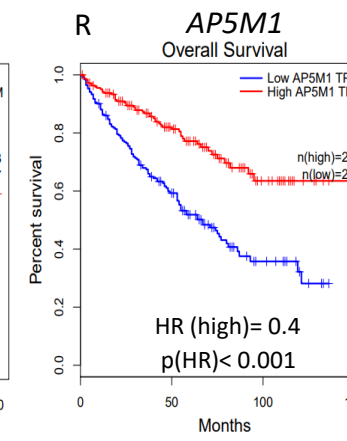
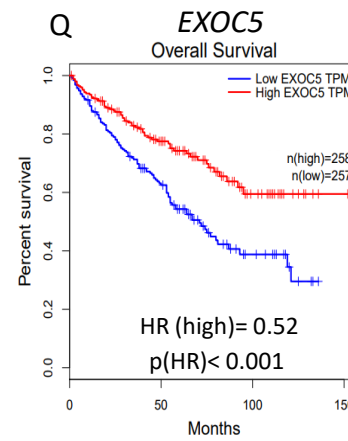
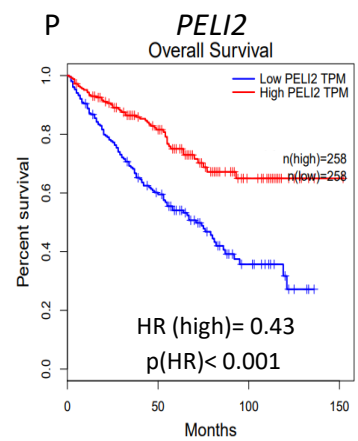
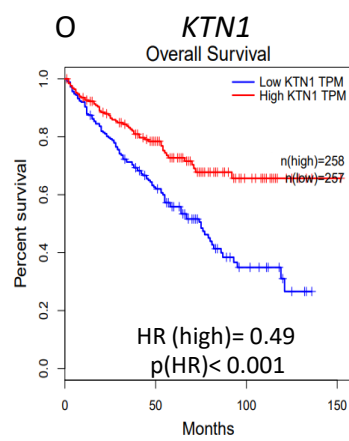
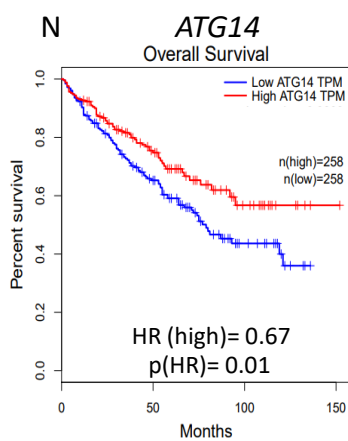
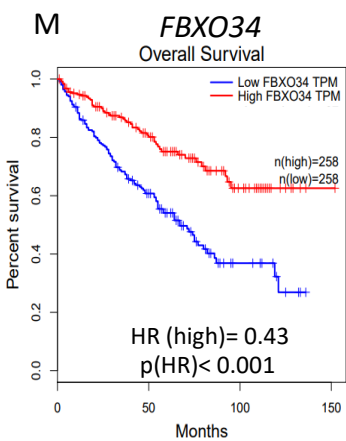
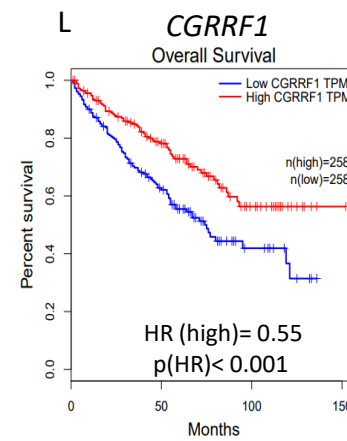
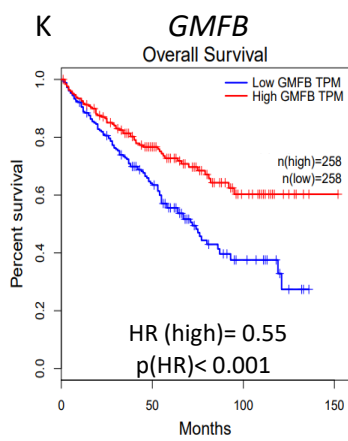
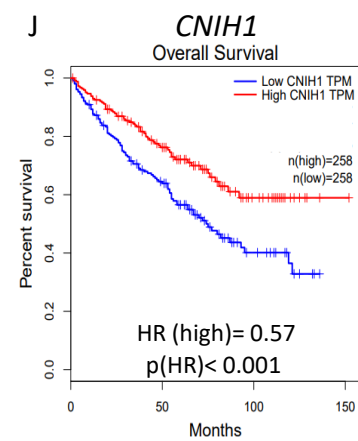
