The adrenergic-specific long non-coding RNA NESPR controls survival of neuroblastoma cells

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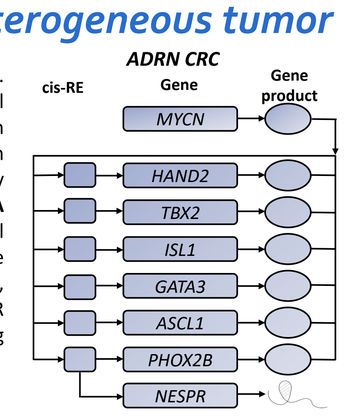
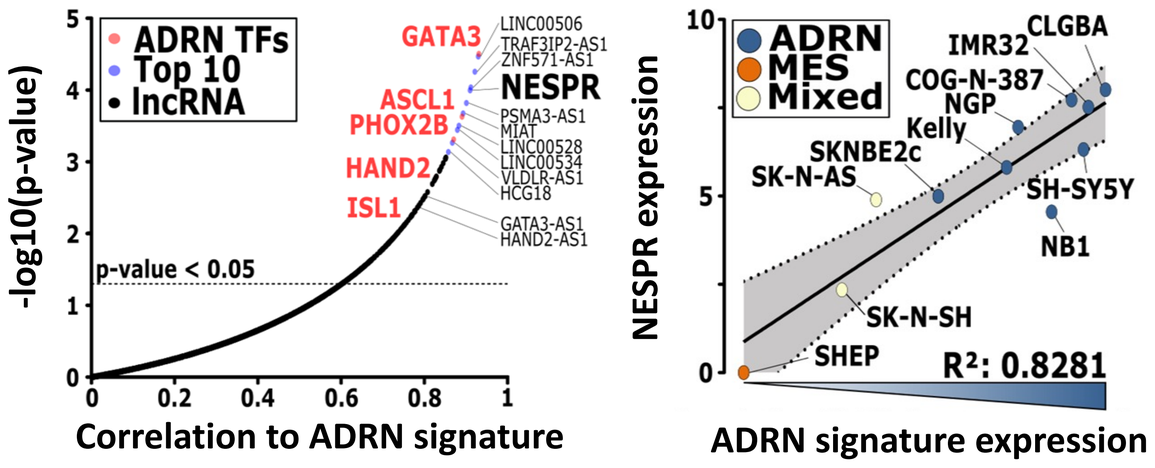
Introduction: neuroblastoma is a heterogeneous tumor

Neuroblastoma (NB) is a childhood cancer of the sympathetic nervous system. Recent studies have shown that neuroblastoma tumors are composed of two cell identities, i.e. the **adrenergic (ADRN)** and mesenchymal (MES) identity. Both identities are driven by a **core regulatory transcriptional circuitry (CRC)**, which acts as an autoregulatory positive feedforward loop, to delineate the cell identity through regulation of its target genes. We identified the **long non-coding RNA NESPR** to be specifically expressed in neuroblastoma cells of the adrenergic cell identity. We show that NESPR is contained within an insulated gene neighborhood with the adrenergic core regulatory transcription factor **PHOX2B**, and that NESPR regulates PHOX2B expression *in cis*. Knockdown of NESPR decreased neuroblastoma cell proliferation and induced cell death, highlighting NESPR's importance in the survival of the adrenergic neuroblastoma cells

