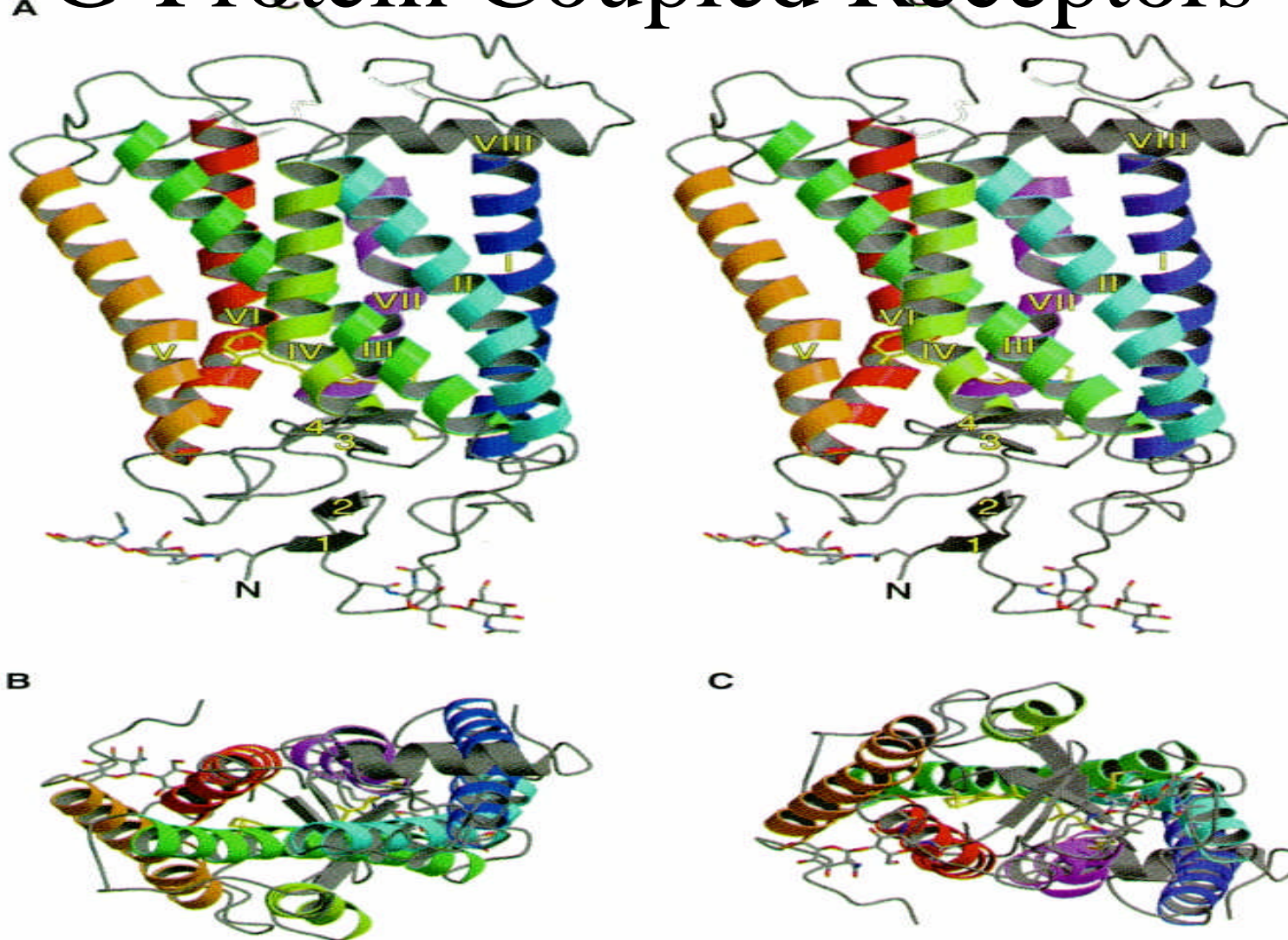
