

Alternative splicing modulation as a therapeutic tool

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Generalitat
de Catalunya



worldwide
cancer research



"la Caixa" Foundation Caixa Capital Risc

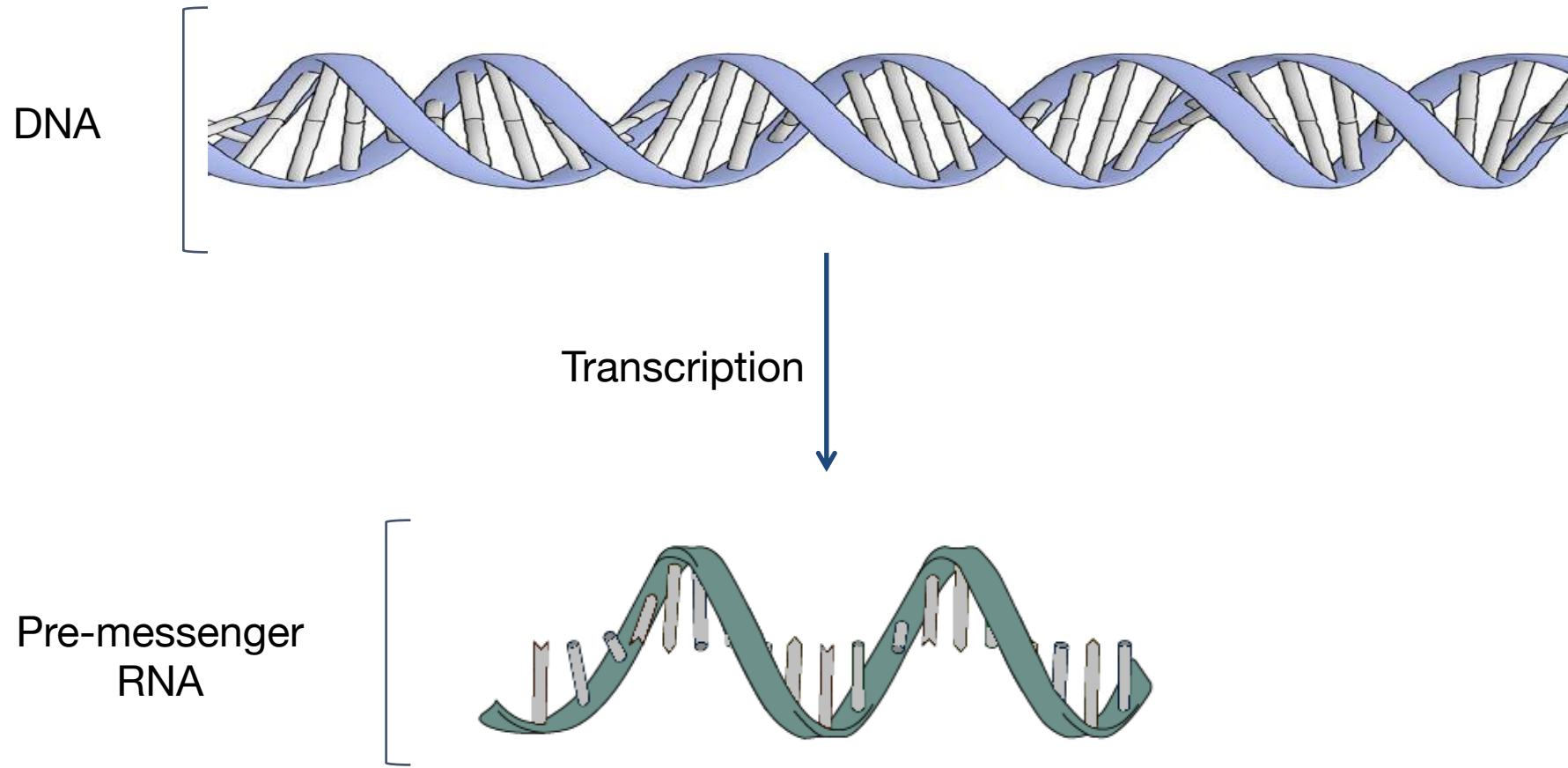


European
Research
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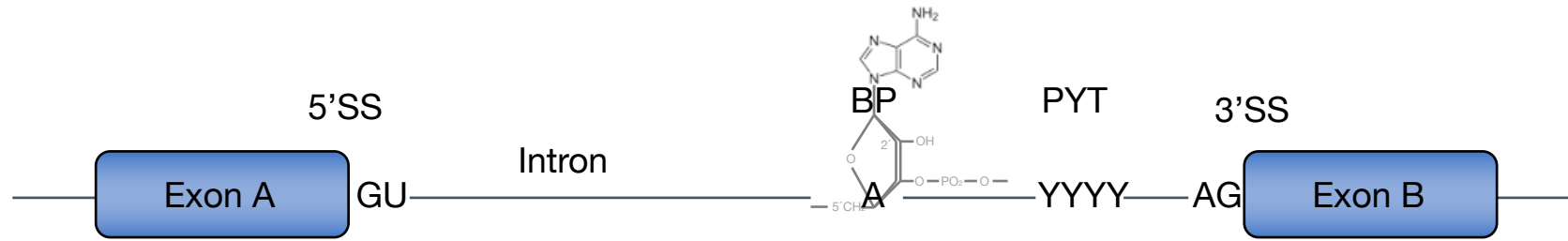


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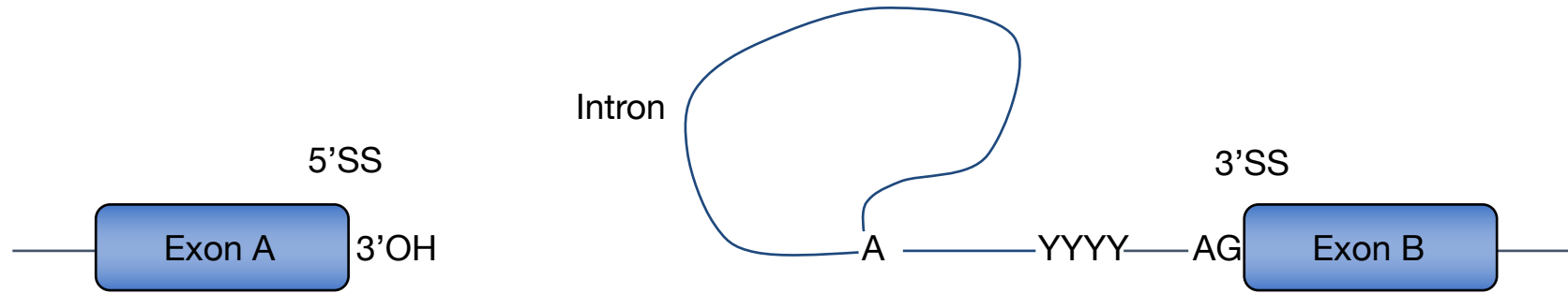
Gene expression