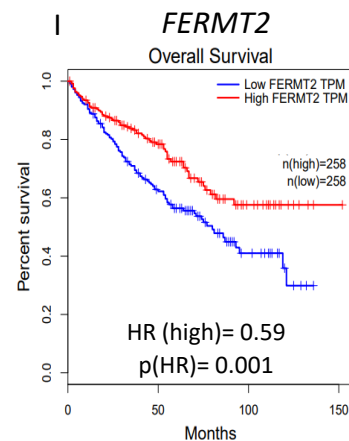
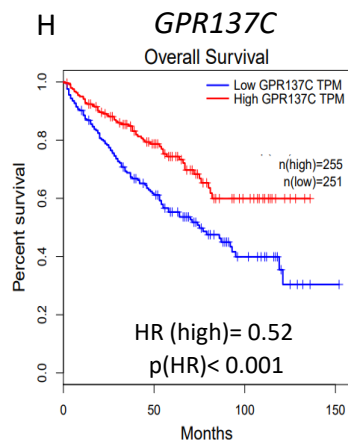
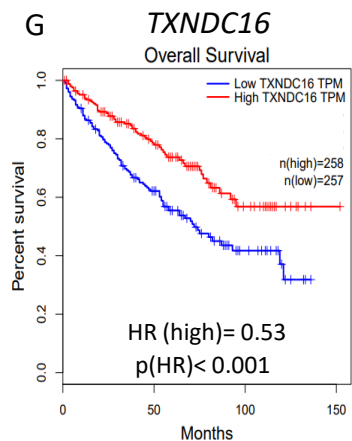
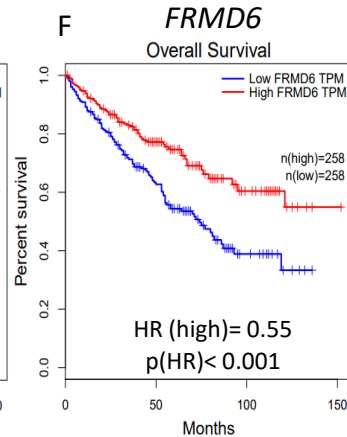
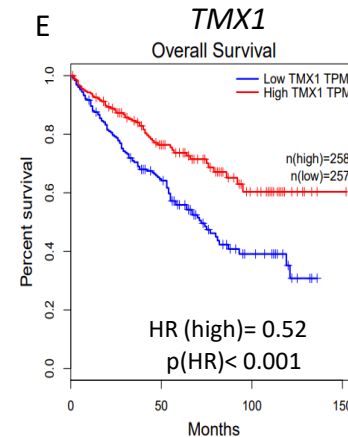
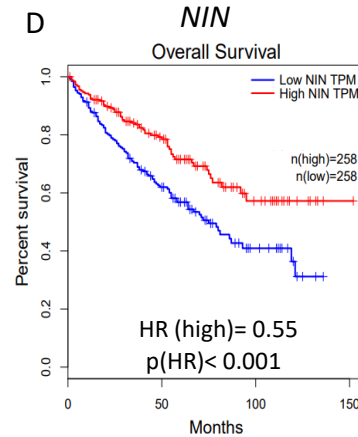
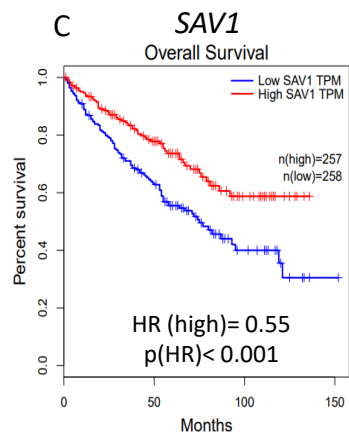
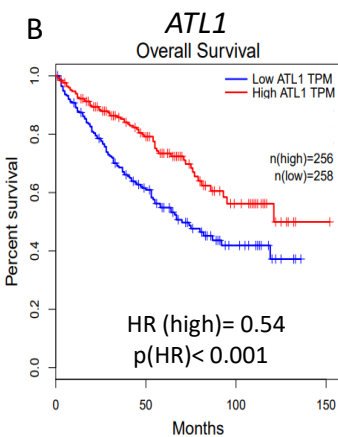
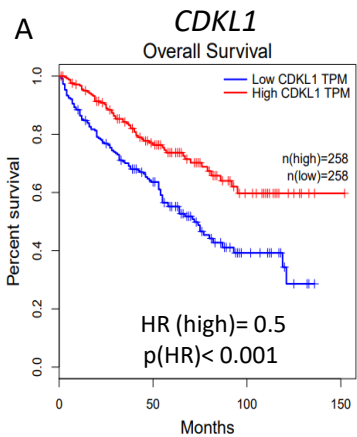


