Società Italiana di Urologia dal 1908

L'ECCELLENZA NEL TRATTAMENTO DEI TUMORI RENALI IN ITALIA

12 Dicembre 2024

Una Hotels Decò

Via Giovanni Amendola, 57 Roma

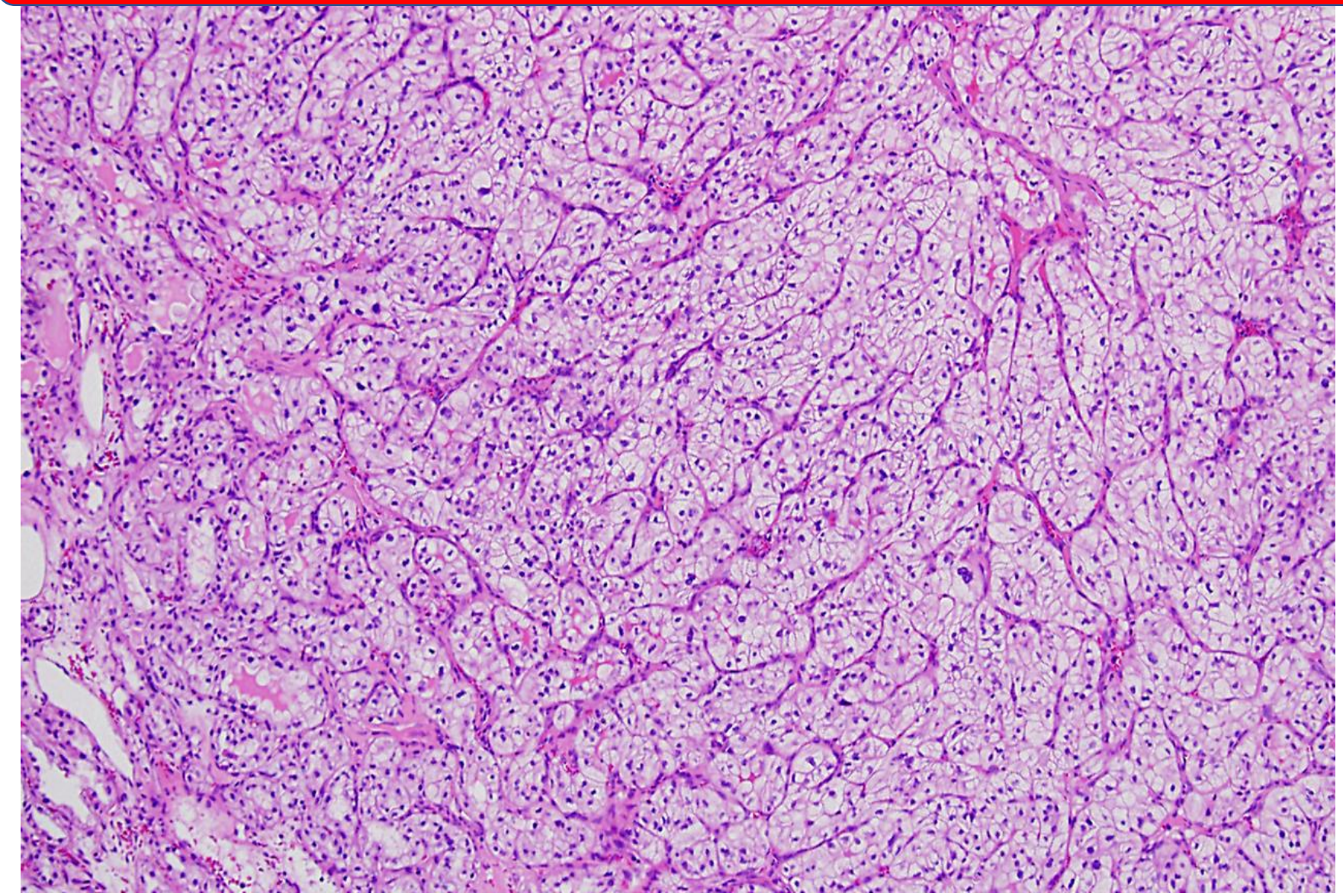
orario 10.30-17.00

12.00-12.20 Fattori prognostici moderni e tradizionali - M. Brunelli

histotyping means prognostication sec. WHO 2022
ex clear cell renal cell carcinoma
ex papillary renal cell carcinoma
ex chromophobe renal cell carcinoma, ex oncocytoma
grading, staging
molecular directions

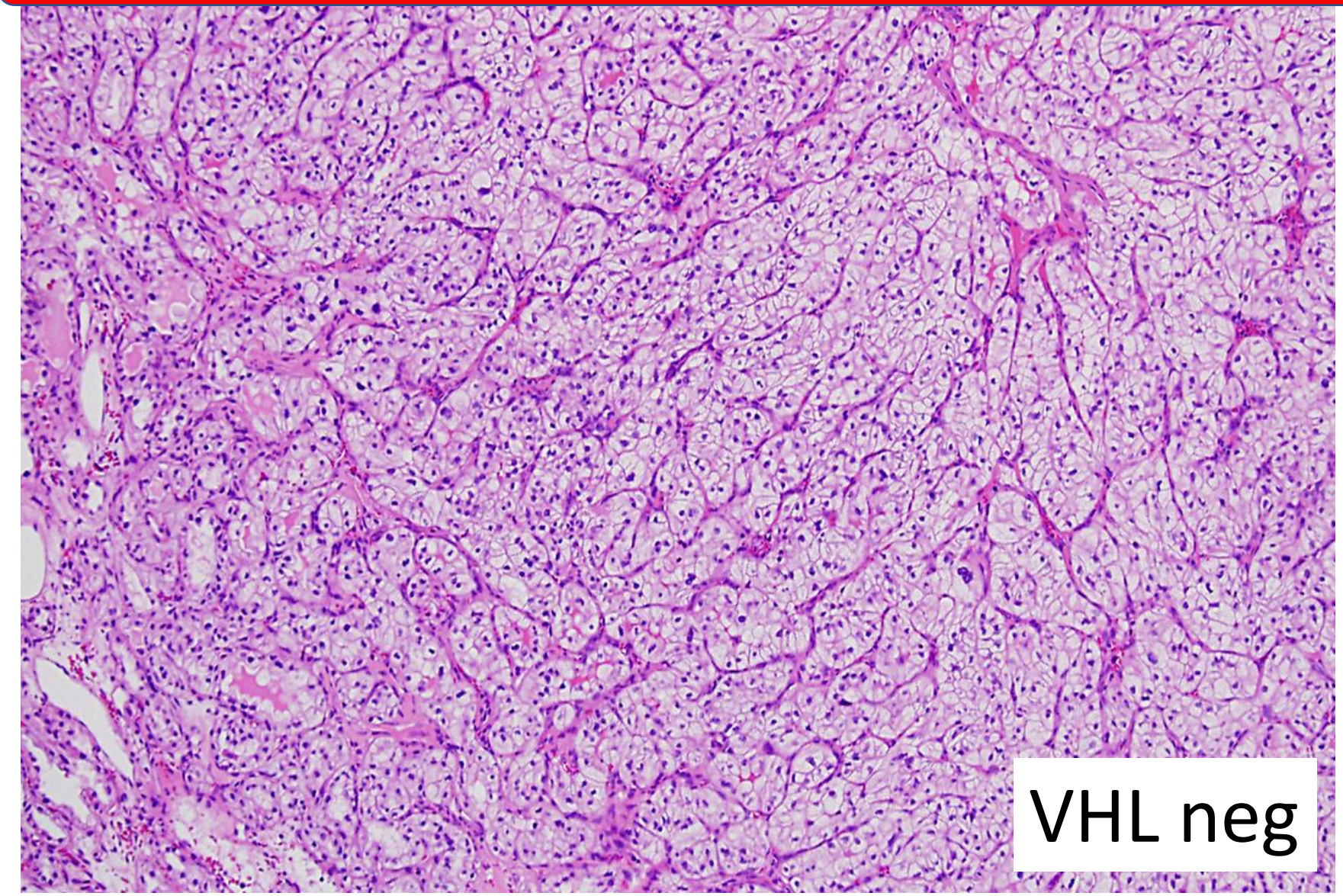
clear cell versus ex clear cell RCC

clear cell renal cell carcinoma

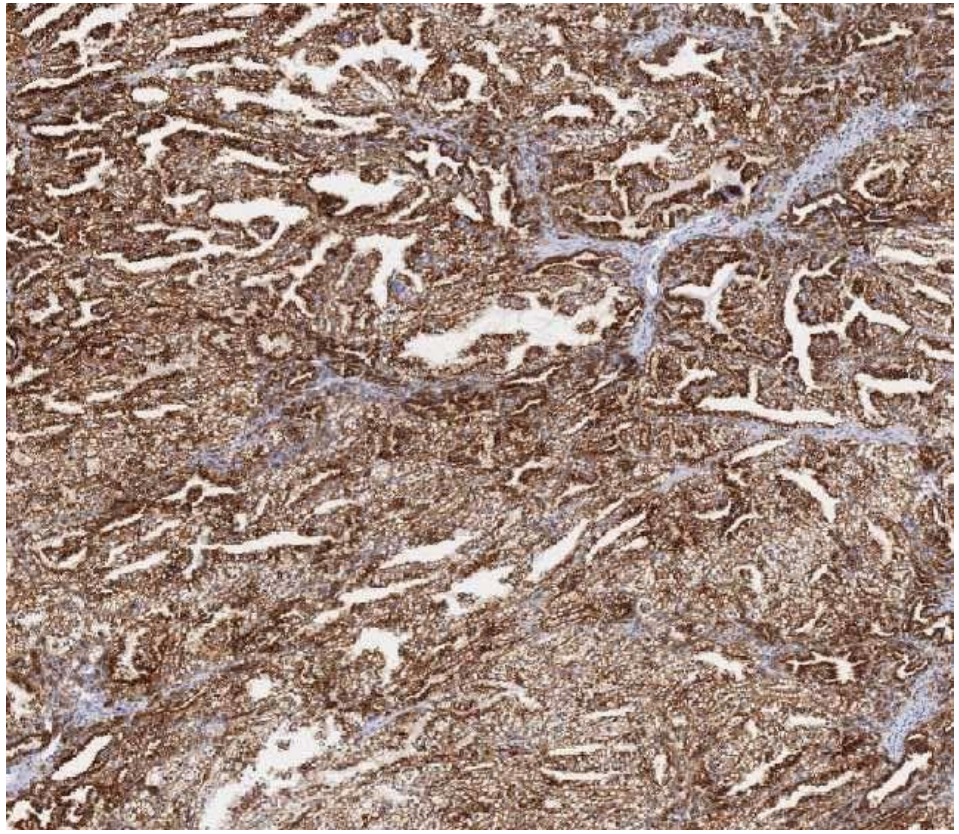


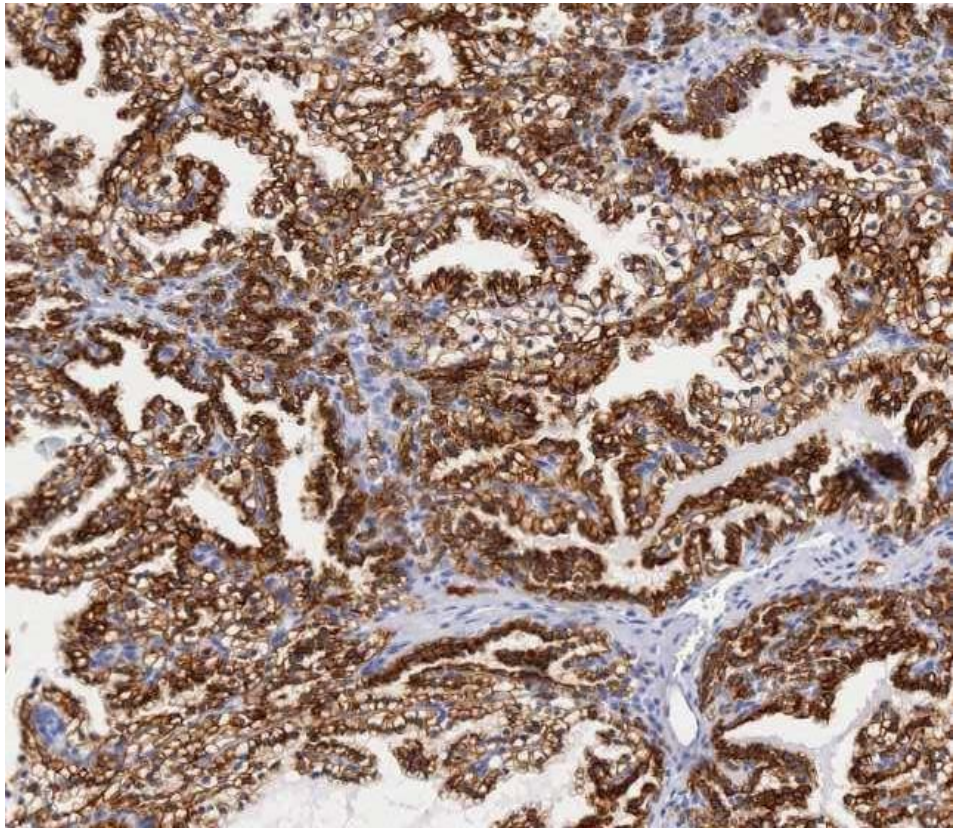
GROSS EXAMINATION

clear cell renal cell carcinoma VHL neg



CK7 diffusely immunoexpressed





WHO 2016

All without evidence of disease

Prognosis and predictive factors

For the cases reported to date, no local recurrence or metastasis has been documented {1549,2590}.

