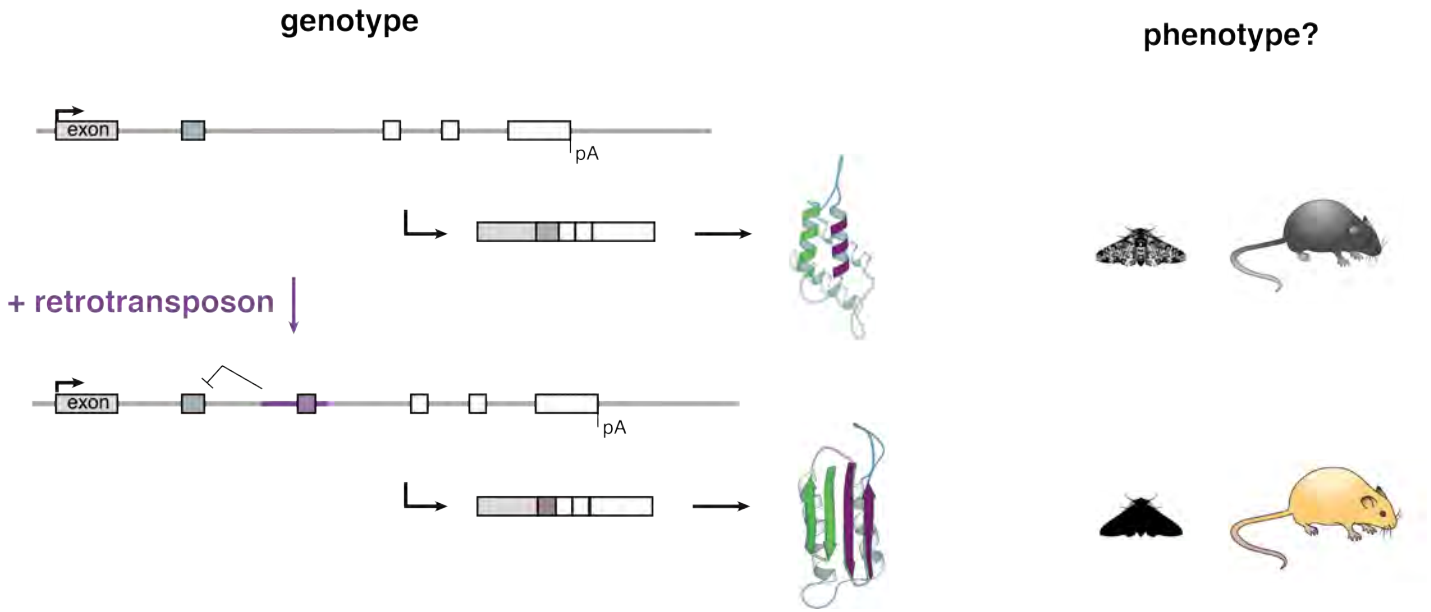
RNA-binding proteins limit and constrain emergence of retrotransposon-derived exons



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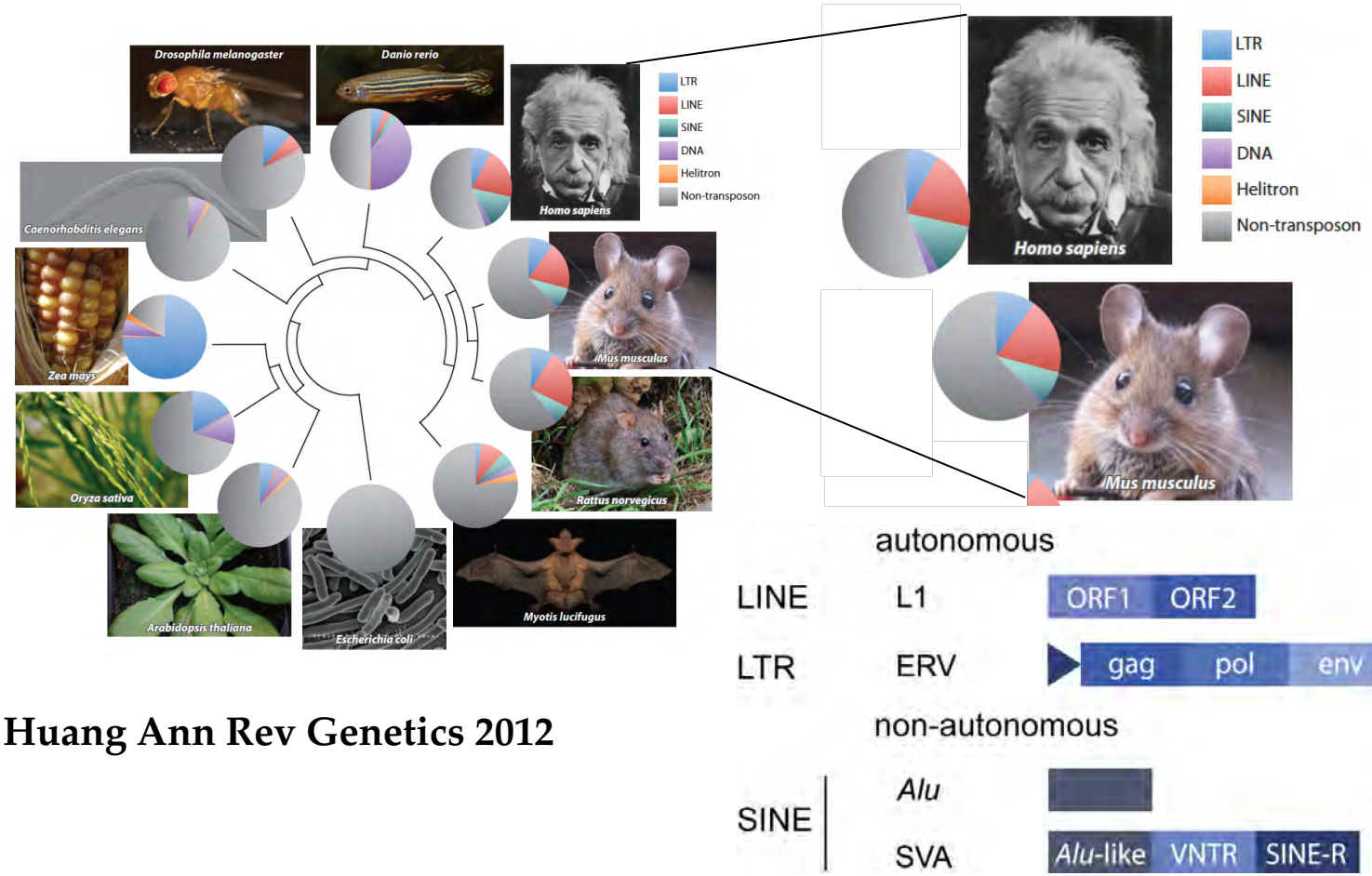
Retrotransposons are pervasive in mammalian genomes



