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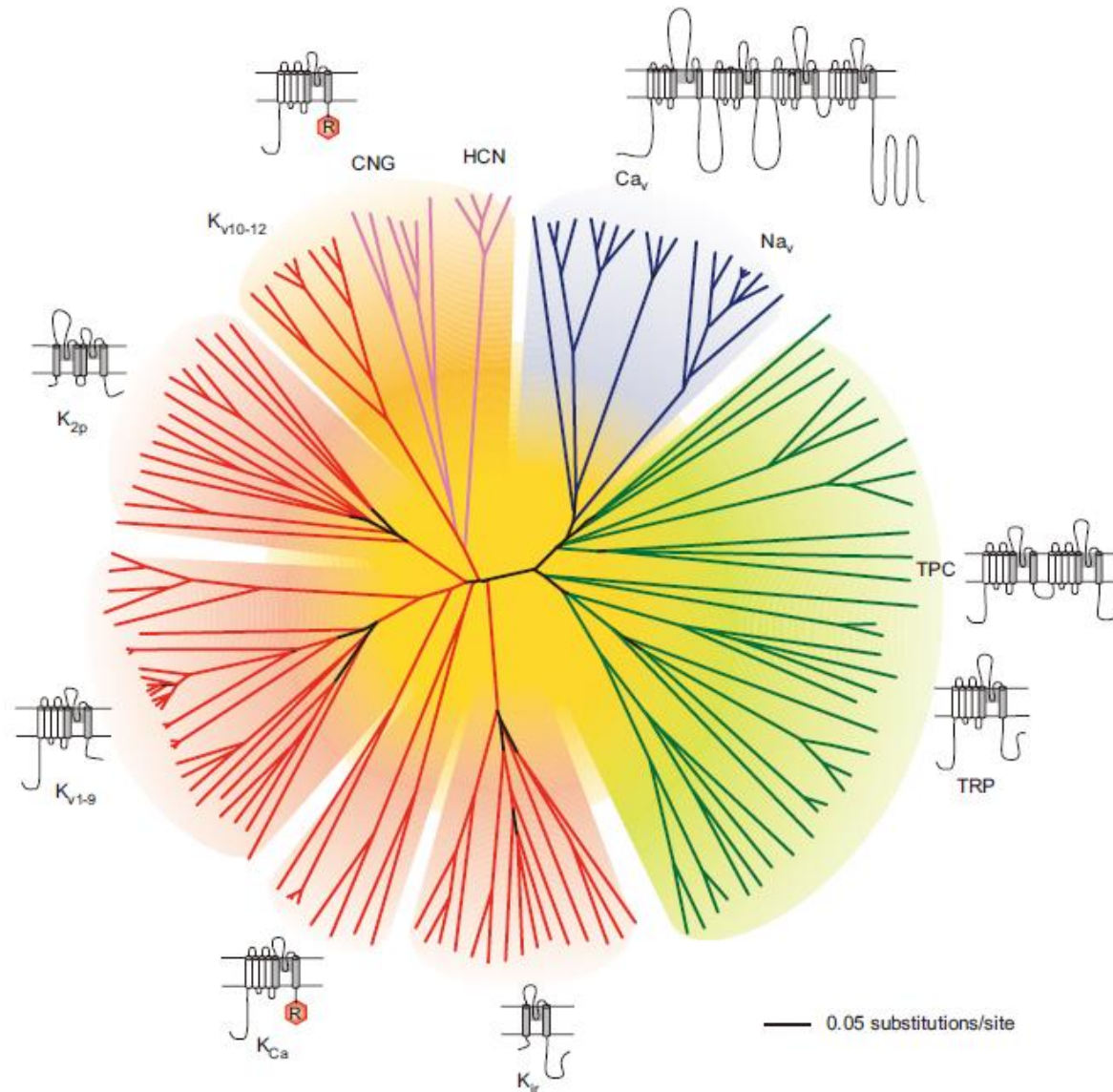
Applied Bioinformatics Course

双孔道蛋白TPC1特征分析

The analysis of the Two pore calcium channel protein 1 (TPC1) protein

Group 09 曹磊
陆明傲
孙含笑
施开宇

TPCs mean what?



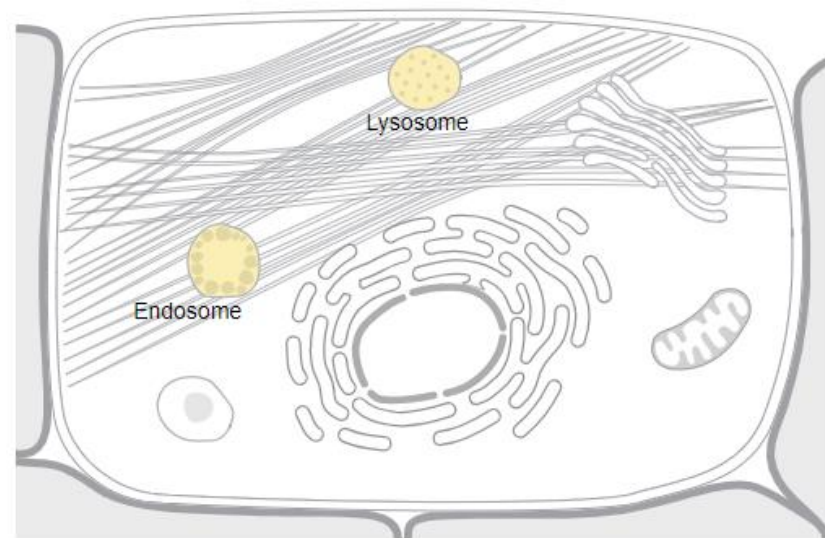
TPC1_HUMAN

Molecular function

- Identical protein binding
- NAADP-sensitive calcium-release channel activity
- Voltage-gated calcium channel activity

Biological process

- Ion transmembrane transport
- Positive regulation of autophagy
- Regulation of ion transmembrane transport

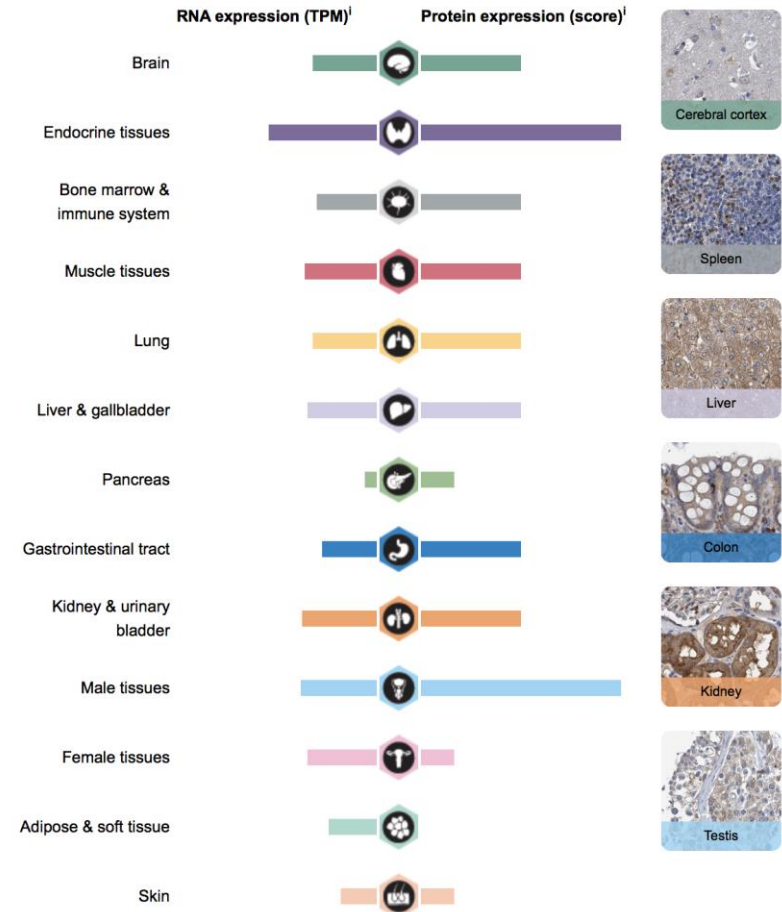


MmTPC1 Sequence and Expression

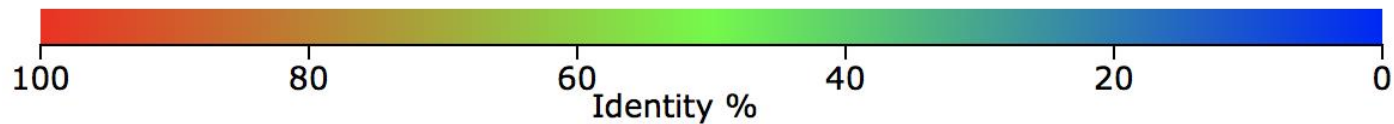
Chr 12 (NC_000012.12): 113,213,329 - 113,306,340

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 LLSLCEAPAVPALRLGIYVHATLELFALMVVVFELCMKLRWLGLHTFIRHKRTMVKTSVL
 VVQFVEAIVVLVRQMSHVRVTRALRCIFLVDCRYCGGVRRLNRQIFQSLPPFMDILLLLL
 FFMIIIFAILGFYLFSPNPSDPYFSTLENSIVSLFVLLTTANFPDVMMPYSYRNWPWSCVFF
 IVYLSIELYFIMNLLLAVVFDTFNDIEKRKFKSLLLHKRTAIQHAYRLLISQRRPAGISY
 RQFEGLMRFYKPRMSARERYLTFKALNQNTPLLSLKDFYDIYEVAALKWKAKKNREHW
 DELPRTALLIFKGINILVKSQAFQYFMYLVVAVNGVWILVETFMLKGGNFFSKHVPWSYL
 VFLTIYGVELFLKVAGLGPVEYLSSGWNLFDFSVTVFAFLGLLALALNMEPFYFIVLVRP
 LQLLRLFKLKERYRNVDTMFELLPRMASLGLTLLIFYYSFAIVGMEFFCGIVFPNCNT
 STVADAYRWRNHTVGNRTVVEEGYYLNNFDNILNSFVTLFELTVVNNWYIIMEGVTSQT
 SHWSRLYFMTFYIVTMVMTIIVAFILEAFVFRMNYSRKNQDSEVDGGITLEKEISKEEL
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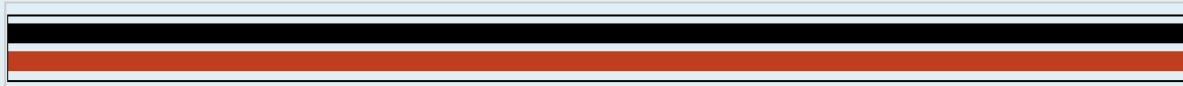
816 Amino acids



