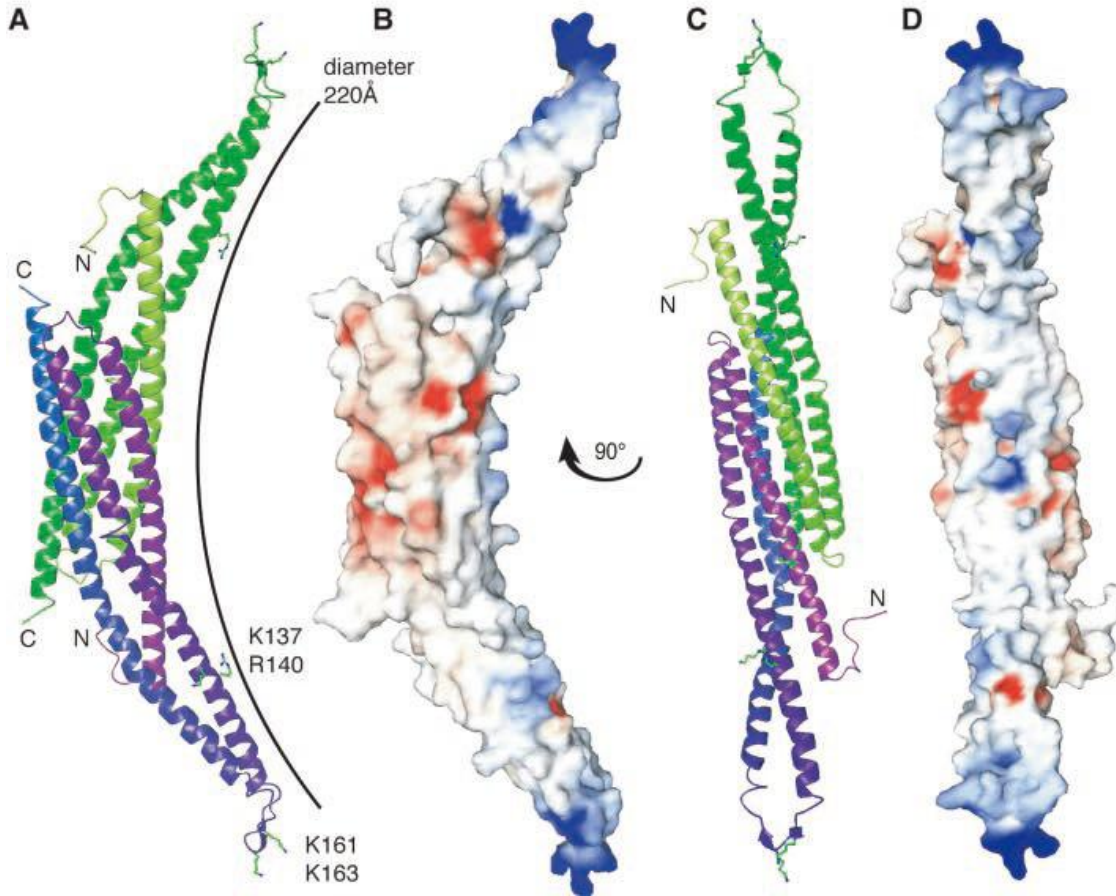
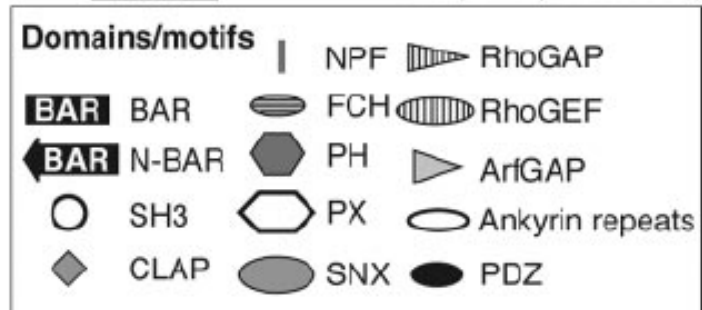
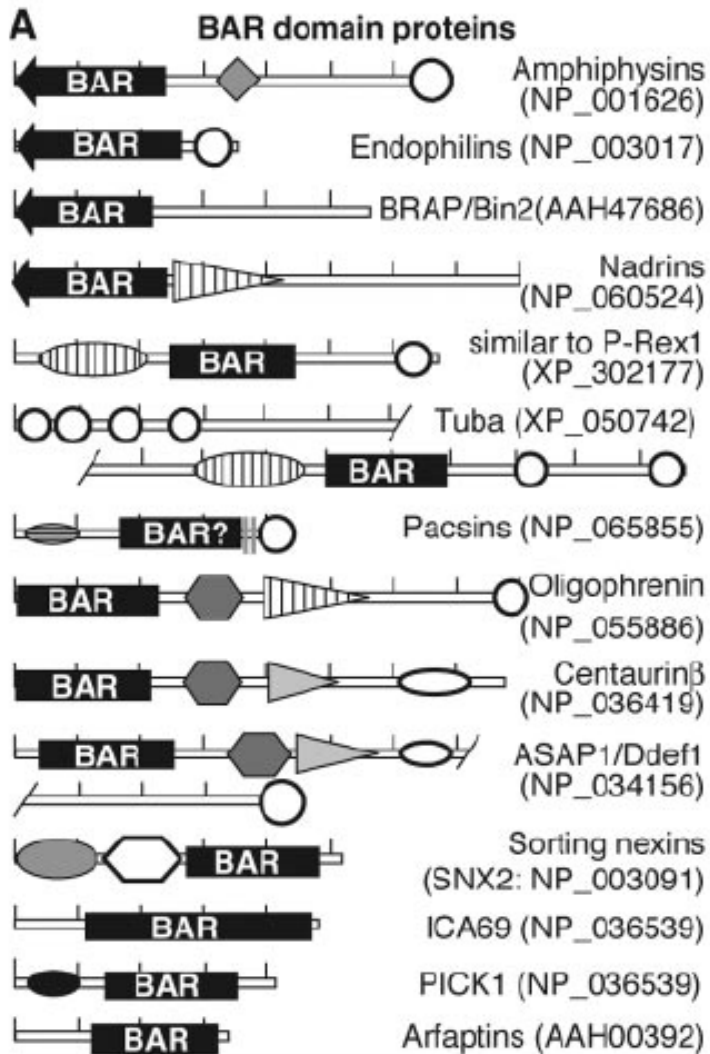


