Transcriptome profiling of HIF-1α and HIF-2α CRISPR/Cas9 knock-out cell lines reveal distinct response pathways to hypoxia

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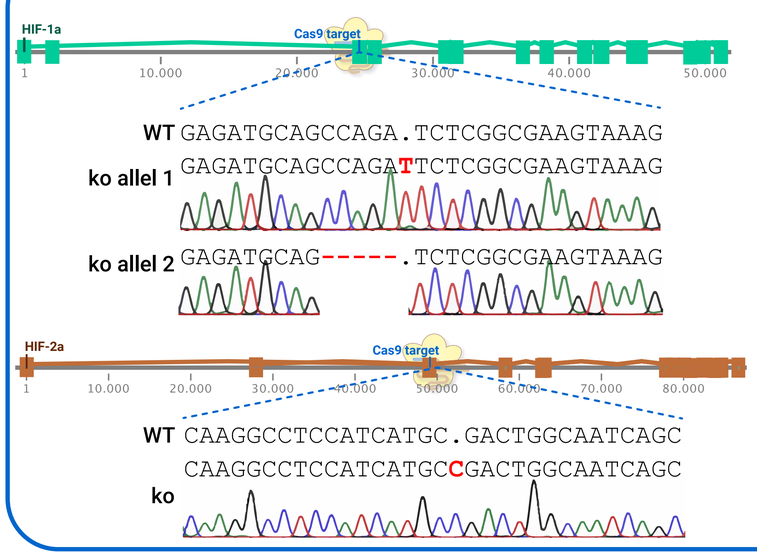
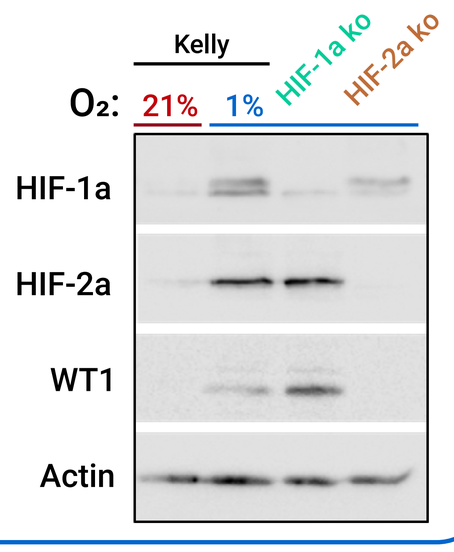
Background and aim

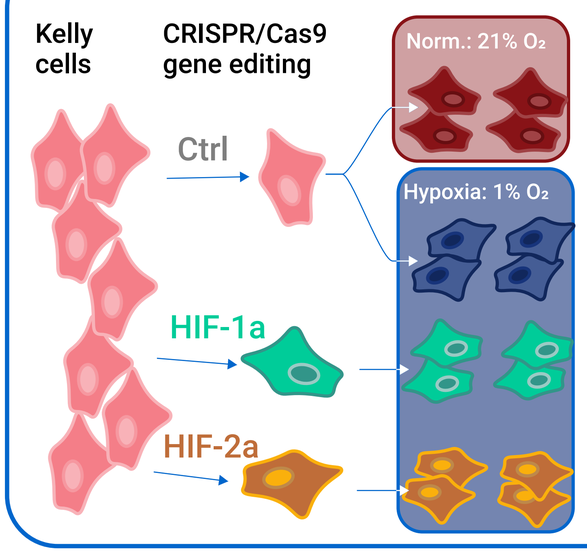
- Neuroblastoma is the most common extracranial, solid childhood tumor accounting for approximately 15% of pediatric cancer deaths (Louis and Shohet, Annu. Rev. Med., 2015).
- Neuroblastoma arises from neural crest-derived sympathoadrenal precursor cells that fail to differentiate normally during embryonic development.
- Recent findings indicate that tumor hypoxia correlates with a highly dedifferentiated neuroblastoma phenotype and unfavorable clinical outcome (Jögi et al., Proc. Natl. Acad. Sci. U S A, 2002; Påhlman and Mohlin, Cell Tissue Res., 2018).
- By combining CRISPR/Cas9 genome editing to delete HIF1α and HIF2α with RNA deep sequencing, we aimed at identifying hypoxia-regulated transcriptional networks in Kelly neuroblastoma cells.