MmTPC1 Sequence Blast



TPC1_MOUSE - Two pore calcium channel protein 1 *Mus musculus* (Mouse) - [View alignment](#)



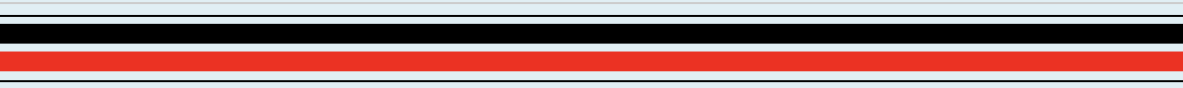
E-value: 0.0
Score: 3,847
Ident.: 90.9%

A0A0G2K997_RAT - Two pore calcium channel protein 1 - *Rattus norvegicus*... - [View alignment](#)



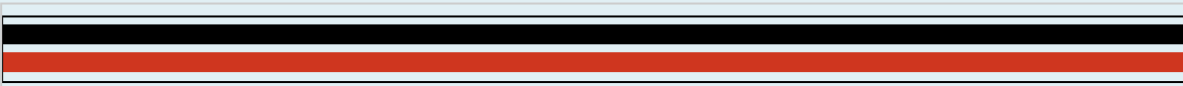
E-value: 0.0
Score: 3,083
Ident.: 89.6%

A0A2J8XKN2_PONAB - TPCN1 isoform 1 - *Pongo abelii* (Su... - [View alignment](#)



E-value: 0.0
Score: 4,199
Ident.: 99.6%

A0A287BJ75_PIG - Two pore segment channel 1 *Sus scrofa* (Pig) - [View alignment](#)

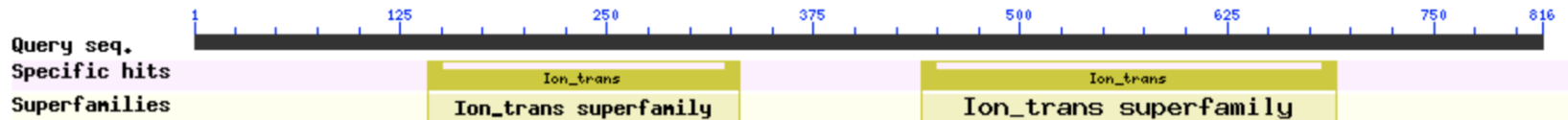


E-value: 0.0
Score: 3,972
Ident.: 93.9%

MmTPC1 Domains

Graphical summary

 Zoom to residue level

[show extra options »](#)




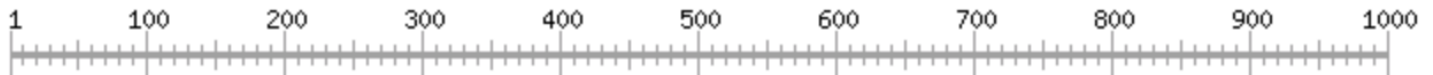


List of domain hits



+	Name	Accession	Description	Interval	E-value
[+]	Ion_trans	pfam00520	Ion transport protein; This family contains sodium, potassium and calcium ion channels. This ...	440-691	1.48e-25
[+]	Ion_trans	pfam00520	Ion transport protein; This family contains sodium, potassium and calcium ion channels. This ...	142-330	1.49e-16

ruler:



USERSEQ1



[PS00307](#) **LECTIN_LEGUME_BETA** *Legume lectins beta-chain signature* :

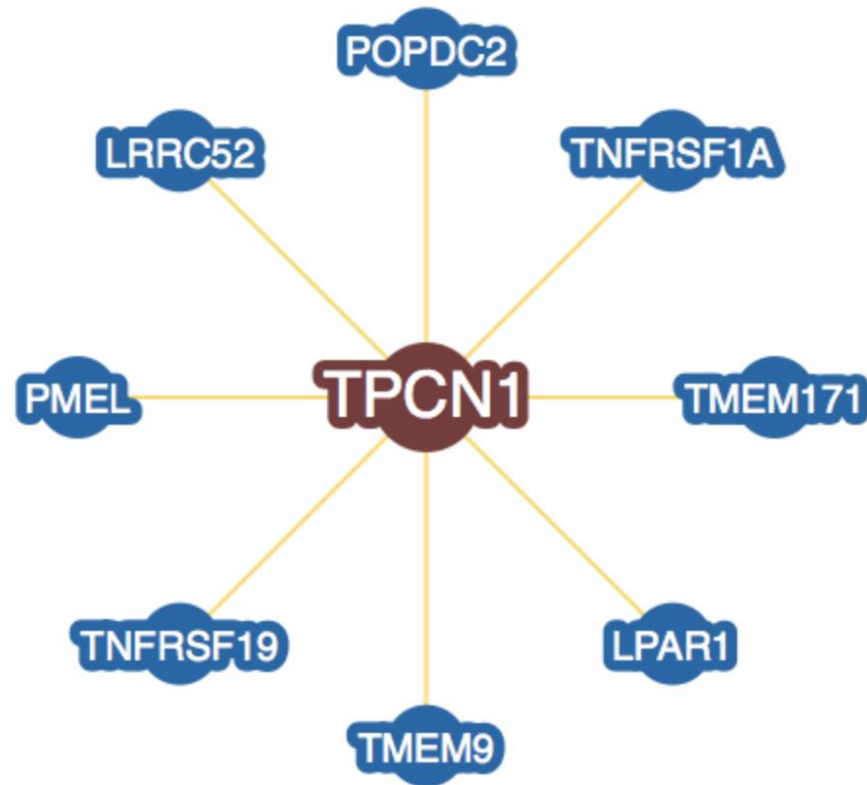
316 - 322: [confidence level: (-1)] LAVVFDT

MmTPC1 Sequence Analysis

		220	230	240	250	260	270		
sp Q6YLX9 TPC1_WHEAT	N	PDVW	VHAYKI	PRWYS	LFFIVYV	LVVYFLTNL	LAVIYD	FEKQFAKQLVQVDSIRKNI	
sp Q6S5H8 TPC1_HORVU	N	PDVW	VPAKYI	SRWYS	LFFIVYV	LVVYFLTNL	LAVIYD	FEKQFAKQLVQVDAIRKNI	
sp Q5QM84 TPC1_ORYSJ	N	PDVW	VPAKYK	SRWSS	LFFIVYV	LVVYFLTNL	LAVIYD	FEKQLAKQVSAQDCTRKSI	
sp Q94KI8 TPC1_ARATH	N	PDVW	IPAYKS	SRWSS	VFFVLYV	LIGVYFV	TNL	LAVVYD	FEKQLAKQVSGMDQMKRRM
sp Q9EQJ0 TPC1_MOUSE	F	PDV	MPSY	SRNPWS	CVFFIVYLS	IELYFIMNL	LAVVFD	FENDIEKHKFKSLLLHKRTA	
sp Q9WTN5 TPC1_RAT	F	PDV	MPSY	SRNPWS	CVFFIVYLS	IELYFIMNL	LAVVFD	FENDIEKHKFKSLLLHKRTA	
sp Q9ULQ1 TPC1_HUMAN	F	PDV	MPSY	SRNPWS	CVFFIVYLS	IELYFIMNL	LAVVFD	FENDIEKRRKFKSLLLHKRTA	

