

Ibuprofen disrupts a WNK1/GSK3 β /SRPK1 protein complex required for expression of tumor-related splicing variant RAC1B in colorectal cells

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Ibuprofen inhibits RAC1B splicing

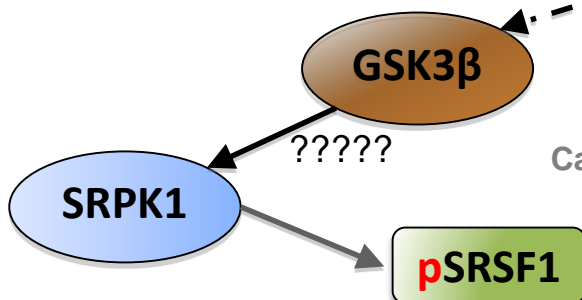
Ibuprofen Inhibits Colitis-Induced Overexpression of Tumor-Related Rac1b¹

Paulo Matos^{*,2}, Larissa Kotelevets^{†,‡,2},
Vânia Gonçalves^{*}, Andreia Henriques^{*},
Philippe Zerbib[§], Mary Pat Moyer[¶], Eric Chastre^{†,‡}
and Peter Jordan^{*}

Ibuprofen

Inhibitory
phosphorylation

Greenspan(2011)
Cancer Prev Res 4(1):161-7



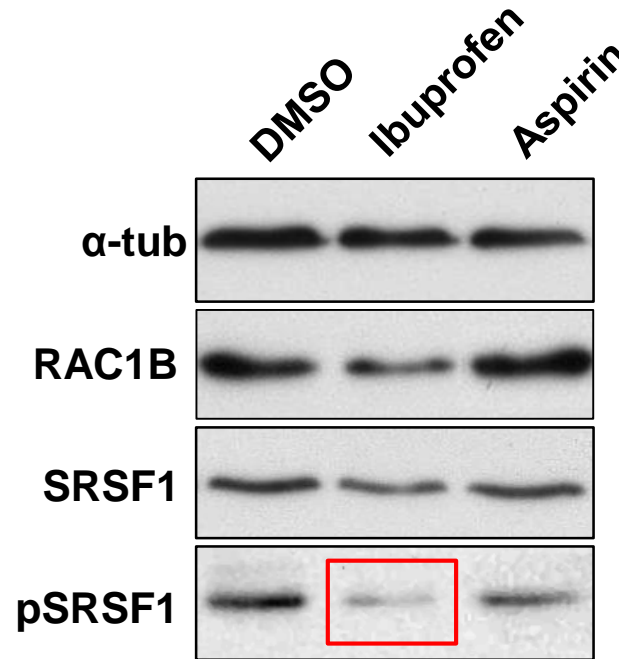
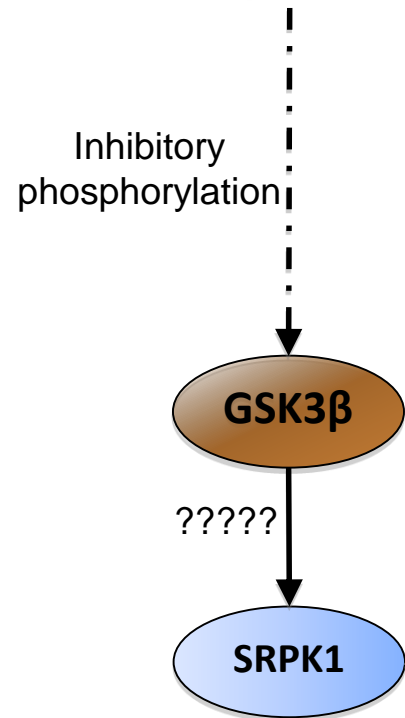
SRSF3

RAC1 pre-mRNA

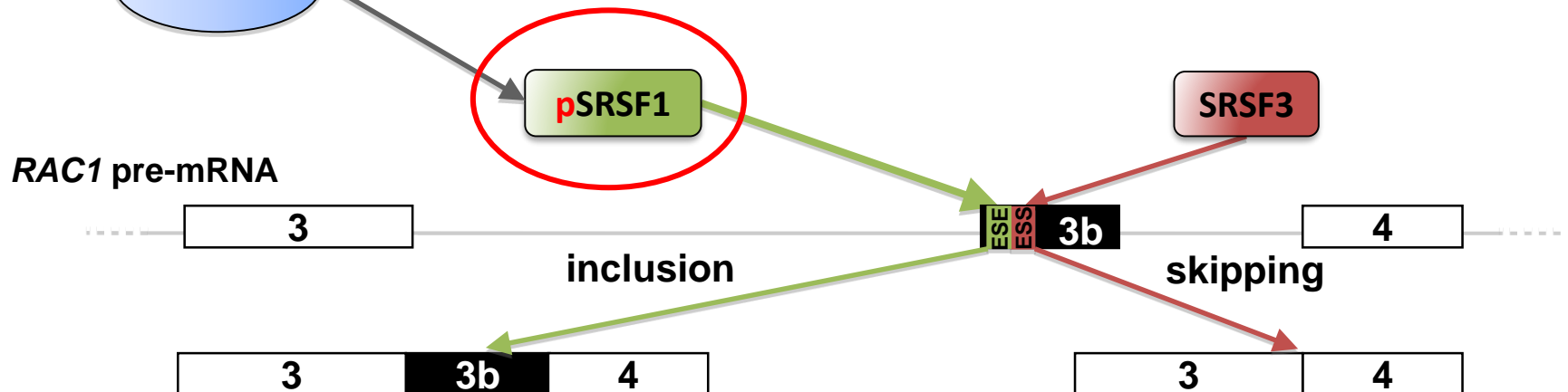


How does ibuprofen interfere with RAC1B splicing ?

Ibuprofen



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Inhibitory phosphorylation

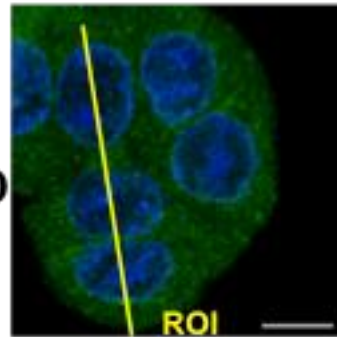
GSK3 β

?????