RNA splicing

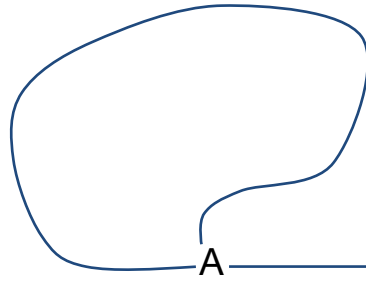


RNA splicing



RNA splicing

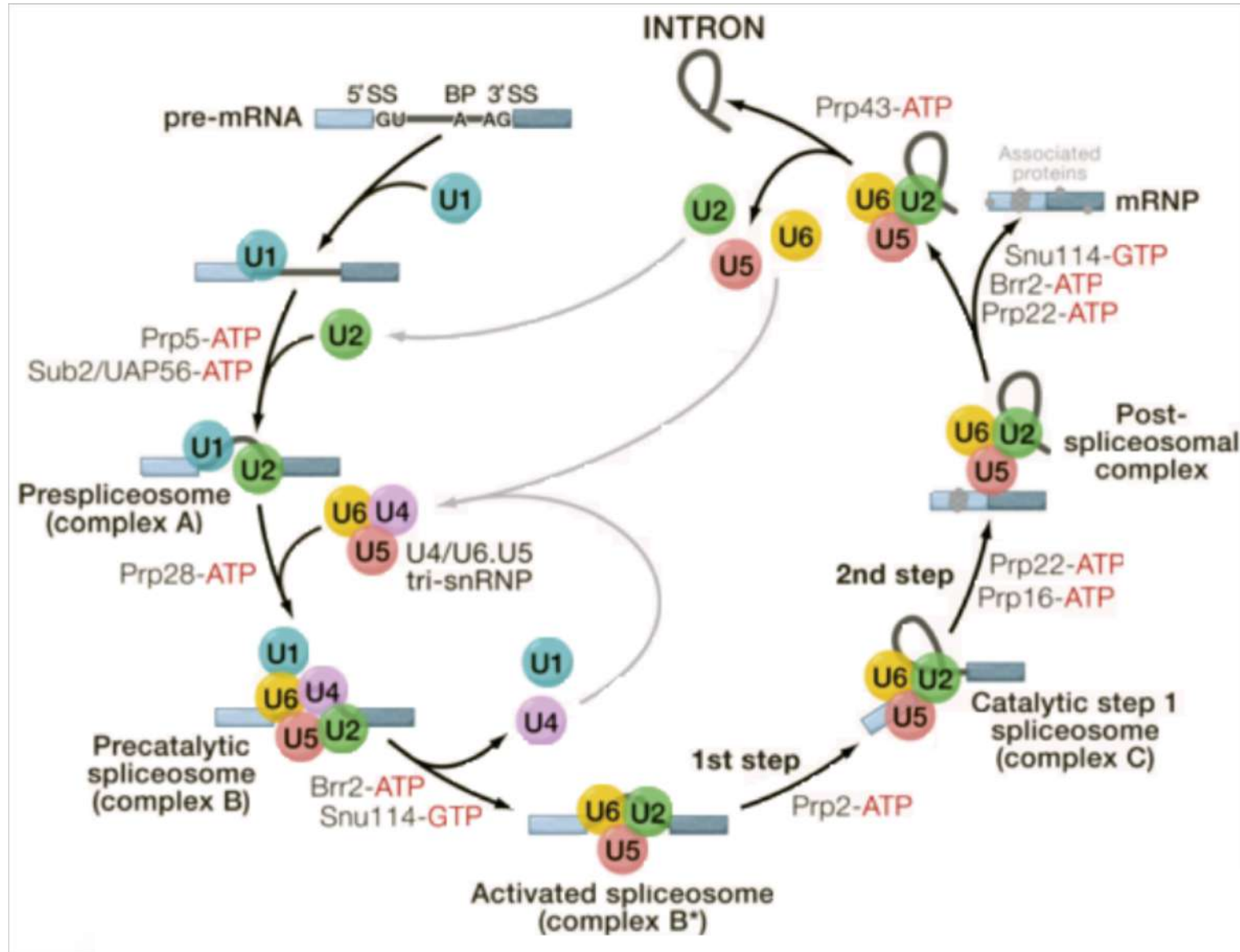
Lariat



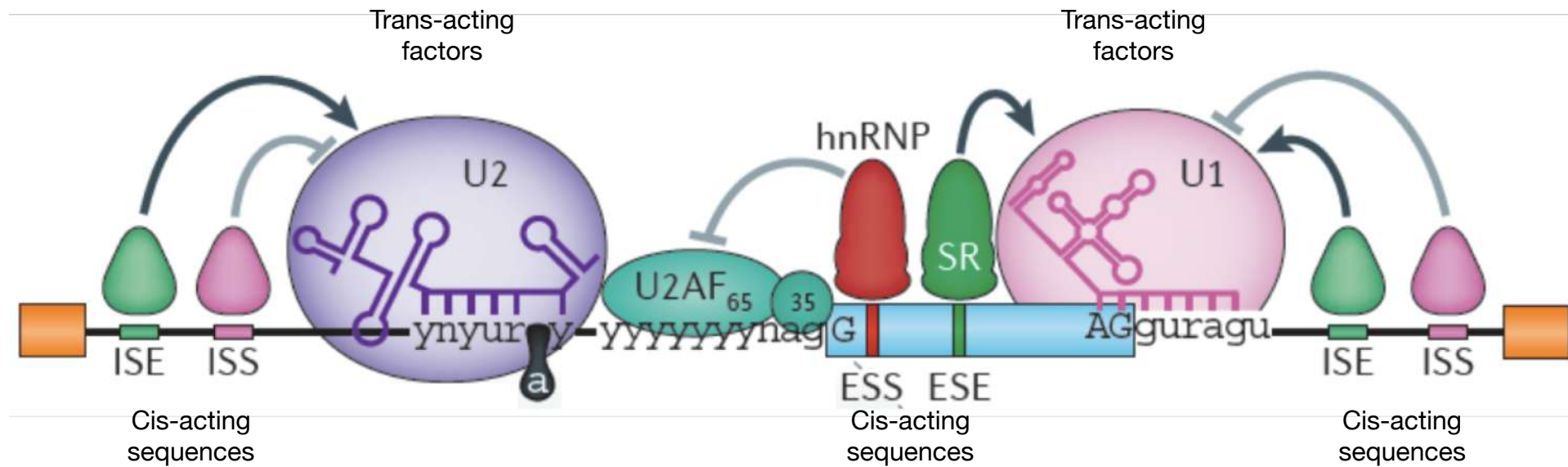