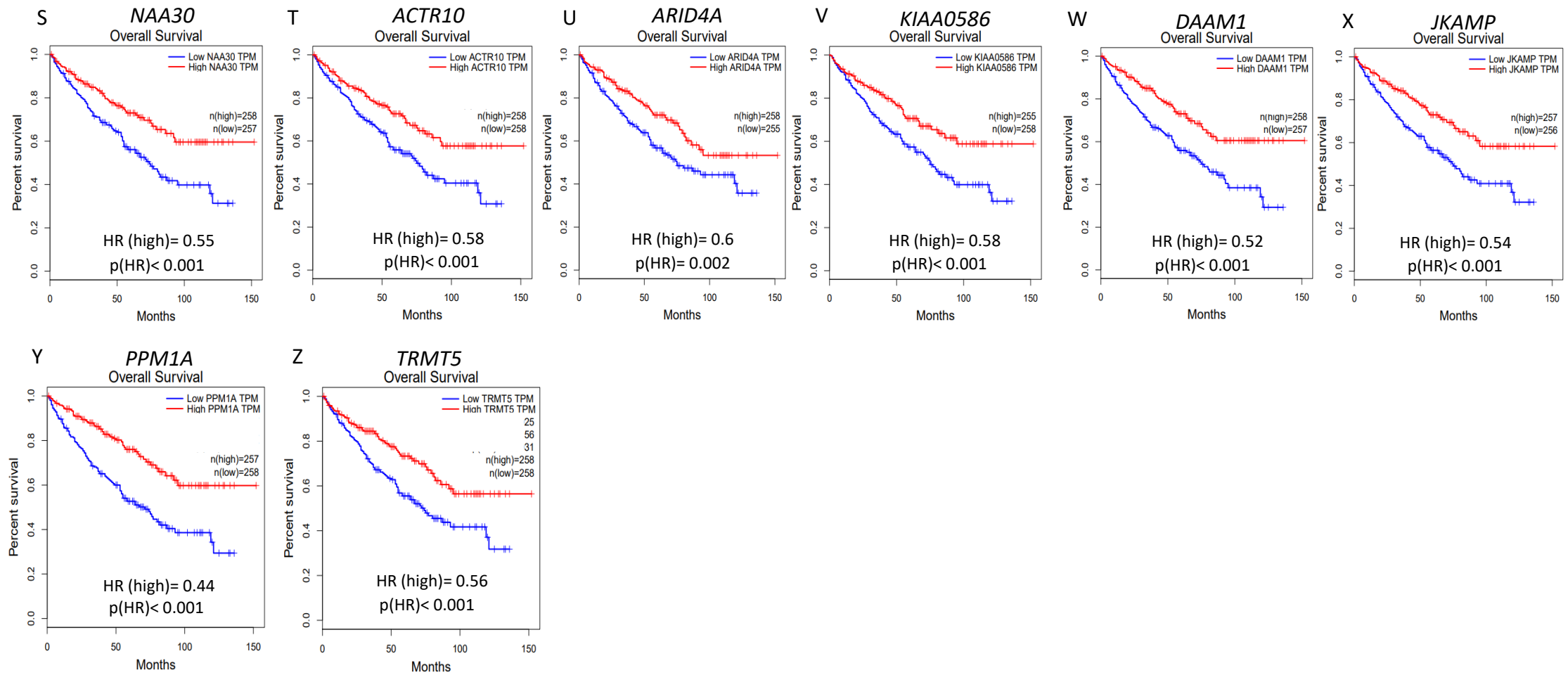
HIF1 $\alpha$  is not a target of 14q deletion in clear cell renal cancer

