

human NPSR	1	MPANF	.....	TEGSFDS	....	SGTG	.....	QT	.....	LDSSPV	..	ACTETVTFTEVVEGK
chimpanzee NPSR	1	MPANF	.....	TEGSFDS	....	SGTG	.....	QT	.....	LDSSPV	..	ACTETVTFTEVVEGK
gorilla NPSR	1	MPANF	.....	TEGSFDS	....	SGTG	.....	QT	.....	LDSSPV	..	ACTETVTFTEVVEGK
marmoset NPSR	1	MPANF	.....	TESSLDS	....	NGTR	.....	QT	.....	PDSSPV	..	ACTETVTFTEVVEGK
orangutan NPSR	1	MPANF	.....	TEGSFDS	....	SGTG	.....	QT	.....	LDSSPV	..	ACTETVTFTEVVEGK
macaque NPSR	1	MPANF	.....	TEGSFDS	....	NGTG	.....	QM	.....	LDSSPV	..	ACTETVTFTEVVEGK
horse NPSR	1	MPANL	.....	TEGSPNS	....	NGTM	.....	QT	.....	LDSSPV	..	LCTGTVTFTEVVEGE
cow NPSR	1	MPANL	.....	TEGSAKS	....	NGTG	.....	QA	.....	LN	..	SPV
dog NPSR	1	MPAHL	.....	AEASPDSSHP	SGAT	.....	.....	QT	.....	LEASPV	..	LCTETVTFTEVVEGE
giant panda NPSR	1	MPANL	.....	TEGSPDSNDAS	SGTT	.....	.....	QT	.....	LDASPV	..	LCTETVTFTEVVEGE
elephant NPSR	1	MPANL	.....	TEGSPDS	....	SGTT	.....	QM	.....	LDSSPA	..	ACSETVTVTEVVEGE
rat NPSR	1	MPANL	.....	TEGSFHA	....	NQTV	.....	PM	.....	LDSSPV	..	ACTEIVTFTEALVAE
mouse NPSR	1	MPANL	.....	TEGSFHA	....	NQTV	.....	PM	.....	LDSSPV	..	ACTEIVTFTEALVAE
rabbit NPSR	1	MPANH	.....	TEGSAPS	....	TQST	.....	LT	.....	QGSSPA	..	TCTETTFTEVVEGE
mouse lemur NPSR	1	MAAHL	.....	TEGSPNS	....	SGTT	.....	QT	.....	LDSSPV	..	ACTETVTVTEVVEGE
bush baby NPSR	1	MPANL	.....	TEGSPNS	....	GGTT	.....	QT	.....	PAPSLV	..	ACDITVTFTEVAEGE
guinea pig NPSR	1	MPSHR	.....	PQDHSSI	....	VAQTAPSLDASS	.....	.....	.....	LDAALV	..	ACTDTVTFTEVVEGE
opossum NPSR	1	MQVNG	.....	TEGSWAV	....	NGTM	.....	EP	.....	LDAQPLDTCA	.....	AEVTTSPEGAEQE
megabat NPSR	1	MPANL	.....	TEGSPNS	....	NGTM	.....	QT	.....	LDSSTA	..	TCFPTT
dolphin NPSR*	1	MPANL	.....	TEGSPKS	....	IGTG	.....	QT	.....	LD	..	SPI
chicken NPSR	1	MEVGP	.....	TAASSSS	....	PAGT	.....	GW	.....	LDVLTV	..	TCTDTVTFTEVLEE
zebra finch NPSR	1	MEVNS	.....	TEASSSS	....	QGGT	.....	SC	.....	LDLTLV	..	TFTETVTFTEVVAEE
lizard NPSR*	1	MDSTFIYII	.....	SSSAYKH	....	HSHK	.....	QC	.....	PFVSK	..	PCFLYVVVTLYSTYGR
frog NPSR	1	MQVSF	.....	AEASDFS	....	NTSS	.....	GT	.....	LNLTLT	..	NCTSANSSADIEEY
lancelet NPSR-like*	1	MPFFS	.....	.....	.....	RYQNRVY	.....	QA	.....	WALEIV	..	ALSTVTTTPPF
acorn worm CCAPR-like*	1	MTSKL	.....	NEMKYAA	....	VMGA	.....	.....	.....	FINTTV	..	YNNTVNNNSTYDIP
water flea CCAPR <sup>+</sup>	1	MGDDD	.....	.....	.....	SCLERTW	.....	.....	.....	FNSDQLAGELN	.....	LCPSPSNSTED
mosquito CCAPR	1	MTASKWATIQDNFVIGHDVVSHPALPRTA	.....	.....	.....	.....	.....	.....	.....	SIVVLPSRSPNTKHAVATRLRPDDDE	.....	.....
fruitfly CCAPR	71	MLAPT	.....	.....	.....	PTTA	.....	.....	.....	TTAAAAATTSPGDSFQAA	.....	AAAAAGDNATSPYAGELD
marine worm CCAPR**	1	MLVLV	.....	LSFEPHL	....	.....	.....	.....	.....	MLLEQFHRNVTSDFIGNLQ	.....	.....
limpet CCAPR**	1	MNHHS	.....	.....	.....	YKYFSVPLSL	.....	VI	.....	LINFCL	..	OCLMEYSYDVILG

