RNA m5C甲基化的研究进展

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Title: Progress in research of RNA m5C methylation

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摘要: RNA 5-甲基胞嘧啶（m5C）甲基化修饰是主要的RNA转录后修饰之一。这种修饰存在于几乎所有类型RNA中，受甲基转移酶、去甲基转移酶及结合蛋白的调控，具有调节核mRNA输出及RNA可变剪切、增加RNA稳定性、调节蛋白质翻译及RNA-蛋白质互相作用、维持RNA正常结构等作用。其水平异常与肿瘤、神经系统缺陷、心血管系统疾病和异常分化等疾病密切相关。为全面了解RNA m5C的研究现状，本文将从RNA m5C的分布特点、调控机制、生物学作用及其与疾病的关系等方面进行综述。

Abstract: RNA m5C methylation modification is one of the major post-transcriptional modifications of RNA and exists in various types of RNA.This modification is present in almost all types of RNA,regulated by methyltransferases,demethyltransferases,and binding proteins.The functions of RNA m5C include regulating nuclear mRNA output and RNA alternative splicing,increasing RNA stability,regulating protein translation and RNA-protein interaction,and maintaining normal RNA structure.The aberrant level of RNA m5C is closely related to tumors,nervous system defects,disease of cardiovascular system and abnormal differentiation.In order to fully understand the research status of RNA m5C,this paper will review the distribution characteristics,regulation mechanism,biological effects of RNA m5C and its relationship with diseases.

参考文献/REFERENCES

[1] Lukas Trixl,Alexandra Lusser.The dynamic RNA modification 5-methylcytosine and its emerging role as an epitranscriptomic mark [J] .PLoS Genet,2013,9(6):e1003602.
[2] Squires JE,Patel HR,Nousch M,et al.Widespread occurrence of 5-methylcytosine in human coding and non-coding RNA [J] .Nucleic Acids Res,2012(40):5023-5033.
[3] Edelheit S,Schwartz S,Mumbach MR.Transcriptome-wide mapping of 5-methylcytidine RNA modifications in bacteria,archaea,and yeast reveals m5C within archaeal mRNAs [J] .PLoS Genet,2013,9(6):e1003602.
[4] Chow CS,Lamichhane TN,Mahto SK.Expanding the nucleotide repertoire of the ribosome with post-transcriptional modifications [J] .ACS Chem Biol,2007 (2) :610-619.
[5] Bujnicki JM,Feder M,Ayres CL,et al.Sequence-structure-function studies of tRNA:m5C methyltransferase Trm4p and its relationship to DNA:m5C and RNA:m5U methyltransferases [J] .Nucleic Acids Res,2004(32):2453-2463.
[6] Liu Y,Santi DV.m5C RNA and m5C DNA methyltransferases use different cysteine residues as catalysts [J] .Proc Natl Acad Sci USA,2000 (97) :8263-8265.
[7] Hussain S,Benavente SB,Nascimento E,et al.The nucleolar RNA methyltransferase Misu (NSun2) is required for mitotic spindle stability [J] .J Cell Biol,2009 (186) :27-40.
[8] Frye M,Watt FM.The RNA methyltransferase Misu (NSun2) mediates Myc-induced proliferation and is upregulated in tumors [J] .Current Biology:CB,2006,16(10):971-981.
[9] Hong B,Brockenbrough JS,Wu P,et al.Nop2p is required for pre-rRNA processing and 60S ribosome subunit

