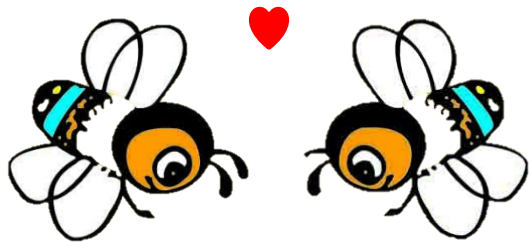


# The ABC's Encounter: Ral and GAP Protein

Ral 和其GAP蛋白的ABC之遇



Speaker: Li Yang  
Zhang YaLei  
Sun ChaoYing  
Xiao Xiong



# Outline

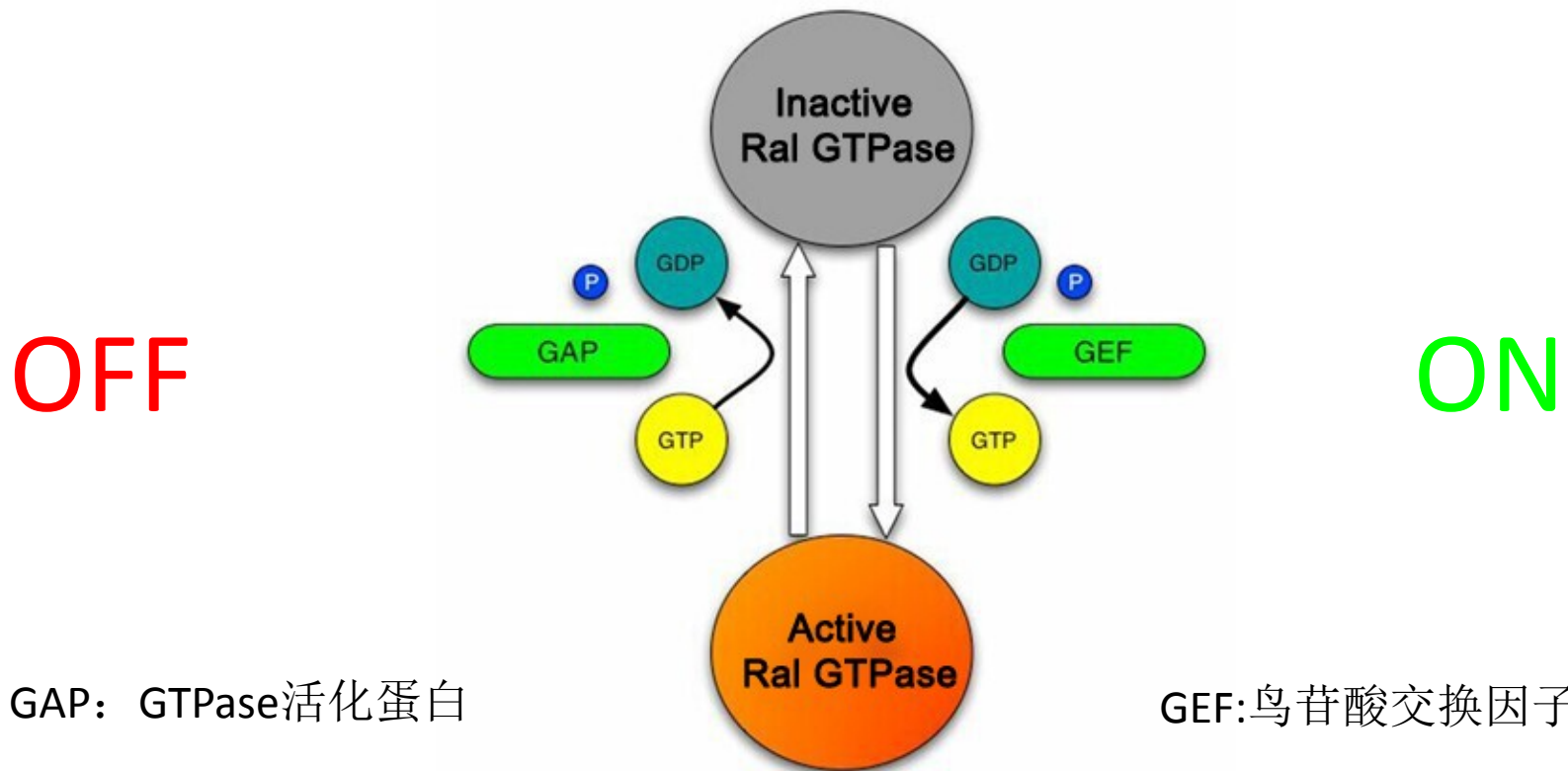
- I. Background Information
- II. General analysis of gene and protein
- III. Structure Prediction
- IV. Prediction of signaling pathway
- V. Summary