Spliced Product



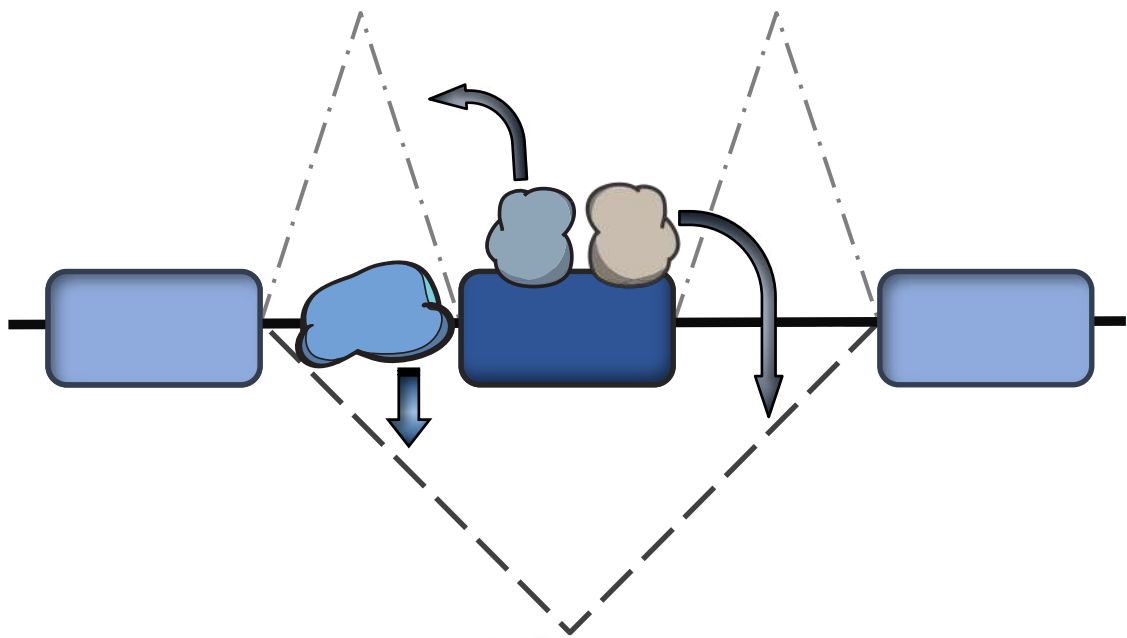
The splicing reaction



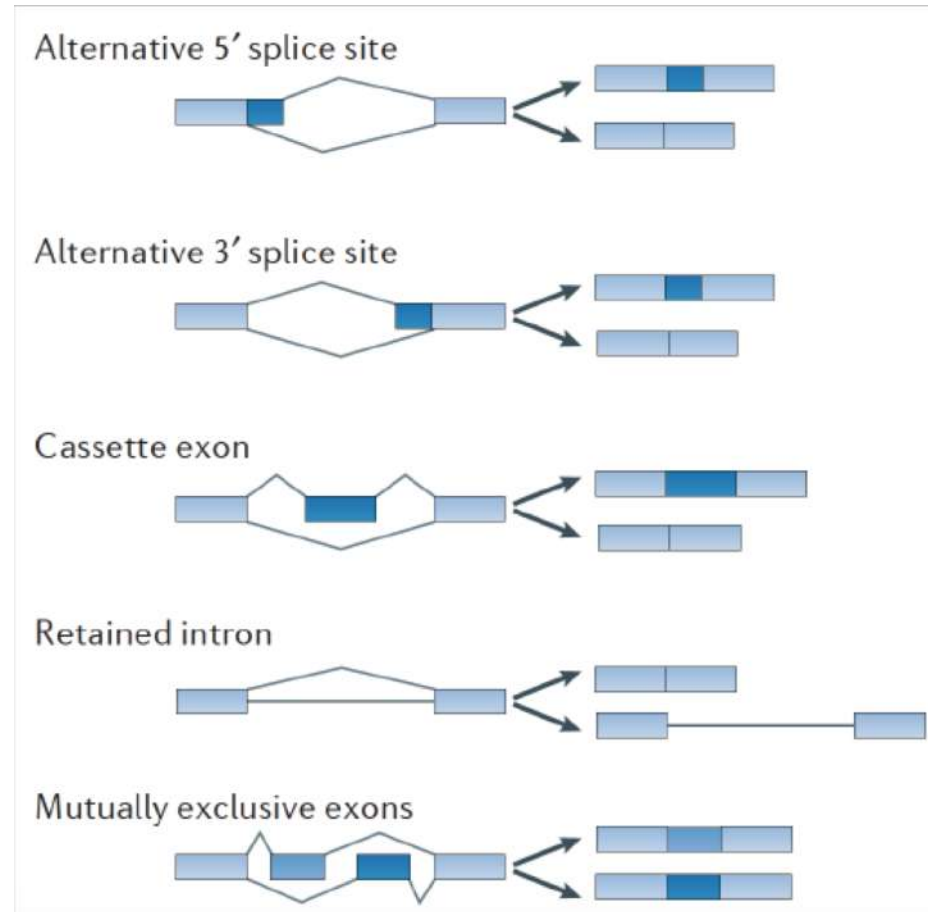
Alternative splicing regulation through cis/trans-acting elements



