Exonización de elementos transponibles

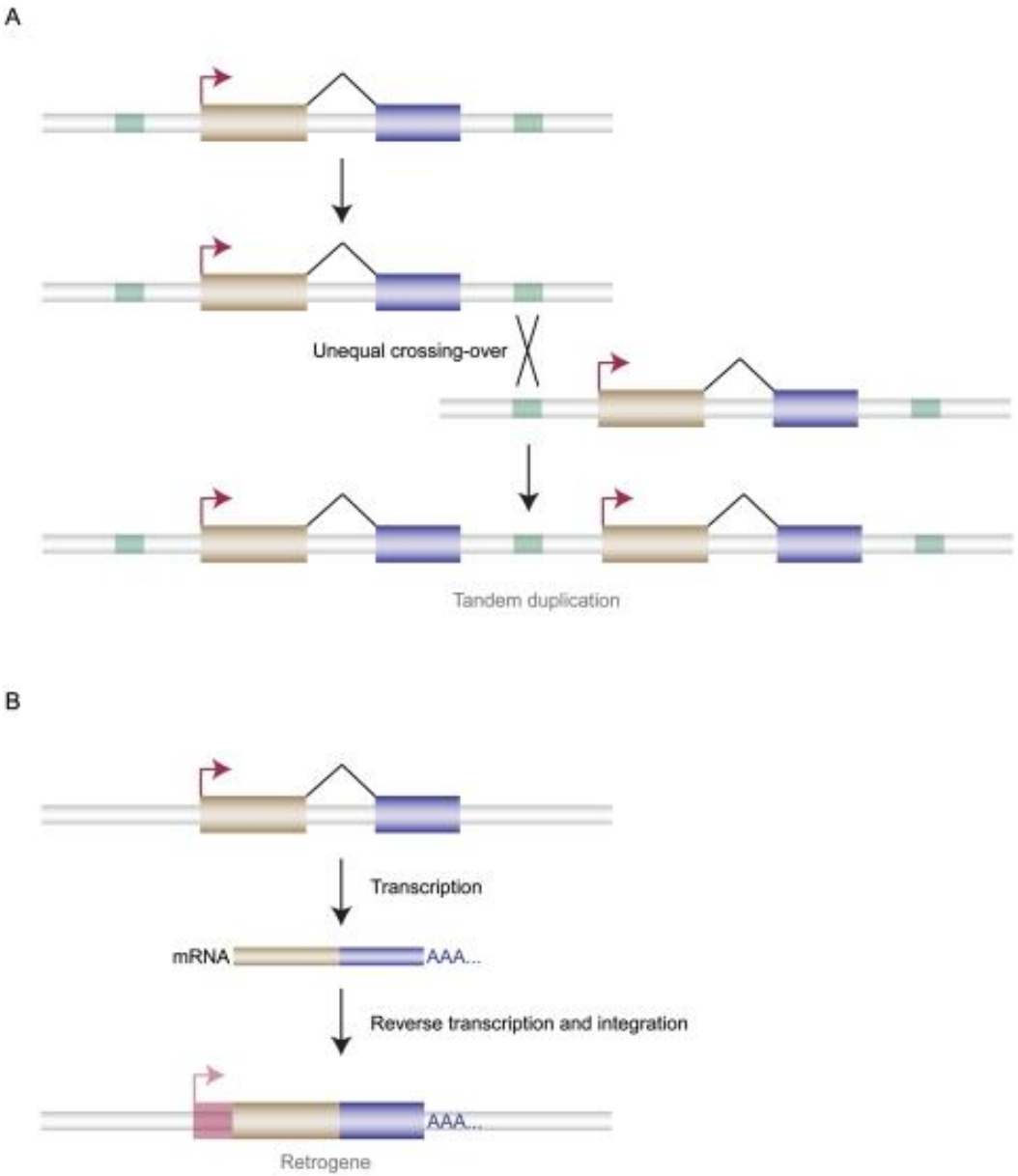
Una fuente de funcionalidad nueva

Duplicación génica

Duplicación génica:

generar una copia de un gen, ya sea en tandem o en otra posición del genoma (recombinación homóloga, transposición, transcripción inversa)