# Outline

- I. Background Information
- II. General analysis of gene and protein
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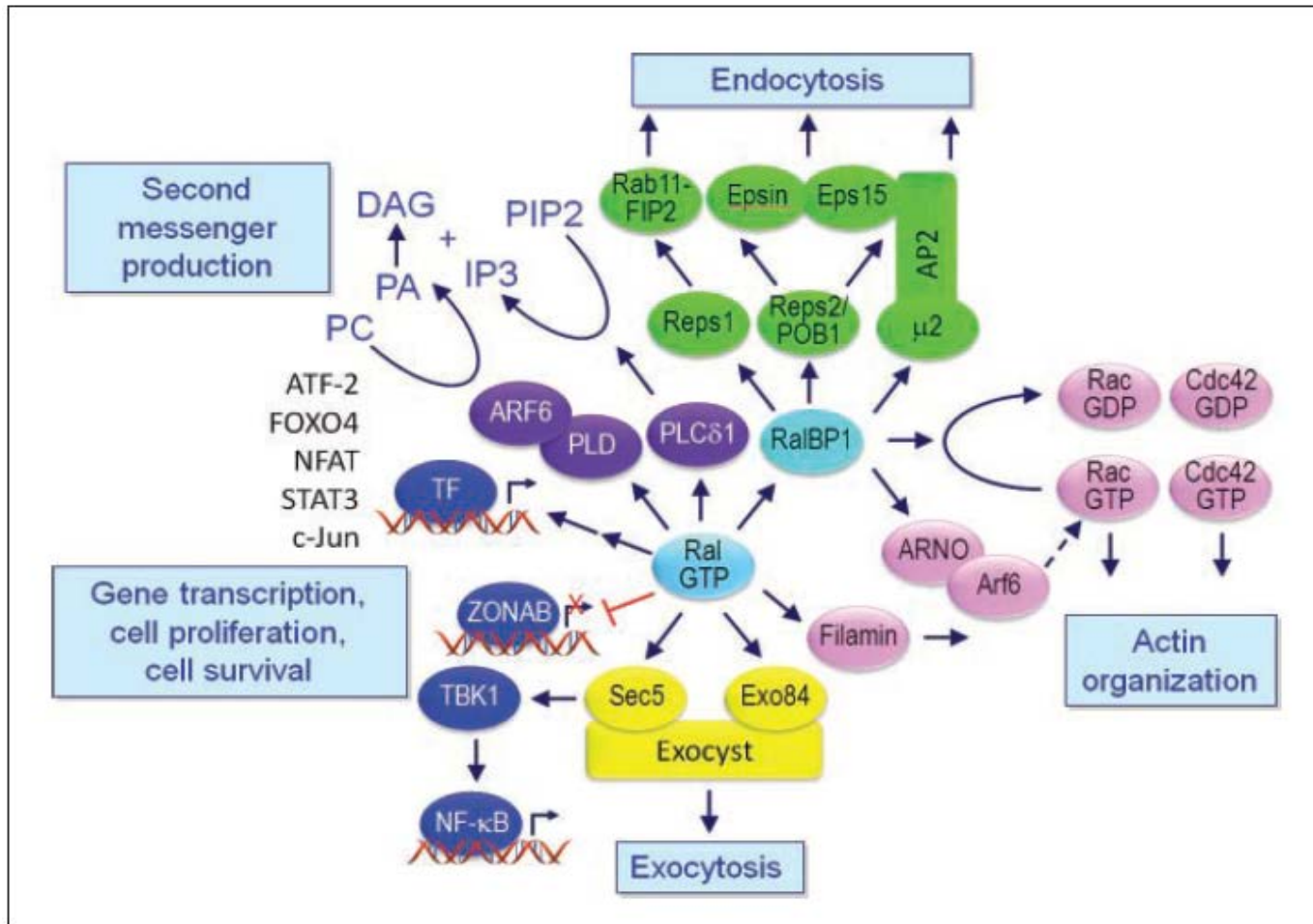
# The Small GTPase: Molecular Switch