Huang Ann Rev Genetics 2012

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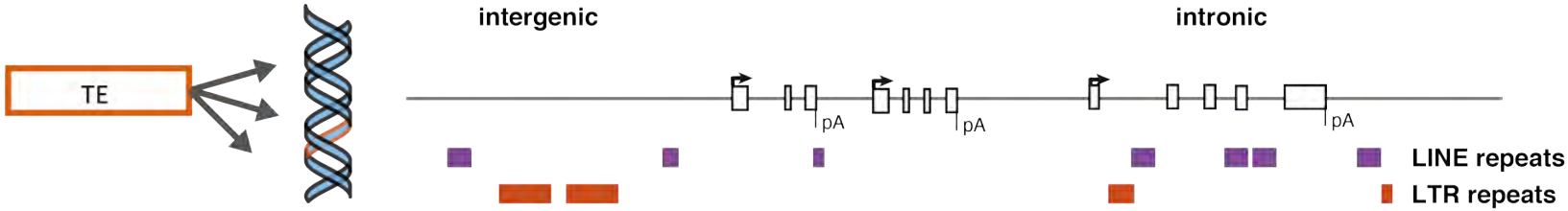
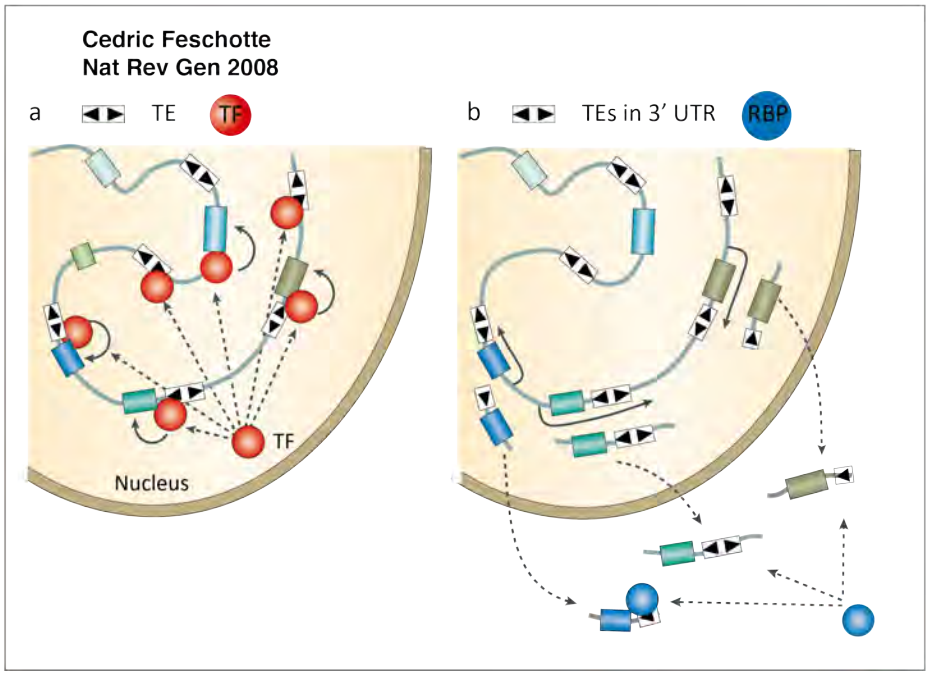
From selfish element to binding site donor





intronic binding sites ?

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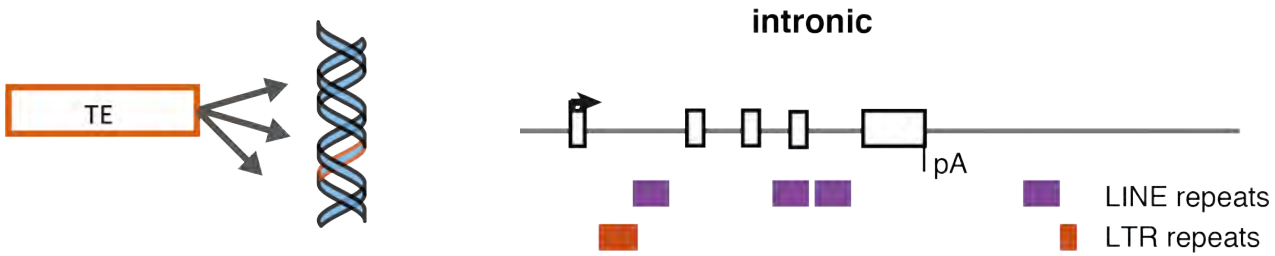
Recognition of repetitive sequences by host factors



Jernej Ule

Federico Agostini

Nick Luscombe

Jan Attig

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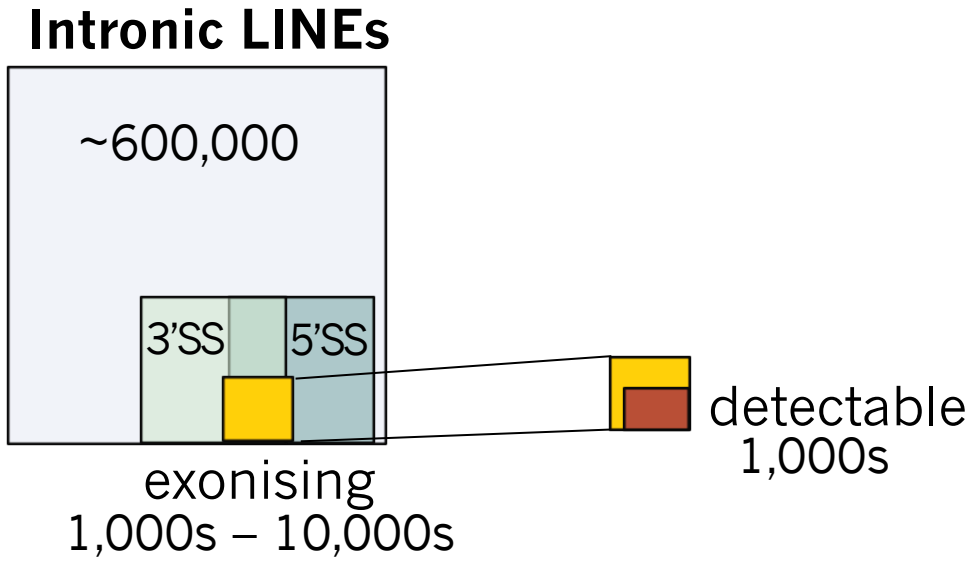
Retrotransposons are rich in splice site sequences