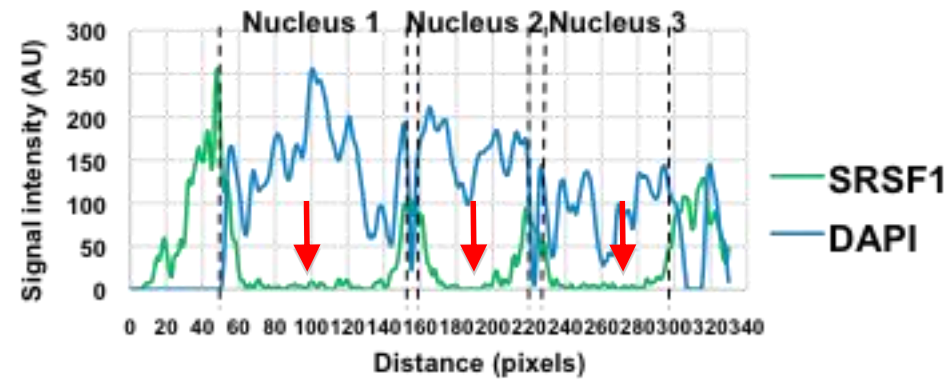
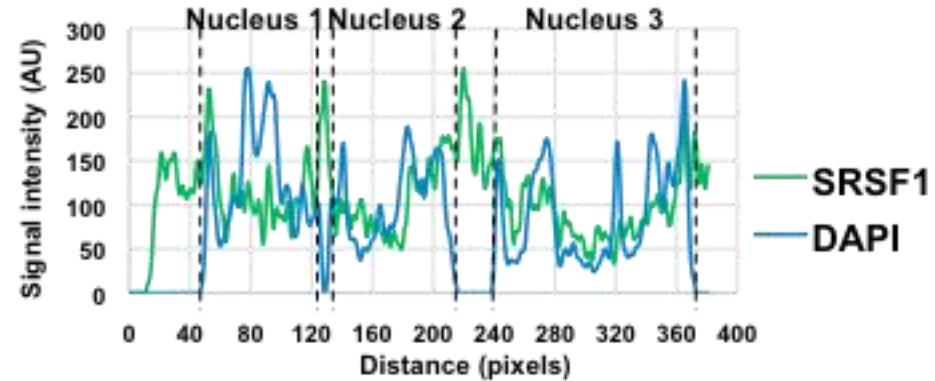
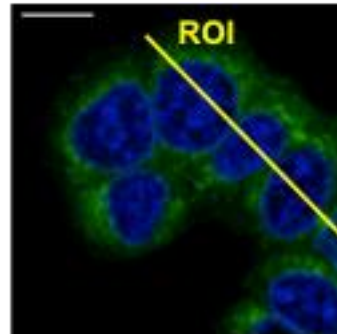
SRPK1

pSRSF1

DMSO



IBU



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RAC1 pre-mRNA

3

inclusion

ESE

ESS

3b

skipping

4

3

3b

4

3

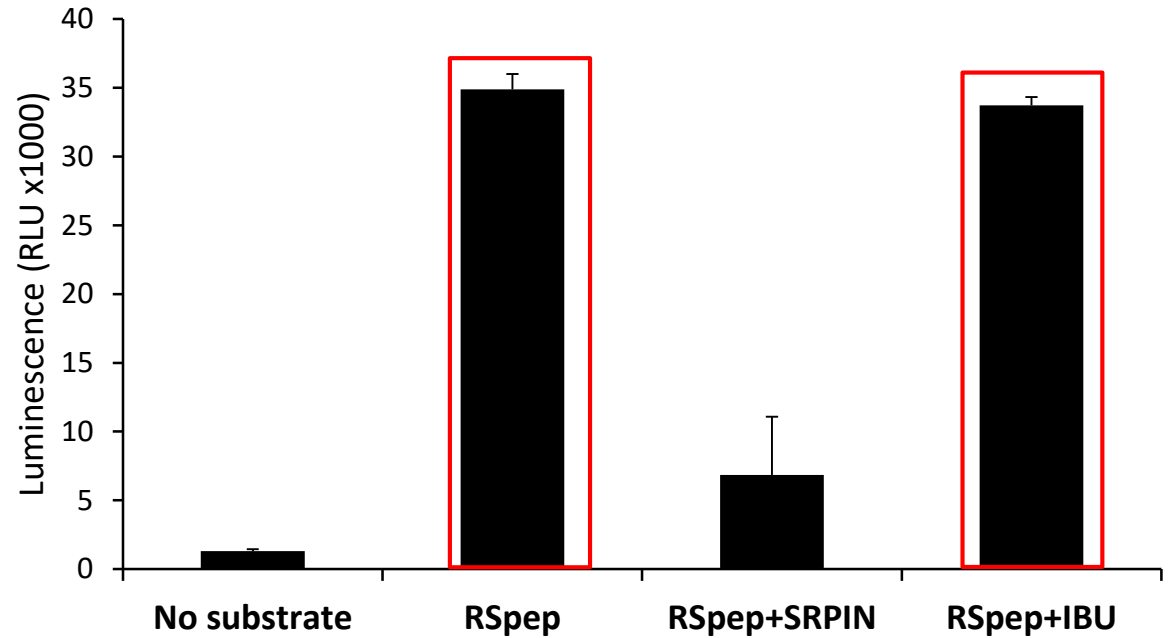
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SRSF3

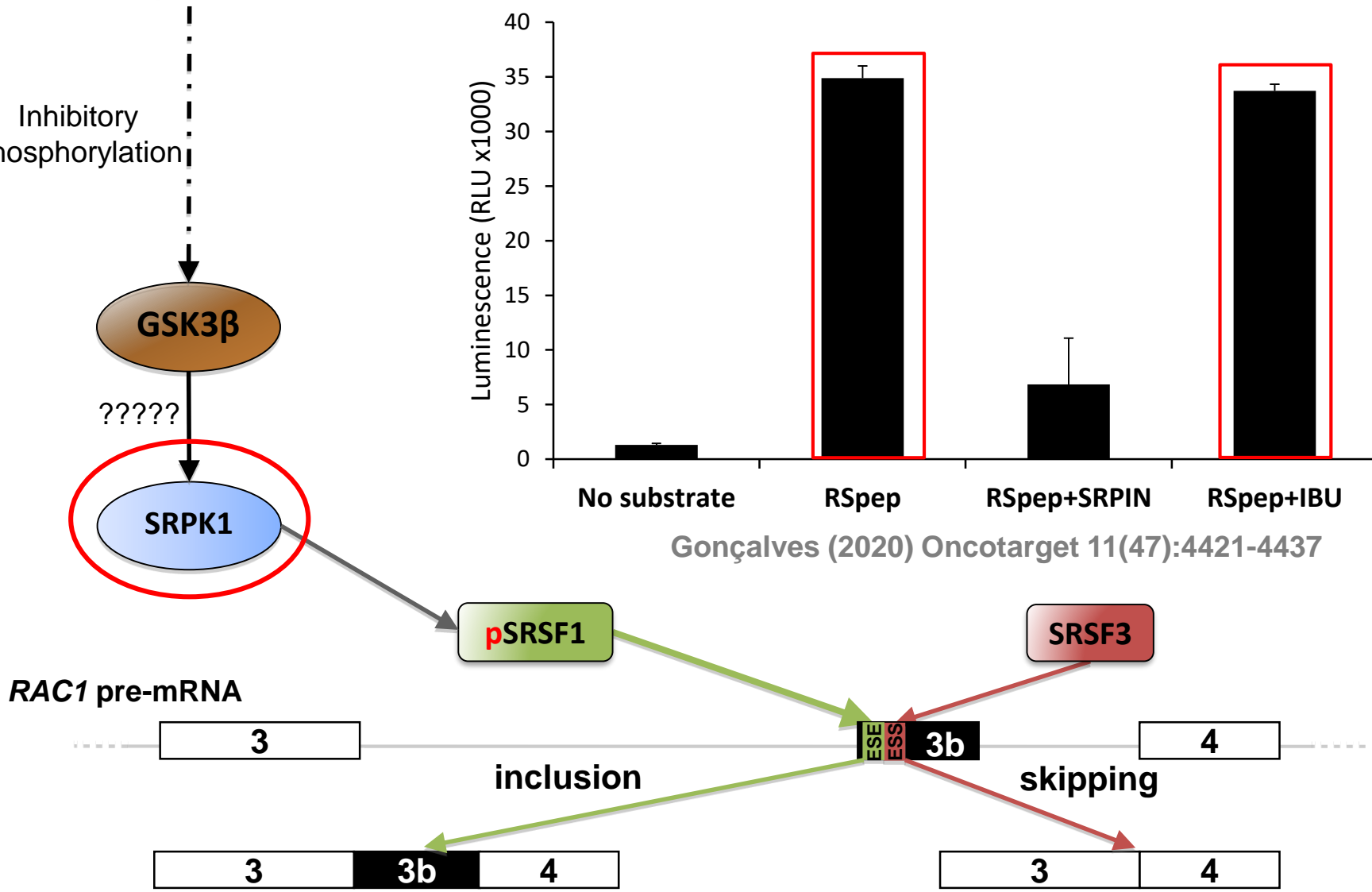
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Ibuprofen

