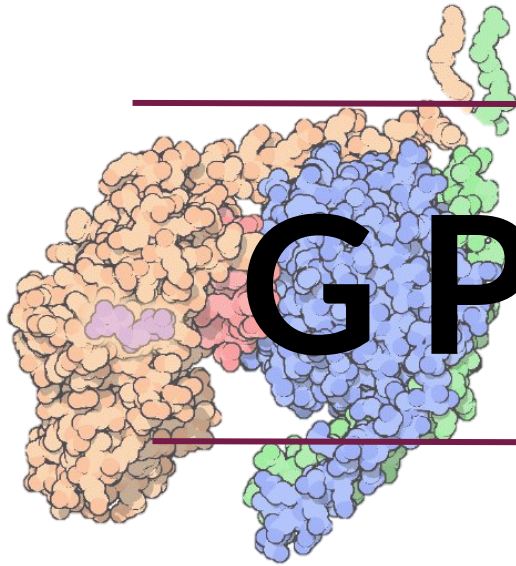




G Proteins

Núria Garcia, Maria Pujol, Irene García, Mònica Biarnés

INDEX

INTRO

- **G proteins**
- Heterotrimeric
- Monomeric - Ras Sp
- Transition GTP-GDP
- Effectors function

EVOLUTION

- *Ras, Rho, Rab, Ran, Arf*
- *G boxes*
- *Eukaryotes*
- *Prokaryotes*

RAS SUPERFAMILY

- **Human Ras**
- G boxes
- Structure
- Superimpositions

ARF1

- Introduction
- Membrane interactions
- N-Myristoylation
- Key structures:
 - GDP-GTP
 - GAF, GEF
 - MG



INTRO

Guanine nucleotide-binding regulatory proteins (G proteins) play an essential role in **cell signaling** coupling cell-surface receptors to various intracellular effectors.

GTPase activity → Cycle between an inactive GDP-bound state and an active GTP-bound state.

FUNCTIONS

- Signal transduction
- Membrane vesicle transport
- Cytoskeletal assembly
- Cell growth
- Protein synthesis

HETEROTRIMERIC

SMALL G PROTEINS or RAS SUPERFAMILY

MONOMERIC

- Small GTPases (20-25 kD)
- **α -subunit homolog**
- 5 families: **Ras, Rho, Rab, Arf and Ran**
- Cytosol/membrane

HETEROTRIMERIC

- Large complexes (~80 kD)
- Subunits: **α , β and γ**
- **α → functional specificity**
- **β and γ → $G\beta\gamma$ subunit**
- Families: **Gs, Gi, Gq and G12/13**
- **GPCRs**
- Cell membrane

HETEROTRIMERIC

INTRO

Family	Types	Signal transduction
G_s	Gs, Golf	+ Adenylate cyclase
G_i	Gi1, Gi2, Gi3, Go, Gt, Gg and Gz	- Adenylate cyclase
G_q	Gq, G11, G14 and G16	+ Phospholipase C
$G_{12/13}$	-	+ Rho family

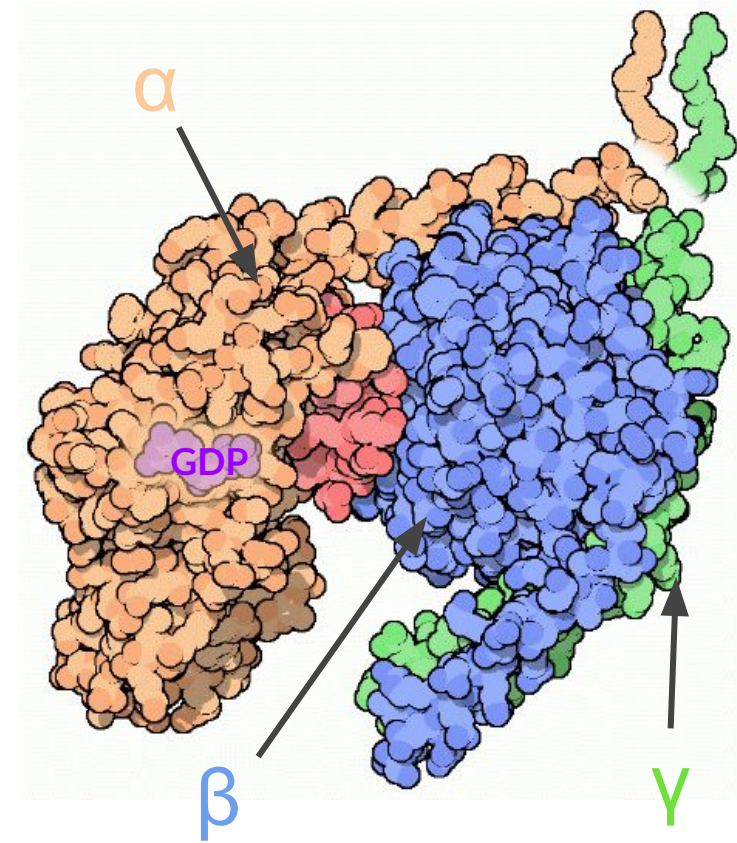
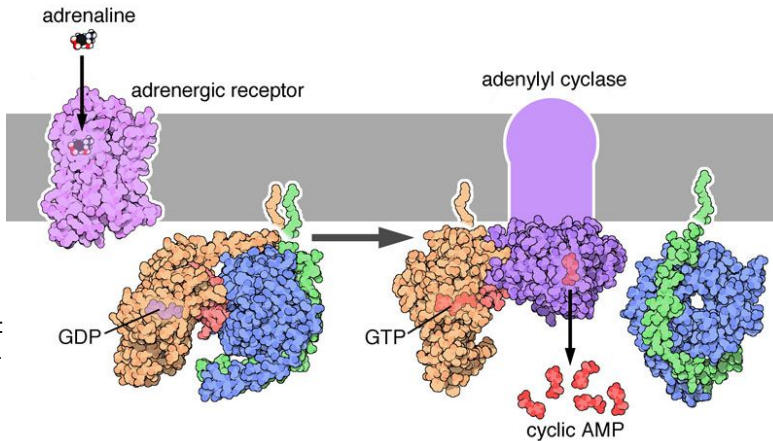


Fig 1. GDP-GTP transition... Extract from: Goodsell D. G Proteins. RCSB Protein Data Bank. 2004;.

DOMAINS

G α

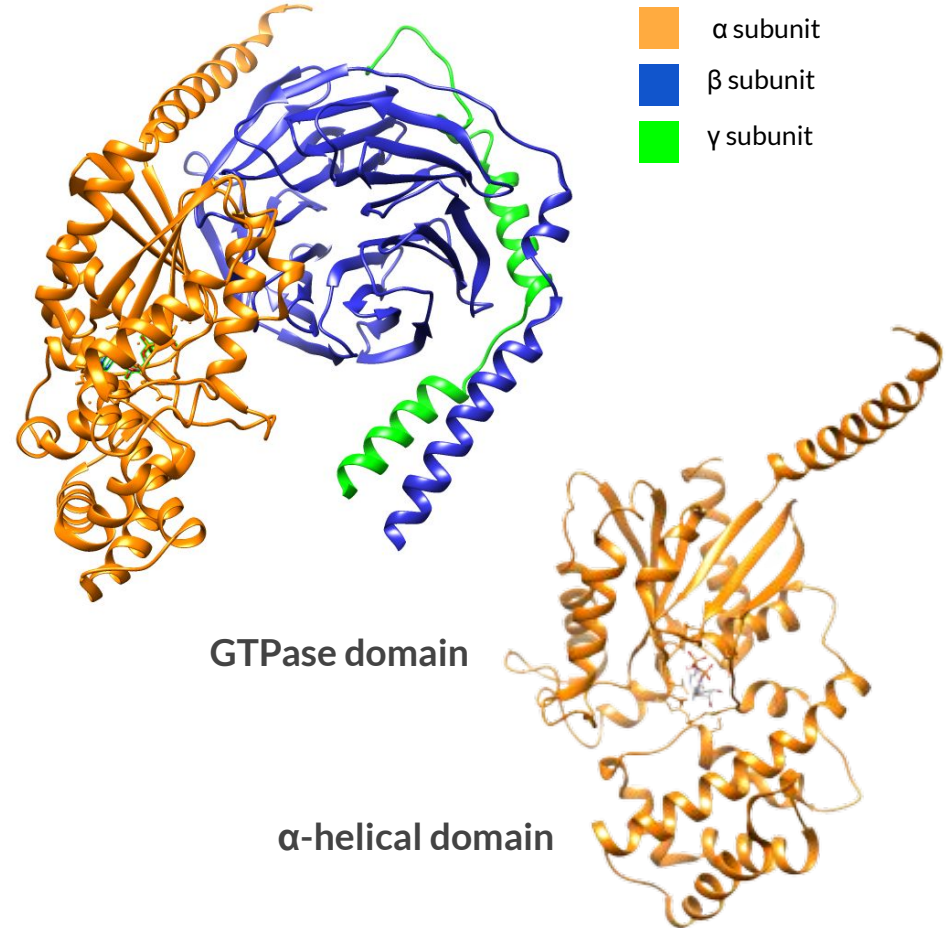
- Ras-like GTPase domain and an α -helical domain
- Switches: I,II,III
- N-terminal and C-terminal domain: protein-protein interactions

G β

- β -propeller domain

G γ

- Interacts with G β through an N-terminal coiled coil



MONOMERIC

INTRO

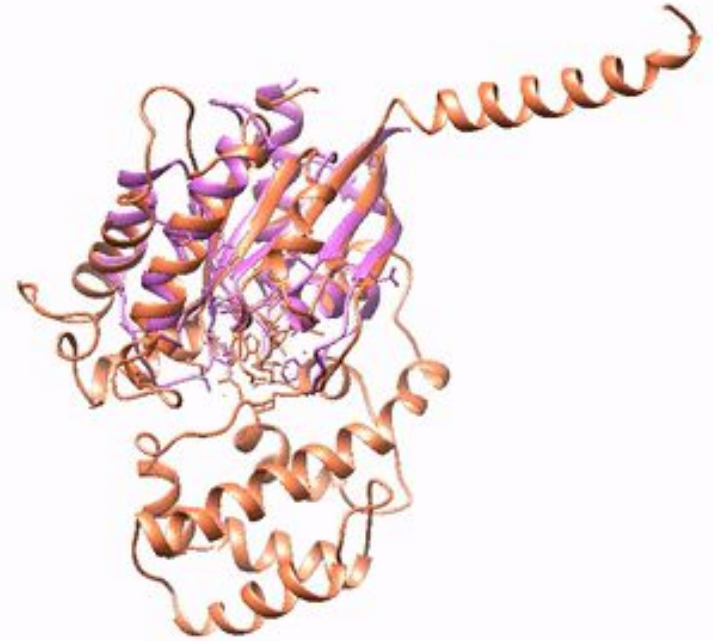
Family	Types	Function
RAS	HRAS, NRAS, KRAS(oncogenic), RRAS,RAP,RAL,RIT...	Cell growth
RHO	RHOA,B,C,D...RAC,ROCK,DIA PH,RND...	Cytoskeletal dynamics
RAB	RAB3A, RABL,RAB1A,RAB35,RAB	Protein trafficking pathways, regulating vesicle formation, movement, and fusion
RAN	RAN	Regulator of nuclear import and export
ARF	ARF1,ARF3,ARF4,ARF5...ARL 4,ARFRP,ARL,SARA...	Vesicle biogenesis, recycling and trafficking

G domain: conserved G box
GDP/GTP-binding motif element

Switches I and II

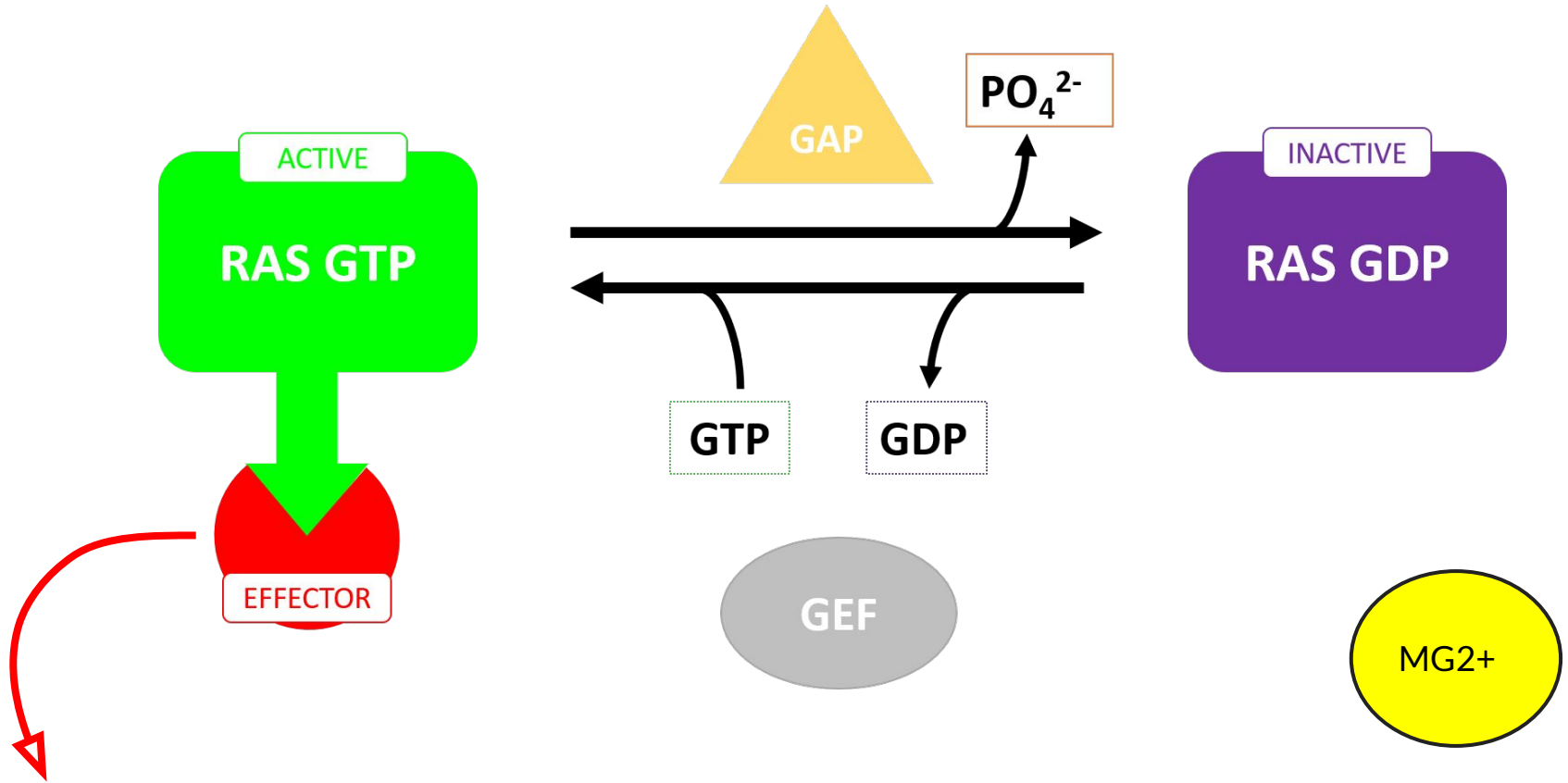
Families are defined by post-translational
modifications

Modulators of a remarkably complex and diverse range of
cellular processes.



Monomeric
Trimeric

RMSD: 1,273 Å



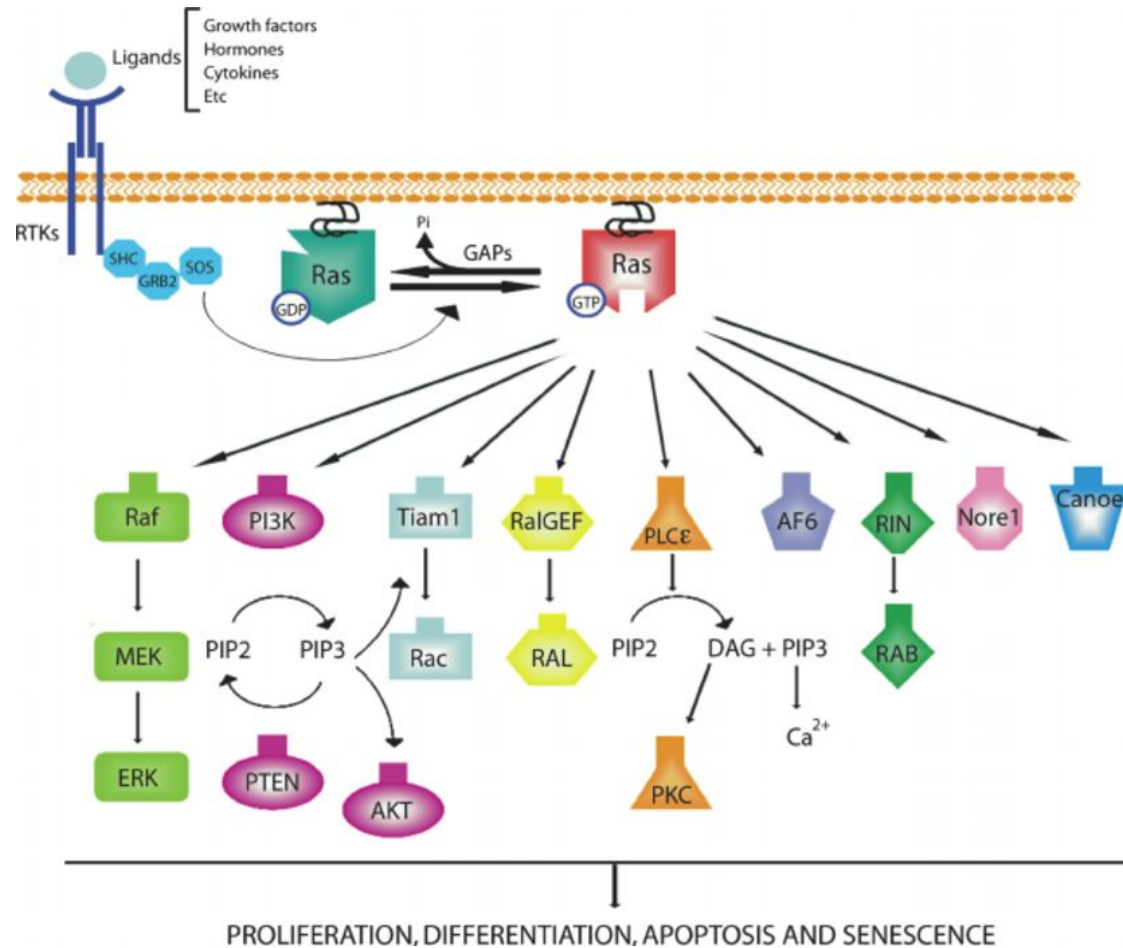
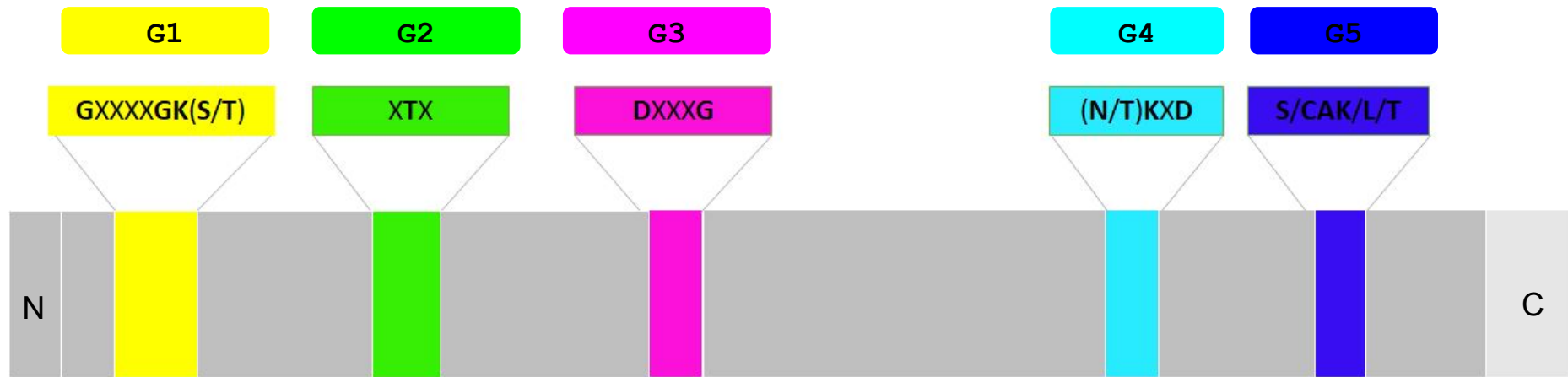


Fig 2. Ras effectors. Extract from: Castellano E, Downward J. Role of RAS in the Regulation of PI 3-Kinase. Current Topics in Microbiology and Immunology. 2010;:143-169.

G BOXES

EVO



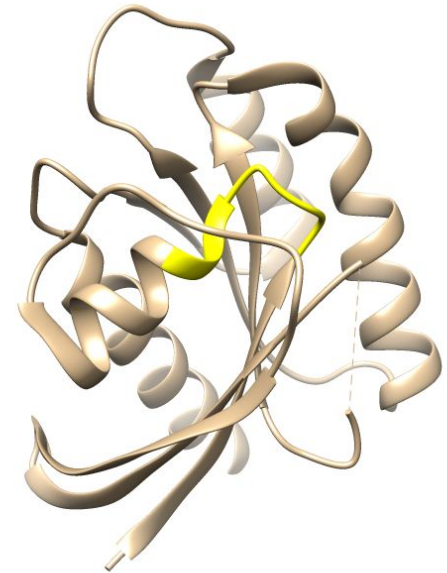
NRAS

G1

MTEYKLVVV**GAGGVGKS**ALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRD
QYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAARTVESRQAQDLARSYG
IPYIETSAKTRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMSCKCVLS

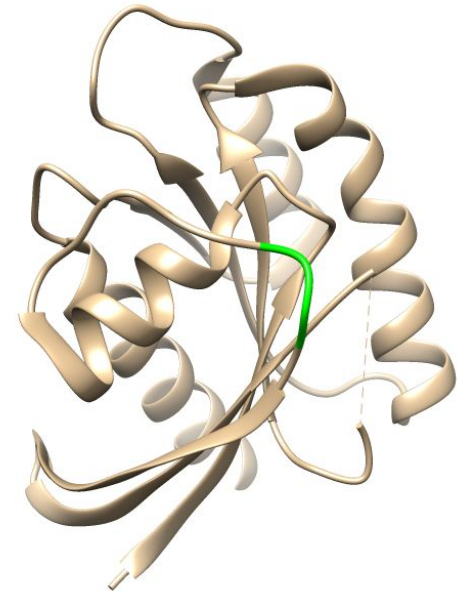
aaaa**GxxxGK (S/T)**

Purine nucleotide binding site



NRAS**G2**

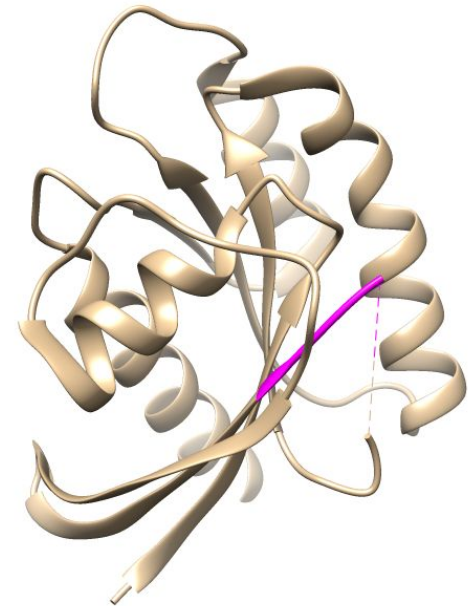
MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYD **PTI**EDSYRKQVVIDGETCLLDILDITAGQEEYSAMRD
QYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAARTVESRQAQDLARSYG
IPYIETSAKTRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMSCKCVLS

XTX**GTP/GDP binding**

NRAS

G3

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDIL **DTAG**QEEYSAMRD
QYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAARTVESRQAQDLARSYG
IPYIETSAKTRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMSCKCVLS

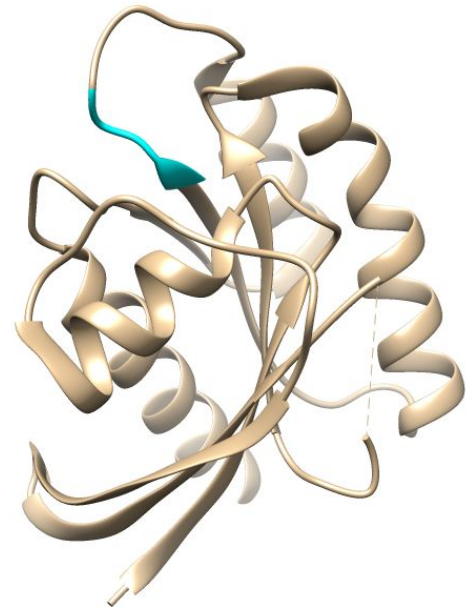
blbb**DxxG**lBinding with Mg²⁺

NRAS

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDITAGQEEYSAMRD
QYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVG **NKCD**LAARTVESRQAQDLARSYG
IPYIETSAKTRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMSCKCVLS

G4**bbbb (N/T) (K/Q) xD**

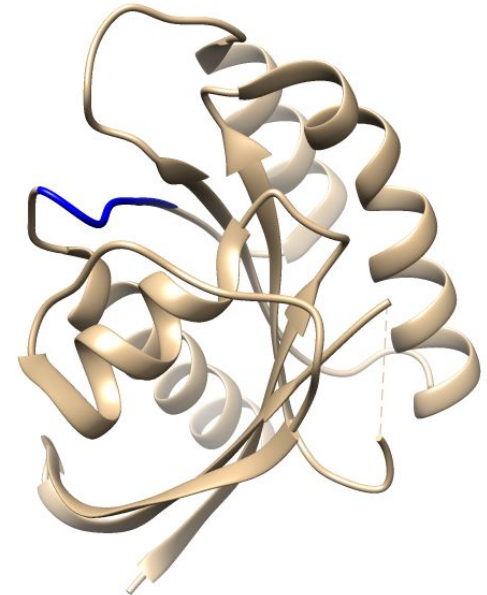
Hydrogen bond contact and stabilization



NRAS

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDITAGQEEYSAMRD
QYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAARTVESRQAQDLARSYG
IPYI **ETSAK**TRQGVEDAFYTLVREIRQHKLRKLNPPDESGPGCMSCKCVLS

G5

bb**E** (A/C/S/T) **SA** (K/L)Indirect associations with the guanine
nucleotide

RAS SUPERFAMILY EVOLUTION IN EUKARYOTES

EVO

RAS (NRAS)

	G1	G2	G3
HUMAN	MTEYKLVVVAGG GVGKS ALTIQLIQNHVDEYDPTIEDSYRKQVVIDGETCLLDILDTAG		
SCROFA	MTEYKLVVVAGG GVGKS ALTIQLIQNHVDEYDPTIEDSYRKQVVIDGETCLLDILDTAG		
MOUSE	MTEYKLVVVAGG GVGKS ALTIQLIQNHVDEYDPTIEDSYRKQVVIDGETCLLDILDTAG		
GALLUS	MTEYKLVVVAGG GVGKS ALTIQLIQNHVDEYDPTIEDSYRKQVVIDGETCLLDILDTAG		
XENOPU	MTEYKLVVVAGG GVGKS ALTIQLIQNHVDEYDPTIEDSYRKQVVIDGETCLLDILDTAG		

	G4
P01111	QEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINLYREQIKRVKSDSDVPMVLVGNKCDL
Q2MJK3	QEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINLYREQIKRVKSDSDVPMVLVGNKCDL
P08556	QEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINLYREQIKRVKSDSDVPMVLVGNKCDL
Q5F352	QEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINLYREQIKRVKSDSDVPMVLVGNKCDL
Q91806	QEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINAYREQIKRVKSDSDVPMVLVGNKCDL

	G5
P01111	PTRTVDTKQAH ELAKSYGIPFIETSA TRQGVEDAFYTLVREIRQYRMKKLNSSDDGTQG
Q2MJK3	PTRTVDTKQAH ELAKSYGIPFIETSA TRQGVEDAFYTLVREIRQYRMKKLNSSDDGTQG
P08556	PTRTVDTKQAH ELAKSYGIPFIETSA TRQGVEDAFYTLVREIRQYRMKKLNSSDDGTQG
Q5F352	PTRTVDTKQAH ELAKSYGIPFIETSA TRQGVEDAFYTLVREIRQYRMKKLNSSDDGTQG
Q91806	PSRTVDTKQAH ELARSYGIPFIETSA TRQGVEDAFYTLVREIHQYRMKKLDSSEDDNQG
	*:*****:***:*****:***:***:*.:.**

P01111 CMGLPCVVM
Q2MJK3 CMGLPCVVM
P08556 CMGSPCVLM
Q5F352 CMGLSCIVM
Q91806 CTRIPCKLM
*: *:

RAB (RAB1A)

	G1	G2
MOUSE	MSSMNPEYDYLFKLLIGDS GVGKS CLLLRFADDTYTESYISTIGVDFKIRTIELDGKTI	
HUMAN	MSSMNPEYDYLFKLLIGDS GVGKS CLLLRFADDTYTESYISTIGVDFKIRTIELDGKTI	
DOG	MSSMNPEYDYLFKLLIGDS GVGKS CLLLRFADDTYTESYISTIGVDFKIRTIELDGKTI	
PIG	MSSMNPEYDYLFKLLIGDS GVGKS CLLLRFADDTYTESYISTIGVDFKIRTIELDGKTI	

	G3
P62821	KLQIWDTAGQERFRTITSSYYRGAGHIIVVYDVTQGSFNNVKQWLQEI DRY ASENVNKL
P62820	KLQIWDTAGQERFRTITSSYYRGAGHIIVVYDVTQGSFNNVKQWLQEI DRY ASENVNKL
P62822	KLQIWDTAGQERFRTITSSYYRGAGHIIVVYDVTQGSFNNVKQWLQEI DRY ASENVNKL
Q52NJ2	KLQIWDTAGQERFRTITSSYYRGAGHIIVVYDVTQGSFNNVKQWLQEI DRY ASENVNKL

	G4	G5
P62821	LVGNKCDLTTKKVVDDYTTAKEFADSLGIPFL ETSA NATNVEQSFMTMAAEIKKRMGP	
P62820	LVGNKCDLTTKKVVDDYTTAKEFADSLGIPFL ETSA NATNVEQSFMTMAAEIKKRMGP	
P62822	LVGNKCDLTTKKVVDDYTTAKEFADSLGIPFL ETSA NATNVEQSFMTMAAEIKKRMGP	
Q52NJ2	LVGNKCDLTTKKVVDDYTTAKEFADSLGIPFL ETSA NATNVEQSFMTMAAEIKKRMGP	

P62821 TAGGAEKSNVKIQSTPVKQSGGGCC
P62820 TAGGAEKSNVKIQSTPVKQSGGGCC
P62822 TAGGAEKSNVKIQSTPVKQSGGGCC
Q52NJ2 TAGGAEKSNVKIQSTPVKQSGGGCC

EVO

G1

HUMAN MAAQGE PQVQFKLVLVGDGGTGKTFVKRHLTGEFEKKYVATLGV EHVPLVFHTNRGPIK
 MOUSE MAAQGE PQVQFKLVLVGDGGTGKTFVKRHLTGEFEKKYVATLGV EHVPLVFHTNRGPIK
 TAURUS MAAQGE PQVQFKLVLVGDGGTGKTFVKRHLTGEFEKKYVATLGV EHVPLVFHTNRGPIK
 DROSOP MAQEGQDIPQFVKCLVLVDGGGTGKTFVKRHMTGEFEKKYVATLGV EHVPLIFHTNRAIGR

** :*: ** *****-*****-*****-*****-*****-*****-*

G3

P62826 FNVWDTAGQEKFGLRGDGGYIIQAQCAIMFDVTSRVTYKNVPNWHRDLVRVCENIPIVLC
P62827 FNVWDTAGQEKFGLRGDGGYIIQAQCAIMFDVTSRVTYKNVPNWHRDLVRVCENIPIVLC
Q3T054 FNVWDTAGQEKFGLRGDGGYIIQAQCAIMFDVTSRVTYKNVPNWHRDLVRVCENIPIVLC
Q9VZ23 FNVWDTAGQEKFGLRGDGGYIQGQCAVIMFDVTSRVTYKNVPNWHRDLVRVCENIPIVLC

G4

P62826 GNKVDIKDRKVKAKSIVFHRKKNLQYYDI SA SNYNFEKPFPLWLARKLIGDPNLEFVAMP
P62827 GNKVDIKDRKVKAKSIVFHRKKNLQYYDI SA SNYNFEKPFPLWLARKLIGDPNLEFVAMP
Q3T054 GNKVDIKDRKVKAKSIVFHRKKNLQYYDI SA SNYNFEKPFPLWLARKLIGDPNLEFVAMP
Q9VZ23 GNKVDIKDRKVKAKSIVFHRKKNLQYYDI SA SNYNFEKPFPLWLARKLVGDPNLEFVAMP

P62826 ALAPPEVVM DPALAAQYEHDLVAQT TALPDEDDDL
P62827 ALAPPEVVM DPALAAQYEHDLVAQT TALPDEDDDL
Q3T054 ALAPPEVVM DPALAAQYEHDLVAQT TALPDEDDDL
Q9VZ23 ALLPPEVKMDKWDQAQIETRLQEAQATALPDEDEL
* *

G1

MOUSE
TAURUS
HUMAN
DROSOP

G2

G3

MQAIKCVVVGDGAVGKTCLLISYTTNAPFGEYIPTVFDNYSANVMVDGKPVNLGLWDTAG
MQAIKCVVVGDGAVGKTCLLISYTTNAPFGEYIPTVFDNYSANVMVDGKPVNLGLWDTAG
MQAIKCVVVGDGAVGKTCLLISYTTNAPFGEYIPTVFDNYSANVMVDGKPVNLGLWDTAG
MQAIKCVVVGDGAVGKTCLLISYTTNAPFGEYIPTVFDNYSANVMVDKPNINLGLWDTAG

G4

P63001
P62998
P63000
P40792

QEDYDRLRLPSYPQTDVFLICFSLVSPASFENVRAKWYPEVRHHCNPNTPIILVGTKL^{DLR}
QEDYDRLRLPSYPQTDVFLICFSLVSPASFENVRAKWYPEVRHHCNPNTPIILVGTKL^{DLR}
QEDYDRLRLPSYPQTDVFLICFSLVSPASFENVRAKWYPEVRHHCNPNTPIILVGTKL^{DLR}
QEDYDRLRLPSYPQTDVFLICFSLVSPASFENVRAKWYPEVRHHCNPNTPIILVGTKL^{DLR}

P63001
P62998
P63000
P40792

DDKDTIEKLKEKKLPITYPQGLAMAKEIGAVKYLECSALTQRGLKTVFDEAIRAVLCPP
DDKDTIEKLKEKKLPITYPQGLAMAKEIGAVKYLECSALTQRGLKTVFDEAIRAVLCPP
DDKDTIEKLKEKKLPITYPQGLAMAKEIGAVKYLECSALTQRGLKTVFDEAIRAVLCPP
DDKNKTIELRDKKLAPITYPQGLAMAKEIGAVKYLECSALTQKGLKTVFDEAIRSVLCPV

RAS SUPERFAMILY EVOLUTION IN EUKARYOTES

EVO

ARF (ARF1)

G1

G2

MOUSE MGNI FANL FKGL FGKKEMRILMVGLDAAGKT TILYKLKLGEIVTTIPTIGFNVETVEYKN
 HUMAN MGNI FANL FKGL FGKKEMRILMVGLDAAGKT TILYKLKLGEIVTTIPTIGFNVETVEYKN
 TAURUS MGNI FANL FKGL FGKKEMRILMVGLDAAGKT TILYKLKLGEIVTTIPTIGFNVETVEYKN
 CEREBI MGLFASKLFSNLFGNKEMRILMVGLDGAGKT TVLYKLKLGEVITTIPTIGFNVETVQYKN
 ** : : : * . * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : *

G3

P84078 ISFTVW DVGGQ DKIRPLWRHYFQNTQGLIFVVDSDNRERVNEAREELMRMLAEDEL RDAV
 P84077 ISFTVW DVGGQ DKIRPLWRHYFQNTQGLIFVVDSDNRERVNEAREELMRMLAEDEL RDAV
 P84080 ISFTVW DVGGQ DKIRPLWRHYFQNTQGLIFVVDSDNRERVNEAREELMRMLAEDEL RDAV
 P11076 ISFTVW DVGGQ DRIRSLWRHYRNTGEVIFVVDSDNDRSRIGEAREVMQRM LNEDEL RNAA
 * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : *

G4

G5

P84078 LLVFANKQDLPNAMAAEITDKLGLHSLRHRNWYIQA TCATSGDGLYEGLDWLSNQLRNQ
 P84077 LLVFANKQDLPNAMAAEITDKLGLHSLRHRNWYIQA TCATSGDGLYEGLDWLSNQLRNQ
 P84080 LLVFANKQDLPNAMAAEITDKLGLHSLRHRNWYIQA TCATSGDGLYEGLDWLSNQLRNQ
 P11076 WLVFANKQDLPEAMSAAEITEKGLHSLRHRNPWFIA TCATSGEGLYEGLEWLSNSLKN S

* : * : * : * : * : * : * : * : * : * : * : * : * : * : * : * : *

P84078 K
 P84077 K
 P84080 K
 P11076 T
 .

