

The neuroblastoma specific lincRNA NESPR controls noradrenergic cell identity

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Eric de Bony

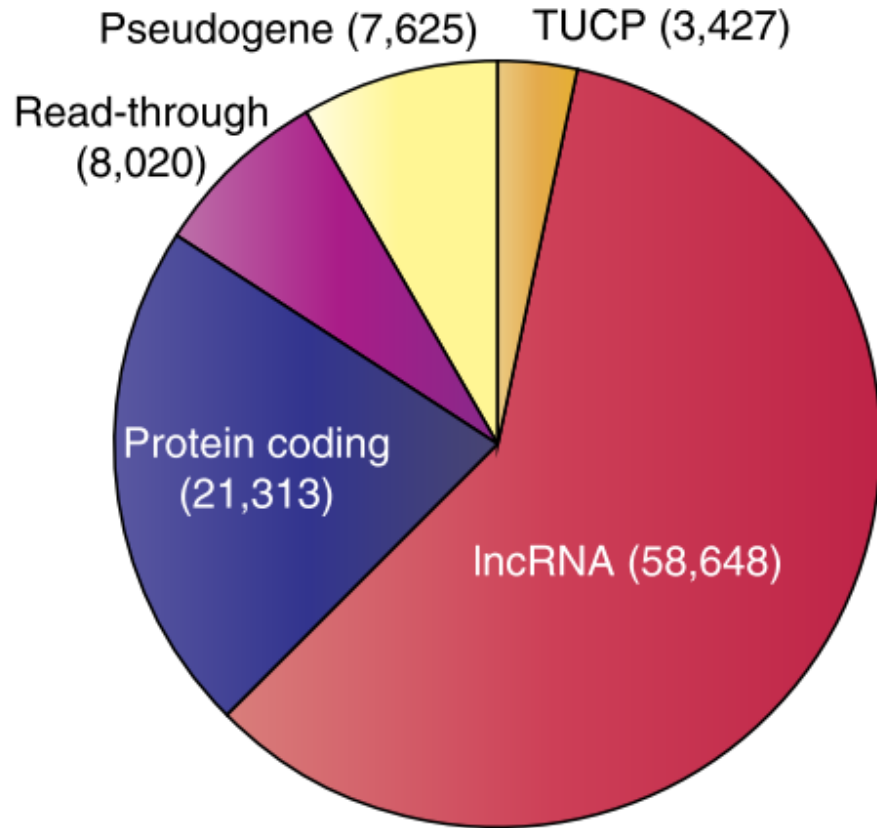


Most of this work was conducted by Dries Rombaut...at home writing his thesis !

