

Bioinformatics Analysis of CDK5

细胞周期蛋白依赖激酶5 的生物信息学分析

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Background

- Alzheimer's Disease
- CDK5 (Cyclin-dependent kinase 5)'s important role in Alzheimer's Disease

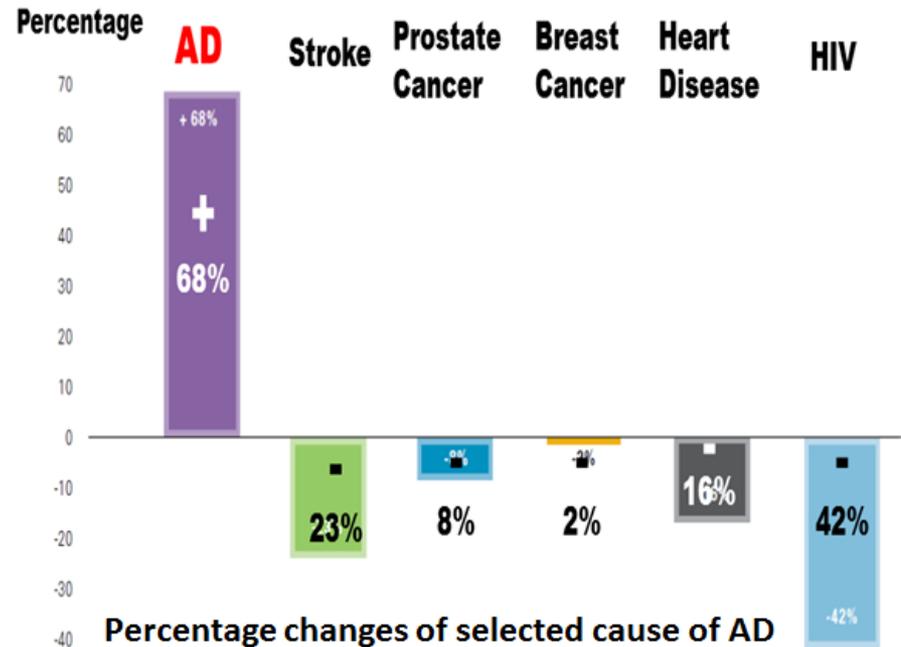
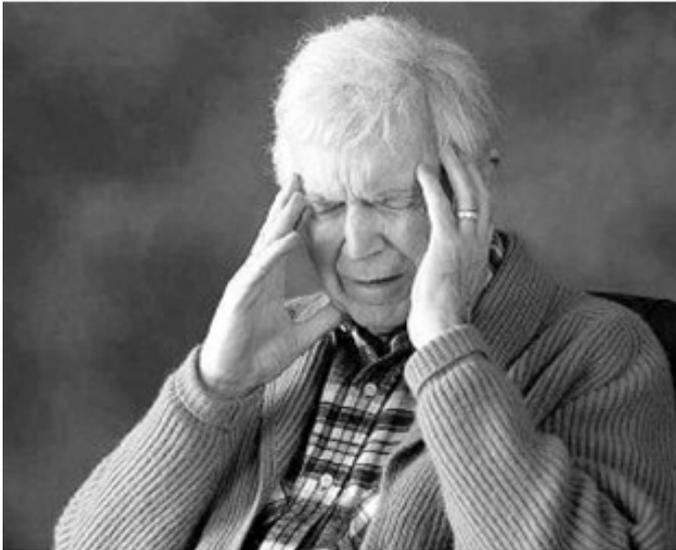
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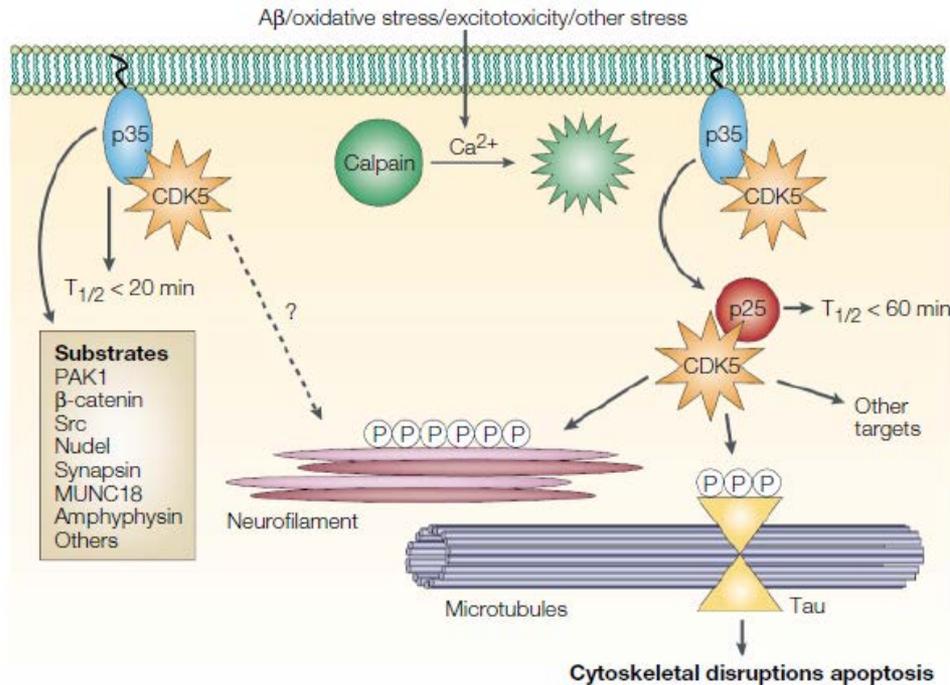
Alzheimer's Disease (阿尔兹海默症)



2013 Alzheimer's Disease Facts and Figures
死亡率变化

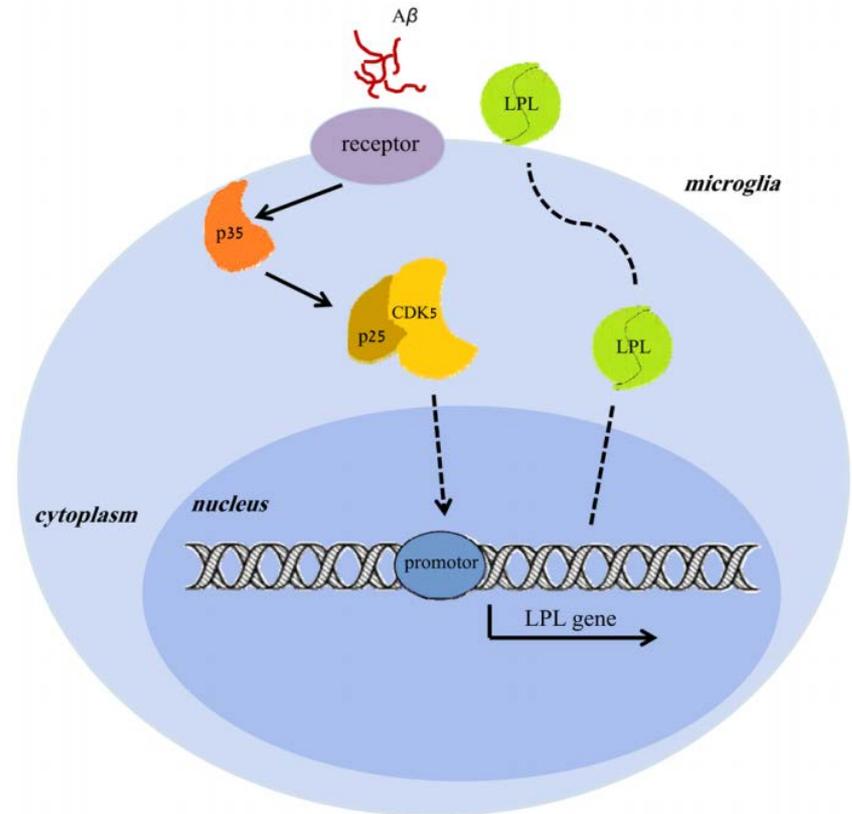
- Money consuming
- Impairment of life quality
- Significant death cause

