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An intron with a constitutive transport element is retained in a *Tap* messenger RNA

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Abstract

Alternative splicing is a key factor contributing to genetic diversity and evolution[1]. Intron retention, one form of alternative splicing, is common in plants[2] but rare in higher eukaryotes[3,4,5,6,7,8], because messenger RNAs with retained introns are subject to cellular restriction at the level of cytoplasmic export and expression[9,10]. Often, retention of internal introns restricts the export of these mRNAs and makes them the targets for degradation by the cellular nonsense-mediated decay machinery if they contain premature stop codons[11,12]. In fact, many of the database entries for complementary DNAs with retained introns represent them as artefacts that would not affect the proteome[11]. Retroviruses are important model systems in studies of regulation of RNAs with retained introns, because their genomic and mRNAs contain one or more unspliced introns[10]. For example, Mason–Pfizer monkey virus overcomes cellular restrictions by using a *cis*-acting RNA element known as the constitutive transport element (CTE)[13]. The CTE interacts directly with the Tap protein (also known as nuclear RNA export factor 1, encoded by *NXF1*), which is thought to be a principal export receptor for cellular mRNA[14], leading to the hypothesis that cellular mRNAs with retained introns use cellular CTE equivalents to overcome restrictions to their expression[10]. Here we show that the *Tap* gene contains a functional CTE in its alternatively spliced intron 10. *Tap* mRNA containing this intron is exported to the cytoplasm and is present in polyribosomes. A small Tap protein is encoded by this mRNA and can be detected in human and monkey cells. Our results indicate that Tap regulates expression of its own intron-containing RNA through a CTE-mediated mechanism. Thus, CTEs are likely to be important elements that facilitate efficient expression of mammalian mRNAs with retained introns.