

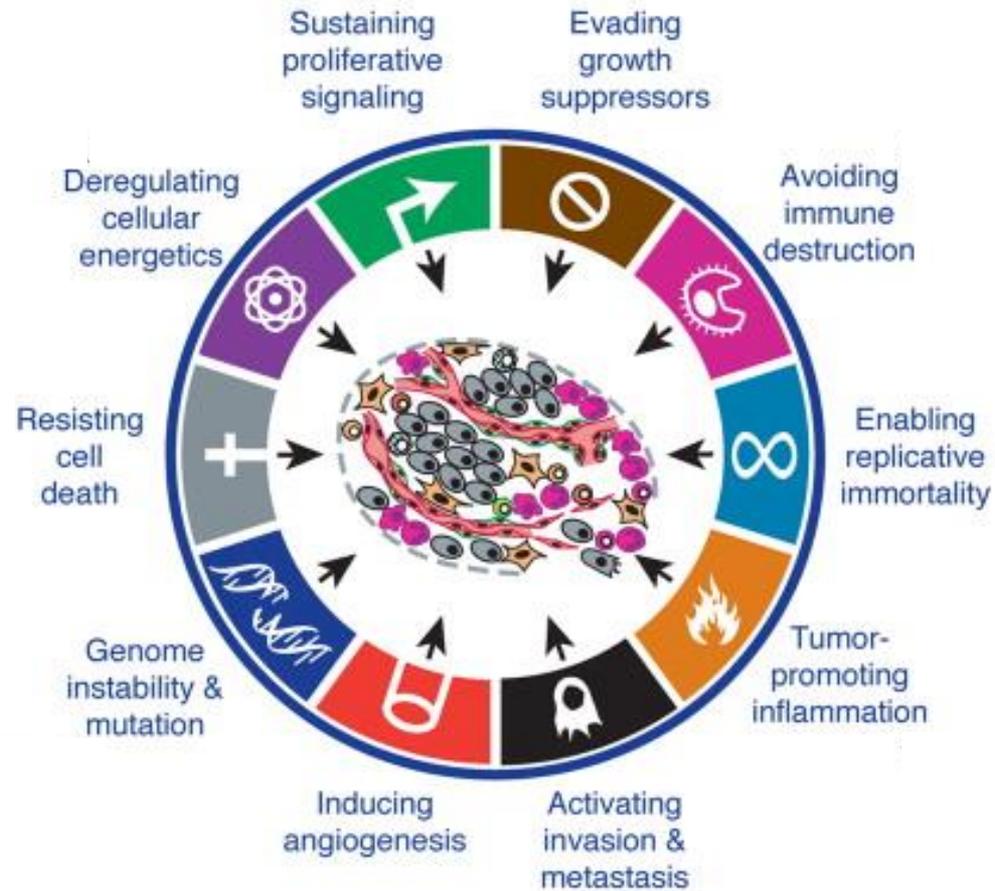
Oncogénèse des cancers du rein : impact sur le diagnostic et la prise en charge

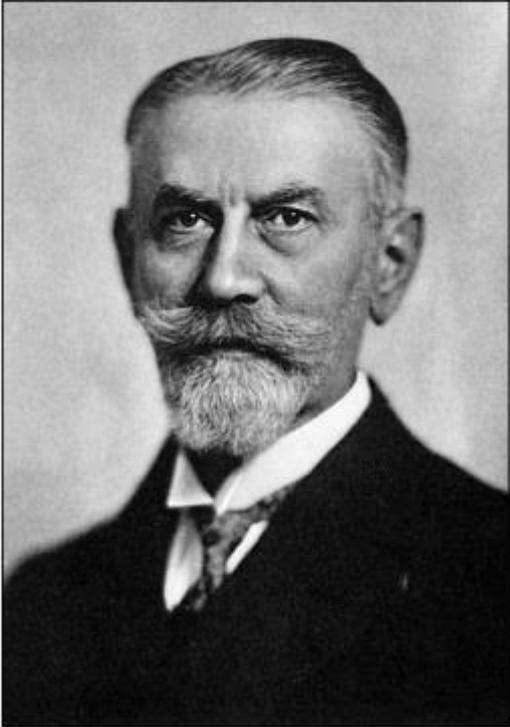
Discuter les avancées en cancérogenèse rénale
et leurs implications en pratique quotidienne

ReIn CaRe

Dr Damien AMBROSETTI
Laboratoire d'Anatomo Pathologie
CHU Nice

Hallmarks Of Cancer

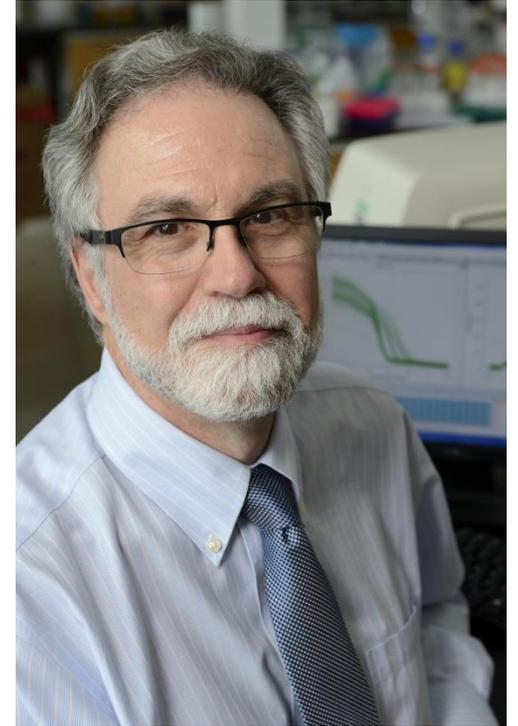




Eugen Von Hippel (1867-1939)

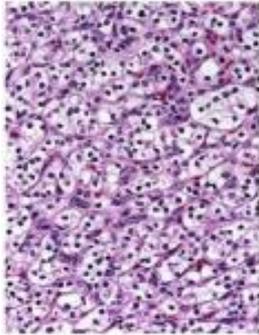


Arvid Lindau (1892-1958)