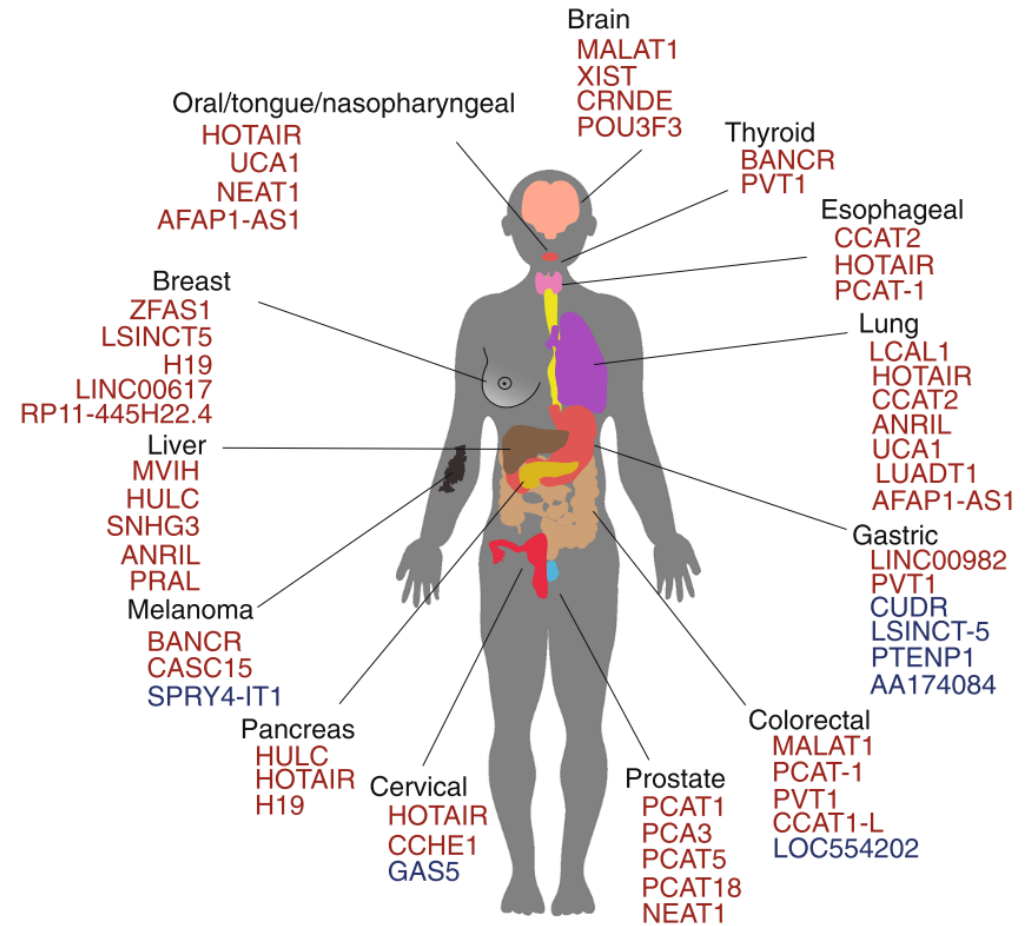


LONG NON-CODING RNAs ARE INVOLVED IN CANCER

59 % of transcriptome arises from lncRNA loci



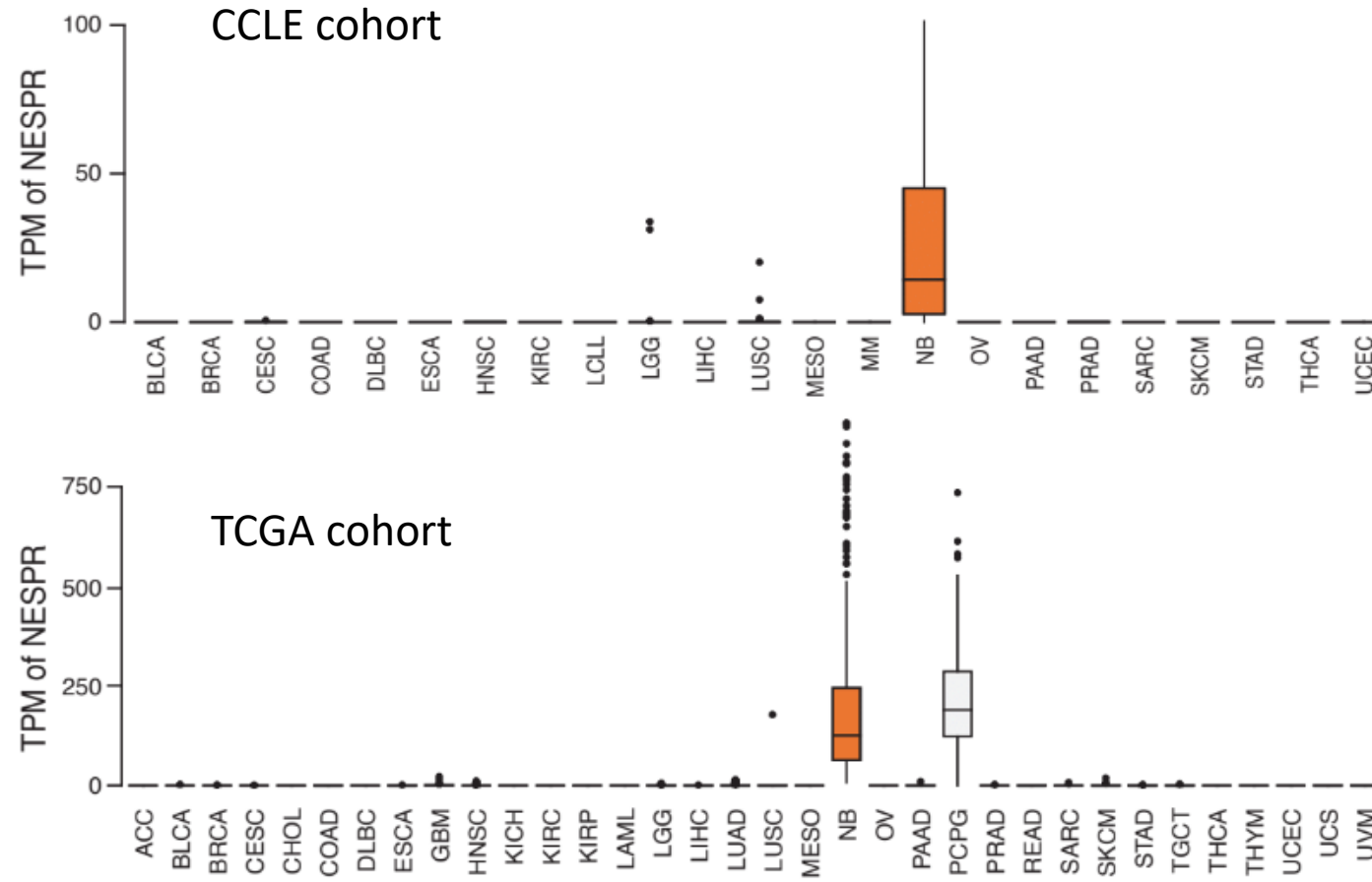
(Iyer et al., Nat. Gen., 2014)



(Guttman & Rinn, Nature 2014)

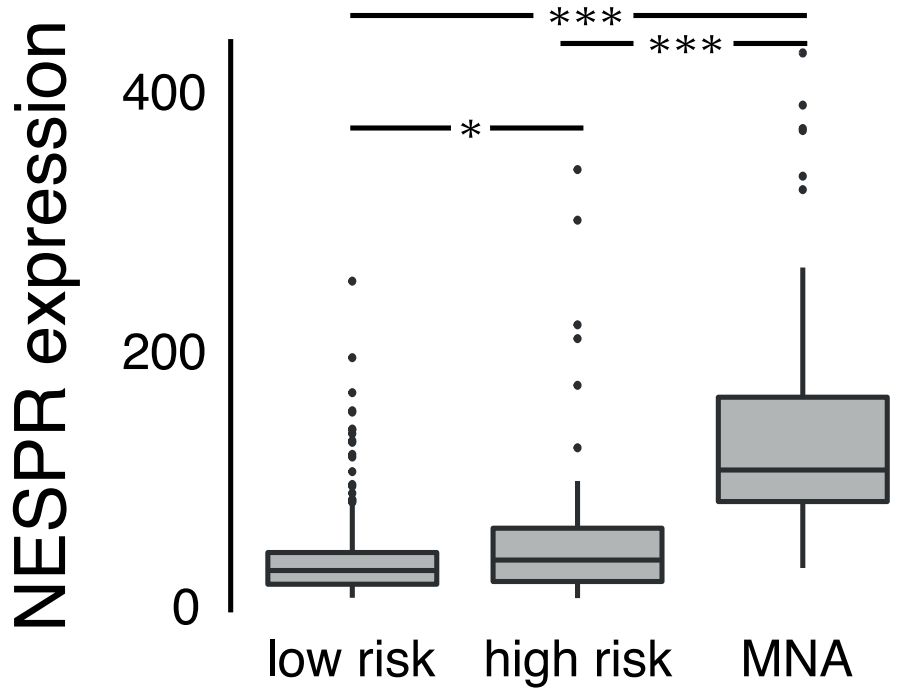
NESPR IS A NEUROBLASTOMA SPECIFIC LNCRNA

