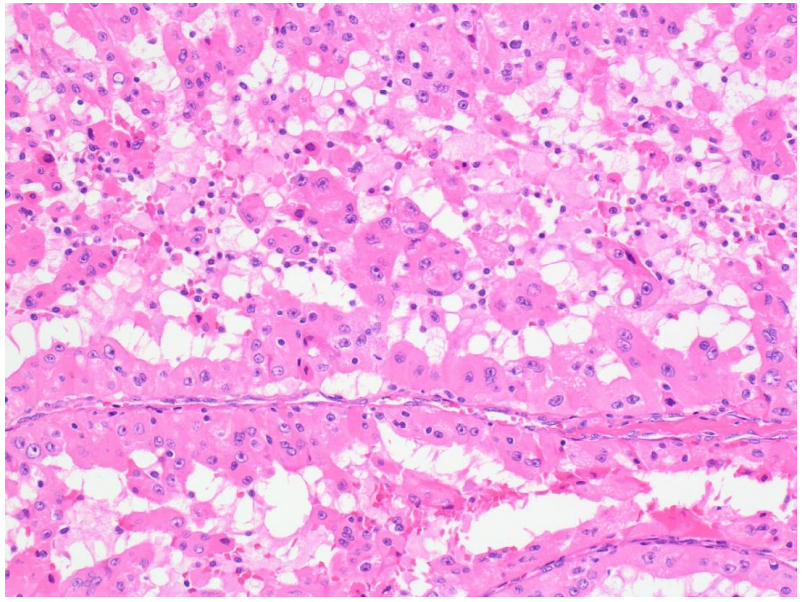


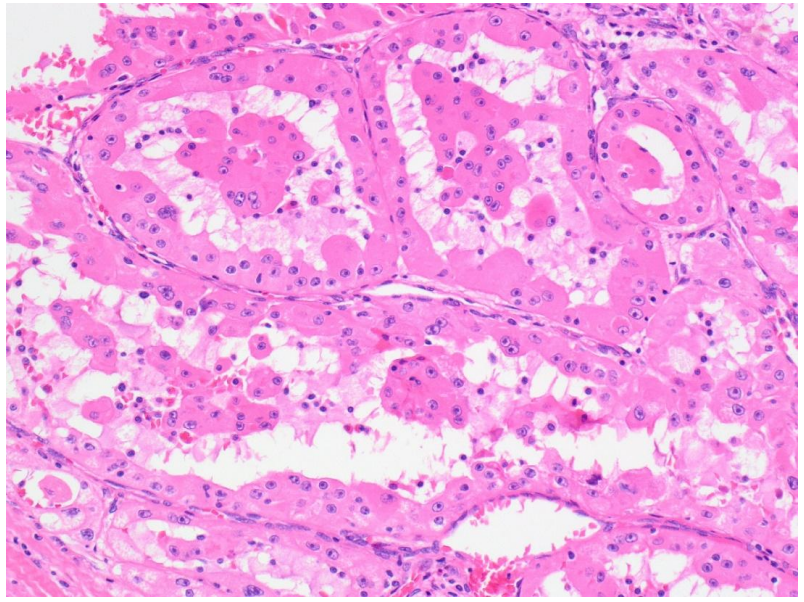
TFEB AMPLIFIED RENAL CELL CARCINOMA

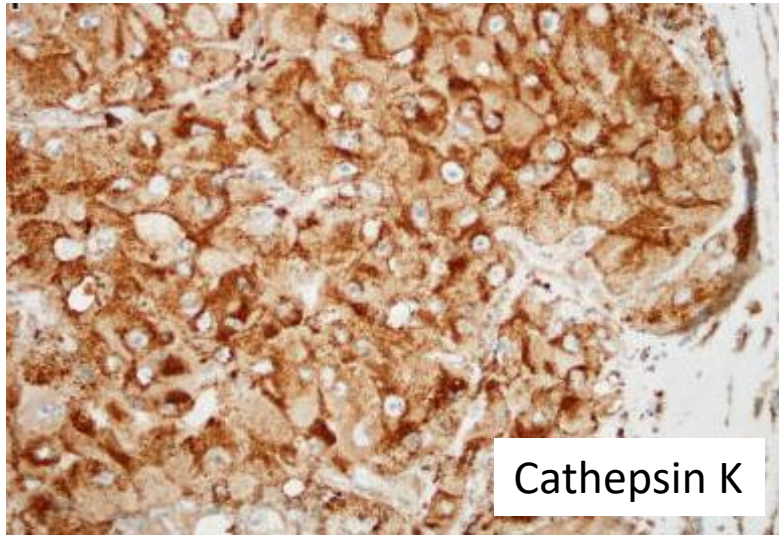




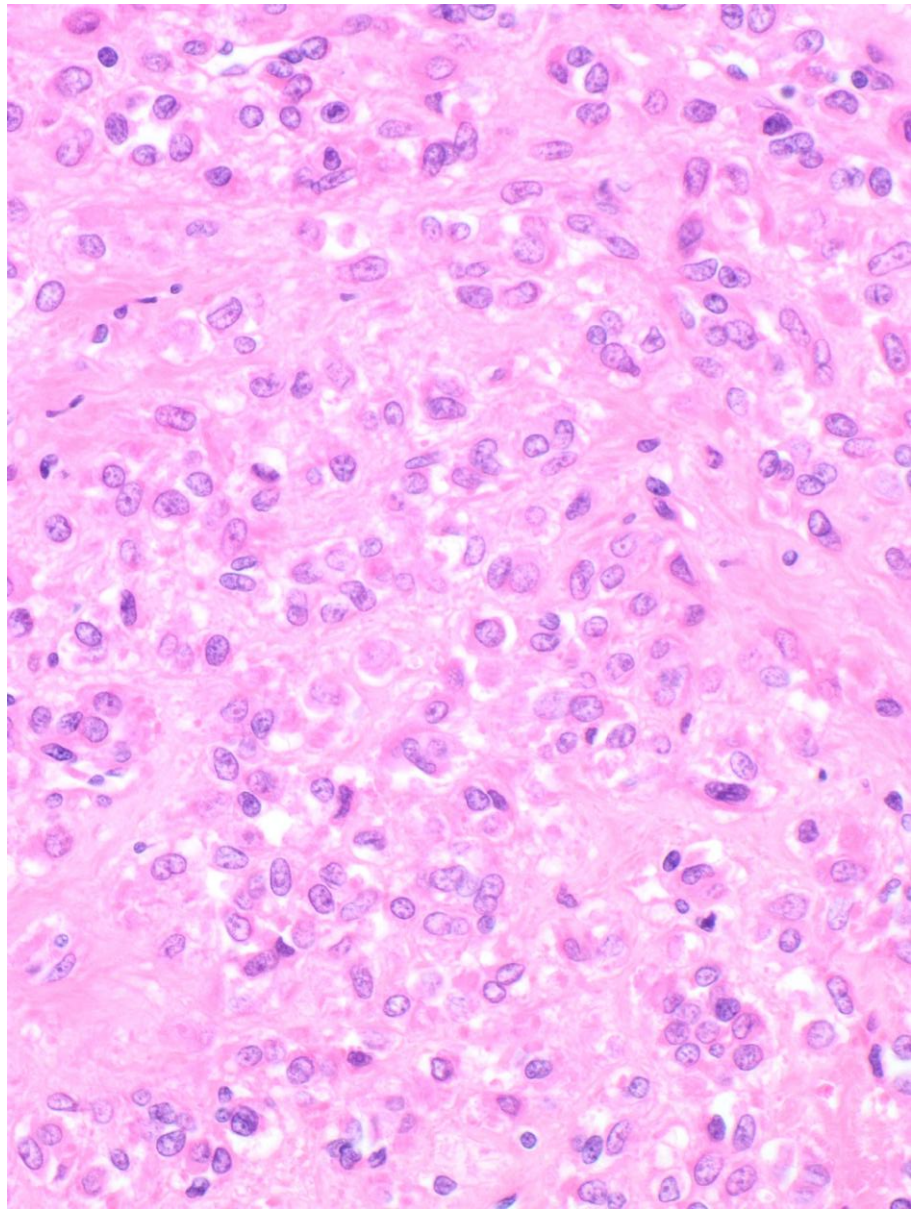