RAS SUPERFAMILY EVOLUTION IN PROKARYOTES

EVO

GTPases not present
in archaea

Obg

Era

Der

Universally
conserved GTPases

YihA

YchF

HflX

IF-2

Ef-Tu

EF-G

Ffh

FtsY

GTPases found in bacterial and
eukaryotic mitochondria and
chloroplasts

MnmE

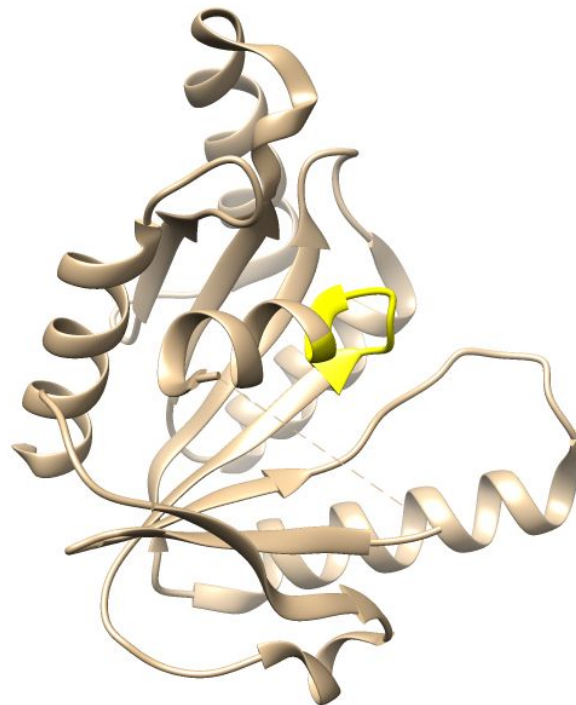
LepA

RAS SUPERFAMILY EVOLUTION IN PROKARYOTES

EVO

G1

→ Yiha_ecoli	028-EVAFAGRSNAGKSSAL-043
→ Yiha_bacillus	025-EIALAGRSNVGKSSFI-040
YchF_ecoli	004-KCGIVGLPNVGKSTLF-019
YchF_bacillus	004-TAGIVGLPNVGKSTLF-019
Hflx_ecoli	199-TVSLVGYTNAGKSTLF-214
Hflx_bacillus	202-QIALVGYTNAGKSTWF-217
IF2_ecoli	393-VTTIMGHVDHGKTSLL-408
IF2_bacillus	221-VVTIMGHVDHGKTLL-236
Eftu_ecoli	014-NVGTIGHVDHGKTTLT-029
Eftu_bacillus	014-NIGTIGHVDHGKTTLT-029
Efg_ecoli	012-NIGISAHIDAGKTTTT-027
Efg_bacillus	012-NIGIMAHIDAGKTTTT-027
Ffh_ecoli	102-VVLMAGLQGAGKTTTSV-117
Ffh_bacillus	103-VIMMVGLQGAGKTTTS-118
Ftsy_ecoli	295-VILMVGVNGVGKTTTI-310
Ftsy_bacillus	122-VILLVGVNGVGKTTTI-137
ras_human	005-KLVVVGAGGVGKSALT-020

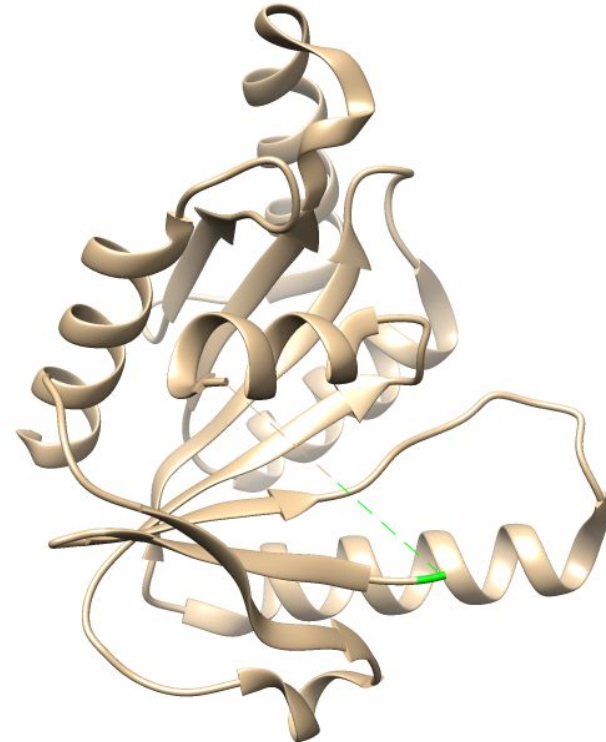


RAS SUPERFAMILY EVOLUTION IN PROKARYOTES

EVO

G2

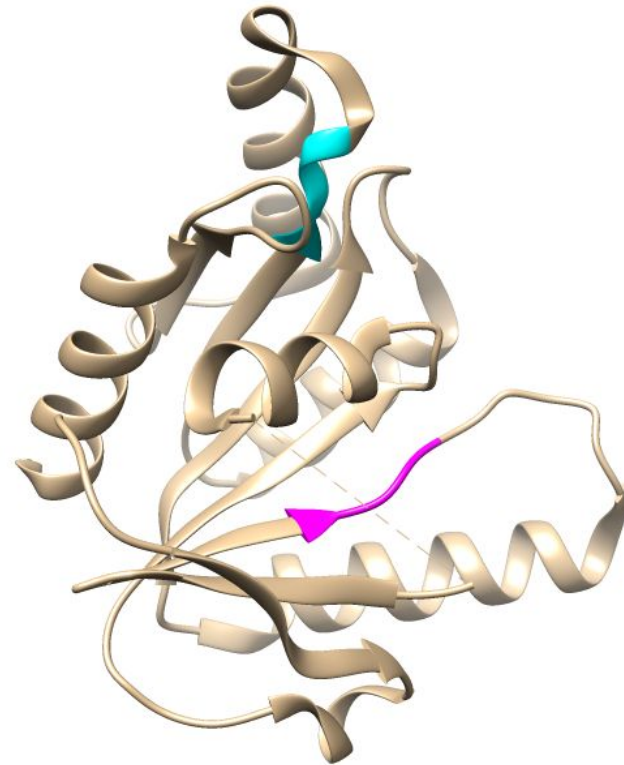
Yiha_ecoli	060-	GR	QL-064
Yiha_bacillus	057-	GK	QT-061
YchF_ecoli	030-	ANFPFC	IEPN-040
YchF_bacillus	030-	ANYPFC	IDPN-040
Hflx_ecoli	227-	QLFATL	-232
Hflx_bacillus	230-	LLFATL	-235
IF2_ecoli	414-TKVASGEAGGI	T	QHIG-429
IF2_bacillus	242-TKVVEGEAGGI	T	QHIG-257
Eftu_ecoli	051-DNAPEEKARGI	T	INTS-066
Eftu_bacillus	052-DGAPEERERGI	T	ISTA-067
Efg_ecoli	051-DWMEQEQRGI	T	ITSA-066
Efg_bacillus	051-DWMEQEQRGI	T	ITSA-066
Ffh_ecoli	138-DVYRPAA		-144
Ffh_bacillus	139-DIYRPAA		-145
Ftsy_ecoli	330-DTFRAAA		-336
Ftsy_bacillus	157-DTFRAGA		-163
ras_human	032-	YDPT	IEDSY-040



RAS SUPERFAMILY EVOLUTION IN PROKARYOTES

EVO

	G3	G4
Yiha_ecoli	074-KRLVDLPGYGLVLL	TKAD-148
→ Yiha_bacillus	071-LHFVDVPGYGIVIA	TKAD-145
YchF_ecoli	068-MEFVDIAGLVMIYIANV	NE-210
YchF_bacillus	068-FEFTDIAGIVLYVANV	SE-210
Hflx_ecoli	247-TVLADTVGFILLVMNK	ID-320
Hflx_bacillus	250-VLLSDTVGFILTAYNKR	D-323
IF2_ecoli	440-ITFLDTPGHAVVAVNK	ID-501
IF2_bacillus	268-ITFLDTPGHAIVAVNK	ID-329
Eftu_ecoli	077-YAHVDCPGHAIVFLNK	CD-139
Eftu_bacillus	078-YAHVDCPGHAVVFLNK	CD-140
Efg_ecoli	084-INIIDTPGHVIAFVNK	MD-145
Efg_bacillus	077-VNIIDTPGHVIVFVNK	MD-138
Ffh_ecoli	186-VLLVDTAGRLGVVL	TKVD-251
Ffh_bacillus	187-YVILDTAGRLGVVL	TKLD-252
Ftsy_ecoli	378-VLIADTAGRLGITL	TKLD-449
Ftsy_bacillus	205-VLICDTAGRLGIAL	TKLD-276
ras_human	053-YLDILDATAGQEVLV	NKCD-119

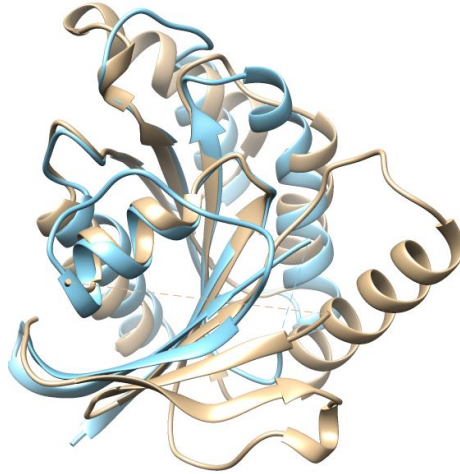


RAS SUPERFAMILY EVOLUTION IN PROKARYOTES

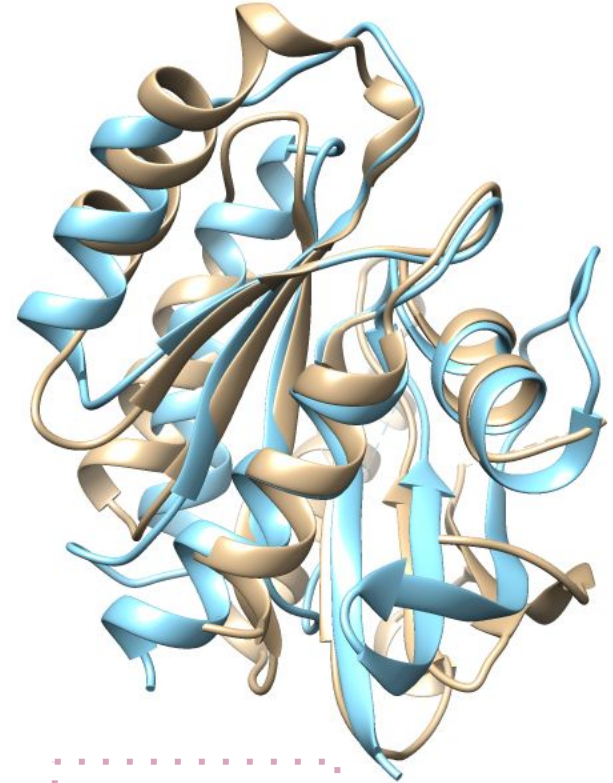
EVO

Nras - Human

YihA - *Bacillus Subtilis*



RMSD: 5.123



RMSD: 0.954



A diagram showing a horizontal rectangular block on the left, colored in a light purple shade. A thin horizontal line extends from the left edge of this block. On the right side of the block, a darker purple hexagon is positioned, partially overlapping the block. Inside the hexagon, the text "RAS SUPERFAMILY" is written in white, bold, uppercase letters.

**RAS
SUPERFAMILY**

HUMAN RAS SUPERFAMILY

RAS

		G1	G2
ARF1	MGNIFANLFKGLFGKKEMRILMV	GLDAAGKT	TTILYKCLKLGEIVTT-IP
RAB1A	-----MSSMNPEDYLFKLLLI	GD	SGVGKSCLLLRFAADDYTESY
NRAS	-----MTEYKLVVVVGAGGVGKS	SALT	IQLIQNHFVDEYDPTIEDSYR-KQVV
RAC1	-----MQAIKCVVVGDGAVGKT	CLL	ISYTTNAFPGEYIPTVFDNYS-ANVM
RAN	-----MAAQGEPPQVQFKLVLV	GDGGTGKT	TFVKRHLTGEFEKKYVATLGVEVHPLVFH
		: : : * . . . * : :	. . . * : .

	G3
ARF1	VEYKNISFTVWDVGGQDKIRPLWRHYFQNTQGLIFVVDSDNRERVNEAREELMRMLAED-
RAB1A	LDGKTIKLIQIWDTAGQERFRTITSSYYRGAGHIIVVYDVTQESFNNVK-QWLQEIDRY-
NRAS	IDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCVFAINNSKSFADIN-LYREQIKRVK
RAC1	VDGKPVNLGLWDTAGQEDYDRLRPLSYPTQDVFLICFSLVSPASFENVRAKWYPEVRHH-
RAN	TNRGPIKFNWDTAGQEKFGGLRDGGYYIAQCAIIMFDVTSRVTYKNVP-NWHRDLVRV-
	: : : * . . . * : :

	G4	G5
ARF1	ELRDAVLLVFANKQDL	LPNA-----MNAAEITDKLGLHSLRHRNWYIQ-----
RAB1A	ASENVNKLVLVGNKCDL	TTTKVVDDYTTAKEFADSLGIPFL
NRAS	DSDDVPMLVLVGNKCDL	PTR-TVDTKQAHELAKSYGIPFI
RAC1	-CPNTPILVGT	TKDLDRDD--KDTIEKLKEKKLTPITYPQGLAMAKEIGAVKYL
RAN	-CENIPIVLCG	NKVDIKDR--KVKAKSIVFHRKKNLQYYDI
	: : : . . * * :	: :

ARF1	-----A	TCA	SGDnGLYEGLDWLSNQLRNQK-----
RAB1A	KK--RMGPGATAGGA	ESNVKIQSTPVKQSGGG	CC-----
NRAS	RQY--RMKKLNSSDDGTG	CGCMGLP	VVM-----
RAC1	QR--GLKTVFDEAIRAVL	PPPVKKRKRC	LLLL-----
RAN	IGDPNLEFVAMPALAPPEV	MDPALAAQYEHDL	LEVAQTALPDEDDL
	. :		



G1 BOX CONSERVATION

RAS

RAS FAM

DIRA1_HUMAN GAGGVGKS
 DIRA2_HUMAN GAGGVGKS
 RAP1A_HUMAN GSGGVGKS
 RAP1B_HUMAN GSGGVGKS
 RAP2A_HUMAN GSGGVGKS
 RAP2C_HUMAN GSGGVGKS
 RAP2B_HUMAN GSGGVGKS
 RASH_HUMAN GAGGVGKS
 RASN_HUMAN GAGGVGKS
 RASK_HUMAN GAGGVGKS
 RRAS_HUMAN GGGGVGKS
 RRAS2_HUMAN GGGGVGKS
 RASM_HUMAN GDGGVGKS
 RALA_HUMAN GSGGVGKS
 RALB_HUMAN GSGGVGKS
 RIT1_HUMAN GAGGVGKS
 RIT2_HUMAN GAGGVGKS
 RASE_HUMAN GASGVGKS
 RHEB_HUMAN GYRSVGKS
 REBL1_HUMAN GYRCVGKT
 RASLC_HUMAN GRRGAGKS
 RASD1_HUMAN GSSKVGKT
 KBR52_HUMAN GQASVGKT
 KBR51_HUMAN GLLSVGKT

* **:

RHO FAM

RAC1_HUMAN GDGAVGKT
 RAC3_HUMAN GDGAVGKT
 RAC2_HUMAN GDGAVGKT
 RHOG_HUMAN GDGAVGKT
 RHOQ_HUMAN GDGAVGKT
 RHOJ_HUMAN GDGAVGKT
 RHOU_HUMAN GDGAVGKT
 RHOV_HUMAN GDGAVGKS
 RHOA_HUMAN GDGACGKT
 RHOC_HUMAN GDGACGKT
 RHOB_HUMAN GDGACGKT
 RND2_HUMAN GDAECGKT
 RND3_HUMAN GDSQCGKT
 RND1_HUMAN GDVQCGKT
 RHOF_HUMAN GDGGCGKT
 RHOD_HUMAN GDGGCGKT
 RHOH_HUMAN GDSAVGKT
 RHBT2_HUMAN GDNAVGT
 RHBT1_HUMAN GDNAVGT

** **:

RAB FAM + RAN

RAB9B_HUMAN GDGGVGK
 RAB9A_HUMAN GDGGVGK
 RAB7A_HUMAN GDSGVGK
 RAB7B_HUMAN GAIGVGK
 RAB32_HUMAN GELGVGK
 RAB38_HUMAN GDLGVGK
 RAB6A_HUMAN GEQSVGK
 RAB41_HUMAN GEQSVGK
 RAB28_HUMAN GEQSVGK
 RAB31_HUMAN GDGASGK
 RB22A_HUMAN GDTGVGK
 RAB5A_HUMAN GDTGVGK
 RAB5B_HUMAN GESAVGK
 RAB24_HUMAN GESAVGK
 RAB21_HUMAN GKEYVGK
 RAB17_HUMAN GEGCVGK
 RAB20_HUMAN GSGSVGK
 RAB34_HUMAN GDMNVGK
 RAB36_HUMAN GDLSVGK
 RAB23_HUMAN GDLYVGK
 RAB8A_HUMAN GNGAVGK
 RAB8B_HUMAN GDSGVGK
 RAB10_HUMAN GDSGVGK
 RAB13_HUMAN GDSGVGK
 RAB15_HUMAN GDSGVGK
 RAB12_HUMAN GDSGVGK
 RB40C_HUMAN GDSGVGK
 RB27A_HUMAN GDSGVGK
 RB27B_HUMAN GSRGVGK
 RAB3A_HUMAN GNSSVGK
 RAB3C_HUMAN GNSSVGK
 RAB3B_HUMAN GDSGVGK
 RAB3D_HUMAN GDSGVGK
 RAB1A_HUMAN GDSGVGK
 RAB1B_HUMAN GDSGVGK
 RAB35_HUMAN GDSGVGK
 RB11A_HUMAN GDSGVGK
 RB11B_HUMAN GESGVGK
 RAB25_HUMAN GNAGTGK
 RAB4A_HUMAN GDMGVGK
 RAB14_HUMAN GDTGVGK
 RAB2A_HUMAN GDTGVGK
 RAB2B_HUMAN GDSTVGK
 RB39A_HUMAN GDSTVGK
 RB39B_HUMAN GDAAVGK
 RAB42_HUMAN GDASVGK
 RAB43_HUMAN GDSNVGK
 RAB19_HUMAN GNAGVGK
 RAB30_HUMAN GNAGVGK
 RAB18_HUMAN GESGVGK
 RBL2B_HUMAN GDSAVGK
 RBL2A_HUMAN GDSAVGK
 RB33B_HUMAN GDSNVGK
 RAN_HUMAN GDGGTGK

* **

ARF FAM

ARL4A_HUMAN GLDCAGK
 ARL4C_HUMAN GLDSAGK
 ARL4D_HUMAN GLDSAGK
 ARF1_HUMAN GLDAAGK
 ARF3_HUMAN GLDAAGK
 ARF4_HUMAN GLDAAGK
 ARF5_HUMAN GLDAAGK
 ARF6_HUMAN GLDAAGK
 ARL1_HUMAN GLDGAGK
 ARL5A_HUMAN GLDNAGK
 ARL5B_HUMAN GLDNAGK
 ARL5C_HUMAN GLDNEGK
 ARL2_HUMAN GLDNAGK
 ARL3_HUMAN GLDNAGK
 ARL6_HUMAN GLDNSGK
 ARL8B_HUMAN GLQYSGK
 ARL8A_HUMAN GLQYSGK
 SAR1A_HUMAN GLDNAGK
 SAR1B_HUMAN GLDNAGK
 ARL9_HUMAN GLDGAGK

** :

RAS FAM

DIRA1_HUMAN PTT
 DIRA2_HUMAN PTV
 RAP1A_HUMAN PTT
 RAP1B_HUMAN PTT
 RAP2A_HUMAN PTT
 RAP2C_HUMAN PTT
 RAP2B_HUMAN PTT
 RASH_HUMAN PTT
 RASN_HUMAN PTT
 RASK_HUMAN PTT
 RRAS_HUMAN PTT
 RRAS2_HUMAN PTT
 RASM_HUMAN PTT
 RALA_HUMAN PTK
 RALB_HUMAN PTK
 RIT1_HUMAN PTT
 RIT2_HUMAN PTT
 RASE_HUMAN PTT
 RHEB_HUMAN PTT
 REBL1_HUMAN PTV
 RASLC_HUMAN PNL
 RASD1_HUMAN PTT
 KBRIS2_HUMAN ETQ
 KBRIS1_HUMAN ETM

RHO FAM

RAC1_HUMAN PTV
 RAC3_HUMAN PTV
 RAC2_HUMAN PTV
 RHOG_HUMAN PTV
 RHOQ_HUMAN PTV
 RHOJ_HUMAN PTV
 RHOU_HUMAN PTA
 RHOV_HUMAN PTA
 RHOA_HUMAN PTV
 RHOC_HUMAN PTV
 RHOB_HUMAN PTV
 RND2_HUMAN PTV
 RND3_HUMAN PTV
 RND1_HUMAN PTV
 RHOF_HUMAN PSV
 RHOD_HUMAN PTV
 RHOH_HUMAN PTV
 RHBT2_HUMAN PTV
 RHBT1_HUMAN PTV

* : .

RAB FAM + RAN

RAB9B_HUMAN ---AFHTL RAB3A_HUMAN VS----TV
 RAB9A_HUMAN ---LFHTL RAB3C_HUMAN VS----TV
 RAB7A_HUMAN ---YKATL RAB3B_HUMAN VS----TV
 RAB7B_HUMAN ---YQATL RAB3D_HUMAN VS----TV
 RAB32_HUMAN ---YRATL RAB1A_HUMAN IS----TL
 RAB38_HUMAN ---YRATL RAB1B_HUMAN IS----TL
 RAB6A_HUMAN ---YQATL RAB35_HUMAN IT----TL
 RAB41_HUMAN ---CQATV RB11A_HUMAN K----STL
 RAB28_HUMAN ---YKQTL RB11B_HUMAN K----STL
 RAB31_HUMAN ---ISPTL RAB25_HUMAN R----TL
 RB22A_HUMAN ---INPTL RAB4A_HUMAN N----HTL
 RAB5A_HUMAN ---QESTL RAB14_HUMAN P----HTL
 RAB5B_HUMAN ---QESTL RAB2A_HUMAN D----LT
 RAB24_HUMAN ---YQNTL RAB2B_HUMAN D----LT
 RAB21_HUMAN ---HITL RB39A_HUMAN S-PACDPTV
 RAB17_HUMAN ---LPTV RB39B_HUMAN ----DPTV
 RAB20_HUMAN ---VSTV RAB42_HUMAN PEPEPEPTV
 RAB34_HUMAN ---YKATL RAB43_HUMAN G----STL
 RAB36_HUMAN ---YKATL RAB19_HUMAN Q----NTL
 RAB23_HUMAN ---YKKT L RAB30_HUMAN G----ATL
 RAB8A_HUMAN IS----TL RAB18_HUMAN AA----TL
 RAB8B_HUMAN IS----TL RBL2B_HUMAN LS----TV
 RAB10_HUMAN IS----TL RBL2A_HUMAN S----TV
 RAB13_HUMAN IS----TL RB33B_HUMAN A----TL
 RAB15_HUMAN IS----TL RAN_HUMAN A----TL
 RAB12_HUMAN KS----TV :
 RB40C_HUMAN AY----SN
 RB27A_HUMAN IT----TV
 RB27B_HUMAN IT----TV

ARF FAM

ARL4A_HUMAN PTK
 ARL4C_HUMAN PTT
 ARL4D_HUMAN PTK
 ARF1_HUMAN PTT
 ARF3_HUMAN PTT
 ARF4_HUMAN PTT
 ARF5_HUMAN PTT
 ARF6_HUMAN PTV
 ARL1_HUMAN PTT
 ARL5A_HUMAN PTT
 ARL5B_HUMAN PTT
 ARL5C_HUMAN PTT
 ARL2_HUMAN PTL
 ARL3_HUMAN PTQ
 ARL6_HUMAN PTT
 ARL8B_HUMAN PTV
 ARL8A_HUMAN PTV
 SAR1A_HUMAN PTL
 SAR1B_HUMAN PTL
 ARL9_HUMAN PTQ

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RAS FAM

DIRA1_HUMAN DTGG
 DIRA2_HUMAN DTGG
 RAP1A_HUMAN DTAG
 RAP1B_HUMAN DTAG
 RAP2A_HUMAN DTAG
 RAP2C_HUMAN DTAG
 RAP2B_HUMAN DTAG
 RASH_HUMAN DTAG
 RASN_HUMAN DTAG
 RASK_HUMAN DTAG
 RRAS_HUMAN DTAG
 RRAS2_HUMAN DTAG
 RASM_HUMAN DTAG
 RALA_HUMAN DTAG
 RALB_HUMAN DTAG
 RIT1_HUMAN DTAG
 RIT2_HUMAN DTAG
 RASE_HUMAN DTAG
 RHEB_HUMAN DTAG
 REBL1_HUMAN DTAG
 RASLC_HUMAN DTAG
 RASD1_HUMAN DTSG
 KBR52_HUMAN DTRG
 KBR51_HUMAN DTRG

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RHO FAM

RAC1_HUMAN DTAG
 RAC3_HUMAN DTAG
 RAC2_HUMAN DTAG
 RHOG_HUMAN DTAG
 RHOQ_HUMAN DTAG
 RHOJ_HUMAN DTAG
 RHOU_HUMAN DTAG
 RHOV_HUMAN DTAG
 RHOA_HUMAN DTAG
 RHOC_HUMAN DTAG
 RHOB_HUMAN DTAG
 RND2_HUMAN DTSG
 RND3_HUMAN DTSG
 RND1_HUMAN DTSG
 RHOF_HUMAN DTAG
 RHOD_HUMAN DTAG
 RHOH_HUMAN DTAG
 RHBT2_HUMAN DTFG
 RHBT1_HUMAN DTFG

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RAB FAM + RAN

RAB9B_HUMAN DTAG
 RAB9A_HUMAN DTAG
 RAB7A_HUMAN DTAG
 RAB7B_HUMAN DTGG
 RAB32_HUMAN DTAG
 RAB38_HUMAN DTAG
 RAB6A_HUMAN DTAG
 RAB41_HUMAN DTAG
 RAB28_HUMAN DTGG
 RAB31_HUMAN DTAG
 RB22A_HUMAN DTAG
 RAB5A_HUMAN DTAG
 RAB5B_HUMAN DTAG
 RAB24_HUMAN DTAG
 RAB21_HUMAN DTAG
 RAB17_HUMAN DTAG
 RAB20_HUMAN DTAG
 RAB34_HUMAN DTAG
 RAB36_HUMAN DTAG
 RAB23_HUMAN DTAG
 RAB8A_HUMAN DTAG
 RAB8B_HUMAN DTAG
 RAB10_HUMAN DTAG
 RAB13_HUMAN DTAG
 RAB15_HUMAN DTAG
 RAB12_HUMAN DTAG
 RB40C_HUMAN DTSG
 RB27A_HUMAN DTAG
 RB27B_HUMAN DTAG

RAB3A_HUMAN DTAG
 RAB3C_HUMAN DTAG
 RAB3B_HUMAN DTAG
 RAB3D_HUMAN DTAG
 RAB1A_HUMAN DTAG
 RAB1B_HUMAN DTAG
 RAB35_HUMAN DTAG
 RB11A_HUMAN DTAG
 RB11B_HUMAN DTAG
 RAB25_HUMAN DTAG
 RAB4A_HUMAN DTAG
 RAB14_HUMAN DTAG
 RAB2A_HUMAN DTAG
 RAB2B_HUMAN DTAG
 RB39A_HUMAN DTAG
 RB39B_HUMAN DTAG
 RAB42_HUMAN DTAG
 RAB43_HUMAN DTAG
 RAB19_HUMAN DTAG
 RAB30_HUMAN DTAG
 RAB18_HUMAN DTAG
 RBL2B_HUMAN DTAG
 RBL2A_HUMAN DTAG
 RB33B_HUMAN DTAG
 RAN_HUMAN DTAG

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ARF FAM

ARL4A_HUMAN DVGG
 ARL4C_HUMAN DVGG
 ARL4D_HUMAN DVGG
 ARF1_HUMAN DVGG
 ARF3_HUMAN DVGG
 ARF4_HUMAN DVGG
 ARF5_HUMAN DVGG
 ARF6_HUMAN DVGG
 ARL1_HUMAN DLGG
 ARL5A_HUMAN DIGG
 ARL5B_HUMAN DIGG
 ARL5C_HUMAN DIVR
 ARL2_HUMAN DVGG
 ARL3_HUMAN DIGG
 ARL6_HUMAN DMSG
 ARL8B_HUMAN DIGG
 ARL8A_HUMAN DIGG
 SAR1A_HUMAN DLGG
 SAR1B_HUMAN DLGG
 ARL9_HUMAN EIGG

::

RAS FAM

DIRA1_HUMAN **NKCD**
 DIRA2_HUMAN **NKCD**
 RAP1A_HUMAN **NKCD**
 RAP1B_HUMAN **NKCD**
 RAP2A_HUMAN **NKVD**
 RAP2C_HUMAN **NKVD**
 RAP2B_HUMAN **NKVD**
 RASH_HUMAN **NKCD**
 RASN_HUMAN **NKCD**
 RASK_HUMAN **NKCD**
 RRAS_HUMAN **NKAD**
 RRAS2_HUMAN **NKAD**
 RASM_HUMAN **NKVD**
 RALA_HUMAN **NKSD**
 RALB_HUMAN **NKSD**
 RIT1_HUMAN **NKSD**
 RIT2_HUMAN **NKID**
 RASE_HUMAN **NKCD**
 RHEB_HUMAN **NKKD**
 REBL1_HUMAN **NKAD**
 RASLC_HUMAN **NKLD**
 RASD1_HUMAN **NKGD**
 KBRIS2_HUMAN **NKCD**
 KBRIS1_HUMAN **NKID**

** *

RHO FAM

RAC1_HUMAN **TKLD**
 RAC3_HUMAN **TKLD**
 RAC2_HUMAN **TKLD**
 RHOG_HUMAN **TKKD**
 RHOQ_HUMAN **TQID**
 RHOJ_HUMAN **TQID**
 RHOU_HUMAN **TQSD**
 RHOV_HUMAN **TQAD**
 RHOA_HUMAN **NKKD**
 RHOC_HUMAN **NKKD**
 RHOB_HUMAN **NKKD**
 RND2_HUMAN **CKLD**
 RND3_HUMAN **CKSD**
 RND1_HUMAN **CKTD**
 RHOF_HUMAN **CKTD**
 RHOD_HUMAN **CKTD**
 RHOH_HUMAN **TQTD**
 RHBT2_HUMAN **CQLD**
 RHBT1_HUMAN **CQLD**

: *

RAB FAM + RAN

RAB9B_HUMAN **NKVD**
 RAB9A_HUMAN **NKID**
 RAB7A_HUMAN **NKID**
 RAB7B_HUMAN **NKID**
 RAB32_HUMAN **NKCD**
 RAB38_HUMAN **NKCD**
 RAB6A_HUMAN **NKTD**
 RAB41_HUMAN **NKID**
 RAB28_HUMAN **NKID**
 RAB31_HUMAN **NKCD**
 RB22A_HUMAN **NKCD**
 RAB5A_HUMAN **NKAD**
 RAB5B_HUMAN **NKAD**
 RAB24_HUMAN **TKSD**
 RAB21_HUMAN **NKID**
 RAB17_HUMAN **NKTD**
 RAB20_HUMAN **NKVD**
 RAB34_HUMAN **SKKD**
 RAB36_HUMAN **TKKD**
 RAB23_HUMAN **NKID**
 RAB8A_HUMAN **NKCD**
 RAB8B_HUMAN **NKCD**
 RAB10_HUMAN **NKCD**
 RAB13_HUMAN **NKCD**
 RAB15_HUMAN **NKAD**
 RAB12_HUMAN **NKLD**
 RB40C_HUMAN **NRLH**
 RB27A_HUMAN **NKSD**
 RB27B_HUMAN **NKAD**

RAB3A_HUMAN **NKCD**
 RAB3C_HUMAN **NKCD**
 RAB3B_HUMAN **NKCD**
 RAB3D_HUMAN **NKCD**
 RAB1A_HUMAN **NKCD**
 RAB1B_HUMAN **NKSD**
 RAB35_HUMAN **NKND**
 RB11A_HUMAN **NKSD**
 RB11B_HUMAN **NKSD**
 RAB25_HUMAN **NKSD**
 RAB4A_HUMAN **NKKD**
 RAB14_HUMAN **NKAD**
 RAB2A_HUMAN **NKSD**
 RAB2B_HUMAN **NKSD**
 RB39A_HUMAN **HKCD**
 RB39B_HUMAN **HKCD**
 RAB42_HUMAN **HKSD**
 RAB43_HUMAN **NKSD**
 RAB19_HUMAN **NKCD**
 RAB30_HUMAN **NKID**
 RAB18_HUMAN **NKID**
 RBL2B_HUMAN **NKID**
 RBL2A_HUMAN **NKID**
 RB33B_HUMAN **NKCD**
 RAN_HUMAN **NKVD**

: .