Gregg L. Semenza

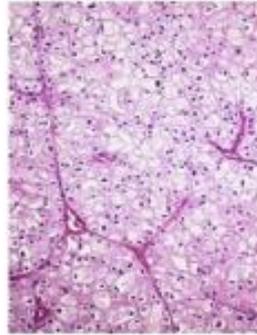
ONE GENE, ONE DISEASE THEORY



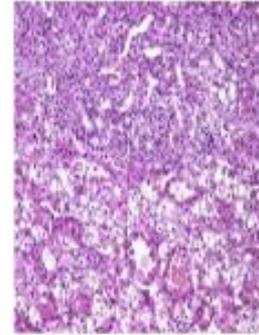
Clear Cell
VHL



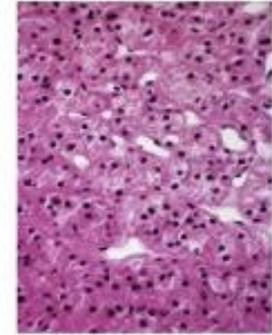
Papillary Type 1
Met



Chromophobe

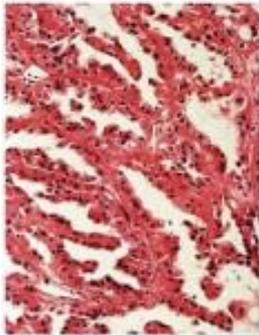


Hybrid

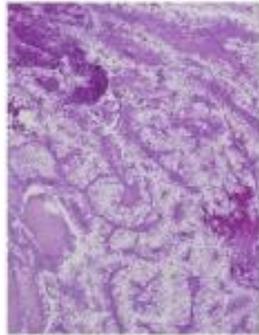


Oncocytoma

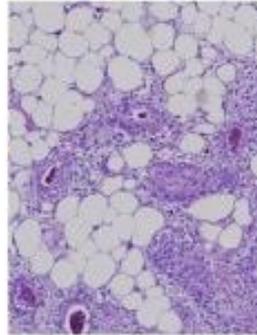
— *FLCN* —



Papillary Type 2
FH



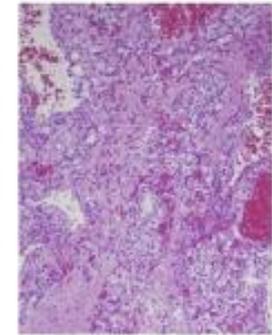
TFE3
TFE3, TFEB, MITF



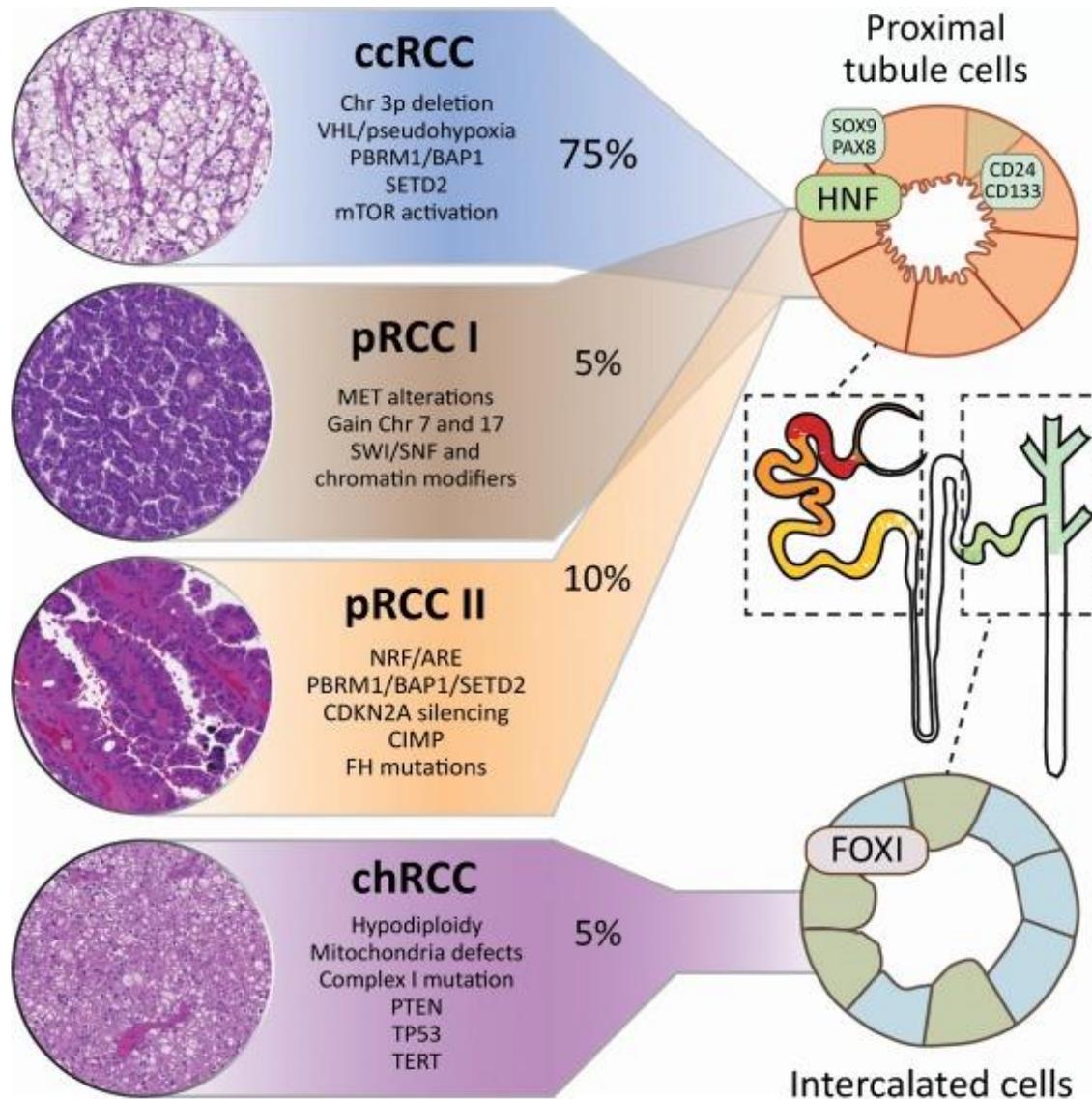
Angiomyolipoma
TSC1, TSC2

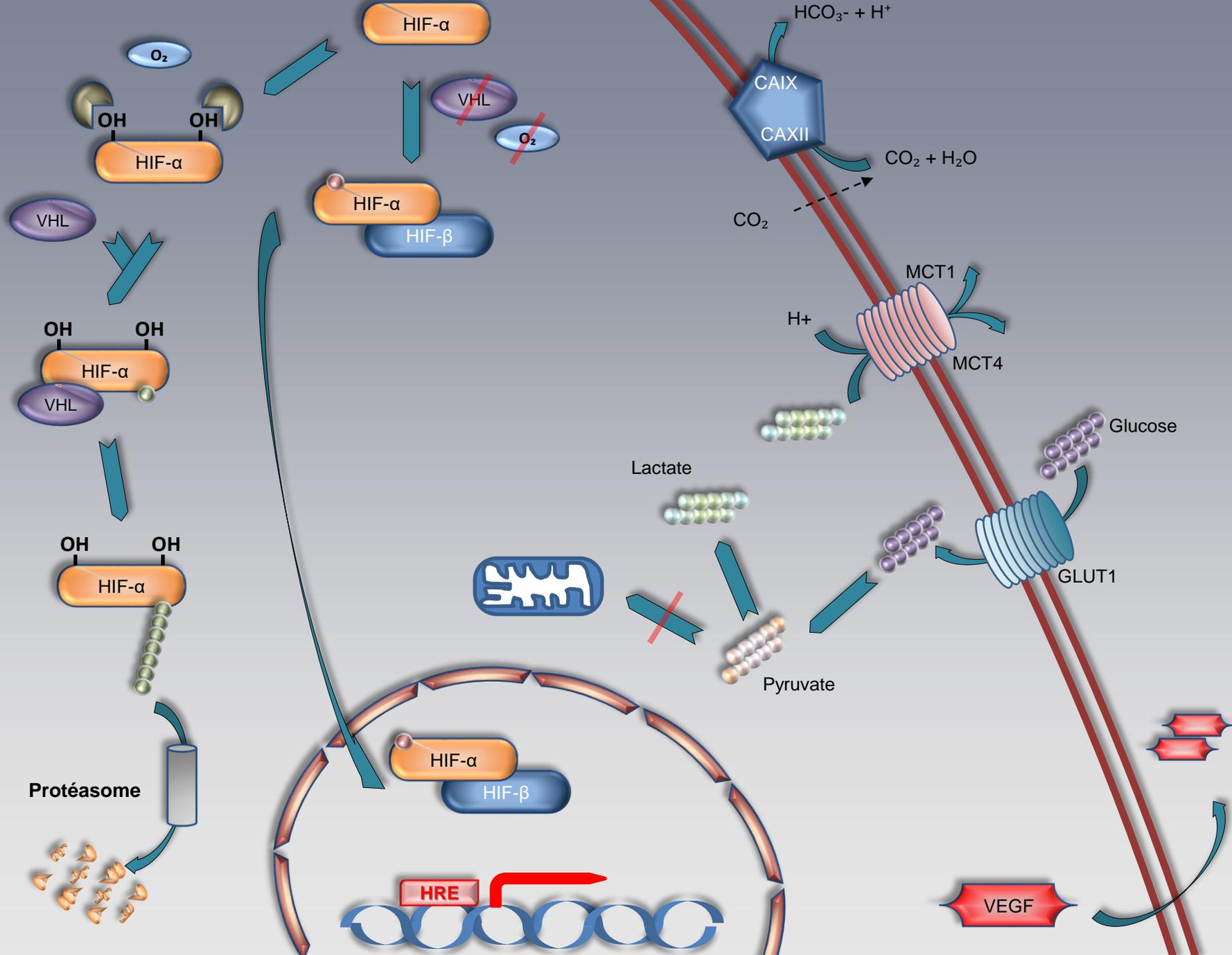


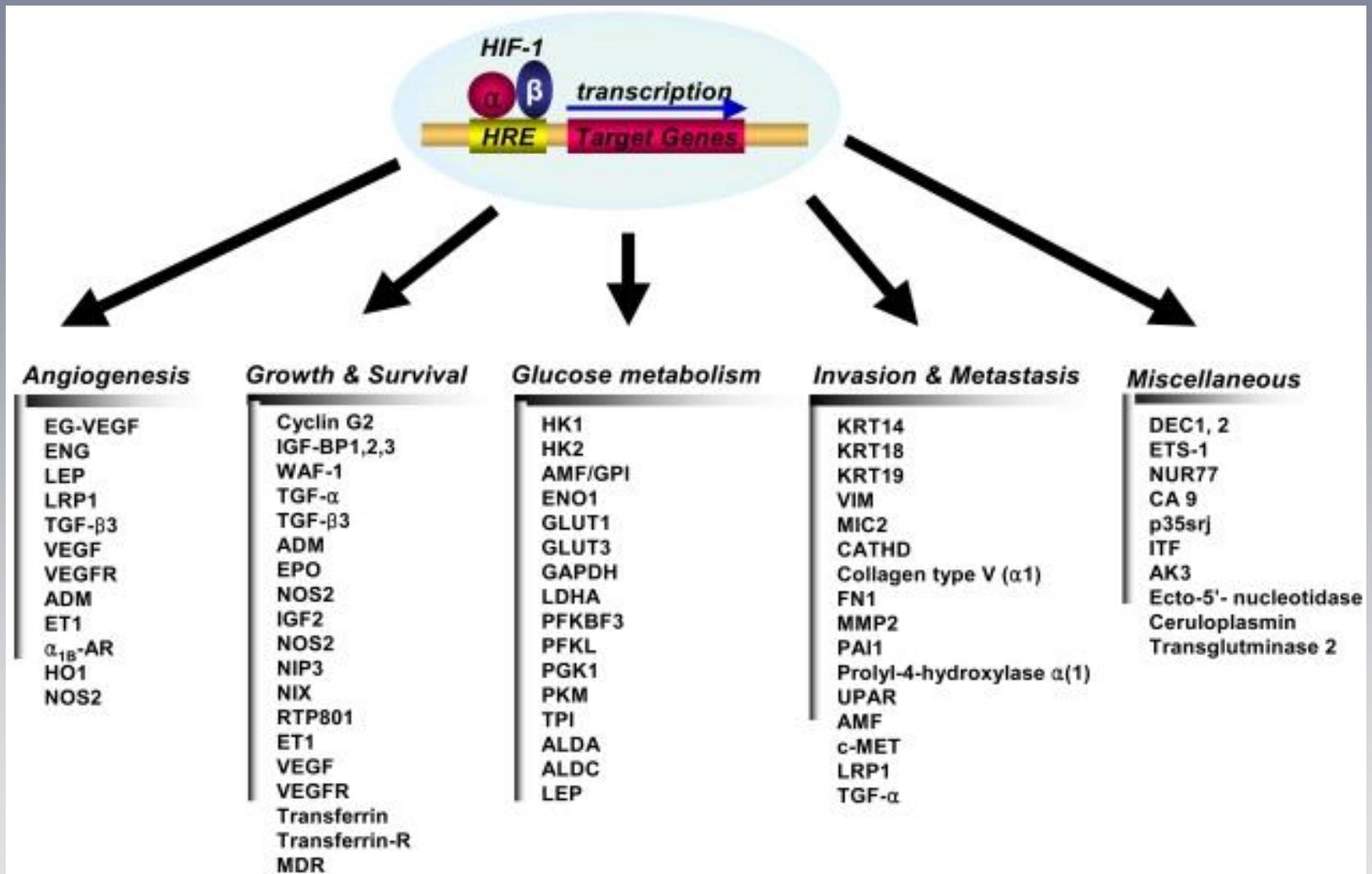
Oncocytic
SDHB, SDHC, SDHD

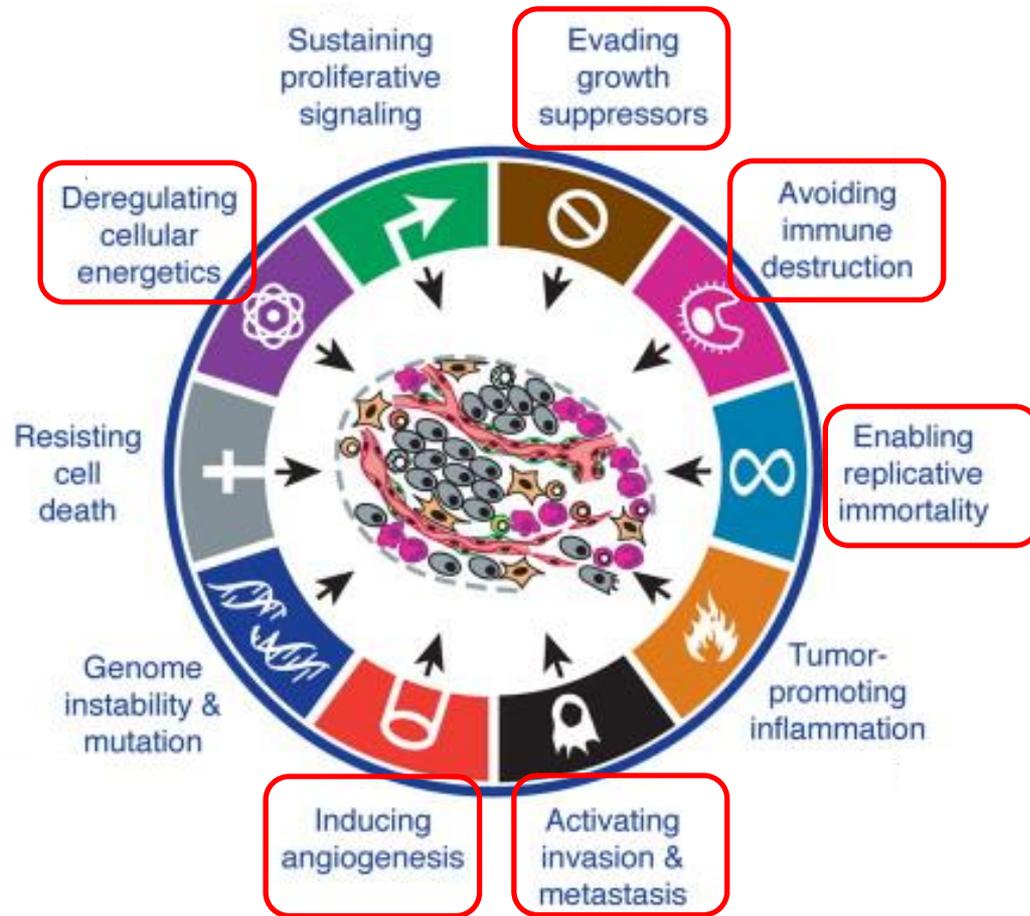


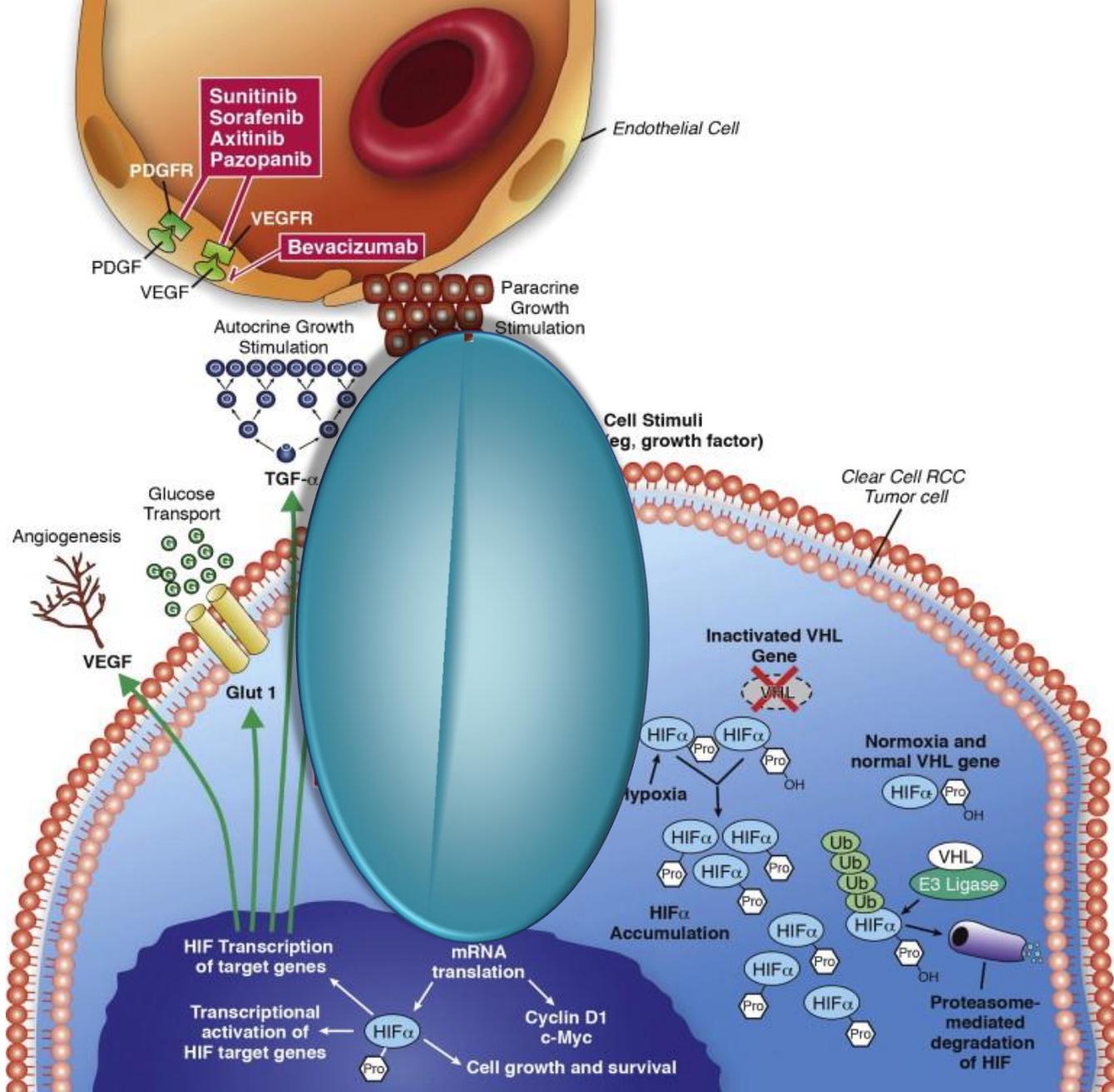
Clear/Chromophobe
PTEN











Shuch B, Amin A, Armstrong AJ, Eble JN, Ficarra V, Lopez-Beltran A, Martignoni G, Rini BI, Kutikov A. Understanding pathologic variants of renal cell carcinoma: distilling therapeutic opportunities from biologic complexity. *Eur Urol.* 2015 Jan;67(1):85-97.

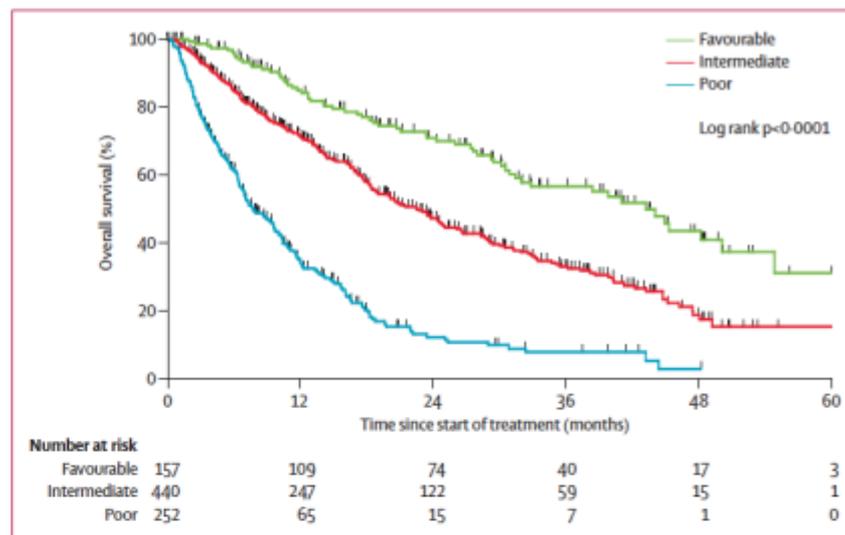
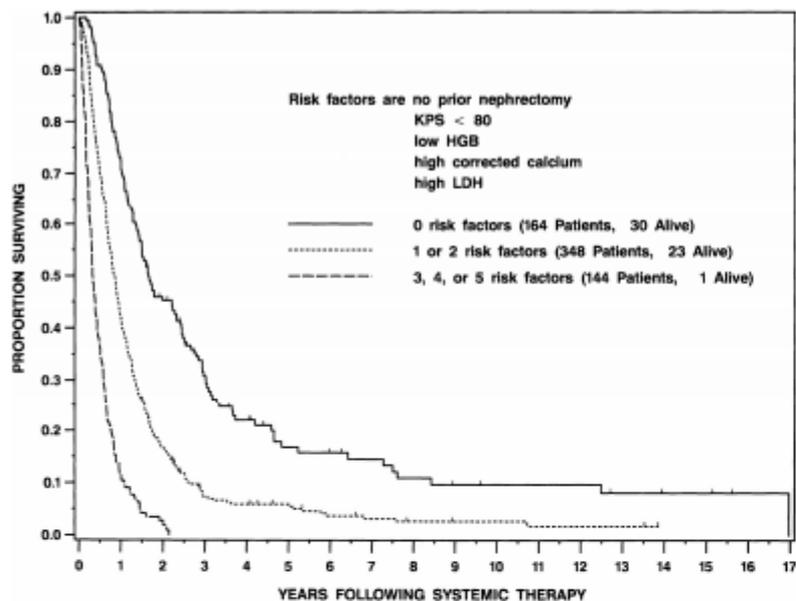
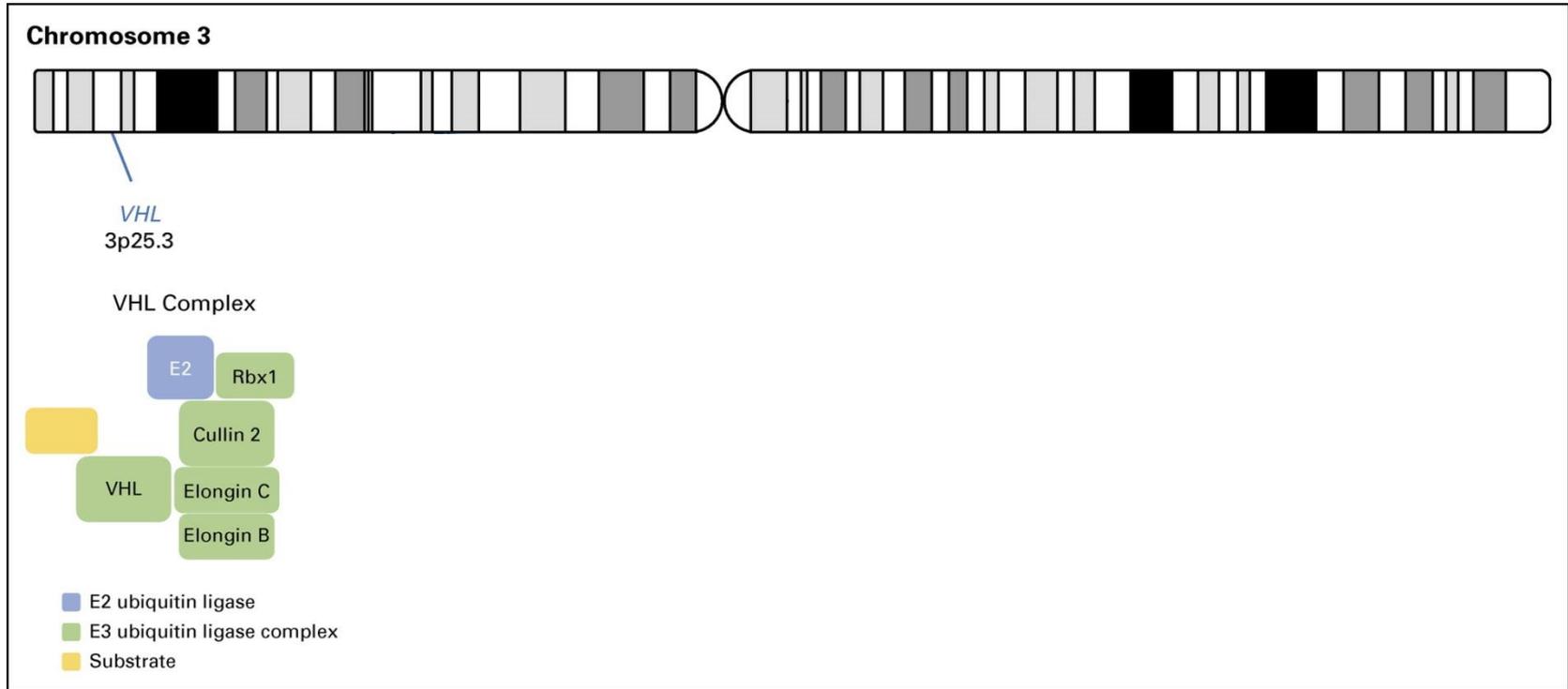


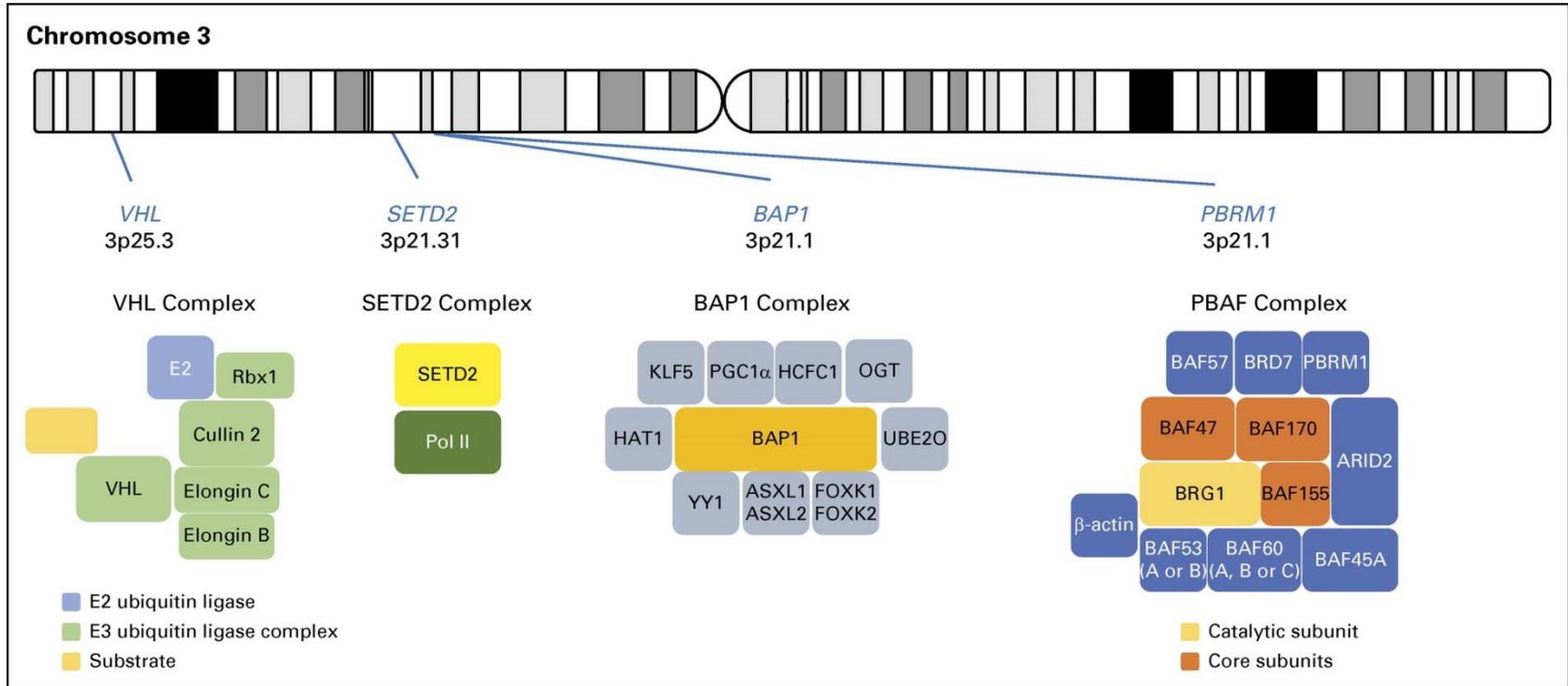
Figure 1: Results of Kaplan-Meier analysis of overall survival for the Database Consortium model