CDK5's important role in AD



Relation with **Tau**
hyperphosphorylation

CDK5参与Tau的超磷酸化



Relation with **Amyloid plaque**

CDK5与Amyloid淀粉样沉淀相关

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- Achieve research using bioinformatics knowledge

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Research with the help of ABC

Research design	Bioinformatics software & methods
Basic information	NCBI, Uniprot, Pubmed (Advanced research)
Sequence Analysis	Needle, Blast
Phylogenetic Tree construction	Mega6.0
Structure Analysis	EMBOSS, ExPASy, Swiss-pdbViewer, Pymol
Protein interaction & pathway	STRING, KEGG pathway

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- Basic analysis of CDK5
- CDK5: Unique member of CDK family
- The structural basis of CDK5 regulation

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CDK5 isoform, location and structure

Pairwise Alignment Result

LENGTH	SCORE	IDENTITY	SIMILARITY	GAPS
292	1360.5	260/292 (89.0%)	260/292 (89.0%)	32/292 (11.0%)

```

1  MQKYEKLEKIGEGTYGIVFKAKNRETHEIVALKRVRLLLLDDEGVPSSAIR  50
   |||||
1  MQKYEKLEKIGEGTYGIVFKAKNRETHEIVALKRVRLLLLDDEGVPSSAIR  50

51  EICLLKELKHKNIIVRLHDVLSHDKKLTLVFEFCDQDLKKYFDSKNGDLDP  100
   |||||
51  EICLLKELKHKNIIVRLHDVLSHDKKLTLVFEFCDQDLKKYFDSKNGDLDP  100

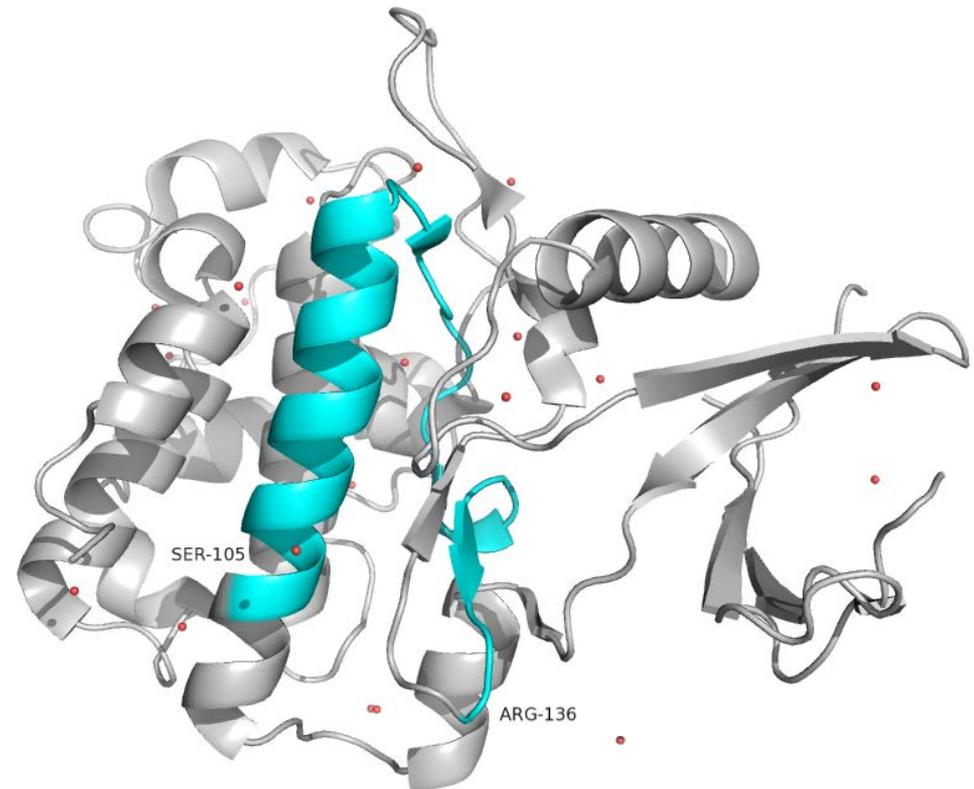
101 EIVKSFLLFQLLKGLGFCHSRNVLHRDLKQPQLLINRNGELKLADFGGLARA  150
     |||||
101 EIVK-----NGELKLADFGGLARA  118

151 FGIPIVRCYSAEIVVILWYRPPDVLPFGAKLYSTSIDMWSAGCIFAELANAGR  200
   |||||
119 FGIPIVRCYSAEIVVILWYRPPDVLPFGAKLYSTSIDMWSAGCIFAELANAGR  168

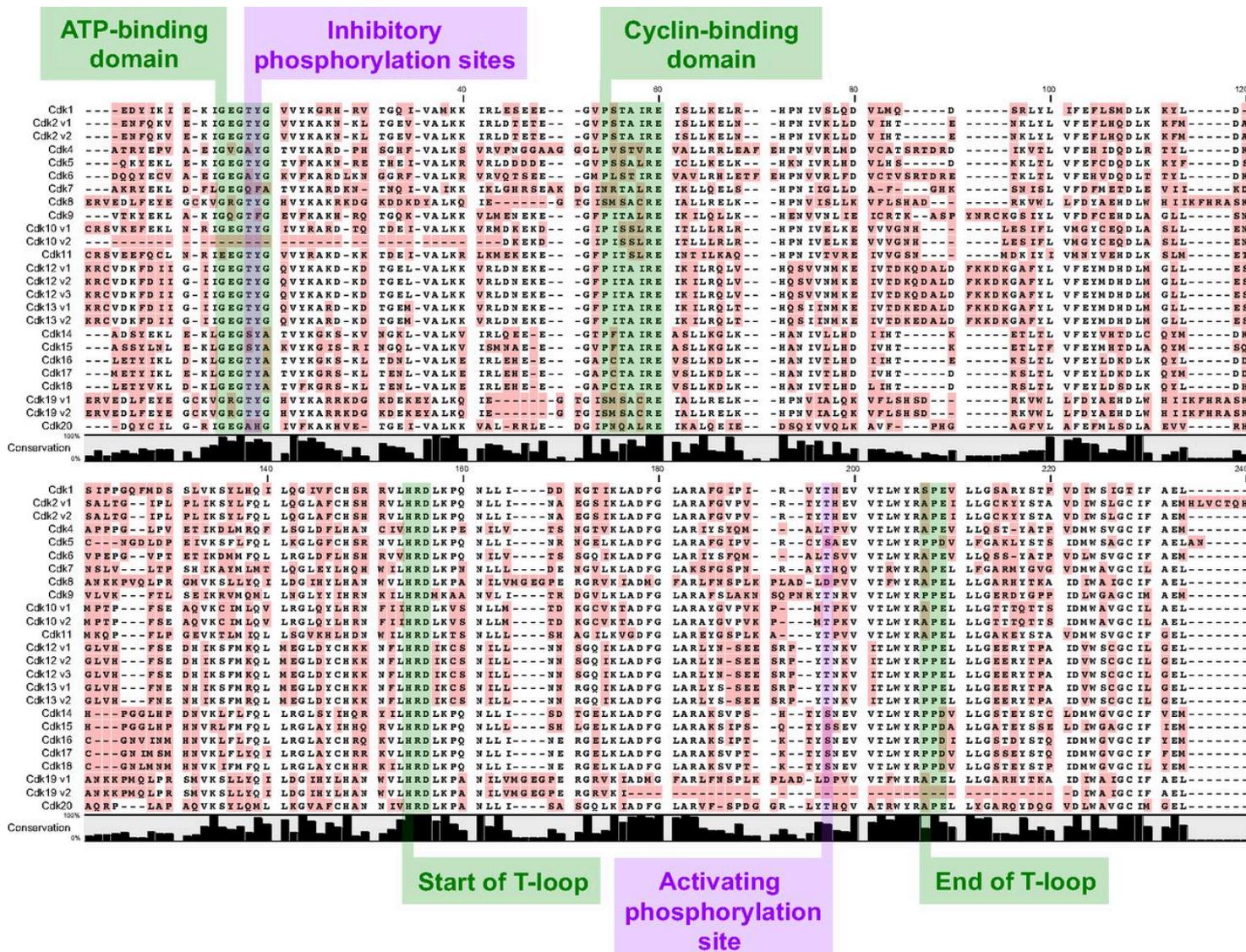
201 PLFPGNDVDDQLKRIFRLLGTPTTEEQWPSMTKLPDYKPYMPYPATTSLVN  250
   |||||
169 PLFPGNDVDDQLKRIFRLLGTPTTEEQWPSMTKLPDYKPYMPYPATTSLVN  218

251 VVPKLNATGRDLLQNLKCNFVQRISAEALQHPYFSDFCPP  292
   |||||
219 VVPKLNATGRDLLQNLKCNFVQRISAEALQHPYFSDFCPP  260
    
```

