核酸表观遗传修饰和检测技术

翁小成

武汉大学 化学与分子科学学院

核酸化学生物学研究团队 （周翔 教授）

2019年07月27日

液体活检与基因检测

RESEARCH ARTICLE

HUMAN GENETICS

RNA sequence analysis reveals macroscopic somatic clonal expansion across normal tissues

Keren Yizhak[1], François Aguet[1], Jaegil Kim[1], Julian M. Hess[1], Kirsten Kübler[1,2,3], Jonna Grimsby[1], Ruslana Frazer[1], Hailei Zhang[1], Nicholas J. Haradhvala[1,2], Daniel Rosebrock[1], Dimitri Livitz[1], Xiao Li[1], Eila Arich-Landkof[1,2], Noam Shoresh[1], Chip Stewart[1], Ayellet V. Segrè[1,3,4], Philip A. Branton[5], Paz Polak[6], Kristin G. Ardlie[1], Gad Getz[1,2,3,7*]

正常细胞存在大量的基因突变（衰老，环境……），仅部分与癌症相关

基于突变的液体活检技术

Science, **2019**, *364*, eaaw0726, 07 Jun

nature
International journal of science

Letter | Published: 14 November 2018

Sensitive tumour detection and classification using plasma cell-free DNA methylomes

Shu Yi Shen, Rajat Singhania, […] Daniel D. De Carvalho

cfMeDIP–seq：

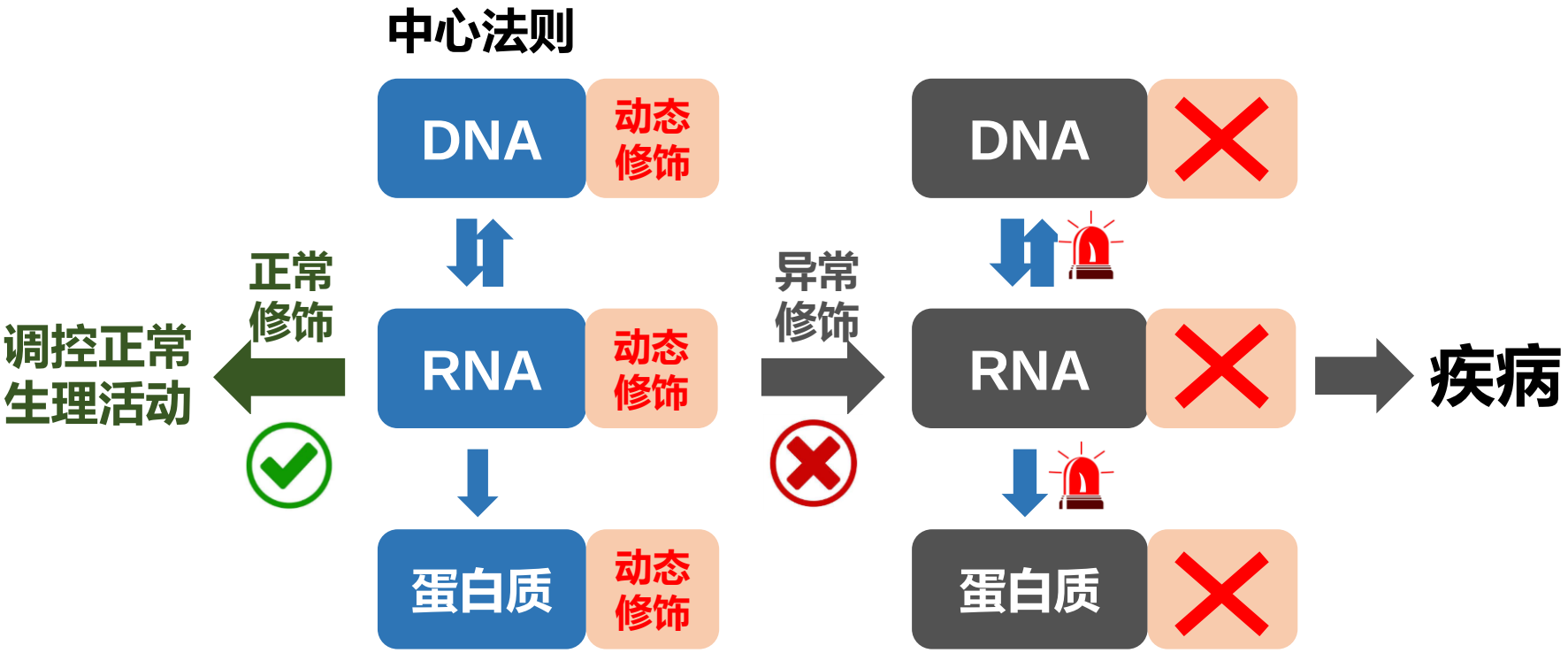
cell-free methylated DNA immunoprecipitation and high-throughput sequencing

cfDNA上的甲基化水平，因为在肿瘤中，DNA甲基化水平会发生显著的变化

基于核酸表观修饰的液体活检技术

Nature, **2018**, *563*, 579-583

表观遗传修饰



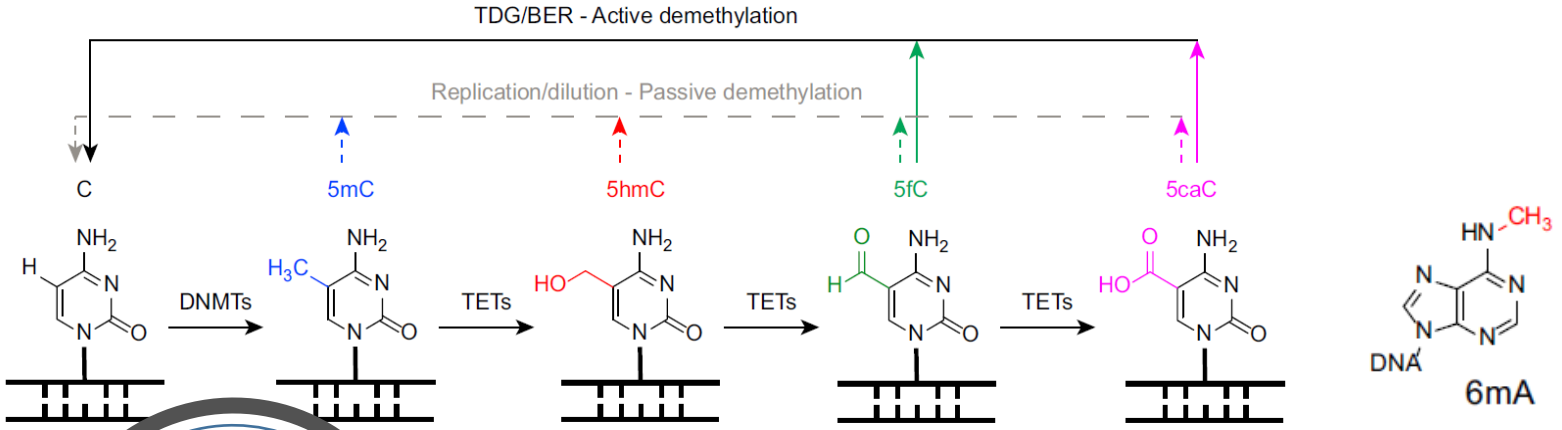
生物大分子动态修饰 ⟺ **早期诊断 疾病治疗**

Chem. Soc. Rev., **2017**, 46, 2844

核酸表观遗传修饰

DNA

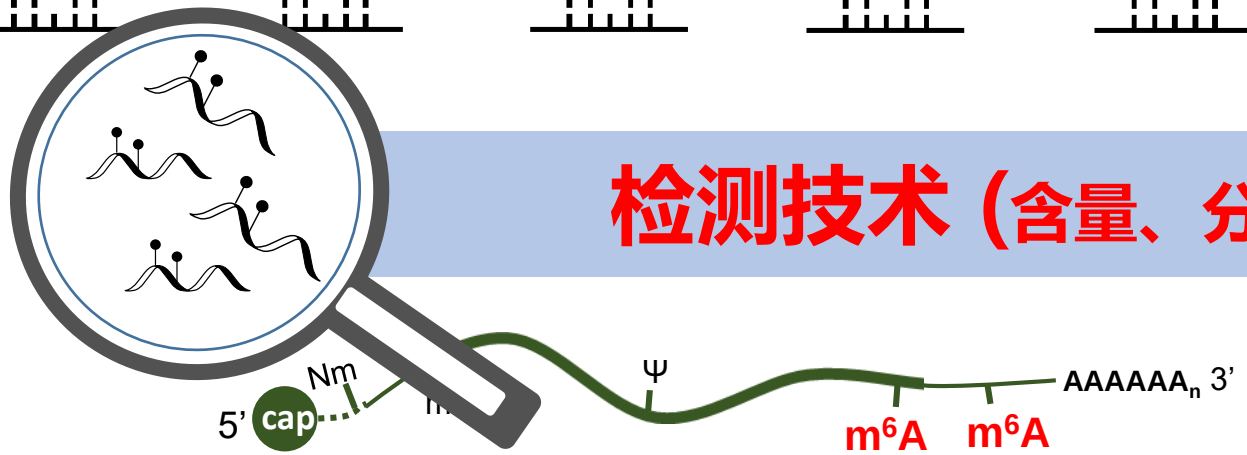
动态修饰

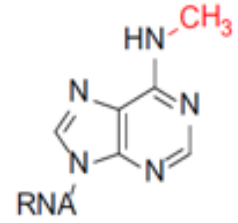


检测技术（含量、分布）

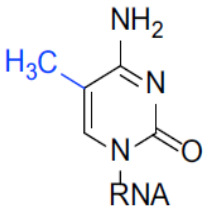
RNA

动态修饰

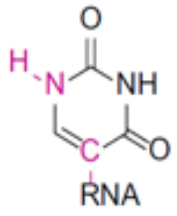




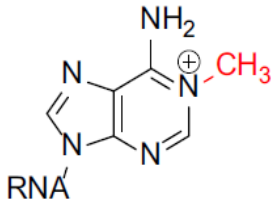
N^6-methyladenosine
m^6A



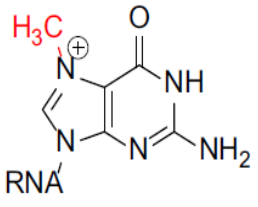
5-methylcytidine
m^5C



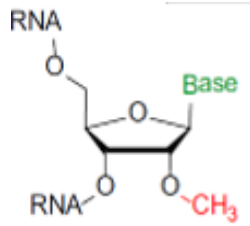
Pseudouridine
Ψ



N^1-methyladenosine
m^1A



N^7-methylguanosine
m^7G



2’-O-methyl
Nm

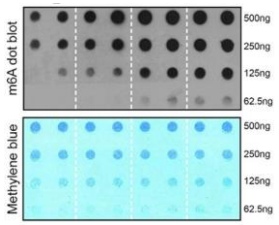
Cell Chem. Biol. **2016**, *23*, 74; *Curr. Opin. Chem. Biol.* **2016**, *30*, 46.

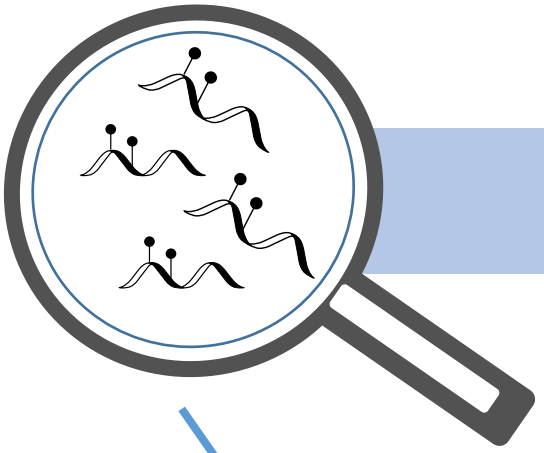
核酸表观遗传修饰

整体含量检测

LC-MS联用

Dot blot
(斑点杂交)





检测技术（含量、分布）

修饰分布检测

全基因组/转录组谱图绘制

目标基因内含量和分布检测

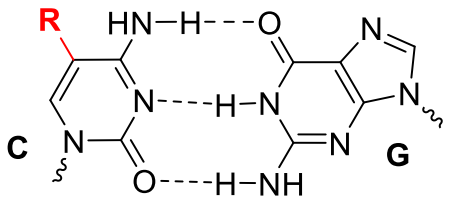
扩增技术

表观遗传扩增技术与常规核酸扩增技术

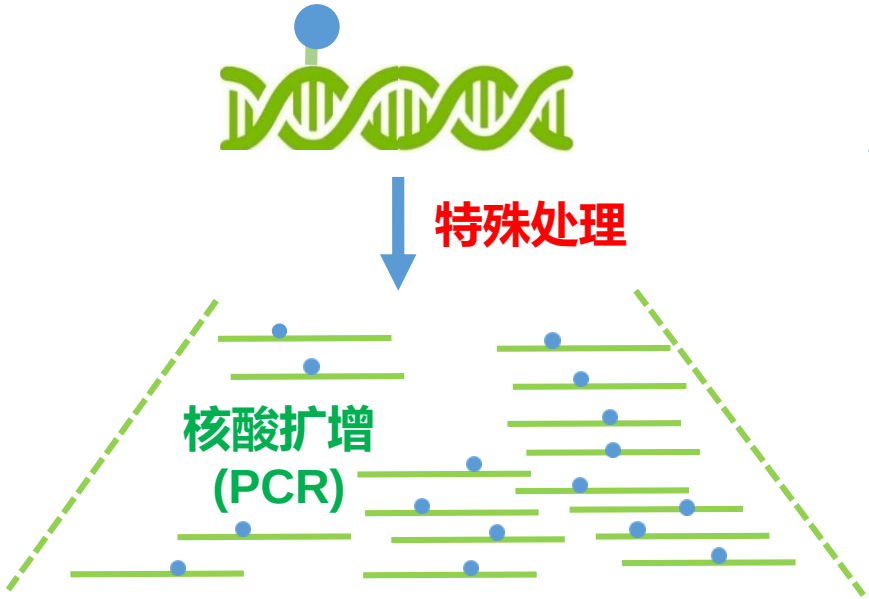
问题：核酸表观修饰碱基的信息扩增过程中丢失

1、修饰基团不在氢键配对位置

2、DNA修饰基团一般较小



R= CH_3, CH_2OH, CHO, COOH



方案：通过前期处理保留修饰碱基信息

+

高通量扩增技术

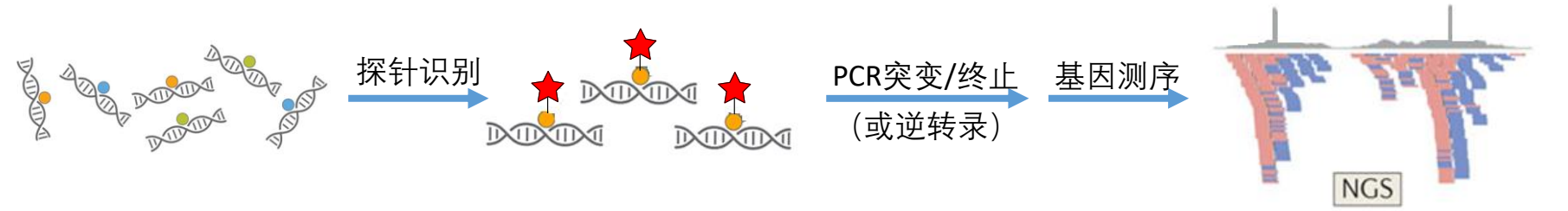
||

核酸表观遗传检测技术

抗体技术 VS 化学技术

抗体免疫沉淀技术	**优点：** • 生物相容性	**缺点：** • 分辨率低（>100bp） • 效率和重现性低 • 昂贵

小分子探针技术	**优点：** • 可达到单碱基分辨率 • 成本低廉，探针稳定	**缺点：** 难以得到高特异性、生物相容性探针分子

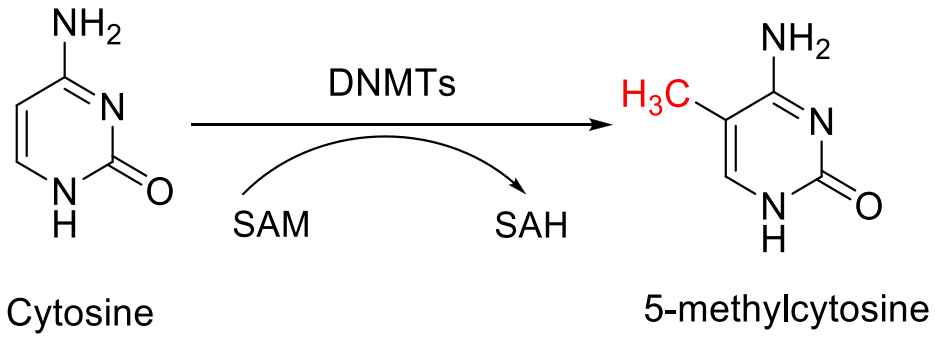


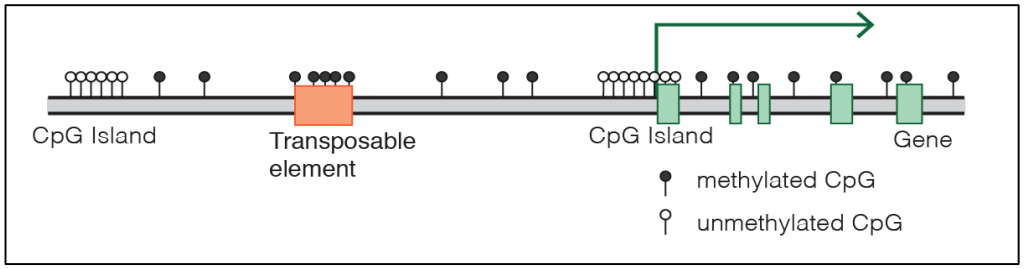
核酸表观遗传修饰

DNA	RNA
5mC	m6A
5hmC	m1A
5fC	PseudoU
5caC	Nm
6mA	m5C
5fU	hm5C
5hmU	m6Am
……	……
特点：主动修饰，调控基因表达	