BIN1 成管特性与其蛋白质结构关系



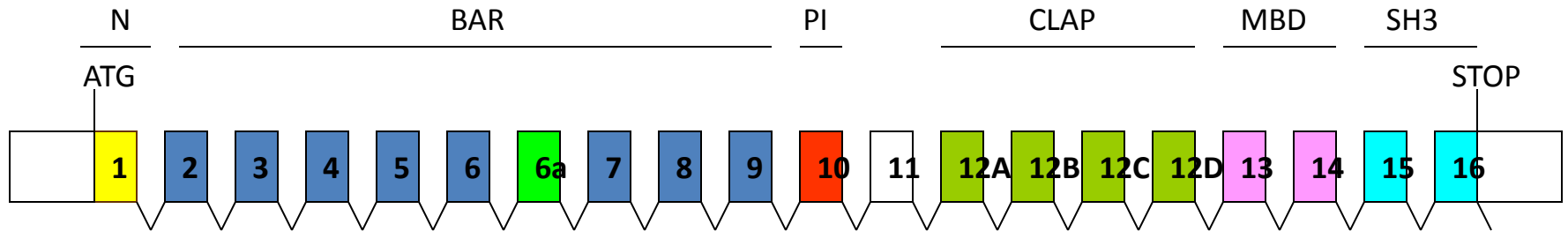
Presented by Wang Qiwei
on behalf of G13,
Members:
Zhu Ying, Zhu Mingyue,
Zheng Zhenggao, Wang Qiwei



BAR super family

The only similarity among proteins in BAR super family is that all of them have a BAR(BIN1-Amphiphysin-Rvs167) domain, which could induce membrane invagination.

And the highlighted protein here is BIN1(bridging integrator 1).



Base on Charlotte Fugier et al.,2011,Nat. Med.(N.Y.)

Human *BIN1* has 20 exons.

N, N-terminal amphipathic helix;

BAR, BIN1-amphiphysin-Rvs167;

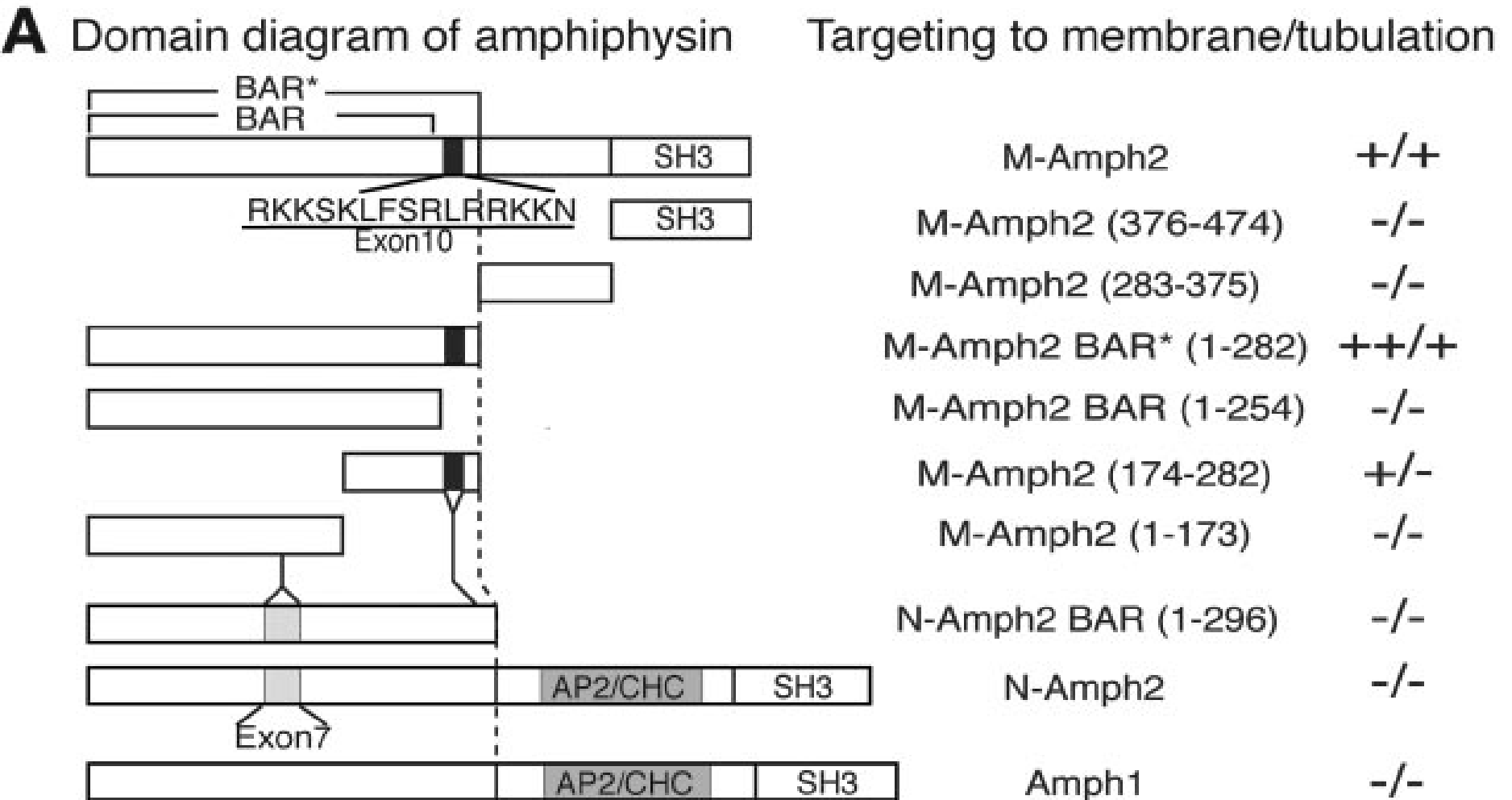
PI, phosphoinositide-binding domain;

CLAP, clathrin-associated protein-binding domain;