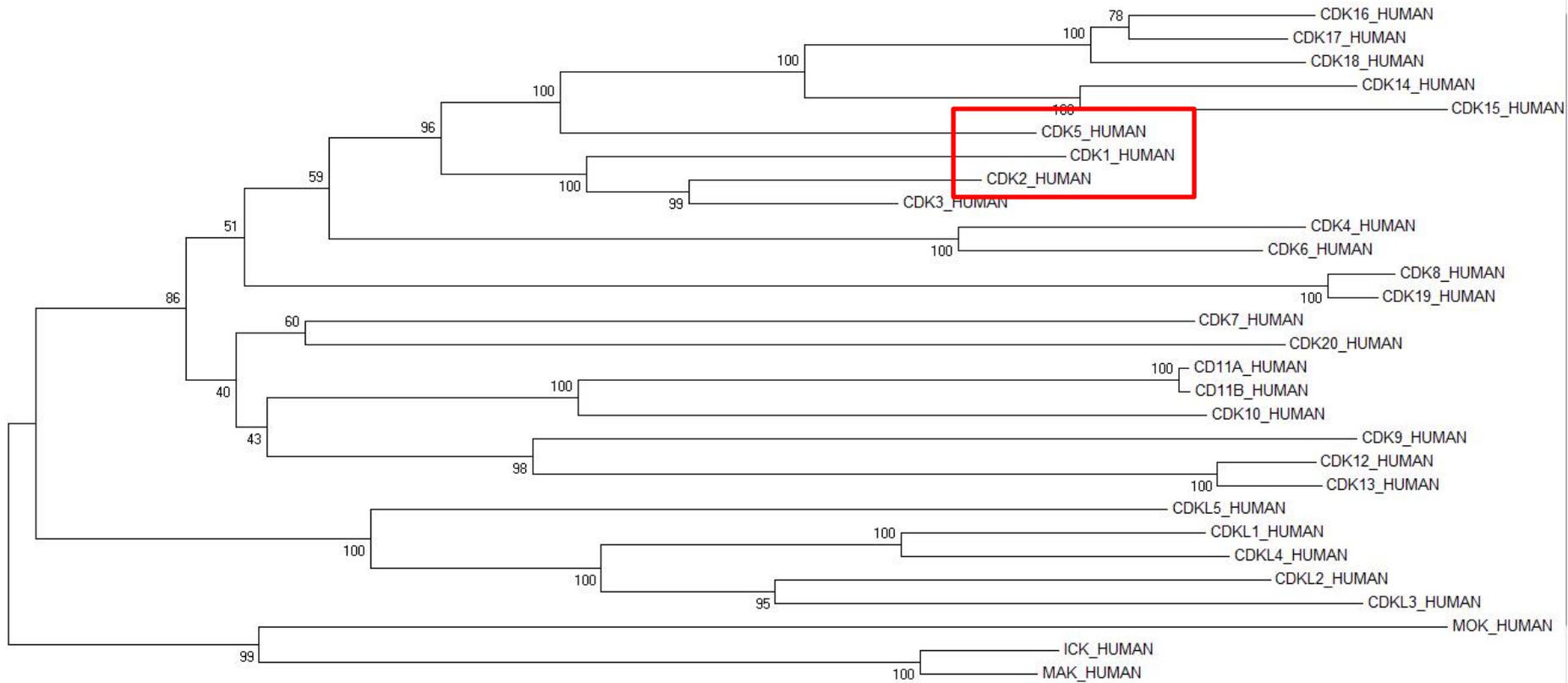
Isoform 1&2 序列比对图



CDK家族蛋白激酶核心区序列比对

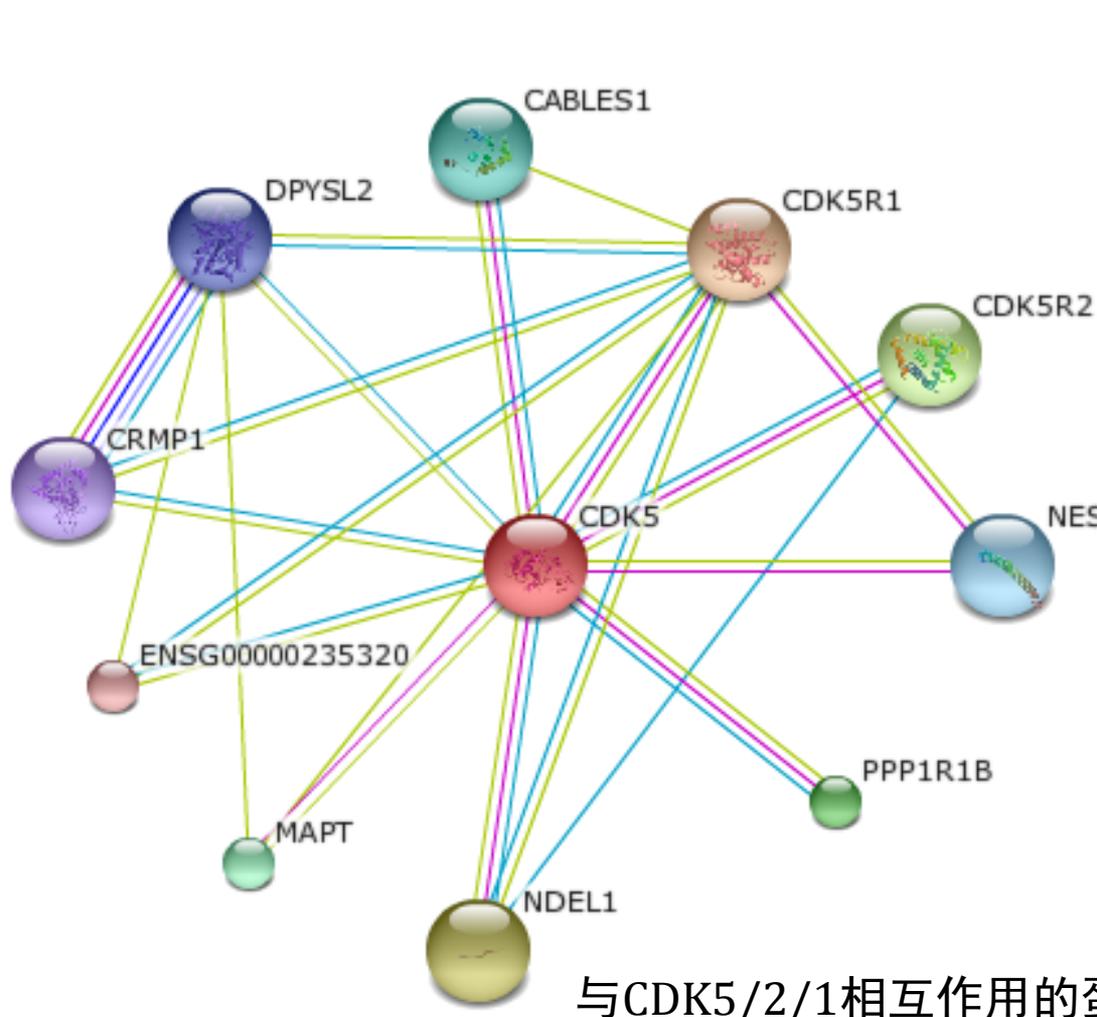


CDK5: unique member of CDK family

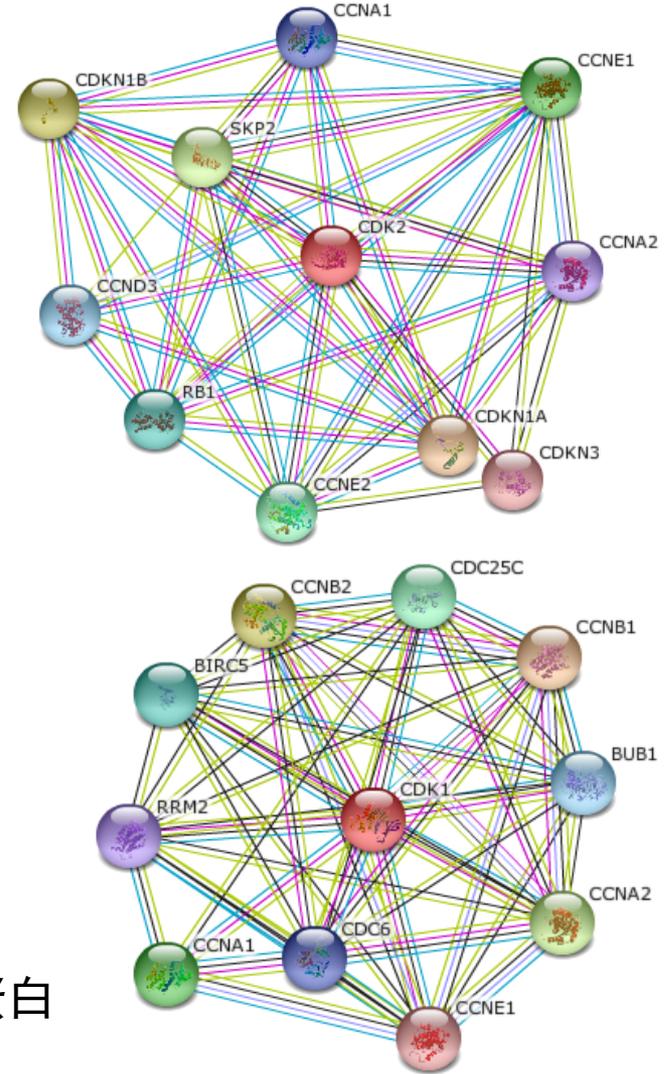