[illegible]



human NPSR 239 IKS KTY.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIIILAFICCCWS

chimpanzee NPSR 239 IKS KTY.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIIILAFVCCWS

gorilla NPSR 239 IKS KTY.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIIILAFICCCWS

marmoset NPSR 239 IKS KTY.ESVI...SN...CSDGK...LCSSY.NRGPISKAKIKAIKYSIVIILAFICCCWS

orangutan NPSR 240 IKS KTY.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIIILAFICCCWS

macaque NPSR 239 IKS KTY.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

horse NPSR 239 TKS KAS.ETVI...SN...CSDGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

cow NPSR 238 VKS KAY.ETVI...SN...CSDGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

dog NPSR 242 IKS KAH.ETVI...SN...CSGGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

giant panda NPSR 242 IKS KAH.ETVI...SN...CLDGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

elephant NPSR 239 IKS KAH.DMVI...SN...CSNGK...LCTSY.NRRLISKAKIKAIKYSVVIILAFICCCWS

rat NPSR 240 IKS KAH.ETVI...SN...CSDGE...LCSSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

mouse NPSR 239 MKS KTH.ETVI...SN...CSDGK...LCSSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

rabbit NPSR 239 VKS KAC.ETVN...SN...CSDGK...LCTSY.NRGLISKAKIKAVKYSAAIILAFICCCWS

mouse lemur NPSR 238 IKS KAH.ETVI...SN...CSGGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

bush baby NPSR 239 IKS KAH.DSVI...SN...CSGGK...LCTSY.NRGLISKAKIKAIKYSIVIILAFICCCWS

guinea pig NPSR 245 MKS KAP.ETVI...SN...YSDGK...LCTSY.NRGPISKAKVKAIKYSIVIVLAFICWS

opossum NPSR 240 IKS KAH.DMII...SN...CSBGK...LCSSY.NRGVISKAKIKAIKYSIVIILAFICWS

megabat NPSR 237 MKS KGH.DESI...SN...CSDGK...LCTSY.NRGLISKAKIKAIKYSMVIIILAFICCCWS

dolphin NPSR\* 235 VKS KAH.ETEI...SS...CSDGK...RCTIS.N.GLISKAKINAIKYSIVIILAFICCCWS

chicken NPSR 239 MKS KAQ.AAIV...SS...CTDGK...TSAGYTSRGFISRAKVKAIKYSIVIVLAFALCWS

zebra finch NPSR 239 MKS KAQ.AAII...SS...CPGGK...TSRGYTSRGFISRAKVKAIKYSIVIILAFILCWS

lizard NPSR\* 247 TKS KAH.AIIV...SN...CSDGK...FCTSY.THRGLISKAKIKAVKYSIVIILAFVLCWS

frog NPSR 240 VKS KGH.AVII...SN...YTDGN...FCTSY.SYHRGLISKAKMKAIKYSIVIVLAFILCWS

lancelet NPSR-like\* 227 KRGGKM.AYEDHIPRSR...ASSGKNFYRIFHLHINNFGTSRAKARTIKLSVAIILAFICCCWS

acorn worm NPSR-like\* 236 RKSKMM.VPAK...RRIFN...EKNGD...SRGLIPAKIKTIKMTLCIVLFSVFCWS

