



# Mining and analysis of homologous proteins of TET enzymes

TET酶同源蛋白挖掘与分析

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# 一、研究背景

## 研究背景

## 定位与互作

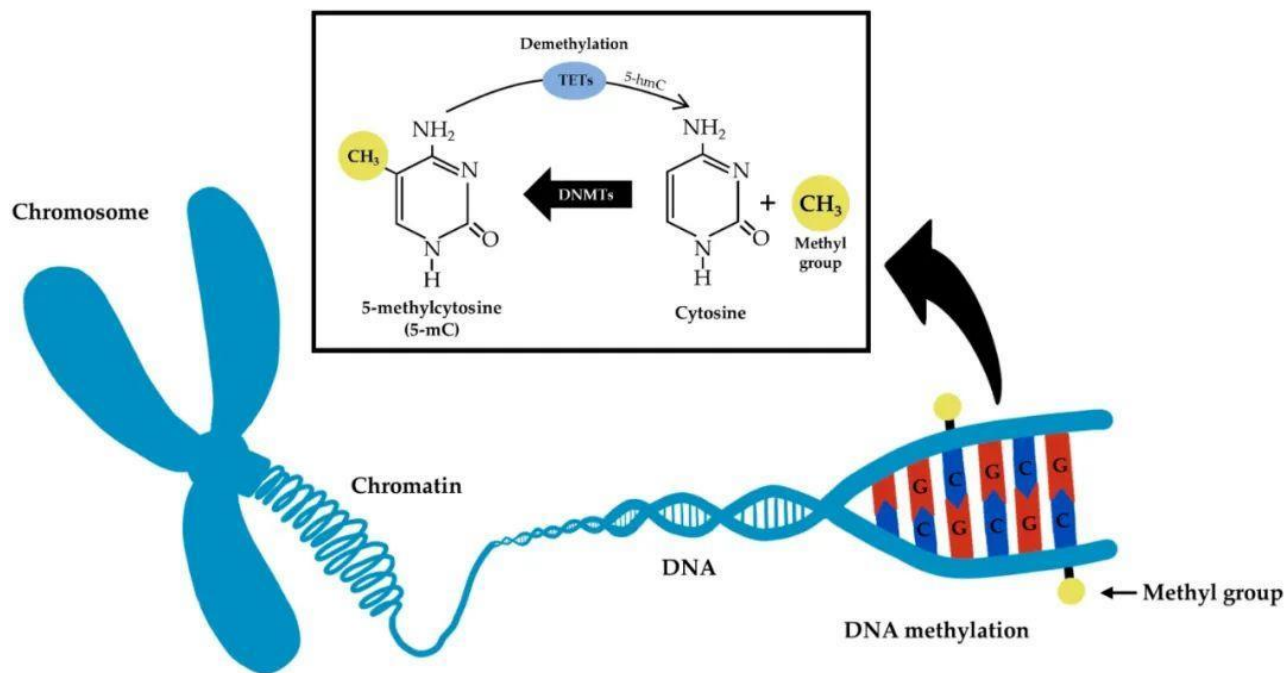
## 序列同源查找

## 进化分析

## 工程潜力

### 1.1 研究背景

**DNA甲基化**是指在DNA分子上（通常位于CpG二核苷酸中的胞嘧啶）添加甲基基团的化学修饰过程。这种表观遗传修饰不改变DNA序列，但可显著影响基因表达，参与多种生命过程：



1. 基因表达调控
2. 基因组稳定性
3. 发育与分化
4. 疾病关联

# 一、研究背景

## 研究背景

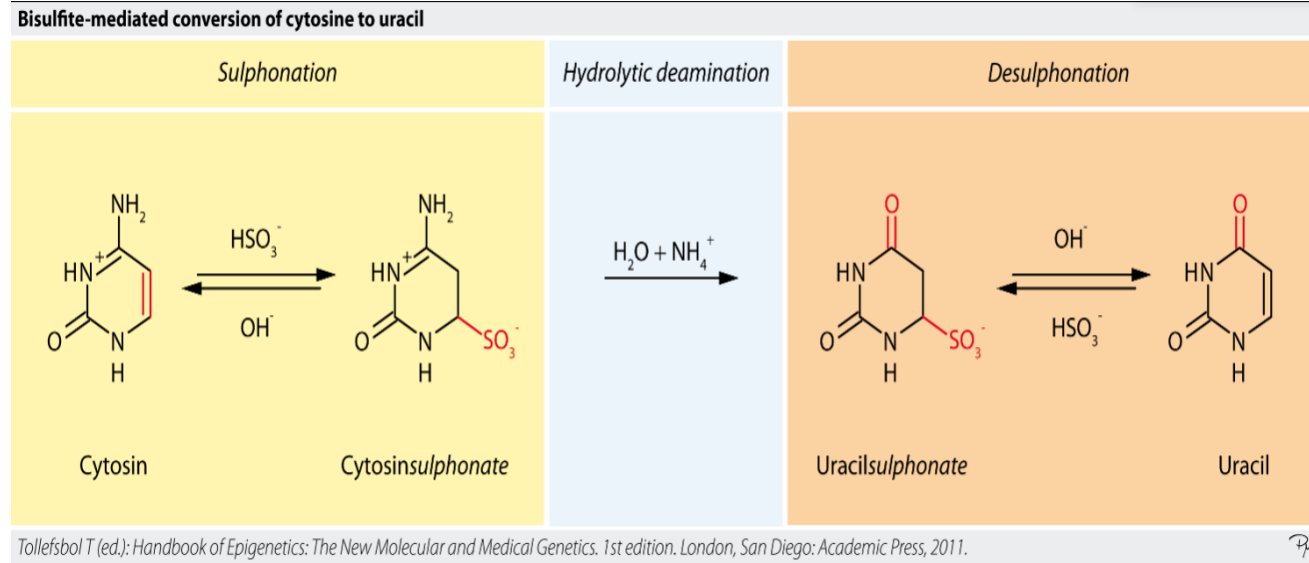
### 1.1 研究背景

定位与互作

