



## 蛋白质基序模式对蛋白互作的影响

# Effect analysis of protein motif pattern on protein-protein interaction and protein-metabolites interaction

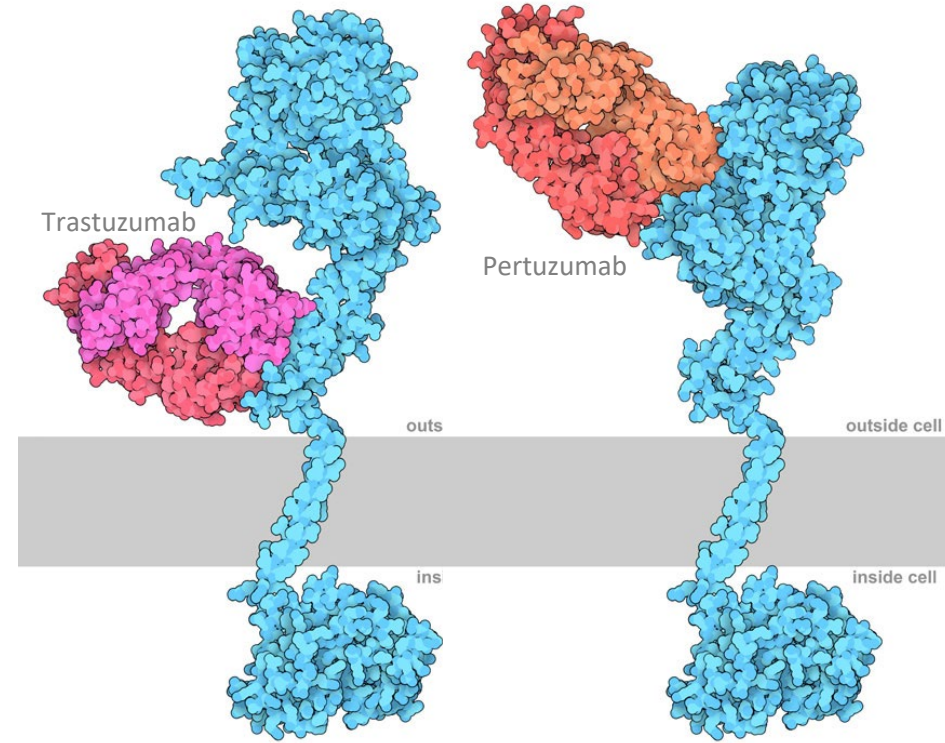
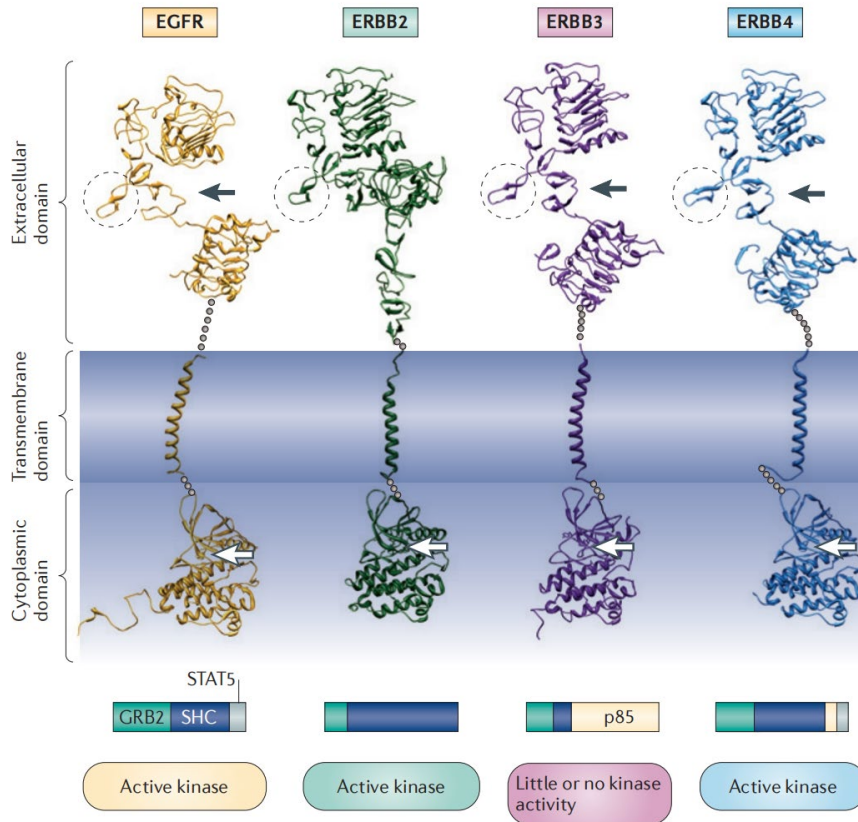
Reporter: G06A\_丁沛文、 G06B\_简舒怡、 G06C\_贾新颖、 G06D\_刘亦成

1. HER2蛋白结构分析及机制探究
2. PDZD8蛋白结构域同源性分析及分子机制探究
3. STING蛋白序列及功能分析
4. RNA结合蛋白内在无序域的序列保守性分析

## HER2蛋白结构分析及机制探究

Reporter:G06A\_丁沛文

# Molecule of the Month: HER2/neu and Trastuzumab



双序列比对:

UniProt登录号: P04626

GenBank登录号: 2064

PDB登录号: 7MN5, 7MN6, 7MN8

Aligned\_sequences: 2  
1:  
2:  
Matrix: EBLOSUM62  
Gap\_penalty: 10.0  
Extend\_penalty: 0.5  
  
Length: 1256  
Identity: 1101/1256 (87.7%)  
Similarity: 1156/1256 (92.0%)  
Gaps: 1/1256 ( 0.1%)  
Score: 5983.0

Aligned\_sequences: 2  
1:  
2:  
Matrix: EBLOSUM62  
Gap\_penalty: 10.0  
Extend\_penalty: 0.5  
  
Length: 1296  
Identity: 634/1296 (48.9%)  
Similarity: 813/1296 (62.7%)  
Gaps: 127/1296 ( 9.8%)  
Score: 3167.5

h\_HER2 与 m\_HER2 蛋白质序列比对

h\_HER1 (EGFR) 与 h\_HER2 蛋白质序列比对

Sbjct	535	RG+ECV++C +L+G PRE+V C+ CHPEC PQ ++TC G D C+ CAHY D P LRGQECVVECRVLQGLPREYVNRHCLPCHPECQFQNGSVTCFGPEADQCVACAHYKDDPP	594
Query	590	HCVKTCFAGVMGENTL-VWKYADAGHVCHLCHPNCTYGCTGPGLEGCTNGPKIP--SI CV CP+GV + + + +WK+ D C C NCT+ C +GCP P SI	646
Sbjct	595	FCVARCPGKVPDLGYMPTWKFPEDEGACQPCINCTHSCVDLDDKGCPEAQASPLTSI	654
Query	647	ATCMVGLLLLLLV-VALGIGLFMRRRHIVRKRTRLRLLQERELVEPLTPSGEAPNQALLR + +VG LL+++ V GI L RR+ +RK T+RRLQE ELVEPLTPSG PNQA +R	705
Sbjct	655	ISAVVGIILLVVVLGVVFGI-LIKRRQKIRKYTMRRLLQETELVEPLTPSGAMPNQAQMR	713
Query	706	ILKETEFKKIKVLGSGAFGTVYKGLWIPEGEKVKIPVAIKELREATSPKANKEILDEAYV ILKETE +K+KVLGSGAFGTVYK+G+WIP+GE VKIPVAIK LRE TSPKANKEILDEAYV	765
Sbjct	714	ILKETELRKRKVLGSGAFGTVYKGIWIPDGENVKIPVAIKVRENTSPKANKEILDEAYV	773
Query	766	MASVDNPHVCRLLGICLTSTVQLITQLMPFGCLLDYVREHKDNIGSQYLLNWCVQIAKGM MA V +P+V RLLGICLTSTVQL+TQLMP+GCLLD+VRE++ +GSQ LLNWC+QIAKGM	825
Sbjct	774	MAGVGSPPYVSRLLGICLTSTVQLVTLMPYGCCLLDHVRNDRGRLGSDLLNWCMIQAKGM	833
Query	826	NYLEDVRLVHRDLAARNVLVKTPQHVKITDFGLAKLLGAEKEYHAEGGKVPKIKWMALES +YLED RLVHRDLAARNVLVK+P HVKITDFGLA+LL +E EYHA+GGKVPKIKWMALES	885
Sbjct	834	SYLEDVRLVHRDLAARNVLVKSPNHVKITDFGLARLLDIDETEHYHAGGKVPKIKWMALES	893
Query	886	ILHRIYTHQSDVWSYGVTVWELMTFGSKPYDGIPIASEISSILEKGERLPQPPICTIDVYM IL R +THQSDVWSYGVTVWELMTFG+KPYDGIPI EI +LEKGERLPQPPICTIDVYM	945
Sbjct	894	ILRRRFTHQSDVWSYGVTVWELMTFGAKPYDGIPIAIPDLLEKGERLPQPPICTIDVYM	953
Query	946	IMVKCWMIDADSRPKFRELIIIEFSKMARDPQRYLVIQGDERMHLPSPTDSNFYRALMDEE IMVKCWMID++ RP+PREL+ EFS+MARDPQR++VIQ ++ + SP DS FYR+L++++	1005
Sbjct	954	IMVKCWMIDSECRPRFRELIVSEFSRMARDPQRFFVIQNEQD-LGPASPLDSTFYRSLLEDD	1012
Query	1006	DMDDVVDADAYLIPQQGFF-----SSPSTSR DM D+VDA+EYL+PQQGFF S R	1031
Sbjct	1013	DMGDLVDAEYLVPPQGFPCDPAPGAGGMVHHRHRSSTSRGGGDLTLGLEPSEEEAPR	1072

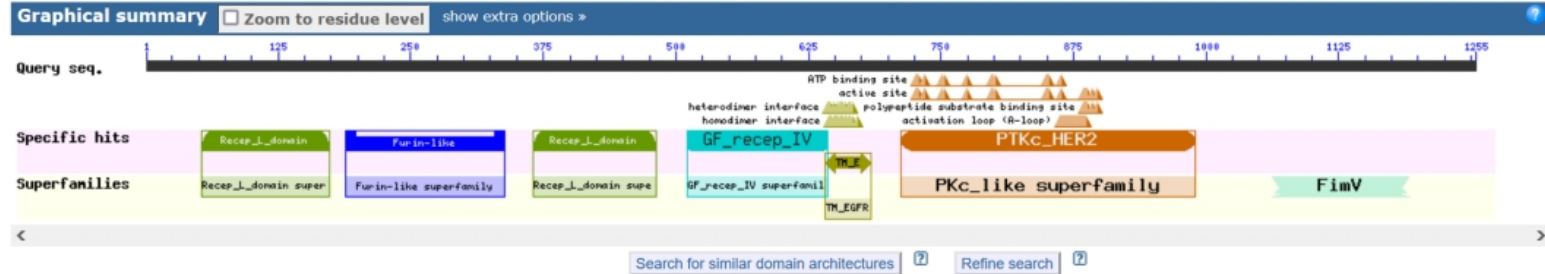
NCBI BLAST分析平台中基于Needleman-Wunsch整体  
比对算法的Global Align序列比对