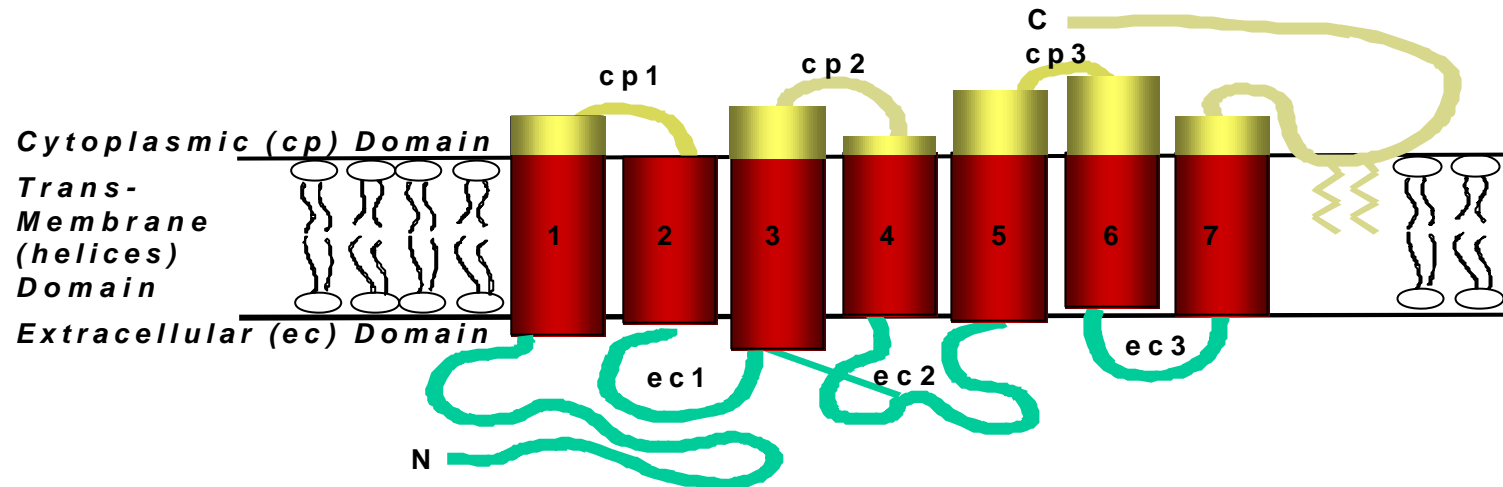


