Diversification and Evolution of the Signal Transduction System : Rapid Divergence of Tissue Specific Genes in Early Evolution of Chordates

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Part 2

Rapid Divergence of Tissue Specific Genes in Early Evolution of Chordates

Introduction

An evolutionary analysis of several protein families based on phylogenetic trees revealed interesting branching patterns characteristic of family members: Divergence of distinct functions by gene duplication predates almost exclusively the divergence of vertebrates and arthropods, whereas in members that are virtually identical in function, but differ only in tissue distribution (tissue specific isoforms), their diversifications had occurred independently in each of vertebrates and arthropods after the separation of the two phyla (Iwabe et al., 1993; Part 1).

Results and Discussion

Figure 1 shows phylogenetic trees of opsin and nicotinic acetylcholine receptor (nAChR) subfamilies. Because members of each subfamily have identical ligand binding specificity and thus are virtually identical in function, but differ only in tissue distributions, they are considered to be tissue specific isoforms. In these trees, the branching point (filled circle in Fig. 1) corresponding to the divergence of fishes and other higher vertebrates was determined by comparing sequences from several vertebrate species and by testing the approximate rate constancy of amino acid substitutions among vertebrate lineages, by which paralogous comparisons were excluded. Tentatively assigning this branching point as a boundary, the whole chordate lineages covering from the divergence (open circle) of chordates and arthropods to modern vertebrates were divided into two periods, the first period (shaded region) and the latter period. On the basis of the phylogenetic trees, the number of gene duplications and the rate of amino acid substitutions were estimated in each of the periods. Similar analyses were performed for 20 different families or subfamilies including opsin and nAChR subfamilies. The results were summarized in Table 1.

Table 1 revealed the following branching patterns characteristic of the tissue specific isoforms: First, in the 18 subfamilies out of 20 analyzed here, the number of gene duplication is larger in the first period than in the latter period; of 67 gene duplications in total, 51 (76%) have been found in the first period. Because the time interval of the first period is only about one half the interval of the latter period (i.e., 200 myrs and 400 myrs, respectively, if vertebrates/arthropods divergence of 600 myrs and fishes/other higher vertebrates divergence of 400 myrs are assumed (Dickerson, 1971)), the rate of gene duplication per year of the first period is estimated to be about six times the corresponding rate of the latter period. This figure may be a minimum estimate, because the number of lineages is apparently smaller in the first period than in the latter period. Second, the evolutionary rate of amino acid substitution is always higher in the first period than in the latter period, and the ratio widely differs for different subfamilies, ranging from 1.8 to 31. Reduced functional constraints in duplicated genes is not responsible for the accelerated amino acid substitutions in the first period, because no appreciable correlation has been observed between copy numbers and evolutionary rates, although we do not exclude a possibility that the former contributes to the latter in part. Third, in spite of such rapid diversification of isoform genes in the early evolution of chordates, the number of isoforms shared between chordates and arthropods is very small, only one or a few in each of 20 subfamilies, except for the case of potassium channels. Although we have no ample data of invertebrate isoforms, it is conceivable that similar branching patterns are also observed in invertebrates, judging from the very limited number of isoforms shared between vertebrates and invertebrates in many subfamilies and the presence of multiple copies of isoforms in arthropod opsins and nAChRs, which had diverged independently from those of vertebrates (Fig. 1).

The frequent duplication of tissue specific isoforms and the rapid rate of amino acid substitutions in the early evolution of chordates are particularly interesting in relation to the rapid phenotypic diversification of chordates at this period, where a variety of tissues and organs had been developed (Romer, 1959). The diversifications at the molecular and phenotypic levels are likely to be evolutionarily linked. There is, however, a possibility that the observed correlation is only an accidental result. To exclude the possibility, we have carried out an similar analysis for another group of isoforms (compartmentalized isoforms), among which they are virtually identical in function, but differ only in localization of intracellular compartments.

Figure 2 shows a phylogenetic tree of members of calcium ATPase subfamily. Three gene duplications leading to four distinct compartmentalized

isoforms showing different intracellular localization evidently predate the divergence of protists and animals. This strongly suggests that diversification of compartmentalized isoform genes had occurred in the early evolution of eukaryotic cells, where several intracellular compartments had been established. Similar branching patterns were also observed in other groups of compartmentalized isoforms analyzed so far, including HSP70, HSP90, ADP ribosylation factor, and *rab* subfamilies; in these subfamilies, three, one, more than four, and more than twelve gene duplications have been observed, respectively, which generate multiple isoforms differing in localization of cellular compartments. In addition all these gene duplications were shown to have occurred during early evolution of protists. It is therefore conceivable that diversifications of compartmentalized isoforms correlate with diversifications of cellular compartments, as in the case of tissue specific isoforms.

Thus it is highly likely that the correlation between genetic variations and phenotypic diversifications during evolution of the common ancestor of chordates and echinoderms and the early stage of chordates is not an accidental result, but has an actual evolutionary meaning. It may be possible to interpret the correlation between diversifications at the two levels in a unified way.

We previously showed that tissue specific genes are constrained against amino acid alternations not only from the structural or functional requirements of individual molecules, but also from higher level as tissues or organs, where they are expressed (Kuma et al., 1993). Lack of function of a tissue results in rapid accumulations of amino acid substitutions in tissue specific genes, as demonstrated by the lens crystallin of blind mole rat (Hendriks, 1987). In addition the number of gene copies are possibly regulated by dosage compensation effect (Allendorf, 1979; Kitagawa et al., 1987). Thus it is conceivable that the relaxation of selective constraints operating at the phenotypic level is responsible for the rapid rate of amino acid substitutions as well as the frequent gene duplications in tissue specific isoforms during the early evolution of chordates. Although we do not exclude a possibility that the Darwinian selection contributes to the genetic diversity in part, our interpretation may be more plausible, because the majority of evolutionary changes at the molecular level are generally thought to be neutral. Furthermore the above interpretation could provide a molecular basis for a widely accepted hypothesis on the rapid evolutionary bursts at high taxonomic level in the Cambrian period; the invasion of new ecological niche is a prerequisite for episodic diversifications of novel body plans, where organisms could survive even in a low state of adaptedness (Simpson, 1967; Kimura, 1991; Valentine, 1977). This implies the relaxation of selective constraint at the phenotypic level. In his four-stage scenario theory of macroevolution (Kimura, 1991), Kimura emphasized the importance of liberation from the preexisting selective constraint at the phenotypic level, followed by sudden increase of neutral variations at the molecular level. If our interpretation is correct, similar evolutionary patterns will be observed in other animal phyla.

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Table 1. Comparisons of the number of gene duplications and evolutionary rates between the first (I) and latter (II) periods in the chordate lineages after the separation from arthropods.

Subfamily	n_0	n_I	n_{II}	v_I/v_{II}
nAChR family				
nAChR	2	10 (5.0)	3 (0.75)	3.6
Rhodopsin family				
opsin	1	6 (3.0)	3 (0.75)	10
mAChR *	1	2 (1.0)	0 (0.0)	5.5
src family				
src	1	4 (2.0)	0 (0.0)	7.2
FGFR *	1	3 (1.5)	1 (0.25)	6.2
raf *	1	2 (1.0)	0 (0.0)	5.5
CDK2 *	1	2 (1.0)	0 (0.0)	4.5
EGFR	1	2 (1.0)	0 (0.0)	3.9
IR *	1	2 (1.0)	2 (0.50)	4.2
erk *	1	1 (0.50)	0 (0.0)	7.0
ras family				
ras	1	3 (1.5)	0 (0.0)	31
*rap*1 (*Krev*)	1	1 (0.50)	0 (0.0)	15
G protein family				
Gαi *	1	2 (1.0)	0 (0.0)	4.3
Gαs *	1	1 (0.50)	0 (0.0)	5.1
Ion-gated channel family				
K^+ channel *	4	3 (1.5)	0 (0.0)	4.3
Na^+ channel	2	1 (0.50)	4 (1.0)	1.8
Ion pump family				
SERCA *	1	2 (1.0)	0 (0.0)	2.6
Na^+ -K^+ pump	1	0 (0.0)	2 (0.50)	1.8
Elongation factor family				
EF-1α *	2	2 (1.0)	1 (0.25)	3.4
Aldolase family				
aldolase *	1	2 (1.0)	0 (0.0)	2.0
Total		51 (25.5)	16 (4.0)	

Table 1. (continued)

Notes - The lineages from the common ancestor of chordates and arthropods to extant vertebrates were subdivided into the first (I) and latter (II) periods, whose boundary was tentatively defined at the time of divergence of fishes and amphibians. n_0, the number of isoforms shared between arthropods and vertebrates. n_I and n_{II}, the numbers of gene duplications occurred in the period I and II, respectively; the number of gene duplications per 100 million years is shown in parenthesis, which has been calculated by assuming 600 million years for the time of divergence of chordates and arthropods, and 400 million years for that of fish and amphibian (Dickerson, 1971). v_I/v_{II}, the average rate v_I of amino acid substitutions in the period I relative to that v_{II} in the period II were calculated from the branch lengths of inferred phylogenetic tree. *, because no fish data were available, the branching point of fish and amphibian was inferred from that of amphibian and mammals, by assuming 400 million years and 350 million years (Dayhoff, 1978) for the divergence times, respectively and the constant rate of vertebrate evolution in the period II. Abbreviations: nAChR, nicotinic acetylcholine receptor; mAChR, muscarinic acetylcholine receptor; FGFR, fibroblast growth factor receptor; EGFR, epidermal growth factor receptor; IR, insulin receptor; $G\alpha i$,G protein α subunit i subtype; $G\alpha s$,G protein α subunit s subtype; SERCA, sarcoplasmic/endoplasmic reticulum type Ca^{2+} ATPase (calcium ion pump). Phylogenetic trees and alignments of the genes listed above are on Appendix C1-18. The list of v_I and v_{II} is on Appendix D.

Figure legends

Figure 1. Phylogenetic trees of (a), opsins and (b), nicotinic acetylcholine receptors (nAChR's) from vertebrates, molluscs and arthropods. Both trees were inferred by neighbor-Joining method (Saitou and Nei, 1987), based on the alignment of sequences for conserved regions [250 sites in a) and 367 sites in b)], where unambiguous alignments are possible. The deepest roots in (a) and (b) were determined by assuming a muscarinic acetylcholine receptor and a serotonin-3 receptor as outgroups, respectively. The number at each node indicates the probability that two lineages are joined together at the node to form a single cluster, which has been estimated by a standard procedure with 1000 times resamplings (Felsenstein, 1985). Filled circle, divergence of fishes and other higher vertebrates; open circle, divergence of chordates and arthropods; Filled rhombus, gene duplication that occurred after the divergence of fishes and other higher vertebrates; open rhombus, gene duplication that occurred before the separation of fishes and other higher vertebrates; Shaded rhombus, gene duplication in arthropod lineages. A double rhombus in (b) represents gene duplication that had occurred before vertebrates/arthropods divergence. A shaded area indicates a period between divergence times shown by the open and closed circles. Sequence data were taken from GenBank database release 77.0, except for *Drosophila* RH4 (Montell et al., 1987); accession numbers of sequences are as follows: (a), human rhodopsin (K02281), chicken rhodopsin (D00702), lamprey rhodopsin (M63632), chicken green (M92038, M88178), *Gecko* P467 (M92035), goldfish green-1 (L11865), goldfish green-2 (L11866), chicken blue (M92037), goldfish blue (L11864), human blue (M13299), chicken violet (M92039), human green (K03494), human red (M13305), chicken iodopsin (X57490), goldfish red (L11867), cave fish R007 (M38630), cave fish G101 (M38624), cave fish G103 (M60945), *Gecko* P521 (M92036), octopus rhodopsin (X07797), *Loligo* rhodopsin (S14332), *Drosophila* RH1 (K02315), *Drosophila*

RH2 (M12896), crayfish opsin (S53494), *Limulus* lateral eye opsin (L03791, L03781), *Drosophila* RH3 (M17718, Y00043), human m1 mAChR (an outgroup, X52068, M35128); (b), human α (Y00762, X02508), chicken α (X07338), *Xenopus* α (X07067), *Xenopus* α1A (X17244), *Torpedo* α (J00963), human α5 (M83712), chicken α5 (J05642), rat β3 (J04636), goldfish nα2 (X14786), goldfish nα3 (M29529), human α3 (M37981), chicken α3 (M37336), goldfish α3 (X54051), rat α6 (L08227), rat α2 (M20297), chicken α2 (X07344) rat α4 (M15682), chicken α4 (X07399), human β2 (X53179), chicken β2 (X53092;X07357), rat b4 (M33953), chicken nα3 (A39218), goldfish β2 (X54052), human β (X14830), *Torpedo* β (J00964), mouse δ (K02582), chicken δ (K02903), *Torpedo* δ (J00965), human γ (M11811), chicken γ (K02904), *Torpedo* γ (J00966, V01394), mouse ε (J04698, X55718), *Drosophila* Dα2 (X52274, X53583), *Drosophila* ALS (X07194), *Drosophila* SBD (X55676), *Drosophil*a ARD (X04016), rat α7 (M85273), chicken α7 (X68586), chicken BgtBP α2 (X52296), mouse 5HT-3 receptor (outgroup, M74425). Alignment of the opsins and nAChRs are on Appendix A1 and A2, respectively.

Figure 2. Phylogenetic tree of calcium ATPases (pump). This tree was inferred by neighbor-joining method (Saitou and Nei, 1987), based on the alignment of 12 sequences from 7 species for conserved regions of 295 sites, where unambiguous alignment is possible. The deepest root was determined by assuming a yeast proton-ATPase as an outgroup. The number at each node indicates the probability that two lineages are joined together at the node to form a single cluster, which has been estimated by a standard procedure with 1000 times resamplings (Felsenstein, 1985). Open circle, divergence of vertebrates and arthropods; closed circle, divergence of protists and other eukaryotes; open rhombus, gene duplications occurred before divergence of protists and other eukaryotes. Data for the localization of Ca^{2+}-ATPases in cells were taken from Ghislain et al. (1990) and Rudolph et al. (1989). Sequence data were taken from GenBank database release 70.0; accession numbers of sequences are as follows: human PMCA1 (J04027), rat SERCA1a (M99223), human SERCA2 (M23114), rat SERCA3 (M30581), *Drosophila* DRSERCA (M62892), tomato Ca^{2+} pump (M96324), *Plasmodium* YEL6 (X55197), rat Ca^{2+} pump (M93017,S43533), *S.cerevisiae* PMR1 (M25488), *S.cerevisiae* PMR2 (M25489), *S.pombe* cta3 (J05634) *S.cerevisiae* PMA1 (outgroup, X03534). Alignment of the pumps are on Appendix B.

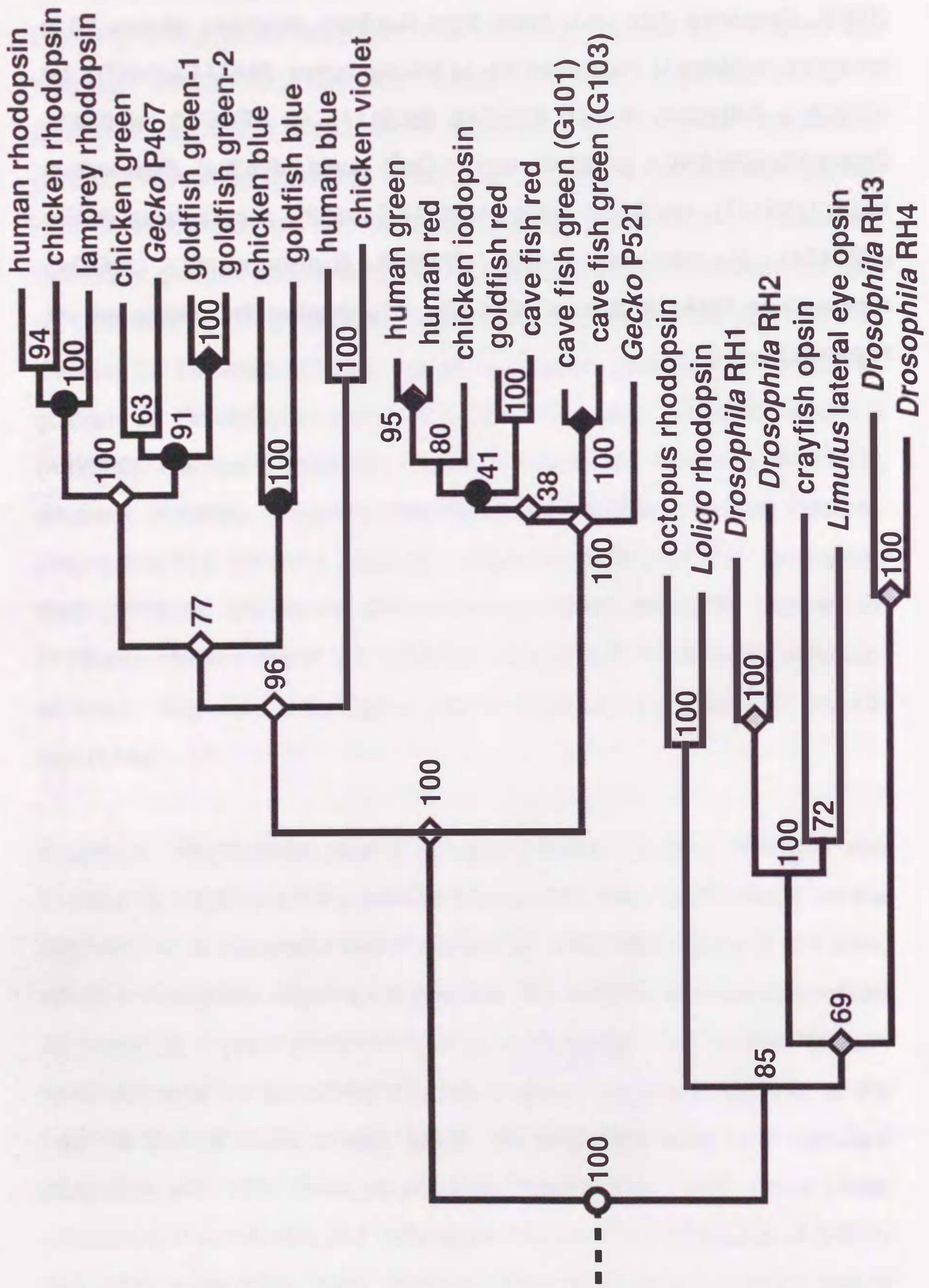

Figure 1(a)

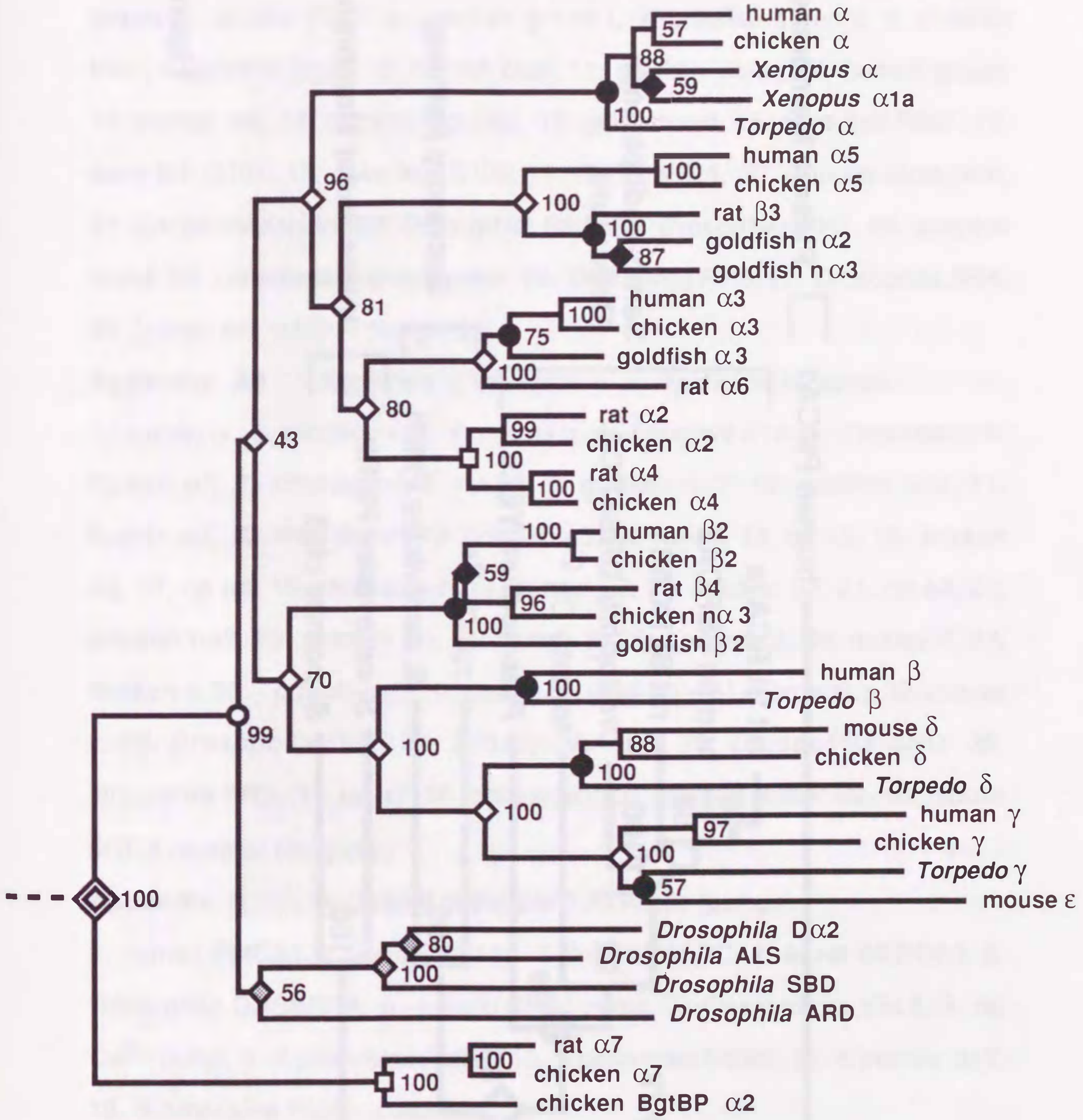

Figure 1(b)

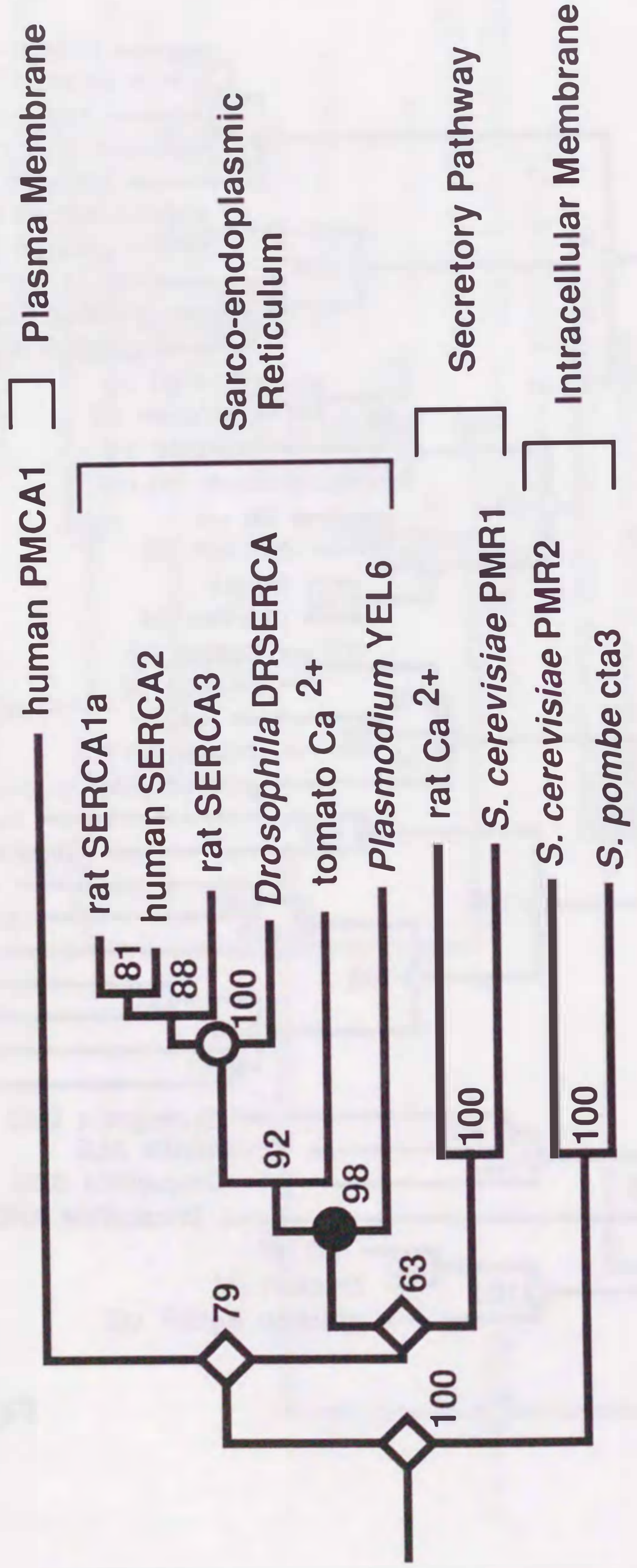

Figure 2

Appendix

Appendix A1 Alignment of the opsins.

1. human rhodopsin, 2. chicken rhodopsin, 3. lamprey rhodopsin, 4. chicken green, 5. *Gecko* P467, 6. goldfish green-1, 7. goldfish green-2, 8. chicken blue, 9. goldfish blue, 10. human blue, 11. chicken violet, 12. human green, 13. human red, 14. chicken iodopsin, 15. goldfish red, 16. cave fish R007, 17. cave fish G101, 18. cave fish G103, 19. *Gecko* P521, 20. octopus rhodopsin, 21. *Loligo* rhodopsin, 22. *Drosophila* RH1, 23. *Drosophila* RH2, 24. crayfish opsin, 25. *Limulus* lateral eye opsin, 26. *Drosophila* RH3, 27. *Drosophila* RH4, 28. human m1 mAChR (outgroup)

Appendix A2 Alignment of the nicotinic acetylcholine receptors.

1. human α, 2. chicken α, 3. *Xenopus* α, 4. *Xenopus* α1A, 5. *Torpedo* α, 6. human α5, 7. chicken α5, 8. rat β3, 9. goldfish nα2, 10. goldfish nα3, 11. human α3, 12. chicken α3, 13. goldfish α3, 14. rat α6, 15. rat α2, 16. chicken α2, 17. rat α4, 18. chicken α4, 19. human β2, 20. chicken β2, 21. rat b4, 22. chicken nα3, 23. goldfish β2, 24. human β, 25. *Torpedo* β, 26. mouse δ, 27. chicken δ, 28. *Torpedo* δ, 29. human γ, 30. chicken γ, 31. *Torpedo* γ, 32. mouse ε, 33. *Drosophila* Dα2, 34. *Drosophila* ALS, 35. *Drosophila* SBD, 36. *Drosophila* ARD, 37. rat α7, 38. chicken α7, 39. chicken BgtBP α2, 40. mouse 5HT-3 receptor (outgroup).

Appendix B Alignment of the Ca^{2+} ATPases (pumps).

1. human PMCA1, 2. rat SERCA1a, 3. human SERCA2, 4. rat SERCA3, 5. *Drosophila* DRSERCA, 6. tomato Ca^{2+} pump, 7. *Plasmodium* YEL6, 8. rat Ca^{2+} pump, 9. *S.cerevisiae* PMR1, 10. *S.cerevisiae* PMR2, 11. *S.pombe* cta3, 12. *S.cerevisiae* PMA1 (outgroup).

Appendix C (1-18) Data were from GenBank Release 77.0. Accession numbers of the data and expressions were in parentheses. Phylogenetic trees were inferred by NJ method (Saitou and Nei, 1987).

Appendix C1 Phylogenetic tree (a) and alignment (b) of muscarinic acetylcholine receptors.

