

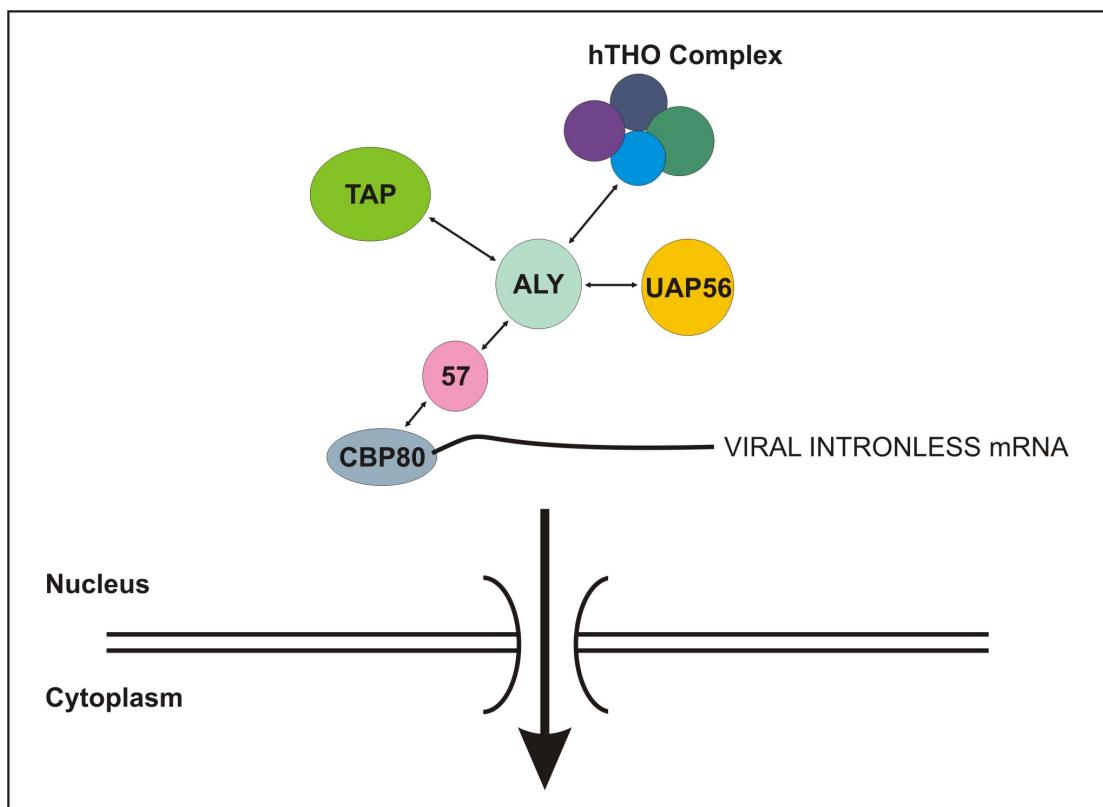
Identification of the ribonucleoprotein complex required for efficient export of herpesvirus intronless mRNAs

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Introduction

The nuclear export of mRNA composes one part of a larger network of molecular events that begin with transcription of the mRNA in the nucleus and end with its translation and degradation in the cytoplasm. During trafficking to the cytoplasm, a nascent mRNA undergoes numerous co-transcriptional processing steps, including 5'-capping, splicing to remove introns and 3'-polyadenylation. Of these events, it has become clear that splicing is particularly important for mRNA nuclear export, as recruitment of multiprotein complexes required for mRNA export are bound to mRNA in a splicing dependent manner. Two multiple protein complexes, namely, hTREX and the EJC bind at separate locations on spliced mRNA. hTREX, which comprises Aly, UAP56 and the multiprotein ThoI complex, is recruited exclusively to the 5'-end of the first exon, providing 5'-polarity and therefore directionality observed in mRNA export.

However, in contrast to the majority of mammalian genes, analysis of herpesvirus genomes has highlighted that most lytically expressed viral genes lack introns. Herpesviruses replicate in the nucleus of the host mammalian cell, and therefore require their intronless mRNAs to be exported out of the nucleus to allow viral mRNA translation in the cytoplasm. This therefore leads to an intriguing question concerning the mechanism by which the viral intronless mRNAs are exported out of the nucleus in the absence of splicing. To circumvent this problem, and to facilitate viral mRNA export, γ -2 herpes viruses encode the ORF 57 protein. ORF 57 interacts with Aly, binds viral RNA, shuttles between the nucleus and the cytoplasm and promotes the nuclear export of viral mRNA.



Assembly of the ribonucleoprotein complex required for efficient export of herpesvirus intronless mRNA

We are currently investigating how an intronless viral mRNP is assembled in KSHV and what role ORF57 plays in that process. We have shown that ORF57 interacts with hTREX and is essential for the recruitment of hTREX onto intronless viral mRNA transcripts. Importantly, ORF57 does not recruit the EJC to intronless viral transcripts. Moreover, we are currently determining how ORF 57 recognises the viral mRNA and allows recruitment of hTREX. This is the first system that has distinguished between hTREX and EJC *in vivo* and demonstrates that recruitment of hTREX alone to mRNA transcripts is sufficient for their nuclear export. Therefore, we believe this viral system is an exciting model to further study mRNA export mechanisms. We propose a model for herpesvirus mRNA export, whereby ORF57 mimics splicing in order to recruit the mRNA export machinery to intronless viral mRNAs.

Publications

Williams, B., Boyne, J.R., Goodwin, D.J., Roaden, L.R., Wilson, S.A. & Whitehouse, A. (2005). The prototype gamma-2 herpesvirus nucleocytoplasmic shuttle protein, ORF 57, transports viral RNA via the cellular mRNA export pathway. *Biochemical Journal*, **387**, 295-308.

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