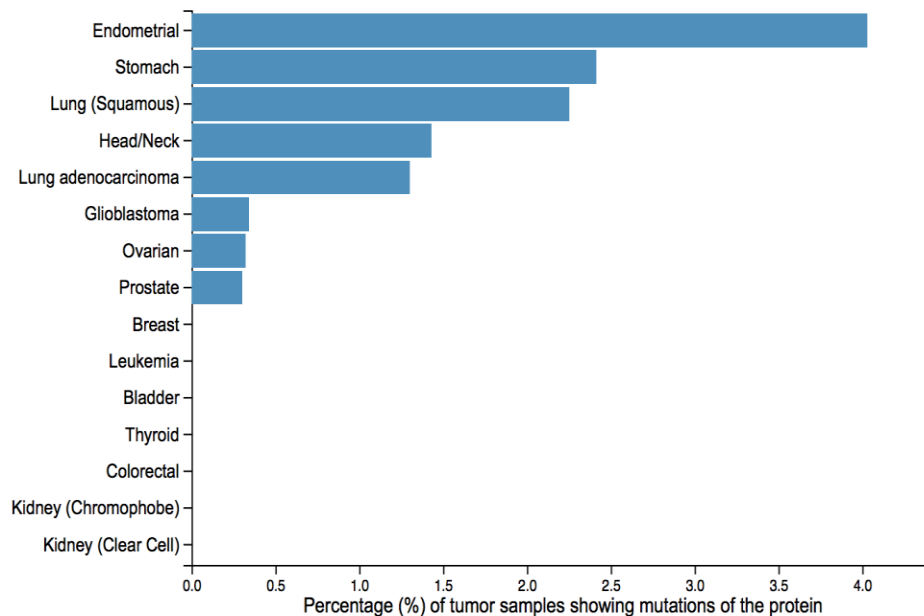
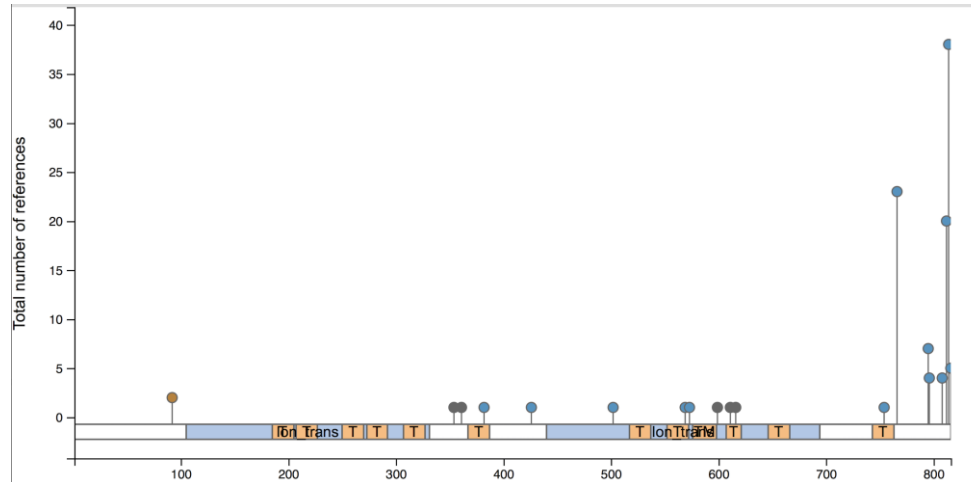
		580	590	600	610	620	630					
sp Q6YLX9 TPC1_WHEAT	V	TLFN	LLVMGNWQ	VW	MESYWQLT	GT	TSWSLIYFVSFYLLISILLLNLI	VAFVLEAF	FAEME			
sp Q6S5H8 TPC1_HORVU	V	TLFN	LLVMGNWQ	VW	MESYWQLT	GT	SSWSLIYFVSFYLLISILLLNLI	VAFVLEAF	FAEME			
sp Q5QM84 TPC1_ORYSJ	V	TLFN	LLVMGNWQ	AW	MESYRQLT	GSYWSLIYFVSFYLLISVLLLNLI	VAFVLEAF	FAEME				
sp Q94KI8 TPC1_ARATH	V	TLFN	LLVMGNWQ	VW	MESYKDLT	GT	TWWSIT	YFVSFYVITILLLNLI	VAFVLEAF	FTELD		
sp Q9EQJ0 TPC1_MOUSE	V	TLF	ELTVVNNWYI	IME	GVTSQT	.	SHWSRLYFMTFYIVTMVVM	T	.	IIVAFI	LEAF	VFRMN
sp Q9WTN5 TPC1_RAT	V	TLF	ELTVVNNWYI	IME	GVTSQT	.	SHWSRLYFMTFYIVTMVVM	T	.	IIVAFI	LEAF	VFRMN
sp Q9ULQ1 TPC1_HUMAN	V	TLF	ELTVVNNWYI	IME	GVTSQT	.	SHWSRLYFMTFYIVTMVVM	T	.	IIVAFI	LEAF	VFRMN