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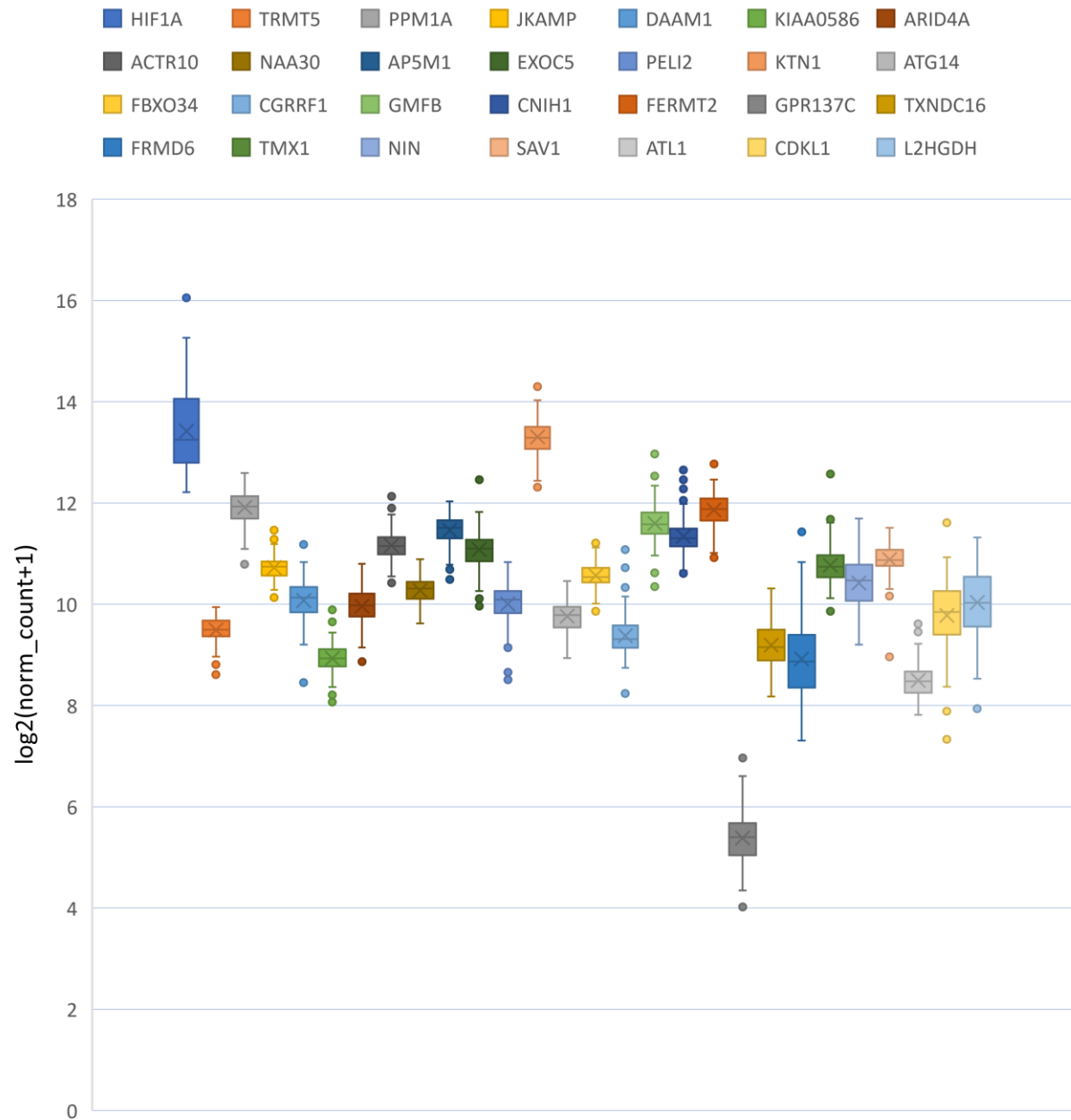
2 Experimental Therapeutics Program, Albert Einstein Cancer Center, Albert  
Einstein College of Medicine, New York 10461