GAP: GTPase活化蛋白

GEF:鸟苷酸交换因子

# The Introduction of Ral's Function





# Outline

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# The Motif Analysis

Name	Start	p-value	Sites [?]	
sp P63321 RALA_MOUSE	15	1.47e-62	KPKGQNSLAL	HKVIMVGS GG V GKSALT LQ FMYDEFV E D Y E P T K A D S Y R K K V V L D G E E V Q I D I L D T A G Q E D
sp P63322 RALA_RAT	15	1.47e-62	KPKGQNSLAL	HKVIMVGS GG V GKSALT LQ FMYDEFV E D Y E P T K A D S Y R K K V V L D G E E V Q I D I L D T A G Q E D
sp P11233 RALA_HUMAN	15	1.47e-62	KPKGQNSLAL	HKVIMVGS GG V GKSALT LQ FMYDEFV E D Y E P T K A D S Y R K K V V L D G E E V Q I D I L D T A G Q E D
sp P48555 RALA_DROME	12	1.47e-62	SKKPTAGPAL	HKVIMVGS GG V GKSALT LQ FMYDEFV E D Y E P T K A D S Y R K K V V L D G E E V Q I D I L D T A G Q E D



G1/PM1

Phosphate binding site

Switch I

Change conformation when GDP-bound state

Name	Start	p-value	Sites [?]	
sp P63321 RALA_MOUSE	65	1.24e-62	VVL D G E E V Q I	D I L D T A G Q E D Y A A I R D N F R S G E G F L C V F S I T E M E S F A A T A D F R E Q I L R V K E D E N V P F L L
sp P63322 RALA_RAT	65	1.24e-62	VVL D G E E V Q I	D I L D T A G Q E D Y A A I R D N F R S G E G F L C V F S I T E M E S F A A T A D F R E Q I L R V K E D E N V P F L L
sp P11233 RALA_HUMAN	65	1.24e-62	VVL D G E E V Q I	D I L D T A G Q E D Y A A I R D N F R S G E G F L C V F S I T E M E S F A A T A D F R E Q I L R V K E D E N V P F L L
sp P48555 RALA_DROME	62	1.58e-55	VVL D G E E V Q I	D I L D T A G Q E D Y A A I R D N F R S G E G F L C V F S I T D D E S F Q A T Q E F R E Q I L R V K N D E S I P F L L