NESPR expression across tumor samples

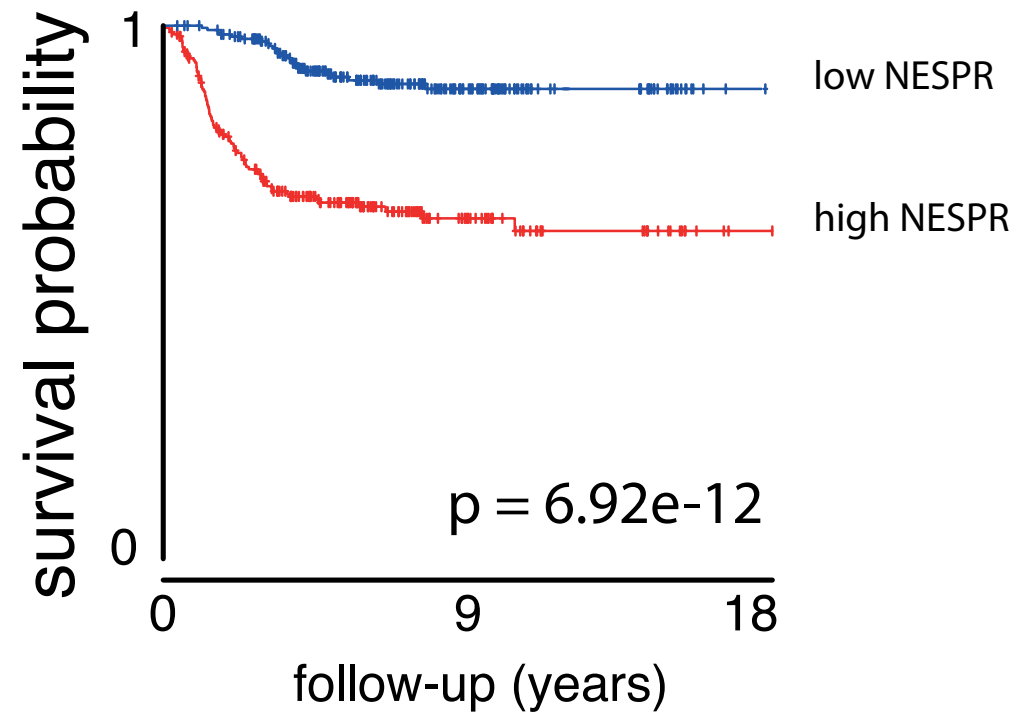


NESPR ASSOCIATES TO POOR OUTCOME AND MYCN AMPLIFICATION

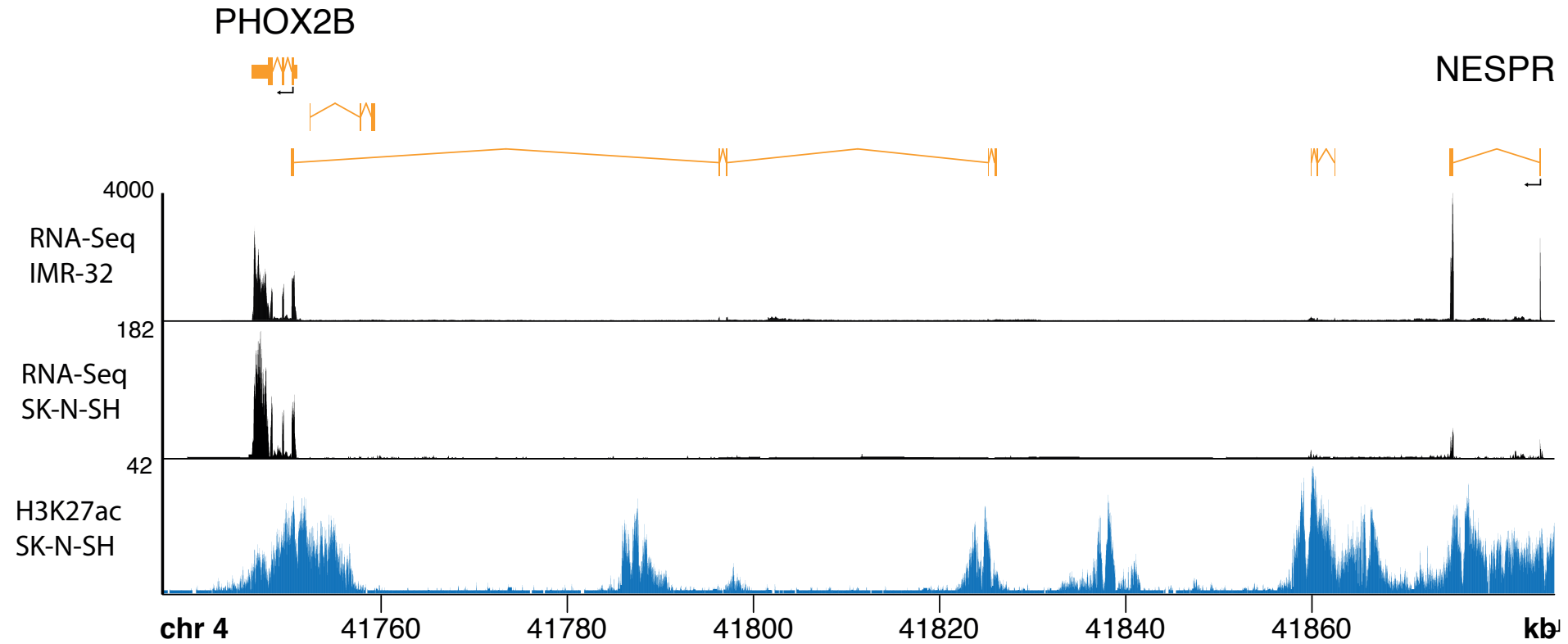