ARF FAM

ARL4A_HUMAN **NKQD**
 ARL4C_HUMAN **NKQD**
 ARL4D_HUMAN **NKQD**
 ARF1_HUMAN **NKQD**
 ARF3_HUMAN **NKQD**
 ARF4_HUMAN **NKQD**
 ARF5_HUMAN **NKQD**
 ARF6_HUMAN **NKQD**
 ARL1_HUMAN **NKQD**
 ARL5A_HUMAN **NKQD**
 ARL5B_HUMAN **NKQD**
 ARL5C_HUMAN **NKQD**
 ARL2_HUMAN **NKQD**
 ARL3_HUMAN **NKQD**
 ARL6_HUMAN **NKMD**
 ARL8B_HUMAN **NKRD**
 ARL8A_HUMAN **NKRD**
 SAR1A_HUMAN **NKID**
 SAR1B_HUMAN **NKID**
 ARL9_HUMAN **NKQD**

** *

NRAS

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDITAGQEEYSAMRDQY

$\beta 1$

$\alpha 1$

$\beta 2$

$\beta 3$

$\alpha 2$

MRTGEGFLCVFAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAARTVESRQAQDLARSYGIPYI

$\beta 4$

$\alpha 3$

$\beta 5$

$\alpha 4$

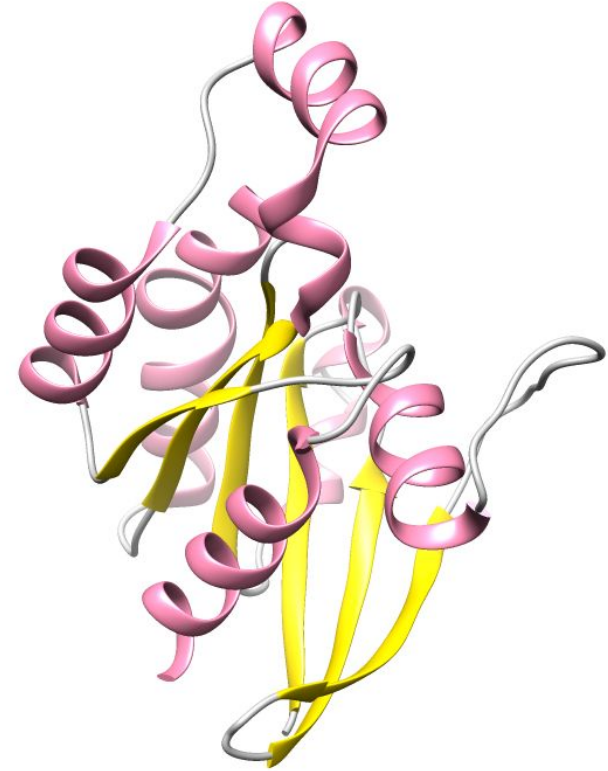
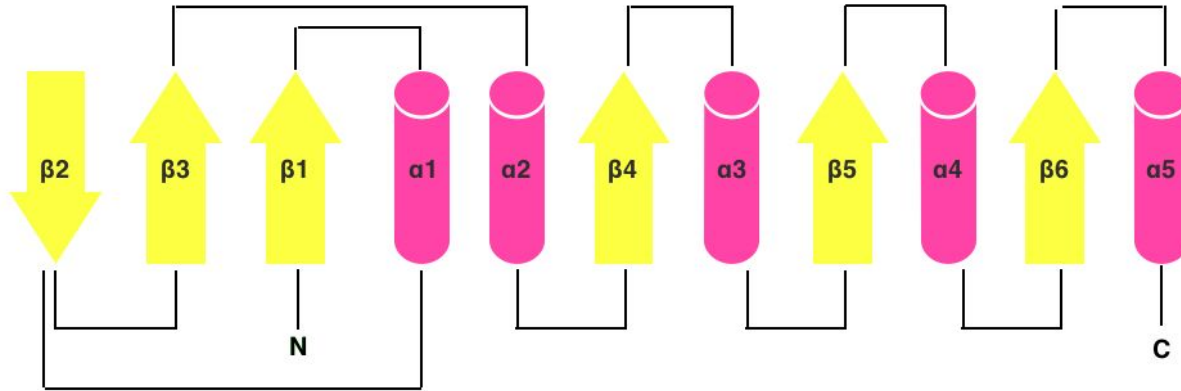
ETSAKTRQGVEDAFYTLVREIRQHKLRLNPPDESGPGCMSCKCVLS

$\beta 6$

$\alpha 5$

RAS SUPERFAMILY COMMON FEATURES: SECONDARY STRUCTURE

RAS

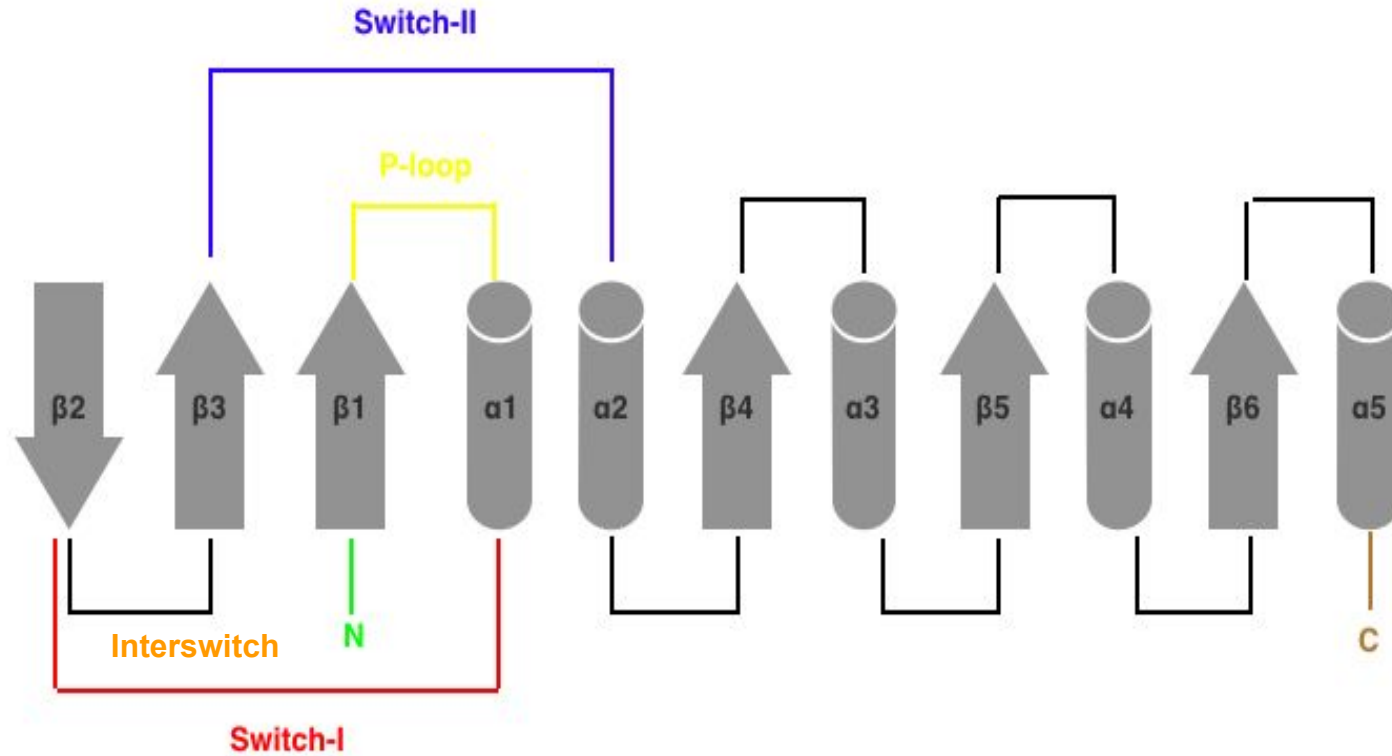


Class. Alpha and beta proteins (a/b)

Fold. 3 layers: a/b/a, parallel or mixed beta-sheets of variable sizes

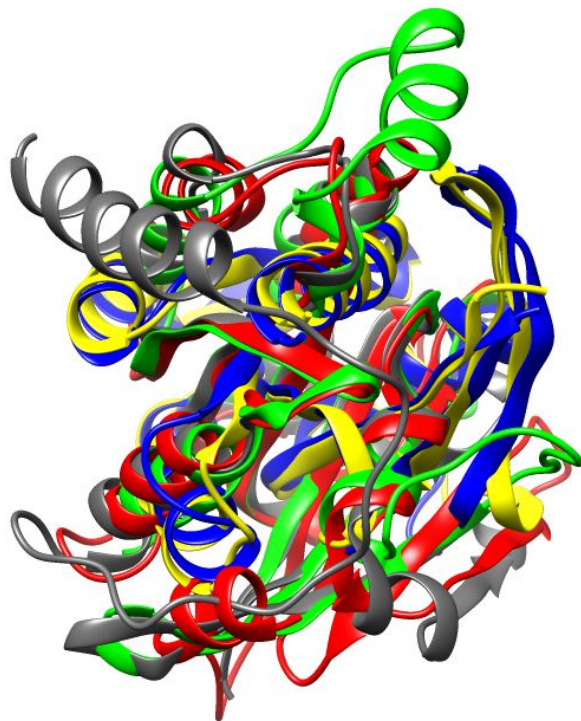
RAS SUPERFAMILY GENERAL STRUCTURE

RAS



RAS SUPERFAMILY SUPERIMPOSITION

RAS



STAMP Structural Alignment of Multiple Proteins

Version 4.4 (May 2010)

by Robert B. Russell & Geoffrey J. Barton

Please cite PROTEINS, v14, 309-323, 1992

Running roughfit.

Sc = STAMP score, RMS = RMS deviation, Align = alignment length

Len1, Len2 = length of domain, Nfit = residues fitted

Secs = no. equivalent sec. strucs. Eq = no. equivalent residues

%I = seq. identity, %S = sec. str. identity

P(m) = P value (p=1/10) calculated after Murzin (1993), JMB, 230, 689-694

(NC = P value not calculated - potential FP overflow)

	No.	Domain1	Domain2	Sc	RMS	Len1	Len2	Align	NFit	Eq.	Secs.	%I	%S	P(m)	
Pair 1	ARF1	RAC1		4.88	1.75	180	176	197	121	120	0	14.17	100.00	3.68e-02	
Pair 2	ARF1	RAN		0.43	2.45	180	200	260	17	0	0	0.00	0.00	1.00e+00	LOW SCORE
Pair 3	ARF1	NRAS		0.36	1.84	180	156	234	8	3	0	0.00	100.00	1.00e+00	LOW SCORE
Pair 4	ARF1	RAB1A		4.79	1.65	180	155	191	110	104	0	18.27	100.00	7.71e-03	
Pair 5	RAC1	RAN		5.10	1.33	176	200	190	136	135	0	25.19	100.00	2.31e-07	
Pair 6	RAC1	NRAS		0.27	1.32	176	156	249	5	3	0	0.00	100.00	1.00e+00	LOW SCORE
Pair 7	RAC1	RAB1A		0.21	100.00	176	155	240	1	0	0	0.00	0.00	1.00e+00	LOW SCORE
Pair 8	RAN	NRAS		1.30	2.08	200	156	222	37	28	0	10.71	100.00	1.00e+00	LOW SCORE
Pair 9	RAN	RAB1A		0.45	2.31	200	155	242	8	0	0	0.00	0.00	1.00e+00	LOW SCORE
Pair 10	NRAS	RAB1A		8.06	1.15	156	155	161	142	139	0	36.69	100.00	3.14e-17	

Reading in matrix file rasrough.mat...

Doing cluster analysis...

Cluster: 1 (NRAS & RAB1A) Sc 8.06 RMS 1.15 Len 161 nfit 142

See file rasrough.1 for the alignment and transformations

Cluster: 2 (RAC1 & RAN) Sc 5.10 RMS 1.33 Len 190 nfit 136

See file rasrough.2 for the alignment and transformations

Cluster: 3 (ARF1 & RAC1 RAN) Sc 6.16 RMS 1.91 Len 206 nfit 129

See file rasrough.3 for the alignment and transformations

Cluster: 4 (NRAS RAB1A & ARF1 RAC1 RAN) Sc 1.17 RMS 3.87 Len 278 nfit 32 LOW SCORE

See file rasrough.4 for the alignment and transformations

RAS SUPERFAMILY SUPERIMPOSITION

RAS



STAMP Structural Alignment of Multiple Proteins

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by Robert B. Russell & Geoffrey J. Barton
Please cite PROTEINS, v14, 309-323, 1992

Sc = STAMP score, RMS = RMS deviation, Align = alignment length
Len1, Len2 = length of domain, Nfit = residues fitted
Secs = no. equivalent sec. strucs. Eq = no. equivalent residues
%I = seq. identity, %S = sec. str. identity
P(m) = P value (p=1/10) calculated after Murzin (1993), JMB, 230, 689-694
(NC = P value not calculated - potential FP overflow)

	No.	Domain1	Domain2	Sc	RMS	Len1	Len2	Align	NFit	Eq.	Secs.	%I	%S	P(m)
Pair 1	1	ARF1	RAC1	4.83	1.86	180	176	198	123	121	0	13.22	100.00	5.61e-02
Pair 2	2	ARF1	RAN	4.60	1.92	180	200	179	130	128	0	18.75	100.00	1.05e-03
Pair 3	3	ARF1	NRAS	4.82	1.92	180	156	188	119	112	0	17.86	100.00	4.03e-03
Pair 4	4	ARF1	RAB1A	4.79	1.65	180	155	191	110	104	0	18.27	100.00	7.71e-03
Pair 5	5	RAC1	RAN	5.16	1.36	176	200	189	138	136	0	25.74	100.00	8.98e-08
Pair 6	6	RAC1	NRAS	6.87	1.26	176	156	179	142	140	0	32.14	100.00	4.90e-13
Pair 7	7	RAC1	RAB1A	6.72	1.17	176	155	179	136	134	0	26.12	100.00	6.10e-08
Pair 8	8	RAN	NRAS	5.36	1.27	200	156	178	131	129	0	24.03	100.00	2.10e-06
Pair 9	9	RAN	RAB1A	5.14	1.23	200	155	181	126	126	0	30.16	100.00	2.30e-10
Pair 10	10	NRAS	RAB1A	8.01	1.15	156	155	162	142	138	0	36.96	100.00	2.21e-17

Reading in matrix file rasfit_OK.mat...

Doing cluster analysis...

Cluster: 1 (NRAS & RAB1A) Sc 8.00 RMS 1.15 Len 162 nfit 142

See file rasfit_OK.1 for the alignment and transformations

Cluster: 2 (RAC1 & NRAS RAB1A) Sc 7.54 RMS 1.11 Len 184 nfit 141

See file rasfit_OK.2 for the alignment and transformations

Cluster: 3 (RAN & RAC1 NRAS RAB1A) Sc 6.15 RMS 1.14 Len 201 nfit 131

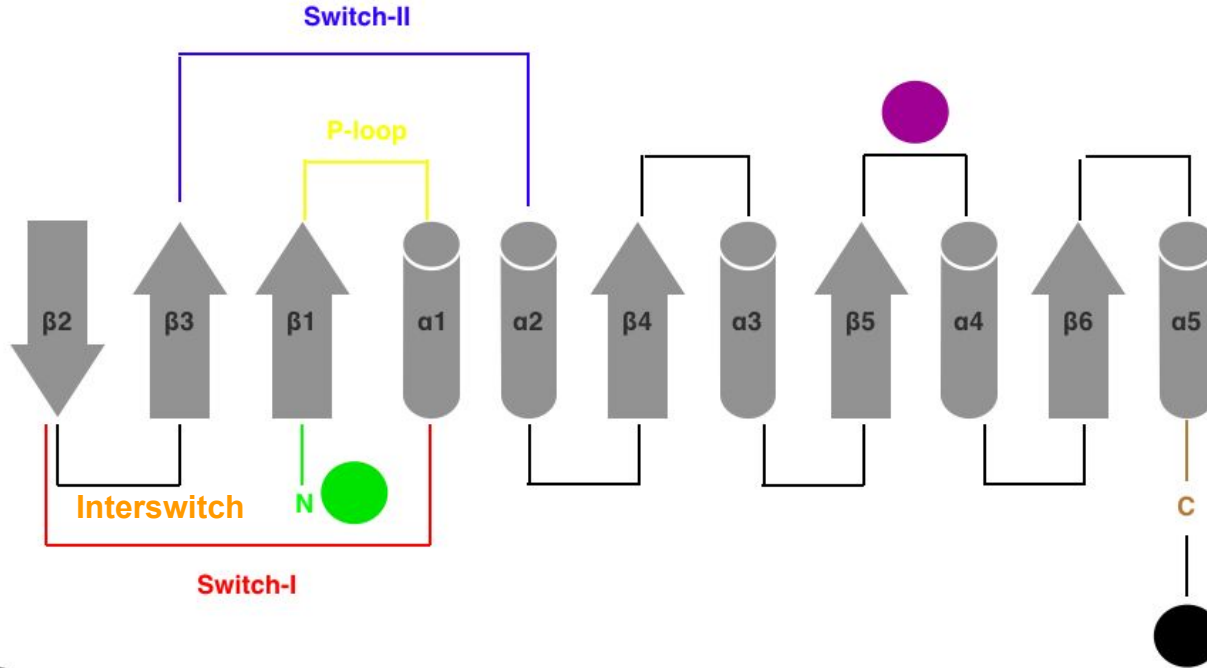
See file rasfit_OK.3 for the alignment and transformations

Cluster: 4 (ARF1 & RAN RAC1 NRAS RAB1A) Sc 5.29 **RMS 1.83** Len 213 nfit 119

See file rasfit_OK.4 for the alignment and transformations

RAS FAMILIES SPECIFIC STRUCTURAL CHANGES

RAS

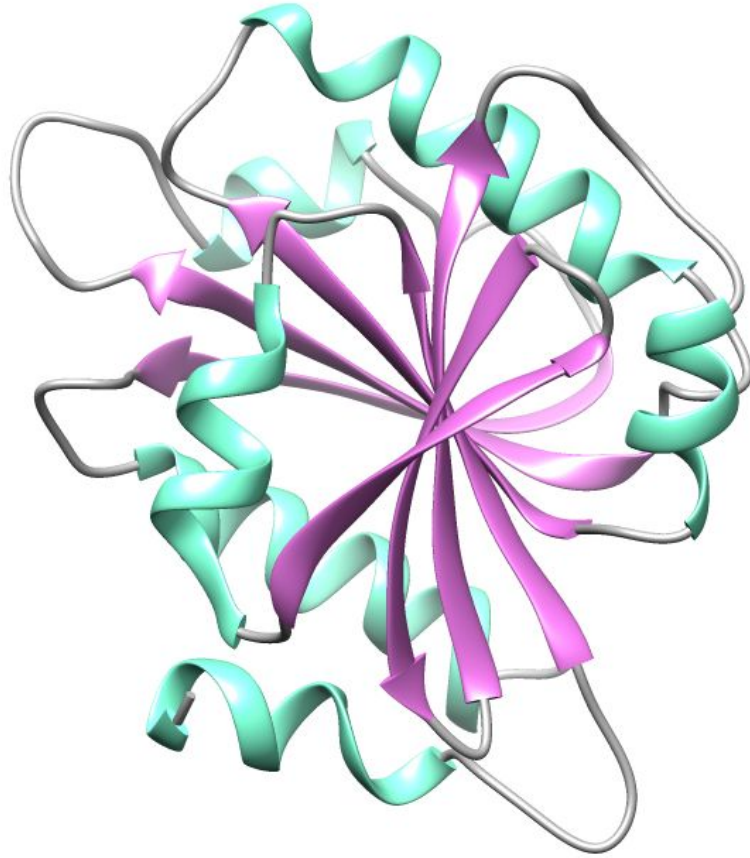


● RHO, RAS, RAB: Cysteine isoprenylation

● RAS, RHO: Cysteine palmitoylation

● ARF, RAS: glycine myristoylation

ARF1



ADP-ribosylation factor 1

Ubiquitous and essential

Vesicular transport (Golgi)

Reversible association with membrane

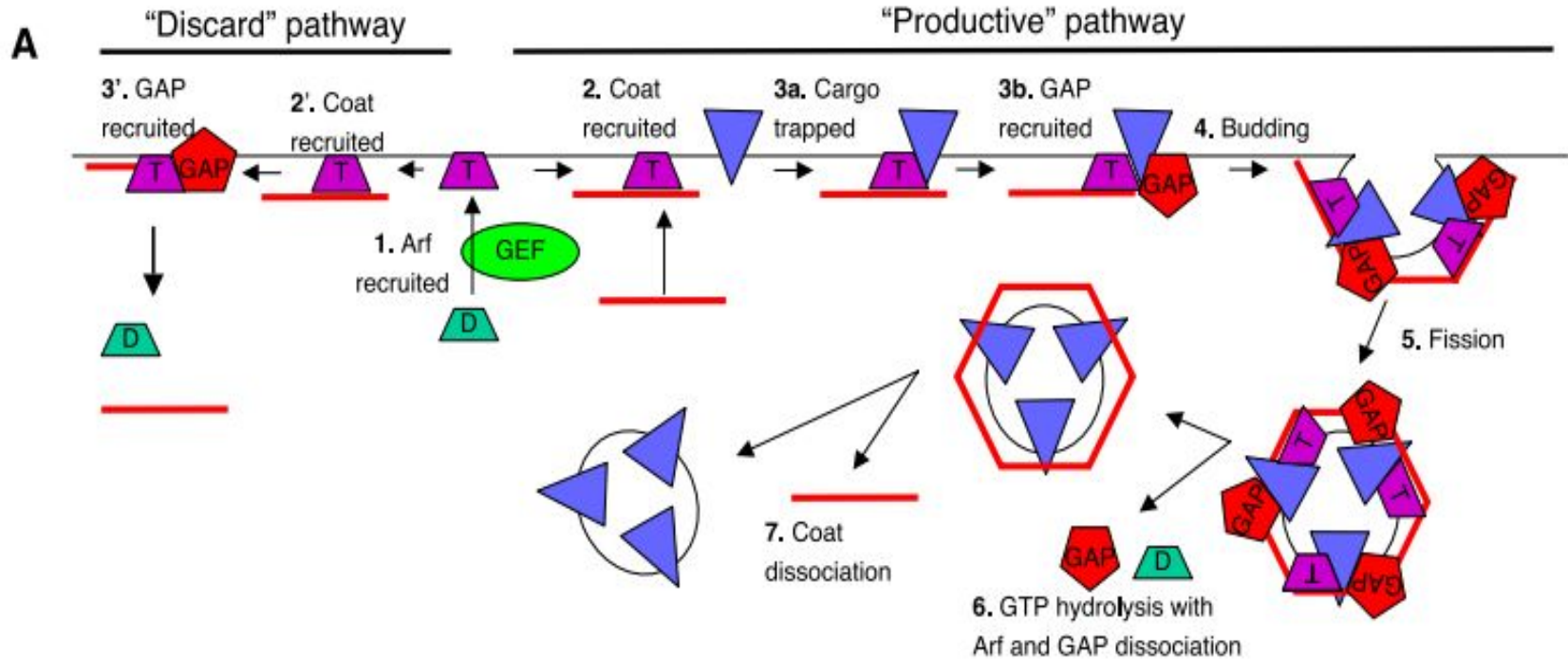
Localization: cytosol/membrane

CLASS I → Arf1, Arf2, Arf3

CLASS II → Arf4, Ar

CLASS III → Arf6





Randazzo P, Hirsch D. Arf GAPs: multifunctional proteins that regulate membrane traffic and actin remodelling. Cellular Signalling. 2004;16(4):401-413.

CLASS: Alpha and beta proteins (a/b)

FOLD: P-loop containing nucleoside triphosphate hydrolases
3 layers: a/b/a, parallel or mixed beta-sheets of variable sizes

SUPERFAMILY: P-loop containing nucleoside triphosphate hydrolases
division into families based on beta-sheet topologies

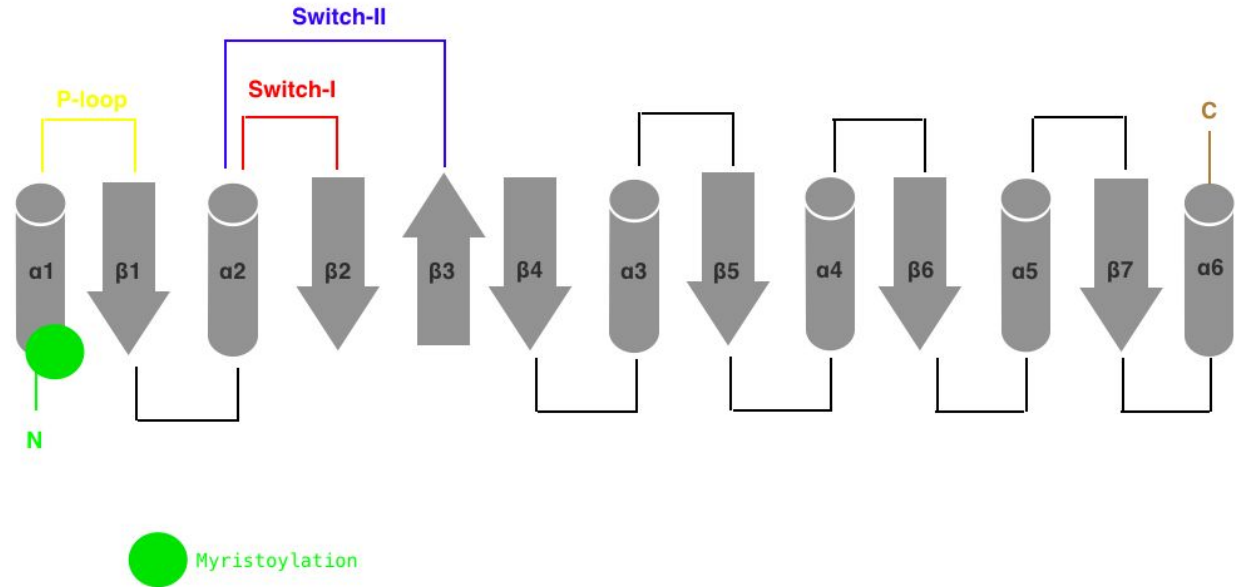
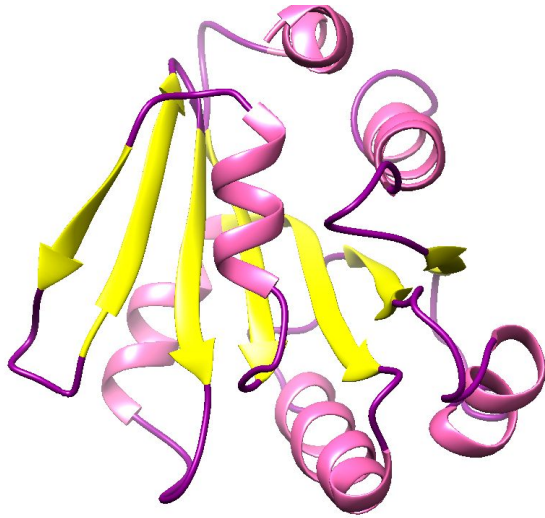
FAMILY: G proteins
core: mixed beta-sheet of 6 strands, order 231456; strand 2 is antiparallel to the rest

PROTEIN: ADP-ribosylation factor

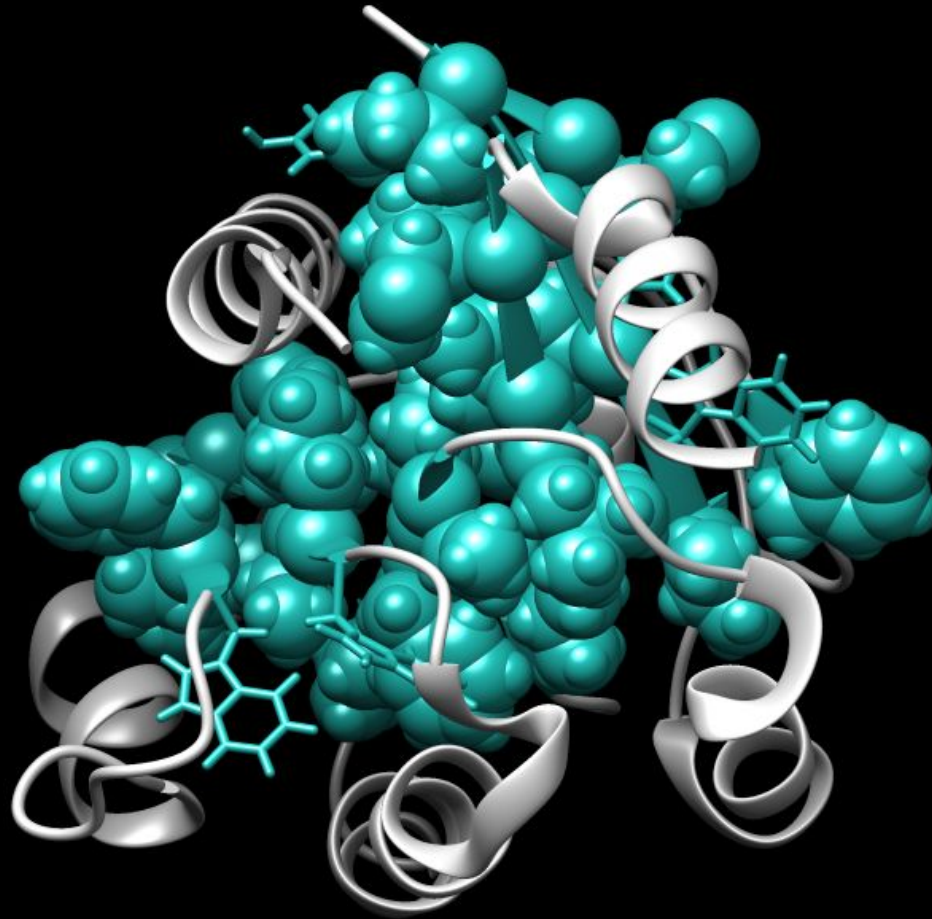
SPECIES: Human (Homo sapiens), ARF1
Uniprot: P32889

ARF SECONDARY STRUCTURE

ARF1

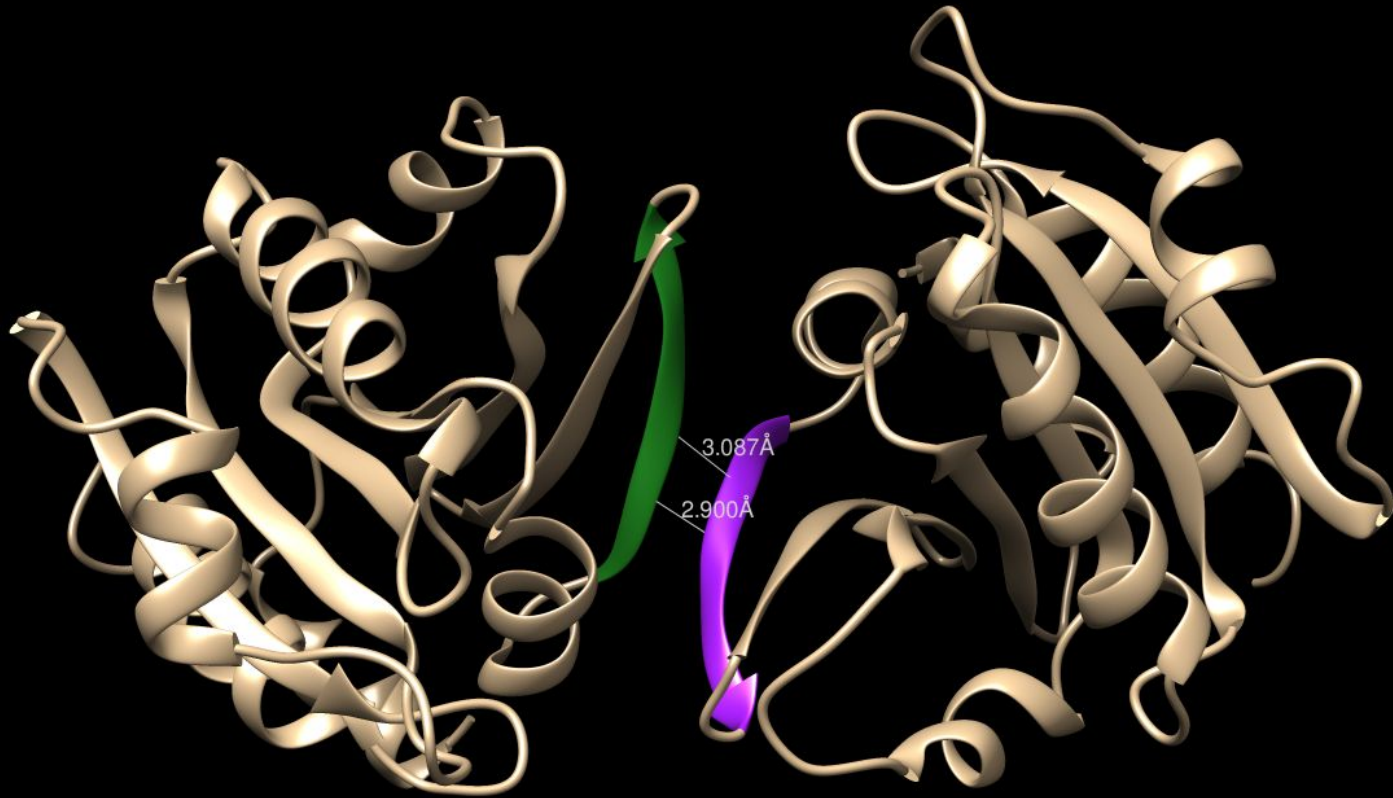


■ BETA-SHEET



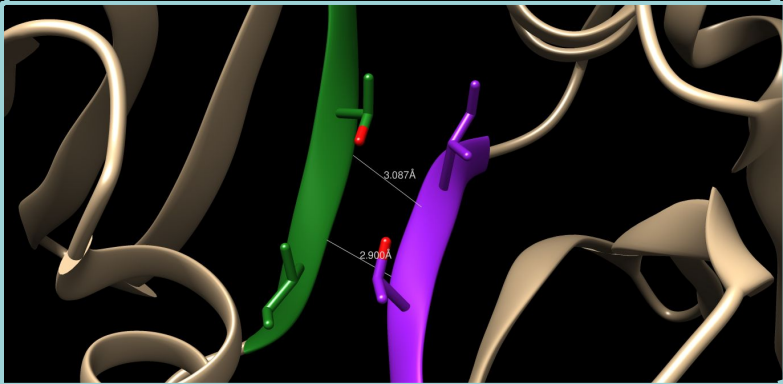
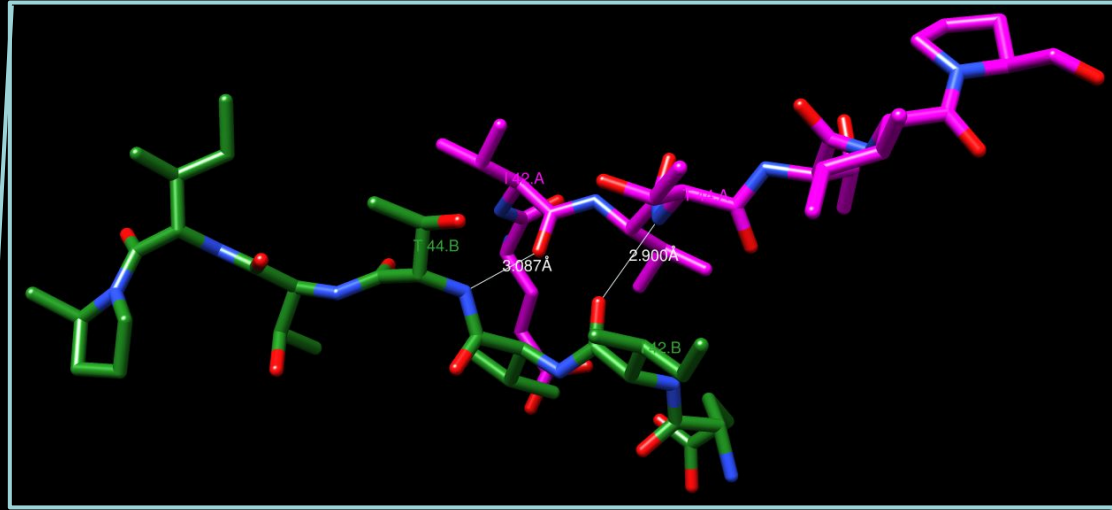
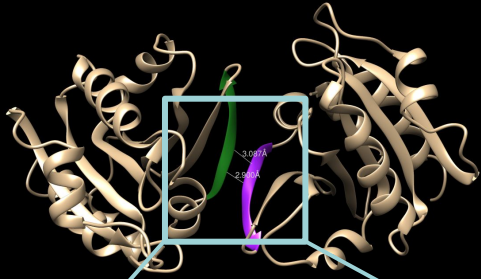
ABOUT DIMERIZATION