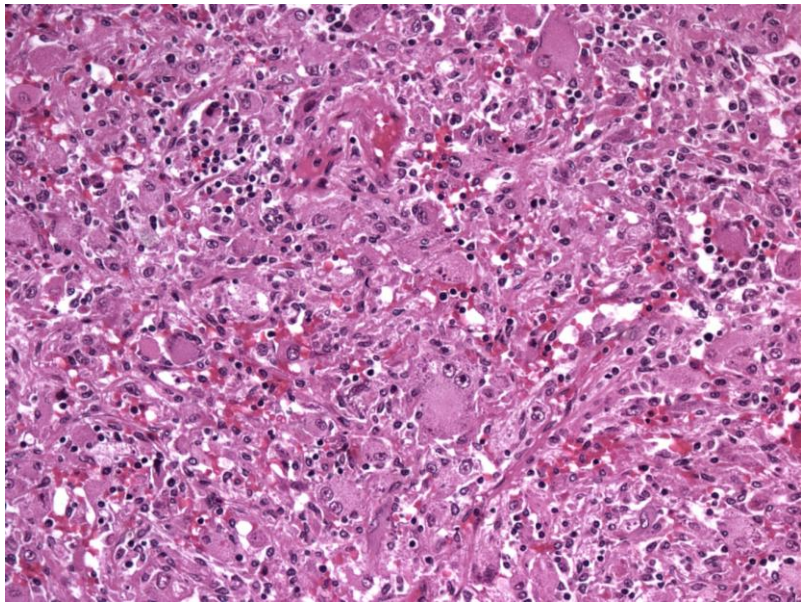


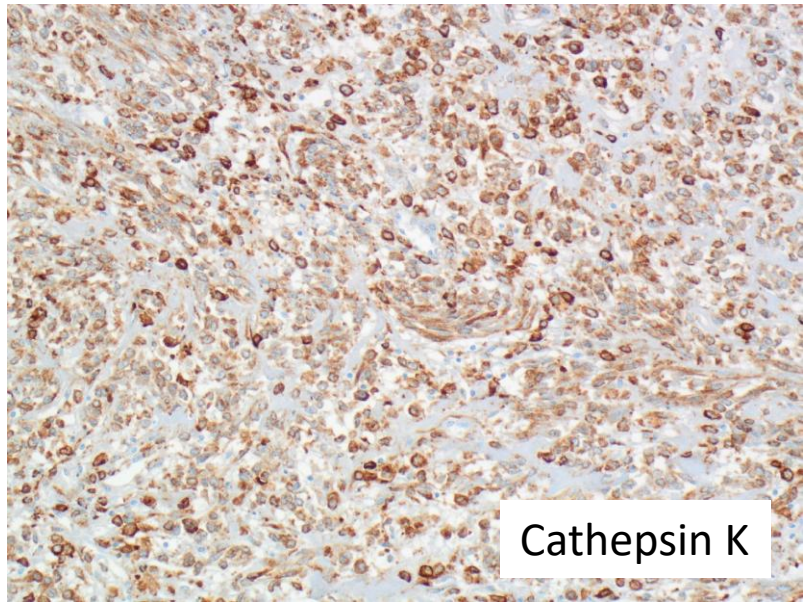


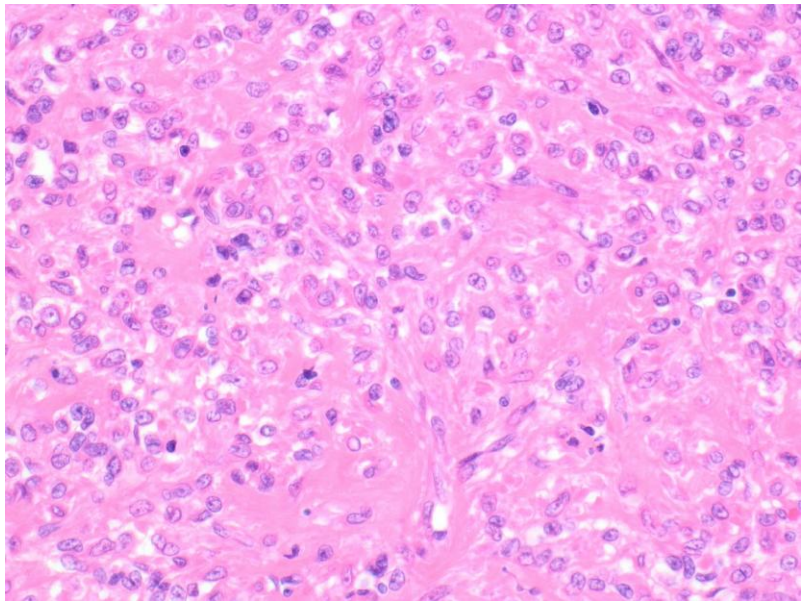


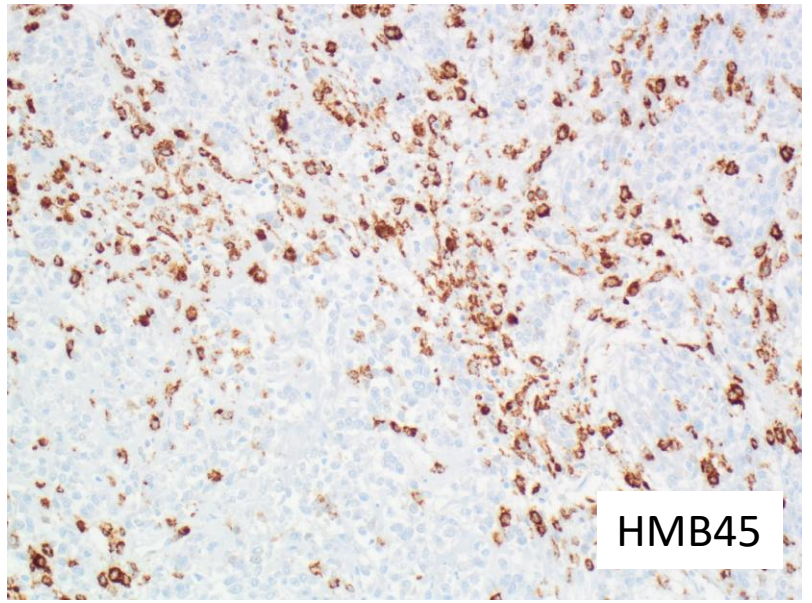
