

Papers of the Week

Trans-splicing Promotes Translation ♦

Many organisms use trans-splicing to join two separately transcribed RNAs. In spliced leader (SL) trans-splicing, a 22-bp leader sequence with a 2,2,7-trimethylguanosine (TMG) cap (rather than the usual monomethylguanosine (m^7G) cap) is joined to the 5' end of another RNA molecule to form a mature mRNA with an unusual cap structure. The nematode *Caenorhabditis elegans* uses two types of spliced leader sequences, SL1 and SL2. The major function of SL2 trans-splicing is to resolve polycistronic transcripts into functional monocistronic mRNAs. However, up until now, the functional significance of SL1 addition was unknown.

To study the effects of SL1 trans-splicing on translation, Sabbi Lall and colleagues designed a cell-free translation system using embryonic extracts from the nematode *Ascaris suum*. Using this system, the investigators found that addition of either the TMG-cap or SL1 sequence alone has a detrimental effect on protein synthesis, but together they promote translation of mRNA. Lall *et al.* also discovered that the *Ascaris* initiation factor eIF4E-3 can bind to both TMG and m^7G -capped RNA and that the SL sequence tends to trans-splice close to the start codon in a diversity of nematode species. From their data, the authors propose that trans-splicing of the SL1 leader sequence may aid in generation of an optimal 5'-UTR length as well as provide a specific sequence context for translation of TMG-capped transcripts. This work strongly supports the notion that the cap structure, the spliced leader, and the spacing to the start codon are all important determinants of nematode translation efficiency.

♦ See referenced article, *J. Biol. Chem.* 2004, **279**, 45573–45585

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