ARF1



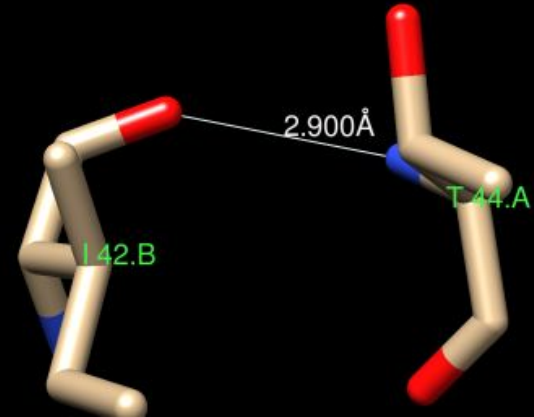
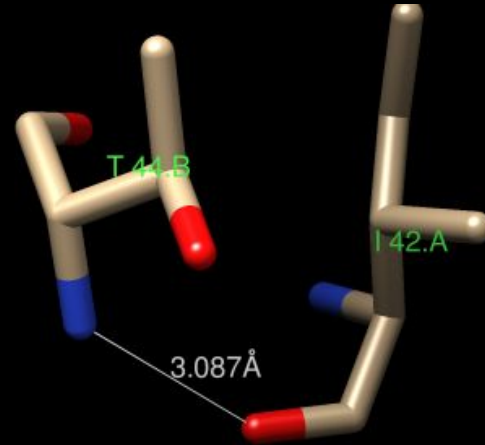
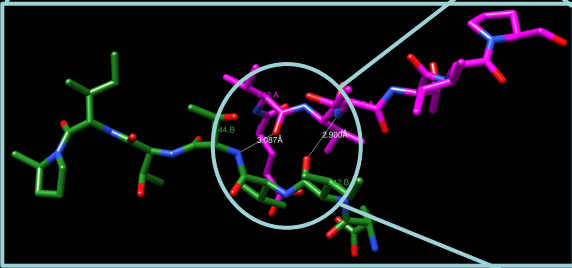
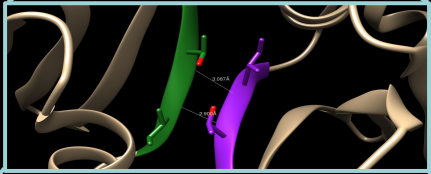
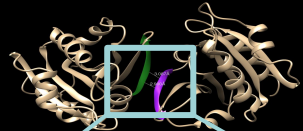
ABOUT DIMERIZATION

ARF1



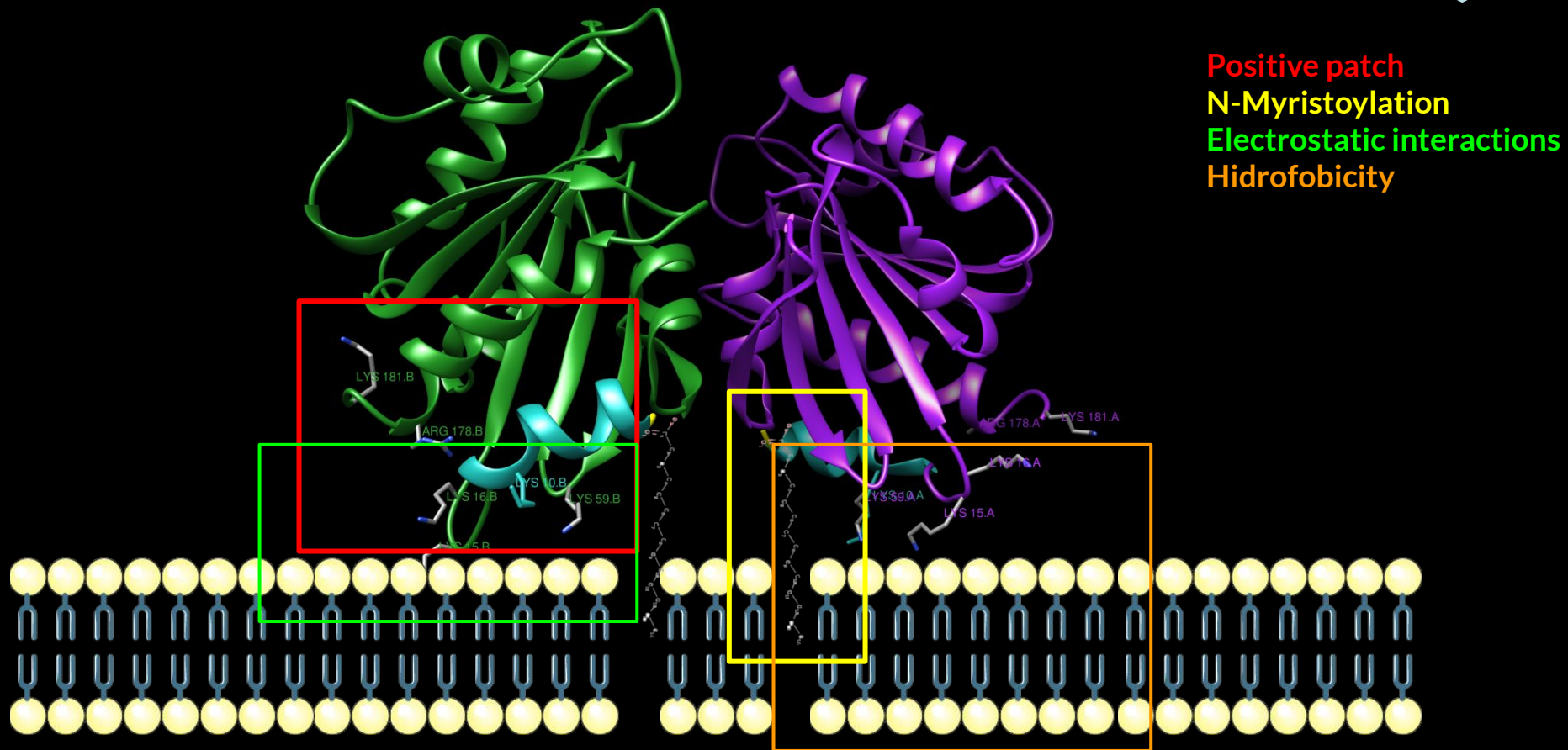
ABOUT DIMERIZATION

ARF1



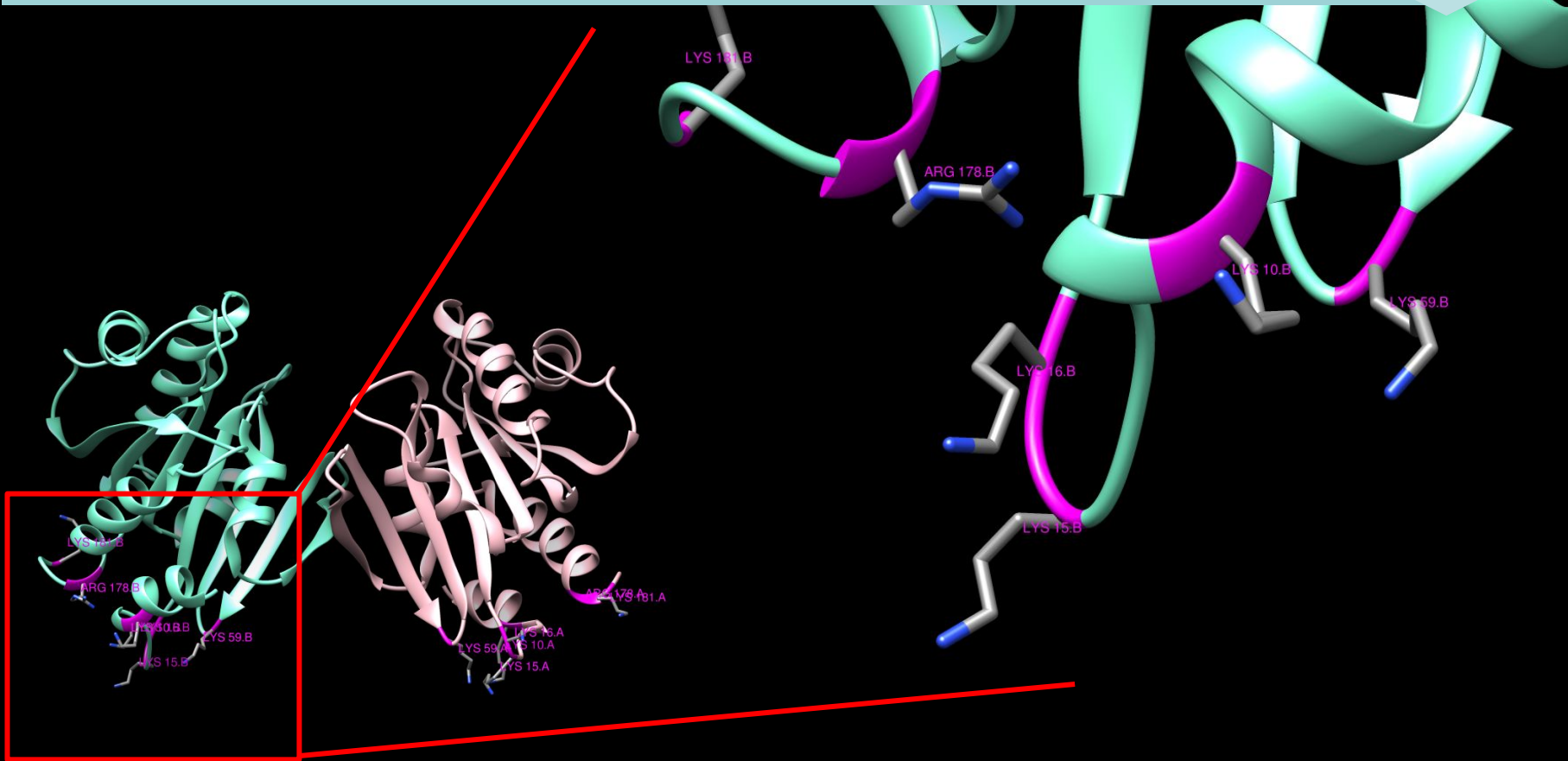
MEMBRANE ASSOCIATION

ARF1



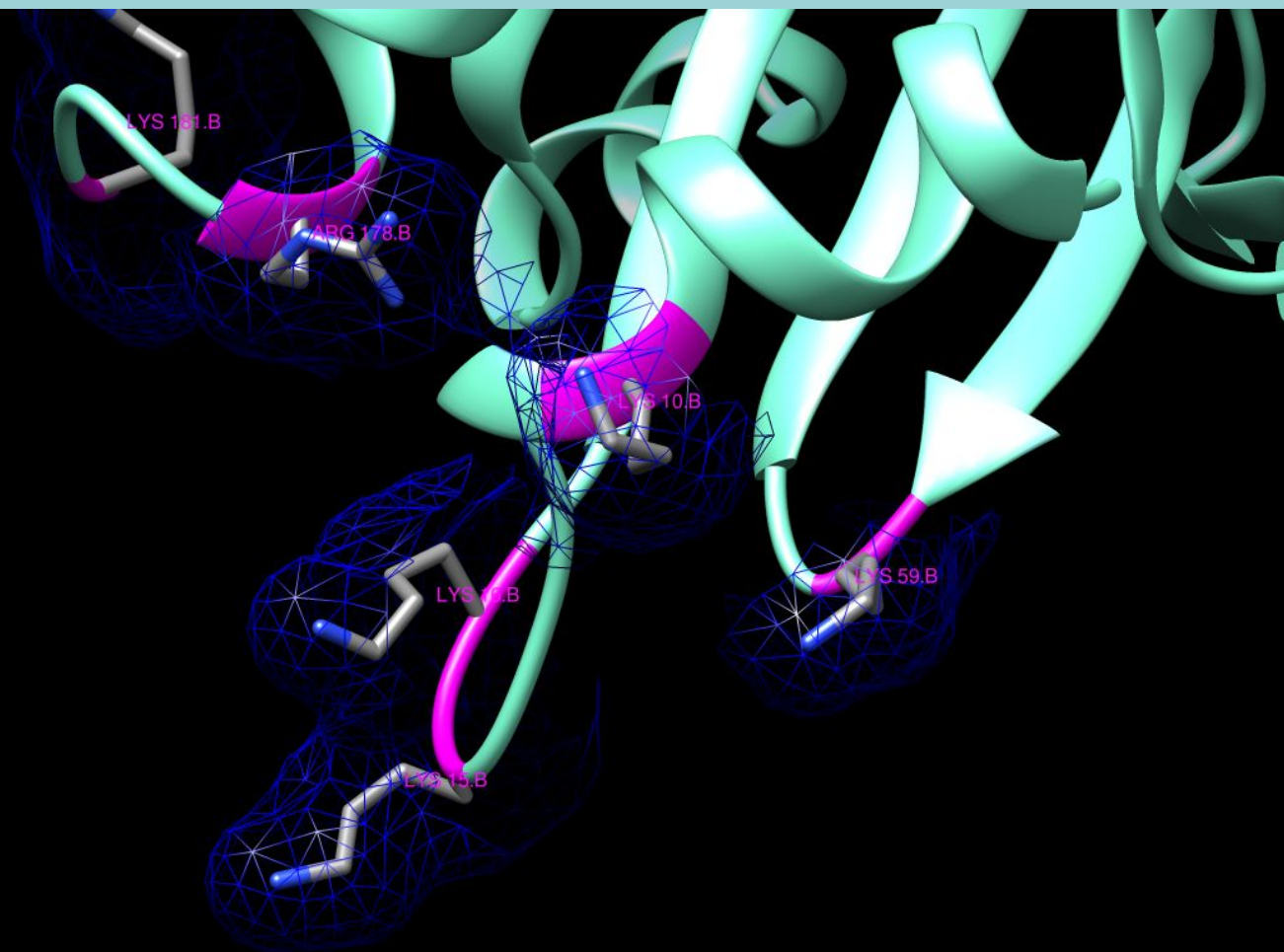
POSITIVE PATCH

ARF1



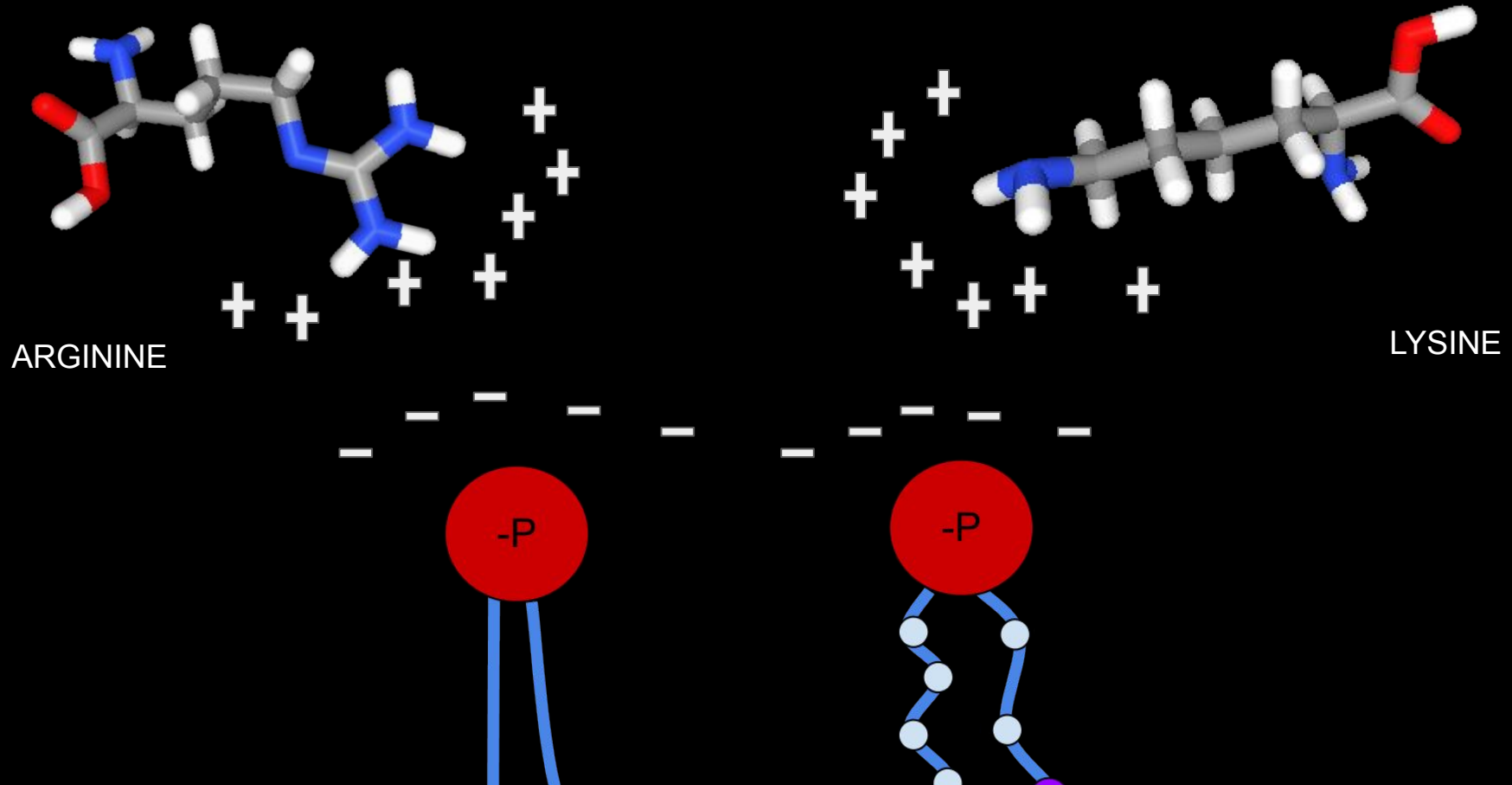
POSITIVE PATCH

ARF1



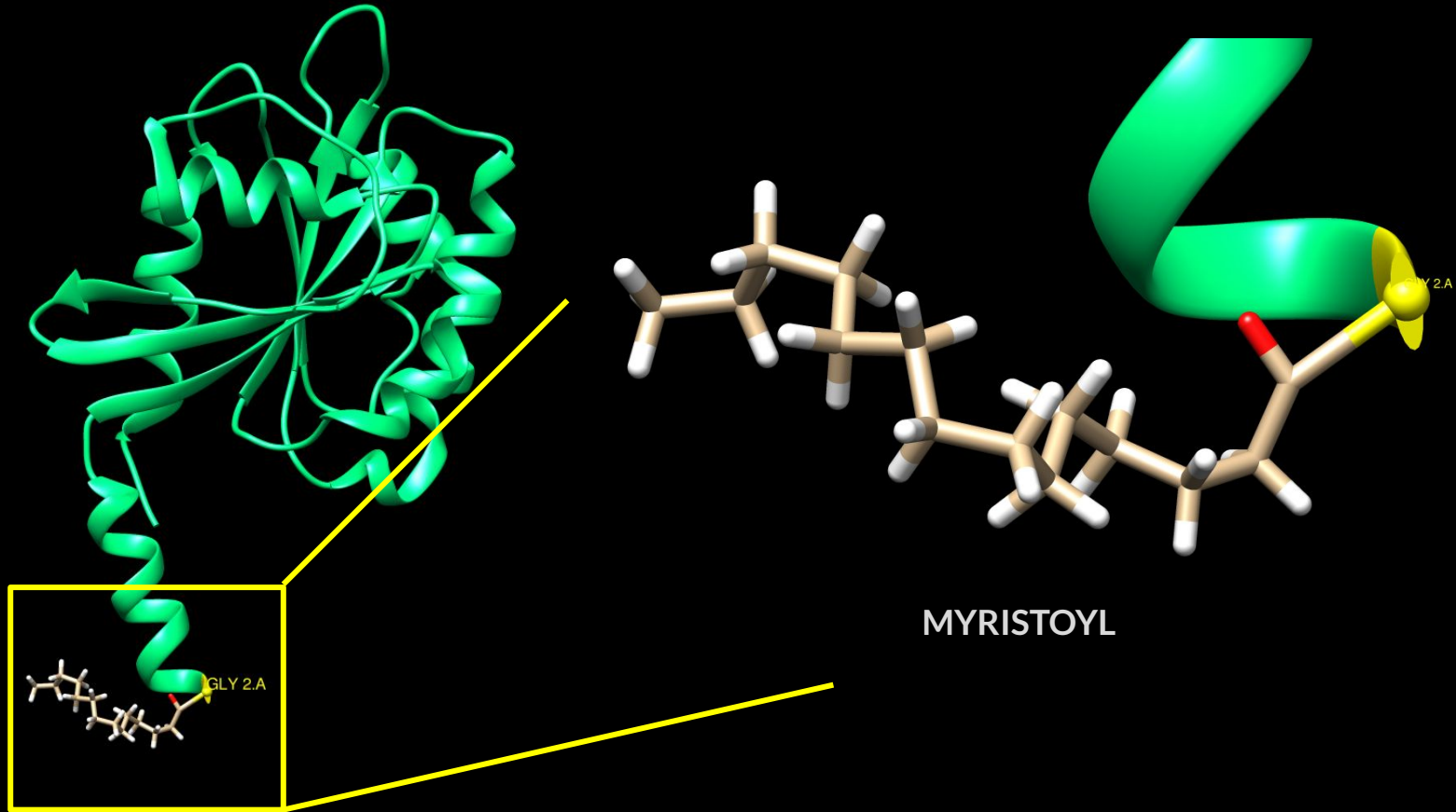
POSITIVE PATCH

ARF1



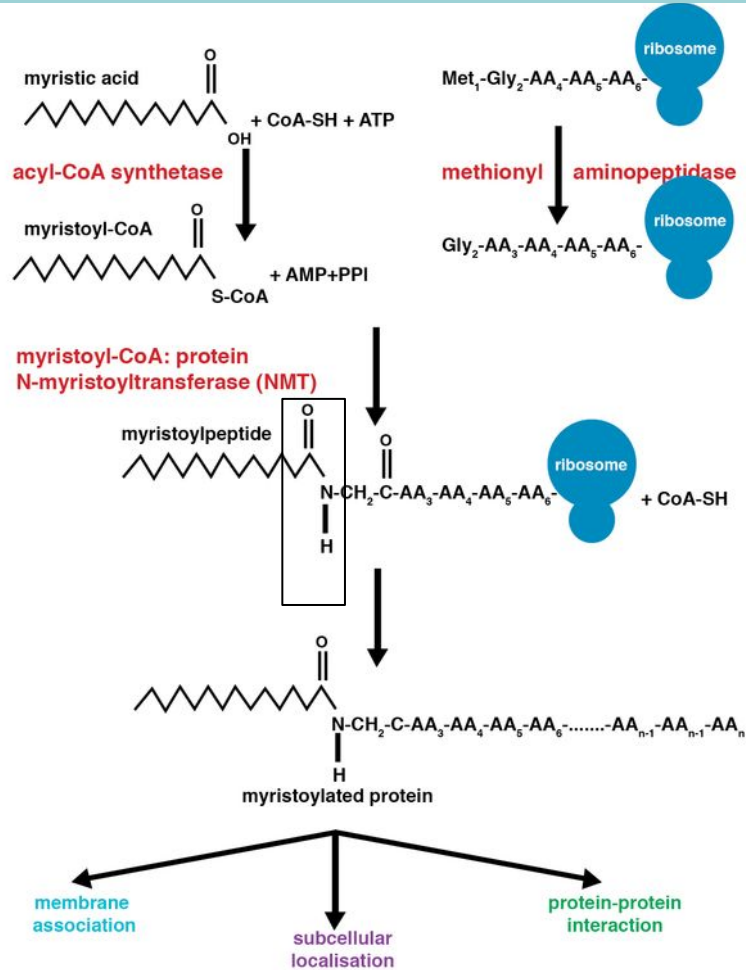
N-MYRISTOYLATION

ARF1



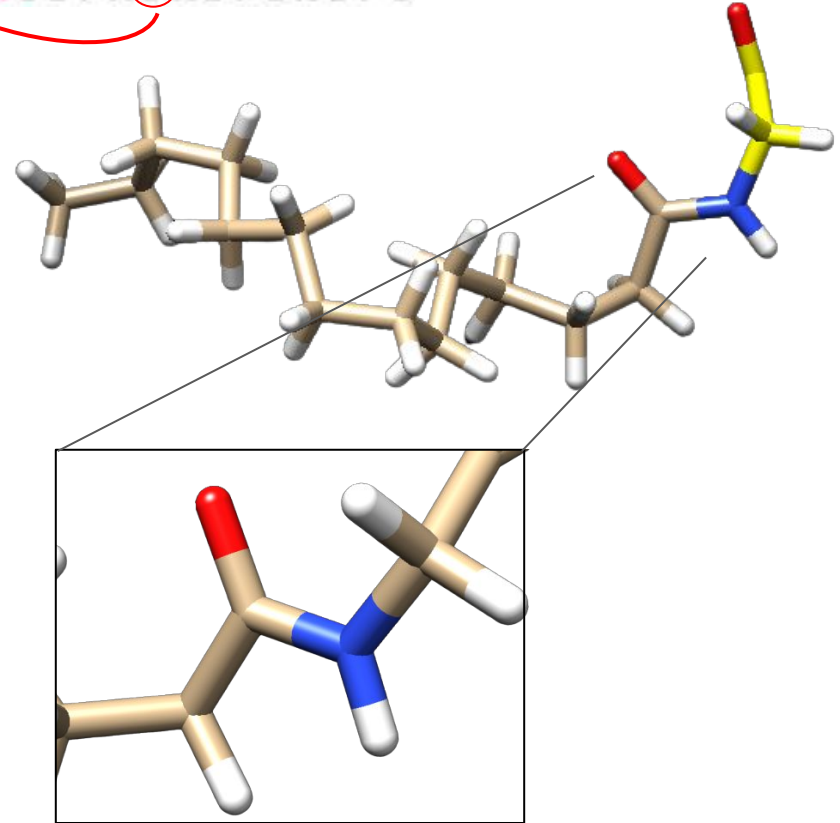
N-MYRISTOYLATION

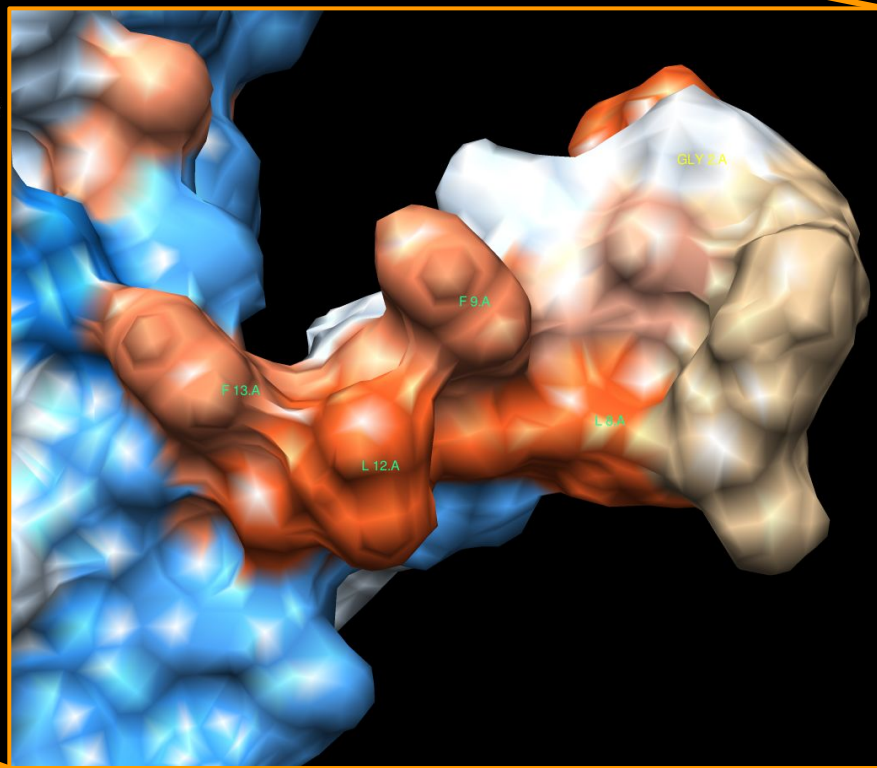
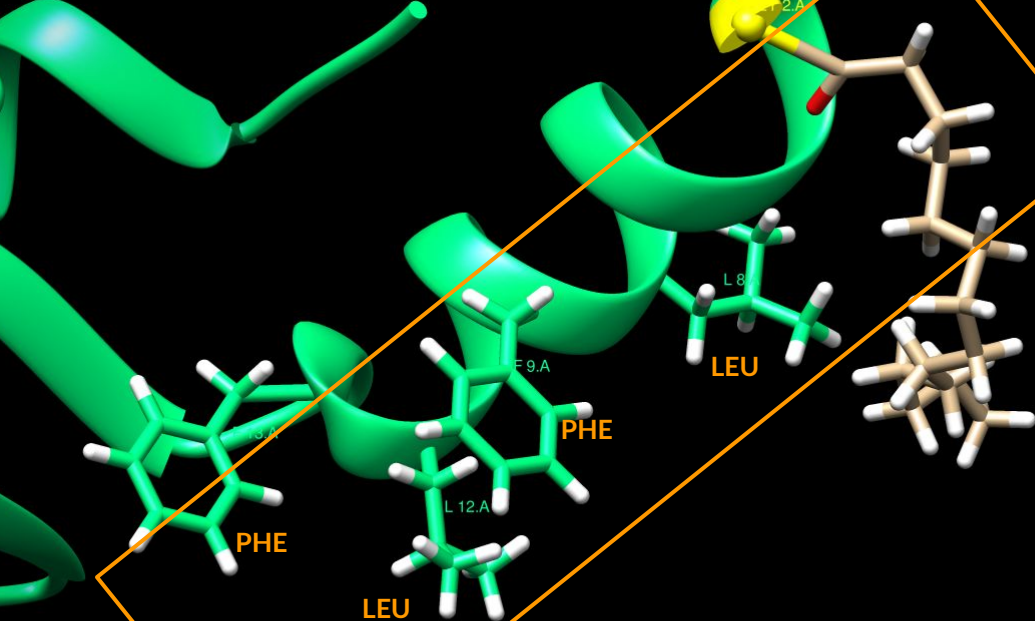
ARF1