water flea CCAPR+ 203 VQSAIF.LGIN...RAGGSAGTAMLDEQE...SRA.SSRGIIPRAKIKTVKMTFVIVLFLCWA

mosquito CCAPR 248 AKGAIM.GPVD...RTRNGMA...DLA...SRA.SSRGIIPRAKIKTVKMTFVIVLFLCWS

fruitfly CCAPR 313 AKGSIF.VPTD...RA.GFG...GAA...TRA.SSRGIIPRAKIKTVKMTLTVFVFLCWS

marine worm CCAPR++ 234 SKNGVS.TTSN...KR...QLSKRGR...ESTT.SSRGMIPKARIKTIKMTFAIVTVFIICVW

limpet CCAPR++ 236 SKQGSRRDGM...ETHNLPR...IGVGSREHMVCRRTNSNRGIIPQAKIKTIKMTLTVIIVFLCWS

HELIX 8		
.....Q		
human NPSR	344	.....IRLRQL.....QEAALMLCPQR.....E.NWK.....GTWP
chimpanzee NPSR	344	.....IPLRQL.....QEAALTLCPQR.....Q.NWK.....GTWP
gorilla NPSR	344	.....NSSVYLLACDVSVLWALVPTSEKESCE.SWRRKGAKITG..FQND
marmoset NPSR	344	.....SSTVYLLACDVAVLWGLVLPGGKENCE.SLRRKGAKITG..FQND
orangutan NPSR	345	.....RRS.....QDSRMTFRERT.....E.RHE.....MQIL
macaque NPSR	344	.....RRS.....QDSRMTFRERT.....E.RHE.....MQIL
horse NPSR	344	.....QRS.....QDSRMTYQERT.....E.RHE.....MQVL
cow NPSR	343	.....QRS.....RDSRMTCRERT.....E.KHE.....MQVL
dog NPSR	347	.....QTS.....RGSRKTFRERT.....Q.RHE.....MQVL
giant panda NPSR	347	.....RTS.....RDSRMTFRERT.....Q.RHE.....MQVL
elephant NPSR	344	.....RKS.....RDSRMTQERT.....E.RHE.....MQVL
rat NPSR	345	.....QRS.....QDSRMTYRERS.....E.RHE.....MQIL
mouse NPSR	344	.....QRS.....QDSRMTYRERS.....E.RHE.....MQIL
rabbit NPSR	344	.....RRS.....QDSRMTCRERT.....E.RHE.....MQTL
mouse lemur NPSR	343	.....RNSVYLLACDASSVHWAVLTSKGEGCE..WRKKGAKITG..FQSD
bush baby NPSR	341	.....NSSAYLLAD.DASVLTWVLTSGKEGCE..RKE...AKITG..FQND
guinea pig NPSR	350	.....QKS.....QVSRMTCRERS.....E.RHE.....LQFL
opossum NPSR	345	.....RRN.....AGGTFQDKT.....E.RHE.....MRMR
megabat NPSR	343	.....NSSAYLLAS.AVIHWALVLGSGGK.....AKITG..FQDD
dolphin NPSR*	339	.....NSSAYLLASDVSVHWAVLTSRKEGCE..WWG.....
chicken NPSR	345	.....RRT.....RRLEGTFRDRS.....DGGQE.....MQVL
zebra finch NPSR	345	.....RRT.....QRLGGTFRERS.....DGGQQ.....MQVL
lizard NPSR*	353	.....RRR.....SGNLGTFRERT.....E.GQE.....MQVL
frog NPSR	346	.....RNS.....GKLGGTIRDKT.....E.GIE.....MQVV
lancelet NPSR-like*+	342	.....RRA.....LKHFKMLKAFH.....LKNHF.....VEEG
acorn worm NPSR-like <sup>+</sup>	339	.....MVTVVREVLSLMTNIHNRN.....GYSNF.....RNIV
water flea CCAPR <sup>+</sup>	347	.....ETLTAYNGIWNKTS.....IFPFHFQNGHTI...
mosquito CCAPR	371	SPDGGSQGAGMRNGTVLNGNARLQNHNSSDSMRTLTTSLTISQRSC...IRP.SRVVIVERPKAAL..
fruitfly CCAPR	431	SYRNNSQQN..RCHTV...GRRL..HNSCDSMRTLTTSLTVSRRST...NKANARVIIICERPKNKVITY
marine worm CCAPR*+	341	.....ETLSVAIRKLEKLYKKSCTTSSSHLLFQKAPV.....LRVAFT
limpet CCAPR*+	350	.....SRLSSCDYSMTQDYESVSVTFTIRLTRELECT.....
▲		
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human NPSR	369	GVPSWALPR
chimpanzee NPSR	369	GVPSWALPR
gorilla NPSR	386	VPGEN.REA
marmoset NPSR	386	VPGEN...R
orangutan NPSR	367	SKPEF...I
macaque NPSR	366	SKPEF...I
horse NPSR	366	SKPEF...I
cow NPSR	365	SKPEF...M
dog NPSR	369	SKPEF...I
giant panda NPSR	369	PKPEF...I
elephant NPSR	366	SKPEF...I
rat NPSR	367	SKPEF...I
mouse NPSR	366	SKPEF...I
rabbit NPSR	366	AKPEF...L
mouse lemur NPSR	384	IPGED...G
bush baby NPSR	379	IPREN...R
guinea pig NPSR	372	SKPEF...I
opossum NPSR	365	PKPEF...I
megabat NPSR	375	VPREN...R
dolphin NPSR*	369	...R...K
chicken NPSR	368	SKPEY...I
zebra finch NPSR	368	SKPEC...I
lizard NPSR*	375	SKPEY...I
frog NPSR	368	SRPEY...L
lancelet NPSR-like*+	365	SVFLC...L
acorn worm NPSR-like <sup>+</sup>	367	NRAMY...I
water flea CCAPR <sup>+</sup>	373	..LKK...D
mosquito CCAPR	433	.AMSQ...V
fruitfly CCAPR	489	PAMSE...V
marine worm CCAPR*+	380	SLLLV...L
limpet CCAPR*+	383	.....S

Note: Secondary structure elements marked on top of the alignment correspond to that predicted for the human NPSR sequence. Transmembrane regions are named TM1 to TM7; extracellular and intracellular loops are named ECL1, 2, 3 and ICL1, 2, 3, respectively. The upright triangle symbol in blue corresponds to Type I divergence sites and star symbol in green corresponds to Type II divergence sites. Numbers on the left of the sequences correspond to the amino acid residue position for each sequence. Intron positions are marked in blue boxes. N-terminal region of the fruitfly CCAPR sequence has been trimmed to align with rest of the sequences. Sequences corrected manually at the N and C- termini are represented with \* and + at the end of their sequence names.

Figure S3