- rare exon formation from retrotransposal insertions

Alu-exons

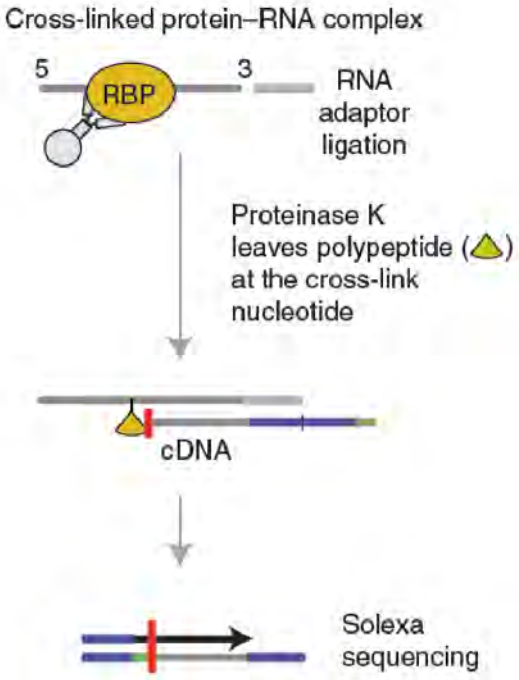
Sorek et al, *Genome Res* 2002
Lev-Maor et al, Science 2003
Attig et al, eLife 2016

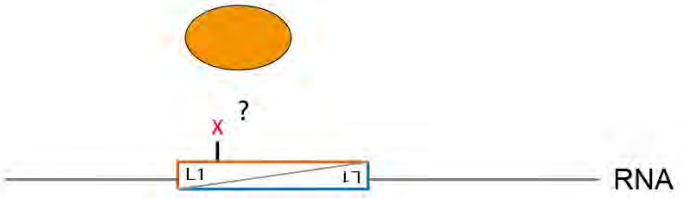
Splicing at LINEs?

Belancio et al, *NAR* 2008

Recognition of repetitive sequences by host factors

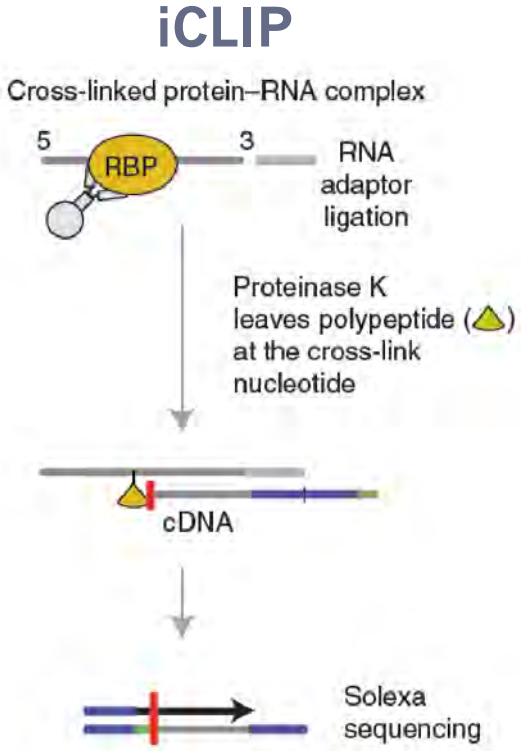
iCLIP





modified from
Konig et al, NSMB, 2010

Recognition of repetitive sequences by host factors



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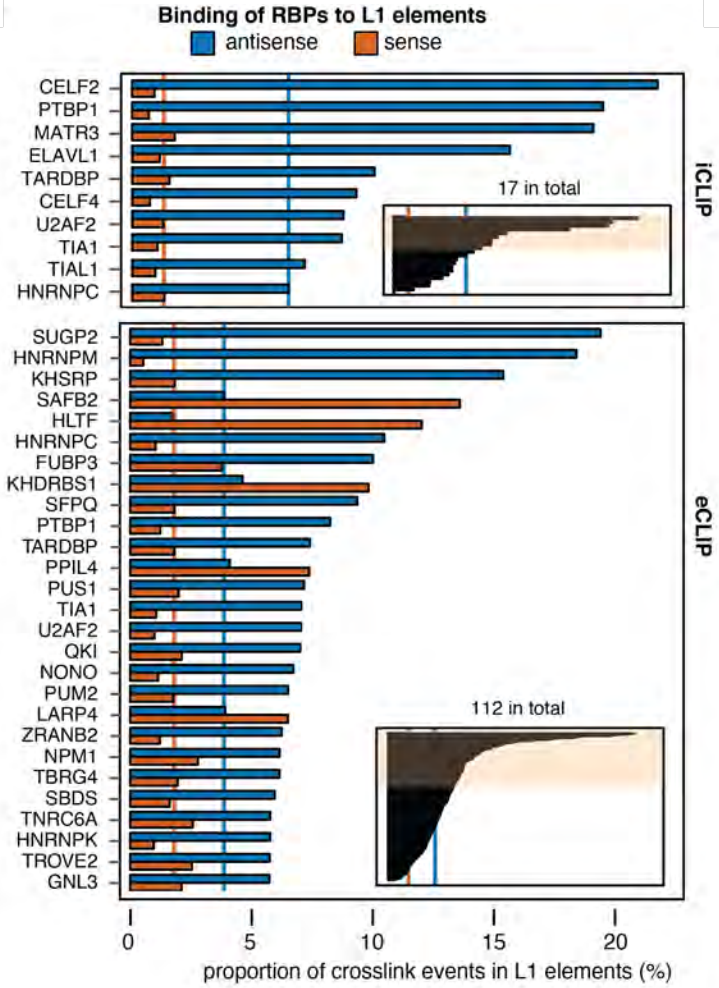
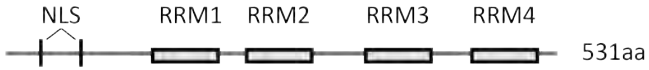