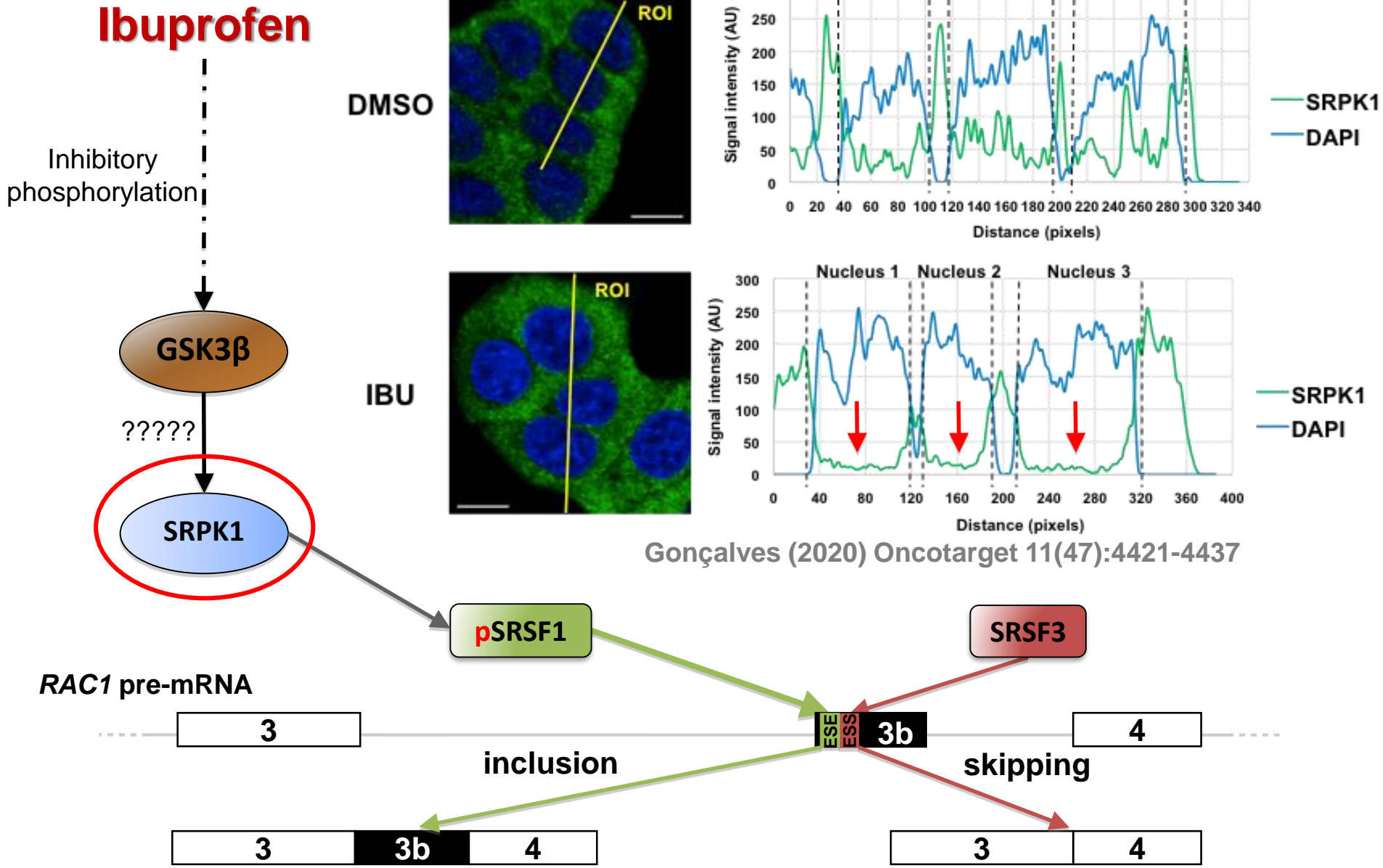
SRPK1 activity measured as ATP consumption