→Dos copias de un gen, una mantiene la función original, la otra evoluciona, generalmente librado de la presión selectiva



Exonización

Incorporación de una secuencia nueva (intrónica o no-traducida) en la región codificadora de un gen → crear una proteína nueva mediante el splicing alternativo

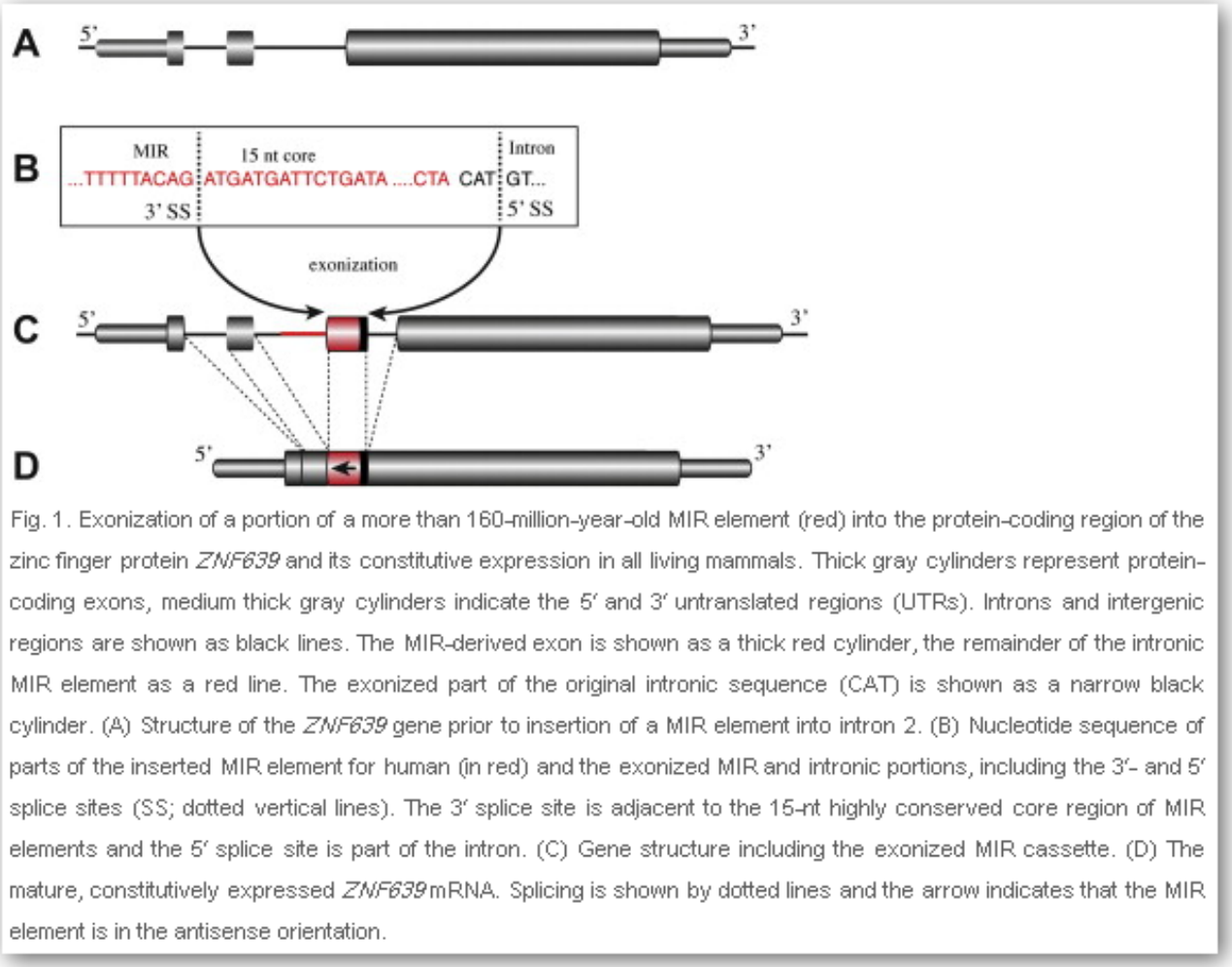


Fig. 1. Exonization of a portion of a more than 160-million-year-old MIR element (red) into the protein-coding region of the zinc finger protein *ZNF639* and its constitutive expression in all living mammals. Thick gray cylinders represent protein-coding exons, medium thick gray cylinders indicate the 5′ and 3′ untranslated regions (UTRs). Introns and intergenic regions are shown as black lines. The MIR-derived exon is shown as a thick red cylinder, the remainder of the intronic MIR element as a red line. The exonized part of the original intronic sequence (CAT) is shown as a narrow black cylinder. (A) Structure of the *ZNF639* gene prior to insertion of a MIR element into intron 2. (B) Nucleotide sequence of parts of the inserted MIR element for human (in red) and the exonized MIR and intronic portions, including the 3′- and 5′ splice sites (SS; dotted vertical lines). The 3′ splice site is adjacent to the 15-nt highly conserved core region of MIR elements and the 5′ splice site is part of the intron. (C) Gene structure including the exonized MIR cassette. (D) The mature, constitutively expressed *ZNF639* mRNA. Splicing is shown by dotted lines and the arrow indicates that the MIR element is in the antisense orientation.