1.human m1 (X52068, M35128; brain), 2. human m3 (hM4) (X15266; brain, pancreas), 3. human m5 (M80333; brain), 4. human m2 (M16404, X15264; brain, heart), 5. chicken m2 (M73217; brain, heart), 6. human m4 (hM3) (X15265; brain), 7. chicken m4 (J05218; brain, heart), 8. *Xenopus* m4 (X65865; ovary), 9. *Drosophila* mAChR (M23412; head), 10. bovine histamine-H1 receptor (D10197) (outgroup).

Appendix C2 Phylogenetic tree (a) and alignment (b) of *src*.

1. human *src* (K03218; ubiquitous, brain), 2. *Xenopus src* (M23422), 3. human *yes* (M15990; brain, kidney), 4. *Xiphophorus yes* (X54970), 5. human *fyn* (M14333; monocyte), 6. *Xiphophorus fyn* (X54971) 7. human *fgr* (M19722; brain, T-cell), 8. human *hck* (M16591; granulocyte) 9. human *lyn* (M16038; B cell, spleen), 10. mouse *lck* (M12056; T cell, spleen), 11. chicken *tkl* (J03579), 12. mouse *blk* (M30903; B-cell), 13. *Drosophila src* (M11917; brain, eye), 14. hydra STK (M25245) (outgroup).

Appendix C3 Phylogenetic tree (a) and alignment (b) of fibroblast growth factor receptors (FGFR).

1. mouse bFGFR (M28998; brain), 2. chicken bFGFR (M24637), 3. *Xenopus* bFGFR (M61687), 4. human *bek* (X52832; brain), 5. chicken *cek3* (M35196), 6. human FGFR3 (M58051; intestinum, lung, brain, calvarial bone, growth plate, skin), 7. human FGFR4 (X57205; fetal adrenal gland, lung, liver, pancreas, small intestine, smooth muscle, spleen), 8. salamander FGFR (X65059), 9. *Drosophila* FGFR (X57746), 10. human *ret* (X12949) (outgroup).

Appendix C4 Phylogenetic tree (a) and alignment (b) of *raf*.

1. human *c-raf* (X03484; ubiquitous, muscle, brain), 2. *Xenopus c-raf* (X12948), 3. human *B-raf* (X54072; brain), 4. human *A-raf* (X04790; epididymis, ovary, kidney, urinary bladder), 5. *Drosophila D-raf* (X07181), 6. *Dictyostelium* DPYK2 (M33784) (outgroup).

Appendix C5 Phylogenetic tree (a) and alignment (b) of CDK2.

1. human CDK2 (X61622), 2. goldfish *cdc2* (S40289), 3. *Xenopus* Eg1 (X14227), 4. human CDK3 (X66357), 5. *Drosophila cdc2c* (X57486), 6. human *cdc2* (X05360) (outgroup), 7. *Xenopus cdc2* (M60681) (outgroup), 8. *Drosophila cdc2* (X57485) (outgroup), 9. *Saccharomyces cdc2* (X00257) (outgroup).

Appendix C6 Phylogenetic tree (a) and alignment (b) of epidermal growth factor receptors (EGFR).

1. human EGFR (X00663; epidermal tissue, placenta), 2. chicken EGFR (M10066), 3. *Xiphophorus* EGFR-like protein (X16891), 4. human *c-erb-B-2* (X03363; fetus epidermal tissue, term placenta, 20-week placenta, liver, kidney, lung, brain), 5. human *c-erb-B-3* (M29366; term placenta, postnatal skin, stomach, lung, kidney, brain), 6. *Drosophila* EGFR-like protein (K03054), 7. *Schistosoma* EGFR-like (M86396) (outgroup).

Appendix C7 Phylogenetic tree (a) and alignment (b) of insulin receptors (IR).

1. human insulin receptor (X02160; ubiquitous), 2. human insulin-like growth factor-1 receptor (IGF1R) (X04434), 3. *Xenopus* XTK-1A (X64659), 4. *Xenopus* XTK-1B (X64660), 5. bovine isulin-like growth factor-1 receptor (IGF1R) (X54980), 6. *Xenopus* XTK-2 (X64661), 7. human insulin receptor related protein (IRR), 8. *Drosophila* insulin receptor-like protein (M14778), 9. human ROS1 (M34353) (outgroup).

Appendix C8 Phylogenetic tree (a) and alignment (b) of *erk*.

1. human *erk2* (M84489; ubiquitous), 2. *Xenopus* Xp42 (M60977), 3. human *erk1* (M84490; lung), 4. *Drosophila erk* (S40154), 5. *Candida erk* (M76585) (outgroup).

Appendix C9 Phylogenetic tree (a) and alignment (b) of *ras*.

1. human K-*ras* (L00048; endocrine gland, brain), 2. *Xenopus ras* (M34657), 3. goldfish *ras* (M26734), 4. human H-*ras*-1 (V00574, J00277; ubiquitous), 5.

chicken H-*ras*-1 (X03578), 6. human N-*ras* (L00043, X02751; ubiquitous, bone marrow, thymus, testis), 7. Drosophila Dm*ras*85D (M16429), 8. Artemia p21 (M27887), 9. *Caenorhabditis let-60* (M55535), 10. *Saccharomyces RAS1* (K01970) (outgroup).

Appendix C10 Phylogenetic tree (a) and alignment (b) of *rap* (*Krev*).

1. human *Krev*-1 (X12533; ubiquitous), 2. *Discopyge* o-*Krev* (M38395; ubiquitous), 3. human *rap1b* (NBRF Release 36.0, S01952), 4. *Drosophila Rap1* (M80535), 5. *Dictyostelium Ddrap1* (X54291) (outgroup).

Appendix C11 Phylogenetic tree (a) and alignment (b) of Gαi.

1. human i1 (M17219; nearly ubiquitous, brain), 2. *Xenopus* i1 (X56089), 3. human i3 (J03005, M20604, J03198, M27543, J03238; nearly ubiquitous), 4. *Xenopus* i3 (X56090), 5. human i2 (M20593, X04828; ubiquitous), 6. *Lymnaea* i (Z15095), 7. *Drosophila* G1 (M23094), 8. human o2 (M60165) (outgroup), 9. human z (J03260) (outgroup), 10. human t2 (D10384) (outgroup).

Appendix C12 Phylogenetic tree (a) and alignment (b) of Gαs.

1. human s-1 (M21142, X04408; ubiquitous), 2. *Xenopus* s (X56091), 3. rat olf (M26718; olfactory neuroepithelium), 4. *Drosophila* s-S (M33998, M23233; brain), 5. *Lymnaea* s (Z15096), 6. *Schistosoma* s (M81085) (outgroup).

Appendix C13 Phylogenetic tree (a) and alignment (b) of K^+ channels.

1. mouse MK2 (M30440), 2. *Xenopus XSha2* (NBRF Release 36.0, JH0313), 3. mouse MBK1 (Y00305), 4. human HPCN3 (M55515), 5. human HPNC2 (M55514), 6. human HBK2 (X17622; brain), 7. human HPCN1 (M55513), 8. *Drosophila Shaker* (M17211), 9. *Drosophila ShB* (X07132), 10. Aplysia AK01-A (M95914), 11. rat drk1 (X16476) (outgroup).

Appendix C14 Phylogenetic tree (a) and alignment (b) of Na^+ channels.

1. rat I (X036389; brain), 2. rat II (X03639; brain), 3. rat III (Y00766; brain), 4. human SkM1 (M81758; skeletal muscle), 5. human hH1 (M77235; heart), 6. *Electrophorus* (X01119), 7. human hNav2.1 (M91556; heart, uterus), 8. *Drosophila para* (M32078), 9. *Loligo* (D14525), 10. *Drosophila* (60D-E) (ref. 1), 11. human Ca^{2+} channel N-type alpha-1.1 (M94172) (outgroup).

ref. 1 = Science *237*, 744-749 (1987).

Appendix C15 Phylogenetic tree (a) and alignment (b) of Ca^{2+} pumps (SERCA).

1. rat 1a (M99223; heart), 2. chicken 1 (M26064), 3. *Rana* 1 (X63009), 4. human 2 (M23114; muscle, brain, kidney, stomach), 5. chicken 2 (M66385, S51963), 6. rat 3 (M30581; ubiquitous, intestine, spleen, lung), 7. *Drosophila* (M62892), 8. *Artemia* (X51674), 9. tomato Ca^{2+} pump (M96324) (outgroup).

Appendix C16 Phylogenetic tree (a) and alignment (b) of Na^+-K^+ pumps.

1. human 1 (X04297, D00099; fetal kidney > adult kidney), 2. chicken 1 (J03230), 3. *Xenopus* 1 (ref. 1), 4. *Bufo* 1 (Z11798, S43455), 5. *Catostomus* 1 (X58629), 6. human 2 (J05096; brain, fetal heart), 7. chicken 2 (M59959; heart, brain), 8. human 3 (M37457; fetal brain, adult brain, heart, skeletal muscle), 9. chicken 3 (M59960), 10. *Torpedo* 1 (X02810), 11. *Drosophila* Da-47 (X14476), 12. *Artemia* (1) (S63410), 13. *Artemia* (2) (Y07513), 14. hydra (M75140) (outgroup).

ref. 1 = Am. J. Physiol. 256, F1034-F1043 (1989).

Appendix C17 Phylogenetic tree (a) and alignment (b) of EF-1α.

1. human (X03558, J04617; ubiquitous), 2. *Xenopus* S (M25504; ubiquitous), 3. rat statin-related protein (M62751), 4. *Xenopus* 42Sp48 (X56699; oocyte, tailbud), 5. *Xenopus* O (M75873, M67485, X52976; oocyte, early embryo), 6. *Onchocerca* (M64333), 7. *Drosophila* F1 (X06869, M11744), 8. *Bombyx* (D13338), 9. *Drosophila* F2 (X06870), 10. *Apis* (X52884), 11. *Artemia* (X03349), 12. *Saccharomyces* A (X00779, X01638, M15666, M10992, M15667) (outgroup).

Appendix C18 Phylogenetic tree (a) and alignment (b) of aldolases. 1. human A (M11560; muscle), 2. human B (K01177; liver), 3. chicken B (M10946), 4. human C (X05196; brain), 5. chicken C (ref. 1), 6. *Xenopus* C (ref. 2), 7. *Drosophila* (X60064), 8. maize (M16220) (outgroup).

ref. 1 = Biochem. Int. *20*, 921-929 (1990).

ref. 2 = from Prof. Katuji Hori (personal communication).

Appendix D Comparison of the evolutionary rates between the first (I) and latter (II) periods in the chordate lineages after the separation from arthropods.

opsin (1)

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 1. (37) SMLAAYMFLLIVLGFPINFLTLYVTVQHKKLRTPLNYILLNLAVADLFMVLGGF TSTLYTSLHGYFVFGPTGCNLEGFFATLGGEIALWS
 2. (37) SALAAYMFMLILLGFPVNFLTLYVTIQHKKLRTPLNYILLNLVVADLFMVFGGF TTTMYTSMNGYFVFGVTGCYIEGFFATLGGEIALWS
 3. (37) SALAAYMFFLILVGFPVNFLTLFVTVQHKKLRTPLNYILLNLAMANLFMVLFGF TVTMYTSMNGYFVFGPTMCSIEGFFATLGGEVALWS
 4. (37) RLVCCYIFFLISTGLPINLLTLLVTFKHKKLRQPLNYILVNLAVADLFMACFGF TVTFYTAWNGYFVFGPVGCAVEGFFATLGGQVALWS
 5. (37) KVLSFYMFFLIAAGMPLNGLTLFVTFQHKKLRQPLNYILVNLAAANLVTVCCGF TVTFYASWYAYFVFGPIGCAIEGFFATIGGQVALWS
 6. (37) KILALYLFFLMSMGLPINGLTLVVTAQHKKLRQPLNFILVNLAVAGTIMVCFGF TVTFYTAINGYFVLGPTGCAVEGFMATLGGEVALWS
 7. (37) KLLAVYMFFLICLGLPINGLTLICTAQHKKLRQPLNFILVNLAVAGAIMVCFGF TVTFYTAINGYFALGPTGCAVEGFMATLGGEVALWS
 8. (44) RAMAAFMFLLIALGVPINTLTIFCTARFRKLRSHLNYILVNLALANLLVILVGS TTACYSFSQMYFALGPTACKIEGFAATLGGMVSLWS
 9. (41) MAMSVFMFFIFIGGASINILTILCTIQFKKLRSHLNYILVNLSIANLFVAIFGS PLSFYSFFNRYFIFGATACKIEGFLATLGGMVGLWS
10. (34) YLQAAFMGTVFLIGFPLNAMVLVATLRYKKLRQPLNYILVNVSFGGFLLCIFSV FPVFVASCNGYFVFGRHVCALEGFLGTVAGLVTGWS
11. (32) YLQTAFMGIVFAVGTPLNAVVLWVTVRYKRLRQPLNYILVNISASGFVSCVLSV FVVFVASARGYFVFGKRVCELEAFVGTHGGLVTGWS
12. (53) HLTSVWMIFVVIASVFTNGLVLAATMKFKKLRHPLNWILVNLAVADLAETVIAS TISVVNQVYGYFVLGHPMCVLEGYTVSLCGITGLWS
13. (53) HLTSVWMIFVVTASVFTNGLVLAATMKFKKLRHPLNWILVNLAVADLAETVIAS TISIVNQVSGYFVLGHPMCVLEGYTVSLCGITGLWS
14. (50) NLTSLWMIFVVAASVFTNGLVLVATWKFKKLRHPLNWILVNLAVADLGETVIAS TISVINQISGYFILGHPMCVVEGYTVSACGITALWS
15. (50) NLATVWMFFVVVASTFTNGLVLVATAKFKKLRHPLNWILVNLAVADLAETLLAS TISVTNQFFGYFILGHPMCIFEGFTVSVCGIAGLWS
16. (50) NLATCWMFFVVVASTVTNGLVLVASAKFKKLRHPLNWILVNLAIADLLETLLAS TISVCNQFFGYFILGHPMCVFEGFTVATCGIAGLWS
17. (48) NVSSLWMIFVVIASVFTNGLVIVATAKFKKLRHPLNWILVNLAIADLGETVLAS TISVINQIFGYFILGHPMCVFEGWTVSVCGITALWS
18. (50) NLASLWMIIVVIASIFTNSLVIVATAKFKKLRHPLNWILVNLAIADLGETVLAS TISVFNQVFGYFVLGHPMCIFEGWTVSVCGITALWS
19. (52) NLVSFFMIIVVIASCFTNGLVLVATAKFKKLRHPLNWILVNLAFVDLVETLVAS TISVFNQIFGYFILGHPLCVIEGYVVSSCGITGLWS
20. (35) YSVGIFIGVVGIIGILGNGVVIYLFSKTKSLQTPANMFIINLAMSDLSFSAINGFPLKTISAFMKKWIFGKVACQLYGLLGGIFGFMSINT
21. (34) YSLGIFIAICGIIGCVGNGVVIYLFTKTKSLQTPANMFIINLAFSDFTFSLVNGFPLMTISCFMKYWVFGNAACKVYGLIGGIFGLMSIMT
22. (50) KILTAYMIMIGMISWCGNGVVIYIFATTKSLRTPANLLVINLAISDFGIMITNT PMMGINLYFETWVLGPMMCDIYAGLGSAFGCSSIWS
23. (57) KILGLFTLAIMIISCCGNGVVVYIFGGTKSLRTPANLLVLNLAFSDFCMMASQS PVMIINFYYETWVLGPLWCDIYAGCGSLFGCVSIWS
24. (53) PLLLIFMLFTGILCLAGNFVTIWVFMNTKSLRTPANLLVVNLAMSDFLMMFTMF PPMMVTCYYHTWTLGPTFCQVYAFLGNLCGCASIWT
25. (47) SILGVAMIILGIICVLGNGMVIYLMMTTKSLRTPTNLLVVNLAFSDFCMMAFMM PTMTSNCFAETWILGPFMCEVYGMAGSLFGCASIWS
26. (58) YLLGTLYIFFTLMSMLGNGLVIWVFSAAKSLRTPSNILVINLAFCDFMMMVKT  PIFIYNSFHQGYALGHLGCQIFGIIGSYTGIAAGAT
27. (54) YMLGVFYIFLFCASTVGNGMVIWIFSTSKSLRTPSNMFVLNLAVFDLIMCLKA  PIFIYNSFHRGFALGNTWCQIFASIGSYSGIGAGMT
28. (25) AFIGITTGLLSLATVTGNLLVLISFKVNTELKTVNNYFLLSLACADLIIGTFSM NLYTTYLLMGHWALGTLACDLWLALDYVASNASVMN
consensus                 N            L    N                                 G   C
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Appendix A1

opsin (2)

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       1. LVVLAIERYVVVCKPMS NFRFGENHAIMGVAFTWVMALACAAPPLA GWSRYIPEGL (15) NNESFVIYMFVVHFTIPMIIIFFCYGQLVFTV
       2. LVVLAVERYVVVCKPMS NFRFGENHAIMGVAFSWIMAMACAAPPLF GWSRYIPEGM (15) NNESFVIYMFVVHFMIPLAVIFFCYGNLVCTV
       3. LVVLAIERYIVICKPMG NFRFGNTHAIMGVAFTWIMALACAAPPLV GWSRYIPEGM (15) NNESYVVYMFVVHFLVPFVIIFFCYGRLLCTV
       4. LVVLAIERYIVVCKPMG NFRFSATHAMMGIAFTWVMAFSCAAPPLF GWSRYMPEGM (15) HNESYVLYMFVIHFIIPVVVIFFSYGRLICKV
       5. LVVLAIERYIVICKPMG NFRFSATHAIMGIAFTWFMALACAGPPLF GWSRFIPEGM (15) HNESYVIYMFIVHFTVPMVVIFFSYGRLVCKV
       6. LVVLAIERYIVVCKPMG SFKFSSSHAFAGIAFTWVMALACAAPPLF GWSRYIPEGM (15) NNESYVIYMFVCHFILPVAVIFFTYGRLVCTV
       7. LVVLAIERYIVVCKPMG SFKFSSTHASAGIAFTWVMAMACAAPPLV GWSRYIPEGI (15) NNESYVLYMFICHFILPVTIIFFTYGRLVCTV
       8. LAVVAFERFLVICKPLG NFTFRGSHAVLGCVATWVLGFVASAPPLF GWSRYIPEGL (15) HNESYVLFLFTFCFGVPLAIIVFSYGRLLITL
       9. LAVVAFERWLVICKPLG NFTFKTPHAIAGCILPWISALAASLPPLF GWSRYIPEGL (15) NNESYVMFLFCFCFAVPFGTIVFCYGQLLITL
      10. LAFLAFERYIVICKPFG NFRFSSKHALTVVLATWTIGIGVSIPPFF GWSRFIPEGL (15) RSESYTWFLFIFCFIVPLSLICFSYTQLLRAL
      11. LAFLAFERYIVICKPFG NFRFSSRHALLVVVATWLIGVGVGLPPFF GWSRYMPEGL (15) RSEYYTWFLFIFCFIVPLSLIIFSYSQLLSAL
      12. LAIISWERWMVVCKPFG NVRFDAKLAIVGIAFSWIWAAVWTAPPIF GWSRYWPHGL (15) GVQSYMIVLMVTCCITPLSIIVLCYLQVWLAI
      13. LAIISWERWLVVCKPFG NVRFDAKLAIVGIAFSWIWSAVWTAPPIF GWSRYWPHGL (15) GVQSYMIVLMVTCCIIPLAIIMLCYLQVWLAI
      14. LAIISWERWFVVCKPFG NIKFDGKLAVAGILFSWLWSCAWTAPPIF GWSRYWPHGL (15) GVQSYMVVLMVTCCFFPLAIIILCYLQVSLAI
      15. LTVISWERWVVVCKPFG NVKFDAKWASAGIIFSWVWSAIWCAPPIF GWSRFWPHGL (15) GVQSYMIVLMITCCIIPLAIIILCYIAVWLAI
      16. LTVISWERWVVVCKPFG NVKFDGKMATAGIVFTWVWSAVWCAPPIF GWSRYWPHGL (15) GVQSYMIVLMITCCFIPLGIIILCYIAVWWAI
      17. LTIISWERWVVVCKPFG NVKFDGKWAAGGIIFSWVWAIIWCTPPIF GWSRYWPHGL (15) GVASYMITLMLTCCILPLSIIIICYIFVWSAI
      18. LTIISWERWVVVCKPFG NVKFDGKWAAGGIIFAWTWAIIWCTPPIF GWSRYWPHGL (15) GVASYMVTLLLTCCILPLSVIIICYIFVWNAI
      19. LAIISWERWFVVCKPFG NIKFDSKLAIIGIVFSWVWAWGWSAPPIF GWSRYWPHGL (15) GCQSFMLTLMITCCFLPLFIIIVCYLQVWMAI
      20. MAMISIDRYNVIGRPMAASKKMSHRRAFLMIIFVWMWSIVWSVGPVF NWGAYVPEGI (13) STRSFILCMYFCGFMLPIIIIAFCYFNIVMSV
      21. MTMISIDRYNVIGRPMSASKKMSHRKAFIMIIFVWIWSTIWAIGPIF GWGAYTLEGV (13) TTRSNILCMYIFAFMCPIVVIFFCYFNIVMSV
      22. MCMISLDRYQVIVKGMA GRPMTIPLALGKIAYIWFMSSIWCLAPAF GWSRYVPEGN (13) NPRSYLIFYSIFVYYIPLFLICYSYWFIIAAV
      23. MCMIAFDRYNVIVKGIN GTPMTIKTSIMKILFIWMMAVFWTVMPLI GWSAYVPEGN (13) NPRSYLITYSLFVYYTPLFLICYSYWFIIAAV
      24. MVFITFDRYNVIVKGVA GEPLSTKKASLWILTIWVLSITWCIAPFF GWNRYVPEGN (13) LSRSYLYDYSTWVYYLPLLPI YCYVSIIKAV
      25. MVMITLDRYNVIVRGMA AAPLTHKKATLLLLFVWIWSGGWTILPFF GWSRYVPEGN (13) SSASYVVIYGLAVYFLPLITMIYCYFFIVHAV
      26. NAFIAYDRFNVITRPME  GKMTHGKAIAMIIFIYMYATPWVVACYTETWGRFVPEGY (13) DTRLFVACIFFFSFVCPTTMITYYYSQIVGHV
      27. NAAIGYDRYNVITKPMN  RNMTFTKAVIMNIIWLYCTPWVVLPLTQFWDRFVPEGY (13) DTRLFVGTIFFFSFVCPTLMILYYYSQIVGHV
      28. LLLISFDRYFSVTRPLSYRAKRTPRRAALMIGLAWLVSFVLWAPAIL FWQYLVGERT (11) SQPIITFGTAMAAFYLPVTVMCTLYWRIYRET
consensus        R                                         W                              P      Y
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Appendix A1 (Continued)

opsin (3)

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       1. ( 15) AEKEVTRMVIIMVIAFLICWVPYASVAFYIFTHQGSNFGPIFMTIPAFFAKSAAIYNPVIYIMMNKQFRNCMLTTI ( 27)
       2. ( 15) AEKEVTRMVIIMVIAFLICWVPYASVAFYIFTNQGSDFGPIFMTIPAFFAKSSAIYNPVIYIVMNKQFRNCMITTL ( 30)
       3. ( 15) AEKEVTRMVVLMVIGFLVCWVPYASVAFYIFTHQGSDFGATFMTLPAFFAKSSALYNPVIYILMNKQFRNCMITTL ( 32)
       4. ( 15) AEKEVTRMVILMVLGFMLAWTPYAVVAFWIFTNKGADFTATLMAVPAFFSKSSSLYNPIIYVLMNKQFRNCMITTI ( 34)
       5. ( 15) AEKEVTRMVILMVLGFLLAWTPYAATAIWIFTNRGAAFSVTFMTIPAFFSKSSSIYNPIIYVLLNKQFRNCMVTTI ( 34)
       6. ( 15) AEREVTKMVILMVFGFLIAWTPYATVAAWIFFNKGADFSAKFMAIPAFFSKSSALYNPVIYVLLNKQFRNCMLTTI ( 28)
       7. ( 15) AEREVTKMVILMVLGFLVAWTPYATVAAWIFFNKGAAFSAQFMAIPAFFSKTSALYNPVIYVLLNKQFRSCMLTTL ( 28)
       8. ( 15) ADREVTKMVVVMVLGFLVCWAPYTAFALWVVTHRGRSFEVGLASIPSVFSKSSTVYNPVIYVLMNKQFRSCMLKLL ( 33)
       9. ( 15) AEREVTKMVVVMVLGFLVCWAPYASFSLWIVSHRGEEFDLRMATIPSCLSKASTVYNPVIYVLMNKQFRSCMMKMV ( 26)
      10. ( 15) AEREVSRMVVVMVGSFCVCYVPYAAFAMYMVNNRNHGLDLRLVTIPSFFSKSACIYNPIIYCFMNKQFQACIMKMV ( 30)
      11. ( 15) AEREVSRMVVVMVGSFCLCYVPYAALAMYMVNNRDHGLDLRLVTIPAFFSKSACVYNPIIYCFMNKQFRACIMETV ( 31)
      12. ( 15) AEKEVTRMVVVMVLAFCFCWGPYAFFACFAAANPGYPFHPLMAALPAFFAKSATIYNPVIYVFMNRQFRNCILQLF ( 27)
      13. ( 15) AEKEVTRMVVVMIFAYCVCWGPYTFFACFAAANPGYAFHPLMAALPAYFAKSATIYNPVIYVFMNRQFRNCILQLF ( 27)
      14. ( 15) AEKEVSRMVVVMIVAYCFCWGPYTFFACFAAANPGYAFHPLAAALPAYFAKSATIYNPIIYVFMNRQFRNCILQLF ( 28)
      15. ( 15) AEKEVSRMVVVMIFAYCFCWGPYTFCACFAAANPGYAFHPLAAAMPAYFAKSATIYNPIIYVFMNRQFRVCIMQLF ( 23)
      16. ( 15) AEKEVSRMVVVMIMAYCFCWGPYTFFACFAAANPGYAFHPLAAAMPAYFAKSATIYNPVIYVFMNRQFRVCIMQLF (  7)
      17. ( 15) AEKEVSRMVVVMILAFIVCWGPYASFATFSAVNPGYAWHPLAAAMPAYFAKSATIYNPIIYVFMNRQFRSCIMQLF ( 21)
      18. ( 15) AEKEVSRMVVVMILAFILCWGPYASFATFSALNPGYAWHPLAAALPAYFAKSATIYNPIIYVFMNRQFRSCIMQLF ( 21)
      19. ( 15) AEREVSRMVVVMIVAFCICWGPYASFVSFAAANPGYAFHPLAAALPAYFAKSATIYNPVIYVFMNRQFRNCIMQLF ( 29)
      20. ( 27) AEMKLAKISMVIITQFMLSWSPYAIIALLAQFGPAEWVTPYAAELPVLFAKASAIHNPIVYSVSHPKFREAIQTTF (124)
      21. ( 27) AEMKLAKISIVIVTQFLLSWSPYAVVALLAQFGPIEWVTPYAAQLPVMFAKASAIHNPMIYSVSHPKFRERIASNF (122)
      22. ( 28) AEGKLAKVALVTITLWFMAWTPYLVINCMGLFKFEGL TPLNTIWGACFAKSAACYNPIVYGISHPKYRLALKEKC ( 29)
      23. ( 28) AEGKLAKVALTTISLWFMAWTPYLVICYFGLFKIDGL TPLTTIWGATFAKTSAVYNPIVYGISHPKYRIVLKEKC ( 30)
      24. ( 28) AECRLAKIAMTTVALWFIAWTPYLLINWVGMFARSYL SPVYTIWGYVFAKANAVYNPIVYAISHPKYRAAMEKKL ( 30)
      25. ( 29) AECRLAKVAMMTVGLWFMAWTPYLIISWAGVFSSGTRLTPLATIWGSVFAKANSCYNPIVYGISHPRYKAALYQRF ( 33)
      26. ( 29) AEIRIAKAAITICFLFFCSWTPYGVMSLIGAFGDKTLLTPGATMIPACACKMVACIDPFVYAISHPRYRMELQKRC ( 30)
      27. ( 29) AEIRIAKAAITICFLFFVSWTPYGVMSLIGAFGDKSLLTQGATMIPACTCKLVACIDPFVYAISHPRYRLELQKRC ( 29)
      28. (143) KEKKAARTLSAILLAFILTWTPYNIMVLVSTFCKDCV PETLWELGYWLCYVNSTINPMCYALCNKAFRDTFRLLL ( 27)
consensus                            PY                                  P  Y
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Appendix A1 (Continued)

nAChR (1)

