

19 de
mayo
de
2011

CONSOLIDANDO PUENTES

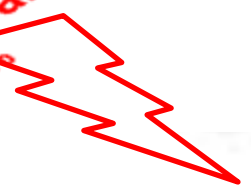


Los tumores renales de la edad pediátrica

De la célula al gene

Por qué los niños no son adultos pequeños?

Exposición del medio ambiente
70-85%



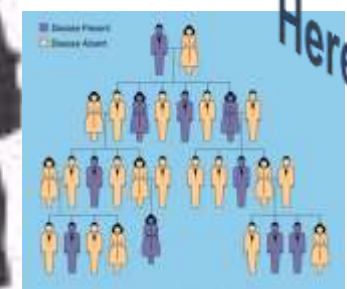
Tejidos mais diferenciados



Alta rotación de la célula

Presença de "células embrionarias"?

Herencia



Los tumores renales de la edad pediátrica

De la célula al gene

Por qué los niños no son adultos pequeños?

Cáncer

Cáncer

Carcinoma de células renales

Células claras

Del 3p-VHL

Wilms

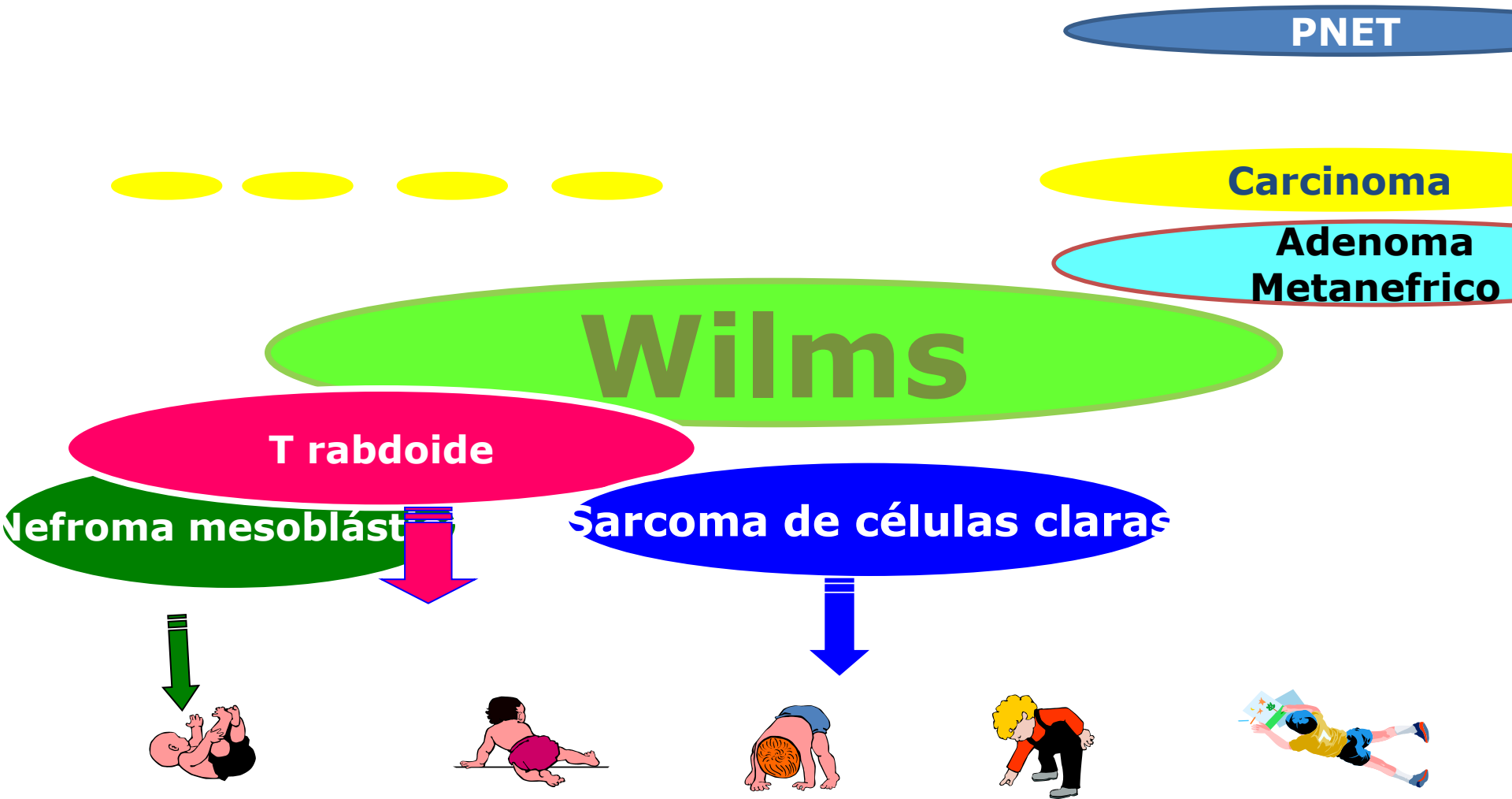
Carcinoma de células renales

Papilar

MITF



Grupo de edad



Edad



Clínica y imagen

Fondo

Cohesión y disposición celular

Subtipo celular

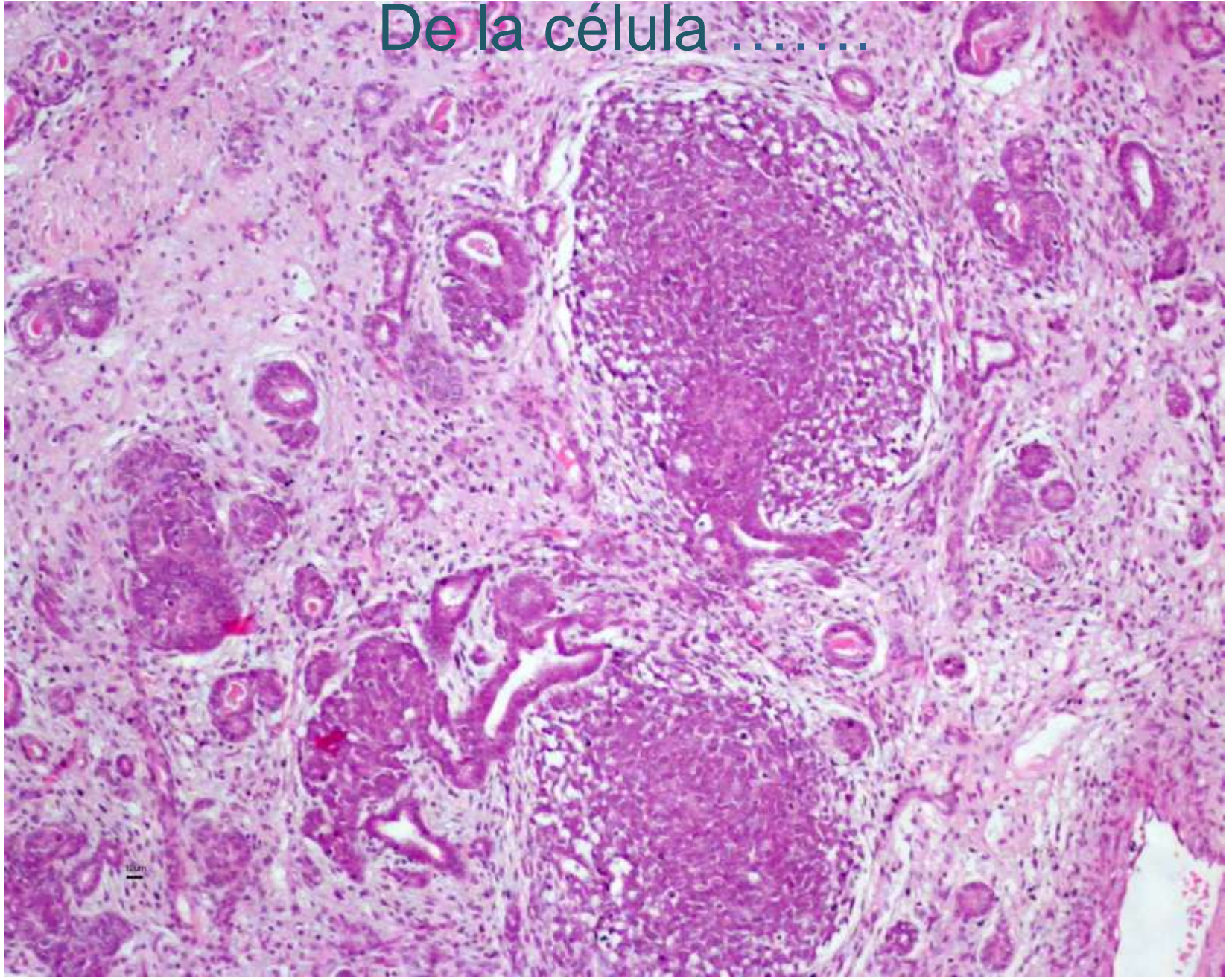
Núcleo e citoplasma

Diagnóstico citológico