比对结果总分值 (NW Score) 2069;  
相同位点 (Identities) 比例629/1277和百分比49%;  
正分值 (Positives) 比例807/1277和百分比63%;  
空位 (Gaps) 比例89/1277和百分比6%。

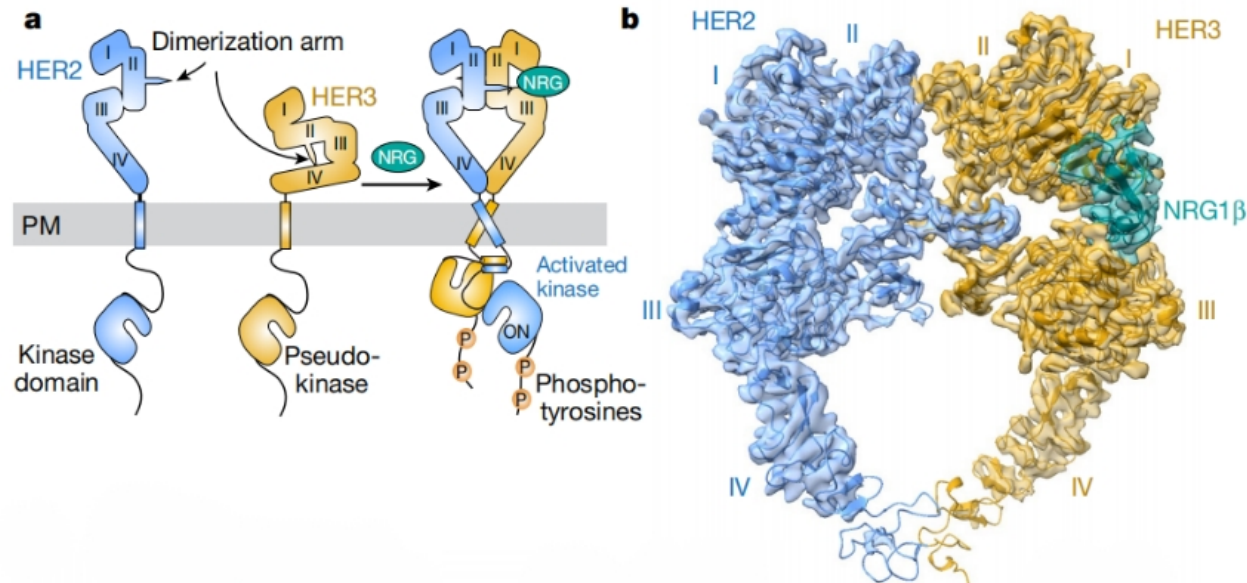
## Conserved domains on [sp|P04626]

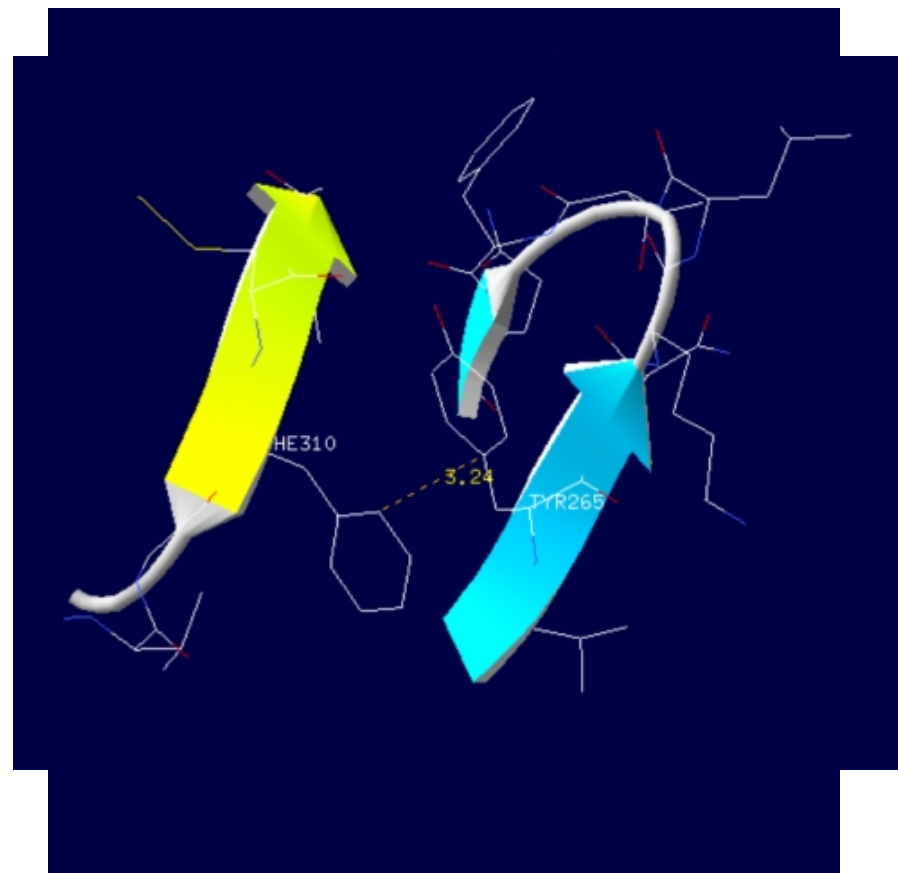
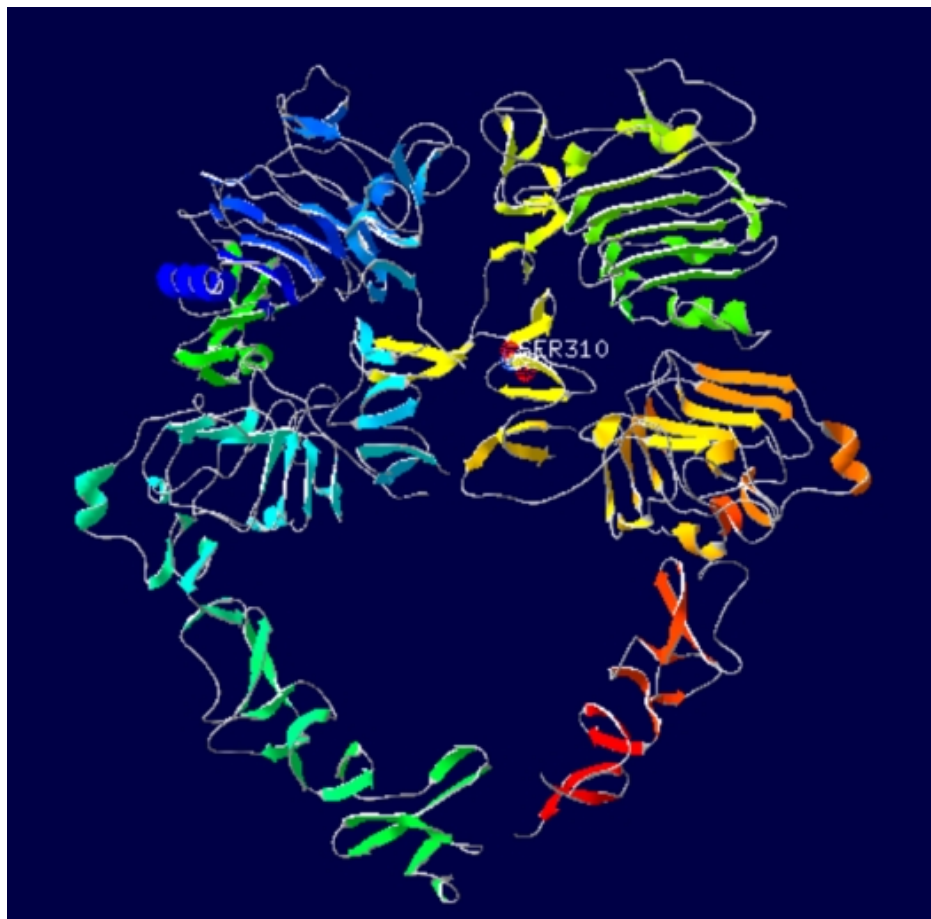
ERBB2\_HUMAN Receptor tyrosine-protein kinase erbB-2 OS=Homo sapiens OX=9606 GN=ERBB2 PE=1 SV=1

View **Concise Results**



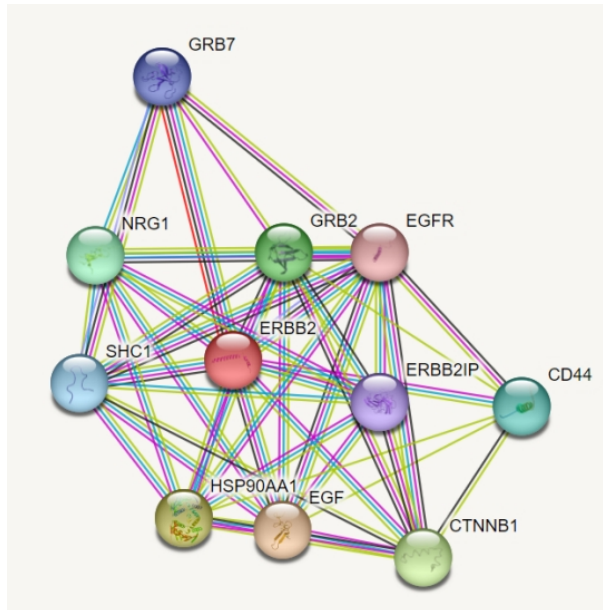
Name	Accession	Description	Interval	E-value
PTKc_HER2	cd05109	Catalytic domain of the Protein Tyrosine Kinase, HER2; PTKs catalyze the transfer of the ...	712-990	0e+00
GF_recep_IV	pfam14843	Growth factor receptor domain IV; This is the fourth extracellular domain of receptor tyrosine ...	511-643	4.56e-60
Furin-like	pfam00757	Furin-like cysteine rich region;	189-338	4.60e-41
Recept_L_domain	pfam01030	Receptor L domain; The L domains from these receptors make up the bilobal ligand binding site. ...	52-173	3.21e-32
Recept_L_domain	pfam01030	Receptor L domain; The L domains from these receptors make up the bilobal ligand binding site. ...	366-482	1.14e-20
TM_ErbB2	cd12094	Transmembrane domain of ErbB2, a Protein Tyrosine Kinase; PTKs catalyze the transfer of the ...	641-684	3.18e-07
FimV super family	cl34561	Ttp pilus assembly protein FimV [Cell motility, Extracellular structures];	1063-1192	2.09e-03