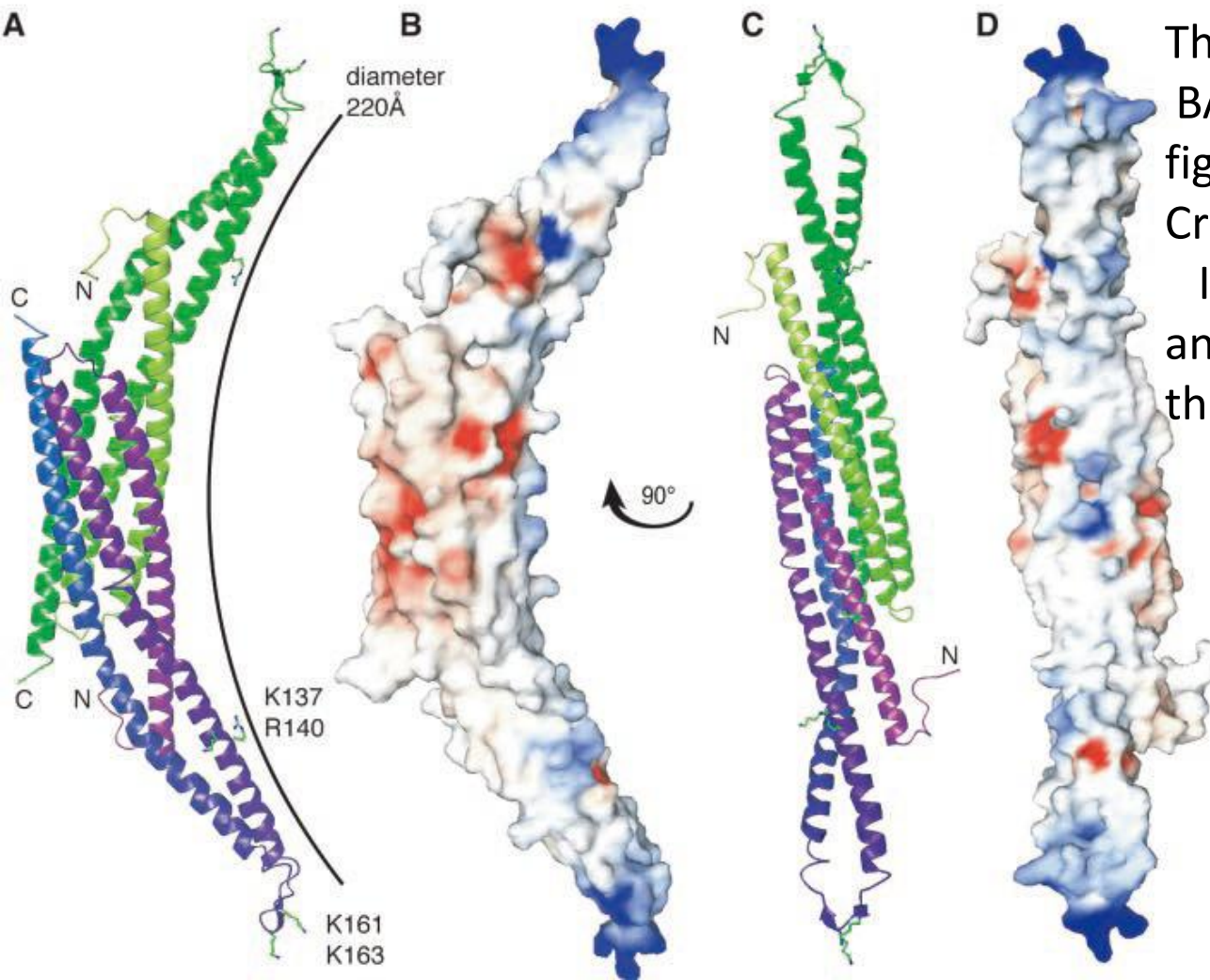
MBD, Myc-binding domain;

SH3, Src homology 3 domain.

Tubulation function of BIN1

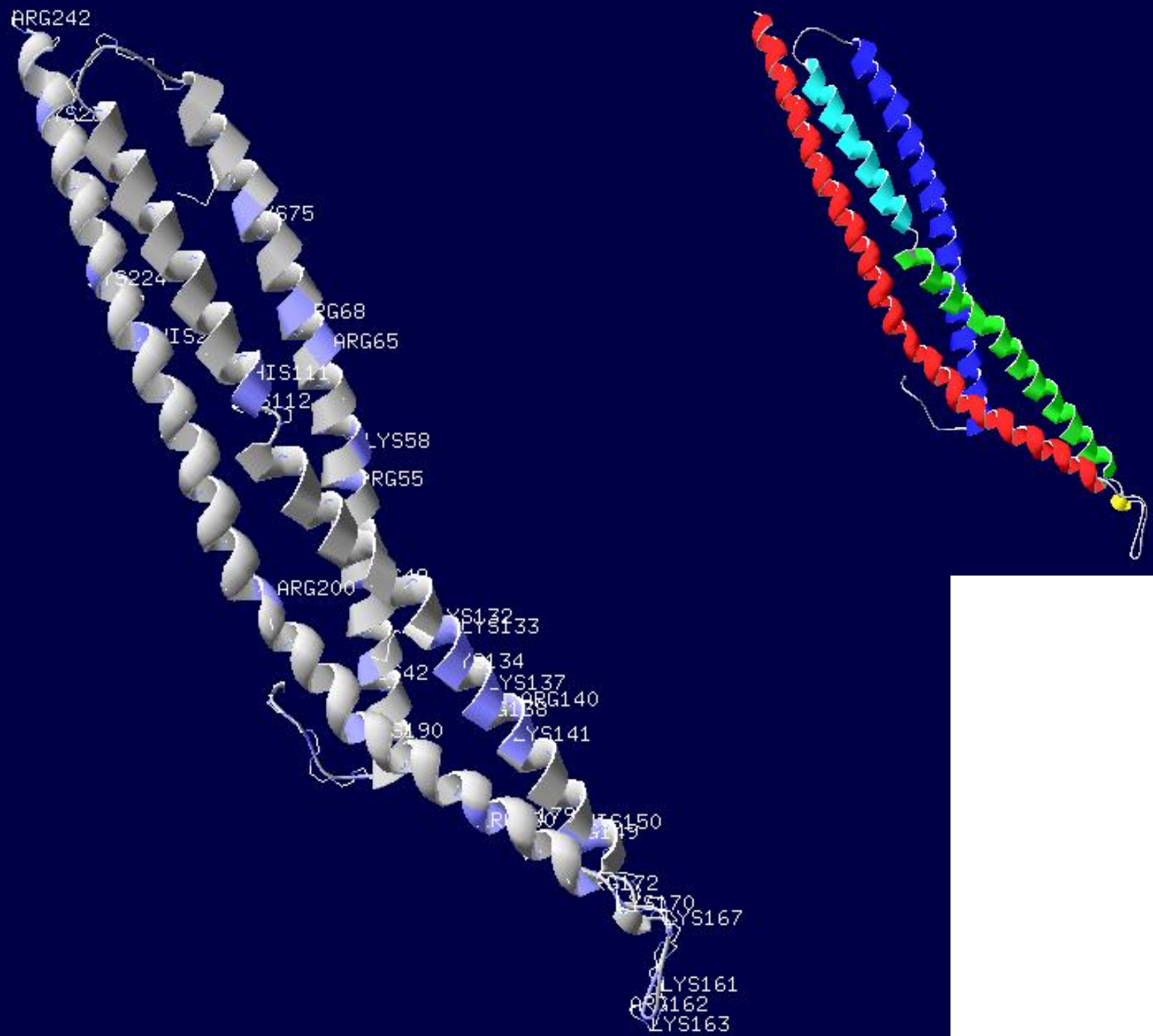


The function of BAR domain: feeling membrane curvature



The 3D structure of the BAR domain has been figured out by X-ray Crystallography.