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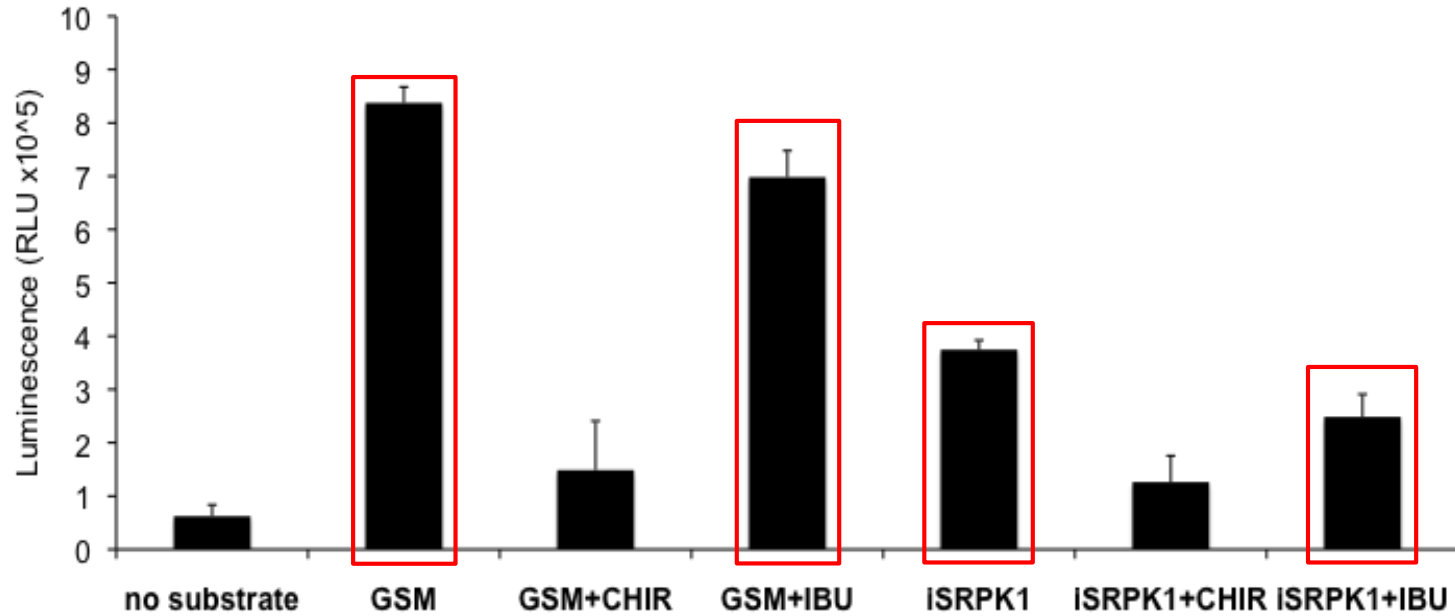
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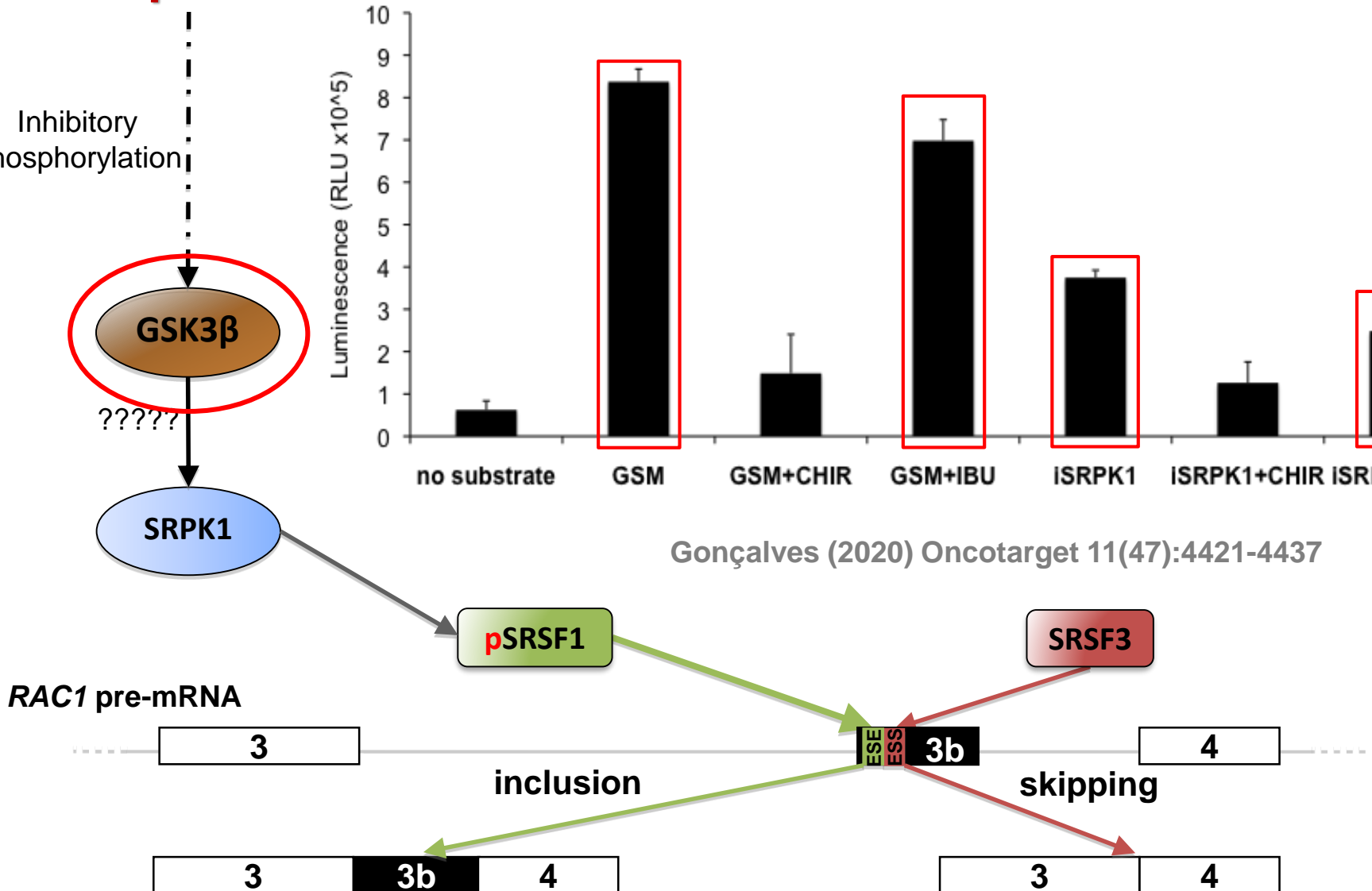
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Ibuprofen

GSK3β activity measured as ATP consumption

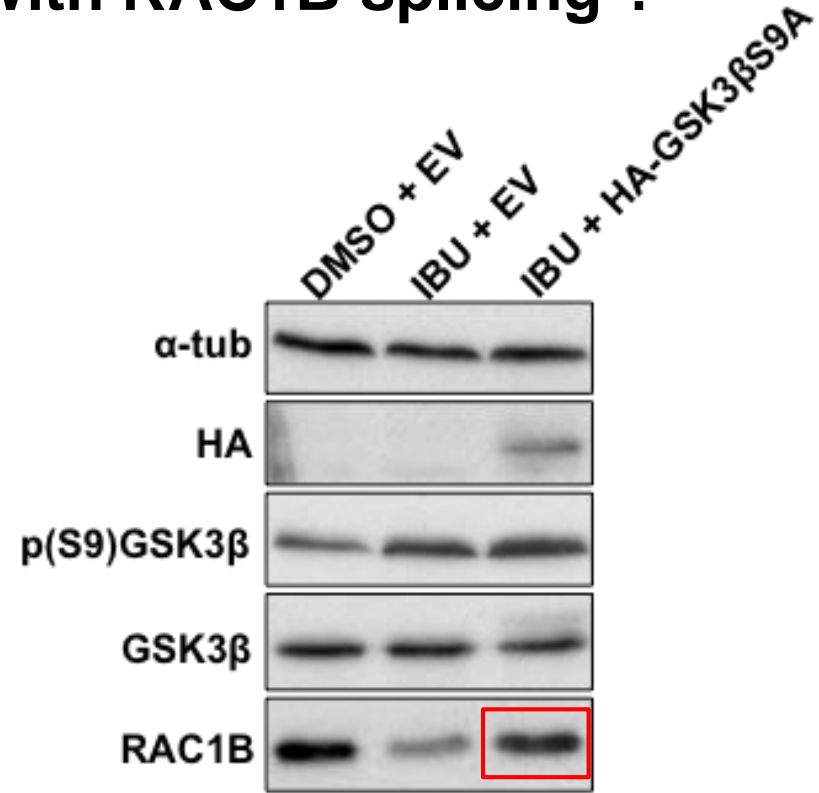
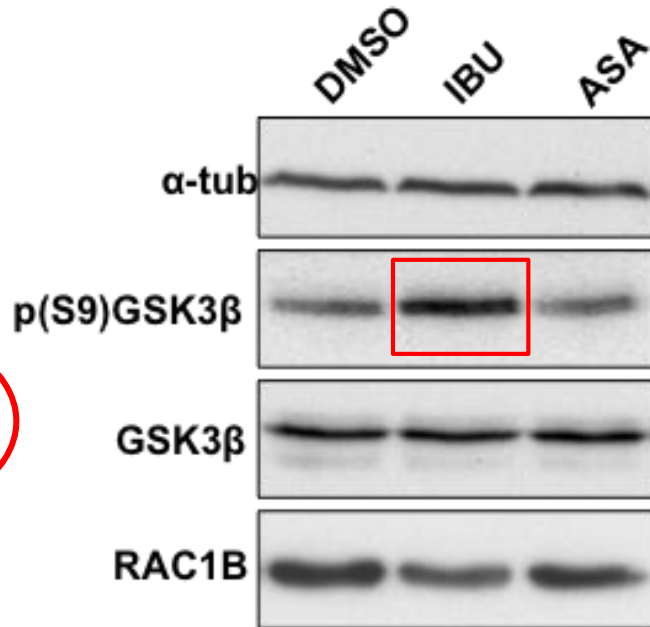
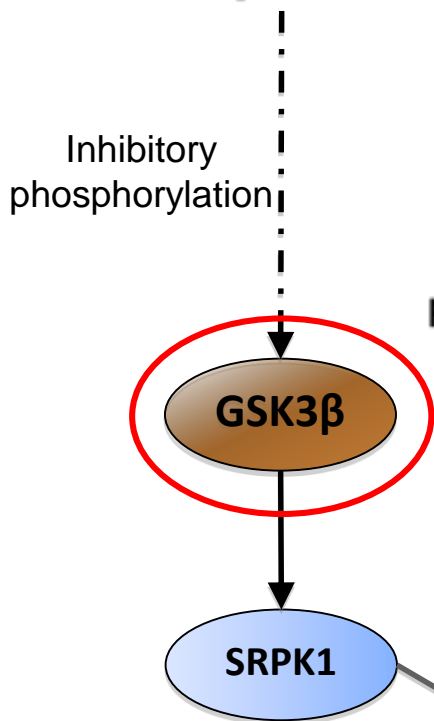