EPITHELIOID ANGIOMYOLIPOMA



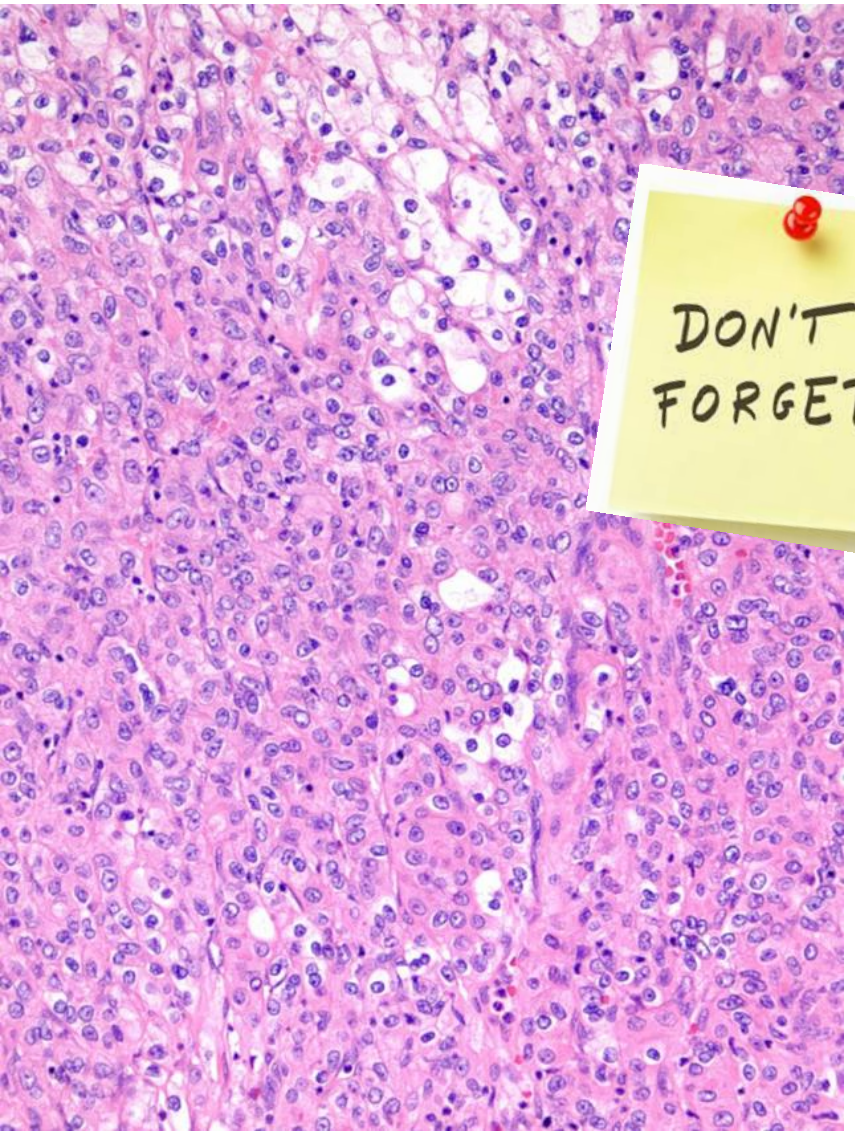


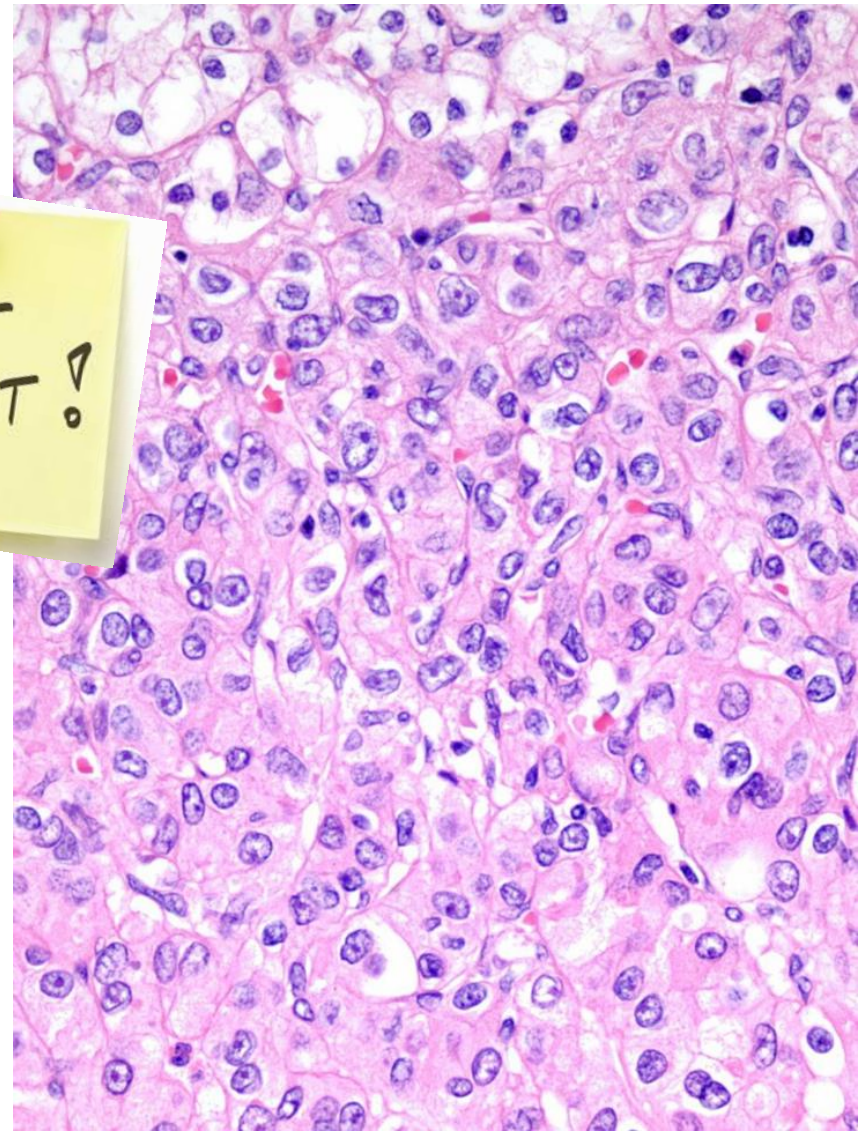


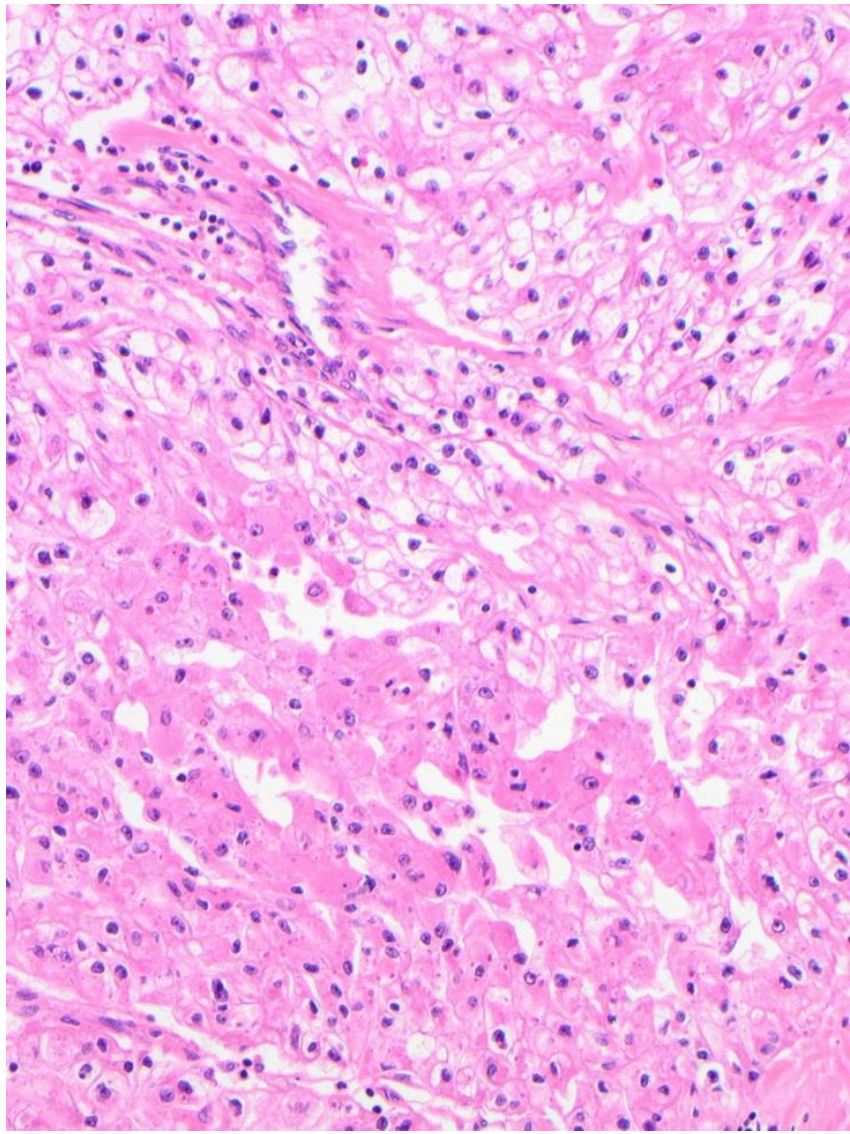




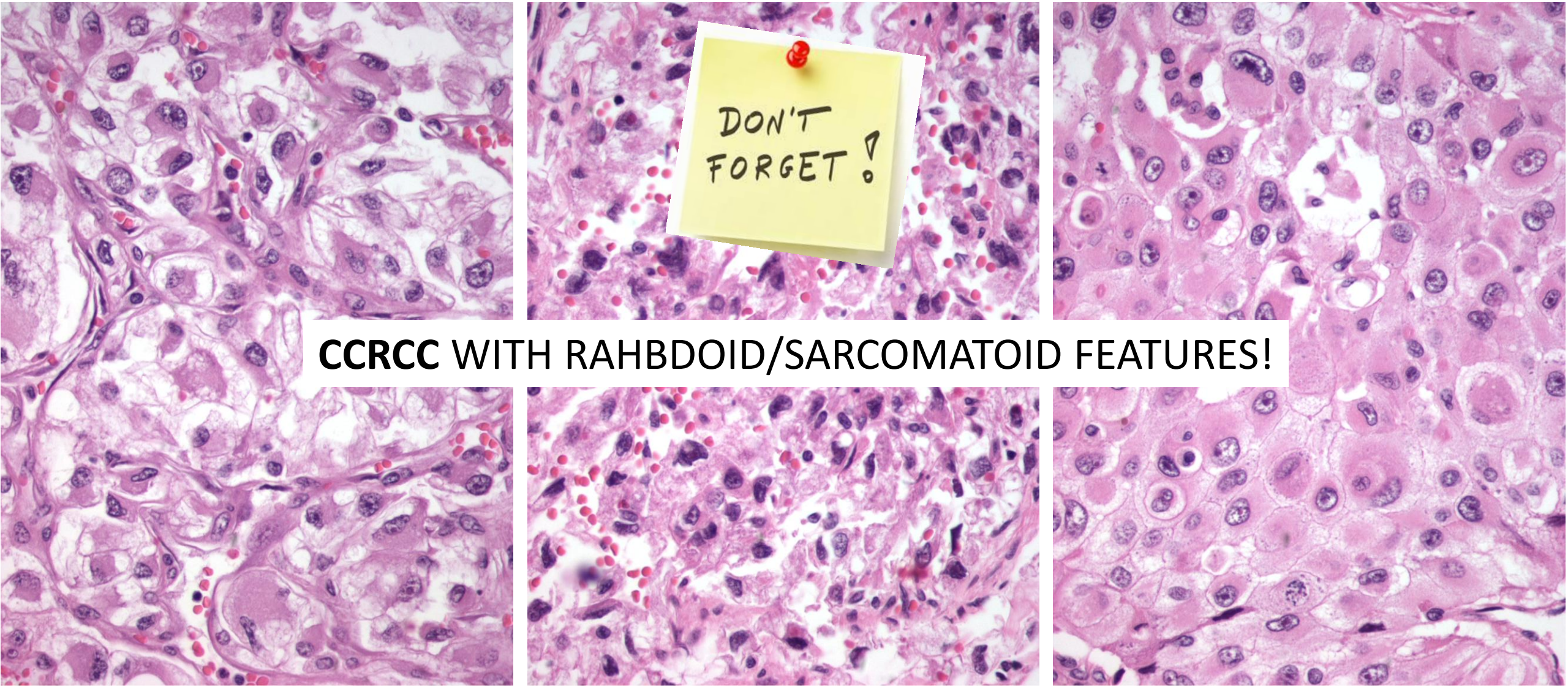