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       1. (28) AKLF  KDYSSVVRPVEDHRQVVEVTVGLQLIQLINVDEVNQIVTTNVRLKQQWVDYNLKWNPDDYGGVKKIHIPSEKIWRPDLVLYNNADGDFAIVKFTKVLLQYTGHITWTPPAIFKSYCEIIVTHFP
       2. (27) DDLF  REYSKVVRPVENHRDAVVVTVGLQLIQLINVDEVNQIVTTNVRLKQQWTDINLKWNPDDYGGVKQIRIPSDDIWRPDLVLYNNADGDFAIVKYTKVLLEHTGKITWTPPAIFKSYCEIIVTYFP
       3. (28) GDLF  ANYNKVVRPVETYKDQVVVTVGLQLIQLINVDEVNQIVSTNIRLKQQWRDVNLKWDPAKYGGVKKIRIPSSDVWSPDLVLYNNADGDFAISKDTKILLEYTGKITWTPPAIFKSYCEIIVTYFP
       4. (28) NDLF  KSYNKVVRPVKAFKDKVVVTVGLQLIQLINVNEVNQIVTTNVRLKQQWEDVHLKWDPEDYGGIKKVRIPSSDIWRPDIVLYNNADGDFAIVQETKVLLDYTGKIIWLPPAIFKSYCEMIVTYFP
       5. (32) ANLL  ENYNKVIRPVEHHTHFVDITVGLQLIQLISVDEVNQIVETNVRLRQQWIDVRLRWNPADYGGIKKIRLPSDDVWLPDLVLYNNADGDFAIVHMTKLLLDYTGKIMWTPPAIFKSYCEIIVTHFP
       6. (51) KDLF  QDYERWVRPVEHLNDKIKIKFGLAISQLVDVDEKNQLMTTNVWLKQEWIDVKLRWNPDDYGGIKVIRVPSDSSWTPDIVLFDNADGRFEGTS TKTVIRYNGTVTWTPPANYKSSCTIDVTFFP
       7. (37) KHLF  EDYQRWVRPVEHLNDTIKIKFGLAISQLVDVDEKNQLMTTNVWLKQEWIHVKLRWNPEDYAGITSIRVPSDSIWIPDIVLYDNADGRFEGTS TKTVVKYDGTIAWTPPVNYKSSCTIDVTFFP
       8. (39) RHLF  QGYQKWVRPVLNSSDIIKVYFGLKISQLVDVDEKNQLMTTNVWLKQEWTDQKLRWNPEEYGGINSIKVPSESLWLPDIVLFENADGRFEGSLMTKAIVKSSGTVSWTPPASYKSSCTMDVTFFP
       9. (35) RELF  QGYQRWVRPVQHANHSVKVRFGLKISQLVDVDEKNQLMTTNVWLWQEWLDYKLRWNPENYGGITSIRVPSESIWLPDIVLYENADGRFEGSLMTKAIVRYNGMITWTPPASYKSACTMDVTFFP
      10. (36) RNLF  RGYQKWVRPILHANDTITVRFGLKISQLVDVDEKNHLMTTNVWLWQEWTDYKLRWNPEDYGGITSIRVPSETIWLPDIVLYENADGRFEGSLMTKAIVRFNGTIMWTPPASYKSSCTMDVTFFP
      11. (37) ERLF  EDYNEIIRPVANVSDPVIIHFEVSMSQLVKVDEVNQIMETNLWLKQIWNDYKLKWNPSDYGGAEFMRVPAQKIWKPDIVLYNNAVGDFQVDDKTKALLKYTGEVTWIPPAIFKSSCKIDVTYFP
      12. (30) AALF  KNYNQFVRPVKNASDPVIIQFEVSMSQLVKVDEVNQIMETNLWLKHIWNDYKLRWNPVDYGGAEFIRVPSGQIWKPDIVLYNNAVGDFQVDDKTKALLKYTGDVTWIPPAIFKSSCKIDVTYFP
      13. (31) RRLF  RRYNQFIRPVENVSDPVTVEFEVSISQLVKVDEVNQIMETNLWLRHIWNDYKLKWLPAEFDGIEFIRVPSNKIWRPDIVLYNNAVGDFLVEDKTKALLKYDGTITWVPPAIFKSSCPMDITYFP
      14. (38) HTLF  AHYNRFIRPVENVSDPVTVHFELAITQLANVDEVNQIMETNLWLRHVWKDYRLCWDPTEYDGIETLRVPADNIWKPDIVLYNNAVGDFQVEGKTKALLKYDGVITWTPPAIFKSSCPMDITFFP
      15. (40) KHLF  GGYNRWARPVPNTSDVVIVRFGLSIAQLIDVDEKNQMMTTNVWLKQEWNDYKLRWDPAEFGNVTSLRVPSEMIWIPDIVLYNNADGEFAVTHMTKAHLFFTGTVHWVPPAIYKSSCSIDVTFFP
      16. (38) KHLF  TGYNRWSRPVPNTSDVVIVKFGLSIAQLIDVDEKNQMMTTNVWLKQEWSDYKLRWNPEDFDNVTSIRVPSEMIWIPDIVLYNNADGEFAVTHMTKAHLFSNGKVKWVPPAIYKSSCSIDVTYFP
      17. (39) KRLF  SGYNKWSRPVGNISDVVLVRFGLSIAQLIDVDEKNQMMTTNVWVKQEWHDYKLRWDPGDYENVTSIRIPSELIWRPDIVLYNNADGDFAVTHLTKAHLFYDGRVQWTPPAIYKSSCSIDVTFFP
      18. (36) KKLF  SGYNKWSRPVANISDVVLVRFGLSIAQLIDVDEKNQMMTTNVWVKQEWHDYKLRWDPQEYENVTSIRIPSELIWRPDIVLYNNADGDFAVTHLTKAHLFYDGRIKWMPPAIYKSSCSIDVTFFP
      19. (33) EHLLDPSRYNKLIRPATNGSELVTVQLMVSLAQLISVHEREQIMTTNVWLTQEWEDYRLTWKPEEFDNMKKVRLPSKHIWLPDVVLYNNADGMYEVSFYSNAVVSYDGSIFWLPPAIYKSACKIEVKHFP
      20. (26) EYLLDPTRYNKLIRPATNGSQLVTVQLMVSLAQLISVHEREQIMTTNVWLTQEWEDYRLTWKPEDFDNMKKVRLPSKHIWLPDVVLYNNADGMYEVSFYSNAVISYDGSIFWLPPAIYKSACKIEVKHFP
      21. (30) DDLLNKTRYNNLIRPATSSSQLISIRLELSLSQLISVNEREQIMTTSIWLKQEWTDYRLAWNSSCYEGVNILRIPAKRVWLPDIVLYNNADGTYEVSVYTNVIVRSNGSIQWLPPAIYKSACKIEVKHFP
      22. (11) NHLLSPDRYNKLIRPAVNSSQLVSIELQVSLAQLISVNEREQIMTTNVWLNQEWIDYRLAWKPSDYEGINMLRIPAKHIWLPDIVLYNNADGTYEVSLYTNAIVQNNGSIRWLPPAIYKSACKIEVKHFP
      23. ( 3) DFLLGPERYNKLIRPAVNKSQQVTIGIKVSLAQLISVNEREQIMTTNVWLTQEWTDYRLVWDPNEYEGIKKLRIPSQHIWLPDIVLYNNADGVYEVSFYCNAVVSNTGDIFWLPPAIYKSACAIEVRNFP
      24. (31) EKLF  SGYDSSVRPAREVGDRVRVSVGLILAQLISLNEKDEEMSTKVYLDLEWTDYRLSWDPAEHEGIDSLRITAESVWLPDVVLLNNNDGNFDVALDISVVVSSDGSVRWQPPGIYRSSCSIQVTYFP
      25. (32) SVLF  ETYNPKVRPAQTVGDKVTVRVGLTLTNLLILNEKIEEMTTNVFLNLAWTDYRLQWDPAAYEGIKDLRIPSSDVWQPDIVLMNNNDGSFEITLHVNVLVQHTGAVSWQPSAIYRSSCTIKVMYFP
      26. (32) QHLFNEKGYDKDLRPVARKEDKVDVALSLTLSNLISLKEVEETLTTNVWIDHAWVDSRLQWDANDFGNITVLRLPPDMVWLPEIVLENNNDGSFQISYACNVLVYDSGYVTWLPPAIFRSSCPISVTYFP
      27. (26) HHLFEERGYNKEVRPVASADEVVDVYLALTLSNLISLKEVDETLTTNVWVEQSWTDYRLQWNTSEFGGVDVLRLLPEMLWLPEIVLENNNDGLFEVAYYCNVLVYNTGYVYWLPPAIFRSACPINVNFFP
      28. (29) NDLLIVNKYNKHVRPVKHNNEVVNIALSLTLSNLISLKETDETLTSNVWMDHAWYDHRLTWNASEYSDISILRLPPELVWIPDIVLQNNNDGQYHVAYFCNVLVRPNGYVTWLPPAIFRSSCPINVLYFP
      29. (30) ADLM  QNYDPNLRPAERDSDVVNVSLKLTLTNLISLNEREEALTTNVWIEMQWCDYRLRWDPRDYEGLWVLRVPSTMVWRPDIVLENNVDGVFEVALYCNVLVSPDGCIYWLPPAIFRSACSISVTYFP
      30. (30) QDLM  TNYNRHLRPALRGDQVIDVTLKLTLTNLISLNEREETLTTNVWIEMQWSDYRLRWDPDKYDDIQQLRVPSAMVWLPDIVLENNIDGTFEITLYTNVLVYPDGSIYWLPPAIYRSSCSIHVTYFP
      31. (25) EKLL  GDYDKRIIPAKTLDHIIDVTLKLTLTNLISLNEKEEALTTNVWIEIQWNDYRLSWNTSEYEGIDLVRIPSELLWLPDVVLENNVDGQFEVAYYANVLVYNDGSMYWLPPAIYRSTCPIAVTYFP
      32. (28) HHLF  DNYDPECRPVRRPEDTVTITLKVTLTNLISLNEKEETLTTSVWIGIDWHDYRLNYSKDDFAGVGILRVPSEHVWLPEIVLENNIDGQFGVAYDSNVLVYEGGYVSWLPPAIYRSTCAVEVTYFP
      33. (49) DDLL  SNYNRLIRPVSNNTDTVLVKLGLRLSQLIDLNLKDQILTTNVWLEHEWQDHKFKWDPSEYGGVTELYVPSEHIWLPDIVLYNNADGEYVVTTMTKAILHYTGKVVWTPPAIFKSSCEIDVRYFP
      34. (29) DDLL  SNYNRLIRPVGNNSDRLTVKMGLRLSQLIDVNLKNQIMTTNVWVEQEWNDYKLKWNPDDYGGVDTLHVPSEHIWHPDIVLYNNADGNYEVTIMTKAILHHTGKVVWKPPAIYKSFCEIDVEYFP
      35. (15) DDLL  SNYNRLIRPVVNNTETLTVWLGLKLSQLIEVNLKNQVMTTNLWVKQRWFDYKLRWDPEEYGGVEQLYVPSEHIWVPDIVLYNNWDGNYEVTLMTKATLKYTGEVFWEPPAIYKSSCEMNVEYFP
      36. (32) RDLF  RGYNKLIRPVQNMTQKVGVRFGLAFVQLINVNEKNQVMKSNVWLRLVWYDYQLQWDEADYGGIGVLRLPPDKVWKPDIVLFNNADGNYEVRYKSNVLIYPTGEVLWVPPAIYQSSCTIDVTYFP
      37. (30) KELV  KNYNPLERPVANDSQPLTVYFSLSLLQIMDVDEKNQVLTTNIWLQMSWTDHYLQWNMSEYPGVKNVRFPDGQIWKPDILLYNSADERFDATFHTNVLVNASGHCQYLPPGIFKSSCYIDVRWFP
      38. (30) KELL  KNYNPLERPVANDSQPLTVYFTLSLMQIMDVDEKNQVLTTNIWLQMYWTDHYLQWNVSEYPGVKNVRFPDGLIWKPDILLYNSADERFDATFHTNVLVNSSGHCQYLPPGIFKSSCYIDVRWFP
      39. (38) RDLL  RNYNRLERPVMNDSQPIVVELQLSLLQIIDVDEKNQVLITNAWLQMYWVDIYLSWDQYEYPGVQNLRFPSDQIWVPDILLYNSADERFDATFHTNVLVNYSGSCQYIPPGILKSTCYIDVRWFP
      40. (42) DHLL  ANYKKGVRPVRDWRKPTTVSIDVIMYAILNVDEKNQVLTTYIWYRQYWTDEFLQWTPEDFDNVTKLSIPTDSIWVPDILINEFVDVGKSPNIPYVYVHH RGEVQNYKPLQLVTACSLDIYNFP
consensus        L     Y     P                                      W                         W P                         G             C      FP
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Appendix A2

nAChR (2)

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       1. FDEQNCSMKLGTWTYDGSVVAINPESDQ ( 2) LSNFMESGEWVIKESRGWKHSVTYSC (4) PYLDITYHFVMQRLPLYFIVNVIIPCLLFSFLTGLVFYLPTDS GEKMTLSISVLLSLTVFLLVIVELIP
       2. FDQQNCSMKLGTWTYDGTMVVINPESDR ( 2) LSNFMESGEWVMKDYRGWKHWVYYAC (4) PYLDITYHFLMQRLPLYFIVNVIIPCLLFSFLTGFVFYLPTDS GEKMTLSISVLLSLTVFLLVIVELIP
       3. FDQQNCSMKFGTWTYDGSLLVINPERDR ( 2) LSNFMASGEWMMKDYRCWKHWVYYTC (4) PYLDITYHFVLQRLPLYFIVNVIIPCLLFSFLTGLVFYLPTDS GEKMTLSISVLLSLTVFLLVIVELIP
       4. FDLQNCSMKLGTWTYDGTLVVINPENDR ( 2) LSNFMESGEWYMKDYRCWKHWVYYDC (4) PYLDITYHFLLQRLPLYFIVNVVIPCLLFSFLTGLVFYLPTDS GEKITLSVSVLLSLVVFLLVIVELIP
       5. FDQQNCTMKLGIWTYDGTKVSISPESDR ( 2) LSTFMESGEWVMKDYRGWKHWVYYTC (4) PYLDITYHFIMQRIPLYFVVNVIIPCLLFSFLTGLVFYLPTDS GEKMTLSISVLLSLTVFLLVIVELIP
       6. FDLQNCSMKFGSWTYDGSQVDIILEDQD ( 2) KRDFFDNGEWEIVSATGSKGNRTDSC (1) WYPYVTYSFVIKRLPLFYTLFLIIPCIGLSFLTVLVFYLPSNE GEKICLCTSVLVSLTVFLLVIEEIIP
       7. FDLQNCSMKFGSWTYDGSQVDIILEDYE ( 2) KRDFFDNGEWEIVTATGSKGNRTDGC (1) WYPFVTYSFIIRRLPLFYTLFLIIPCIGLSFLTVLVFYLPSNE AEKISLCTSVLVSLTVFLLVIEEIIP
       8. FDRQNCSMKFGSWTYDGTMVDLILINEN ( 2) RKDFFDNGEWEILNAKGMKGNRREGF (1) SYPFVTYSFVLRRLPLFYTLFLIIPCLGLSFLTVLVFYLPSDE GEKLSLSTSVLVSLTVFLLVIEEIIP
       9. FDRQNCSMKFGSWTYDGNMVKLVLINQQ ( 2) RSDFFDNGEWEILSATGVKGSRQDSH (1) SYPYITYSFILKRLPLFYTLFLIIPCLGLSFLTVLVFYLPSDE GEKVSLSTSVLVSLTVFLLVIEEIIP
      10. FDRQNCSMKFGSWTYDGTMVDLTLLDAY ( 2) RKDFFDNGEWEILNATGQRGSRRDGI (1) SYPYVTYSFILKRLPLFYTLFLIIPCLGLSFLTVLVFYLPSDE GEKLLLSTSVLVSLTVFLLVIEEIIP
      11. FDYQNCTMKFGSWSYDKAKIDLVLIGSS ( 2) LKDYWESGEWAIIKAPGYKHDIKYNC (3) IYPDITYSLYIRRLPLFYTINLIIPCLLISFLTVLVFYLPSDC GEKVTLCISVLLSLTVFLLVITETIP
      12. FDYQNCTMKFGSWSYDKAKIDLVLIGST ( 2) LKDYWESGEWAIIKAPGYKHDIKYNC (3) IYTDITYSLYIRRLPLFYTINMIIPCLLISFLTVLVFYLPSDC GEKVTLCISVLLSLTVFLLVITETIP
      13. FDYQNCSMKFGSWTYDKAKIDLVLIGSK ( 2) LKDFWESGEWEIIDAPGYKHDIKYNC (3) IYPDITYSFYIRRLPLFYTINLIIPCLLISFLTILVFYLPSDC GEKVTLCISVLLSLTVFLLVITETIP
      14. FDHQNCSLKFGSWTYDKAEIDLLIIGSK ( 2) MNDFWENSEWEIVDASGYKHDIKYNC (3) IYTDITYSFYIRRLPMFYTINLIIPCLFISFLTVLVFYLPSDC GEKVTLCISVLLSLTVFLLVITETIP
      15. FDQQNCKMKFGSWTYDKAKIDLEQMERT ( 2) LKDYWESGEWAIINATGTYNSKKYDC (3) IYPDVTYYFVIRRLPLFYTINLIIPCLLISCLTVLVFYLPSEC GEKITLCISVLLSLTVFLLLITEIIP
      16. FDQQNCKMKFGSWTYDKAKIDLENMEHH ( 2) LKDYWESGEWAIINAIGRYNSKKYDC (3) IYPDITFYFVIRRLPLFYTINLIIPCLLISCLTVLVFYLPSDC GEKITLCISVLLSLTVFLLLITEIIP
      17. FDQQNCTMKFGSWTYDKAKIDLVSIHSR ( 2) QLDFWESGEWVIVDAVGTYNTRKYEC (3) IYPDITYAFIIRRLPLFYTINLIIPCLLISCLTVLVFYLPSEC GEKVTLCISVLLSLTVFLLLITEIIP
      18. FDQQNCKMKFGSWTYDKAKIDLVSMHSH ( 2) QLDYWESGEWVIINAVGNYNSKKYEC (3) IYPDITYSFIIRRLPLFYTINLIIPCLLISCLTVLVFYLPSEC GEKITLCISVLLSLTVFLLLITEIIP
      19. FDQQNCTMKFRSWTYDRTEIDLVLKSEV ( 2) LDDFTPSGEWDIVALPGRRNENPDDS (0) TYVDITYDFIIRRKPLFYTINLIIPCVLITSLAILVFYLPSDC GEKMTLCISVLLALTVFLLLISKIVP
      20. FDQQNCTMKFRSWTYDRTEIDLVLKSEV ( 2) LDDFTPSGEWDIVALPGRRNENPDDS (0) TYVDITYDFIIRRKPLFYTINLIIPCILITSLAILVFYLPSDC GEKMTLCISVLLALTVFLLLISKIVP
      21. FD QNCTLKFRSWTYDHTEIDMVLKSPT ( 2) MDDFTPSGEWDIVALPGRRTVNPQDP (0) SYVDVTYDFIIKRNALFYTINLIIPCVLITSLAILVFYLPSDC GEKMTLCISVLLALTFFLLLISKIVP
      22. FDQQNCTLKFRSWTYDHTEIDMVLKTSM ( 2) MDDFTPSGEWDIVALPGRRTENPLDP (0) NYVDVTYDFIIKRKPLFYTINLIIPCVLITSLAILVFYLPSDC GEKMTLCISVLLALTVFLLLISKIVP
      23. FDQQNCTLKFRSWTYDRTELDLVLTSDF ( 2) RDDYTPSGEWDIVSLPGRKNEDPNDL (0) TYLDITYDFVIKRKPLFYTINLIIPCVLITSLAILVFYLPSDC GEKVTLCMSVLLALTVFLLLISKIVP
      24. FDWQNCTMVFSSYSYDSSEVTLQTGLGP (11) EGTFIENGQWENIHKPSRLIQPPGDP (6) QRQEVIFYLIIRRKPLFYLVNVIAPCILITLLAIFVFYLPPDA GEKMGLSIFALLTLTVFLLLLADKVP
      25. FDWQNCTMVFKSYTYDTSEVTLQHALDA (12) KDAFTENGQWSIEHKPSRKNWRSDDP (0) SYEDVTFYLIIQRKPLFYIVYTIIPCILISILAILVFYLPPDA GEKMSLSISALLAVTVFLLLLADKVP
      26. FDWQNCSLKFSSLKYTAKEITLSLKQEE (14) PEGFTENGEWEIVHRAAKLNVDPSVP (4) NHQDVTFYLIIRRKPLFYIINILVPCVLISFMINLVFYLPGDC GEKTSVAISVLLAQSVFLLLISKRLP
      27. FDWQNCTLKFSSLAYNAQEINMHLKEES (16) PEGFTENGEWEIIHRPARKNIHPSYP (4) EHQDITFYLIIKRKPLFYVINIVTPCVLIAFMAILVFYLPADS GEKMTLVISVLLAQSVFLLLVSQRLP
      28. FDWQNCSLKFTALNYDANEITMDLMTDT (14) PEAFTENGEWEIIHKPAKKNIYPDKF (4) NYQDVTFYLIIRRKPLFYVINFITPCVLISFLASLAFYLPAES GEKMSTAISVLLAQAVFLLLTSQRLP
      29. FDWQNCSLIFQSQTYSTNEIDLQLSQED (10) PEAFTENGEWAIQHRPAKMLLDPAAP (4) GHQKVVFYLLIQRKPLFYVINIIAPCVLISSVAILIHFLPAKAGGQKCTVAINVLLAQTVFLFLLAKKVP
      30. FDWQNCTMVFQSQTYSANEINLLLTVEE (10) PEAFTENGEWAIKHRPARKIINSGRF (5) QYQQVIFYLIIQRKPLFYIINIIVPCVLISSMAVLVYFLPAKAGGQKCTVSINVLLAQTVFLFLIAQKVP
      31. FDWQNCSLVFRSQTYNAHEVNLQLSAEE (10) PEDFTENGEWTIRHRPAKKNYNWQLT (4) DFQEIIFFLIIQRKPLFYIINIIAPCVLISSLVVLVYFLPAQAGGQKCTLSISVLLAQTIFLFLIAQKVP
      32. FDWQNCSLIFRSQTYNAEEVEFIFAVDD (11) TAAFTENGEWAIDYCPGMIRRYEGGS (4) GETDVIYTLIIRRKPLFYVINIIVPCVLISGLVLLAYFLPAQAGGQKCTVSINVLLAQTVFLFLIAQKIP
      33. FDQQTCFMKFGSWTYDGDQIDLKHISQK (12) LREYYPSVEWDILGVPAERHEKYYPC (3) PYPDIFFNITLRRKTLFYTVNLIIPCVGISYLSVLVFYLPADS GEKIALCISILLSQTMFFLLISEIIP
      34. FDEQTCFMKFGSWTYDGYMVDLRHLKQT (11) LQDYYISVEWDIMRVPAVRNEKFYSC (3) PYLDIVFNLTLRRKTLFYTVNLIIPCVGISFLSVLVFYLPSDS GEKISLCISILLSLTVFFLLLAEIIP
      35. YDEQICFMKFGSWTYNGAQVDLKHLDQI (11) LTEFYLSVEWDILEVPATKNEEYYPD (3) PFSDITFKLTMRRKTLFYTVNLIVPCVALTFLTVLVFYLPSDS GEKVTLCISILVSLTVFFLLLAEIIP
      36. FDQQTCIMKFGSWTFNGDQVSLALYNNK ( 4) LSDYWKSGTWDIIEVPAYLNVYEGDS (3) TETDITFYIIIRRKTLFYTVNLILPTVLISFLCVLVFYLPAEA GEKVTLGISILLSLVVFLLLVSKILP
      37. FDVQQCKLKFGSWSYGGWSLDLQMQEAD ( 0) ISSYIPNGEWDLMGIPGKRNEKFYEC (3) PYPRCTYTVTMRRTTLYYGLNLLIPCVLISALALLVFLLPADS GEKISLGITVLLSLTVFMLLVAEIMP
      38. FDVQKCNLKFGSWTYGGWSLDLQMQEAD ( 0) ISGYISNGEWDLVGIPGKRTESFYEC (3) PYPDITFTVTMRRRTLYYGLNLLIPCVLISALALLVFLLPADS GEKISLGITVLLSLTVFMLLVAEIMP
      39. FDVQKCDLKFGSWTHSGWLIDLQMLEAD ( 0) ISNYISNGEWDLVGVPGKRNELYYEC (3) PYPDVTYTITMRRRTLYYGLNLLIPCVLISGLALLVFLLPADS GEKISLGITVLLSLTVFMLLVAEIMP
      40. FDVQNCSLTFTSWLHTIQDINITLWRSP ( 6) KSIFINQGEWELLEVFPQFKEFSIDI (2) SYAEMKFYVIIRRRPLFYAVSLLLPSIFLMVVDIVGFCLPPDS GERVSFKITLLLGYSVFLIIVSDTLP
consensus  D Q C                                     W                                 R           P             LP              L     F        P
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Appendix A2 (Continued)

nAChR (3)