A G-Protein Coupled Receptors



2-D representation

A .

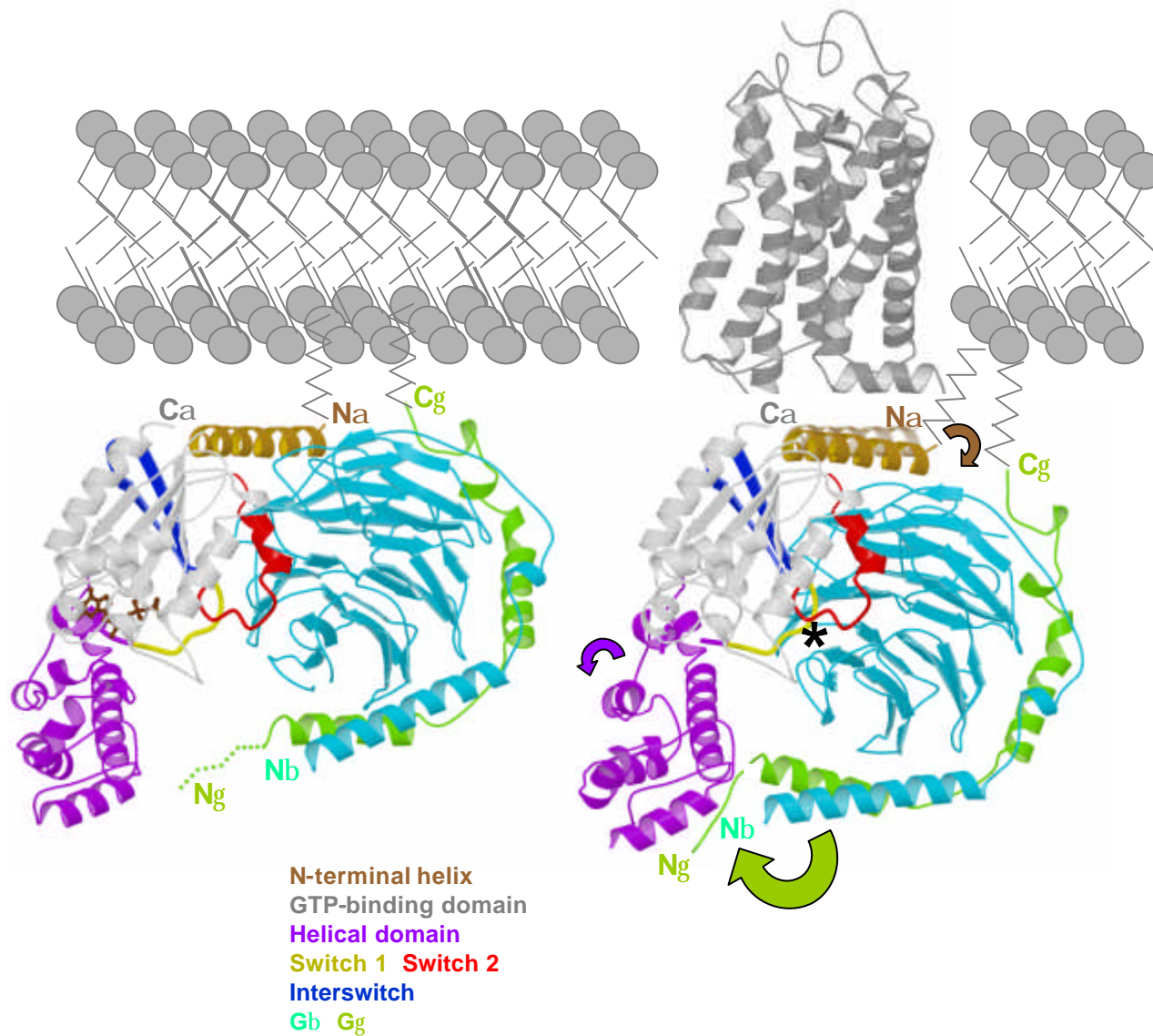


B .



- Segments contributing to extracellular (ec) domain
- Segments contributing to transmembrane (helices) domain
- Segments contributing to cytoplasmic (cp) domain

3-D representation



G-Protein Coupled Receptors (GPCR)

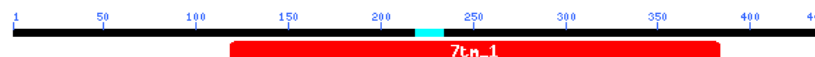
- Endothelin Receptors (endothelins)
- C-X-C Chemokine Type 3 Receptors (chemokines)
- Cysteinyl-leukotriene Receptors (cysteinyl-Leukotrienes)
- Protein Activated Receptors (Thrombin, trypsin)