NESPR expression across tumor types



NESPR expression correlates to survival

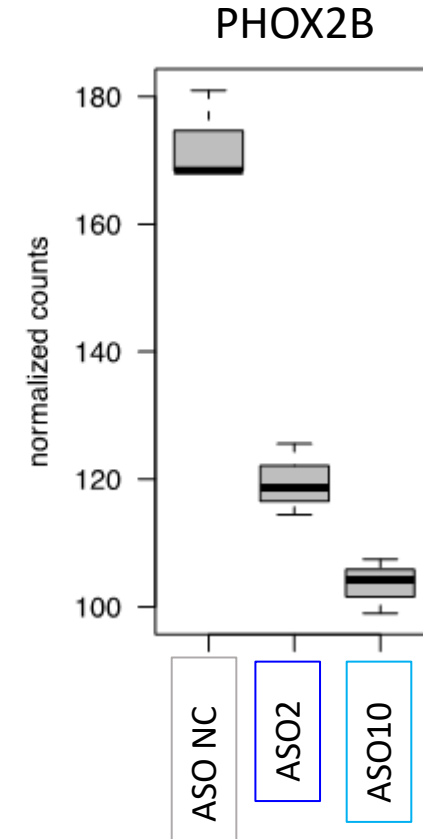
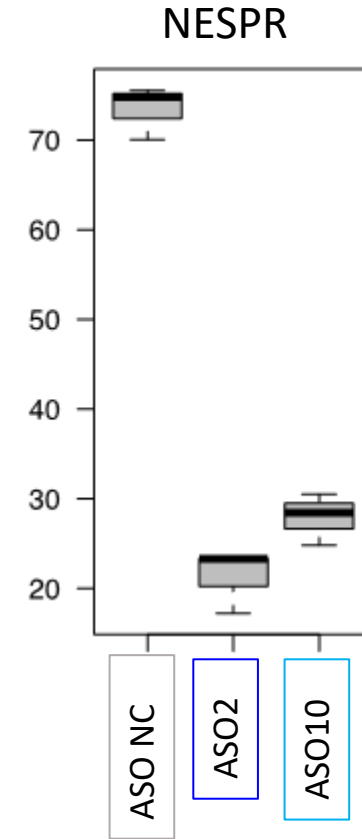
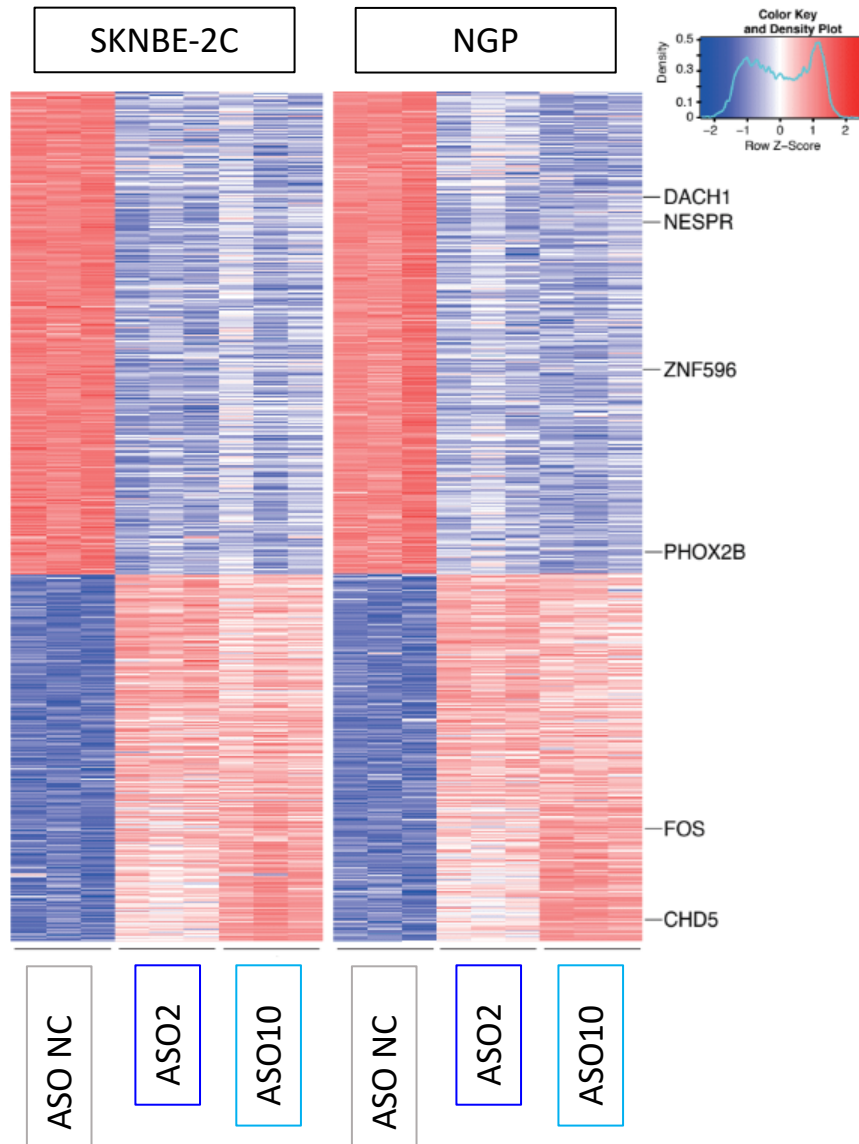