MmTPC1 Interactions

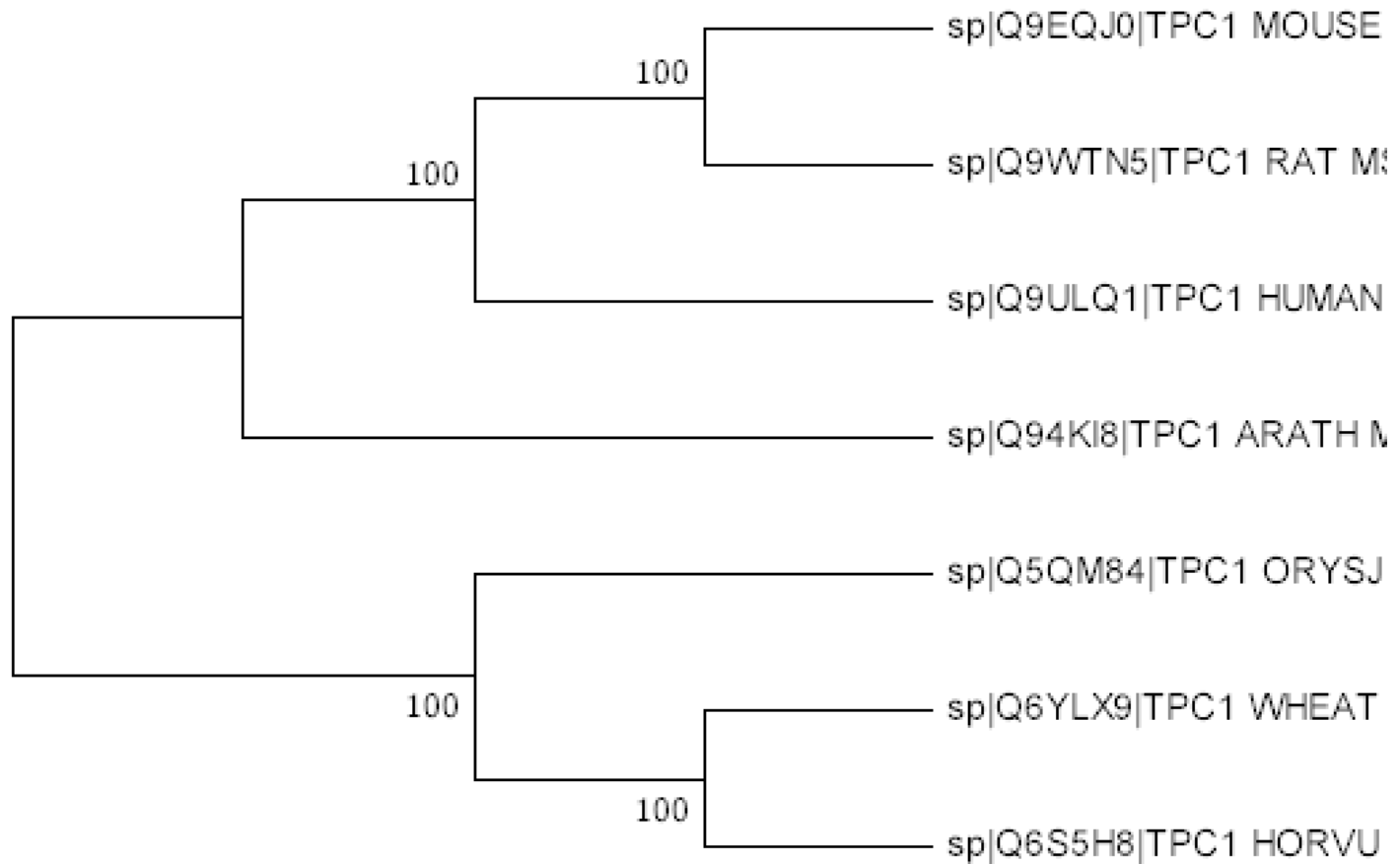


Human TCP1

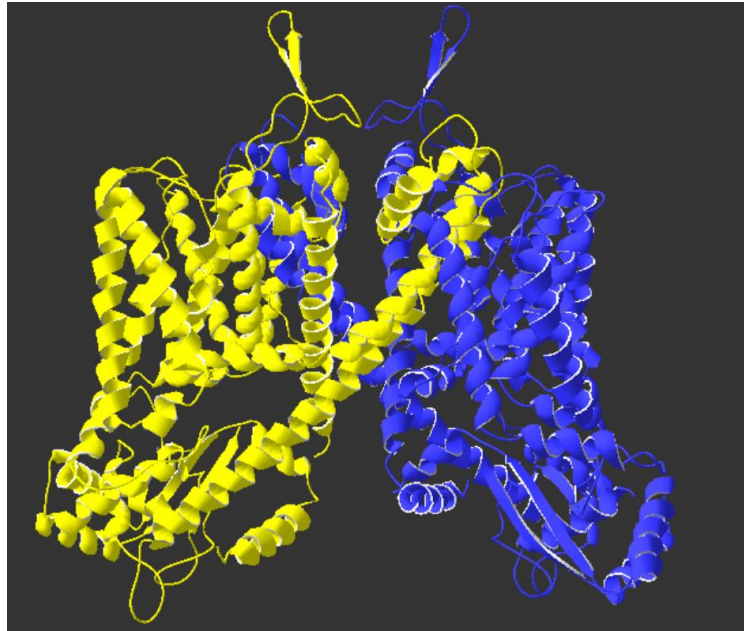
MmTPC1 PTM and Mutations



TPC1 Phylogeny

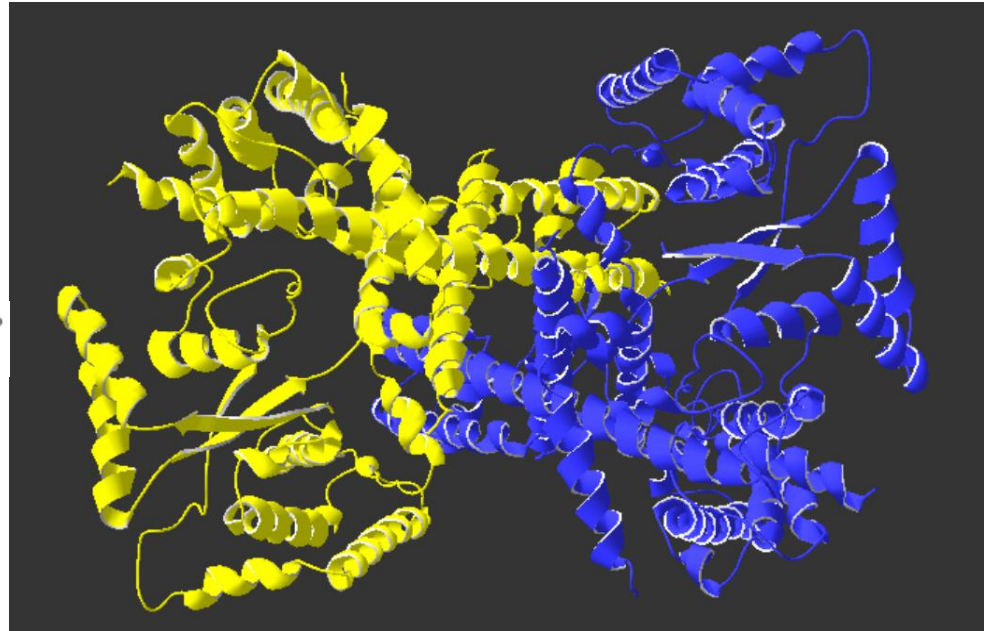


Structure Overview of MmTPC1



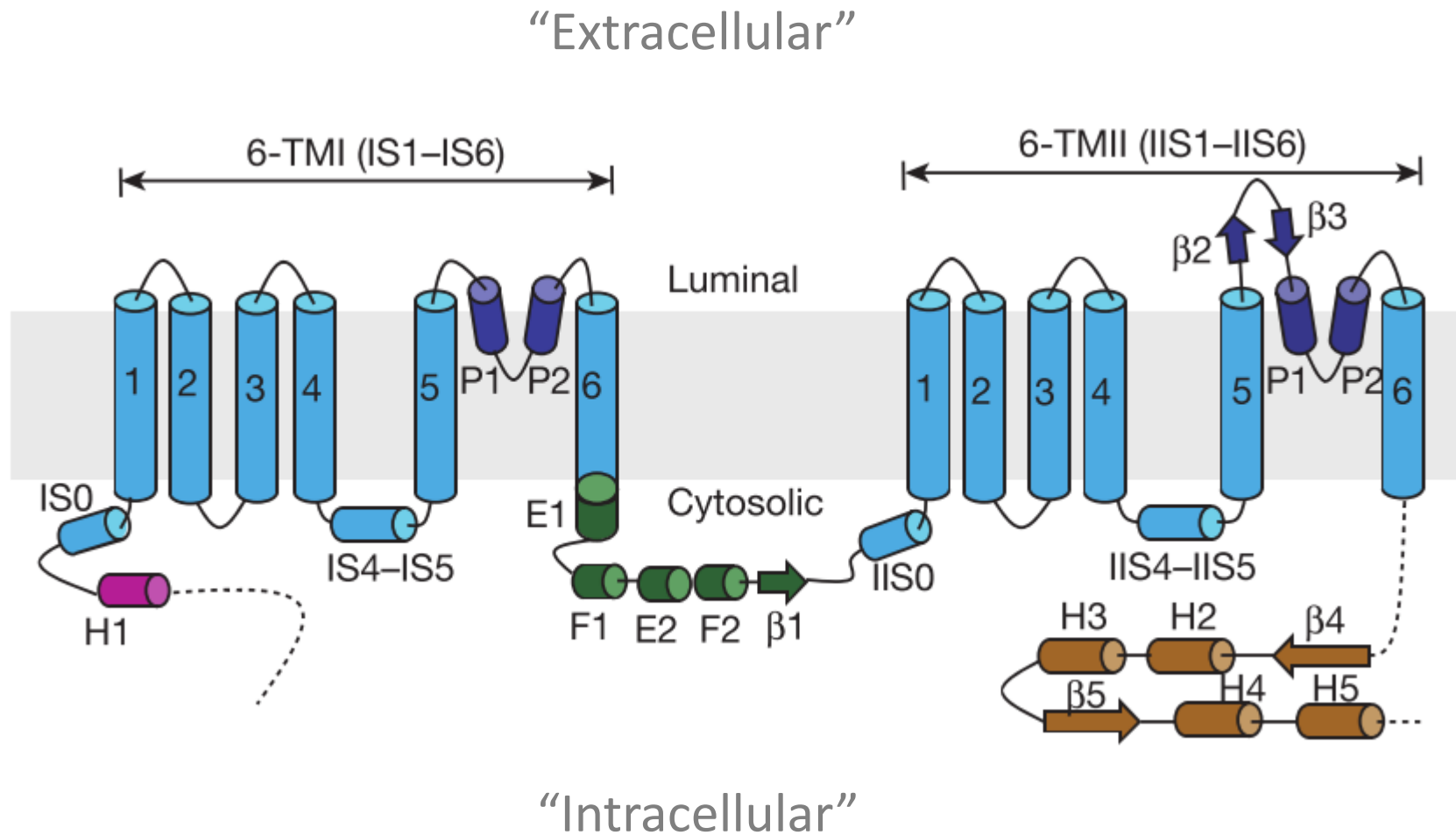
Side view

90°

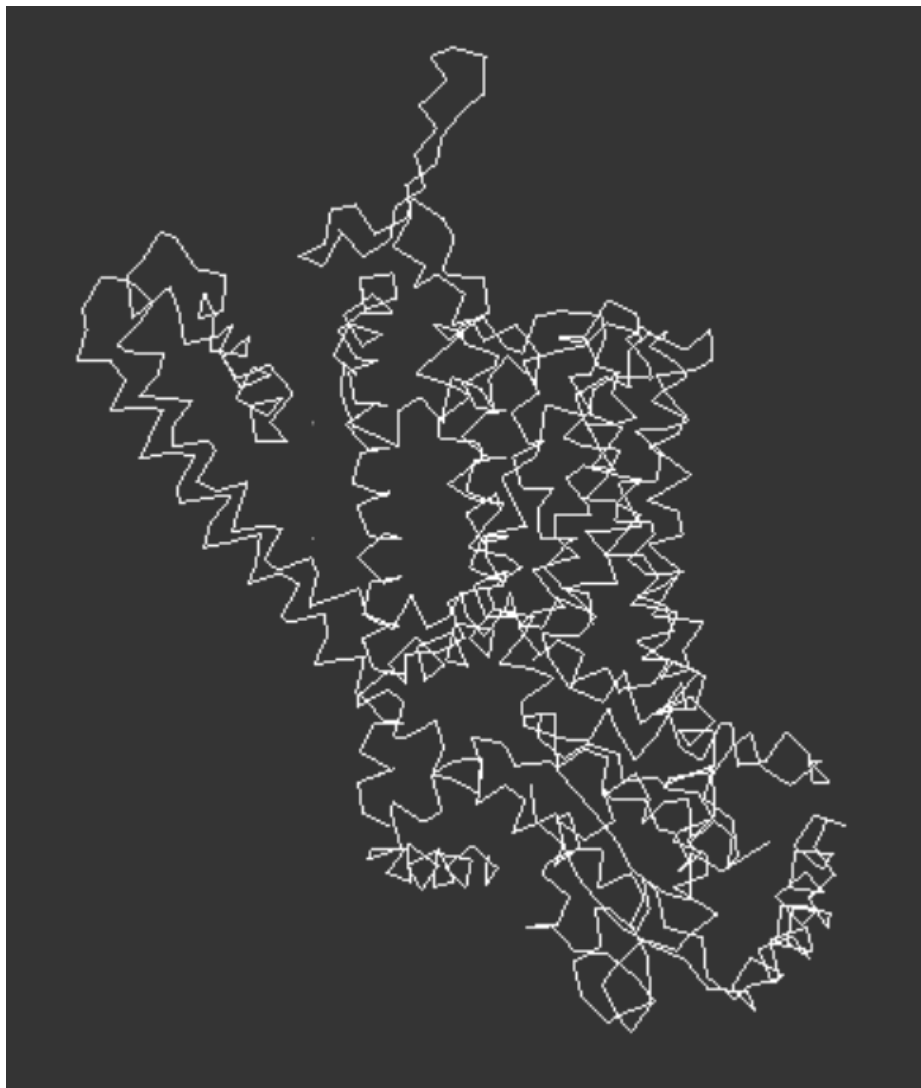


Top view

Two Homologous Domains



Homodimer

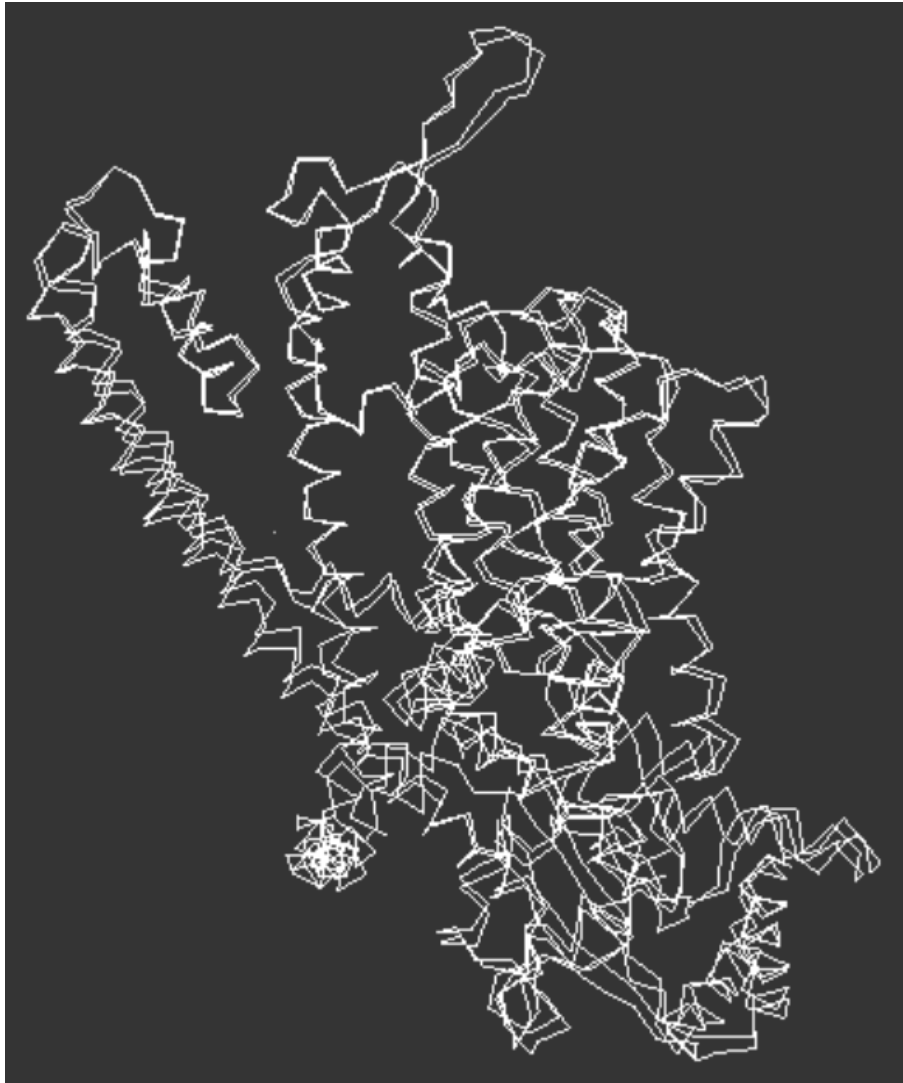


Iterative magic fit

nb atoms involved: 723 RMS: 0.00

PDB: 6C96 (the apo state)

