

Summary for general public

tRNAs are RNA adaptor molecules composed of 76-90 nucleotides that serve as physical links between mRNA and the amino acid sequence of proteins. They have a very specific secondary structure, often referred to as a "cloverleaf." Unique structural features are conserved in tRNAs in order for recognition their cognate tRNA synthetases to aminoacylate given tRNA with the specified amino acid corresponding to its anticodon. All tRNAs have an L-shaped tertiary structure that allows them to fit ribosome binding sites.

Beyond canonical tRNAs, a number of larger RNAs contain so-called "tRNA-like structures," defined either as RNA that have a secondary or tertiary structure that closely resembles the canonical features of tRNA or an RNA that interacts with one or more tRNA-specific enzymes. tRNA-like structures have been identified in eukaryotic mRNAs and lncRNAs, including introns and regulatory regions. tRNA-like structures are parts of longer polymerase II transcripts whereas nuclear tRNA genes are transcribed by RNA polymerase III. Primary tRNA transcripts undergo maturation beginning at removal of the 5' leader sequence that is catalyzed by RNase P. Several tRNA-like structures with regulatory potential have been reported in the literature as RNase P substrates.

RNA polymerase III activity is under the control of Maf1 protein, a general negative regulator that is conserved in eukaryotes from yeast to humans. Maf1 suppresses canker development in citrus plants and functions as a tumor suppressor in humans. Studies of the control of Maf1 activity have focused on Maf1 phosphorylation that is mediated by cell signaling and the mode of Maf1 interaction with the Pol III complex. Under repressive conditions, dephosphorylated Maf1 binds to Pol III and impairs the recruitment of Pol III to a DNA promoter. Unique properties of repression by Maf1 in human cells have been recently deciphered by resolving the RNA polymerase III structure at the atomic level.

Here, we focus on the regulation of *MAF1* gene expression by using yeast *Saccharomyces cerevisiae* as a model eukaryotic organism. *MAF1* is among 5% of the yeast genes that contain introns. Immediately downstream of the 3' splice site in the second exon of *MAF1*, we identified a tRNA-like structure. Because Maf1 controls tRNA transcription, the tRNA-like structure could be potentially used for competitive feedback regulation using tRNA identity rules. The planned experiments in this proposal address the potential regulatory effect of a tRNA-like sequence in terms of *MAF1* mRNA cleavage by RNase P, intron excision and Maf1 translation. The regulatory mechanism that we plan to decipher is possibly conserved in eukaryotes because the tRNA-like sequence has been identified in the intron of the *MAF1* gene from *Arabidopsis* plant.