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工程潜力



**亚硫酸氢盐方法**是 DNA 甲基化分析的金标准技术，其核心原理是未甲基化的胞嘧啶 (C) 被转化为尿嘧啶 (U)，而甲基化胞嘧啶 (5mC) 保持不变，经 PCR 后 U 变为 T，通过测序可区分甲基化状态

# 一、研究背景

研究背景

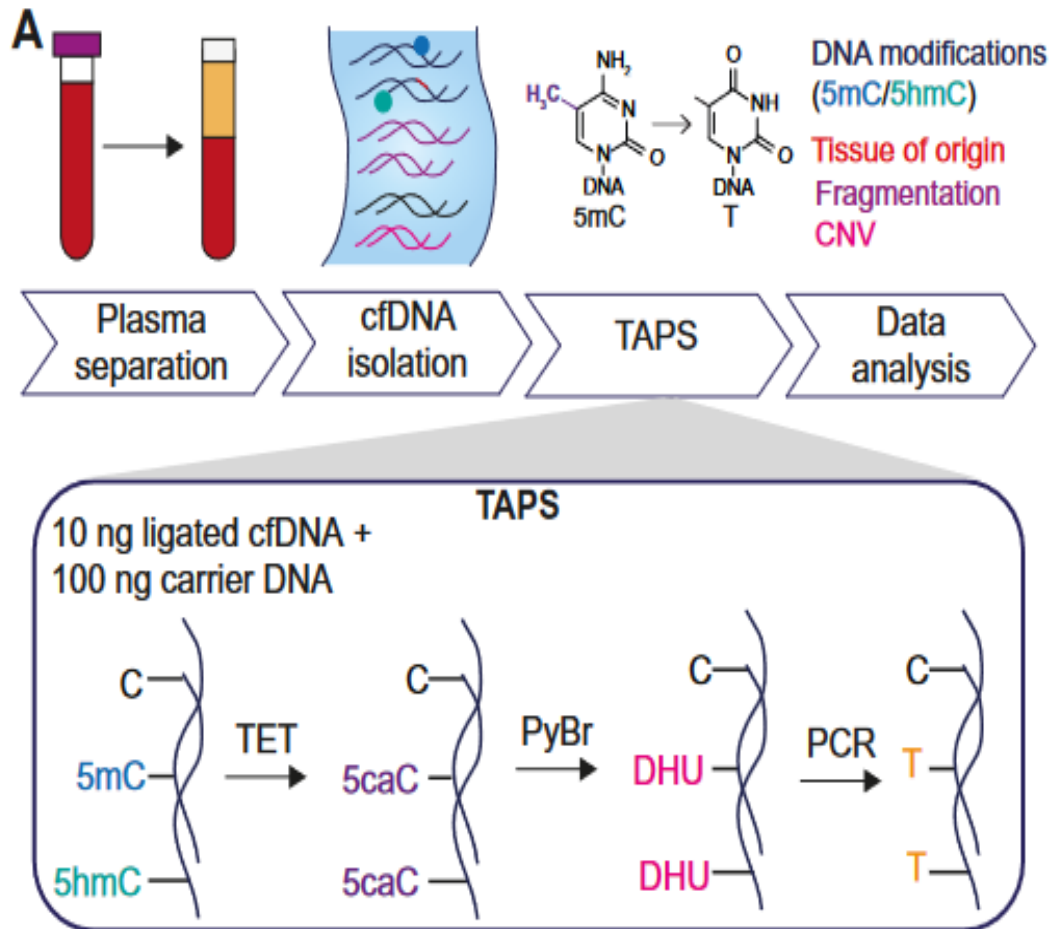
定位与互作

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## 1.1 研究背景



DNA甲基化是表观遗传调控的关键机制，与癌症、神经退行性疾病、发育异常等密切相关。

技术比较:

a. 甲基化测序的“金标准”亚硫酸氢盐法存在固有缺陷

b. 新兴解决方案:TAPS法: 一种无损、信息保全的新方法。TAPS的性能高度依赖于其关键酶——TET酶(ten-eleven translocation)的效率