	Immunotherapy era ¹	Targeted agents era ²
Median OS of good risk patients	20 months	43.2 months (95% CI: 31.4–50.1)
Median OS of intermediate risk patients	10 months	22.5 months (95% CI: 18.7–25.1)
Median OS of poor risk patients	4 months	7.8 months (95% CI: 6.5–9.7)

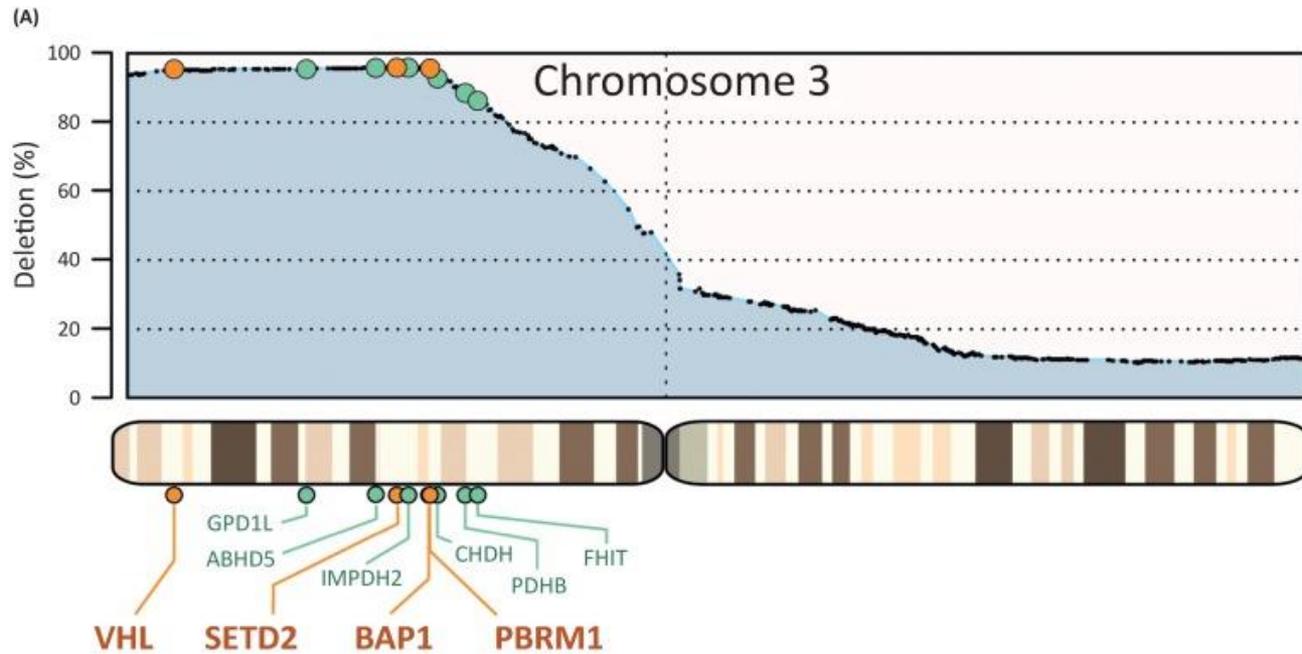
1. Motzer RJ, et al. *J Clin Oncol* 1993;11:1368-75; 2. Heng DY, et al. *Lancet Oncol* 2013;14:141-8.



Hsieh JJ, Le VH, Oyama T, Ricketts CJ, Ho TH, Cheng EH.
 Chromosome 3p Loss-Orchestrated VHL, HIF, and Epigenetic Deregulation in Clear Cell Renal Cell Carcinoma.
 J Clin Oncol. 2018 Oct 29



Hsieh JJ, Le VH, Oyama T, Ricketts CJ, Ho TH, Cheng EH.
 Chromosome 3p Loss-Orchestrated VHL, HIF, and Epigenetic Deregulation in Clear Cell Renal Cell Carcinoma.
 J Clin Oncol. 2018 Oct 29



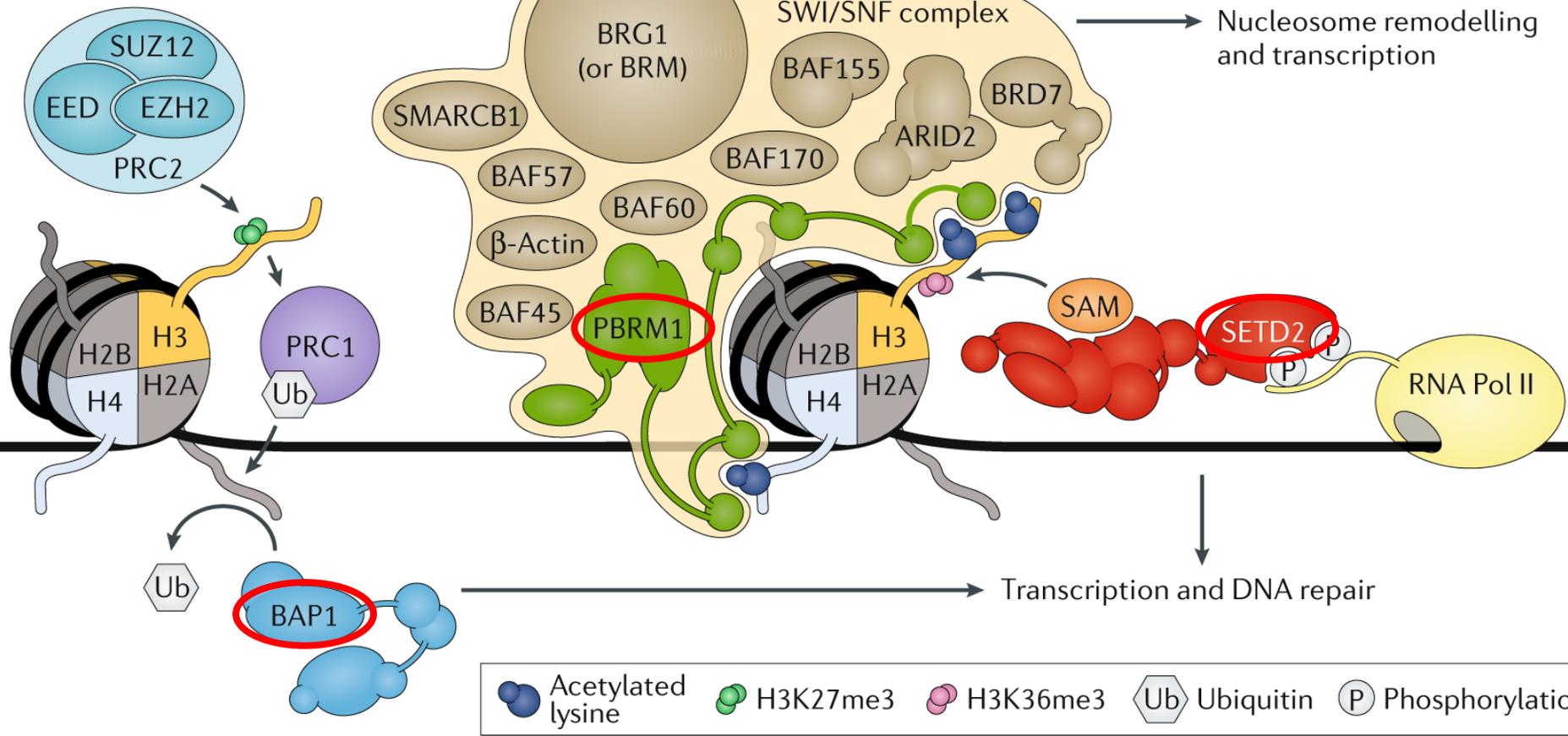
Lindgren D, Sjölund J, Axelson H.
 Tracing Renal Cell Carcinomas back to the Nephron.
 Trends Cancer. 2018 Jul;4(7):472-484

Target gene repression

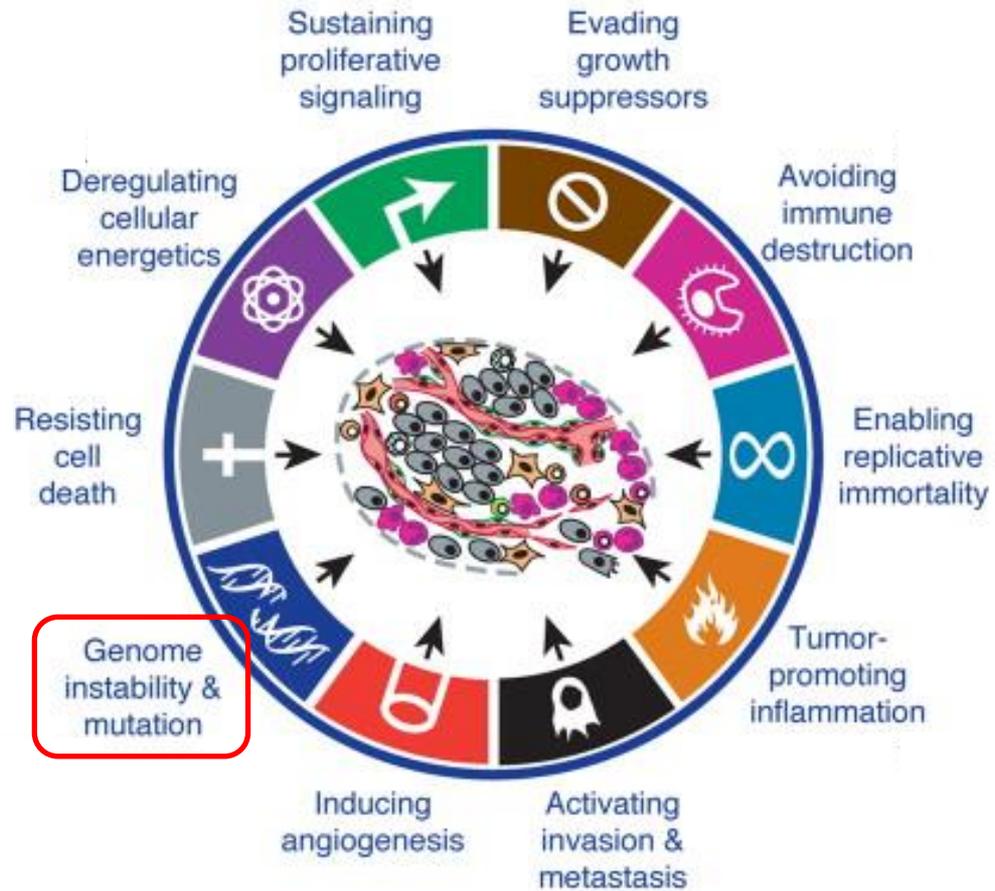
PBAF

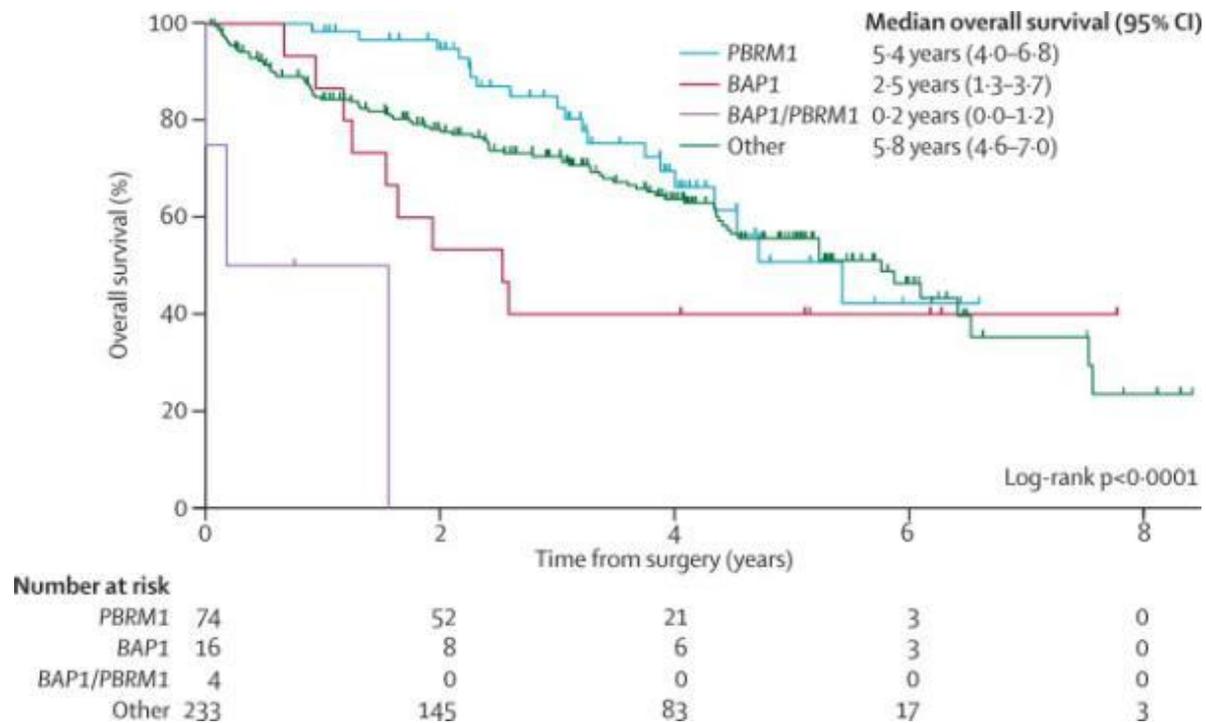
Nucleosome remodelling and transcription

Transcription and DNA repair

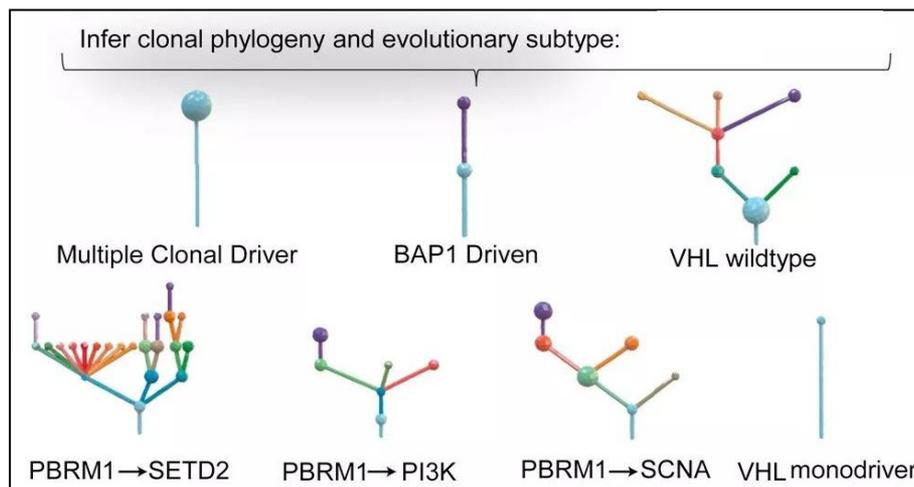
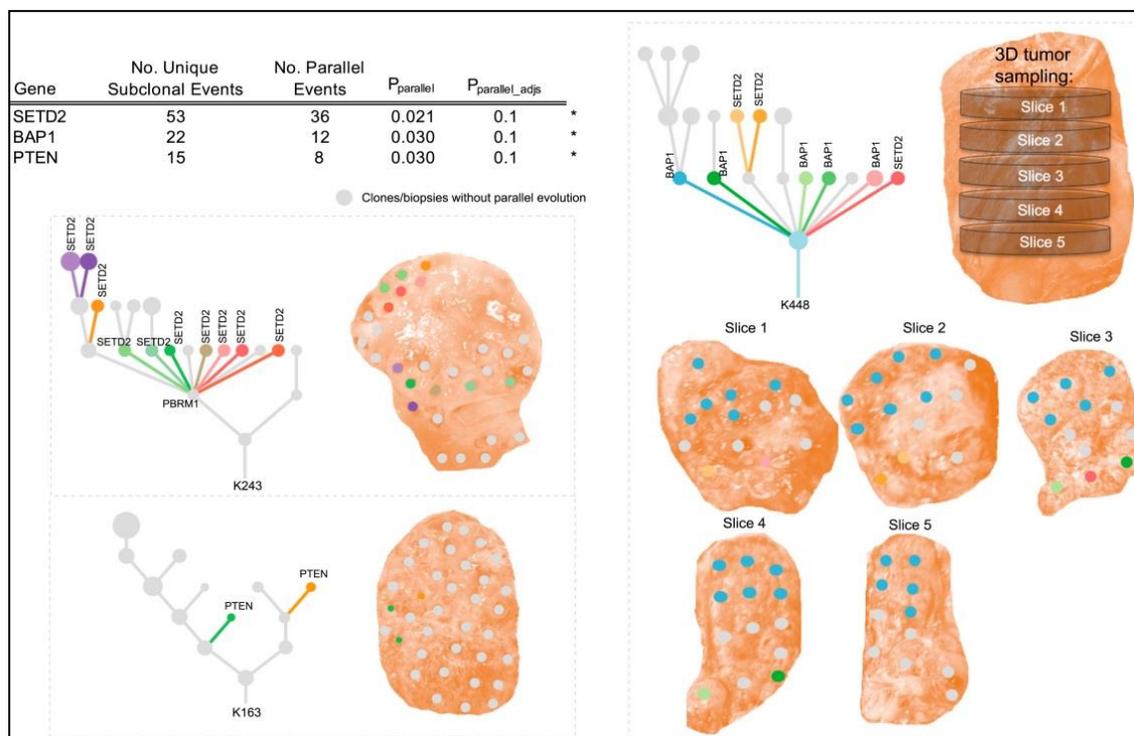