# ERBB2 association networks

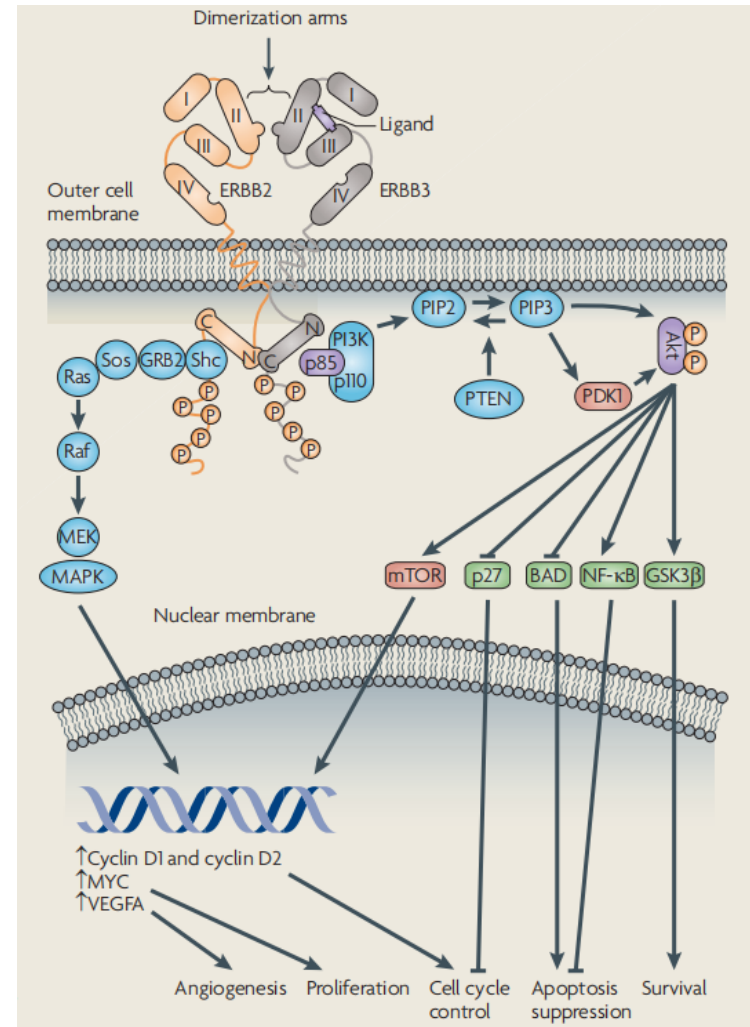
STRING:



KEGG:

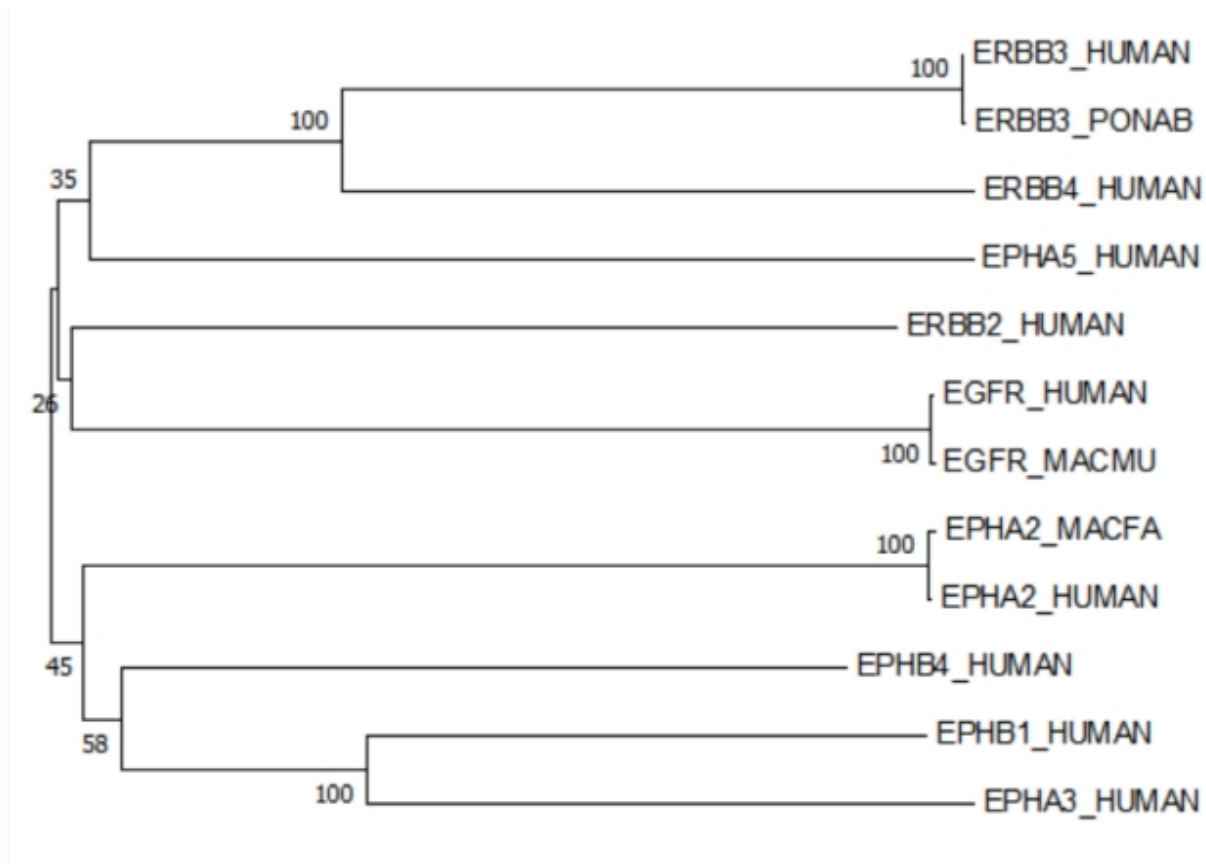
**KEGG** Homo sapiens (human): 2064 [Help](#)

Entry	2064	CDS	T01001
Symbol	ERBB2, CD340, HER-2, HER-2/neu, HER2, MLN_19, MLN-19, NEU, NGL, TKR1, VSCN2, c-ERB-2, c-ERB2, p185(erbB2)		
Name	(RefSeq) erb-b2 receptor tyrosine kinase 2		
KO	K05083 receptor tyrosine-protein kinase erbB-2 [EC:2.7.10.1]		
Organism	hsa Homo sapiens (human)		
Pathway	<ul style="list-style-type: none"> <li>hsa01521 EGFR tyrosine kinase inhibitor resistance</li> <li>hsa01522 Endocrine resistance</li> <li>hsa01524 Platinum drug resistance</li> <li>hsa04010 MAPK signaling pathway</li> <li>hsa04012 ErbB signaling pathway</li> <li>hsa04020 Calcium signaling pathway</li> <li>hsa04066 HIF-1 signaling pathway</li> <li>hsa04151 PI3K-Akt signaling pathway</li> <li>hsa04510 Focal adhesion</li> <li>hsa04520 Adherens junction</li> <li>hsa04530 Tight junction</li> <li>hsa05200 Pathways in cancer</li> <li>hsa05205 Proteoglycans in cancer</li> <li>hsa05206 MicroRNAs in cancer</li> <li>hsa05212 Pancreatic cancer</li> <li>hsa05213 Endometrial cancer</li> <li>hsa05215 Prostate cancer</li> <li>hsa05219 Bladder cancer</li> <li>hsa05223 Non-small cell lung cancer</li> <li>hsa05224 Breast cancer</li> <li>hsa05226 Gastric cancer</li> <li>hsa05230 Central carbon metabolism in cancer</li> </ul>		





MEGA7 :