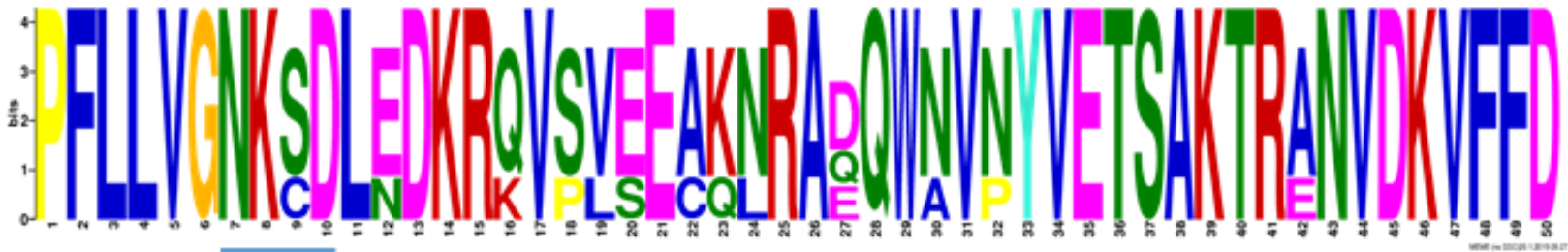
G3/PM3

Switch II

Change conformation when GTP-bound state

# The Motif Analysis

Name	Start	p-value	Sites ?
sp P63321 RALA_MOUSE	121	2.73e-61	ILRVKEDENV P FLLVGNKSDLEDKRQVSVEEAKNRADQWNVNYVETS AKTRANVDKVF FD LMREIRARKM
sp P63322 RALA_RAT	121	2.73e-61	ILRVKEDENV P FLLVGNKSDLEDKRQVSVEEAKNRADQWNVNYVETS AKTRANVDKVF FD LMREIRARKM
sp P11233 RALA_HUMAN	121	9.61e-61	ILRVKEDENV P FLLVGNKSDLEDKRQVSVEEAKNR AEQWNVNYVETS AKTRANVDKVF FD LMREIRARKM
sp P48555 RALA_DROME	118	7.67e-48	ILRVKNDESI P FLLVGNKCDLNDKRK VPLSE CQLRAQQWAVPYVETS AKTRENVDKVF FD LMREIRSRKT



G4

G5

Guanine base-binding specificity

Guanine base binding site

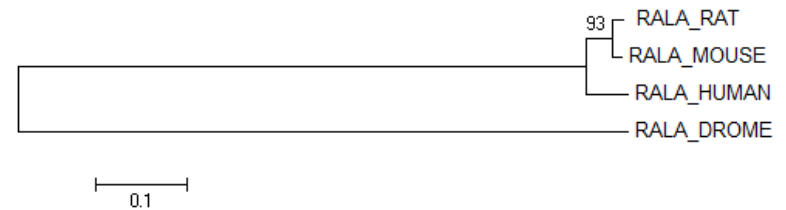
Important motif of Rala for function is highly conserved.





# Evolutionary Tree of Rala and GAP

Species	Accession	Length/Identity
Human/DROME	P11233/P48555	206/201(80.0%)
Mouse/DROME	P63321/P48555	206/201 (80.0%)
Rat/DROME	P63322/P48555	206/201 (80.0%)



Species	Accession	Length/Identity
Human/DROME	Q2PPJ7/Q9VB98	1873/1958(33.0%)
Mouse/DROME	A3KGS3/Q9VB98	1872/1958(33.0%)
Rat/DROME	P86411/Q9VB98	1872/1958(34.0%)



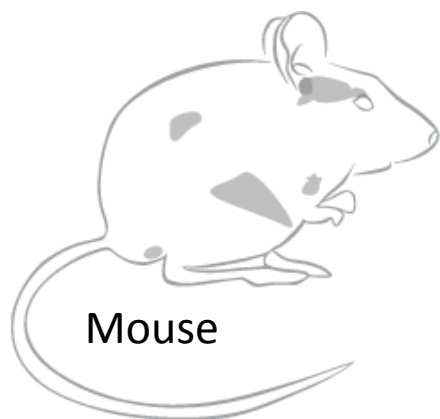


# Tissue Expression



Rat

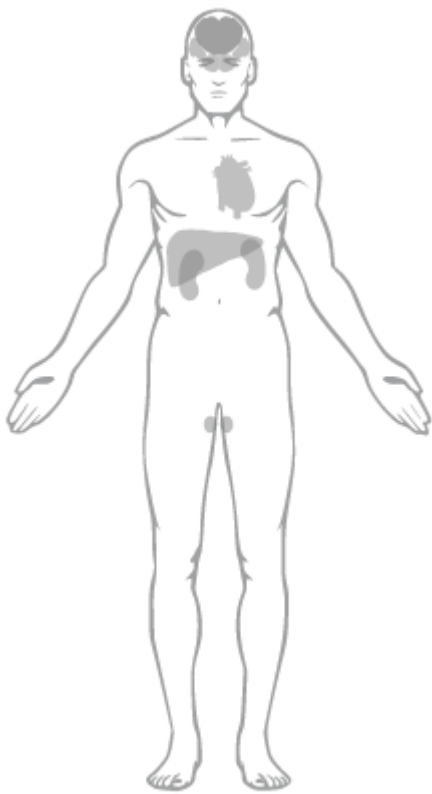
Gene	adrenal gland	brain	gastrocnemius	heart	kidney	liver	lung	spleen	testis	thymus
<u>Rala</u>	16	21	12	13	13	11	26	26	58	34