NESPR IS EXPRESSED FROM THE PHOX2B SUPER-ENHANCER



CORE NORADRENERGIC REGULATORS ARE REGULATED BY NESPR

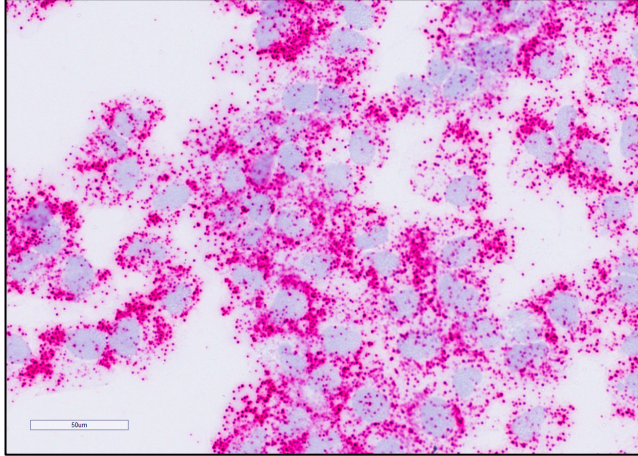
NESPR knock-down in neuroblastoma cell lines



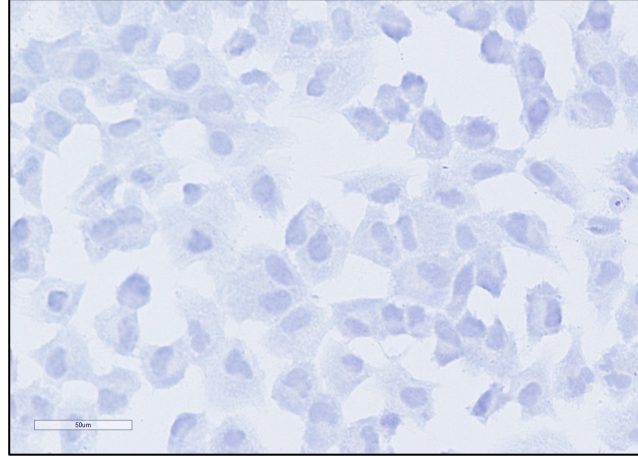
- NESPR knockdown impairs expression of **neuroblastoma cell identity genes**
- Including PHOX2B, DACH1, ZNF596, FOS...

NON-NORADRENERGIC CELL LINE LACKS NESPR TRANSCRIPT

SHEP-PPIB (pos Ct probe)

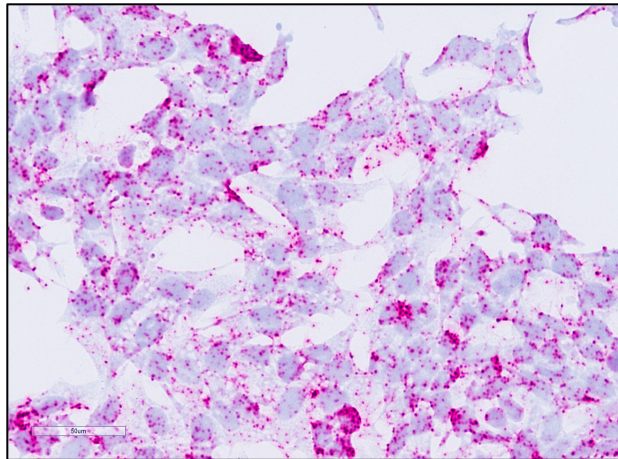


SHEP-NESPR

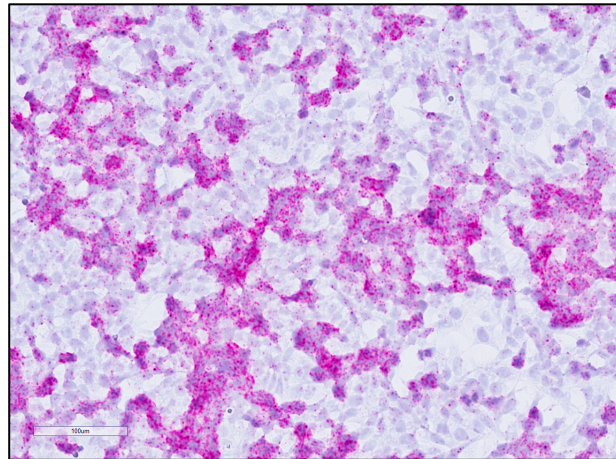


Neural crest cell

SKNBE2C-PPIB (pos Ct probe)