Attig, Agostini et al,
Cell, *in press*

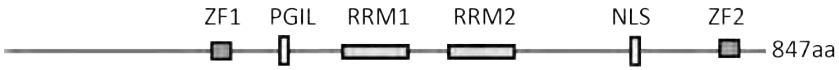
Jan Attig

Consequences of RBP binding to LINEs

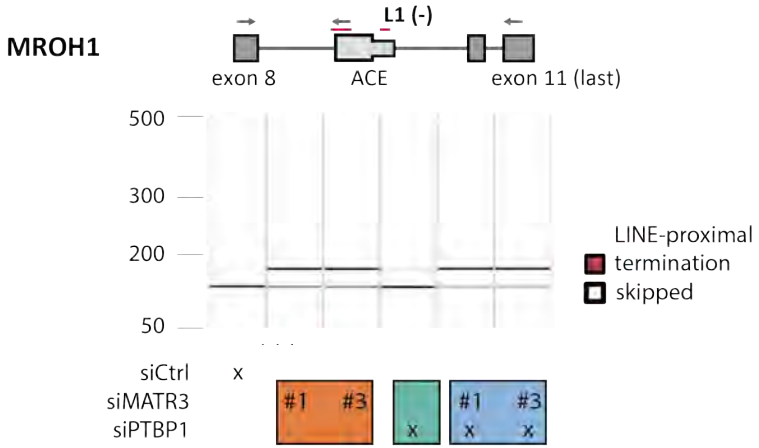
PTBP1



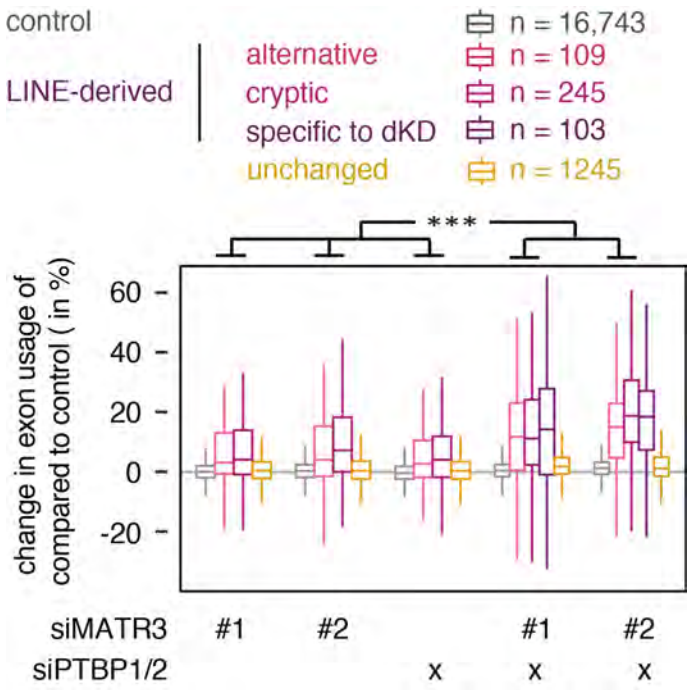
MATR3



RT-PCR, MROH1



RNA-seq



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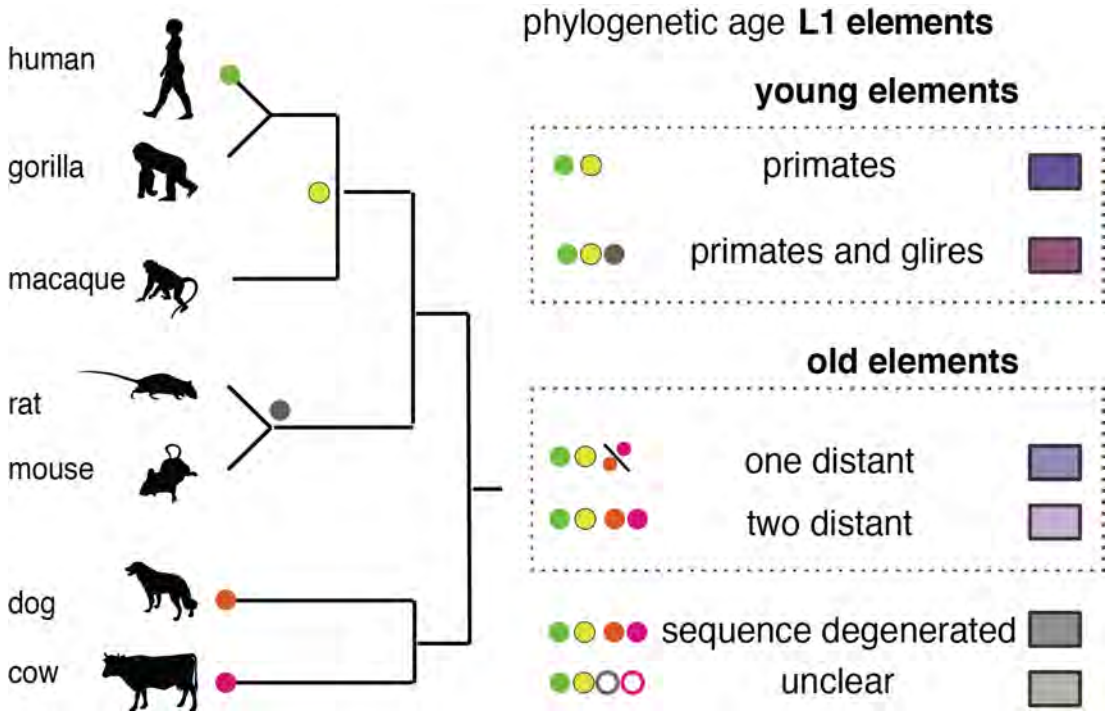
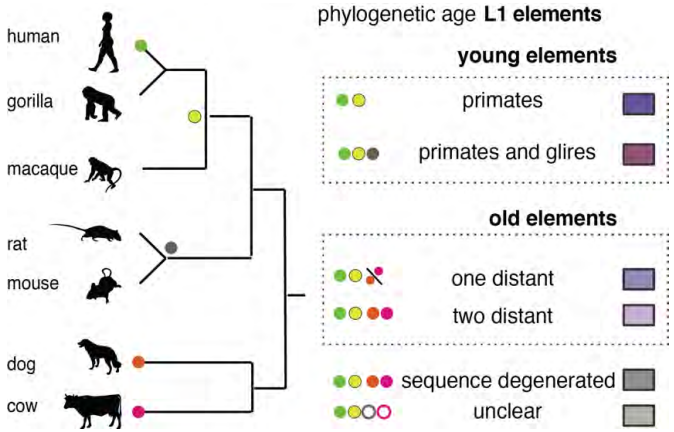
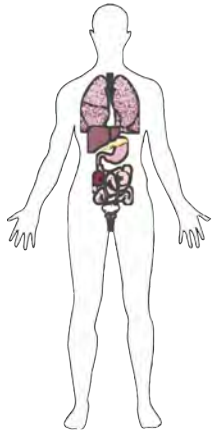
Is regulation conferred through L1 consensus sequence ?

- estimate age of L1 elements genome-wide

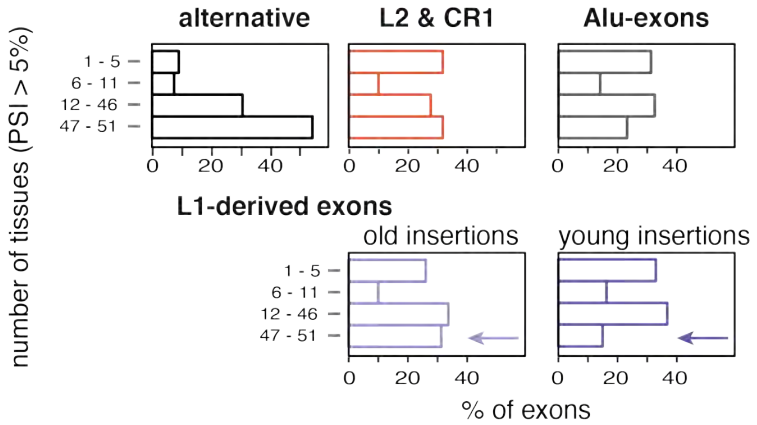


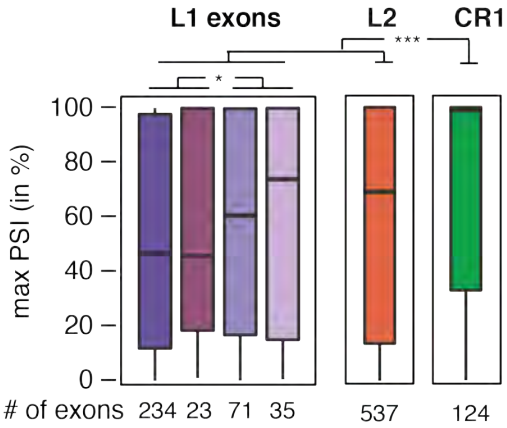
Evolutionary age determines RBP binding and exonisation