EOSINOPHILIC CLEAR CELL RENAL CELL CARCINOMA





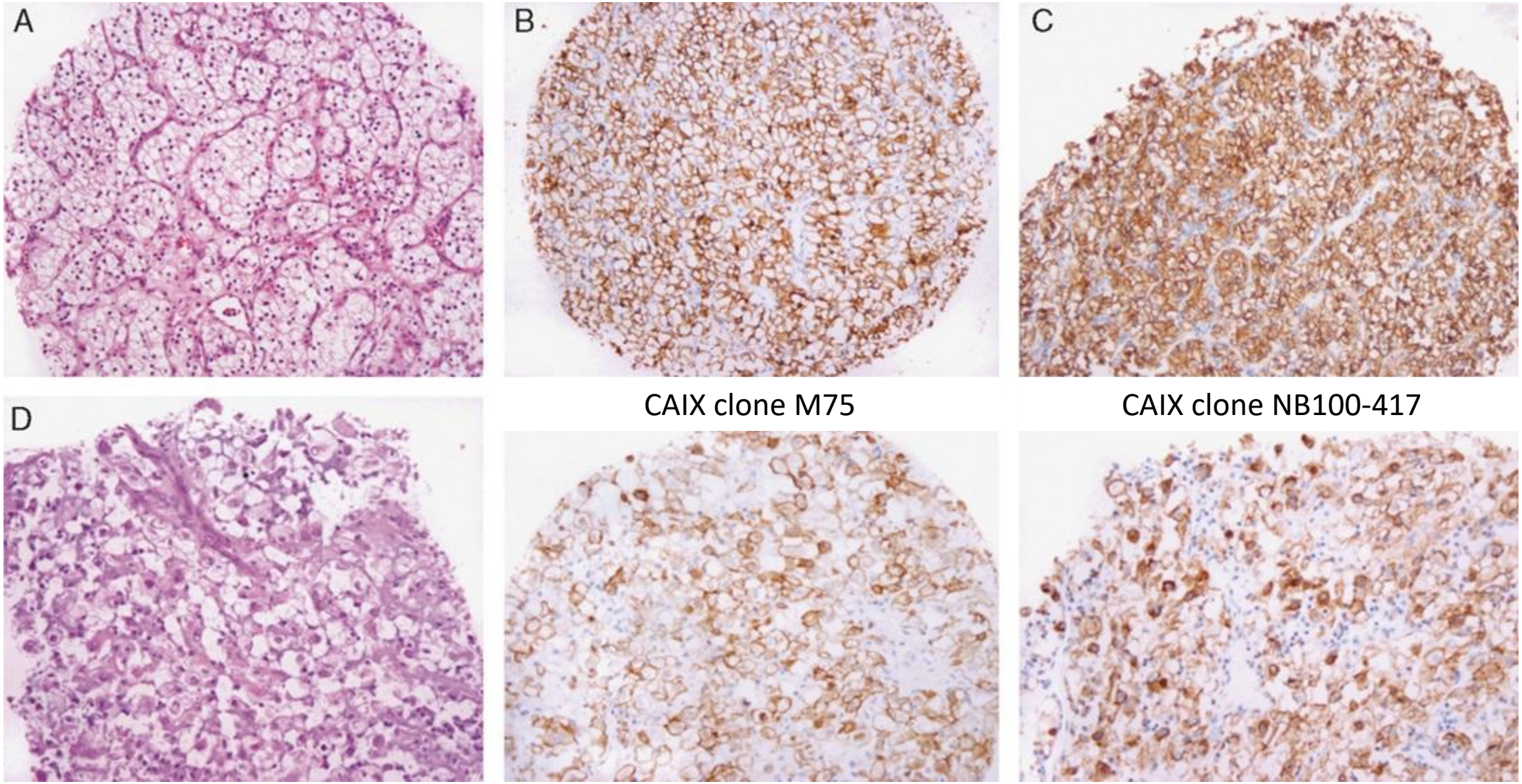


EOSINOPHILIC CLEAR CELL RENAL CELL CARCINOMA



CCRCC WITH RAHBDOID/SARCOMATOID FEATURES!