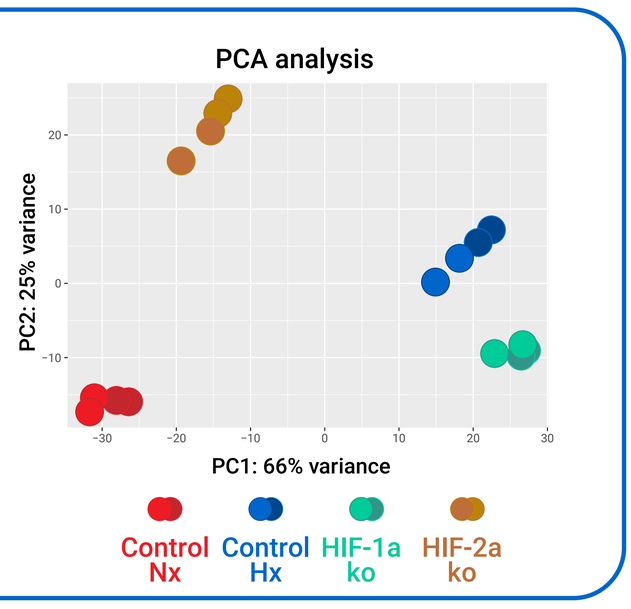
Generation of HIF-1a & HIF-2a knock-out cell lines