Mouse

Gene	brain	cerebellum	heart	kidney	liver	testis
<u>Rala</u>	20	21	15	20	9	12

# Tissue Expression



	cerebellum	frontal lobe	heart	kidney	liver	prefrontal cortex	temporal lobe	testis
Gene								
<b>RALA</b>	8	9	7	6	4	11	8	8



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# Structure Prediction

## Model Results



Model 01  ▾

Oligo-State

MONOMER

Template	Seq Identity	Coverage
<b>3brw_1.A</b>	21.36%	<input type="range" value="21.36"/>

Model-Template Alignment



Model 03  ▾

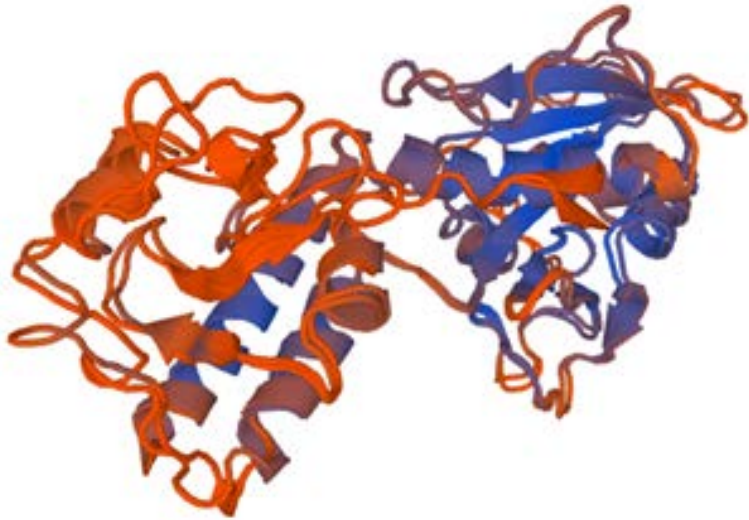
Oligo-State

MONOMER (matching prediction)

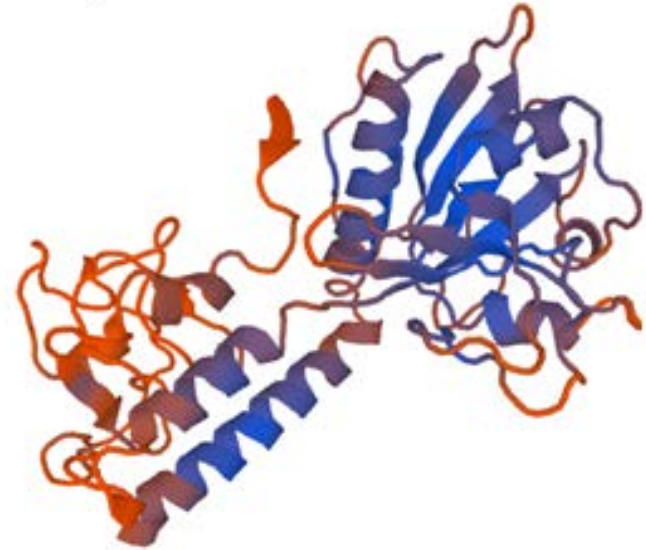
Template	Seq Identity	Coverage
<b>1srq_2.A</b>	21.68%	<input type="range" value="21.68"/>