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 1. STSSAVPLIGKYMLFTMVFVIASIIITVIVINTHHRSPST H VMPNWVRKVFIDTIPNIMF ( 45) EVKSAIEGIKYIAETMKSDQESNNAAAEWKYVAMVMDHILLGVFMLVCIIGTLAVFAGRL ( 7)
 2. STSSAVPLIGKYMLFTMVFVIASIIITVIVINTHHRSPST H TMPPWVRKIFIDTIPNIMF ( 45) DVKNAIEGIKYIAETMKSDQESSNAADEWKFVAMVLDHLLLVIFMLVCIIGTLAVFAGRL ( 7)
 3. STSSAVPLIGKYMLFTMVFVIASIIITVIVINTHHRSPST H TMPPWVRKIFIETIPNIMF ( 45) DVKSAIEGIKYIAETMKSDQESNKASEEWKFVAMVLDHILLAVFMTVCVIGTLAVFAGRI ( 7)
 4. STSSAVPLIGKYMLFTMVFVIASIVITVIVINTHHRSPST H IMPQWLKKIFIETIPRVMF ( 45) DVKSAIEGAKYVAETMKSDQESTKASEEWKFVAMVLDHLLLAVFMIVCIIGTLAIFAGRL ( 7)
 5. STSSAVPLIGKYMLFTMIFVISSIIITVVVINTHHRSPST H TMPQWVRKIFIDTIPNVMF ( 45) DVKSAIEGVKYIAEHMKSDEESSNAAEEWKYVAMVIDHILLCVFMLICIIGTVSVFAGRL ( 7)
 6. SSSKVIPLIGEYLVFTMIFVTLSIMVTVFAINIHHRSSST HNAMAPLVRKIFLHTLPKLLS ( 26) TLEAALDSIRYITTHIMKENDVREVVEDWKFIAQVLDRMFLWTFLFVSIVGSLGLFVPVI (17)
 7. SSSKVIPLIGEYLVFTMIFVTLSIVITVFAINIHHRSSST HNAMAPWVRKIFLHKLPKLLC ( 26) TLEAALDSIRYITRHVMKENEVREVVEDWKFIAQVLDRMFLWAFLLVSIIGSLVLFIPVI (17)
 8. SSSKVIPLIGEYLLFIMIFVTLSIIVTVFVINVHHRSSSTYH PMAPWVKRLFLQRLPRWLC ( 42) FLEKASESIRYISRHVKKEHFISQVVQDWKFVAQVLDRIFLWLFLIASVLGSILIFIPAL ( 8)
 9. SSSKVIPLIGEYLLFIMIFVTLSIIVTIFVINVHHRSSATYH PMSPWVRSLFLQRLPHLLC ( 40) LLEQATNSVRYISRHIKKEHFIREVVQDWKFVAQVLDRIFLWTFLTVSVLGTILIFTPAL (12)
10. SSSKVIPLIGEYLLFIMIFVTFSIIVTLFVINVHHRSSATYH PMAPWVKSLFLQRLPRLLC ( 49) LLEKATHSVHYISRHIKKEHFIREVVQDWKFVAQVLDRIFLWVFLTASVLGTILIFTPAL ( 6)
11. STSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHYRTPTT H TMPSWVKTVFLNLLPRVMF ( 84) EIKEAIQSVKYIAENMKAQNEAKEIQDDWKYVAMVIDRIFLWVFTLVCILGTAGLFLQPL ( 6)
12. STSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHYRTPKT H TMPVWVRTIFLNLLPRIMF ( 84) EMRDAIESVKYIAENMKMQNEAKEIQDDWKYVAMVIDRIFLWVFILVCILGTAGLFLQPL ( 6)
13. STSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHYRTPMT H TMPSWVRTVFLRALPRVML (100) EIKQAIESVKYIAENMRSRNKAKEVEDDWKYVAMVIDRIFLWVFVLVCVLGTLGLFLQPL ( 5)
14. STSLVIPLVGEYLLFTMIFVTLSIVVTVFVLNIHYRTPAT H TMPKWVKTMFLQVFPSILM ( 72) DVEDVIDSVQFIAENMKSHNETKEVEDDWKYMAMVVDRVFLWVFIIVCVFGTVGLFLQPL ( 7)
15. STSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHHRSPST H NMPNWVRVALLGRVPRWLM ( 90) QIQKALEGVHYIADRLRSEDADSSVKEDWKYVAMVVDRIFLWLFIIVSFLGTIGLFLPPF ( 5)
16. STSLVIPLIGEYLLFTMIFVTLSIIITVFVLNVHHRSPST H TMPHWVRSFFLGFIPRWLF (109) SILRALEGVQYIADHLRAEDADFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPY ( 5)
17. STSLVIPLIGEYLLFTMIFVTLSIVITVFVLNVHHRSPRT H TMPAWVRRVFLDIVPRLLF (206) ALTRAVEGVQYIADHLKAEDTDFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPW ( 5)
18. STSLVIPLIGEYLLFTMIFVTLSIIITVFVLNVHHRSPRT H TMPDWVRRVFLDIVPRLLF (205) ALKLAVEGVHYIADHLRAEDADFSVKEDWKYVAMVIDRIFLWMFIIVCLLGTVGLFLPPW ( 5)
19. PTSLDVPLVGKYLMFTMVLVTFSIVTSVCVLNVHHRSPTT H TMAPWVKVVFLEKLPALLF ( 74) GLREAVDGVRFIADHMRSEDDDQSVSEDWKYVAMVIDRLFLWIFVFVCVFGTIGMFLQPL (20)
20. PTSLDVPLVGKYLMFTMVLVTFSIVTSVCVLNVHHRSPTT H TMPPWVRTLFLRKLPALLF ( 70) GLEEAVEGVRFIADHMRSEDDDQSVSEDWKYVAMVIDRLFLWIFVFVCVFGTVGMFLQPL (20)
21. PTSLDIPLIGKYLLFTMVLVTFSIVTTVCVLNVHHRSPST H TMASWVKECFLHKLPTFLF ( 80) DLQEALEGVSFIAQHLESDDRDQSVIEDWKFVAMVVDRLFLWVFVFVCILGTMGLFLPPL (10)
22. PTSLDVPLIGKYLMFTMVLVTFSIVTSVCVLNVHHRSPST H TMPPWVKLVFLERLPAYLF ( 74) EVQEAIDGVSFIAEHMKSDDNDQSVIEDWKYVAMVVDRLFLWIFVLVCVLGTVGLFLQPL (10)
23. PTSLAVPLIGKYLMFTMVLVTFSIVTSVCVLNVHHRSPST H YMPEWVKCVFLHKLPAFLL ( 65) DVDEAIDGVRFIAEHMKIEDDDEGIIEDWKYVAMVIDRLFLWIFILVCVVGTLGLFVQPL (16)
24. ETSLSVPIIIKYLMFTMVLVTFSVILSVVVLNLHHRSPHT H QMPLWVRQIFIHKLPLYLR ( 72) ELREVVSSISYIARQLQEQEDHDALKEDWQFVAMVVDALFLWTFIIFTSVGTLVIFLDAT (10)
25. ETSLSVPIIIRYLMFIMILVAFSVILSVVVLNLHHRSPNT H TMPNWIRQIFIETLPPFLW ( 68) DLKEAVEAIKYIAEQLESASEFDDLKKDWQYVAMVADRLFLYVFFVICSIGTFSIFLDAS (10)
26. ATSMAIPLVGKFLLFGMVLVTMVVVICVIVLNIHFRTPST H VLSEGVKKFFLETLPKLLH ( 73) EMKPAVDGANFIVNHMRDQNSYNEEKDNWNQVARTVDRLCLFVVTPVMVVGTAWIFLQGV (24)
27. ATSHAIPLIGKYLLFIMLLVTAVVVICVVVLNFHFRTPST H VMSDWVRGVFLEILPRLLH ( 70) HLKPTLDEANFIVKHMREKNSYNEEKDNWNRVARTLDRLCLFLITPMLVVGTLWIFLMGI (24)
28. ETALAVPLIGKYLMFIMSLVTGVIVNCGIVLNFHFRTPST H VLSTRVKQIFLEKLPRILH ( 78) EIKSGIDSTNYIVKQIKEKNAYDEEVGNWNLVGQTIDRLSMFIITPVMVLGTIFIFVMGN (24)
29. ETSQAVPLISKYLTFLLVVTILIVVNAVVVLNVSLRSPHT H SMARGVRKVFLRLLPQLLR ( 80) AIQACVEACNLIACARHQQSHFDNGNEEWFLVGRVLDRVCFLAMLSLFICGTAGIFLMAH (21)
30. ETSQAVPLIGKYLTFLMVVTVVIVVNAVIVLNVSLRTPNT H SMSQRVRQVWLHLLPRYLG ( 78) EIRACVEACNHIANATREQNDFSSENEEWILVGRVIDRVCFFIMASLFVCGTIGIFLMAH (19)
31. ETSLNVPLIGKYLIFVMFVSMLIVMNCVIVLNVSLRTPNT H SLSEKIKHLFLGFLPKYLG ( 77) EIKSCVEACNFIAKSTKEQNDSGSENENWVLIGKVIDKACFWIALLLFSIGTLAIFLTGH (18)
32. ETSLSVPLLGRYLIFVMVVATLIVMNCVIVLNVSLRTPTT H ATSPRLRQILLELLPRLLG ( 63) EIRCCVDAVNFVAESTRDQEATGEELSDWVRMGKALDNVCFWAALVLFSVGSTLIFLGGY (15)
33. STSLALPLLGKYLLFTMLLVGLSVVITIIILNIHYRKPST H KMRPWIRSFFIKRLPKLLL (113) ELEKAIHNVMFIQHHMQRQDEFNAEDQDWGFVAMVMDRLFLWLFMIASLVGTFVILGEAP (28)
34. PTSLTVPLLGKYLLFTMMLVTLSVVVTIAVLNVNFRSPVT H RMAPWVQRLFIQILPKLLC (121) EMEKTIEGSRFIAQHVKNKDKFESVEEDWKYVAMVLDRMFLWIFAIACVVGTALIILQAP (32)
35. PTSLAVPLLGKYLLFTMILVSLSVWTTVCVLNIHFRSPST H NMSRLVRKLFLHFMPKLMM ( 65) EVLQALRAVRFIAQHIKDADKDNEIVEDWKFVSMVLDRFFLWLFTLSCVFGTLAIICQSP (35)
36. PTSLVLPLIAKYLLFTFIMNTVSILVTVIIINWNFRGPRT H RMPMYIRSIFLHYLPAFLF ( 93) EASKATEAVEFIAEHLRNEDLYIQTREDWKYVAMVIDRLQLYIFFIVTTAGTVGILMDAP (18)
37. ATSDSVPLIAQYLPSTMIIVGLSVVVTVIVLRYHHHDPDG G KMPKWTRIILLNWCAWFLR ( 87) DLAKILEEVRYMPTAYRCQDESEVICSEWKFAACVVDRLCLMAFSVFTIICTIGILMSAP (11)
38. ATSDSVPLIAQYFASTMIIVGLSVVVTVIVLQYHHHDPDG G KMPKWTRVILLNWCAWFLR ( 87) DLAKILEEVRYIANRFRDQDEEEAICNEWKFAASVVDRLCLMAFSVFTIICTIGILMSAP (11)
39. ATSDSVPLIAQYFASIMVIVGLSVVVTVLVLQFHHHDPQA G KMPRWVRVILLNWCAWFLR ( 88) VIVKILEEVQFIAMRFRKQDEGEEICSEWKFAAAVIDRLCLVAFTLFAIICTFTILMSAP (11)
40. ATI GTPLIGVYFVVCMALLVISLAETIFIVRLVHKQDLQ R PVPDWLRHLVLDRIAWILC ( 63) AVRGLLQELSSIRHFLEKRDEMREVARDWLRVGYVLDRLLFRIYLLAVLAYSITLVTLWS ( 5)
consensus P                                                                                          W       D
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Appendix A2 (Continued)

Ca^{2+} pump (1)

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 1. (203) QIPVADITVGDIAQVKYGDLLPADGILI  QGNDLKIDESSLTGESDHVKK ( 7) LLSGTHVREGSGRMVVTAVGVNSQTGII
 2. (138) RIKARDIVPGDIVEVAVGDKVPADIRILSIKSTTLRVDQSILTGESVSVIK (18) LFSGTNIAAGKAVGIVATTGVSTEIGKI
 3. (138) RIKAKDIVPGDIVEIAVGDKVPADIRLTSIKSTTLRVDQSILTGESVSVIK (18) LFSGTNIAAGKAMGVVVATGVNTEIGKI
 4. (138) RIRARDIVPGDIVEVAVGDKVPADLRLIEIKSTTLRVDQSILTGESVSVTK (18) LFSGTNIASGKALGVAVATGLHTELGKI
 5. (138) KVRAKEIVPGDLVEVSVGDKIPADIRITHIYSTTLRIDQSILTGESVSVIK (18) LFSGTNVAAGKARGVVIGTGLSTAIGKI
 6. (144) DFPAKELVPGDIVELRVGDKVPADMRVATLKSSTLRVEQSSLTGESMPVTK (18) VFAGTTVVNGSCICIVVNTGMCTEIGKI
 7. (142) IIDSKYLTVGDIIELSVGNKTPADARIVKIFSTSIKAEQSMLTGESCSVDK (20) LFSSTAIVAGRCTAVVIKIGMNTEIGNI
 8. (148) HTLARDLVPGDTVCLSVGDRVPADLRLF  EAVDLSIDESSLTGETTPCSK (19) AFMGTLVRCGKAKGIVIGTGENSEFGEV
 9. (162) HVLASTLVPGDLVHFRIGDRIPADIRII  EAIDLSIDESNLTGENEPVHK (26) AYMGTLVKEGHGKGIVVGTGTNTSFGAV
10. (139) TINSKDVVPGDICLVKVGDTIPADLRLI  ETKNFDTDESLLTGESLPVSK (20) AFSSSAVVKGRAKGIVIKTALNSEIGKI
11. (132) AIDSHLLVPGDVVVLKTGDVVPADLRLV  ETVNFETDEALLTGESLPVIK (20) AYSSSIVTKGRAKGICYATGMQTQIGAI
12. (189) EIPANEVVPGDILQLEDGTVIPTDGRIVT EDCFLQIDQSAITGESLAVDK ( 5) TFSSSTVKRGEGFMVVTATGDNTFVGRA
consensus          GD      G   P D                  TGE     K     G                G

 1. (132) FIIGVTVLVVAVPEGLPLAVTISLAYSVKKMMKDNNLVRHLDACETMGNATAICSDKTGTLTMNRMTV ( 90) FNSVRKSMS
 2. ( 60) FKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTTNQMSV (123) FSRDRKSMS
 3. ( 60) FKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTTNQMSV (123) FSRDRKSMS
 4. ( 60) FKIAVALAVAAIPEGLPAVITTCLALGTRRMARKNAIVRSLPSVETLGCTSVICSDKTGTLTTNQMSV (123) FSRDRKSMS
 5. ( 60) FKIAVAVAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTTNQMSV (123) FSRDRKSMS
 6. ( 69) FKIAVALAVAAIPEGLPSVITTCLALGTRKMAQKNAIVRKLQSVETLGCTTVICSDKTGTLTTNQMSV (128) FDRVRKSMG
 7. ( 61) FKISVALAVAAIPEGLPAVITTCLALGTRRMVKKNAIVRKLQSVETLGCTTVICSDKTGTLTTNQMTA (219) FTRERKLMS
 8. ( 50) FTISVSLAVAAIPEGLPIVVTVTLALGVMRMVKKRAIVKKLPIVETLGCCNVICSDKTGTLTKNEMTV ( 91) FSSEQKWMA
 9. ( 50) FQISVSLAVAAIPEGLPIIVTVTLALGVLRMAKRKAIVRRLPSVETLGSVNVICSDKTGTLTSNHMTV ( 93) FNSKRKLMA
10. ( 77) AIYAICVALSMIPSSLVVVLTITMSVGAAVMVSRNVIVRKLDSLEALGAVNDICSDKTGTLTQGKMLA (155) FDSTVKRMS
11. ( 83) SIYAISLGISIIPESLIAVLSITMAMGQKNMSKRRVIVRKLEALEALGGVTDICSDKTGTITQGKMIT (116) FDSEIKRMA
12. ( 50) LRYTLGITIIGVPVGLPAVVTTTMAVGAAYLAKKQAIVQKLSAIESLAGVEILCSDKTGTLTKNKLSL ( 60) FDPVSKKVT
consensus             P  L                     V  L   E        CSDKTGT T             F    K
```

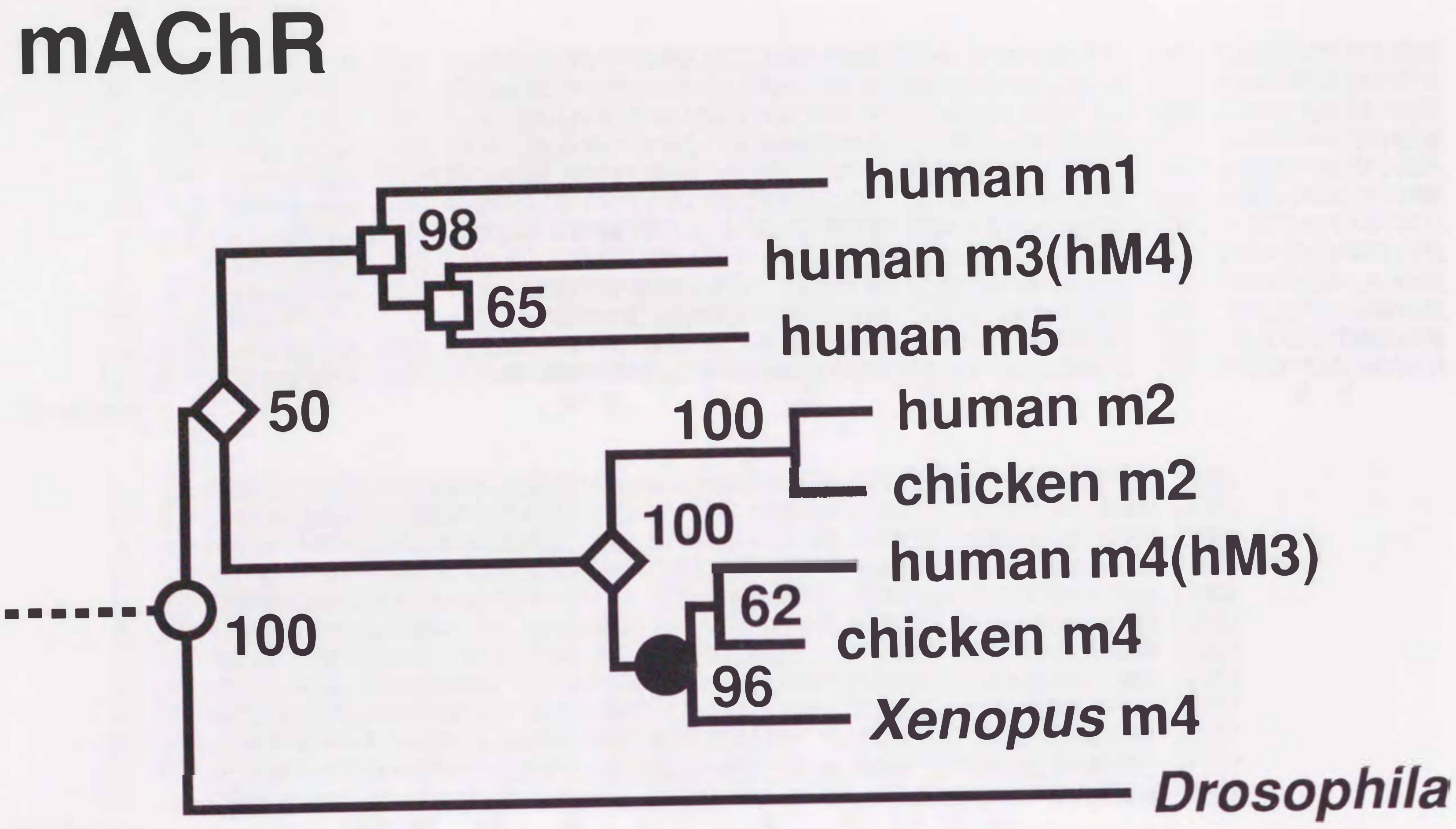
Appendix B

Ca^{2+} pump (2)

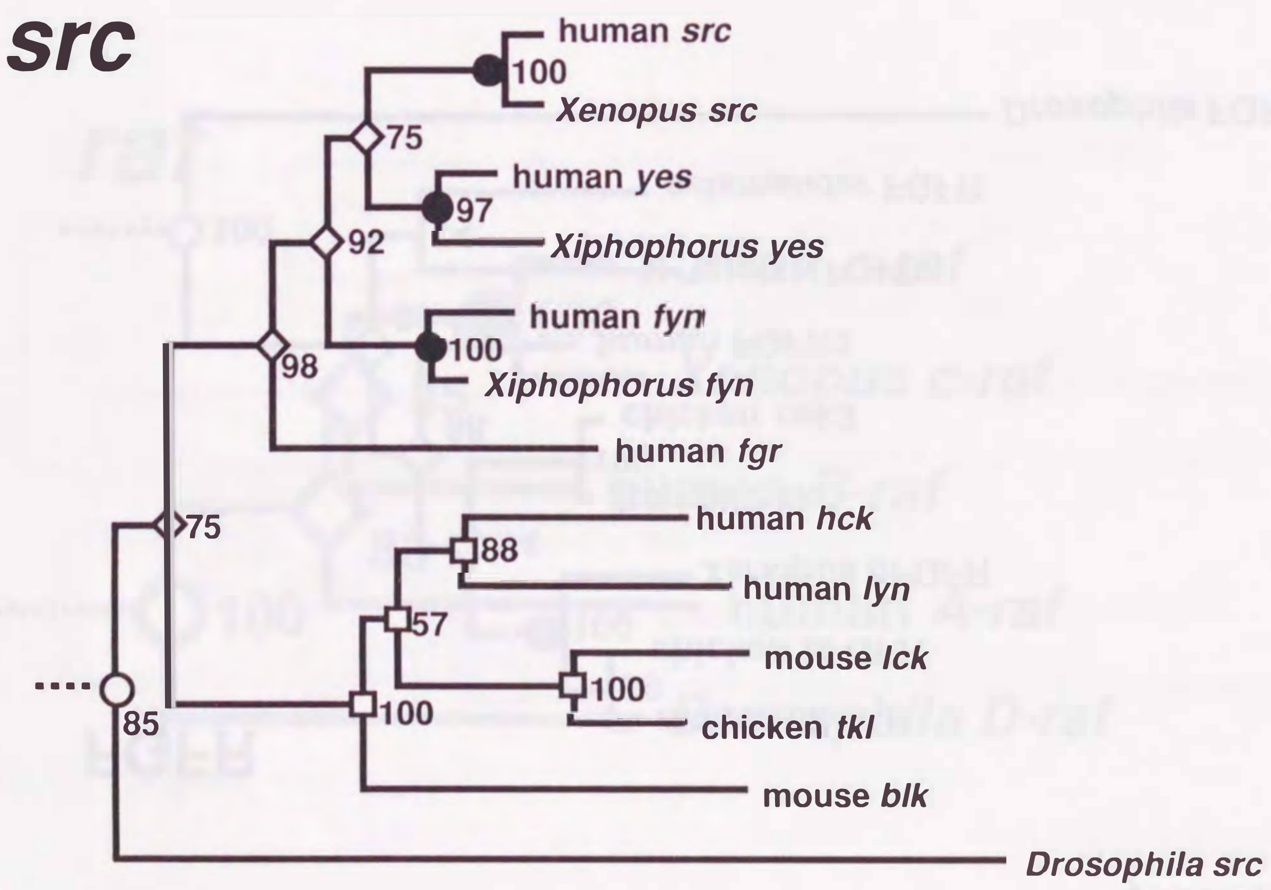
```
      1. (12) FSKGASEIIL (67) CIAVVGIEDPVRPEVPDAIKKCQRAGITVRMVTGDNINTARAIATKCGI (40) LARSSPTDKHTLVKGI
      2. (17) FVKGAPEGVI (70) FVGVVGMLDPPRKEVTGSIQLCRDAGIRVIMITGDNKGTAIAICRRIGI (34) FARVEPSHKSKIVEYL
      3. (16) FVKGAPEGVI (70) FVGCVGMLDPPRIEVASSVKLCRQAGIRVIMITGDNKGTAVAICRRIGI (34) FARVEPSHKSKIVEFL
      4. (17) FVKGAPESVI (70) FVGCVGMLDPPRPEVAACITRCSRAGIRVVMITGDNKGTAVAICRRLGI (34) FARVEPAHKSRIVENL
      5. (17) FVKGAPEGVL (70) FVGVVGMLDPPRKEVFDSIVRCRAAGIRVIVITGDNKATAEAICRRIGV (34) FSRVEPQHKSKIVEFL
      6. (12) LVKGAFESLL (78) FVGVVGLRDPPREEVHRAVNDCRRAGIKIMVITGDNKSTAEAVCREIQL (36) FSRAEPRHKQEIVRML
      7. (12) YCKGAPENII (66) YIGGLGIIDPPRKYVGKAISLCHLAGIRVFMITGDNIDTAKAIAKEINI (37) FCRTEPKHKKNIVKIL
      8. (15) FMKGAYEQVI (50) LLGLVGIIDPPRTGVKEAVTTLIASGVSIKMITGDSQETAIAIASRLGL (30) FYRASPRHKMKIIKSL
      9. (13) YVKGAFERIL (63) FTGLIGMNDPPRPNVKFAIEQLLQGGVHIIMITGDSENTAVNIAKQIGI (32) FARATPEHKLNIVRAL
     10. (13) YGKGAFESII (72) FLGLIGIYDPPRNETAGAVKKFHQAGINVHMLTGDFVGTAKAIAQEVGI (40) IARCSPQTKVRMIEAL
     11. (12) YAKGAVERIL (60) FVSLVGIYDPPRTESKGAVELCHRAGIRVHMLTGDHPETAKAIAREVGI (39) IARCAPQTKVKMIEAL
     12. (12) CVKGAPLSAL (44) ILGVMPCMDPPRDDTAQTVSEARHLGLRVKMLTGDAVGIAKETCRQLGL (32) FAEVFPQHKYRVVEIL
consensus       KGA                   DP R             G      TGD    A                    P  K
```