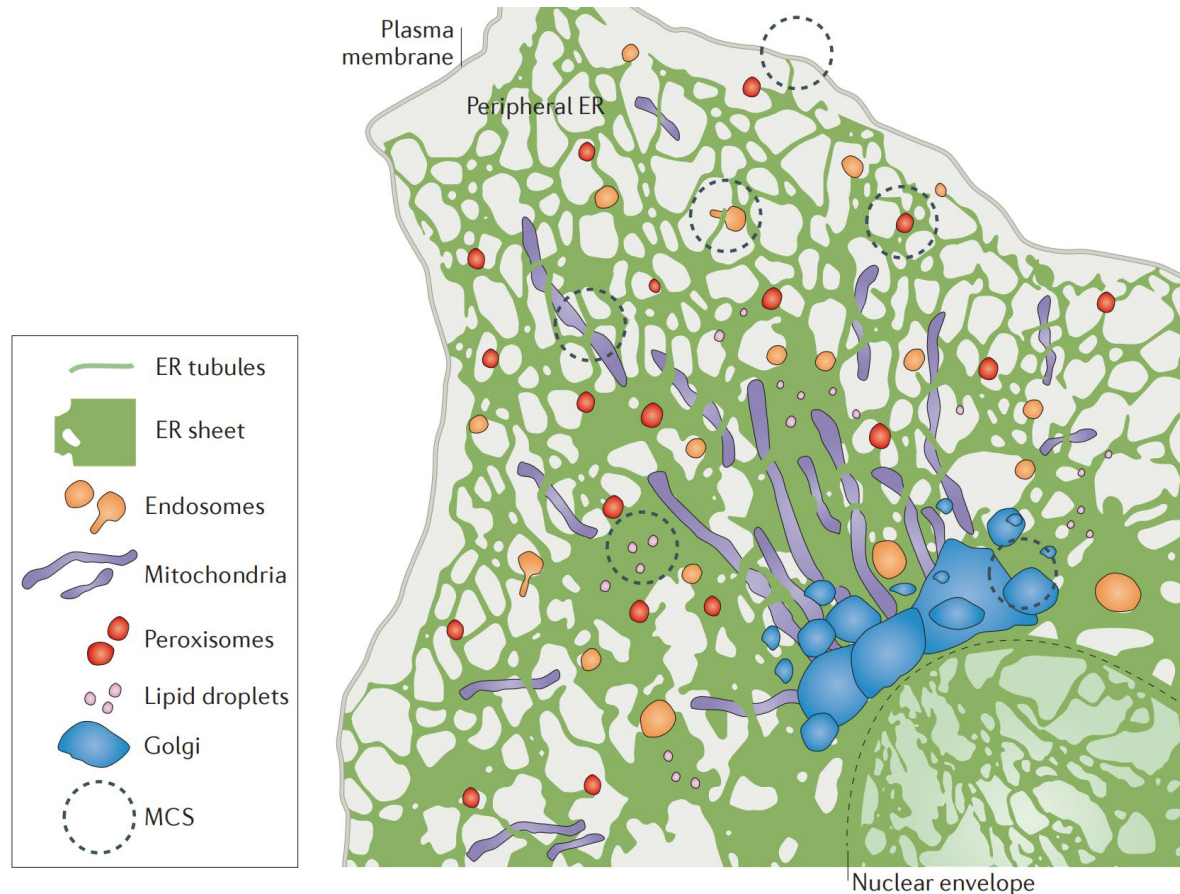


## PDZD8蛋白结构域同源性分析及分子机制探究

Reporter:G06B\_简舒怡

## PDZD8 (PDZ domain containing 8)

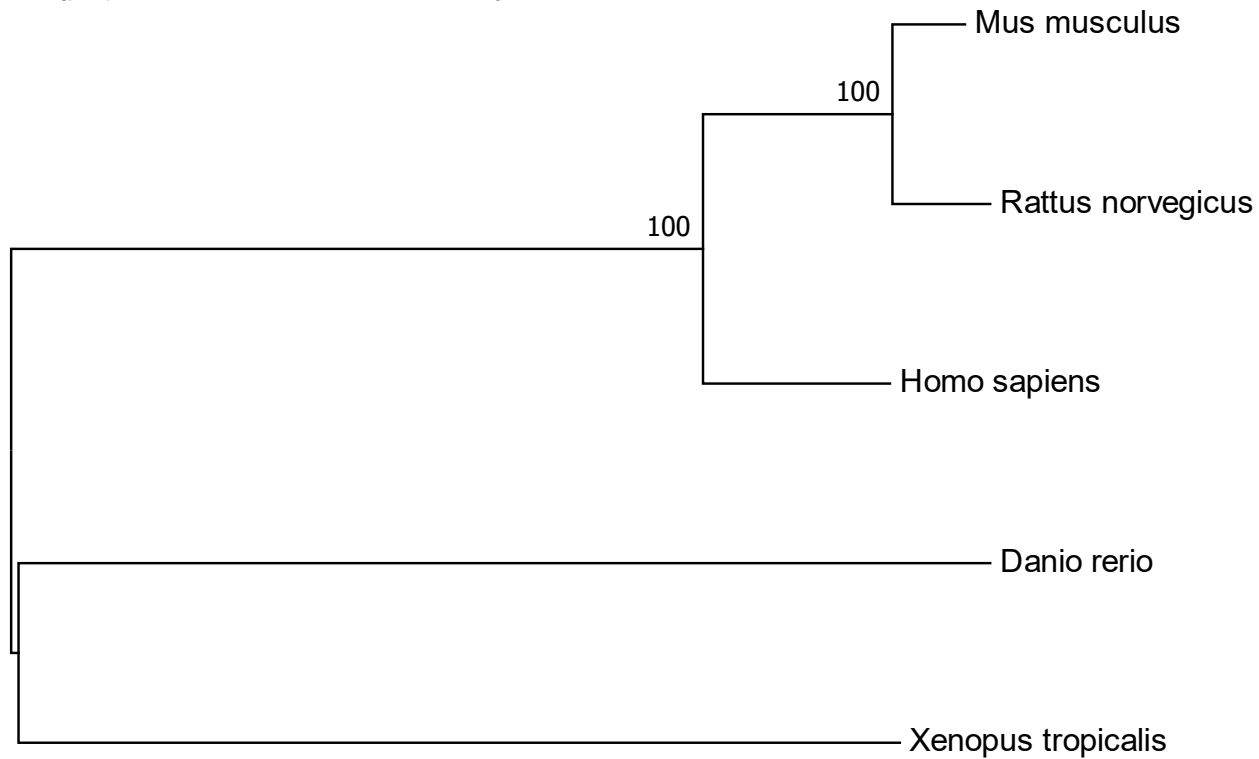
Molecular tethering protein that connects endoplasmic reticulum and mitochondria membranes. It localizes to **ER-mitochondria** and ER-late endosome contacts.



使用Uniprot中的Align功能对比序列相似性

Danio rerio	100.00%	58.80%	57.96%	57.05%	56.79%
Xenopus tropicalis	58.80%	100.00%	60.52%	58.89%	58.05%
Homo sapiens	57.96%	60.52%	100.00%	86.75%	86.11%
Mus musculus	57.05%	58.89%	86.75%	100.00%	95.29%
Rattus norvegicus	56.79%	58.05%	86.11%	95.29%	100.00%

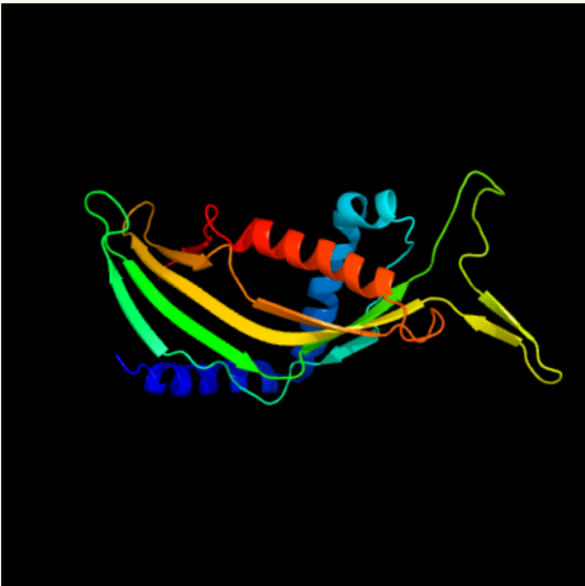
使用MEGA 7.0建立的进化树



0.050

## 使用Phyre2对PDZD8\_HUMAN的SMP-LTD结构域进行同源建模

Top model



Model (left) based on template [c5yk7A](#)

Top template information

**PDB header:**lipid transport  
**Chain:** A: **PDB Molecule:**maintenance of mitochondrial morphology protein 1;  
**PDBTitle:** crystal structure of mdm12-mmm1 complex  
**PDB Entry:** [PDBe](#) [RCSB](#) [PDBj](#)

Confidence and coverage

Confidence: 100.0% Coverage: 90%

183 residues ( 90% of your sequence) have been modelled with 100.0% confidence by the single highest scoring template.


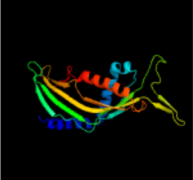
3D viewing

[Interactive 3D view in JSmol](#)

For other options to view your downloaded structure offline see the [FAQ](#)

Image coloured by rainbow N → C terminus

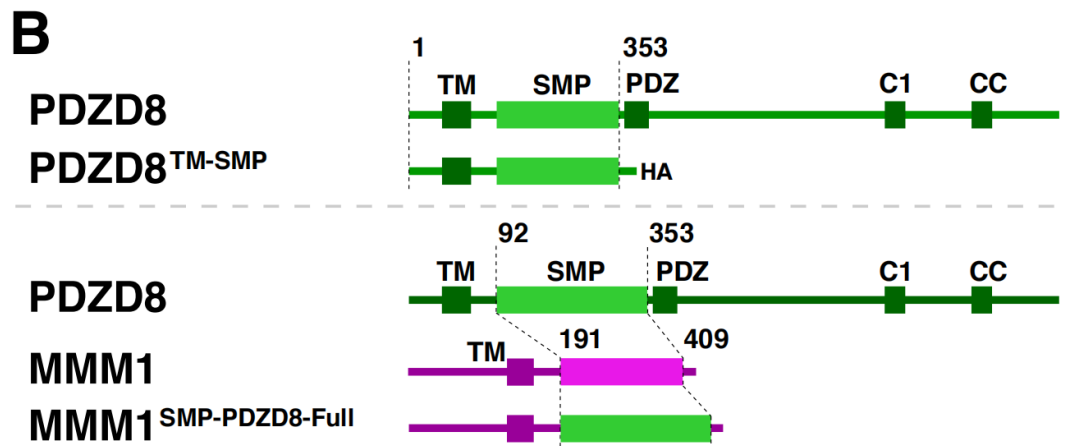
Model dimensions (Å): **X:**62.146 **Y:**64.289 **Z:**39.387

#	Template	Alignment Coverage	3D Model	Confidence	% i.d.	Template Information
1	<a href="#">c5yk7A</a> <input checked="" type="radio"/> <input type="checkbox"/>	 <div style="border: 1px solid #ccc; padding: 2px; font-size: x-small;">Alignment</div>		100.0	19	<p><b>PDB header:</b>lipid transport  <b>Chain:</b> A: <b>PDB Molecule:</b>maintenance of mitochondrial morphology protein 1;  <b>PDBTitle:</b> crystal structure of mdm12-mmm1 complex  <b>PDB Entry:</b> <a href="#">PDBe</a> <a href="#">RCSB</a> <a href="#">PDBj</a></p>

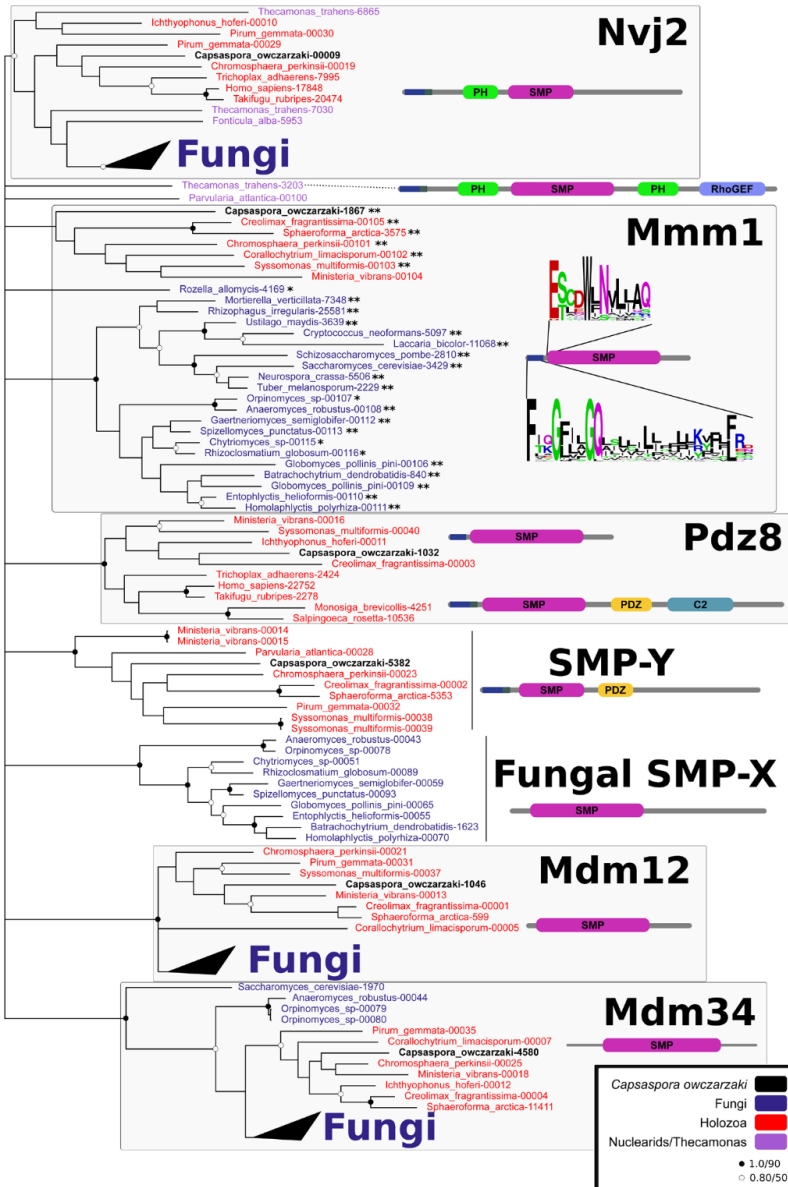
## ER-mitochondria tethering by PDZD8 regulates $\text{Ca}^{2+}$ dynamics in mammalian neurons

Yusuke Hirabayashi,<sup>1,2,3,4\*</sup> Seok-Kyu Kwon,<sup>1,2,3\*</sup> Hunki Paek,<sup>1,2,3</sup>  
Wolfgang M. Pernice,<sup>5</sup> Maëla A. Paul,<sup>1,2,3</sup> Jinoh Lee,<sup>1,2,3</sup> Parsa Erfani,<sup>1,2,3</sup>  
Ashleigh Raczkowski,<sup>7</sup> Donald S. Petrey,<sup>8,9</sup> Liza A. Pon,<sup>5,6</sup> Franck Polleux<sup>1,2,3†</sup>

SMP domains from yeast MMM1 represent a structural and functional ortholog of the SMP domain of metazoans PDZD8.