Pathol. Oncol. Res. (2018) 24:447–456
DOI 10.1007/s12253-017-0271-x

REVIEW

The Tumor Entity Denominated "*clear cell-papillary renal cell carcinoma*" According to the WHO 2016 new Classification, have the Clinical Characters of a Renal Cell Adenoma as does Harbor a Benign Outcome

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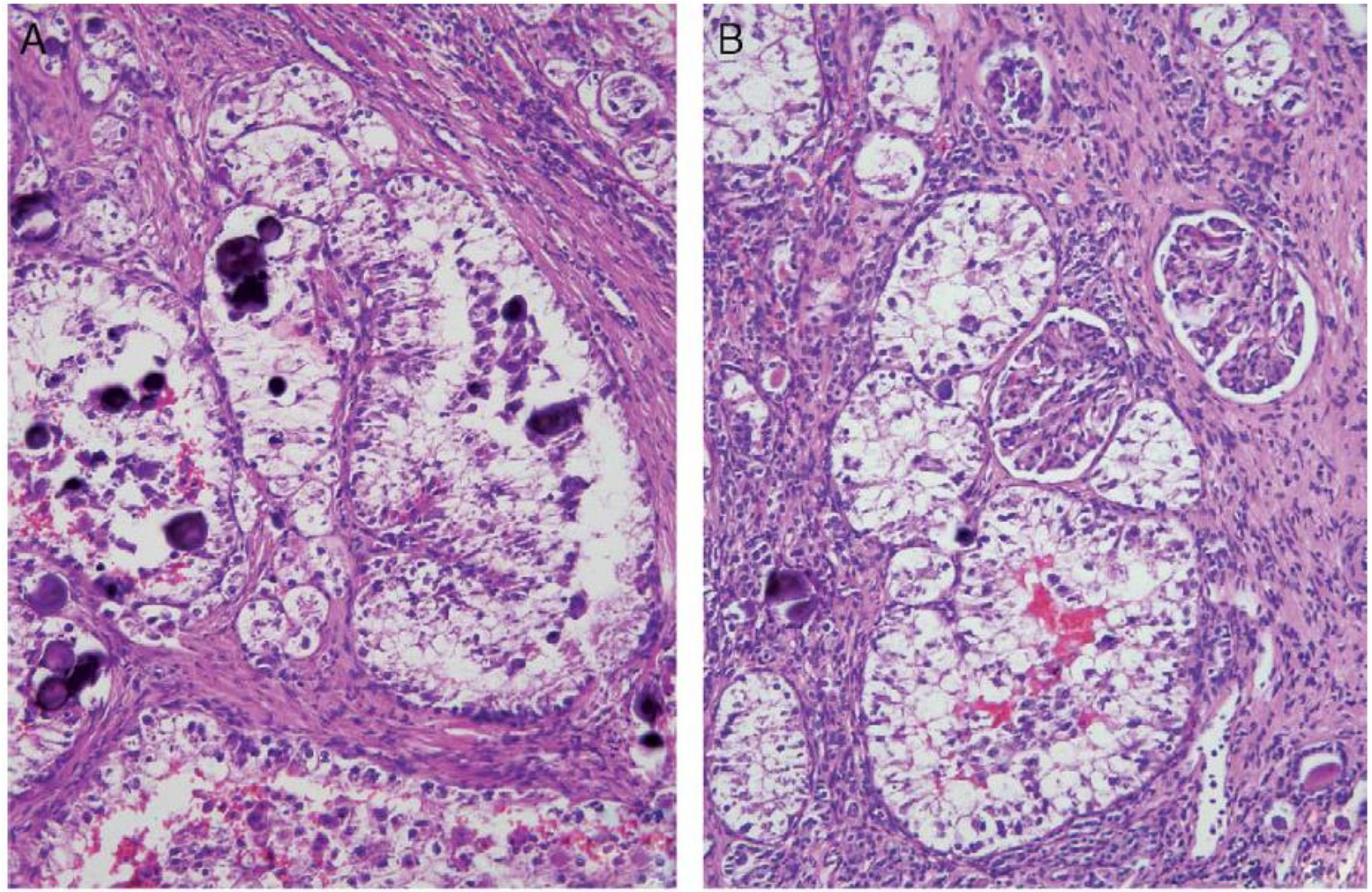
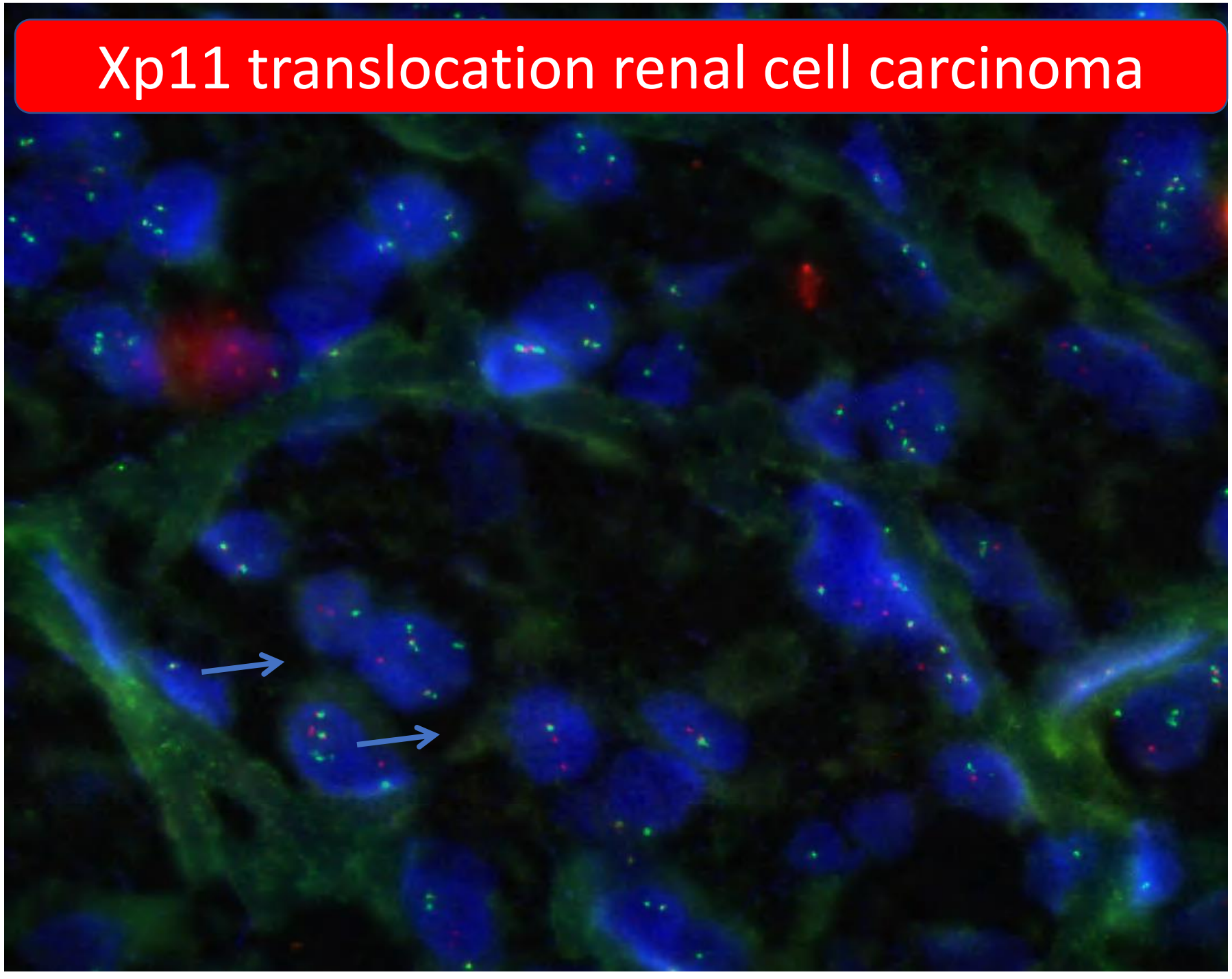
clear cell papillary renal cell tumor

clear cell versus ex clear cell RCC


A
B

Xp11 translocation renal cell carcinoma

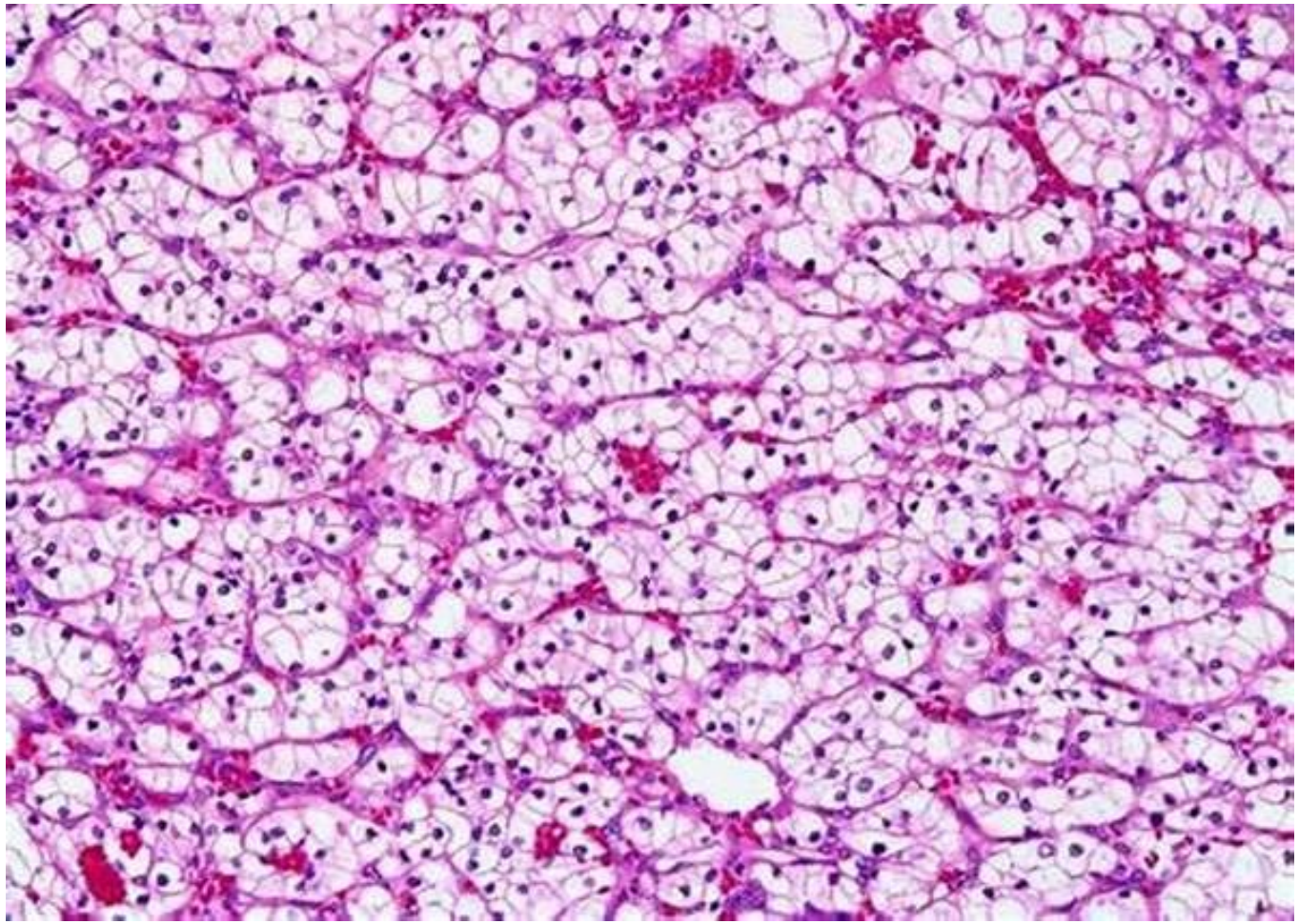


Adult Xp11 translocation renal cell carcinoma

1	68/F/R	pT1bNXMX stage I (5 cm primary)	Molecularly confirmed *ASPL-TFE3* type 1 fusion. t(X;17)(p11;q25)
2	23/F/R	pT1aNXMX stage I (2.8 cm primary)	Cytogenetically confirmed t(X;1)(p11;p34) (*PSF-TFE3* fusion)
3	28/F/R	pT3aNXMX stage III (21 cm primary)	NED 4 mo: cystic and extensively necrotic neoplasm
4	27/F/R	pT1bNXMX stage I (5.5 cm primary)	Biphasic small cell/large cell mimicking t(6;11) renal carcinoma
5	34/F/L	pT1N1M1 stage IV (6.5 cm primary, 3/4 lymph nodes positive, lung metastasis)	Probable *ASPL-TFE3* RCC
6	38/M/L	pT3bN2MX stage IV (8.3 cm primary)	DOD 3 mo; probable *ASPL-TFE3* RCC
7	29/M/?	Stage IV (spinal metastasis)	DOD 10 mo; probable *ASPL-TFE3* RCC
8	20/F/?	Stage IV (supraclavicular lymph node metastasis)	Probable *ASPL-TFE3* RCC
9	47/F/R	pT1bNxMx stage I (5 cm primary)	NA
10	78/M/L	pT3bN2MX stage IV (10 cm primary, 11/15 positive lymph nodes)	Probable *ASPL-TFE3* RCC
11	26/F/R	pT3aNXMX stage III (6 cm primary)	NA
12	37/F/?	pT1aNXMX stage I (2.8 cm primary, partial nephrectomy)	Probable *ASPL-TFE3* RCC
13	28/F/R	pT1bN2MX stage IV (5.8 cm primary, 3/8 positive lymph nodes)	NA
14	58/F/R	pT1bN2MX stage IV (4.8 cm primary, 3/6 positive lymph nodes)	Probable *ASPL-TFE3* RCC
15	63/F/R	pT1NXMX stage I (3.3 cm primary)	Favor *ASPL-TFE3* RCC. Calcified on plain film, thought to be lithiasis until contrast CT was performed; patient underwent ESWL
16	34/M/R	pT3N2MX stage IV (8.8 cm primary)	Developed epidural metastasis at 6 y; probable *ASPL-TFE3* RCC
17	22/F/R	pT1aNXMX stage I (2.1 cm primary, partial nephrectomy)	NED 6 mo
18	33/M/R	pT1bN0M1 stage IV (6.1 cm primary, spinal metastasis)	Developed liver metastasis at 1 y, alive with disease (spinal metastases); probable *ASPL-TFE3* RCC
19	25/M/L	pT2NXMX stage II (9 cm)	Hematuria
20	44/F/L	pT3bN2MX stage IV (7.5 cm primary)	NA
21	29/F/R	pT1bNXMX stage I (6 cm primary)	NA
22	27/F/R	pT2NXMX stage II (7 cm primary)	NA
23	26/F/L	pT2NOMX stage II (7.5 cm primary)	NED 3 y
24	22/F/?	pT1bN2MX stage IV (6 cm primary, 7 lymph nodes positive)	Probable *ASPL-TFE3* RCC protruded into renal pelvis, causing xanthogranulomatous pyelonephritis.
25	32/F/L	pT3aN2MX stage IV (3.5 cm primary, 3 lymph nodes positive)	Cytogenetically confirmed t(X;3)(p11;q23), morphologically similar to *ASPL-TFE3* RCC
26	77/F/L	pT1bNXMX stage I (5 cm primary)	Cystic lesion, present for 13 y by imaging, spindle cell areas
27	38/M/?	pT3N2M1 Stage IV (13 cm primary)	Metastasis to esophagus 1 y after diagnosis
28	30/F/?	pT2N1M1 stage IV (9 cm primary; adrenal, retroperitoneal, mediastinal, cervical nodal	Poor response to interleukin therapy and radiation therapy