```
      1. (5) SDQRQVVAVTGDGTNDGPALKKADVGFAMGIAGTDVAKEASDIILTDDNFTSIVKAVMWGRNVYDSI (368)
      2. (0) QSYDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNM (237)
      3. (0) QSFDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNM (286)
      4. (0) QSFNEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKSAAEMVLSDDNFASIVAAVEEGRAIYNNM (242)
      5. (0) QSMNEISAMTGDGVNDAPALKKAEIGIAMG SGTAVAKSAAEMVLADDNFSSIVSAVEEGRAIYNNM (245)
      6. (0) KEMGEIVAMTGDGVNDAPALKLADIGIAMGITGTEVAKEASDMVLADDNFSTIVSAVAEGRSIYNNM (265)
      7. (0) KDLGETVAMTGDGVNDAPALKSADIGIAMGINGTQVAKEASDIILADDNFNTIVEAIKEGRCIYNNM (260)
      8. (0) QKNGSVVAMTGDGVNDAVALKAADIGVAMGQTGTDVCKEAADMILVDDDFQTIMSAIEEGKGIYNNI (220)
      9. (0) RKRGDVVAMTGDGVNDAPALKLSDIGVSMGRIGTDVAKEASDMVLTDDDFSTILTAIEEGKGIFNNI (215)
     10. (0) HRRKKFCTMTGDGVNDSPSLKMANVGIAMGINGSDVSKEASDIVLSDDNFASILNAVEEGRRMTDNI (279)
     11. (0) HRRKAFVAMTGDGVNDSPSLKQANVGIAMGQNGSDVAKDASDIVLTDDNFSSIVNAIEEGRRMFDNI (279)
     12. (0) QNRGYLVAMTGDGVNDAPSLKKADTGIAVE GATDAARSAADIVFLAPGLSAIIDALKTSRQIFHRM (230)
consensus             TGDG ND   LK    G             A            I  A
```

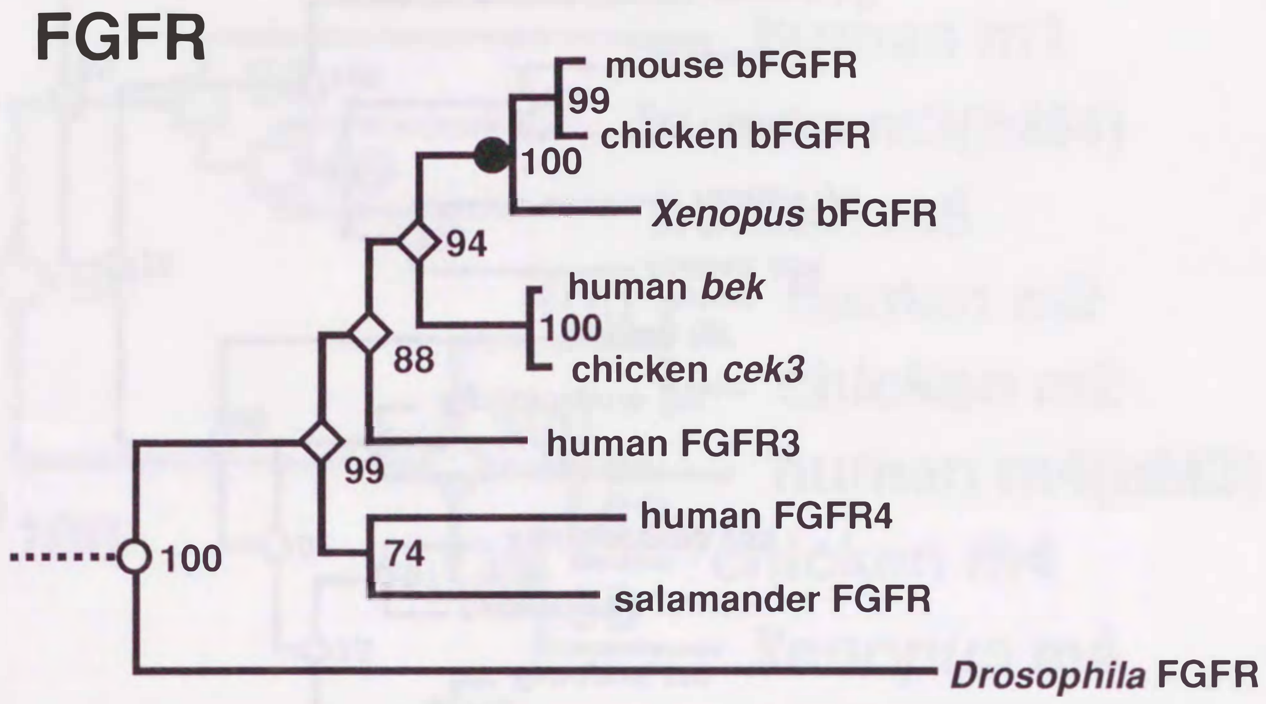
Appendix B (Continued)



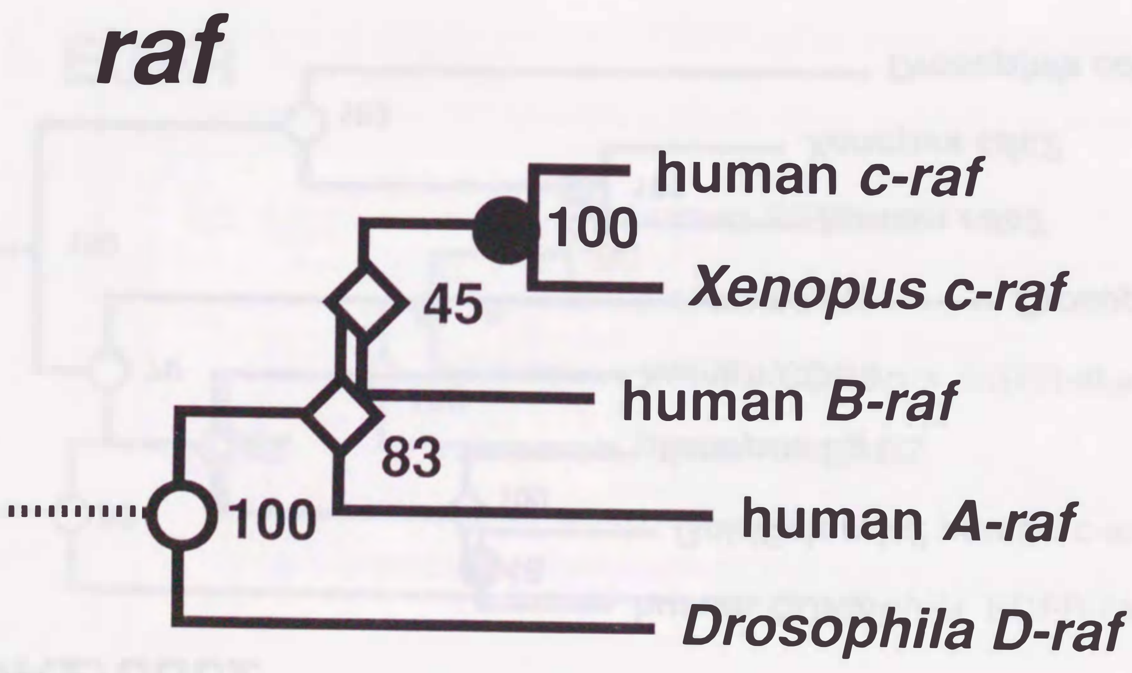
Appendix C1(a)



Appendix C2(a)

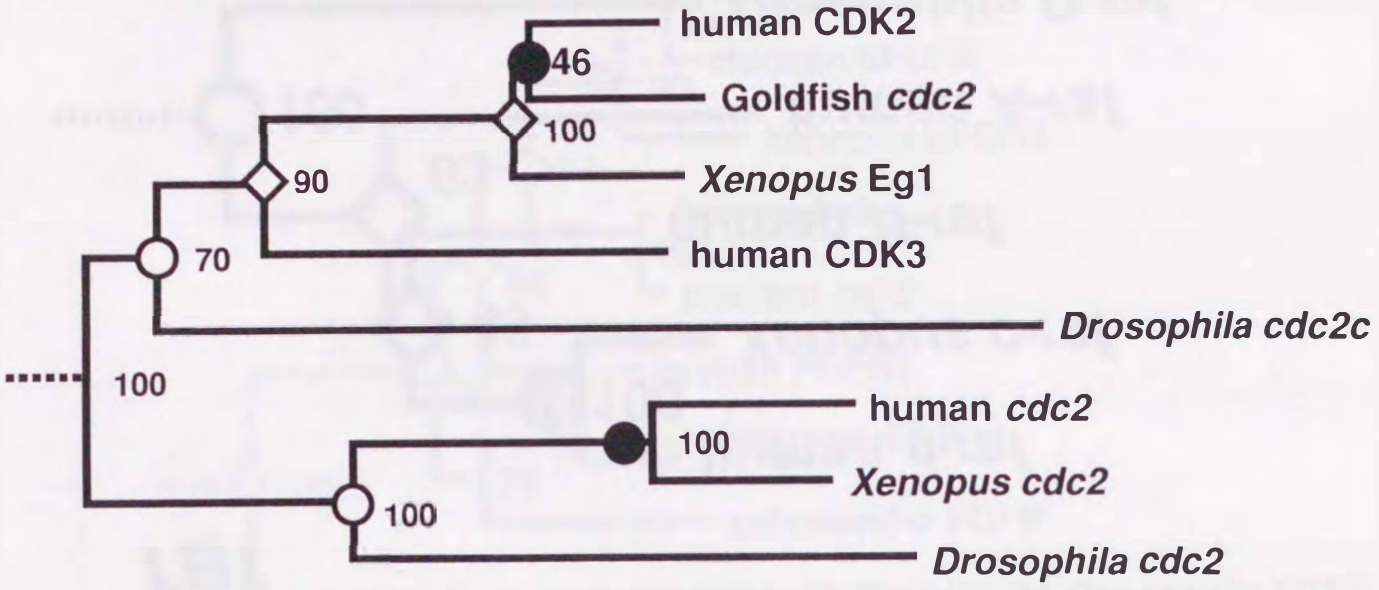


Appendix C3(a)



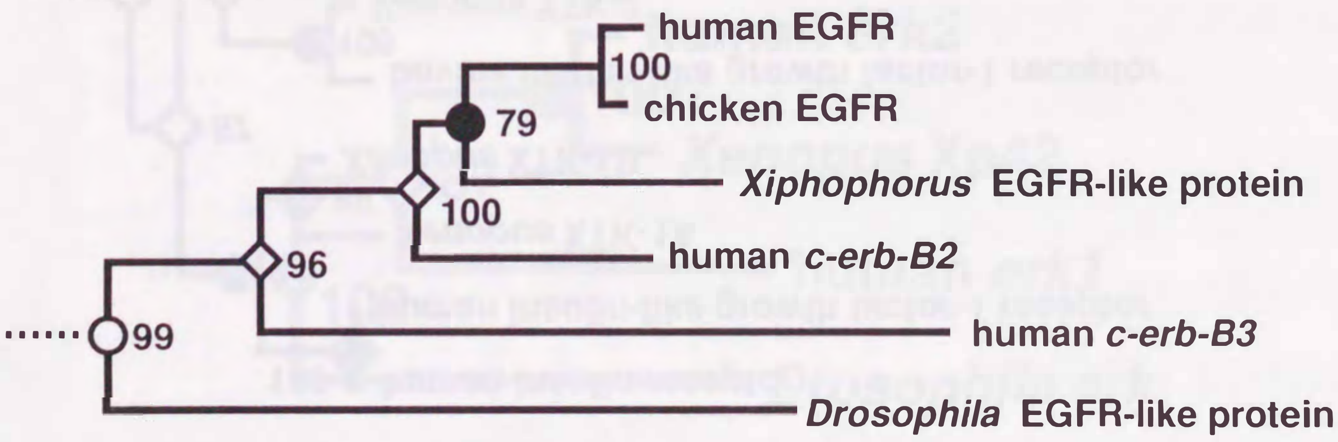
Appendix C4(a)

CDK2/*cdc2*



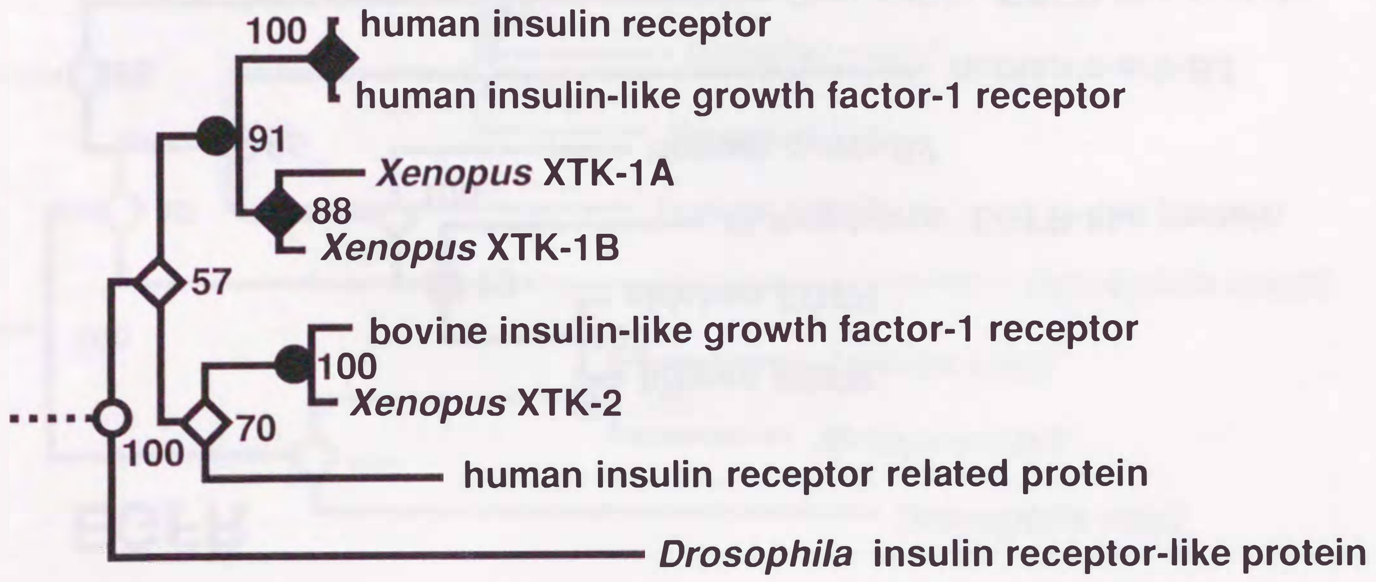
Appendix C5(a)

EGFR



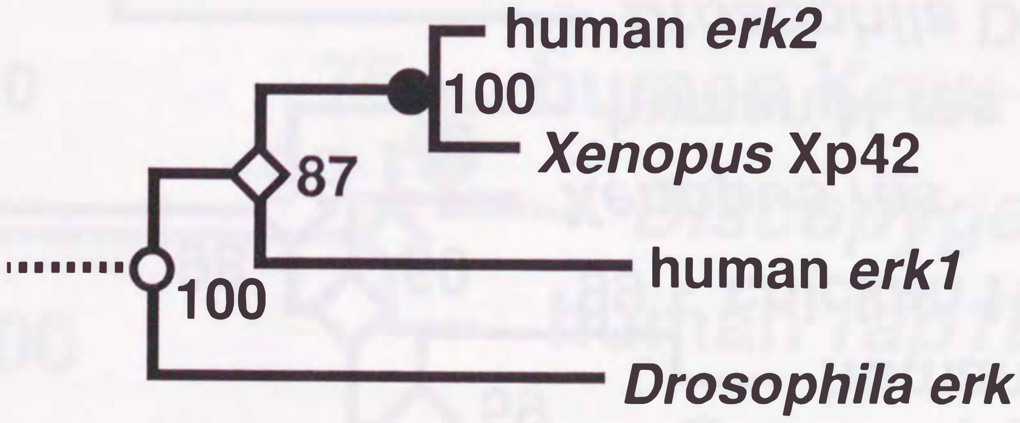
Appendix C6(a)

IR (insuline receptor)

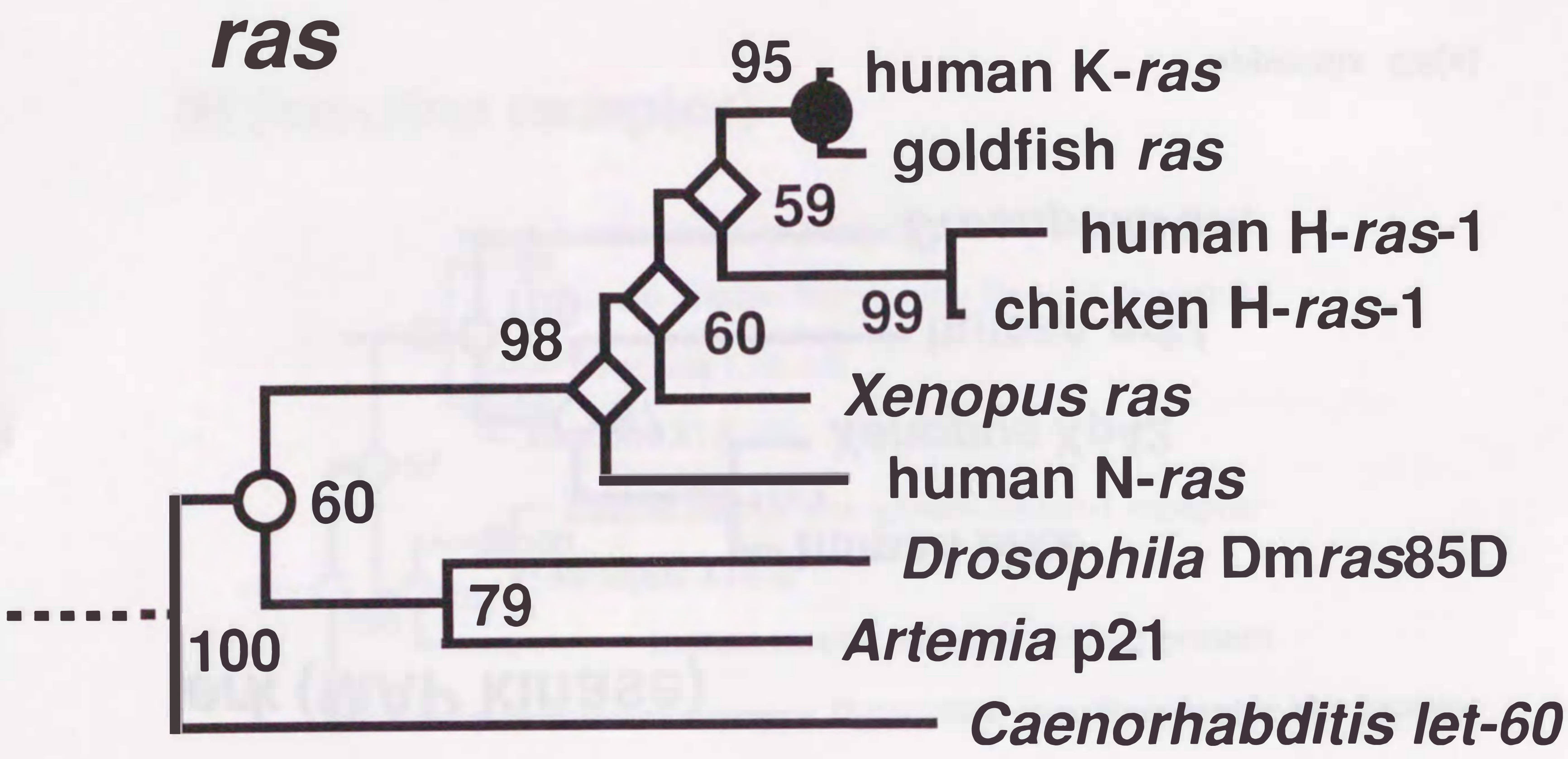


Appendix C7(a)

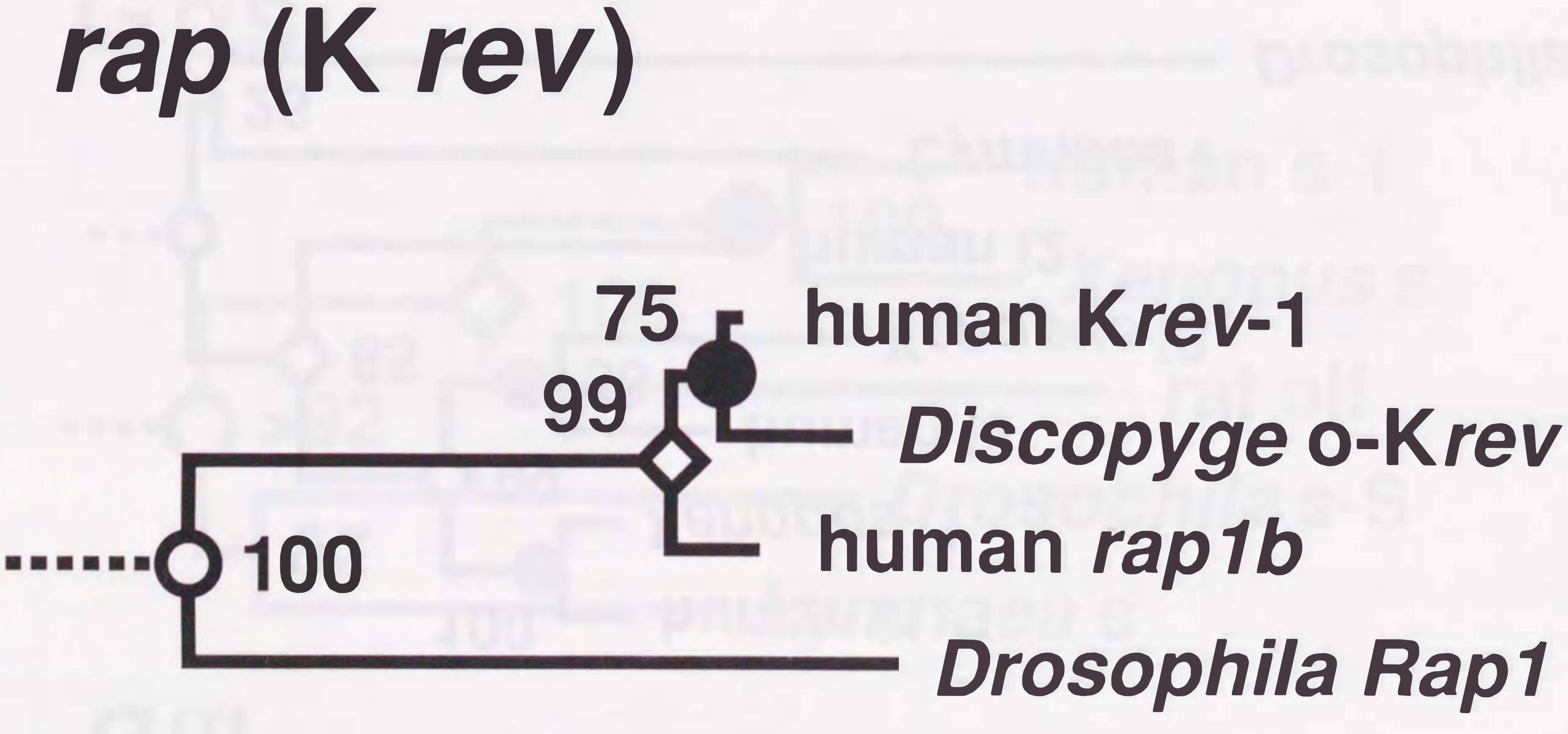
erk (MAP kinase)



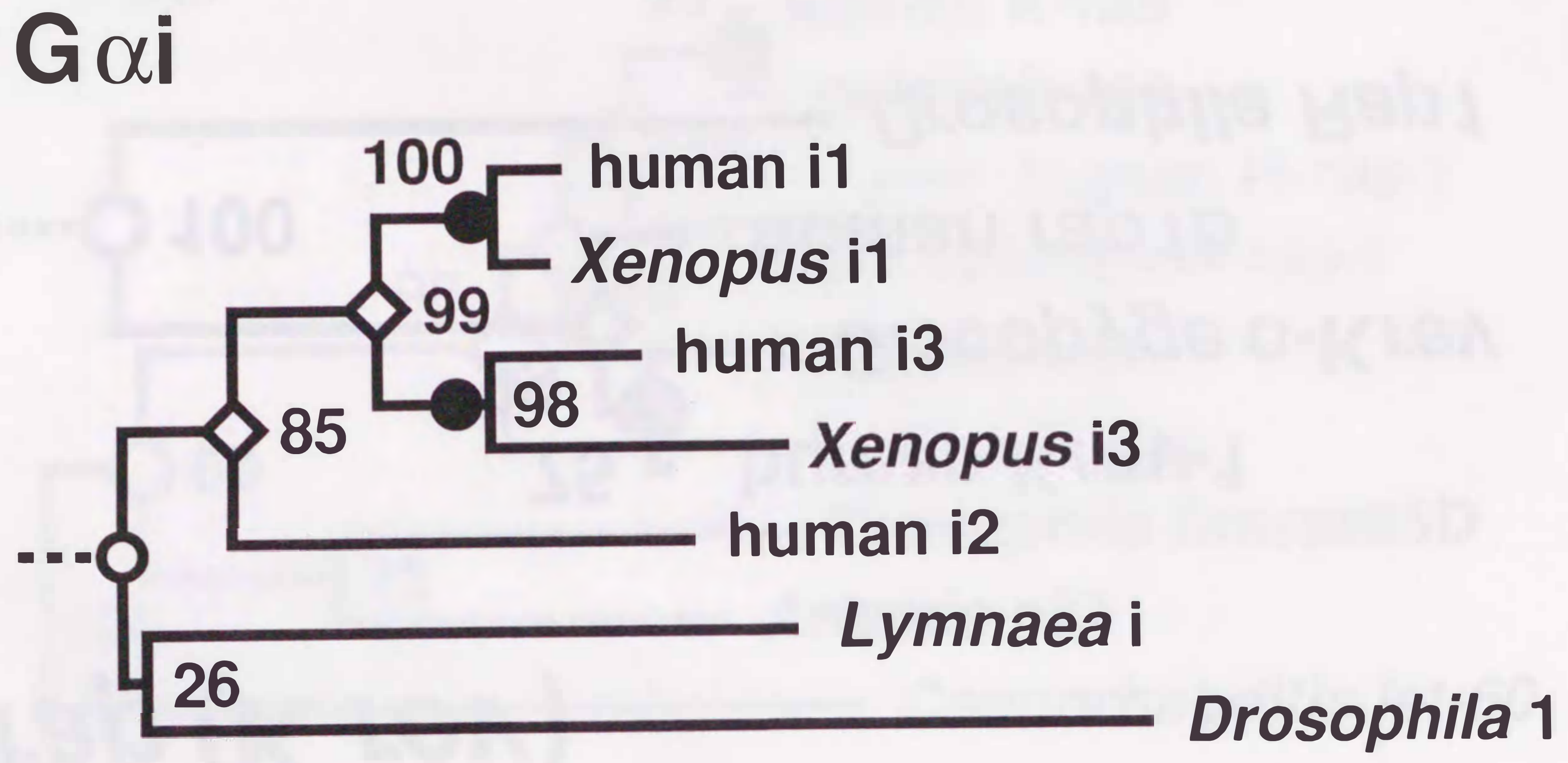
Appendix C8(a)



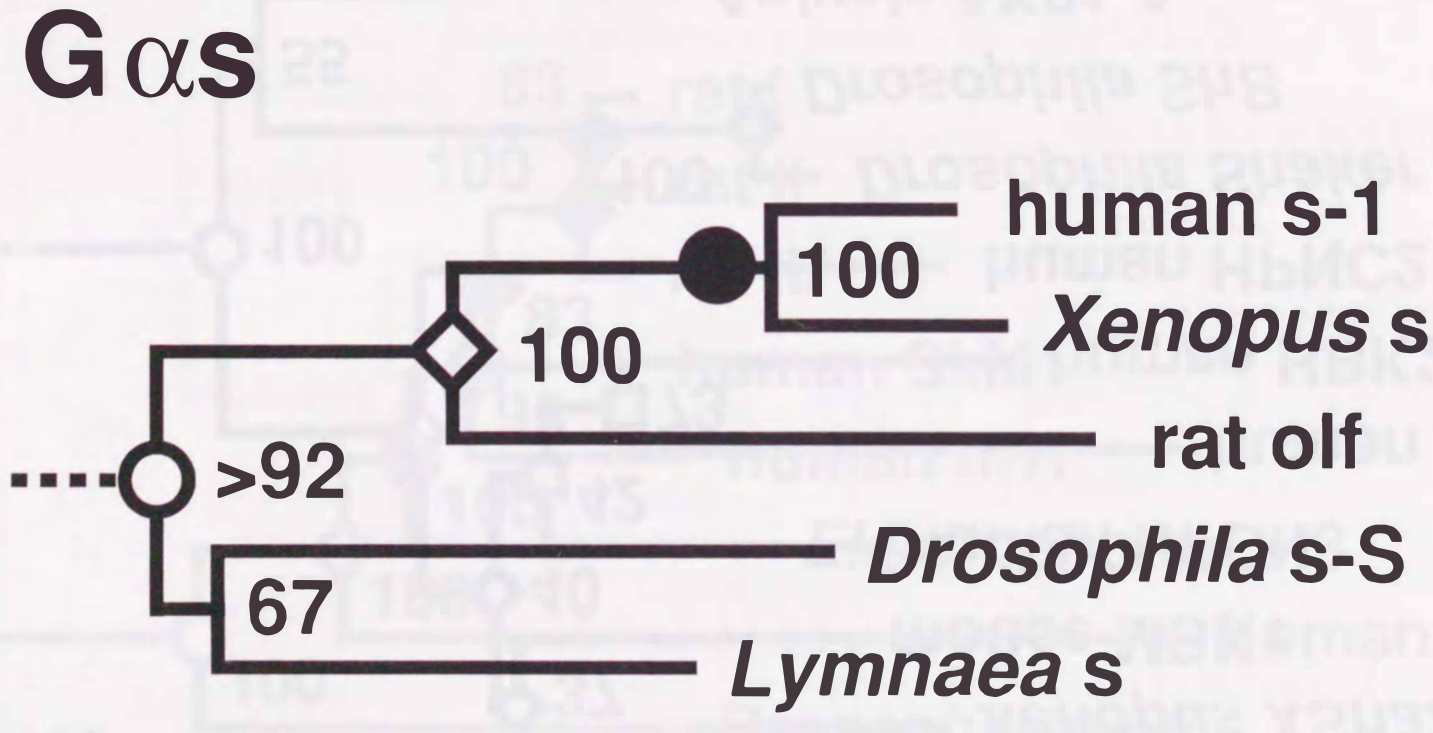
Appendix C9(a)



Appendix C10(a)

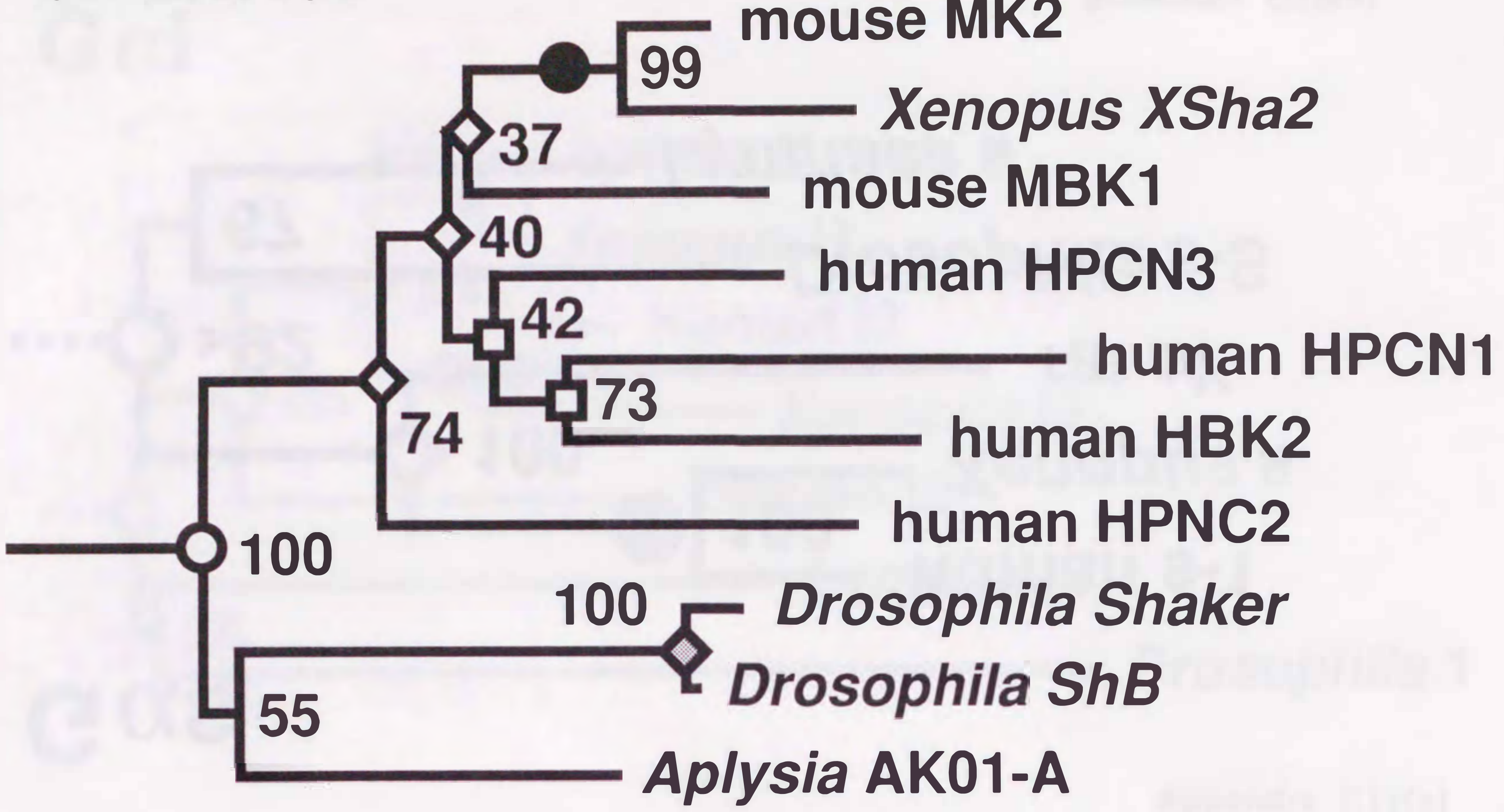


Appendix C11(a)



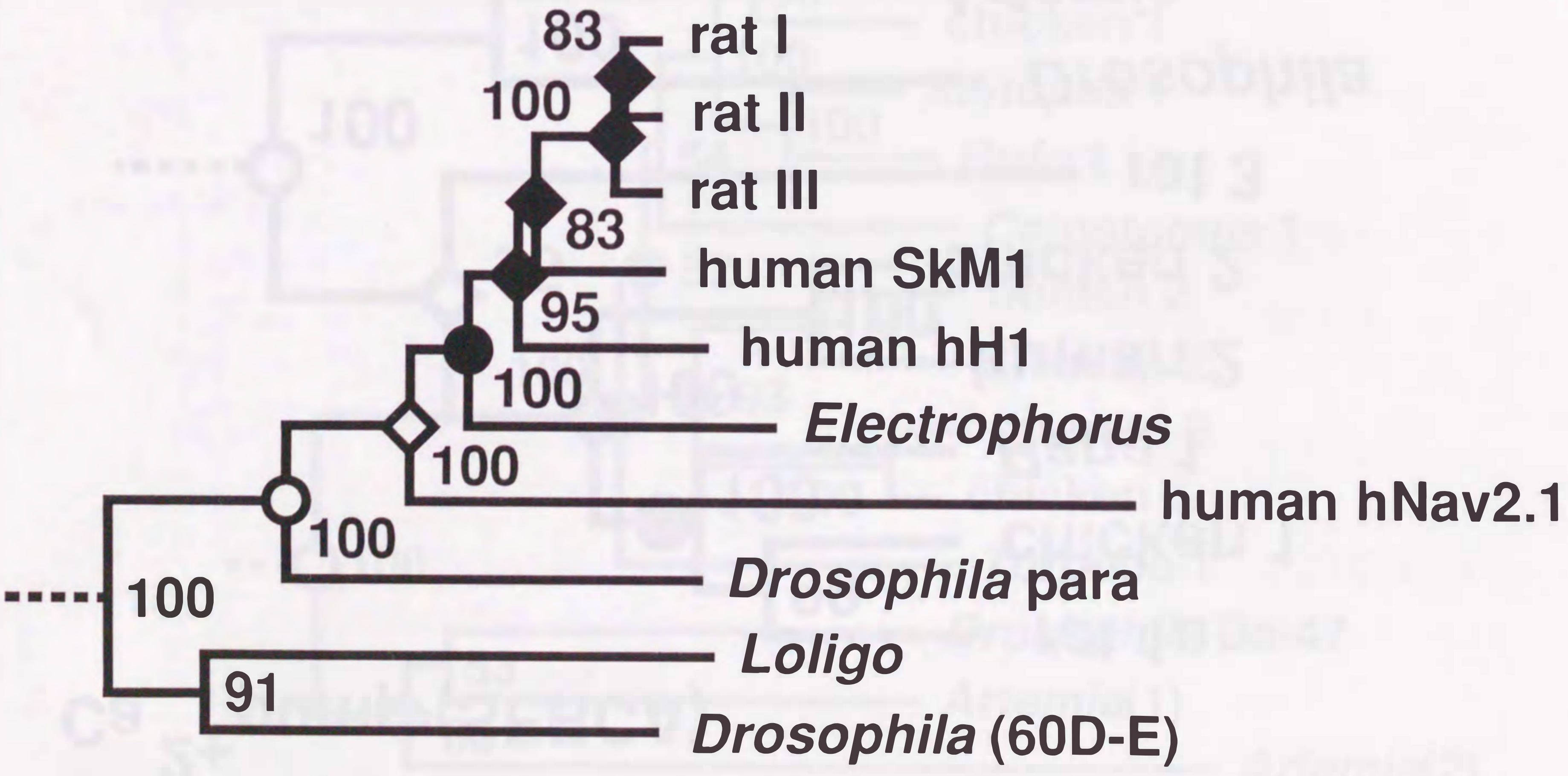
Appendix C12(a)

K$^+$-channel

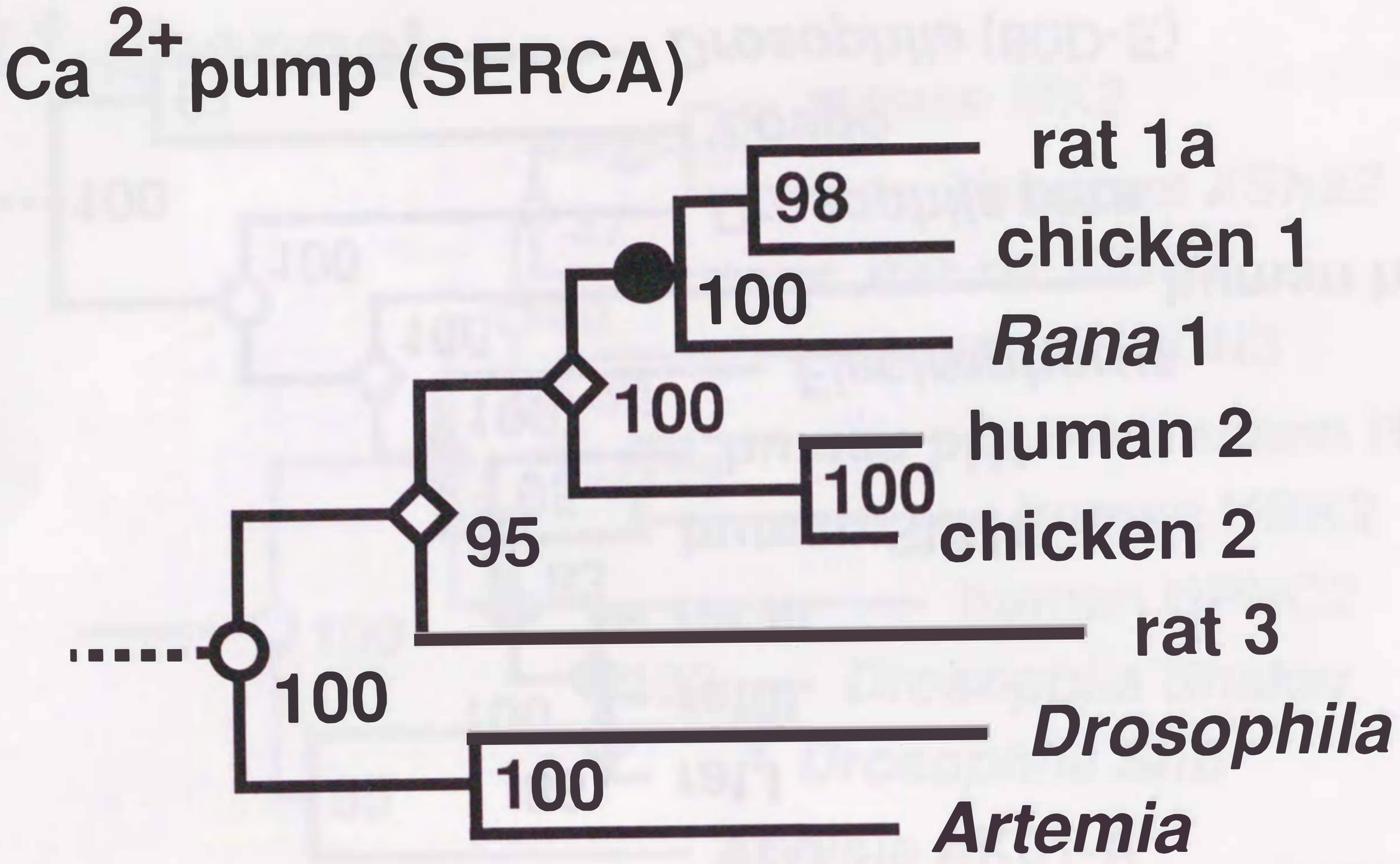


Appendix C13(a)

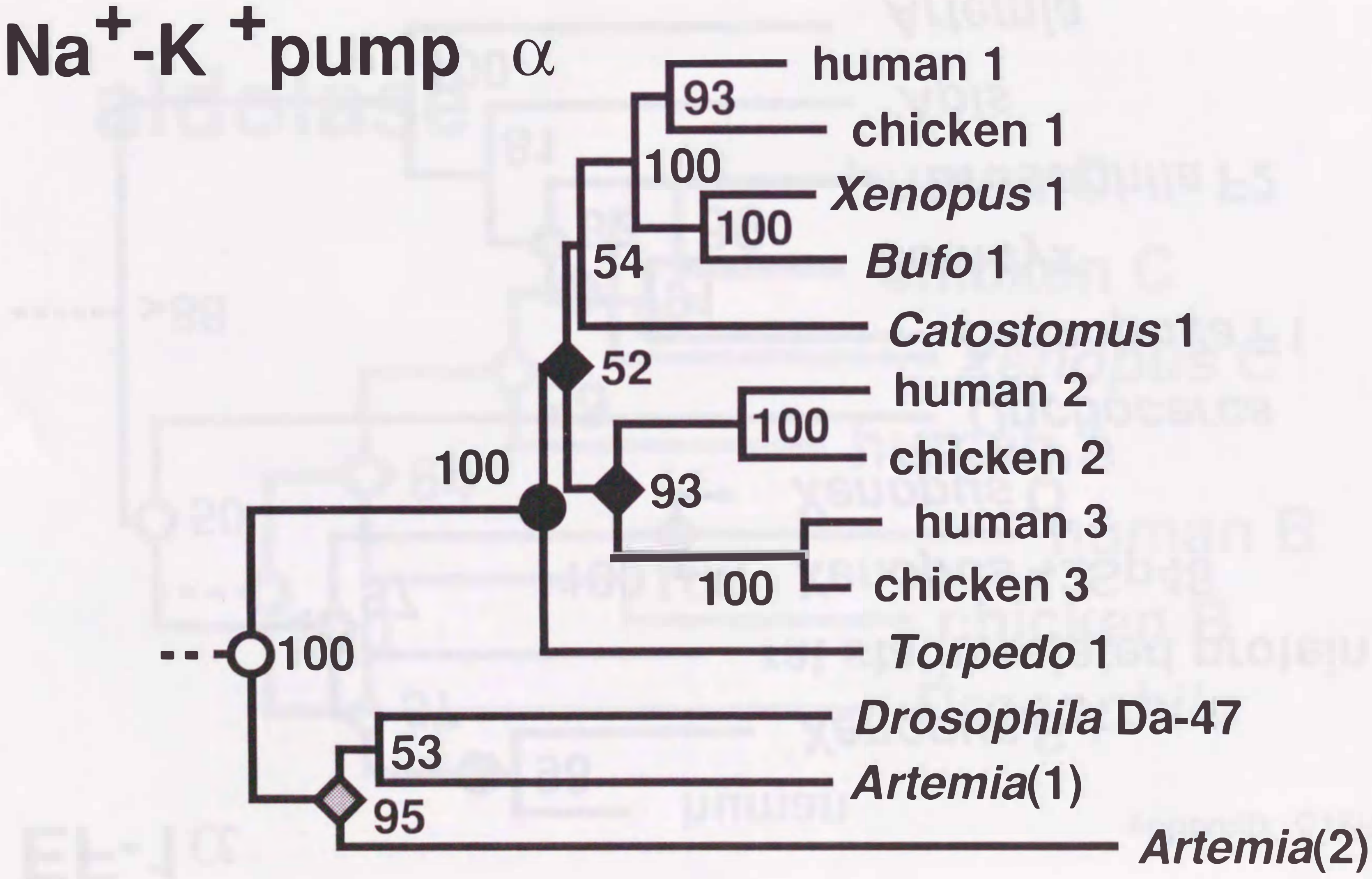
Na$^+$-channel



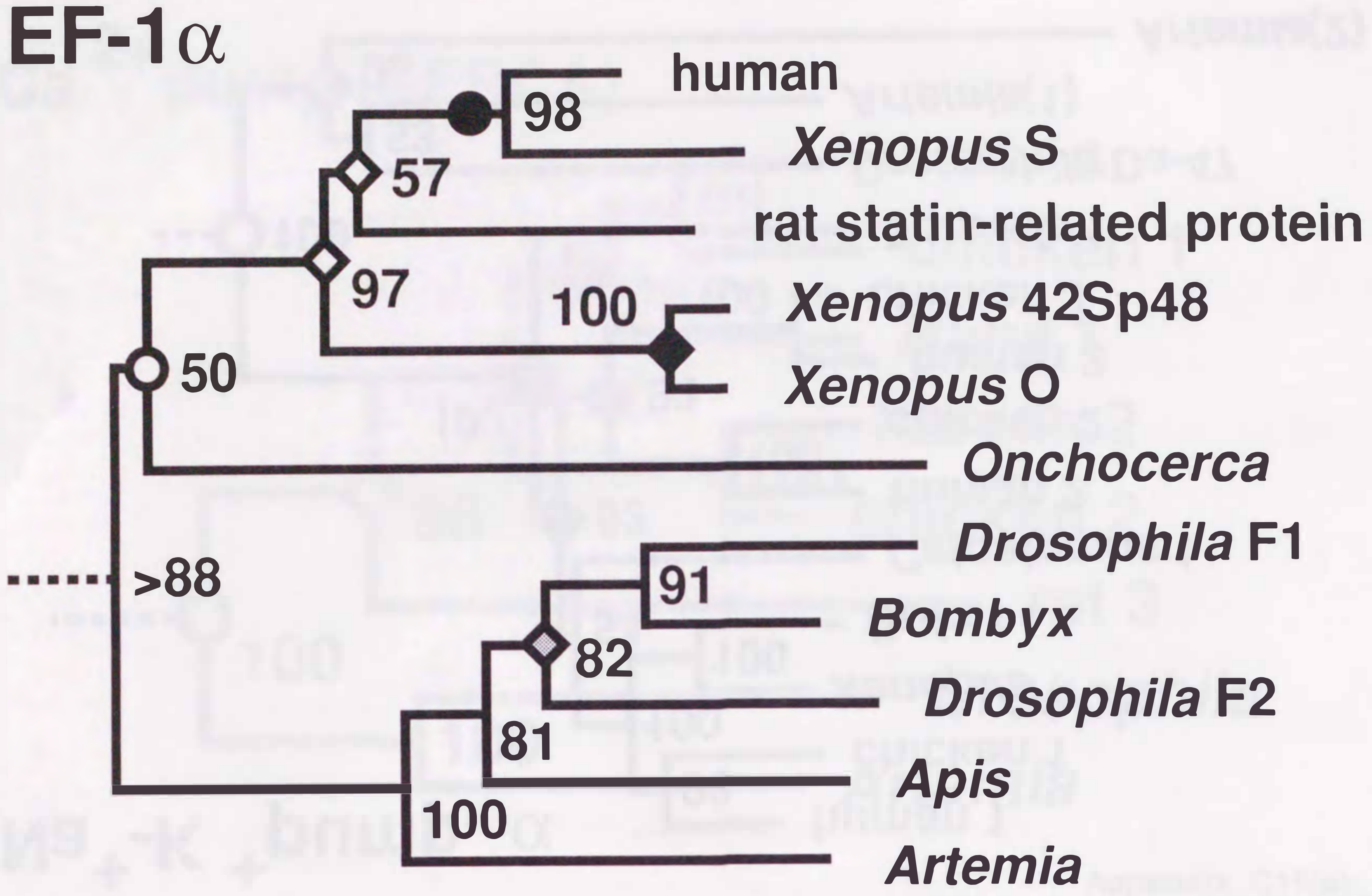
Appendix C14(a)



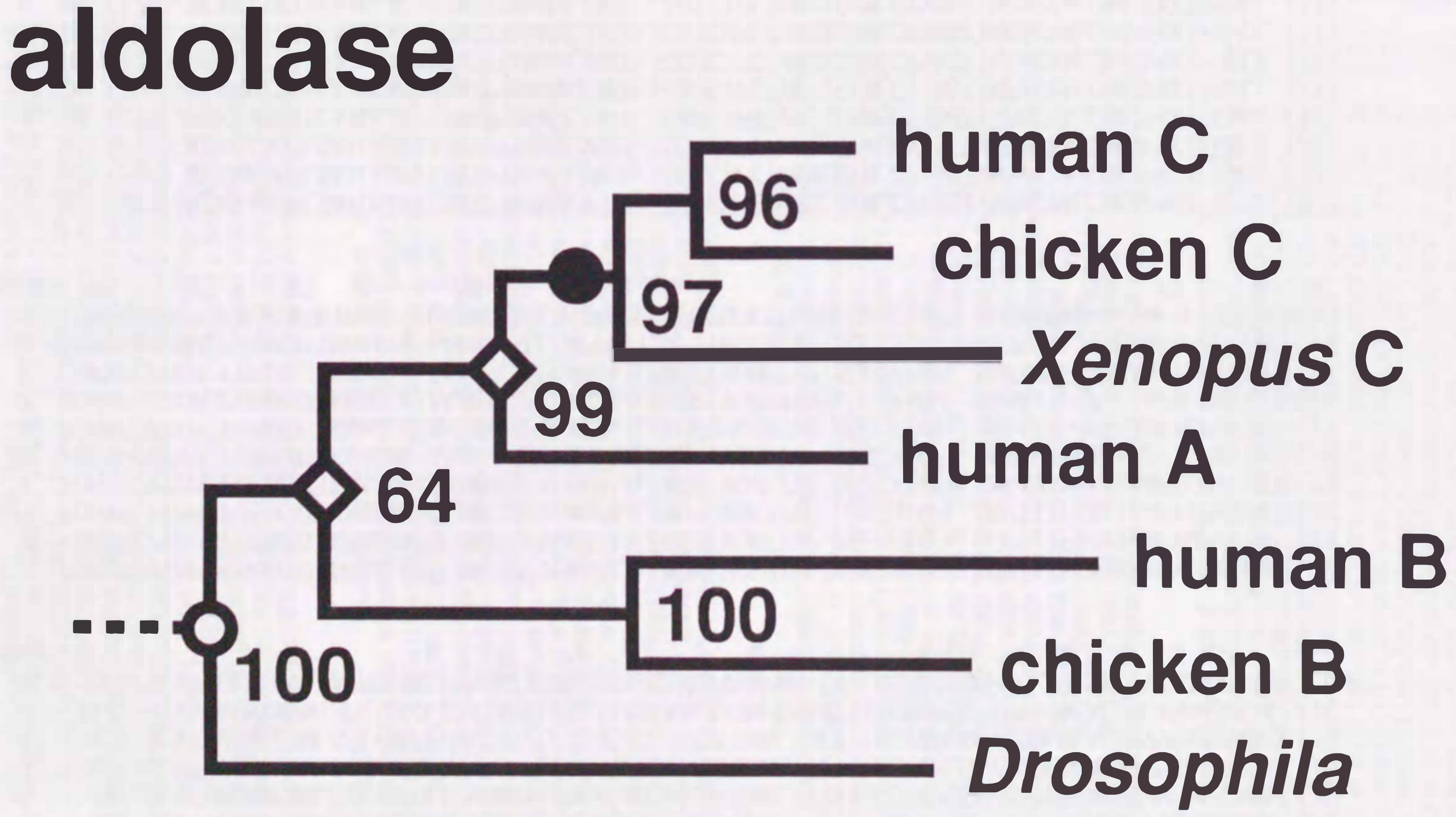
Appendix C15(a)



Appendix C16(a)



Appendix C17(a)



Appendix C18(a)

mAChR