Los tumores renales de la edad pediátrica

De la célula

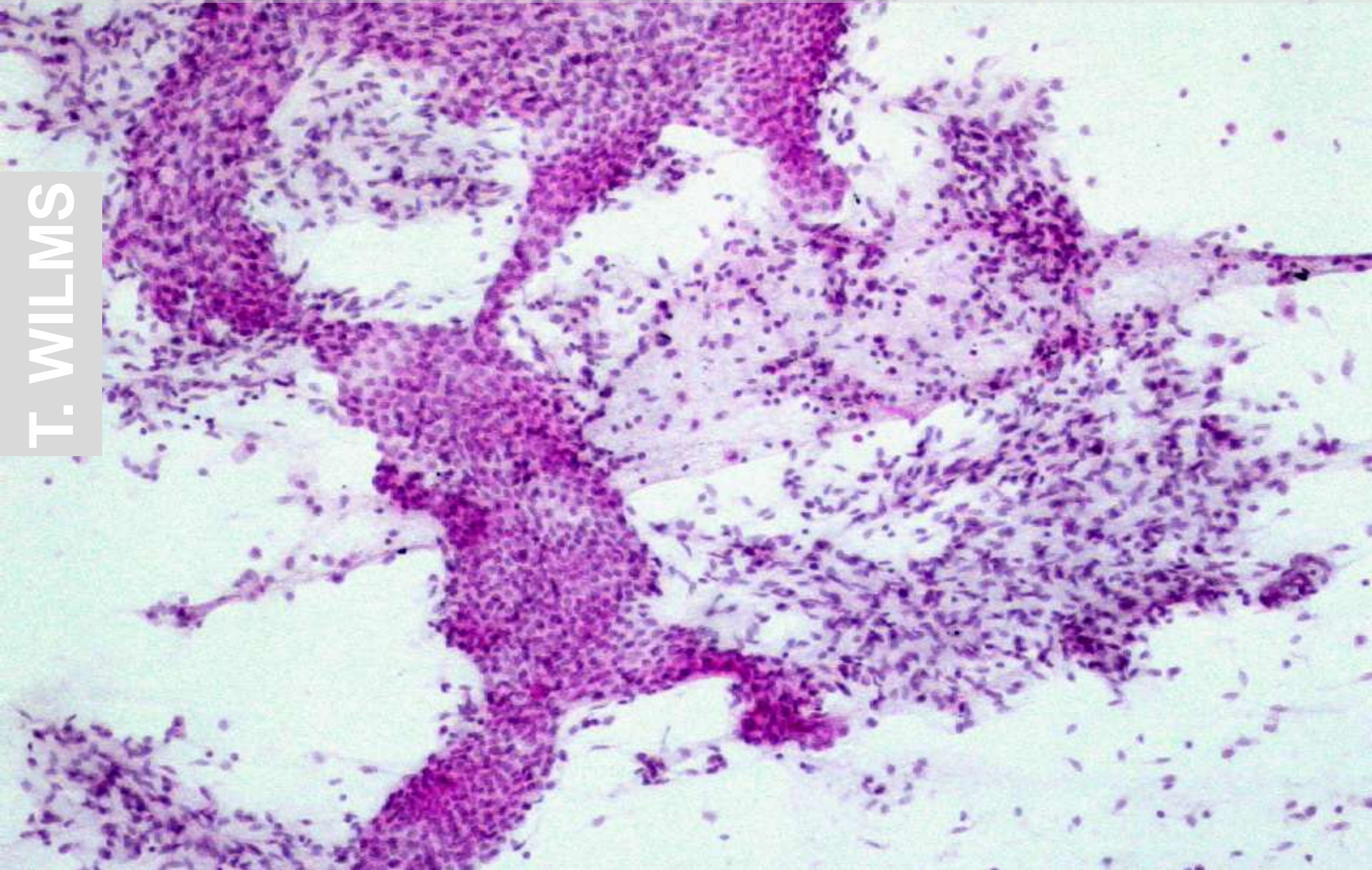
T. WILMS



Los tumores renales de la edad pediátrica

De la célula

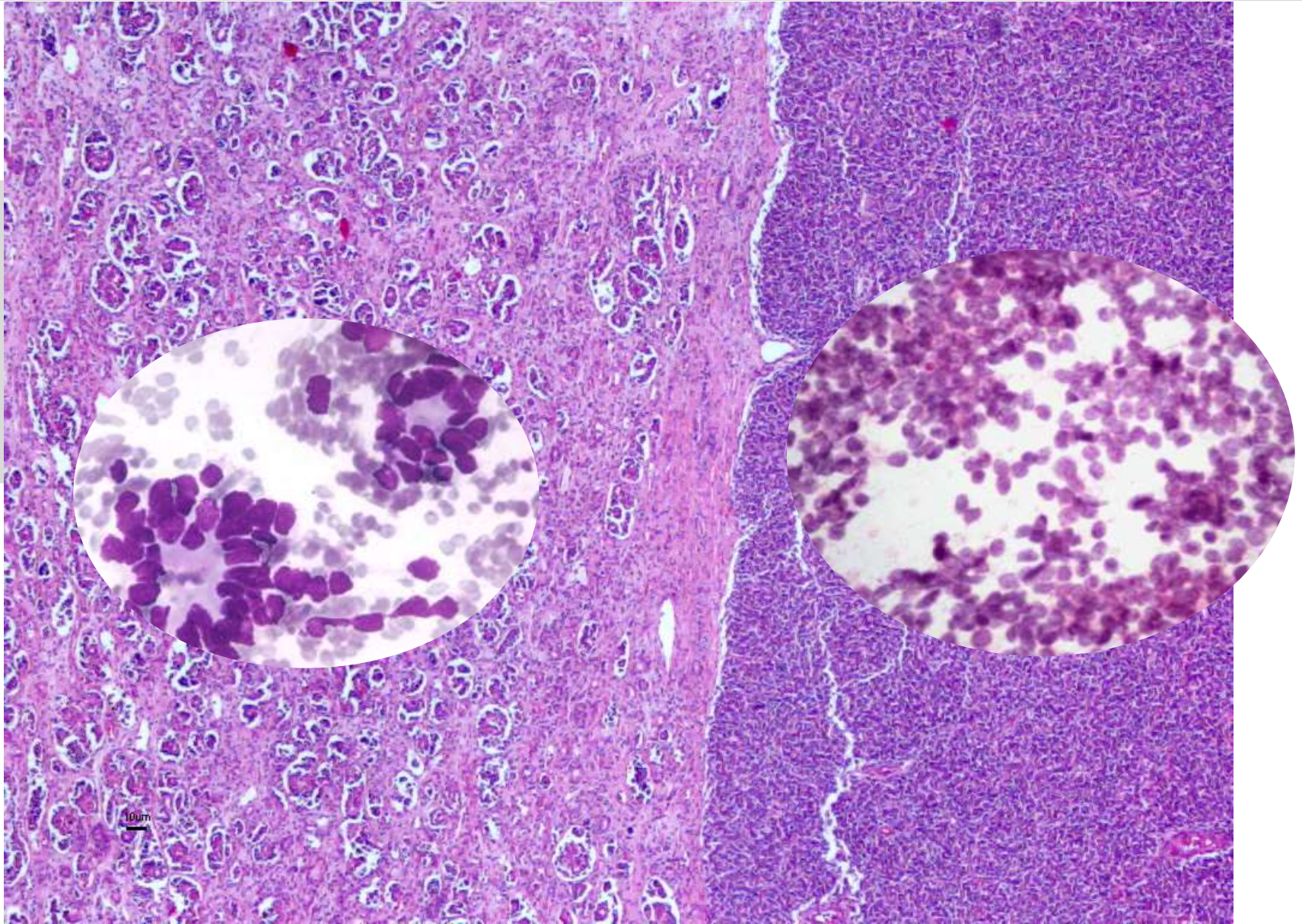
T. WILMS



Los tumores renales de la edad pediátrica

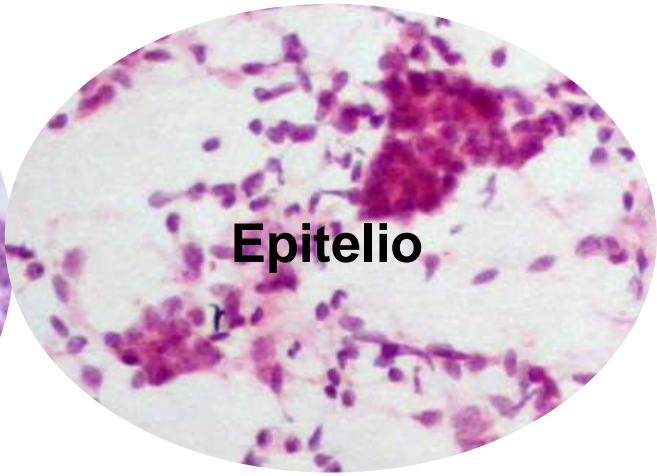
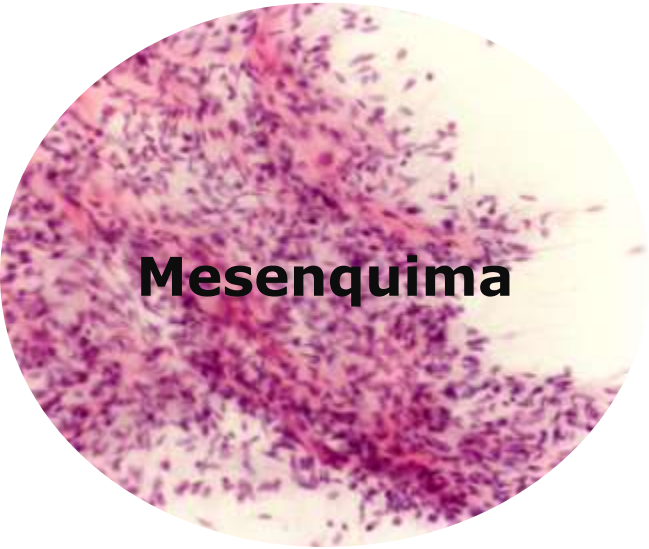
De la célula

T. WILMS



Los tumores renales de la edad pediátrica
De la célula

T. WILMS



Diagnóstico diferencial

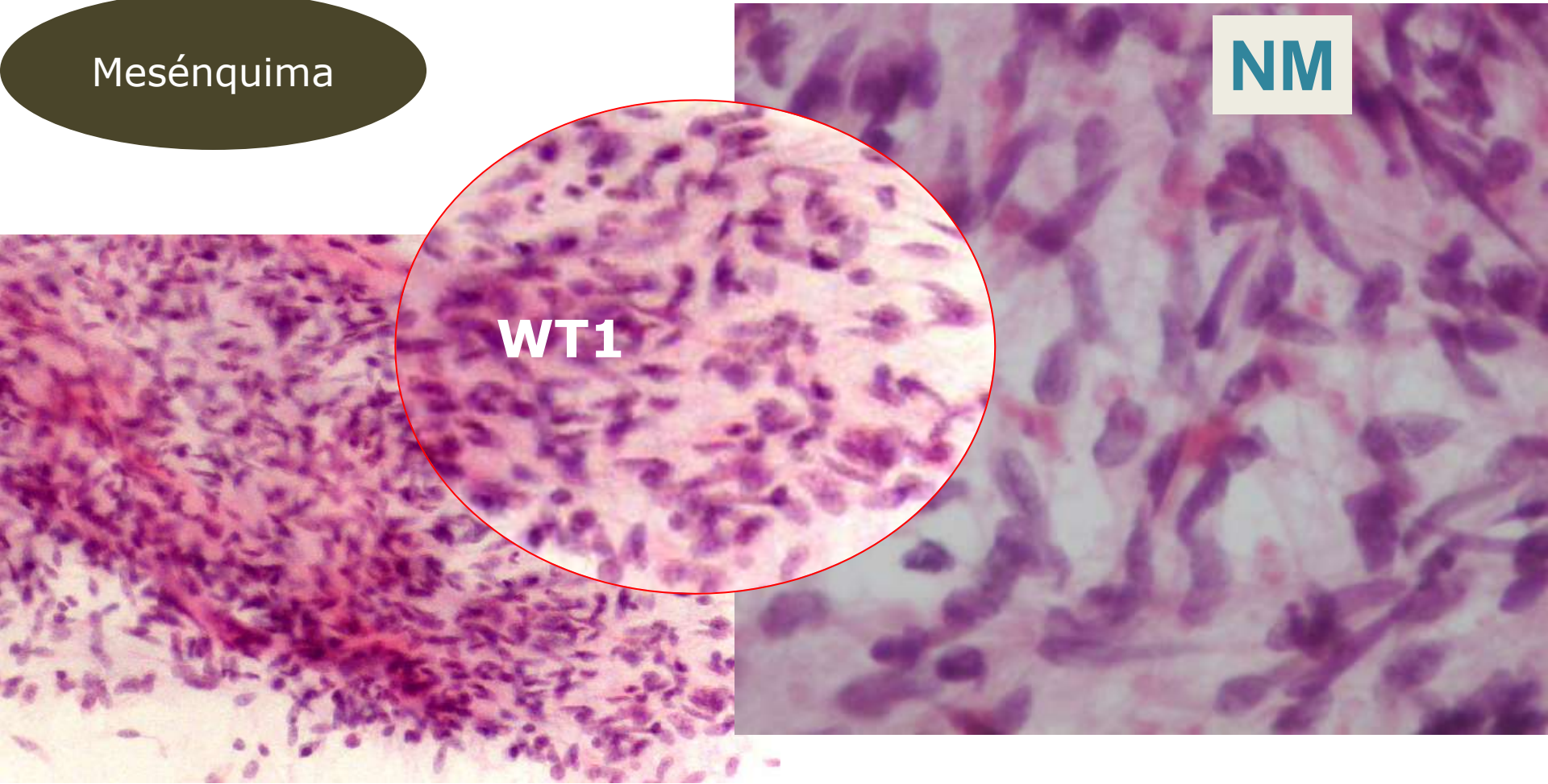
Nefroma mesoblástico
Sarcoma de células claras

Adenoma metanéfrico
Carcinoma papilar
Epitelio renal

T. Células pequeñas red azules
Linfoma
T. Rabdoide
Sarcoma de células claras

T. WILMS

Mesénquima



Tipo de tumor

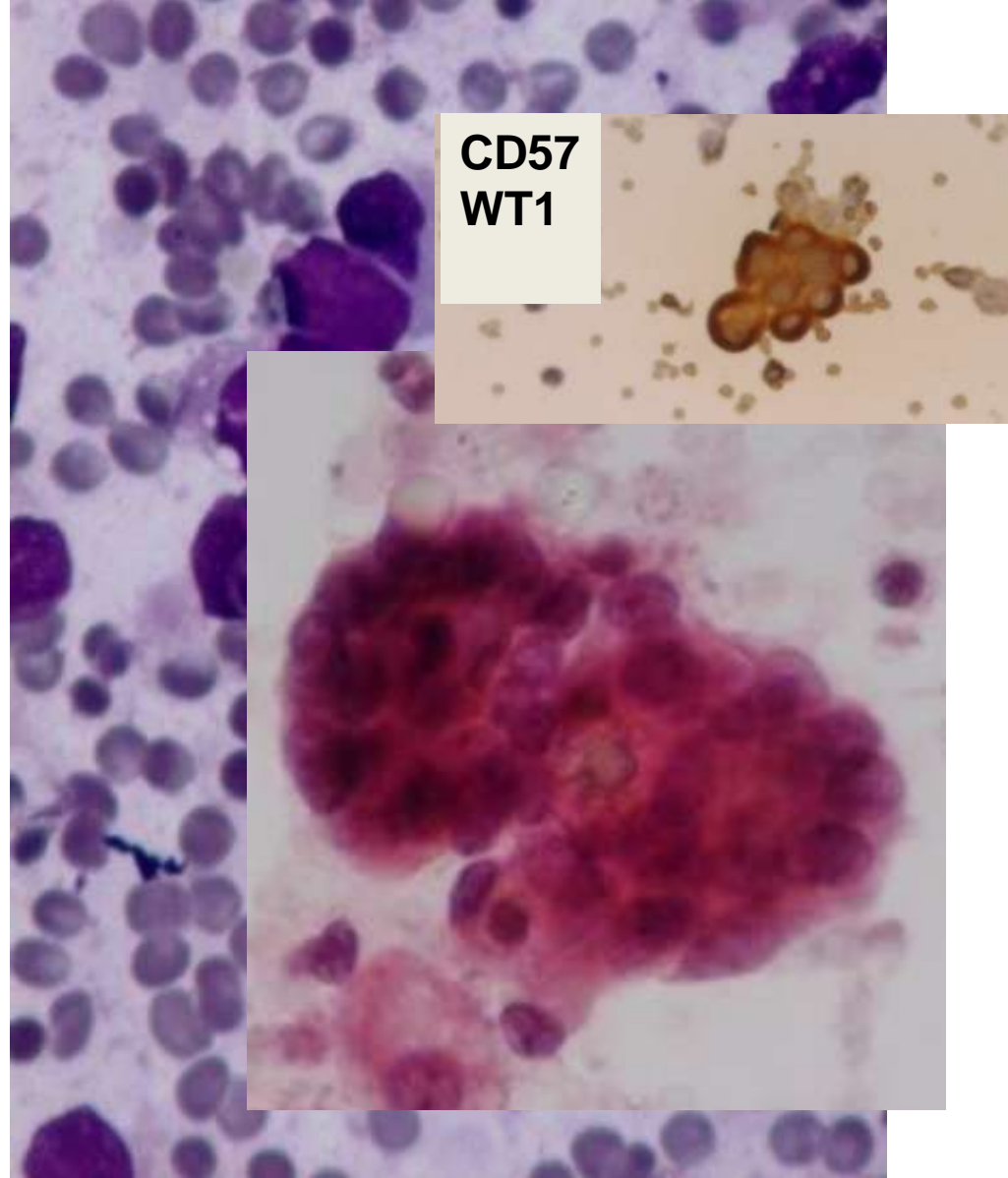
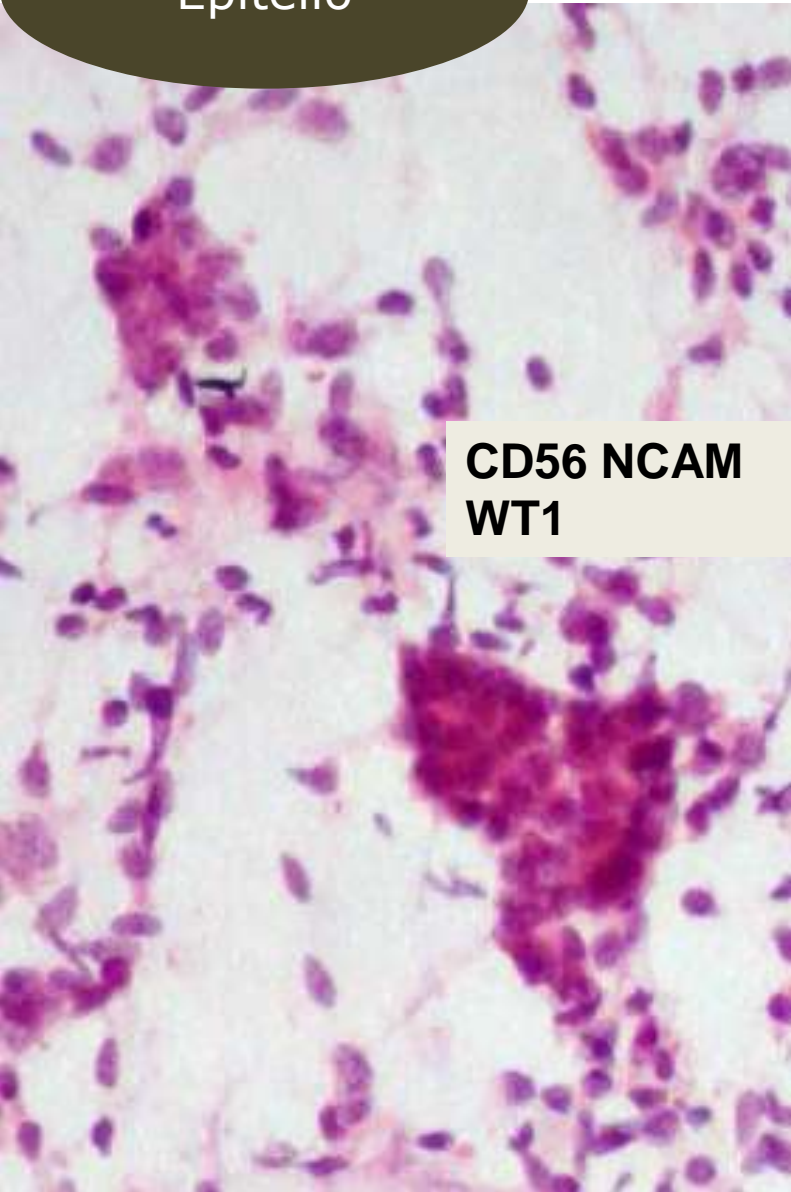
Fibrosarcoma congénito / nefroma mesoblástico