It's a banana-shaped dimer and could feel the curvature of the membrane.



物种中BIN1 序列搜寻

Protein Name	Species	Common Name	UniProt Entry	Length
BIN1	<i>Homo sapiens</i>	Human	O00499	593
BIN1	<i>Mus musculus</i>	Mouse	O08539	588
BIN1	<i>Rattus norvegicus</i>	Rat	O08839	588
BIN1	<i>Bos taurus</i>	Bovine	E1BNG8	584
BIN1	<i>Meleagris gallopavo</i>	Common turkey	G1NGS1	687
BIN1	<i>Canis familiaris</i>	Dog	F1PJ63	659
Uncharacterized protein	<i>Xenopus tropicalis</i>	Western clawed frog	F7ENL6	559
Uncharacterized protein	<i>Ailuropoda melanoleuca</i>	Giant panda	G1MEW9	668
Uncharacterized protein	<i>Monodelphis domestica</i>	Gray short-tailed opossum	F7FBY3	598
Uncharacterized protein	<i>Oryctolagus cuniculus</i>	Rabbit	G1T894	578
Uncharacterized protein	<i>Sus scrofa</i>	Pig	F1RXZ3	407
Uncharacterized protein	<i>Loxodonta africana</i>	African elephant	G3U552	452
Uncharacterized protein	<i>Nomascus leucogenys</i>	Northern white-cheeked gibbon	G1S0D1	595
Uncharacterized protein	<i>Gorilla gorilla gorilla</i>	Lowland gorilla	G3RIZ8	591

不同物种中 BIN1 序列比对

LYS → ASN

Positive
Negative

ARG → GLN

1	MAEMGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	60	000499	BIN1_HUMAN
1	---MGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	57	G3RIZ8	G3RIZ8_GORGO
1	MAEMGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	60	G1S0D1	G1S0D1_NOMLE
1	---MGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	57	E1BNG8	E1BNG8_BOVIN
1	MAEMGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	60	O08539	BIN1_MOUSE
1	MAEMGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	60	O08839	BIN1_RAT
1	-----QVLQKLGKADETKDEQFEQCVQNFNKQLVSGTW	33	G1T894	G1T894_RABIT
1	MAELGSKGVTAGKIASNVQKKLTRAQEKVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	60	F7FBY3	F7FBY3_MONDO
1	-----QVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	33	F1PJ63	F1PJ63_CANFA
1	-----QVLQKLGKADETKDEQFEQCVQNFNKQLSEGTR	33	F1RXZ3	F1RXZ3_PIG
1	-----QVLQKLGKADETKDEQFEQCVQNFNKQLTEGTR	33	G1MEW9	G1MEW9_AILME
1	-----QVLQKLGKADETKDEQFEQCVQNFNKQLTRGQW	33	G3U552	G3U552_LOXAF
1	----EKKWKTVIPSWTFNPLNKGIIYKVLQKLGKADETKDEQFEQCVQNFNKQLSEGTR	55	G1NGS1	G1NGS1_MELGA
1	-----VLQKLGKADETKDEQFEQCVQNFNKQLTEGSK	32	F7ENL6	F7ENL6_XENTR
1	----MTENKGIMLAKSVQKHAGRAKEKILQNLGKVDRTADEIFDDHLNNFNRRQASANR	55	Q7KLE5	Q7KLE5_DROME

61	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEANKIA-----ENND-L	109	000499	BIN1_HUMAN
58	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEANKIA-----ENND-L	106	G3RIZ8	G3RIZ8_GORGO
61	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEANKIA-----EVSVMQ	110	G1S0D1	G1S0D1_NOMLE
58	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEASKIA-----ENND-L	106	E1BNG8	E1BNG8_BOVIN
61	LQKDLRITYLASVKAMHEASK--KLSECLQEVYE-PEWPGRDEANKIA-----ENND-L	109	O08539	BIN1_MOUSE
61	LQKDLRITYLASVKAMHEASK--KLSECLQEVYE-PEWPGRDEANKIA-----ENND-L	109	O08839	BIN1_RAT
34	QEREVRVELARLAGLQATGVGAGLSPCPQGPFR--PPWLGREDPSSLLTLTLWPTQNNND-L	91	G1T894	G1T894_RABIT
61	LQKDLRITYLASVKAMHEASK--KLTECLQEVYE-PDWPGREETNKIA-----ENND-L	109	F7FBY3	F7FBY3_MONDO
34	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEANKIA-----ENND-L	82	F1PJ63	F1PJ63_CANFA
34	LQKDLRITYLASVKAMHEASK--KLNECLQEVYE-PDWPGRDEANKIA-----ENND-L	82	F1RXZ3	F1RXZ3_PIG
34	LQKDLRITYLASVKAMHEASK--KLNECLQEMYE-PDWPGRDEANKIA-----ENND-L	82	G1MEW9	G1MEW9_AILME
34	QKELAHGGSLGAVVAHPACP--RPSQCWWYVWGGECWSPSHRGGCSR----CWSWAGHV	87	G3U552	G3U552_LOXAF
56	LQKDLRITYLASVKAMHEASK--KLTECLQEVYE-PDWPGRDDTNKIA-----ENND-L	104	G1NGS1	G1NGS1_MELGA
33	LLFDIKSSRLPSPAMHEASK--KLTECLLDVYE-PDWPGREETNKIA-----ENND--	80	F7ENL6	F7ENL6_XENTR
56	LQKEFNYYIRCVRAAQAASK--TLMDSVCEIYE-PQWSGYDALQAQT-----GASES	104	Q7KLE5	Q7KLE5_DROME