```
 1. ( 35) SLATVTGNLLVLISFKVNTELKTVNNYFLLSLACADLIIGTFSMNLYTTYLLMGHWALGTLACDLWLALDYVASNASVMNLLLIS
 2. ( 78) ALVTIIGNILVIVSFKVNKQLKTVNNYFLLSLACADLIIGVISMNLFTTYIIMNRWALGNLACDLWLAIDYVASNASVMNLLVIS
 3. ( 40) SLITIVGNVLVMISFKVNSQLKTVNNYYLLSLACADLIIGIFSMNLYTTYILMGRWALGSLACDLWLALDYVASNASVMNLLVIS
 4. ( 33) SLVTIIGNILVMVSIKVNRHLQTVNNYFLFSLACADLIIGVFSMNLYTLYTVIGYWPLGPVVCDLWLALDYVVSNASVMNLLIIS
 5. ( 36) SLVTIIGNILVMVSIKVNRHLQTVNNYFLFSLACADLIIGIFSMNLYTLYTVIGYWPLGPVVCDLWLALDYVVSNASVMNLLIIS
 6. ( 42) SLVTVVGNILVMLSIKVNRQLQTVNNYFLFSLACADLIIGAFSMNLYTVYIIKGYWPLGAVVCDLWLALDYVVSNASVMNLLIIS
 7. ( 52) SLVTVVGNILVMLSIKVNRQLQTVNNYFLFSLACADLIIGVFSMNLYTVYIIKGYWPLGAVVCDLWLALDYVVSNASVMNLLIIS
 8. ( 43) SLVTVVGNILVMLSIKVNRQLQTVNNYFLFSLACADLIIGVFSMNLYSLYIIKGYWPLGPIVCDLWLALDYVVSNASVMNLLIIS
 9. (114) STVTVAGNVMVMISFKIDKQLQTISNYFLFSLAIADFAIGAISMPLFAVTTILGYWPLGPIVCDTWLALDYLASNASVLNLLIIS
10. ( 38) SLVTVGLNLLVLYAVRSERKLHTVGNLYIVSLSVADLIVGVVVMPMNILYLLMSRWSLGRPLCLFWLSMDYVASTASIFSVFILC
consensus    T   N  V         L T  N    SL  AD   G   M           W LG   C  WL  DY  S AS
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```
       1. FDRYFSVTRPLSYRAKRTPRRAALMIGLAWLVSFVLWAPAILFWQYLVGERTVL AGQCYIQFL SQPIITFGTAMAAFYLPVTVMCTLYW
       2. FDRYFSITRPLTYRAKRTTKRAGVMIGLAWVISFVLWAPAILFWQYFVGKRTVP PGECFIQFL SEPTITFGTAIAAFYMPVTIMTILYW
       3. FDRYFSITRPLTYRAKRTPKRAGIMIGLAWLISFILWAPAILCWQYLVGKRTVP LDECQIQFL SEPTITFGTAIAAFYIPVSVMTILYC
       4. FDRYFCVTKPLTYPVKRTTKMAGMMIAAAWVLSFILWAPAILFWQFIVGVRTVE DGECYIQFF SNAAVTFGTAIAAFYLPVIIMTVLYW
       5. FDRYFCVTKPLTYPVKRTTKMAGMMIAAAWVLSFILWAPAILFWQFIVGGRTVP DKDCYIQFF SNPAVTFGTAIAAFYLPVIIMTVLYW
       6. FDRYFCVTKPLTYPARRTTKMAGLMIAAAWVLSFVLWAPAILFWQFVVGKRTVP DNQCFIQFL SNPAVTFGTAIAAFYLPVVIMTVLYI
       7. FDRYFCVTKPLTYPARRTTKMAGLMIAAAWILSFILWAPAILFWQFIVGKRTVH ERECYIQFL SNPAVTFGTAIAAFYLPVVIMTVLYI
       8. LERXFCVTKPLTYPARRTTKMAGLMIAAAWLLSFELWAPAILFWQFIVGQRTVP SGECYIQFL SNPAVTFGTAIAAFYLPVVIMTILYI
       9. FDRYFSVTRPLTYRAKRTTNRAAVMIGAAWGISLLLWPPWIYSWPYIEGKRTVP KDECYIQFIETNQYITFGTALAAFYFPVTIMCFLYW
      10. IDRYRSVQQPLKYLRYRTKTRASITILAAWFLSFLWIIP ILGWRHFQPKTPEPREDKCETDFY NVTWFKVMTAIINFYLPTLLMLWFYA
consensus   R      PL Y   RT   A   I  AW  S     P I  W              C   F          TA   FY P   M   Y
```

```
       1. RI (147) KEKKAARTLSAILLAFILTWTPYNIMVLVSTF  CKDCVPETLWELGYWLCYVNSTINPMCYALCNKAFRDTFRLLL (27)
       2. RI (230) KEKKAAQTLSAILLAFIITWTPYNIMVLVNTF  CDSCIPKTFWNLGYWLCYINSTVNPVCYALCNKTFRTTFKMLL (31)
       3. RI (219) KERKAAQTLSAILLAFIITWTPYNIMVLVSTF  CDKCVPVTLWHLGYWLCYVNSTVNPICYALCNRTFRKTFKMLL (22)
       4. HI (171) REKKVTRTILAILLAFIITWAPYNVMVLINTF  CAPCIPNTVWTIGYWLCYINSTINPACYALCNATFKKTFKHLL (11)
       5. QI (168) REKKVTRTILAILLAFIITWTPYNVMVLINSF  CASCIPGTVWTIGYWLCYINSTINPACYALCNATFKKTFKHLL (11)
       6. HI (175) RERKVTRTIFAILLAFILTWTPYNVMVLVNTF  CQSCIPDTVWSIGYWLCYVNSTINPACYALCNATFKKTFRHLL (11)
       7. HI (176) REKKVTRTIFAILLAFILTWTPYNVMVLINTF  CETCVPETVWSIGYWLCYVNSTINPACYALCNATFKKTFKHLL (11)
       8. HI (179) REKKVTRTIFAILLAFIITWTPYNVMVLINTF  CQTCIPETIWYIGYWLCYVNSTINPACYALCNATFKKTFKHLL (11)
       9. RI (402) QESKAAKTLSAILLSFIITWTPYNILVLIKPLTTCSDCIPTELWDFFYALCYINSTINPMCYALCNATFRRTYVRIL (18)
      10. KI (198) RERKAAKQLGFIMAAFIICWIPYFIFFMVIAF  CESCCNQHVHMFTIWLGYINSTLNPLIYPLCNENFKKTFKKIL ( 4)
consensus  I        E K       I   FI  W PY           C  C           L Y NST NP  Y LCN  F  T    L
```

Appendix C1(b)

src

