N6-methyl-riboadenosine (N6-methyl rA; m6A) is a common, fairly abundant RNA modification found in the mRNA of most eukaryotes (1,2); it has also been observed in tRNA, rRNA snRNA and in long non-coding RNA (3). While the biological importance of this modification remains poorly understood, results from a number of research studies suggest that regulation of m6A levels in mRNA may have significant effects on subsequent gene expression. The modification mainly appears in exons, 3′-UTRs and near stop codons. Within 3′-UTRs, N6-methyl-rA is associated with miRNA binding sites (4). The modification itself is catalyzed by a N6-methyl-rA methyltransferase complex that contains the METTL3 subunit (5). Silencing this methyltransferase dramatically affects N6-methyl-A cellular levels, gene expression and alternative RNA splicing patterns (6). The FTO and ALKBH5 genes, implicated in obesity risk, encode two different N6-methyl-rA demethylases; silencing of FTO with siRNA results in increased levels of N6-methyl-rA in poly(A) RNA (6), while FTO overexpression results in decreased levels (4). Moreover, modulation of the activities of these three enzymes can alter the expression of thousands of genes at the cellular level. This suggests that N6-methyl-rA plays an important role in RNA metabolism and as an epigenetic marker (7).

References