lymph-nodal homing

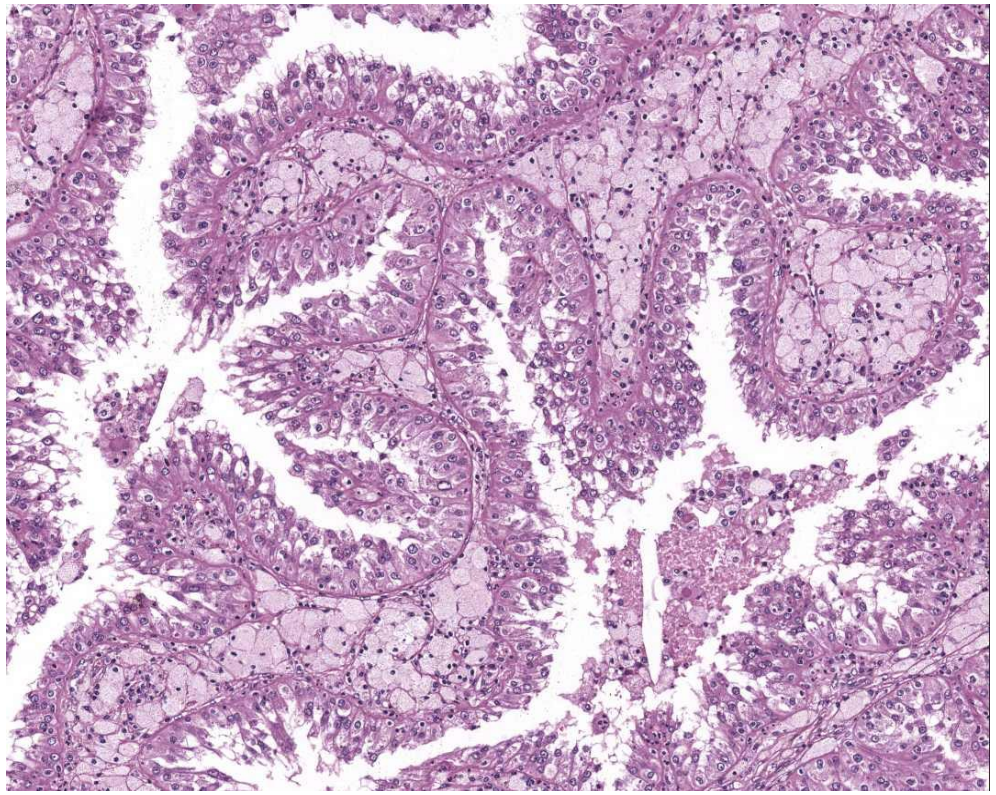
1997: clear cell renal cell carcinoma

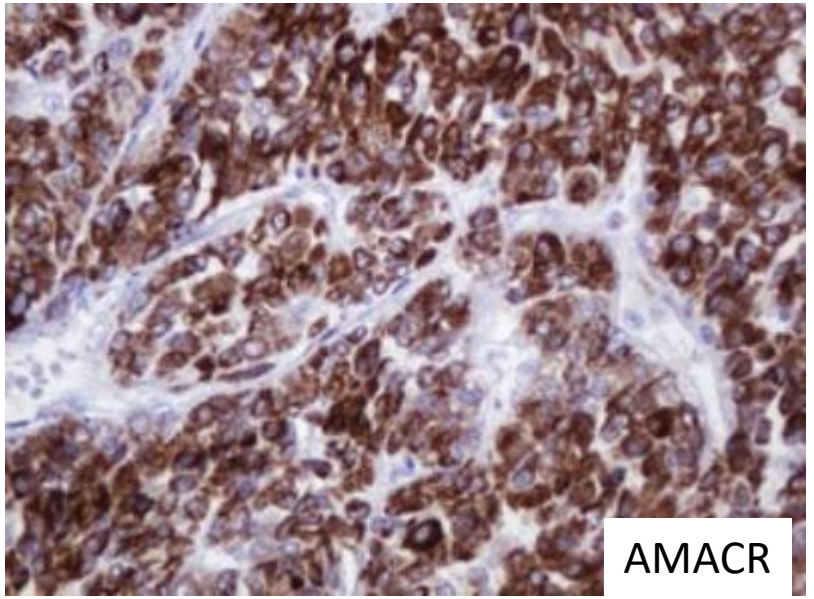


75-80% of RCCs are clear cell histotype

most VHL mutation

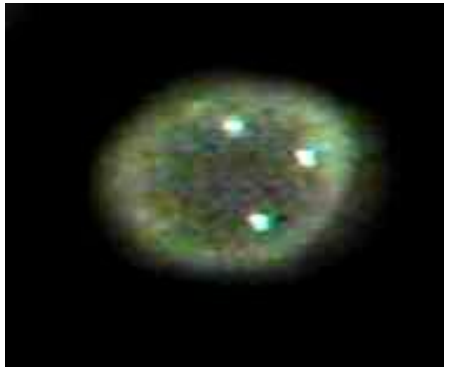
papillary renal carcinoma

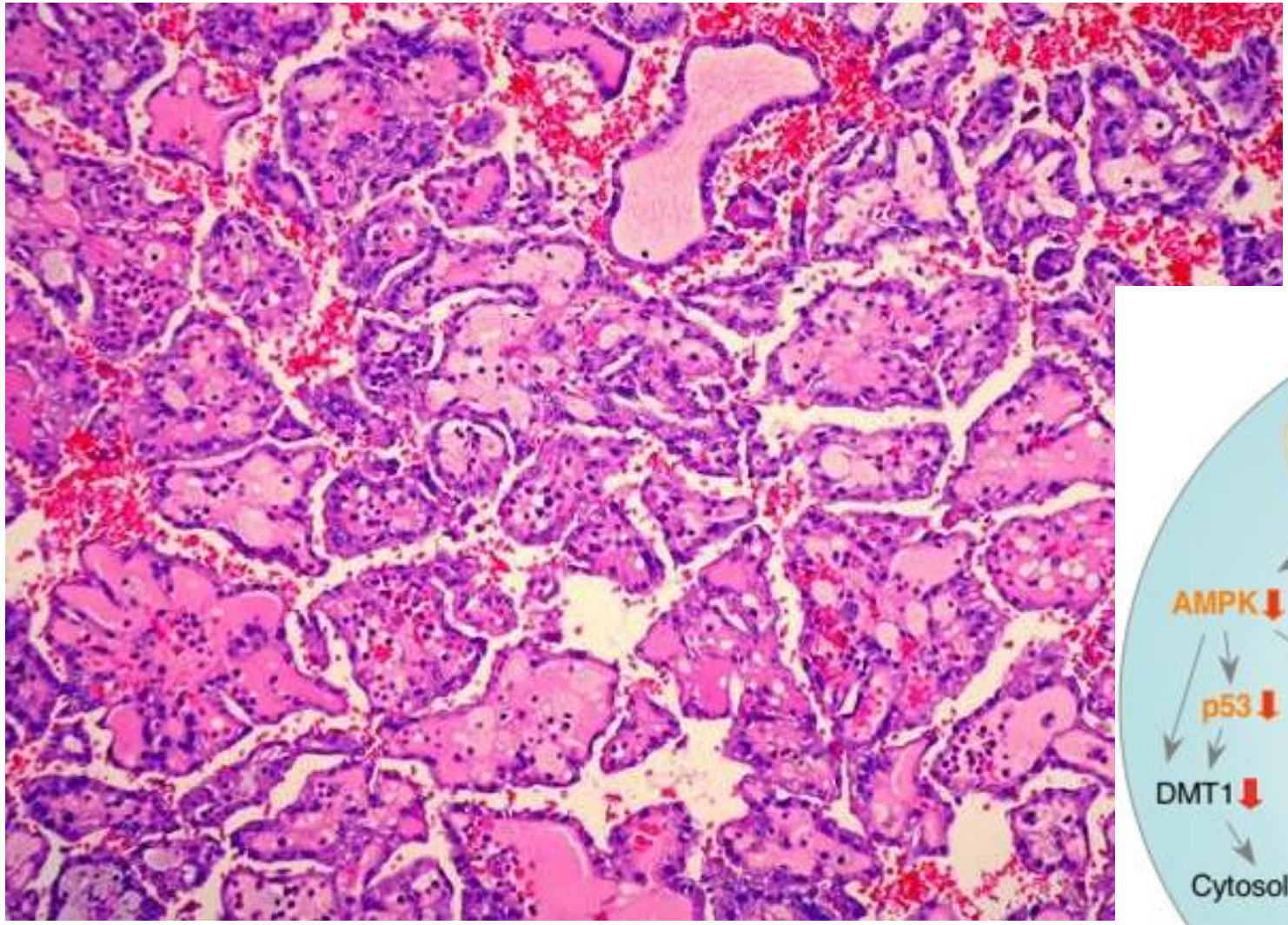


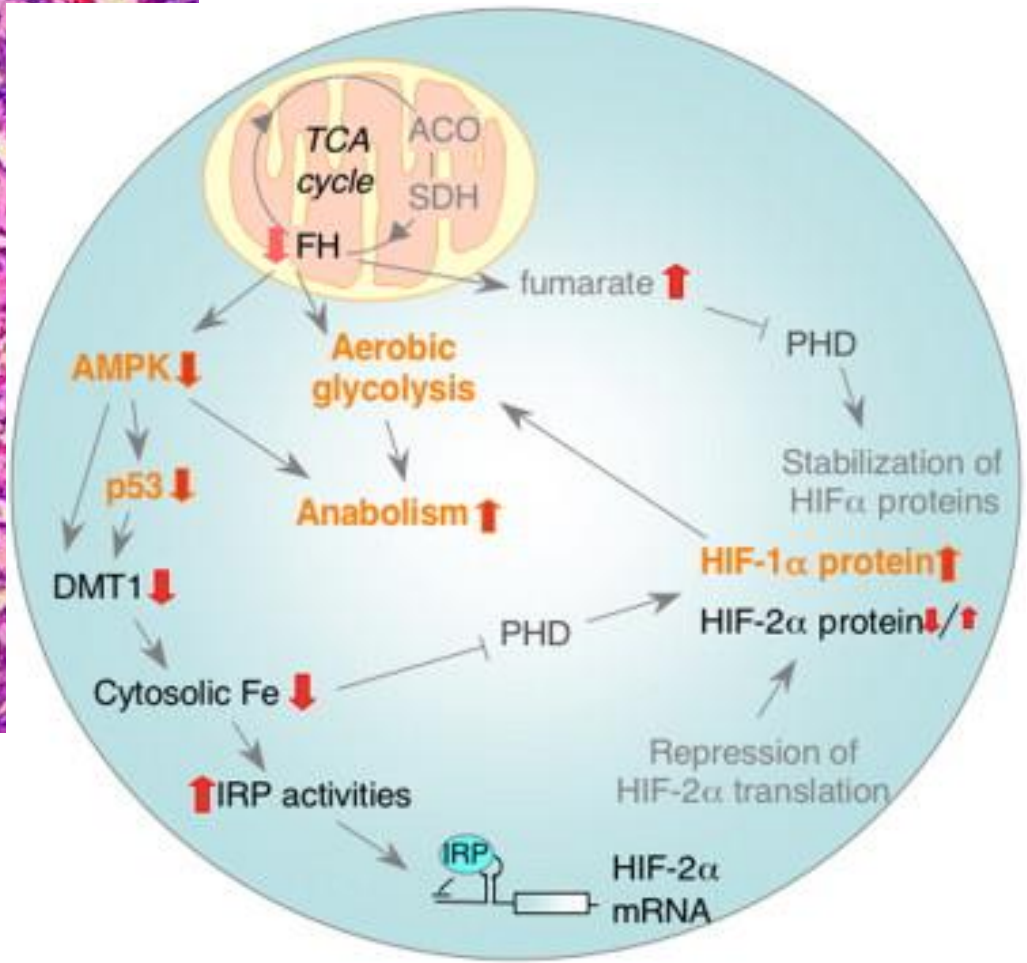


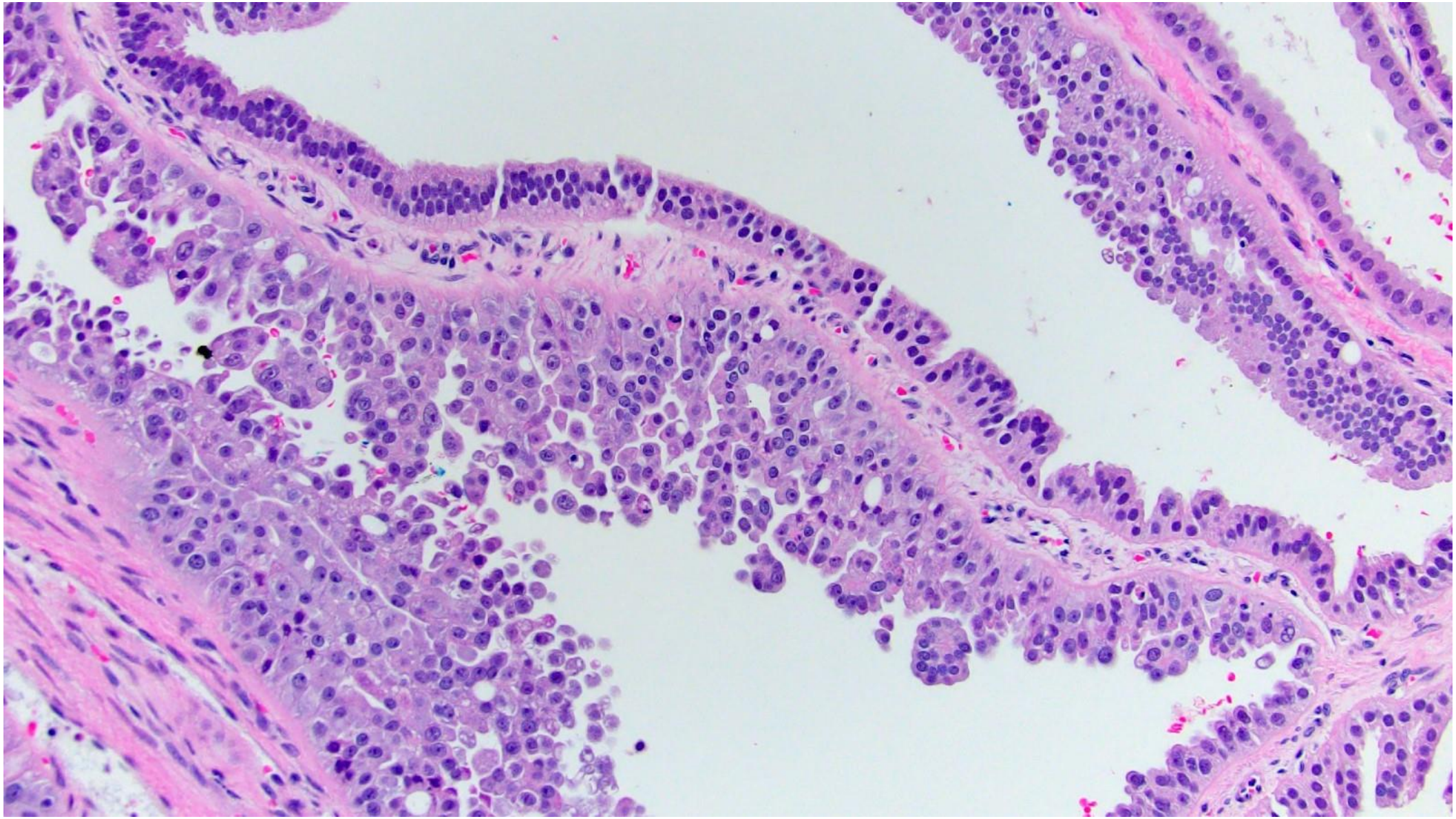
AMACR

trisomy of chromosome 7






TCA cycle
ACO
SDH
FH
fumarate
PHD
AMPK
Aerobic glycolysis
Stabilization of HIFα proteins
p53
Anabolism
HIF-1α protein
DMT1
HIF-2α protein
PHD
Cytosolic Fe
Repression of HIF-2α translation
IRP activities
IRP
HIF-2α mRNA



FH-renal cell carcinoma

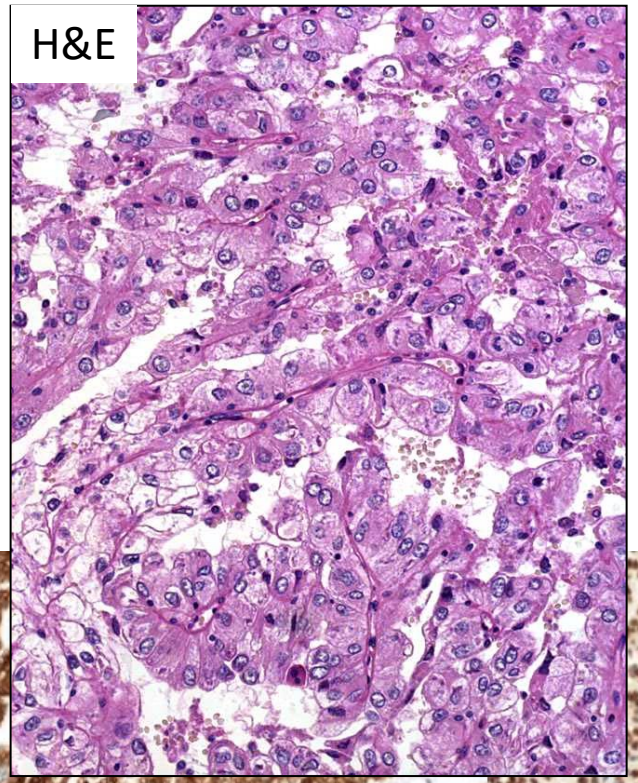
Clinical characteristics of 9 genetically confirmed HLRCC patients with renal tumors