CAIX expression in Clear Cell Renal Cell Carcinoma



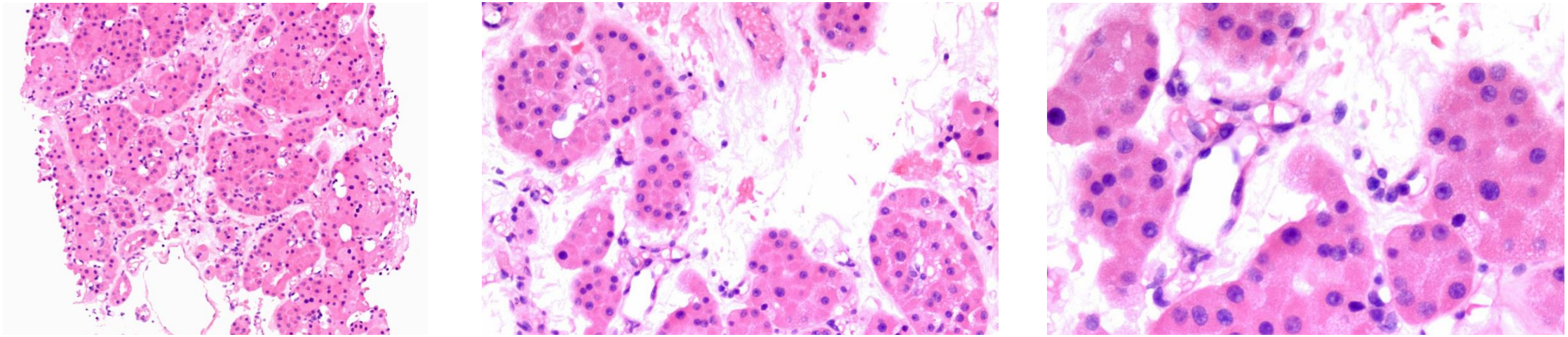
Al-Ahmadie et al. Am J Surg Pathol 2008

RENAL TUMOR WITH EOSINOPHILIC CYTOPLASM

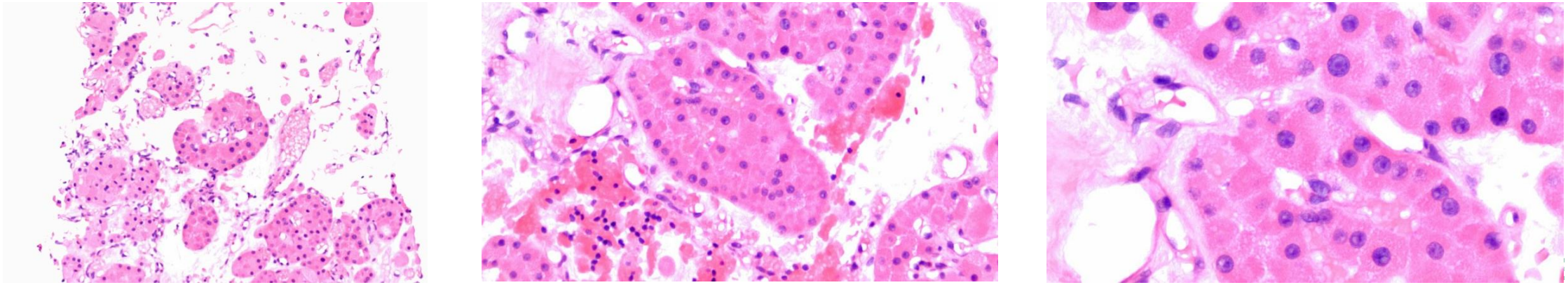
Tumor type	CK7	CD117	CK20	GATA3	Cathepsin K	Vimentin	HMB45/Melan A	SDHB
Oncocytoma	**-/+**	**+**		-	-	-/+		+
Hybrid oncocytic tumor	-/+	+			+/-			+
LOT	**+**	**-**	-	+	-	-	-	+
EVT	**-/+**	**+**	-		**+/-**	-	-	+
ChRCC	**+**	**+/-**	-	-/+	-	-	-	+
ESC-RCC	-/+	-	+/-		+	+	-/+	+
SDH-deficient RCC	-	-	-					**-**