Domain Maps of some G-Protein- coupled Receptors

Endothelin Receptor A



Endothelin Receptor B



Cysteinyl-leukotriene Receptor 1



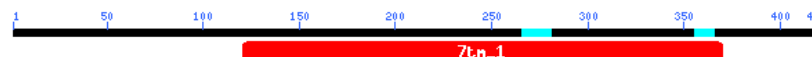
Cysteinyl-leukotriene Receptor 2



C-X-C Chemokine Receptor type 3 A



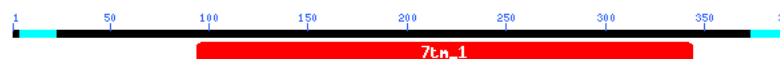
C-X-C Chemokine Receptor type 3 B



Proteinase Activated Receptor 1



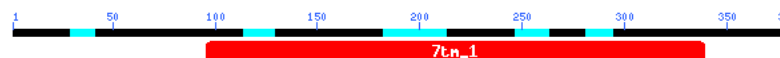
Proteinase Activated Receptor 2



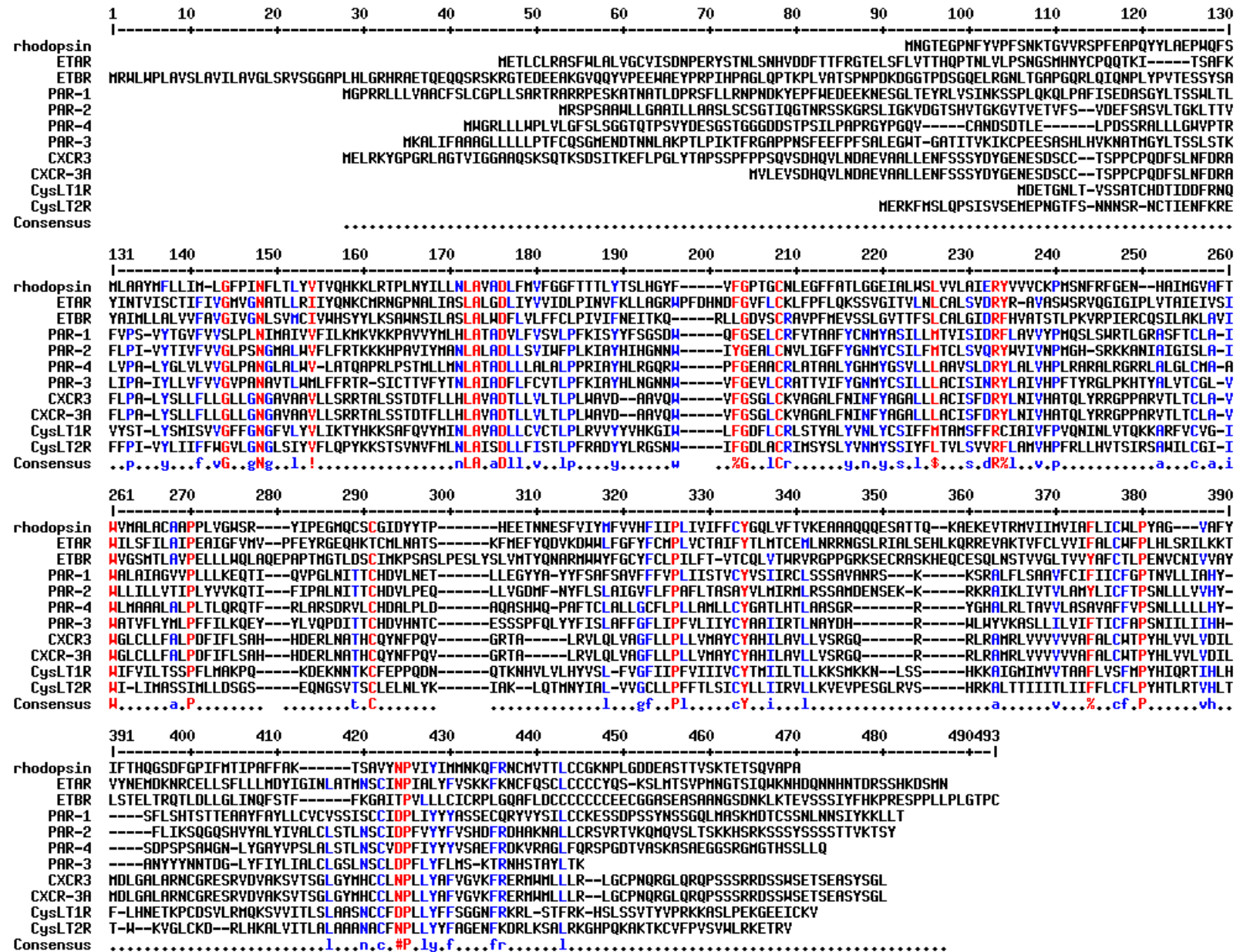
Proteinase Activated Receptor 3



Proteinase Activated Receptor 4



Comparison between sequences (with Mutlialin)



N-terminal part (alignment)

	1	10	20	30	40	50	60	70	80	90	100	
CXCR3A												
CXCR3-B												
ETBR												
CysLT2R												
ETAR												
PAR1												
PAR3												
PAR2												
bRhodopsin												
CysLT1R												
PAR4												
Consensus												

No conserved residues in general sequence : ligand binding site!