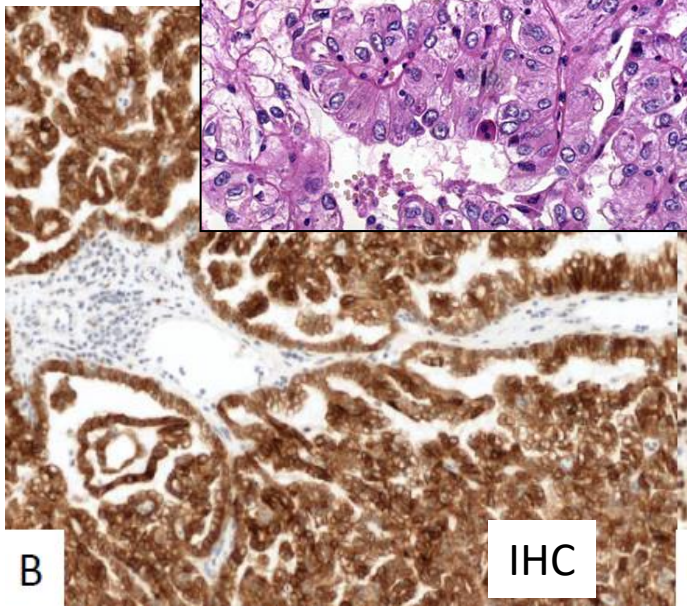
Pt	Sex	Age	Symptoms	Leiomyoma	Family Hx at Presentation	Kidney Mass	Size (cm)	pT	Metastasis	Follow-Up (Month)
1	F	37	Flank pain	Uterine at 32	None	L /solitary	4.9	pT3a	RPLNs	DOD (44)
2	M	38	Flank pain, hematuria	None	None	R/solitary	12.5	pT3a	RPLNs, adrenal, liver, lung, bone	DOD (28)
3	F	32	Abdominal discomfort	Uterine (imaging only)	N/A (adopted)	R/ solitary	9.2	pT3a	RPLNs, lung, liver	DOD (23)
4	M	24	Flank pain	None	Mother ovarian ca	L /solitary	5	pT3a	RPLNs, lung	AWD (10)
5	M	61	Flank pain, hematuria	None	Father RCC, mother breast ca, daughter fibroid	L /two masses	15; 3	pT3a	RPLNs, adrenal, liver	DOD (8)
6	M	42	Flank pain, hematuria	None	None	L /solitary	6.5	pT3a	RPLNs, adrenal, liver	DOD (8)
7	M	34	Incidental renal mass	None	Father non-small cell lung ca	L /solitary	12.2	pT3a	RPLNs	AWD (10)
8	F	30	Flank pain	None	None	R /solitary	6.7	pT3a	RPLNs, adrenal	AWD (12)
9	F	25	Flank pain	Yes (but not identified initially)	Mother RCC	R/solitary	11.5	pT3a	RPLNs	NED (6)

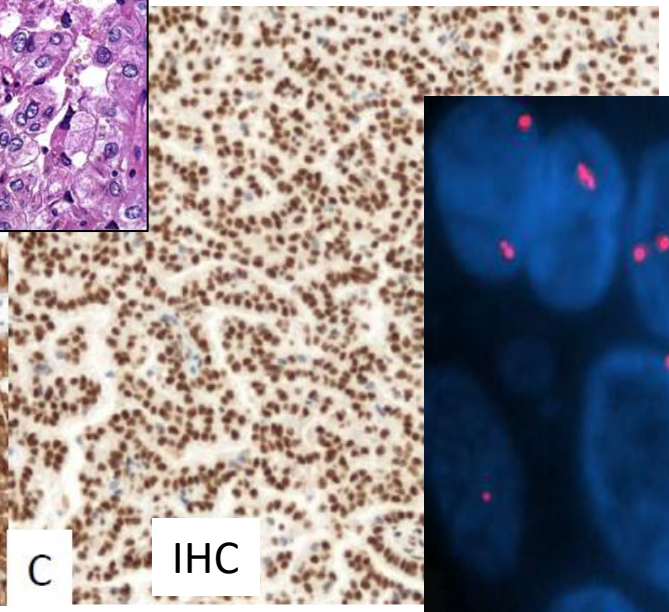
RPLNs: retroperitoneal lymph nodes; DOD: death of disease; AWD: alive with disease; RCC: renal cell carcinoma; ca:cancer

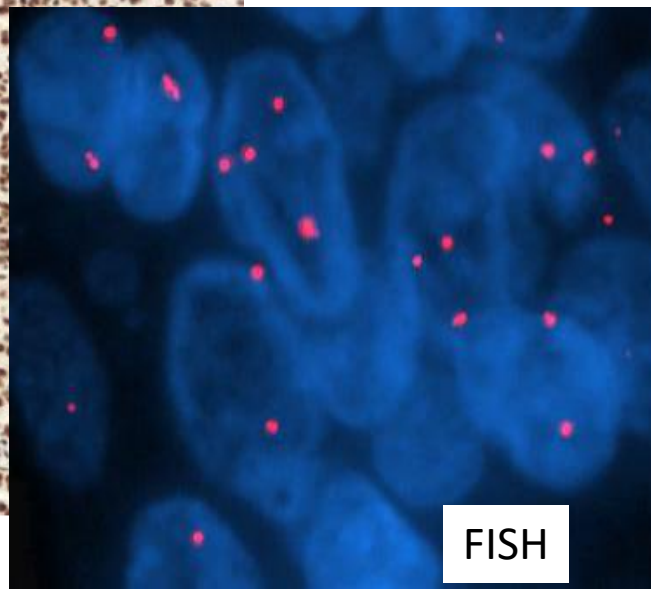
patients died of disease

FH-RCC

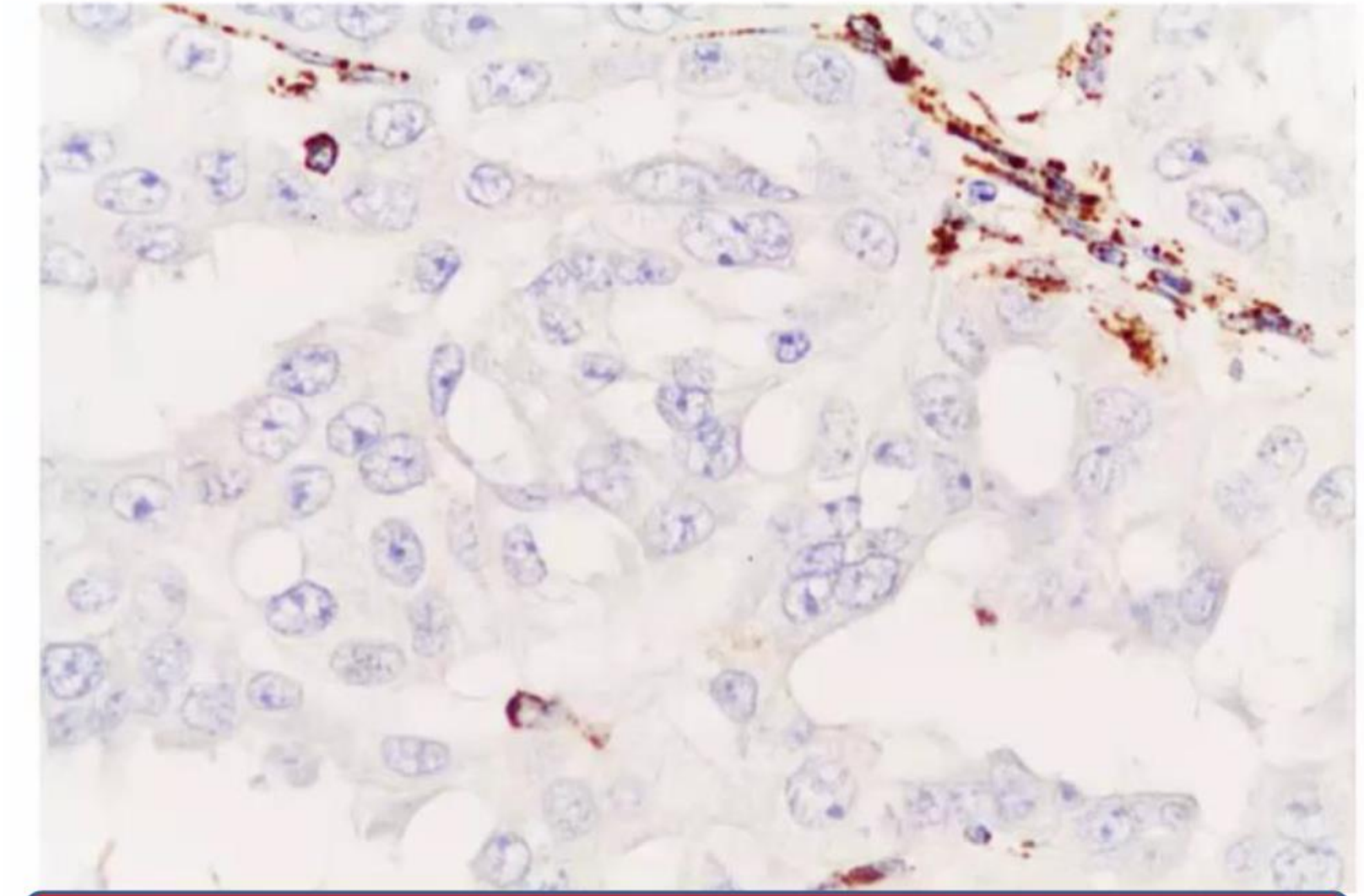






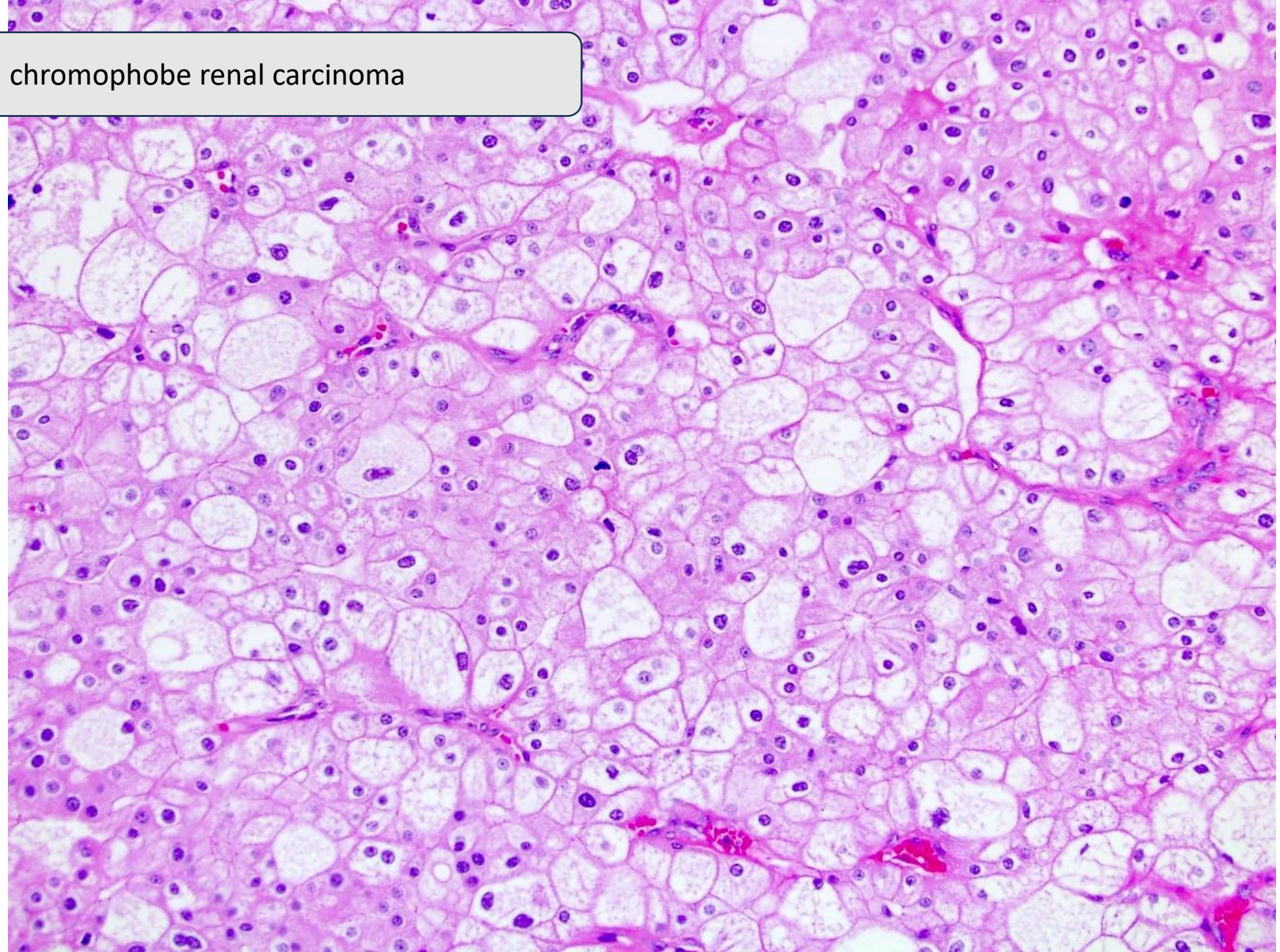


Immunohistochemistry

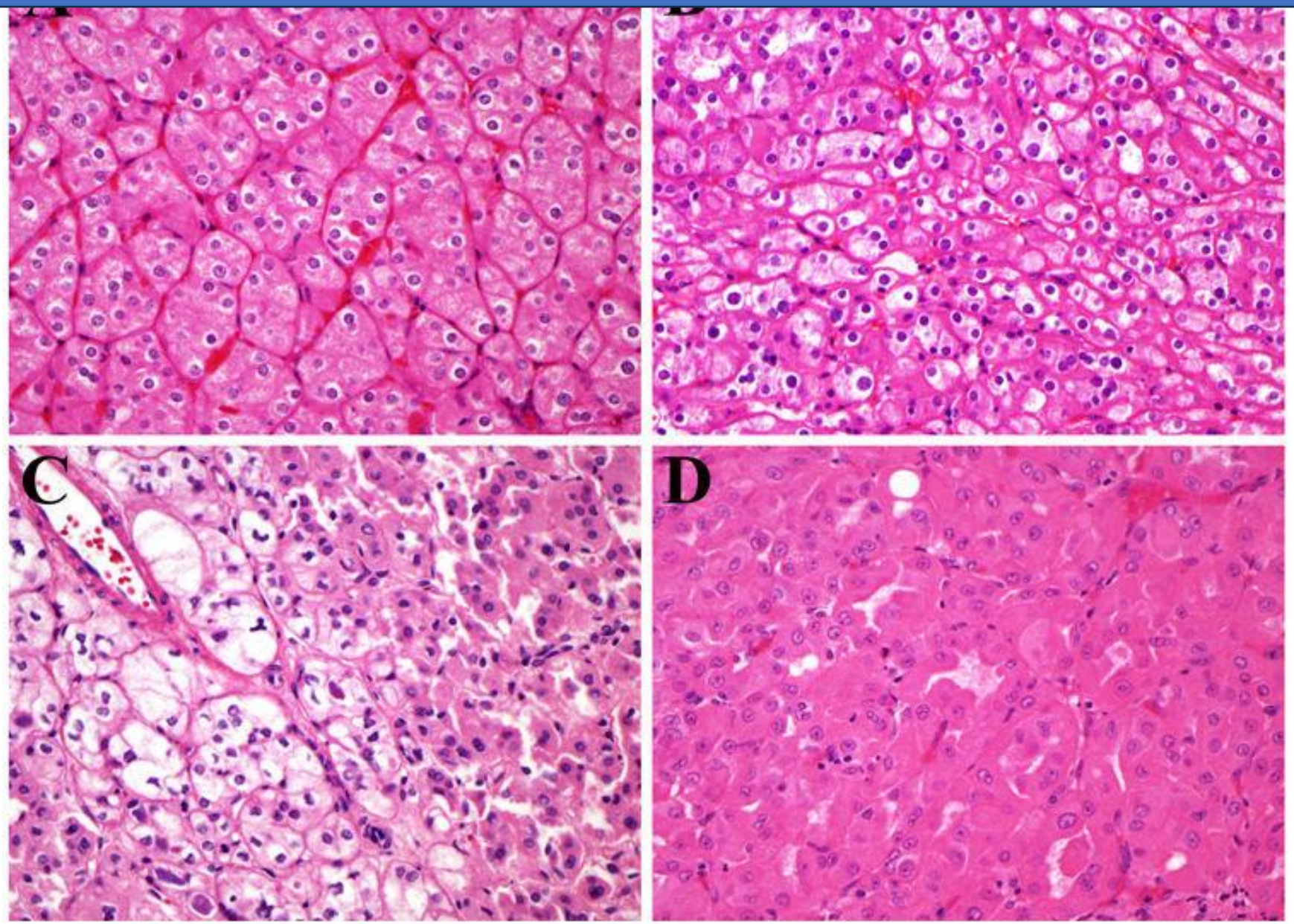


fumarate hydratase (FH)