人源CDK家族成员系统发育树

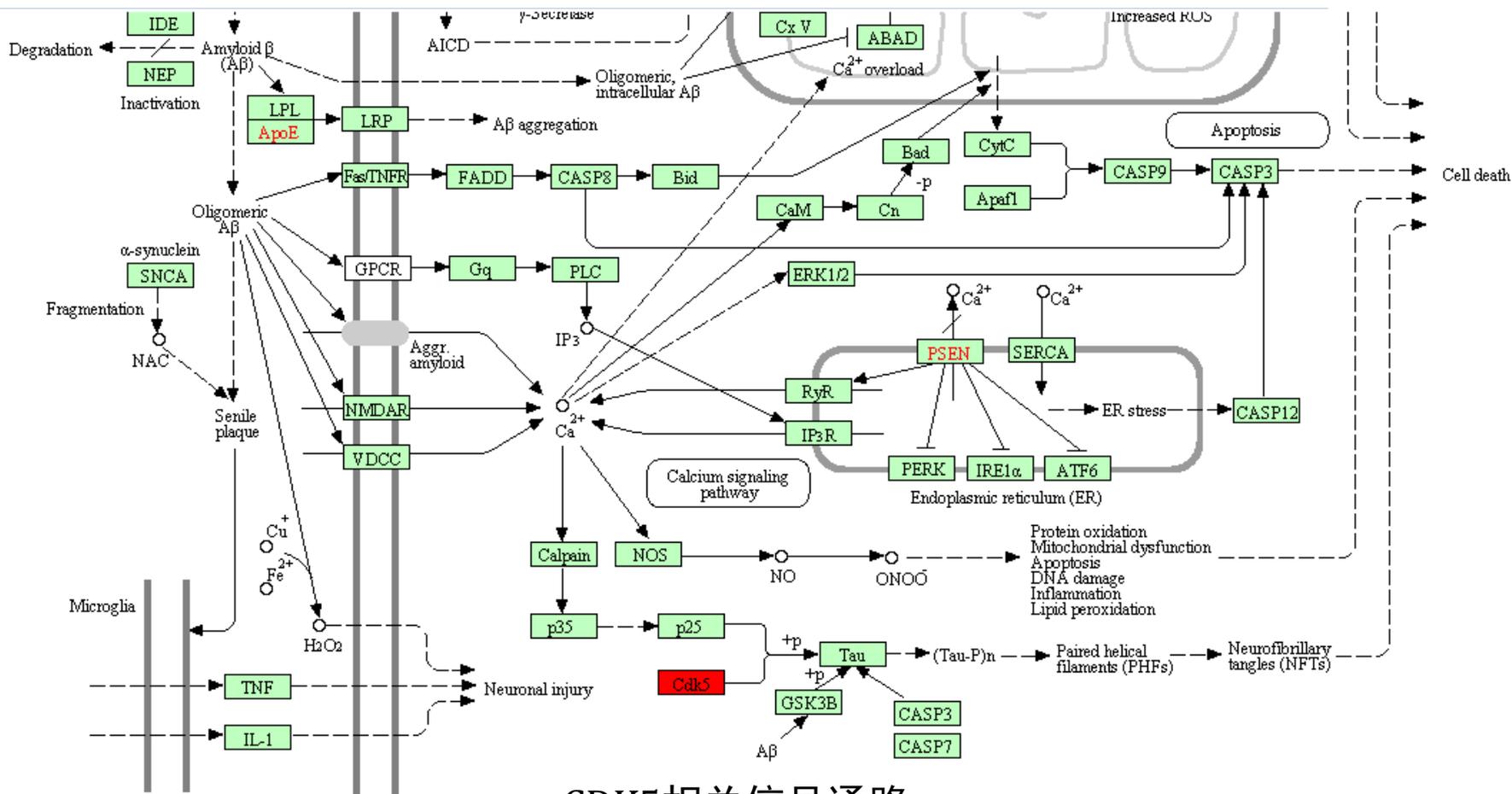
CDK5 doesn't interact with cyclins



与CDK5/2/1相互作用的蛋白



CDK5-related pathways analysis

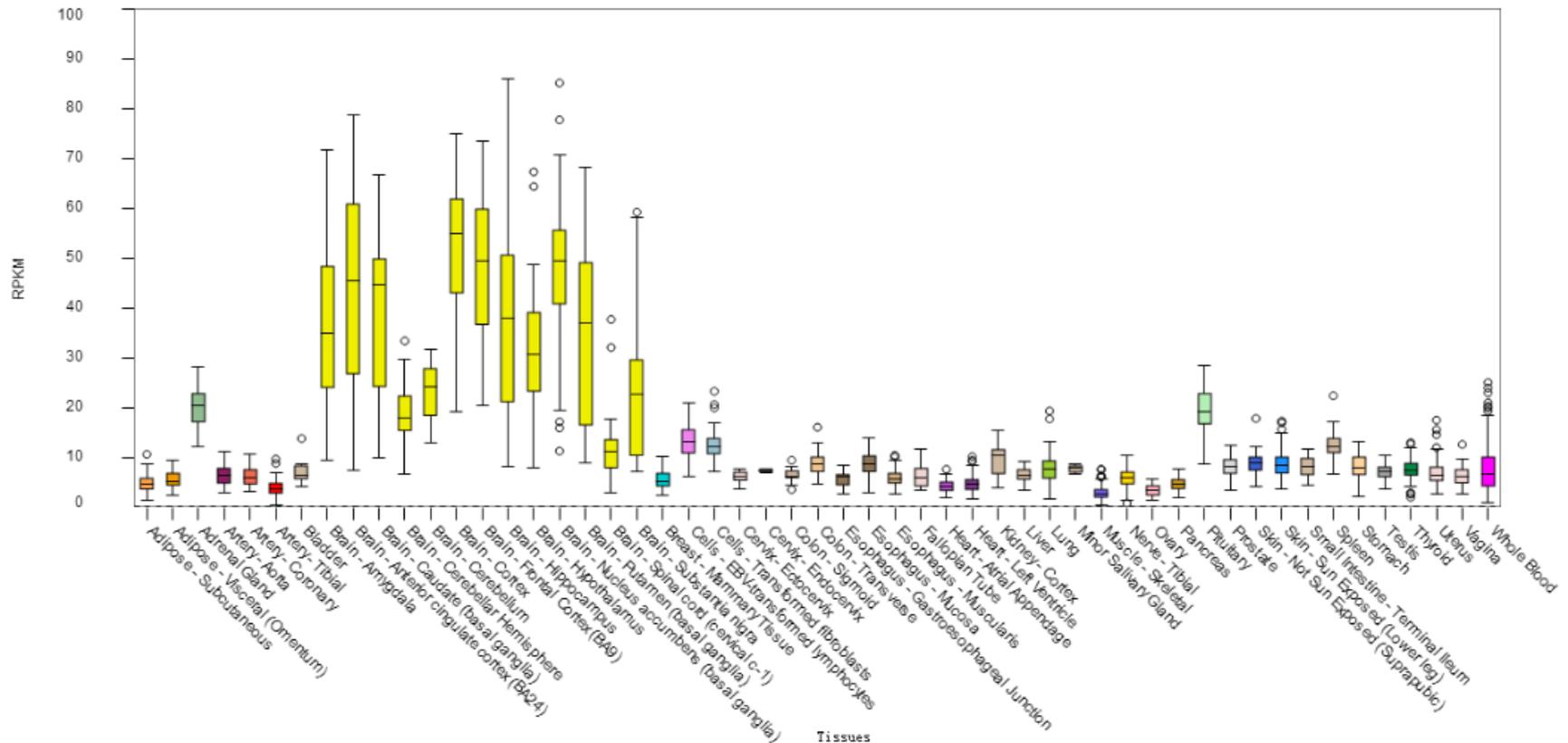


