Format: Abstract

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Intronic antisense Alu elements have a negative splicing effect on the inclusion of adjacent downstream exons.

Nakama M[1], Otsuka H[2], Ago Y[2], Sasai H[2], Abdelkreem E[3], Aoyama Y[4], Fukao T[5].

Author information

Abstract

Alu elements occupy 10% of the human genome. However, although they contribute to genomic and transcriptomic diversity, their function is still not fully understood. We hypothesized that intronic Alu elements may contribute to alternative splicing. We therefore examined their effect on splicing using minigene constructs including exon 9-exon 11 inclusive of ACAT1 with truncated introns 9 and 10. These constructs contained a suboptimal splice acceptor site for intron 9. Insertion of AluY-partial AluSz6-AluSx, originally located in ACAT1 intron 5, in an antisense direction within intron 9 had a negative effect on exon 10 inclusion. This effect was additive with that of an exonic splicing enhancer mutation in exon 10, and was canceled by the substitution of G for C at the first nucleotide of exon 10 which optimized the splice acceptor site of intron 9. A sense AluY-partial AluSz6-AluSx insertion had no effect on exon 10 inclusion, and one antisense AluSx insertion had a similar effect to antisense AluY-partial AluSz6-AluSx insertion. The shorter the distance between the antisense Alu element and exon 10, the greater the negative effect on exon 10 inclusion. This distance effect was more evident for suboptimal than optimal splice sites. Based on our data, we propose that intronic antisense Alu elements contribute to alternative splicing and transcriptomic diversity in some genes, especially when splice acceptor sites are suboptimal.

KEYWORDS: Alternative splicing; Alu elements; Minigene splicing experiment; Splicing factor

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MeSH terms, Substances

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