RNAseq
GTEx consortium





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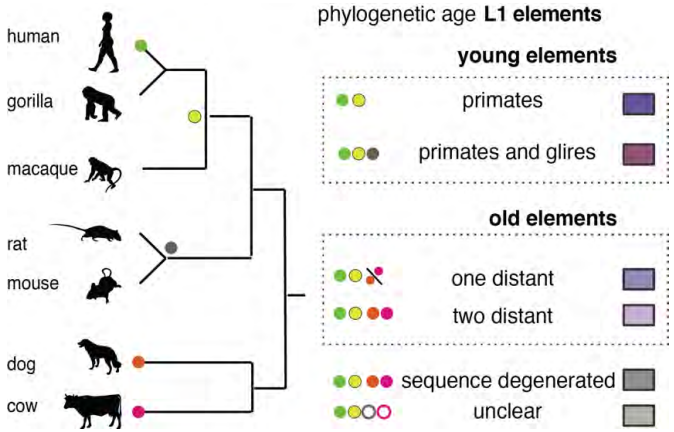
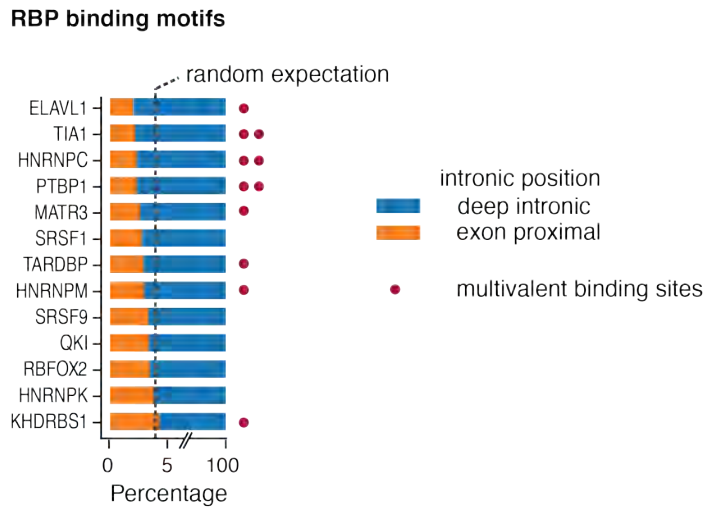
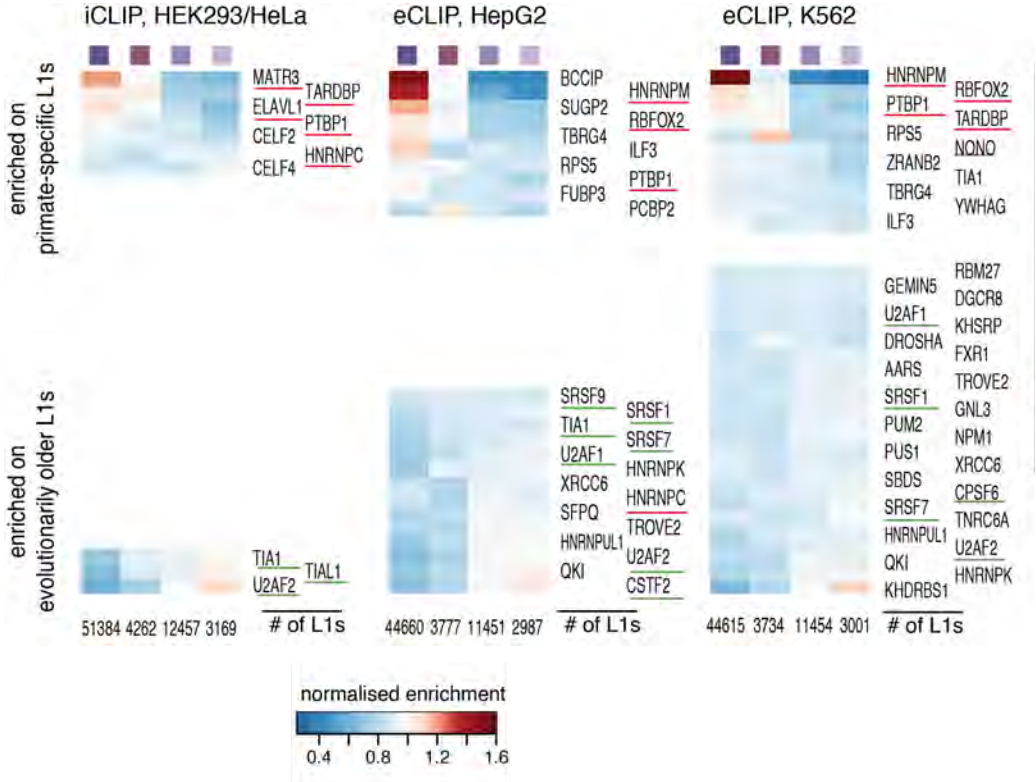
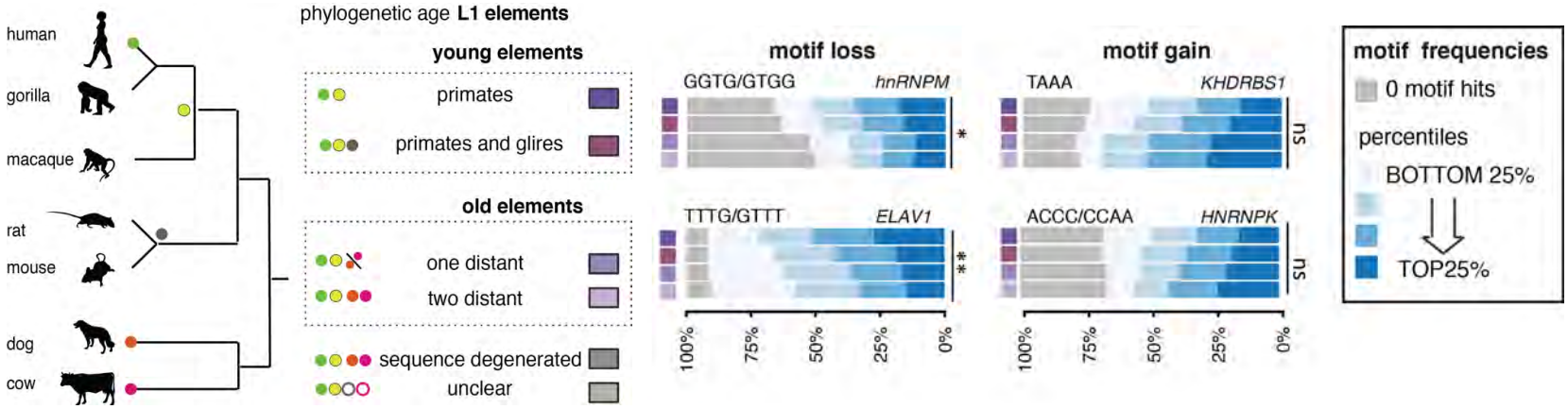
Evolutionary age determines RBP binding and exonisation