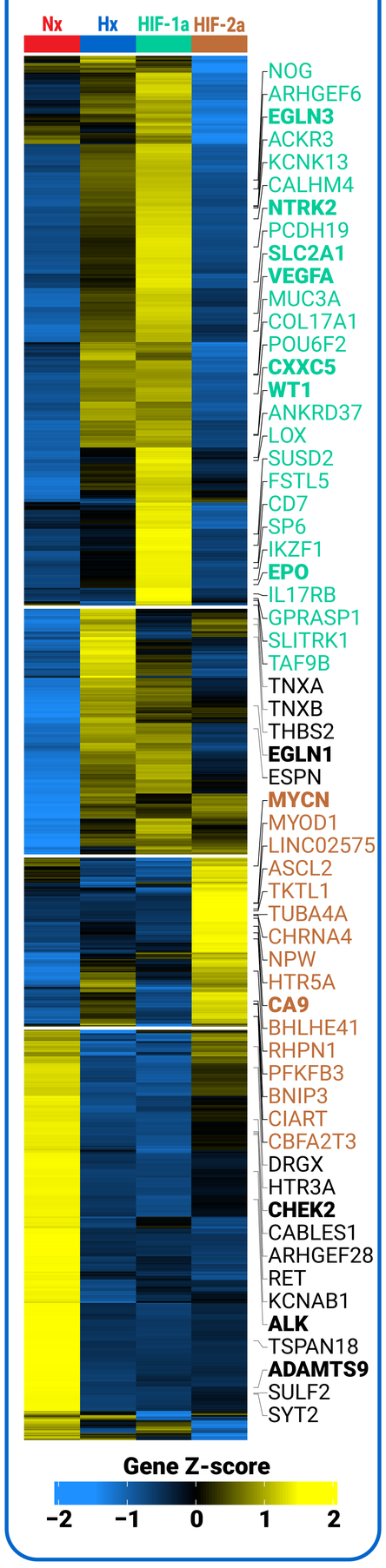


RNA-Seq experiment

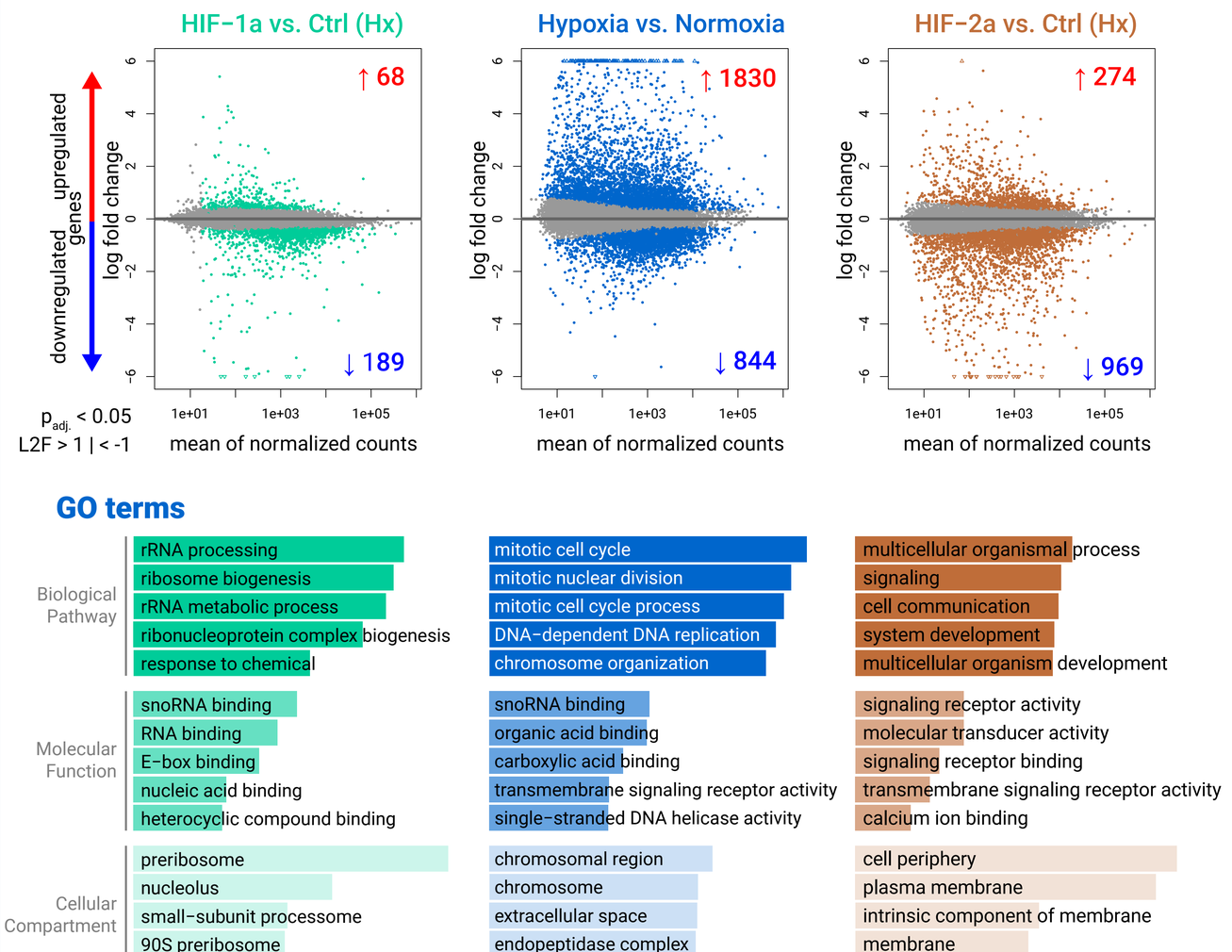




DE genes (counts)