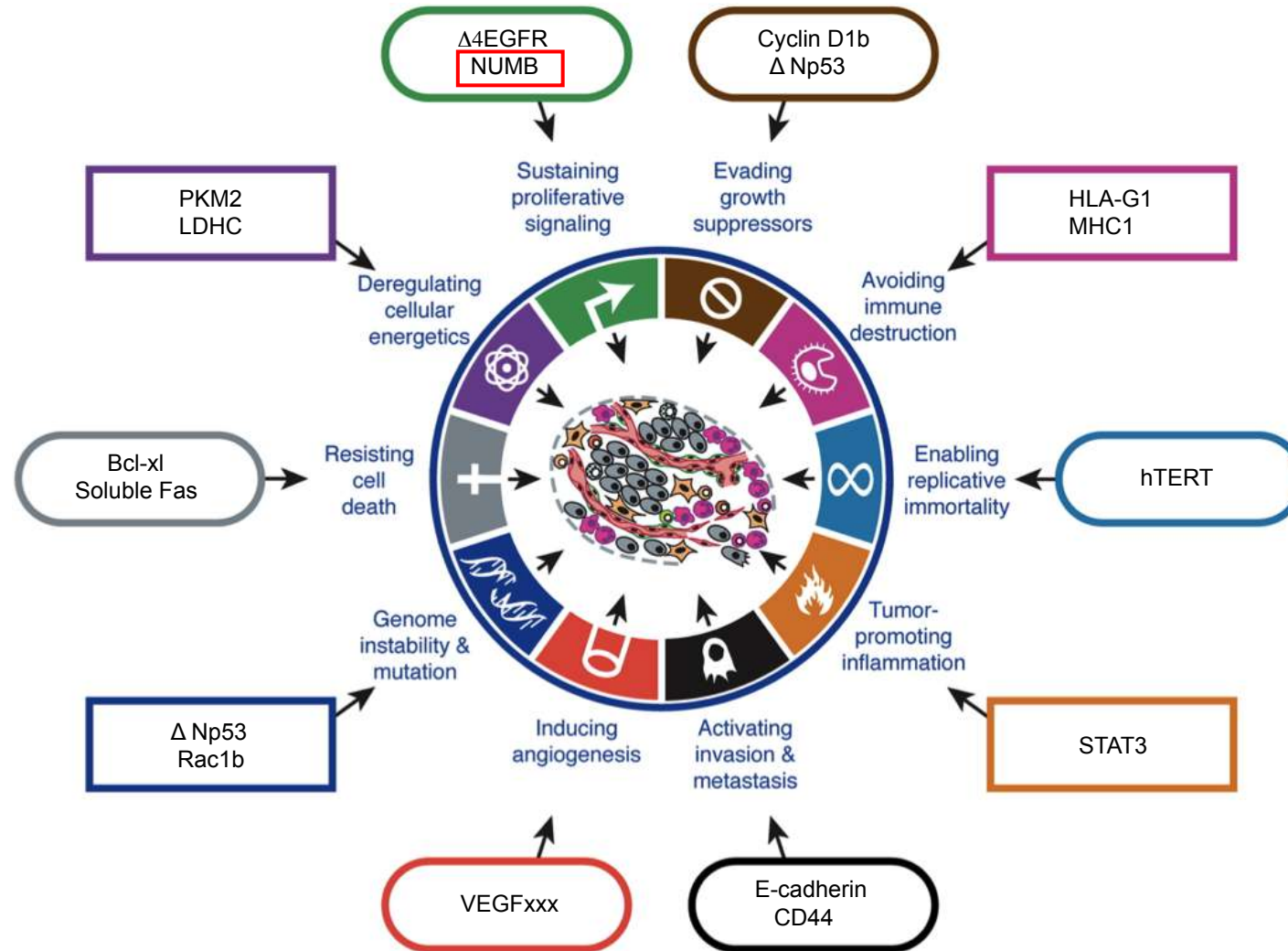
The combinatorial effects of splicing factors will determine the splicing outcome



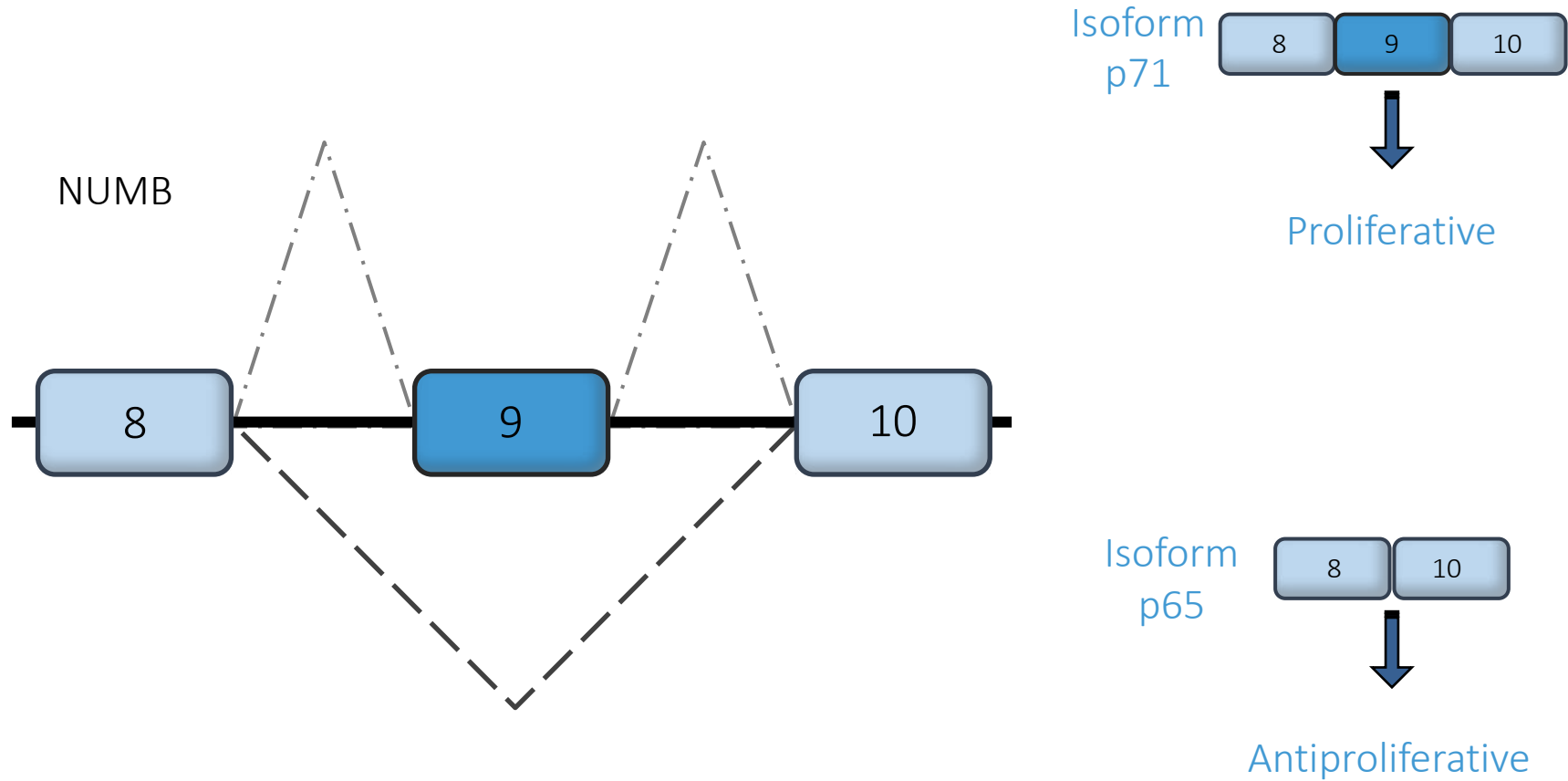
Different types of alternative splicing events



