# Biosynthesis and function of 1-methyladenosine in transfer RNA

James T. Anderson and Louis Droogmans

## Abstract

Determining the function of single nucleotide modifications in tRNA has been elusive because so many tRNA modification enzymes are not essential for cell viability, making it difficult to do functional studies *in vivo*. The enzyme that catalyzes the formation of 1-methyladenosine modification at position 58 ($m^1A58$) in most yeast tRNAs is essential for yeast cell viability, which has made it possible to explore the role of this single modification in tRNA structure and function. In addition to reviewing the role of $m^1A$ in tRNAs from prokaryotes to eukaryotes and mitochondria to cytoplasm, this chapter discusses the importance of $m^1A58$ in maintaining the 3-dimensional structure of yeast initiator $tRNA^{Met}$. Exploiting the genetics available in yeast, it has been discovered that initiator $tRNA^{Met}$ lacking $m^1A58$ is eliminated from cells by 3' polyadenylation and 3' to 5' exonuclease degradation.

## 1 Introduction

The free base, 1-methyladenine, was identified 43 years ago (Dunn 1961), and shortly following its discovery, the 1-methyladenosine mononucleotide was purified from RNA (Dunn 1963). The first demonstration of 1-methyladenosine ($m^1A$) in tRNA came after purification and sequence determination of $tRNA^{Phe}$ from yeast (RajBhandary et al. 1966); nearly four decades later the number of tRNAs known to possess $m^1A$ stands at 264 out of 564 tRNA sequences (Sprinzl et al. 1998). The reported positions of $m^1A$ in tRNA are 9, 14, 22, (57 transiently) and 58, with the major proportion of the 264 tRNAs containing $m^1A$ at position 58 in the TΨC loop (Fig. 1). The significance of $m^1A$ modification at this position is underscored by its occurrence in tRNAs from the three domains of life (Bacteria, Archaea, and Eukaryota). The postulate which has emerged from this knowledge is that $m^1A$ is a primordial RNA modification that plays a significant role in tRNA function and or structure (Björk 1995). In support of this, $m^1A$ being one of a few methylated nucleosides bearing a positive electrostatic charge (together with 7-methylguanosine and 3-methylcytidine), indicates that it could make a significant contribution to tRNA structure stability through an electro-chemical interaction, reviewed in (Agris 1996). The goal of this review is to summarize what is known

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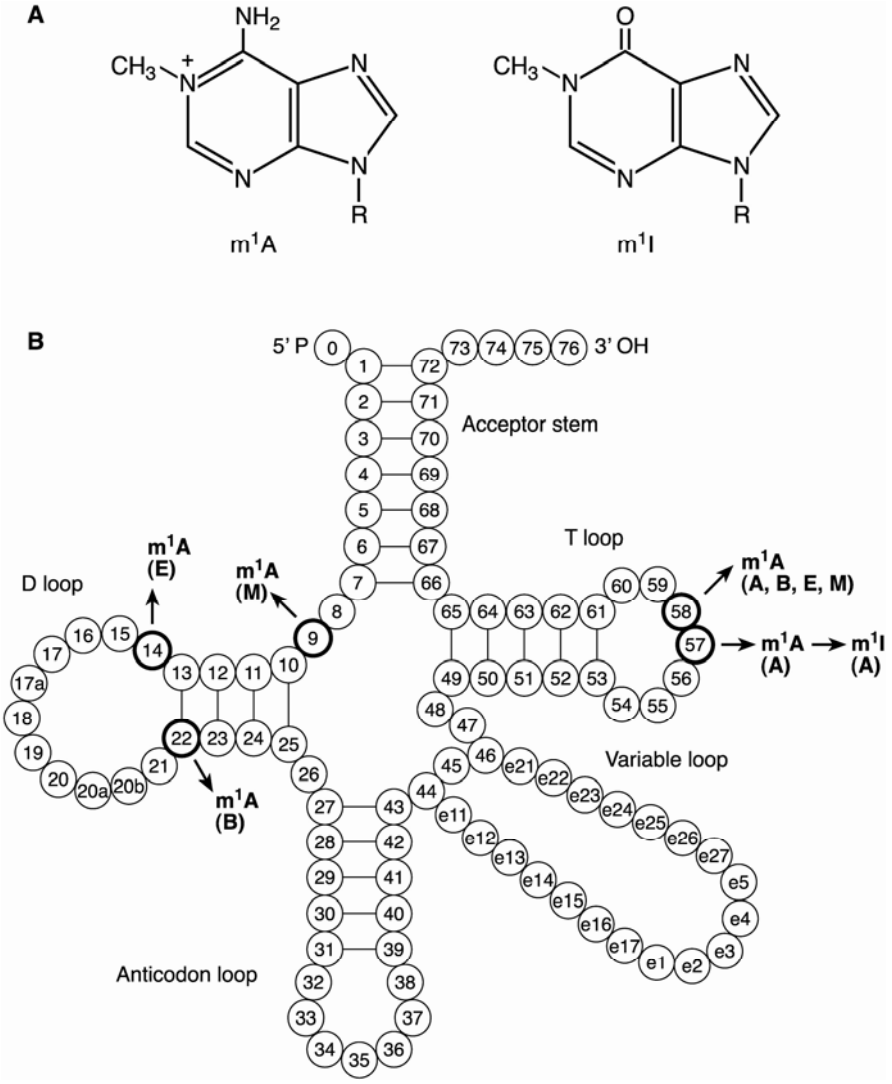


**Fig. 1.** Location of 1-methyladenosine ($m^1A$) in tRNA from the three domains of life. A. Formula of $m^1A$ and 1-methylinosine ($m^1I$), the deamination product of $m^1A$. R represents ribose. B. Cloverleaf structure of tRNA with the occurrence and positions of $m^1A$. The letters A, B, and E refer to the three domains of life (A, Archaea; B, Bacteria; E, Eukaryota), while M refers to mitochondria. $m^1A$ has not been detected in any sequenced chloroplast tRNAs. $m^1A57$ is the intermediate in $m^1I57$ formation in archaeal tRNAs.

about the function of $m^1A$ in tRNA and to highlight interesting questions that remain unanswered about $m^1A$ and its role in tRNA function with particular attention being paid to recent genetic studies in yeast.