寻找具有更高催化效率或更佳稳定性的TET酶，以提升TAPS技术的整体性能

## 二、亚细胞定位与互作分析

研究背景

定位与互作

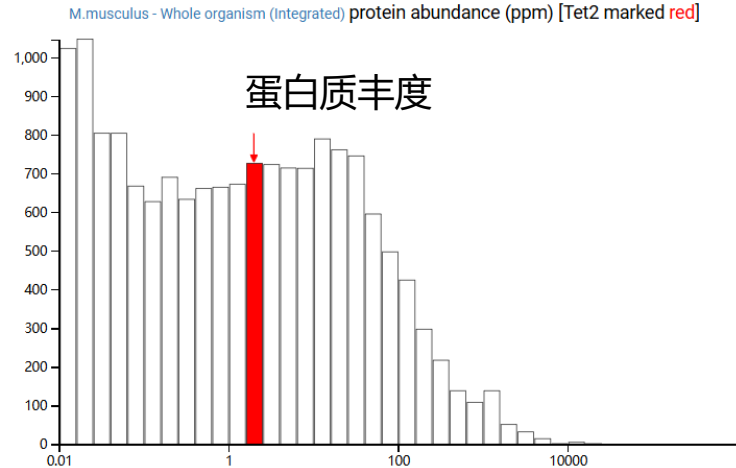
序列同源查找

进化分析

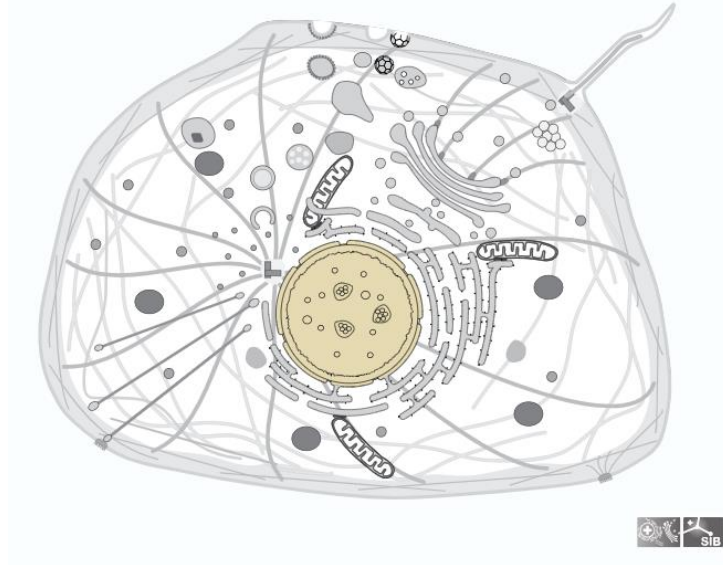
工程潜力

### 2.1 亚细胞定位分析

Protein Abundance Histogram



Nucleus



- **该TET酶蛋白质丰度低**：符合“催化剂”和“信号调节器”的身份
- **该TET酶定位在细胞核**：与“参与DNA去甲基化”和“介导O-GlcNAc转移酶OGT招募至活性基因CpG富集的转录起始位点，从而促进OGT介导的组蛋白H2B GlcNA酰化”等功能相对应
- **可见，该TET酶在细胞核中发挥重要作用**