CDK5相关信号通路

Not in cell cycle, but in AD

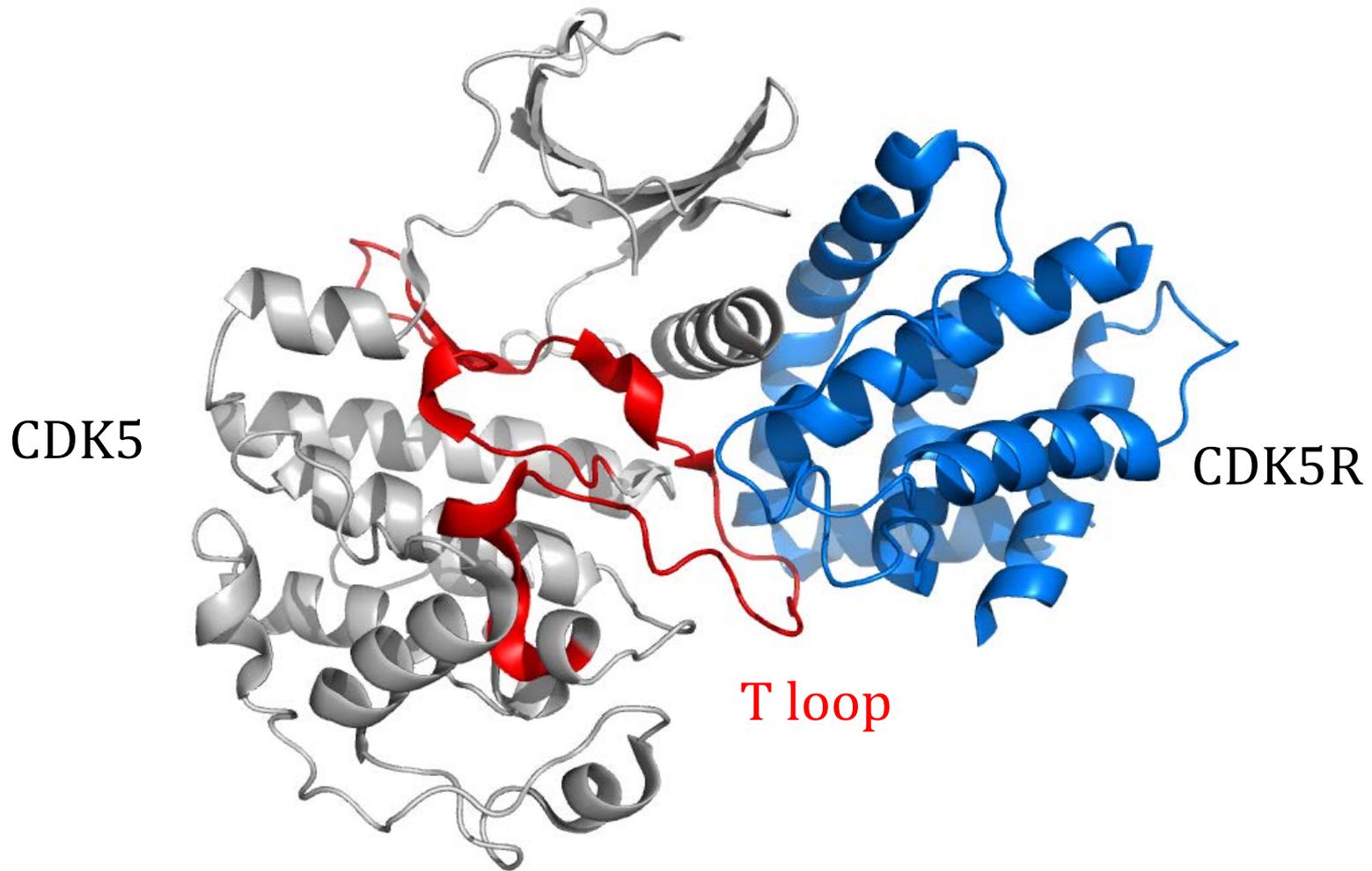
High expression of CDK5 in brain

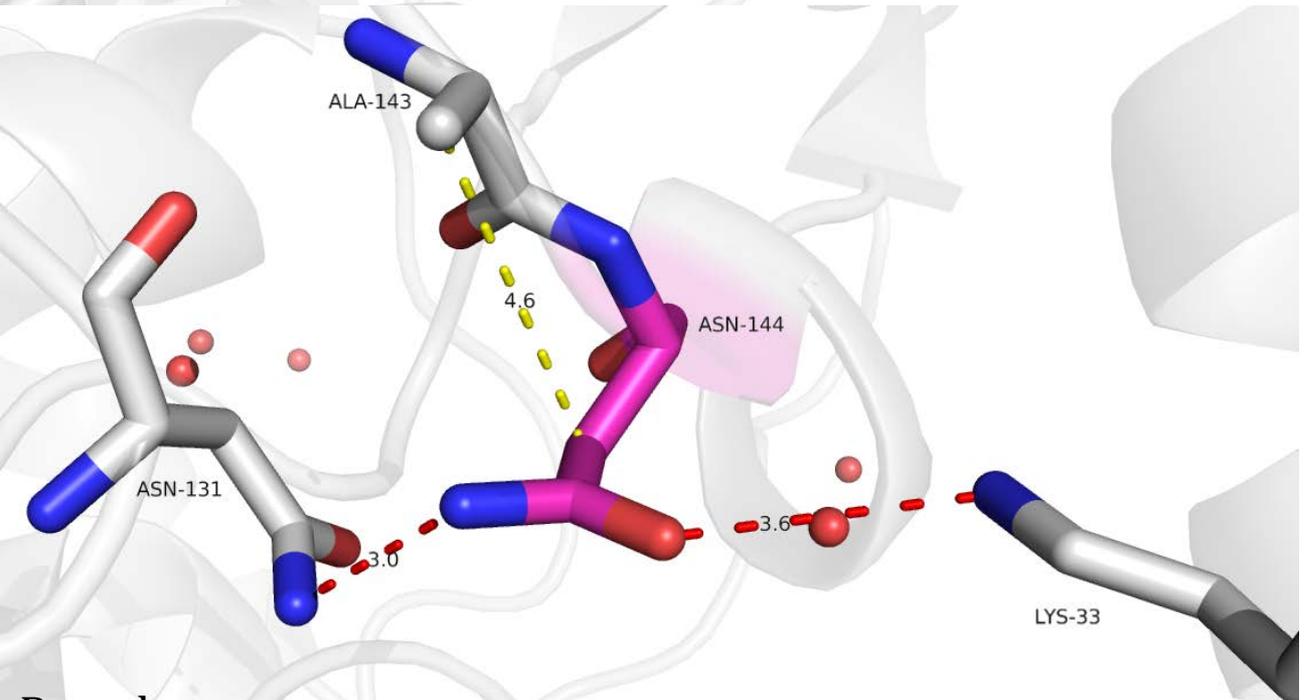