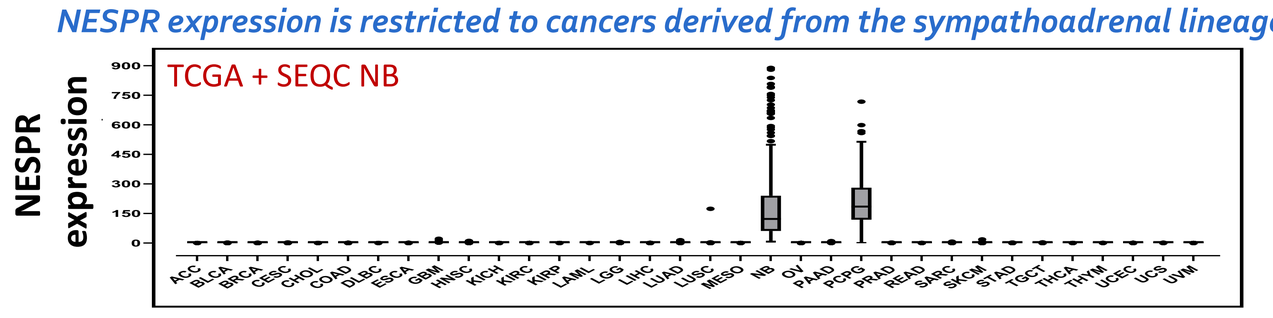


NESPR is a adrenergic-specific long non-coding RNA

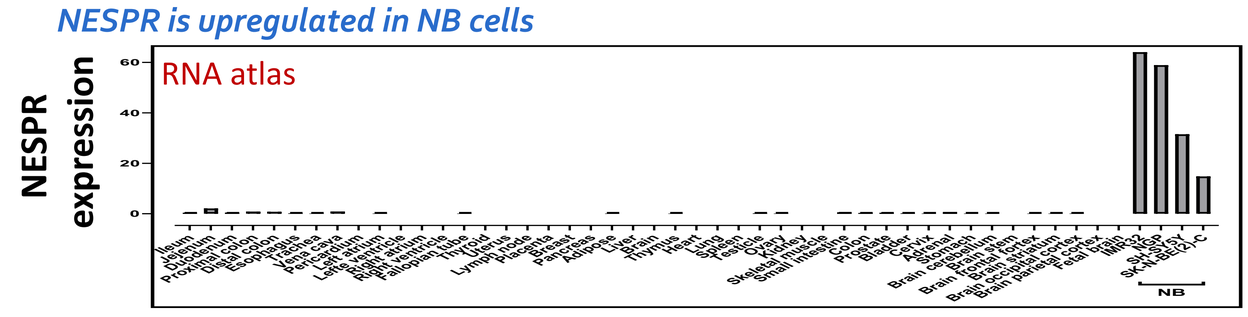


NESPR acts as a lineage survival oncogene in NB

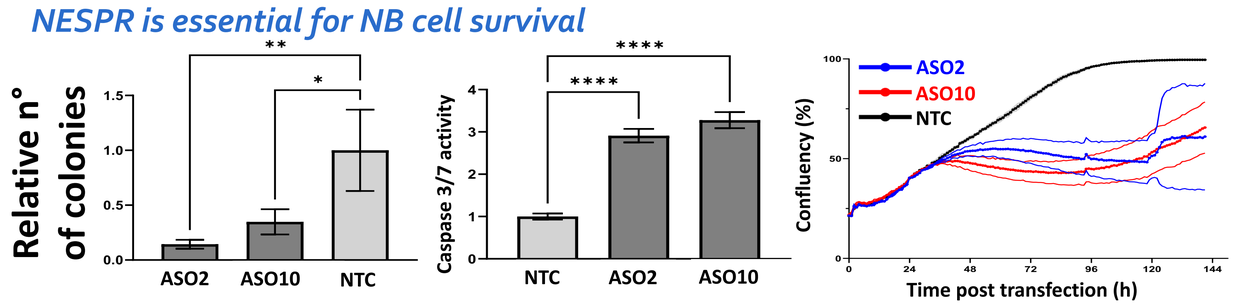
NESPR expression is restricted to cancers derived from the sympathoadrenal lineage