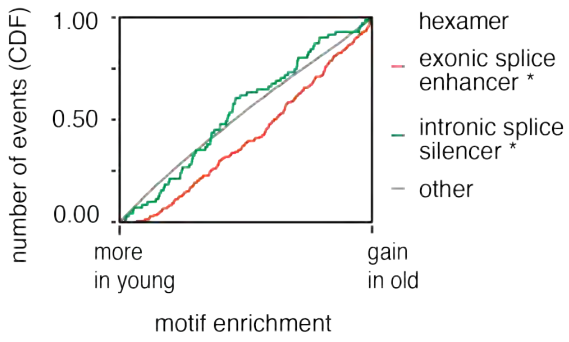


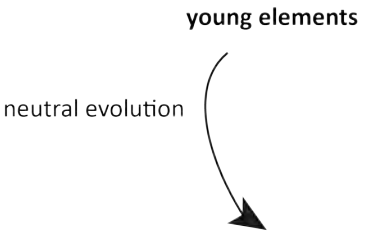


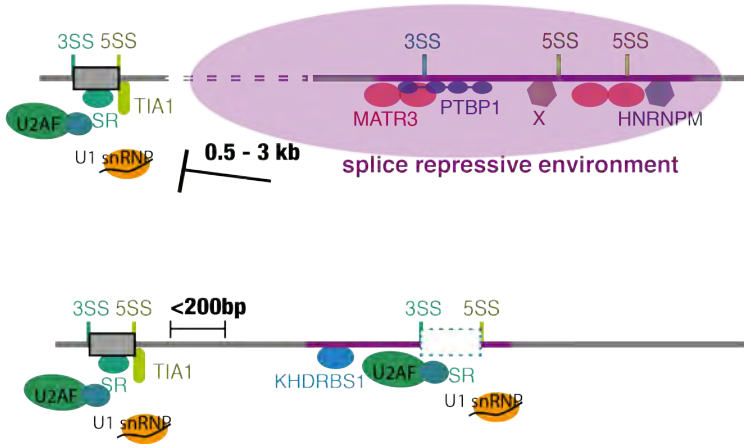


Evolutionary age determines RBP binding and exonisation





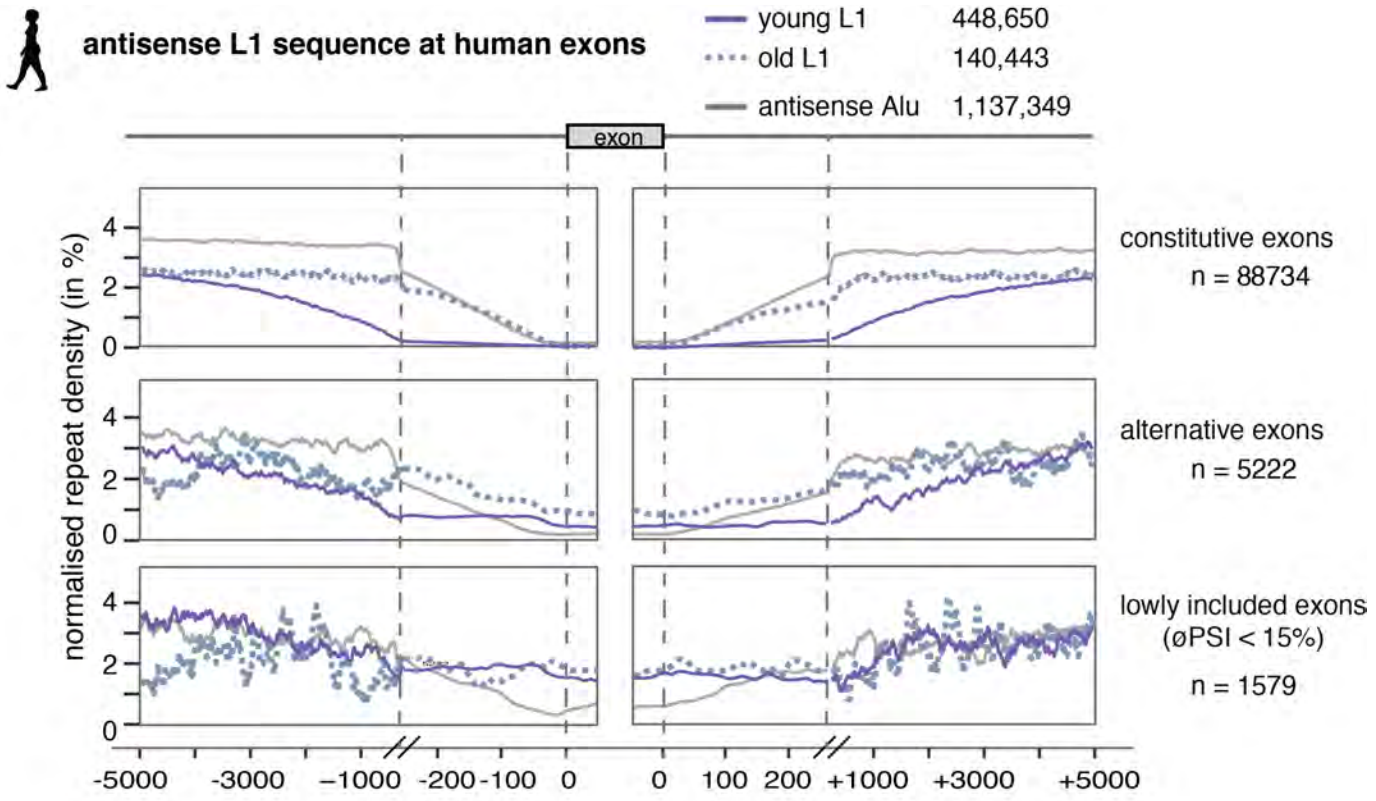




***Wang et al. NSMB 2013,**
Fairbrother et al. Science 2002

Attig, Agostini et al, Cell, *in press*