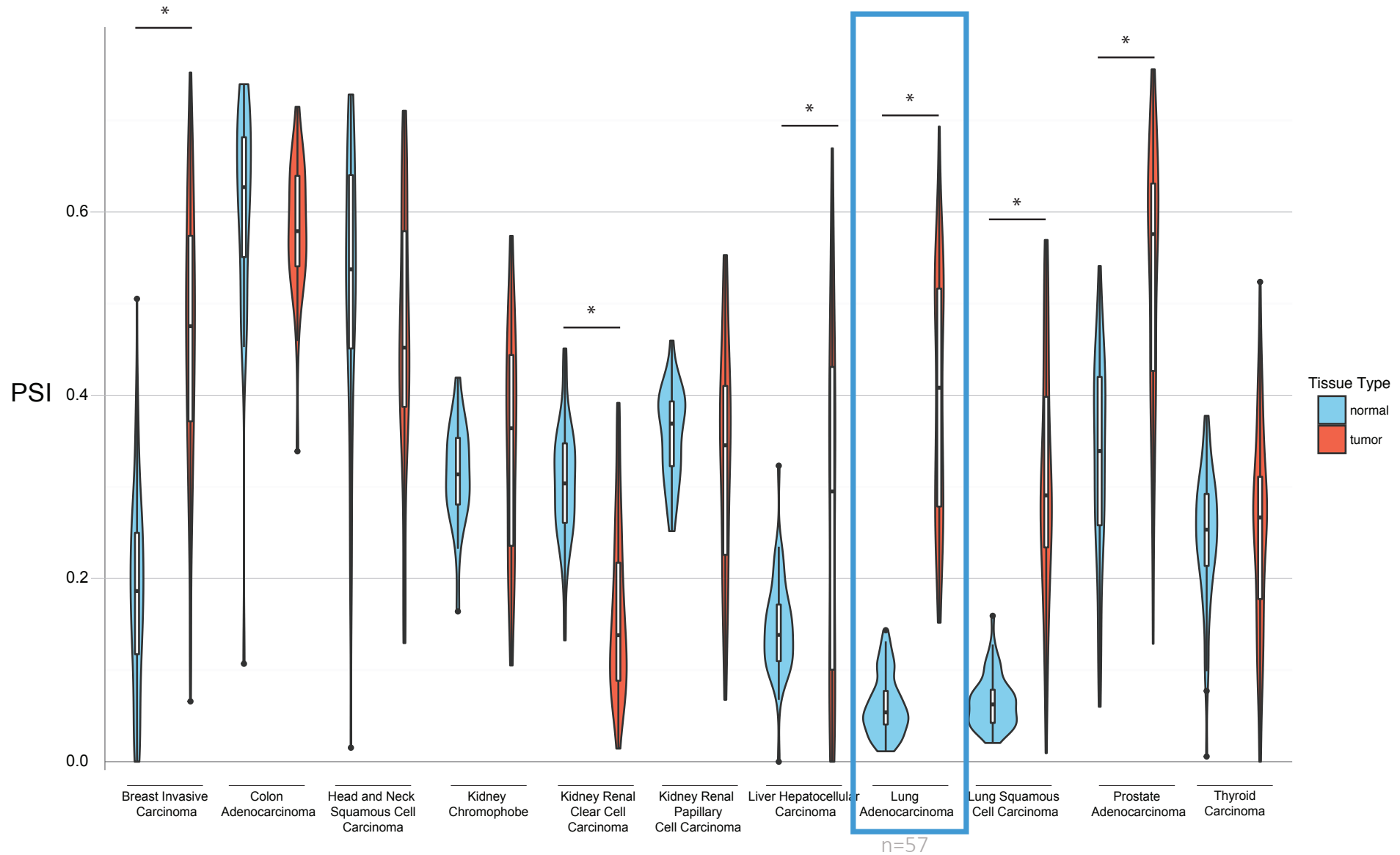
Alterations in RNA splicing and cancer



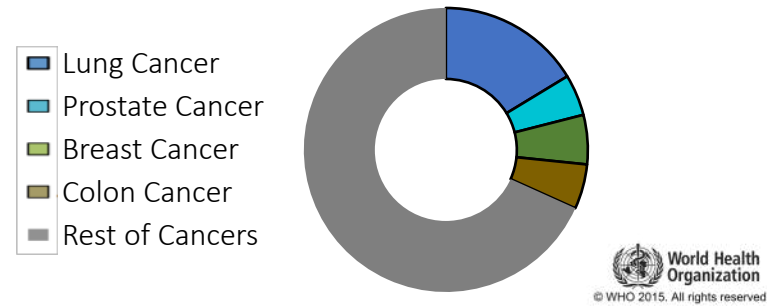
Cell proliferation is controlled by NUMB alternative splicing



Elevated NUMB inclusion in tumor samples

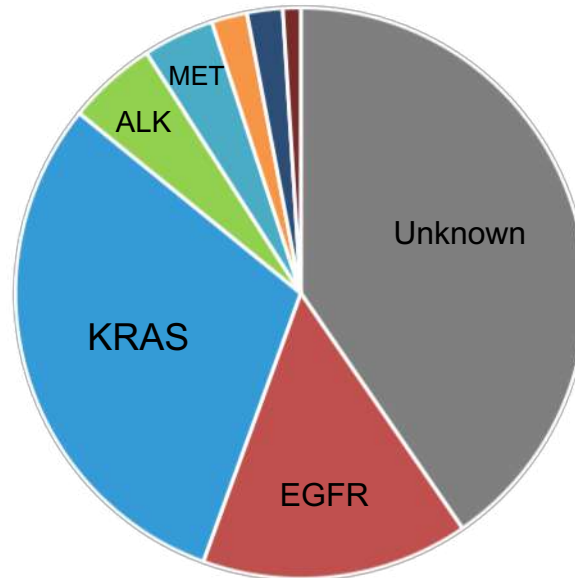


The oncological unmet need: lung cancer



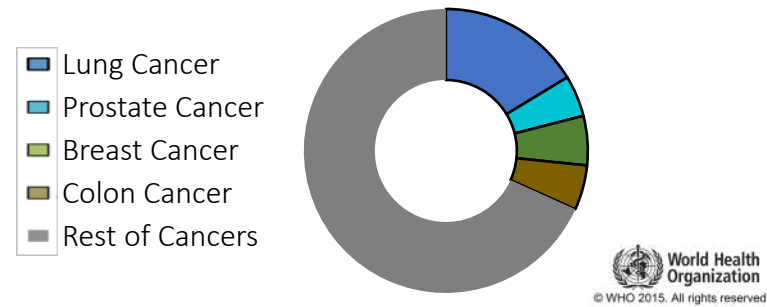
1.8 million diagnoses per year and 1.6 million death per year