核酸损伤：被动修饰，造成基因组不稳定和错误表达

DNA 甲基化 5-甲基胞嘧啶(5mC)





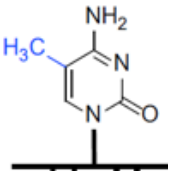
- **DNA甲基转移酶：**

  DNMT3A, DNMT3B, DNMT3L
- **DNA甲基化结合蛋白：MeCP2, MBD1-4**
- **DNA擦除蛋白：TET家族蛋白**

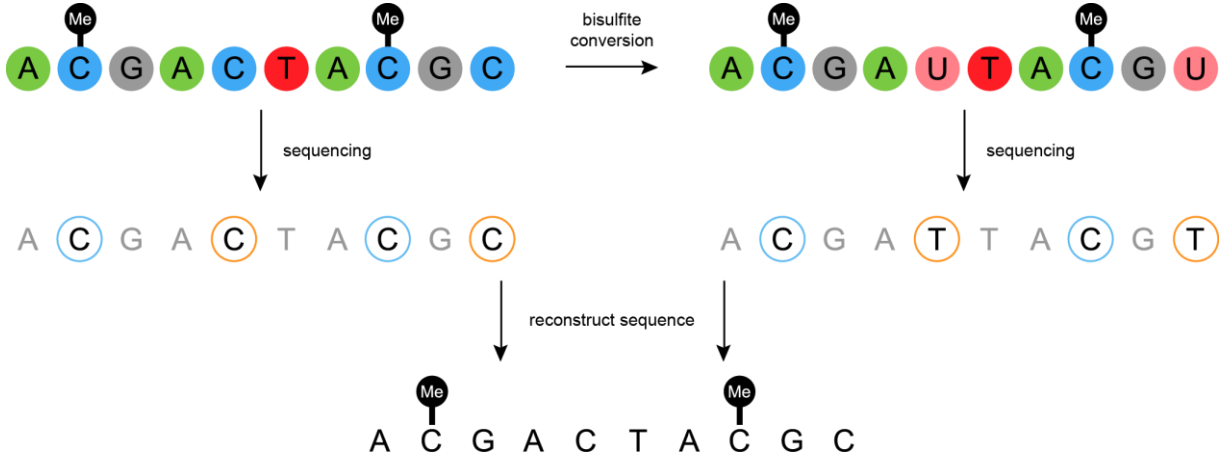
癌症
阿尔兹海默症
AD
糖尿病
肥胖
……

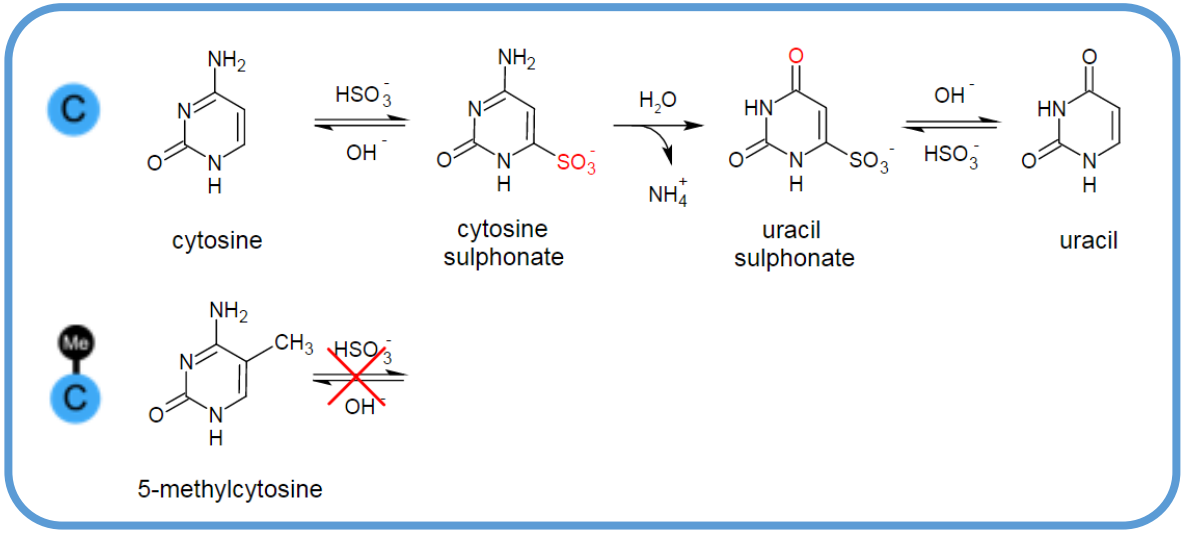
Nat. Rev. Genet. **2012**, *13*, 484; *Nat. Rev. Genet.* **2008**, *9*, 465; *Chem. Soc. Rev.* **2017**, 46, 2844.

DNA 5mC seq



- **化学转化法**: 亚硫酸氢钠转化法 (bisulfite conversion, BS-seq)

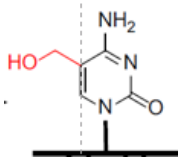




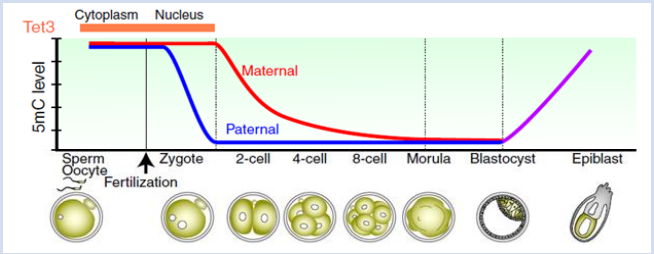
- **限制性内切酶法:**
  HpaII / MspI
- **甲基化DNA富集技术:**
  5-mC 抗体 or_甲基结合蛋白

Nucleic Acids Res. **1994**, *22*, 2990

DNA 5-羟甲基胞嘧啶(5hmC)的发现



问题重重



胚胎分化过程中，基因组DNA甲基化**短时间内**需要经历重塑 (清洗、重建) 过程

DNA去甲基化酶?

群雄逐鹿

nature
International journal of science

Article | Published: 18 February 1999

A mammalian protein with specific demethylase activity for mCpG DNA

Sanjoy K. Bhattacharya, Shyam Ramchandani, Nadia Cervoni & Moshe Szyf

Nature **397**, 579–583 (18 February 1999) | Download Citation

探索中.....

Cell

Leading Edge

Minireview

The Colorful History of Active DNA Demethylation

Steen K.T. Ooi[1] and Timothy H. Bestor[1,*]
[1]Department of Genetics and Development, College of Physicians and Surgeons of Columbia University,
*Correspondence: thb12@columbia.edu
DOI 10.1016/j.cell.2008.06.009

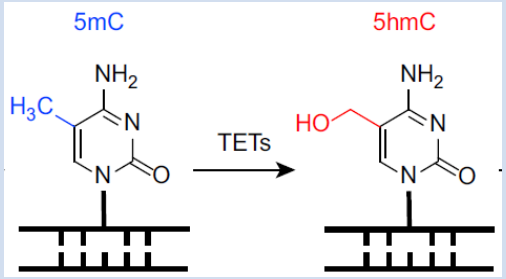
水落石出

The Nuclear DNA Base 5-Hydroxymethylcytosine Is Present in Purkinje Neurons and the Brain

Skirmantas Kriaucionis and Nathaniel Heintz*

Conversion of 5-Methylcytosine to 5-Hydroxymethylcytosine in Mammalian DNA by MLL Partner TET1

Mamta Tahiliani,[1] Kian Peng Koh,[1] Yinghua Shen,[2] William A. Pastor,[1] Hozefa Bandukwala,[1] Yevgeny Brudno,[2] Suneet Agarwal,[3] Lakshminarayan M. Iyer,[4] David R. Liu,[2]* L. Aravind,[4]* Anjana Rao[1]*

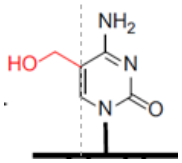


Science, **2009**, 929-930
Science, **2009**, 930-935

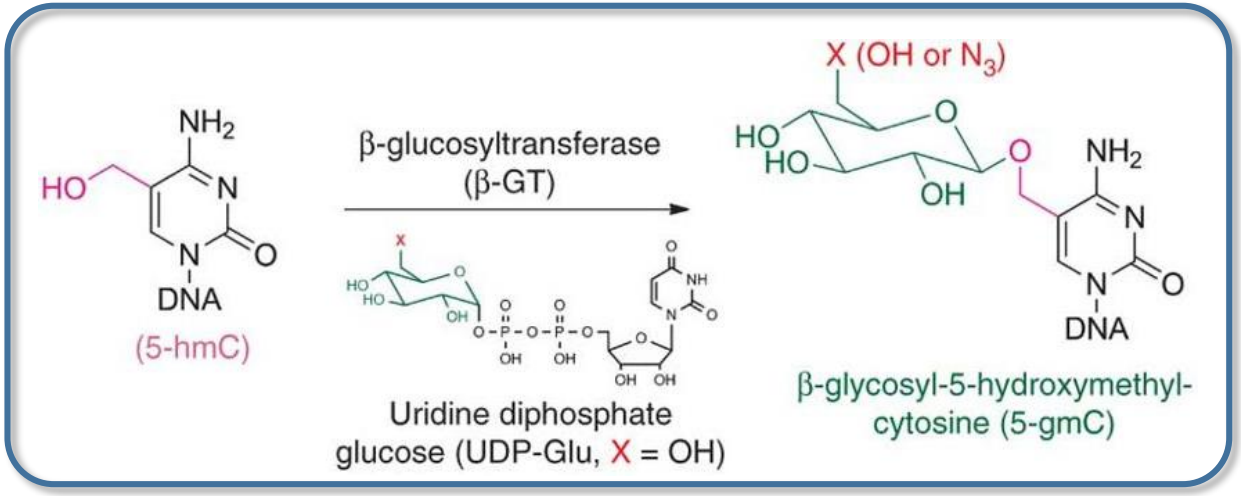
5hmC工作:

Nature 18 Jul 2010; *Nature* 30 Mar 2011; *Nature* 03 Apr 2011; *Nature* 13 April 2011; *Cell* 14 April 2011

DNA 5hmC-seq

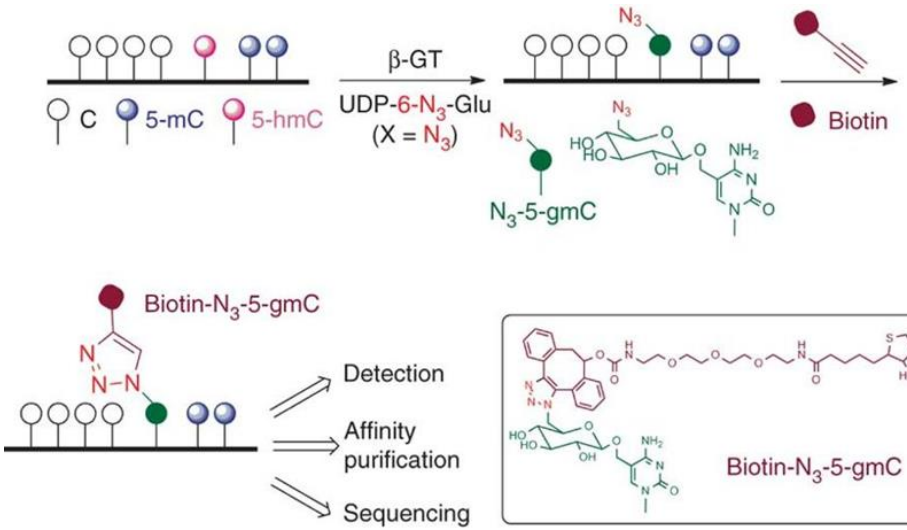


- 通过β-GT/UDP-N_3-Glu选择性修饰5hmC



芝加哥大学
何川教授

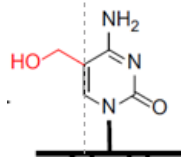
- 5hmC富集检测技术



Nat. Biotechnol. **2011**, *29*, 68-72.

Cell Res. **2018,** *25*, 597-600
Cell Res. **2017**, *27*, 1243-1257
Mol. Cell **2016**, *63*, 711-719
Cell. **2014**, *157*, 979-991
Cell. **2013**, *153*, 773-784
Nat. Protoc. **2012**, *7*, 2159-2170
Cell **2012**, *149*, 1368-1380
Nat. Methods. **2011**. *9*, 75-77.

DNA 5hmC-seq – 单碱基分辨率



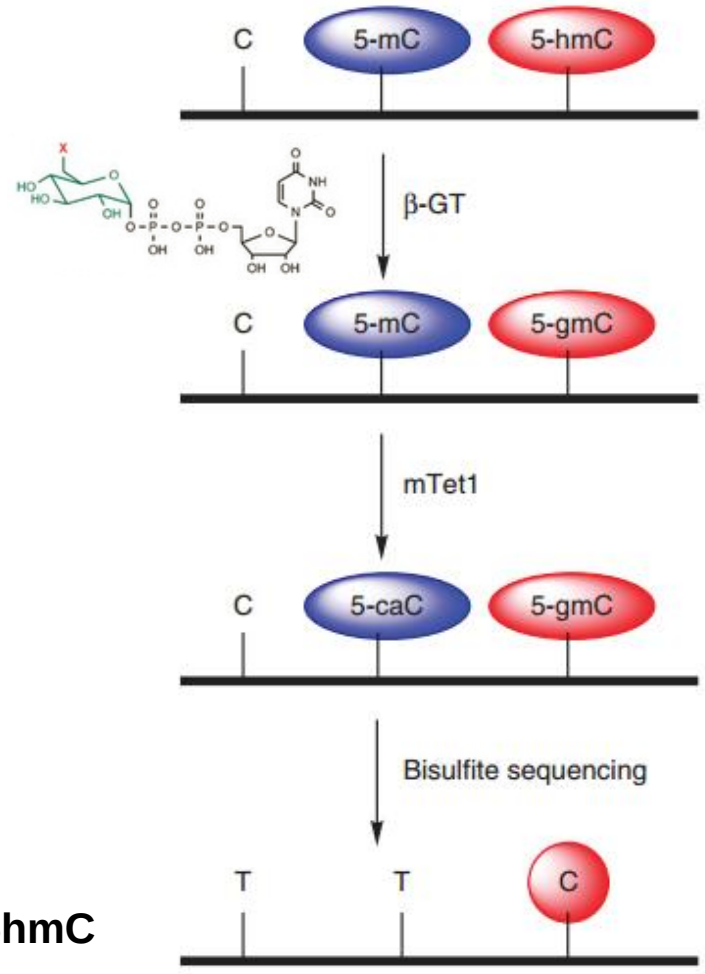
	C	5mC	5hmC	5fC	5caC
测序	C	C	C	C	C
BS-seq	U	C	C	U	U

TAB-Seq

Step 1:
保护5hmC

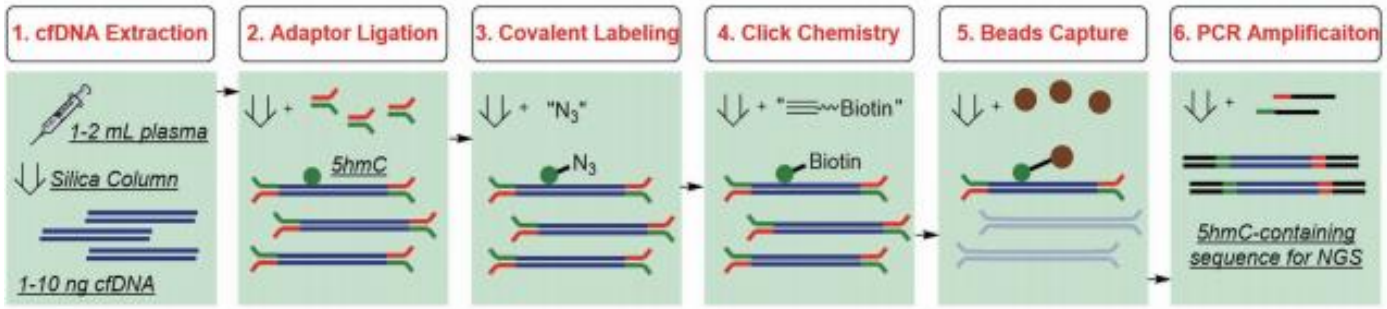
Step 2:
氧化5mC成5caC，
5hmC不受影响

Step3:
BS-seq区分5mC和5hmC



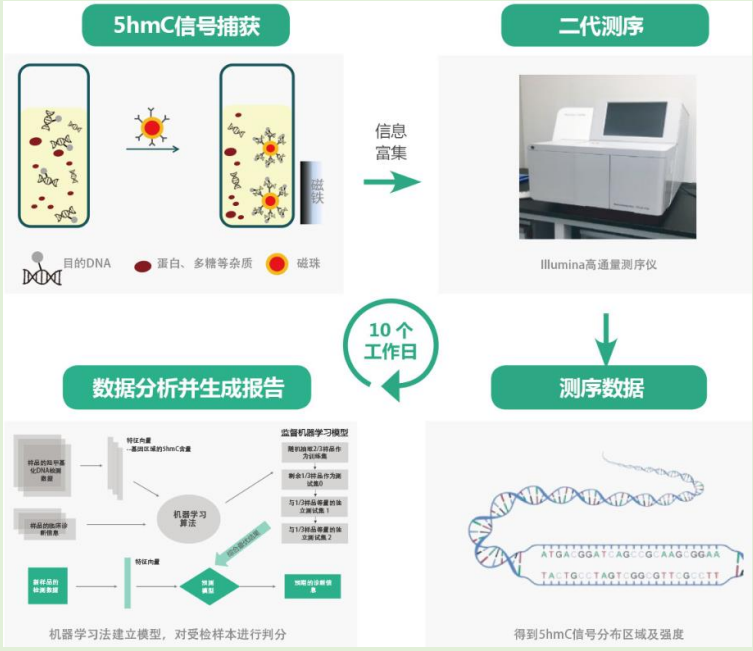
Nat. Protoc. **2012**, *7*, 2159-2170
Cell. **2012**, *149*, 1368-1380