Apo and PtdIns(3,5)P2-bound state



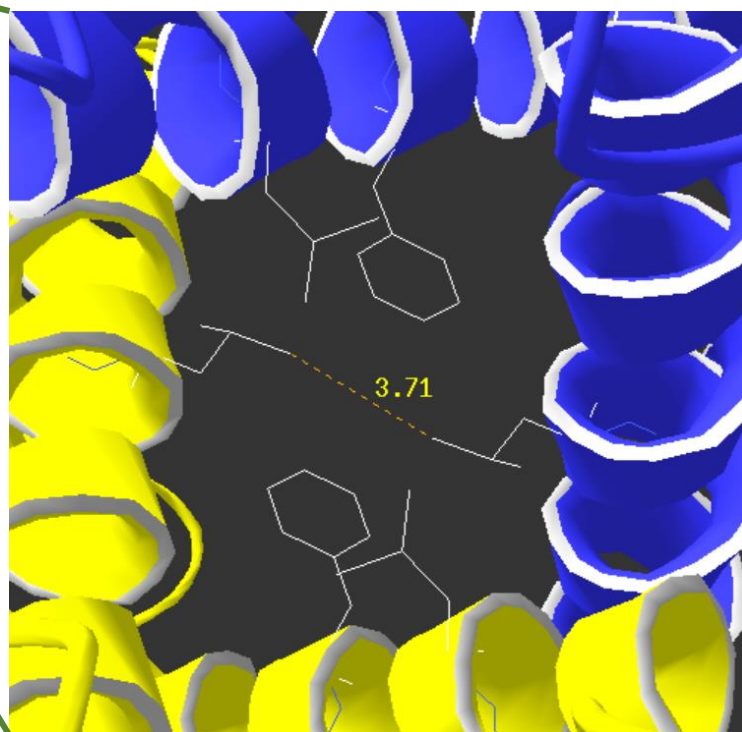
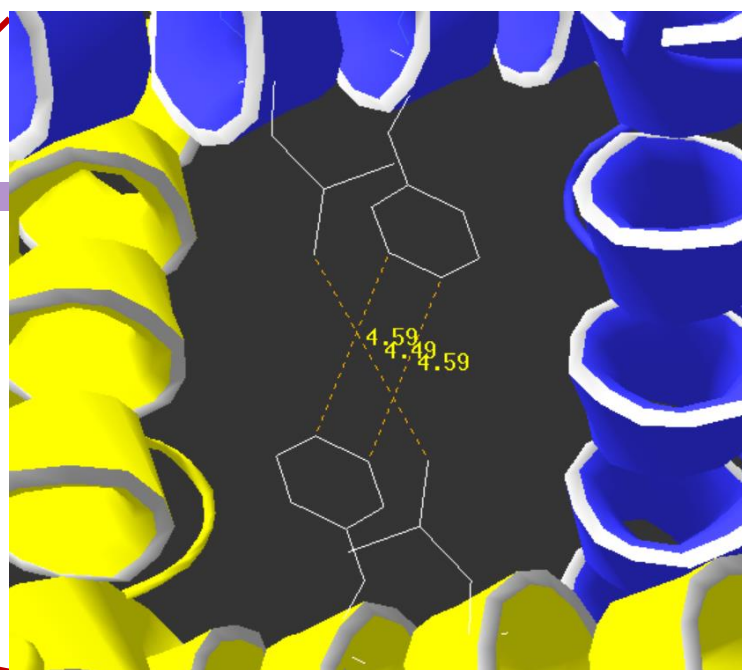
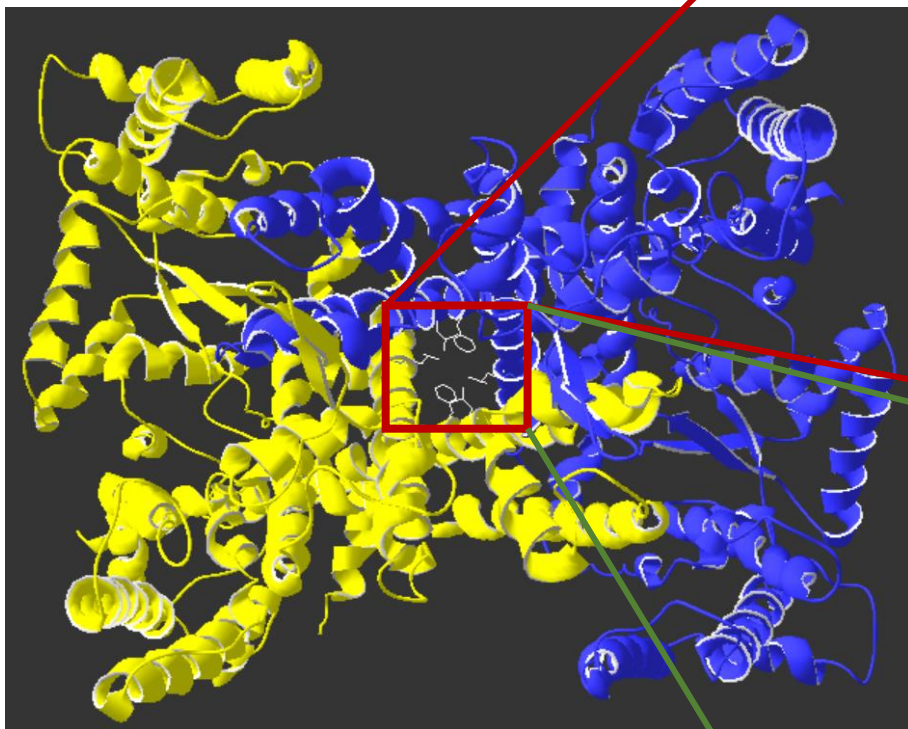
Iterative magic fit

nb atoms involved: 669 RMS: 1.38

PDB: 6C96 (the apo state)

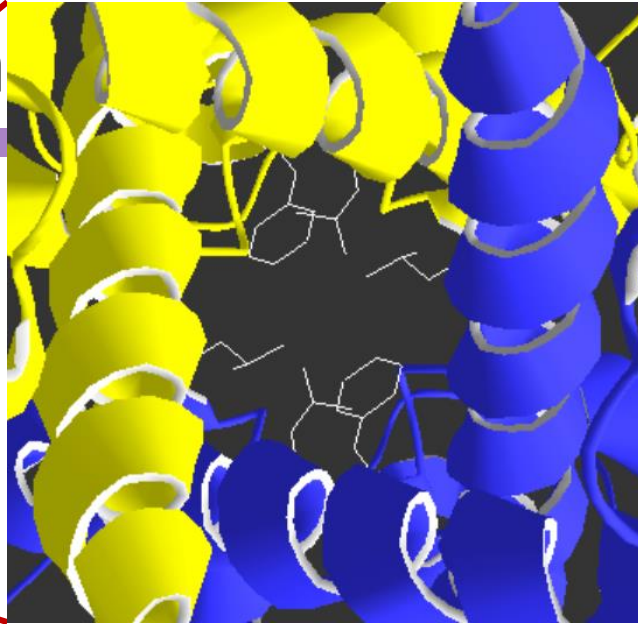
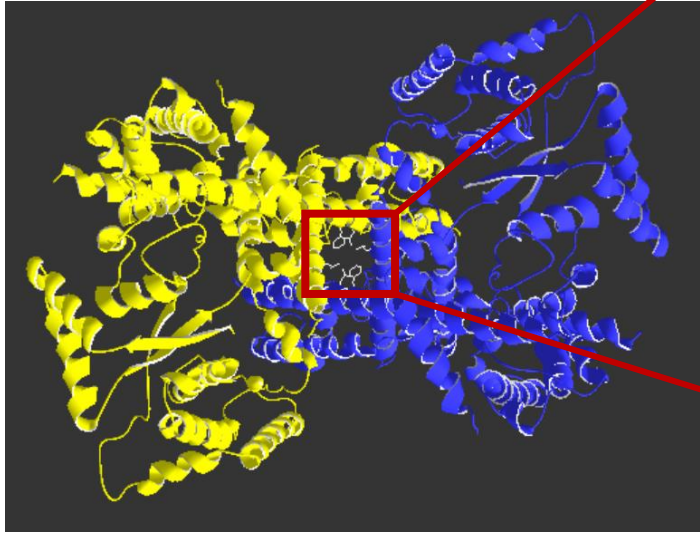
PDB: 6C9A (PtdIns(3,5)P2-bound state)

Gate (closed)