_ G X X X S/T

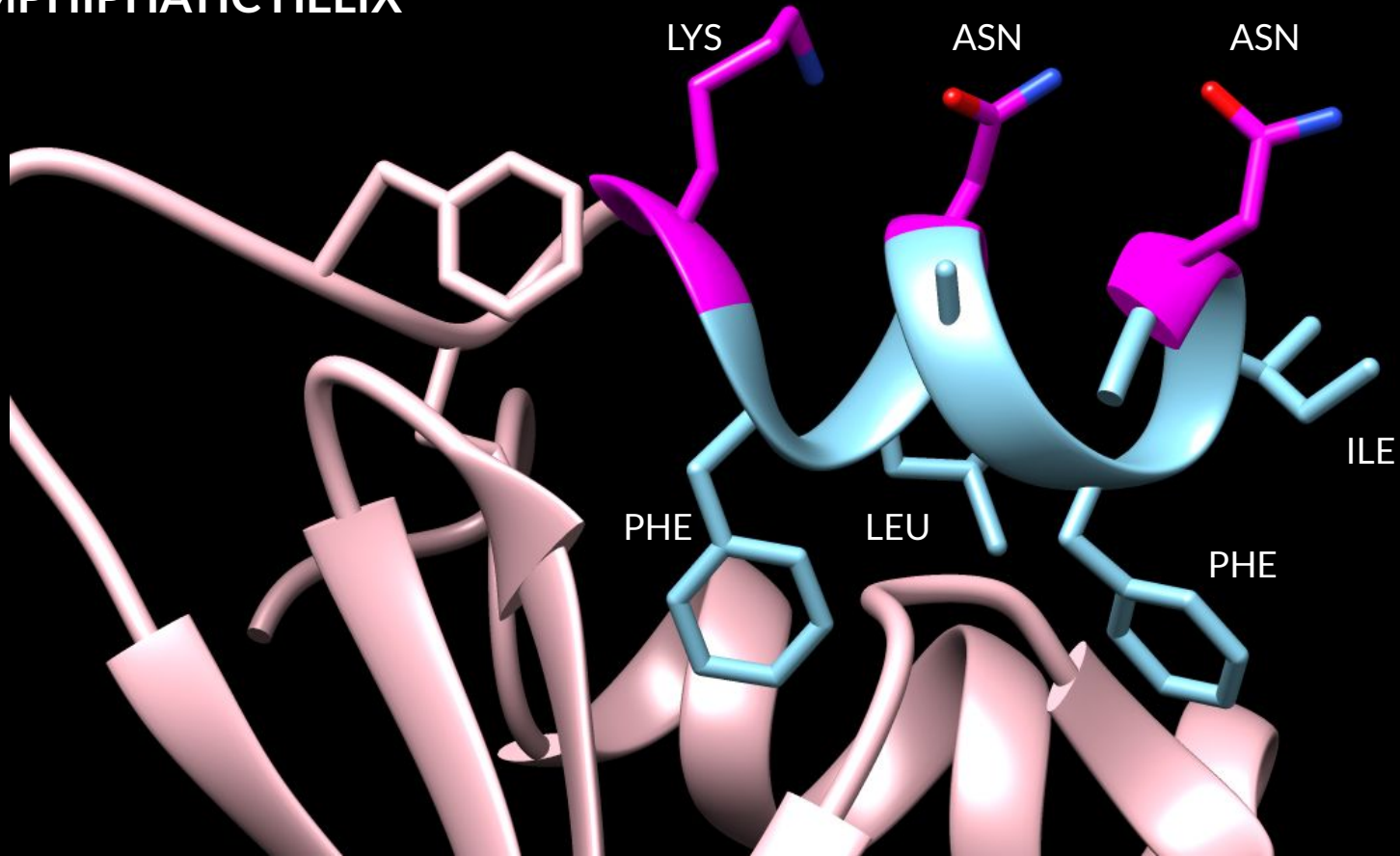
X G L F A S K L F S N L F G

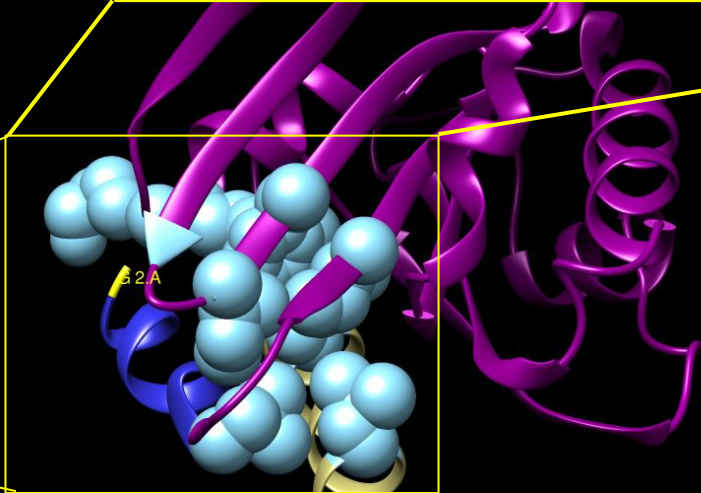
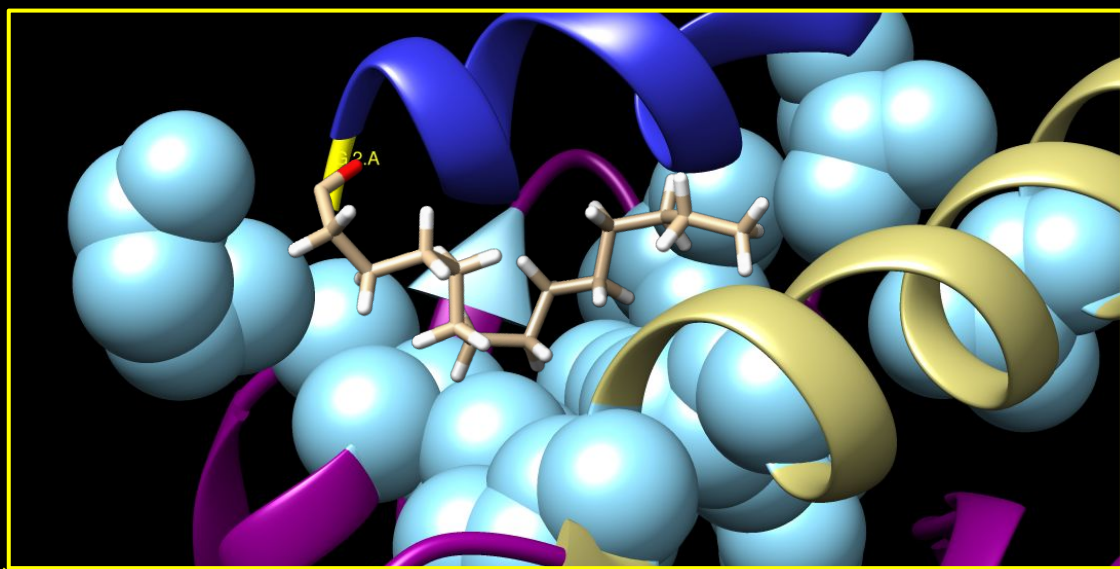
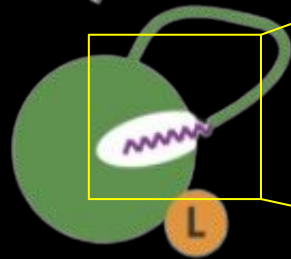
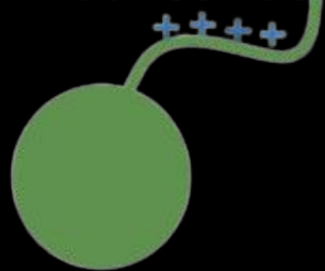
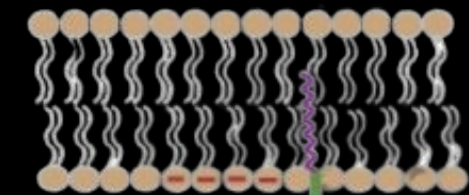




HIDROFOBICITY

AMPHIPHATIC HELIX



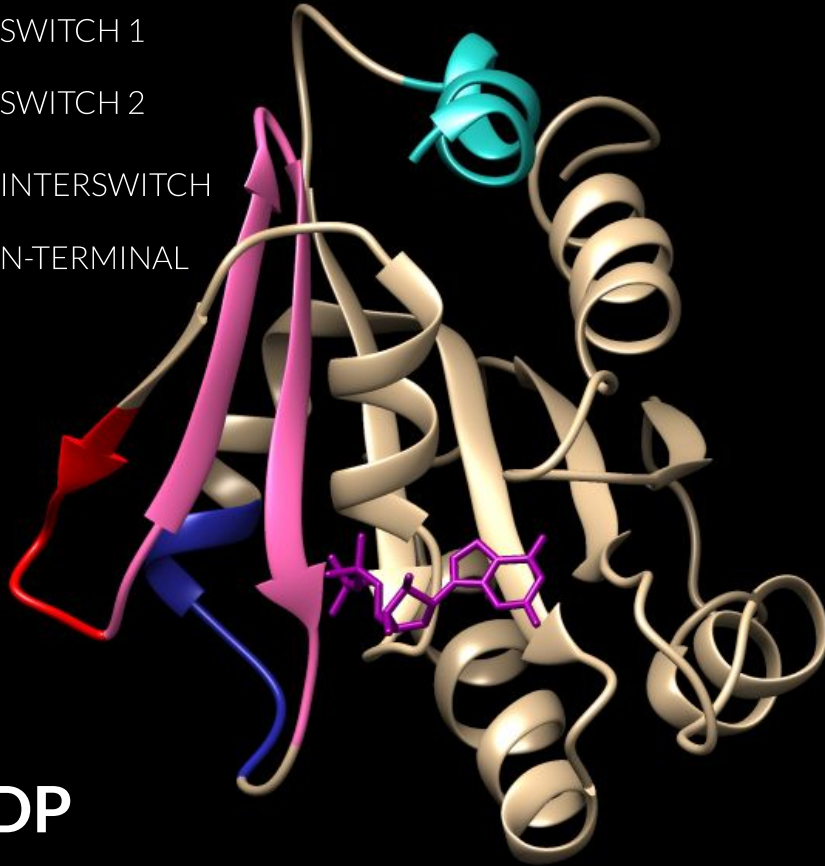


KEY STRUCTURAL FEATURES FOR GTP-GDP TRANSITION

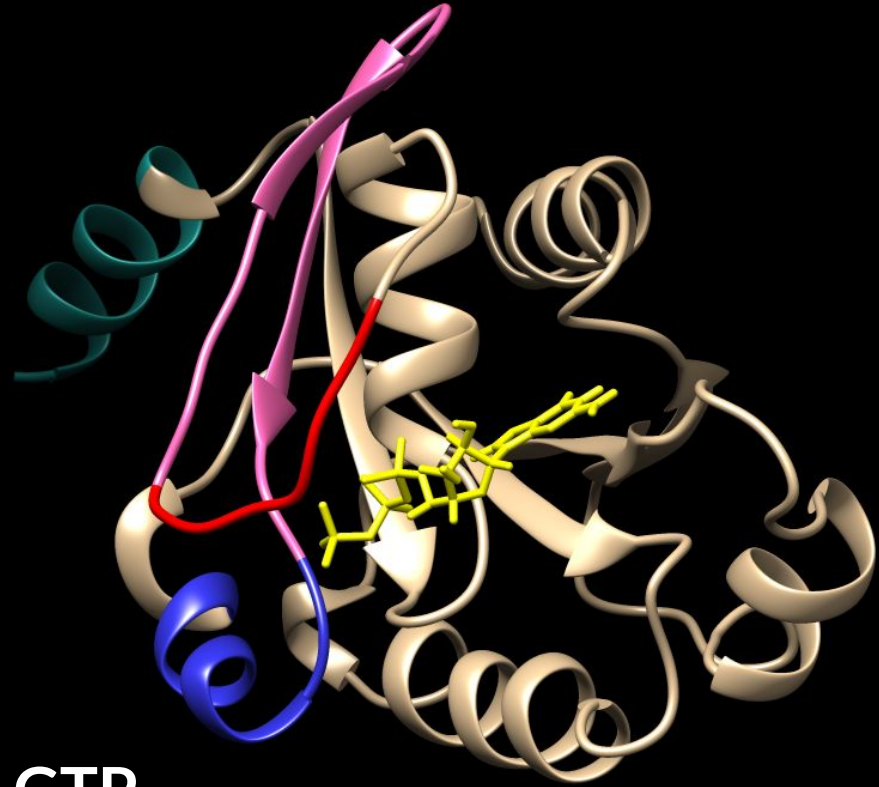
ARF1

- SWITCH 1
- SWITCH 2
- INTERSWITCH
- N-TERMINAL

GDP

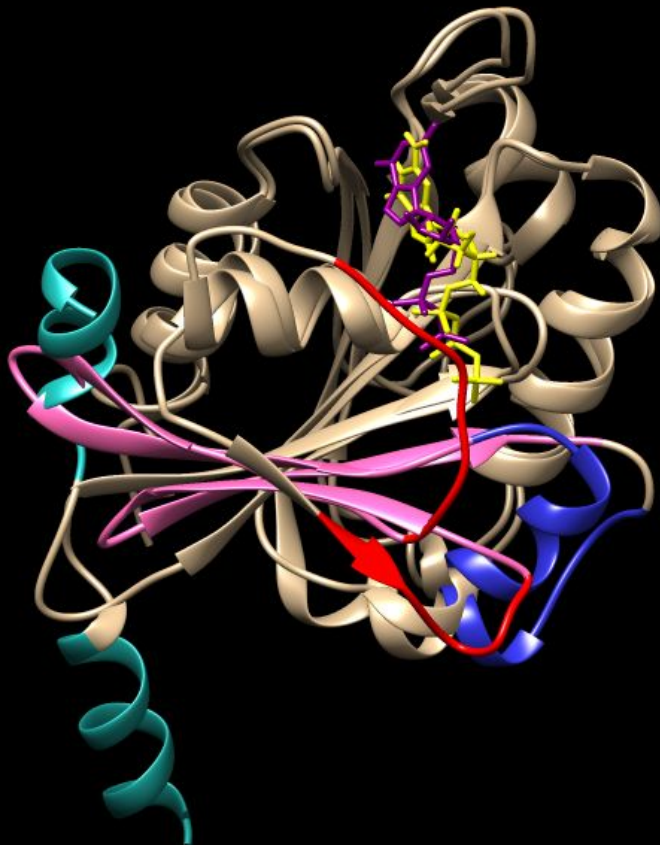


GTP



GTP-GDP SUPERIMPOSITION

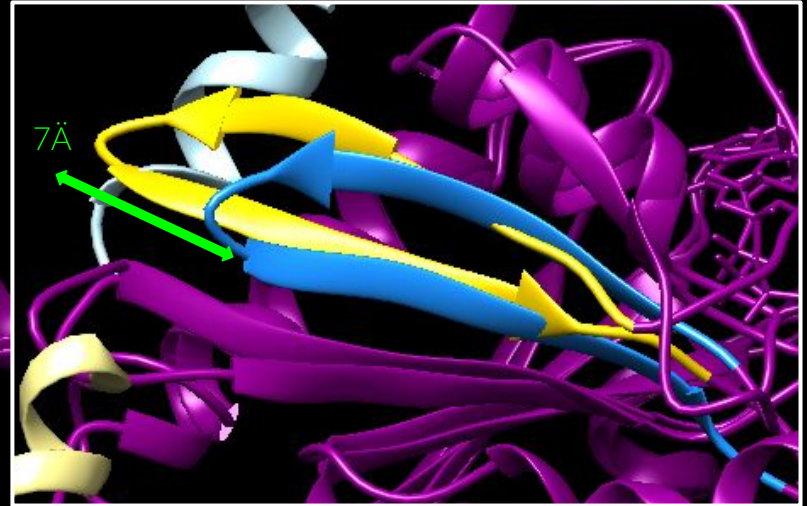
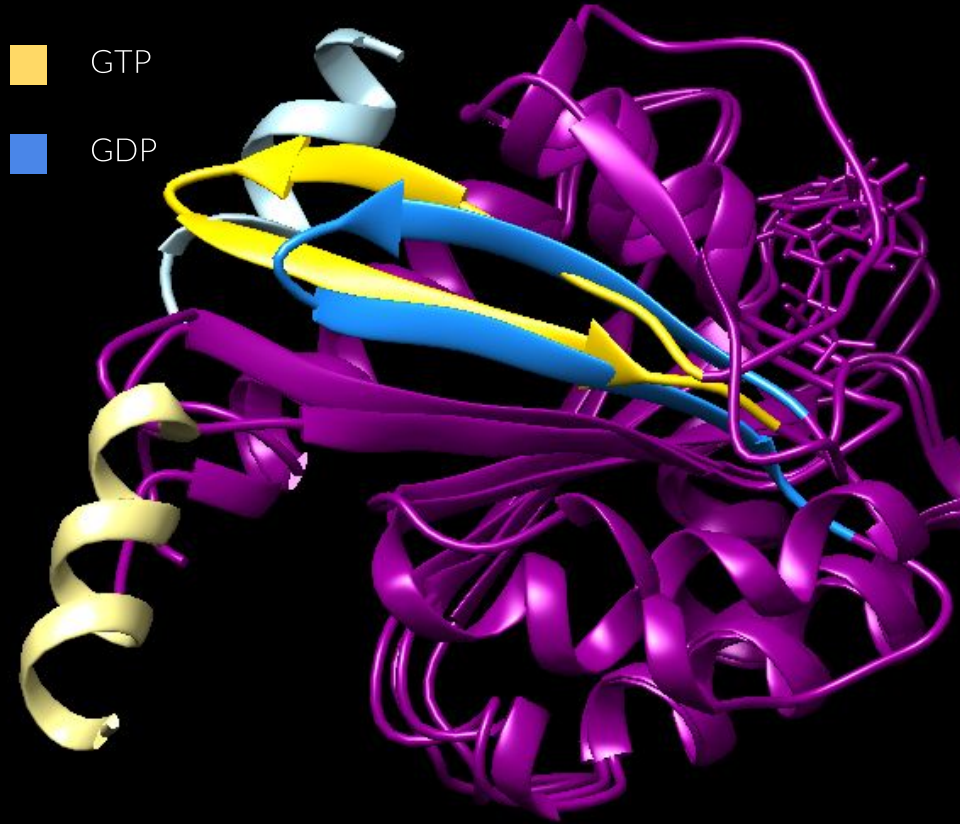
ARF1



RMSD: 1.070

INTERSWITCH

ARF1

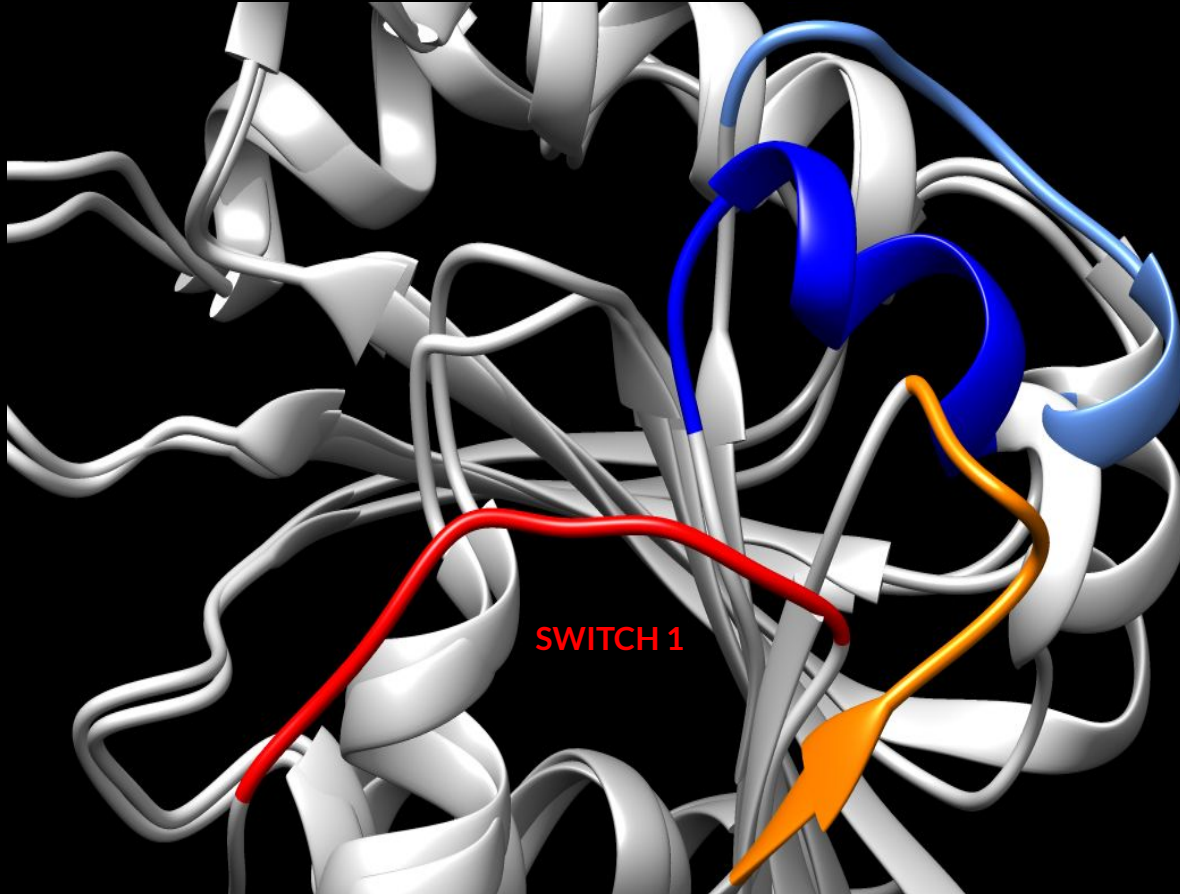


SWITCH 1 AND SWITCH 2 IN GDP-GTP

ARF1

■ GTP
■ GDP

■ GTP
■ GDP



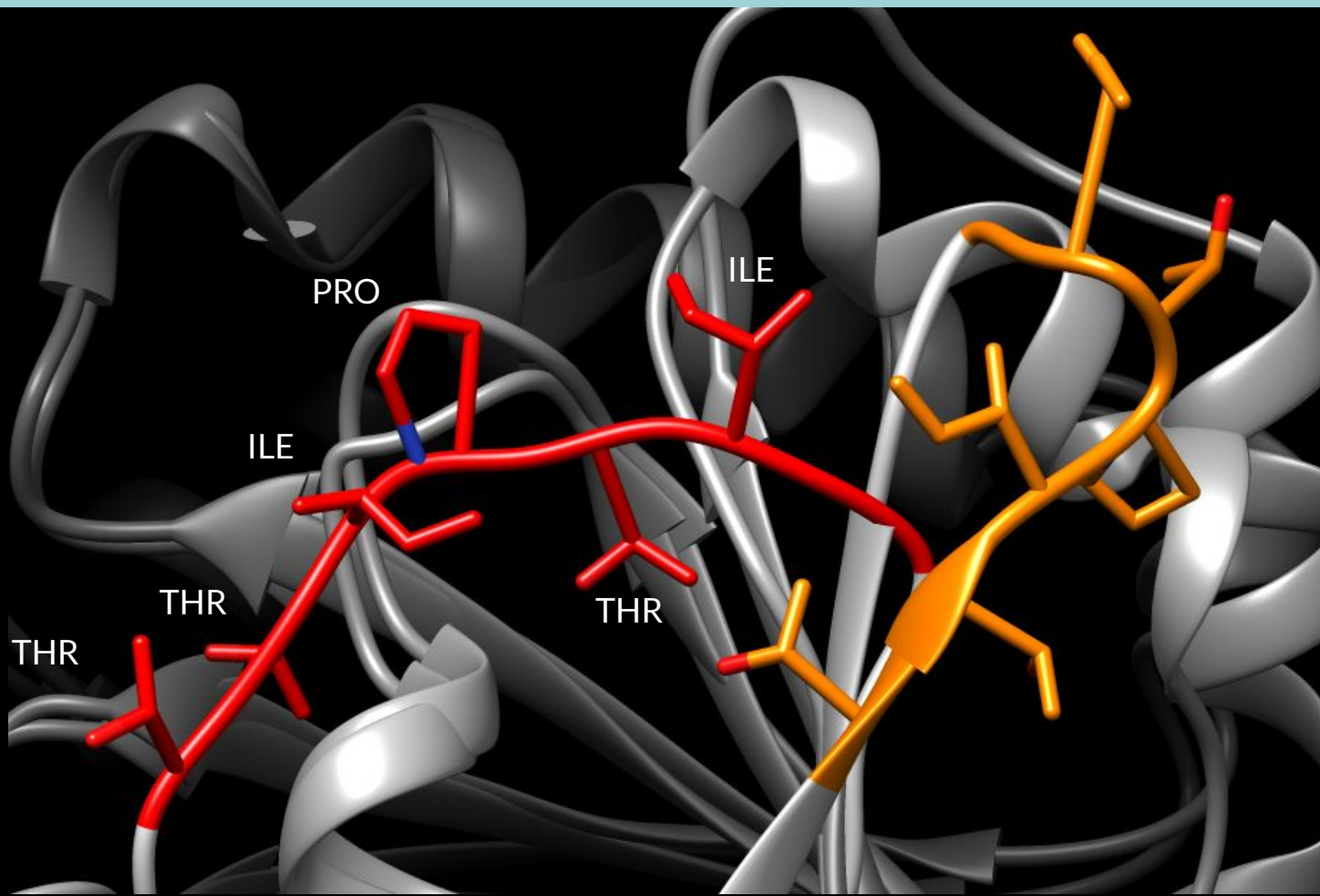
SWITCH 1

SWITCH 2

SWITCH 1

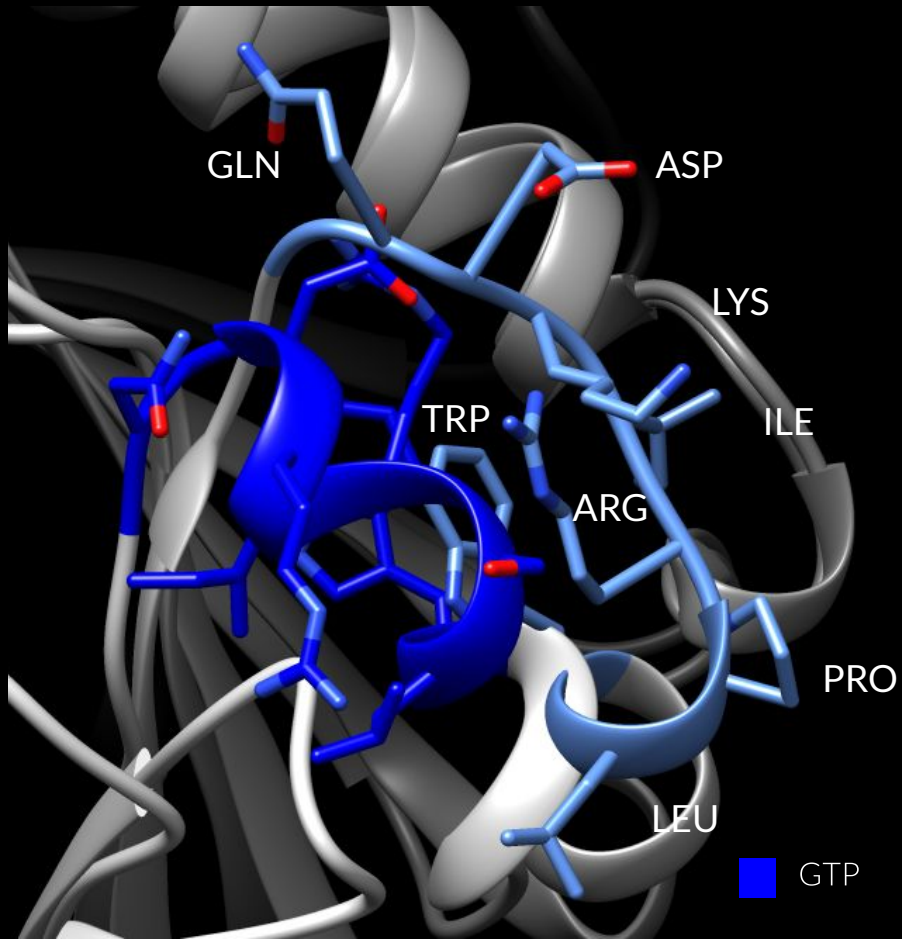
ARF1

■ GTP
■ GDP

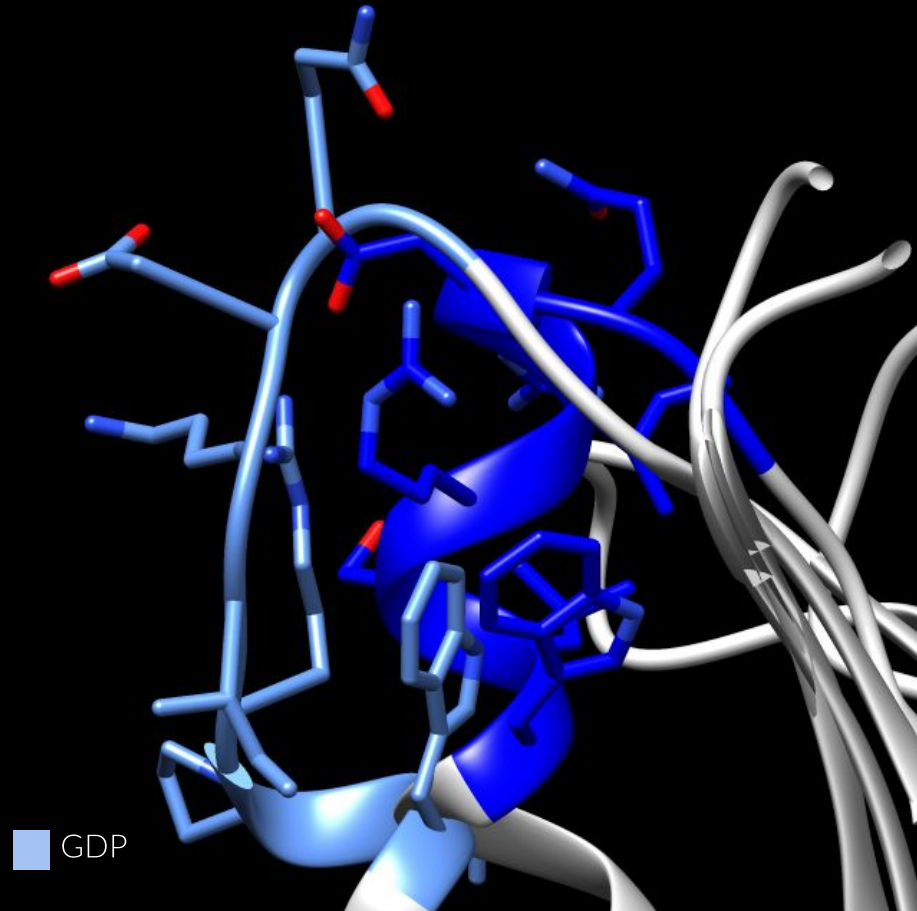


SWITCH 2

ARF1



GTP



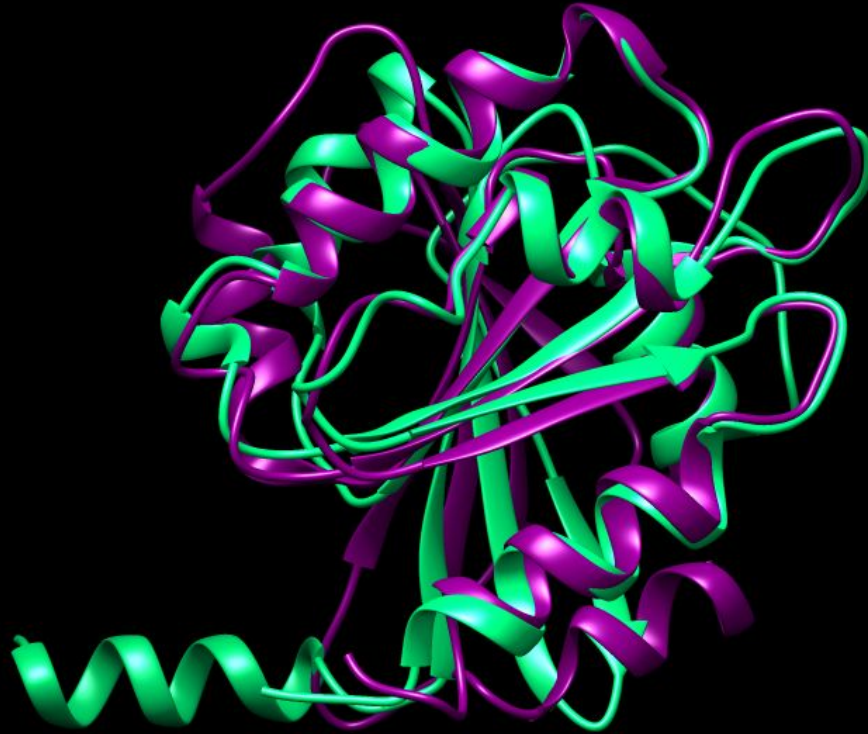
GDP

GTP-GDP SUPERIMPOSITION

ARF1

■ Arf1-GTP

■ Arf1-GDP



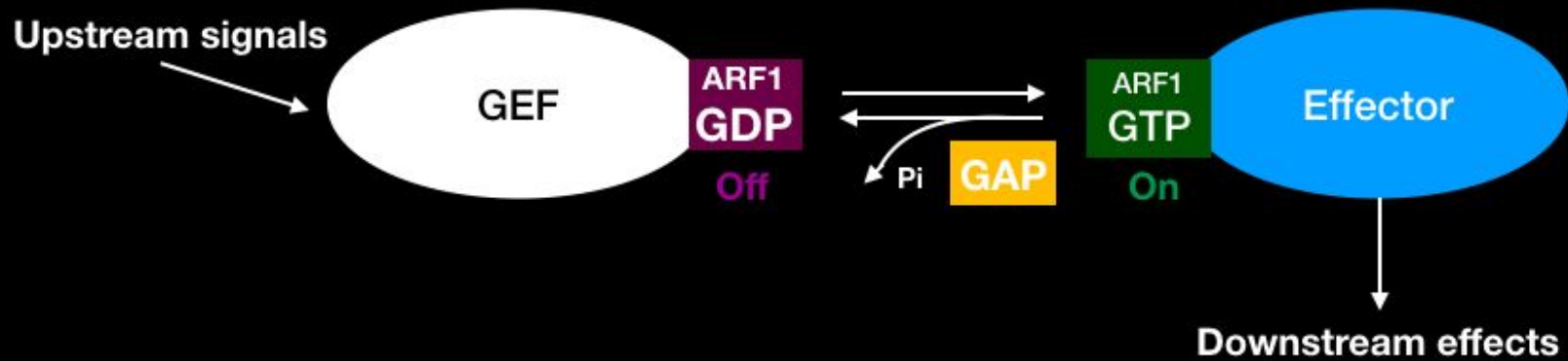
RMSD: 1.070

SUPERIMPOSITION GDP-GTP ALIGNMENT

ARF1

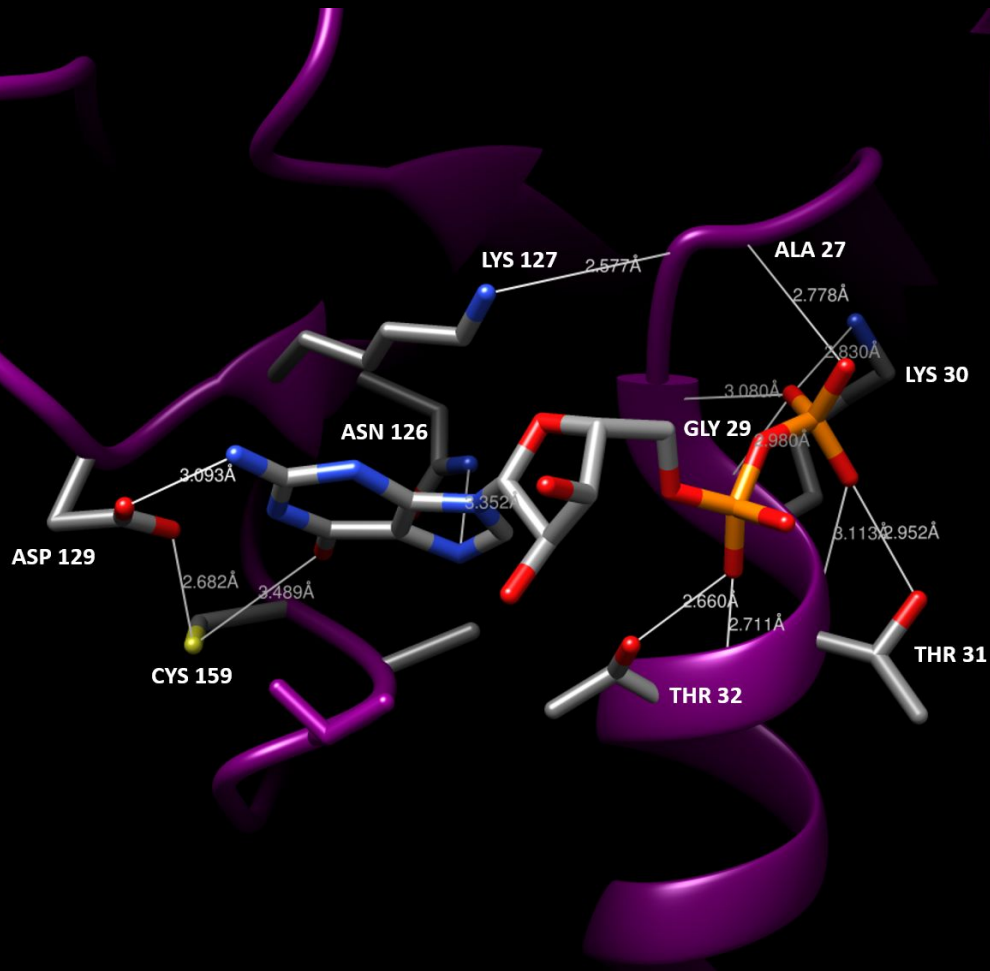
Consensus	1	- G l i a a k L F k	11	g L F G k K E M R I	21	L M V G L D a A G K	31	T T i L Y K L K L G	41	E i i T T I P T I G
Conservation		■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■
1hur.pdb (#0) chain B	2	- G N I F A N L F K		G L F G K K E M R I		L M V G L D A A G K		T T I L Y K L K L G		E I V T T I P T I G
2ksq20.pdb (#1) chain A	1	X G L F A S K L F S		N L F G N K E M R I		L M V G L D G A G K		T T V L Y K L K L G		E V I T T I P T I G
Consensus	51	F N V E c V q Y k N	61	I S F T V W D V G G	71	Q D k I R p L W R H	81	Y y q N T q G I I F	91	V V D S N D R s R i
Conservation		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■
1hur.pdb (#0) chain B	51	F N V E T V E Y K N		I S F T V W D V G G		Q D K I R P L W R H		Y F Q N T Q G L I F		V V D S N D R E R V
2ksq20.pdb (#1) chain A	51	F N V E C V Q Y C N		I S F T V W D V G G		Q D R I R S L W R H		Y Y C N T E G V I F		V V D S N D R S R I
Consensus	101	g E A R E e m q R M	111	L a E D E L c d A a	121	I L V F A N K Q D L	131	P e A M s A A E I T	141	e K L G L H S i R h
Conservation		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■
1hur.pdb (#0) chain B	101	N E A R E E L M R M		L A E D E L R D A V		L L V F A N K Q D L		P N A M N A A E I T		D K L G L H S L R H
2ksq20.pdb (#1) chain A	101	G E A R E V M Q R M		L N E D E L C N A A		W L V F A N K Q D L		P E A M S A A E I T		E K L G L H S I R N
Consensus	151	R p W y I Q A T C A	161	T S G e G L Y E G L	171	e W L S N q L k N q	181	k		
Conservation		■ ■ ■ ■ ■		■ ■ ■ ■ ■		■ ■ ■ ■ ■				
1hur.pdb (#0) chain B	151	R N W Y I Q A T C A		T S G D G L Y E G L		D W L S N Q L R N Q		K		
2ksq20.pdb (#1) chain A	151	R P W F I Q A T C A		T S G E G L Y E G L		E W L S N C L K N S		T		