DNA 5hmC-seq

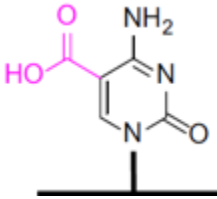


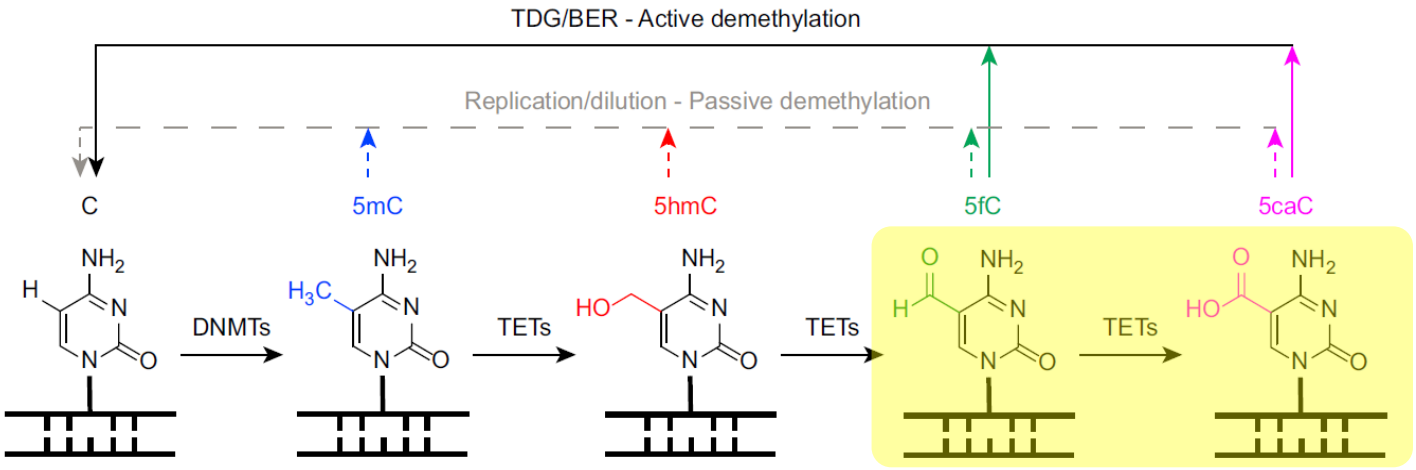
Mol. Cell **2016**, *63*, 711-719; *Cell Res.* **2017**, *27*, 1243-1257

5hmC优势：1. 相对5mC信息更集中，背景更低； 2. 技术稳定，条件温和



DNA 5-醛基胞嘧啶 (5fC)，5-羧基胞嘧啶 (5caC)





DNA主动去甲基化过程 → **新碱基 5fC & 5caC** → **难点 丰度低**

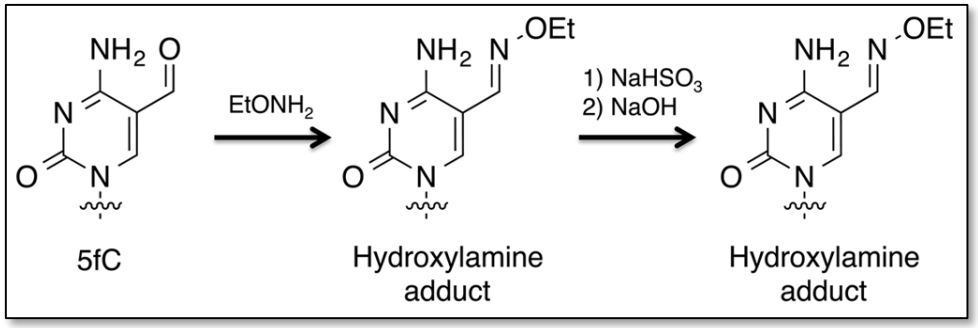
Modification	Tissues and cell lines	Relative abundance
5hmC	Mouse ESC	0.1% of cytosine
	Mouse brain tissue	0.4~0.7% of cytosine
	Other mouse tissues	0.02~0.3% of cytosine
	Human cancer cells	0.03~0.1% of guanine
5fC	Mouse ESC	20 ppm of cytosine
	Mouse tissues	3-20 ppm of cytosine
5caC	Mouse ESC	3 ppm of cytosine

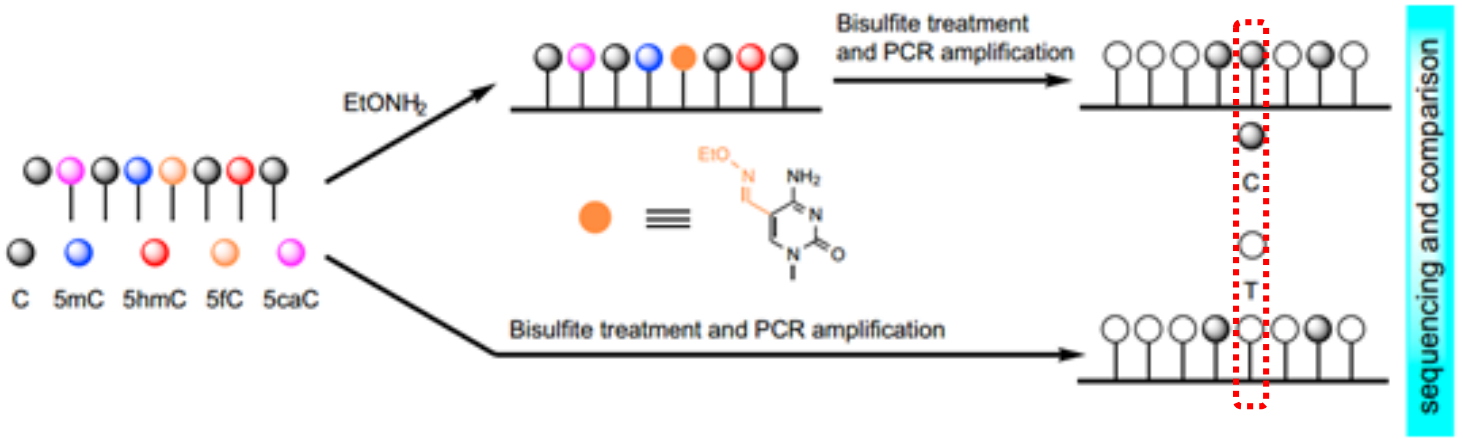
Ito, S. *et al. Science* **333**, 1300-1303 (2011)
Guo, J.U. *et al. Cell* **145**, 423-434 (2011)
Quivoron, C. *et al. Cancer Cell* **20**, 25-38 (2011)
Hackett, J.A. *et al. Trends Genet.* **28**, 164-174 (2012)

DNA 5fC-seq：bisulfite-dependent 单碱基分辨率

	C	5mC	5hmC	5fC	5caC
测序	C	C	C	C	C
BS-seq	U	C	C	U	U

fCAB-Seq



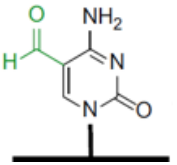


1. 5fC与羟胺反应，BS不能转化成U，测序读成 T

2. Control, 无羟胺，5fC被BS转化成U，测序读成 C

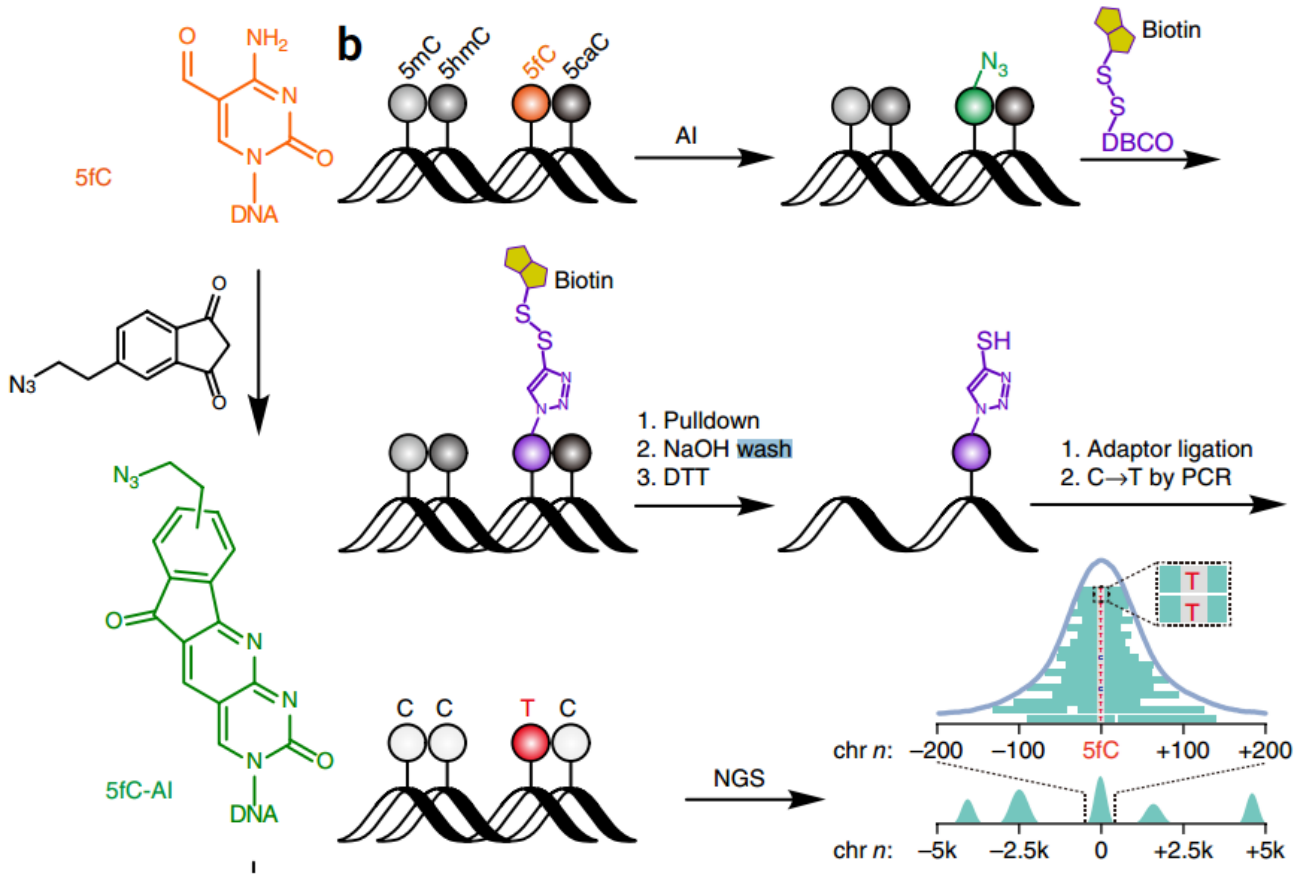
Cell. **2013**, *153*, 678-691

DNA 5fC-seq： bisulfite-independent 单碱基分辨率



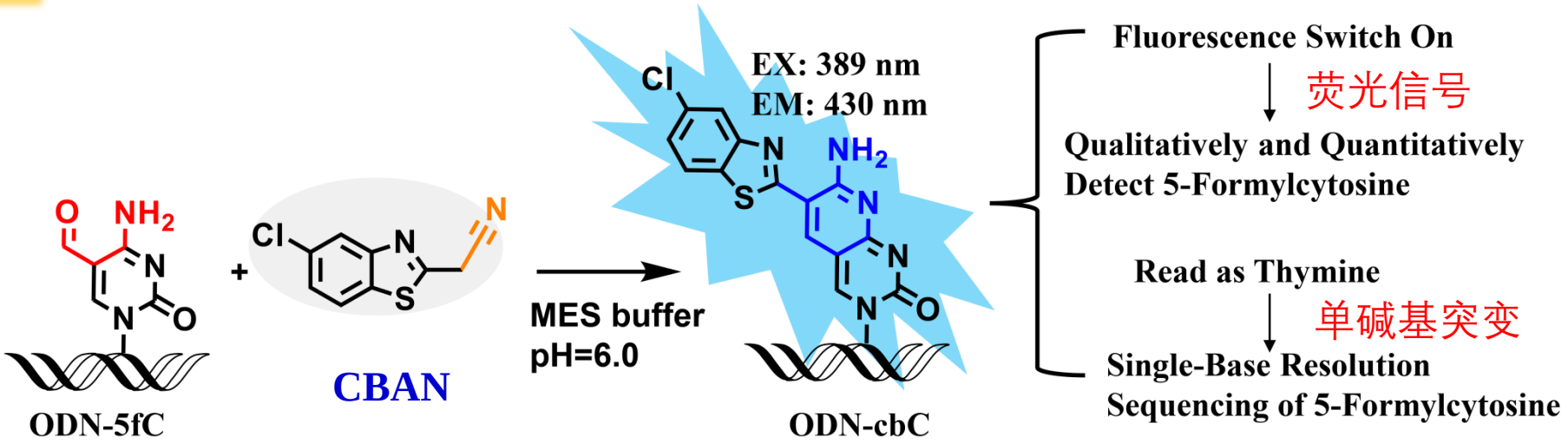
5fC → 特异性探针 → 化学标记 → 改变氢键信息 → PCR突变

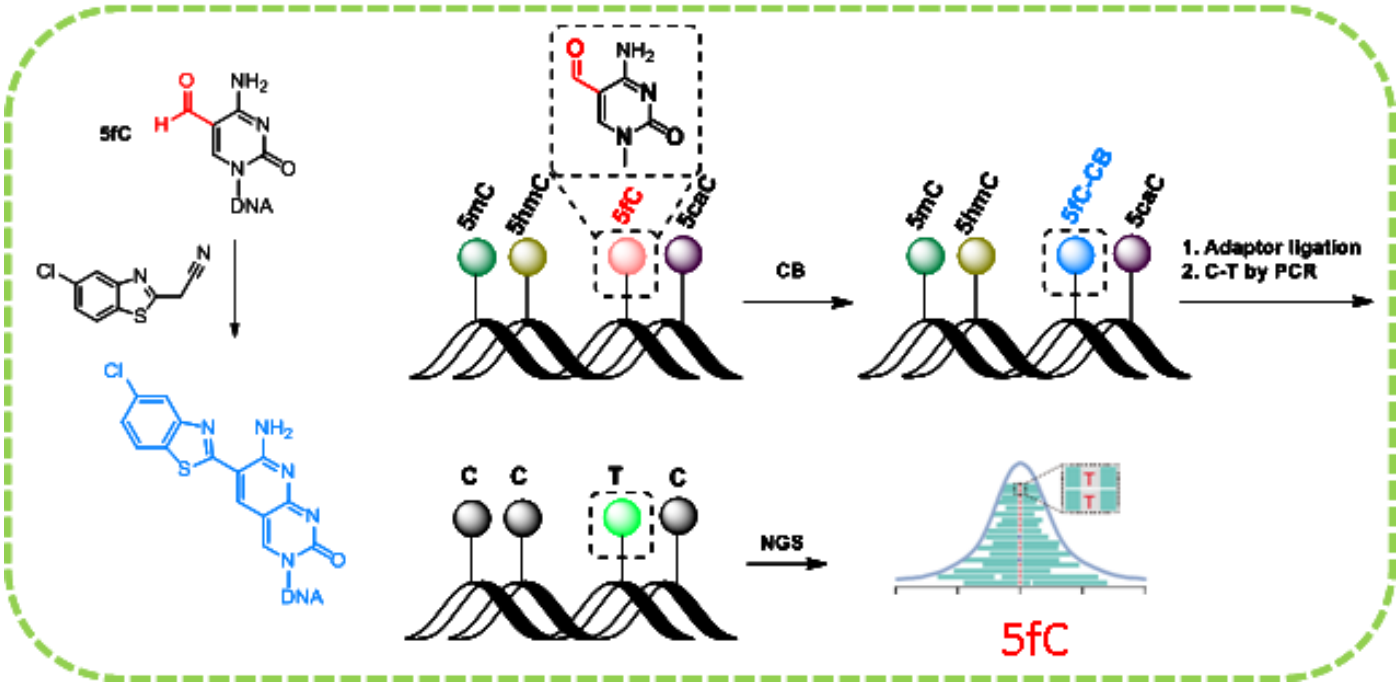
fC-CET



Nat. Methods, **2015**, *12*, 1047-1050

荧光标记和单碱基分辨的5-醛基胞嘧啶(5fC)检测技术

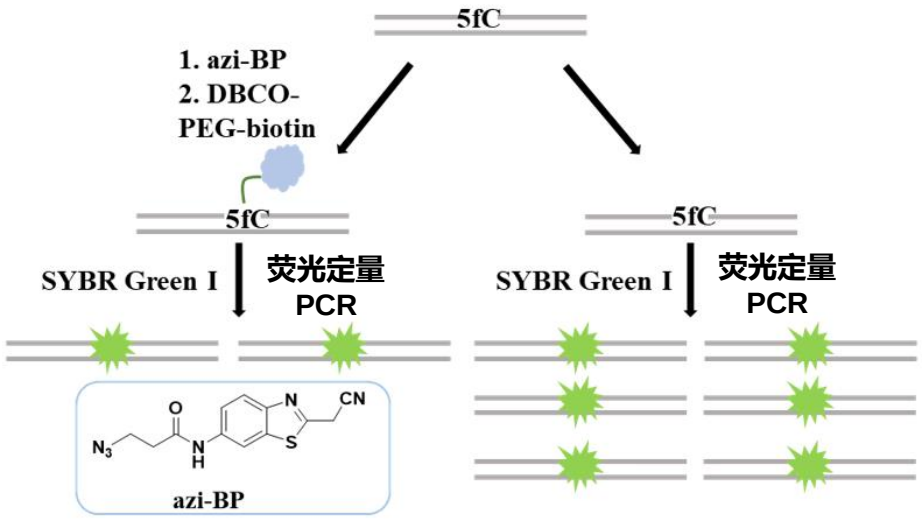


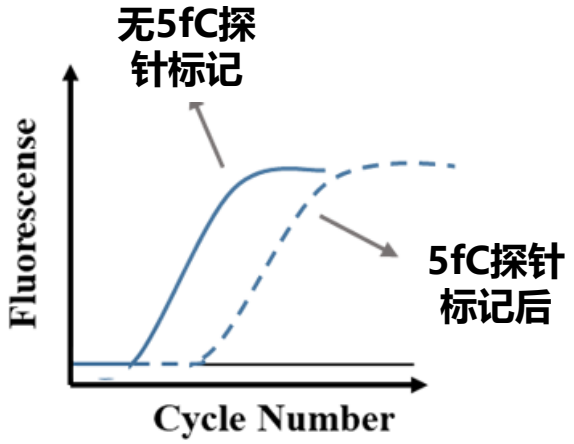


Liu CX#, Wang YF#, ……Weng XC, Zhou, X*, *Chem. Sci.*, **2017**, *8*, 7443.