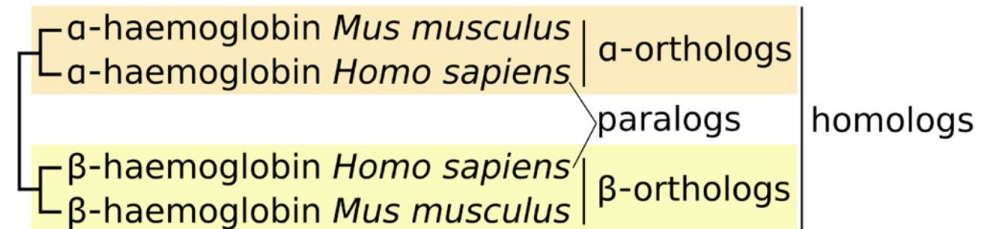
# PDZD8蛋白结构域同源性分析及分子机制探究



## CORRESPONDENCE

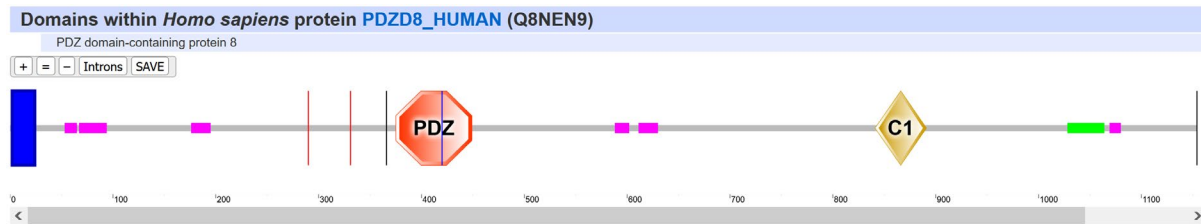
**PDZD8 is not the 'functional ortholog' of Mmm1, it is a paralog [version 1; referees: 2 approved]**

Jeremy G. Wideman <sup>1,2</sup>, Dario L. Balacco <sup>3</sup>, Tim Fieblinger <sup>2,4</sup>,  
Thomas A. Richards <sup>1</sup>





## 利用SMART对PDZD8进行结构域分析



### Confidently predicted domains, repeats, motifs and features:

Name	Start ▲	End	E-value
transmembrane region	2	24	N/A
low complexity	53	65	N/A
low complexity	67	94	N/A
low complexity	176	195	N/A
PDZ	375	449	4.98e-10
low complexity	588	602	N/A
low complexity	611	630	N/A
C1	841	891	0.00000231
coiled coil	1028	1064	N/A
low complexity	1069	1080	N/A




Click on a row to highlight the feature in the diagram above. Click the feature name for more information.

## PTMs

### Posttranslational modifications

PTM annotation is taken from [PTMcode](#), a re

There are **24** PTMs annotated in this protein:

PTM	Count
 Phosphorylation	20
 Ubiquitination	2
 Acetylation	2

Information Architecture Interactions PTMs Orthology

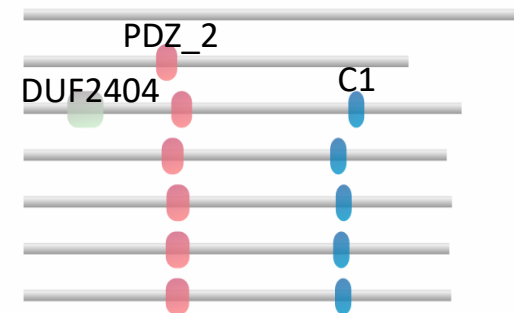
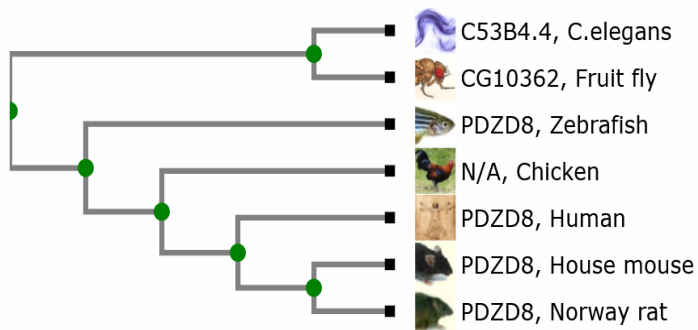
### Orthologous groups

Orthology information is taken from [eggNOG](#), a database of orthologous groups of genes. Orthologous groups containing this protein are listed below.

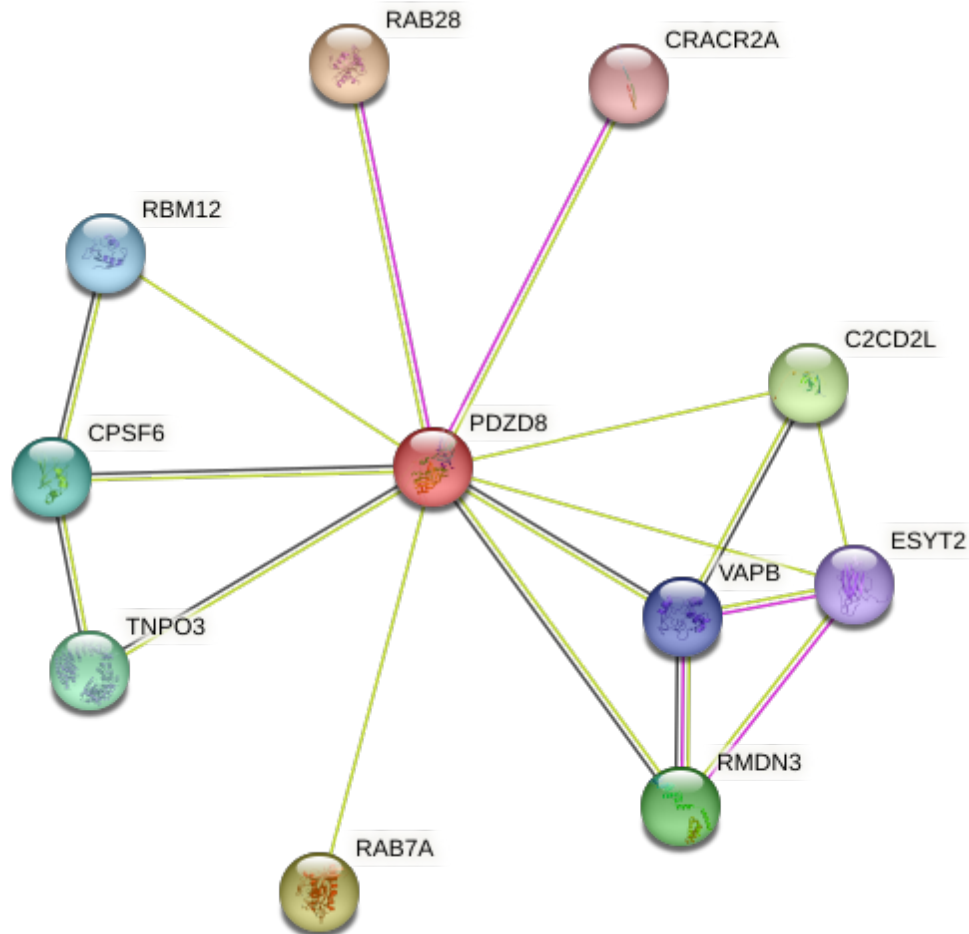
This protein is named **ENSP00000334642** in eggNOG.

Orthologous group	Description	Taxonomic class
ENOG4109W1U	PDZ domain containing 8	<i>Bilateria</i> (no rank)
ENOG410DHAX	PDZ domain containing 8	<i>Chordata</i> (phylum)
ENOG410RXHZ	PDZ domain containing 8	<i>Hominidae</i> (family)
ENOG410UJE5	PDZ domain containing 8	<i>Mammals</i> (class)
ENOG410V702	PDZ domain containing 8	<i>Animals</i> (kingdom)
ENOG410ZV0K	intracellular signal transduction	<i>All organisms</i> (no rank)
ENOG4112PN4	PDZ domain containing 8	<i>Opisthokonts</i> (no rank)
ENOG4116FAF	PDZ domain containing 8	<i>Primates</i> (order)
ENOG411AXXQ	PDZ domain containing 8	<i>Supraprimates</i> (superorder)
ENOG411CS11	PDZ domain containing 8	<i>Vertebrates</i> (no rank)
KOG3532	PDZ domain containing 8	<i>Eukaryotes</i> (superkingdom)