110	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	166	000499	BIN1_HUMAN
107	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	163	G3RIZ8	G3RIZ8_GORGO
111	VALPFSGGLVSAVPLCRALWGLLPALRSRIAKRGRKLVYDYSARHHYESLQT--AKKK	168	G1S0D1	G1S0D1_NOMLE
107	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	163	E1BNG8	E1BNG8_BOVIN
110	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	166	O08539	BIN1_MOUSE
110	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	166	O08839	BIN1_RAT
92	LWMDYHQK-LVDQALLTMDTYLGQFPDIKVRGGSGLVALGSGEEEKACLGLGS--GAQG	148	G1T894	G1T894_RABIT
110	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	166	F7FBY3	F7FBY3_MONDO
83	LWLDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	139	F1PJ63	F1PJ63_CANFA
83	LWMDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	139	F1RXZ3	F1RXZ3_PIG
83	LWLDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHYESLQT--AKKK	139	G1MEW9	G1MEW9_AILME
88	LWLPRHKD-VFQALFSLPCLSPQ---SRIAKRGRKLVYDYSARHHYESLQT--AKKK	140	G3U552	G3U552_LOXAF
105	LWTDYHQK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHFEALQT--AKKK	161	G1NGS1	G1NGS1_MELGA
81	LWTDYHEK-LVDQALLTMDTYLGQFPDIKSRIAKRGRKLVYDYSARHHFESLQN--AKKK	137	F7ENL6	F7ENL6_XENTR
105	LWADFAHK-LGQVLIPLNTYTGFPEMKKKVEKRNKRLIYDYGRRHSFQNLQANANKRK	163	Q7KLE5	Q7KLE5_DROME

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228 G1S0D1 G1S0D1_NOMLE
223 E1BNG8 E1BNG8_BOVIN
226 O08539 BIN1_MOUSE
226 O08839 BIN1_RAT
208 G1T894 G1T894_RABIT
226 F7FBY3 F7FBY3_MONDO
168 F1PJ63 F1PJ63_CANFA
168 F1RXZ3 F1RXZ3_PIG
168 G1MEW9 G1MEW9_AILME
169 G3U552 G3U552_LOXAF
190 G1NGS1 G1NGS1_MELGA
192 F7ENL6 F7ENL6_XENTR
192 Q7KLE5 Q7KLE5_DROME

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273 G3RIZ8 G3RIZ8_GORGO
278 G1S0D1 G1S0D1_NOMLE
273 E1BNG8 E1BNG8_BOVIN
276 O08539 BIN1_MOUSE
276 O08839 BIN1_RAT
260 G1T894 G1T894_RABIT
276 F7FBY3 F7FBY3_MONDO
218 F1PJ63 F1PJ63_CANFA
218 F1RXZ3 F1RXZ3_PIG
218 G1MEW9 G1MEW9_AILME
219 G3U552 G3U552_LOXAF
240 G1NGS1 G1NGS1_MELGA
244 F7ENL6 F7ENL6_XENTR
250 Q7KLE5 Q7KLE5_DROME

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321 E1BNG8 E1BNG8_BOVIN
324 O08539 BIN1_MOUSE
324 O08839 BIN1_RAT
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264 F1PJ63 F1PJ63_CANFA
266 F1RXZ3 F1RXZ3_PIG
266 G1MEW9 G1MEW9_AILME
267 G3U552 G3U552_LOXAF
289 G1NGS1 G1NGS1_MELGA
293 F7ENL6 F7ENL6_XENTR
310 Q7KLE5 Q7KLE5_DROME

BIN1 SNP 位点搜寻

NCBI Resources How To



National Center for
Biotechnology Information

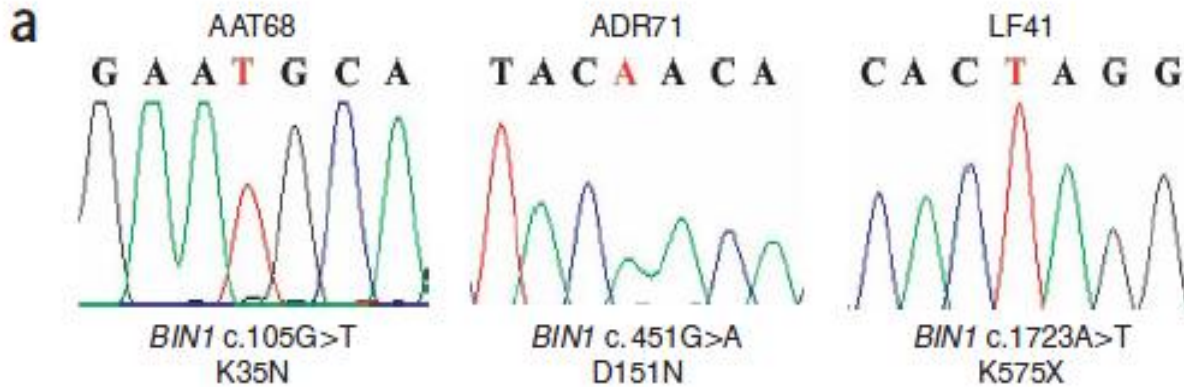
OMIM



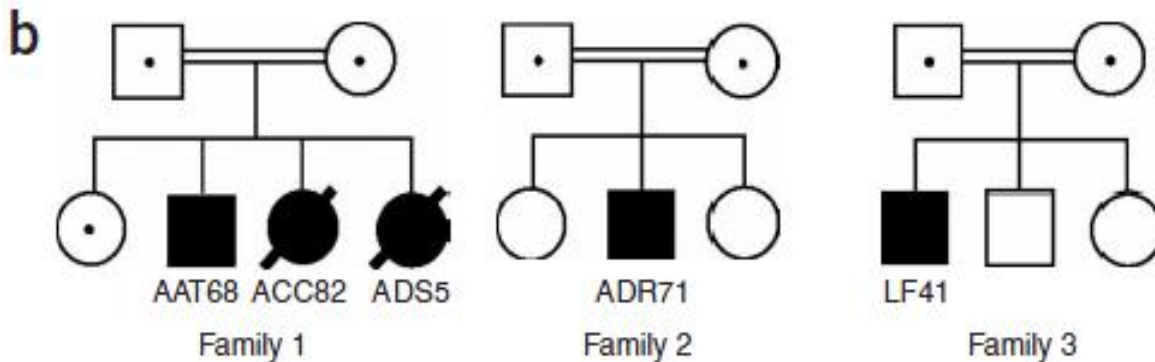
bridging integrator 1

Number	Phenotype	Mutation	dbSNP
0.0001	MYOPATHY, CENTRONUCLEAR, AUTOSOMAL RECESSIVE	BIN1, LYS35ASN	[rs121909273]
0.0002	MYOPATHY, CENTRONUCLEAR, AUTOSOMAL RECESSIVE	BIN1, ASP151ASN	[rs121909274]
0.0003	MYOPATHY, CENTRONUCLEAR, AUTOSOMAL RECESSIVE	BIN1, LYS575TER	[rs121909275]
0.0004	MYOPATHY, CENTRONUCLEAR, AUTOSOMAL RECESSIVE	BIN1, ARG154GLN	-