## 二、亚细胞定位与互作分析

研究背景

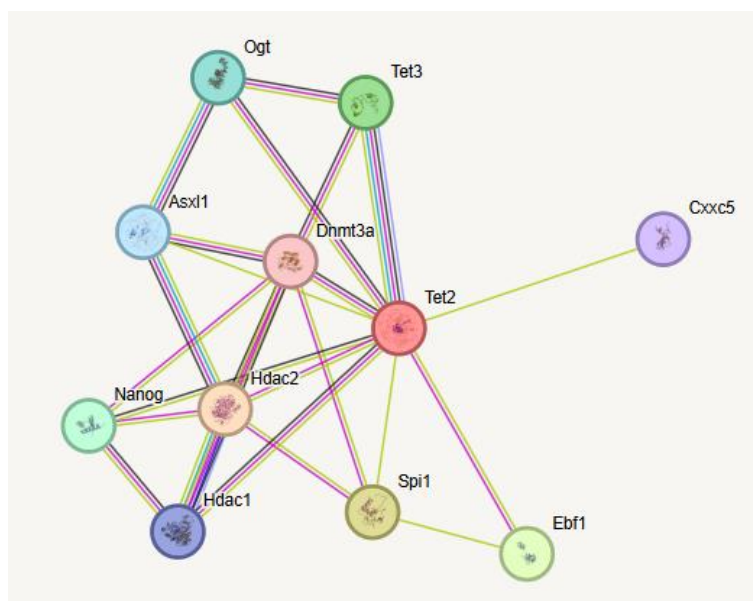
### 2.1 TET酶的蛋白互作网络分析

定位与互作

序列同源查找

进化分析

工程潜力



	Neighborhood	Gene Fusion	Cooccurrence	Coexpression	Experiments	Databases	Textmining [Homology]	Score
Hdac2					●		●	0.992
Spi1							●	0.965
Ebf1					●		●	0.950
Tet3				●	●	●	●	0.947
Nanog				●			●	0.940
Ogt				●	●		●	0.936
Asxl1							●	0.920
Hdac1				●	●		●	0.915
Cxxc5							●	0.900
Dnmt3a				●	●		●	0.898

- TET酶与多种甲基化相关的蛋白互作，共同构成生物体中的甲基化调控通路。



# 三、序列同源查找

研究背景

## Interpro查找功能序列

定位与互作

序列同源查找

进化分析

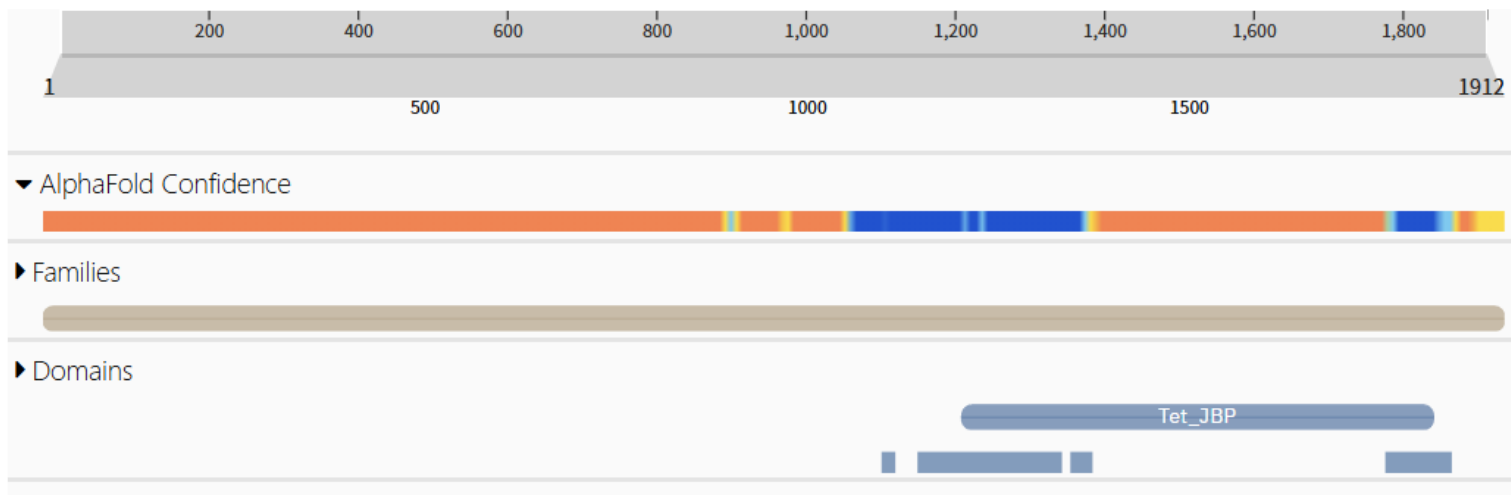
工程潜力

Entry matches to this protein<sup>1</sup>



Feature Display Mode <sup>?</sup>

Summary  Full





# 三、序列同源查找

研究背景

定位与互作

序列同源查找

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## BLASTP 同源查找

select all 10 sequences selected [GenPept](#) [Graphics](#) [Distance tree of results](#) [Multiple alignment](#) [MSA Viewer](#)