Negative selection against LINE sequences impacts exon structure



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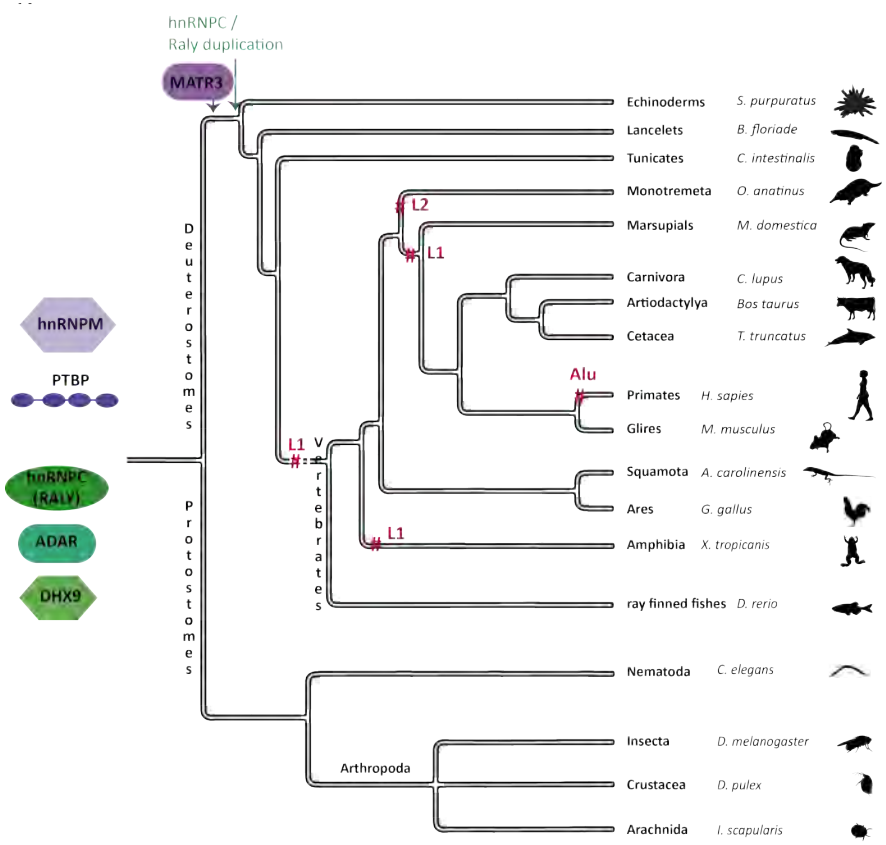
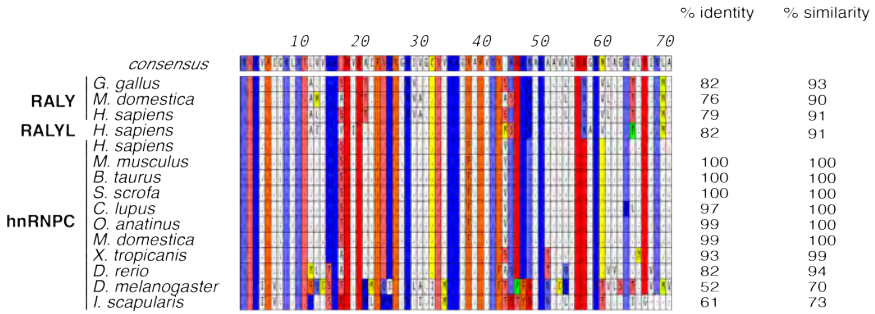
Evolutionary perspective

Why do LINEs carry splice-repressive motifs ?

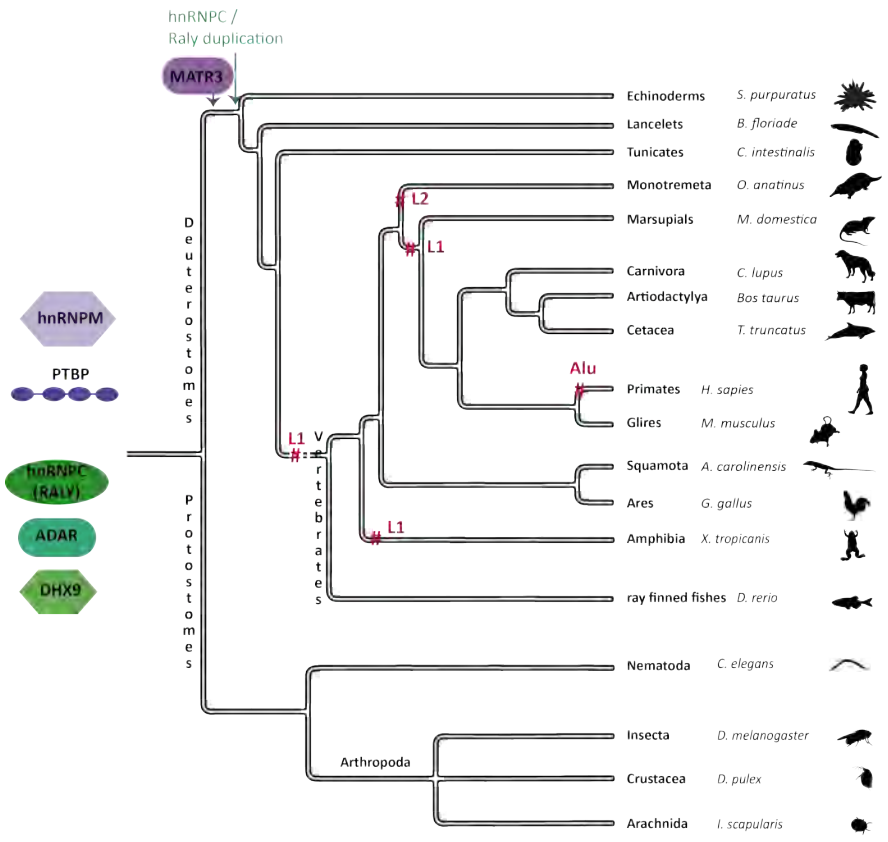
Splice-repressors are present at emergence of novel sequences