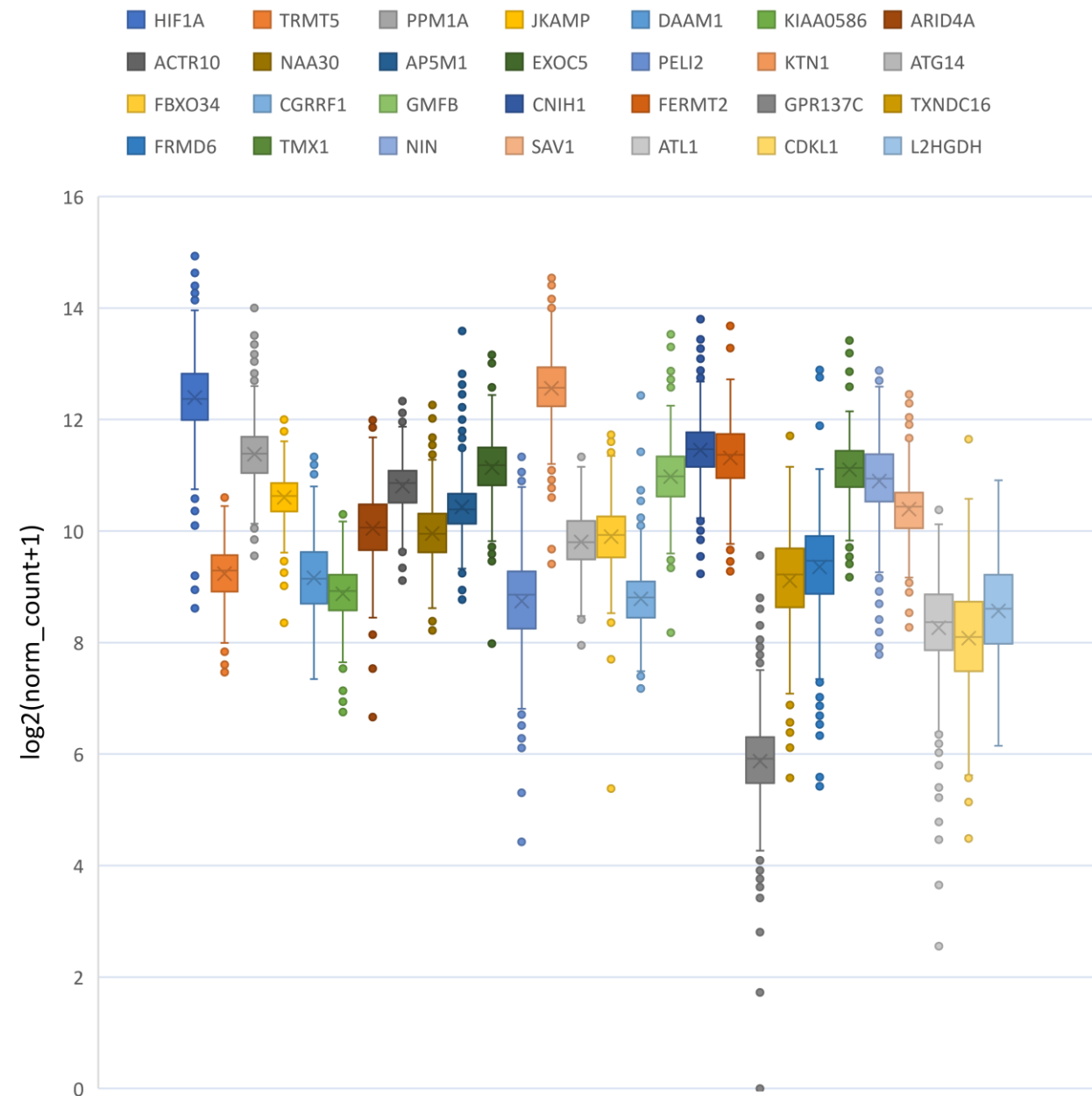


**Figure S1. A–Z:** 26 genes between the loci of *L2HGDH* at 14q21.3 and *HIF1A* at 14q23.1, whose lower gene expression is significantly associated with inferior survival in ccRCC (log-rank  $p < 0.05$ ) but are yet to be functionally characterized. The figures show survival curves based on higher or lower expression of the gene, separated by median (TCGA). Hazard ratios are depicted, as well as the p values for hazard ratio. These 26 genes are also deleted in  $\geq 95\%$  of ccRCC 14q deletions involving the *HIF1A* locus. (Of note, for comparison of effect size, HR (high) value for *L2HGDH*, a fully characterized 14q ccRCC tumor suppressor, is 0.42. Only one of the 26 genes (*AP5M1*) has a HR (high) value lower than that of *L2HGDH*)