特定基因区域5fC定量检测

定量检测





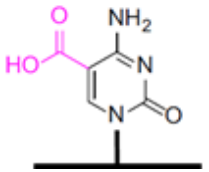
影响PCR效率，增加PCR循环数

化学探针辅助实现特定基因区域内5fC的快速方便和精准检测

特定基因片段 → 化学探针 → 荧光定量PCR → 5fC快速定量检测 → 存在修饰 → 一代测序 → 5fC位点精准识别

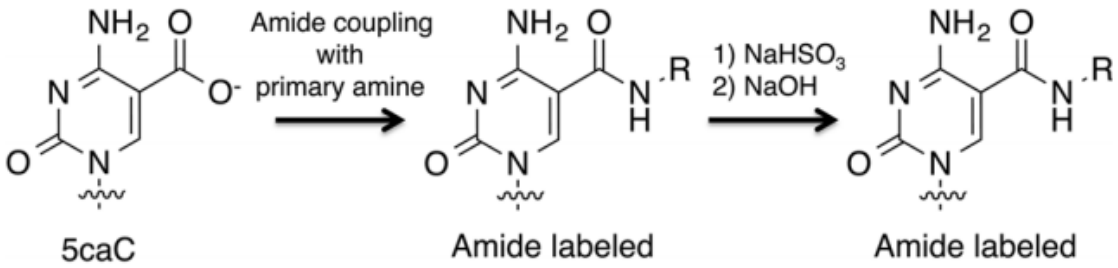
Wang YF#, Liu CX#, Zhang X#,....., **Weng XC*,** Zhou X*, *Chem. Sci.* **2018,** *9,* 3723

DNA 5caC



	C	5mC	5hmC	5fC	5caC
测序	C	C	C	C	C
BS-seq	U	C	C	U	U

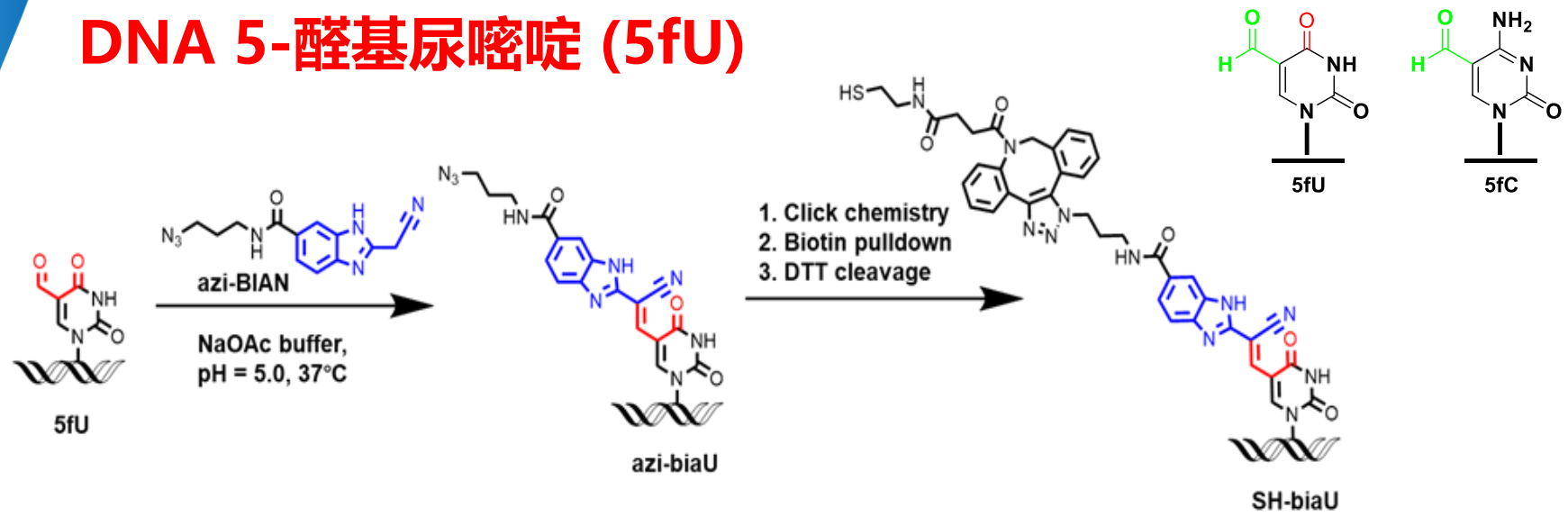
CAB-Seq

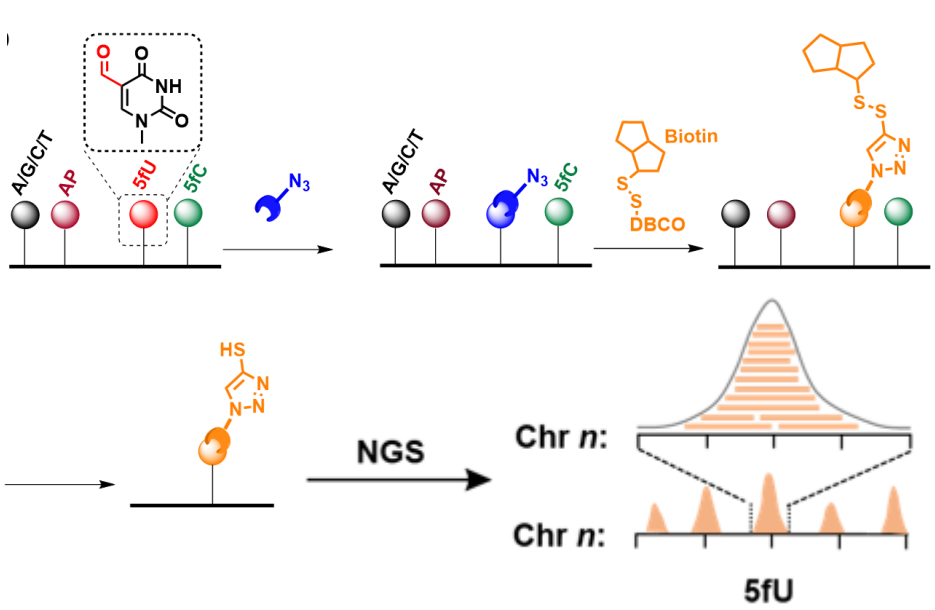


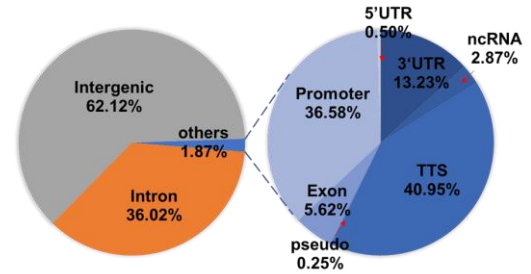
Base	BS-Seq	CAB-Seq
C	T	T
5mC	C	C
5hmC	C	C
5fC	T	T
5caC	T	C
C read out:	5mC + 5hmC	5mC + 5hmC + 5caC

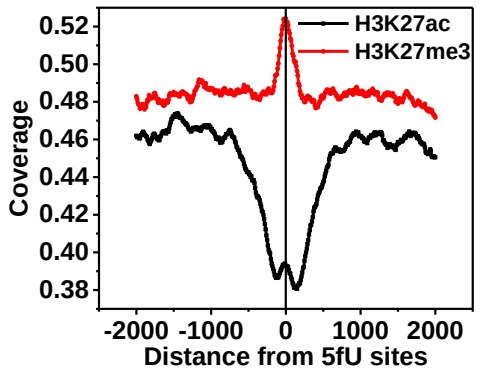
J. Am. Chem. Soc. **2013**, *135*, 9315−9317
Cell Res. **2015**, *25*, 386-389

DNA 5-醛基尿嘧啶 (5fU)









Our groups, *iScience* **2018**, *9*, 423-432

RNA表观遗传修饰

RNA表观遗传学

RNA modified nucleotides

JBC **1960**, *235*, 1488

At least 140 alternative nucleotide forms (tRNA, rRNA, snRNA)

m6A in mRNA

PNAS **1974**, *71*, 3971

FTO m6A demethylase

NCB **2011**, *7*, 855

m6A Demethylase Methyltransferase Binding Protein

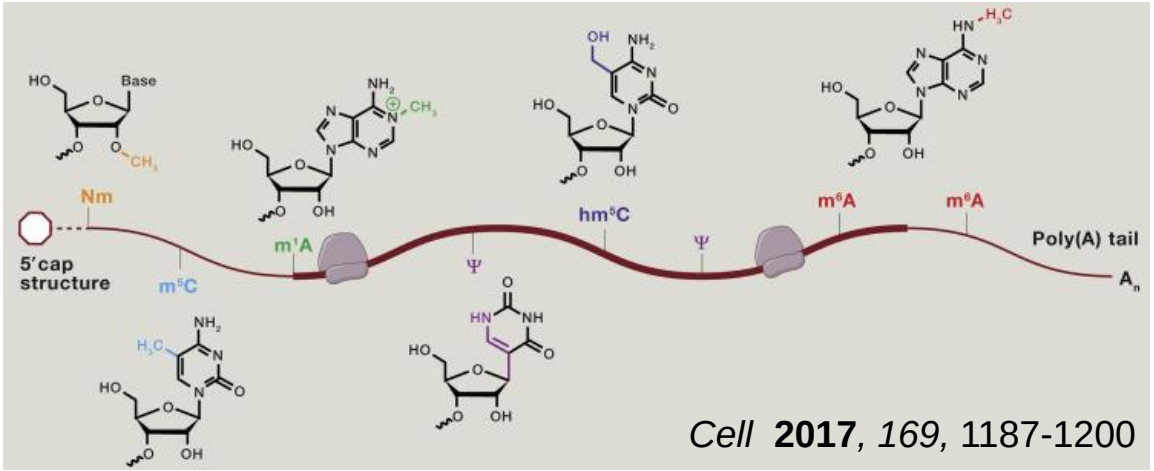
芝加哥大学
何川教授

m6A Function

m6A & disease

Other RNA Modified Bases

- 动态
- 酶催化
- 有规律



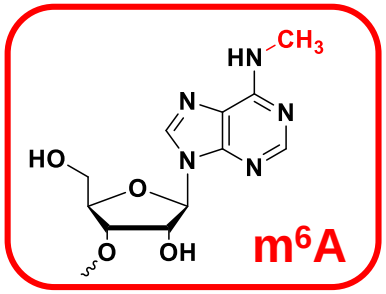
Cell **2017**, *169*, 1187-1200

RNA m6A

相关酶的成功鉴定：

M3/M14/WTAP/VIRMA/ZC3H13
METTL16
FTO, ALKBH5
YTHDF1,2,3; YTHDC1,2

Nat. Chem. Biol. **2011**, *7*, 885.
Mol. Cell. **2013**, 18
Nature **2014**, *505*, 117
Nat. Chem. Biol. **2014**, *10*, 93
Cell **2015**, *161*, 1388
Cell Res. **2017**, *27,* 315
Elife **2017**, *6,* e31311
Cell Res. **2017**, *27,* 1115
Cell Discov. **2018,** *4,* 10
Mol. Cell **2018,** *69,* 1028
Mol. Cell **2018,** *71,* online



植物，微生物：

MTA, FIP37,
ECT2, ALKBH10B

Plant Cell. **2008**, *20,* 1278
Nucleic Acids Res. **2015**, *43*, 6557
Developmental Cell **2016**, *38*, 186
Plant Cell. **2017**, *29,* 2995
Plant Cell. **2018**, doi: 10.1105/tpc.17.00854

各种功能：

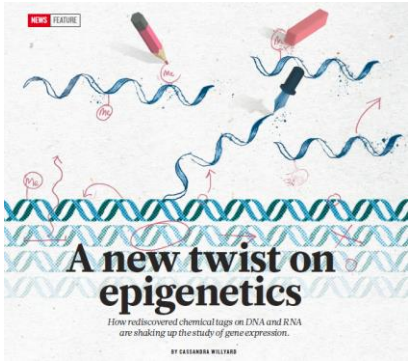
Pri-miRNAs processing, RNA structural switches, DNA damage response, T cell homeostasis, maternal mRNA clearance, learning and memory, Anti-tumour immunity, histone modification, phase separation

Nature **2015**, *519*, 482; *Nature* **2015**, *518*, 560
Nature **2017**, *543*, 573; *Nature* **2017**, *548*, 338
Nature **2017**, *542*, 475; *Nature* **2018**, *563*, 249
Nature **2019**, *566*, 270; *Nature* **2019**, *567*, 414
Nature **2019**. *571* , 424

疾病相关：

Leukemia; Glioblastoma; lung cancer; HIV; Zika Virus Infection

Cancer Cell **2017**, *31*, 127; *Cancer Cell* **2017**, *31*, 591; *Mol Cell* **2016**, *62*, 335; *eLife* **2016***;5:*e15528*.*
Cell Host & Microbe **2016***, 20,* 666

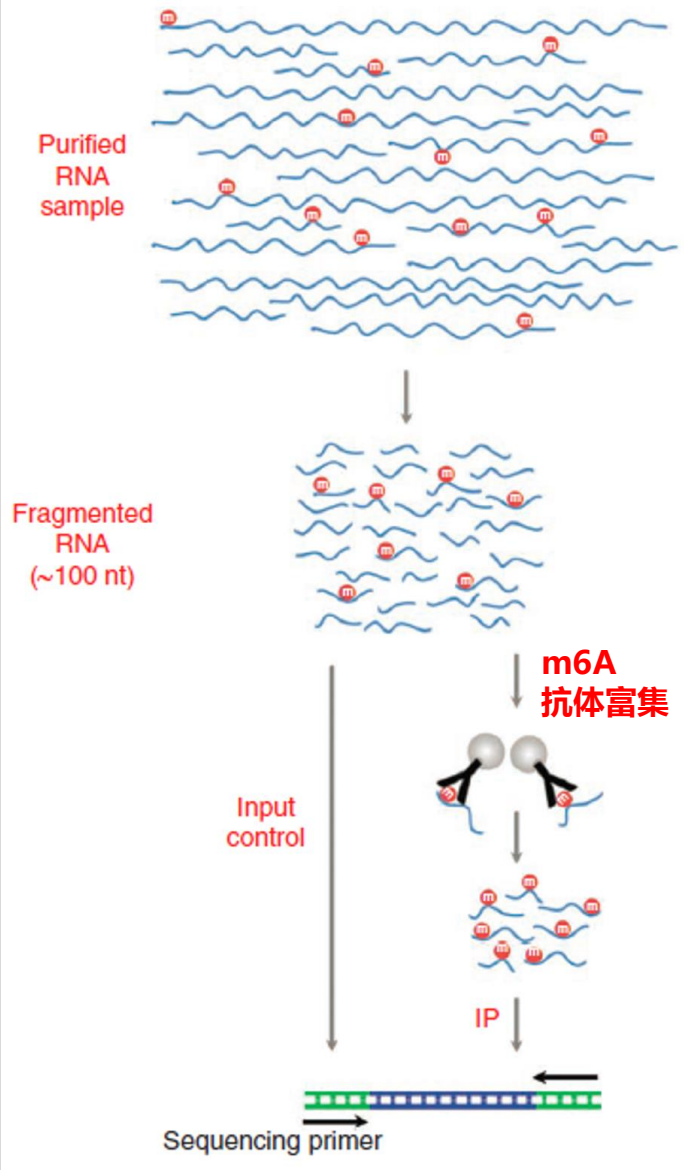


- scientific **gold rush**
- we are only in the **beginning** of the story
- as the **techniques improve**, scientists will be able to see these marks more clearly.

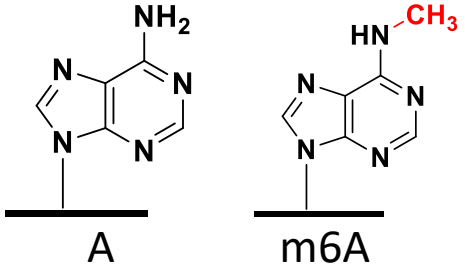
Nature, **2017**, *542*, 406-408

RNA m6A-seq antibody-dependent

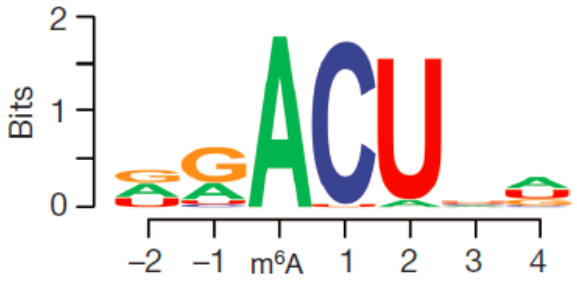
m6A-seq or MeRIP-seq



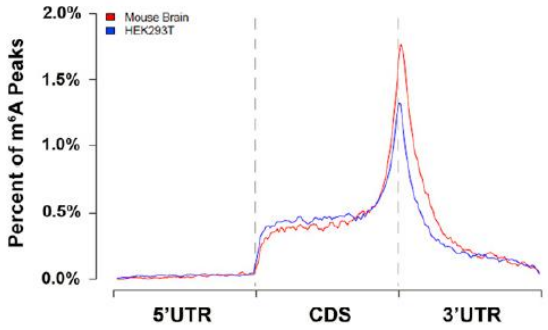
Nature, **2012**, *485*, 201; *Cell*, **2012**, *149*, 1635



- 保守motif



- 特征分布规律

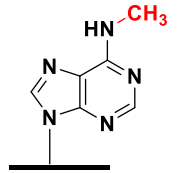


潜在生物功能!