Citogenética

t(12;15)(p13;q25)

T. WILMS

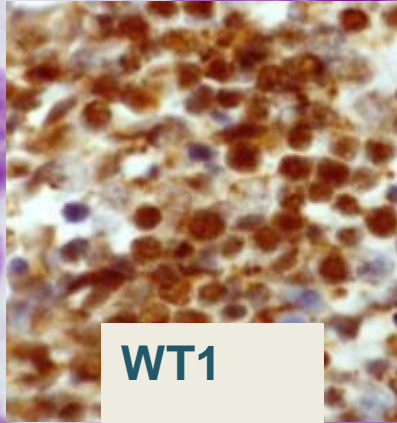
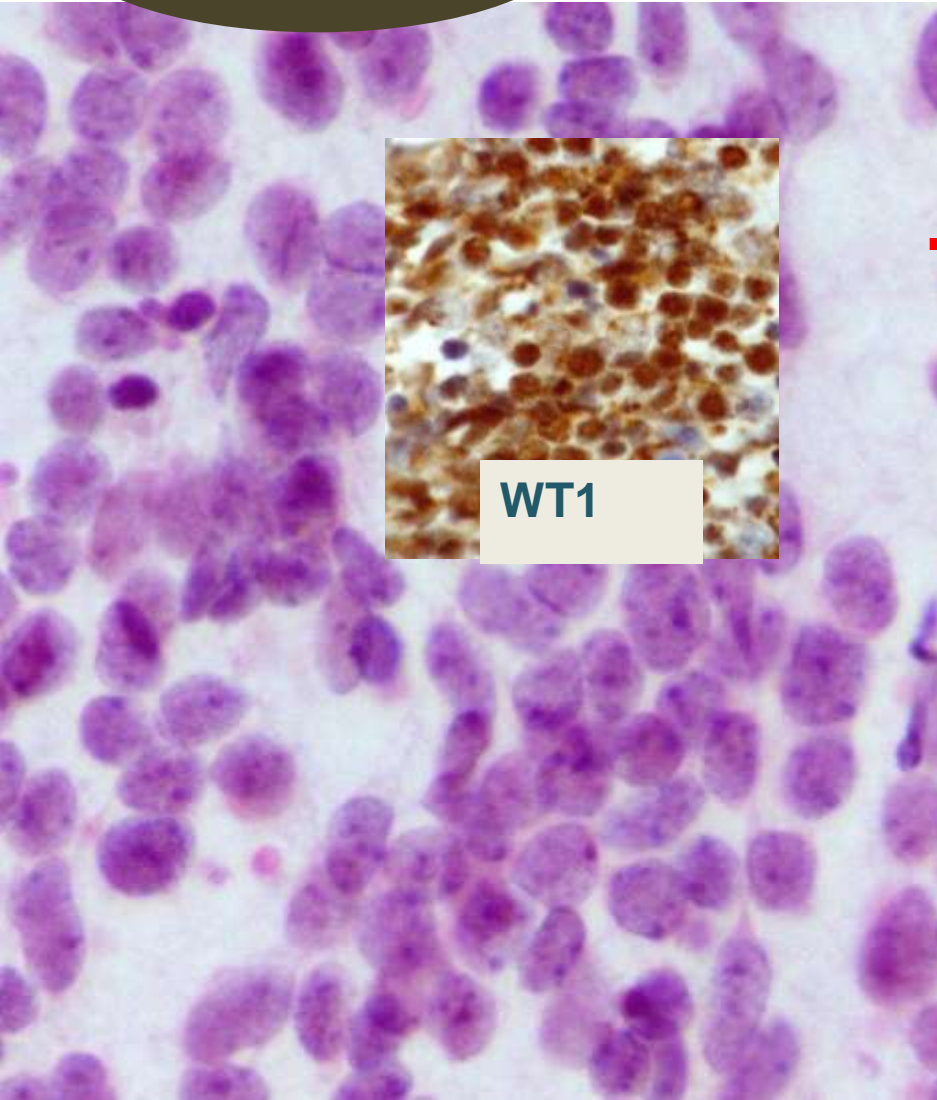
Epitelio