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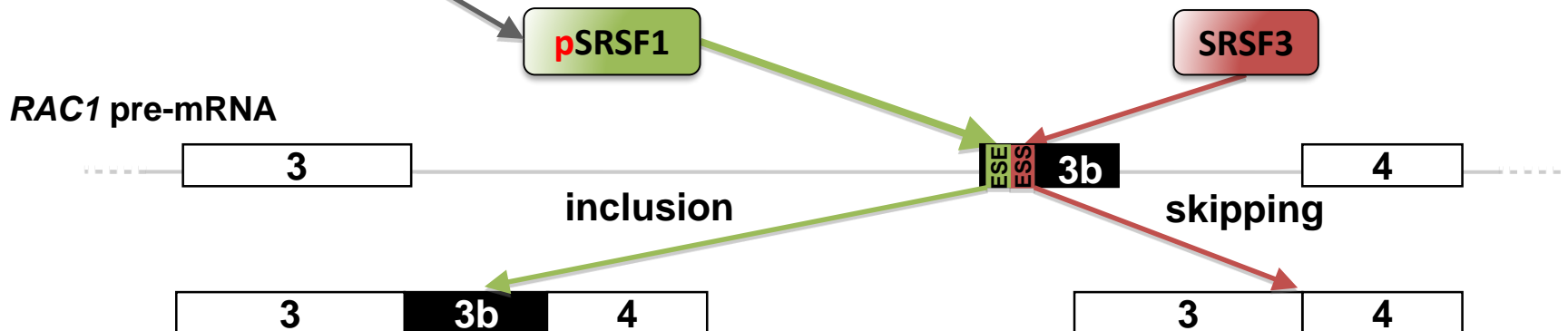


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Ibuprofen



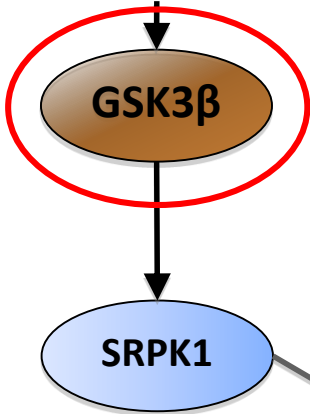
Gonçalves (2020) Oncotarget 11(47):4421-4437



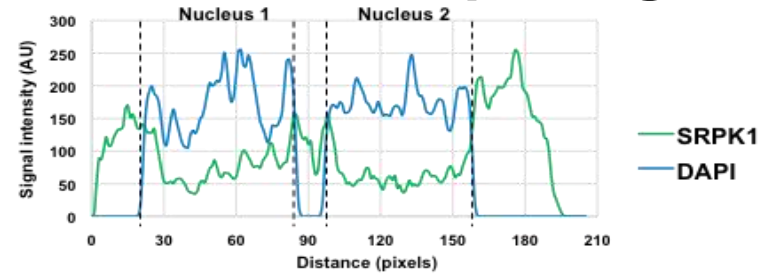
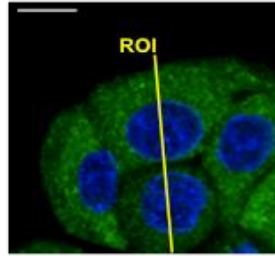
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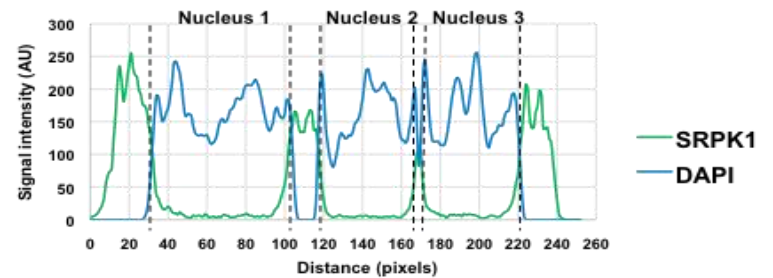
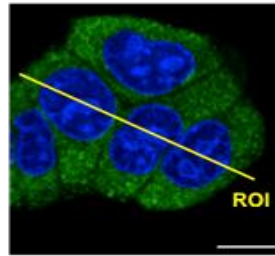
Inhibitory phosphorylation



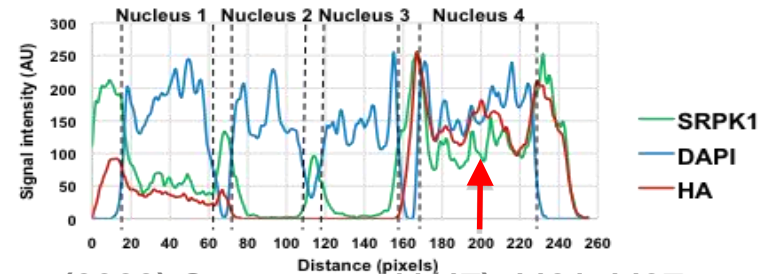
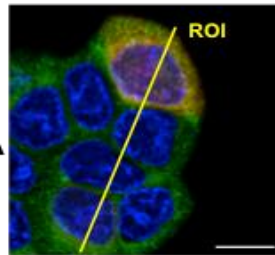
DMSO + EV