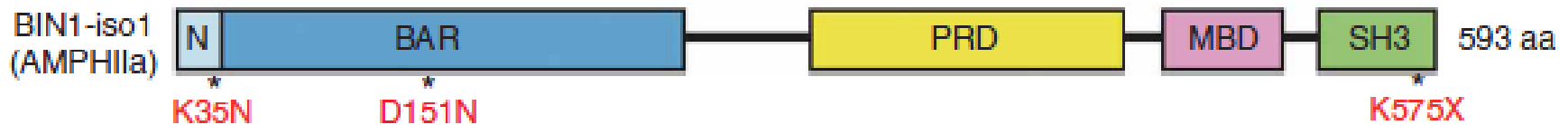
BIN1 mutation and human disease



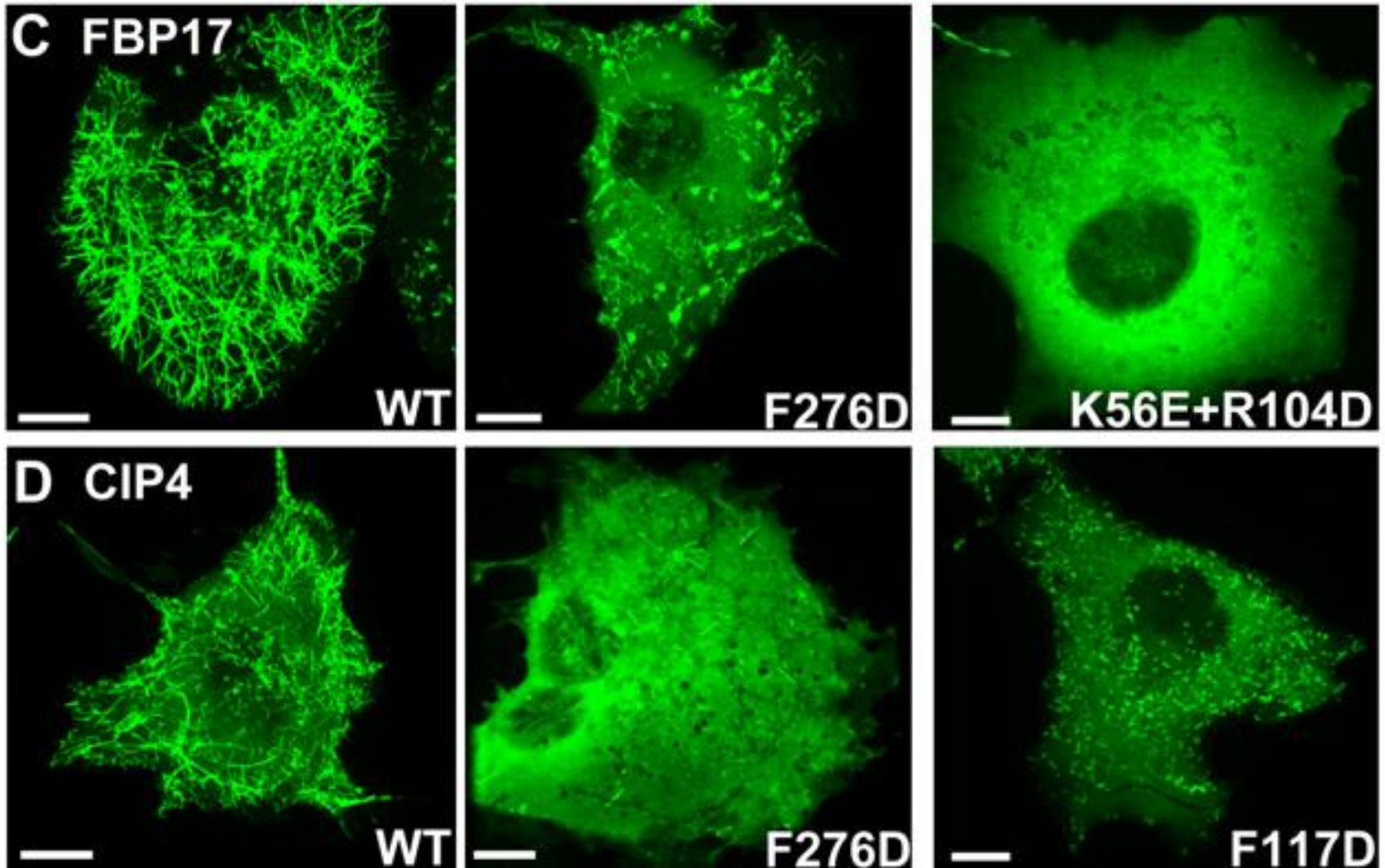
BIN1 mutations are found in patients with recessive centronuclear myopathy.