Adenoma Metanérico

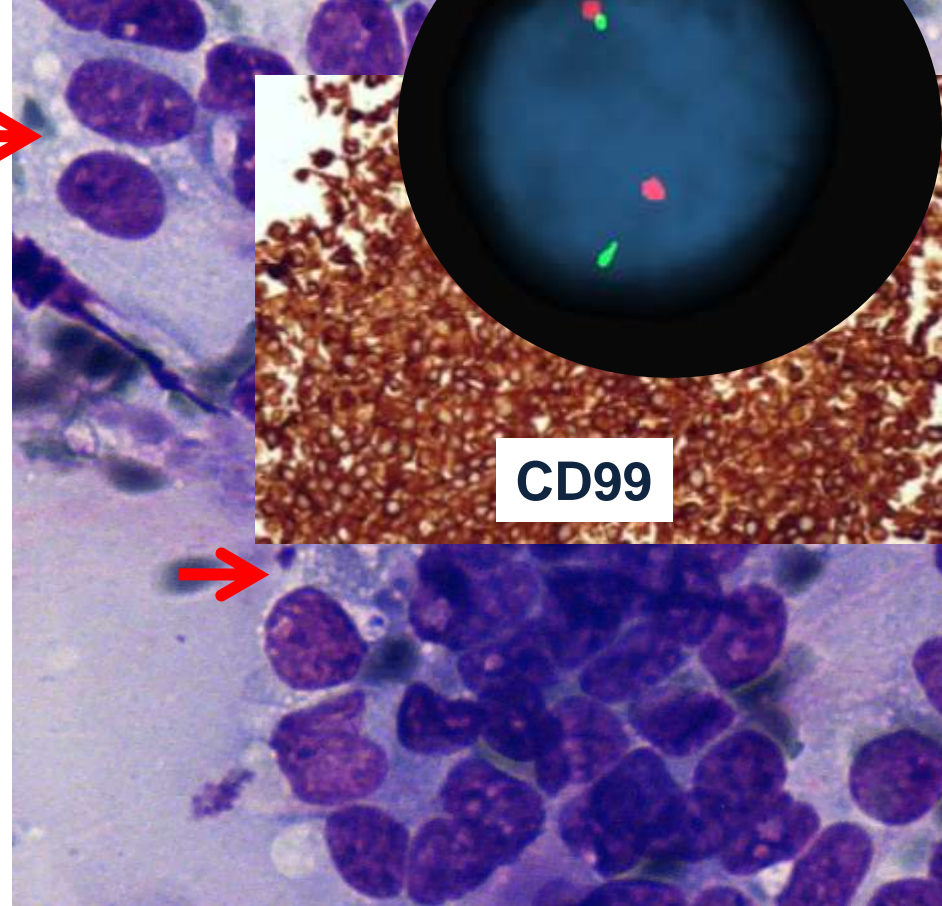
T. WILMS

Blastema

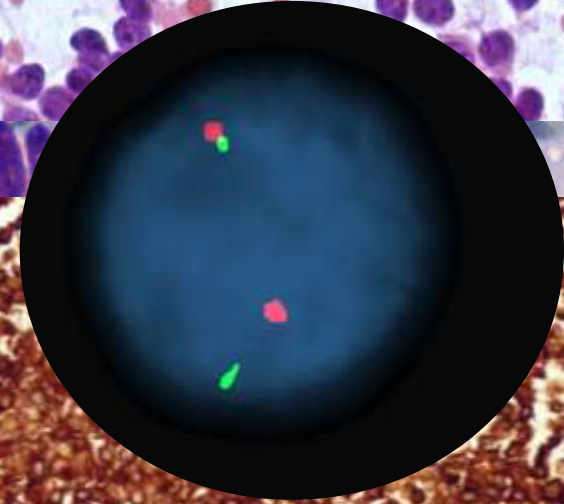


WT1

PNET

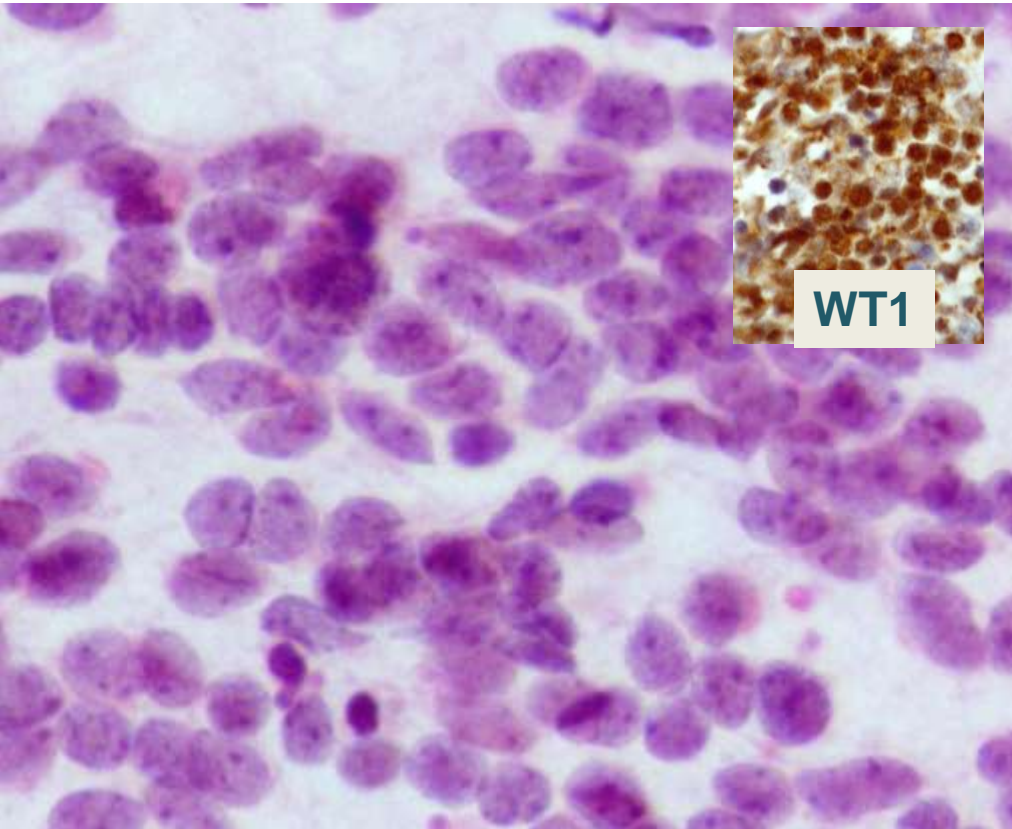


CD99

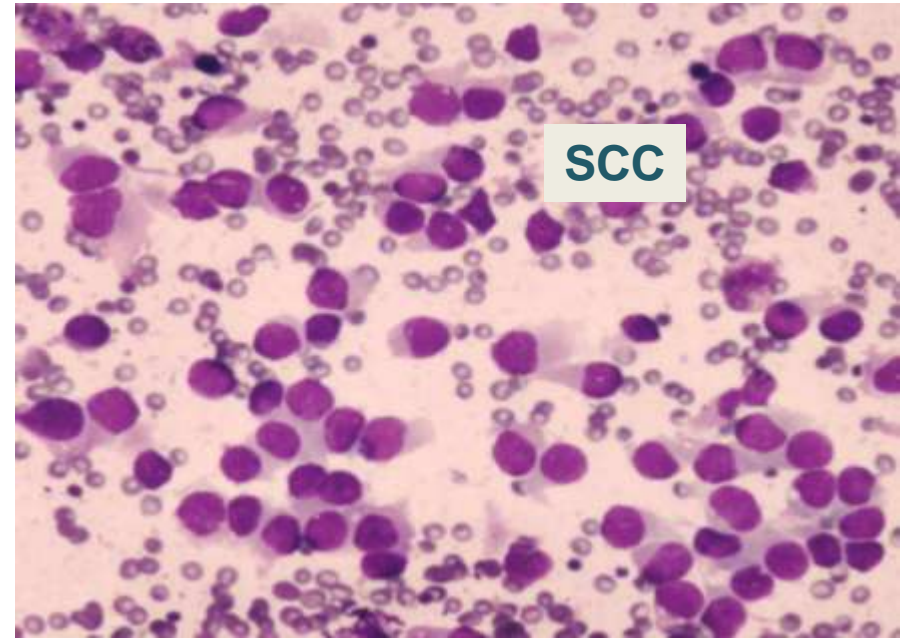


T. WILMS

Blastema



WT1



SCC



T rabdoide

Del cromossoma 22
INI1 negativo

Los tumores renales de la edad pediátrica de la célula **al gene**

Los tumores renales de la edad pediátrica

De la célula al gene

T. WILMS

Esporádicos

90%

**(Denys-Drash)
(WAGR)**

Beckwith-Wiedemann

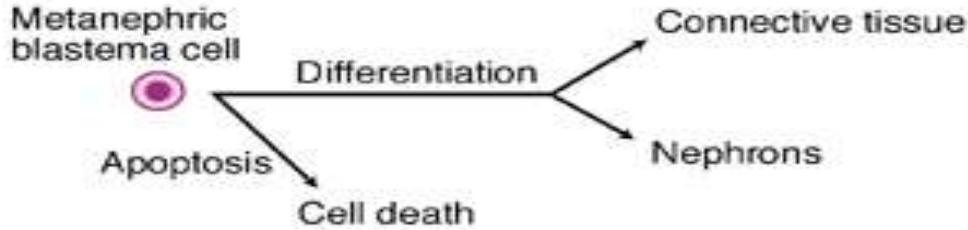
**Formas familiares
1-2%**

**Otros Síndromes
•Perlman**

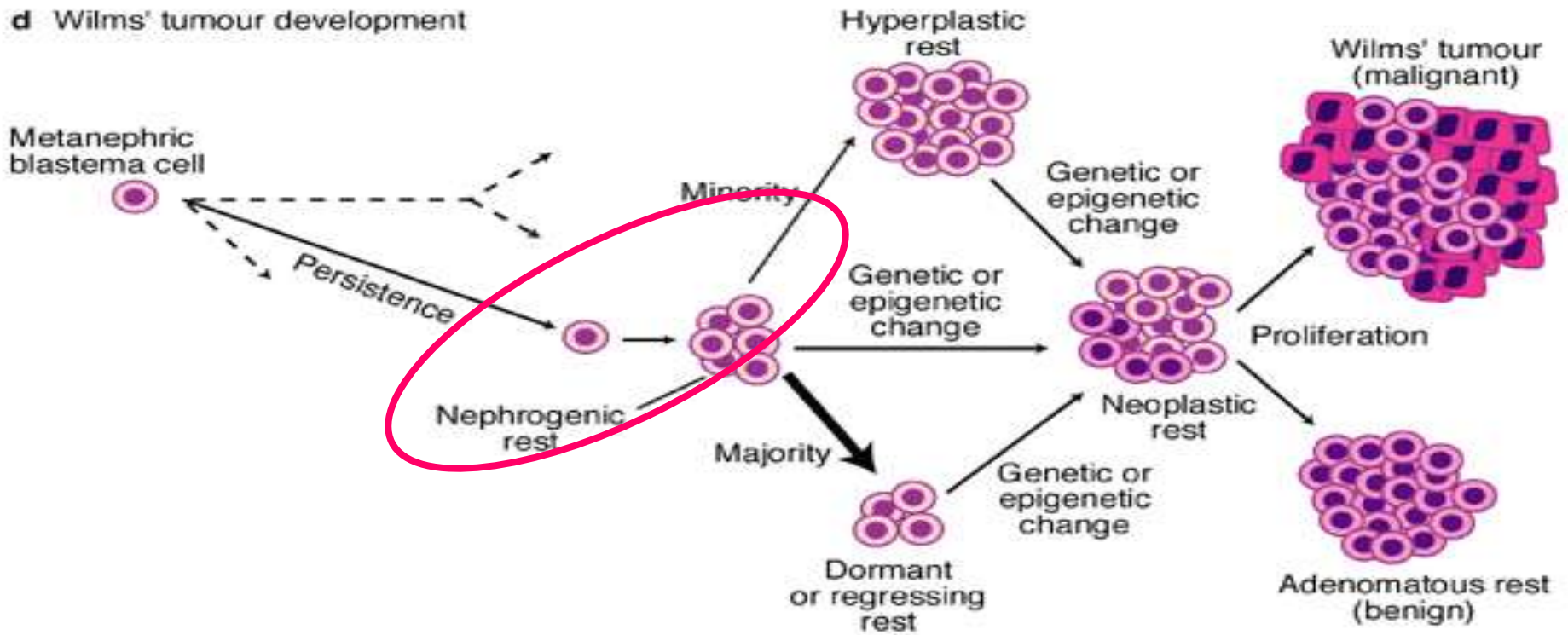
Los tumores renales de la edad pediátrica

De la célula al gene

c Normal cell development



d Wilms' tumour development

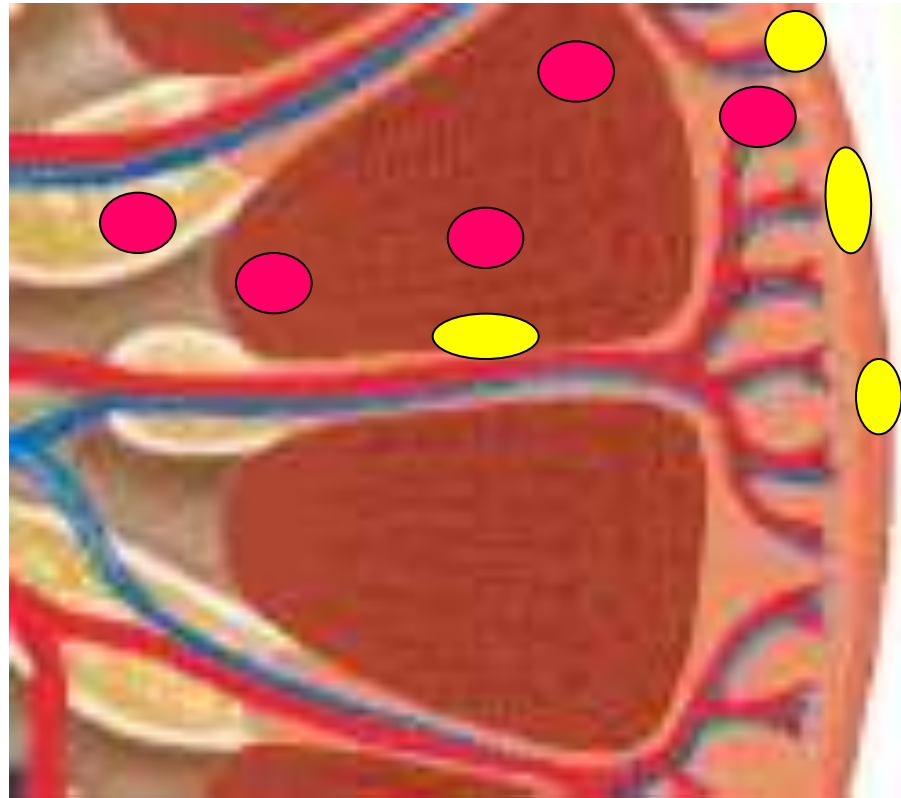


Kidney development and Wilms' tumourigenesis

Los tumores renales de la edad pediátrica
De la célula al gene

Restos nefrogénicos

En el 30% de los riñones con Wilms



ILNR

Intralobular nephrogenic rests

PLNR

Peri lobular nephrogenic rests

Los tumores renales de la edad pediátrica

De la célula al gene

PLNR

ILNR

- Mujeres
- jóvenes y adolescentes
- Asiáticos / Caucásicos
- Hemi-hipertrofia/BW
- Dif nefrogénica epitelial con blastema
- Wt2- IGF 2

- Varones
- bebés o "jóvenes"
- Caucásico
- WARG/DD
- Diferenciación mesenquimatosa predominante

IGF II (LOI)