### A. TCGA Normal kidney tissue (n=129)

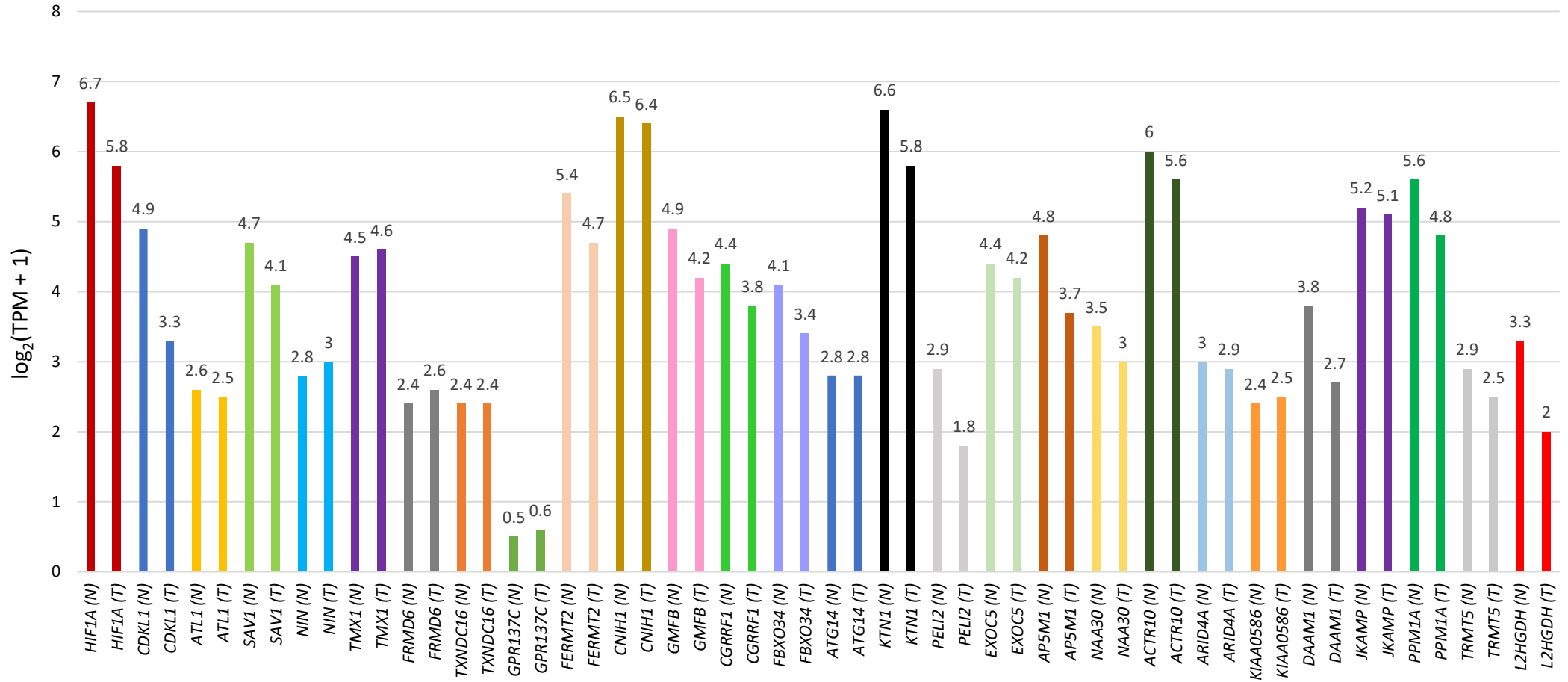


### B. TCGA KIRC (n=530)

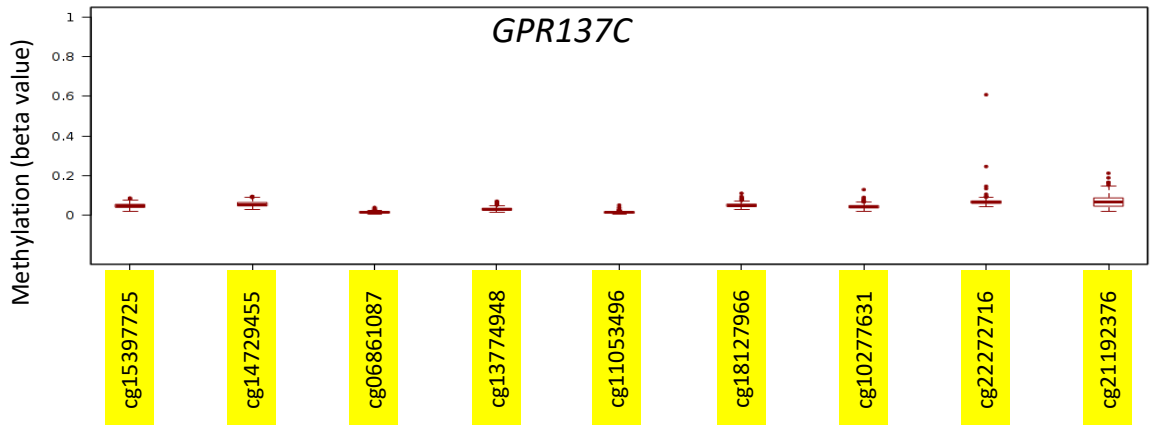
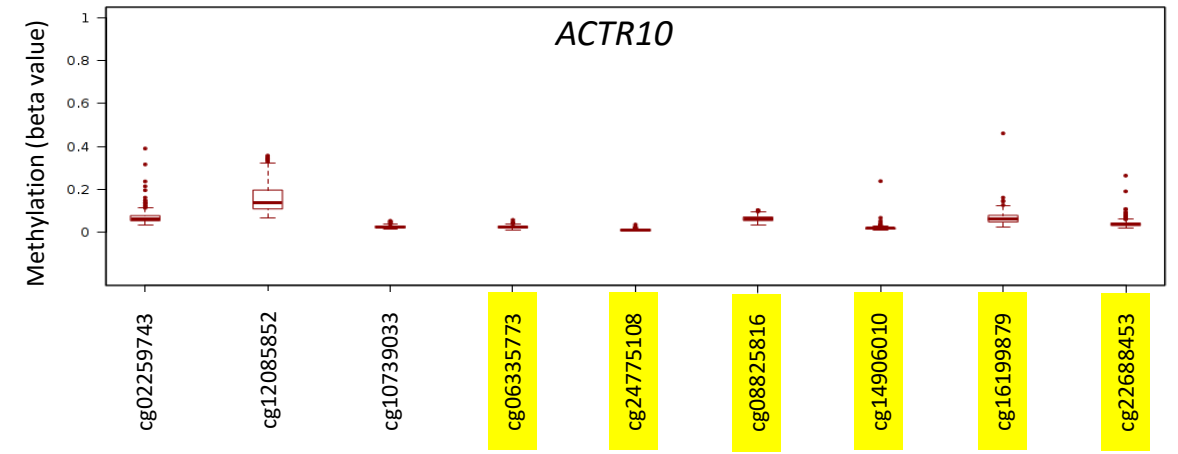
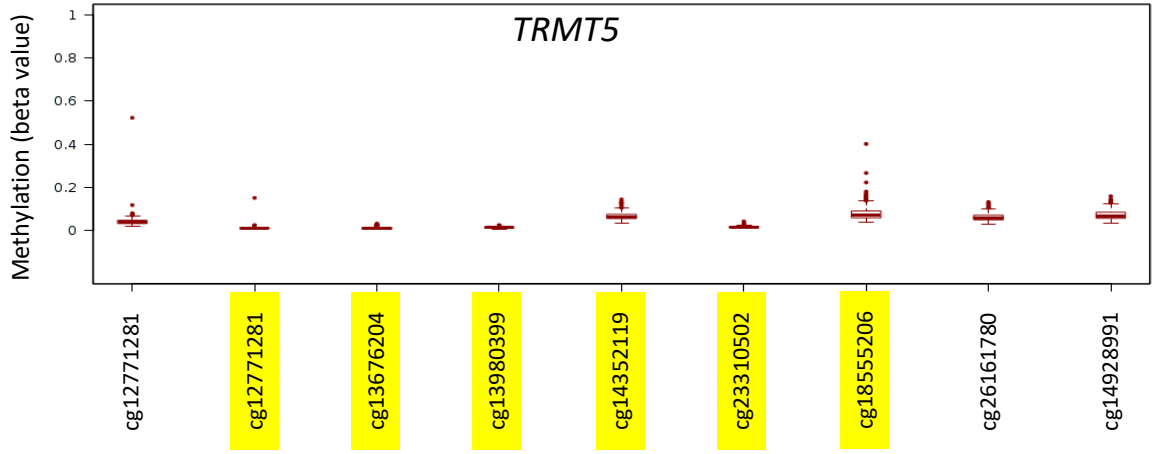
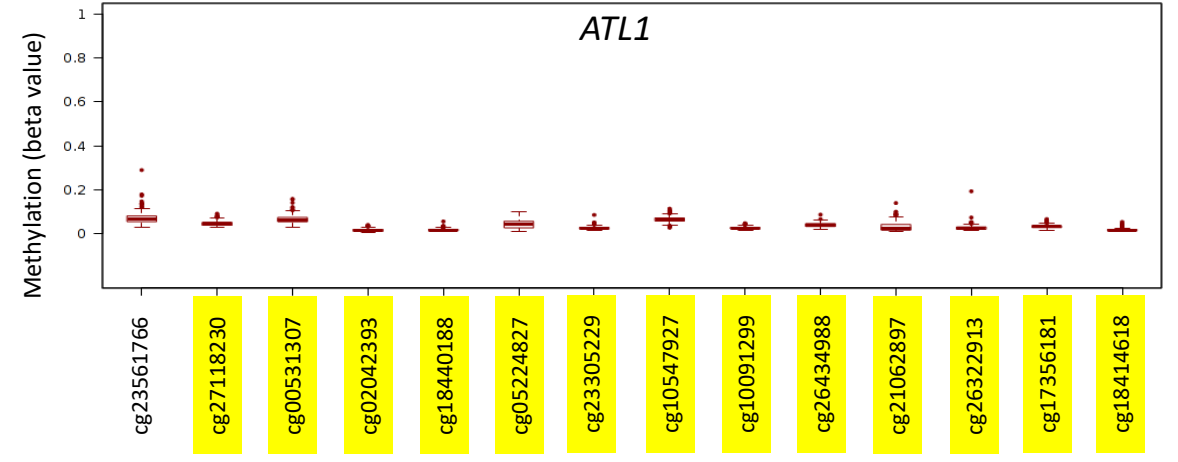