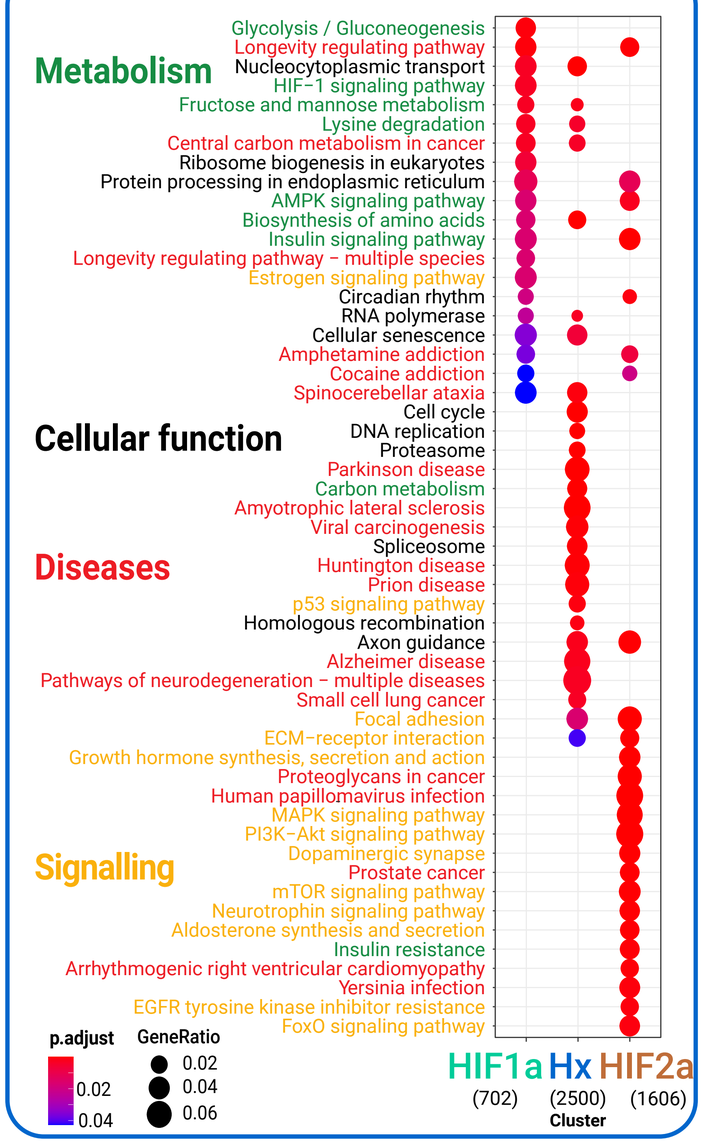


RNA-seq results

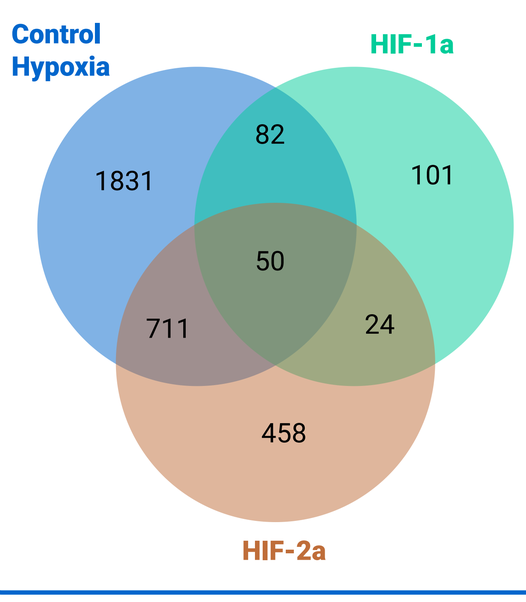


GO terms

KEGG terms enrichment

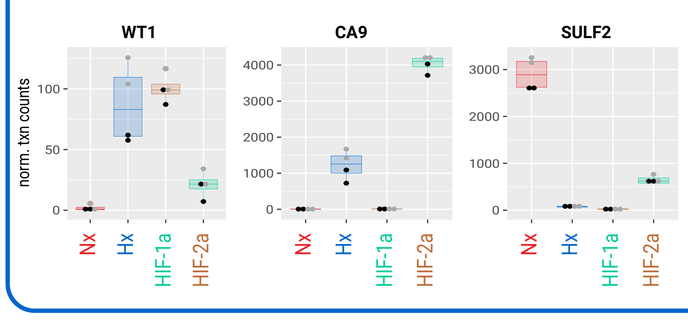


Overlap



Conclusions

- The combinatorial use of CRISPR/Cas9 genome editing and transcriptome sequencing is a valuable tool to detect novel HIF target genes in Kelly neuroblastoma cells.
- Targeting HIF-dependent signalling mechanisms might represent a promising novel approach for the treatment of neuroblastoma.



Neuroblastoma and Hypoxia