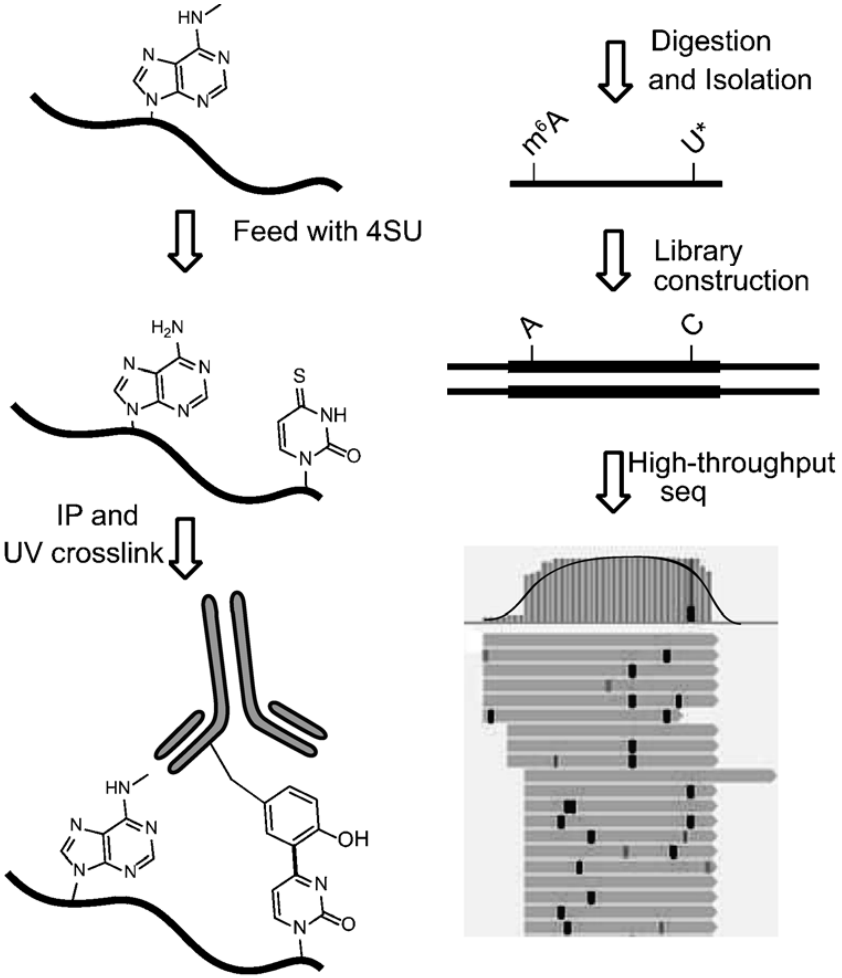
Fragmented RNA ~100nt

更好的检测技术?

RNA m6A-seq antibody-dependent

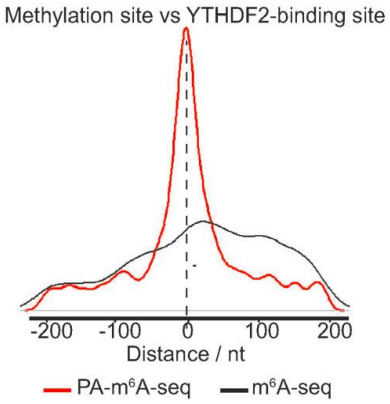


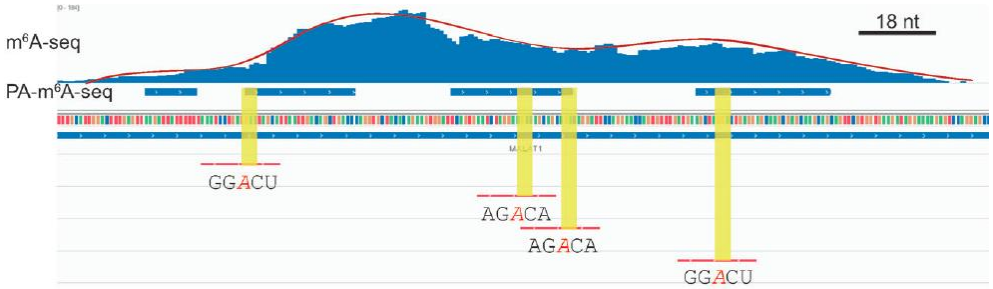
PA-m6A-seq: photo-crosslinking-assisted m6A sequencing



Steps:

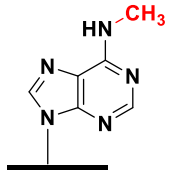
1. 4-thiouridine (4SU) treatment
2. Photo-crosslinking
3. RNase T1 Digestion
4. Library construction



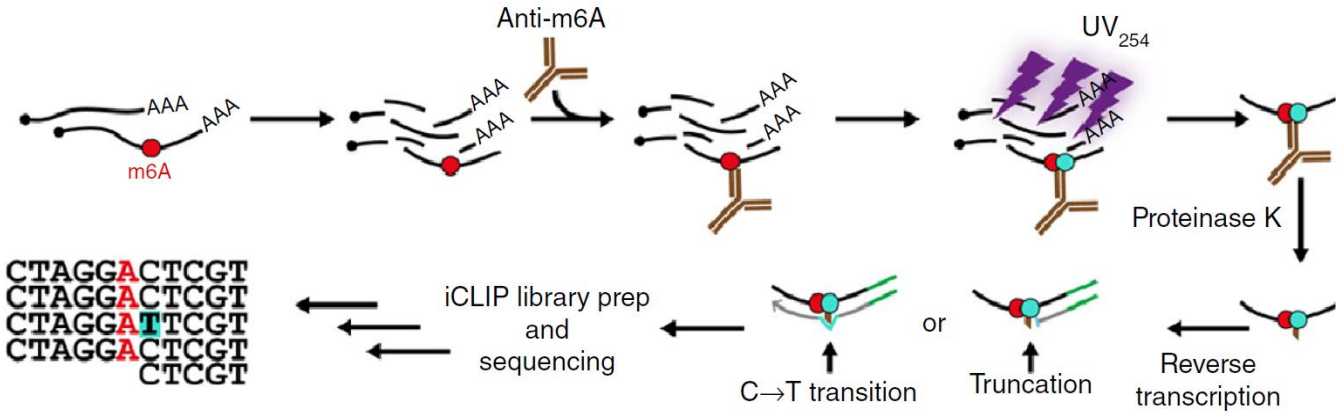


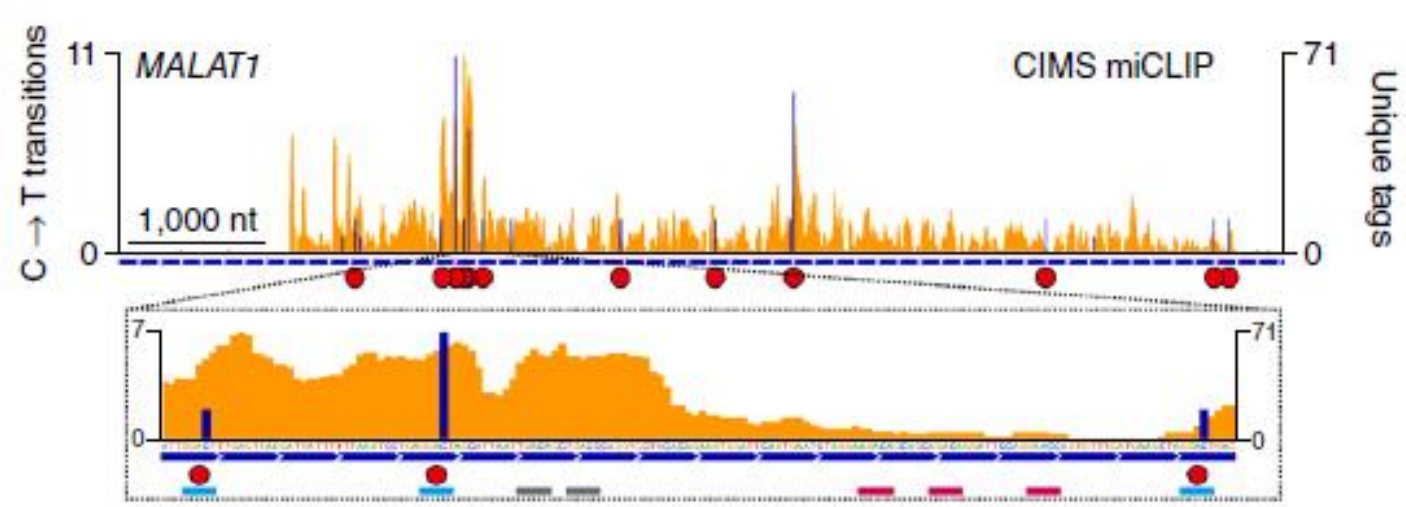
Angew. Chem. Int. Ed. **2015**, *54*, 1587 –1590

RNA m6A-seq antibody-dependent



miCLIP: m6A individual-nucleotide-resolution cross-linking and immunoprecipitation





Nat. Methods, **2015**, *12*, 767–772

RNA m6A-seq antibody-independent

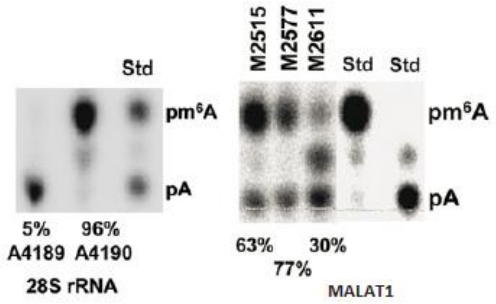
Disadvantages of m6A-antibody:

1. Low resolution;
2. Low IP efficiency
3. Poor repeatability
4. High cost

Antibody-independent m6A mapping methods?

SCARLET method

- TLC with ^{32}P



RNA. **2013**, *19*, 1848

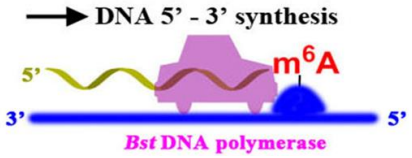
DNA polymerase with reverse transcriptase activity

- *Tth* DNA polymerase

J. Am. Chem. Soc. **2013**, *135*, 19079

- *Bst* DNA polymerase

Chem. Sci., **2016**, *7*, 1440

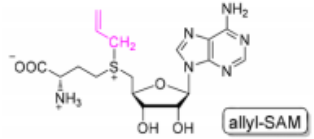


Selective DNA ligase for m6A

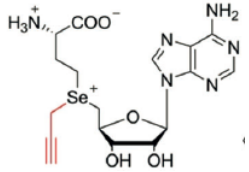
Chem. Sci., **2018**, *9*, 3354

SAM analogue

- N6 -Allyladenosine



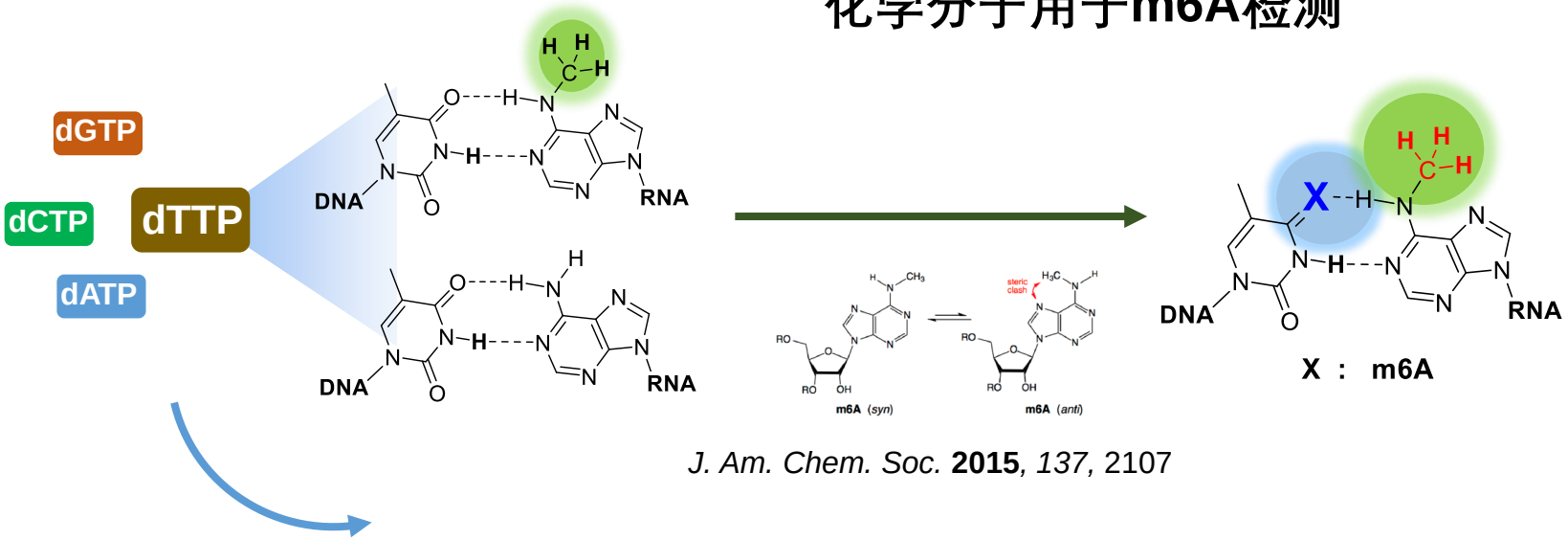
J. Am. Chem. Soc. **2017**, *139*, 17213



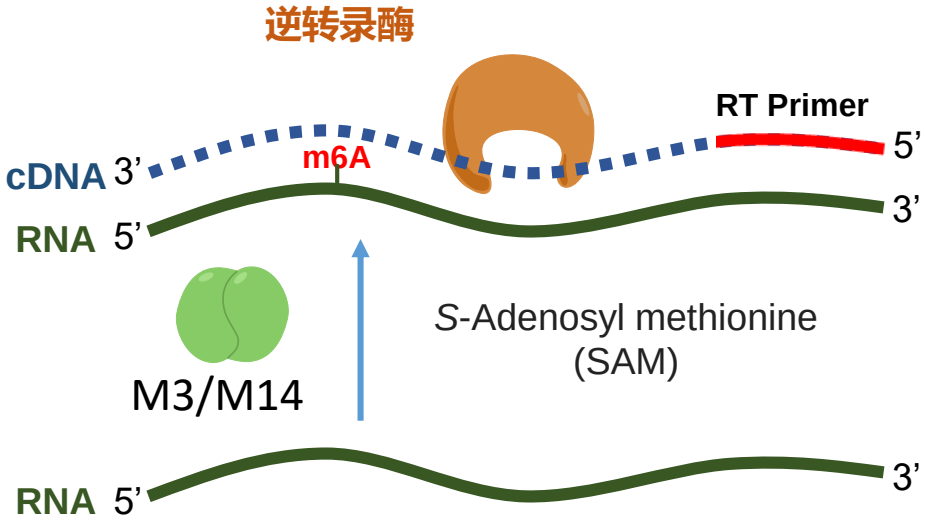
Angew. Chem. Int. Ed., **2018**, *57*, 6342