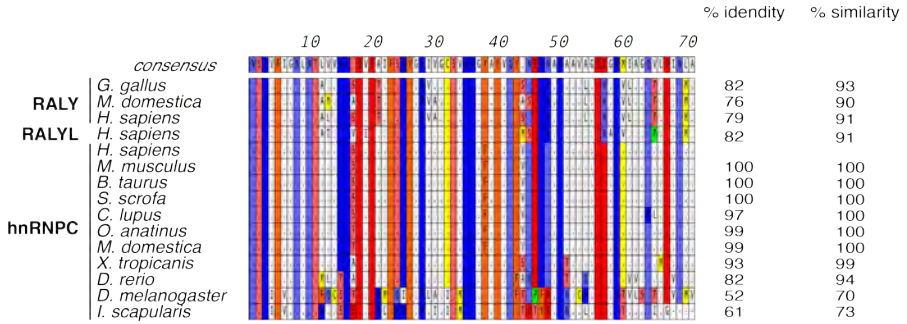


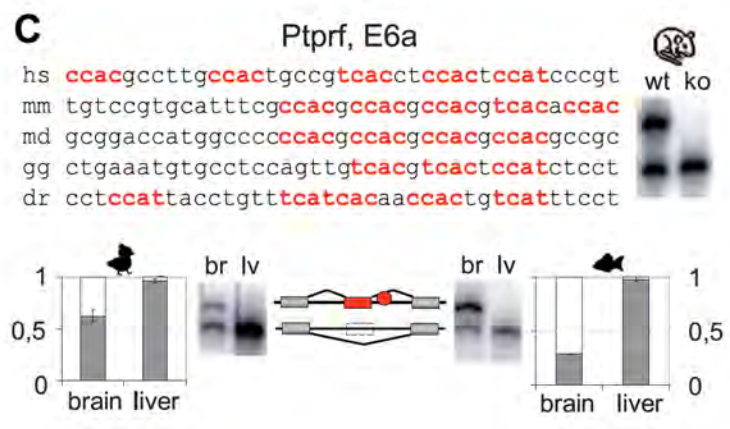


Attig and Ule, *in prep*.

Splice-repressors are present at emergence of novel sequences



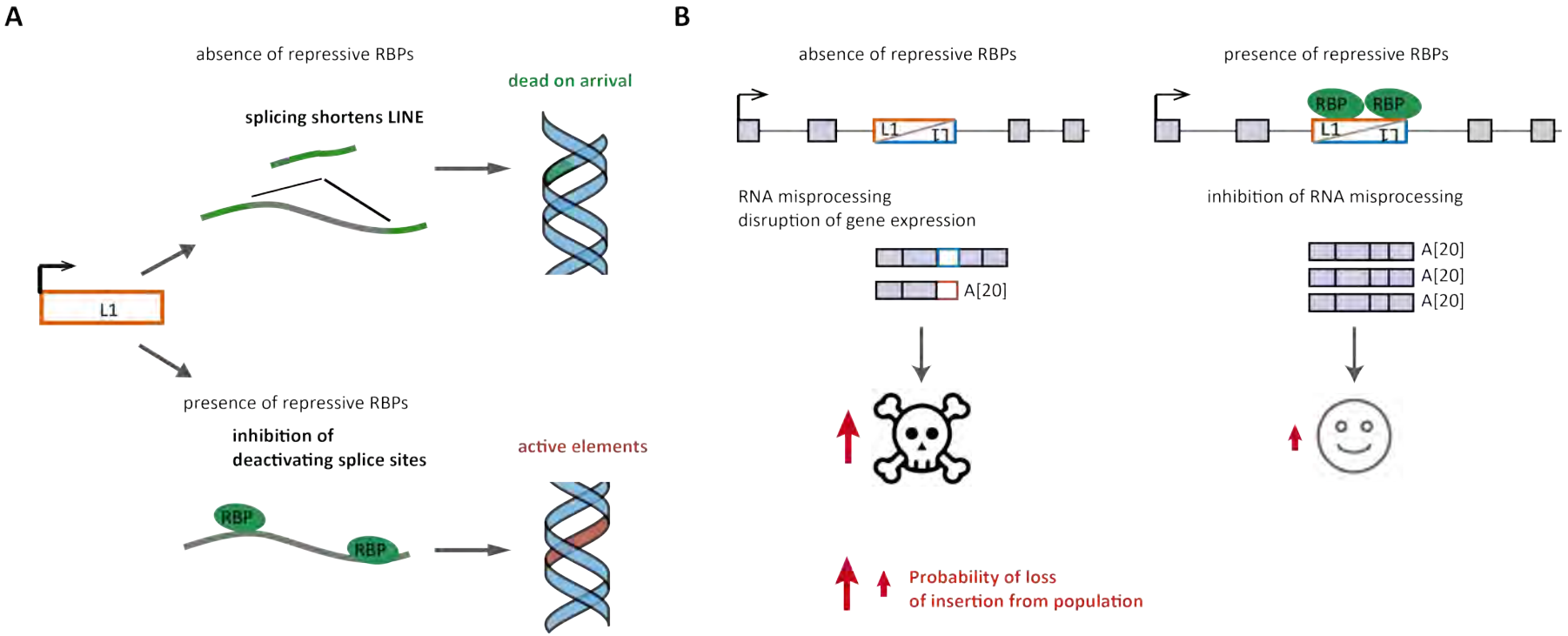




Attig and Ule, *in prep*.

Possible reasons for splice-repressor persistence in L1s

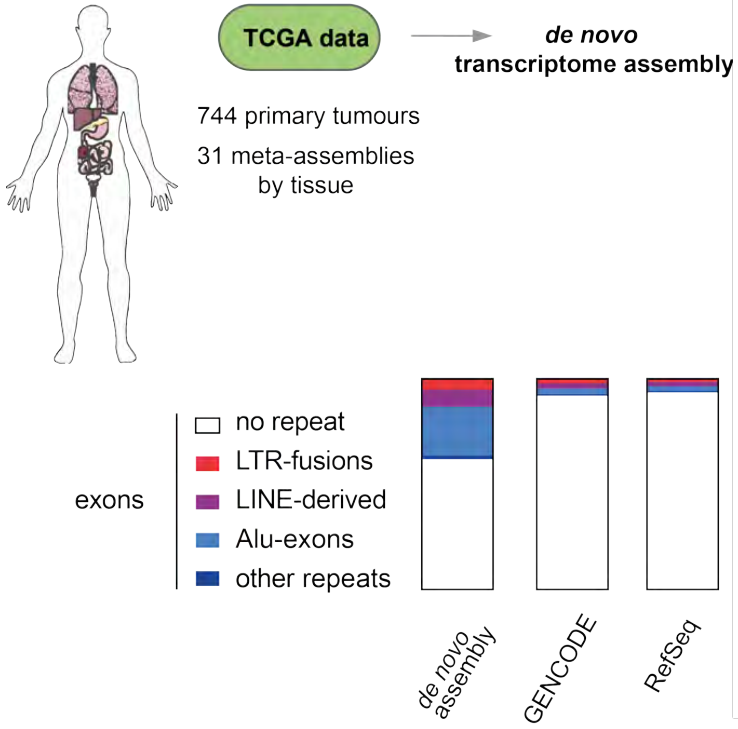
- Maintenance of retrotransposition competent L1s ?



Attig and Ule, *in prep.*

Future prospects

Are retroelements ‘unmasked’ in pathology ?



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IMB Mainz

Rickie Patani
University College London

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Buchmann institute

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