```
 1. (262) WEIPRESLRLEVKLGQGCFGEVWMGTWNGTTRVAIKTLKPGTMSPEAFLQEAQVMKKLRHE
 2. (258) WEIPRDSLRLELKLGQGCFGEVWMGTWNGTTRVAIKTLKPGTMSPEAFLQEAQVMKKLRHE
 3. (269) WEIPRESLRLEVKLGQGCFGEVWMGTWNGTTKVAIKTLKPGTMMPEAFLQEAQIMKKLRHD
 4. (270) WEIPRESLRLDVRLGQGCFGEVWMGTWNGTTKVAIKTLKPGTMSPEAFLEEAQIMKKLRHD
 5. (263) WEIPRESLQLIKRLGNGQFGEVWMGTWNGNTKVAIKTLKPGTMSPESFLEEAQIMKKLKHD
 6. (263) WEIPRESLQLIKRLGNGQFGEVWMGTWNGTTKVAVKTLKPGTMSPESFLEEAQIMKKLRHD
 7. (255) WEISRSSITLERRLGTGCFGDVWLGTWNGSTKVAVKTLKPGTMSPKAFLEEAQVMKLLRHD
 8. (233) WEIPRESLKLEKKLGAGQFGEVWMATYNKHTKVAVKTMKPGSMSVEAFLAEANVMKTLQHD
 9. (239) WEIPRESIKLVKRLGAGQFGEVWMGYYNNSTKVAVKTLKPGTMSVQAFLEEANLMKTLQHD
10. (237) WEVPRETLKLVERLGAGQFGEVWMGYYNGHTKVAVKSLKQGSMSPDAFLAEANLMKQLQHP
11. (184) WEVPRESLKLVEKLGAGQFGEVWMGFYNGHTKVAIKNLKQGSMSPSAFLAEANLMKNLQHP
12. (227) WEIPRQSLKLVRKLGSGQFGEVWMGYYKNNMKVAIKTLKEGTMSPEAFLGEANVMKTLQHE
13. (276) YEIPRSEIQLLRKLGRGNFGEVFYGKWRNSIDVAVKTLREGTMSTAAFLQEAAIMKKFRHN
14. (232) WEIPRESLRLNRKLGAGQFGEVWAGVWNNTTQVAVKTLKPGTMSPASFLDEAGVMKKLRHK
consensus  E  R    L   LG G FG V          VA K    G M    FL EA  MK   H
```

```
       1. KLVQLYAVVSE EPIYIVTEYMSKGSLLDFLKGETGKYL RLPQLVDMAAQIASGMAYVERMNYVHR
       2. KLVQLYAVVSE EPIYIVTEYMSKGSLLDFLKGEMGRYL RLPQLVDMAAQIASGMAYVERMNYVHR
       3. KLVPLYAVVSE EPIYIVTEFMSKGSLLDFLKEGDGKYL KLPQLVDMAAQIADGMAYIERMNYIHR
       4. KLVPLYAVVSE EPIYIVTEFMGKGSLLDFLKEGDGKHL KLPQLVDMASQIADGMAFIERMNYIHR
       5. KLVQLYAVVSE EPIYIVTEYMNKGSLLDFLKDGEGRAL KLPNLVDMAAQVAAGMAYIERMNYIHR
       6. KLVQLYAVVSE EPIYIVTEYMSKGSLLDFLKDGEGRAL KLPNLVDMAAQVAAGMAYIERMNYIHR
       7. KLVQLYAVVSE EPIYIVTEFMCHGSLLDFLKNPEGQDL RLPQLVDMAAQVAEGMAYMERMNYIHR
       8. KLVKLHAVVTK EPIYIITEFMAKGSLLDFLKSDEGSKQ PLPKLIDFSAQIAEGMAFIEQRNYIHR
       9. KLVRLYAVVTREEPIYIITEYMAKGSLLDFLKSDEGGKV LLPKLIDFSAQIAEGMAYIERKNYIHR
      10. RLVRLYAVVTQ EPIYIITEYMENGSLVDFLKTPSGIKL NVNKLLDMAAQIAEGMAFIEEQNYIHR
      11. RLVRLYAVVTK EPIYIITEYMEKGSLVDFLKTSEGIKL SINKLLDMAAQIAEGMAFIEAKNYIHR
      12. RLVRLYAVVTR EPIYIVTEYMARGCLLDFLKTDEGSRL SLPRLIDMSAQVAEGMAYIERMNSIHR
      13. RLVALYAVCSQEEPIYIVQEYMSKGSLLDFLREGDGRYL HFEDLIYIATQVASGMEYLESKQLIHR
      14. HLVQLYAICSDREPIYIVTEYMSGGSLLDYLSKGEGVNL QLPTLIDMAAQVASGMAFLEAQGYIHR
consensus  LV L A     EPIYI  E M  G L D L    G        L     Q A GM   E     HR
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       1. DLRAANILVGENLVCKVADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILL
       2. DLRAANILVGENLVCKVADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILL
       3. DLRAANILVGENLVCKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILQ
       4. DLRAANILVADNLVCKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILL
       5. DLRSANILVGNGLICKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILL
       6. DLRSANILVGDNLVCKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVWSFGILL
       7. DLRAANILVGERLACKIADFGLARLIKDDEYNPCQGSKFPIKWTAPEAALFGRFTIKSDVWSFGILL
       8. DLRAANILVSASLVCKIADFGLARVIEDNEYTAREGAKFPIKWTAPEAINFGSFTIKSDVWSFGILL
       9. DLRAANVLVSESLMCKIADFGLARVIEDNEYTAREGAKFPIKWTAPEAINFGCFTIKSDVWSFGILL
      10. DLRAANILVSDTLSCKIADFGLARLIEDNEYTAREGAKFPIKWTAPEAINYGTFTIKSDVWSFGILL
      11. DLRAANILVSEALCCKIADFGLARLIEDNEYTAREGAKFPIKWTAPEAINYGTFTIKSDVWSFGILL
      12. DLRAANILVSETLCCKIADFGLARII DSEYTAQEGAKFPIKWTAPEAIHFGVFTIKADVWSFGVLL
      13. DLAARNVLIGENNVAKICDFGLARVIADDEYCPKQGSRFPVKWTAPEAIIYGKFSIKSDVWSYGILL
      14. DLAARNILVGENYICKVADFGLARLIEDDEYTAHEGAKFPIKWTAPEAALYNRFTIKSDVWSFGILM
consensus DL   N L       K  DFGLAR I D EY    G  FP KWTAPEA     F IK DVWS G L
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       1. TELTTKGRVPYPGMVNREVLDQVERGY (7) CPESLH DLMCQCWRKEPEERPTFEYLQAFL (17)
       2. TELTTKGRVPYPGMVNREVLDQVERGY (7) CPESLH DLMFQCWRKDPEERPTFEYLQAFL (17)
       3. TELVTKGRVPYPGMVNREVLEQVERGY (7) CPESLH ELMNLCWKKDPDERPTFEYIQSFL (17)
       4. TELVTKGRVPYPGMVNREVLEQVDRGY (7) CPESLH EMMRQCWKKEPDERPTFEYIQSFL (17)
       5. TELVTKGRVPYPGMNNREVLEQVERGY (7) CPISLH ELMIHCWKKDPEERPTFEYLQSFL (17)
       6. TELVTKGRVPYPGMNNREVLEQVERGY (7) CPASLH ELMLQCWKKDPEERPTFEYLQAFL (17)
       7. TELITKGRIPYPGMNKREVLEQVEQGY (7) CPASLY EAMEQTWRLDPEERPTFEYLQSFL (17)
       8. MEIVTYGRIPYPGMSNPEVIRALERGY (7) CPEELY NIMMRCWKNRPEERPTFEYIQSVL (15)
       9. YEIVTYGKIPYPGRTNADVMTALSQGY (7) CPDELY DIMKMCWKEKAEERPTFDYLQSVL (15)
      10. TEIVTHGRIPYPGMTNPEVIQNLERGY (7) CPEELY HLMMLCWKERPEDRPTFDYLRSVL (15)
      11. TEIVTYGRIPYPGMTNPEVIQNLERGY (7) CPQELY ELMMQCWKEQPEERPTFEYMKSVL (15)
      12. MVIVTYGRVPYPGMSNPEVIRSLEHGY (7) CPPELYNDIITECWRGRPEERPTFEFLQSVL (15)
      13. MELFTYGQVPYPGMHSREVIENIERGF (9) FPDNIY QLLLQCWDAVPEKRPTFEFLNHYF (16)
      14. AEIVTKGRIPYPGMTNAQTIAEVEKGY (7) CPEPLY NIMLQTWNKDPENRPTFDYLQGVL (19)
consensus     T G  PYPG            G       P           W      RPTF
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Appendix C2(b)

FGFR

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       1. (462) YELPEDPRWELPRDRLVLGKPLGEGCFGQVVLAEAIGLDKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASK
       2. (460) YELPEDPRWELPRDRLILGKPLGEGCFGQVVLAEAIGLDKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASK
       3. (456) YELPEDPRWEVARDRLILGKPLGEGCFGQVVMAEAIGLDKEKPNKVTKVAVKMLKSDASEKDLSDLISEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYTSK
       4. (465) YELPEDPKWEFPRDKLTLGKPLGEGCFGQVVMAEAVGIDKDKPKEAVTVAVKMLKDDATEKDLSDLVSEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASK
       5. (467) YELPEDPKWEFPRDKLTLGKPLGEGCFGQVVMAEAVGIDKDRPKEAVTVAVKMLKDDATEKDLSDLVSEMEMMKMIGKHKNIINLLGACTQDGPLYVIVEYASK
       6. (456) LELPADPKWELSRARLTLGKPLGEGCFGQVVMAEAIGIDKDRAAKPVTVAVKMLKDDATDKDLSDLVSEMEMMKMIGKHKNIINLLGACTQGGPLYVLVEYAAK
       7. (451) LDLPLDPLWEFPRDRLVLGKPLGEGCFGQVVRAEAFGMDPARPDQASTVAVKMLKDNASDKDLADLVSEMEVMKLIGRHKNIINLLGVCTQEGPLYVIVECAAK
       8. (470) FDLPLDSKWEFPRERLVLGKPLGEGCFGQVVRAEAYGINKDQPDKAITVAIKIVKDKGTDKELSDLISEMELMKLMGKHKNIINLLGVCTQDGPLYMIVEYASK
       9. (435) YEFPLDSNWEIPRQQLSLGSILGEGAFGRVVMAEAEGLPRSPQLAETIVAVKMVKEEHTDTDMASLVREMEVMKMIGKHINIINLLGCCSQGGPLWVIVEYAPH
      10. (454) FKILEDPKWEFPRKNLVLGKTLGEGEFGKVVKATAFHL KGRAGYT TVAVKMLKENASPSELRDLLSEFNVLKQV NHPHVIKLYGACSQDGPLLLIVEYAKY
consensus            D  WE  R  L LG  LGEG FG VV A A             VA K  K          L  E    K    H   I L G C Q GPL   VE
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       1. GNLREYLQARRPPGLE ( 9) EEQLSSKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHIDYYKKTTNGRLPVKWMAPEALFDRIYTH
       2. GNLREYLQARRPPGME ( 9) EEQLSFKDLVSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHHIDYYKKTTNGRLPVKWMAPEALFDRIYTH
       3. GNLREYLRARRPPAME ( 9) DQLLSFKDLVSCAYQVARGMDYLASKKCIHRDLAARNVLVTEDNIMKIADFGLARDIHHIDYYKKTTNGRLPVKWMAPEALFDRIYTH
       4. GNLREYLRARRPPGME ( 9) EEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLAARNVLVTENNVMKIADFGLARDINNIDYYKKTTNGRLPVKWMAPEALFDRVYTH
       5. GNLREYLRARRPPGME ( 9) EEQMTFKDLVSCTYQLARGMEYLASQKCIHRDLAARNVLVTENNVMKIADFGLARDINNIDYYKKTTNGRLPVKWMAPEALFDRVYTH
       6. GNLREFLRARRPPGLD ( 9) EEQLTFKDLVSCAYQVARGMEYLASQKCIHRDLAARNVLVTEDNVMKIADFGLARDVHNLDYYKKTTNGRLPVKWMAPEALFDRVYTH
       7. GNLREFLRARRPPGPD ( 9) EGPLSFPVLVSCAYQVARGMQYLESRKCIHRDLAARNVLVTEDNVMKIADFGLARGVHHIDYYKKTSNGRLPVKWMAPEALFDRVYTH
       8. GNLREFLRARRPPSPD ( 9) EEQLSFQDLVSCSYQVARGMAYLESKRCIHRDLAARNVLVTGENVMKIADFGLARGVHDIDYYKKTSNGRLPVKWMAPEALFDRVYTH
       9. GNLKDFLKQNRPGAPQ (16) TQHLGEKELTKFAFQIARGMEYLASRRCIHRDLAARNVLVSDGYVMKIADFGLARDIQDTEYYRKNTNGRLPIKWMXP SRCRRRSTT
      10. GSLRGFLRESRKVGPG (17) ERALTMGDLISFAWQISQGMQYLAEMKLVHRDLAARNILVAEGRKMKISDFGLSRDVYEEDSYVKRSQGRIPVKWMAIESLFDHIYTT
consensus G L   L   R                   L     Q   GM YL      HRDLAARN LV     MKI DFGL R       Y K   GR P KWM          T
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       1. QSDVWSFGVLLWEIFTLGGSPYPGV PVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDHIV (4) NQEYLDLSIPLDQYSPSFPD (40)
       2. QSDVWSFGVLLWEIFTLGGSPYPGV PVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRIV (4) NQEYLDLSVPLDQYSPGFPA (39)
       3. QSDVWSFGVLLWEIFTLGGSPYPGV PMEELFKLLKEGHRMDKPTNCTNELYMMMKDCWHAMPSQRPTFNQLVEDLDRIL (4) NQEYLDLSMPVNQYSPCFPD (37)
       4. QSDVWSFGVLMWEIFTLGGSPYPGI PVEELFKLLKEGHRMDKPANCTNELYMMMRDCWHAVPSQRPTFKQLVEDLDRIL (4) NEEYLDLSQPLEQYSPSYPD (36)
       5. QSDVWSFGVLMWEIFTLGGSPYPGI PVEELFKLLKEGHRMDKPANCTNELYMMMRDCWQAVPSQRPTFKQLVEDLDRIL (4) NEEYLDLSGPLEQYSPSYPD (36)
       6. QSDVWSFGVLLWEIFTLGGSPYPGI PVEELFKLLKEGHRMDKPANCTHDLYMIMRECWHAAPSQRPTFKQLVEDLDRVL (4) TDEYLDLSAPFEQYSPGGQD (30)
       7. QSDVWSFGILLWEIFTLGGSPYPGI PVEELFSLLREGHRMDRPPHCPPELYGLMRECWHAAPSQRPTFKQLVEALDKVL (3) SEEYLDLRLTFGPYSPSGGD (32)
       8. QSDVWSFGVLTWEIFTLGGSPYPGI PVEELFKLLREGHRMDKPSNCTHELYMLMRECWHAAPSQRPTFKQLVETLDRIL (3) AEEYLDLSMPFEQYSPACED (34)
       9. HSDVWSYGVLLWEIMTYGDQPYPHILSAEELYSYLITGQRMEKPAKCSLNIYVVMRQCWHFQSCARPTFAELVESFDGIL (7) NDAYLDLSMPMLETPPSSGD (25)
      10. QSDVWSFGVLLWEIVTLGGNPYPGI PPERLFNLLKTGHRMERPDNCSEEMYRLMLQCWKQEPDKRPVFADISKDLEKMM (2) RRDYLDLAASTPSDSLIYDD (83)
consensus  SDVWS G L WEI T G  PYP     E L   L  G RM  P  C    Y  M  CW      RP F                   YLDL
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Appendix C3(b)

raf

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       1. (353) RIGSGSFGTVYKGKWHG DVAVKILKVVDPTPEQFQA FRNEVAVLRKTRHVNILLFMGYMTKDNL
       2. (344) RIGSGSFGTVYKGKWHG DVAVKILKVTDPTPEQLQA FRNEVAVLRKTRHVNILLFMGYMTKDNL
       3. (460) RIGSGSFGTVYKGKWHG DVAVKMLNVTAPTPQQLQA FKNEVGVLRKTRHVNILLFMGYSTKPQL
       4. (314) RIGTGSFGTVFRGRWHG DVAVKVLKVSQPTAEQAQA FKNEMQVLRKTRHVNILLFMGFMTRPGF
       5. (360) RIGSGSFGTVYRAHWHG PVPVKTLNVKTPSPAQLQA FKNEVAMLKKTRHCNILLFMGCVSKPSL
       6. (112) KVGEGAFSEVWEGWWKGIHVAIKKLKII GDEEQFKERFIREVQNLKKGNHQNIVMFIGACYKPA
consensus         G G F  V    W G  V  K L        Q    F  E   L K  H NI  F G
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       1. AIVTQWCEGSSLYK (21) AQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLATVKSRWSGSQQVEQ
       2. AIVTQWCEGSSLYY (21) AQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLATVKTRWSGSQQVEQ
       3. AIVTQWCEGSSLYH (21) AQGMDYLHAKSIIHRDLKSNNIFLHEDLTVKIGDFGLATVKSRWSGSHQFEQ
       4. AIITQWCEGSSLYH (21) AQGMDYLHAKNIIHRDLKSNNIFLHEGLTVKIGDFGLATVKTRWSGAQPLEQ
       5. AIVTQWCEGSSLYK (21) AQGMDYLHAKNIIHRDLKSNNIFLHEDLSVKIGDFGLATAKTRWSGEKQANQ
       6. CIITEYMAGGSLYN (26) ALGLLHLHSITIVHRDLTSQNILLDELGNIKISDFGLSAEKSREGSMTMTNG
consensus  I T    G SLY       A G   LH    I HRD  S NI L E    KI DFGL   K R
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       1. PTGSVLWMAPEVIRMQDNNPFSFQSDVYSYGIVLYELMTGELPYSHINNRDQIIFMVGRGYASP (80)
       2. LTGSILWMAPEVIRMQDNNPFSFQSDVYSYGIVLYELMTGELPYSHIRDRDQIIFLVGRGGVVP (80)
       3. LSGSILWMAPEVIRMQDKNPYSFQSDVYAFGIVLYELMTGQLPYSNINNRDQIIFMVGRGYLSP (90)
       4. PSGSVLWMAAEVIRMQDPNPYSFQSDVYAYGVVLYELMTGSLPYSHIGCRDQIIFMVGRGYLSP (77)
       5. PTGSILWMAPEVIRMQELNPYSFQSDVYAFGIVMYELLAECLPYGHISNKDQILFMVGRGLLRP (91)
       6. GICNPRWRPPELTK  NLGHYSEKVDVYCFSLVVWEILTGEIPFSDLDGS QRSAQVAYAGLRP (81)
consensus       W   E          S   DVY    V  E      P        Q    V      P
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Appendix C4(b)

CDK2

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   1. (1) ENFQKVEKIGEGTYGVVYKARNKLTGE   VVALKKIRLDTETEGVPSTAIREISLLKELNHPNIVKLLDVIHTE NKLYLVFEFLHQDLKKFMD
   2. (1) ESFQKVEKIGEGTYGVVYKAKNKVTGE   TVALKKIRLDTETEGVPSTAIREISLLKELNHPNIVKLHDVIHTE NKLYLVFEFLHQDLKRFMD
   3. (1) ENFQKVEKIGEGTYGVVYKARNRETGE   IVALKKIRLDTETEGVPSTAIREISLLKELNHPNIVKLLDVIHTE NKLYLVFEFLNQDLKKFMD
   4. (1) DMFQKVEKIGEGTYGVVYKAKNRETGQ   LVALKKIRLDLEMEGVPSTAIREISLLKELKHPNIVRLLDVVHNE RKLYLVFEFLSQDLKKYMD
   5. (5) DNFQRAEKIGEGTYGIVYKARSNSTGQ   DVALKKIRLEGETEGVPSTAIREISLLKNLKHPNVVQLFDVVISG NNLYMIFEYLNMDLKKLMD
   6. (1) EDYTKIEKIGEGTYGVVYKGRHKTTGQ   VVAMKKIRLESEEEGVPSTAIREISLLKELRHPNIVSLQDVLMQD SRLYLIFEFLSMDLKKYLD
   7. (1) DEYTKIEKIGEGTYGVVYKGRHKATGQ   VVAMKKIRLENEEEGVPSTAIREISLLKELQHPNIVCLLDVLMQD SRLYLIFEFLSMDLKKYLD
   8. (1) EDFEKIEKIGEGTYGVVYKGRNRLTGQ   IVAMKKIRLESDDEGVPSTAIREISLLKELKHENIVCLEDVLMEE NRIYLIFEFLSMDLKKYMD
   9. (5) ANYKRLEKVGEGTYGVVYKALDLRPGQGQRVVALKKIRLESEDEGVPSTAIREISLLKELKDDNIVRLYDIVHSDAHKLYLVFEFLDLDLKRYME
consensus       EK GEGTYG VYK      G     VA KKIRL    EGVPSTAIREISLLK L   N V L D         Y  FE L  DLK

   1. (10) LIKSYLFQLLQGLAFCHSHRVLHRDLKPQNLLINTEGAIKLADFGLARAFGVPVRTYTHEVVTLWYRAPEILLGSKYYSTAVDIWSLGCIFAEM
   2. (10) LVKSYLFQLLQGLAFCHSHRVLHRDLKPQNLLINAQGEIKLADFGLARAFGVPVRTYTHEVVTLWYRAPEILLGCKYYSTAVDIWSLGCIFAEM
   3. (10) LVKSYLFQLLQGLAFCHSHRVLHRDLKPQNLLINSDGAIKLADFGLARAFGVPVRTFTHEVVTLWYRAPEILLGCKFYSTAVDIWSLGCIFAEM
   4. (10) LIKSYLFQLLQGVSFCHSHRVIHRDLKPQNLLINELGAIKLADFGLARAFGVPLRTYTHEVVTLWYRAPEILLGSKFYTTAVDIWSIGCIFAEM
   5. ( 9) LIKSYMHQILDAVGFCHTNRILHRDLKPQNLLVDTAGKIKLADFGLARAFNVPMRAYTHEVVTLWYRAPEILLGTKFYSTGVDIWSLGCIFSEM
   6. (11) LVKSYLYQILQGIVFCHSRRVLHRDLKPQNLLIDDKGTIKLADFGLARAFGIPIRVYTHEVVTLWYRSPEVLLGSARYSTPVDIWSIGTIFAEL
   7. (11) LVKSYLYQILQGIVFCHSRRVLHRDLKPQNLLIDSKGVIKLADFGLARAFGIPVRVYTHEVVTLWYRAPEVLLGSVRYSTPVDVWSIGTIFAEI
   8. (11) LVRSYLYQITSAILFCHRRRVLHRDLKPQNLLIDKSGLIKVADFGLGRSFGIPVRIYTHEIVTLWYRAPEVLLGSPRYSCPVDIWSIGCIFAEM
   9. (11) IVKKFMMQLCKGIAYCHSHRILHRDLKPQNLLINKDGNLKLGDFGLARAFGVPLRAYTHEIVTLWYRAPEVLLGGKQYSTGVDTWSIGCIFAEM
consensus         Q       CH  R  HRDLKPQNLL    G  K  DFGL R F  P R  THE VTLWYR PE LLG   Y   VD WS G IF E

   1.     VTRRALFPGDSEIDQLFRIFRTLGTPDEVVWPGVTSMPDYKPSFPKWARQDFSKVVPPLDEDGRSLLSQMLHYDPNKRISAKAALAHPFFQD (10)
   2.     ITRKALFPGDSEIDQLFRIFRTLGTPDESIWPGVTSMPDYKPSFPKWARQDLSKVVPPLDEDGRDLLGQMLIYDPNKRISAKNALVHRFFRD (10)
   3.     ITRRALFPGDSEIDQLFRIFRTLGTPDEVSWPGVTTMPDYKSTFPKWIRQDFSKVVPPLDEDGRDLLAQMLQYDSNKRISAKVALTHPFFRD ( 9)
   4.     VTRKALFPGDSEIDQLFRIFRMLGTPSEDTWPGVTQLPDYKGSFPKWTRKGLEEIVPNLEPEGRDLLMQLLQYDPSQRITAKTALAHPYFSS (17)
   5.     IMRRSLFPGDSEIDQLYRIFRTLSTPDETNWPGVTQLPDFKTKFPRWEGTNMPQ  PITEHEAHELIMSMLCYDPNLRISAKDALQHAYFRN (25)
   6.     ATKKPLFHGDSEIDQLFRIFRALGTPNNEVWPEVESLQDYKNTFPKWKPGSLASHVKNLDENGLDLLSKMLIYDPAKRISGKMALNHPYFND ( 8)
   7.     ATKKPLFHGDSEIDQLFRIFRALGTPNNEVWPEVESLQDYKNSFPKWKGGSLSANVKNIDKDGLDLLAKMLIYDPAKRISARKALLHPYFDD (13)
   8.     ATRKPLFQGDSEIDQLFRMFRILKTPTEDIWPGVTSLPDYKNTFPCWSTNQLTNQLKNLDANGIDLIQKMLIYDPVHRISAKDILEHPYFNG ( 8)
   9.     CNRKPIFSGDSEIDQIFKIFRVLGTPNEAIWPDIVYLPDFKPSFPQWRRKDLSQVVPSLDPRGIDLLDKLLAYDPINRISARRAAIHPYFQE ( 1)
consensus       F GDSEIDQ    FR L TP    WP      D K  FP W                   L   L YD   RI       H F
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Appendix C5(b)

EGFR

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   1. ( 712) KKIKVLGSGAFGTVYKGLW IPEGEKVK (0) IPVAIKELREAT ( 0) SPKAN KEILDEAYVMASVDNPHVCRLLGICLTSTVQ LIT
   2. ( 196) KKVKVLGSGAFGTVYKGLW IPEGEKVK (0) IPVAIKELREAT ( 0) SPKAN KEILDEAYVMASVDNPHVCRLLGICLTSTVQ LIT
   3. ( 709) KKDRVLGSGAFGTVYKGLW NPDGENIR (0) IPVAIKVLREAT ( 0) SPKVN QEVLDEAYVMASVDHPHVCRLLGICLTSAVQ LVT
   4. ( 720) RKVKVLGSGAFGTVYKGIW IPDGENVK (0) IPVAIKVLRENT ( 0) SPKAN KEILDEAYVMAGVGSPYVSRLLGICLTSTVQ LVT
   5. ( 709) RKLKVLGSGVFGTVHKGVW IPEGESIK (0) IPVCIKVIEDKS ( 0) GRQSF QAVTDHMLAIGSLDHAHIVRLLGLCPGSSLQ LVT
   6. ( 763) RKGGVLGMGAFGRVYKGVW VPEGENVK (0) IPVAIKELLKST ( 0) GAESS EEFLREAYIMASEEHVNLLKLLAVCMSSQMM LIT
   7. (1020) FNSAPLGTGSFGAVYKGVWKVPKHALLR (8) LDVAIKVILNDS (28) SVRANIEELLQEAKIMASVMHRHCLPLIGICLSSERHCLVS
consensus         LG G FG V KG W  P             V IK                                      L   C  S    L