方案设计

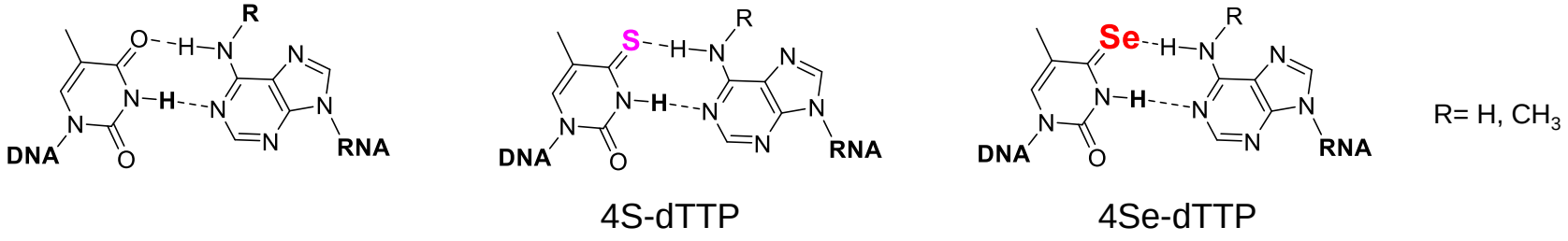
Our Strategy
化学分子用于m6A检测



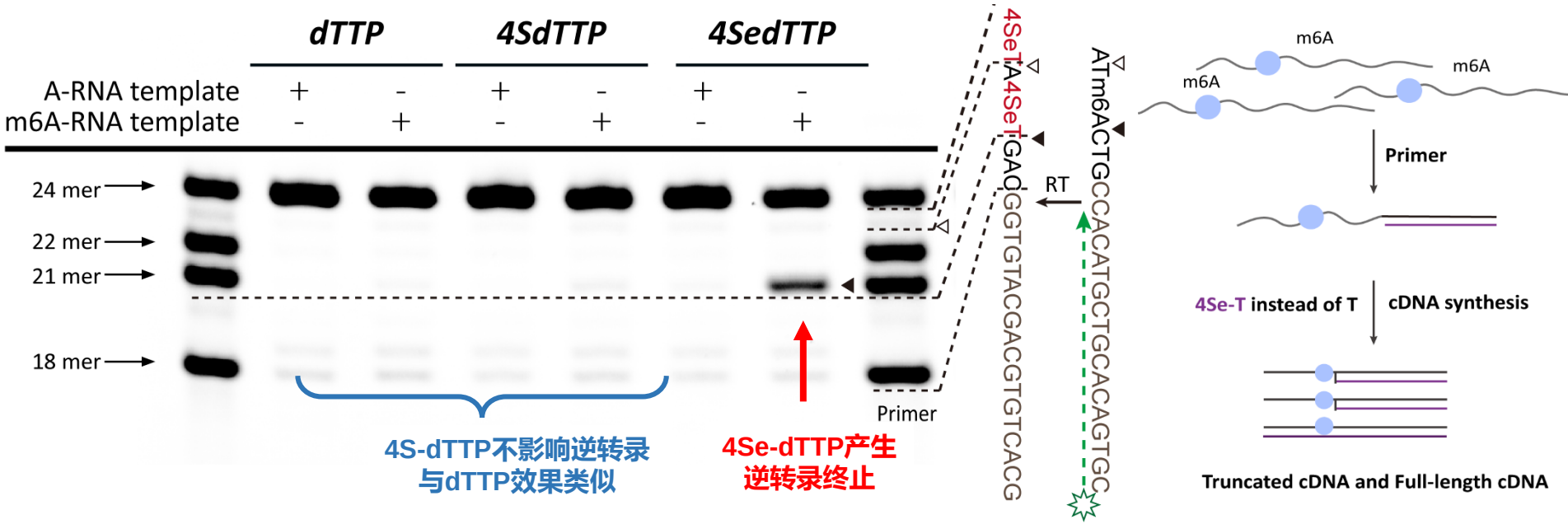
J. Am. Chem. Soc. **2015**, *137*, 2107



4Se-dTTP引入导致m6A位点逆转录终止

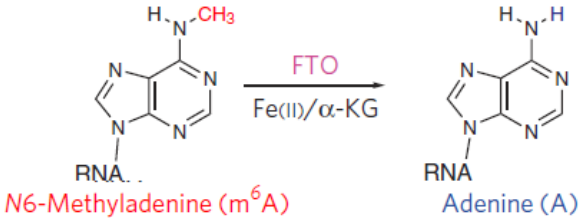


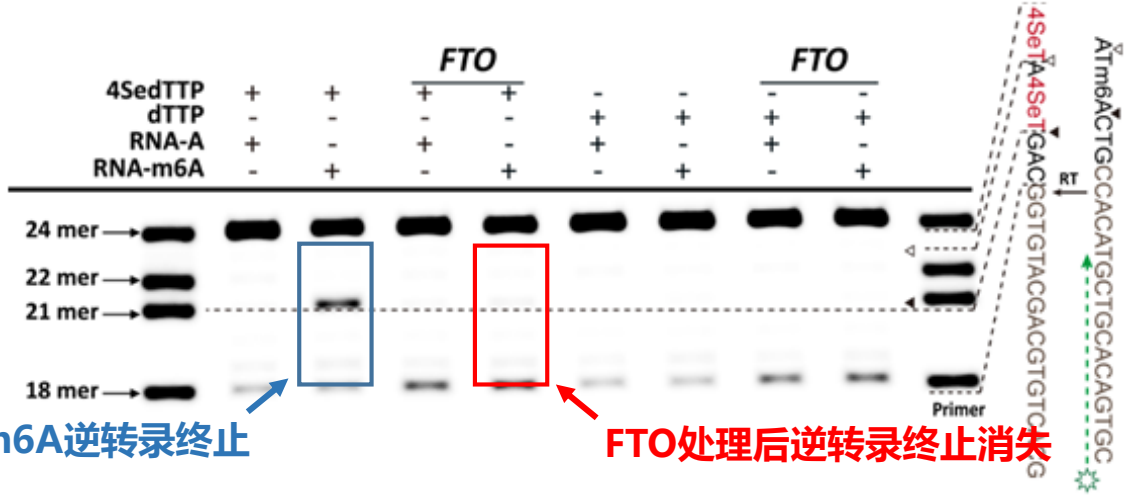
4S-dTTP　　4Se-dTTP

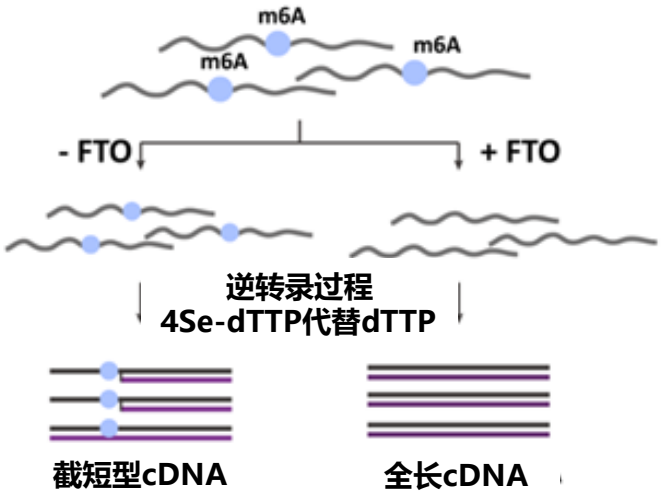


可以完成多碱基的延伸，摆脱之前单碱基延伸策略的限制

FTO去甲基化制备A位点对照 (用于未知位点检测)







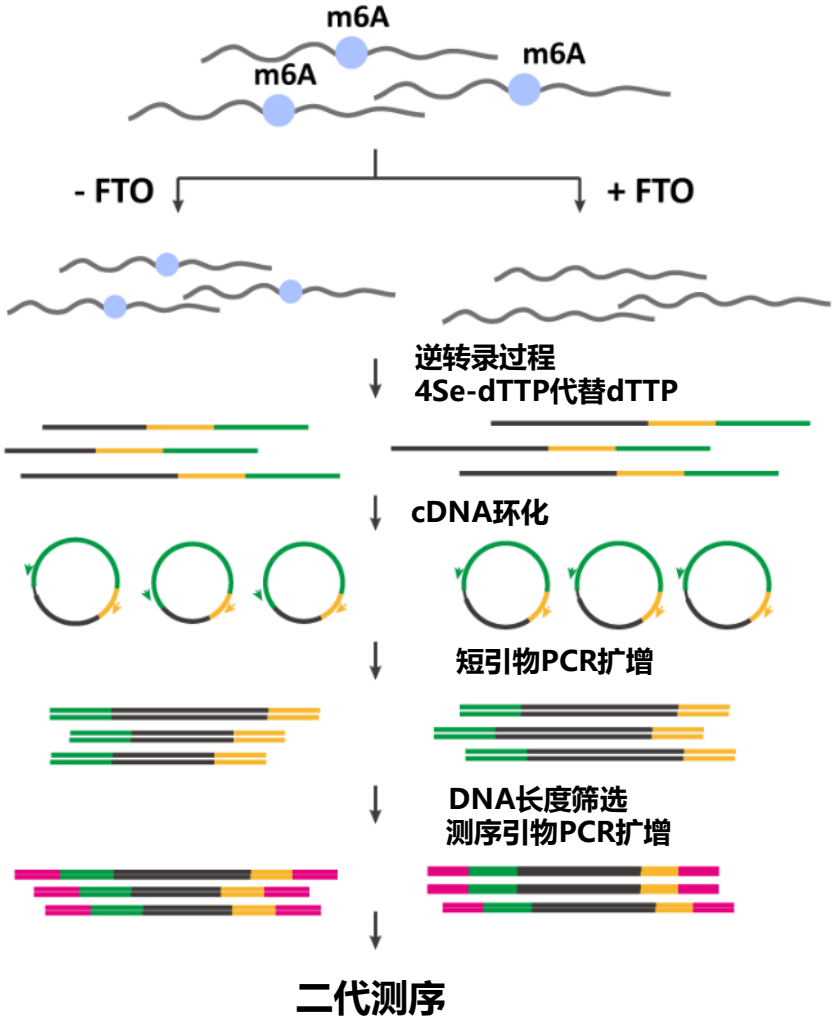
举例：

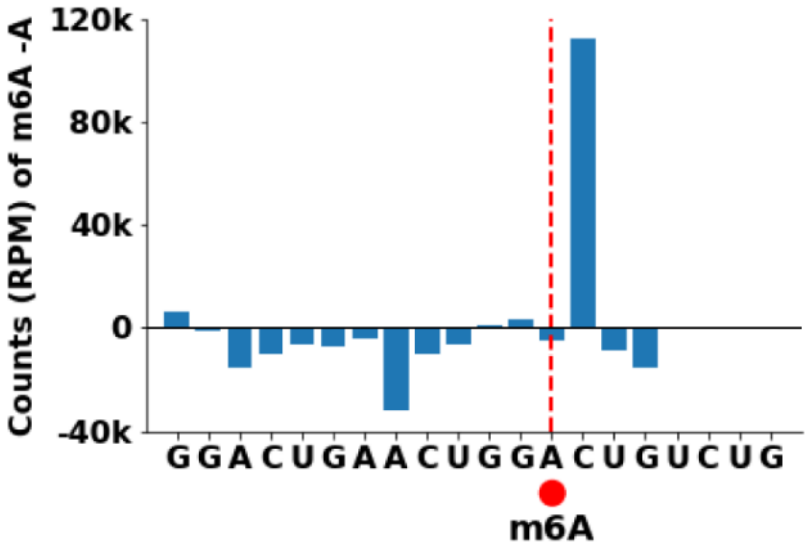
m6A引起逆转录终止

序列	5’-AUCGGGm6ACUAUCACCUGA-3’
无FTO处理测得序列	CUAUCACCUGA
FTO处理测得序列	AUCGGGACUAUCACCUGA

FTO处理后逆转录终止消失，测成A

不依赖抗体的RNA m6A单碱基分辨率检测技术

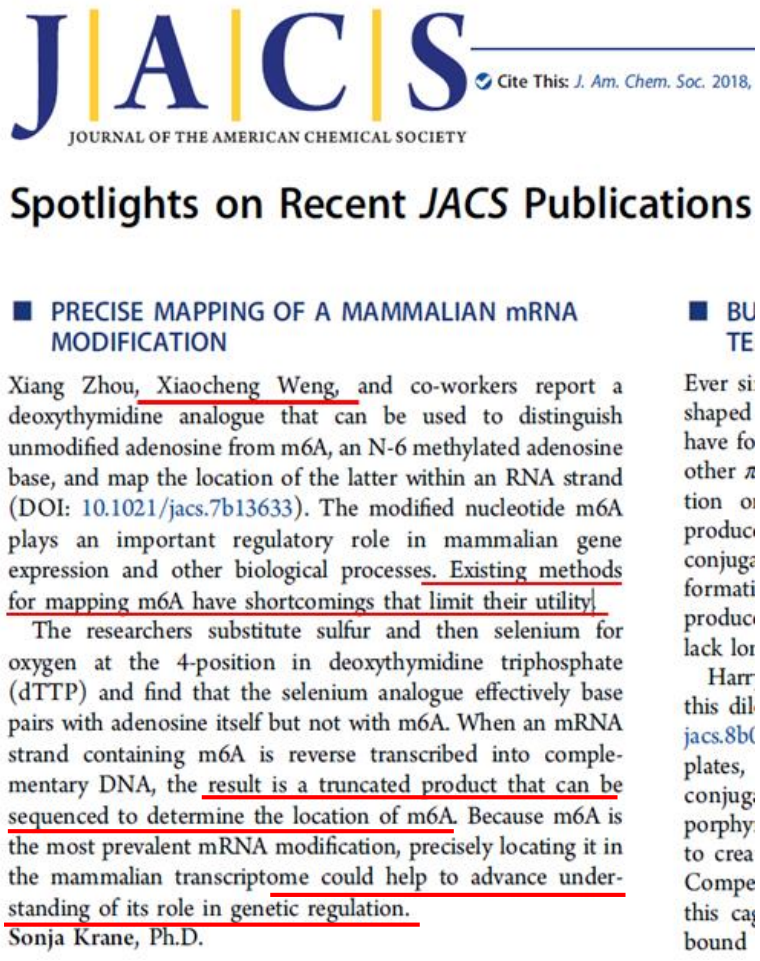




- 开发了一种不依赖抗体的m6A单碱基分辨率检测新技术 (4Se-dTTP辅助)
- 通过条件优化，有望实现转录组m6A单碱基分辨率高通量测序

Hong TT#, Yuan YS#,……Weng XC*, Zhou X*, *J. Am. Chem. Soc.* **2018,** *140*, 5886

作为JACS封面文章 (Front Cover) 发表，并被选为JACS“Spotlight”



JACS

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Cite This: *J. Am. Chem. Soc.* 2018,

Spotlights on Recent *JACS* Publications

■ PRECISE MAPPING OF A MAMMALIAN mRNA MODIFICATION

Xiang Zhou, Xiaocheng Weng, and co-workers report a deoxythymidine analogue that can be used to distinguish unmodified adenosine from m6A, an N-6 methylated adenosine base, and map the location of the latter within an RNA strand (DOI: 10.1021/jacs.7b13633). The modified nucleotide m6A plays an important regulatory role in mammalian gene expression and other biological processes. Existing methods for mapping m6A have shortcomings that limit their utility.

The researchers substitute sulfur and then selenium for oxygen at the 4-position in deoxythymidine triphosphate (dTTP) and find that the selenium analogue effectively base pairs with adenosine itself but not with m6A. When an mRNA strand containing m6A is reverse transcribed into complementary DNA, the result is a truncated product that can be sequenced to determine the location of m6A. Because m6A is the most prevalent mRNA modification, precisely locating it in the mammalian transcriptome could help to advance understanding of its role in genetic regulation.

Sonja Krane, Ph.D.

■ BU TE

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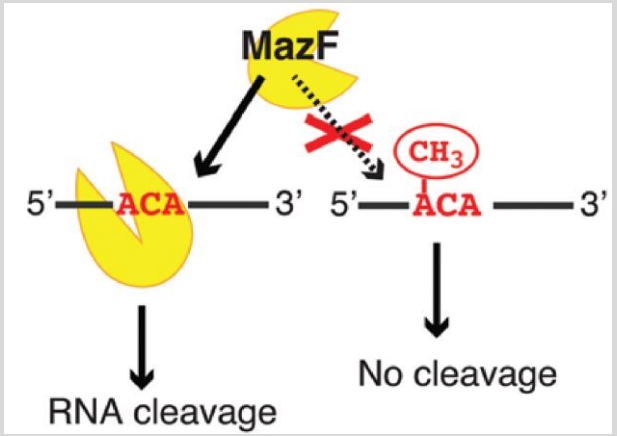
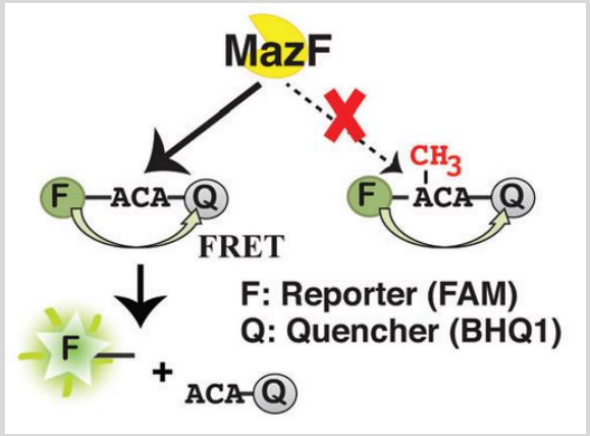
Compe
this ca
bound

Hong TT#, Yuan YS#,……Weng XC*, Zhou X*, *J. Am. Chem. Soc.* **2018,** *140*, 5886

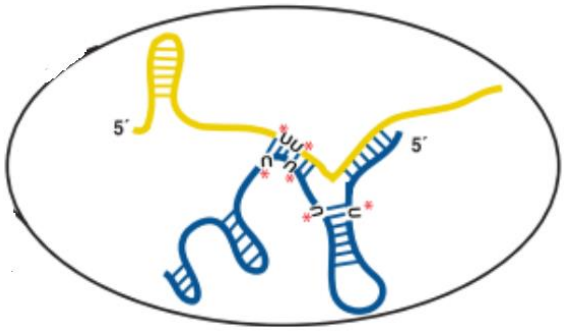
MazF-based m6A-seq (antibody-independent)



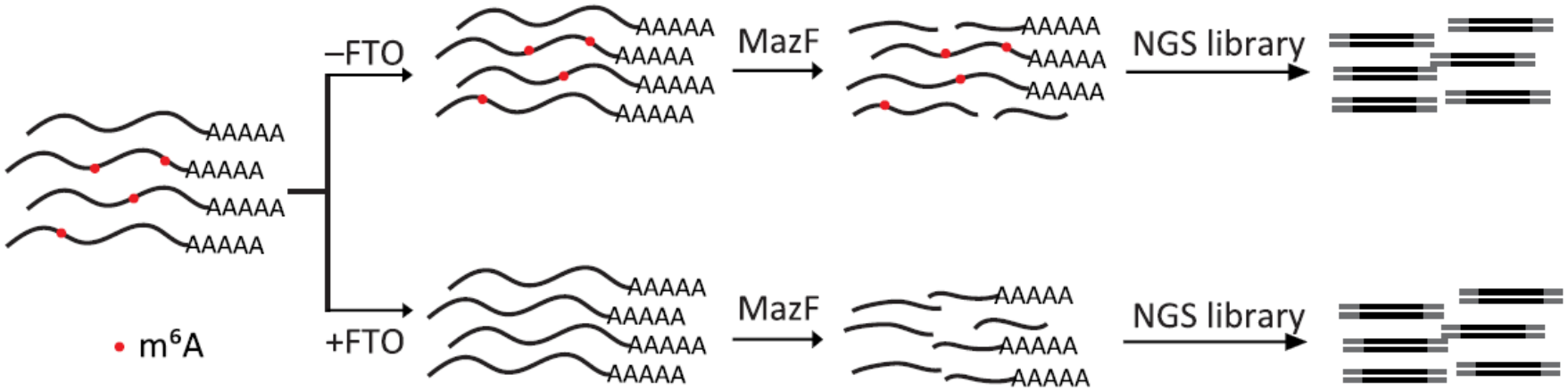


Chem. Commun., **2017**, *53*, 12930-12933

RNA 结构



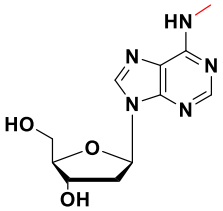
MAZTER-seq / m6A-REF-seq:



Cell, **2019**, 27 June, doi.org/10.1016/j.cell.2019.06.013
Sci. Adv. **2019**; *5* : eaax0250