Wt2

30-50%

WTX
30%

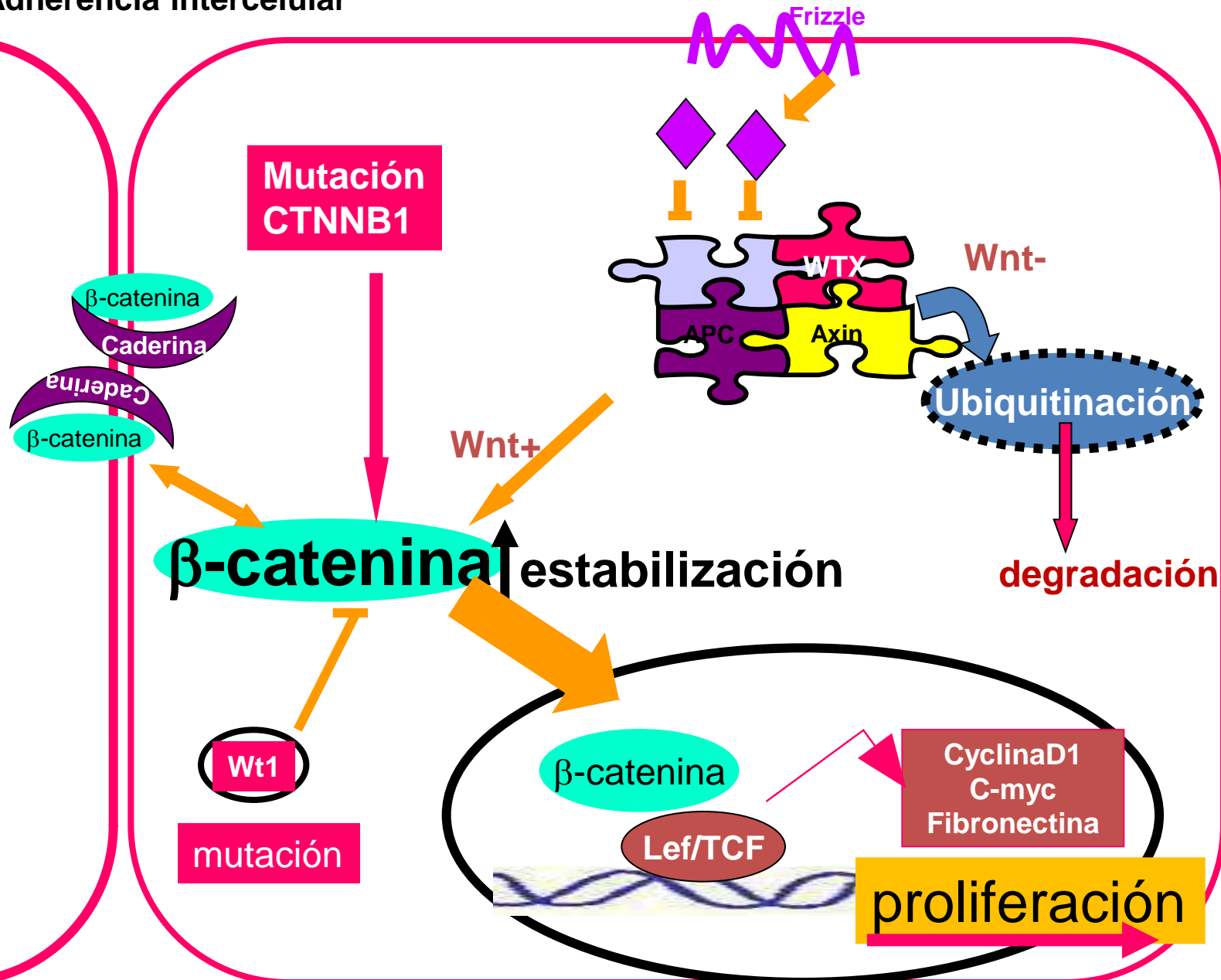
Mutación / LOH

Wt1

10%

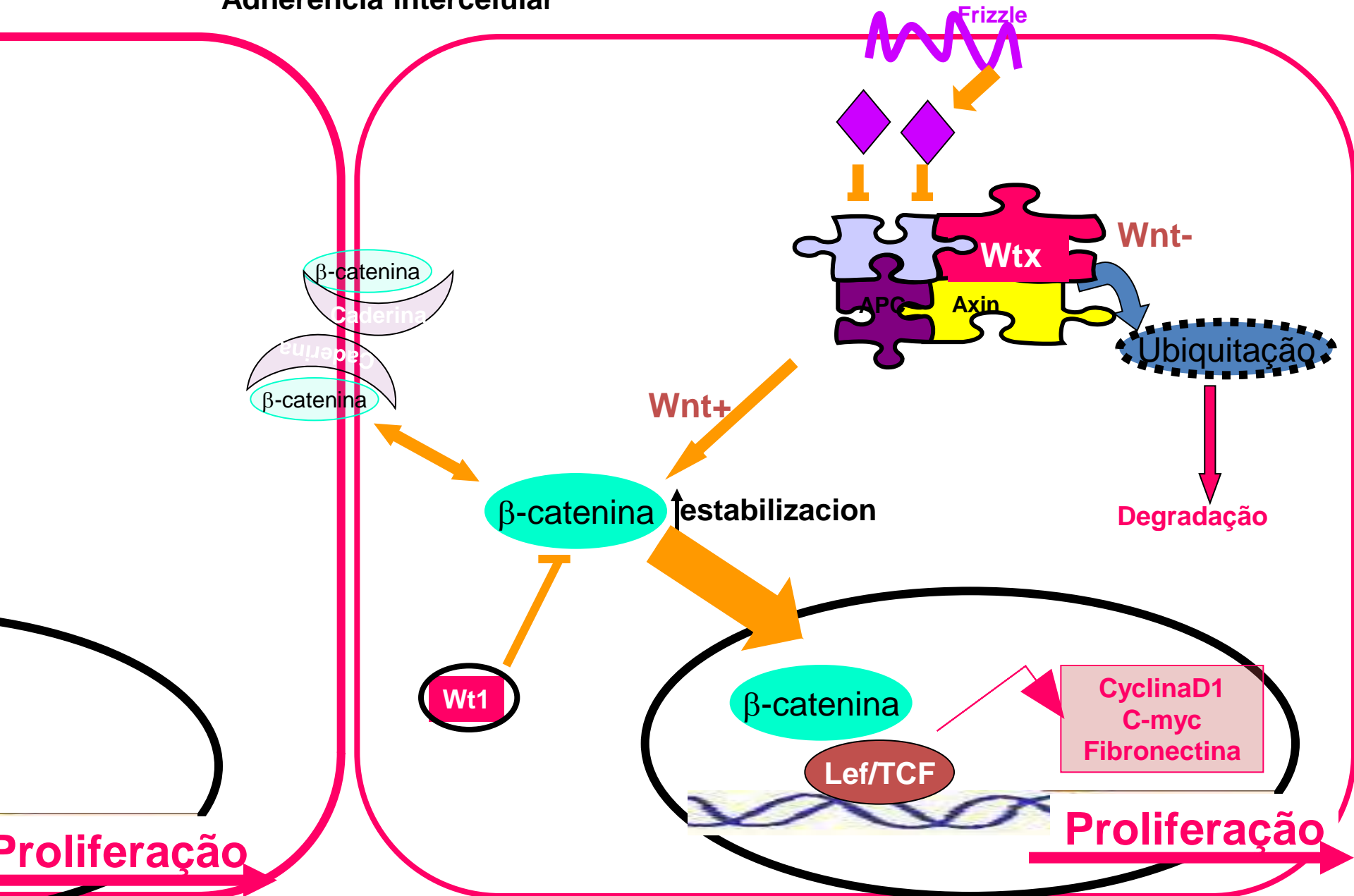
Wnt pathway-Wilms

Adherencia intercelular



Wnt pathway

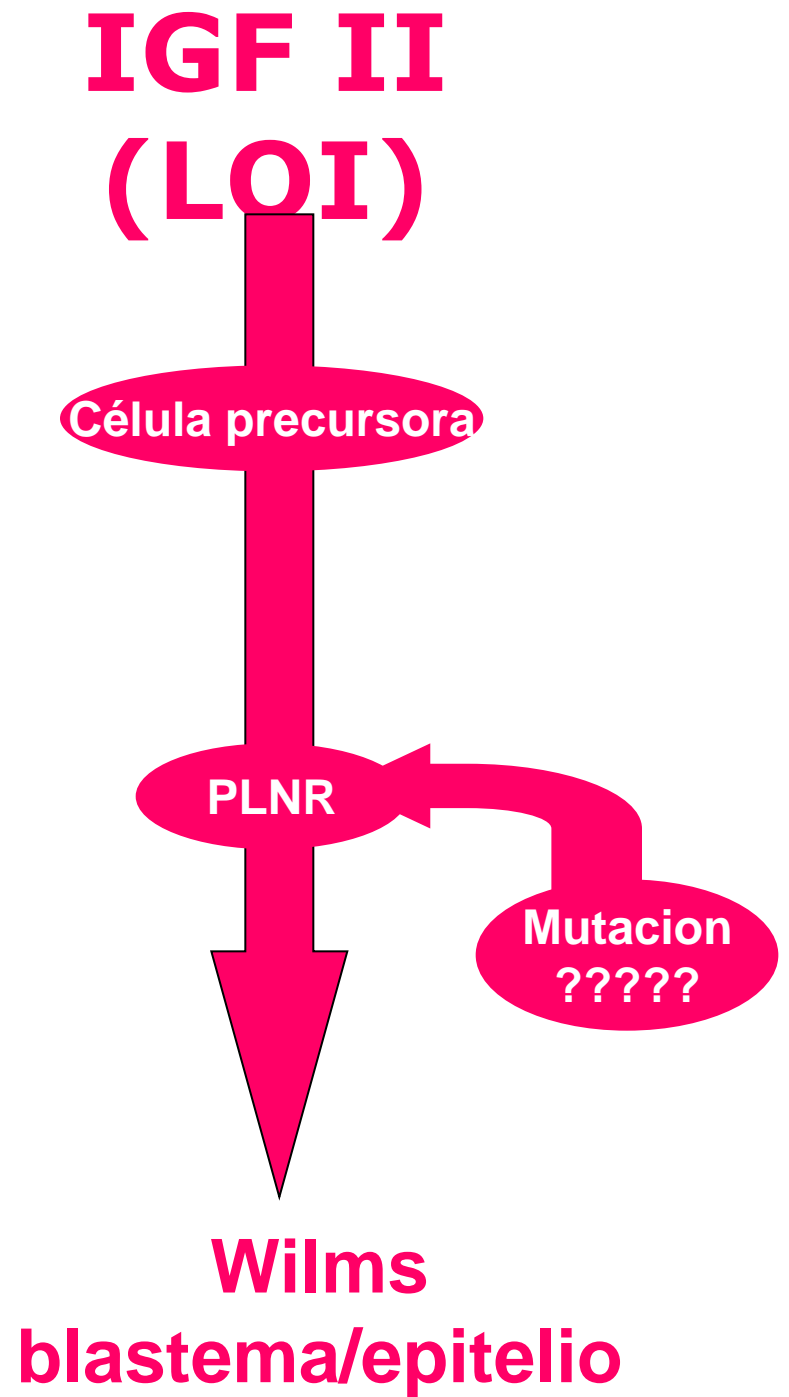
Adherencia intercelular



- Mutaciones WT1 y beta-catenina (CTNNB1) parecen coexistir (50-75%)
- Mutaciones del CTNNB1 parecen surgir en células precursoras células capaces de diferenciación mesenquimatosas
- Las mutaciones del WT1 son precursoras de las mutaciones del gen CTNNB1

- WTX por lo general participa en el mecanismo de degradación de b-catenina
- WTX puede tener un papel modulador de WT1 en la diferenciación celular
- WTX parece contribuir a cerca de 30% de los tumores de Wilms y pueden o no estar asociada con la mutación de WT1 y CTNNB1

Wt2



Wt2 e IGFII (LOI)



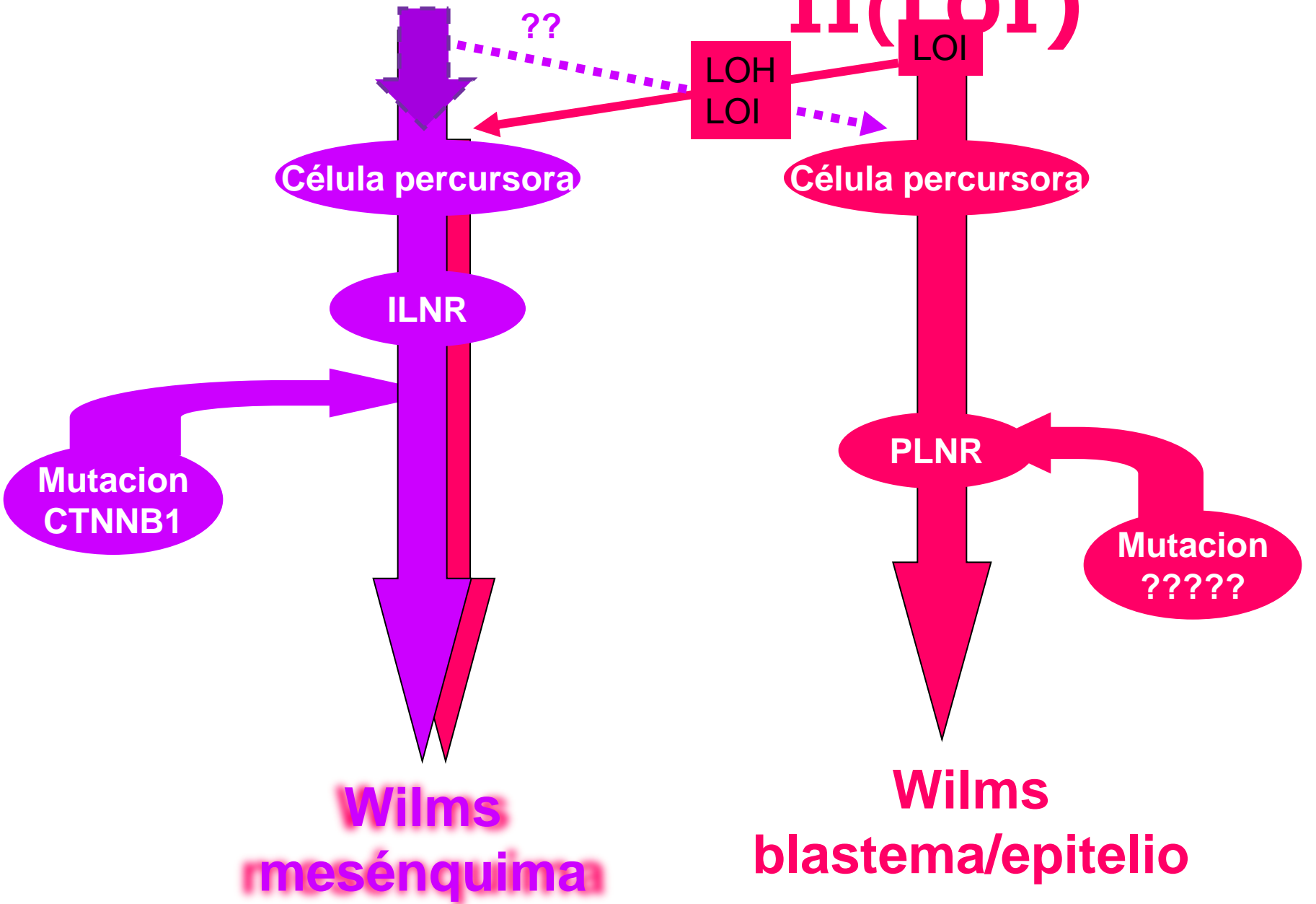
Hemi-hipertrofia

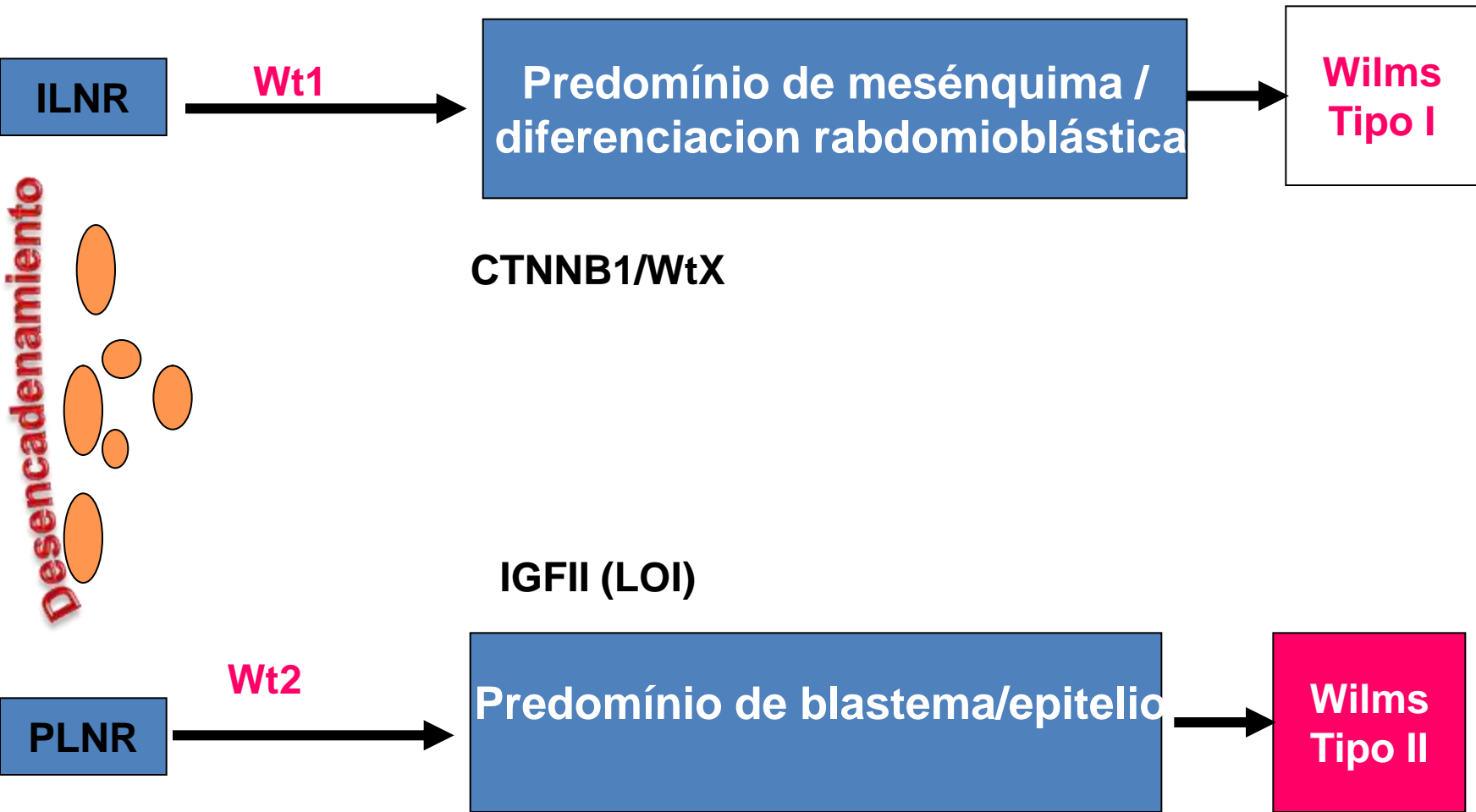
IGFII (LOH) es un fenómeno precoz en la génesis del tumor de Wilms

Wt2 - IGF

Wt1

II(LOI)





Los tumores renales de la edad pediátrica- De la célula al gene

Carcinoma renal

Por qué los niños no son adultos pequeños?

Carcinomas de células claras

Carcinomas de padrão papilar

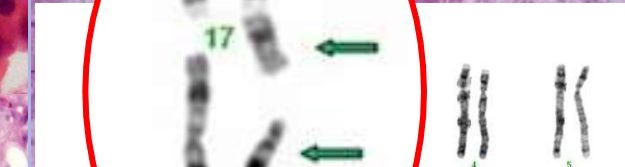
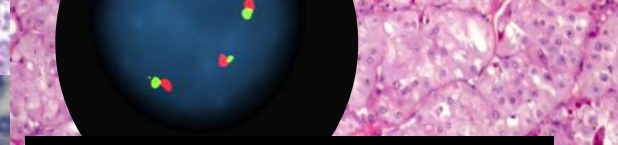
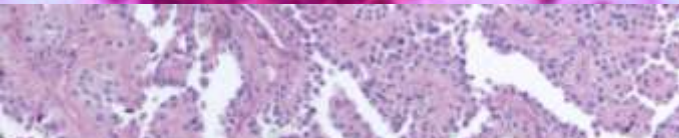
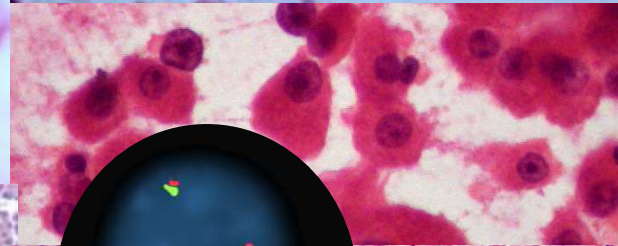
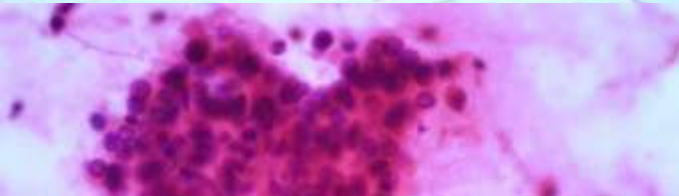
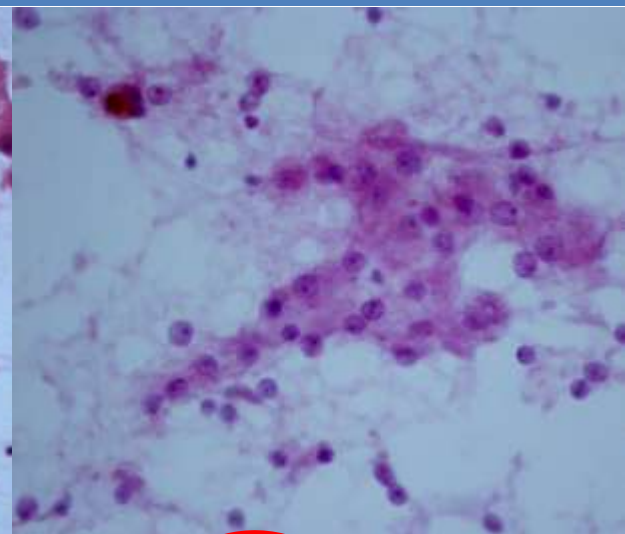
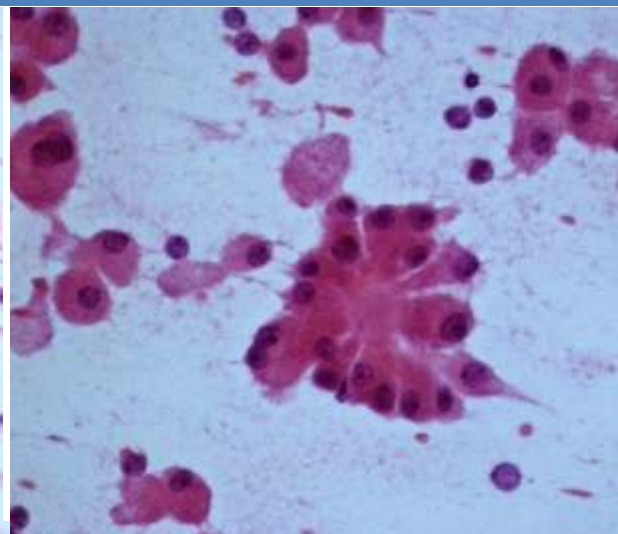
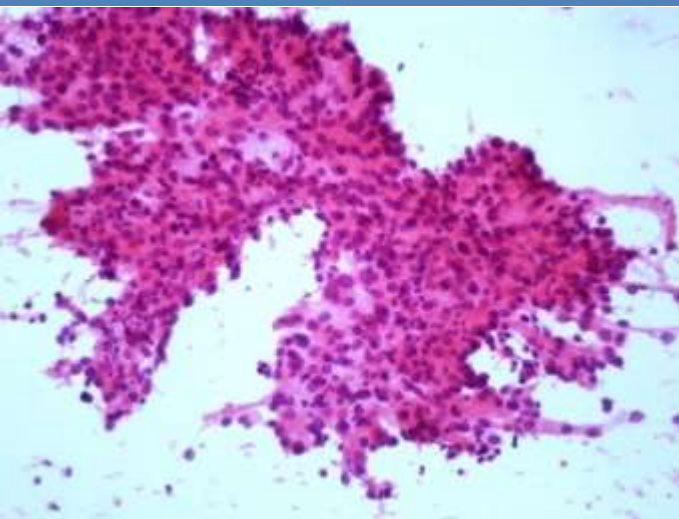
**Del 3p
Von Hippel Lindau**