	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET2; AltName: Full=Protein Ayu17-449 [Mus musculus]</a>	<a href="#">Mus musculus</a>	1296	1296	100%	0.0	100.00%	1912	<a href="#">Q4JK59.3</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET2 [Homo sapiens]</a>	<a href="#">Homo sapiens</a>	680	680	100%	0.0	59.94%	2002	<a href="#">Q6N021.3</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase tet3-A [Xenopus laevis]</a>	<a href="#">Xenopus laevis</a>	240	335	39%	1e-66	62.01%	1925	<a href="#">A0A1L8GSA2.1</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase tet3 [Xenopus tropicalis]</a>	<a href="#">Xenopus tropicalis</a>	238	336	39%	9e-66	62.57%	1901	<a href="#">A0JP82.1</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET3 [Mus musculus]</a>	<a href="#">Mus musculus</a>	235	332	39%	7e-65	63.13%	1803	<a href="#">Q8BG87.4</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET3 [Homo sapiens]</a>	<a href="#">Homo sapiens</a>	234	331	47%	2e-64	52.16%	1795	<a href="#">O43151.4</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase tet3-B [Xenopus laevis]</a>	<a href="#">Xenopus laevis</a>	232	329	39%	6e-64	61.45%	1915	<a href="#">K9JHZ4.1</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET1; AltName: Full=CXXC-type zinc finger protein 6; AltName: ...</a>	<a href="#">Homo sapiens</a>	231	333	47%	1e-63	52.10%	2136	<a href="#">Q8NFU7.2</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET1; AltName: Full=CXXC-type zinc finger protein 6; AltName: ...</a>	<a href="#">Mus musculus</a>	205	294	40%	1e-54	50.46%	2039	<a href="#">Q3URK3.3</a>
<input checked="" type="checkbox"/>	<a href="#">RecName: Full=Methylcytosine dioxygenase TET; AltName: Full=DNA 6mA demethylase; AltName: Full=DNA ...</a>	<a href="#">Drosophila mela...</a>	191	274	41%	6e-50	48.95%	2860	<a href="#">M9NEY8.1</a>



# 三、序列同源查找

研究背景

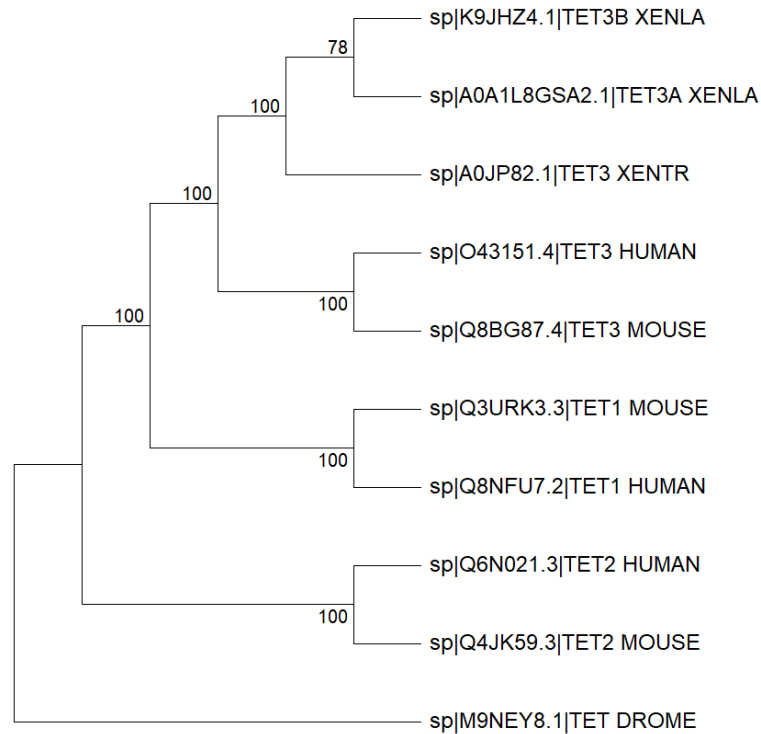
同源查找

定位与互作

序列同源查找

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Species/Abbrv	Sequence
1. sp Q3URK3.3 TET1 MOUSE	-----NCKDAMSVTISGGECDHLLKGRNNTLLFKPGLNCRSG--AEPTIFNHPNTHSAGSRPHPEKVPNKEP-----KDGSPVQPSLLS
2. sp Q8NFU7.2 TET1 HUMAN	-----NHKNAMSSVATDMSCDHLKGRSNVLFVQQPGFNCSSIPHSSHSIIHHASIHNEGDQPKTPENIPSKEP-----KDGSPVQPSLLS
3. sp K9JHZ4.1 TET3B XENLA	HHKRNLFVDSNTEACTQEQQ-----NWWVPNSQQAPVS-----KTTEKPVKERKKRRQ--SPSQKQ-----VEPKPKPP----
4. sp O43151.4 TET3 HUMAN	HHKRSLFLEQVHDTISFPAPSEPSAPGWPPPS--SPVP-----RLPDRPPKEKKKKLP--TFAGGP-----VGTAKAAPGIKF
5. sp Q8BG87.4 TET3 MOUSE	HHKRNLFLEQAQDASFPTSTEPQAPGWVAPPG--SPAP-----RPPDKPPKEKKKPP--TFAGGP-----VGAEKITPGIKI
6. sp A0JP82.1 TET3 XENTR	HHKRNLFVDPNAMEACTQEQQ-----NWWVPSSQQAPVS-----KTTEKPVKERKKRRQ--SPSQKQ-----VEPKPKPQ----
7. sp AOA1L8GSA2.1 TET3A XENLA	HHKRNLFVDPNTEACAQEQQ-----NWWVPKSQKLPVS-----KTTEKPVKERKKRRQRSPSQKQ-----VEPKPKPP----
8. sp Q6N021.3 TET2 HUMAN	-----PVLKQHLNQQASETEPFPSNSHLLQHKPHKQAAQTQPSQSSHLPC-----NQQQQQKLQIKNKEEILQTFPHPQSN-----NDQQREGSFFGC
9. sp Q4JK59.3 TET2 MOUSE	-----HLSQQATEQRLSG--FLQHTPQTQASQTPASQNSNFPQI--CQQQQQQQLQRKNKEQMPQTFSHLQGS-----NDKQREGSCFCG
10. sp M9NEY8.1 TET DROME	SLDFTQTQSYAYPSNGYVQSGLGFDPNYGRSPYAAPVQRYDFQSQQLSTAPSAINQVGLQSVAGFAPSYAGQVSAAPVPPSQQQQQQQQQQQHGLGADLNKTMGNDTPGYPRVSSVPPRSLNCNGYSGDYSC