IBU + EV

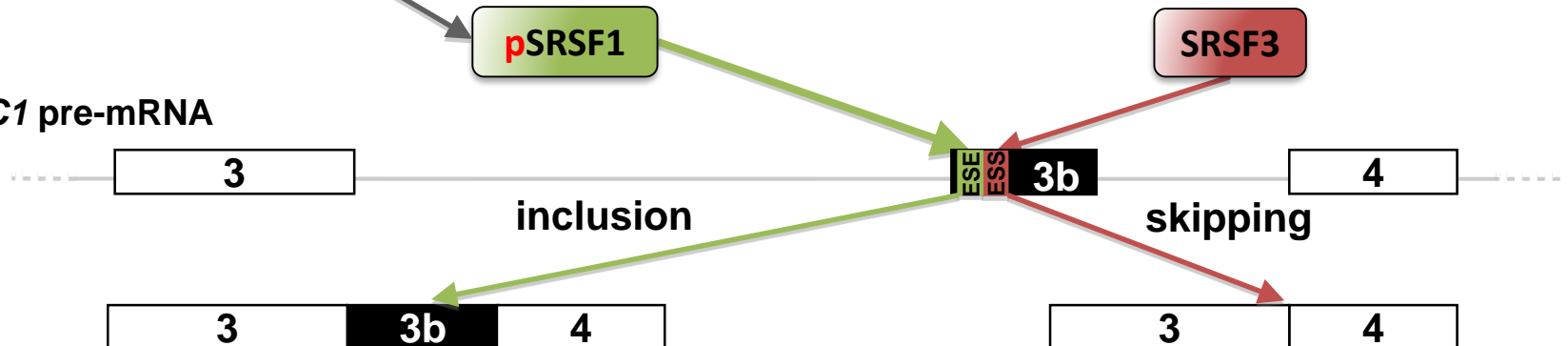


IBU + HA-GSK3βS9A



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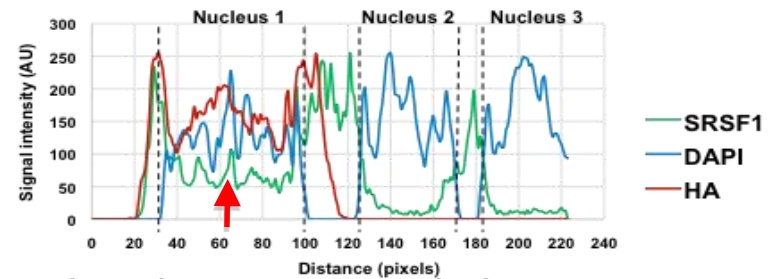
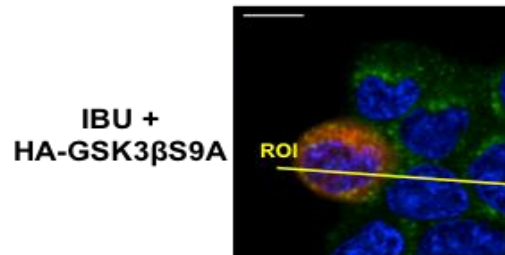
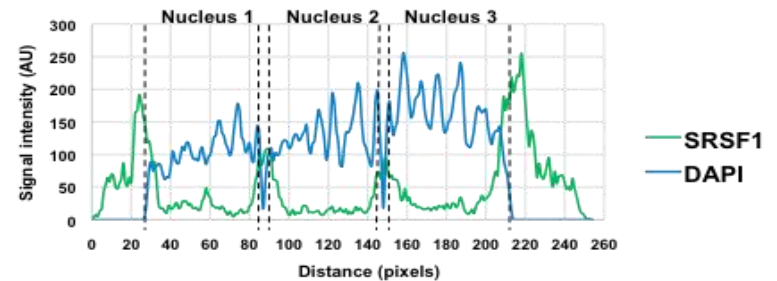
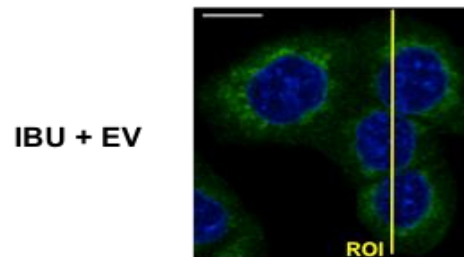
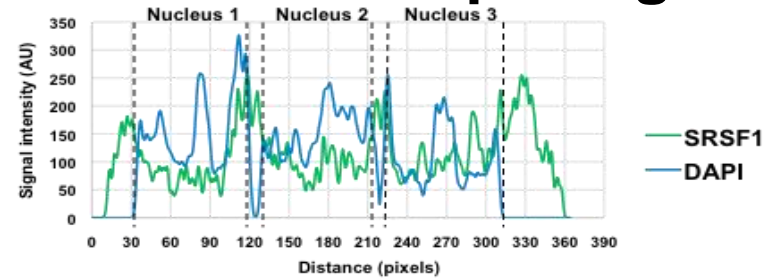
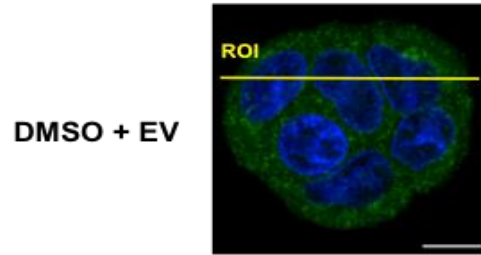
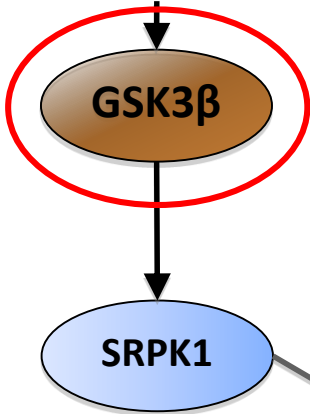
RAC1 pre-mRNA