DNA 6mA

早期：6mA以较高丰度存在于原核生物



DNA 6mA

2015 Cell Volume 161, Issue 4 May 07, 2015

DNA Methylation on N^6-Adenine in *C. elegans* **线虫**

Eric Lieberman Greer, Mario Andres Blanco, Lei Gu, Erdem Sendinc, Jianzhao Liu, David Aristizábal-Corrales, Chih-Hung Hsu, L. Aravind, Chuan He, Yang Shi

Full-Text HTML | PDF

N^6-Methyldeoxyadenosine Marks Active Transcription Start Sites in *Chlamydomonas* **绿藻**

Ye Fu, Guan-Zheng Luo, Kai Chen, Xin Deng, Miao Yu, Dali Han, Ziyang Hao, Jianzhao Liu, Xingyu Lu, Louis C. Doré, Xiaocheng Weng, Quanjiang Ji, Laurens Mets, Chuan He

Full-Text HTML | PDF

N^6-Methyladenine DNA Modification in *Drosophila* **果蝇**

Guoqiang Zhang, Hua Huang, Di Liu, Ying Cheng, Xiaoling Liu, Wenxin Zhang, Ruichuan Yin, Dapeng Zhang, Peng Zhang, Jianzhao Liu, Chaoyi Li, Baodong Liu, Yuewan Luo, Yuanxiang Zhu, Ning Zhang, Shunmin He, Chuan He, Hailin Wang, Dahua Chen

Full-Text HTML | PDF

DNA methylation on N(6)-adenine in mammalian embryonic stem cells. *Nature*, **2016,** *532*, 329-333

Abundant DNA 6mA methylation during early embryogenesis of zebrafish and pig. *Nat. Commun.*, **2016**, *7*, 13052

Quantitative LC–MS Provides No Evidence for m^6dA or m^4dC in the Genome of Mouse Embryonic Stem Cells and Tissues. *Angew Chem Int Ed Engl*, **2017**, *56*, 11268-11271

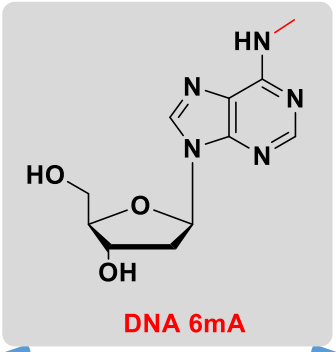
N^6-Methyladenine DNA Modification in the Human Genome. *Mol Cell*, **2018**, *71*, 306-318

N6-methyladenine DNA Modification in Glioblastoma *Cell*, **2018**, https://doi.org/10.1016/j.cell.2018.10.006

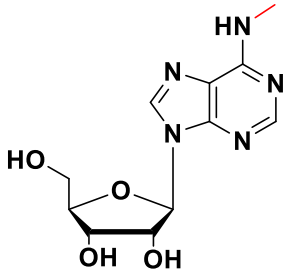
DNA N^6-methyladenine: a new epigenetic mark in eukaryotes?

Nature Reviews Molecular Cell Biology, **2015**, ***16***, 705–710

DNA 6mA 检测

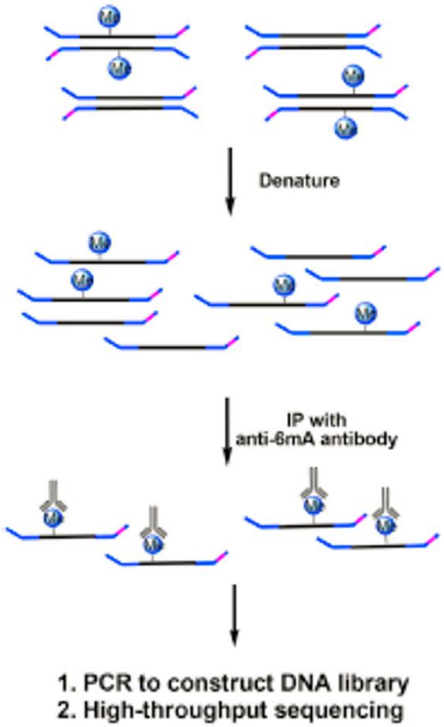


DNA 6mA



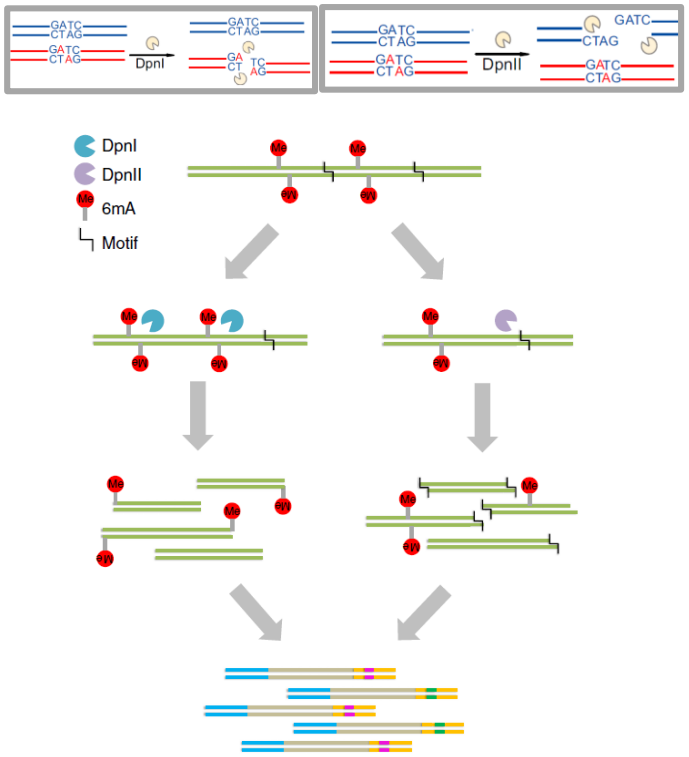
RNA m6A

Anti-m6A抗体



Cell, **2015**, *161*, 879

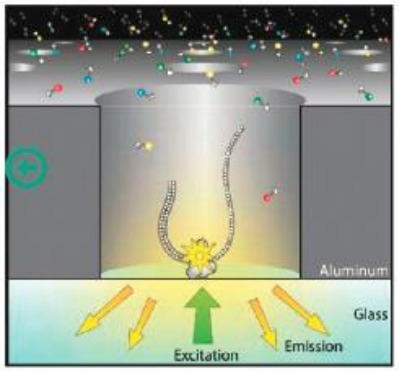
限制性内切酶



Nat Commun, **2016**, *7*, 11301

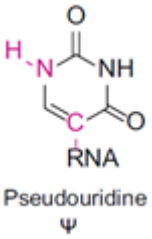
三代测序

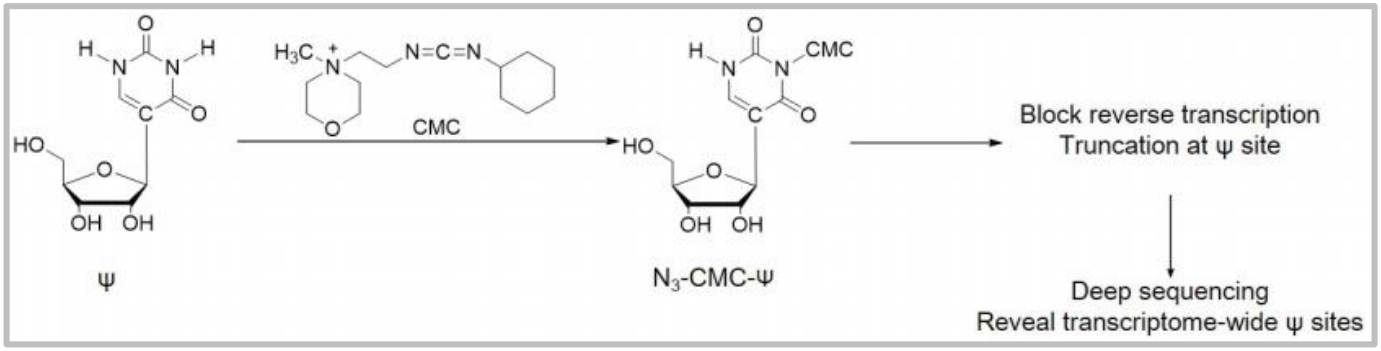
SMRT测序: PacBio

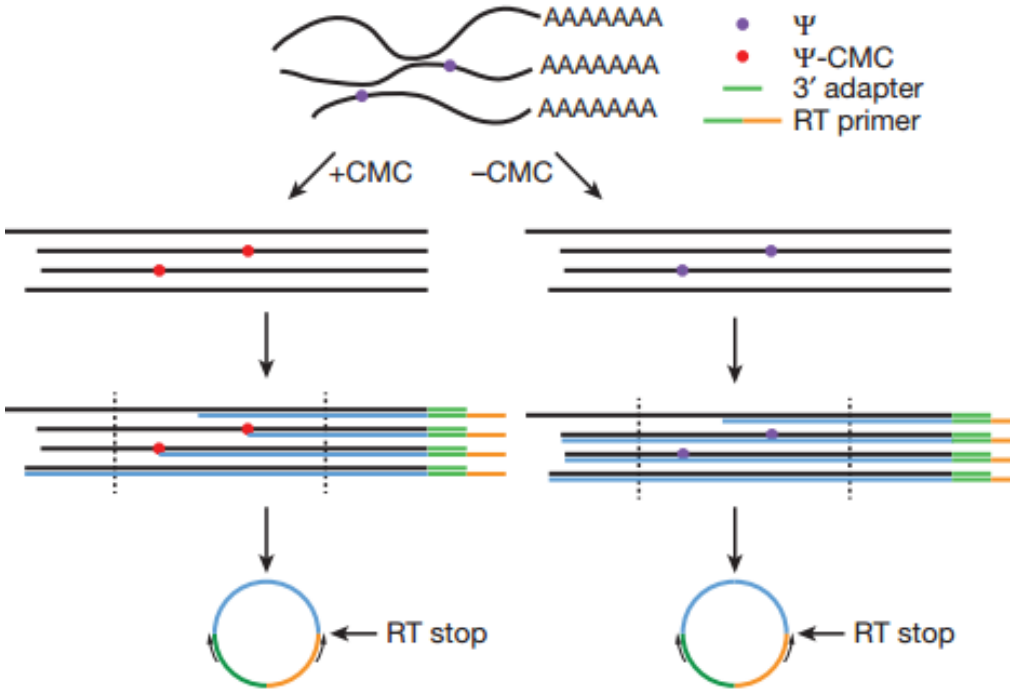


Mol Cell, **2018**, *71*, 306

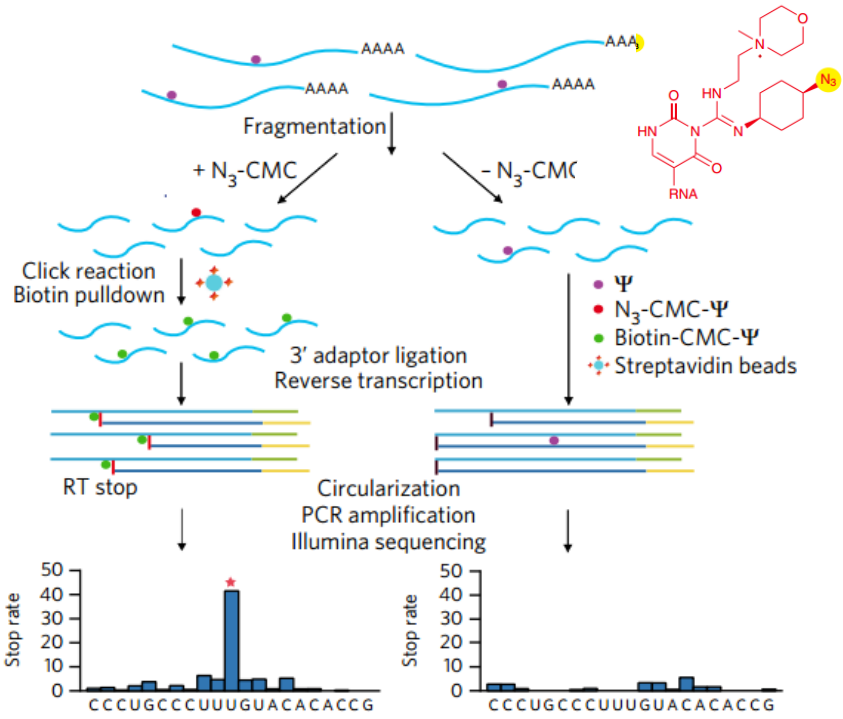
RNA PseudoUridine (Ψ)





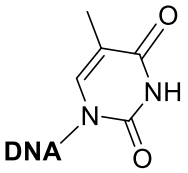


Nature, **2014**, *515*, 143-146
Cell, **2014**, *159*, 148-162.



Nat. Chem. Biol. **2015**, *11*, 592–597

RNA m1A



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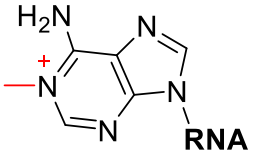
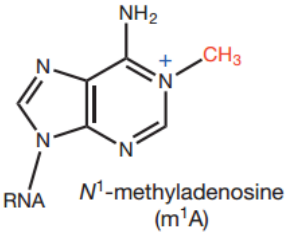
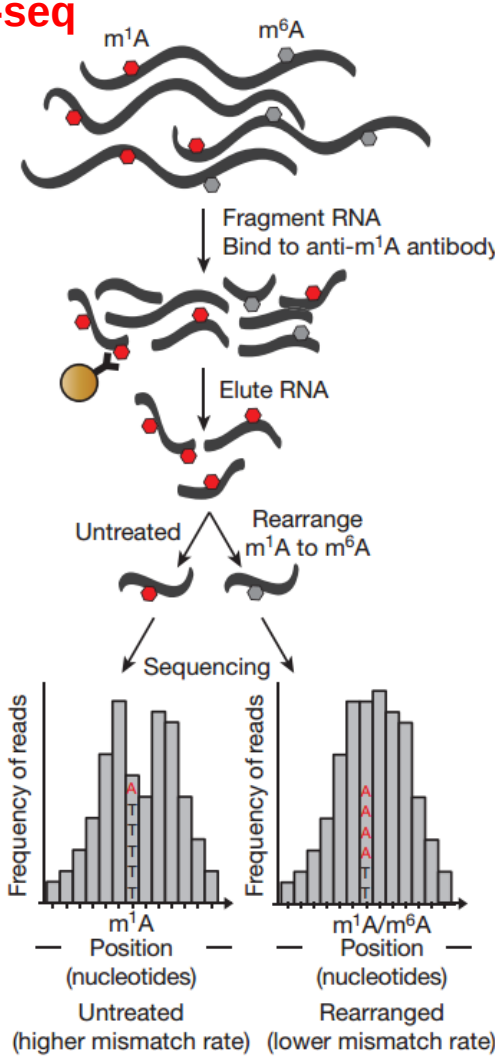


m^{1}A (影响氢键配对)

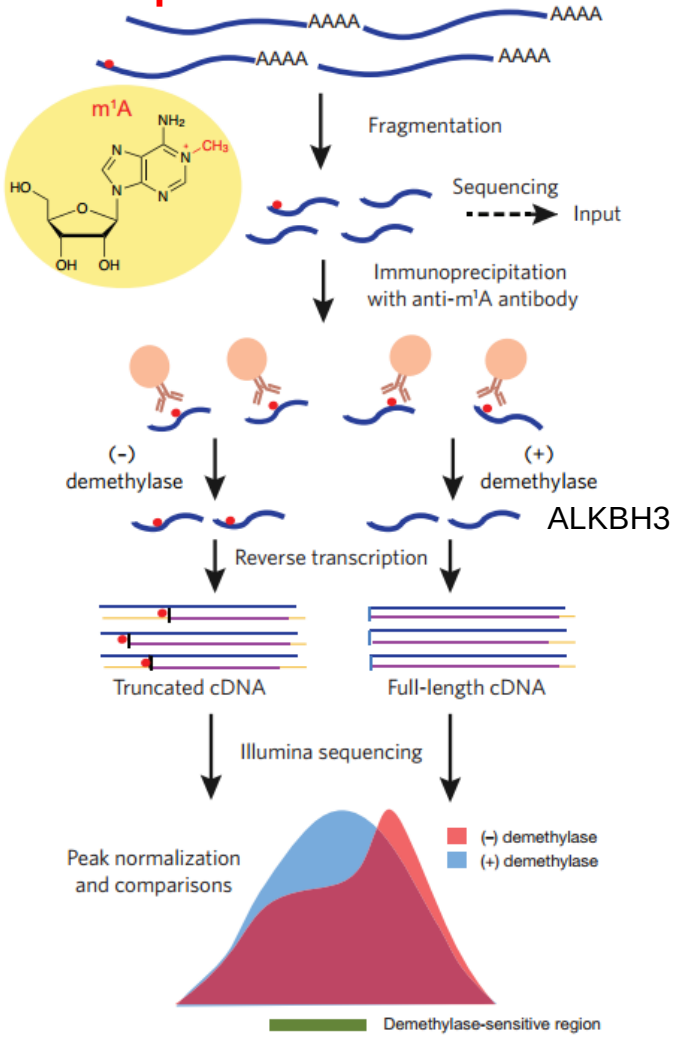


m1A-seq



Nature, **2016**. *530*, 441–446 (10 February 2016)

m1A-ID-seq



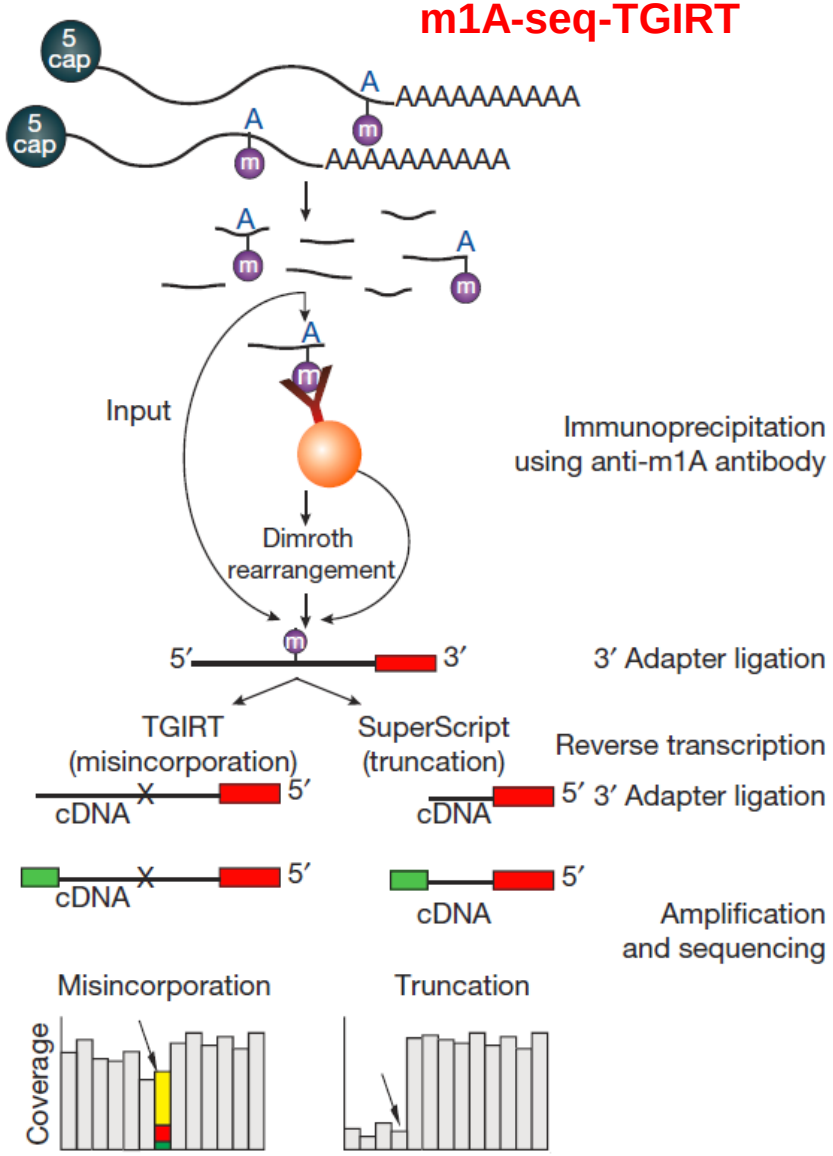
Nat. Chem. Biol. **2016,** *12*, 311–316 (10 February 2016)