Model-Template Alignment

# Structure Prediction

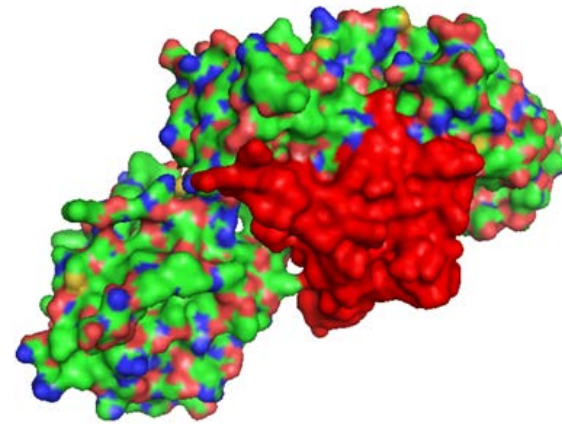
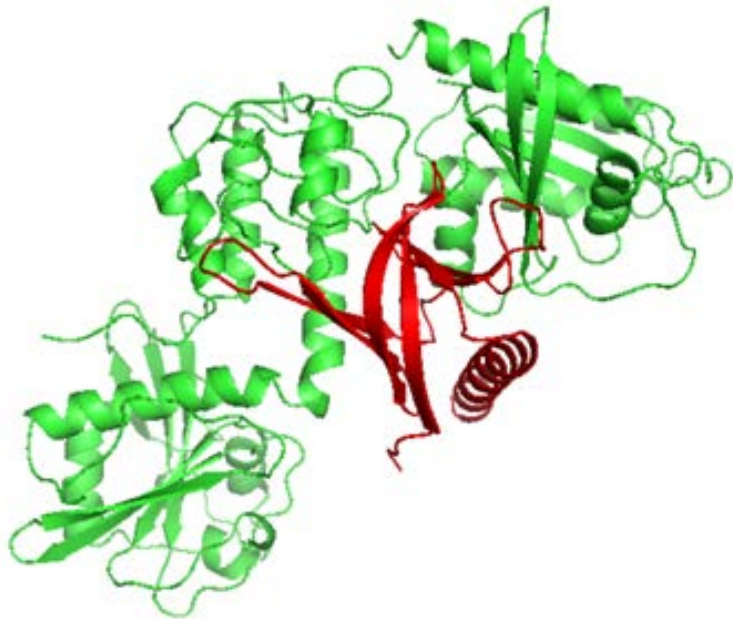


Proteins Comparison



Prediction Structure

# Structure Prediction



```
181 186 191 196 201 206 211  
LVEYEADHMAQLQRVHGFMLNDCLLVATWLPQR
```

```
241 246 251 256  
DMFKLLMFPESTRIFQAENAI
```

GAP

The interaction between Rala and GAP

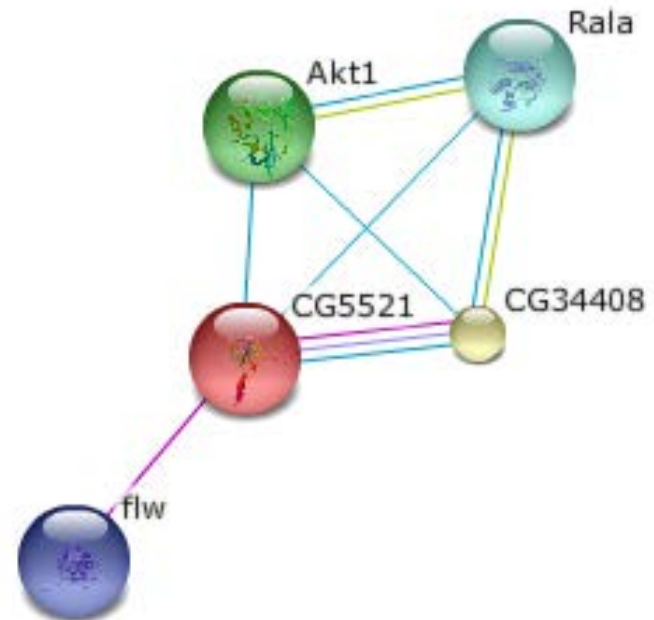
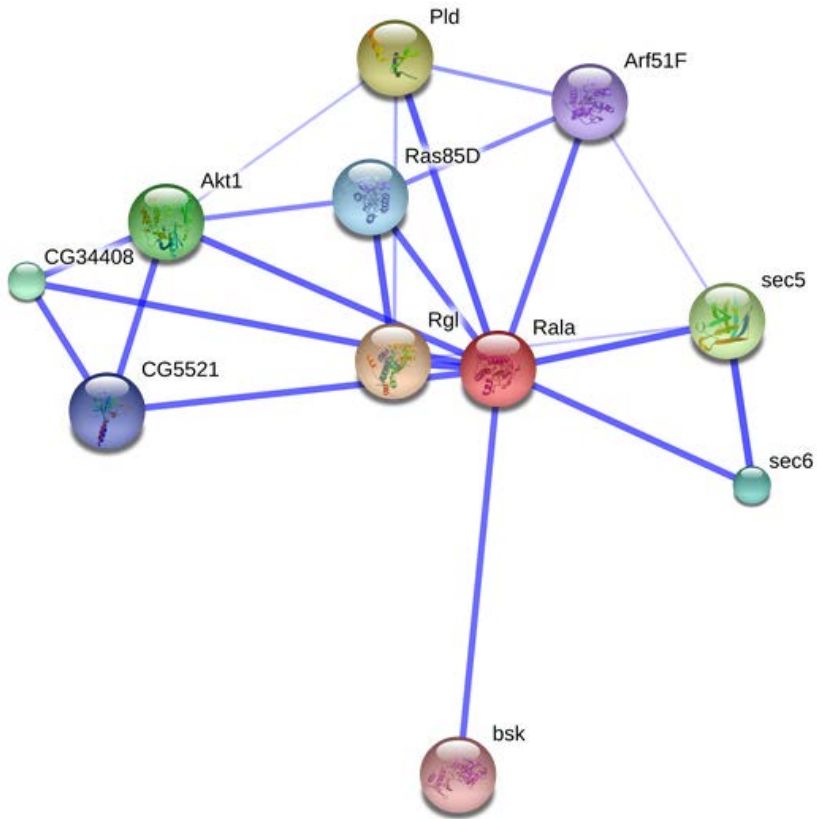