Chimera



GDP BINDING SITE

ARF1

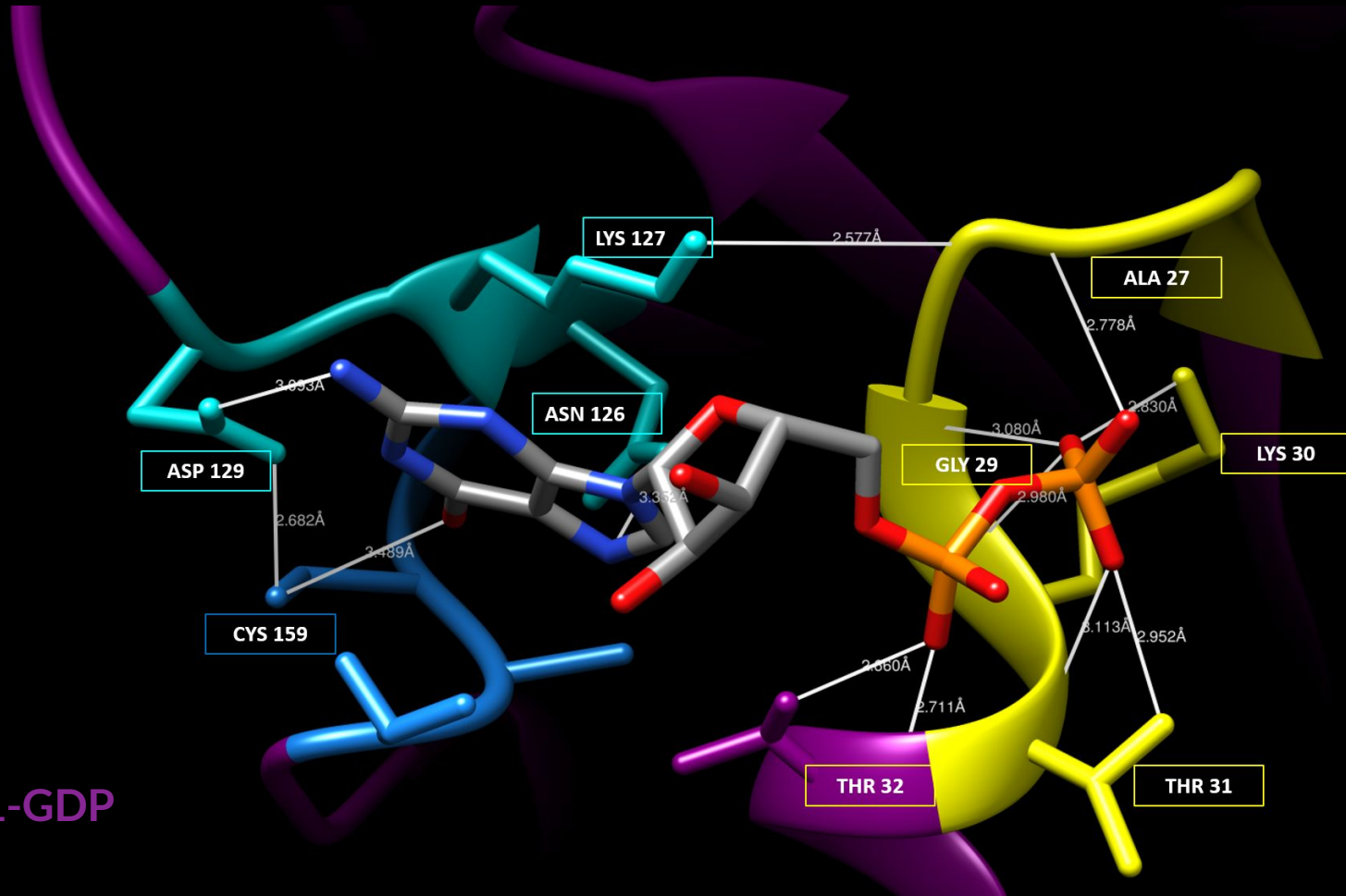


Arf1-GDP

GDP BINDING SITE vs G BOXES

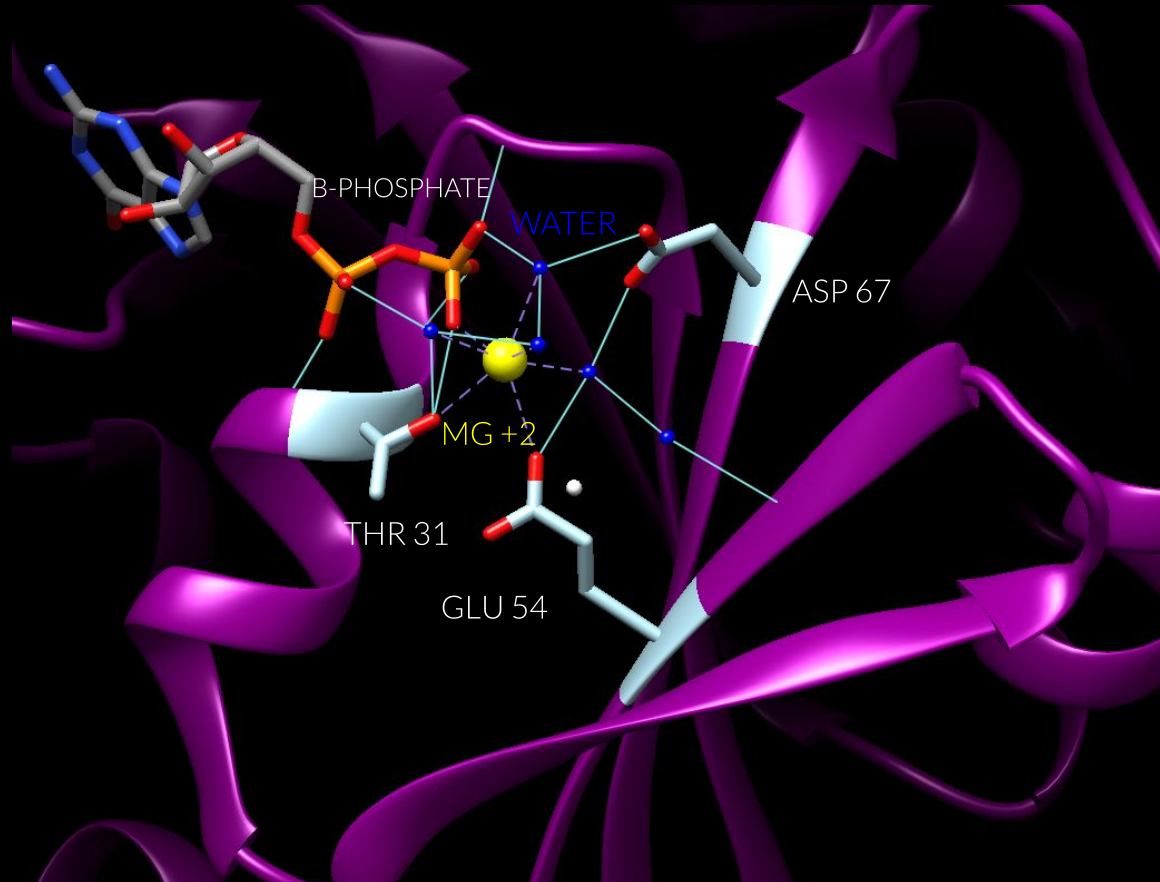
ARF1

- G1
- G2
- G3
- G4
- G5
- Arf1-GDP



MAGNESIUM INTERACTIONS IN GDP-STATE

ARF1



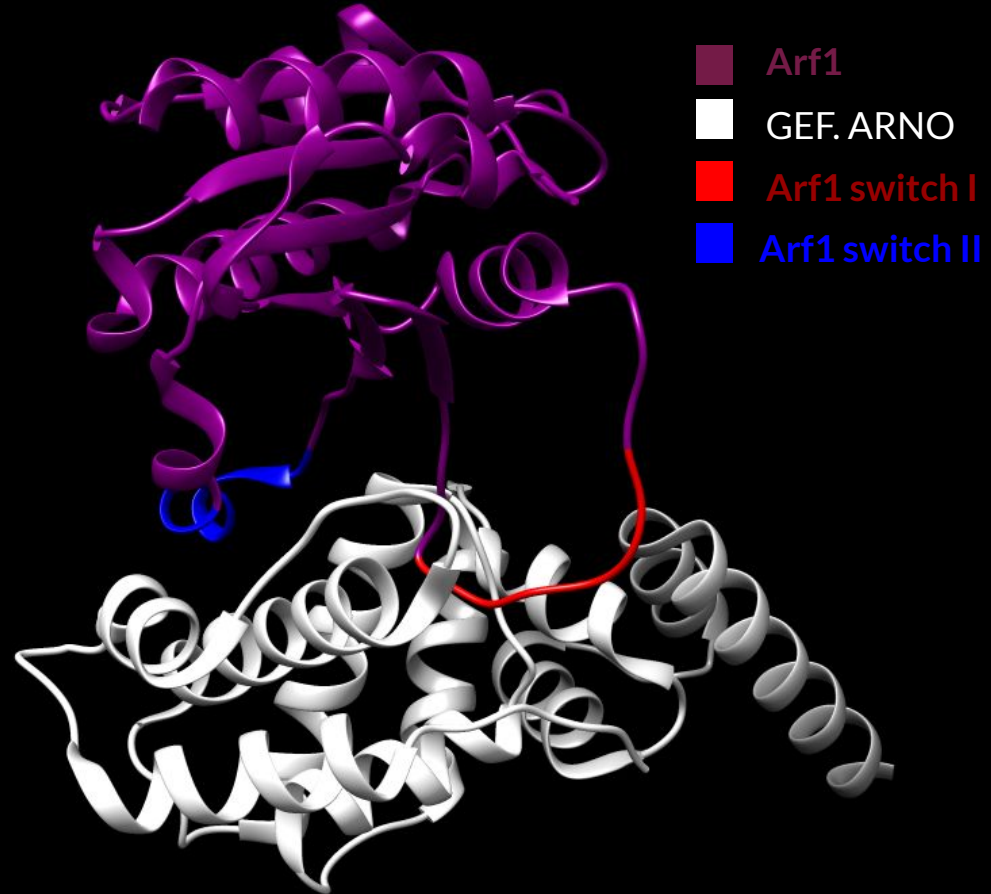
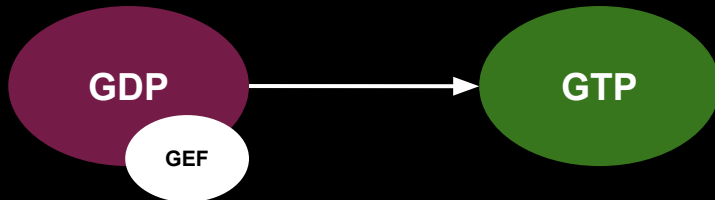
ARF1-GDP REGULATING FACTORS: GEF

ARF1

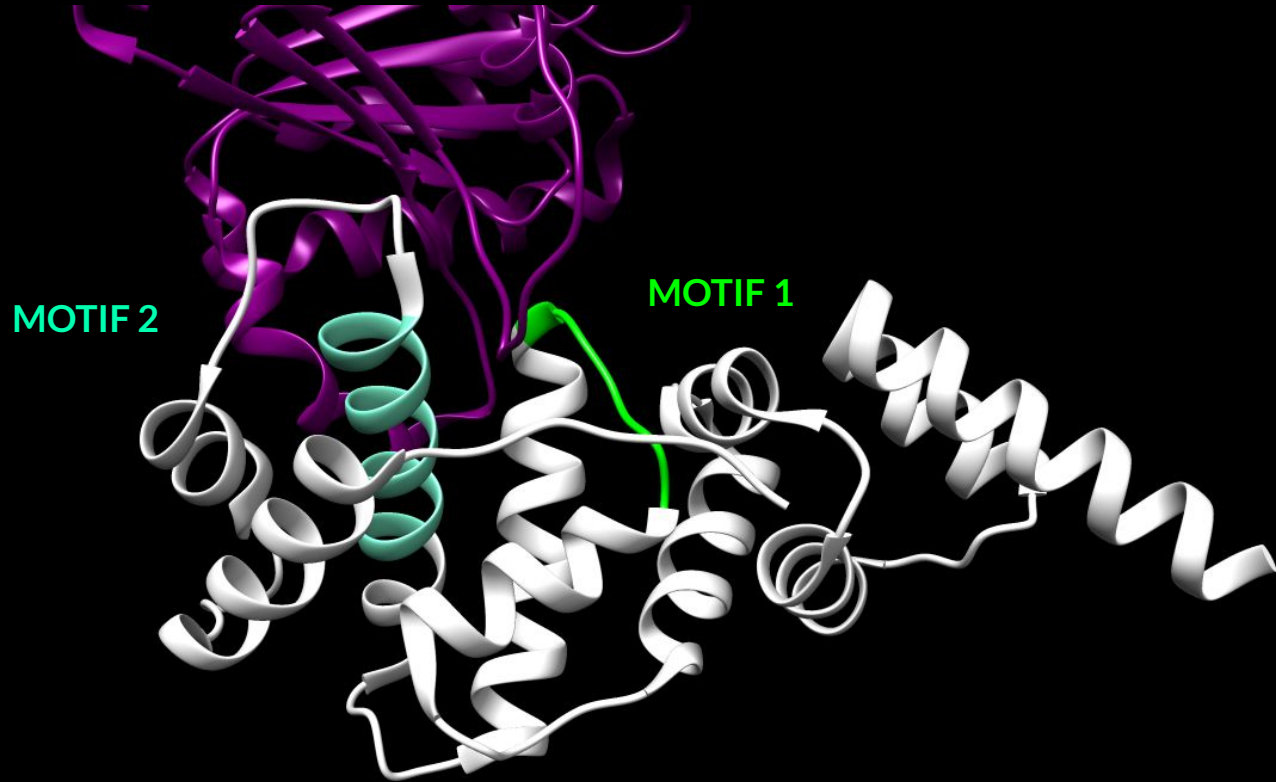
Guanine nucleotide exchange factors (GEF)

Sec7 domain

200 conserved amino acids



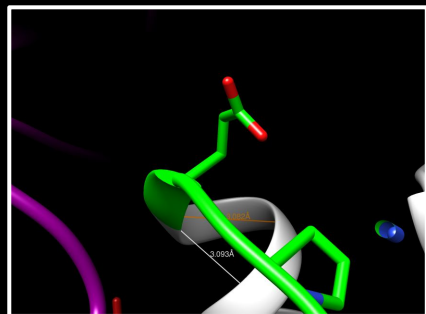
- Arf1
- GEF. ARNO
- Arf1 switch I
- Arf1 switch II



ARF1-GDP REGULATING FACTORS: GEF

ARF1

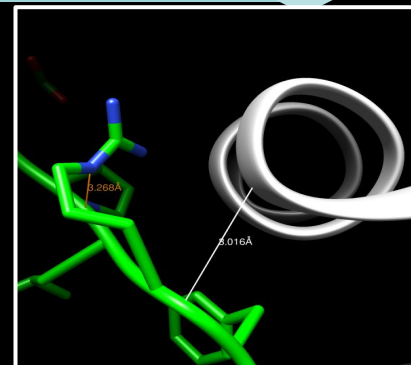
- Arf1
- GEF. ARNO
- Arf1 switch I
- Arf1 switch II



ASN 52

GLU156

3.093Å



LYS108

ARG 152

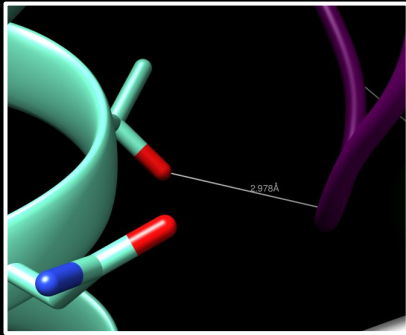
3.016Å

Arf1 - GEF stabilizing residues
(motif 1)

ARF1-GDP REGULATING FACTORS: GEF

ARF1

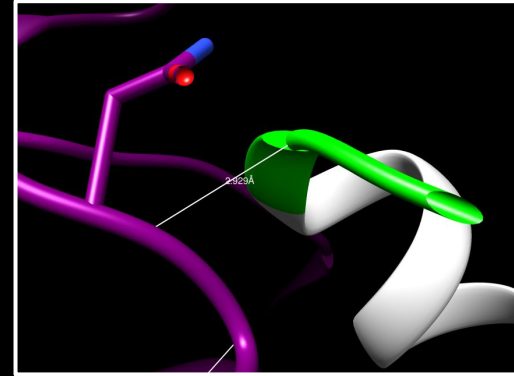
- Arf1
- GEF. ARNO
- Arf1 switch I
- Arf1 switch II



GLY 50

THR 197

2.978Å



ASN 52

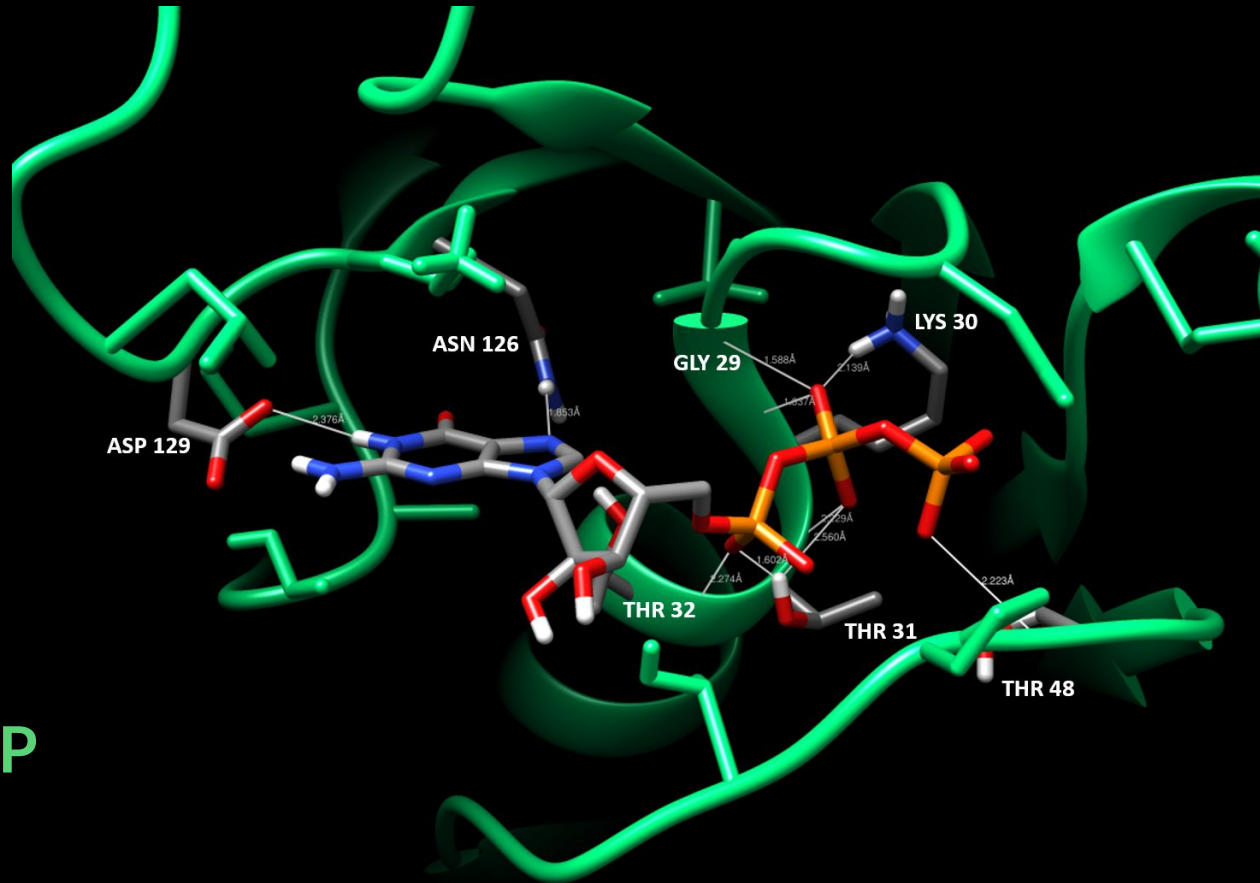
GLY158

2.929Å

Arf1 - GEF stabilizing residues
(motif 1 and motif 2)

ARF1-GTP: BINDING SITE

ARF1

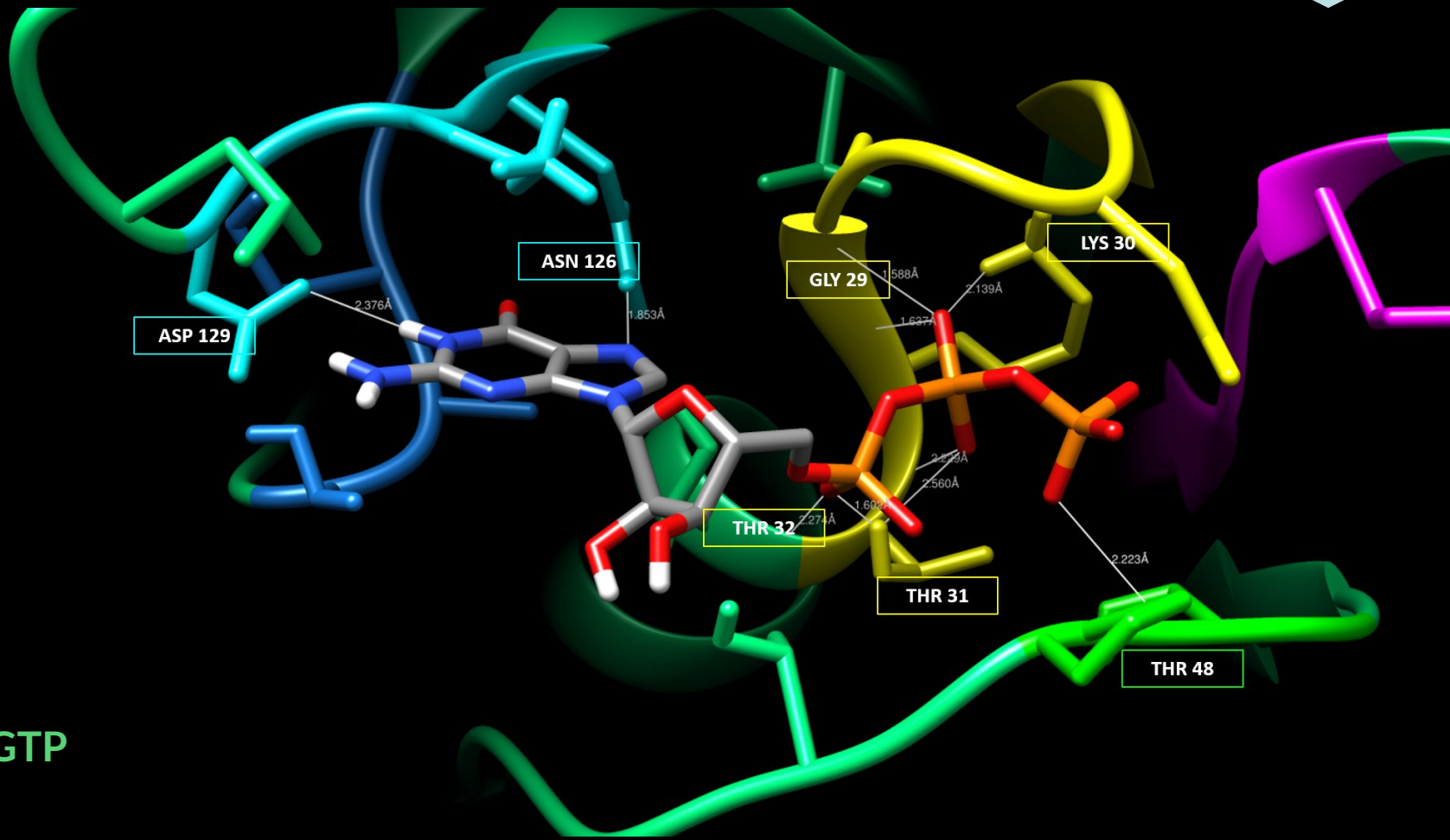


Arf1-GTP

ARF1-GTP: GTP BINDING SITE vs G BOXES

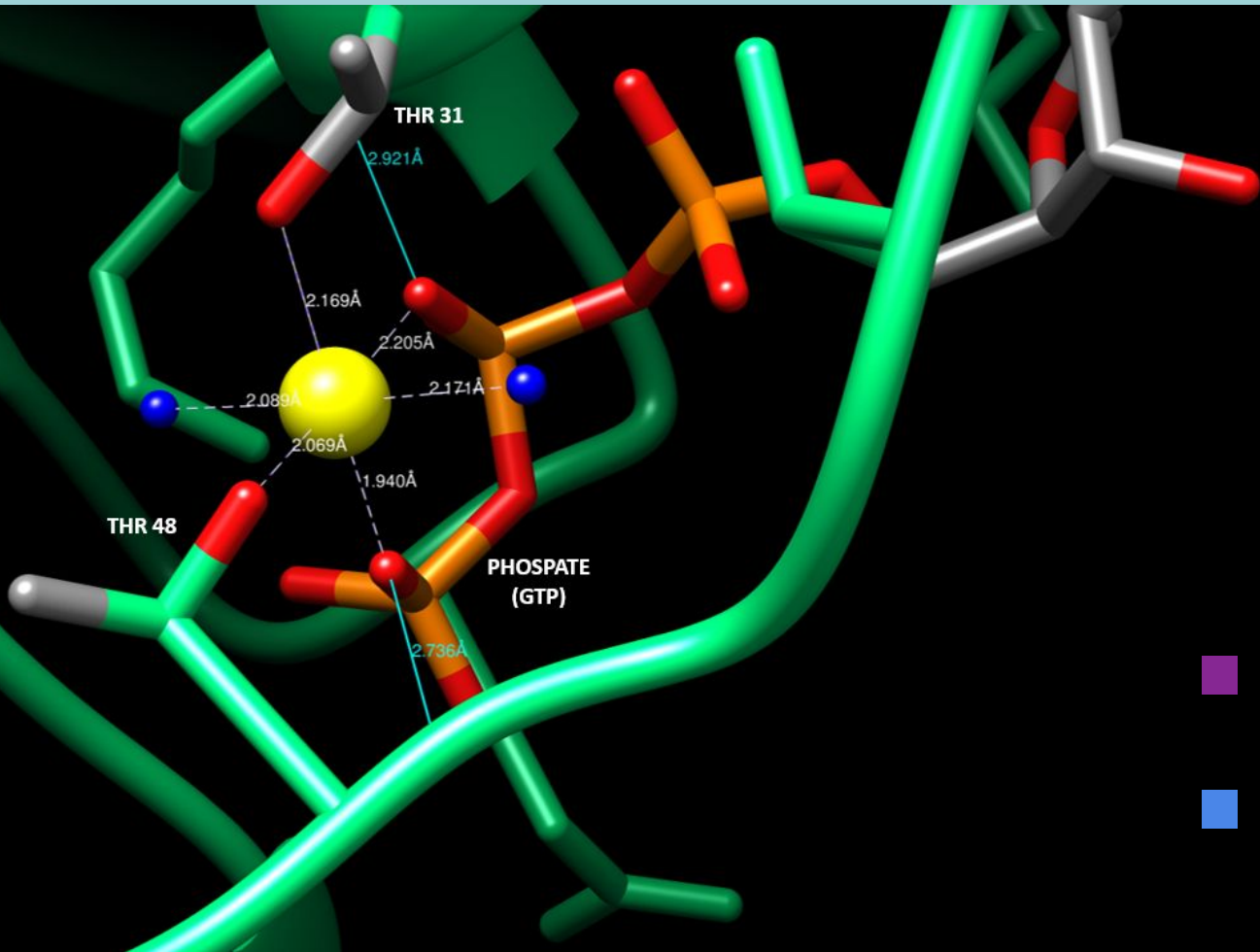
ARF1

- G1
- G2
- G3
- G4
- G5
- Arf1-GTP



MAGNESIUM INTERACTIONS IN GTP STATE

ARF1



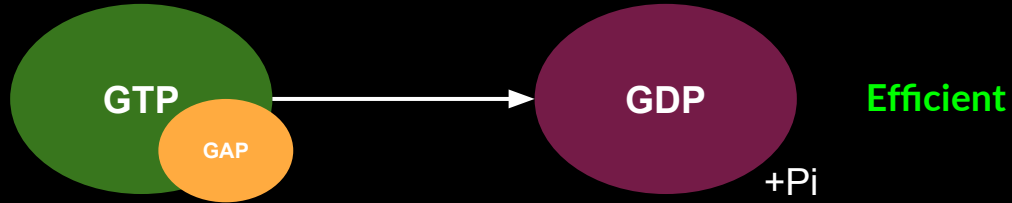
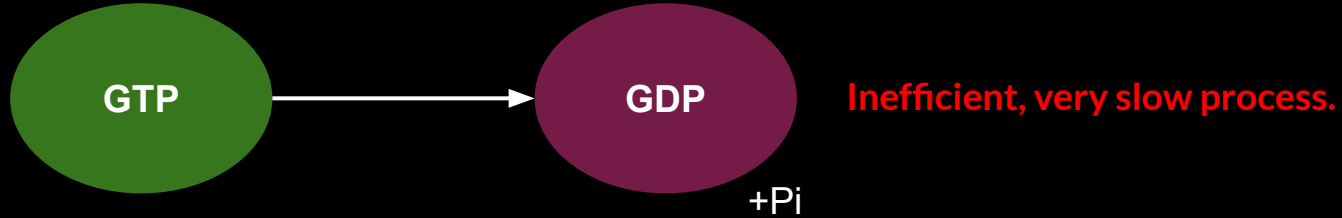
- Arf1-GTP (*Mus musculus*)
- Arf1-GDP (*Homo sapiens*)



RMSD: 0.518

GTP HYDROLYSIS

ARF1

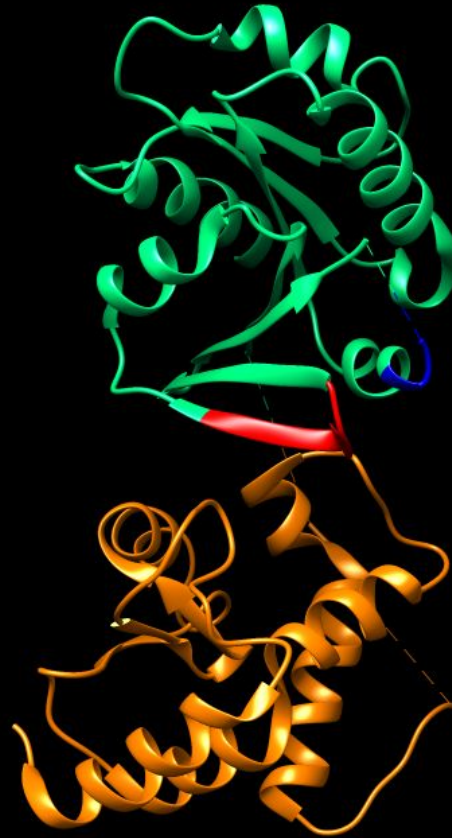


Lower transition state energy

GDP-like environment

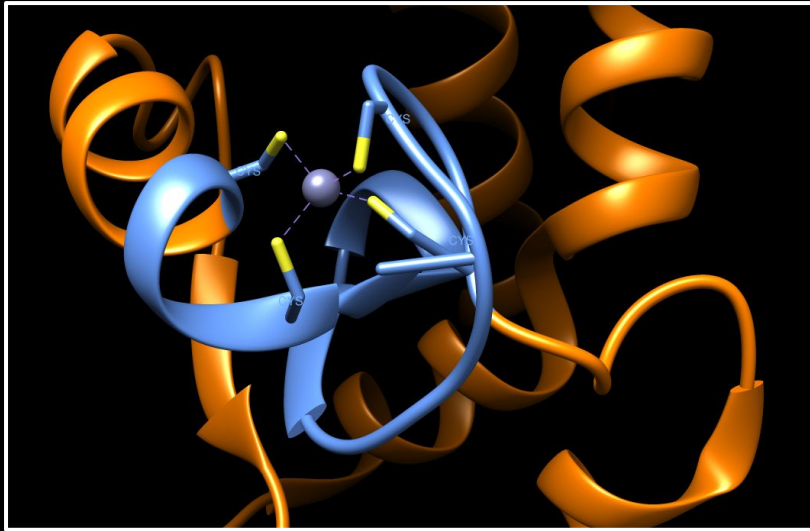
ARFGAP1-ARF1

- Arf1
- GAP1
- Arf1 switch I
- Arf1 switch II



ARFGAP1-ARF1

■ Arf1 ■ GAP1 domain
■ GAP1



Zn finger



ARFGAP1-ARF1

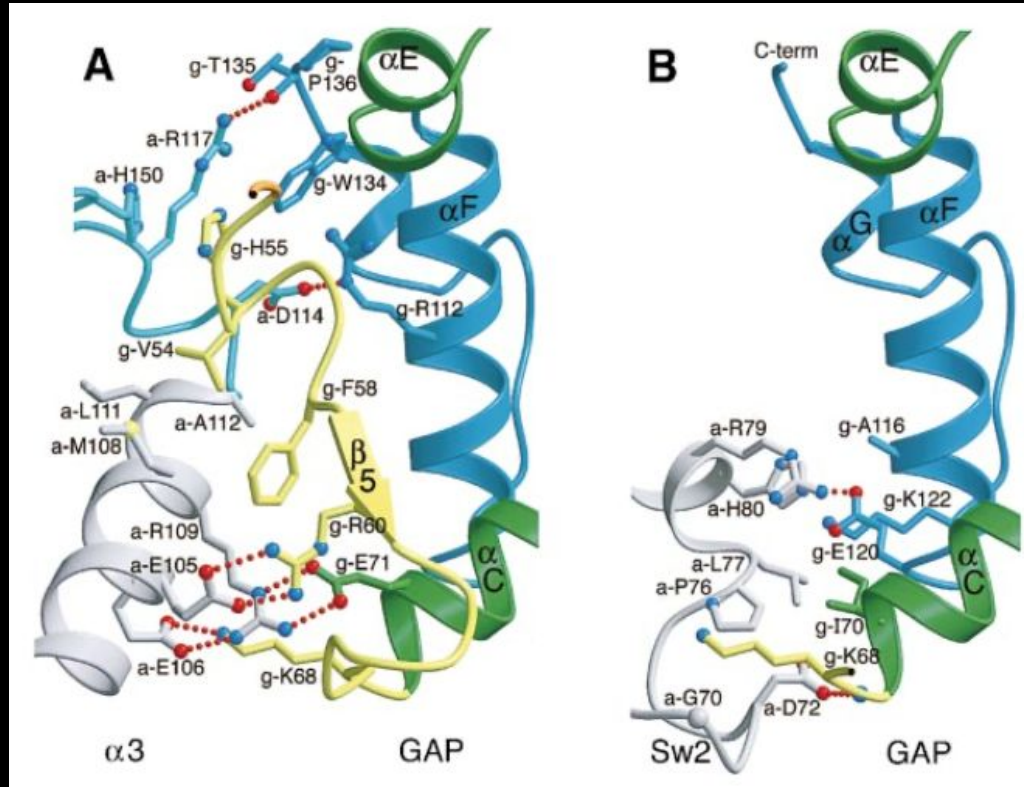


Fig 3. Goldberg J. Structural and Functional Analysis of the ARF1-ARFGAP Complex Reveals a Role for Coatomer in GTP Hydrolysis. Cell. 1999;96(6):893-902.