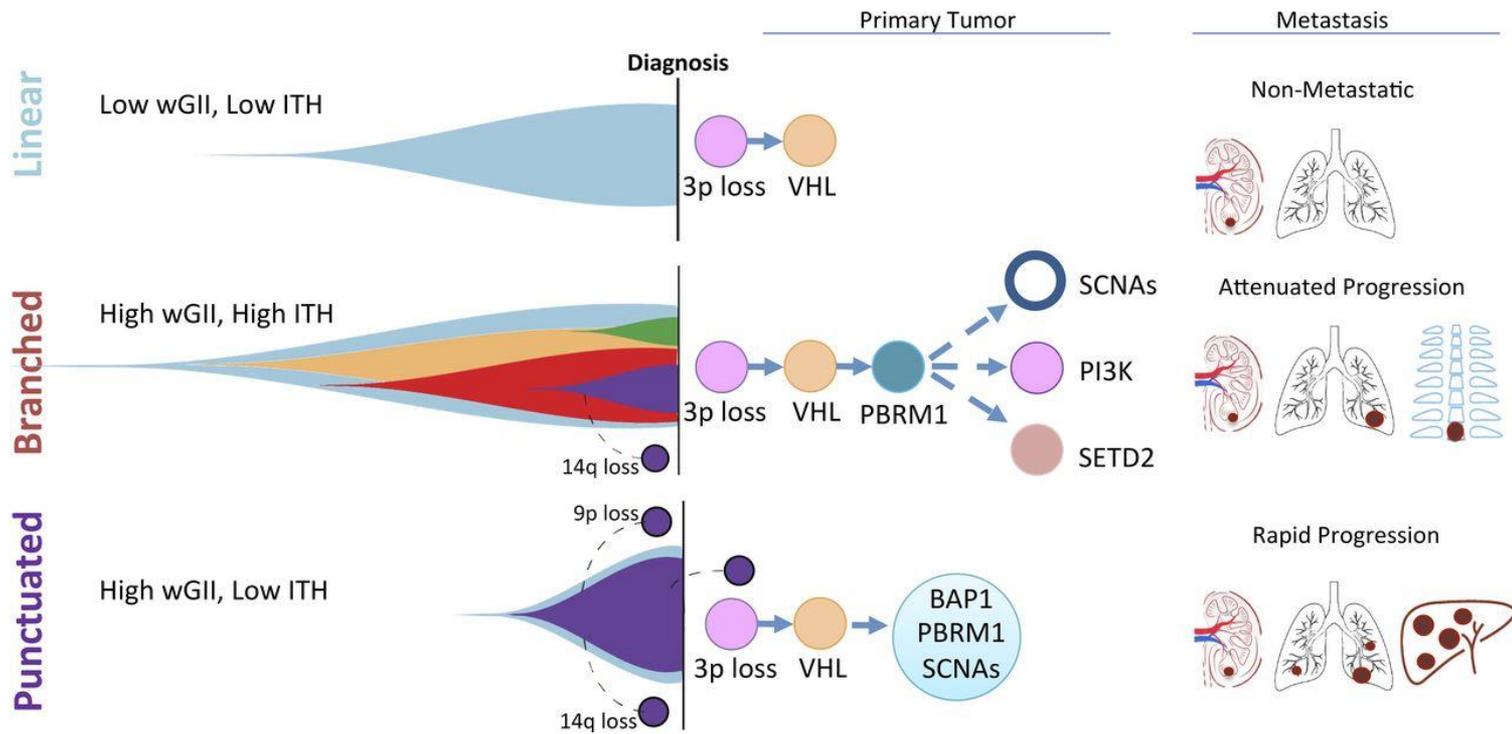
de Cubas AA, Rathmell WK.
 Epigenetic modifiers: activities in renal cell carcinoma.
 Nat Rev Urol. 2018 Oct;15(10):599-614

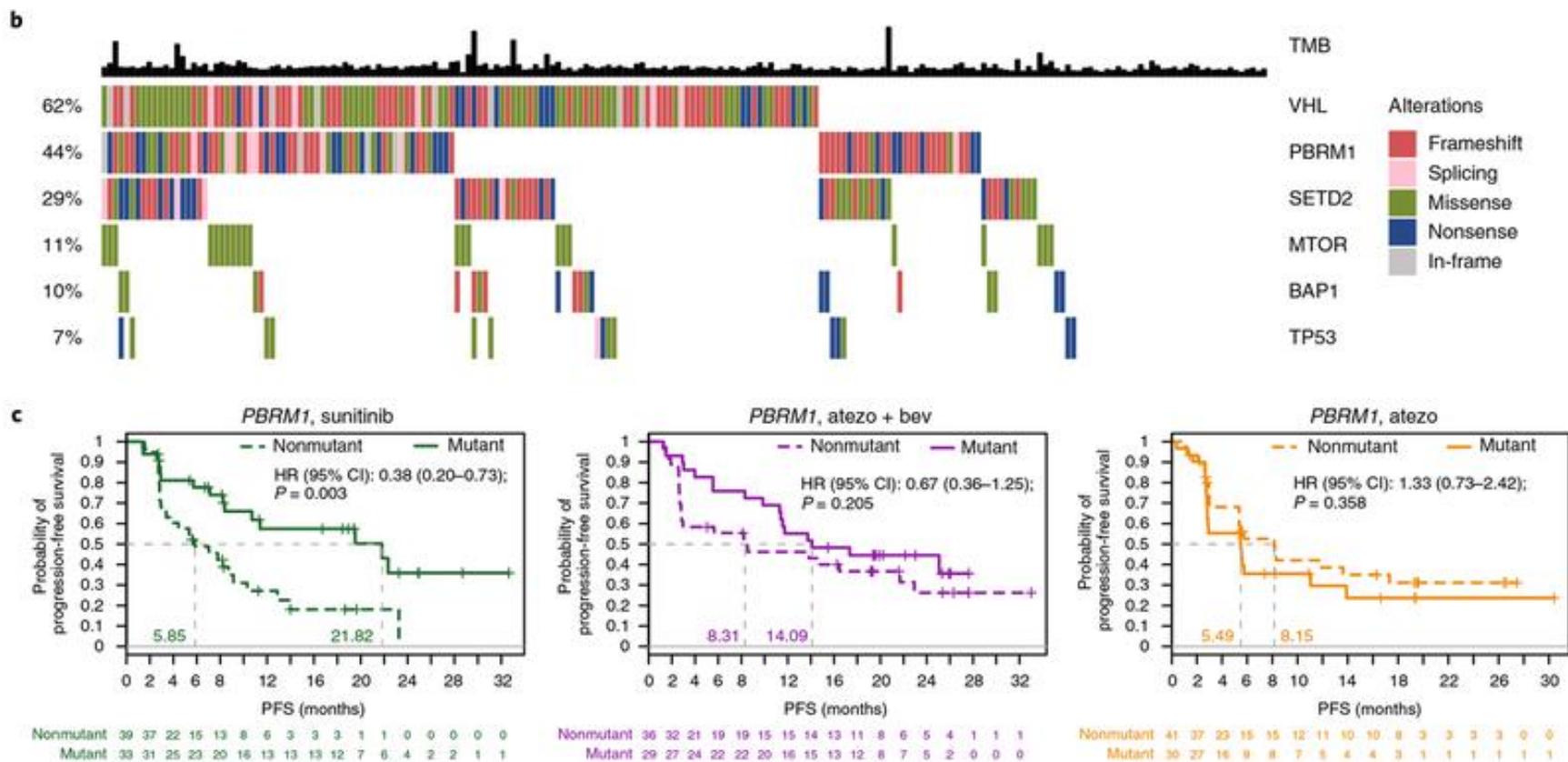




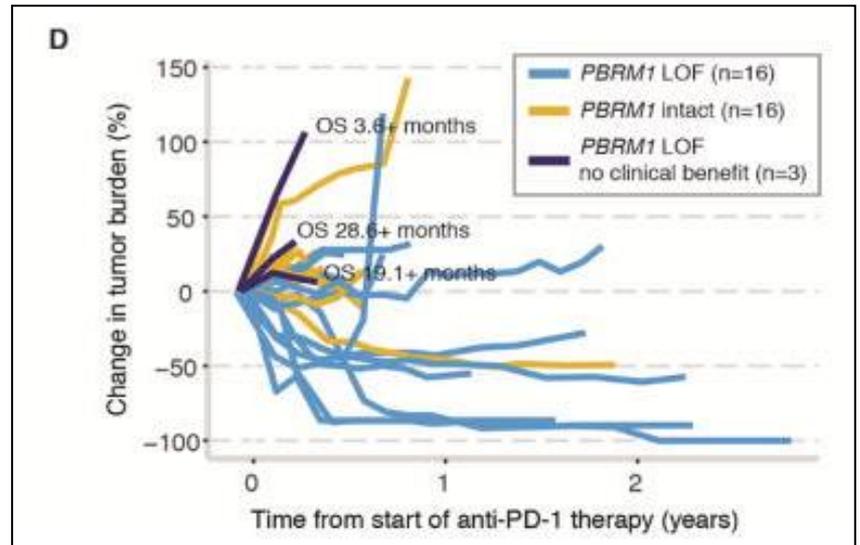
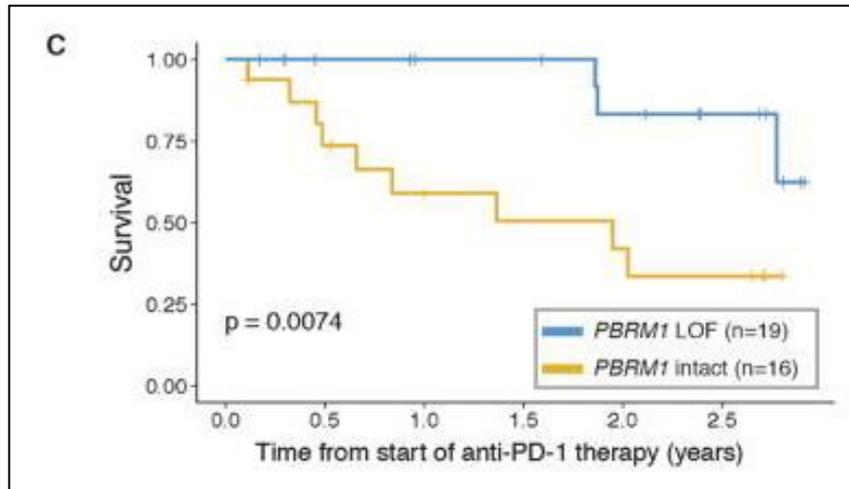
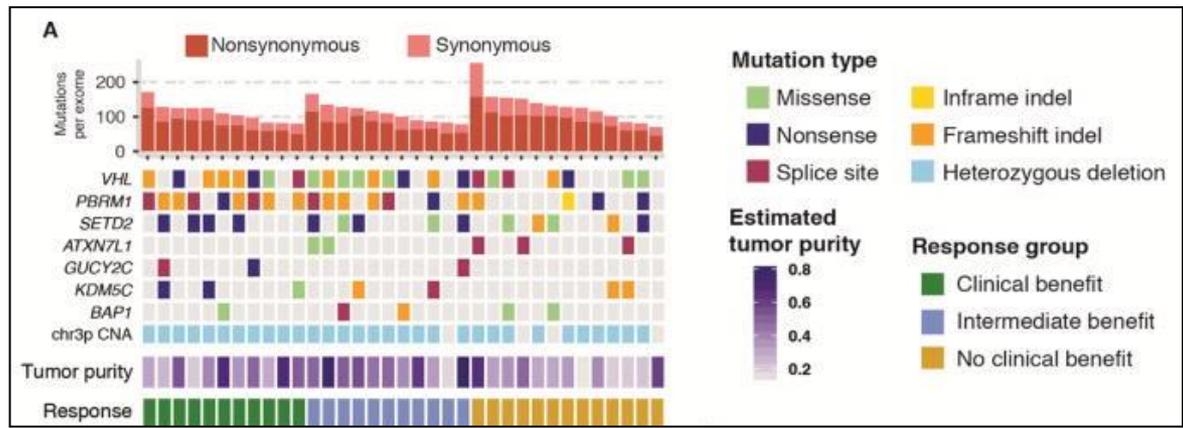
Kapur P, Peña-Llopis S, Christie A, Zhrebker L, Pavía-Jiménez A, Rathmell WK et al.
 Effects on survival of BAP1 and PBRM1 mutations in sporadic clear-cell renal-cell carcinoma: a retrospective analysis with independent validation.
 Lancet Oncol. 2013 Feb;14(2):159-167.