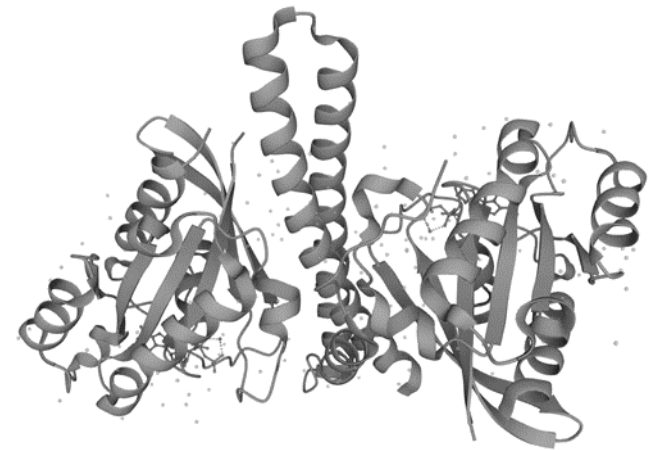
## TreeFam网站分析结果



## STRING网站分析结果



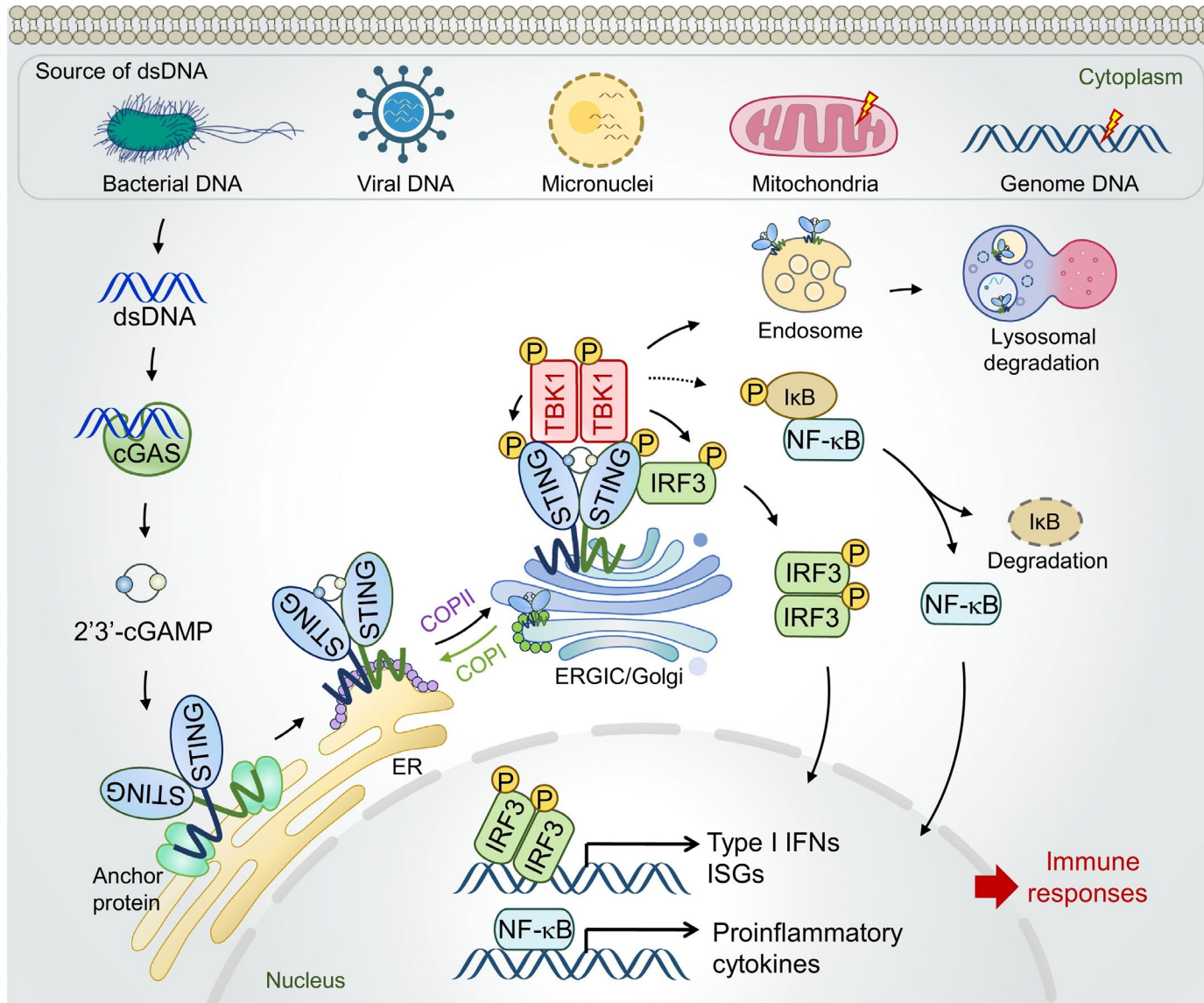
Crystal structure of the PDZD8 coiled-coil domain - Rab7 complex



## STING蛋白序列及功能分析

Reporter:G06C\_贾新颖

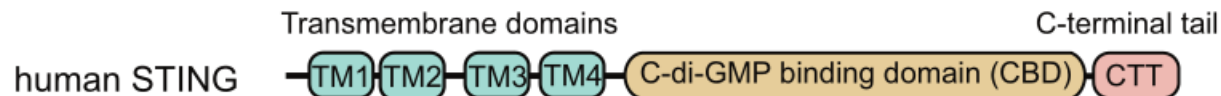
# cGAS-STING Pathway



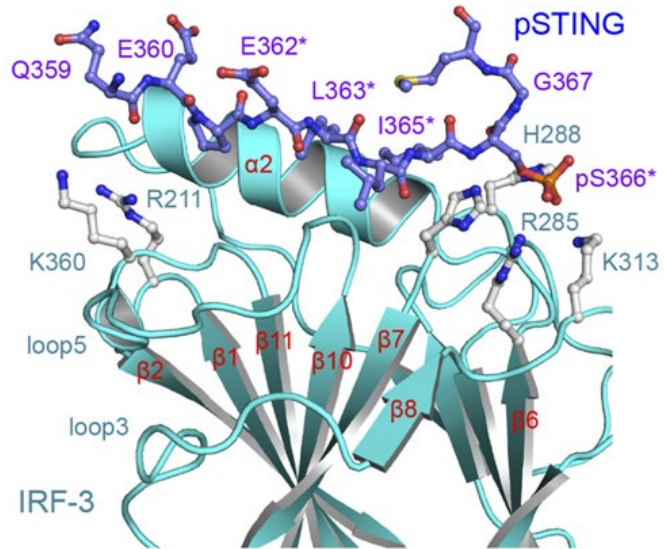
# Regions and motif of STING

▶ Region	1-190	Mediates interaction with ZDHHC1 and ZDHHC11	2 Publications	BLAST	Add
▶ Region	153-340	Cyclic dinucleotide-binding domain (CBD)	1 Publication	BLAST	Add
▶ Region	340-379	C-terminal tail (CTT)	1 Publication	BLAST	Add
▶ Region	341-370	Disordered	Automatic Annotation	BLAST	Add
▶ Compositional bias	346-362	Polar residues	Automatic Annotation	BLAST	Add
▶ Motif	363-366	pLxIS motif	1 Publication	BLAST	Add

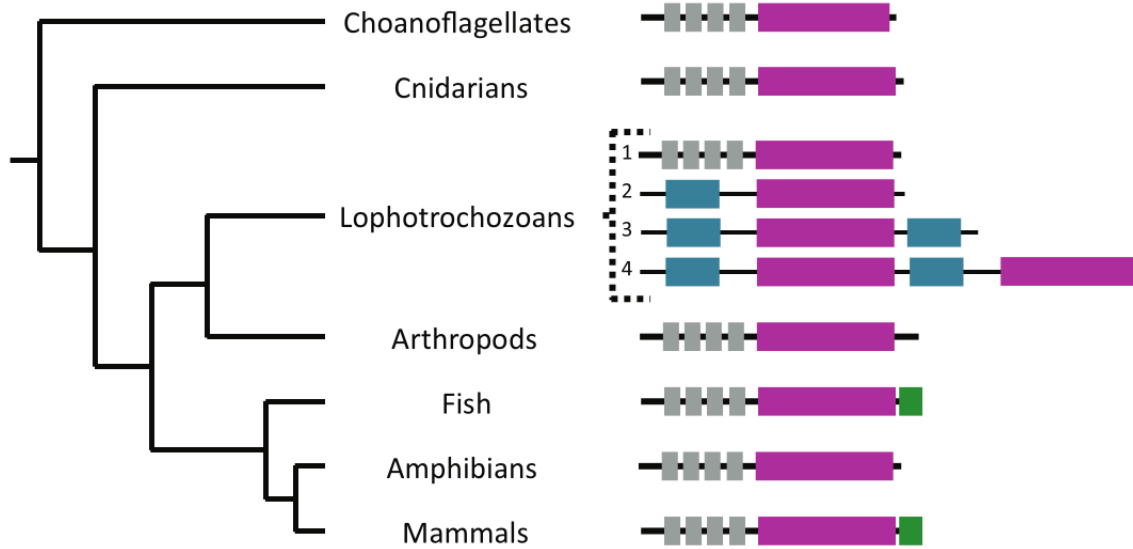
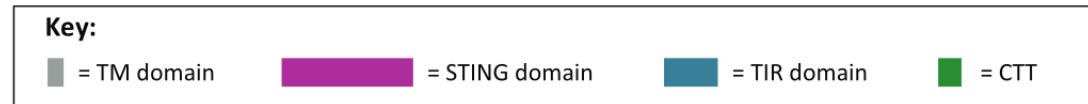
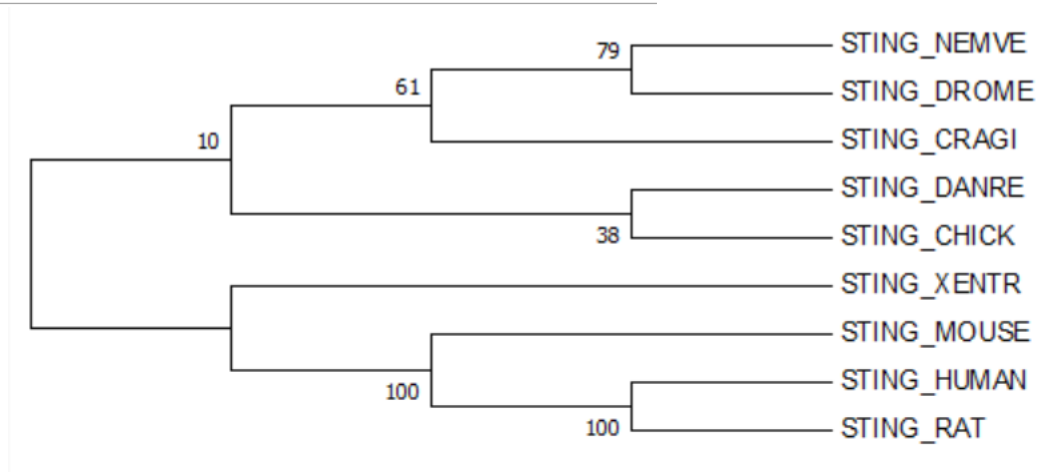
与TBK1相互作用