Alterations in lung adenocarcinoma



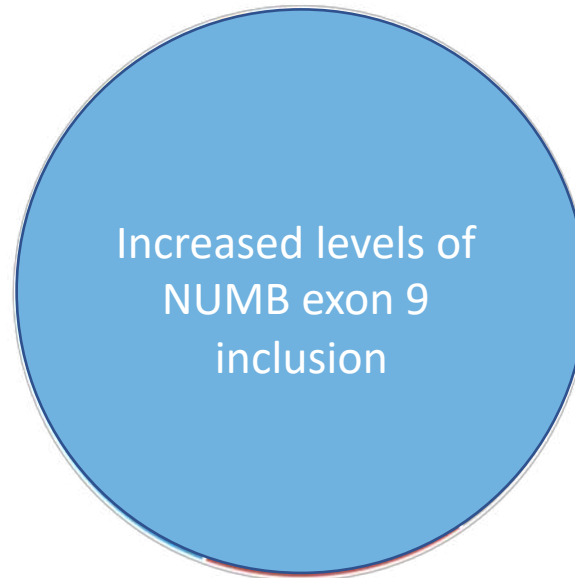
Chan BA, Hughes BG
Transl Lung Cancer Res; 2015

The oncological unmet need: lung cancer



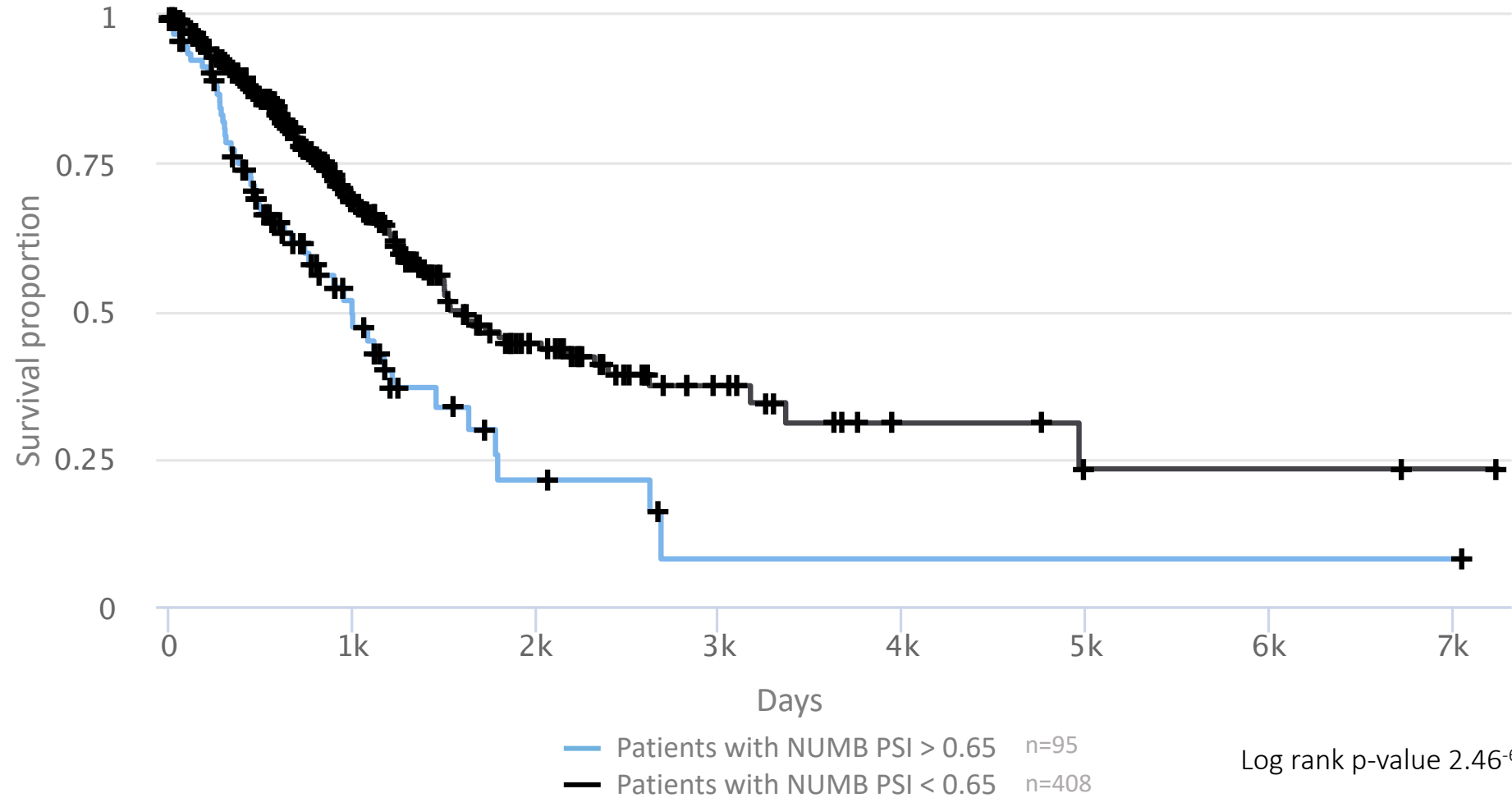
1.8 million diagnoses per year and 1.6 million death per year

Alterations in lung adenocarcinoma

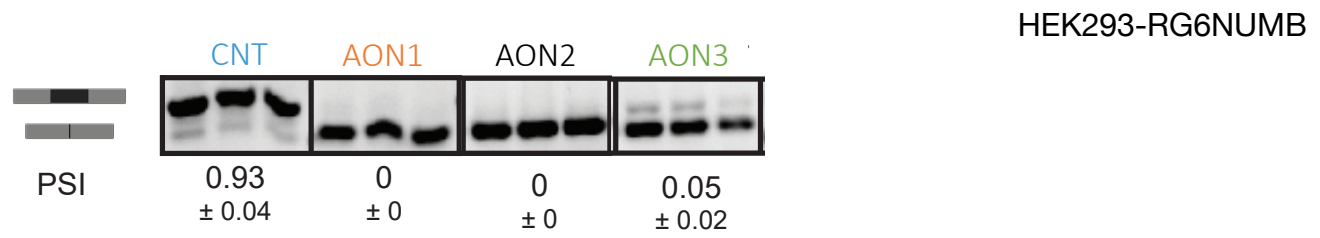
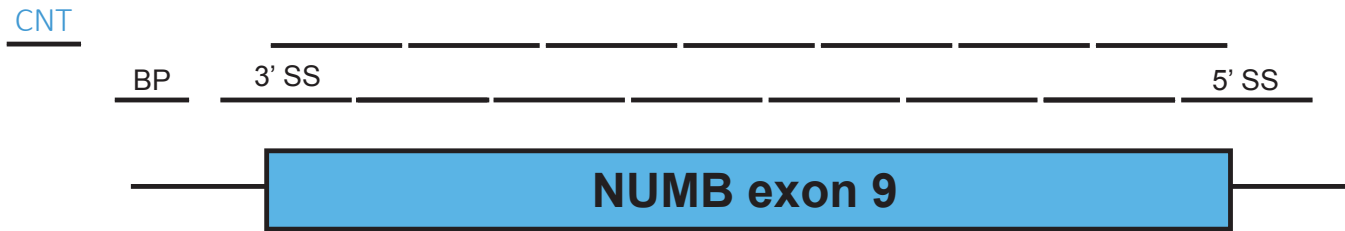