ACD-RCC	**-**	**-**	**-**	**-**				+
TFEB amplified					+/-	+	+	+
Epithelioid AML	-	-	-	-	+	+	+	+

RENAL TUMORS ON NEEDLE BIOPSY

Multiple R renal masses in a 62 year-old gentleman

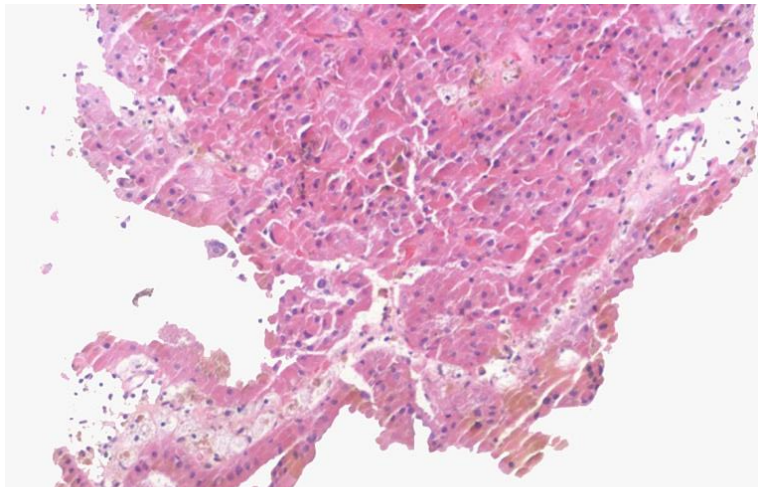
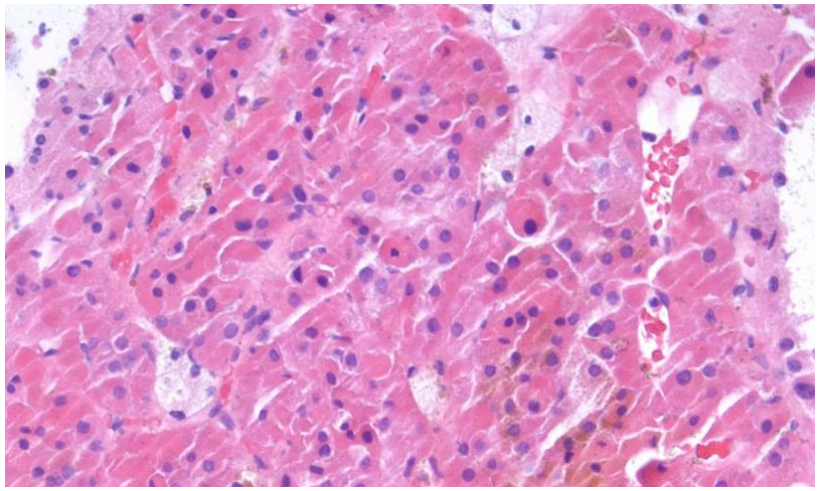
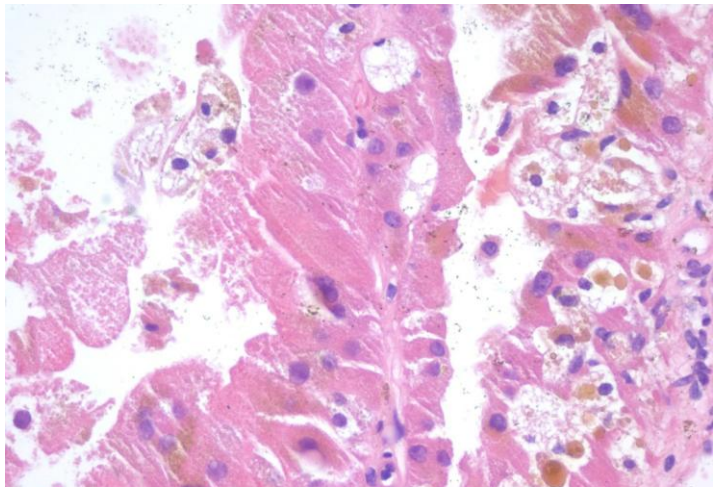


Oncocytic renal neoplasm of low malignant potential (ORNLMP)

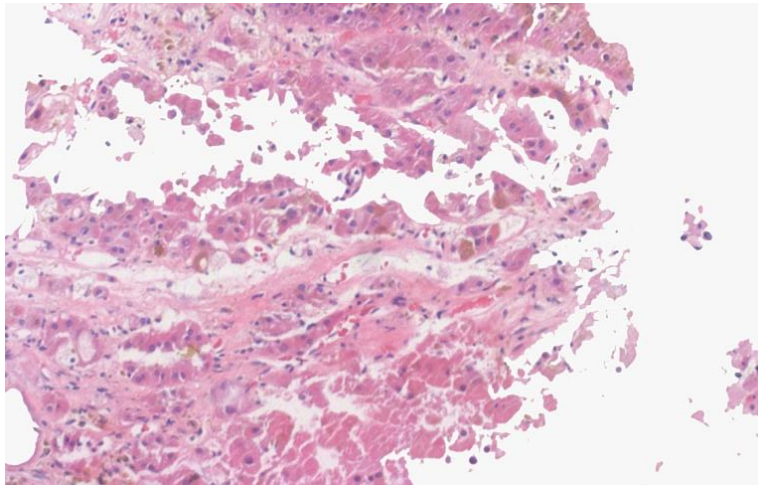
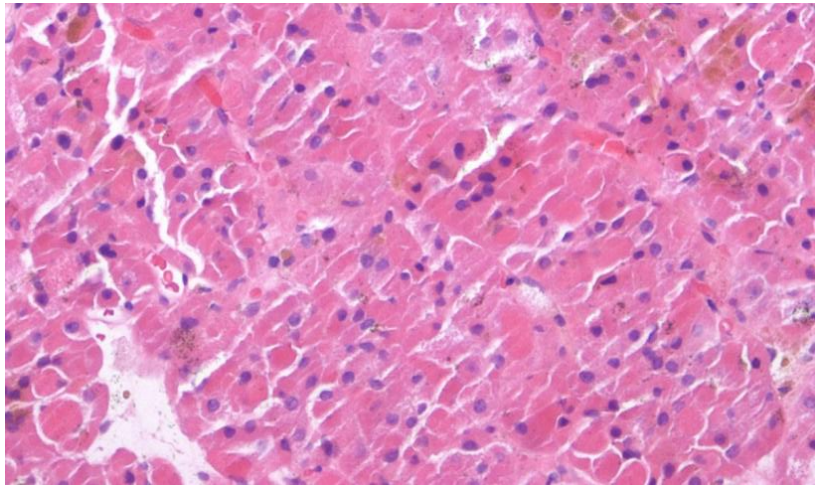
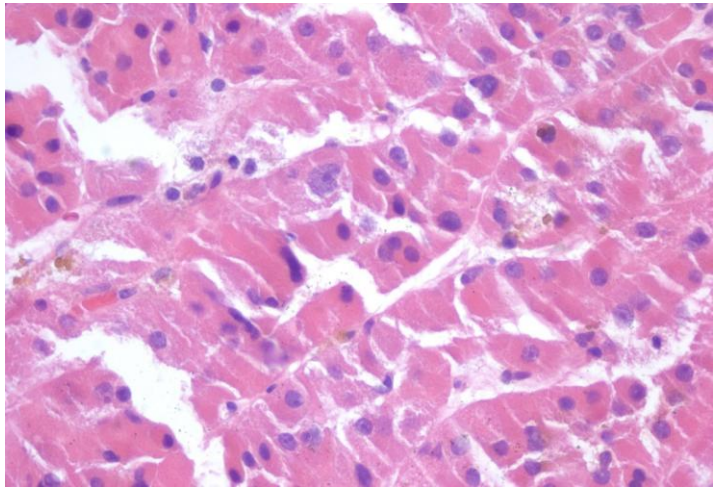