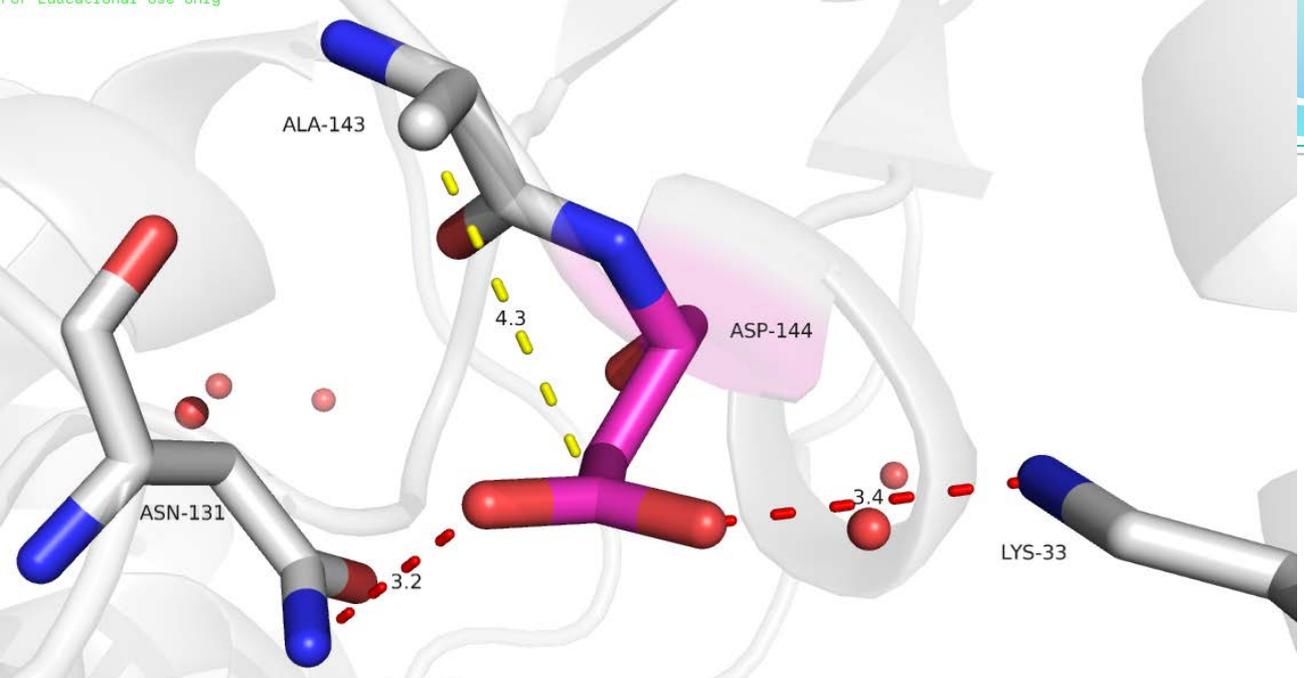
CDK5 Gene View



CDK5在不同组织中的表达差异

Activated form: CDK5-p25 complex

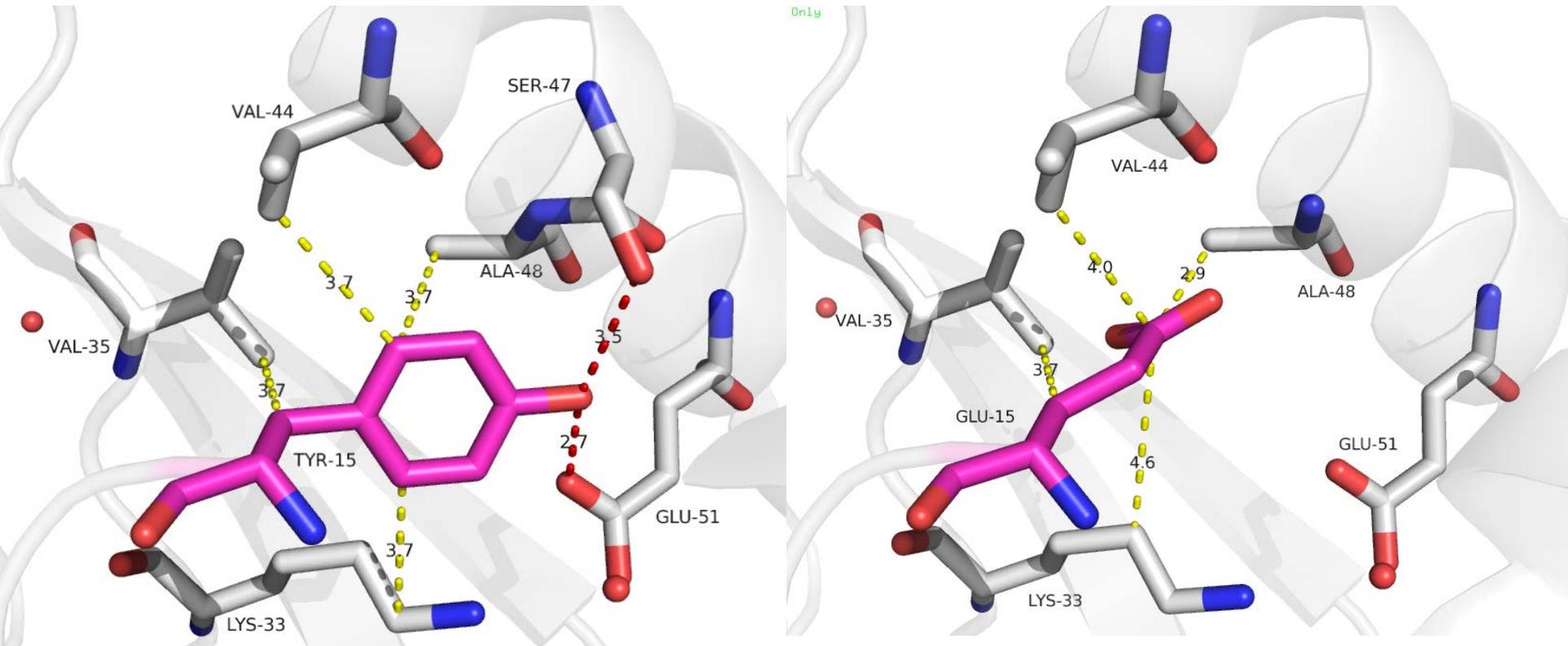




Potential key site mutation analysis (1)