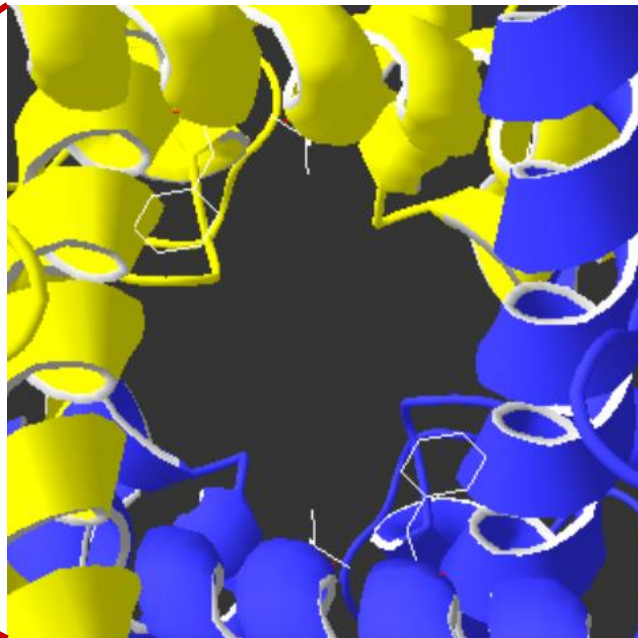
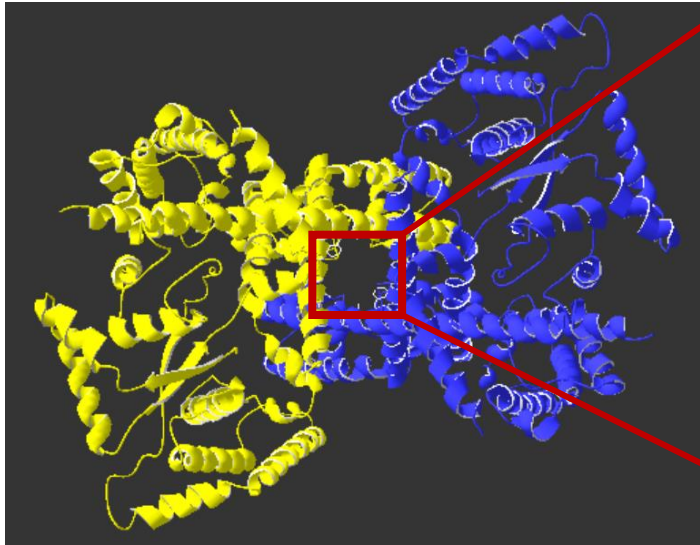


PDB: 6C96 (the apo state)

Gate (closed Vs. open)

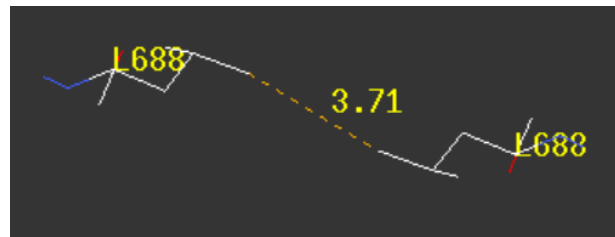
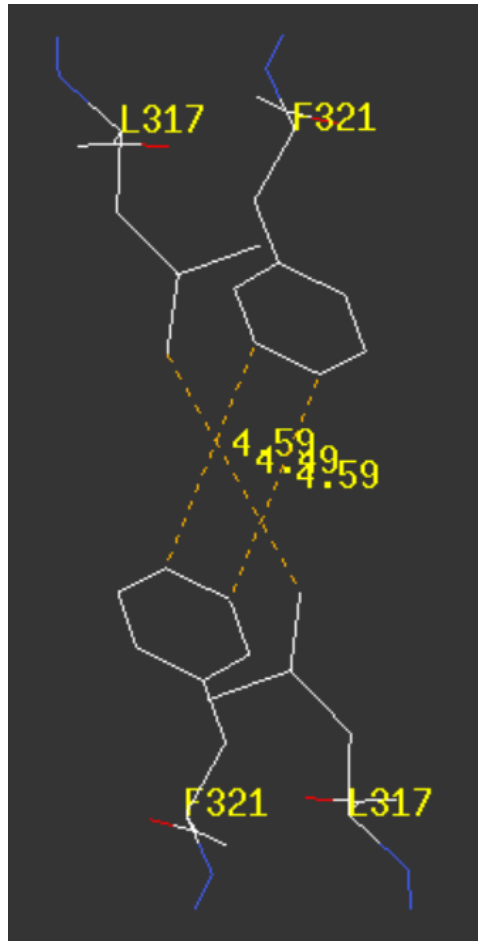


PDB: 6C96
the apo state

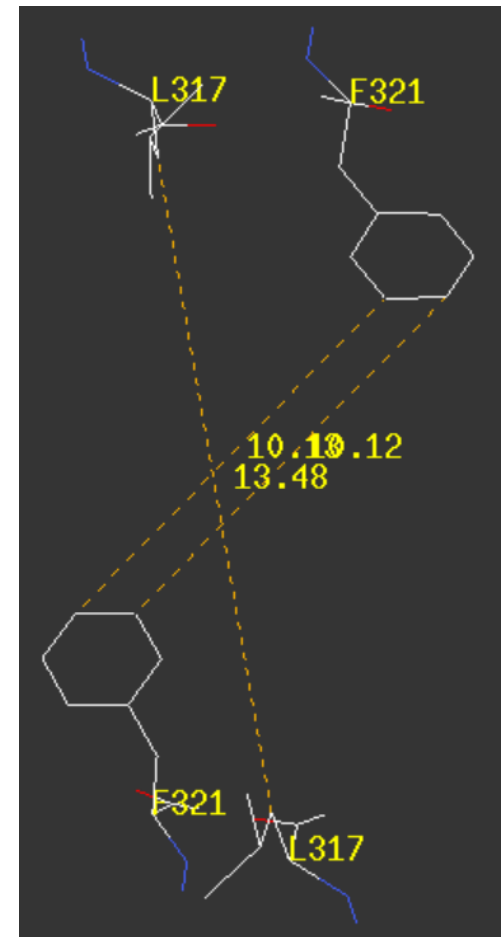
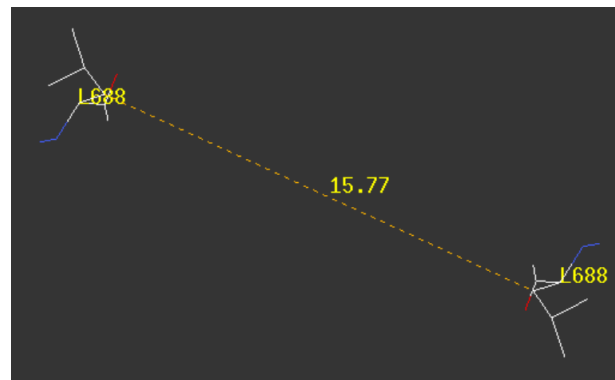


PDB: 6C9A
PtdIns(3,5)P2-
bound state

Residues involved



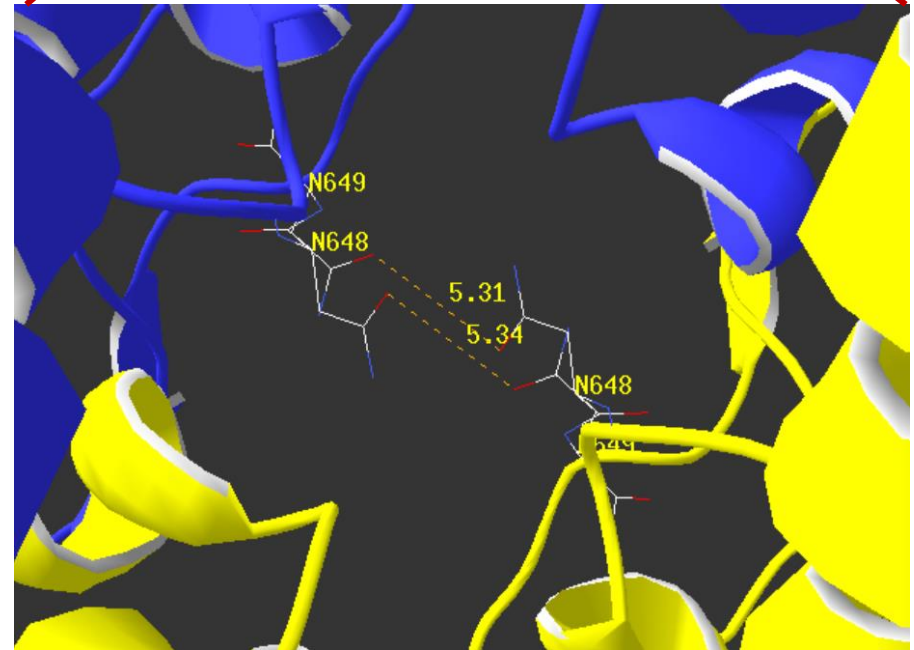
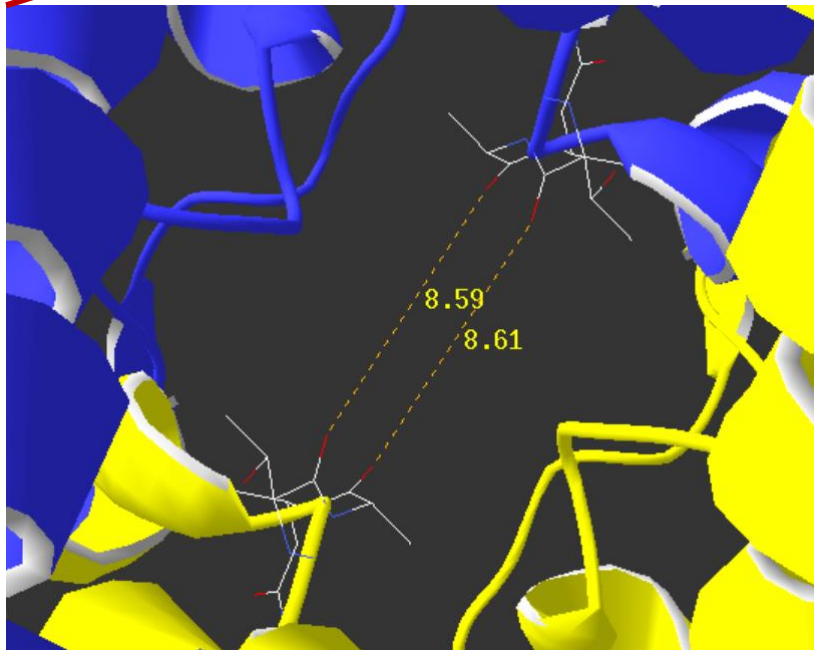
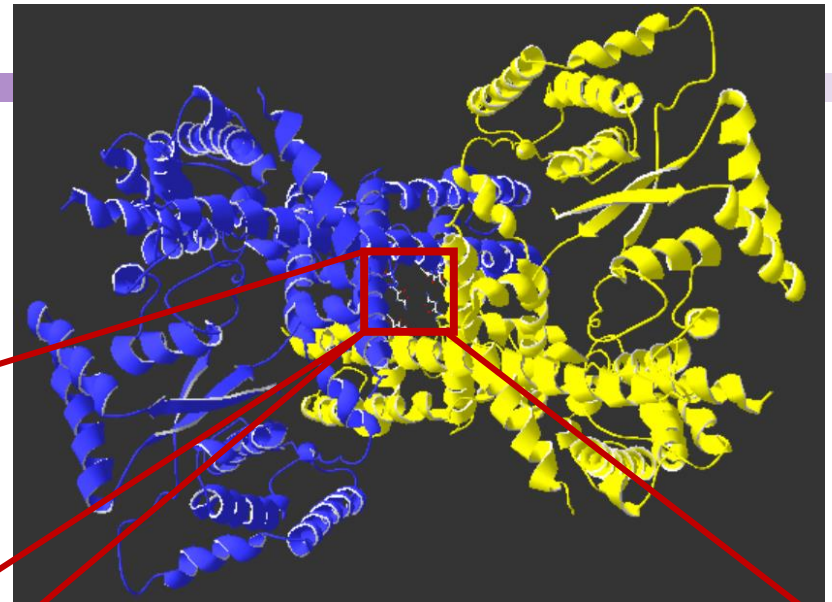
PDB: 6C96 (the apo state)