Chan BA, Hughes BG
Transl Lung Cancer Res; 2015

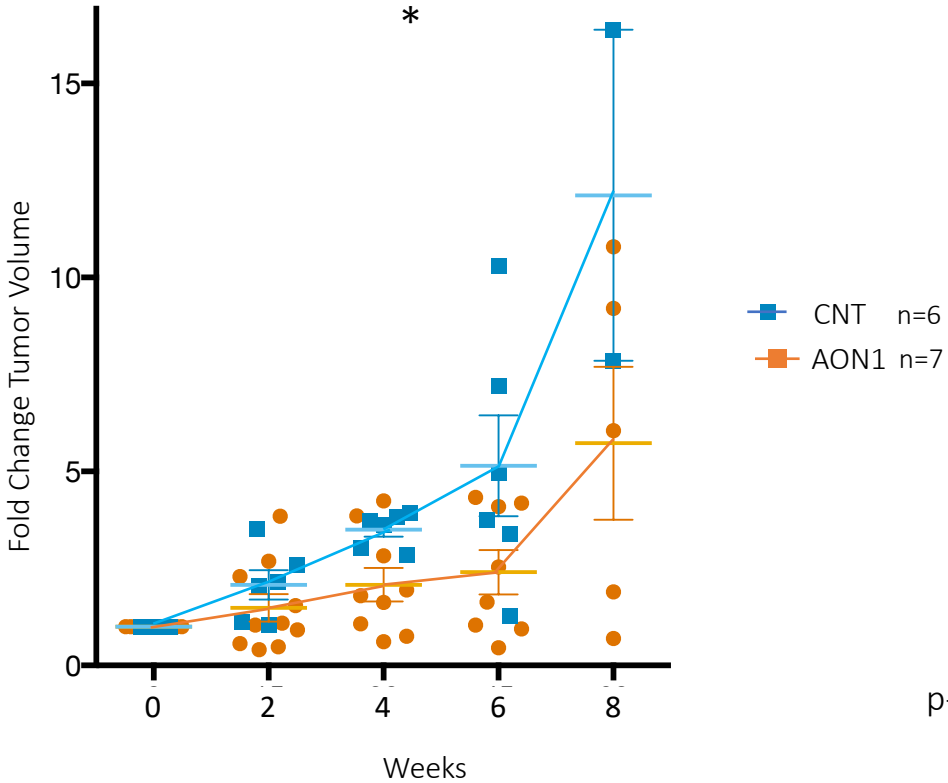
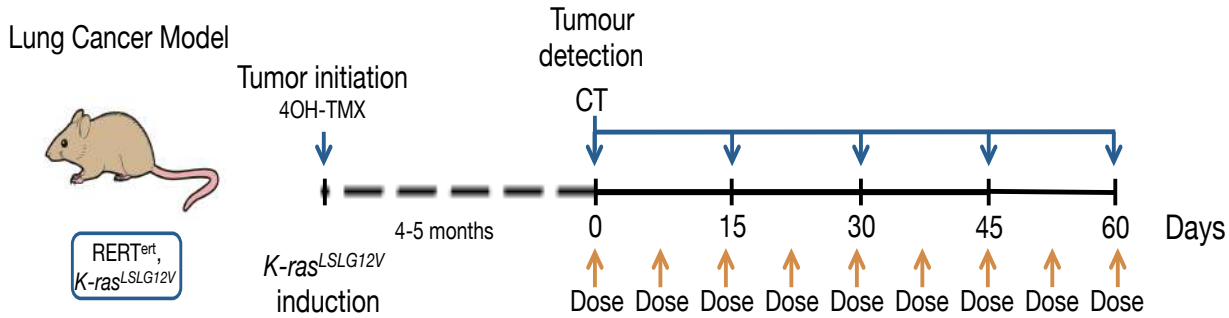
Patient survival predicted by NUMB inclusion



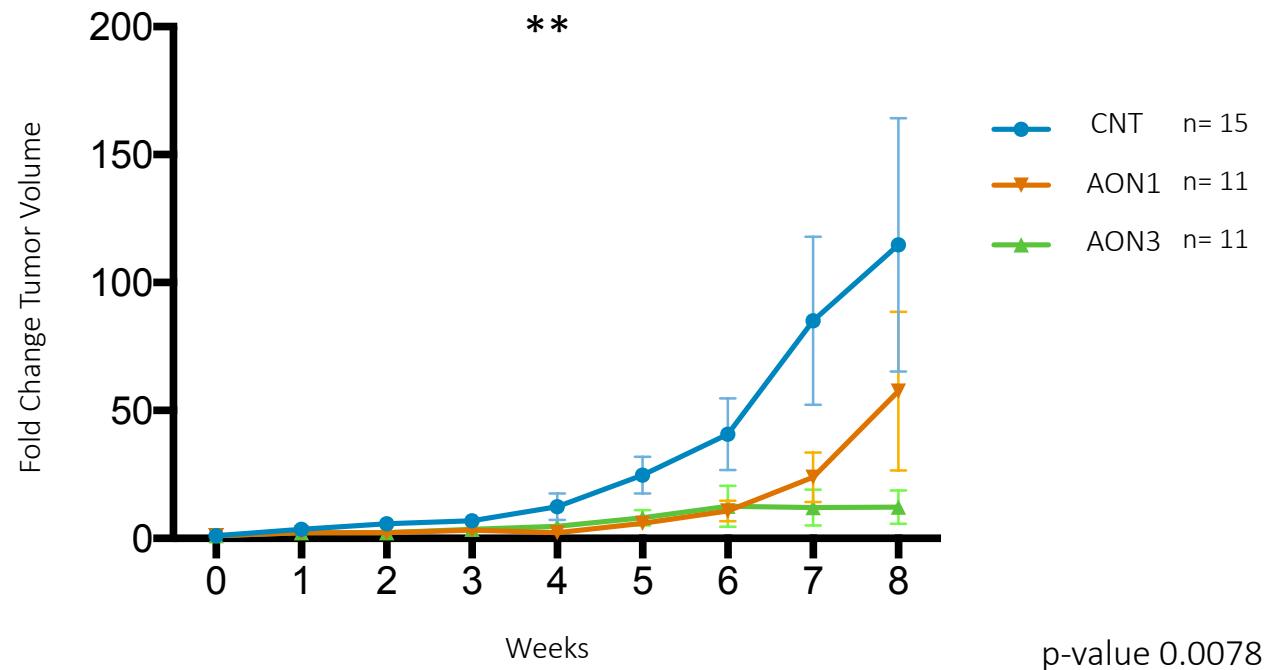
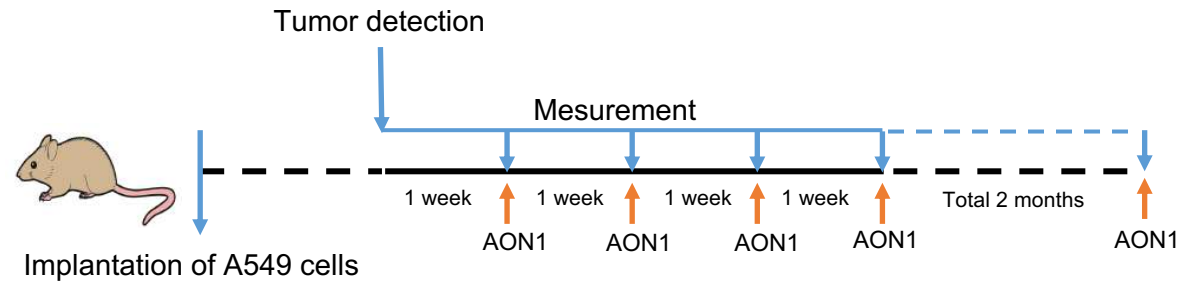
Three key regulatory regions were identified