# Interaction between STING and IRF3



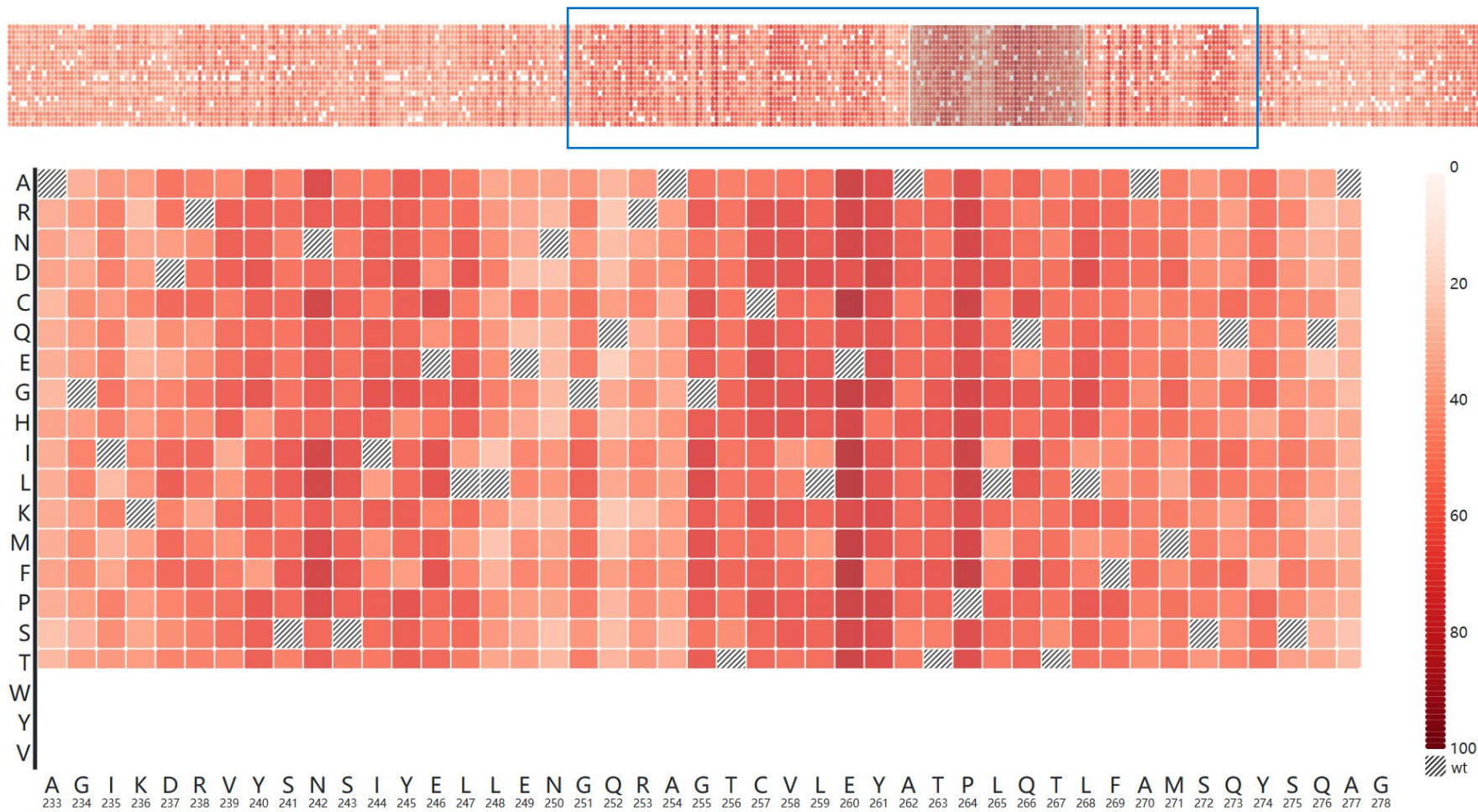
# Evolution of STING





# Mutation Sensitivity of STING

C-di-GMP binding domain



不可替代突变主要位于负责结合核苷酸的结构域

## STING-associated vasculopathy, infantile-onset (SAVI)

3 Publications


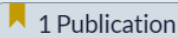
**Note** | The disease is caused by variants affecting the gene represented in this entry

**Description** | An autoinflammatory disease characterized by early-onset systemic inflammation and cutaneous vasculopathy, resulting in severe skin lesions. Violaceous, scaling lesions of fingers, toes, nose, cheeks and ears progress to acral necrosis in most of the patients. Some patients have severe interstitial lung disease.


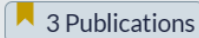
**See also** | MIM:[615934](#) 

### Natural variants in SAVI

VARIANT ID POSITION(S) CHANGE DESCRIPTION

VAR\_071878 147 **V>L** in SAVI; [dbSNP:rs587777611](#)  

VAR\_071879 154 **N>S** in SAVI; [dbSNP:rs587777609](#)  

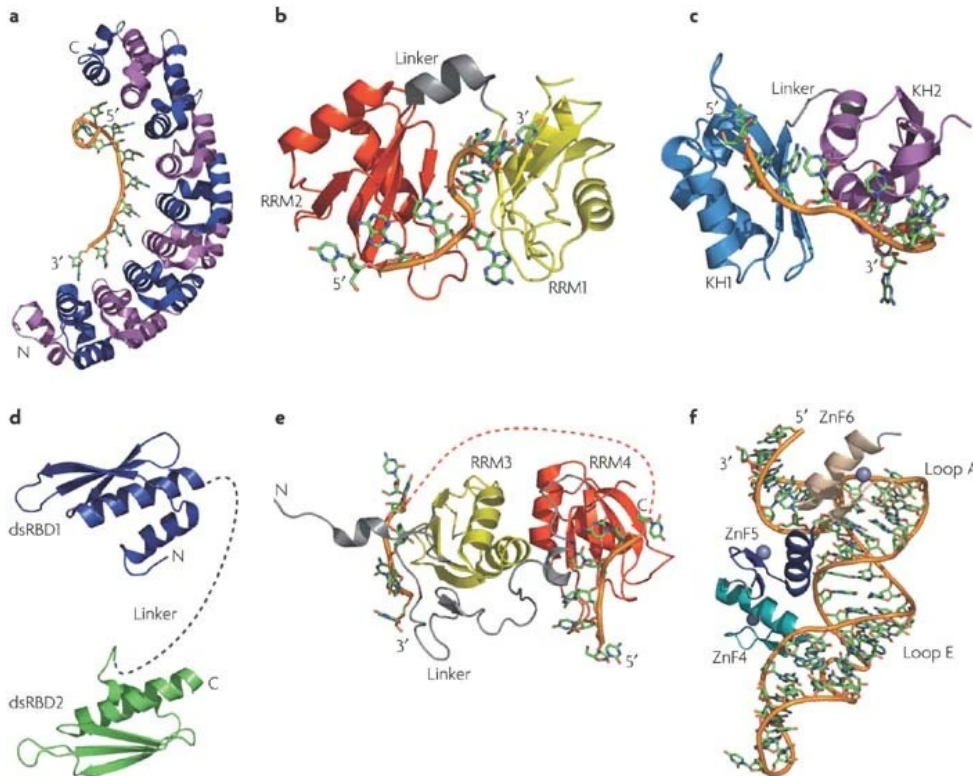
VAR\_071880 155 **V>M** in SAVI; constitutively active mutant that promotes the production of type I interferon in absence of cGAMP ligand; [dbSNP:rs587777610](#)  