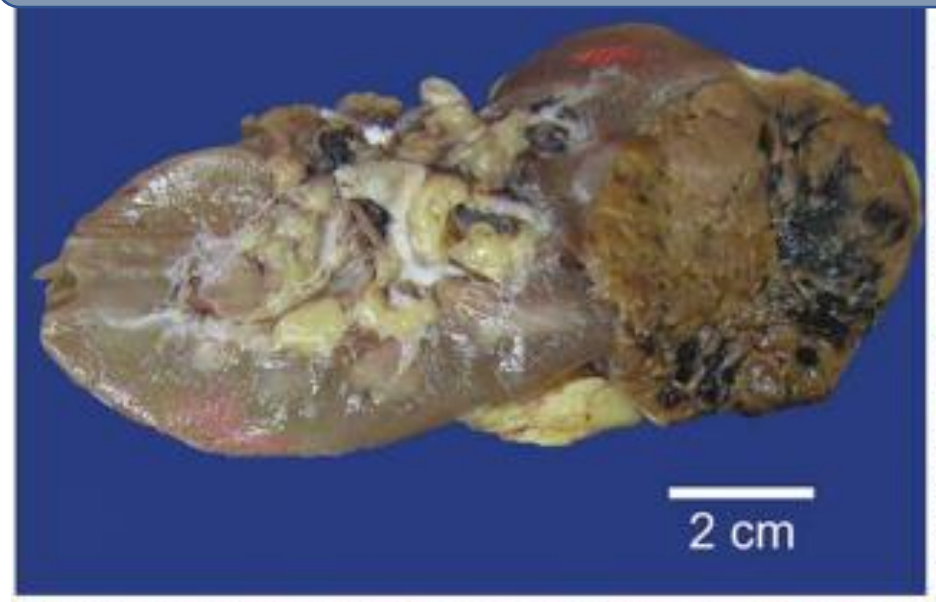
chromophobe renal carcinoma

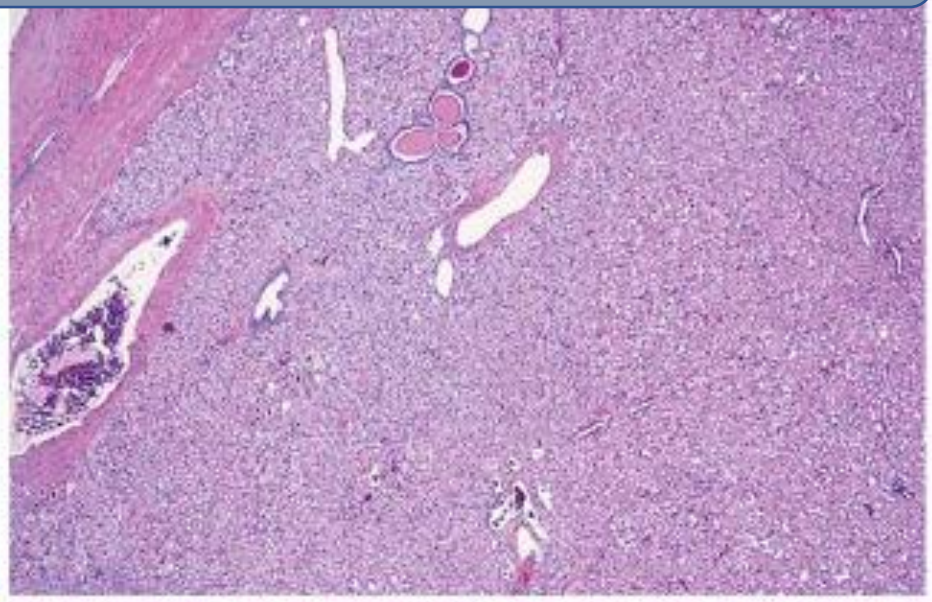


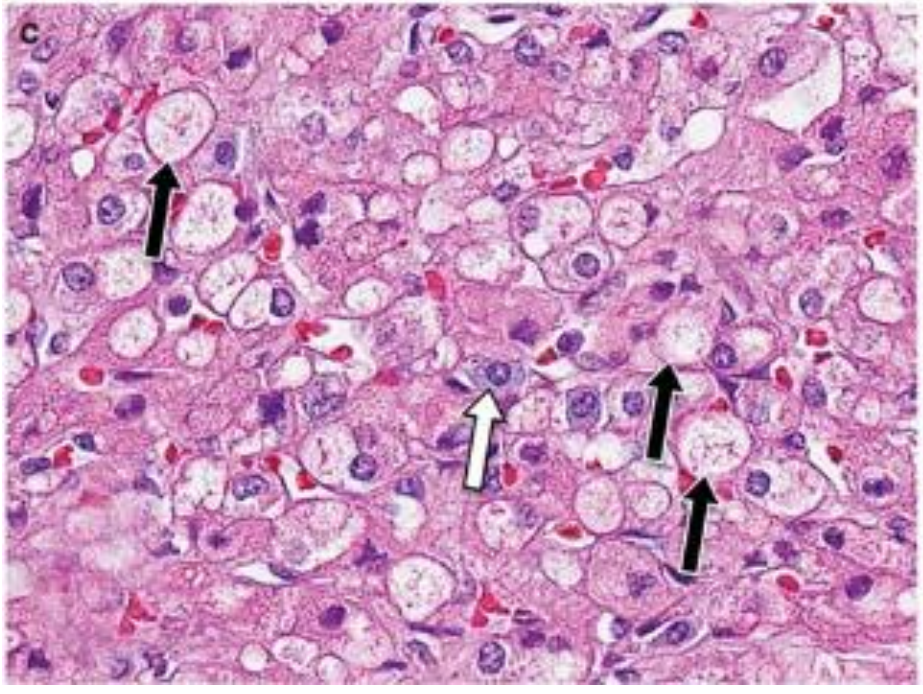
low grade eosinophilic renal cell neoplasms

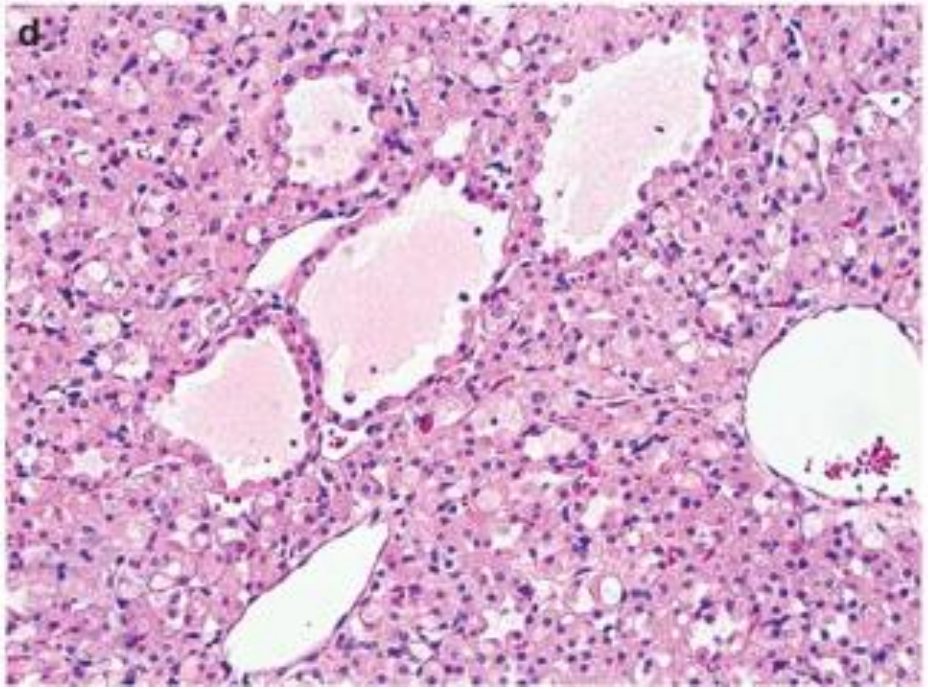


Oncocytic renal neoplasms









Low grade oxyphilic renal neoplasm

Histol Histopathol (2022) 37: 405-413

http://www.hh.um.es

Histology and Histopathology
From Cell Biology to Tissue Engineering

REVIEW **Open Access**

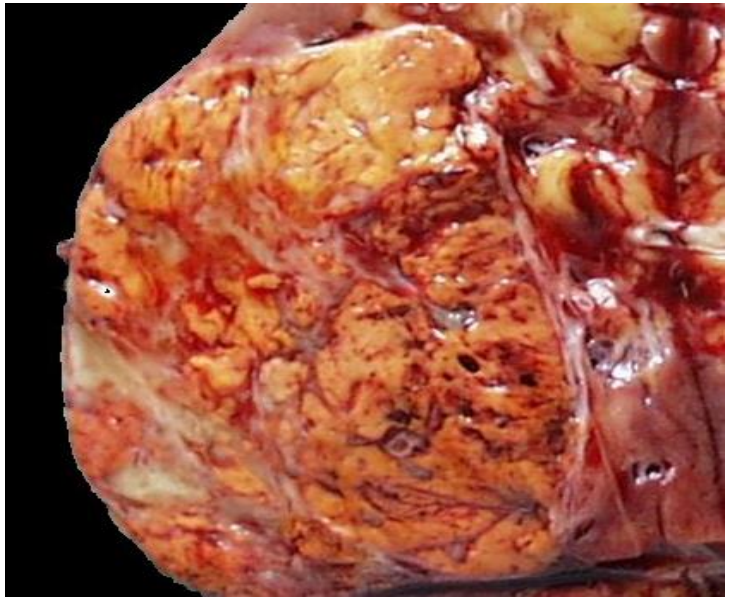
Low-grade oncocytic tumor (LOT) - a new renal entity ready for a prime time: An updated review

Mehdi Mansoor, Farshid Siadat and Kiril Trpkov

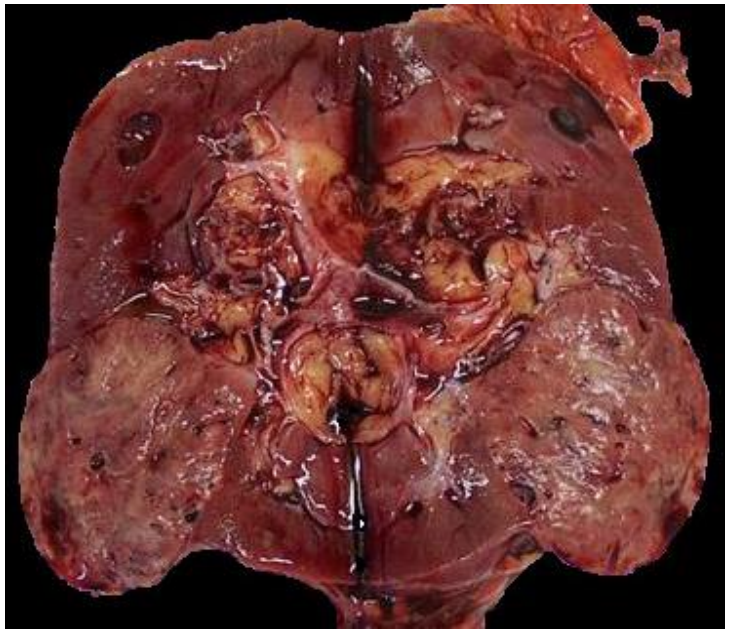
Department of Pathology and Laboratory Medicine, Cumming School of Medicine, University of Calgary and Alberta Precision Laboratories, Calgary, AB, Canada