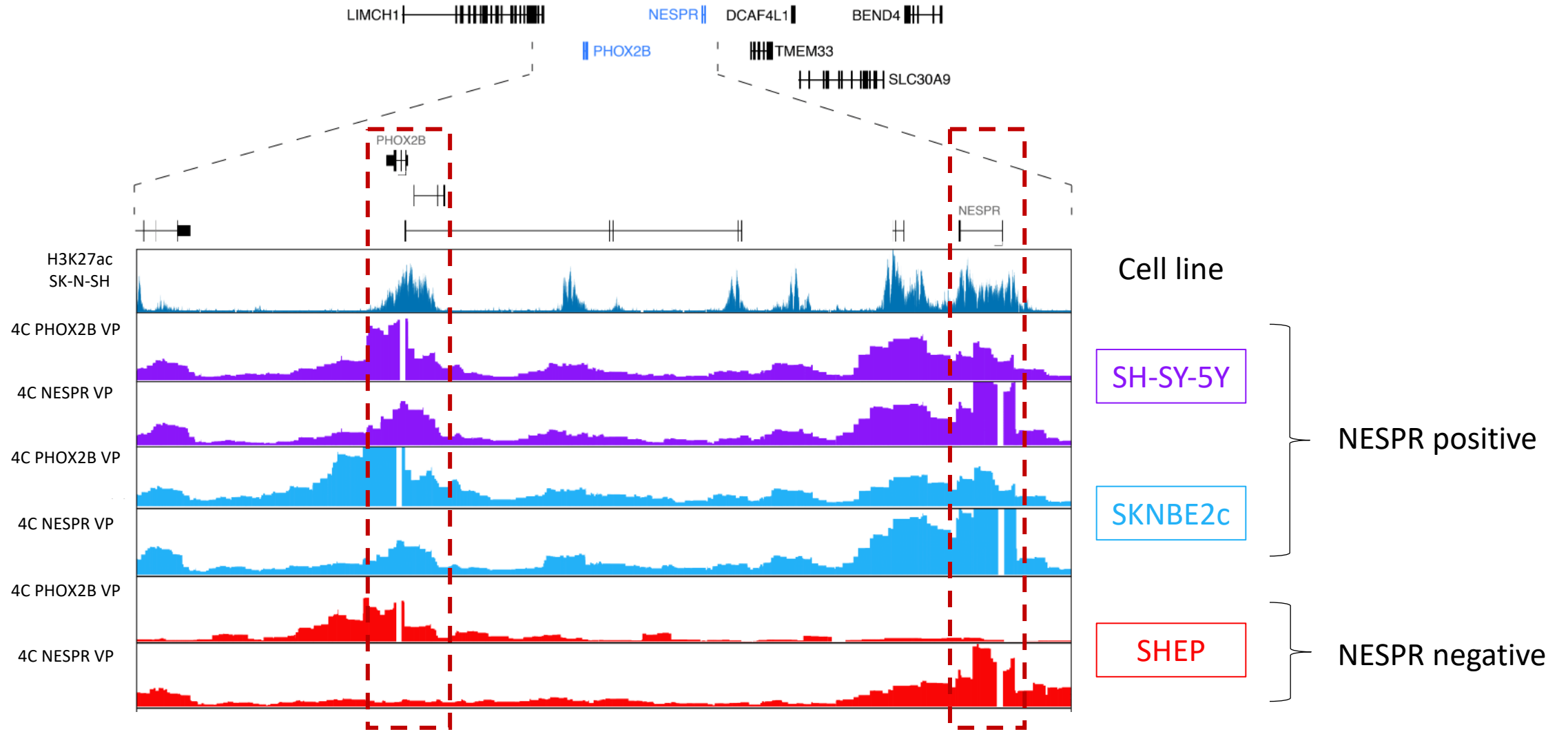


SKNBE2C-NESPR



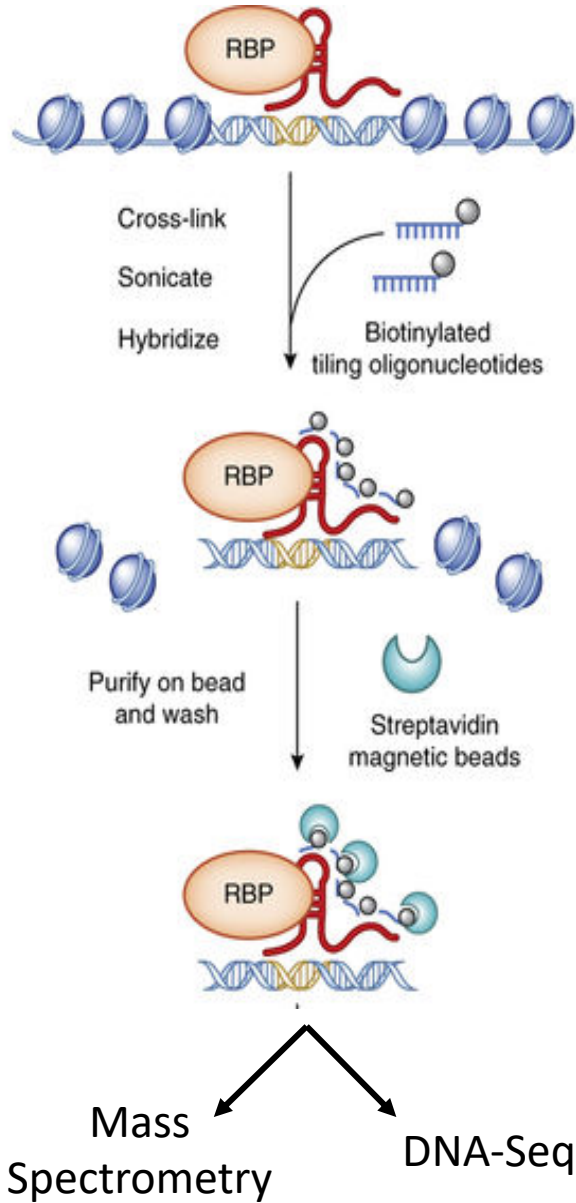
noradrenergic

CHROMATIN LOOPING AT NESPR & PHOX2B LOCI



NESPR and PHOX2B loci interact

NESPR BINDING SITES OVERLAP WITH CORE REGULATORY TFs