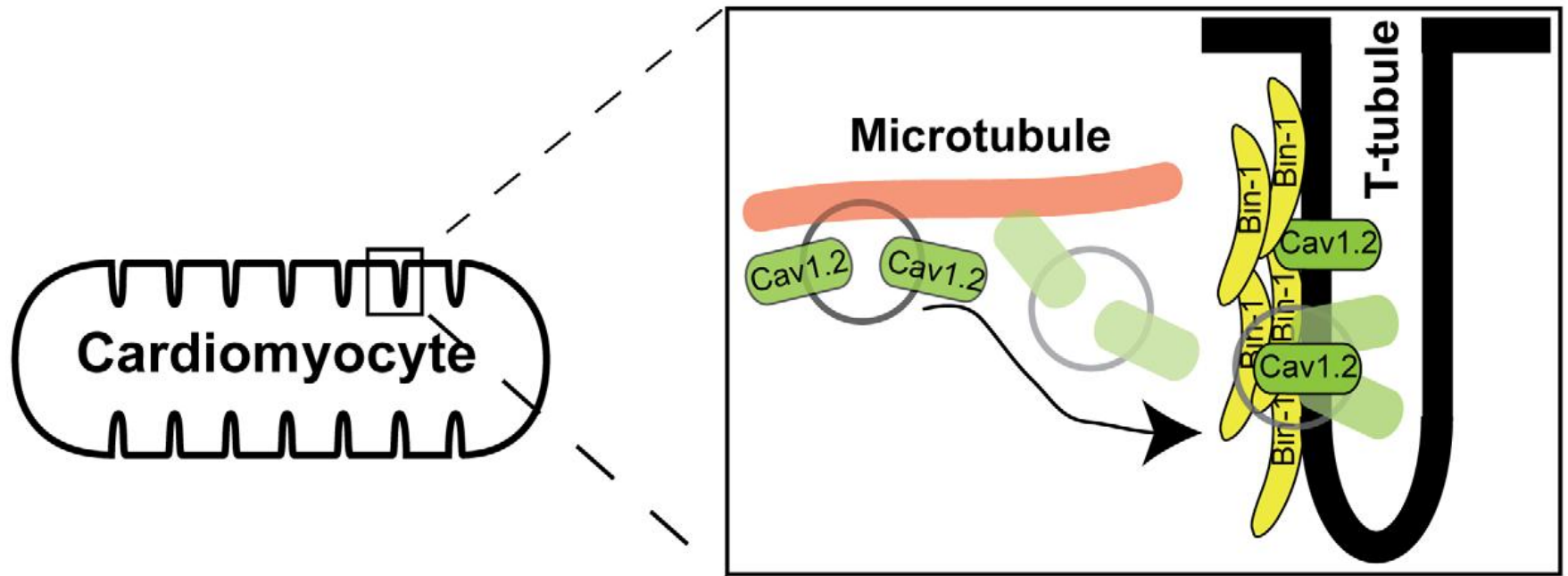
The first two mutations cause aa changes in BAR domain and the third one result in premature stop codon



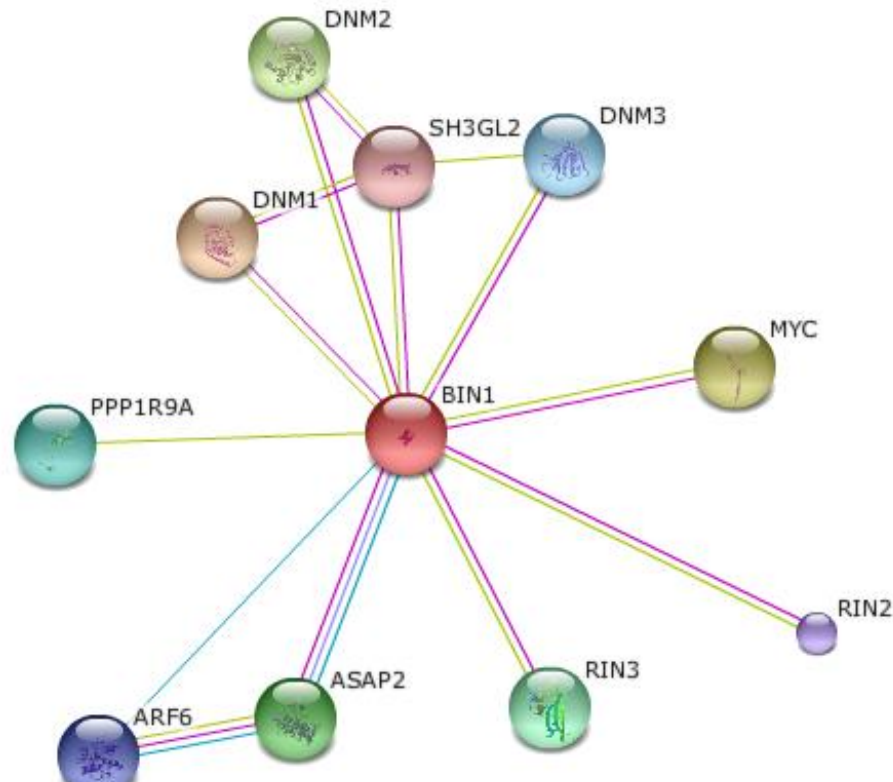
Tubulation induced by FBP17 and CIP4



BIN1 recruit LCC to T-tubule



Predicted Functional Partners of BIN1



Your Input:

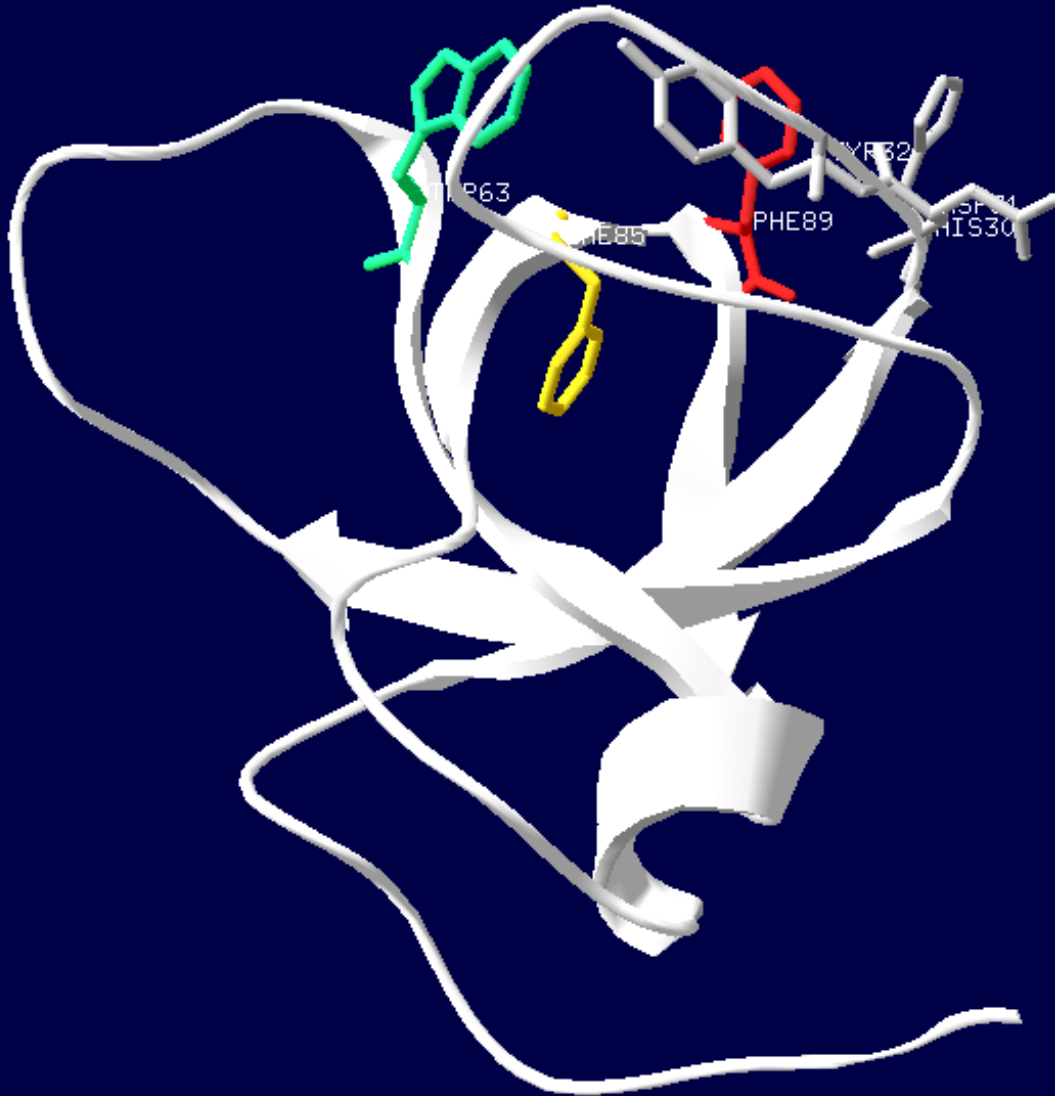
- BIN1 bridging integrator 1; May be involved in regulation of synaptic vesicle endocytosis. May act as a tumor suppressor and inhibits malignant cell transformation (593 aa) (*Homo sapiens*)