Exonización de elementos transponibles

- La estructura génica en eucariotas (intrón – exón) facilita la incorporación de exones nuevos (exaptación a nivel del genoma) desde el espacio intrónico
- En *C. elegans* (nematodo) solo se conocen 12 exones derivados de elementos transponibles mientras en humanos son cerca de 1800 → intrones mas cortos en invertebrados y actividad retro-transposicional mas baja
- Los elementos SINE (Alus y MIRs) son predestinados para la exonización: (i) en orientación antisentido (antisense orientation) preexisten sitios de splicing canónico AG (acceptor) y (ii) la secuencia inversa complementaria de la cola poli-A de las Alus (cola poli-pirimidina) son señales importantes para el espliceosoma
- Como mínimo el 5% de todos los exones alternativos tiene su origen en una Alu
- Aproximadamente el 85% de las Alus exonizadas se exonizan en orientación antisentido (19 de 23 posibles sitios canónicos se encuentran en la orientación antisentido)

Case study

Communication

From "Junk" to Gene: *Curriculum vitae* of a Primate Receptor Isoform Gene

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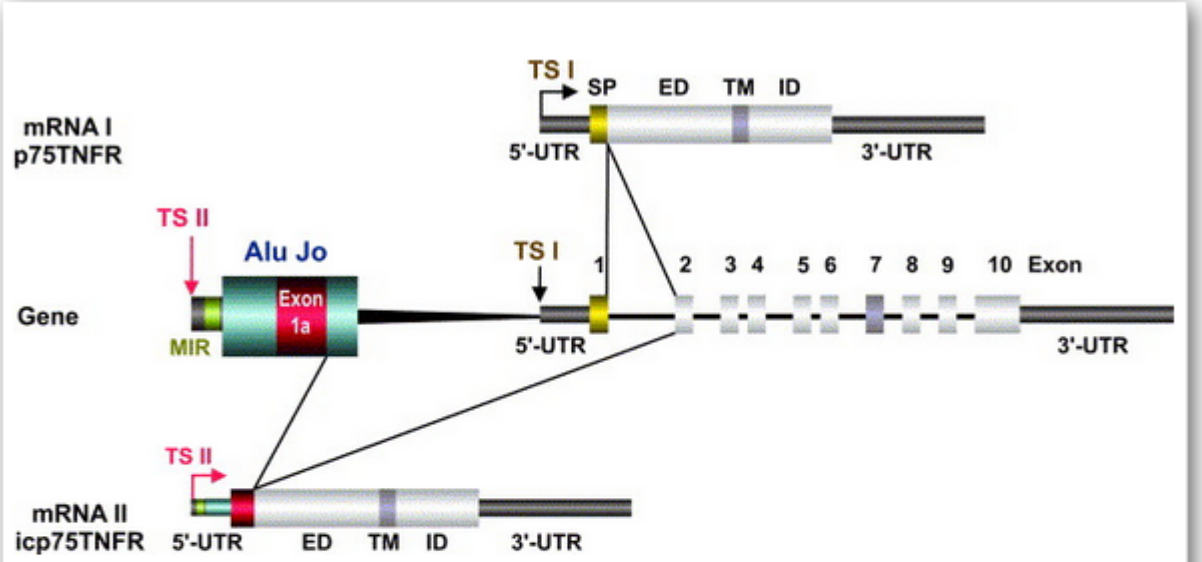