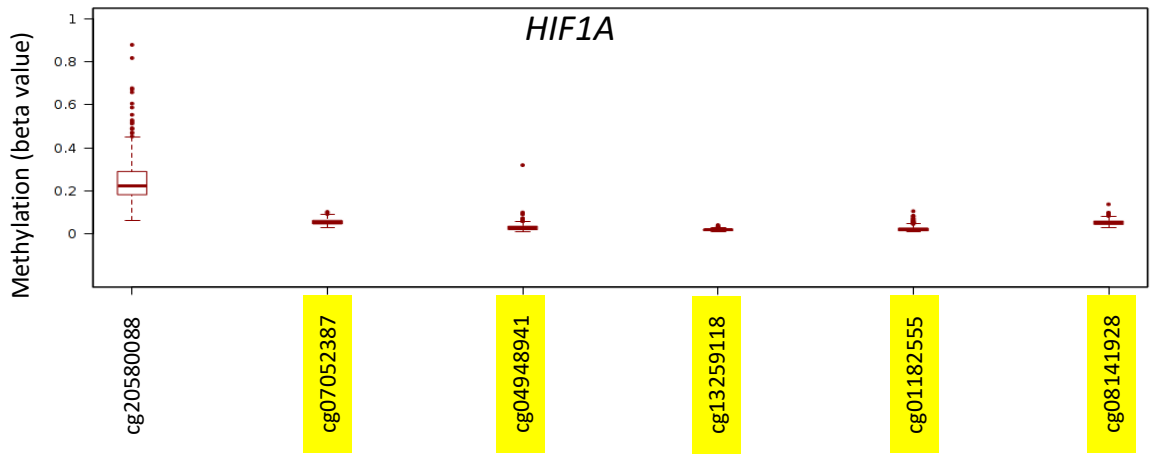


**Figures S2A,B.** Expression of the 26 genes depicted in Table 1 in  $\log_2(\text{norm\_count}+1)$  units (along with the two genes *HIF1A* and *L2HGDH*). TCGA normal kidney tissue (**S2A**, n=129) and TCGA KIRC (**S2B**, n=530).