# 三、序列同源查找

研究背景

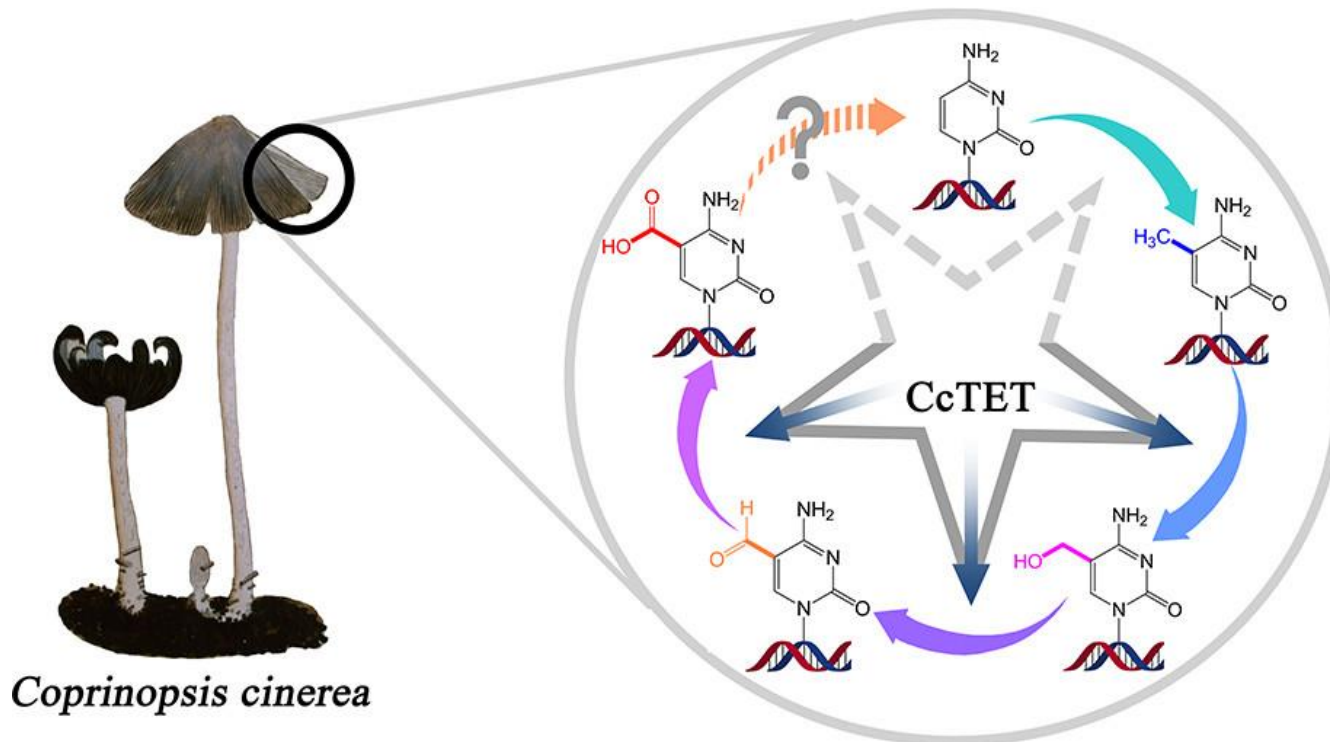
同源查找

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# 三、序列同源查找

研究背景

## PSI-BLAST 同源查找

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	Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession	Select for PSI blast	Used to build PSSM	New adde
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET2; AltName: Full=Protein Ayu17-449 [Mus...	Mus musculus	948	948	100%	0.0	100.00%	1912	Q4JK59.3	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET2 [Homo sapiens]	Homo sapiens	914	914	100%	0.0	59.08%	2002	Q6N021.3	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET3 [Homo sapiens]	Homo sapiens	445	445	100%	3e-138	32.46%	1795	Q43151.4	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET3 [Mus musculus]	Mus musculus	344	470	51%	2e-102	49.40%	1803	Q8BG87.4	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET1; AltName: Full=CXXC-type zinc finger pr...	Homo sapiens	344	465	60%	2e-102	43.22%	2136	Q8NFU7.2	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase tet3-A [Xenopus laevis]	Xenopus laevis	329	448	47%	4e-97	50.65%	1925	A0A1L8GSA2.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase tet3-B [Xenopus laevis]	Xenopus laevis	329	451	52%	6e-97	53.99%	1915	K9JHZ4.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase tet3 [Xenopus tropicalis]	Xenopus tropi...	326	453	53%	5e-96	52.65%	1901	A0JP82.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET; AltName: Full=DNA 6mA demethylase; Al...	Drosophila m...	287	393	72%	1e-82	32.30%	2860	M9NEY8.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Methylcytosine dioxygenase TET1; AltName: Full=CXXC-type zinc finger pr...	Mus musculus	281	393	59%	1e-80	44.19%	2039	Q3URK3.3	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
<input checked="" type="checkbox"/>	RecName: Full=Protein piccolo; AltName: Full=Aczonin; AltName: Full=Multidomain presyn...	Rattus norveg...	63.3	118	24%	6e-09	26.67%	5085	Q9JKS6.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Protein piccolo; AltName: Full=Aczonin; AltName: Full=Brain-derived HLMN...	Mus musculus	62.5	62.5	39%	1e-08	22.99%	5068	Q9QYX7.4	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Nik-related protein kinase; AltName: Full=Nck-interacting kinase-like embry...	