Predicted Functional Partners:

Partner	Description
DNM1	dynamain 1; Microtubule-associated force-producing protein involved in producing microtubule bun [...] (864 aa)
MYC	v-myc myelocytomatosis viral oncogene homolog (avian); Participates in the regulation of gene t [...] (454 aa)
DNM2	dynamain 2; Microtubule-associated force-producing protein involved in producing microtubule bun [...] (870 aa)
ASAP2	ArfGAP with SH3 domain, ankyrin repeat and PH domain 2; Activates the small GTPases ARF1, ARF5 [...] (1006 aa)
RIN3	Ras and Rab interactor 3; Potential Ras effector protein. May function as a guanine nucleotide [...] (985 aa)
PPP1R9A	protein phosphatase 1, regulatory (inhibitor) subunit 9A; Binds to actin filaments (F-actin) an [...] (1098 aa)
DNM3	dynamain 3; Microtubule-associated force-producing protein involved in producing microtubule bun [...] (859 aa)
ARF6	ADP-ribosylation factor 6; GTP-binding protein that functions as an allosteric activator of the [...] (175 aa)
RIN2	Ras and Rab interactor 2; Ras effector protein. May function as an upstream activator and/or do [...] (944 aa)
SH3GL2	SH3-domain GRB2-like 2; Implicated in synaptic vesicle endocytosis. May recruit other proteins [...] (352 aa)

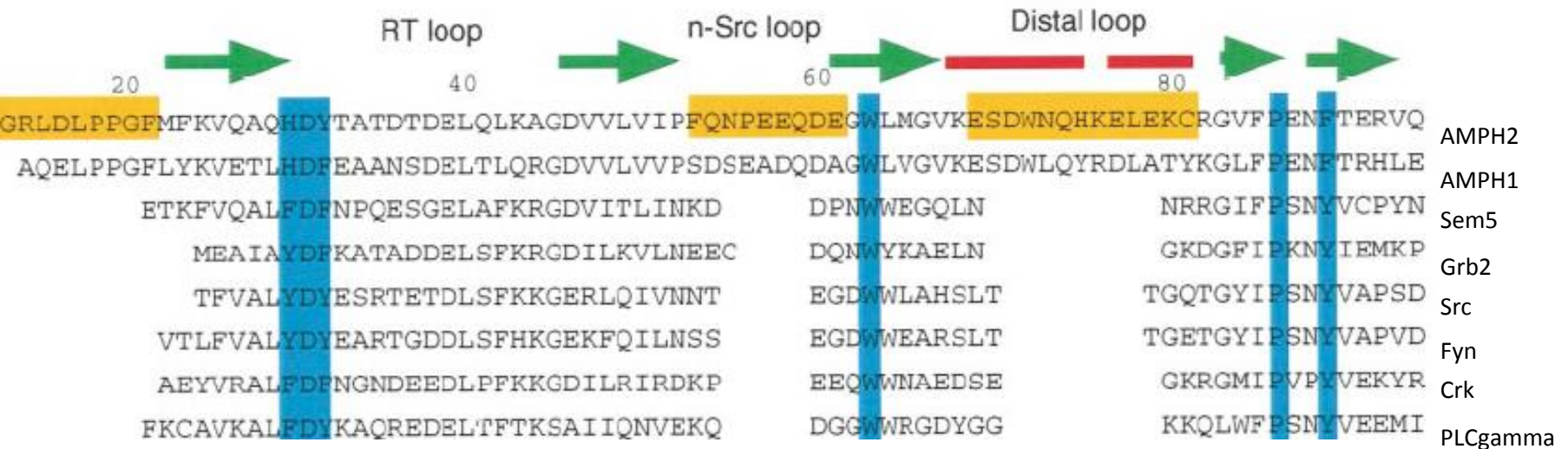
Neighborhood	Gene Fusion	Cooccurrence	Coexpression	Experiments	Databases	Textmining	[Homology]	Score
				●	●	●	●	0.982
				●	●	●	●	0.979
				●	●	●	●	0.974
				●	●	●	●	0.959
				●	●	●	●	0.922
				●	●	●	●	0.911
				●	●	●	●	0.909
				●	●	●	●	0.899
				●	●	●	●	0.896
				●	●	●	●	0.892

SH3 domain structure of BIN1



Residues labeled here are Conservative amino acids that interactive with dynamin. They are HIS30, ASP31, TYR32, TRP63, PHE85, PHE89.

Conservative residues in SH3 domain in different proteins



30, 31, 32, 63, 85, 89 are conservative.

Future Plan

1. Searching novel proteins that could interact with BIN1
2. Searching BIN1 mutations in cardiomyopathy patients.

Acknowledgments

Prof. Luo

Zhu Ying

Zhu Mingyue,

Zheng Zhenggao