synthesis in yeast [J] .Mol Cell Biol,1997 (17) :378-388.
[10] Nakano S,Suzuki T,Kawarada L,et al.NSUN3 methylase initiates 5-formylcytidine biogenesis in human mitochondrial tRNA(Met) [J] .Nat Chem Biol,2016 (12) :546-551.
[11] Metodiev MD,Spahr H,Loguercio Polosa P,et al.NSUN4 is a dual function mitochondrial protein required for both methylation of 12S rRNA and coordination of mitoribosomal assembly [J] .PLoS Genet,2014 (10) :e1004110.
[12] Camara Y,Asin-Cayuela J,Park CB,et al.MTERF4 regulates translation by targeting the methyltransferase NSUN4 to the mammalian mitochondrial ribosome [J] .Cell Metab,2011 (13) :527-539.
[13] Schosserer M,Minois N,Angerer TB,et al.Methylation of ribosomal RNA by NSUN5 is a conserved mechanism modulating organismal lifespan [J] .Nat Commun,2015 (6) :6158.
[14] Haag S,Warda AS,Kretschmer J,et al.NSUN6 is a human RNA methyltransferase that catalyzes formation of m5C72 in specific tRNAs [J] .RNA,2015 (21) :1532-1543.
[15] Aguilo F,Li S,Balasubramaniyan N,et al.Deposition of 5-methylcytosine on enhancer RNAs enables the coactivator function of PGC-1α [J] .Cell Rep,2016 (14) :479-492.
[16] Goll MG,Kirpekar F,Maggert KA,et al.Methylation of tRNAAsp by the DNA methyltransferase homolog Dnmt2 [J] .Science,2006 (311) :395-398.
[17] Fu L,Guerrero CR,Zhong N,et al.Tet-mediated formation of 5-hydroxymethylcytosine in RNA [J] .J Am Chem Soc,2014 (136) :11582-11585.
[18] Yang X,Yang Y,Sun BF,et al.5-methylcytosine promotes mRNA export - NSUN2 as the methyltransferase and ALYREF as an m5C reader [J] .Cell Res,2017,27(5):606-625.
[19] Zhang X,Liu Z,Yi J,et al.The tRNA methyltransferase NSun2 stabilizes p16INK4 mRNA by methylating the 3′-untranslated region of p16 [J] .Nat Commun,2012(3):712.
[20] SUN Huiying,HAO Yajuan,PING Xiaoli,et al.Research progress in dynamic RNA methylation modification and its regulation mechanism [J] .Life Science,2016,28(5):540-550. [孙慧颖,郝亚娟,平晓丽,等.动态RNA甲基化修饰及其调控机制研究进展 [J] .生命科学,2016,28(5):540-550.]
[21] Hoernes TP,Clementi N,Faserl K,et.al.Nucleotide modifications within bacterial messenger RNAs regulate their translation and are able to rewire the genetic code [J] .Nucleic Acids Research,2016,44(2):852-862.
[22] Agris PF.Bringing order to translation:The contributions of transfer RNA anticodon-domain modifications [J] .EMBO Rep,2008(9):629-635.
[23] Lukas Trixl, Alexandra Lusser.The dynamic RNA modification 5-methylcytosine and its emerging role as an epitranscriptomic mark [J] .PLoS Genet,2013,9(6):e1003602.
[24] Chernyakov I,Whipple JM,Kotelawala L,et al.Degradation of several hypomodified mature tRNA species in Saccharomyces cerevisiae is mediated by Met22 and the 5′-3′ exonucleases Rat1 and Xrn1 [J] .Gene Dev,2008(22):1369-1380.
[25] Shanmugam R,Fierer J,Kaiser S,et al.Cytosine methylation of tRNA-asp by DNMT2 has a role in translation of proteins containing poly-asp sequences [J] .Cell Discovery,2015(1):15010.
[26] Schaefer M,Pollex T,Hanna K,et al.RNA methylation by Dnmt2 protects transfer RNAs against stress-induced cleavage [J] .Genes and Development,2010,24(15):1590-1595.
[27] Tuorto F,Liebers R,Musch T,et al.RNA cytosine methylation by Dnmt2 and NSun2 promotes tRNA stability and protein synthesis [J] .Nature Structural & Molecular Biology,2012,19(9):900-905.
[28] Tuorto F,Herbst F,Alerasool N,et al.The tRNA methyltransferase Dnmt2 is required for accurate polypeptide synthesis during haematopoiesis [J] .The EMBO Journal,2015,34(18):2350-2362.
[29] Haag S,Warda AS,Kretschmer J,et al.NSUN6 is a human RNA methyltransferase that catalyzes formation of m5C72 in specific tRNAs [J] .RNA (New York,NY),2015,21(9):1532-1543.
[30] Sharma S,Lafontaine DLJ."View from a bridge":A new perspective on eukaryotic rRNA base modification [J] .Trends in Biochemical Sciences,2015,40(10):560-575.
[31] Amort T,Soulieere MF,Wille A,et al.Long non-coding RNAs as targets for cytosine methylation [J] .RNA Biology,2013,10(6):1003-1008.
[32] Amort T,Rieder D,Wille A,et.al.Distinct 5-methylcytosine profiles in poly(A) RNA from mouse embryonic stem cells and brain [J] .Genome Biology,2017,18(1):1.
[33] David R,Burgess A,Parker B,et al.Transcriptome-wide mapping of RNA 5-Methylcytosine in Arabidopsis mRNAs and non-coding RNAs [J] .The Plant Cell,2017,29(3):445-460.
[34] Khan MA,Rafiq MA,Noor A,et al.Mutation in NSUN2,which encodes an RNA methyltransferase,causes autosomal-recessive intellectual disability [J] .American Journal of Human Genetics,2012.90(5):856-863.
[35] Flores JV,Cordero-Espinoza L,Oeztuerk-Winder F,et al.Cytosine-5 RNA methylation regulates neural stem cell differentiation and motility [J] .Stem Cell Reports,2017,8(1):112-124.
[36] Trixl L,Amort T,Wille A,et al.RNA cytosine methyltransferase Nsun3 regulates embryonic stem cell differentiation by promoting mitochondrial activity [J] .Cellular and Molecular Life Sciences:CMLS,2018,75(8):1483-1497.
[37] Luo Y,Feng J,Xu Q,et al.NSun2 deficiency protects endothelium from inflammation via mRNA methylation of ICAM-1 [J] .Circulation Research,2016,118(6):944-956.
[38] Ghanbarian H,Wagner N,Polo B,et al.Dnmt2/Trdmt1 as mediator of RNA polymerase II transcriptional activity in cardiac growth [J] .PLoS One,2016,11(6):e0156953.
[39] Harris T,Marquez B,Suarez S,et al.Sperm motility defects and infertility in male mice with a mutation in Nsun7,a member of the sun domain-containing family of putative RNA methyltransferases [J] .Biology of

Reproduction,2007,77(2):376-382.
[40] Jhiang SM,Yaneva M,Busch H.Expression of human proliferation-associated nucleolar antigen p120 [J] .Cell Growth & Differentiation,1990, 1(7):319-324.
[41] Li C,Wang S,Xing Z,et.al.A ROR1-HER3-lncRNA signalling axis modulates the Hippo-YAP pathway to regulate bone metastasis [J] .Nature Cell Biology,2017,19(2):106-119.

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