位于或靠近CBD的关键位点突变后导致STING自激活，引起自身免疫病SAVI  
选择147、154、155位突变产生实验所需的自激活突变体

## RNA结合蛋白内在无序域的序列保守性分析

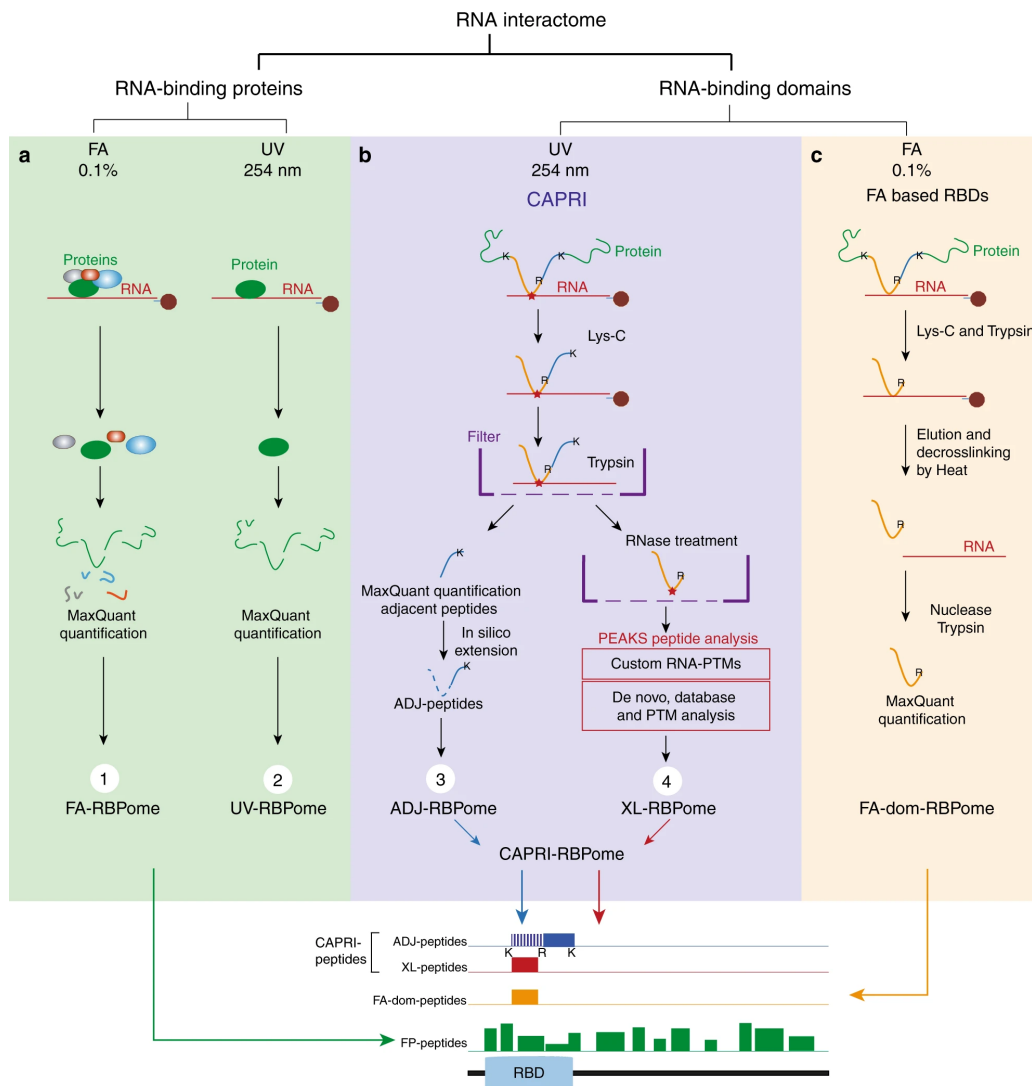
Reporter:G06D\_刘亦成

# RNA-protein interface is crucial for function of RBP

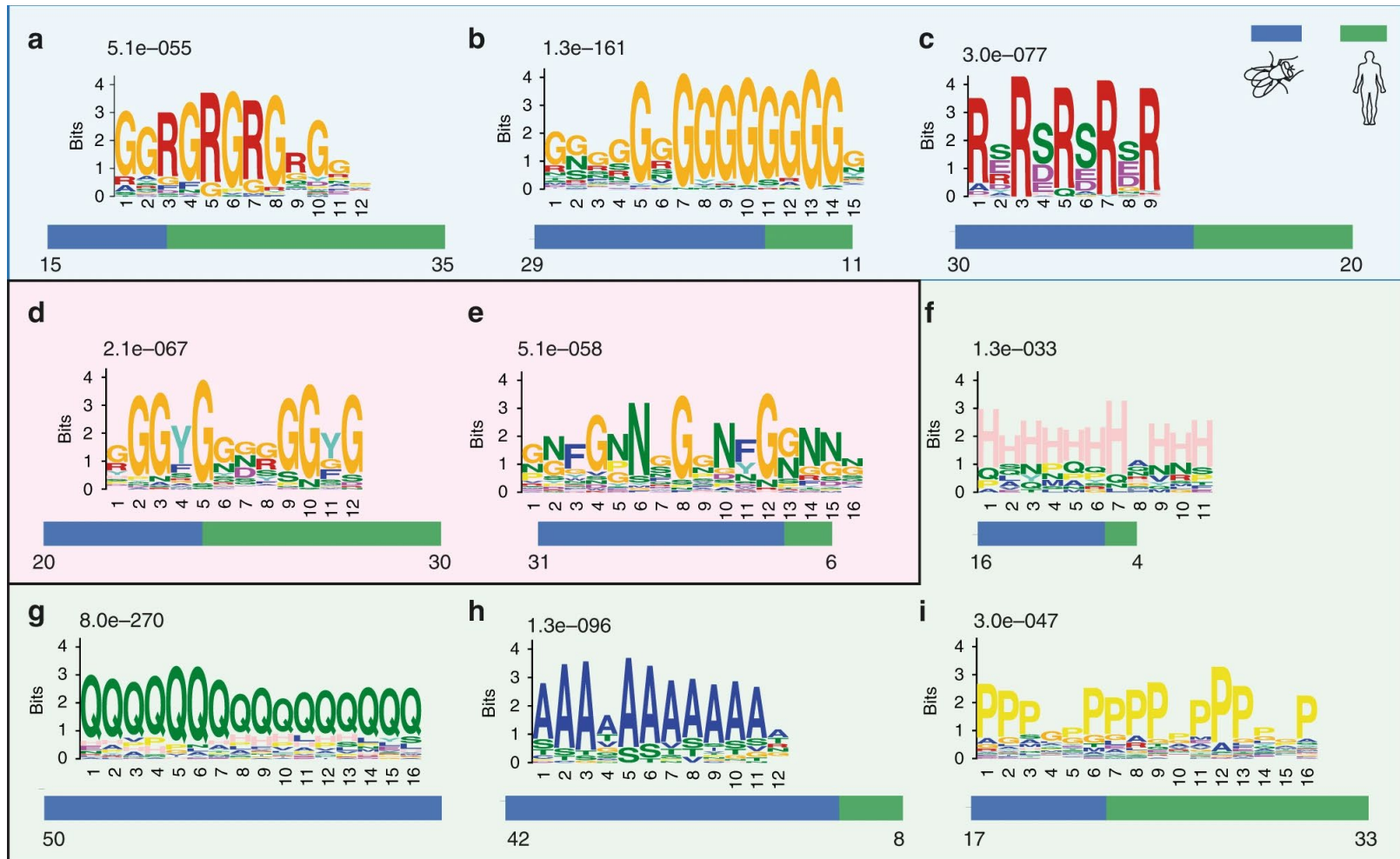


Domain	Topology	RNA-recognition surface
RRM	$\alpha\beta$	Surface of $\beta$ -sheet
KH (type I and type II)	$\alpha\beta$	Hydrophobic cleft formed by variable loop between $\beta 2$ , $\beta 3$ and GXXG loop. Type II: same as type I, except variable loop is between $\alpha 2$ and $\beta 2$
dsRBD	$\alpha\beta$	Helix $\alpha 1$ , N-terminal portion of helix $\alpha 2$ , and loop between $\beta 1$ and $\beta 2$
ZnF-CCHH	$\alpha\beta$	Primarily residues in $\alpha$ -helices
ZnF-CCCH	Little regular secondary structure	Aromatic side chains form hydrophobic binding pockets for bases that make direct hydrogen bonds to protein backbone
S1	$\beta$	Core formed by two $\beta$ -strands with contributions from surrounding loops
PAZ	$\alpha\beta$	Hydrophobic pocket formed by OB like $\beta$ -barrel and small $\alpha\beta$ motif
PIWI	$\alpha\beta$	Highly conserved pocket, including a metal ion that is bound to the exposed C-terminal carboxylate

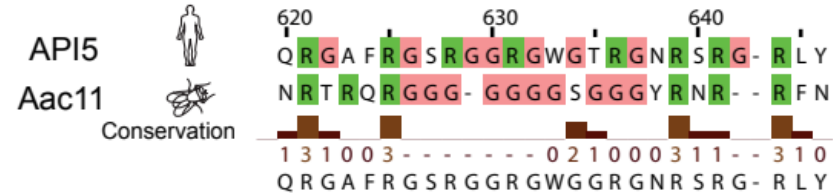
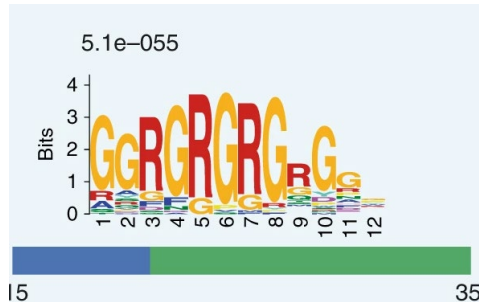
# Methods developed to find RNA-binding peptides



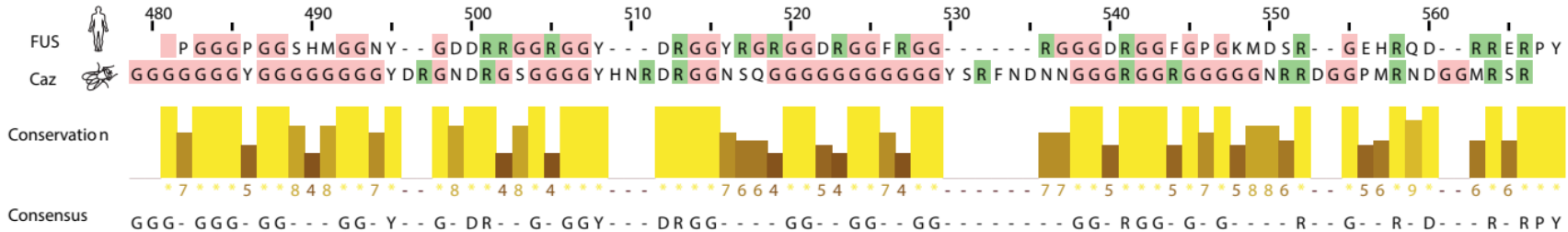
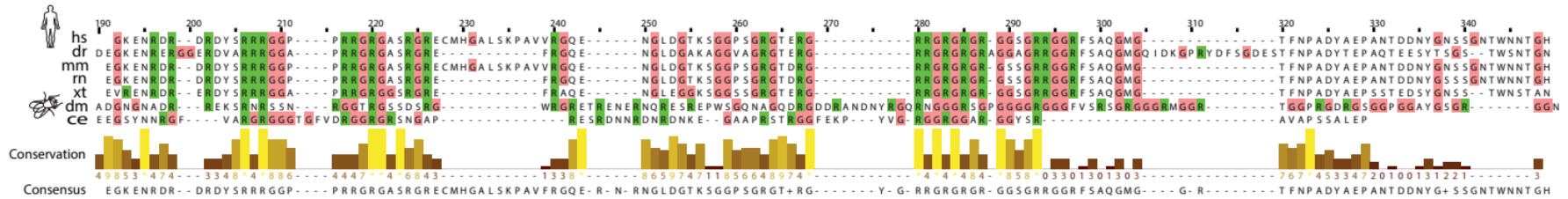
# Conservation sequence character in unstructured segments



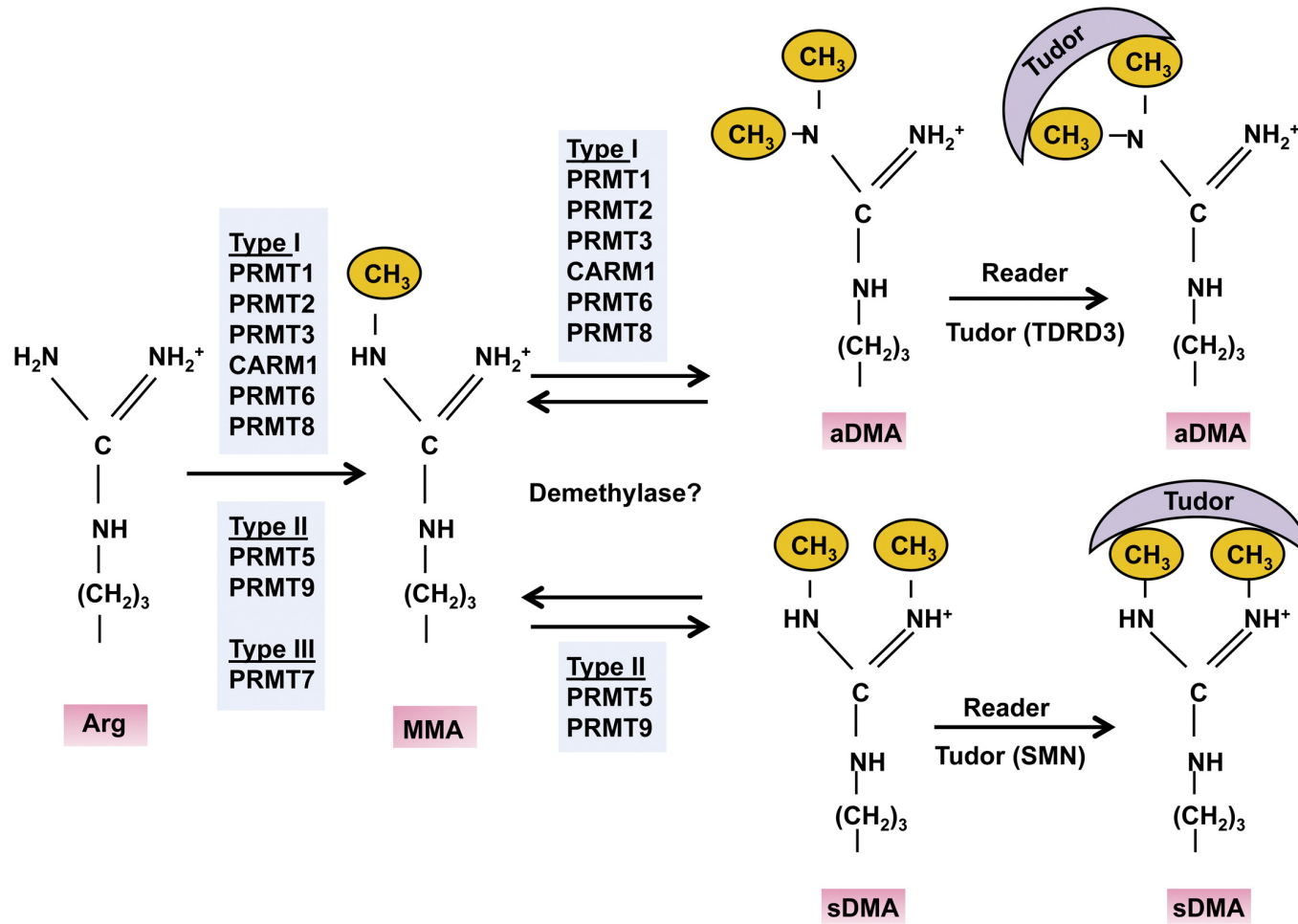
# Evolutionary conservation between *Drosophila* and humans



UBAP2L RG repeat conservation



# Chemical basis of RGG region





- 在本课程中我们了解并学习了多个数据库和生物信息分析方法，并以自己的研究方向甚至课题为中心进行实践，获取与课题相关的信息，从而对课题的进行起到更好的引领和启发作用。
- 另外abc网站也是非常实用的生信分析工具数据库，网站中还有很多好的资源值得我们进一步的学习。
- 时间安排上除了正常的课时，罗老师还会找时间给同学补课并为我们补充农科院同学的内容，非常感谢老师！

**Thanks for listening!**