Figure 1. Structure of the *p75TNFR* gene (center) and the two p75TNFR mRNA splice variants. mRNA I and mRNA II originate at the transcriptional start sites TSI and TSII, respectively. Introns are depicted as thin lines, 5′ and 3′ untranslated regions (5′ UTR and 3′ UTR) of the terminal exons as grey bars (intermediate thickness) and protein-coding regions of exons as thick bars. The extracellular domain (ED), transmembrane domain (TM), and intracellular domain (ID) are indicated. The part of exon 1 in mRNA I that contributes the signal peptide (SP) is highlighted in yellow. The proximal portion of the gene is enlarged. A mammalian interspersed repeat (MIR, green) precedes the Alu Jo element (blue), part of which contributes the ATG start codon of mRNA II (at the left border of the protein coding domain, shown in red, of exon 1a). The right border of the exon 1a protein-coding domain (red) is determined by a 5′ splice site. The differential splicing of the first exons of the alternative transcripts to exon 2 is indicated by the respective lines.

(a)

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Alu Jo      RGCCGGGCGC GGTGGCTCAC GCCTGTAATC CCAGCACTTT GGGAGGCC-G AGGCGGGAGG ATCGCTTGAG ---------- 69
hicp75TNFR  GGCCGAGTGC AGTGGCTCAC ACCTATAATC CCAGCACCTT GGGAGGCCAG AGGCGGGAAG ATCACTTGAG GGTGGGAAGA 80

Alu Jo      ---------C CCAGGAGTTC GAGACCAGCC TGGGCAAC ATAGCGAGAC CCCGTCTCTA CAAAAAATAC AAAAATTAGC 138
hicp75TNFR  ACACGTGAGC TCAGGAGTTC GAGACCAGCC TGGACAAC ATGGCGAAAC CCCATCTCTA 7 bp del TAA AGAAATCAGC 151

Alu Jo      CGGGCGTGGT GGCGCGCGCC TGTAGTCCCA GCTACTCGGG AGGCTGAG GCAGGAGGAT CGCTTGAGCC CAGGAGTTCG 216
hicp75TNFR  CTAGCATGGT GGCCCGAGCC TGTAGTCCCA GCTACTCGGG AGGCTGAG GTGGGAGGAT CGCTTGAGCG CAGGAGTTGG 229

Alu Jo      AGGCTGCAGT GAGCTATGAT CGCGCCACTG CACTCCAGCC TGGGCGACAG AGCGAGACCC TGTCTCAAAA AAAAAAAAAA 296
hicp75TNFR  AGGCTGCAGT GAGCTATG-- ---------- ---------- --GGTGAAAG AGTGAGACCT TGTCTCAAAA AAAATTAAAA 285