Motif discovery

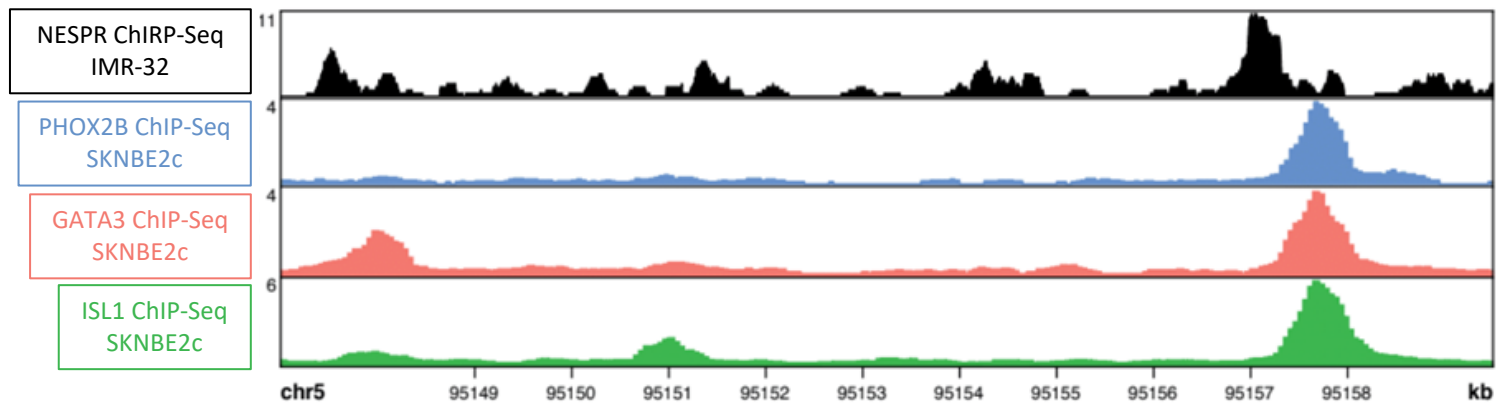
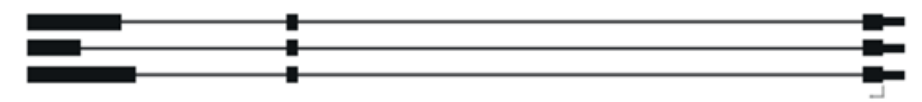


- ISL1 motif
- 1010 peaks (32.13%)
- pvalue = 1.10^{-22}



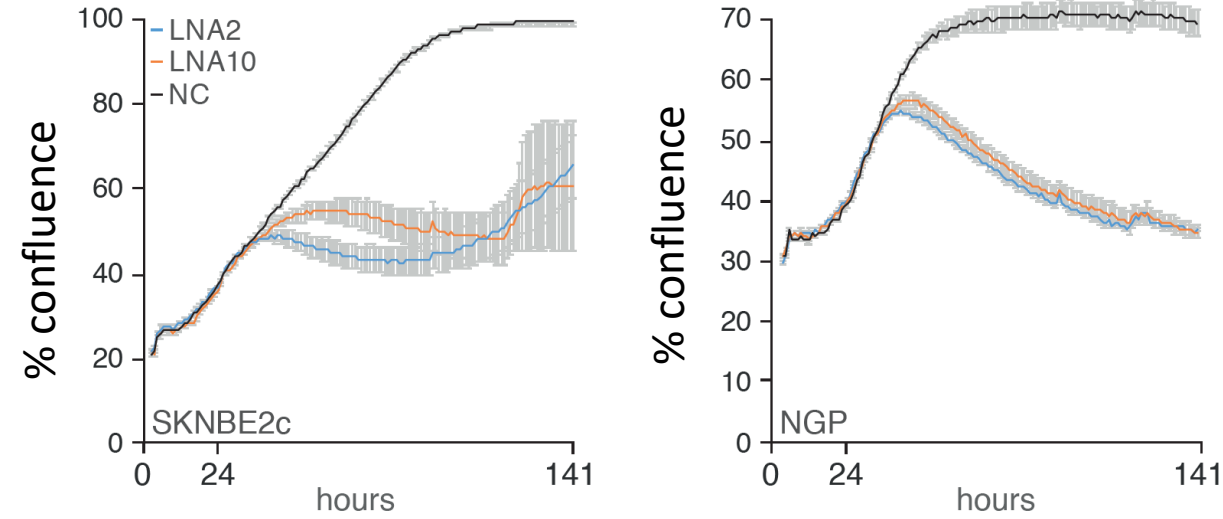
- GATA3 motif
- 790 peaks (25.14%)
- pvalue = 1.10^{-12}