PDB: 6C9A (PtdIns(3,5)P2-bound state)

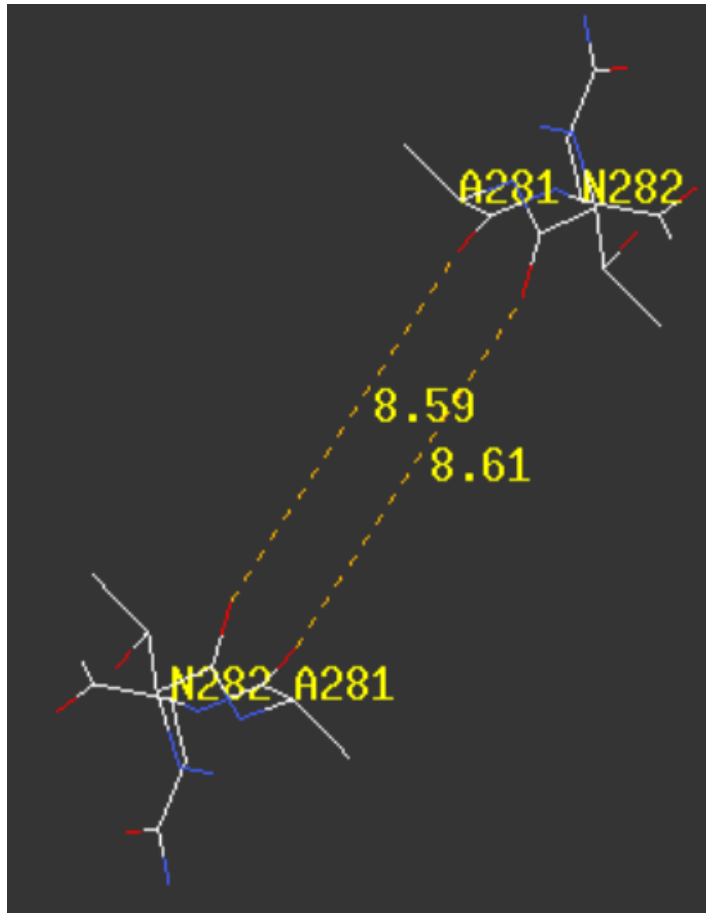
Filter Domain

PDB: 6C96 (the apo state)