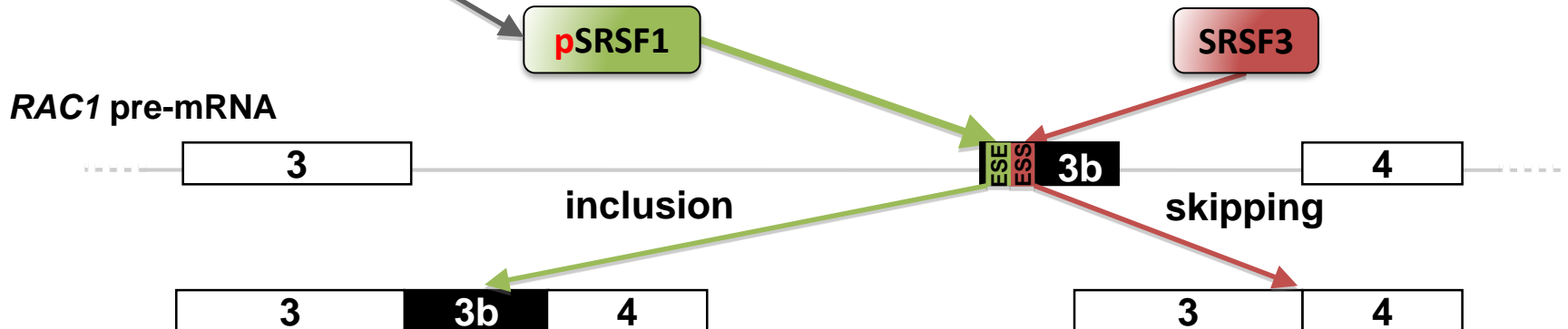
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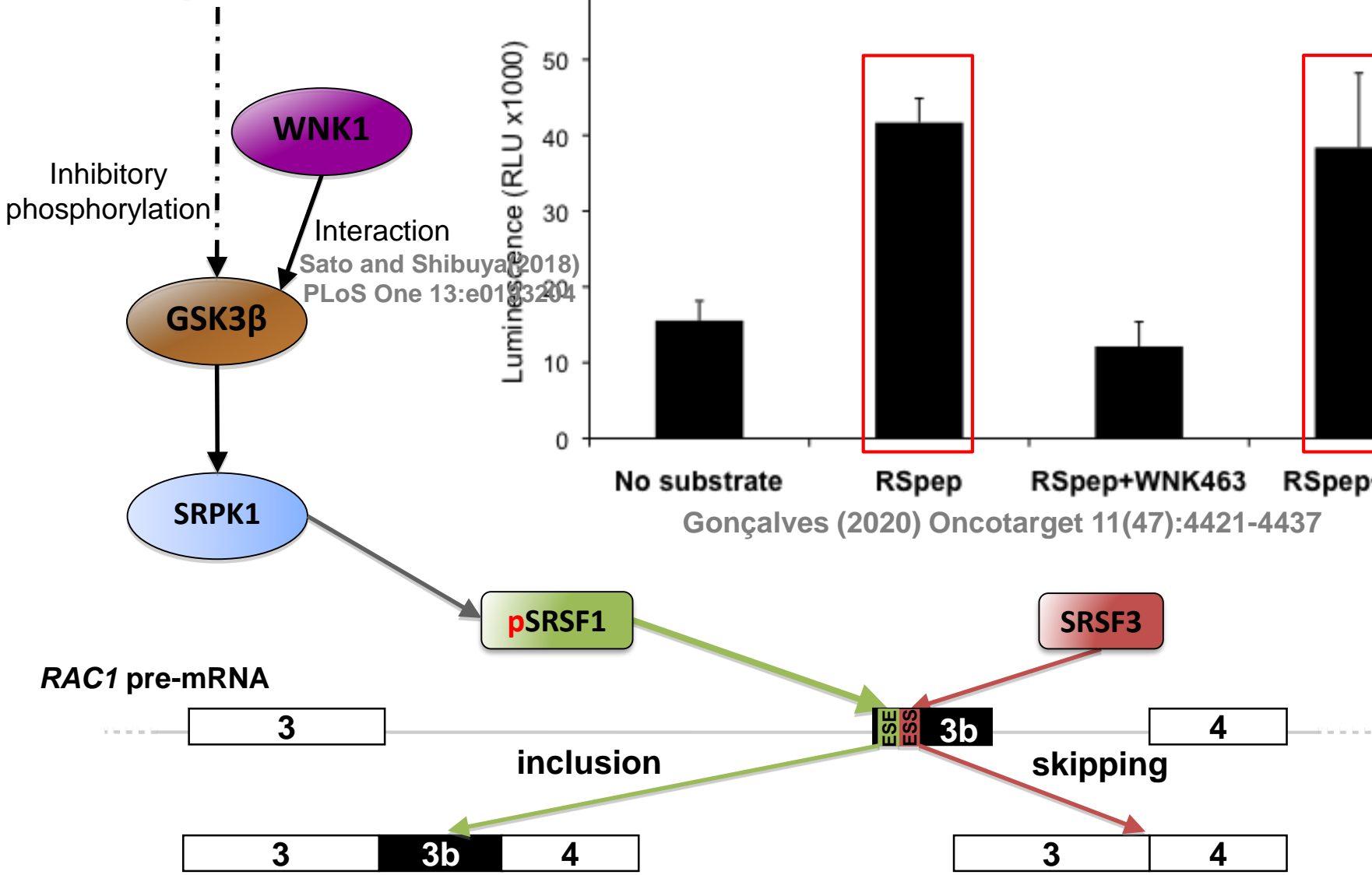


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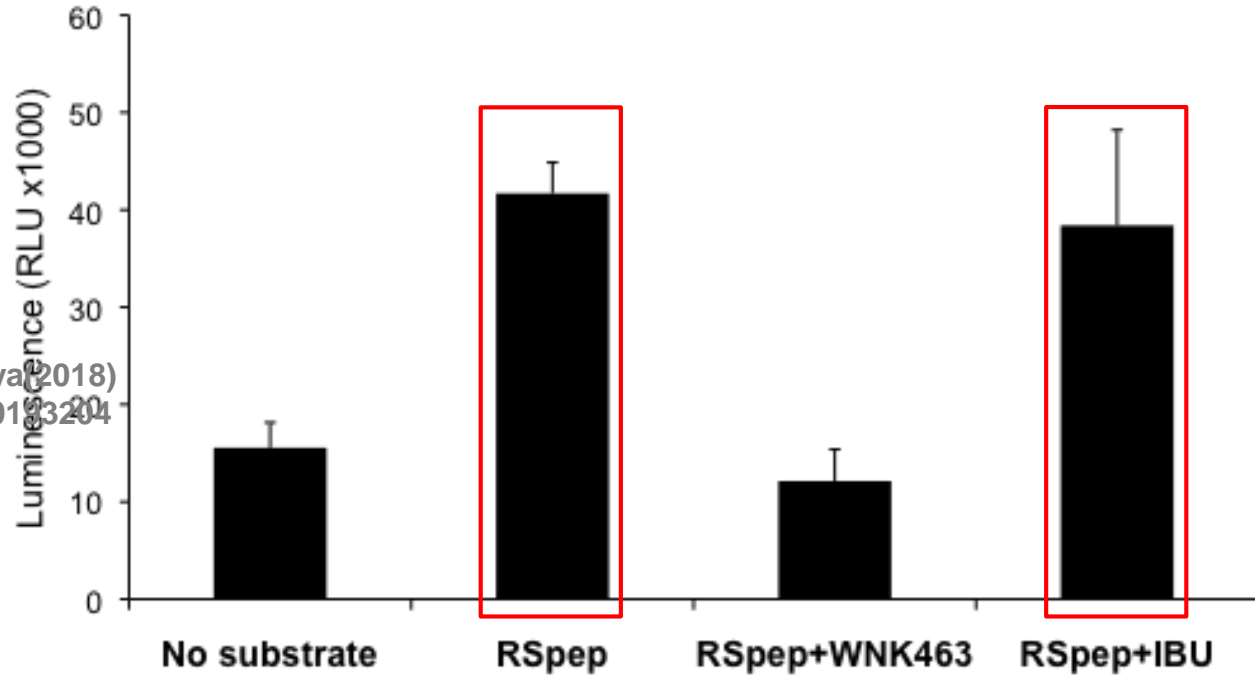