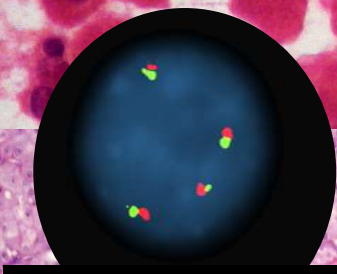
**MITF- 20-74%
de los carcinomas renales pediátricos**

**En pacientes con neuroblastoma
Esclerosis tuberosa,
Von Hippel Lindau....**

niño 16 años niño - 12 años- Escl Tub niño 1 año

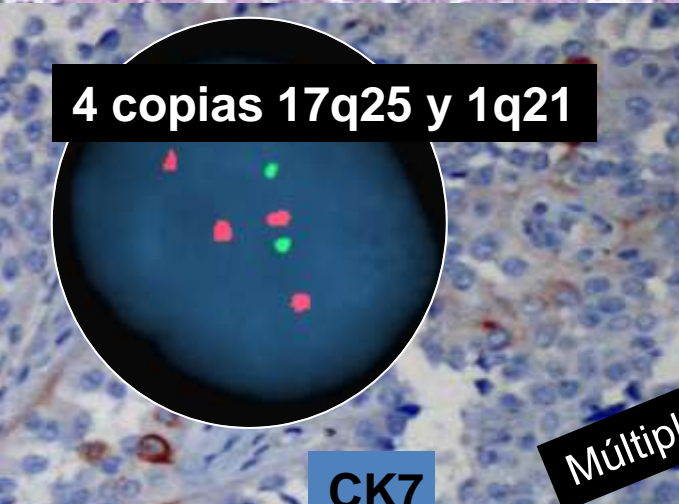
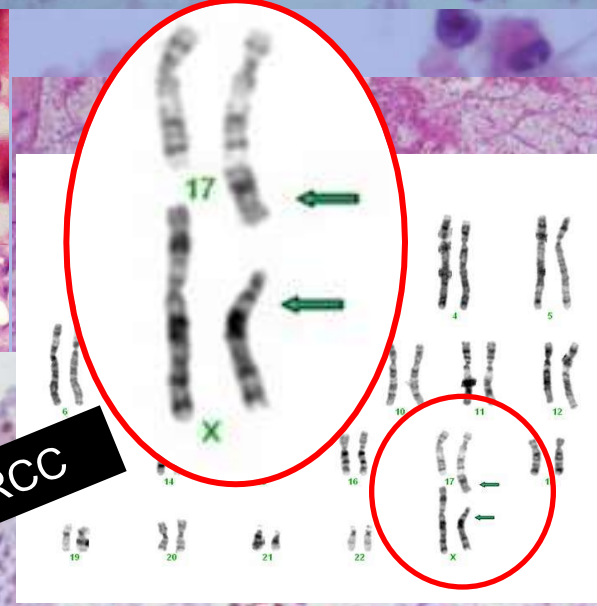
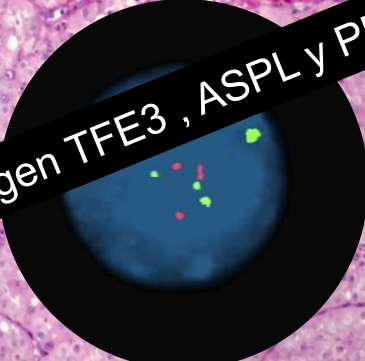


4 copias 17q25 y 1q21

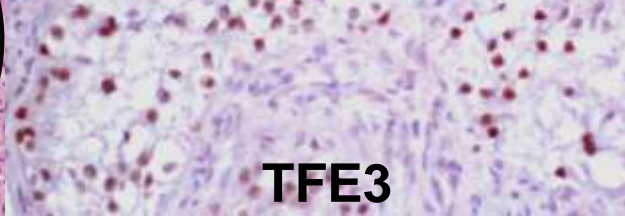


4 copias del gen TFEB

Múltiples copias del gen TFE3, ASPL y PRCC



CK7

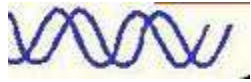


TFE3

MIT y MET

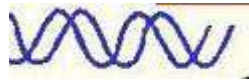
MITF

Xp11.2



TFE3

6q21



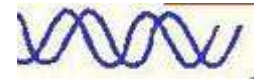
TFEB

7q31.2

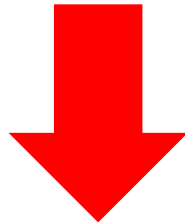
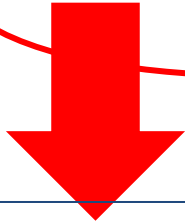


TFEC

3p14.2



MITF



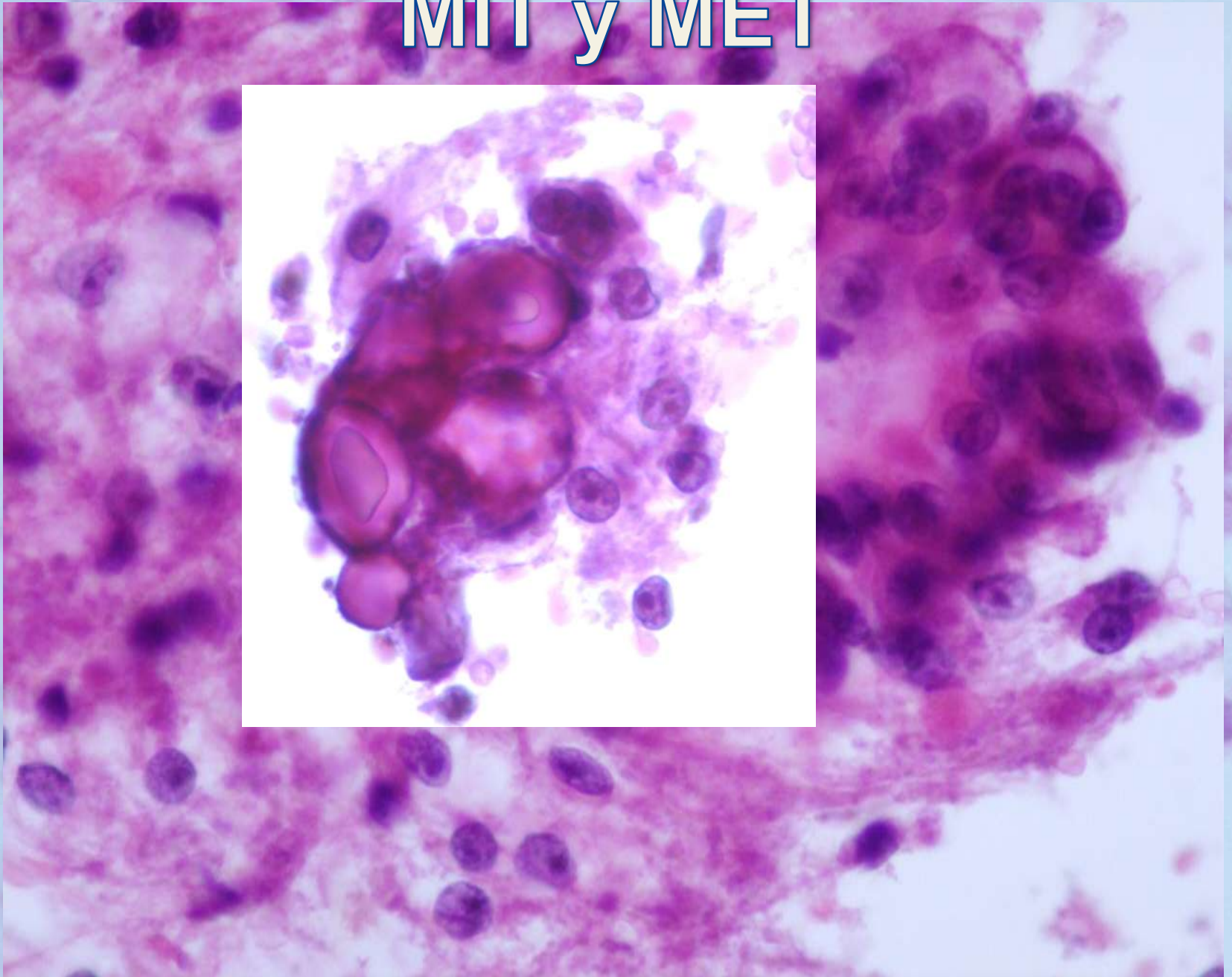
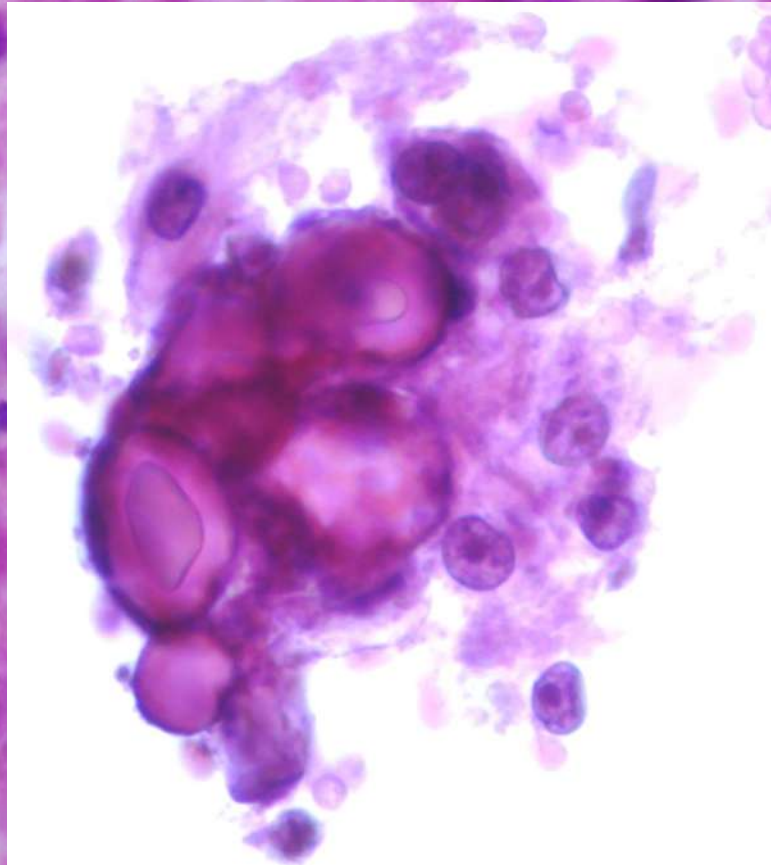
T(X;17)(p11.2;q25)
TFE3; ASPL

T(X;1)(p11.2;q34)
TFE3; PSF

T(6;11)
TFEB: *alpha*



MIT y MET



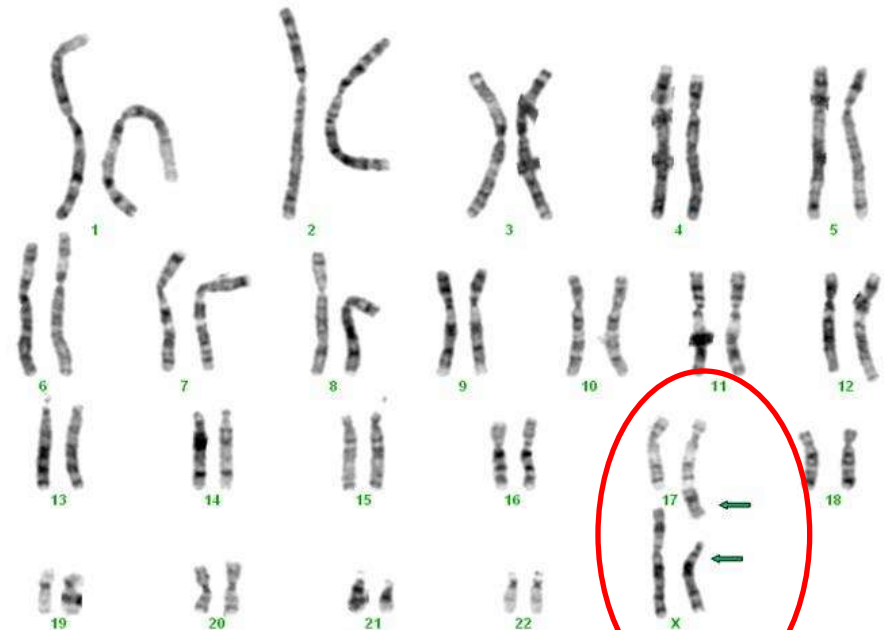
TFE3

CD10+
Caderina E +
CK7-
EMA -

Estadios avanzados
supervivencia?

cristales romboides

TF



Esclerosis tuberosa

- Angiomiolipomas (10 años) 75-80%
- Quistes renales 17%
- Carcinoma de células renales <5%
- Oncocitoma