Mus musculus	56.3	56.3	27%	6e-07	15.43%	1455	Q9R0G8.2	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Protein piccolo; AltName: Full=Aczonin [Homo sapiens]	Homo sapiens	54.0	104	35%	4e-06	24.76%	5142	Q9Y6V0.5	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Pollen-specific leucine-rich repeat extensin-like protein 1; Short=AtPEX1; S...	Arabidopsis th...	52.9	52.9	24%	7e-06	20.69%	956	Q9LJ64.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Protein lifeguard 1; AltName: Full=Glutamate (NMDA) receptor-associated p...	Homo sapiens	52.1	52.1	22%	8e-06	26.09%	371	Q7Z429.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Protein lifeguard 1; AltName: Full=Glutamate (NMDA) receptor-associated p...	Bos taurus	51.7	51.7	23%	9e-06	26.24%	366	Q32L53.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Protein piccolo; AltName: Full=Aczonin [Gallus gallus]	Gallus gallus	52.9	104	33%	9e-06	19.89%	5120	Q9PU36.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=COPII coat assembly protein sec16; AltName: Full=Protein transport protein...	Aspergillus fis...	50.2	50.2	35%	6e-05	20.61%	1835	A1DLN3.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Axotactin; Flags: Precursor [Drosophila melanogaster]	Drosophila m...	49.8	49.8	32%	8e-05	16.98%	2179	M9PE65.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Stress response protein nst1 [Aspergillus niger CBS 513.88]	黑曲霉 Aspergillus ni...	49.4	49.4	59%	8e-05	19.02%	1201	A2R7P5.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Stress response protein NST1 [Coccidioides immitis RS]	粗球孢子菌 Coccidioides i...	47.1	47.1	32%	4e-04	19.05%	1235	Q1E1H4.2	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=Global transcription regulator sge1 [Fusarium fujikuroi IMI 58289]	水稻病菌 Fusarium fujik...	45.9	45.9	15%	6e-04	28.26%	333	S0E3H0.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
<input checked="" type="checkbox"/>	RecName: Full=COPII coat assembly protein sec16; AltName: Full=Protein transport protein...	Aspergillus fu...	46.3	46.3	35%	8e-04	18.94%	1832	Q4WD95.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