NESPR is upregulated in NB cells

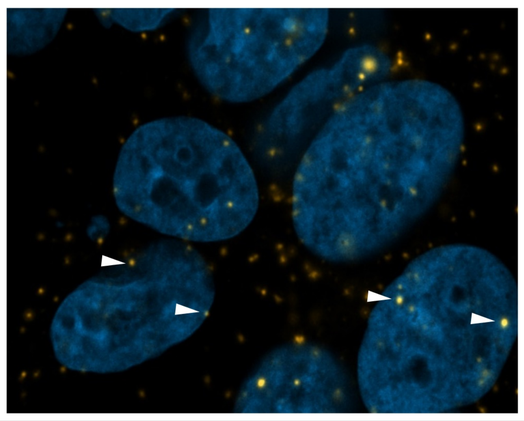


NESPR is essential for NB cell survival

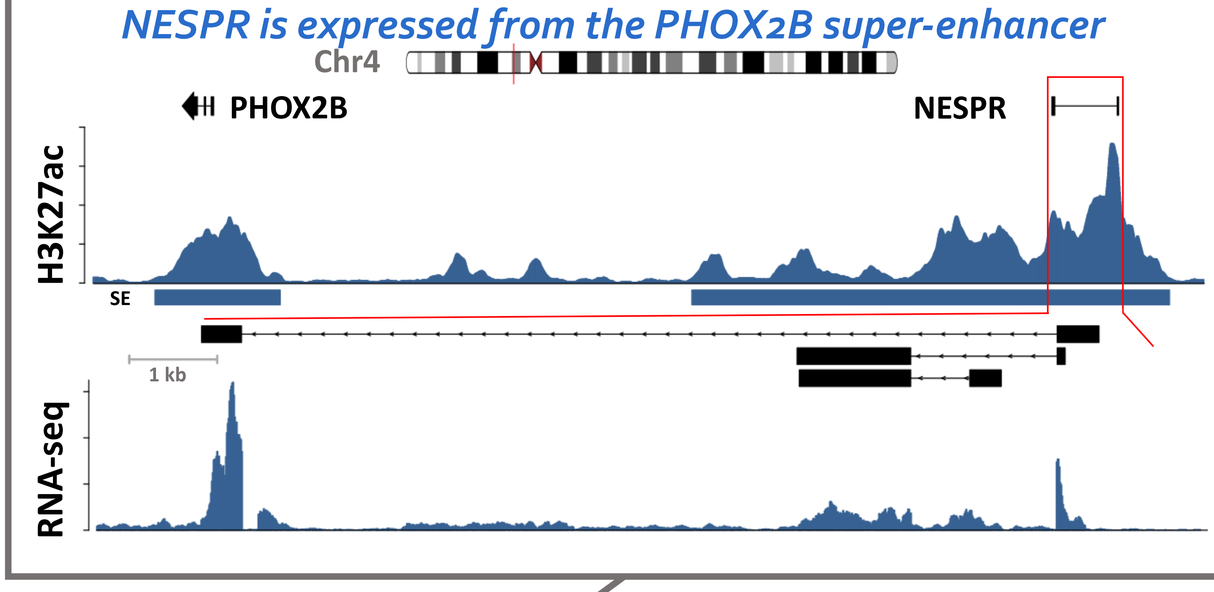


Understanding NESPR's mode-of-action – a multi omics approach

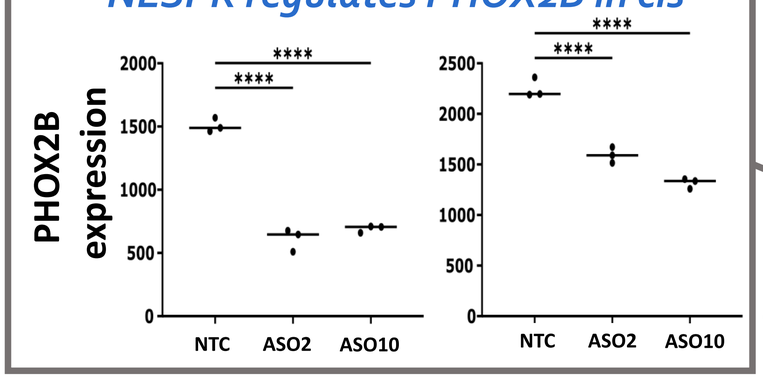
Nuclear NESPR concentrates in distinct foci