But some conservation between homologues.

Comparison of intra cellular loops

Loop 1

	1	10	14									
	-----+-----											
ETAR	R	I	I	Y	Q	N	K	C	M	R		
ETBR	Y	K	N	K	C	M	R	N	G	P	N	
rhodopsin	T	V	Q	H	K	K	L	R	T	P	L	N
cysLTR1	K	T	Y	H	K	K	S	A				
cysLTR2	L	Q	P	Y	K	K	S	T				
PAR-1	L	K	M	K	Y	K	K	P	A			
PAR-2	F	R	T	K	K	K	H	P	A			
CXCR3A	R	R	T	A	L	S	S	T				
PAR-3	F	R	T	R	S	I	C	T				
PAR-4	T	Q	A	P	R							
Consensus											

Loop 2

	1	10	20	24																					
	-----+-----+-----																								
ETAR	D	R	Y	R	A	V	A	S	H	S	R	V	Q	G	I	G	I	P	L	Y	T	A	I	E	
ETBR	D	R	Y	R	A	V	A	S	H	S	R	I	K	G	I	G	V	P	K	A	T				
CXCR3A	D	R	Y	L	N	I	V	H	A	T	Q	L	Y	R	G	P	P	A	R	V	T				
PAR-1	D	R	F	L	A	V	Y	Y	P	H	Q	S	L	S	A	R	T	L	G	R					
PAR-4	D	R	Y	L	A	L	V	H	P	L	R	A	R	A	L	R	G	R	R	L					
PAR-3	N	R	Y	L	A	I	V	H	P	F	T	Y	R	G	L	P	K								
PAR-2	Q	R	Y	H	V	I	V	N	P	H	G	H	S	R	K	K	A	N	I						
rhodopsin	E	R	Y	V	V	V	C	K	P	H	S	N	F	R	F	G	E	N	H						
cysLTR1	P	V	Q	N	I	N	L	Y	T	Q	K	K	A	R											
cysLTR2	R	L	L	H	V	T	S	I	R																
Consensus	.r	y	l	p																			

Loop 3

	1	10	20	29																										
	-----+-----+-----																													
ETAR	T	C	E	M	L	N	R	R	N	G	S	L	R	I	A	L	S	E	H	L	K	Q	R	R	E	V	A	K		
ETBR	T	C	E	M	L	R	K	K	S	G	-	H	Q	I	A	L	N	D	H	L	K	Q	R	R	E	V	A	K	T	
rhodopsin	K	E	A	A	A	Q	Q	Q	E	S	A	T	T	Q	K	A	E	K	E	V	T									
CXCR3A	C	Y	A	H	I	L	A	V	L	L	Y	S	R	G	Q	R	R	L	A	M	R									
PAR-1	C	Y	V	S	I	I	R	C	L	S	S	A	V	A	N	R	S	K	K	S	R	A								
PAR-2	A	Y	V	L	H	I	R	M	L	R	S	S	A	N	D	E	N	S	E	K	K	R	K	R	A					
PAR-3	C	Y	A	A	I	I	R	T	L	N	A	Y	D	H	R	M														
cysLTR2	R	V	L	L	K	V	E	V	P	E	S	G	L	R	V	S	H	R	K	A										
PAR-4	H	T	L	A	A	S	G	R	R	Y	G	H	A	L	R															
cysLTR1	T	L	L	K	K	S	H	K	K	N	L	S	S	H	K															
Consensus	l	s	k																							