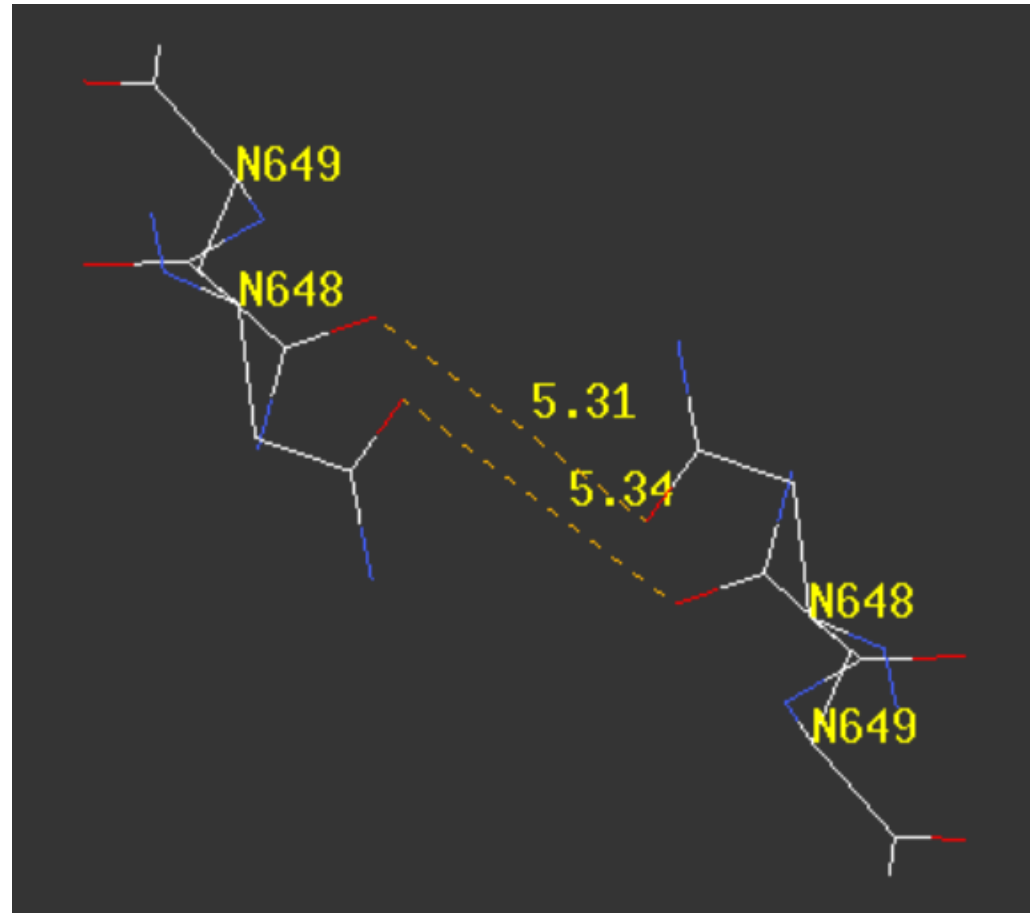


Residues involved

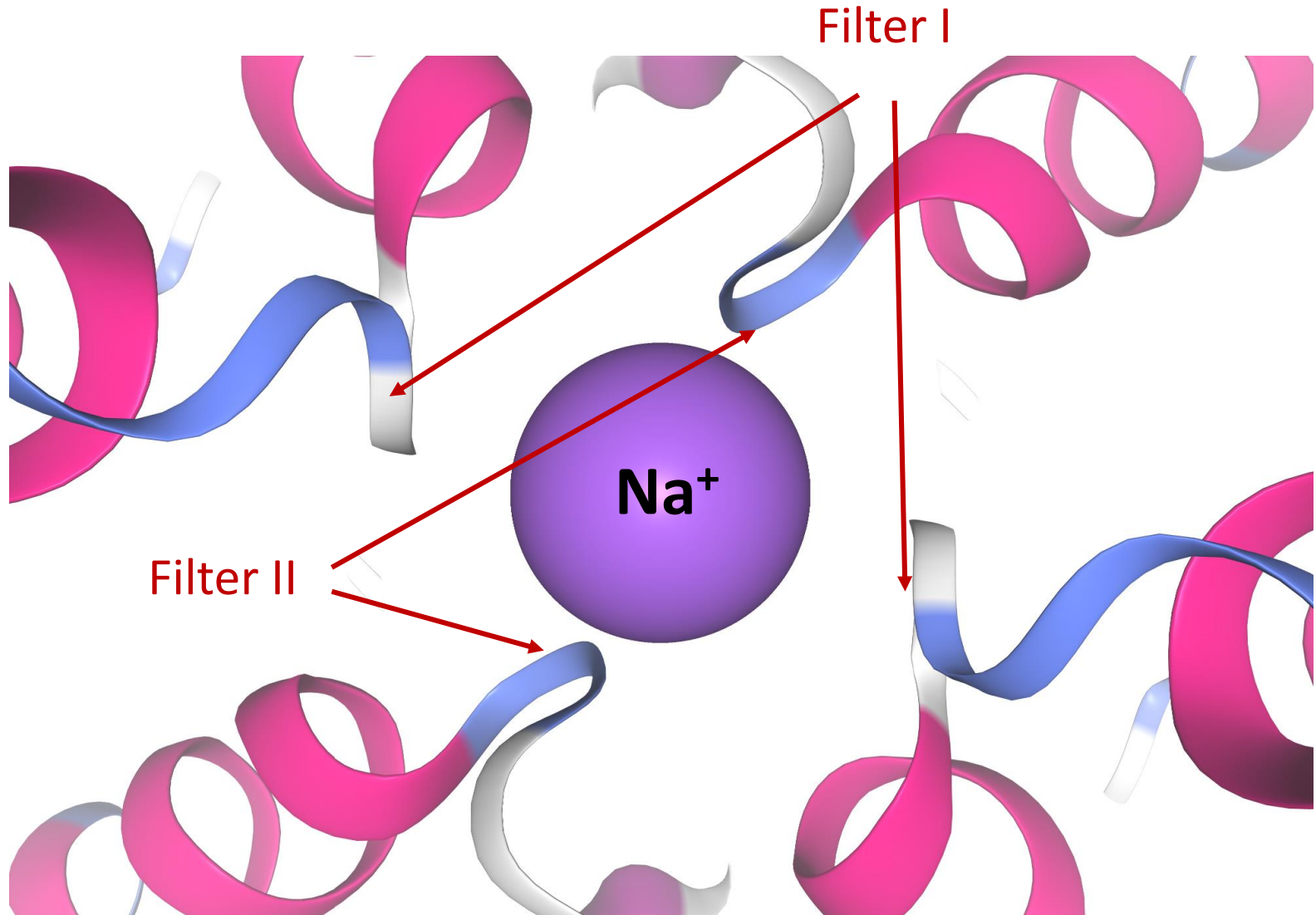
Filter I



Filter II

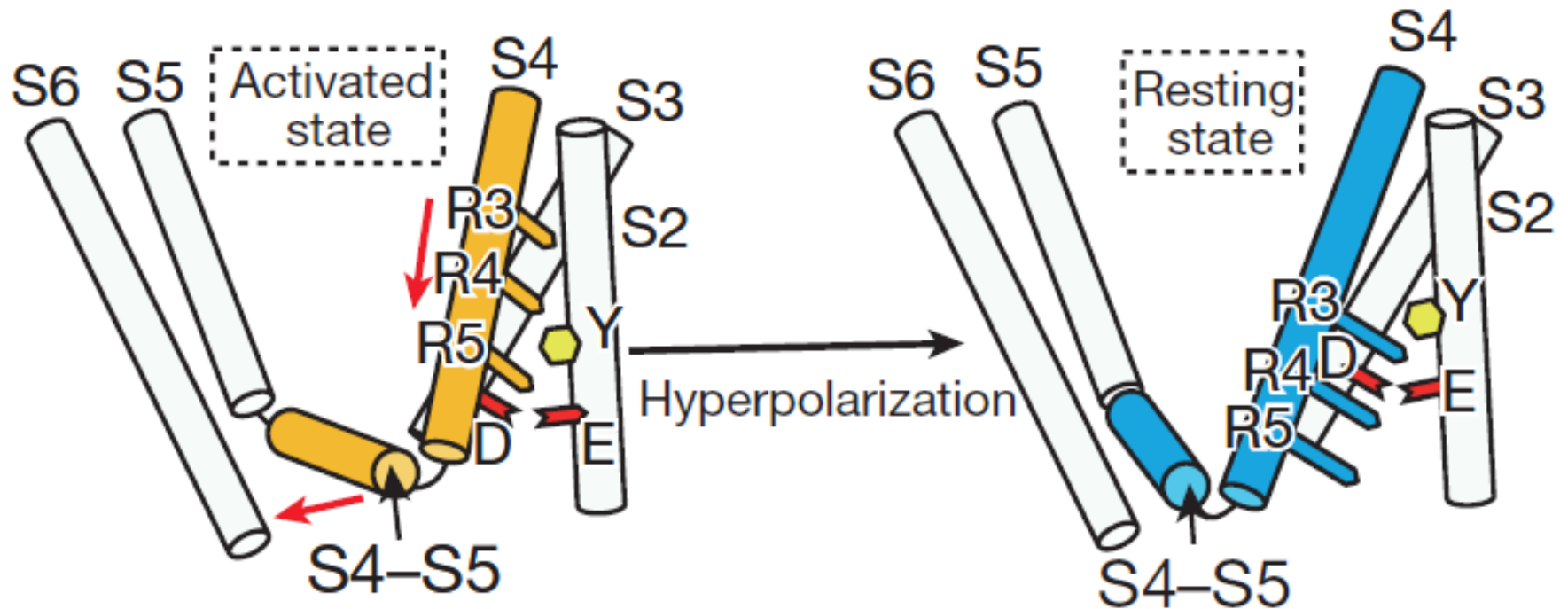


Filter Domain

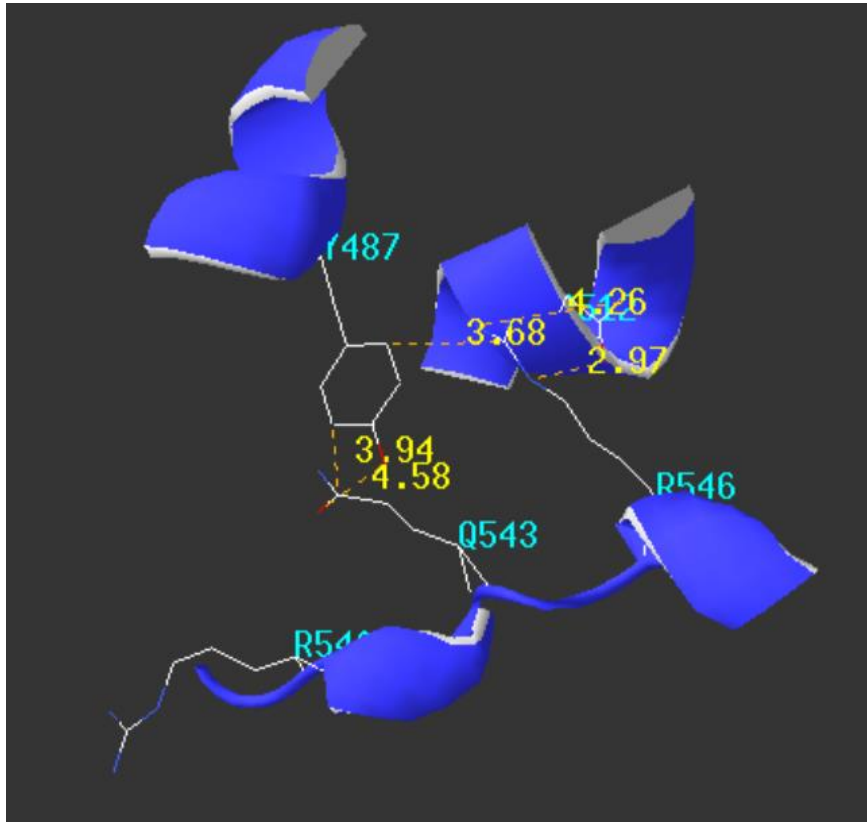


PDB: 6C96 (the apo state)

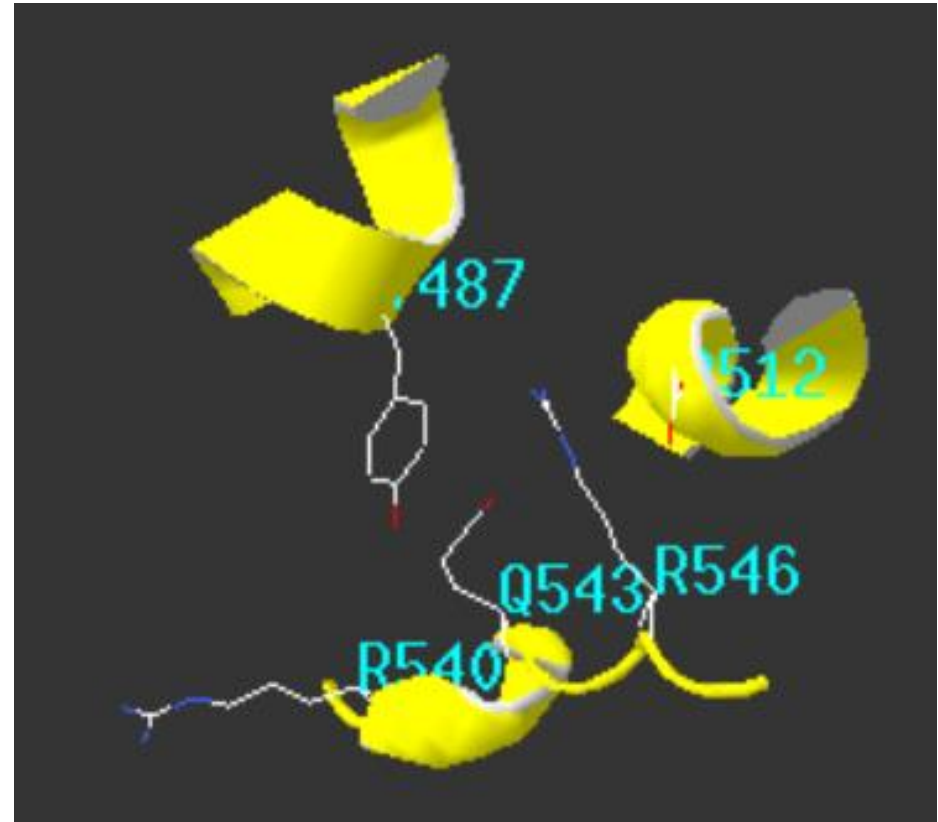
Voltage-sensing Domain



Voltage-sensing Domain



PDB: 6C9A (PtdIns(3,5)P2-bound state)



PDB: 6C96 (the apo state)



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Thanks for you listening!

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