TSC1/TSC2

Célula progenitora renal

diferenciación mesenquimal

diferenciación epitelial

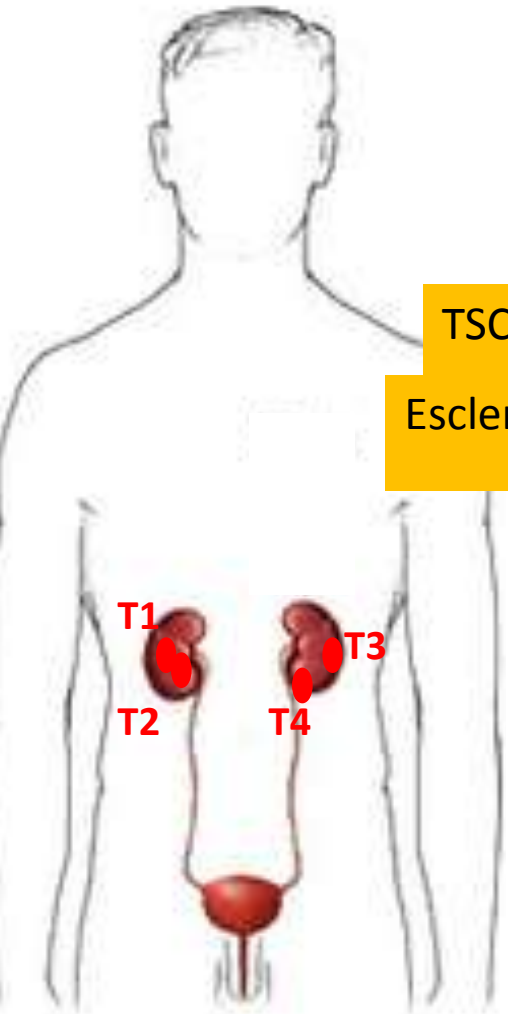
Angiomiolipoma

**RCC
Oncocitoma**

Distinctive morphology of renal cell carcinomas in tuberous sclerosis

43 años
Esclerose tuberosa

Scheiner A et al- Int J Surg Pathol 2009



TSC1/TSC2

Esclerose tuberosa

- Células granulares eosinofílicas
- heterogeneidad del perfil inmunológico

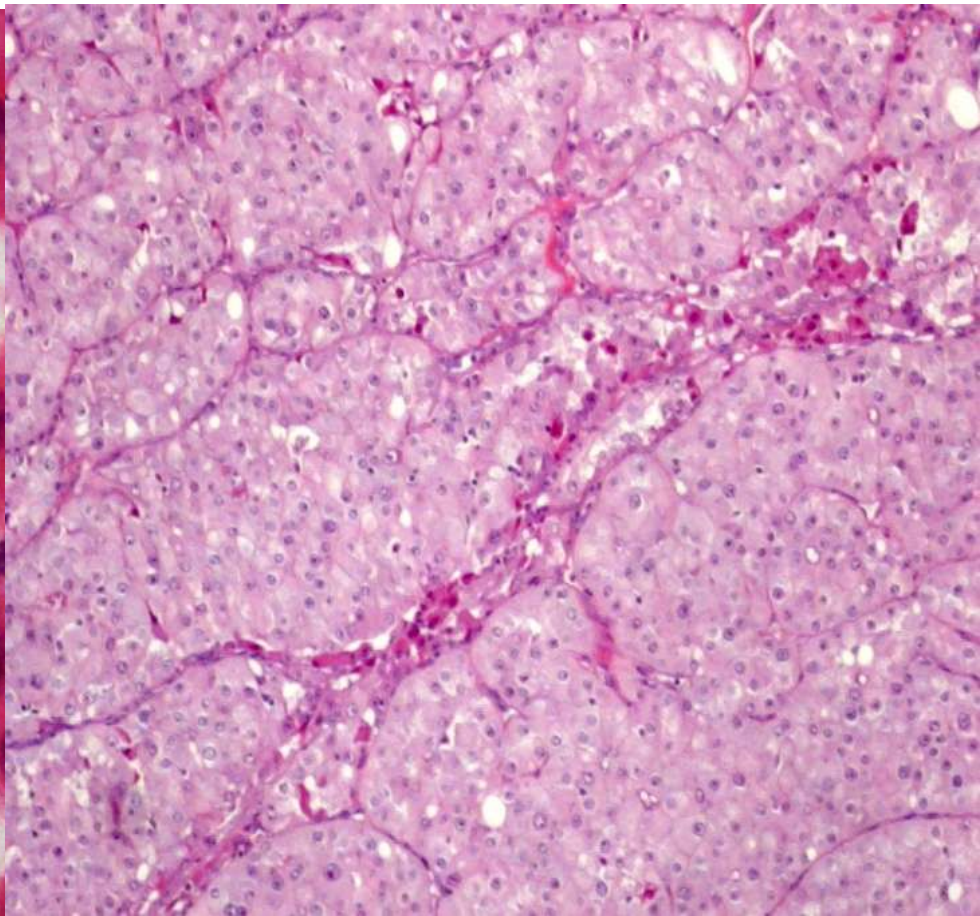
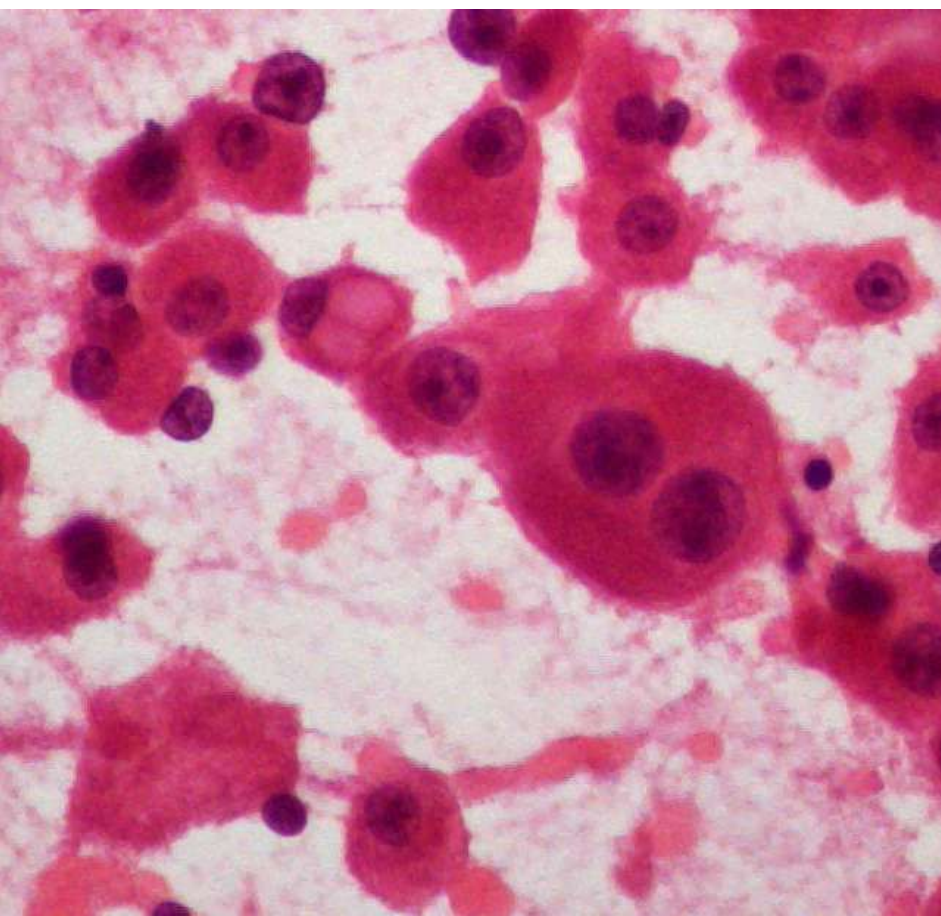
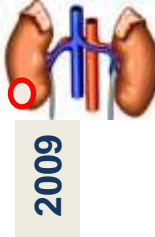
Carcinoma Renal

Perfil comum
AE1/AE3 +
CD10 +

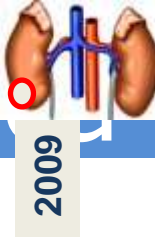
Perfil variável

- CK7
- RCC
- Vimentina
- CD117
- AMARC

niño - 12 años- esclerosis tuberosa

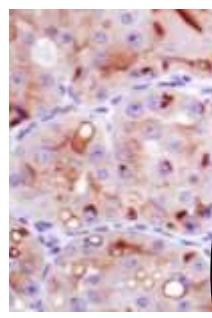


Histo Alteraciones moleculares químicas

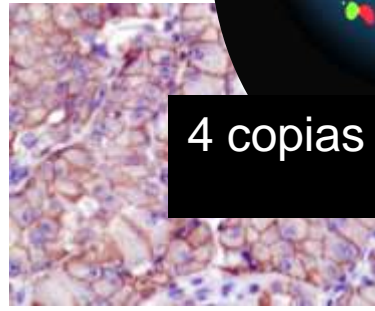


POSITIVOS

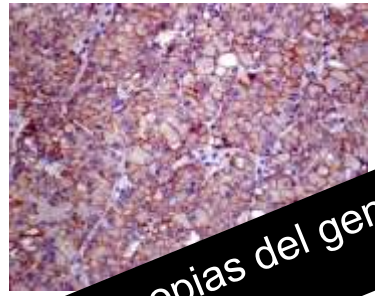
CD10 (focal)



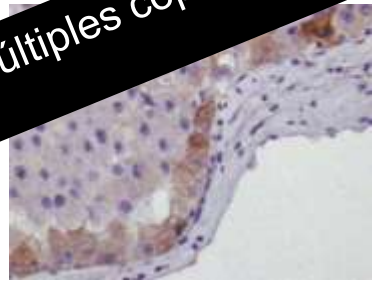
Cadherina E



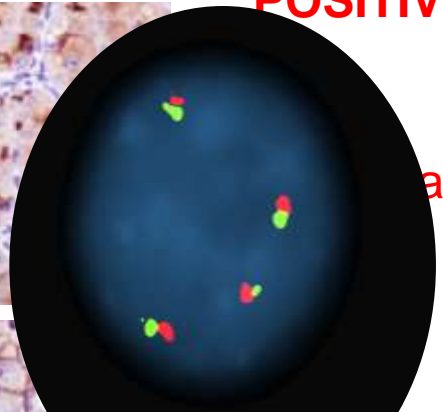
CD117 (focal)



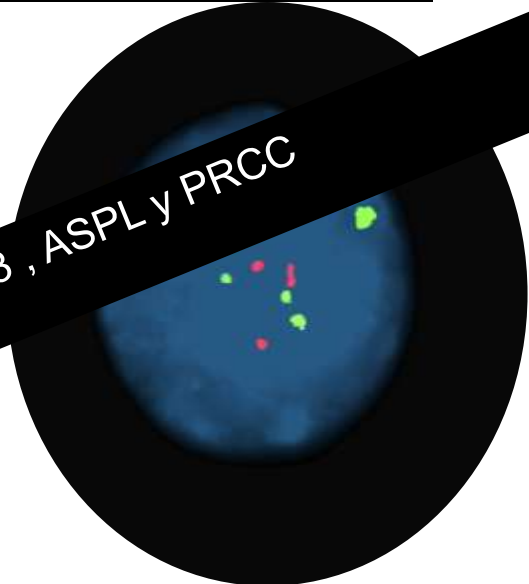
EMA (focal)