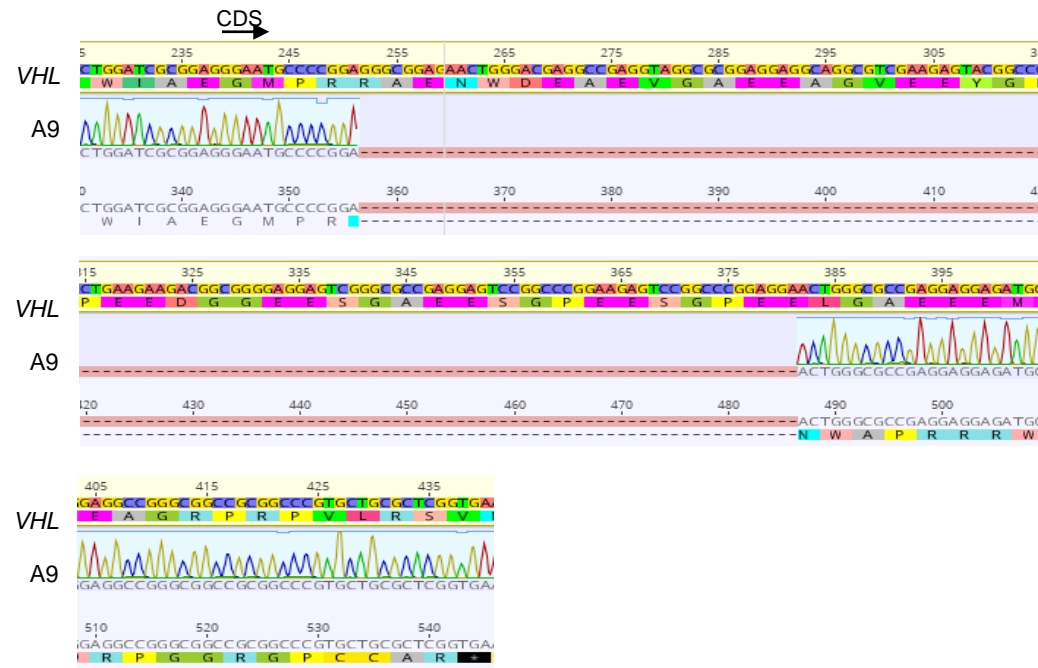
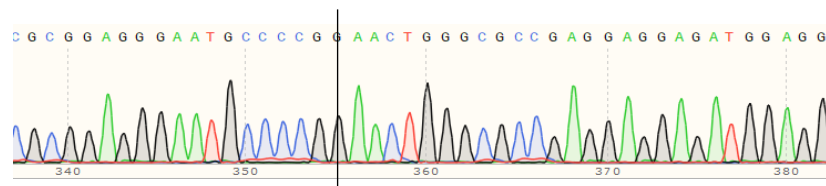
### TCGA KIRC & Normal Kidney



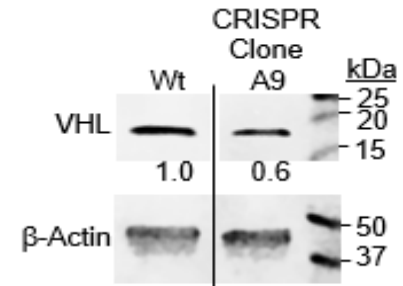
**Figure S2C.** Expression of the 28 genes in TCGA KIRC and normal kidney in log<sub>2</sub> (TPM+1) units to facilitate comparison of expression between genes. Of all the 28 genes, *L2HGDH* (far right) has the greatest percentage reduction in expression in tumor compared to normal (40% reduction), followed by *PELI2* (38%) and *CDKL1* (33%). *HIF1A* is among the higher expressed genes, both in tumor and normal tissue.



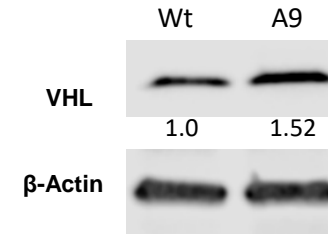
**Figure S3.** CpG island probes are highlighted. Non- CpG island probes are not. Probes for 1000bp upstream and 500 bp downstream from TSS of each gene depicted. Low methylation beta values seen for all the 5 analyzed genes, including *HIF1A*. TCGA KIRC (n= 324).

**A****B****C**

10/24/2019

**D**

11/13/2019



**Figure S4. A.** Alignment to VHL genomic sequence shows 130 bp deletion in Exon 1 resulting in a frame-shift and introduction of an early stop codon. **B.** Sanger sequence of deleted region. **C, D.** A9 clone western blot done 3 weeks apart, revealing increased VHL expression (compensation by the preserved allele) over time. Figure S4C represents non-contiguous lanes from a single blot. (*The A9 clone was generated as a part of another project in the lab; this particular observation turned out relevant for the discussion section of this manuscript*)