RNA m1A

单碱基分辨率

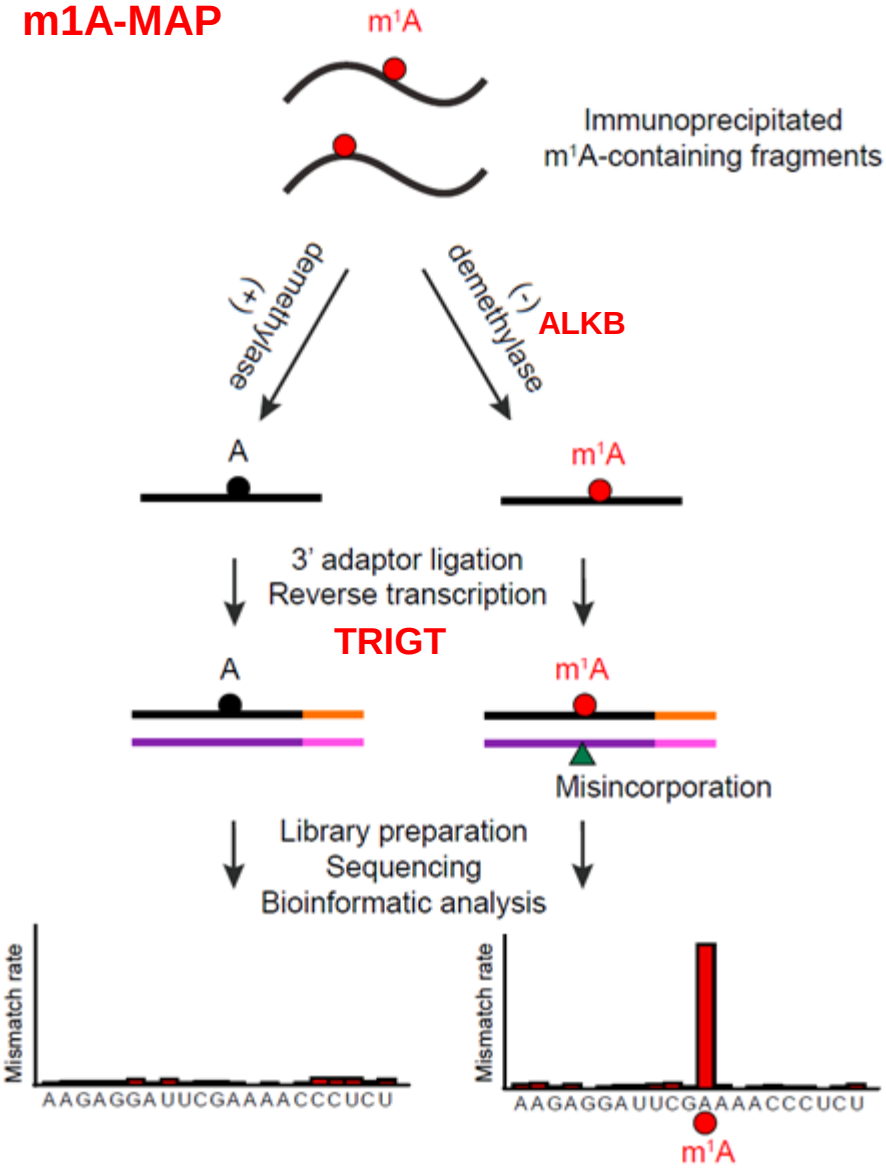
TGIRT： Highly processive reverse transcriptase

m1A-seq-TGIRT



Nature. **2017**, *551*, 251–255 (09 Nov 2017)

m1A-MAP

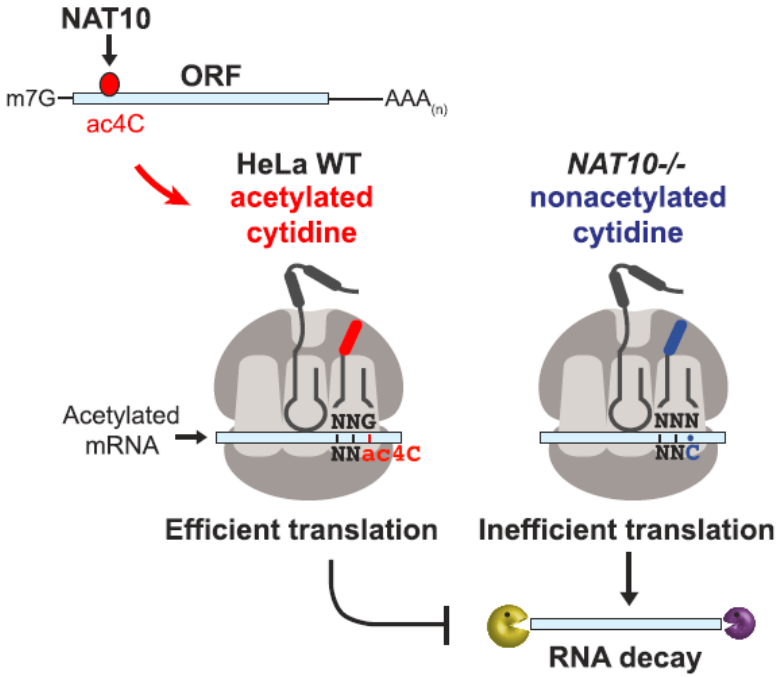


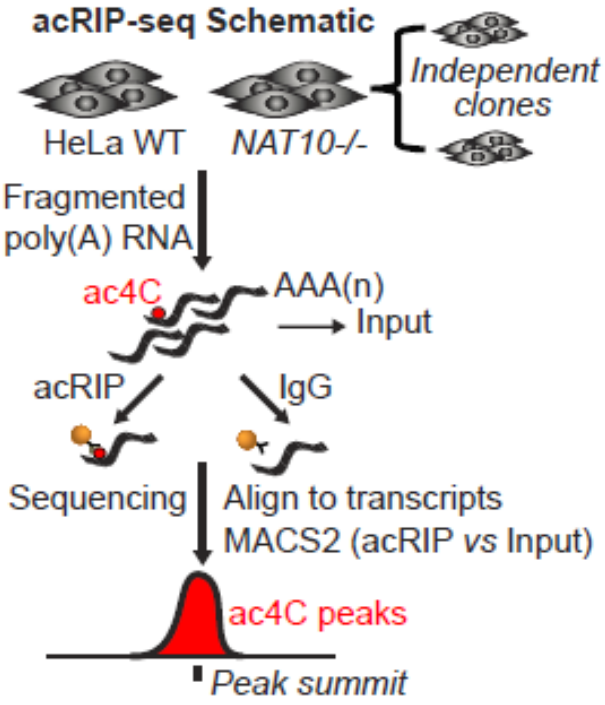
Mol Cell. **2017,** *68*, 993–1005 (7 Dec 2017)

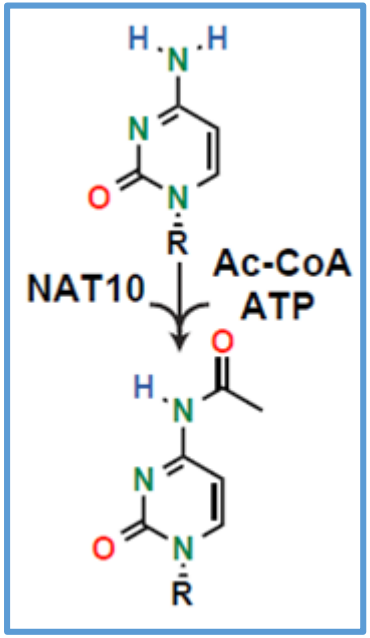
新修饰： RNA ac4C

Cell

Acetylation of Cytidine in mRNA Promotes Translation Efficiency







Cell, **2018**, 15 Nov, DOI:https://doi.org/10.1016/j.cell.2018.10.030

新修饰: DNA 5-glyceryl-methylcytosine (5gmC)

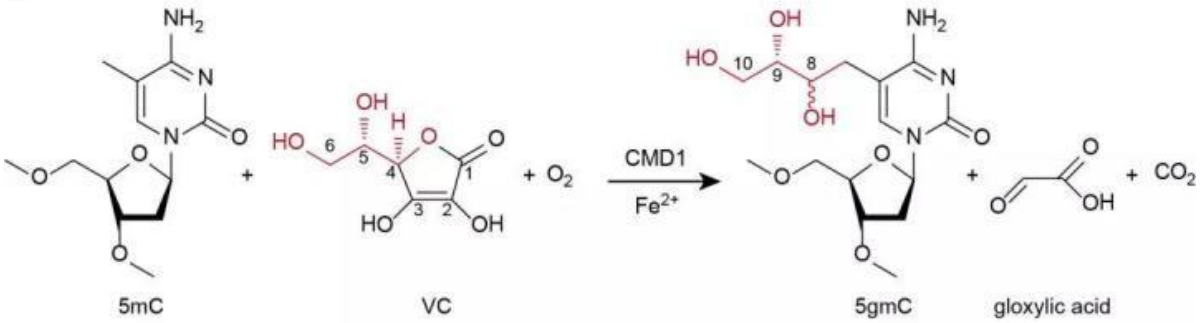
Letter | Published: 01 May 2019

nature
International journal of science

A vitamin-C-derived DNA modification catalysed by an algal TET homologue

Jian-Huang Xue, Guo-Dong Chen, [...] Guo-Liang Xu

a



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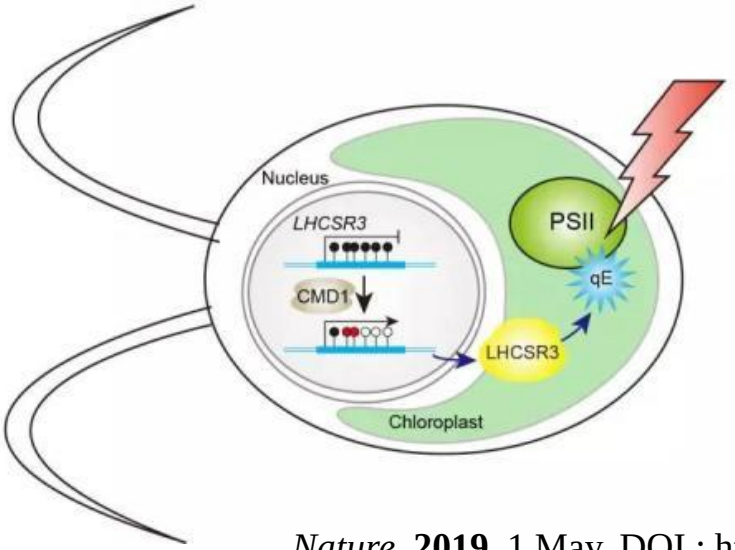


莱茵衣藻（*C. reinhardtii*）中，TET同源蛋白可以将维生素C的半个分子的碳基骨架转移到DNA上，从而产生一种全新的DNA表观修饰。

Nature, **2019**, 1 May, DOI : https://doi.org/10.1038/s41586-019-1160-0

Take home message

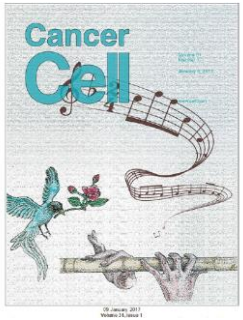
修饰种类多，疾病种类多

退可守

检测技术

功能研究

临床诊治



RNA m6A与白血病

Cancer Cell, **2017**, *31*, 127

进可攻

1

Epi proColon®

FDA批准第一个结直肠癌血液检测试剂—Epi proColon (Epigenomics)

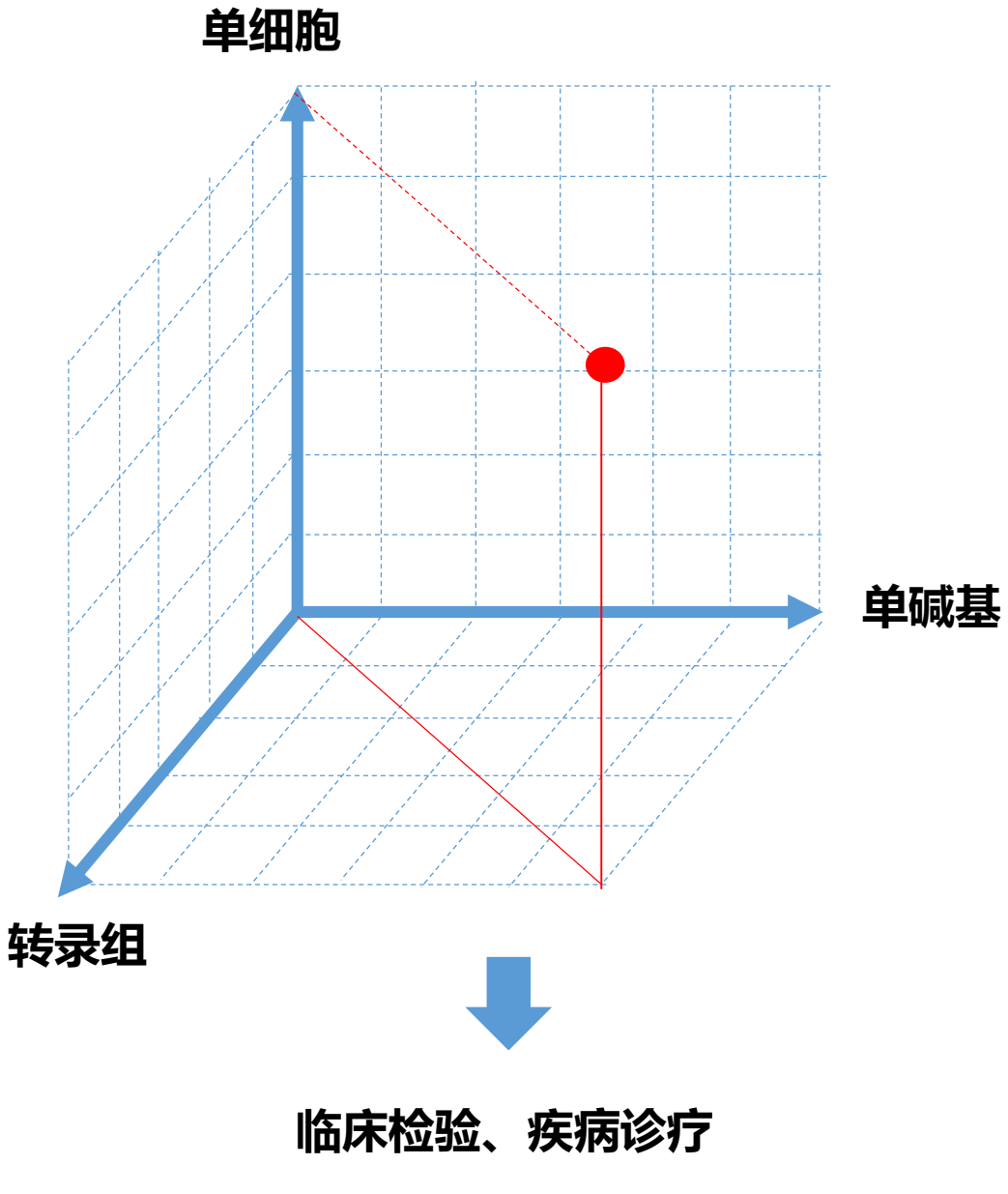
EpiproColon是一种针对甲基化Septin9基因的血液检测方法，它在结直肠癌细胞中高度甲基化，在正常组织中不会甲基化

2

地西他滨通过抑制DNA甲基转移酶减少甲基化来抑制肿瘤细胞增殖并防止耐药发生，适用于治疗骨髓增生异常综合征

总结及目标

Works in our group		
DNA	5mC	√
	5hmC	√
	5fC	√
	5caC	√
	5fU	√
	dU	√
mRNA	m6A	√
	m1A	√
	pseudoU	
	5mC	
	5hmC	
To be continued……		



谢谢各位老师！
敬请批评指正！