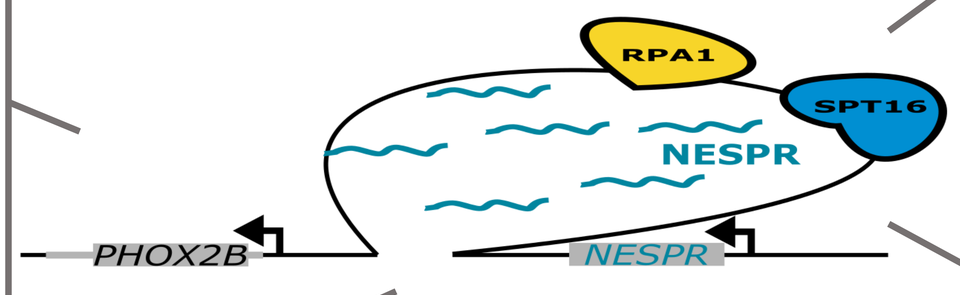


NESPR is expressed from the PHOX2B super-enhancer

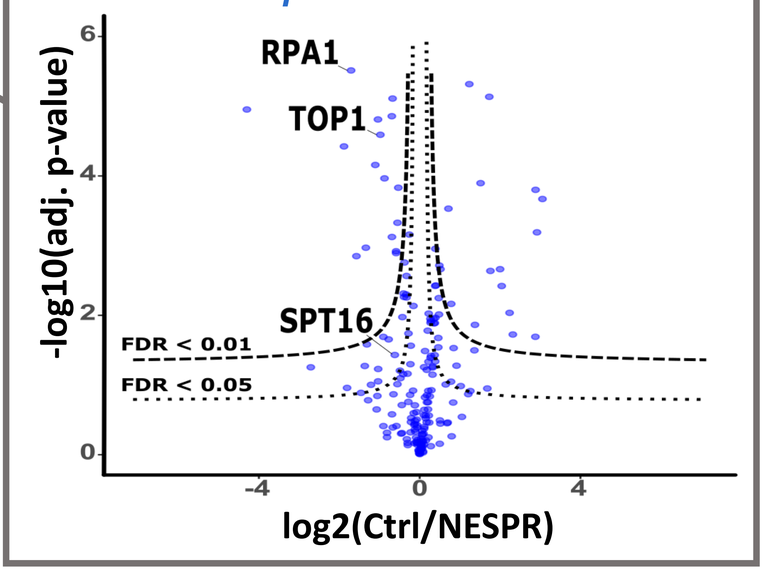


NESPR regulates PHOX2B in cis

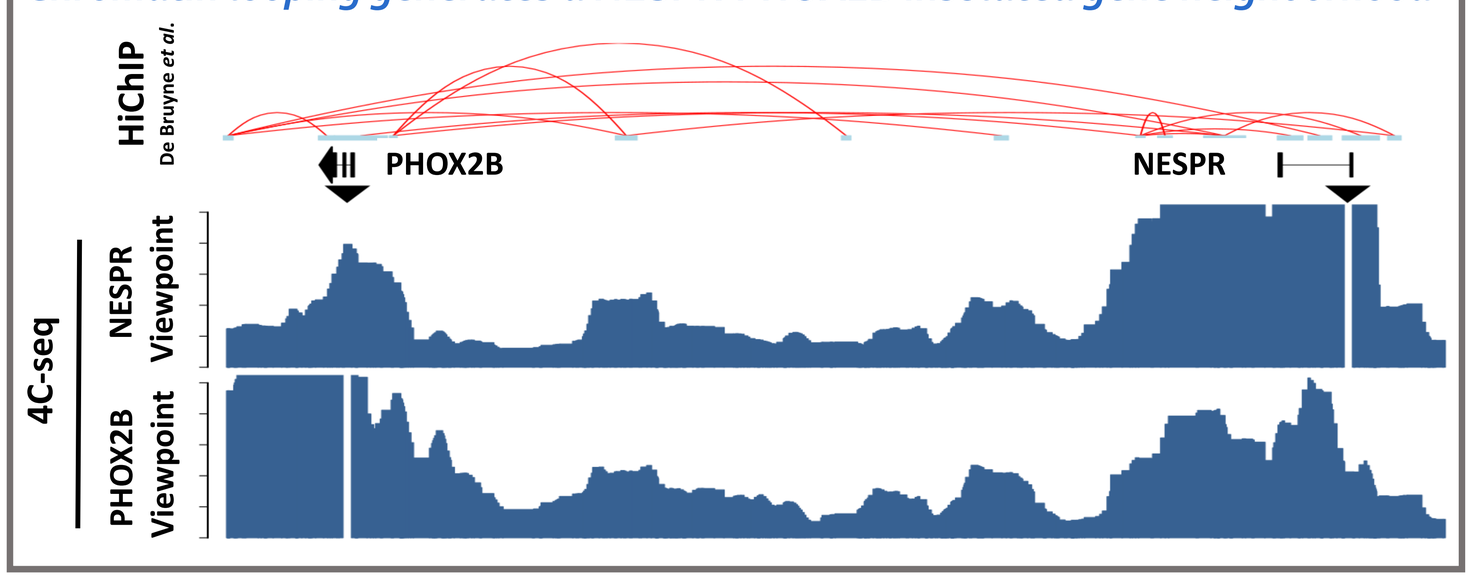




NESPR interacts with transcriptional co-activators



Chromatin looping generates a NESPR-PHOX2B insulated gene neighborhood



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