RENAL TUMORS ON NEEDLE BIOPSY

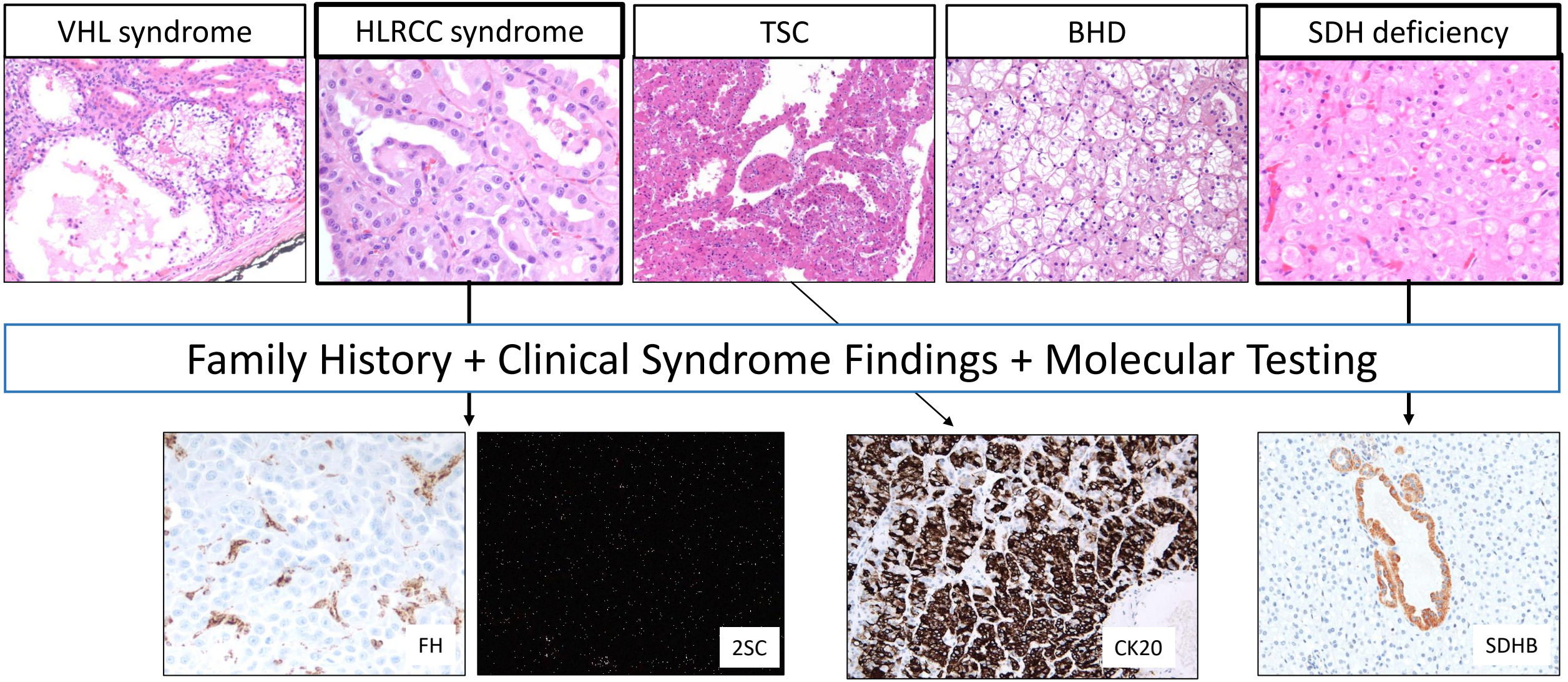
L renal mass in a 73 year-old gentleman

Renal cell carcinoma with eosinophilic features

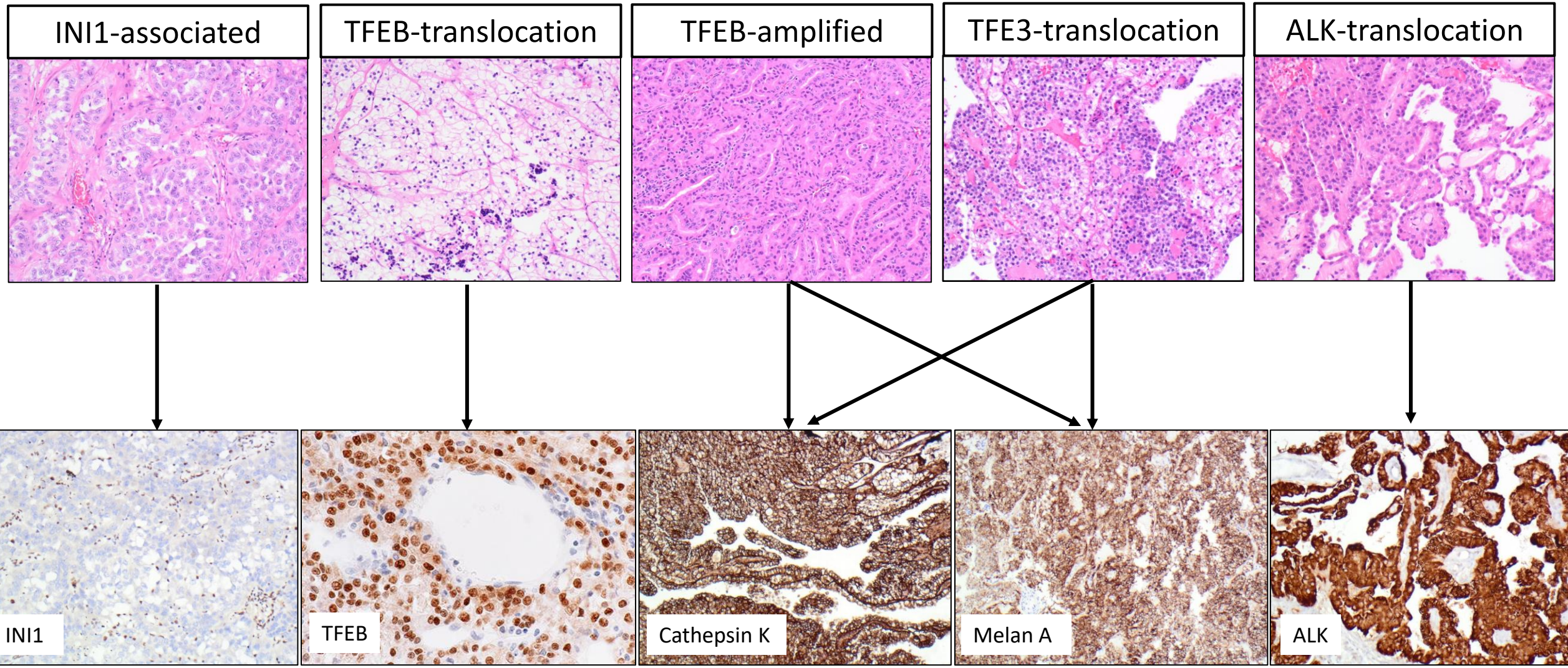




Hereditary Renal Tumors – Tissue Biomarkers

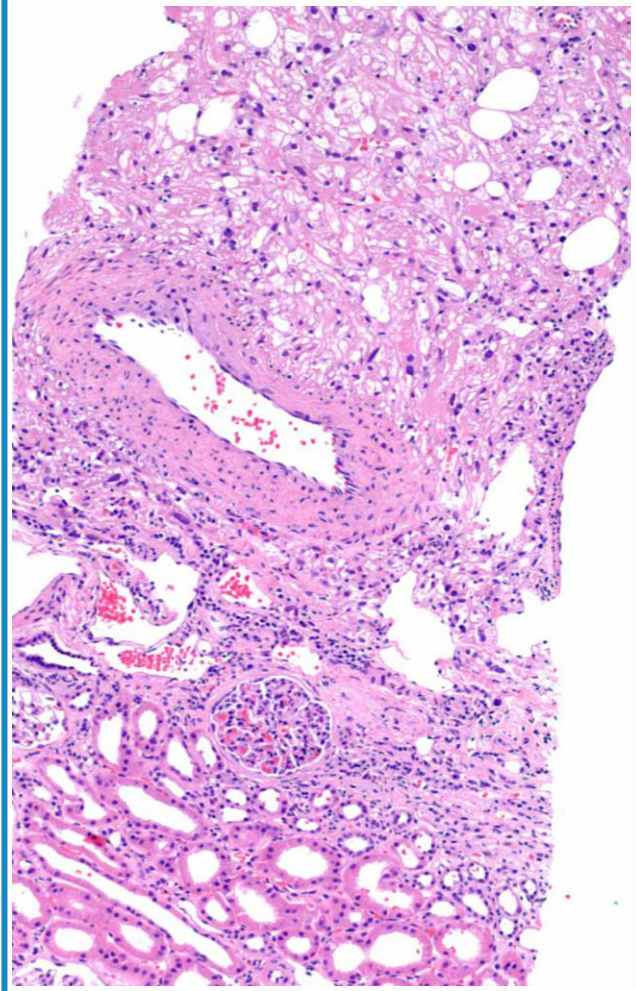


FH= fumarate hydratase; 2SC=2-succinocysteine; SDHB=succinate dehydrogenase B

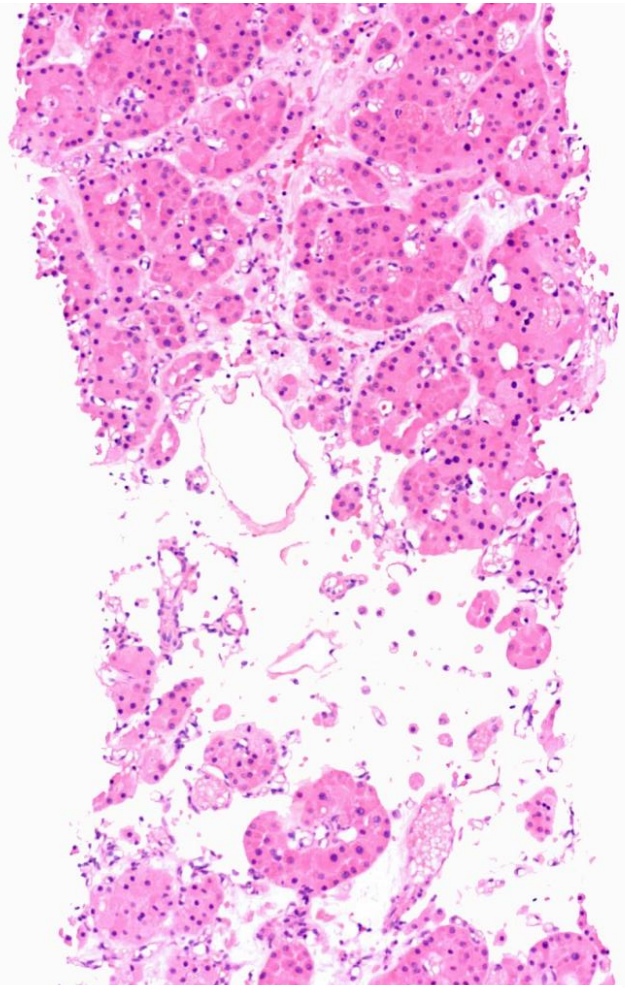
Molecularly Defined Renal Tumors – Tissue Biomarkers