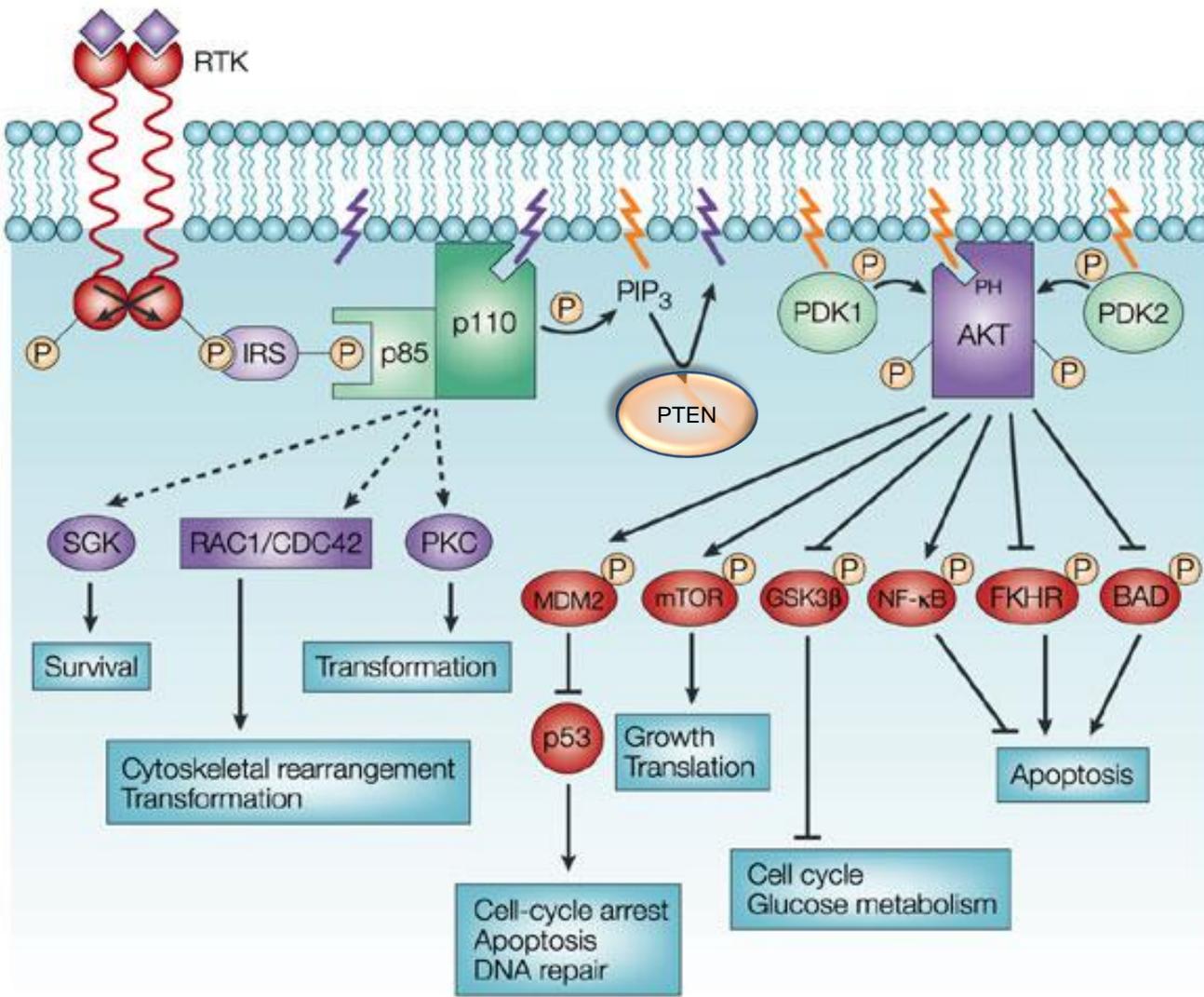


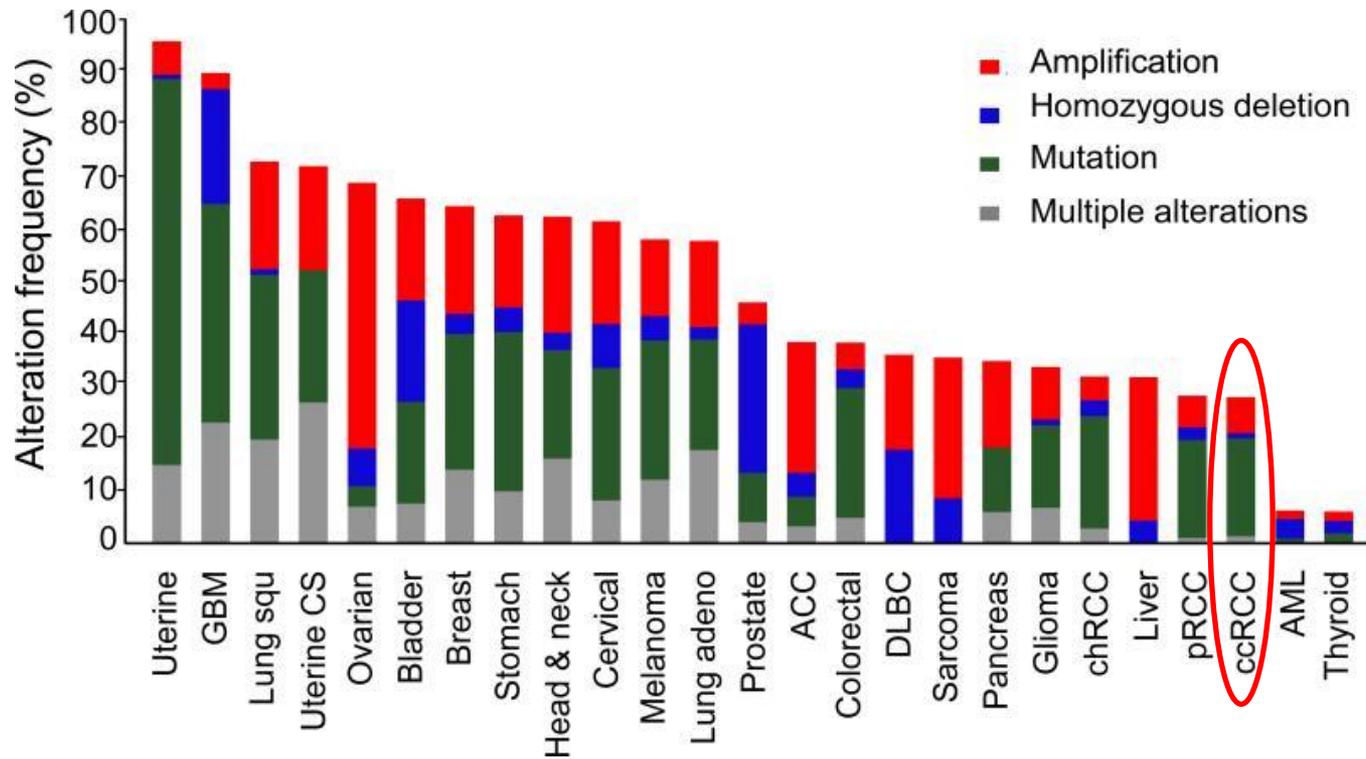




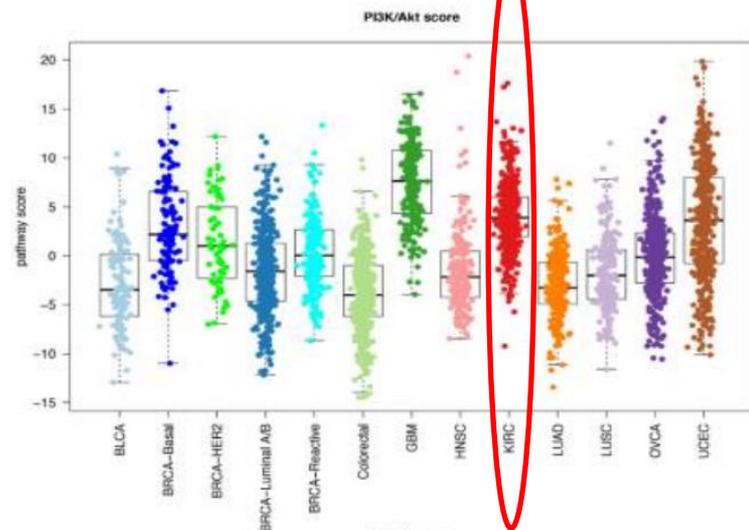
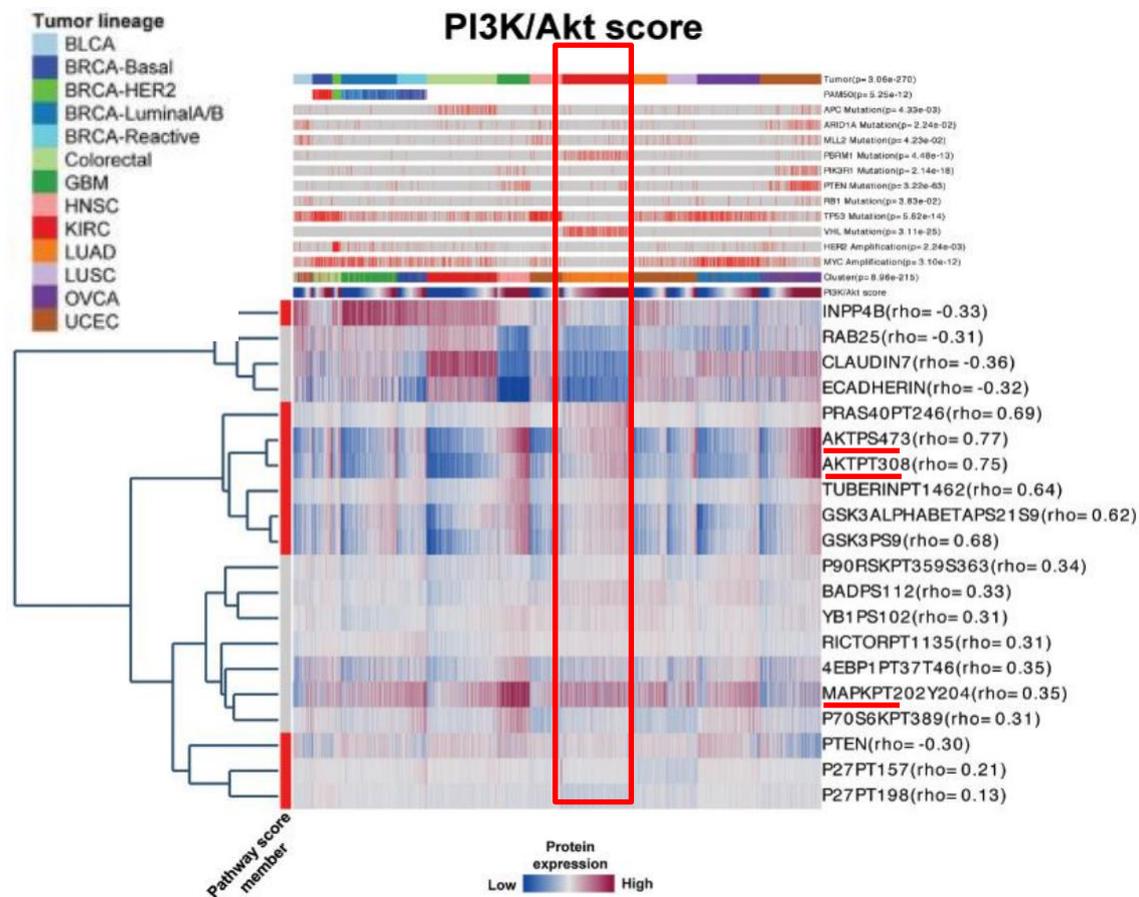
McDermott DF, Huseni MA, Atkins MB, Motzer RJ, Rini BI, Escudier B, et al.
 Clinical activity and molecular correlates of response to atezolizumab alone or in combination with bevacizumab versus sunitinib in renal cell carcinoma.
 Nat Med. 2018 Jun;24(6):749-757

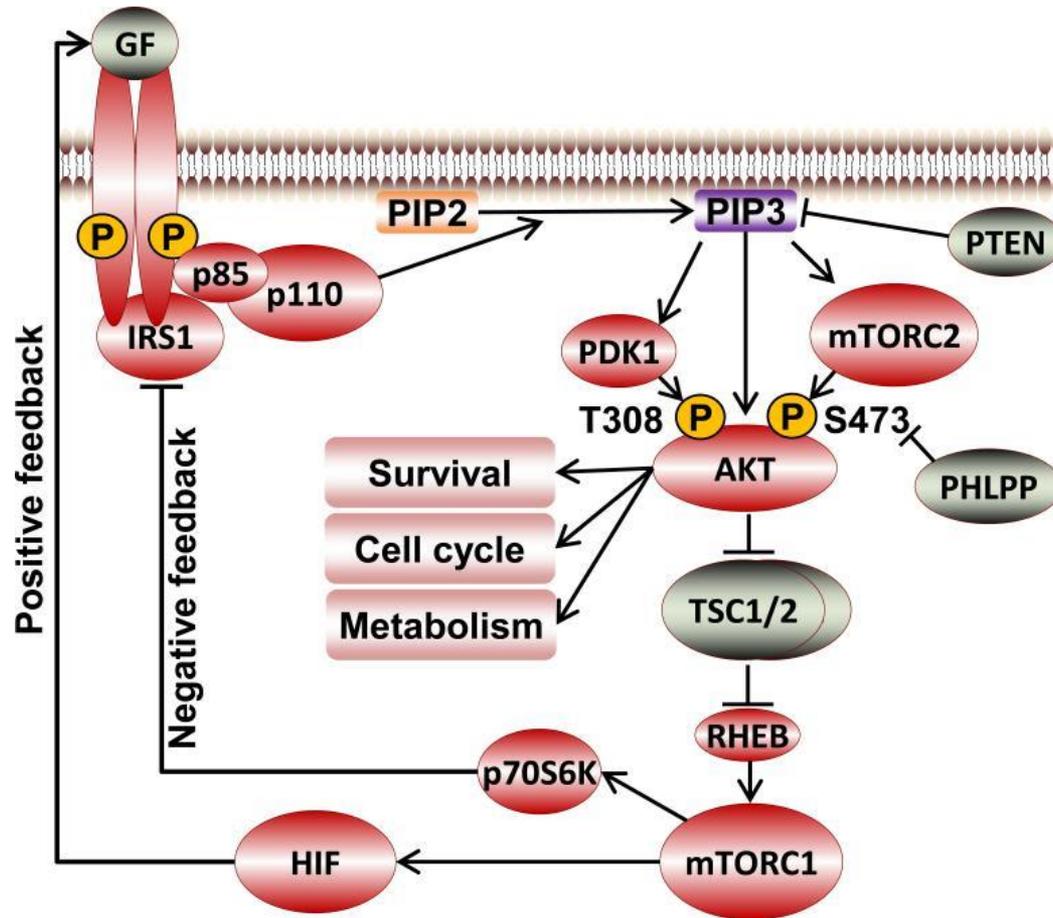


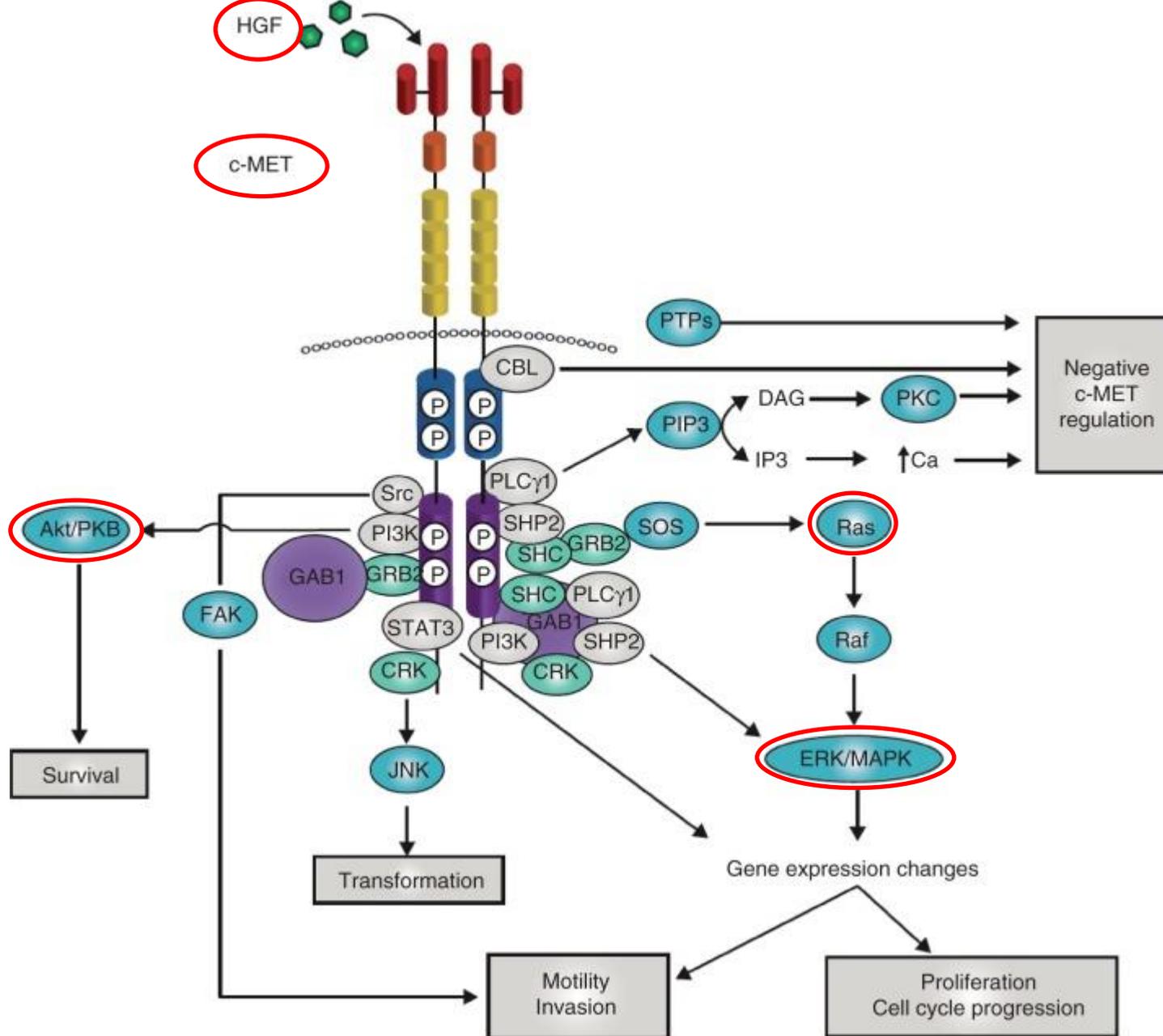




Genetic alteration frequency of 20 representative components of the PI3K/AKT pathway across 25 cancer types in The Cancer Genome Atlas (TCGA) database at cBioPortal.