TAKE-HOME MESSAGES

- G boxes are conserved in all small GTPases, not only in human, but in a lot of other species.
- Monomeric G proteins share the fold of the alpha subunit of trimeric G proteins.
- Mg^{2+} ion is important for the function and structure.
- The transition from the GTP-active state to the GDP-inactive state needs collaboration of auxiliary molecules (GAPs).
- The exchange of the GDP for a GTP in the inactive proteins also needs an auxiliary molecule (GEF).
- Arf1 is a particular small GTPase which has specific features such as a myristoylation in the N-terminus.
- Arf1 is involved in many key cellular process, such as vesicular trafficking.



THANK YOU
FOR YOUR ATTENTION!!!
ANY QUESTIONS?

Núria Garcia, Maria Pujol, Irene García, Mònica Biarnes

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1. How is the general structural of Ras proteins?

- a. 4 beta strands and 4 alpha helices
- b. 6 beta strands and 5 alpha helices**
- c. 10 beta strands and no alpha helices
- d. 2 beta strands and 1 alpha helix
- e. A single beta propeller

2. How many small GTPases are conserved in all domains of life?

- a. All of them
- b. 20
- c. 10
- d. 8**
- e. None

3. What subunit of the trimeric G proteins is present in the monomeric GTPases?

- a. G alpha**
- b. G beta
- c. G gamma
- d. G delta
- e. None

4. Which inorganic ion is involved in the stabilization of the union between the guanine nucleotide and the G protein?

- a. Chloride ion (Cl⁻)
- b. Magnesium ion (Mg²⁺)**
- c. Iodide ion (I⁻)
- d. Sodium ion
- e. None

5. Which post-translational modification is present both in Arf and Ras families?

- a. Cysteine palmitoylation
- b. Cysteine isoprenylation
- c. Glycine myristoylation**
- d. Glycine isoprenylation
- e. Cysteine myristoylation

6. Choose the incorrect option:

- a. When G protein is bound to a GTP it is in its active state.
- b. Without GAP the monomeric G protein is unable to hydrolyse the GTP.**
- c. Both of them are incorrect
- d. GEF is responsible for GDP to GTP exchange.
- e. All of them are incorrect

7. Which are the main structures that present a conformational change in the GDP-GTP transition?

1. N-terminal
2. Switch 1 and Switch 2
3. Interswitch
4. C-terminal

a. 1,2,3

b. 2 i 4

c. 1 i 3

d. 1,2,3 i 4

e. 4

9. Choose the correct affirmation:

- a. There are 5 G boxes conserved across species and across the members of the same subfamily
- b. The G1 box is implicated in the purine nucleoside binding
- c. Both a and c are correct.
- d. The G2 box is implicated in the GDP/GTP binding site.

e. All of them are correct

8. Arf-1 main function is involved in:

a. Vesicle trafficking

- b. Cell growth
- c. Reproduction
- d. DNA repair
- e. Glycosylation

10. A key feature that enhance the association of Arf1 to the membrane is:

a. Positive patch

- b. Hydrophilic interactions
- c. Both a and b are correct
- d. Polybasic region
- e. All of them are incorrect



EXTRA

RAS FAMILY ALIGNMENT

RAS

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DIRA1_HUMAN      -MPSNDYRVVVFGAGGVGKSSLVLRFBVG--TFRDTYIPTIEDTYRQVISCD-KSVCTLQ
DIRA2_HUMAN      -MPSNDYRVAVFGAGGVGKSSLVLRFBVG--TFRESYIPTVEDTYRQVISCD-KSICTLQ
RAP1A_HUMAN      ---MREYKLVVLGSGGVGKSALTQVFVQG--IFVEKYDPTIEDSYRKQVEVD-CQQCMLE
RAP1B_HUMAN      ---MREYKLVVLGSGGVGKSALTQVFVQG--IFVEKYDPTIEDSYRKQVEVD-AQQCMLE
RAP2A_HUMAN      ---MREYKVVLGSGGVGKSALTQVFVTG--TFIEKYDPTIEDFYRKEIEVD-SSPSVLE
RAP2C_HUMAN      ---MREYKVVLGSGGVGKSALTQVFVTG--TFIEKYDPTIEDFYRKEIEVD-SSPSVLE
RAP2B_HUMAN      ---MREYKVVLGSGGVGKSALTQVFVTG--SFIEKYDPTIEDFYRKEIEVD-SSPSVLE
RASH_HUMAN       ---MTEYKLVVVGAGGVGKSALTIQLIQN--HFVDEYDPTIEDSYRKQVVID-GETCLLD
RASN_HUMAN       ---MTEYKLVVVGAGGVGKSALTIQLIQN--HFVDEYDPTIEDSYRKQVVID-GETCLLD
RASK_HUMAN       ---MTEYKLVVVGAGGVGKSALTIQLIQN--HFVDEYDPTIEDSYRKQVVID-GETCLLD
RRAS_HUMAN       -MSSETHKLVVVGSGGVGKSALTIQFIQS--YFVSDYDPTIEDSYTKICSVD-GIPARLD
RRAS2_HUMAN      -MAQEKYRLVVVGSGGVGKSALTIQFIQS--YFVTDYDPTIEDSYTKQCVID-DRAARLD
RASM_HUMAN       -MALPTYKLVVVGSGGVGKSALTIQFFQK--IFVPDYDPTIEDSYLKHTEID-NQWAILD
RALA_HUMAN       -MALALHKVIMVGSGGVGKSALTQLQFMYD--EFVEDYEPTKADSYRKKVVLG-GEEVQID
RALB_HUMAN       -MALALHKVIMVGSGGVGKSALTQLQFMYD--EFVEDYEPTKADSYRKKVVLG-GEEVQID
RIT1_HUMAN       -MDSREYKLVMLGAGGVGKSSAMTMQFISH--RFPEDHDPTIEDAYKIRIRID-DEPANLD
RIT2_HUMAN       -MESREYKVVMLGAGGVGKSSAMTMQFISH--QFPDYHDPTIEDAYKTQVRID-NEPAYLD
RASE_HUMAN       -MELPEYKAVVVGASGVGKSALTIQLNHQ--CFVEDHDPTIQDSYWKELTLD-SGDCILN
RHEB_HUMAN       MPQSKSRKIAILGYRSVGKSSLTIQFVEG--QFVDSYDPTIENTFTKLITVN-GQEYHLQ
REBL1_HUMAN      MPLVRYRKVVILGYRCVGKTSLAHQFVEG--EFSEGYDPTVENTYSKIVTLG-KDEFHLH
RASLC_HUMAN      MSPLEVN-LAILGRRGAGKSALTQVFLTK--RFISEYDPNLEDTYSSEETVD-HQPVHLR
RASD1_HUMAN      -MKKNCYRMVILGSSKVGKTAIVSRLTG--RFEDAYTPTIEDFHRKFYSIR-GEVYQLD
KBR52_HUMAN      --MGKSCKVVVCGQASVGKTSILEQLLYGNHVVGSEMIETQEDIYVGSJETDRGVREQVR
KBR51_HUMAN      --MGKGCKVVVCGLLSVGKTTAILEQLLYGNHTIGMEDCETMEDVYMASVETDRGVKEQLH

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RAS FAMILY ALIGNMENT

RAS

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DIRA1_HUMAN      ITDTTGS HQFPAMQRLSISKGHAFILVFSVTSKQSLEELGPIYKLIVQIK-----GSVE
DIRA2_HUMAN      ITDTTGS HQFPAMQRLSISKGHAFILVYSITSRQSLLEELKPIYEQICEIK-----GDVE
RAP1A_HUMAN      ILDTAGTEQFTAMRDLYMKNQGQGFALVYSITAQSTFNDLQDLREQILRVK-----DTED
RAP1B_HUMAN      ILDTAGTEQFTAMRDLYMKNQGQGFALVYSITAQSTFNDLQDLREQILRVK-----DTDD
RAP2A_HUMAN      ILDTAGTEQFASMRDLYIKNGQGFI LVYSLVNQQSFQDIKPMRDQIIRVK-----RYEK
RAP2C_HUMAN      ILDTAGTEQFASMRDLYIKNGQGFI LVYSLVNQQSFQDIKPMRDQIVRVK-----RYEK
RAP2B_HUMAN      ILDTAGTEQFASMRDLYIKNGQGFI LVYSLVNQQSFQDIKPMRDQIIRVK-----RYER
RASH_HUMAN       ILDTAGQEEYSAMRDQYMRTGEGFLCVFAINNTKSFEDIHQYREQIKRVK-----DSDD
RASN_HUMAN       ILDTAGQEEYSAMRDQYMRTGEGFLCVFAINNSKSFADINLYREQIKRVK-----DSDD
RASK_HUMAN       ILDTAGQEEYSAMRDQYMRTGEGFLCVFAINNTKSFEDIHHYREQIKRVK-----DSED
RRAS_HUMAN       ILDTAGQEEFGAMREQYMRAGHGFL LVFAINDRQSFNEVGKLFQTQILRVK-----DRDD
RRAS2_HUMAN      ILDTAGQEEFGAMREQYMRAGHGFL LVFSVTDGRGSFEEIYKFQRQILRVK-----DRDE
RASM_HUMAN       VLDTAGQEEFSAMREQYMRGTGDGFLIVYSVTDKASF EHVDRFHQLILRVK-----DRES
RALA_HUMAN       ILDTAGQEDYAAIRDNYFRSGEGFLCVFSITEMESFAATADFREQILRVK-----EDEN
RALB_HUMAN       ILDTAGQEDYAAIRDNYFRSGEGFL LVFSITEHESFTATAEFREQILRVK-----AEED
RIT1_HUMAN       ILDTAGQAEFTAMRDQYMRAGEGFI ICYSITDRRSFHEVREFKQLIYRVR-----RTDD
RIT2_HUMAN       ILDTAGQAEFTAMREQYMRGGEGFI ICYSVTDRQSFQEAAKFELIFQVR-----HTYE
RASE_HUMAN       VLDTAGQAIHRALRDQCLAVCDGVLGVFALDDPSSLIQL----QQIWATW-----GPHP
RHEB_HUMAN       LVDTAGQDEYSIFPQTYSIDINGYILVYSVTSIKSF EVIKVIHGKLLDMV-----GKVQ
REBL1_HUMAN      LVDTAGQDEYSILPYSFIIGVHGYYLVYSVTSLSHSFQVIESLYQKLHEGH-----GKTR
RASLC_HUMAN      VMDTADLDTPRNCER-YLNWAHAFLVYVSVD SRQSFDSSSSYLELLALHA-----KETQ
RASD1_HUMAN      ILDTSGNHPPFAMRRLSILTGDFILVFSLDNRDSFE EVQRLRQQILDTSKSLKNKTEN
KBR52_HUMAN      FYDTRGLRDGAELPRHCFSDTGYYLVYSTDSRESFQRV ELLKKEIDKSK-----DKKE
KBR51_HUMAN      LYDTRGLQEGVELPKHYFSFADGFVLVYSVNNLESFQRV ELLKKEIDKFK-----DKKE

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RAS FAMILY ALIGNMENT

RAS

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DIRA1_HUMAN      D-IPVMLVGNKCDET-QREVDTREAAVAQEWK--CAFMENTSAC-MNYNVKELFQELLTL
DIRA2_HUMAN      S-IPIMLVGNKCDESPSREVQSSEAEALARTWK--CAFMENTSAC-LNHNVKELFQELLNL
RAP1A_HUMAN      --VPMILVGNKCDLEDERVVGKEQGQNLARQWCN-CAFLESSAK-SKINVNEIFYDLVRQ
RAP1B_HUMAN      --VPMILVGNKCDLEDERVVGKEQGQNLARQWNN-CAFLESSAK-SKINVNEIFYDLVRQ
RAP2A_HUMAN      --VPVILVGNKVDLESEREVSSSEGRALAEWG--CPFMETSAC-SKTMVDELFAEIVRQ
RAP2C_HUMAN      --VPLILVGNKVDLEPEREVMSSSEGRALAEWG--CPFMETSAC-SKSMVDELFAEIVRQ
RAP2B_HUMAN      --VPMILVGNKVDLEGEREVSYGEGKALAEWS--CPFMETSAC-NKASVDELFAEIVRQ
RASH_HUMAN       --VPMVLVGNKCDLAA-RTVESRQAQDLARSYG--IPYIETSAC-TRQGVEDAFYTLVRE
RASN_HUMAN       --VPMVLVGNKCDLPT-RTVDTKQAHELAKSYG--IPFIETSAC-TRQGVEDAFYTLVRE
RASK_HUMAN       --VPMVLVGNKCDLPS-RTVDTKQADLARSYG--IPFIETSAC-TRQRVEDAFYTLVRE
RRAS_HUMAN       --FPVVLVGNKADLESQRQVPRSEASAFGASHH-VAYFEASAK-LRLNVDEAFEQLVRA
RRAS2_HUMAN      --FPMILIGNKADLDHQRQVTQEEGQQLARQLK--VTYMEASAK-IRMNVDAQAFHELVRV
RASM_HUMAN       --FPMILVNKVDLMHLRKITREQGKEMATKHN--IPYIETSADPPLNVDKAFHDLVRV
RALA_HUMAN       --VPFLLVGNKSDLEDKRQVSVEEAKNRAEQWN--VNYVETSAC-TRANVDKVF FDLMRE
RALB_HUMAN       K-IPLLVGNKSDLEERRQVPVEEARSKAEEWG--VQYVETSAC-TRANVDKVF FDLMRE
RIT1_HUMAN       --TPVVLVGNKSDLKQLRQVTKEEGLALAREFS--CPFFETSAA-YRYYIDDV FHALVRE
RIT2_HUMAN       --IPLVLVGNKIDLEQFRQVSTEEGLSLAQEYN--CGFFETSAA-LRFCIDDAFHGLVRE
RASE_HUMAN       A-QPLVLVGNKCDLVTTAGDAHAHAHAALAHSWG--AHFVETSAC-TRQGVEEAFSLLVHE
RHEB_HUMAN       --IPIMLVGNKCDLHMERVISYEEGKALAESWN--AAFLESSAK-ENQTAVDV FFRRIIE
REBL1_HUMAN      --VPVVLVGNKADLSPEREVQAVEGKKLAESWG--ATFMESAR-ENQLTQGIFTKVIQE
RASLC_HUMAN      RSIPALLLGNKLDMAQYRQVTKAEGVALAGRFG--CLFFEVSACLD FEFVQHFHEAVRE
RASD1_HUMAN      VDVPLVICGNKGDRDIFYREVDQREIEQLVGDDPQRCAYFEISAK-KNSSLDQMFRALFAM
KBR2_HUMAN       --VTIVVLGNKCDLQEQRVDPDVAQHWAKSEK--VKLWEVSVA-DRRSLLEPFVYLASK
KBR1_HUMAN       --VAIVVLGNKIDLSEQRQVDAEVAQQWAKSEK--VRLWEVTVT-DRKTLIEPFTLLASK

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RAB + RAN FAMILY ALIGNMENT

RAS

	G1	G2
RAB9B_HUMAN	--MSGKSLLLKVILLG	DDGGVGKSSLMNRYVTNKFD
RAB9A_HUMAN	--MAGKSLLFKVILLG	DDGGVGKSSLMNRYVTNKFD
RAB7A_HUMAN	--MTRKKVLLKVILLG	DDGGVGKSSLMNQYVYVKKFSN
RAB7B_HUMAN	--MNRKKVDLKLII	GAIVGKTSLLHQYVHKTFYEE
RAB32_HUMAN	--MATREHLFKVL	IGELGVGKTSIKRYVHQLFSQ
RAB38_HUMAN	--MQHKEHLKVL	IGDLGVGKTSIIKRYVHQNFSH
RAB6A_HUMAN	--MSNPLRKFVL	IGEQSVGKTSILTRFMYDSFNT
RAB41_HUMAN	--MSQSLCKSKLL	IGEQSVGKTSIISRFMYSFGCA
RAB28_HUMAN	--MSSQDRQLKIV	LGDSGKTSLTTCFAQETFGKQ
RAB31_HUMAN	--MA--IRELKVCL	LDGTGVGKSSIVCRFVQDHFDHN
RB22A_HUMAN	--MA--IRELKVCL	LDGTGVGKSSIVCRFVQDHFDHN
RAB5A_HUMAN	--MANKICQFLVL	IGESAVGKSSLVRFVKGQFHEF
RAB5B_HUMAN	--MTSKICQFLVL	IGESAVGKSSLVRFVKGQFHEY
RAB24_HUMAN	--MSGQRVDVVM	LGKEYVGKTSIVRYVHDFLVGP
RAB21_HUMAN	--MAGRAVSFKV	LLGEGCVGKTSILVLRVCENKFNDK
RAB17_HUMAN	--MASQPRVFL	VLVLLGSGSVGKSSALRYVKNDFKSI
RAB28_HUMAN	---	MRKPDQSKIVLLGDMNVGKTSILQRYMERRFPDT
RAB34_HUMAN	--MNVGFKISKV	IVVGDLSVGKTCILNRFCKDTFDKN
RAB36_HUMAN	--MVVGLKLSKV	VVVVGDLYVGKTSILHRFCKNVDFRD
RAB23_HUMAN	--MLDMEVAIKM	VVVGNGAVGKSSMIQRYCKGIFTKD
RAB8A_HUMAN	--MAKTYDYLFK	LLLLIGDSGVGKTCVLFRRFSEDAFNSTFIS
RAB8B_HUMAN	--MAKTYDYLFK	LLLLIGDSGVGKTCVLFRRFSEDAFNSTFIS
RAB18_HUMAN	--MATYDILLFK	LLLLIGDSGVGKTCVLFRRFSDAFNSTFIS
RAB13_HUMAN	--MAKAYDHLFK	LLLLIGDSGVGKTCILIRFAEDNFNNTYIS
RAB15_HUMAN	--MAKQYDVLFR	LLLLIGDSGVGKTCVLFRRFSEDAFNSTFIS
RAB12_HUMAN	--MDPADFKLV	QVIIIGSRGVGKTSIMERFTDFTCEACKS
RB48C_HUMAN	--MGSYDYLLFK	LLVVGDSGVGKGEILESQDGAESPAY
RB27A_HUMAN	--MSDYDYLLFK	LALGDSGVGKTSVLQYTDGKFNKFI
RB27B_HUMAN	--MTDYDYLLFK	LALGDSGVGKTTFLYRYTDNKNFNPFI

	G1	G2
RAB3A_HUMAN	--MANFDYMFKILII	GNSSVGKTSFLFRYADDSFTPAFVS
RAB3C_HUMAN	--MRNFDYMFKILII	GNSSVGKTSFLFRYADDSFTSAFVS
RAB3B_HUMAN	--MANFDYMFKILII	GNSSVGKTSFLFRYADDSFTPAFVS
RAB3D_HUMAN	--MANFDYMFKILII	GNSSVGKTSFLFRYADDSFTPAFVS
RAB1A_HUMAN	--MS-EYDYLKLL	LLIGDSGVGKSCVLLRFADDTYTESYIS
RAB1B_HUMAN	--MNPEDYDLKLL	LLIGDSGVGKSCVLLRFADDTYTESYIS
RAB35_HUMAN	--MA-DYDHLFKLL	LLIGDSGVGKSSLLRFADNTFSGSYIS
RB11A_HUMAN	--MGEYDYLKVV	LLIGDSGVGKSNLRSRFRTRNEFNLESK
RB11B_HUMAN	--MGEYDYLKVV	LLIGDSGVGKSNLRSRFRTRNEFNLESK
RAB25_HUMAN	--MGDYNFVFKVV	LLIGESGVGKTNLRSRFRTRNEFSHDSR
RAB4A_HUMAN	--MSTYDFLFKFL	LVIGNAGTGKSCVLLHQFTEKKFKDDSN
RAB14_HUMAN	--MANSYIFKYII	IGDMGVGKSCVLLHQFTEKKFMADCP
RAB2A_HUMAN	---	MAYAYLFKYIIGDGTGVGKSCVLLQFQDKRFQPVHD
RAB2B_HUMAN	---	MTYAYLFKYIIGDGTGVGKSCVLLQFQDKRFQPVHD
RB39A_HUMAN	METI-WIYQFRL	IVIGDSTVGKSCVLLHRFTQGRFPGLRS-PACD
RB39B_HUMAN	MEAI-WLYQFRL	IVIGDSTVGKSCVLLHRFTQGRFAQVS
RAB42_HUMAN	MEAEGRYQFRV	ALLGDAAVGKTSLLRSYVAGAPGAPEPEPEPE
RAB43_HUMAN	--MAQYDFLFK	LVLLVGDASVGKTCVQVRFKTFGAFSERQG
RAB19_HUMAN	--MHNFDYLFKIL	LLIGDSNVGKTCVQVHFQKSGVYTETQQ
RAB30_HUMAN	--MSDYDFLKII	LVIGNAGVGKTCVLRFTQGLFPFGQ
RAB18_HUMAN	--MDVDLTTLKIL	LLIGESGVGKSSLLRFDDTDFDPELA
RB12B_HUMAN	--MADADDNVKII	CLGDSAVGKSKLMERFLMDGFPQQLS
RB12A_HUMAN	--MADADDNVKII	CLGDSAVGKSKLMERFLMDGFPQQLS
RB33B_HUMAN	--MAARSRLF	KIIVIGDSNVGKTCVLRFCAGRFPORTER
RAN_HUMAN	--MAEPQVQFKL	VLVGGDGTGKTTFKRHLTGFEKKYV

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RAB + RAN FAMILY ALIGNMENT

RAS

G3

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RAB9B_HUMAN GRF-----VTLQIWDTAGQERFKS-LRTPFYRGADCCLLTF5VDDRQSFENLGNWQ
RAB9A_HUMAN GHF-----VTMQIWDTAGQERFRS-LRTPFYRGSDCCLLTF5VDDSQSFQNL5NWK
RAB7A_HUMAN DRL-----VTMQIWDTAGQERFQS-LGVAFYRGADCCVLVFDVTPNTFKTLD5WR
RAB7B_HUMAN DTT-----LKLQIWDTAGQERFRS-MVSTFYKGSQGCILAFDVTDLSEFALDIWR
RAB32_HUMAN RTL-----VRLQLWDTAGQERFGN-MTRVYYKEAVGAFVVDISRSSTFEAVLKWK
RAB38_HUMAN ETV-----VRLQLWDTAGQERFGN-MTRVYYREAMGAFIVFDVTRPATFEAVAKWK
RAB6A_HUMAN RT-----VRLQLWDTAGQERFRS-LIPSYIRDSTVAVVVDITNVNSFQQTTKWI
RAB41_HUMAN QI-----VQLQLWDTAGQERFHS-LIPSYIRDSTIAVVVDITNVNSFKETDKW
RAB28_HUMAN NLN-----VTLQIWDTAGQETIGGK-MLDKYIYGAQGVLLVVDITNYQSFENLEDWY
RAB31_HUMAN EL-----HKFLIWDTAGQERFHS-LAPMYRYGSAAAIVVDITKQSFYTLKKW
RB22A_HUMAN EL-----HKFLIWDTAGQERFRA-LAPMYRYGSAAAIVVDITKEETSTLKNW
RAB5A_HUMAN TT-----VKFEIWDTAGQERYHS-LAPMYRYGAQAAIVVDITNEESFARAKNW
RAB5B_HUMAN TT-----VKFEIWDTAGQERYHS-LAPMYRYGAQAAIVVDITNQETFARAKTW
RAB24_HUMAN RT-----VTLGIWDTAGSERYEA-MSRIYYRGAKAAIVCYDLTDSSFERAKFW
RAB21_HUMAN KR-----VNLAIWDTAGQERFHA-LGPIYYRDSNGAILVYDITDEDSFQVKKNW
RAB17_HUMAN TS-----LKLEIWDTAGQEKYHS-VCHLYFRGANAALLVYDITRKDSFLKAQQWL
RAB28_HUMAN -----YNISIWDTAGREQFHG-LGSMYCRGAAIILTYDVNHRQSLVELEDRF
RAB34_HUMAN IP-----FSLQIWDTAGQERFKC-IASYYRGAAQIIIVFNLDVASFLEHTKQWL
RAB36_HUMAN IP-----YSLQIWDTAGQEKFKC-IASYYRGAAQIITAFDLTDVQLEHTRQWL
RAB23_HUMAN ED-----VRLMLWDTAGQEEFDA-ITKAYYRGAAQCVLVFSTTDRESFEAVSSWR
RAB8A_HUMAN K-----RIKLQIWDTAGQERFRT-ITTAYYRGAMGIMLVYDITNEKSFQDNRNWI
RAB8B_HUMAN K-----KIKLQIWDTAGQERFRT-ITTAYYRGAMGIMLVYDITNEKSFQDNIKNWI
RAB10_HUMAN K-----KIKLQIWDTAGQERFHT-ITTSYYRGAMGIMLVYDITNGKSFENISKWL
RAB13_HUMAN K-----KIKLQIWDTAGQERFRT-ITTAYYRGAMGIMLVYDITDEKSFENIQNM
RAB15_HUMAN I-----KVRIQIWDTAGQERYQT-ITKQYYRGAQGIFLVYDISSESYQIMKW
RAB12_HUMAN K-----KIRLQIWDTAGQERFNS-ITSAYYRSAGIILVYDITKKEFTDDLPKWM
RB40C_HUMAN R-----RVKLELWDTAGQGRFC-IFRSYSRGAQGILLVYDITNRW5FDGDRWI
RB27A_HUMAN SGPDGATGRGRIHLQLWDTAGQERFRS-LTTAFFRDAMGFLLLFDLTNEQSF5LNRNWI
RB27B_HUMAN QGPNSSSGKAFKVLQLWDTAGQERFRS-LTTAFFRDAMGFLLMFDLTSQSF5LNRNWI
    
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G3

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RAB3A_HUMAN K-----RIKLQIWDTAGQERYRT-ITTAYYRGAMGIFILMYDITNEESFNAVQDWS
RAB3C_HUMAN K-----RIKLQIWDTAGQERYRT-ITTAYYRGAMGIFILMYDITNEESFNAVQDWS
RAB3B_HUMAN K-----RVKLQIWDTAGQERYRT-ITTAYYRGAMGIFILMYDITNEESFNAVQDWA
RAB3D_HUMAN K-----RIKLQIWDTAGQERYRT-ITTAYYRGAMGIFILMYDIANQESFAAVQDWA
RAB1A_HUMAN K-----TIKLQIWDTAGQERFRT-ITSSYYRGAGHGIIVVYDVTQESFNNVKQWL
RAB1B_HUMAN K-----TIKLQIWDTAGQERFRT-ITSSYYRGAGHGIIVVYDVTQESYANVKQWL
RAB35_HUMAN E-----KVKLQIWDTAGQERFRT-ITSTYYRGTHGVIVVYDVTSAESFVNVKRWL
RB11A_HUMAN GK-----TIKAQIWDTAGQERYRA-ITSAYYRGAVGALLVYDIAKHLTYENVERWL
RB11B_HUMAN GK-----TIKAQIWDTAGQERYRA-ITSAYYRGAVGALLVYDIAKHLTYENVERWL
RAB25_HUMAN TA-----AVKAQIWDTAGQERYRA-ITSAYYRGAVGALLVFDLTKHQTAVVERWL
RAB4A_HUMAN GK-----YVKLQIWDTAGQERFRS-VTRSYRGAAAGALLVYDITRETYNALTNLWL
RAB14_HUMAN GQ-----KIKLQIWDTAGQERFRA-VTRSYRGAAAGALLVYDITRRSYNHLSSWL
RAB2A_HUMAN GK-----QIKLQIWDTAGQESFRT-ITSSYYRGAAAGALLVYDITRRDFTNHLTTLWL
RAB2B_HUMAN GK-----QIKLQIWDTAGQESFRT-ITSSYYRGAAAGALLVYDITRRDFTNHLTTLWL
RB39A_HUMAN GK-----RIKLQIWDTAGQERFRS-ITRSYYRNSVGGFLVFDITNRRSF5HVKDWL
RB39B_HUMAN GK-----RIKLQIWDTAGQERFRS-ITRSYYRNSVGGLLFDITNRRSF5QNVHEWL
RAB42_HUMAN GP-----RVKLQIWDTAGQERFRT-ITRSYYRNVGALLVYDITNRKSF5HIDQWLH
RAB43_HUMAN GK-----RVKLQIWDTAGQERFRT-ITQSYRSANGAILAYDITKRSSF5LSPHWI
RAB19_HUMAN GK-----KVQMQLWDTAGQERFRT-ITQSYRSANAAIAYDITRRSTF5EIPHWI
RAB30_HUMAN GE-----KVKLQIWDTAGQERFRS-ITQSYRSANALILTYDITCEESF5RCLPEWL
RAB18_HUMAN NK-----AKLAIWDTAGQERFRT-LTPSYRGAGVILVYDVTTRDFTVFLDNWL
RBL2B_HUMAN RT-----ILVDFIWDTAGQERFQS-MHASYYHKAHACIMVFDVQRKVYRNLT5WY
RBL2A_HUMAN KT-----ILVDFIWDTAGQERFQS-MHASYYHKAHACIMVFDIQKVTYRNLT5WY
RB33B_HUMAN ER-----IKIQLWDTAGQERFRKSMVQHYRN5HVVVYD5MTNMA5F5H5LPSWI
RAN_HUMAN GP-----IKFNVLWDTAGQEKFGG-LRDGYIIQAQCAIMFDVTSRVTYKNV5PNWH
    
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RAB + RAN FAMILY ALIGNMENT

RAS

G4

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RAB9B_HUMAN KEFIYYADVDPHFPPFVVLGNKVDKEDR-----QVTT
RAB9A_HUMAN KEFIYYADVDPKESFPFVILGNKIDISER-----QVST
RAB7A_HUMAN DEFLLQASPRDPENFPFVVLGNKIDLENR-----QVAT
RAB7B_HUMAN GDVLAKIVPME-QSYPMVLLGNKIDLADR-----KVPQ
RAB32_HUMAN SLDLSKVHLPNGSPIPAVLLANKCDQNKDS-----SQSP
RAB38_HUMAN NDLDKSLSLPNGKPVSVVLLANKCDQGKDV-----LMNG
RAB6A_HUMAN DDVR---TERGSDVIMLVGNKTDLAD-----KRQVSI
RAB41_HUMAN EHVR---AERGGDVIMLLGNKIDLON-----KRQVTA
RAB28_HUMAN TVVKKVS-EESQTPLVALVGNKIDLEH-----MRTIKP
RAB31_HUMAN KELK----EHGPNIVMAIAGNKCDLSO-----IREVPL
RB22A_HUMAN KELR---QHGPPIVVAIAGNKCDLID-----VREVME
RAB5A_HUMAN KELQ---RQASPNIVIALSGNKADLAN-----KRAVDF
RAB5B_HUMAN KELQ---RQASPSIVIALAGNKADLAN-----KRMVEY
RAB24_HUMAN KELR---SLEEG-CQIYLCGTKSLLLE-----DRRRRRVDF
RAB21_HUMAN KELR---KMLGNEICLCIVGNKIDLEK-----ERHYSI
RAB17_HUMAN KDLEE---ELHPGEVLVMLVGNKTDLSQ-----EREVTF
RAB20_HUMAN LGLT---DTASKDCLFAIVGNKVDLTEEGALAGQEECSPNMDAGDRVSPRAPKQVQL
RAB34_HUMAN ADALK---ENDPSSVLLFLVGSKKDLSTP-----AQYALME
RAB36_HUMAN EDALR---ENEAGSCFIFLVGTKKDLLSG-----AAEQAE
RAB23_HUMAN EKVVA---EVG--DIPTVLVGNKIDLLD-----DSCIKN
RAB8A_HUMAN RNIEE---HA-SADVEKMILGNKCDVNDK-----RQVSK
RAB8B_HUMAN RNIEE---HA-SSDVERMILGNKCDMDK-----RQVSK
RAB10_HUMAN RNIDE---HA-NEDVERMILLGNKCDMDK-----RVVVPK
RAB13_HUMAN KSIKE---NA-SAGVERLLGNKCDMEAK-----RKVQK
RAB15_HUMAN SDVDE---YA-PEGVQKILIGNKADDEEQK-----RQVGR
RAB12_HUMAN KMIDK---YA-SEDAELLVGNKLDCTD-----REITR
RB40C_HUMAN KEIDE---HA-PG-VPRIVLGNRLHLAFK-----RQVPT
RB27A_HUMAN SQLQM---HAYCENPDIVLCGNKSDLEDQ-----RVVKE
RB27B_HUMAN SQLQA---NAYCENPDIVLIGNKADLPDQ-----REVNE
    