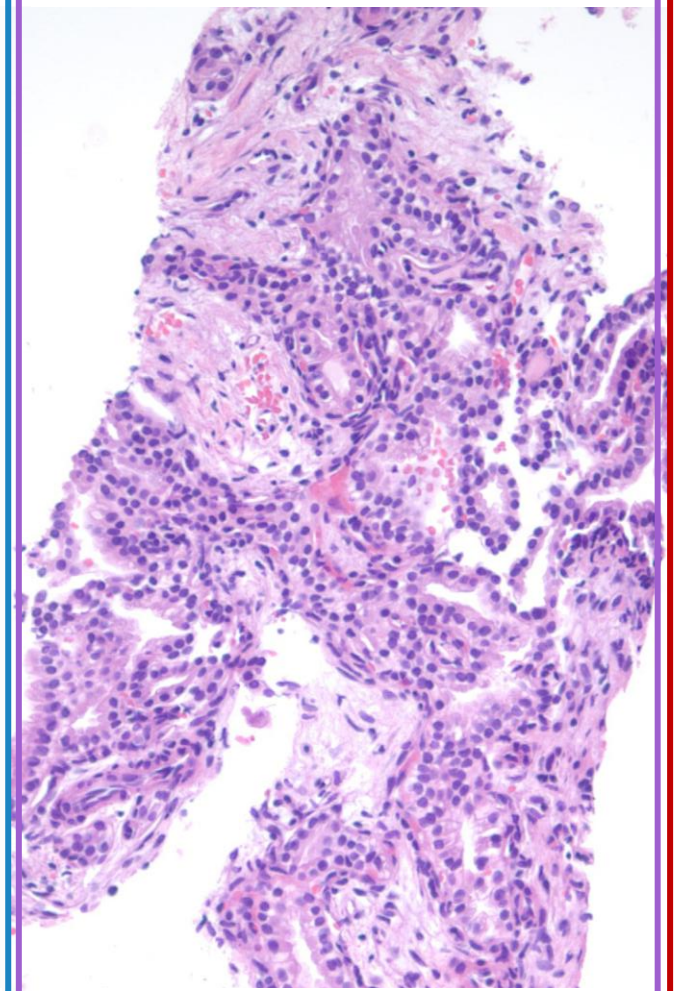
RENAL TUMORS ON NEEDLE BIOPSY



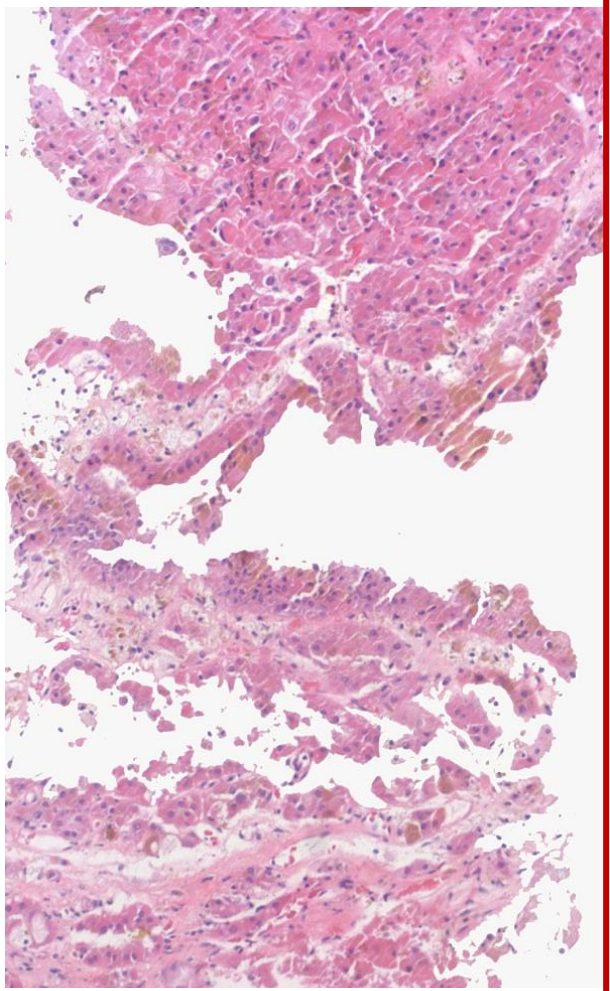
Angiomyolipoma



ORNLMP

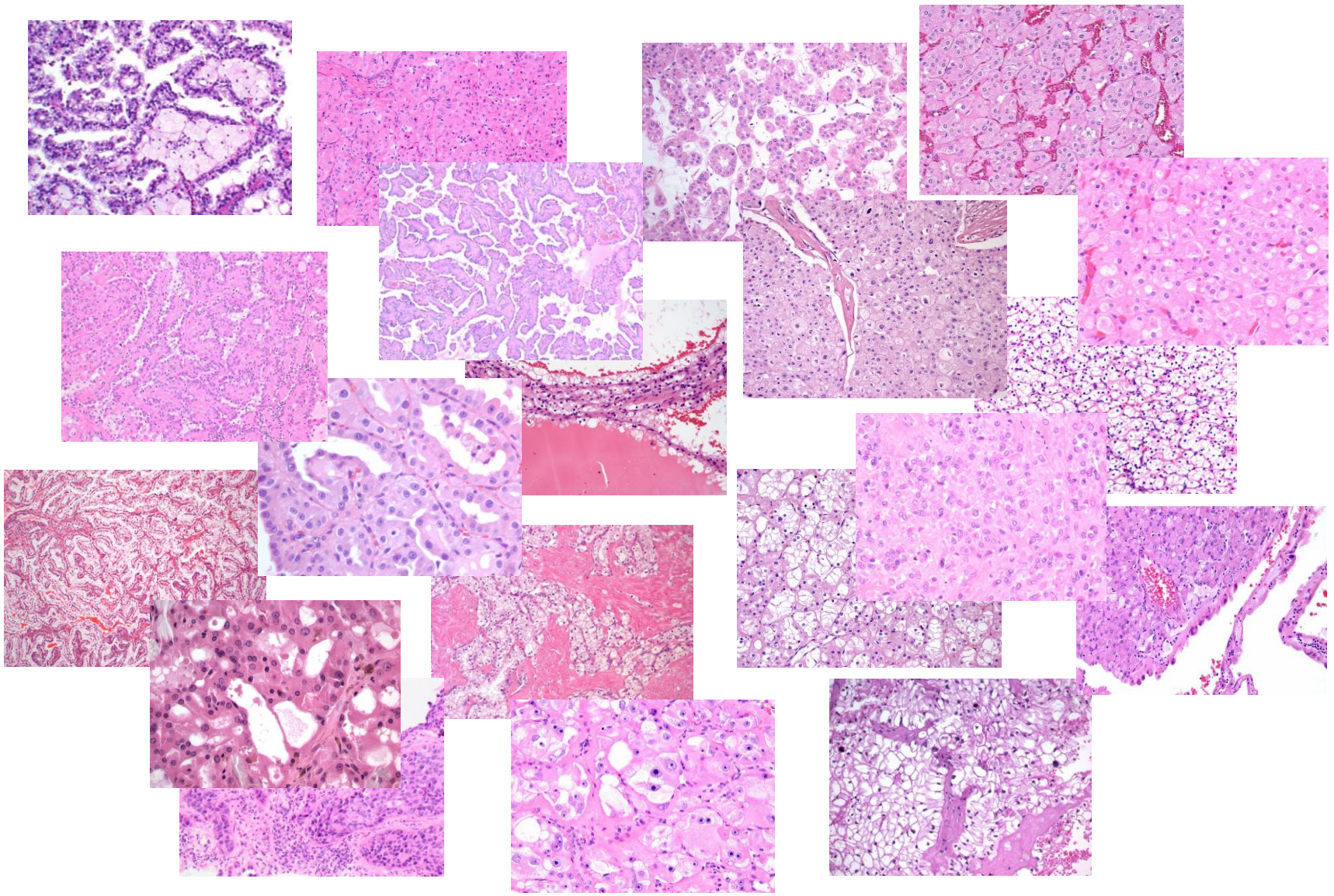


Clear cell papillary tumor ?



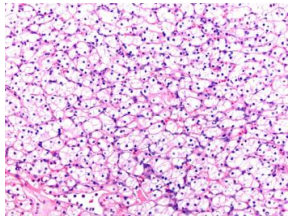
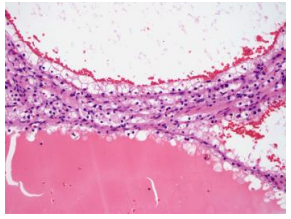
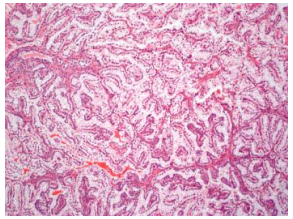
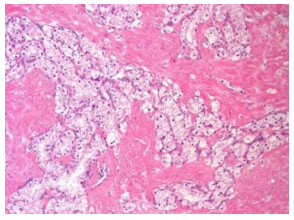
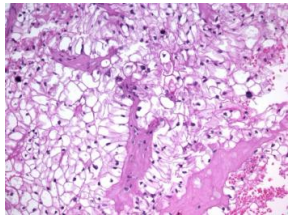
RCC with eosinophilic features

TAKE HOME POINTS

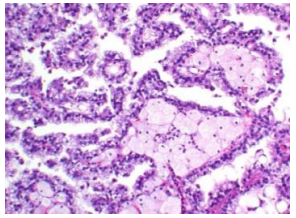
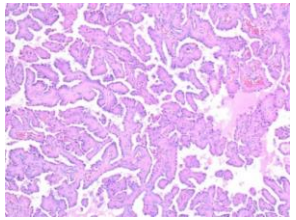
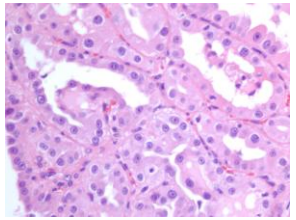
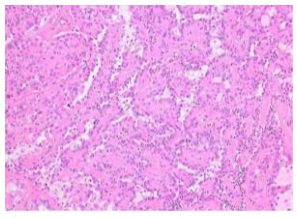
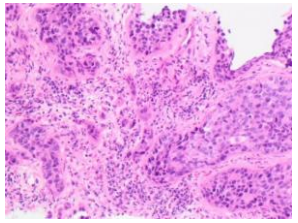


TAKE HOME POINTS

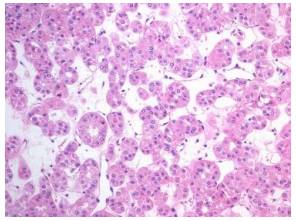
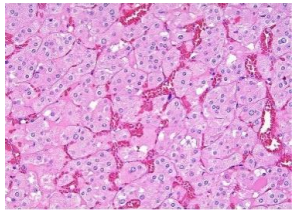
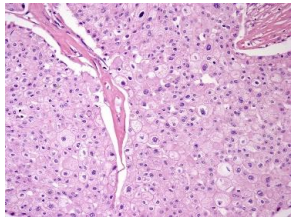
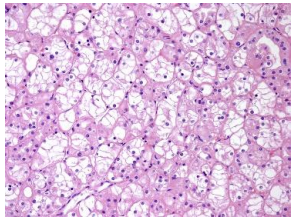
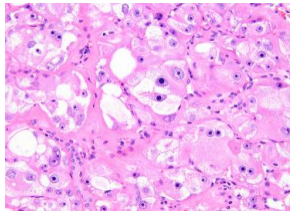
Clear cells

Papillary

Pink

- **Stay calm: common things happen commonly!**
- Review clinical history & gross appearance
- Identify predominant morphologic pattern (clear, papillary, eosinophilic….)
- Is it low-grade or high-grade?
- Exclude things you cannot afford to miss (FH-deficient, ALK, medullary, SDH-deficient, TFEB amplified) with key IHC markers

THANK YOU!

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