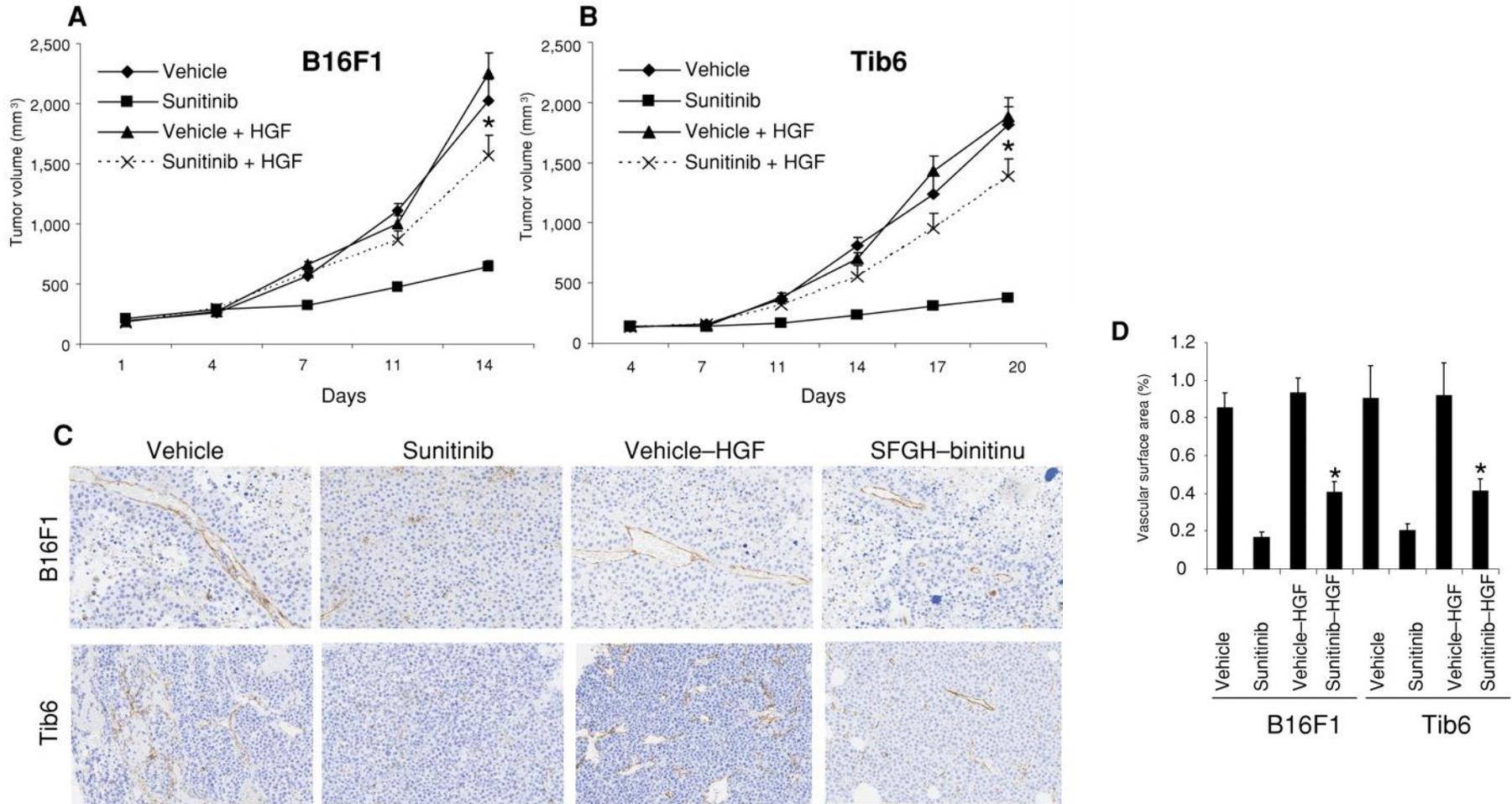


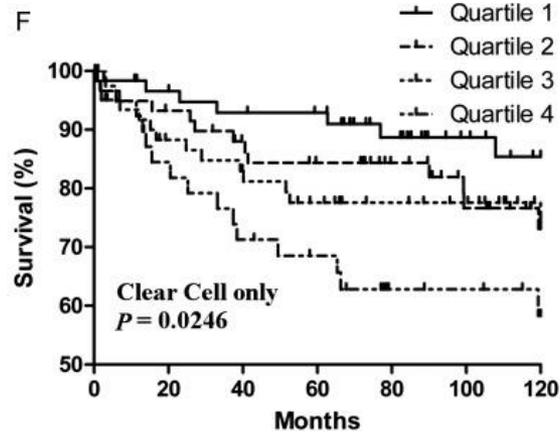
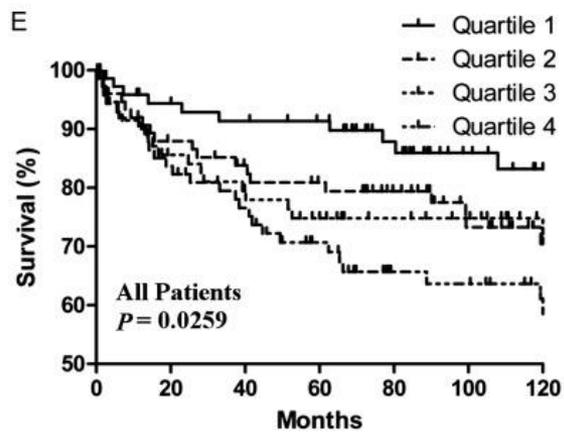
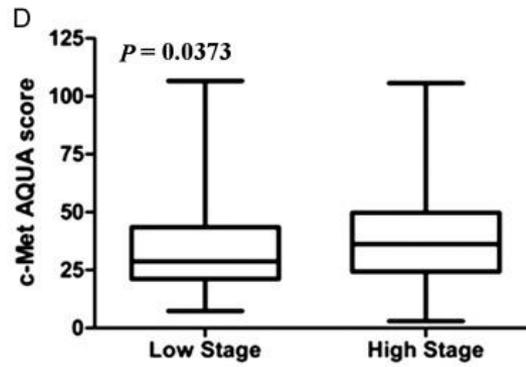
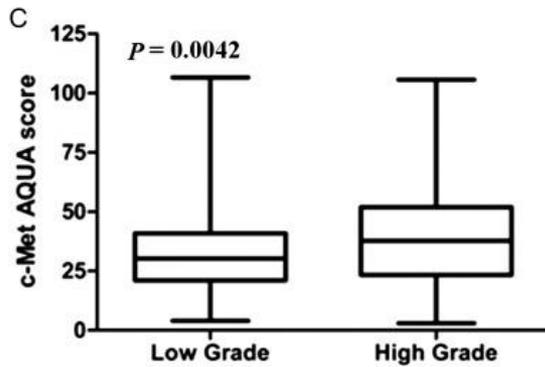
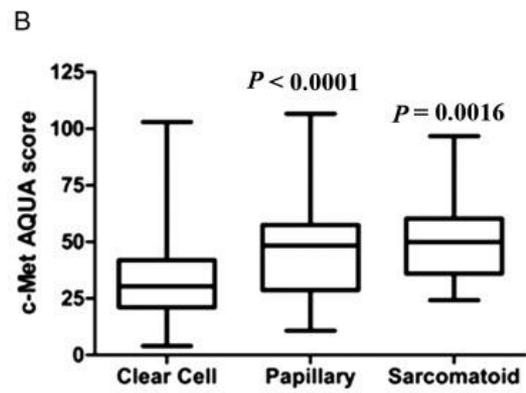
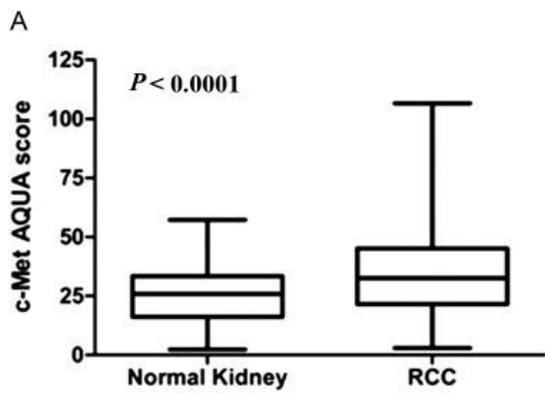


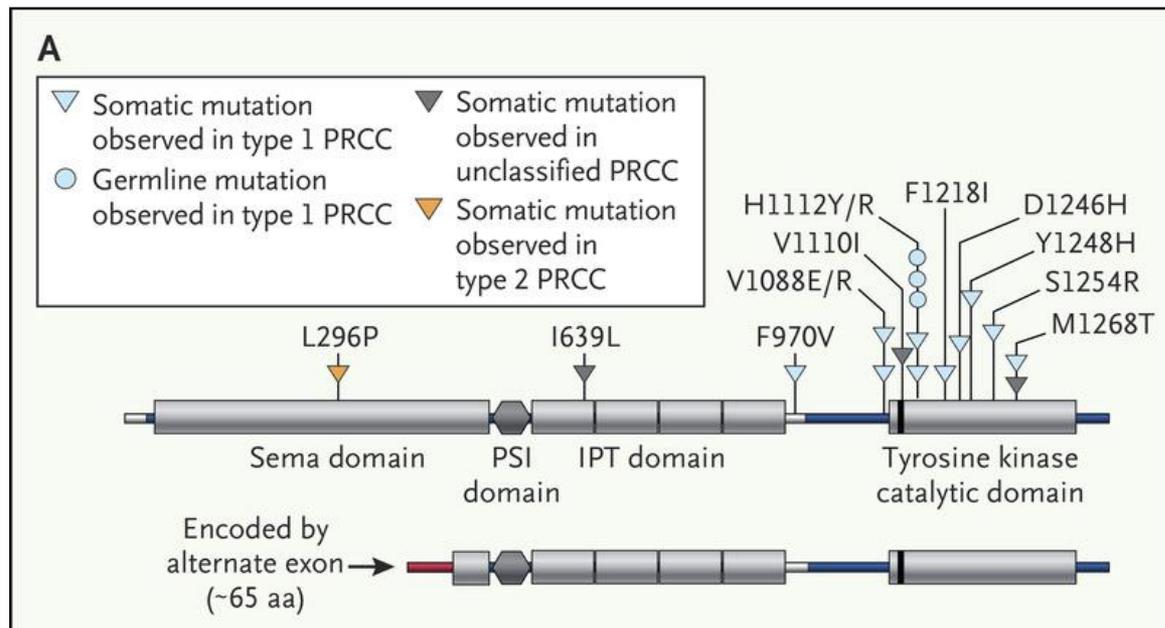
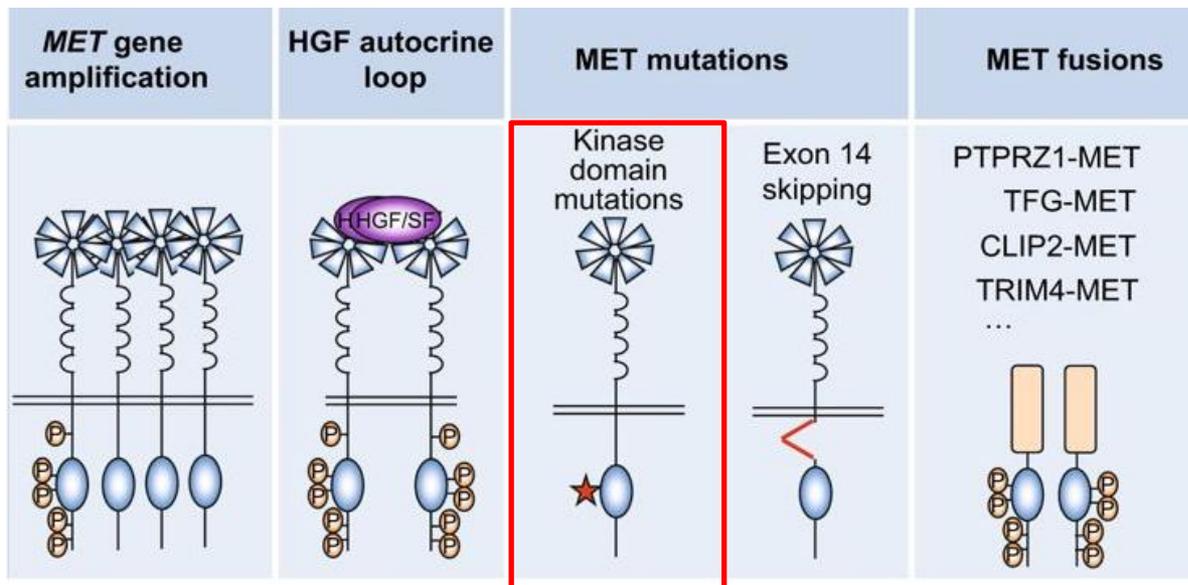


Organ SL, Tsao MS. An overview of the c-MET signaling pathway. Ther Adv Med Oncol. 2011 Nov;3(1 Suppl):S7-S19.

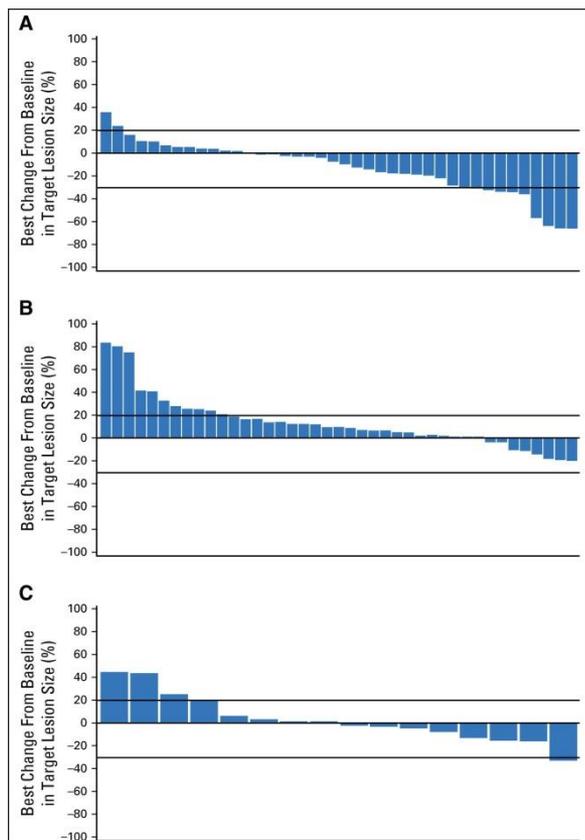
HGF/c-Met acts as an alternative angiogenic pathway in sunitinib-resistant tumors



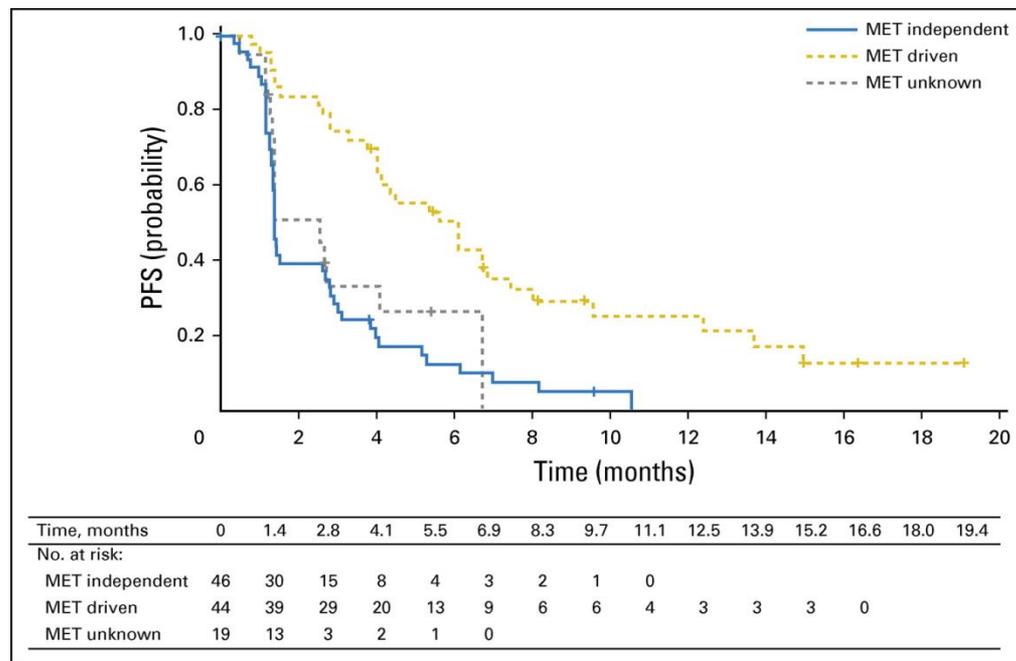


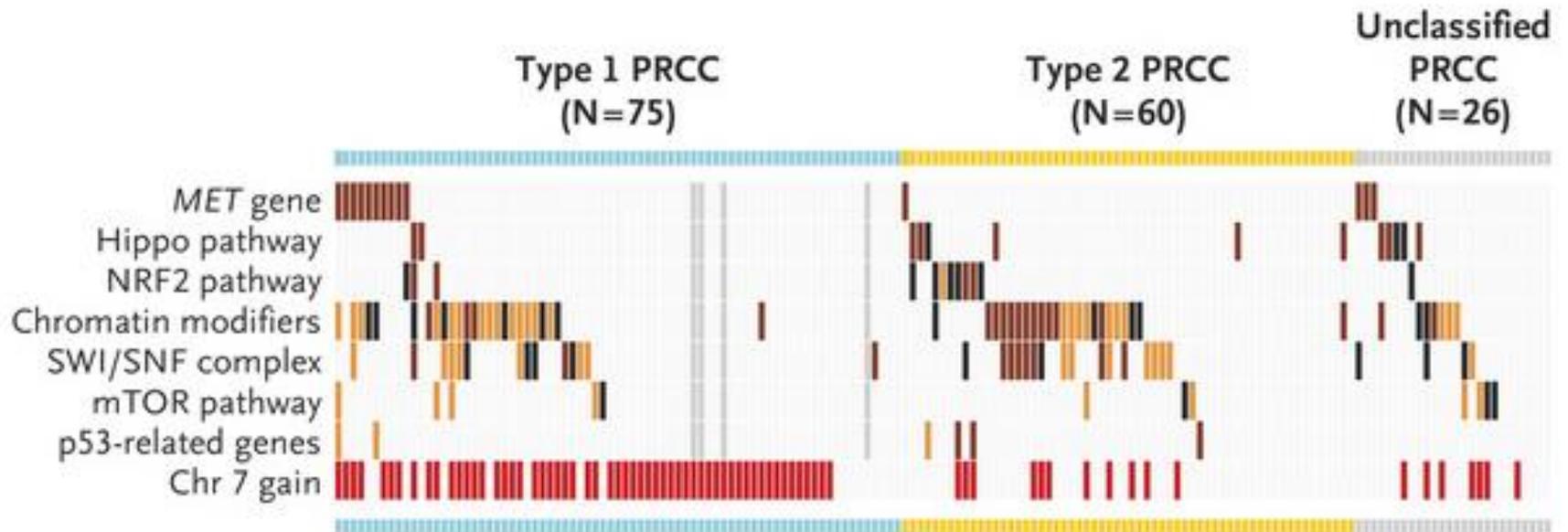


Biomarker-Based Phase II Trial of **Savolitinib** in Patients With Advanced Papillary Renal Cell Cancer

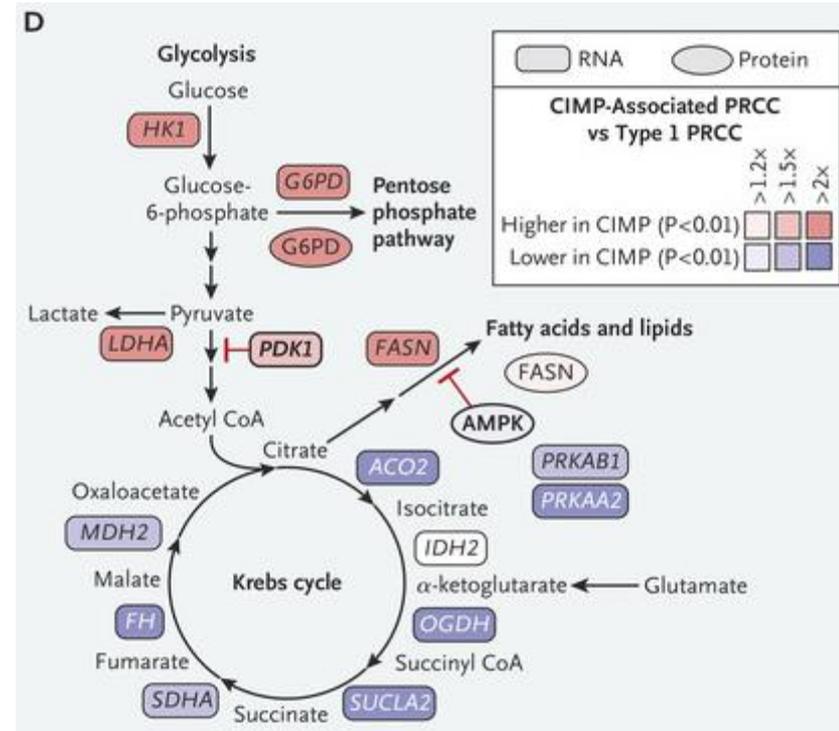
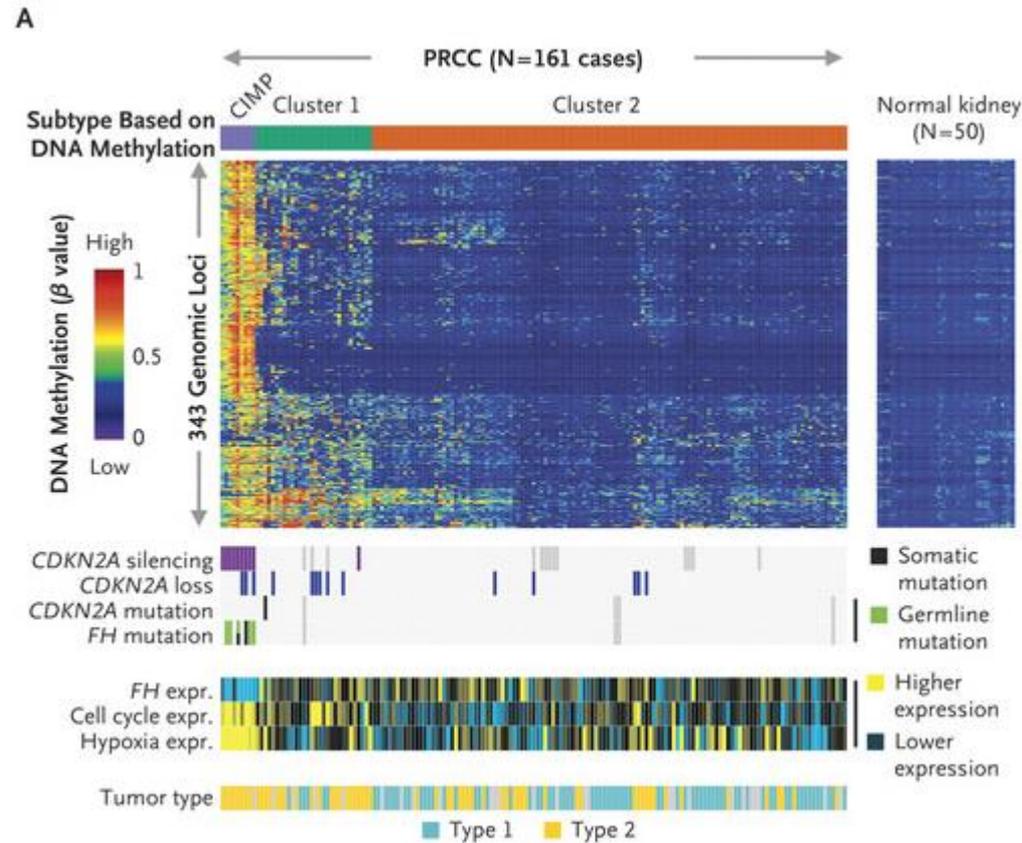