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# Protein Interaction



# Protein Interaction

<u>Interactor</u>	<u>Experimental Evidence Code</u>
ANK2	Two-hybrid 
CG11076	Two-hybrid 
CG12470	Two-hybrid 
CG13367	Two-hybrid 
CG30115	Two-hybrid 
CG32532	Two-hybrid 
CHORD	Two-hybrid 
RLIP	Two-hybrid 
RLIP	Two-hybrid 
WNT5	Two-hybrid 
BSK	Phenotypic Suppression 

<u>Interactor</u>	<u>Experimental Evidence Code</u>
BSK	Phenotypic Suppression 
EIF3-S9	Two-hybrid 
EXO84	Two-hybrid 
EY	Two-hybrid 
HEP	Phenotypic Suppression 
HEP	Phenotypic Suppression 
METL	Two-hybrid 
SEC5	Two-hybrid 
SISA	Two-hybrid 
VIMAR	Two-hybrid 

# Protein Interaction

Interactor	Experimental Evidence Code	Interactor	Experimental Evidence Code
ANK2	Two-hybrid	BSK	Phenotypic Suppression
CG11076	Two-hybrid	EIF3-S9	Two-hybrid
CG12470	Two-hybrid	EXO84	Two-hybrid
CG13367	Two-hybrid	EY	Two-hybrid
CG30115	Two-hybrid	HEP	Phenotypic Suppression
CG32532	Two-hybrid	HEP	Phenotypic Suppression
CHORD	Two-hybrid	METL	Two-hybrid
RLIP	Two-hybrid	SEC5	Two-hybrid
RLIP	Two-hybrid	SISA	Two-hybrid
WNT5	Two-hybrid	VIMAR	Two-hybrid

红色边框圈出的为功能未知的蛋白，紫色边框为对于果蝇生殖发育有重要意义的基因。



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# Summary

1. Background Information
2. General Analysis of Gene and Protein
3. Structure Prediction
4. Singaling Prediction



# Summary

1. Background Information

2. General Analysis of Gene and Protein

**NCBI Uniprot**

3. Structure Prediction

4. Singaling Prediction



# Summary

1. Background Information

2. General Analysis of Gene and Protein

3. Structure Prediction

**MEME MEGA6 ClustalW**

4. Singaling Prediction



# Summary

1. Background Information

2. General Analysis of Gene and Protein

3. Structure Prediction

4. Singaling Prediction

**Pymol SwissModel ZDock**





# Summary

1. Background Information

2. General Analysis of Gene and Protein

**String BioGRID**

3. Structure Prediction

4. Singaling Prediction



Thanks!