GLRX

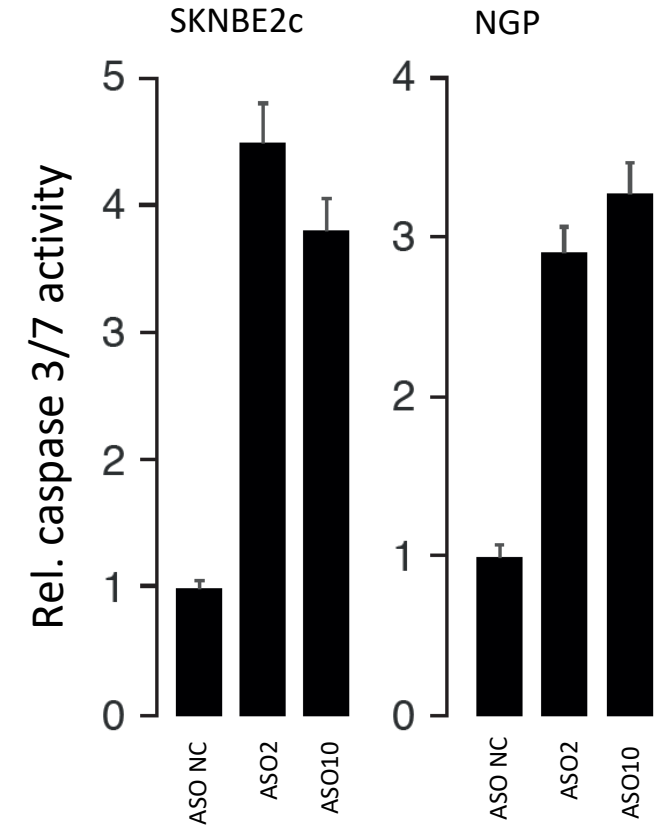


NESPR KNOCK-DOWN IMPAIRS PROPER CELL BEHAVIOR

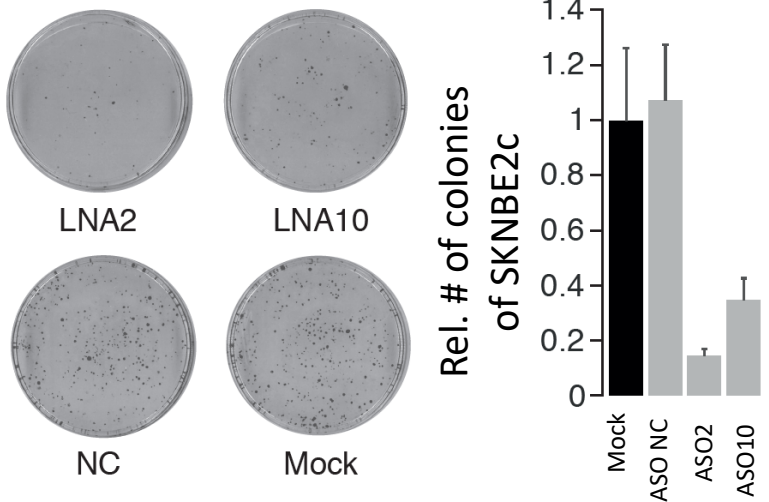
Proliferation



Apoptosis



Colony formation assay



CONCLUSIONS & PERSPECTIVE

NESPR shows neuroblastoma-specific expression

NESPR regulates PHOX2B

Noradrenergic TFs and NESPR binding sites overlap

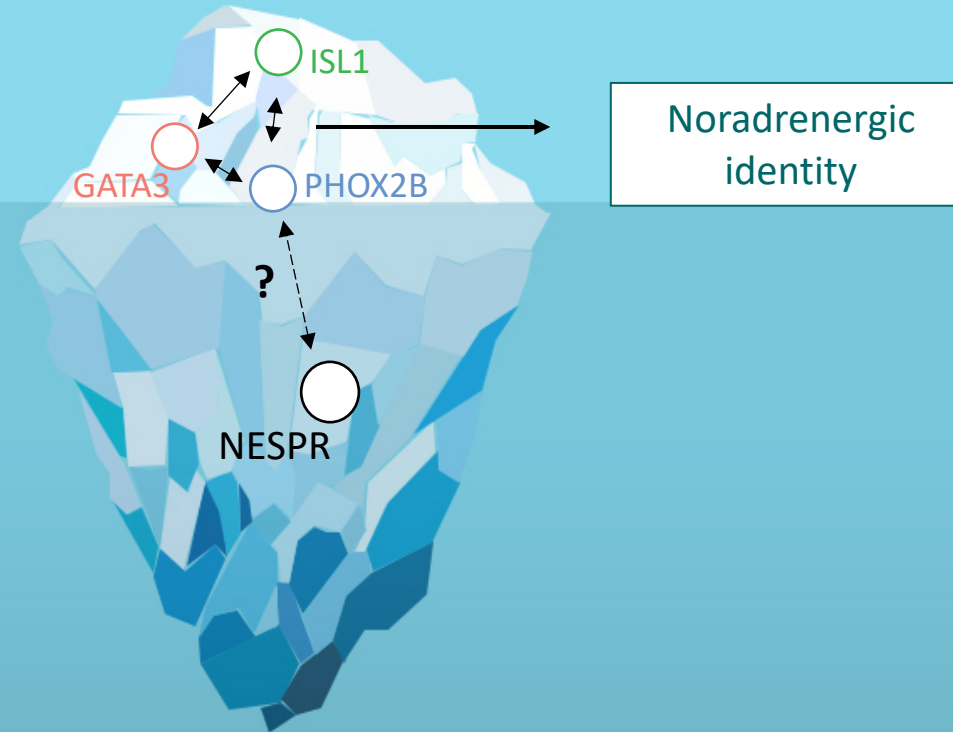


Find its protein partners

Investigate NESPR's role at binding sites

Evaluate ASO treatment *in vivo*

Extended molecular network = new pressure points



Acknowledgements



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Dries Rombaut

Tiago Franca Brazao

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Bieke Decaesteker

Frank Speleman

Louis Delhaye

Sven Eyckerman

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Roberto Ciaccio

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