

Ribosomes are versatile molecular machines tasked with decoding the genetic information encoded within mRNAs. High-resolution structural models of ribosomes portray the view that these splendid machines are homogeneous and unchanging entities. However, recent data challenge this view. In fact, emerging evidence suggest that the translation machinery is manifestly changeable, and ribosomal RNA and proteins could be dynamically altered post-transcriptionally to fine-tune translational efficiency in response to changing cellular needs. Furthermore, a diverse and growing set of accessory proteins, chaperones, enzymes, and surveillance factors are specifically recruited to the ribosome to ensure optimal efficiency and fidelity of the translation process. We have endeavored to shed new light on a fascinating ribosome quality control system that involves a versatile RNA, tmRNA, endowed with the combined structural and functional properties of a tRNA and an mRNA. In association with SmpB, its essential protein co-factor, tmRNA orchestrates a unique process called *trans*-translation, whereby alanine-charged tmRNA engages the stalled ribosome and acts as a tRNA to transfer the incomplete nascent polypeptide to itself. The tmRNA-engaged ribosome switches its mRNA template and resumes translation, in *trans*, on a short open reading frame encoded by tmRNA. Translation terminates on a stop codon provided by the mRNA-like segment of tmRNA, enabling ribosome rescue and recycling of the translation machinery. The ribosome-associated nascent polypeptide is thus appended with a short 11-residue tag, or degron, which targets it for degradation by C-terminus-specific proteases. I will discuss our recent efforts in deciphering when and how tmRNA-tagged proteins are captured and what roles tmRNA and the translation machinery play in the selective capture and guided proteolysis of marked proteins.