(A) MET-driven PRCC (n = 40); (B) MET-independent PRCC (n = 41); and (C) MET status unknown (n = 16)

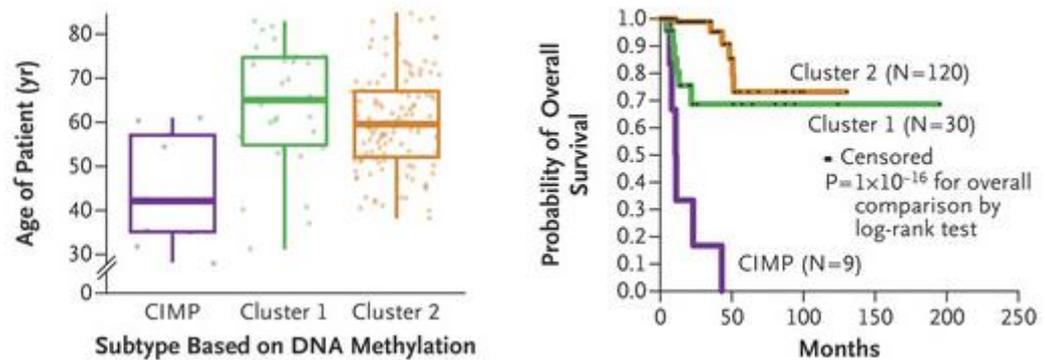


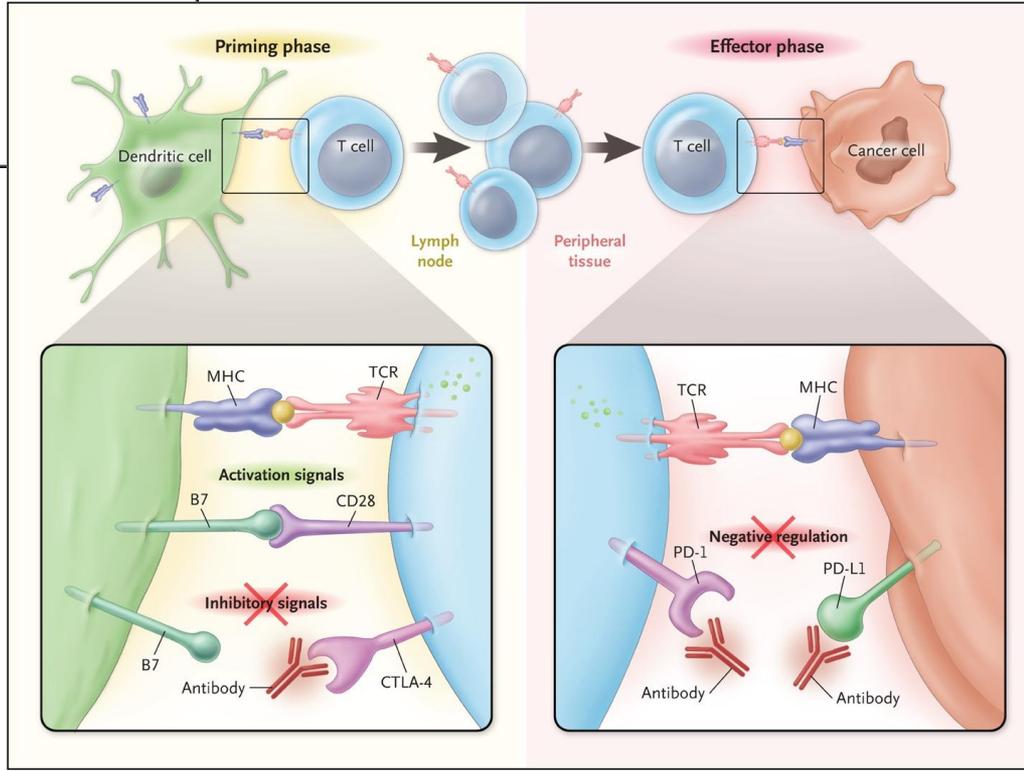
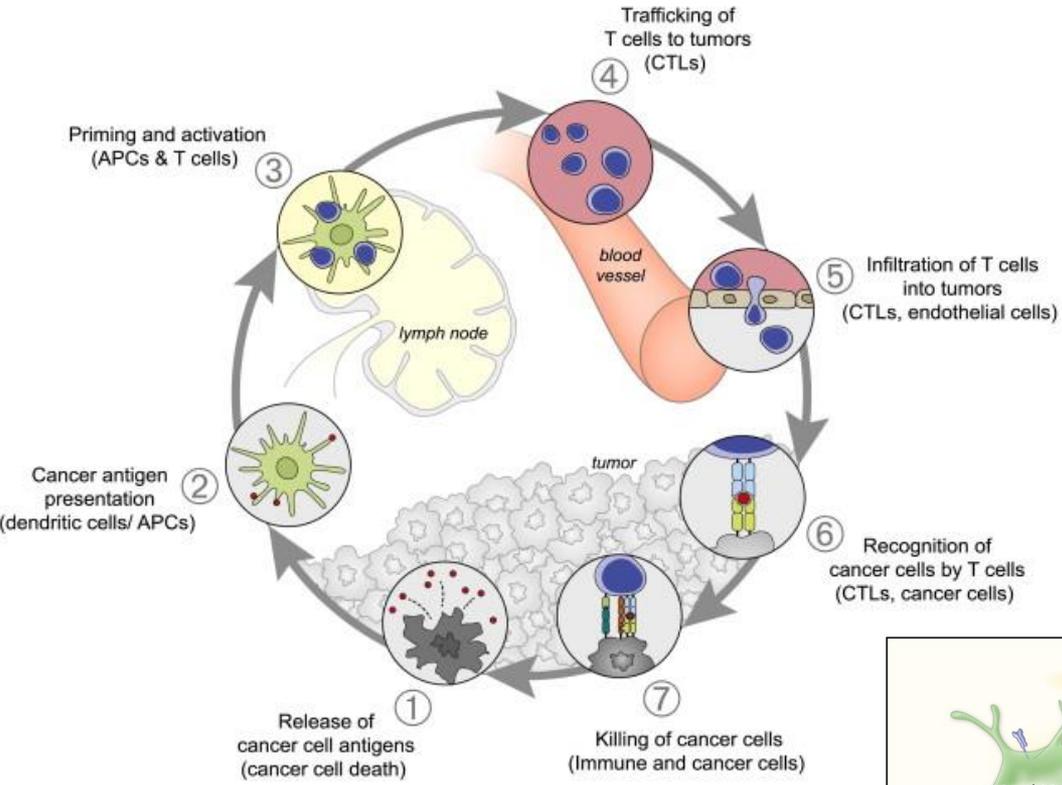


CpG Island Methylator Phenotype (CIMP) in Type 2 Tumors



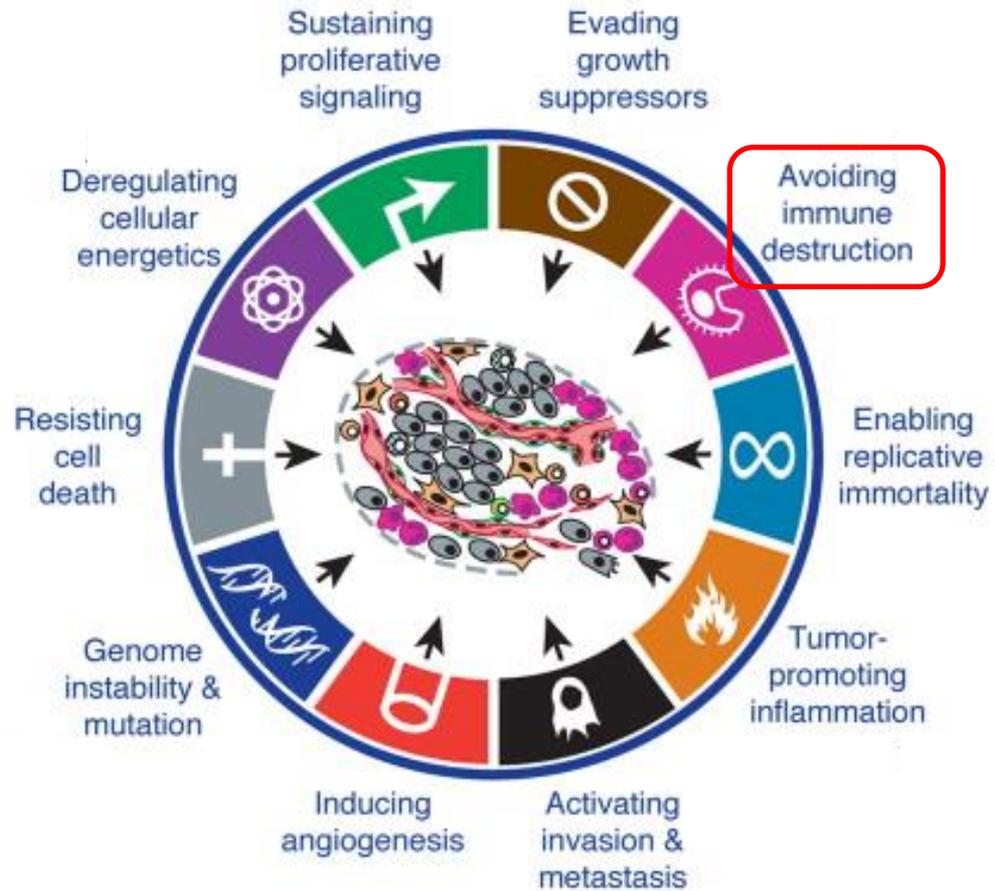
B



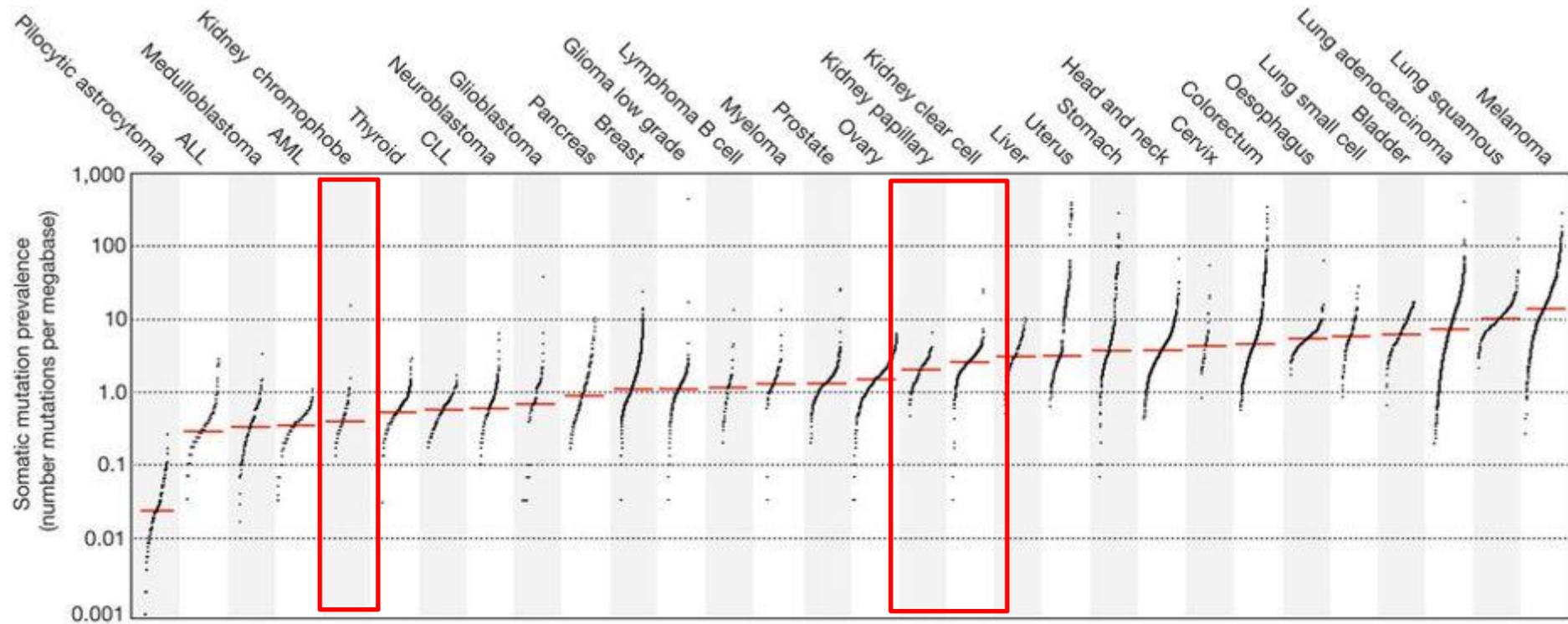


Chen DS, Mellman I. Oncology meets immunology: the cancer-immunity cycle. *Immunity*. 2013 Jul 25;39(1):1-10.

Ribas A. Tumor immunotherapy directed at PD-1. *N Engl J Med*. 2012 Jun 28;366(26):2517-9.