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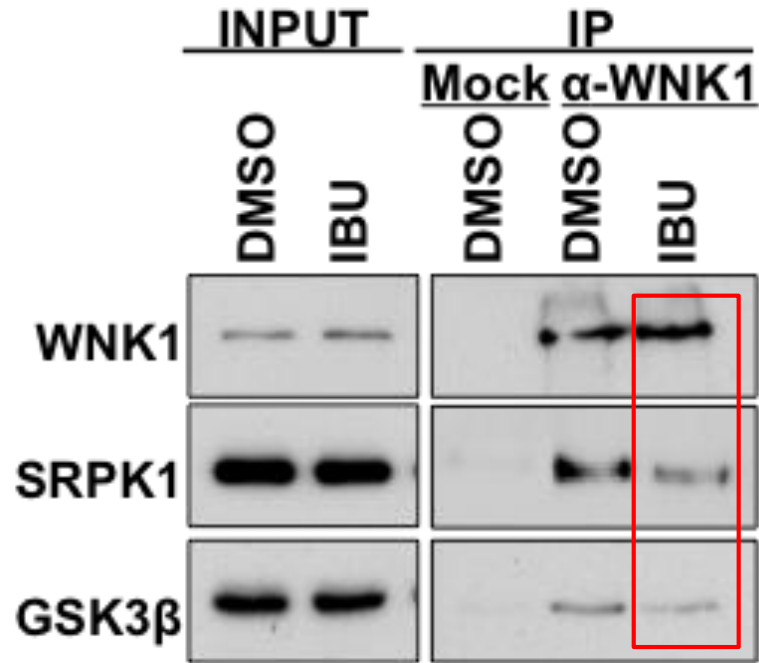
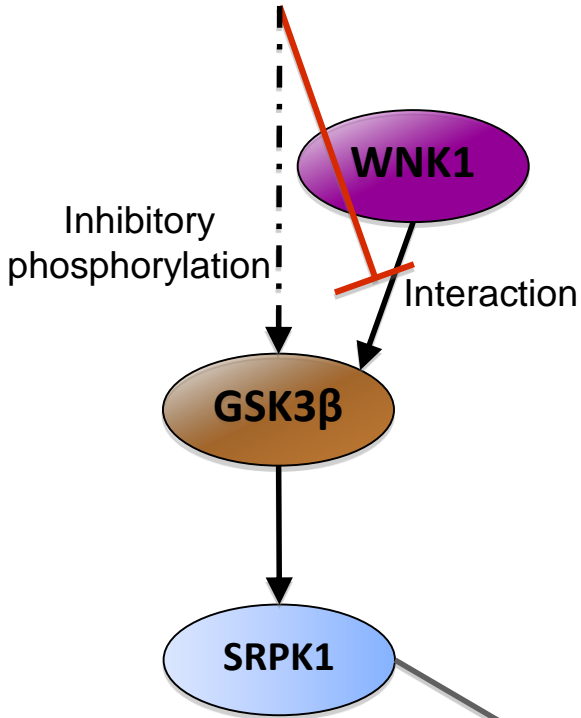
WNK1 activity measured as ATP consumption



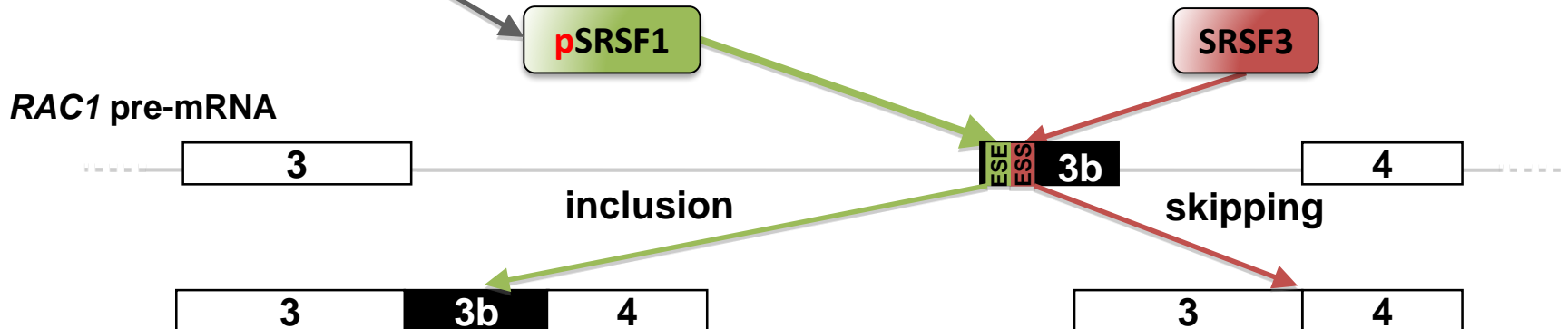
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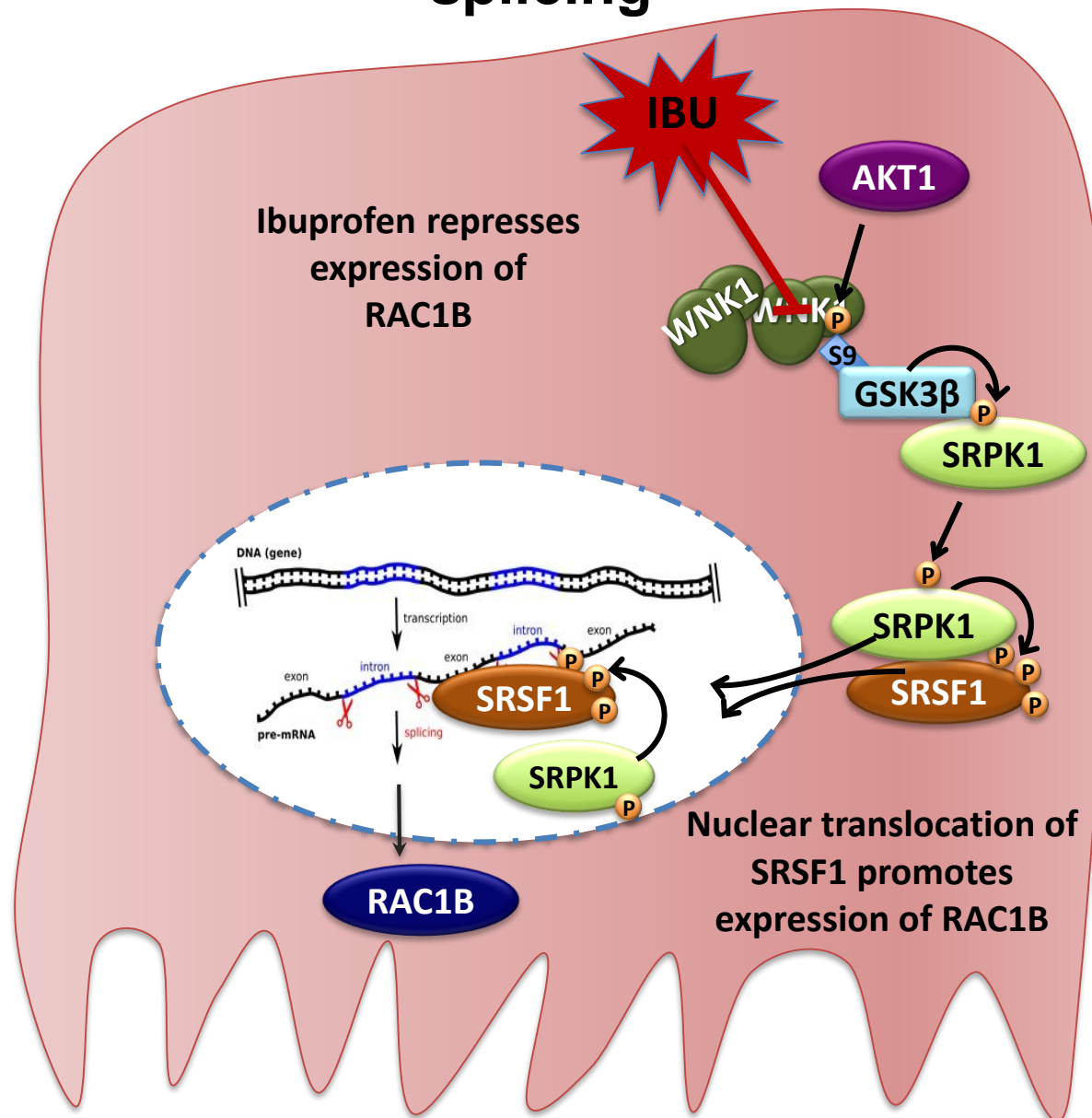
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Proposed model for how ibuprofen interferes with RAC1B splicing



Acknowledgments

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MARATONA
da saúde