gross: orienteering

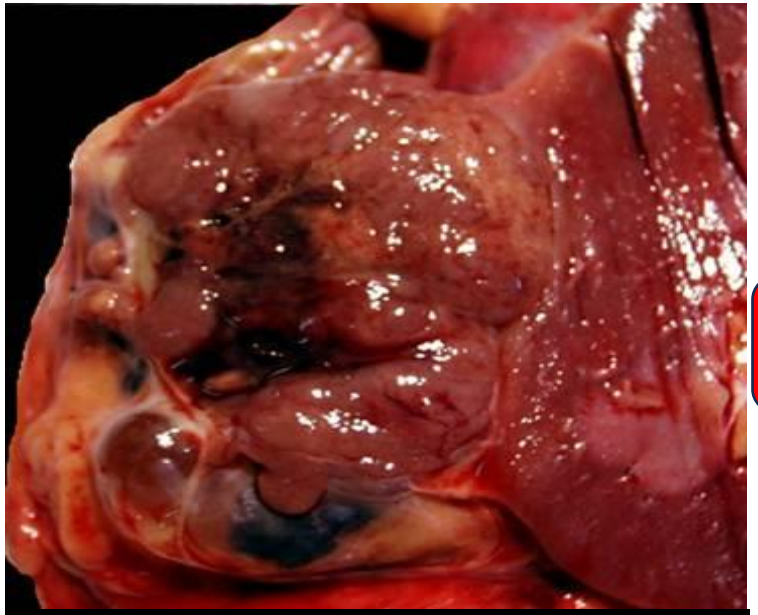
clear cell papillary renal tumor 5-9%



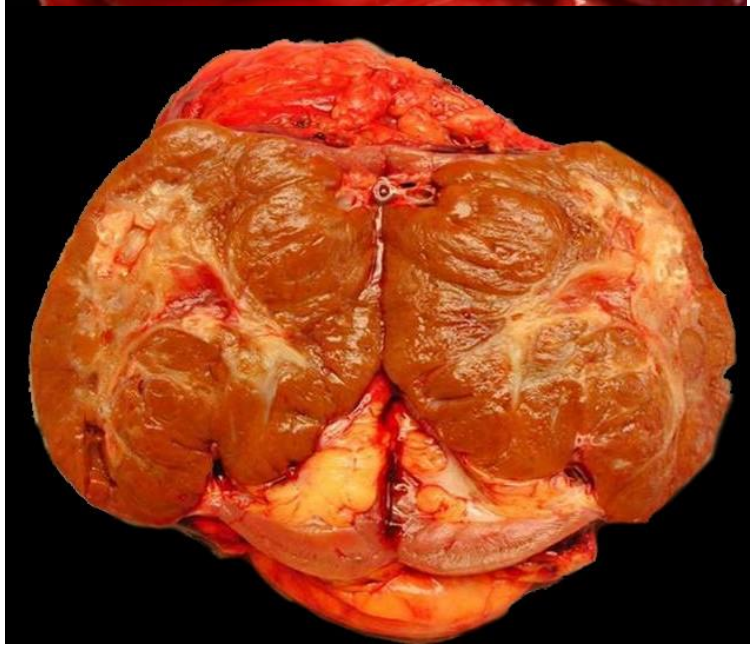
Xp/TFE RCCs



TFEB-RCCs



FH-RCCS



LOT

grading

nucleolar grade for clear cell RCCs and papillary RCcs

carcinoma and papillary renal cell carcinoma {677}

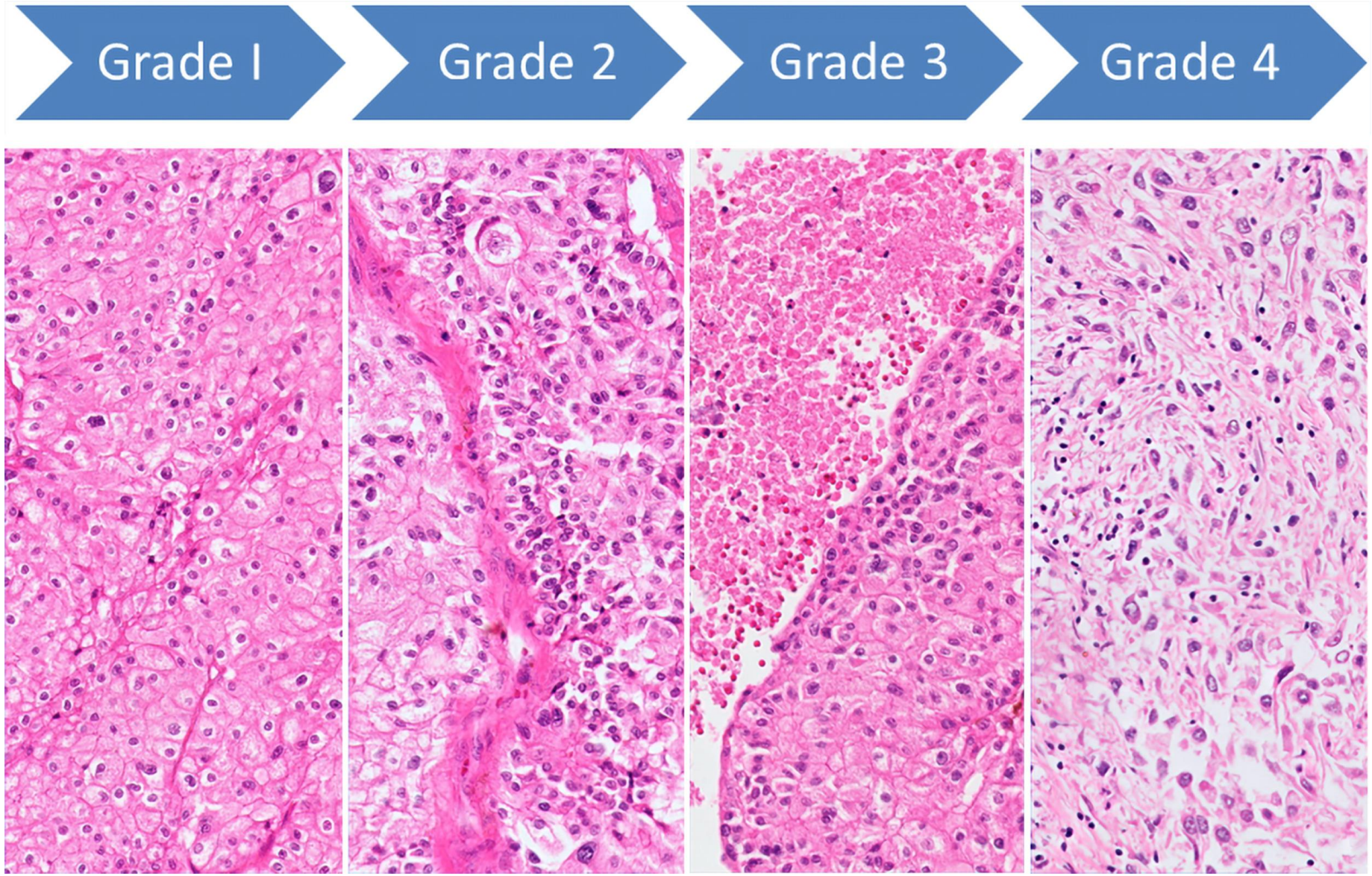
Grade	Description
Grade 1	Nucleoli are absent or inconspicuous and basophilic at ×400 magnification.
Grade 2	Nucleoli are conspicuous and eosinophilic at ×400 magnification and visible but not prominent at ×100 magnification.
Grade 3	Nucleoli are conspicuous and eosinophilic at ×100 magnification.
Grade 4	There is extreme nuclear pleomorphism, multinucleate giant cells, and/or rhabdoid and/or sarcomatoid differentiation.

grading applicable

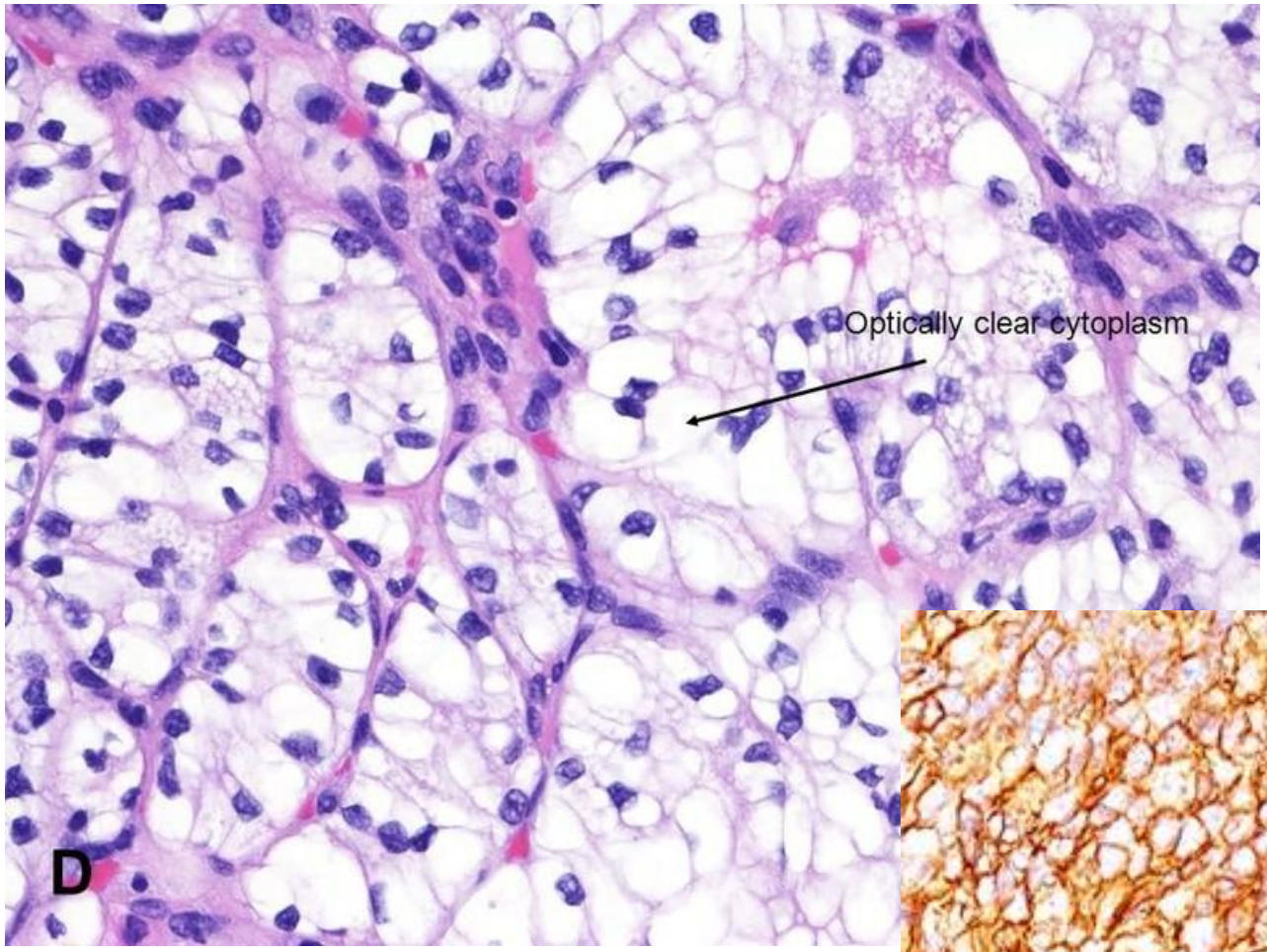
clear cell RCCs
papillary RCCs

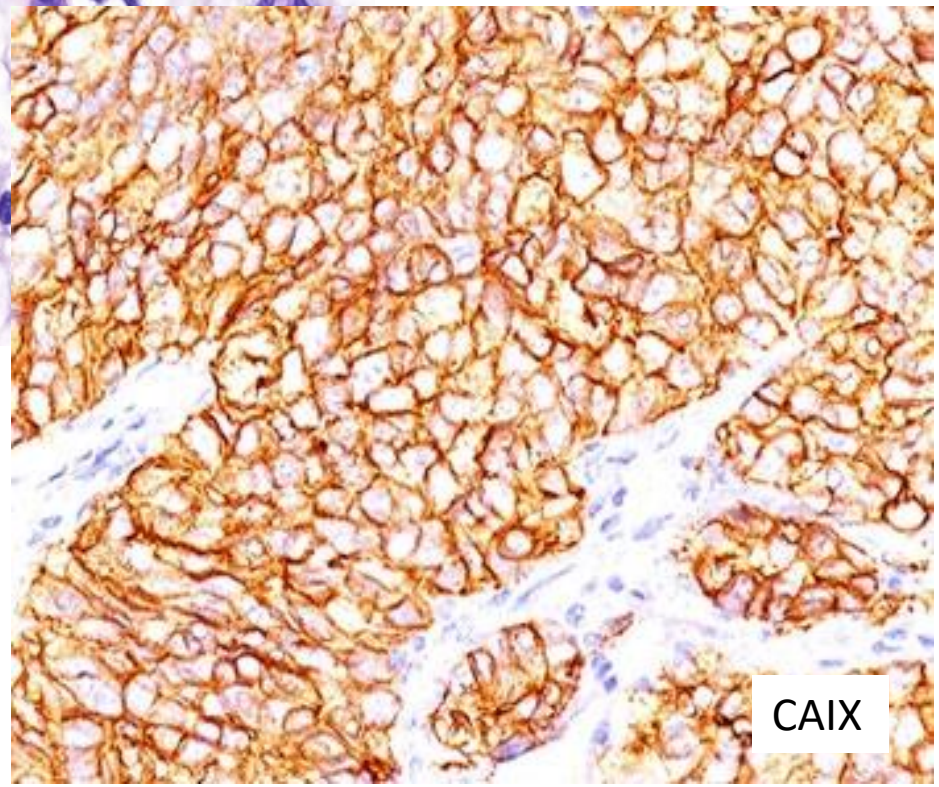
no translocation Xp/TFE3 RCCs
no FH-RCCS
no clear cell papillary renal tumor
no LOT