Alu Jo      AAAAAA--                                                                              302
hicp75TNFR  AATAAGAA                                                                              293
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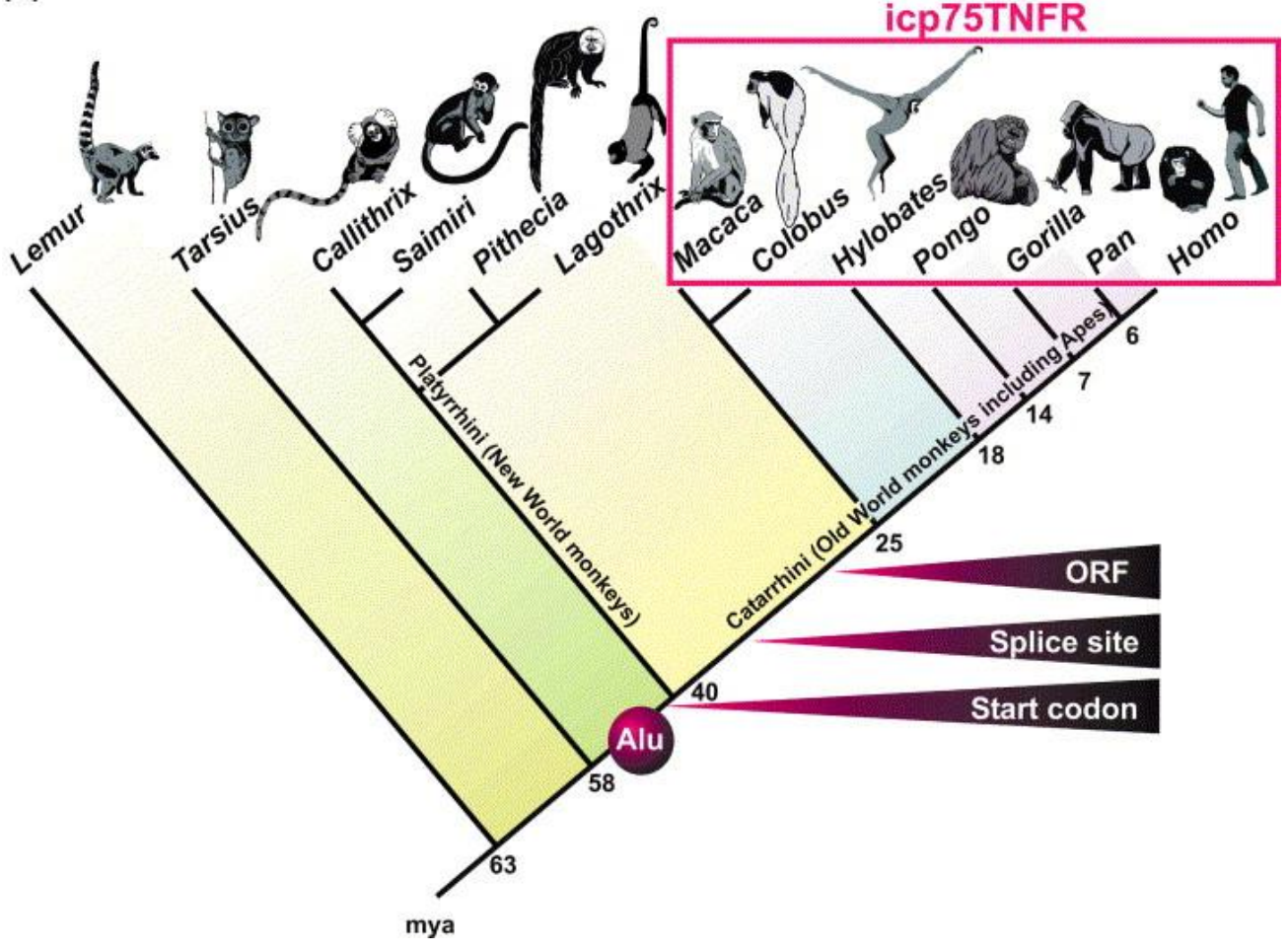
(b)



Publicaciones relevantes

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