Abstract

The N6-methylation of adenosine (m^6A) is the most abundant modification in eukaryotic mRNA. This modification is deposited on RNA co-transcriptionally by the methyltransferase complexes and can also be "erased" by specific demethylases. The existence of m^6A demethylases makes the modification reversible and potentially dynamic, therefore, m^6A could have a function in gene expression regulation. Since the discovery of the first m^6A demethylase FTO, the m^6A has become a hot-topic in RNA-biology research. m^6A is found in mRNAs but also in various non-coding RNAs. Analysis of m^6A distribution on mRNAs revealed the enrichment of m^6A in proximity of a stop codon, in 3' UTRs and possibly around 5' and 3' splice-sites. So far two m^6A methyltransferases have been discovered in vertebrates, METTL3/METTL14 complex is the major methyltransferase and METTL16 deposits m^6A just on a specific subset of RNAs. Additionally, two m^6A demethylases are known – FTO and ALKBH5. Finally, members of protein family with a so-called YTH RNA binding domain were identified as m^6A binding proteins. m^6A serves as a signal affecting various steps of RNA metabolism such as mRNA splicing, nuclear export, translation or RNA degradation. Some of the effects are clearly mediated by the m^6A binding proteins, but also other mechanisms can be involved. m^6A presence on RNA can also modify the RNA secondary structure, changing the accessibility of the RNA to various RNA-binding proteins, this regulatory mechanism is called m^6A switch.