烟曲霉



# 四、进化分析

研究背景

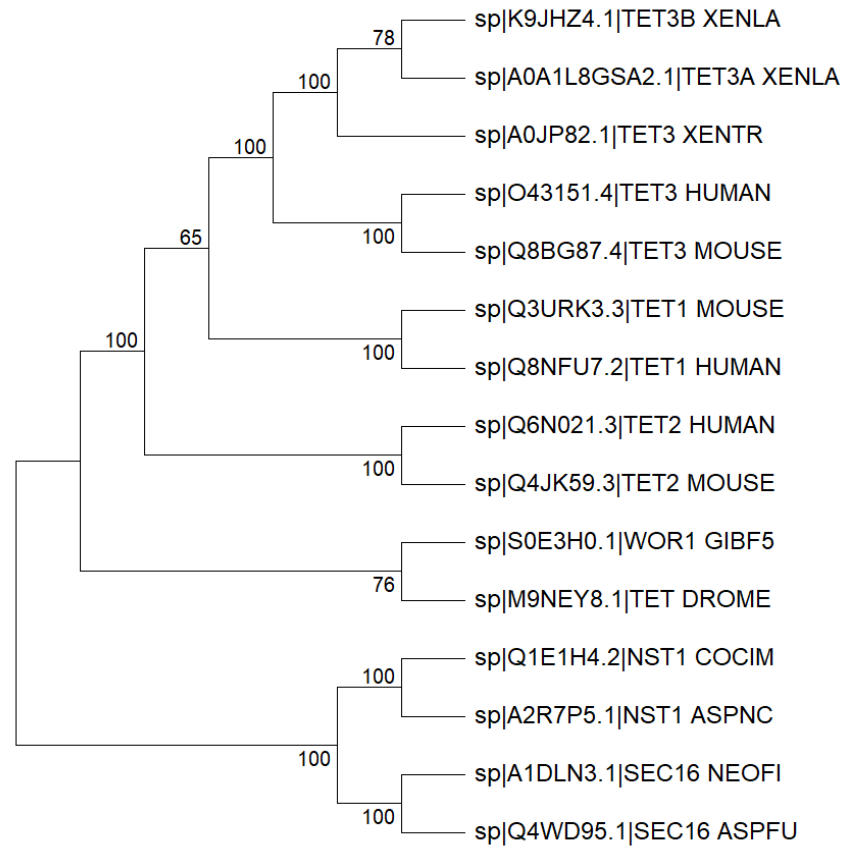
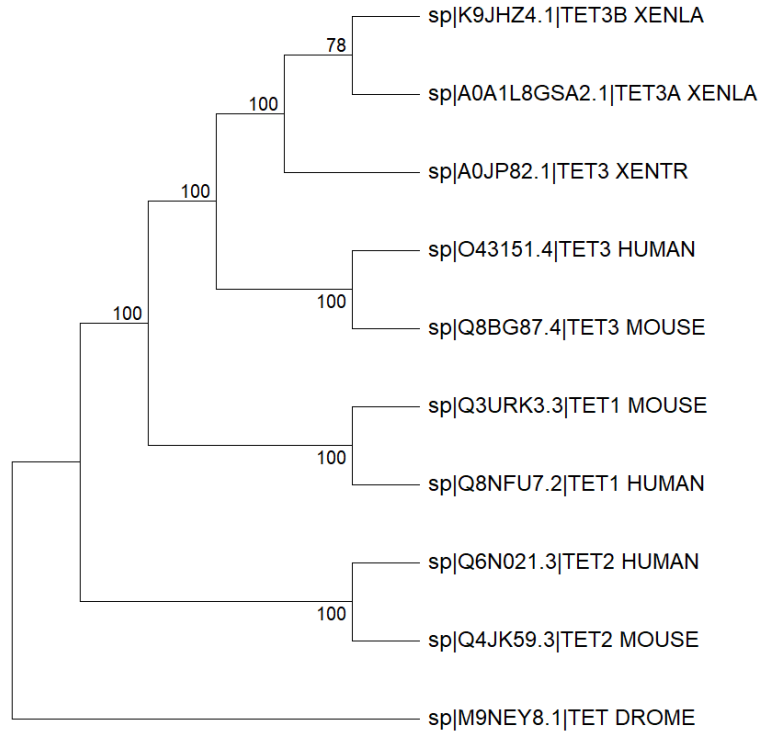
定位与互作

序列同源查找

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## 系统发生树构建



# 五、功能互作与工程潜力分析

研究背景

## 5.2 工程潜力分析

定位与互作

序列同源查找

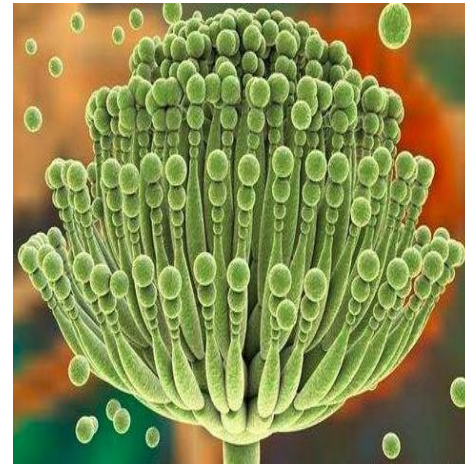
进化分析

工程潜力



**酿酒酵母系统**

- 系统纯净：背景干净
- 改造平台优越：应用广泛



**霉菌系统**

- 文献支撑：cctet
- 更易表达

# 小组成员及分工



G09B宋星月：前期文献调研

G09D赵毅：TET蛋白序列比对和同源性分析

G09A丘萍：TET蛋白理化性质分析以及互作网络分析

G09C李鹭成：思路梳理及PPT润色与讲解



# 汇报结束!

Mining and analysis of homologous proteins of TET  
enzymes

汇报人：C李骞成

小组成员：A丘萍 B宋星月 D赵毅