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G4

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RAB3A_HUMAN TQIKT---YS-WDNAQVLLVGNKCDMEDE-----RVVSS
RAB3C_HUMAN TQIKT---YS-WDNAQVILVGNKCDMEDE-----RVIST
RAB3B_HUMAN TQIKT---YS-WDNAQVILVGNKCDMEDE-----RVVPT
RAB3D_HUMAN TQIKT---YS-WDNAQVILVGNKCDLEDE-----RVVPA
RAB1A_HUMAN QEIDR---YA-SENVNKLVLGNKCDLTTK-----KVVDY
RAB1B_HUMAN QEIDR---YA-SENVNKLVLGNKCDLTTK-----KVVDN
RAB35_HUMAN HEIN---QN-CDDVCRILVGNKNDOPER-----KVVET
RB11A_HUMAN KELRD---HADS-NIVIMLVGNKCDLRHL-----RAVPT
RB11B_HUMAN KELRD---HADS-NIVIMLVGNKCDLRHL-----RAVPT
RAB25_HUMAN KELYD---HAEA-TIVVMLVGNKCDLSQA-----REVPT
RAB4A_HUMAN TDARM---LASQ-NIVIILCGNKCDLAD-----REVTF
RAB14_HUMAN TDARN---LTNP-NTVILIGNKADLEAQ-----RDVTY
RAB2A_HUMAN EDARQ---HSNS-NMVIMLIGNKCDLESR-----REVKK
RAB2B_HUMAN EDARQ---HSNS-NMVIMLIGNKCDLESR-----RDVKK
RB39A_HUMAN EEAKM---YVQPFRIVFLVGNKCDLASQ-----RQVTR
RB39B_HUMAN EETKV---HVQPYQIVFVLVGNKCDLDTQ-----RQVTR
RAB42_HUMAN QEVMA---TQGPDKVIFLLVGNKCDLQST-----RCVSA
RAB43_HUMAN EDVRK---YAGS-NIVQLLIGNKCDLSEL-----REVSL
RAB19_HUMAN HEIEK---YGAA-NVIMLIGNKCDLWEK-----RHLVF
RAB30_HUMAN REIEQ---YASN-KVITVLVGNKIDLAE-----REVSK
RAB18_HUMAN NELET---YCTRNDIVNMLVGNKIDKENR-----EVDK
RBL2B_HUMAN TELRE---FRP--EIPCIVVANKIDINV-----TQKSF
RBL2A_HUMAN TELRE---FRP--EIPCIVVANKIDINV-----TQKSF
RB33B_HUMAN EECKQ---HLLANDIPRILVGNKCDLRS-----TQVPT
RAN_HUMAN RDLVR---VCENIPILVGNKVDIKDR-----KVKA
    
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RAB + RAN FAMILY ALIGNMENT

RAS

G5

G5

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RAB9B_HUMAN EEAQTWCM-----ENGDPYPLETSAKDDTNVTVAEEAVRQVLAVEEQLE--
RAB9A_HUMAN EEAQAWCR-----DNGDPYPFETSAKDATNVAAAFEEAVRRVLATEDRSD--
RAB7A_HUMAN KRAQAWCY-----SKNNIPYFETSAAEAINVEQAFQTIARNALKQETEVE--
RAB7B_HUMAN EVAQGWCR-----EK-DIPYFVTSAKNDINNVQAFEMLASRALSR-YQSI--
RAB32_HUMAN SQVDQFCF-----EHGFAGWFETSAKDNINIEEAAARFLVEKILVNHQSFP--
RAB38_HUMAN LKMDQFCF-----EHGFVGNFETSAKENINIDEASRCLVKHILANECDL--
RAB6A_HUMAN EEEGRKAK-----ELNVMFIETSAGYNNVQFLRRVAAALPGMES-----
RAB41_HUMAN EQGEEKSR-----NLNVMFIETSARTGYNVKKLFRRVASALLSTR-----
RAB28_HUMAN EKHLRFQF-----ENGFSHFVTSAKTGDVSFLCFQKVAEEILGIKLNKA--
RAB31_HUMAN KDAKEYAE-----SIGAIVFETSAKNAINIEELFQGISRQIPPLDPHEN--
RB22A_HUMAN RDAKDYAD-----SIHAIFVETSAKNAININELFIEISRRIPSTDANLP--
RAB5A_HUMAN QEAQSYAD-----DNSLLFMETSAKTSMNVNEIFMAIAKKLPKNPQNPN--
RAB5B_HUMAN EEAQYAD-----DNSLLFMETSAKTAMNVNDLFIAIAKKLPKSEPQNL--
RAB24_HUMAN HDVQDYAD-----NIKAQLFETSSTKGQSVDELQKVAEDYVSVAAFQV--
RAB21_HUMAN QEAEYSYAE-----SVGAKHYFETSARKNGIEELFDLCKRMIETAQVDE--
RAB17_HUMAN QEGKEFAD-----SQKLLFMETSAKLNHQVSEVFNTVAQELLQRSDEEG--
RAB20_HUMAN EDAVALYKKILKYKMLDEQDVPAAEQMCFETSARTGYNVDLLFETLFDLVPMILQQR--
RAB34_HUMAN KDALQVAF-----EMKAEYNAVSSLTGENVREFFFRVAA-----LTFEANV--
RAB36_HUMAN ADAVHLAR-----EMQAEYVSVSARTGENVKAFFSRVAA-----LAFEQSV--
RAB33_HUMAN EEAEALAK-----RLKLRFYRTSVKEDLMNVNEVFYLAEKYLQKLKQOI--
RAB8A_HUMAN ERGEKLALDY-----GIKFMETSAKANINVENAFTLARDIAKAM-----
RAB8B_HUMAN ERGEKLALDY-----GIKFLETSASSANVEEAFFTLARDIMTKL-----
RAB10_HUMAN GKGEQIAREH-----GIRFFETSAKANINIEKAFLLTAEIDILRKT-----
RAB13_HUMAN EQADKLAREH-----GIRFFETSASSMNVDEAFSSLARDILLKS-----
RAB15_HUMAN EQGQQLAKEY-----GMDFYETSQTNLNKIESFTRLTELVLQAH-----
RAB12_HUMAN QQGKEFAQQIT-----GMRFCETSARKDNFNVDEIFLKLVDIDILKKM-----
RB40C_HUMAN EQARAYAEKN-----CMTFFEVSPLCNFMVIESFTLSRIVLMRHGMKIIW-----
RB27A_HUMAN EEAIALAKEY-----GIPYFETSAAAGTNISSQAIEMLLDLIMKRM-----
RB27B_HUMAN RQARELADKY-----GIPYFETSAAATGQNVKEVAFETLLDLIMKRM-----

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RAB3A_HUMAN ERGRQLADHL-----GFEFFETSAKDNINNVKQTFERLVDVICEKM-----
RAB3C_HUMAN ERGQHLGEQL-----GFEFFETSAKDNINNVKQTFERLVDICDKM-----
RAB3B_HUMAN EKGQLLAELQ-----GFDFETSAKENISVRQAFERLVDICDKM-----
RAB3D_HUMAN EDGRRLLADDL-----GFEFFETSAKENINNVKQVFERLVDVICEKM-----
RAB1A_HUMAN TTAKEFADSL-----GIPFLETSAKNATNVEQSFMTMAAEIKKRM-----
RAB1B_HUMAN TTAKEFADSL-----GIPFLETSAKNATNVEQAFMTMAAEIKKRM-----
RAB35_HUMAN EDAYKFAQGM-----GIQLFETSAKENVNVEEMFNCITELVLRAK-----
RB11A_HUMAN DEARAFAEKNG-----LS-FIETSALDSTNVVEEAFQTILTEIYRIVS-----
RB11B_HUMAN DEARAFAEKNN-----LS-FIETSALDSTNVVEEAFKNILTEIYRIVS-----
RAB25_HUMAN EEARMFAENNG-----LL-FLETSALDSTNVLEAFETVLKEIFAKVS-----
RAB4A_HUMAN LEASRFAQENE-----LM-FLETSALTGENVVEEAFVQCARKILNKIE-----
RAB14_HUMAN EEAKQFAEENG-----LL-FLETSARTGENVEDAFLEAAKKIYQNIQ-----
RAB2A_HUMAN EEEGAFAREHG-----LI-FMETSARTASNVEEAFINTAKEIYKIQ-----
RAB2B_HUMAN EEEGAFAREHG-----LI-FMETSARTACNVVEEAFINTAKEIYRQIQ-----
RB39A_HUMAN EEAEKLSADCG-----MK-YIETSAKDATNVEESFTILTRDIYELIK-----
RB39B_HUMAN HEAEKLAAYG-----MK-YIETSARDAINVEKAFDLTRDIYELVK-----
RAB42_HUMAN QEAEELAASLG-----MA-FVETSVMNCNVDLAFDTLADAIQQAQ-----
RAB43_HUMAN AEQSLAEHYD-----ILCAIETSAKSSNVVEEAFRLVATELIMRHG-----
RAB19_HUMAN EDACTLAKEYG-----LLAVLETSAKESKNIEEVFLMAKELIARNS-----
RAB30_HUMAN QRAEEFSEAQD-----MY-YLETSAKESDNVEKFLDLACRLISEAR-----
RAB18_HUMAN NEGLKFAKH-----MLFIETSARTCDGVQCAFEELVEKIIQTPG-----
RBL2B_HUMAN NFAKKFSPLPYFVSAAD-----GTNVVKLFMDAIRLAVSYKQNSQDFMDEIFQELN-----
RBL2A_HUMAN NFAKKFSPLPYFVSAAD-----GTNVVKLFMDAIRLAVSYKQNSQDFMDEIFQELN-----
RB33B_HUMAN DLAQKFAD-----THSMPLFETSARK-----NPNDNDHVEAIFMTLAH-----
RAN_HUMAN KSIVFHRKK-----NLQYYDTSAKSNYNFEKFPWLWLARKLIGDPNLEFVA

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RHO FAMILY ALIGNMENT

RAS

CLUSTAL 2.1 multiple sequence alignment

	G1	G2
RAC1_HUMAN	-----MQAIKCVVV GDGAVGKT CLLISYTTNA-----	FPGEYI PTV FDN----
RAC3_HUMAN	-----MQAIKCVVV GDGAVGKT CLLISYTTNA-----	FPGEYI PTV FDN----
RAC2_HUMAN	-----MQAIKCVVV GDGAVGKT CLLISYTTNA-----	FPGEYI PTV FDN----
RHOG_HUMAN	-----MQSIKCVVV GDGAVGKT CLLICYSYTTNA-----	FPKEYI PTV FDN----
RHOQ_HUMAN	-----MAPGALMLKCVVV GDGAVGKT CLLMSYANDA-----	FPEEYV PTV FDH----
RHOJ_HUMAN	-----MNDEKKMLKCVVV GDGAVGKT CLLMSYANDA-----	FPEEYV PTV FDH----
RHOU_HUMAN	-----MPAEGRGVKCVLV GDGAVGKT SLVVSYYTTNG-----	YPTEYI PTA FDN----
RHOV_HUMAN	-----MPPPELGIVKCVLV GDGAVGKSS LIVSYTCNG-----	YPARYR PTA LDT----
RHOA_HUMAN	-----MAAIRK--KLIVIV GDGACGKT CLLIVFSKDQ-----	FPEVYV PTV FEN----
RHOC_HUMAN	-----MAAIRK--KLIVIV GDGACGKT CLLIVFSKDQ-----	FPEVYV PTV FEN----
RHOB_HUMAN	-----MAAIRK--KLIVIV GDGACGKT CLLIVFSKDE-----	FPEVYV PTV FEN----
RND2_HUMAN	-----MEGQSGRCKIVVV GDGACGKT ALLQVFAKDA-----	YPGSYV PTV FEN----
RND3_HUMAN	-----MKNQNVKCKIVVV GDGACGKT ALLHVFAKDC-----	FPEYV PTV FEN----
RND1_HUMAN	-----MKPVVARCKLVLV GDVQCGKT AMLQVLAKDC-----	YPETYV PTV FEN----
RHOF_HUMAN	-----MDPGRKELKIVIV GDGGCGKT SLLMVYSQGS-----	FPEHYA PSV FEK----
RHOD_HUMAN	-----MTPGVRSVKVVVLV GDGGCGKT SLLMVFAKDA-----	FPEYV PTV FER----
RHOH_HUMAN	-----MLSSIKCVLV GDGAVGKT SLLVRFSTSET-----	FPEAYK PTV YEN----
RHBT2_HUMAN	---MD---PNVETIKCVVV GDNAV GKTRLICARACNATLTQYQLLATHV PTV WAIDQYR	
RHBT1_HUMAN	MDADMDYERPENVETIKCVVV GDNAV GKTRLICARACNTTLTQYQLLATHV PTV WAIDQYR	
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RHO FAMILY ALIGNMENT

RAS

G3

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RAC1_HUMAN  -----YSANVMVDGKPVNLGLWDTAGQEDYDRLRPLSYPQTDVFLICFSLVSPASFENV
RAC3_HUMAN  -----YSANVMVDGKPVNLGLWDTAGQEDYDRLRPLSYPQTDVFLICFSLVSPASFENV
RAC2_HUMAN  -----YSANVMVDSKPVNLGLWDTAGQEDYDRLRPLSYPQTDVFLICFSLVSPASYENV
RHOG_HUMAN  -----YSAQSAVDGRTVNLNLWDTAGQEEYDRLRPLSYPQTNVFVICFSIASPPSYENV
RHOQ_HUMAN  -----YAVSVTVGGKQYLLGLYDTAGQEDYDRLRPLSYPMTDVFLICFSVNPASFQNV
RHOJ_HUMAN  -----YAVTVTVGGKQHLGLYDTAGQEDYNQLRPLSYPNTDVFLICFSVNPASYHNV
RHOU_HUMAN  -----FSAVVSVDGRPVRLQLCDTAGQDEFDKLRPLCYTNTDIFLLCFSVVSPSSFQNV
RHOV_HUMAN  -----FSVQVLVDGAPVRIELWDTAGQEDFDRLRSLCYPD TDVFLACFSVVQPSSFQNI
RHOA_HUMAN  -----YVADIEVDGKQVELALWDTAGQEDYDRLRPLSYPD TDVILMCFSIDSPDSLENI
RHOC_HUMAN  -----YIADIEVDGKQVELALWDTAGQEDYDRLRPLSYPD TDVILMCFSIDSPDSLENI
RHOB_HUMAN  -----YVADIEVDGKQVELALWDTAGQEDYDRLRPLSYPD TDVILMCFSDSPDSLENI
RND2_HUMAN  -----YTASFEIDKRRIELNMWDTSGSSYYDNVRPLAYPDSDAVLICFDISRPETLDSV
RND3_HUMAN  -----YTASFEIDTQRIELSLWDTSGSPYYDNVRPLSYPDSDAVLICFDISRPETLDSV
RND1_HUMAN  -----YTACLETEEQRVELSLWDTSGSPYYDNVRPLCYSDSDAVLLCFDISRPETVDSA
RHOF_HUMAN  -----YTASVTVGSKVTLNLWDTAGQEDYDRLRPLSYQNTHLVLCYDVMNPTS YDNV
RHOD_HUMAN  -----YMVNLQVKGKPVHLHIWDTAGQDDYDRLRPLFYPDASVLLLCFDVTSPNSFDNI
RHOH_HUMAN  -----TGVDVFMDCIQISLGLWDTAGNDAFRSIRPLSYQQADVVLNMCYSVANHNSFLNL
RHBT2_HUMAN VCQEV LERSRDVVDDVS VSLRLWDTFG--DHHKDRRFAYGRSDVVVLCFSIANPNLSLHHV
RHBT1_HUMAN VCQEV LERSRDVVDEVS VSLRLWDTFG--DHHKDRRFAYGRSDVVVLCFSIANPNLSLNHV

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RHO FAMILY ALIGNMENT

RAS

G4

RAC1_HUMAN	RAKWYPEVRHHCPNTPIILVG TKLD LRDDKDTIEKLKE-KKLTPTITY-----PQGLAMA
RAC3_HUMAN	RAKWYPEVRHHCPHTPILLVG TKLD LRDDKDTIERLRD-KKLAPITY-----PQGLAMA
RAC2_HUMAN	RAKWFPEVRHHCPSTPIILVG TKLD LRDDKDTIEKLKE-KKLAPITY-----PQGLALA
RHOG_HUMAN	RHKWHPEVCHHCPDVPILLVG TKKD LRAQPDTLRRLKE-QGQAPITP-----QQGQALA
RHOQ_HUMAN	KEEWVPELKEYAPNVPFLIG TQID LRDDPKTLARLND-MKEKPICV-----EQGQKLA
RHOJ_HUMAN	QEEWVPELKDCMPHVPYVLIG TQID LRDDPKTLARLLY-MKEKPLTY-----EHGVKLA
RHOU_HUMAN	SEKWVPEIRCHCPKAPIILVG TQSD LRDVKVLIELDK-CKEKPVPE-----EAAKLCA
RHOV_HUMAN	TEKWLPEIRTHNPQAPVLLVG TQAD LRDDVNVLIQLDQGGREGVPVQ-----PQAQGLA
RHOA_HUMAN	PEKWTPEVKHFCPNVPIILVG NKKD LRNDEHTRRELAK-MKQEPVKP-----EEGRDMA
RHOC_HUMAN	PEKWTPEVKHFCPNVPIILVG NKKD LRQDEHTRRELAK-MKQEPVRS-----EEGRDMA
RHOB_HUMAN	PEKWVPEVKHFCPNVPIILV NKKD LRSEHVRTELAR-MKQEPVRT-----DDGRAMA
RND2_HUMAN	LKKWQGETQEFCPNAKVVLVG CKLD MRTDLATLRELSK-QRLIPVTH-----EQGTVLA
RND3_HUMAN	LKKWKGEIQEFCPNTKMLLVG CKSD LRTDVSTLVELSN-HRQTPVSY-----DQGANMA
RND1_HUMAN	LKKWRTEILDYCPSTRVLLIG CKTD LRDLDSTLMELSH-QKQAPISY-----EQGCAIA
RHOF_HUMAN	LIKWFPEVTHFCRGIPMVLIG CKTD LRKDKEQLRKLRA-AQLEPITY-----MQGLSAC
RHOD_HUMAN	FNRWYPEVNHFCCKVPIIVVG CKTD LCKDKSLVNKLRR-NGLEPVTY-----HRGQEMA
RHOH_HUMAN	KNKWIGEIRSNLPCTPVLVVAT TQTD QR-----EMGP-HRASCVNA-----MEGKKLA
RHBT2_HUMAN	KTMWYPEIKHFCPRAPVILVG CQLD LRYADLEAVNRARRPLARPIKPNEILPPEKGREVA
RHBT1_HUMAN	KSMWYPEIKHFCPRTPVILVG CQLD LRYADLEAVNRARRPLARPIKRGDILPPEKGREVA

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RHO FAMILY ALIGNMENT

RAS

G5

RAC1_HUMAN	KEIGAVKYL	ECSA-L	TQRGLKTVFDEAIRAVLCP-----	RAC1_HUMAN	---PPVKKRKRK	LLL-
RAC3_HUMAN	REIGSVKYL	ECSA-L	TQRGLKTVFDEAIRAVLCP-----	RAC3_HUMAN	---PPVKKPGKK	TVF-
RAC2_HUMAN	KEIDSVKYL	ECSA-L	TQRGLKTVFDEAIRAVLCP-----	RAC2_HUMAN	---QPTRQQKRA	SLL-
RHOG_HUMAN	KQIHAVRYL	ECSA-L	QQDGVKEVFAEAVRAVLNP-----	RHOG_HUMAN	---TPIKR-GRS	ILL-
RHOQ_HUMAN	KEIGACCVY	ECSA-L	TRIG-----	RHOQ_HUMAN	---SRCIN---	CLIT-
RHOJ_HUMAN	KAIGAQCYL	ECSA-L	TQKGLKAVFDEAILT-IFH-----	RHOJ_HUMAN	---KRCSEGHS	CSII-
RHOU_HUMAN	EEIKAASYI	ECSA-L	TQKNLKEVFDAAI VAGIQL-----	RHOU_HUMAN	---SKSWWKKY	CFV--
RHOV_HUMAN	EKIRACCYL	ECSA-L	TQKNLKEVFDSAILS AIEL-----	RHOV_HUMAN	---SRCRWKKFF	CFV--
RHOA_HUMAN	NRIGAFGYM	ECSAKT	KDG-VREVFEMATRAALQAR-----	RHOA_HUMAN	-----RGKKKSG	LVL-
RHOC_HUMAN	NRISAFGYL	ECSAKT	KEG-VREVFEMATRAGLQVR-----	RHOC_HUMAN	-----KNKRRRG	PIL-
RHOB_HUMAN	VRIQAYDYL	ECSAKT	KEG-VREVFETATRAALQGS-----	RHOB_HUMAN	-----QNGCIN	CKVL-
RND2_HUMAN	KQVGAVSYV	ECSSRS	SERSVRDVFHVATVASLG-----	RND2_HUMAN	---EIHKDRAKS	NLM-
RND3_HUMAN	KQIGAATYI	ECSALQ	SENSVRDIFHVATLACVN-----	RND3_HUMAN	---DLRKDKAKS	TVM-
RND1_HUMAN	KQLGAEIYL	EGSAFT	SEKSIHSIFRTASMLCLNKPSPLPQKSPVRSLSKRL LHLPSRSEL	RND1_HUMAN	ISSTFKKEKAKS	CSIM-
RHOF_HUMAN	EQIRAALYL	ECSAKF	REN-VEDVFREAAKVALSAQ-----	RHOF_HUMAN	-----RQKKRRL	LLL-
RHOD_HUMAN	RSVGAVAYL	ECSARL	HDN-VHAVFQEA AEVALSSRG-----	RHOD_HUMAN	-RNFWRRTQGF	VVT-
RHOH_HUMAN	QDVRAKGYL	ECSA-L	SNRGVQQVF ECAVRTAVNR-----	RHOH_HUMAN	---RRLFSINE	CKIF-
RHBT2_HUMAN	KELG-IPYY	ETSV-V	QAQFGIKDVFDNAIRAALISR-----	RHBT2_HUMAN	-----RHLQFWKSHLRN	
RHBT1_HUMAN	KELG-LPYY	ETSV-F	DQFGIKDVFDNAIRAALISR-----	RHBT1_HUMAN	-----RHLQFWKSHLKK	
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ARF FAMILY ALIGNMENT

RAS

	G1	G2
ARL4A_HUMAN	---MGDQT-----SILSNLPSFQSFHIVILGLDCAGKTTVLRLQFN--EFVNTVPTKGF	
ARL4C_HUMAN	---MG-----NISSNISAFQSLHIVMLGLDSAGKTTVLRLKFN--EFVNTVPTIGF	
ARL4D_HUMAN	---MGNHLEMAPTASSFLPHFQALHVVVIGLDSAGKTSLLYRLKFK--EFVQSVPTKGF	
ARF1_HUMAN	---MGNIFA----NLFGKLFQKKEMRILMVGLDAAGKTTILYKCLKG--EIVTTIPTIGF	
ARF3_HUMAN	---MGNIFG----NLLKSLIGKKEMRILMVGLDAAGKTTILYKCLKG--EIVTTIPTIGF	
ARF4_HUMAN	---MGLTIS----SLFSRIFGKKQMRILMVGLDAAGKTTILYKCLKG--EIVTTIPTIGF	
ARF5_HUMAN	---MGLTVS----ALFSRIFGKKQMRILMVGLDAAGKTTILYKCLKG--EIVTTIPTIGF	
ARF6_HUMAN	---MG-----KVLSKIFGNKEMRILMLGLDAAGKTTILYKCLKG--QSVTTIPTVGF	
ARL1_HUMAN	---MGGFFS----SIFSSLFGTREMRLIILGLDGAGKTTILYRLQVG--EVVTTIPTIGF	
ARL5A_HUMAN	---MGILFT----RIWR-LFNHQEHKVIIVGLDNAGKTTILYQFSMN--EVVHTSPTIGS	
ARL5B_HUMAN	---MGLIFA----KLWS-LFCNQECHKVIIVGLDNAGKTTILYQFLMN--EVVHTSPTIGS	
ARL5C_HUMAN	---MG-LIA----KLMS-IFGNQEHTVIVGLDNEGKTTILYRFLTN--EVVHMCPTIGS	
ARL2_HUMAN	---MGLLTI----LKKMKQK-ERELRLMLGLDNAGKTTILKKFNGE--DIDTISPTLGF	
ARL3_HUMAN	---MGLLSI----LRKLKSAPDQEVRIILLGLDNAGKTTLLKQLASE--DISHITPTQGF	
ARL6_HUMAN	---MGLLDR----LSVLLGLKKKEVHVLCGLDNSGKTTIINKLKPSNAQSQNILPTIGF	
ARL8B_HUMAN	-MLLISRLL----DWFRSLFWKEEMELTLVGLQYSGKTTTFVNVIASGQ-FSEDMIPTVGF	
ARL8A_HUMAN	MIALFNKLL----DWFKALFWKEEMELTLVGLQYSGKTTTFVNVIASGQ-FNEDMIPTVGF	
SAR1A_HUMAN	--MSFSSVL----QFLG--LYKKSGLVFLGLDNAGKTTLLHMLKDDR-LGQ-HVPTLHP	
SAR1B_HUMAN	--MSFSSVL----QFLG--LYKKTGKLVFLGLDNAGKTTLLHMLKDDR-LGQ-HVPTLHP	
ARL9_HUMAN	---MRPTWK---ALSHPAWPEEKNKQILVLGLDGAGKTSVLHSLASNR-VQHSVAPPTQGF	
	. : **: ***:: :	**

ARF FAMILY ALIGNMENT

RAS

G3

ARL4A_HUMAN	NTEKIKVTLGNSKTVTFHFWDVGGQ	QEKLRPLWKS	YTRCTDGIVFV	VDSVDVERMEEAKTE
ARL4C_HUMAN	NTEKIKLSNGTAKGISCHFWDVGGQ	QEKLRPLWKS	YSRCTDGIIVV	DSVDVDRLEEAKTE
ARL4D_HUMAN	NTEKIRVPLGGSRGITFQVWDVGGQ	QEKLRPLWRS	YTRRTDGLVFV	DAAEAEERLEEAKVE
ARF1_HUMAN	NVETVEY-----KNISFTVWDVGGQ	QDKIRPLWRH	YFQNTQGLIFV	VDSNDRERVNEAREE
ARF3_HUMAN	NVETVEY-----KNISFTVWDVGGQ	QDKIRPLWRH	YFQNTQGLIFV	VDSNDRERVNEAREE
ARF4_HUMAN	NVETVEY-----KNICFTVWDVGGQ	QDRIRPLWKH	YFQNTQGLIFV	VDSNDRERIQEVADE
ARF5_HUMAN	NVETVEY-----KNICFTVWDVGGQ	QDKIRPLWRH	YFQNTQGLIFV	VDSNDRERVQESADE
ARF6_HUMAN	NVETVTY-----KNVKFNVDVGGQ	QDKIRPLWRH	YTYGTQGLIFV	VDCADRDRIDEARQE
ARL1_HUMAN	NVETVTY-----KNLKFQVWDLGGQ	QTSIRPYWRC	YYSNTDAVIYV	VDSCDRDRIGISKSE
ARL5A_HUMAN	NVEEIVI-----NNTRFLMWDLGGQ	QESLRSSWN	TYTNTTEFVIV	VVDSTDREERISVTREE
ARL5B_HUMAN	NVEEIVV-----KNTHFLMWDLGGQ	QESLRSSWN	TYYSNTEFIIL	VDSIDRERLAIITKEE
ARL5C_HUMAN	NVEEIIIL-----PKTHFFMWDLVRF	PEALSFIWNT	YYSNTEFIIL	VIDSTDTRDLLTTREE
ARL2_HUMAN	NIKTLEH-----RGFKLNIWDVGGQ	QKSLRSYWR	NYFESTDGLIW	VVDSADRQRMQDCQRE
ARL3_HUMAN	NIKSVQS-----QGFKLNVWDLGGQ	QRKIRPYWK	NYFENTDILII	VIDSADRKRFEETGQE
ARL6_HUMAN	SIEKFKS-----SSLSFTVFDMSG	QGRYRNLEH	YHYKEGQAIIF	VIDSSDRLRMVVAKEE
ARL8B_HUMAN	NMRKVTK-----GNVTIKIWDLGGQ	QPRFRSMW	ERYCRGVNAIV	YMIDAADREKIEASRNE
ARL8A_HUMAN	NMRKITK-----GNVTIKLWDLGGQ	QPRFRSMW	ERYCRGVS	SAIVYMVDAADQEKIEASKNE
SAR1A_HUMAN	TSEELTI-----AGMTFTTFDLGGQ	HEQARRVW	KNYLPAINGIV	FLVDCADHSRLVESKVE
SAR1B_HUMAN	TSEELTI-----AGMTFTTFDLGGQ	HVQARRVW	KNYLPAINGIV	FLVDCADHERLLESKEE
ARL9_HUMAN	HAVCINT-----EDSQMEFLFIGG	SKPFRSYW	EMYLKGLLLIF	VVDSADHSRLPEAKKY

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ARF FAMILY ALIGNMENT

RAS

G4

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ARL4A_HUMAN LHKITRISENQG--VPVLIVANKQDLRNSLSLSEIEKLLAMG-----ELSSSTP
ARL4C_HUMAN LHKVTKFAENQG--TPLLVIANKQDLPKSLPVAEIEKQLALH-----ELIPATT
ARL4D_HUMAN LHRISRASDNQG--VPVLVLANKQDQPGALSAAEVEKRLAVR-----ELAAATL
ARF1_HUMAN LMRMLAEDELRD--AVLLVFANKQDLPNAMNAAEITDKLGLH-----SLRHRN
ARF3_HUMAN LMRMLAEDELRD--AVLLVFANKQDLPNAMNAAEITDKLGLH-----SLRHRN
ARF4_HUMAN LQKMLLVDELRD--AVLLLFANKQDLPNAMAISEMTDKLGLQ-----SLRNRT
ARF5_HUMAN LQKMLQEDELRD--AVLLVFANKQDMPNAMPVSELTDKLGLQ-----HLRSRT
ARF6_HUMAN LHRINDREMRD--AIILIFANKQDLPDAMKPHEIQEKLGLT-----RIRDRN
ARL1_HUMAN LVAMLEEEELRK--AILVVFANKQDMEQAMTSSEMANSGLP-----ALKDRK
ARL5A_HUMAN LYKMLAHEDLRK--AGLLIFANKQDVKECMTVAEISQFLKLT-----SIKDHQ
ARL5B_HUMAN LYRMLAHEDLRK--AAVLIFANKQDMKGCMATAEISKYLTLS-----SIKDHQ
ARL5C_HUMAN LYKMLAHEALQD--ASVLIFANKQDVKDSMRMVEISHFLTLS-----TIK DHS
ARL2_HUMAN LQSLLVEERLAG--ATLLIFANKQDLPALSSNAIREVLELD-----SIRSHH
ARL3_HUMAN LAELLEEEKLSC--VPVLIFANKQDLLTAAPASEIAEGLNLH-----TIRDRV
ARL6_HUMAN LDTLLNHPDIKHRRIPILFFANKMDLRDAVTSVKVSQLLCLE-----NIKDKP
ARL8B_HUMAN LHNLLDKPQLQG--IPVLVLGNKRDLPNALDEKQLEKMNLS-----AIQDRE
ARL8A_HUMAN LHNLLDKPQLQG--IPVLVLGNKRDLPNALDEKQLEKMNLS-----AIQDRE
SAR1A_HUMAN LNALMTDETISN--VPILILGNKIDRTDAISEEKLREIFGLYGQTTGKGNVTLKELNARP
SAR1B_HUMAN LDSLMTDETIAN--VPILILGNKIDRPEAISEERLREMFGLYGQTTGKGSISLKELNARP
ARL9_HUMAN LHQLIAANPVLP---LVVFANKQDLEAAYHITDIHEALALS-----EVGNDRK
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G5

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ARL4A_HUMAN WHLQPTCAII-GDGLKEGLEKLHDMIKRRKMLRQKKKKR
ARL4C_HUMAN YHVQPAACAI-GEGLTEGMDKLYEMILKRRKSLKQKKKR
ARL4D_HUMAN THVQGCSAVD-GLGLQQGLERLYEMILKRRKAARGGKKRR
ARF1_HUMAN WYIQATCATS-GDGLYEGLDWLSNQLRNQK-----
ARF3_HUMAN WYIQATCATS-GDGLYEGLDWLANQLKNKK-----
ARF4_HUMAN WYVQATCATQ-GTGLYEGLDWLSNELSKR-----
ARF5_HUMAN WYVQATCATQ-GTGLYDGLDWLSHLSKR-----
ARF6_HUMAN WYVQPSCATS-GDGLYEGLTWLTSNYKS-----
ARL1_HUMAN WQIFKTSATK-GTGLDEAMEWLVTLSRSRQ-----
ARL5A_HUMAN WHIQACCAIT-GEGLCQGLEWMSRLKIR-----
ARL5B_HUMAN WHIQSCCAIT-GEGLCQGLEWMTSRIGVR-----
ARL5C_HUMAN WHIQGCCALT-REGLPARLQWMSQAAN-----
ARL2_HUMAN WCIQGCSAVT-GENLLPGIDWLDDISSRIFTAD-----
ARL3_HUMAN WQIQSCSALT-GEQVQDGMNVCKNVNAKKK-----
ARL6_HUMAN WHICASDAIK-GEGLQEGVDWLQDQIQTVKT-----
ARL8B_HUMAN ICCYSTSCKE-KDNIDITLQWLIQHSKSRRS-----
ARL8A_HUMAN ICCYSTSCKE-KDNIDITLQWLIQHSKSRRS-----
SAR1A_HUMAN MEVFMCSVLK-RQGYGEGFRWLQSYID-----
SAR1B_HUMAN LEVFMCSVLK-RQGYGEGFRWMAQYID-----
ARL9_HUMAN MFLGFTYLT-KNGSEIPSTMQDAKDLIAQLAADVQ-----
    
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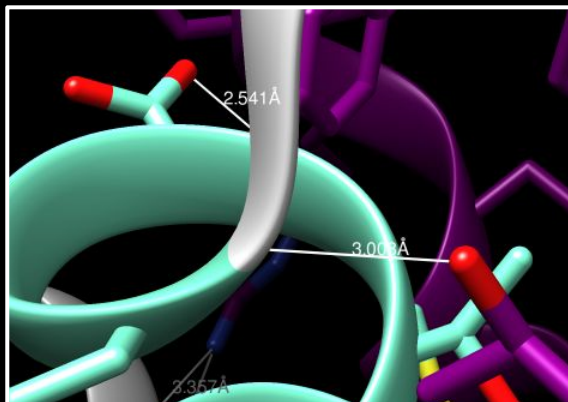
■ Arf1
 ■ GEF.ARNO

Arf1 - GEF interacting residues

ARG 79

GLY 219

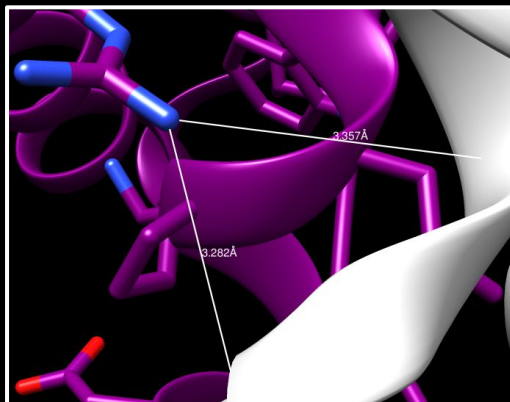
3.282Å



THR 48

ASN 20

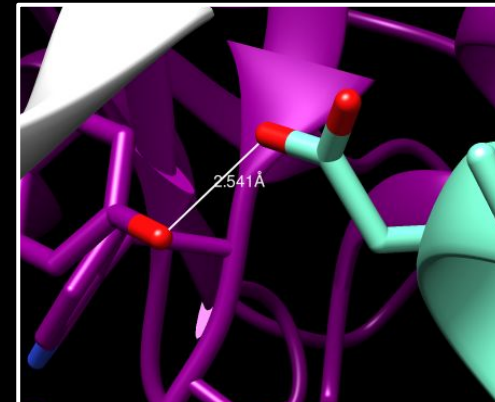
3.008Å



ARG 79

MET 216

3.357Å



TYR 81

ASP 198

2.541Å