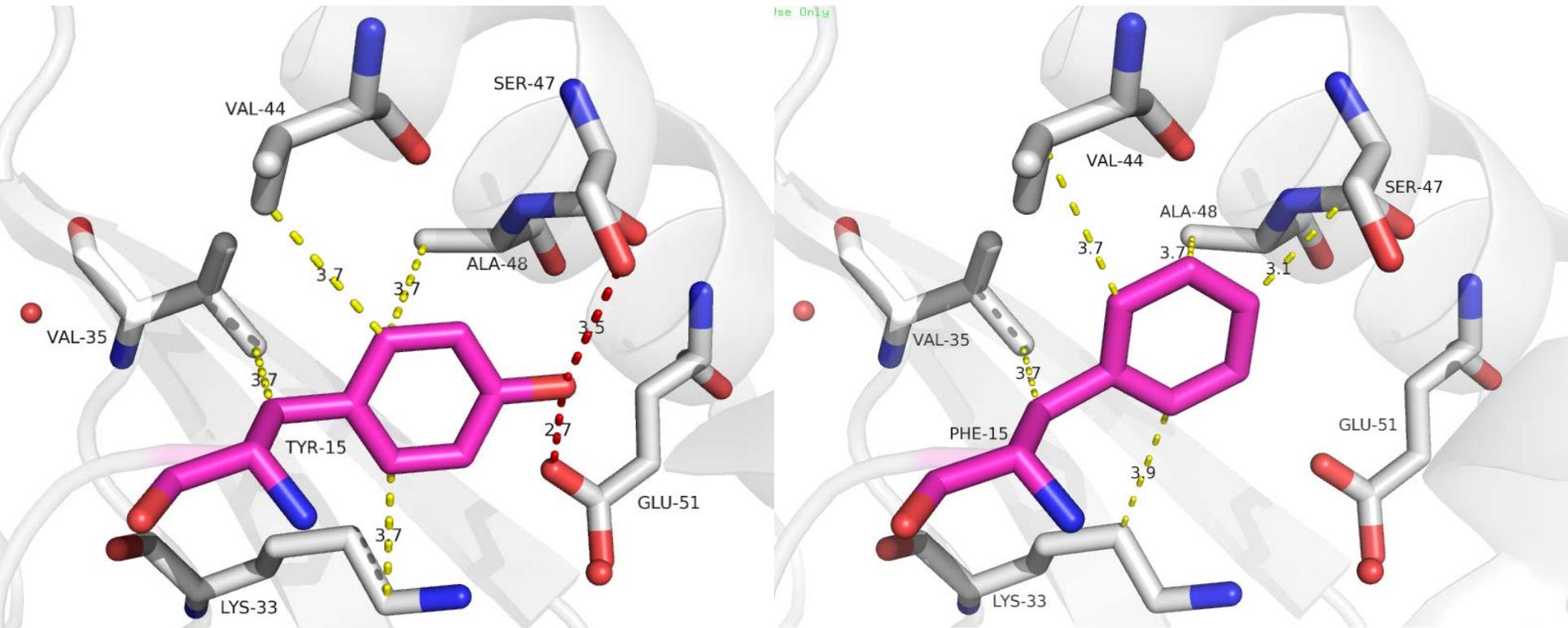
CDK5 D144N

Potential key site mutation analysis (2)



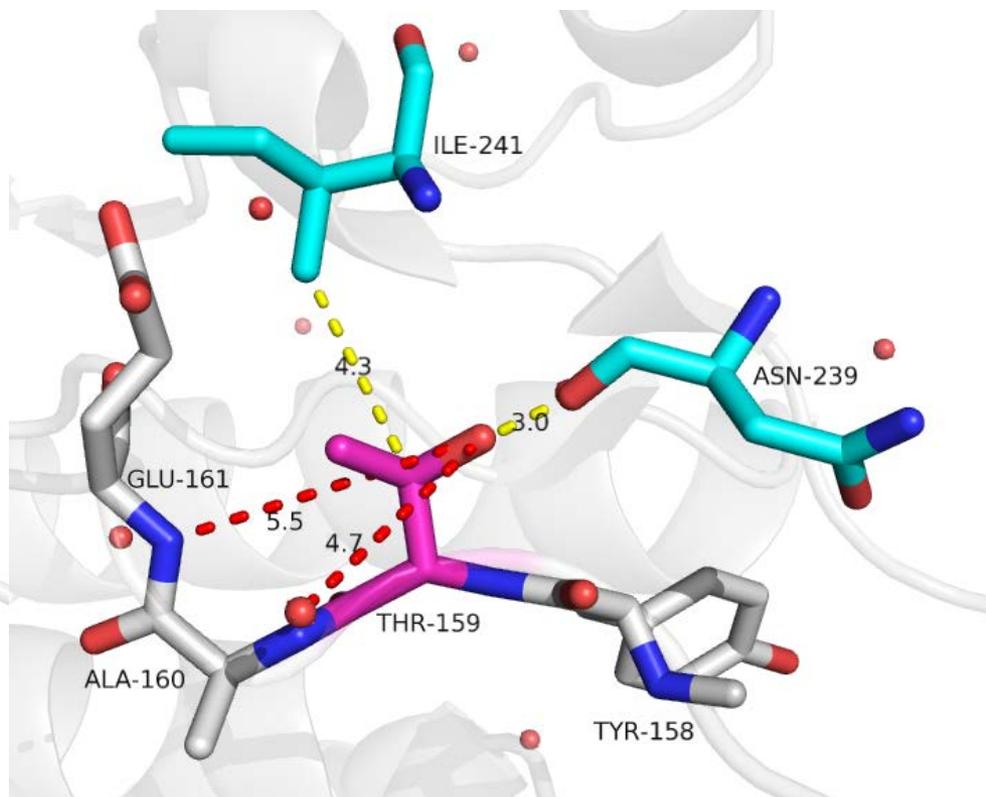
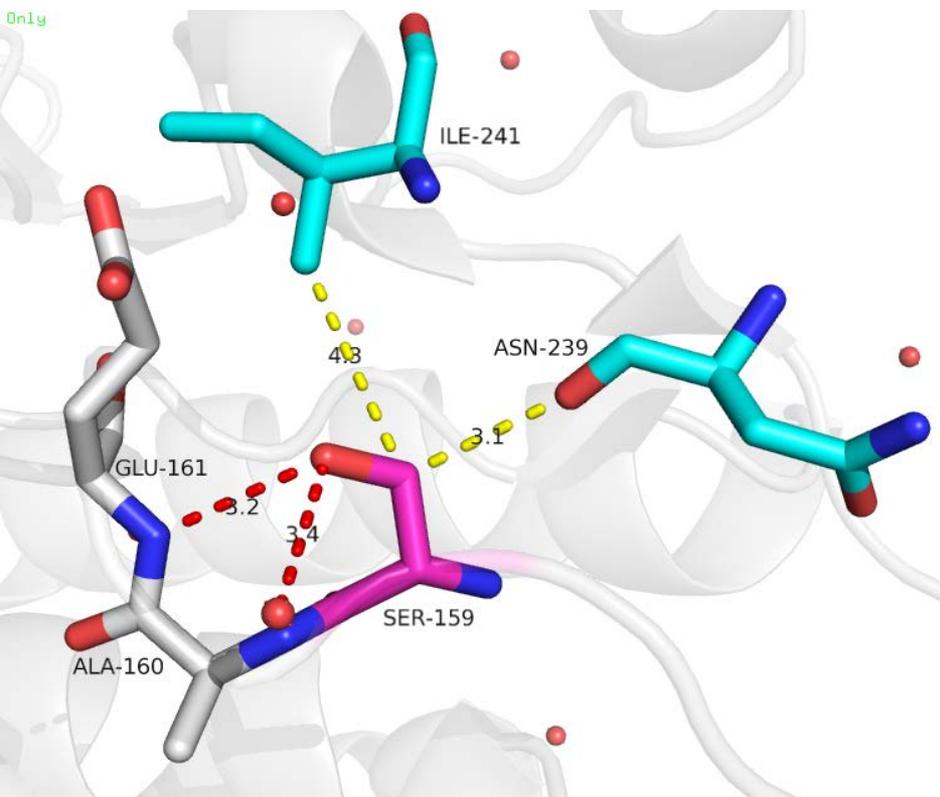
CDK5 Y15E

Potential key site mutation analysis (3)