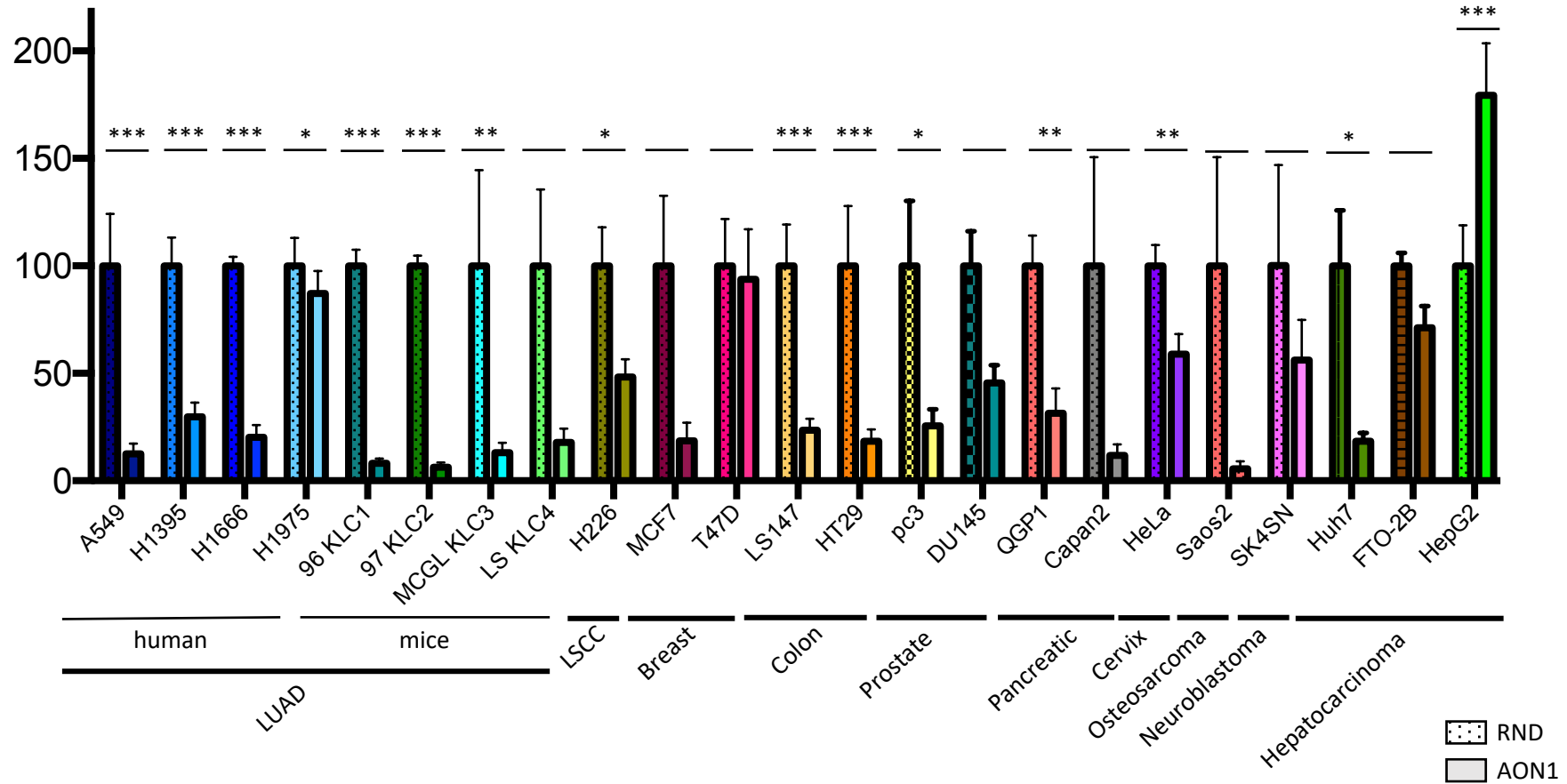
AON1 reduces tumor growth in genetic K-Ras driven mouse model of LUAD



Anti-tumoral effect of AON1 *in vivo* orthotopic LUAD model



AON1 reduces the colony formation capacity of several cell lines



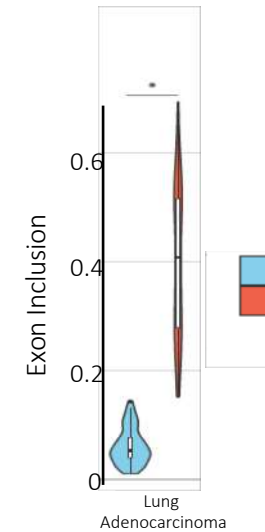
Conclusions



1.8 million diagnoses per year
1.6 million death per year
85% mortality rate

- Lung cancer is an unmet medical need.

- NUMB alternative splicing represents a novel target, altered in all LUAD samples.



- NUMB alternative splicing modulation represents a novel approach, validated *in vivo*, for lung cancer treatment.



Thanks



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