Protein (accession number)	Φ/Ψ/RRXR	Topology	Comments	Reference
Invariant chain Iip35(P04233)	**RRSR**	II	+	Schutze et al, EMBO J, 1994
Kir6.2 (P70673)	**LRKR**	P(C)	+	Zerangue et al, Neuron, 1999
Kir6.1(Q63664)	**LRKR**	P(C)	+	Zerangue et al, Neuron, 1999
SUR1(A56248)	**NRKR**	P(L)	+	Zerangue et al, Neuron, 1999
SUR2 (NP_037172)	**NRKQ**	P(L)	+, weak	Konstas et al, JBC, 2002
EBV gp110 (CAD53463)	**LRRR**	I	+, inm	Lee Virology,1999
$GABA_B$ receptor 1(Q9Z0U4)	**LRSR**	P(C)	+	Margeta-Mitrovic et al, Neuron, 2000
NMDA receptor subunit NR1 (Q05586)	**KRRR**	P(C)	+	Standley et al, Neuron, 2000
mGluR1 (NP_000829)	**FRRK**	P(C)		Chan et al, Mol Cell Neurosci, 2001
HCMV gB (P06473)	**LRHR**	I	+, inm	Meyer et al, JBC, 2000
HSV1 gB (P06437)	**MRKR**	I	+, inm	Meyer et al, BBRC, 2002
KA2 (NP_113696)	**RRRR**	P(C)	+	Ren et al, J Neurosci, 2003
KA1 (Q16099)	**RRRR**	P(C)	+	Ren et al, J Neurosci, 2003
VIPL (Q9H0V9)	**SRKRFY**–COOH	I	+, but see *	Nufer et al, JBC, 2003
5-hydroxytryptamine receptor 3B (NP_006019)	**CRAR**	P(L)	Problematic, see **	Boyd et al, JBC, 2003
Kv4.2 (NP_036413)	**ERKR**	P(N)	-	Shibata et al, JBC, 2003
Glucosidase I (CAD19636)	**RRRR**	II	+	Hardt et al, Glycobiology, 2003
GLT-1 (P43006)	**DRMR**	P(EL)	Extracellular!	Kalandadze et al, J Neurosci, 2004
hGGA1 (O43292)	**VRRR**	P(N)	-	Vainauskas et al, JBC, 2005
V2 vasopressin receptor (P30518)	**RRGR**	P(L)	Exposed upon truncation	Hermosilla et al, Mol Pharmacol. 2001

Table I: Selected examples of R-based signals. These motifs were investigated in the context of the respective protein and in many cases on reporter proteins as well. Topology is indicated as type I, type II, or P (polytopic). Position of R-based signal in the N-terminus (N), cytosolic loop (L), extracellular loop (EL), or C-terminus (C) is indicated. + or - indicate functionality of the signal. inm = inner nuclear membrane.
* Whilst functional, this signal is very difficult to distinguish from a –KKXX type signal as there is one K present, the spacing is correct with respect to the distal C-terminus and the signal is spaced fairly close to the transmembrane segment.
** This signal does not comply with the consensus at all and is located in a very short cytosolic loop. There are no reporter protein experiments to support the function of this motif as a peptide sorting signal.

References

Boyd GW, Doward AI, Kirkness EF, Millar NS & Connolly CN (2003) Cell surface expression of 5-hydroxytryptamine type 3 receptors is controlled by an endoplasmic reticulum retention signal. *J Biol Chem* **278:** 27681-27687

Chan WY, Soloviev MM, Ciruela F & McIlhinney RA (2001) Molecular determinants of metabotropic glutamate receptor 1B trafficking. *Mol Cell Neurosci* **17:** 577-588

Hardt B, Kalz-Fuller B, Aparicio R, Volker C & Bause E (2003) (Arg)3 within the N-terminal domain of glucosidase I contains ER targeting information but is not required absolutely for ER localization. *Glycobiology* **13:** 159-168

Hermosilla R & Schulein R (2001) Sorting functions of the individual cytoplasmic domains of the G protein-coupled vasopressin V(2) receptor in Madin Darby canine kidney epithelial cells. *Mol Pharmacol* **60:** 1031-1039

Kalandadze A, Wu Y, Fournier K & Robinson MB (2004) Identification of motifs involved in endoplasmic reticulum retention-forward trafficking of the GLT-1 subtype of glutamate transporter. *J Neurosci* **24:** 5183-5192

Konstas AA, Dabrowski M, Korbmacher C & Tucker SJ (2002) Intrinsic sensitivity of Kir1.1 (ROMK) to glibenclamide in the absence of SUR2B. Implications for the identity of the renal ATP-regulated secretory K+ channel. *J Biol Chem* **277:** 21346-21351

Lee SK (1999) Four consecutive arginine residues at positions 836-839 of EBV gp110 determine intracellular localization of gp110. *Virology* **264:** 350-358

Margeta-Mitrovic M, Jan YN & Jan LY (2000) A trafficking checkpoint controls GABA(B) receptor heterodimerization. *Neuron* **27:** 97-106

Meyer G, Gicklhorn D, Strive T, Radsak K & Eickmann M (2002) A three-residue signal confers localization of a reporter protein in the inner nuclear membrane. *Biochem Biophys Res Commun* **291:** 966-971

Meyer GA & Radsak KD (2000) Identification of a novel signal sequence that targets transmembrane proteins to the nuclear envelope inner membrane. *J Biol Chem* **275:** 3857-3866

Nufer O, Mitrovic S & Hauri HP (2003) Profile-based data base scanning for animal L-type lectins and characterization of VIPL, a novel VIP36-like endoplasmic reticulum protein. *J Biol Chem* **278:** 15886-15896

Ren Z, Riley NJ, Garcia EP, Sanders JM, Swanson GT & Marshall J (2003) Multiple trafficking signals regulate kainate receptor KA2 subunit surface expression. *J Neurosci* **23:** 6608-6616

Schutze MP, Peterson PA & Jackson MR (1994) An N-terminal double-arginine motif maintains type II membrane proteins in the endoplasmic reticulum. *EMBO J* **13:** 1696-1705

Shibata R, Misonou H, Campomanes CR, Anderson AE, Schrader LA, Doliveira LC, Carroll KI, Sweatt JD, Rhodes KJ & Trimmer JS (2003) A fundamental role for KChIPs in determining the molecular properties and trafficking of Kv4.2 potassium channels. *J Biol Chem* **278:** 36445-36454

Standley S, Roche KW, McCallum J, Sans N & Wenthold RJ (2000) PDZ domain suppression of an ER retention signal in NMDA receptor NR1 splice variants. *Neuron* **28:** 887-898

Vainauskas S & Menon AK (2005) Endoplasmic reticulum localization of Gaa1 and PIG-T, subunits of the glycosylphosphatidylinositol (GPI) transamidase complex. *J Biol Chem*

Zerangue N, Schwappach B, Jan YN & Jan LY (1999) A new ER trafficking signal regulates the subunit stoichiometry of plasma membrane K(ATP) channels. *Neuron* **22:** 537-548