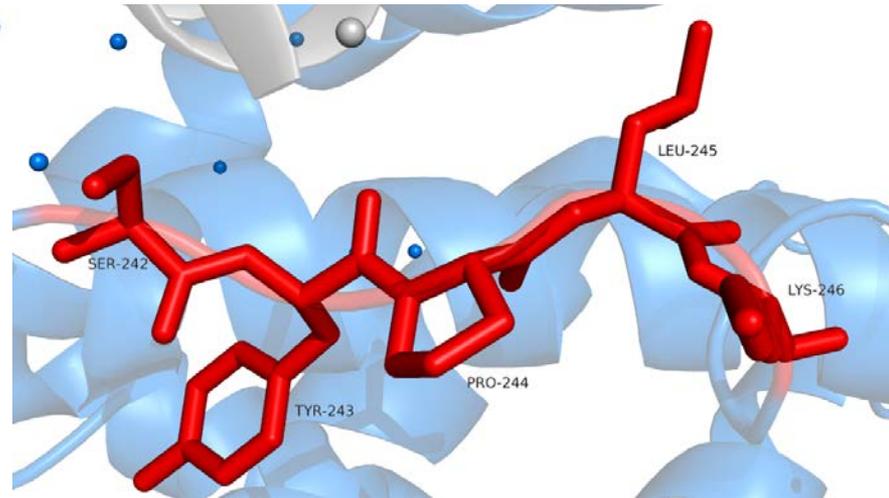
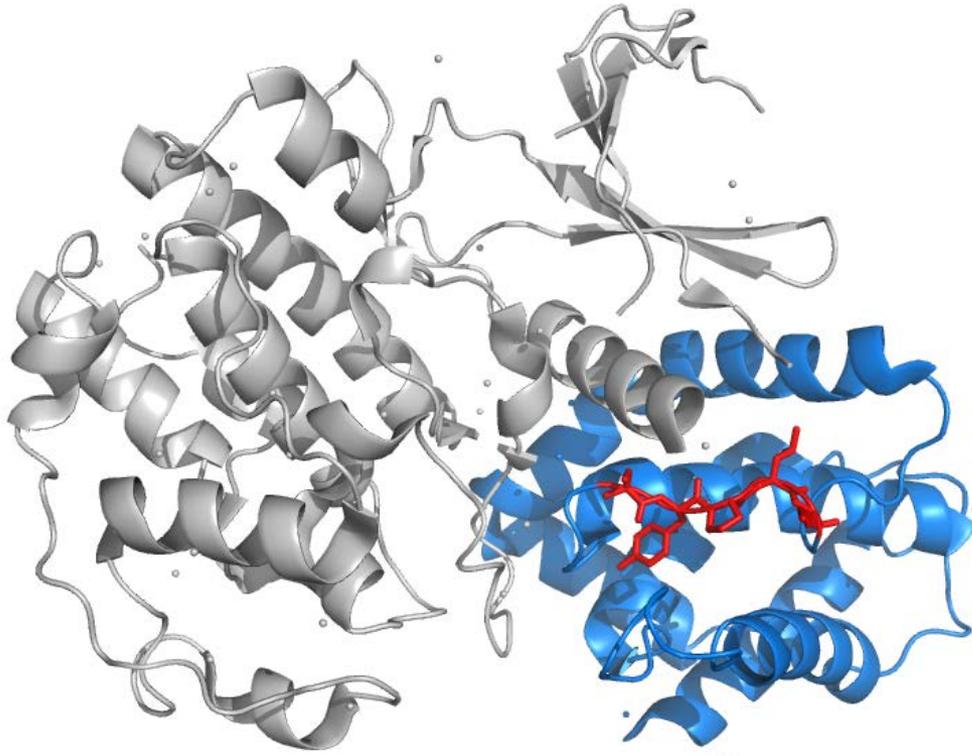


CDK5 Y15F

Confirmed impaired binding activity: S159T



S/T P domain in p35

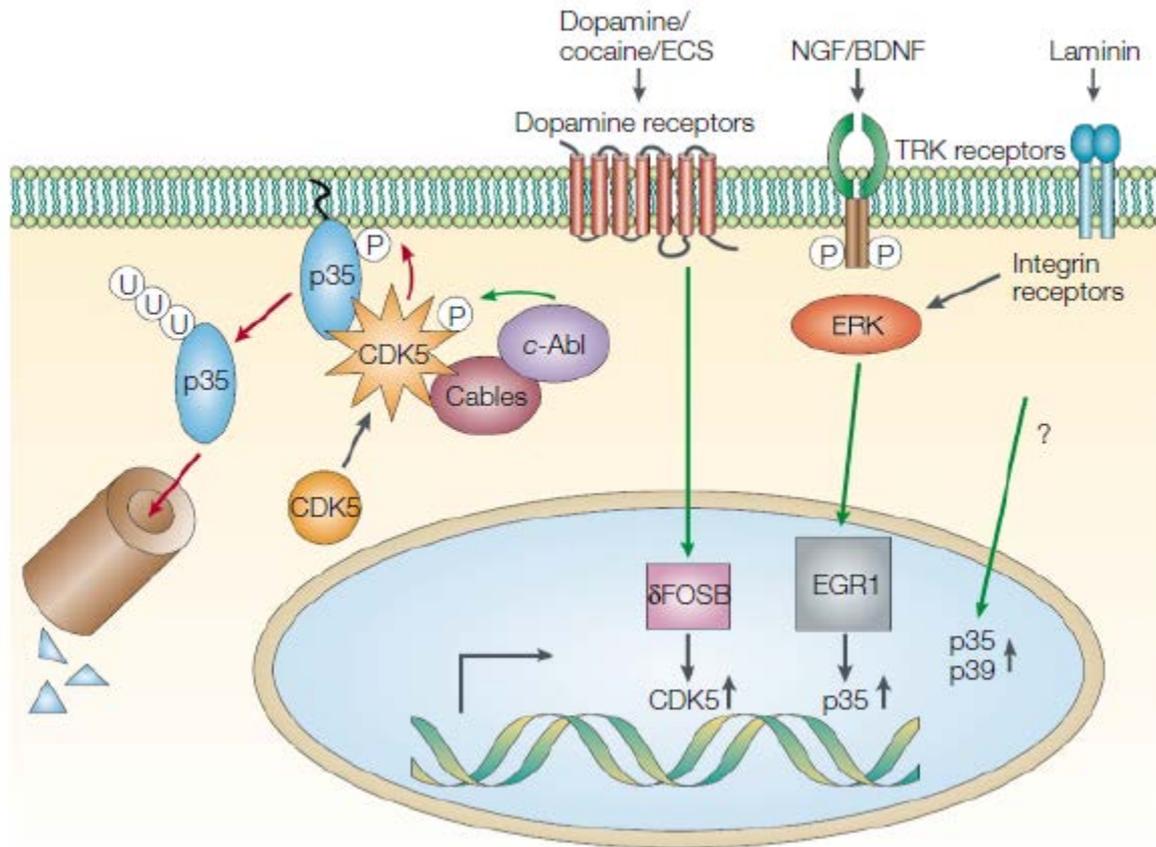


Conserved in different species

✓ NP_003876	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ AAH30792	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ AAH26347	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ NP_001244644	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—SQEDKKRLLLGLD	306
✓ Q28199	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ AAI22780	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSTKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ NP_034001	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNES—GQEDKKRLLLGLD	306
✓ NP_001095286	230	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQVFSDLKNGS—GPEDKKRLLLGLD	306
✓ Q4KYY2	230	LYLSYSYVGNIE SYPLK PFLVESCKEAFWDRCLSVINLMSSKMLQINADPHYFTQAFSDLKNES—GQEDKKRLLLGLD	306
✓ ETE73798	228	LYLSYSYMGNEI SYPLK PFLVESCKEAFWDRCLSIINLMSPKMLQINADPHYFTQVFADLKNES—SQEKNRLLIGLD	304
✓ CBN81694	224	LYLSYSYMGNEI SYPLK PFLVESSKETFWDRCLSIINLMSAKMLQINSDPHYFTQVFADLKNESq—KEEERSRLLIGLD	301
✓ NP_001002515	226	LYLSYSYMGNEI SYPLK PFLVETSKETFWDRCLSIINLMSAKMLQINSDPHYFTQVFADLKNESq—KEEERSRLLIGLD ^[6]	309
✓ AIM47937	227	LYLSYSYMGNEI SYPLK PFLVESCKEVFWDRCLSIINLMSAKMLQINSDPHFFTQVFADLKKESq—SEE—SRLLIGLD	302
✓ NP_001079141	219	LYLSYSYMGNEI SYPLK PFLVEAGKDAFWDRCLCIIDAMSSKMLRINADPHYFTQVFADLKNEN ⁿ —RDEFSRVL—D	292
✓ ETE66392	209	LYLSYSYMGNEI SYPLK PFLVEASKDIFWNRCLHIHAMSAQMLRINADPHYFTQVFADLKNEN ^{nv} AAEDFARVL—D	284

p35的S/T P 结构域高度保守

Negative feedback regulation of CDK5



CDK5-p35的负反馈调控

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Summary

- CDK5 is a unique member of CDK family
 - Similar sequence and activation method
 - Different regulatory subunits and function
- Further research of CDK5 by mutagenesis is promising
- CDK5 is stringently regulated in negative feedback way and this mechanism may be conserved in different species
- Research on CDK5 in AD may cast light on the underlying mechanism

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- TA Wang Zhimin
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