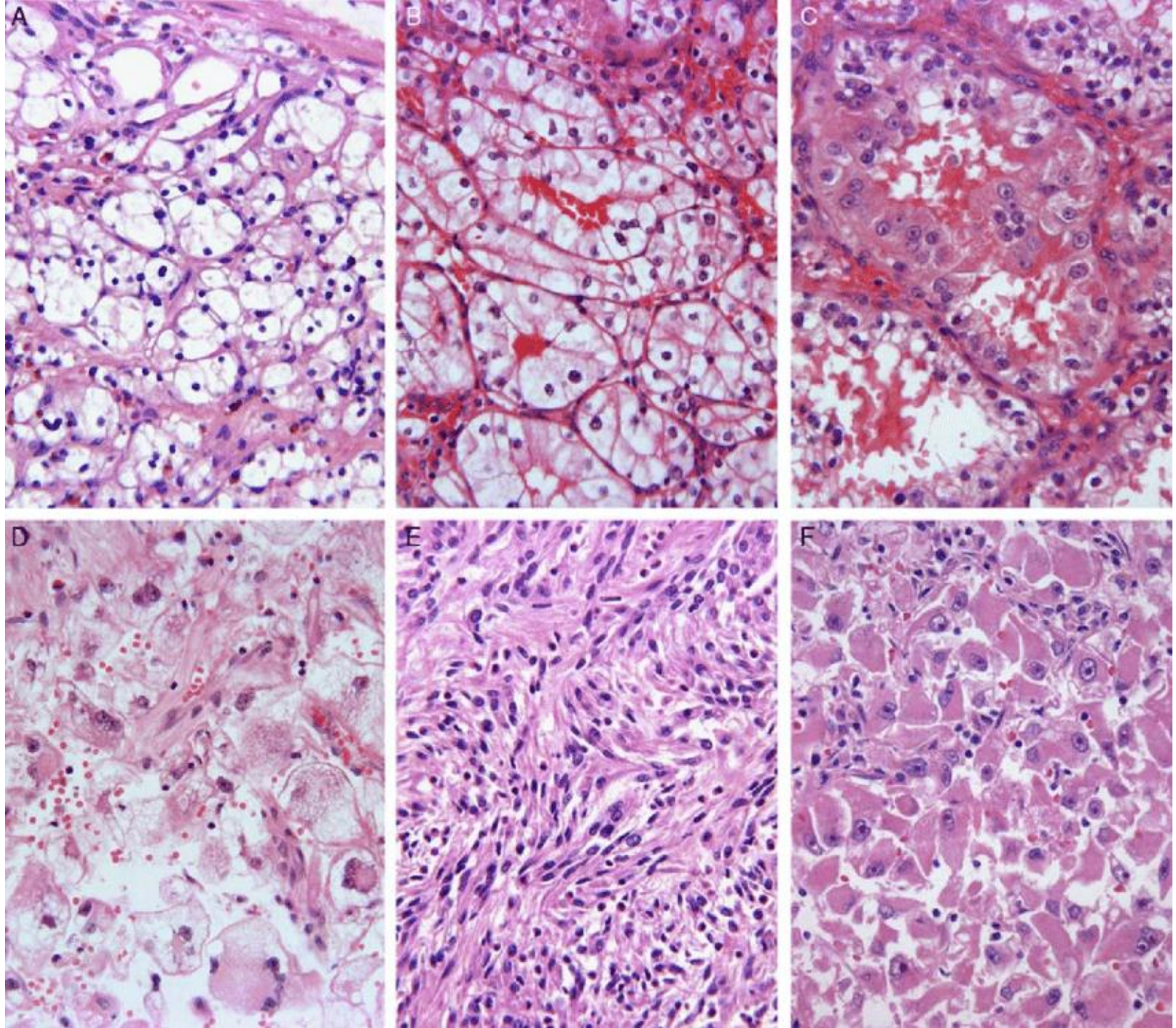
chromophobe renal carcinoma



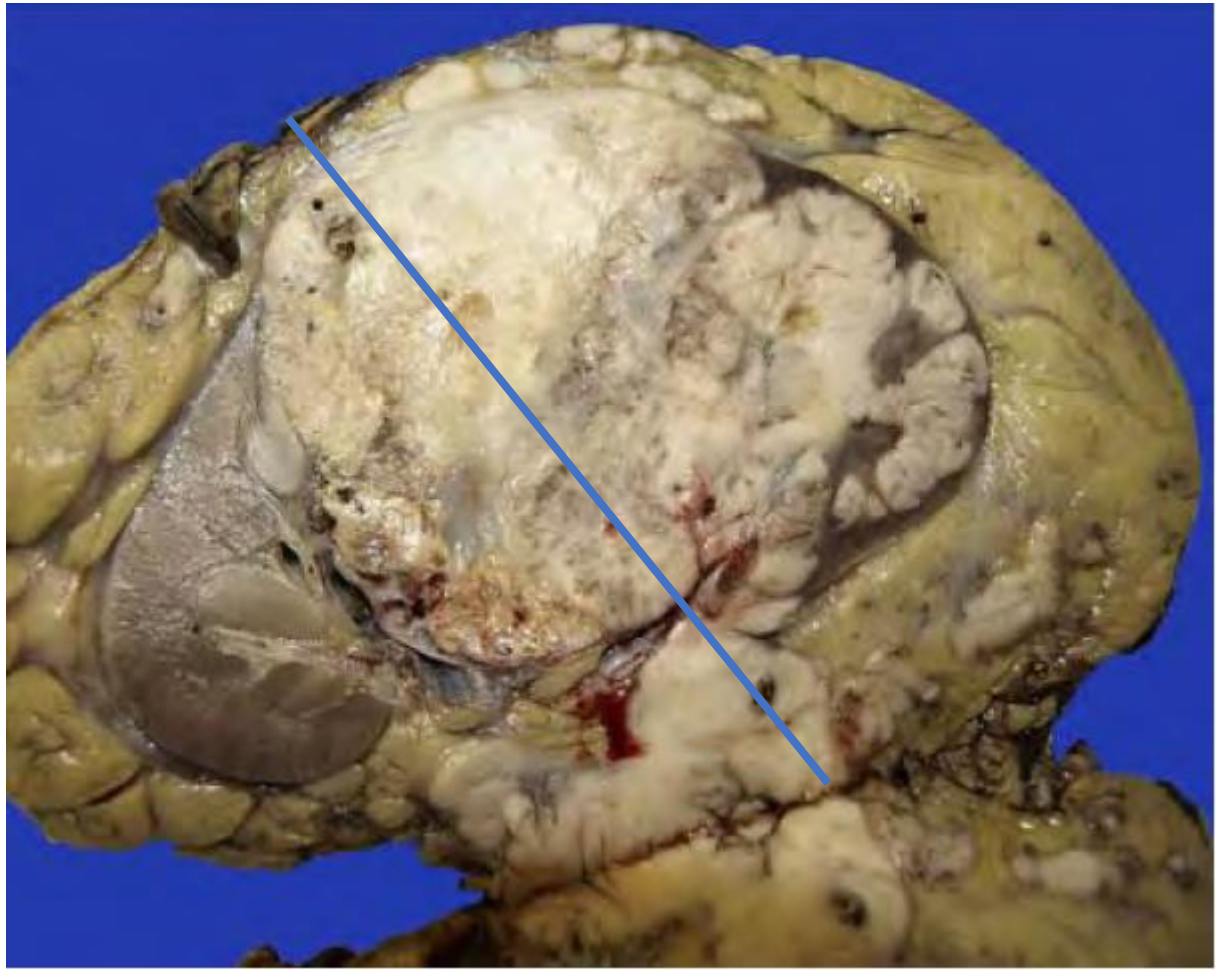
yellowish gross view


Optically clear cytoplasm
D

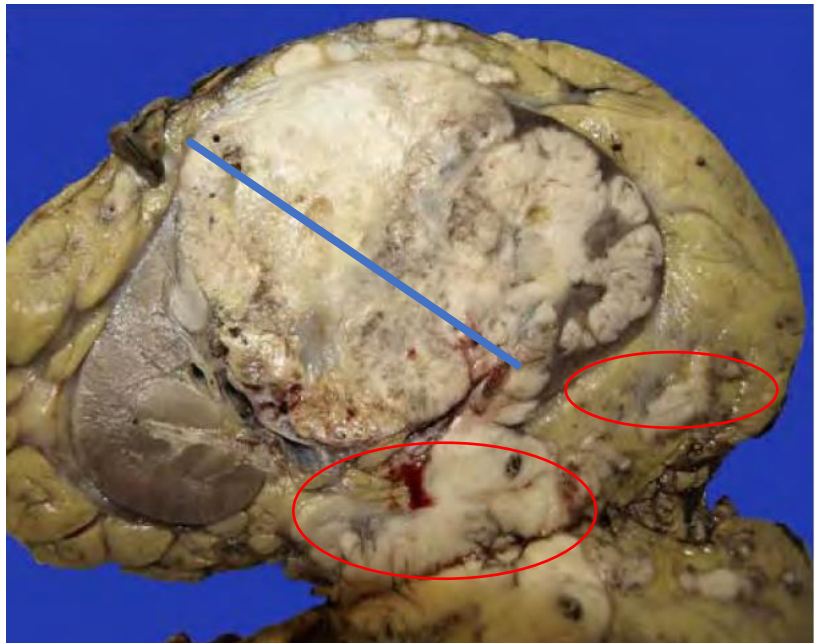

CAIX


A
B
C
D
E
F

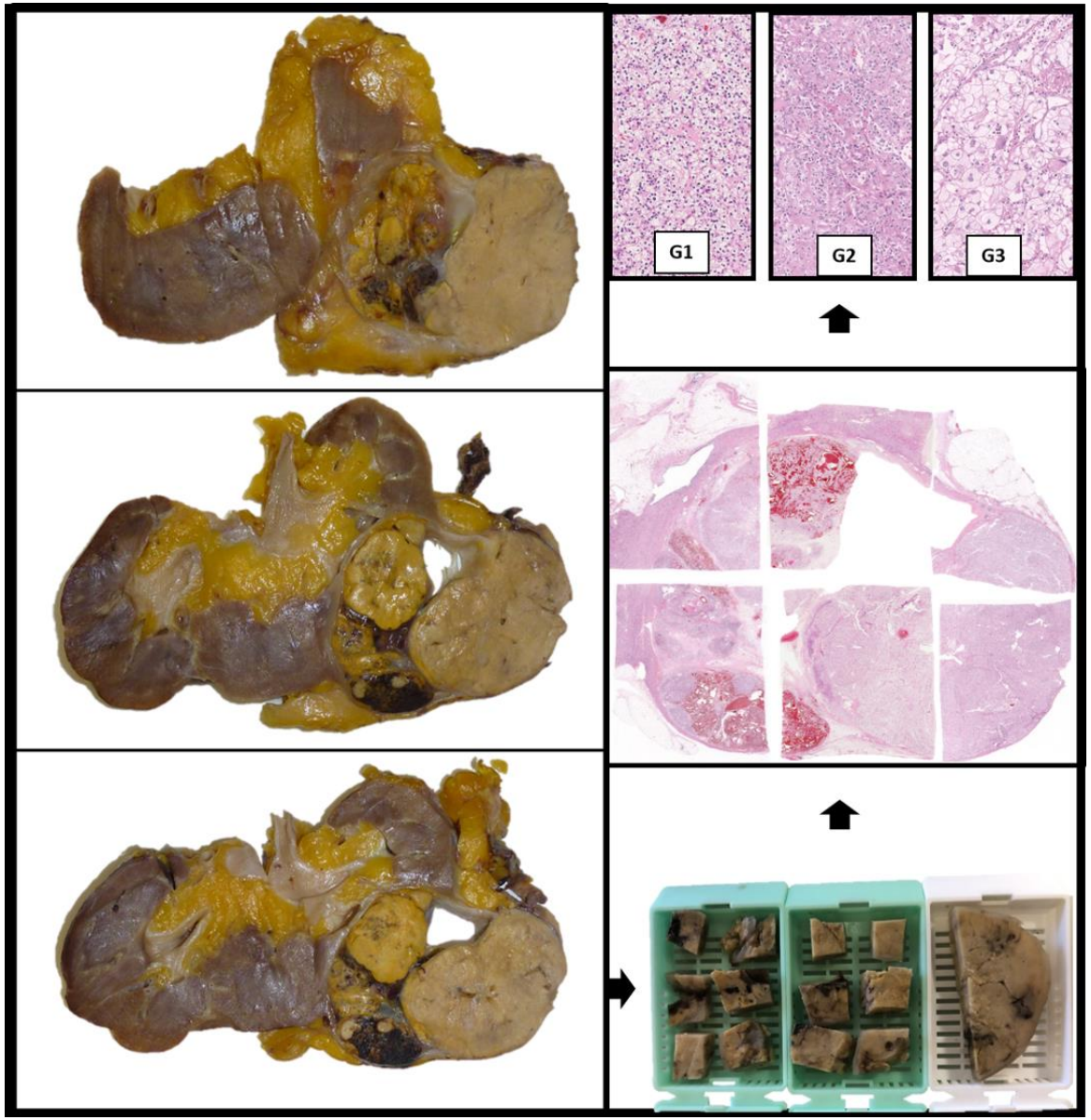
staging



necrosis
G3-G4
sarcomatoid and
rhabdoid features

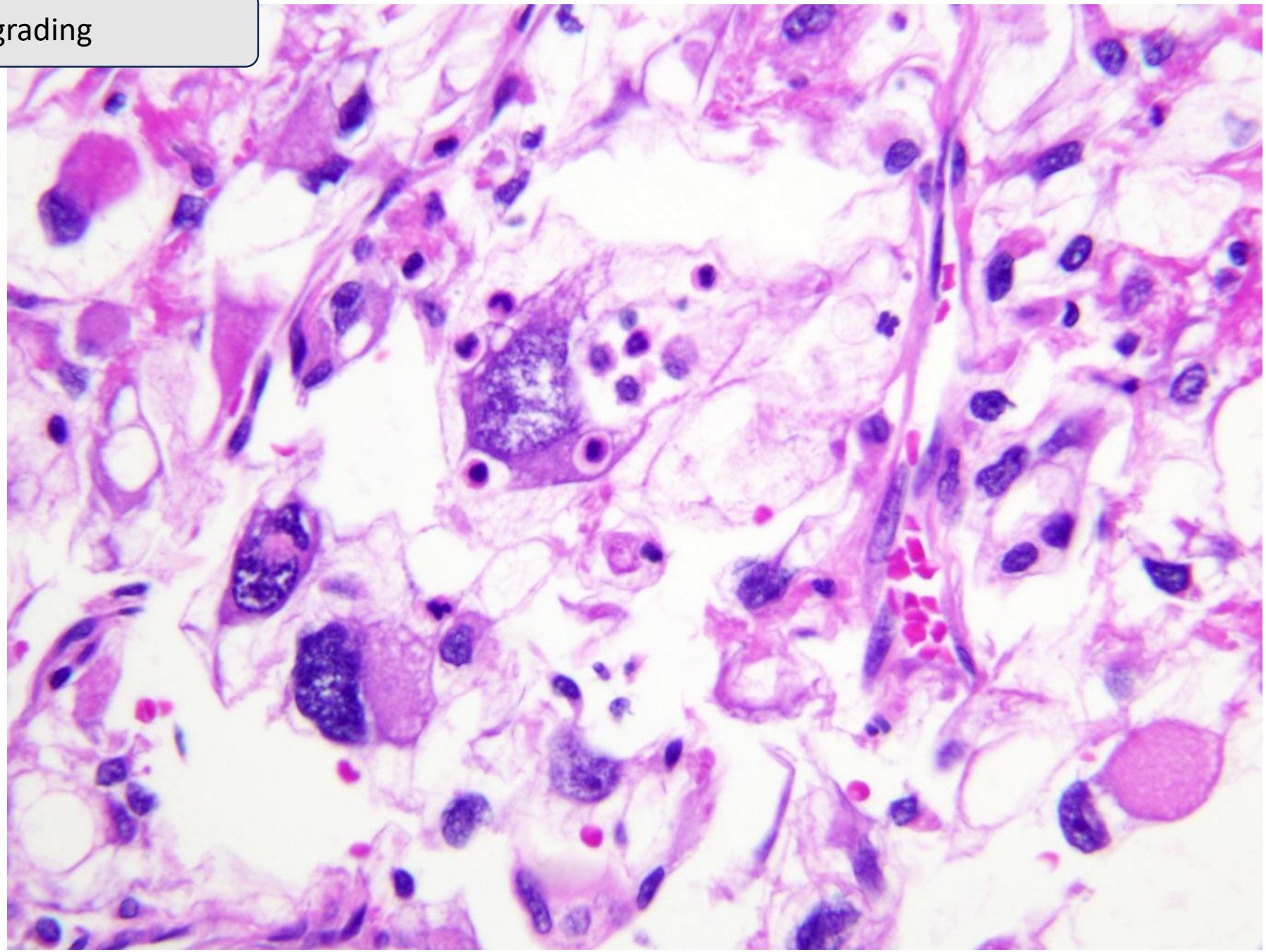


3D fusion gross sampling



Brunelli et al. 2021

ISUP grading



prognostication: traditional versus modern

nature COMMUNICATIONS

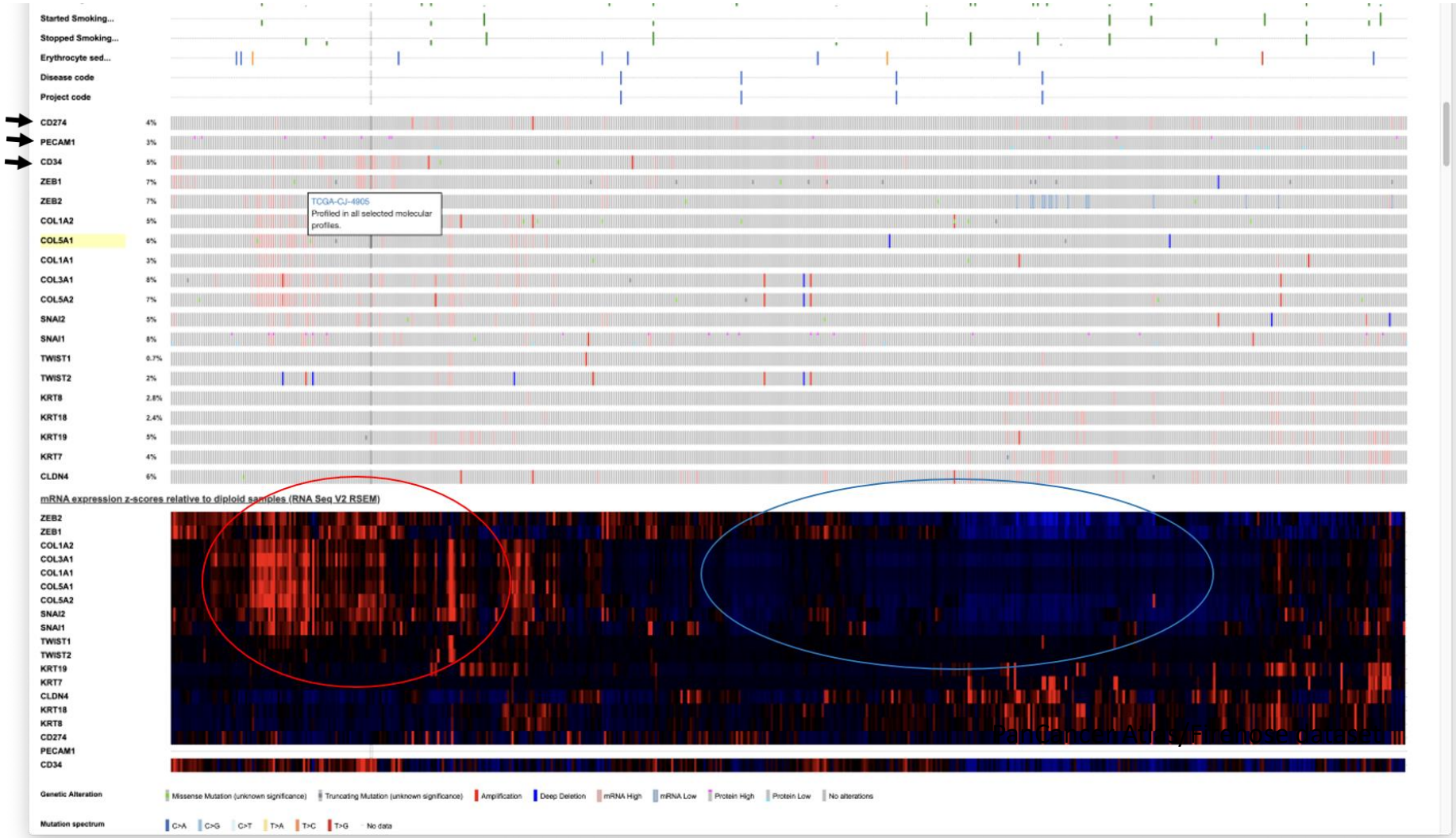
ARTICLE

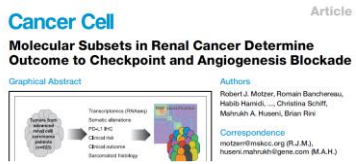
https://doi.org/10.1038/s41467-021-21068-9 OPEN