Comparison of C-terminal sequence

	1	10	20	30	40	50	54
	-----+	-----+	-----+	-----+	-----+	-----+	
ETAR					LLMDYIGINL	ATMNSCINPI	ALYFV
ETBR	SKR	FKNCFK	SCLCC	HCQSFE	EKQSLEE	KQSCLK	FKANDHGYDNFRSSNKYSSS
PAR-2	SHD	FRDHAK	NALLC	--RSV	RTYKQ	HQVSLT	SKKHSRKSSSYSSSSTTVKTSY
PAR-1	SSEC	QRYVYS	ILCC	KESSDP	SSYNSS	GGQLH	ASKHDTCCSNLNNSIYKLLT
CXCR3A	GVK	FRERMM	LLL	--RL	GCPNQ	RGLQR	QPSSSRDSSMSETSEASYSGL
PAR-4	SAE	FRDKY	RAGL	FQR	SPGDT	VASKA	SAEGGSRGHTHSSLLQ
rhodopsin	NKQ	FRNCH	LTTI	CCGK	NPLG	DDEA	SATVSKTETSQVAPA
cysLTR1	SGGN	FRKRL	-ST	FRK-	HSL	SSV	TYVPRKKASLPEKGEEICKV
cysLTR2	AGEN	FKDRL	KSAL	LRK	GHPQ	KAKT	KCVFPVSVMLRKETRY
PAR-3	SKT	RNH	STAY	LTK			
Consensus	fr.....	l.....

TM1 alignment

	1	10	20	27
	-----+-----+-----			
CysLTR1	LYSMISVVGFFGNGFVLYVLI			
CXCR3	AFLPALYSLLFLLGLLGNGAYAAVLLS			
PAR1	LFVPSYVTGVFVYSLPLNIMAIYVFI			
PAR2	VFLPIYTYIVFVYGLPSNGMALWVFL			
PAR3	KLIPAIYLLVFVYGPANAYTLWMLF			
PAR4	LYGLVLYVGLPANGALWVLA			
CysLTR2	IYYLIIFFWGYLGNLSIYVF			
ET2R	YINTVVSCLVFVLGIIGNSTLLRII			
ET1R	YINTVISCTIFIYGMVGNATLL			
Consensusy..vfvvG..gNg...I.v...			

TM2 alignment

	1	10	20	30
	-----+-----+-----			
CysLTR1	FQVYMINLAVADLL-CVCTLP			
CysLTR2	VNVFMLNLAISDLL-FISTLPF			
PAR1	VYYMLHLATAQYL-FVSYLPF			
PAR3	TYFYTNLAIADFL-FCVTLPF			
CXCR3	TFLLHLAVADTL-LVLTLPWA			
PAR2	VIYMANLALADLL-SVIMFPL			
PAR4	LPSTMLLMNLATAQDL-LALAL			
ET2R	ILIASLALGDLHIVIDIPINVKLL			
ET1R	ILIASLALGDLHIVIDIPINVKLL			
ConsensusnLA.aDIL..v..lp.....			

Receptor	IL1	IL2	IL3	C-terminus
par1		cki,pcsk	CaMII,PKA,PKC	CKI,CKII,GSK3
par2		PKC	CKII,PKA,PKC	CaMII, CKI,GSK3, PKA, PKC, PKG
par3	CaMII, PKA,	PKC		CaMII, CKI, S6K, PKA
par4			CKI, PKC	CKI, CKII
CLT1		PKC CKI,	PKC	CaMII, CKI, CKII, S6K, PKA, PKC, PKG
CLT2	PKG	GSK3, PKC	PKA, PKC	CaMII, S6K, PKA
CXCR3	CKI, CKII, GSK3, PKA,			CaMII, CKI, CKII, GSK3, PKA, PKC, PKG
ETAR		CKII	camII,PKA, ,PKC	CKI, CKII, GSK3, PKA, PKC
ETBR			camII,PKA, ,PKG	CKII, GSK3, PKA, PKC
Rhodopsin			CKI, CKII, PKC	CKI, CKII, GSK3

Thanks very much!

The GPCR team:

Joan Campbell-Tofte (Sweden)

Simona Infantino (Switzerland)

Sarah Knight (Ireland)

Jelena Predic (UK)

Jennifer Gillibert (France)