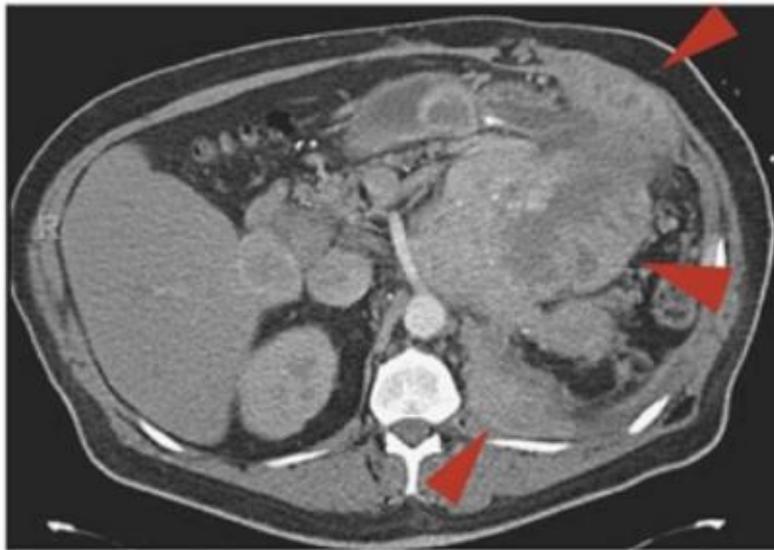
Tumor Mutational Burden



Activity of Anti-Programmed Death 1 (PD-1) Antibody

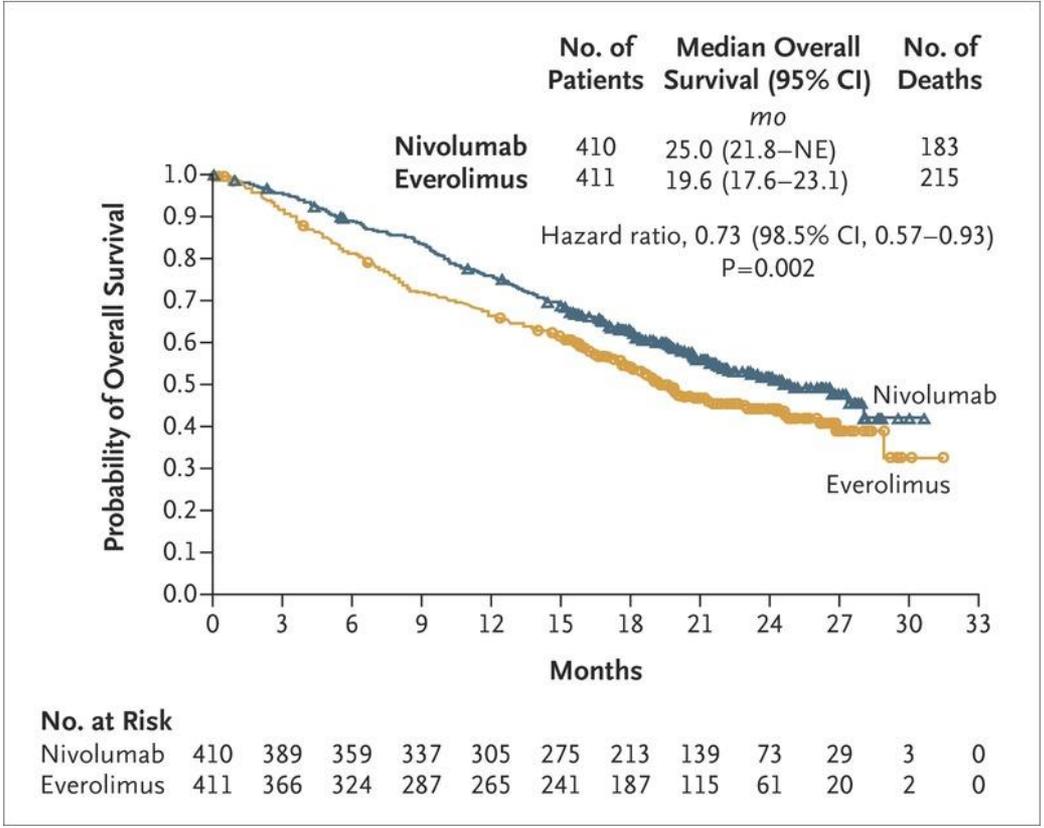
Patient with Renal-Cell Cancer

Before Treatment

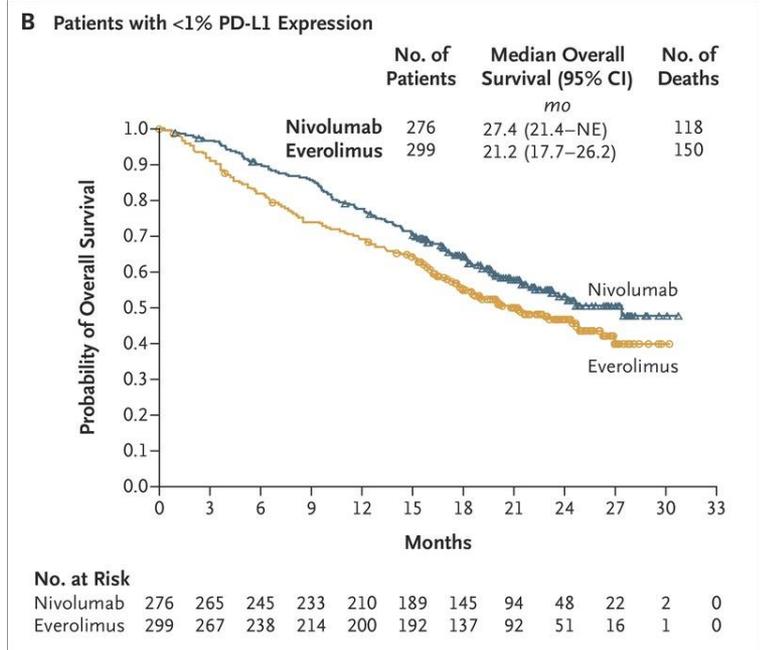
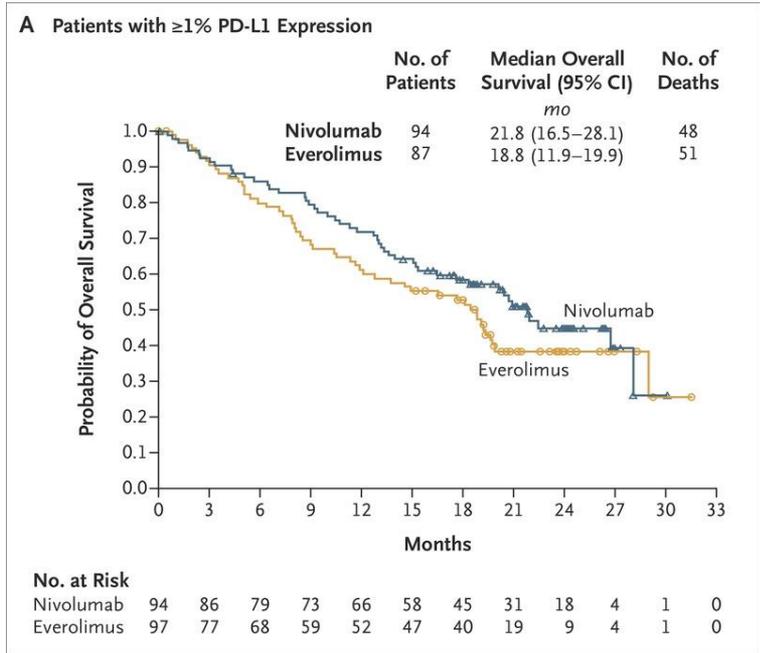
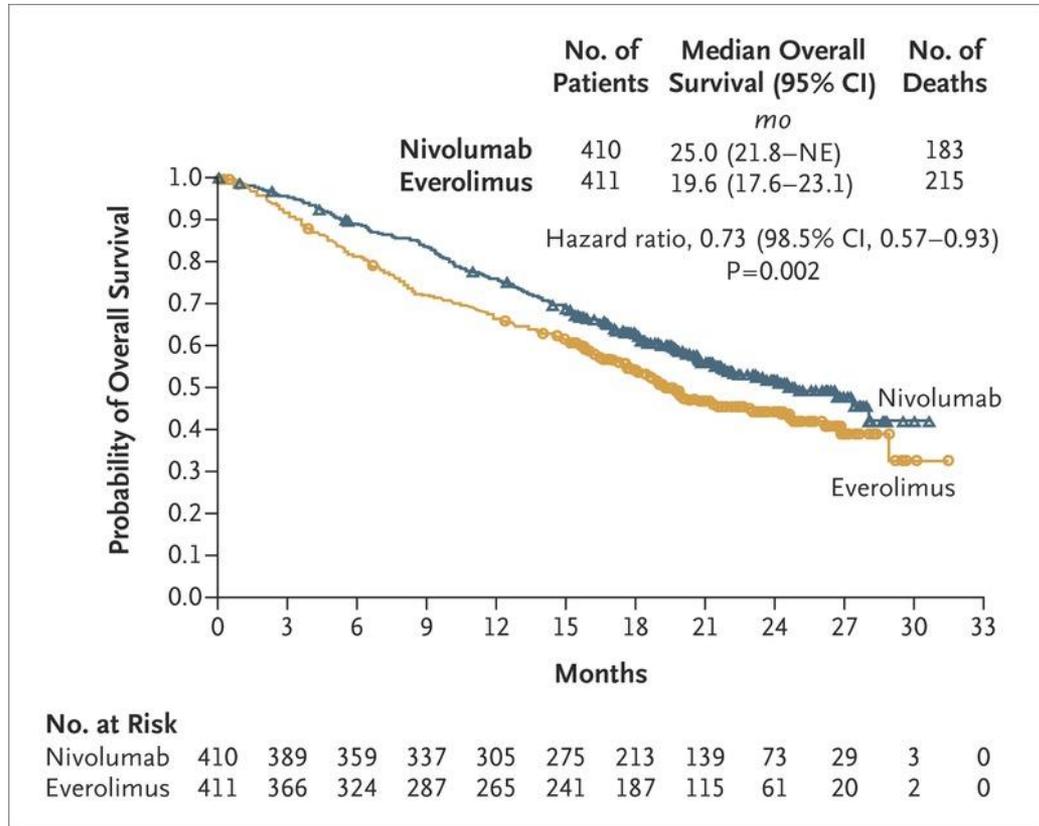


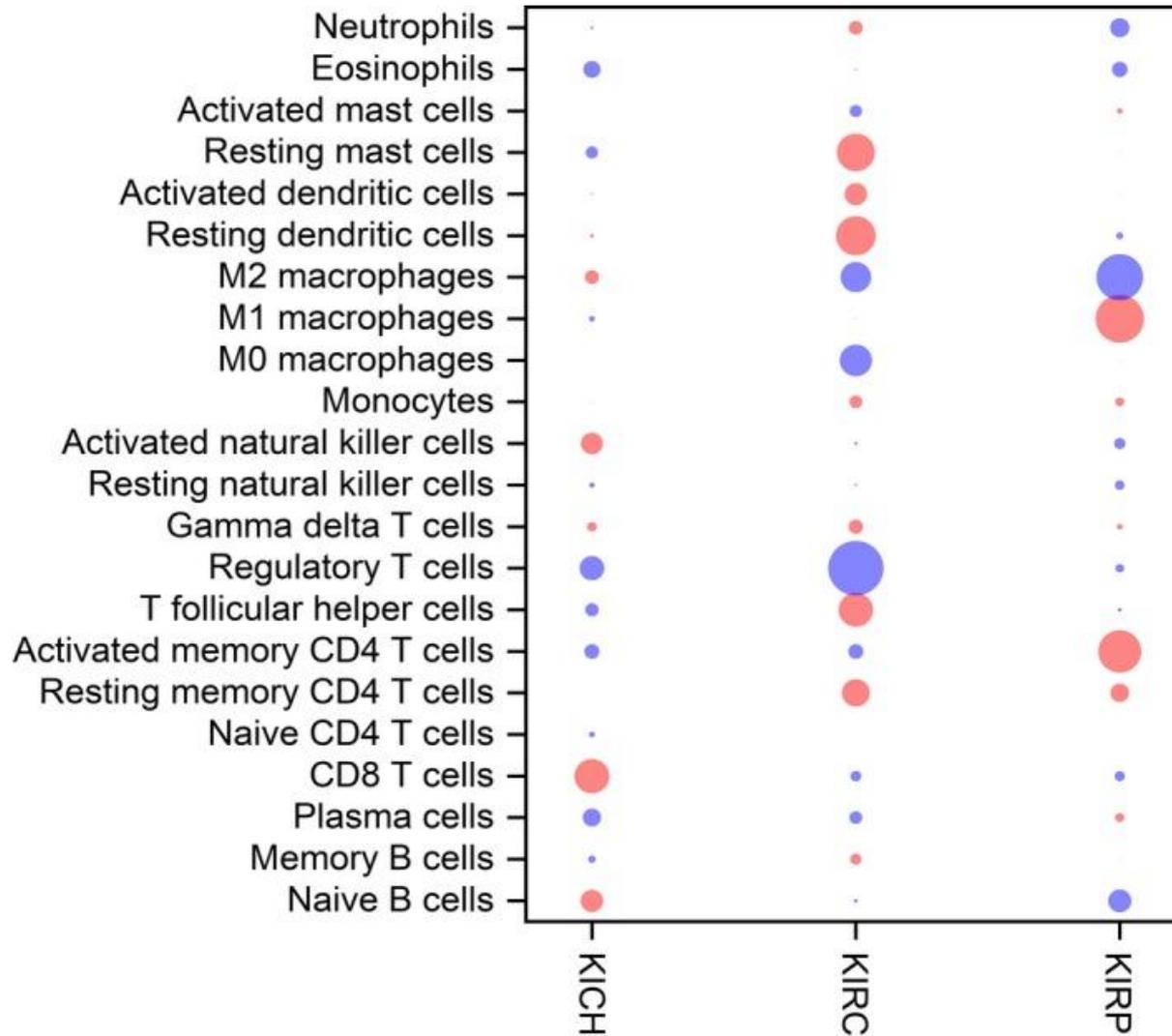
6 Months





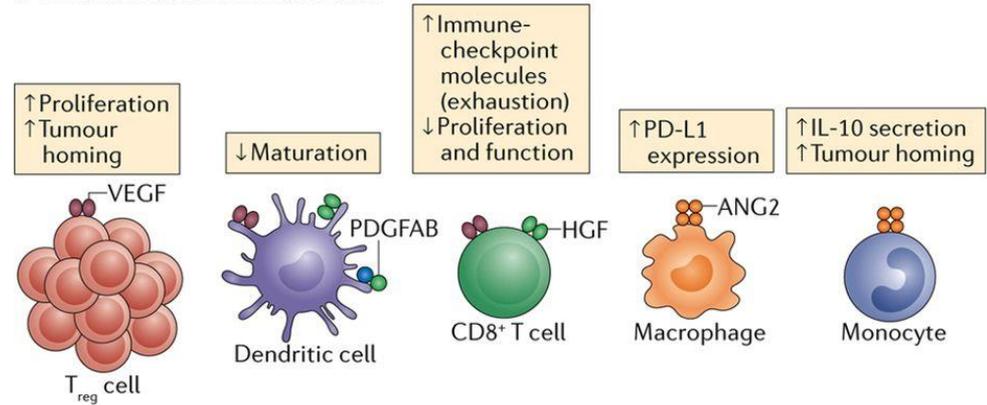
Motzer RJ, Escudier B, McDermott DF, George S, Hammers HJ, et al.
 Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma.
 N Engl J Med. 2015 Nov 5;373(19):1803-13



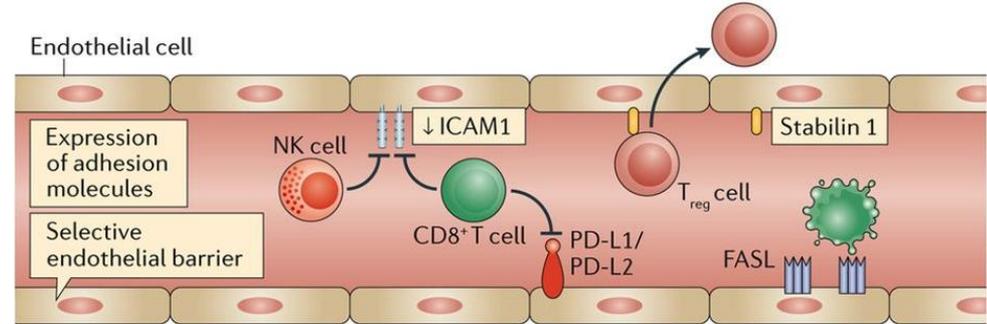


Angiogenesis-modulating factors have effects on the immune system in three established ways.

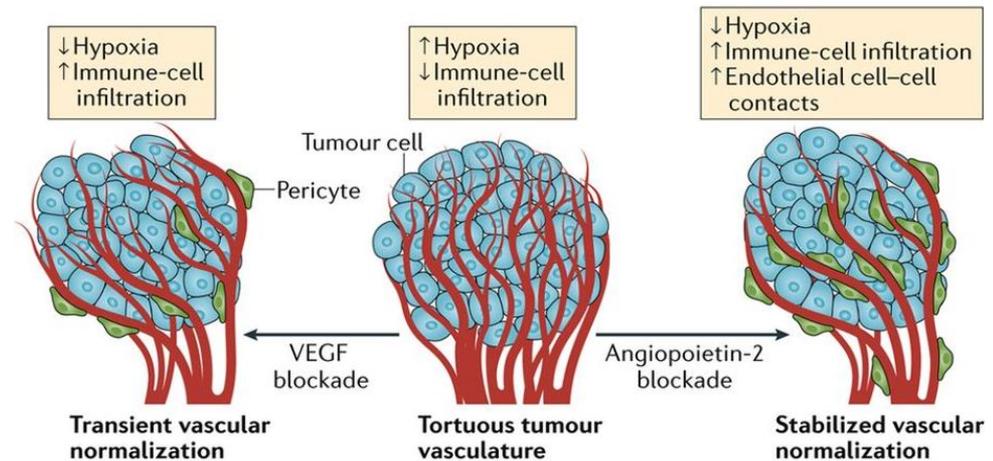
a Direct effects on immune cells

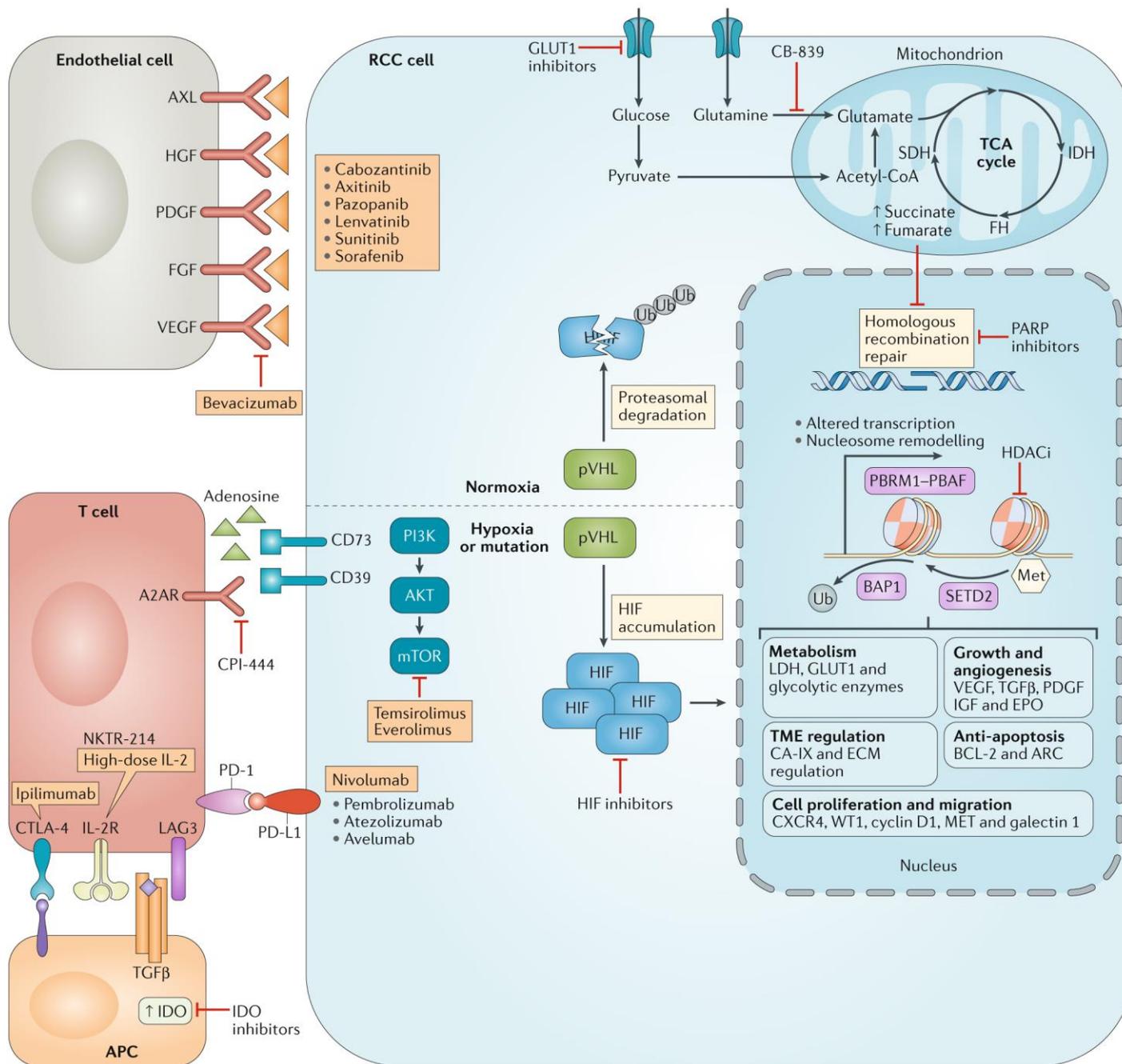


b Indirect effects on endothelium



c Indirect physical effects





Oncogénèse des cancers du rein : impact sur le diagnostic et la prise en charge

Discuter les avancées en cancérogenèse rénale
et leurs implications en pratique quotidienne

ReIn CaRe

Dr Damien AMBROSETTI
Laboratoire d'Anatomo Pathologie
CHU Nice