POSITIVOS



4 copias del gen TFEB



Múltiples copias del gen TFE3 , ASPL y PRCC

NEGATIVOS

Vimentina

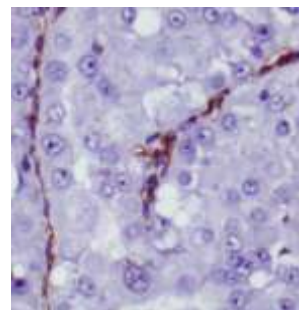
CK7

CAM5.2

45

Fierro coloidal

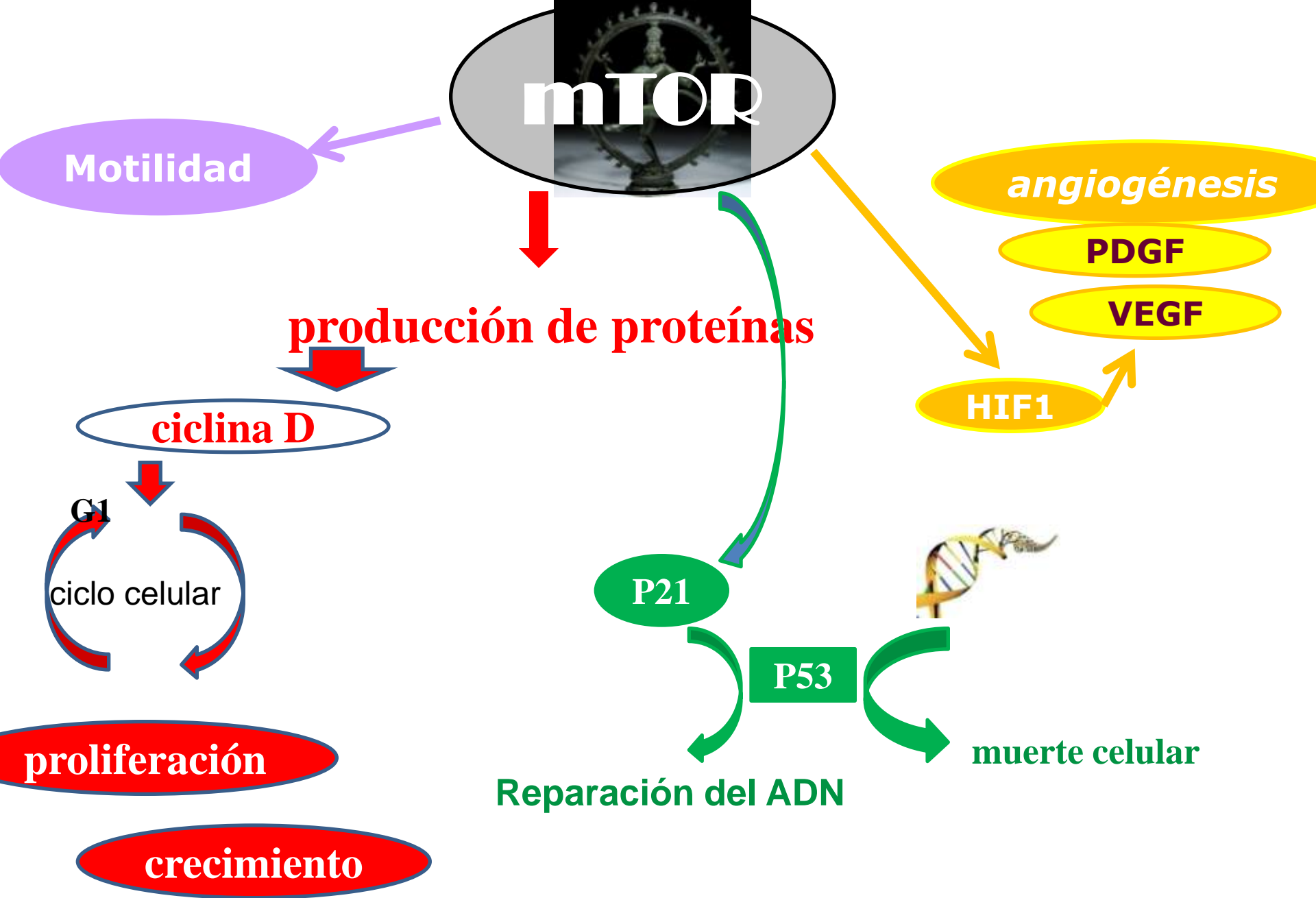
RP



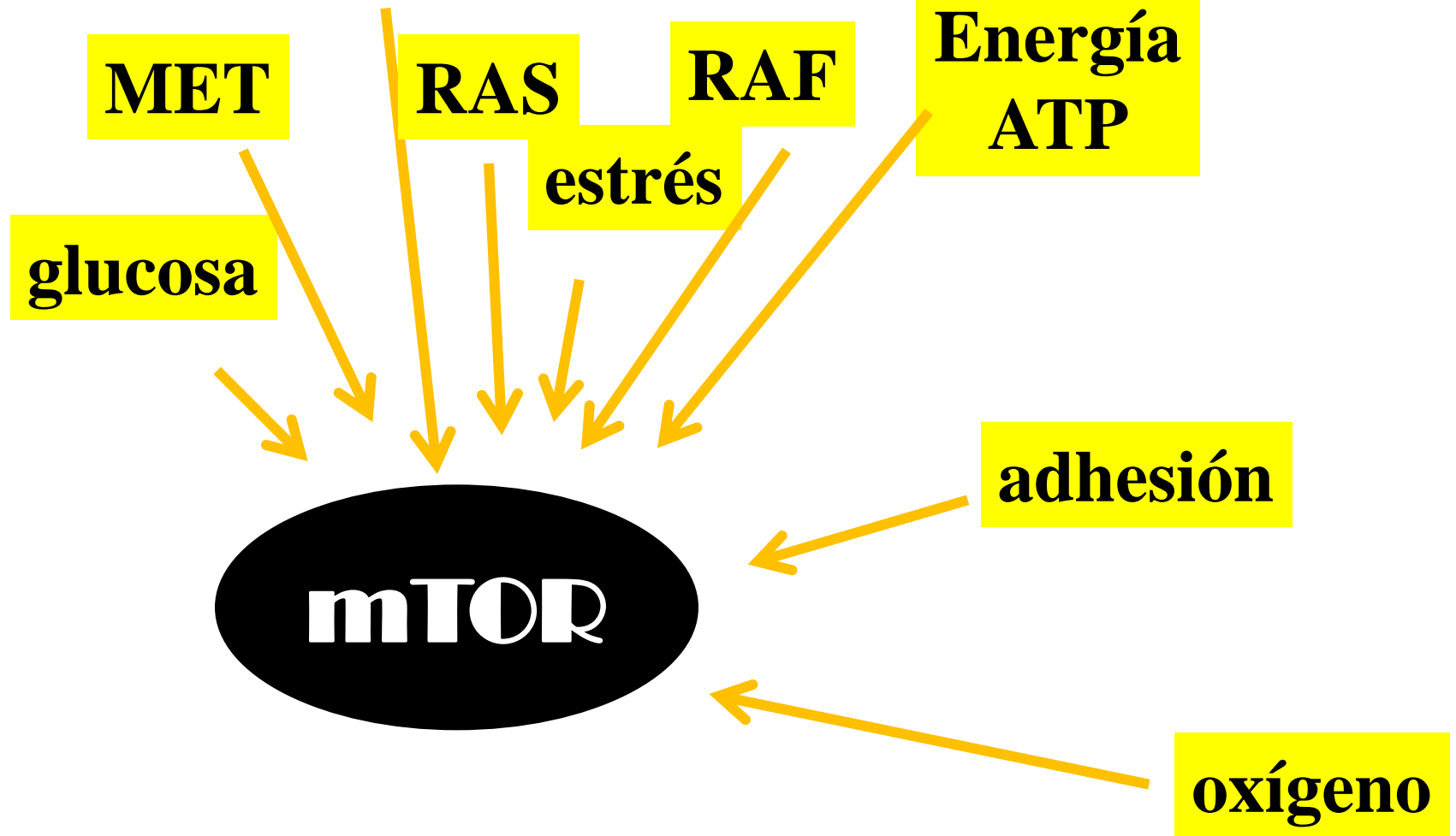
¿Qué hay detrás del carcinoma renal de los niños?



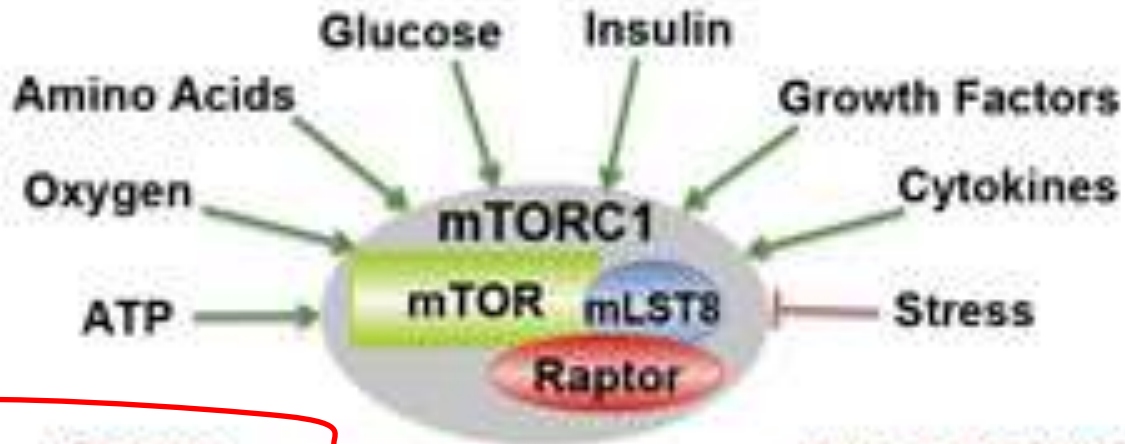
mTOR



**factores de crecimiento
EGFR, HER2, IGF-1R, HGFR**



mTOR complex 1 senses cellular growth conditions and is dysregulated in a wide variety of human diseases



- Cancer
- Neurofibromatosis
- Tuberous Sclerosis Complex
- Cowden Syndrome
- Proteus Syndrome
- Lymphangi leiomyomatosis
- Peutz-Jeghers Syndrome
- Autism Spectrum Disorders
- Epilepsy
- Huntington's Disease
- Alzheimer's Disease
- Polycystic Kidney Disease
- Type-2 Diabetes
- Systemic Lupus Erythematosus
- Obesity
- Autoimmune Lymphoproliferative Syndrome
- Cardiovascular Disease
- Asthma
- Aging

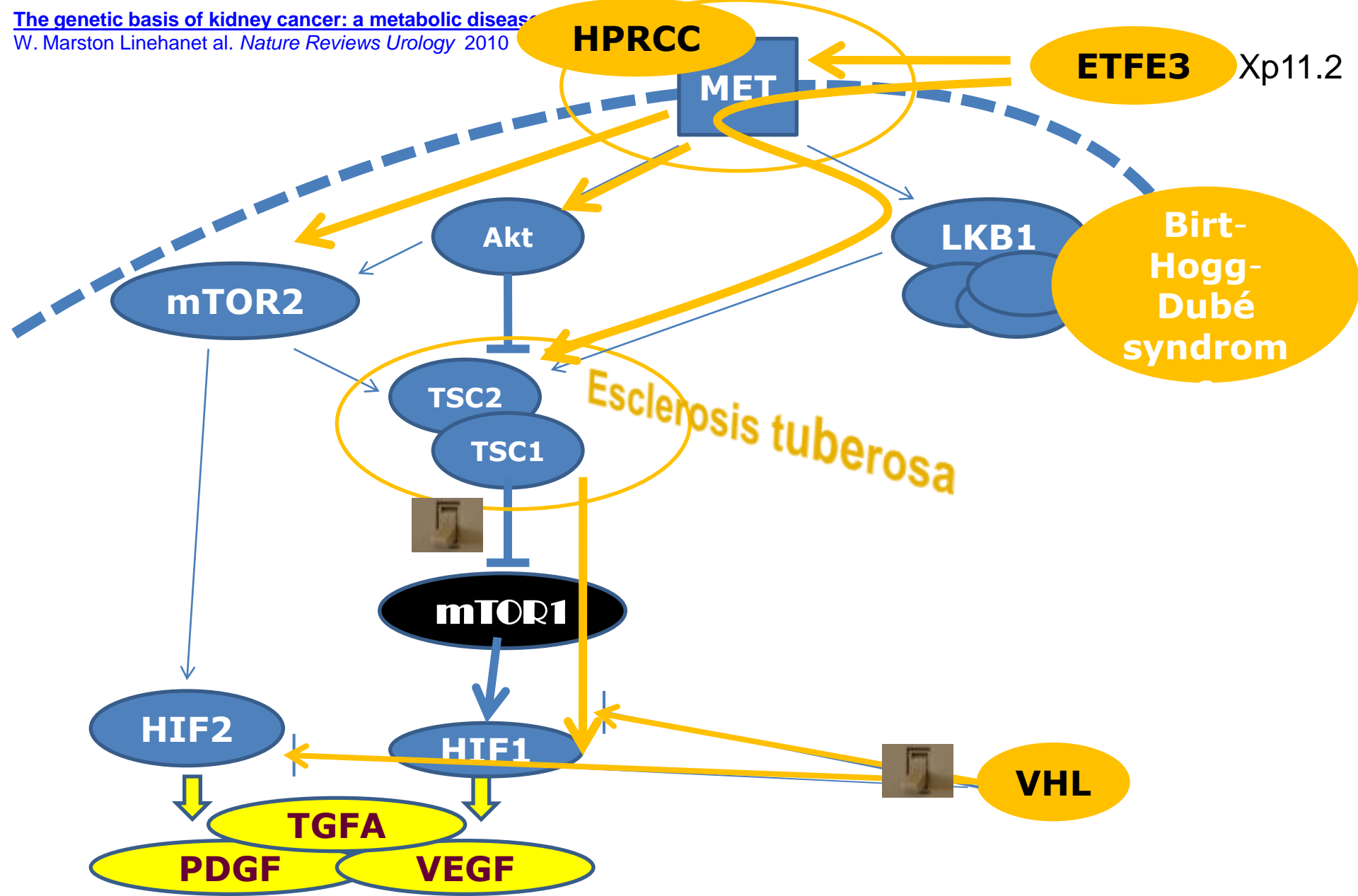
Carcinoma Renal

**Una
enfermedad metabólica**

estrés metabólico

hipoxia

nutrientes



Cancer: Cause & Cure

A 20TH CENTURY PERSPECTIVE

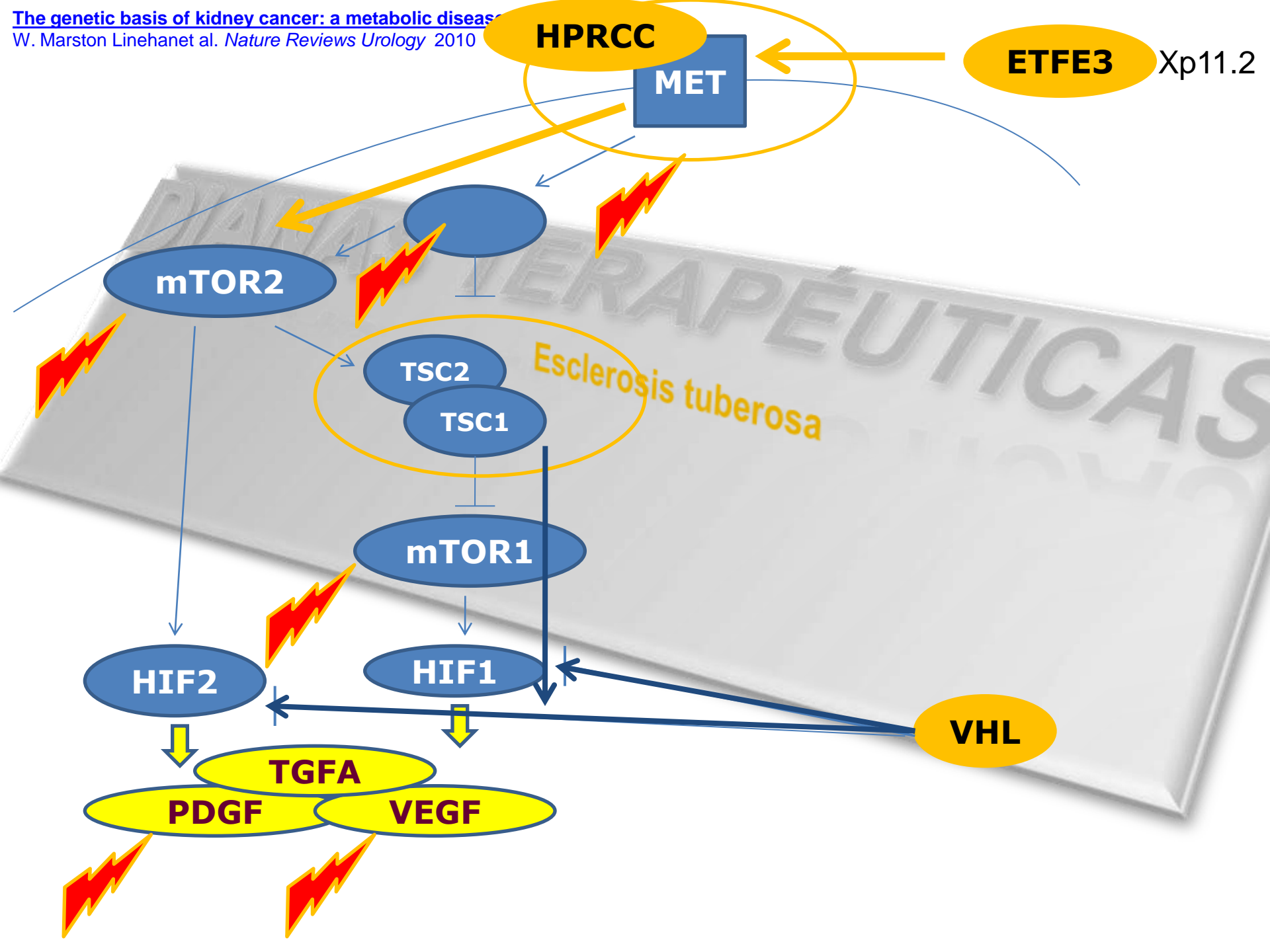
Nature's secrets exposed



A farmer's fascinating account of how agribusiness is disrupting the balance of nature and causing havoc in the food chain.

He explains how anyone can beat cancer without expensive drugs, hospitalisation and doctors, just as he did.

By Percy Weston



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de
2011

CONSOLIDANDO PUENTES





Si tiene cualquier error
es su culpa

Gracias
Carmen Valbuena
por la
traducción al Español

CONSOLIDANDO
PUENTES