Integrative molecular characterization of sarcomatoid and rhabdoid renal cell carcinoma

Ziad Bakouny[1], David A. Braun[1], Sachet A. Shukla[2], Wenting Pan[1], Xin Gao[3], Yue Hou[2], Abdallah Flaifel[4], Stephen Tang[1], Alice Bosma-Moody[1], Meng Xiao He[1], Natalie Vokes[1], Jackson Nyman[1], Wanling Xie[5], Amin H. Nassar[1], Sarah Abou Alaiwi[1], Ronan Flippot[1], Gabrielle Bouchard[1], John A. Steinharter[1], Pier Vitale Nuzzo[1], Miriam Ficial[4], Miriam Sant'Angelo[4], Juliet Forman[1,2,6], Jacob E. Berchuck[1], Shaan Dudani[7], Kevin Bi[1], Jihye Park[1], Sabrina Camp[1], Maura Sticco-Ivins[4], Laure Hirsch[1], Sylvan C. Baca[1], Megan Wind-Rotolo[8], Petra Ross-Macdonald[8], Maxine Sun[1], Gwo-Shu Mary Lee[1], Steven L. Chang[1], Xiao X. Wei[1], Bradley A. McGregor[1], Lauren C. Harshman[1], Giannicola Genovese[9], Leigh Ellis[4,10], Mark Pomerantz[1], Michelle S. Hirsch[4], Matthew L. Freedman[1], Michael B. Atkins[11], Catherine J. Wu[1,6], Thai H. Ho[12], W. Marston Linehan[13], David F. McDermott[14], Daniel Y. C. Heng[7], Srinivas R. Viswanathan[1], Sabina Signoretti[4,10], Eliezer M. Van Allen[1,15]✉ & Toni K. Choueiri[1,15]✉

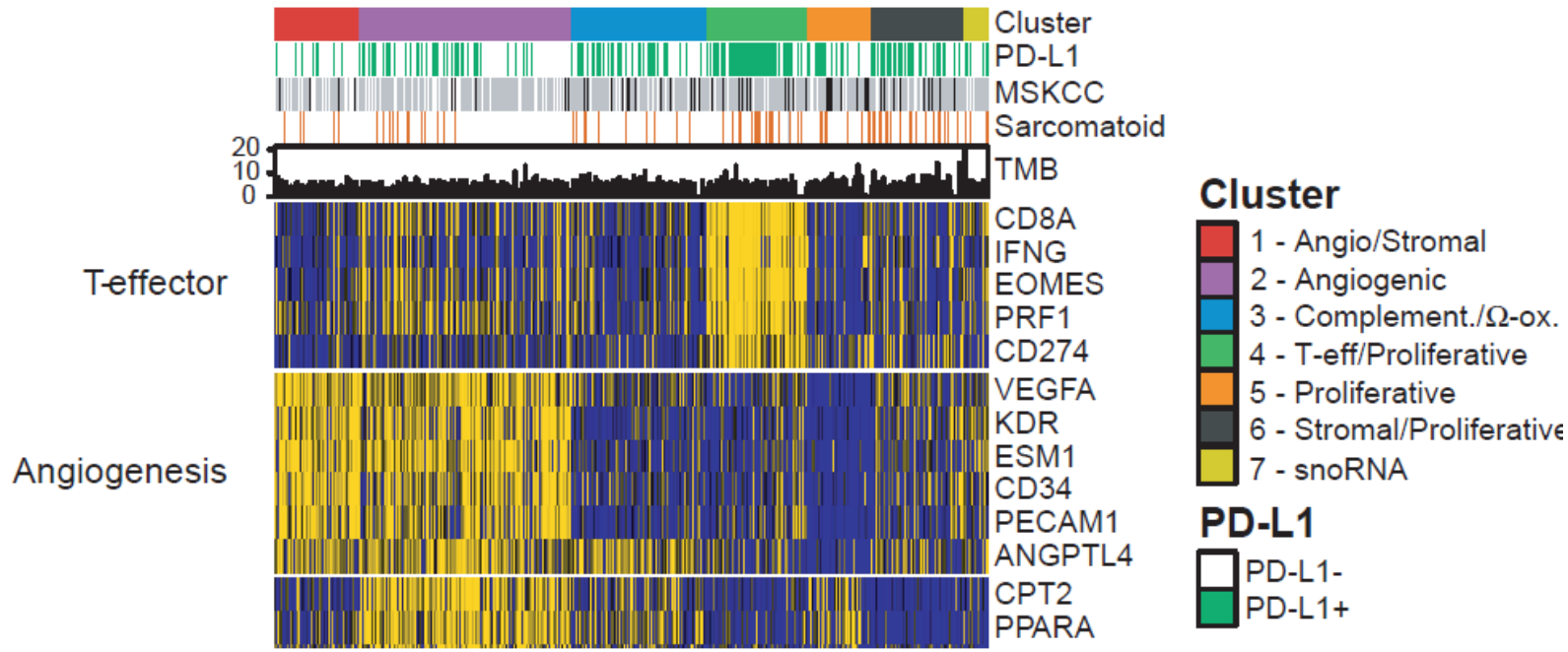
International Public Repository: angiogenetic versus immune signatures





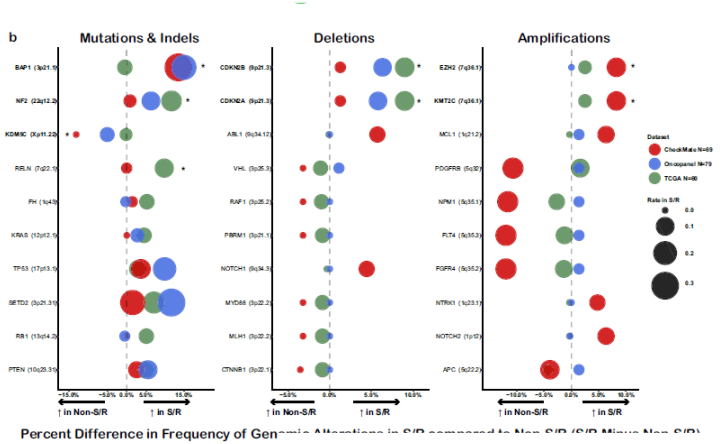
Tumors from 823 patients

C

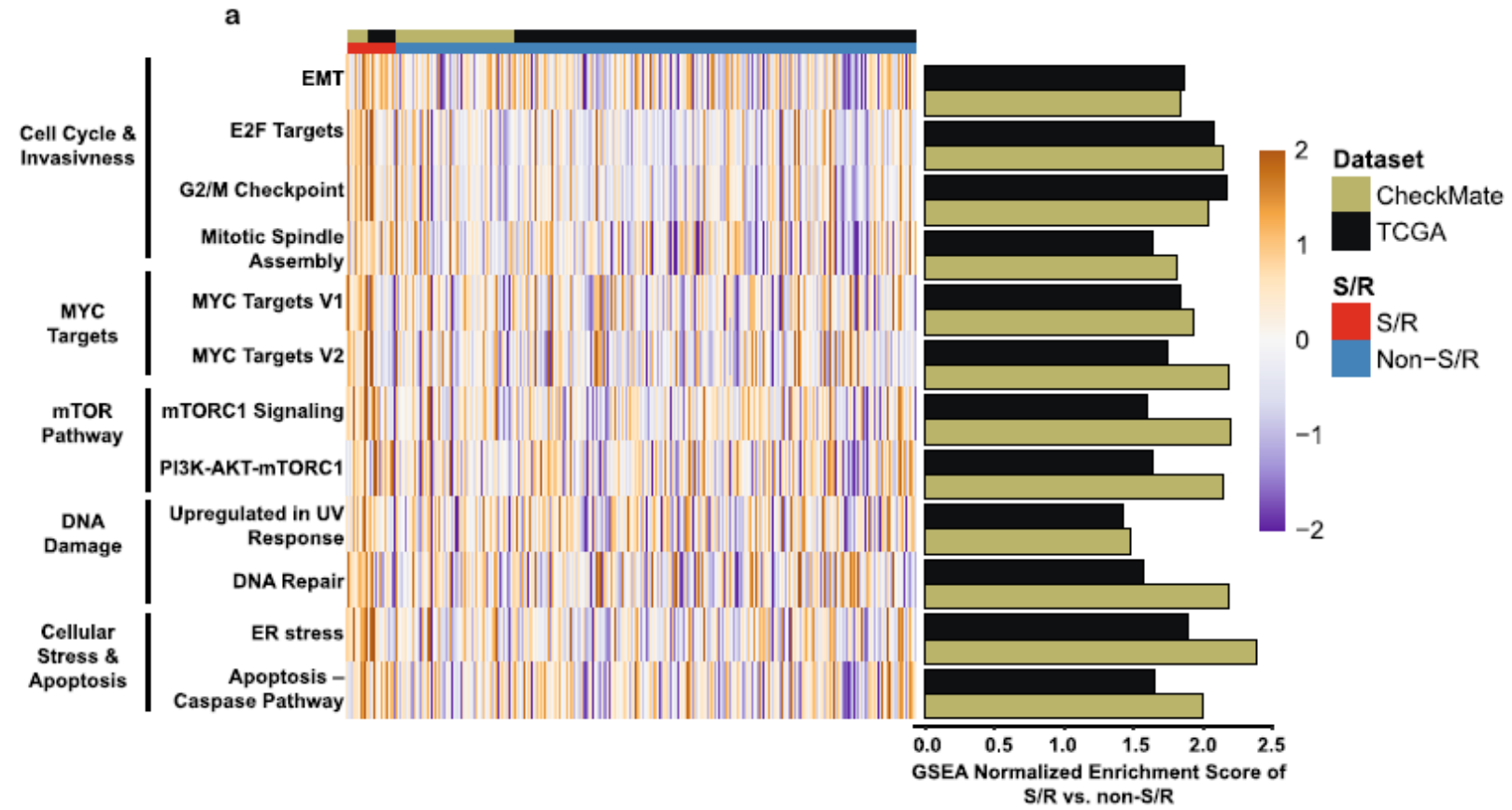


CellPress

	Cluster 1 98/823 (12%)	Cluster 2 245/823 (30%)	Cluster 3 156/823 (19%)	Cluster 4 116/823 (14%)	Cluster 5 74/823 (9%)	Cluster 6 106/823 (13%)	Cluster 7 28/823 (3%)
Pathways	Angiogenesis Stroma	Angiogenesis Fatty acid oxidation	Complement cascade Ω-oxidation	T-effector Cell Cycle Fatty acid synthesis	Cell Cycle Fatty acid synthesis	Stroma Cell Cycle	snoRNA



MYC
BAP-1
CDKN2A/9p
PD-L1
14q



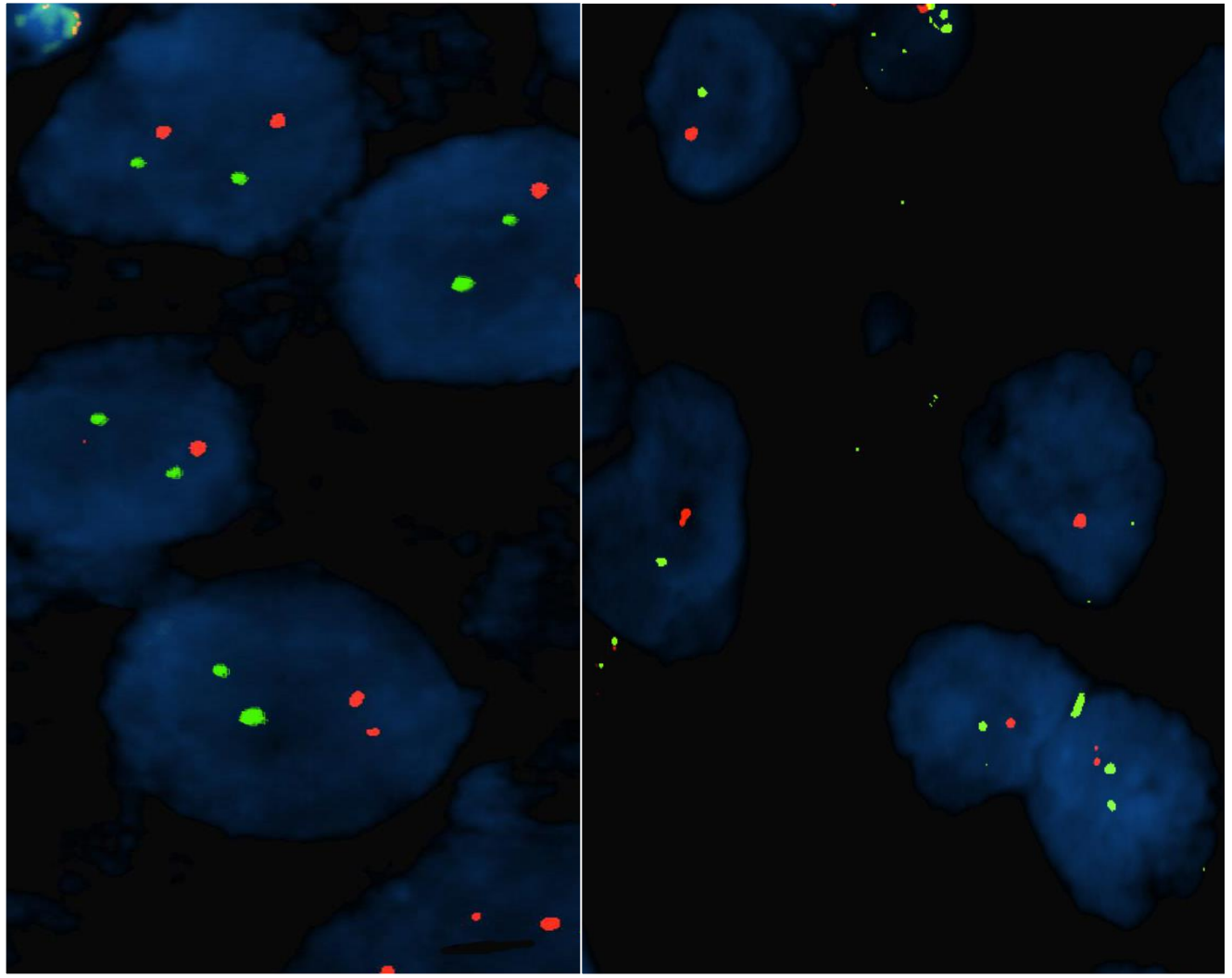
history and modern profiling

External Validation of the Mayo Clinic Stage, Size, Grade and Necrosis (SSIGN) Score to Predict Cancer Specific Survival Using a European Series of Conventional Renal Cell Carcinoma
Ficarra et al. 2006 J Urol

Pathological and genetic markers improve recurrence prognostication with the University of California Los Angeles Integrated Staging System for patients with clear cell renal cell carcinoma
Kroeger et al. European Journal of Cancer 2022

necrosis, sarcomatoid features, rhabdoid features, chromosomal loss 9p, combined chromosomal loss 3p and 14q and microvascular invasion

Losses of chromosome 3/3p



histotyping means prognostication sec. WHO 2022
ex clear cell renal cell carcinoma
ex papillary renal cell carcinoma
ex chromophobe renal cell carcinoma, ex oncocytoma
grading, staging
molecular directions

Società Italiana di Urologia dal 1908

L'ECCELLENZA NEL TRATTAMENTO DEI TUMORI RENALI IN ITALIA

12 Dicembre 2024

Una Hotels Decò

Via Giovanni Amendola, 57 Roma

orario 10.30-17.00

12.00-12.20 Fattori prognostici moderni e tradizionali - M. Brunelli