       1. QLMPFGCLLDYVREHKDNIGSQYLLNWCVQIAKGMNYLEDRRLVHRDLAARNVLVKTPQHVKITDFGLAKLLG AEEKEYHAEGGKVPIKWMALESILH
       2. QLMPYGCLLDYIREHKDNIGSQYLLNWCVQIAKGMNYLEERRLVHRDLAARNVLVKTPQHVKITDFGLAKLLG ADEKEYHAEGGKVPIKWMALESILH
       3. QLMPYGCLLDYVRQHQERICGQWLLNWCVQIAKGMNYLEERHLVHRDLAARNVLLKNPNHVKITDFGLSKLLT ADEKEYQADGGKVPIKWMALESILQ
       4. QLMPYGCLLDHVRENRGRLGSQDLLNWCMQIAKGMSYLEDVRLVHRDLAARNVLVKSPNHVKITDFGLARLLD IDETEYHADGGKVPIKWMALESILR
       5. QYLPLGSLLDHVRQHRGALGPQLLLNWGVQIAKGMYYLEEHGMVHRNLAARNVLLKSPSQVQVADFGVADLLP PDDKQLLYSEAKTPIKWMALESIHF
       6. QLMPLGCLLDYVRNNRDKIGSKALLNWSTQIAKGMSYLEEKRLVHRDLAARNVLVRLLAG EDHDFGLAKLLS SDSNEYKAAGGKMPIKWLALECIRN
       7. IFVELGALDRYVKQHADELNSLTLLSWAEQIADGMSYLEMRGIIHRDLAARNVLVQTREHVQITDFGLAKMLERRDEDSVIVKAGRVPIRWLAIETLQY
consensus      G L               LL W  QIA GM YLE     HR LAARNVL          DFG   L                PI W A E

       1. RIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSILEKGERLPQPPICTIDVYMIMVKCWMIDADSRPKFRELIIEFSKMARDPQRYLVI (229)
       2. RIYTHQSDVWSYGVTVWELMTFGSKPYDGIPASEISSVLEKGERLPQPPICTIDVYMIMVKCWMIDADSRPKFRELIAEFSKMARDPPRYLVI (233)
       3. WTYTHQSDVWSYGVTVWELMTFGSKPYDGIPAKEIASVLENGERLPQPPICTIEVYMIILKCWMIDPSSRPRFRELVGEFSQMARDPSRYLVI (188)
       4. RRFTHQSDVWSYGVTVWELMTFGAKPYDGIPAREIPDLLEKGERLPQPPICTIDVYMIMVKCWMIDSECRPRFRELVSEFSRMARDPQRFVVI (266)
       5. GKYTHQSDVWSYGVTVWELMTFGAEPYAGLRLAEVPDLLEKGERLAQPQICTIDVYMVMVKCWMIDENIRPTFKELANEFTRMARDPPRYLVI (364)
       6. RVFTSKSDVWAFGVTIWELLTFGQRPHENIPAKDIPDLIEVGLKLEQPEICSLDIYCTLLSCWHLDAAMRPTFKQLTTVFAEFARDPGRYLAI (252)
       7. GIYSHKTDVWSYGVTLWEIFTFGKRPYEDVDTVDIKDHVIKGGRLTQPDICTLDVYMVLVKCWMEDYESRPTFIELMRTFNTFCKTPGRYLYI (388)
consensus        DVW  GVT WE  TFG  P               G  L QP IC    Y     CW  D   RP F  L   F      P R   I
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Appendix C6(b)

IR

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       1. ( 6) FGMVYEGNARDIIK GEAETRVAVKTVNESASLRERIEFLNEASVMKGFTCHHVVRLLGVVSKGQPTLVVMELMAH
       2. ( 6) FGMVYEGNARDIIK GEAETRVAVKTVNESASLRERIEFLNEASVMKGFTCHHVVRLLGVVSKGQPTLVVMELMAH
       3. ( 0) FGMVYEGIAKDIIK GEPEVHVAVKTVNESASLRERIEFLNEASVMKSFSCHHVVRLIGVVSKGQPTLVIMGLMTH
       4. ( 0) FGMVYEGIAKDIIK GEPEVRVAVKTVNESASLRERIEFLNEASVMKAFNCHHVVRLLGVVSKGQPTLVIMELMAH
       5. ( 6) FGMVYEGVAKGVVK DEPETRVAIKTVNEAASMRERIEFLNEASVMKEFNCHHVVRLLGVVSQGQPTLVIMELMTR
       6. ( 0) FGMVYEGIAKGVVK DEAETKVAIKTVNEAASMRERIEFLNEASVMKEFNCHHVVRLLGVVSQGQPTLVIMELMTR
       7. ( 6) FGMVYEGLARGLEA GEESTPVALKTVNELASPRECIEFLKEASVMKAFKCHHVVRLLGVVSQGQPTLVIMELMTR
       8. ( 6) FGMVYEGILKSFPP NGVDRECAIKTVNENATDRERTNFLSEASVMKEFDTYHVVRLLGVCSRGQPALVVMELMKK
       9. (35) FGEVYEGTAVDILGVGSGEIKVAVKTLKKGSTDQEKIEFLKEAHLMSKFNHPNILKQLGVCLLNEPQYIILELMEG
consensus      FG VYEG               A KT        E   FL EA  M  F         GV     P      LM
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       1. GDLKSYLRSLRP (12) LQEMIQMAAEIADGMAYLNAKKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY (91)
       2. GDLKSYLRSLRP (12) LQEMIQMAAEIADGMAYLNAKKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY (91)
       3. GDLKSYLRSLRP (12) LKEMIQMAAEISDGMAYLNAKKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY ( 0)
       4. GDLKSYLRSLRP (12) LKEIIQMAAEISDGMAYLNAKKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY ( 0)
       5. GDLKSYLRSLRP (12) LSKMIQMAGEIADGMAYLNANKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY (91)
       6. GDLKSYLRSLRP (12) LKKMIQMAGEIADGMAYLNANKFVHRDLAARNCMVA (4) VKIGDFGMTRDIYETDY ( 0)
       7. GDLKSHLRSLRP (12) LGEMIQMAGEIADGMAYLAANKFVHRDLAARNCMVS (4) VKIGDFGMTRDVYETDY (91)
       8. GDLKSYLRAHRP (24) YGRIYQMAIEIADGMAYLAAKKFVHRPFAARNCMVA (4) VKIGDFGMTRDIYETDY (50)
       9. GDLLTYLRKARM ( 9) LVDLVDLCVDISKGCVYLERMHFIHRDLAARNCLVS (9) VKIGDFGLARDIYKNDY (91)
consensus GDL   LR  R                 I  G  YL    F HR  AARNC V      VKIGDFG  RD Y  DY
```

Appendix C7(b)

erk (MAP kinase)

```
       1. (18) FDVGPRYTNLSYIGEGAYGMVCSAYDNVNKVRVAIKKISPFEHQTYCQRTLREIKILLRFRHENIIGINDIIRAPTIEQMKDV
       2. (21) FDVGPRYTNLSYIGEGAYGMVCSAHCNINKVRVAIKKISPFEHQTYCQRTLREIKILLRFKHENIIGINDIIRAPTIEQMKDV
       3. (22) FDVGPRYTQLQYIGEGAYGMVSSAYDHVRKTRVAIKKISPFEHQTYCQRTLREIQILLRFRHENVIGIRDILRASTLEAMRDV
       4. (31) FEVGPRYIKLAYIGEGAYGMVVSADDTLTNQRVAIKKISPFEHQTYCQRTLREITILTRFKHENIIDIRDILRVDSIDQMRDV
       5. (61) FNVSDHYQILEIVGEGAYGIVCSAIHKPSQQKVAIKKIEPFERSMLCLRTLRELKLLKHFNHENIISILAIQRPINYESFNEI
consensus      F V   Y  L   GEGAYG V SA        VAIKKI PFE    C RTLRE   L  F HEN I I  I R
```

```
       1. YIVQDLMETDLYKLLKTQHLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVA
       2. YIVQDLMETDLYKLLKTQHLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLLNTTCDLKICDFGLARVADPDHDHTGFLTEYVA
       3. YIVQDLMETDLYKLLKSQQLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLINTTCDLKICDFGLARIADPEHDHTGFLTEYVA
       4. YIVQCLMETDLYKLLKTQRLSNDHICYFLYQILRGLKYIHSANVLHRDLKPSNLLLNKTCDLKICDFGLARIADPEHDHTGFLTEYVA
       5. YLIQELMETDLHRVIRTQNLSDDHIQYFIYQTLRALKAMHSANVLHRDLKPLNLLLNSNCDLKICDFGLARSIASQEDNYGFMTEYVA
consensus Y  Q LMETDL      Q LS DHI YF YQ LR LK  HSANVLHRDLKP NLL N  CDLKICDFGLAR      D  GF TEYVA
```

```
       1. TRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLNCIINLKARNYLLSLPHKNKVPWNR
       2. TRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLNCIINLKARNYLLSLPHKNKVPWNR
       3. TRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGILGSPSQEDLNCIINMKARNYLQSLPSKTKVAWAK
       4. TRWYRAPEIMLNSKGYTKSIDIWSVGCILAEMLSNRPIFPGKHYLDQLNHILGVLGSPSRDDLECIINEKARNYLESLPFKPNVPWAK
       5. TRWYRAPEIMLTFQEYTTAIDVWSVGCILAEMLSGRPLFPGRDYHNQLWLIMEVLGTPNMEDYYNIKSKRAREYIRSLPFCKKIPFSE
consensus TRWYRAPEIML    YT  ID WSVGCILAEMLS RP FPG  Y  QL  I   LG P   D   I    AR Y  SLP
```

```
       1. LFPNADS ( 1) ALDLLDKMLTFNPHKRIEVEQALAHPYLEQYYDPSDEP (0) IAEAPFKFDMELDDLPKEKLKELIFEE (10)
       2. LFPNADP ( 1) ALDLLDKMLTFNPHKRIEVEAALAHPYLEQYYDPSDEP (0) VAEAPFKFEMELDDLPKETLKELIFEE ( 9)
       3. LFPKSDS ( 1) ALDLLDRMLTFNPNKRITVEEALAHPYLEQYYDPTDEP (0) VAEEPFTFAMELDDLPKERLKELIFQE (12)
       4. LFPNADA ( 1) ALDLLGKMLTFNPHKRIPVEEALAHPYLEQYYDPGDEP (0) VAEVPFRINMENDDISRDALKSLIFEE (13)
       5. LFANTNN (16) ALDLLEKLLIFNPAKRITVEDALKHPYLQLYHDPNDEP (4) IPEDFFDFDKMKDQLTIEDLKKLLYEE ( 5)
consensus LF           ALDLL   L FNP KRI VE AL HPYL  Y DP DEP       E  F      D      LK L   E
```

Appendix C8(b)

ras

```
       1. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       2. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       3. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       4. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       5. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       6. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLCV
       7. (11) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLLV
       8. ( 0) GGVGKSALTIQLIQNHFVDEYDPTIEDSYRQQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLLV
       9. (14) GGVGKSALTIQLIQNHFVEEYDPTIEDSYRKQVVIDGETCLLDILDTAGQEEYSAMRDQYMRTGEGFLLV
      10. (18) GGVGKSALTIQFIQSYFVDEYDPTIEDSYRKQVVIDDKVSILDILDTAGQEEYSAMREQYMRTGEGFLLV
consensus      GGVGKSALTIQ IQ  FV EYDPTIEDSYR QVVID     LDILDTAGQEEYSAMR QYMRTGEGFL V
```

```
       1. FAINNTKSFEDIHHYREQIKRVKDSEDVPMVLVGNKCDLPS RTVDTKQAQDLARSYGIPFIETSAKTRQ( 39)
       2. FAINNTKSFEDVHHYREQINRVKDSDDVPMVLVGNKCDLPS RTVDTKQAQELAKSYGIPFIETSAKTRQ( 36)
       3. FAINNTKSFEDIHHYREQIKRVKDSEDVPMVLVGNKCDLPS RSVDTKQAQDLARSYGIPFIETSAKTRQ( 33)
       4. FAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLAA RTVESRQAQDLARSYGIPYIETSAKTRQ( 39)
       5. FAINNTKSFEDIHQYREQIKRVKDSDDVPMVLVGNKCDLPA RTVETRQAQDLARSYGIPYIETSAKTRQ( 39)
       6. FAINNSKSFADINLYREQIKRVKDSDDVPMVLVGNKCDLPT RTVDTKQAHELAKSYGIPFIETSAKTRQ( 39)
       7. FAVNSAKSFEDIGTYREQIKRVKDAEEVPMVLVGNKCDLAS WNVNNEQAREVAKQYGIPYIETSAKTRM( 39)
       8. FAVNNAKSFEDISAYREQIKRVKDAEEVPMVLVGNKCDLPT RAVDMSQAREVARQYGIPFVETSAKTRM( 39)
       9. FAVNEAKSFENVANYREQIRRVKDSDDVPMVLVGNKCDLSS RSVDFRTVSETAKGYGIPNVDTSAKTRM( 34)
      10. YSVTSRNSFDELLSYYQQIQRVKDSDYIPVVVVGNKLDLENERQVSYEDGLRLAKQLNAPFLETSAKQAI(151)
consensus        SF     Y  QI RVKD    P V VGNK DL     V        A     P   TSAK
```

Appendix C9(b)

rap (K*rev*)

```
       1. (1) REYKLVVLGSGGVGKSALTVQFVQGIFVEKYDPTIEDSYRKQVEVDCQQCMLEILD
       2. (1) REYKLVVLGSGGVGKSALTVQFVQGIFVEKYDPTIEDSYRKQVEVDCQPCMLEILD
       3. (1) REYKLVVLGSGGVGKSALTVQFVQGIFVEKYDPTIEDSYRKQVEVDAQQCMLEILD
       4. (1) REYKIVVLGSGGVGKSALTVQFVQCIFVEKYDPTIEDSYRKQVEVDGQQCMLEILD
       5. (3) REFKIVVLGSGGVGKSALTVQFVQGIFVEKYDPTIEDSYRKQVEVDSNQCMLEILD
consensus     RE K VVLGSGGVGKSALTVQFVQ IFVEKYDPTIEDSYRKQVEVD   CMLEILD
```

```
       1. TAGTEQFTAMRDLYMKNGQGFALVYSITAQSTFNDLQDLREQILRVK DTEDVPMILVGN
       2. TAGTEQFTAMRDLYMKNGQGFALVYSITAQSTFNDLQDLREQILRVK DTEDVPMILVGN
       3. TAGTEQFTAMRDLYMKNGQGFALVYSITAQSTFNDLQDLREQILRVK DTDDVPMILVGN
       4. TAGTEQFTAMRDLYMKNGQGFVLVYSITAQSTFNDLQDLREQILRVK DTDDVPMVLVGN
       5. TAGTEQFTAMRDLYMKNGQGFVLVYSIISNSTFNELPDLREQILRVK DCEDVPMVLVGN
consensus TAGTEQFTAMRDLYMKNGQGF LVYSI   STFN L DLREQILRVK D  DVPM LVGN
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```
       1. KCDLEDERVVGKEQGQNLARQWCNCAFLESSAKSKINVNEIFYDLVRQINRKTP (14)
       2. KCDLEDERVVGKEQGQNLARQWNNCAFLESSAKSKINVNEIFYDLVRQINRKAP (14)
       3. KCDLEDERVVGKEQGQNLARQWNNCAFLESSAKSKINVNEIFYDLVRQINRKTP (14)
       4. KCDLEEERVVGKELGKNLATQF NCAFMETSAKAKVNVNDIFYDLVRQINKKSP (15)
       5. KCDLHDQRVISTEQGEELARKFGDCYFLEASAKNKVNVEQIFYNLIRQINRKNP (14)
consensus KCDL   RV   E G  LA     C F E SAK K NV  IFY L RQIN K P
```

Appendix C10(b)

Gαi

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       1. ( 8) ERSKMIDRNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEAGYSEEECKQYKAVVYSNTIQSIIAIIRAMGRLKIDFGDSARADDARQLFVLAGAAEE GFMTAELAG
       2. (13) ERSKMIDRNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEAGYSEEECKQYKAVVYSNTIQSIIAIIRAMGRLKIDFGDPSRADDARQLFVLAGAAEE GFMTAELAG
       3. (13) ERSKMIDRNLREDGEKAAKEVKLLLLGAGESGKSTIVKQMKIIHEDGYSEDECKQYKVVVYSNTIQSIIAIIRAMGRLKIDFGEAARADDARQLFVLAGSAEE GVMTPELAG
       4. ( 4) ERSKMIDRNLREDGEKASKEVKLLLLGAGESGKSTIVKQMKIIHEDGYSEEECRQYKVVVYSNTIQSIIAIIRAMGRLRIDFGDVARADDARQLFVLASSAEE GVMSPELAG
       5. (13) ERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEDGYSEEECRQYRAVVYSNTIQSIMAIVKAMGNLQIDFADPSRADDARQLFALSCTAEEQGVLPDDLSG
       6. (13) ERSKQIDKSLRMDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEKGYSQEECLQYKPVVYSNAIQSMIAIIKAMGQLKIQFGHPDRAEDARQFFALAGHADE GEMSAELSG
       7. (14) ERSKNIDRALRAEGERAASEVKLLLLGAGESGKSTIVKQMKIIHDTGYSQEECEEYRRVVFSNTVQSLMVIIRAMGRLKIEFADPSRTDIARQFFTHASAADE GILLPEIVL
       8. (13) ERSKAIEKNLKEDGISAAKDVKLLLLGAGESGKSTIVKQMKIIHEDGFSGEDVKQYKPVVYSNTIQSLAAIVRAMDTLGIEYGDKERKADAKMVCDVVSRMEDTEPFSAELLS
       9. (13) RRSRRIDRHLRSESQRQRREIKLLLLGTSNSGKSTIVKQMKIIHSGGFNLEACKEYKPLIIYNAIDSLTRIIRALAALRIDFHNPDRAYDAVQLFALTGPAESKGEITPELLG
      10. (13) KRSKELEKKLQEDADKEAKTVKLLLLGAGESGKSTIVKQMKIIHQDGYSPEECLEFKAIIYGNVLQSILAIIRAMTTLGIDYAEPSCADDGRQLNNLADSIEE GTMPPELVE
consensus       RS      L           KLLLLG   SGKSTIVKQMKIIH  G               N   S   I  A   L I

       1. VIKRLWKDSGVQACFNRSREYQLNDSAAYYLNDLDRIAQPNYIPTQQDVLRTRVKTTGIVETHFTFKDLHFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLVLAEDEEMNRM
       2. VIKRLWKDGGVQACFNRSREYQLNDSAAYYLNDLDRIAQNSYIPTQQDVLRTRVKTTGIVETHFTFKDLHFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLVLAEDEEMNRM
       3. VIKRLWRDGGVQACFSRSREYQLNDSASYYLNDLDRISQSNYIPTQQDVLRTRVKTTGIVETHFTFKDLYFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLVLAEDEEMNRM
       4. VIQRLWEDSGVQACFSRSREYQLNDSASYYLSDIERIAQGSYIPTQQDVLRTRVKTTGIVETHFTFKDLYFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLLLAEDEEMNRM
       5. VIRRLWADHGVQACFGRSREYQLNDSAAYYLNDLERIAQSDYIPTQQDVLRTRVKTTGIVETHFTFKDLHFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSAYDLVLAEDEEMNRM
       6. IMKRLWKDVGVQECFSRSREYQLNDSAEYYLNALDRISAPGYIPTEQDVLRTRVKTTGIVETHFTFKDLHFKMFDVGGQRSERKKWIHCFEGVTAIIFIVAMSEYDLTLAEDQEMNRM
       7. LMKKLWADGGVQQTFARSREYQLNDSAGYYLNSLDRIAQPNYIPTQQDVLRTRVKTTGIIETHFSCKQLHFKLFDVGGQRSERKKWIHCFEGVTAIIFCVALSGYDLVLAEDEEMNRM
       8. AMMRLWGDSGIQECFNRSREYQLNDSAKYYLDSLDRIGAADYQPTEQDILRTRVKTTGIVETHFTFKNLHFRLFDVGGQRSERKKWIHCFEDVTAIIFCVALSGYDQVLHEDETTNRM
       9. VMRRLWADPGAQACFSRSSEYHLEDNAAYYLNDLERIAAADYIPTVEDILRSRDMTTGIVENKFTFKELTFKMVDVGGQRSERKKWIHCFEGVTAIIFCVELSGYDLKLYEDNQTSRM
      10. VIRRLWKDGGVQACFERAAEYQLNDSASYYLNQLERITDPEYLPSEQDVLRSRVKTTGIIETKFSVKDLNFRMFDVGGQRSERKKWIHCFEGVTCIIFCAALSAYDMVLVEDDEVNRM
consensus     LW D G Q  F R  EY L D A YYL    RI    Y P   D LR R  TTGI E  F  K L F   DVGGQRSERKKWIHCFE VT IIF    S YD  L ED    RM

       1. HESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKIKKSPLTICYPEYAGSNTYEEAAAYIQCQFEDLNKRKD (1) KEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKDCGLF (0)
       2. HESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKIKRSPLTICYPEYPGSNTYEEAAAYIQCQFEDLNKRKD (1) KEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKDCGLF (0)
       3. HESMKLFDSICNNKWFTETSIILFLNKKDLFEEKIKRSPLTICYPEYTGSNTYEEAAAYIQCQFEDLNRRKD (1) KEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKECGLY (0)
       4. HESMKLFDSICNNKWFIDTSIILFLNKKDLFEEKISRSPLTICYPEYSGSNTYEEAAAYIQCQFEDLNRRKD (1) KEIYTHFTCATDTKNVQFVFDAVTDVIIKSNLMECGLY (0)
       5. HESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKITHSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKD (1) KEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKDCGLF (0)
       6. MESMKLFDSICNNKWFTETSIILFLNKKDLFEEKIKKSPLTICFPEYTGANTYEEAAAYIQLQFENLNKKKD (1) KEIYSHFTCATDTNNVQFVFDAVTDVIIKNNLKDCGLF (0)
       7. IESLKLFDSICNSKWFVETSIILFLNKKDLFEEKIKRSPLTICFPEYTGTNTFEEAANYIRMKFENLNKRKD (1) KEIYTHLTCATDTNNVKFVFDAVTDVIIKNNLKQIGLF (0)
       8. HESLKLFDSICNNKWFTDTSIILFLNKKDIFEEKIKKSPLTICFPEYTGPSAFTEAVAYIQAQYESKNKSAH (0) KEIYSHVTCATDTNNIQFVFDAVTDVIIAKNLRGCGLY (0)
       9. AESLRLFDSICNNNWFINTSLILFLNKKDLLAEKIRRIPLTICFPEYKGQNTYEEAAVYIQRQFEDLNRNKE (1) KEIYSHFTCATDTSNIQFVFDAVTDVIIQNNLKYIGLC (0)
      10. HESLHLFNSICNHKFFAATSIVLFLNKKDLFEEKIKKVHLSICFPEYDGNNSYDDAGNYIKSQFLDLNMRKD (1) KEIYSHMTCATDTQNVKFVFDAVTDIIIKENLKDCGLF (0)
consensus  ES  LF SICN   F  TS  LFLNKKD   EKI    L IC PEY G      A  YI       N         KEIY H TCATDT N  FVFDAVTD II  NL   GL
```

Appendix C11(b)

Gαs

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       1. (25) IEKQLQKDKQVYRATHRLLLLGAGESGKSTIVKQMRILHVNGFNGE (15) EKATKVQDIKNNLKEAIE
       2. (25) IEKQLQKDKQVYRATHRLLLLGAGESGKSSIVKQMRILHVNGFNAE ( 0) EKKTKVQDIKNNIKEAIE
       3. (27) IEKQLQKERLAYKATHRLLLLGAGESGKSTIVKQMRILHVNGFNPE ( 0) EKKQKILDIRKNVKDAIV
       4. (28) ISRQLQKDKQLYRATHRLLLLGAGESGKSTIVKQMRILHVDGFSDS ( 0) EKKQKIDDIKKNIRDAIL
       5. (22) IEKQLAKDKLLYRGTHRLLLLGAGESGKSTIVKQMRILHVNGFSPE ( 0) ERKQKIEDIKRNVRDAIL
       6. (24) IEKLIEKEKKNFKSTHRLLLLGAGESGKSTIVKQMRILHIDGFSER ( 0) EKKEKIDAIRKNLRDAIC
consensus      I     K       THRLLLLGAGESGKS IVKQMRILH  GF         E   K   I  N   AI

       1. TIVAAMSNLVPPVELANPENQFRVDYILSVMNVPDFDFPPEFYEHAKALWEDEGVRACYERSNEYQLIDCAQYFL
       2. TIVTAMGNLSPPVELVNPENQFRIDYILNLPNYKDFEFSPEFYEHTKTLWQDEGVRACYERSNEYQLIDCAQYFL
       3. TIISAMSTIIPPVPLANPENQFRSDYIKSIAPITDFEYSQEFFDHVKKLWDDEGVKACFERSNEYQLIDCAQYFL
       4. TITGAMSTLNPPVALEKKENEPRVEYIQDYASSPDFNYPPEFYEHTEELWKDKGVLQTYERSNEYQLIDCAKYFL
       5. TITGAMSTLNPPVQLEHPQNKAKVDYIQDKASQAEFDYPPIFYEYTEILWKDKGVQAAFERSNEYQLIDCAQYFL
       6. SIAGAMGSLKPPVKLELSENRKLRDYILETASKPDFDYPPEFFTYCAKLWKDGGIQETFERSNEYQLIDCAKYFL
consensus  I  AM    PPV L    N     YI        F     F      LW D G     ERSNEYQLIDCA YFL

       1. DKIDVIKQADYVPSDQDLLRCRVLTSGIFETKFQVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIFVVASSSYN
       2. DKIDIVKQNDYTPSDQDLLRCRVLTSGIFETKFQVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIFVVASSSYN
       3. ERIDSVSLVDYTPTDQDLLRCRVLTSGIFETRFQVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIYVAACSSYN
       4. DRVSTIKNPNYTPNEQDILRCRVLTSGIFETRFQVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIFVTACSSYN
       5. DRVHIIRQAEYTPSEQDILRCRVLTSGIFETKFSVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIFVTACSGYN
       6. DKALEVGAPNYIPSEQDILRCRVLTSGIFETKFSVDKVNFHMFDVGGQREERRKWIQCFNDVTAIIFVAACSSYN
consensus           Y P  QD LRCRVLTSGIFET F VDKVNFHMFDVGGQR ERRKWIQCFNDVTAII V A S YN

       1. MVIREDNQTNRLQEALNLFKSIWNNRWLRTISVILFLNKQDLLAEKVLAGKSKIEDYFPEFARYTTP (0) EDA
       2. MVIREDNHTNRLQEALNLFKSIWNNRWLRTISVILFLNKQDLLAEKVNAGKSKIEDYFPEFARYTTP (0) DDA
       3. MVIREDNNTNRLRESLDLFESIWNNRWLRTISIILFLNKQDMLAEKVLAGKSKIEDYFPEYANYTVP (0) EDA
       4. MVLREDPTQNRLRESLDLFKSIWNNRWLRTISIILFLNKQDLLAEKIKAGKSKLSEYFSEFNKYQTP (3) GDA
       5. MVLREDATQNRLKESLDLFKSIWNNRWLRTISVILFLNKQDLLAEKVKAGKSKIEDYFPEYARYQVP (0) PDA
       6. MVLREDPSQNRVKESLELLASIWNNRWLRNISVILFLNKQDLLTEKVLAGKSKIEVYFPHYATYQAP (0) ADT
consensus MV RED   NR  E L L  SIWNNRWLR IS ILFLNKQD L EK  AGKSK   YF     Y  P       D

       1. TPE PGEDPRVTRAKYFIRDEFLRISTASGDGRHYCYPHFTCAVDTENIRRVFNDCRDIIQRMHLRQYELL (0)
       2. TPE VGEDPRVTRAKYFIRDEFLRISTASGDGRHYCYPHFTCAVDTENIRRVFNDCRDIIQRMHLRQYELL (0)
       3. TPD AGEDPKVTRAKFFIRDLFLRISTATGDGKHYCYPHFTCAVDTENIRRVFNDCRDIIQRMHLKQYELL (0)
       4. IME SNDDPEVIRAKYFIRDEFLRISTASGDGKHYCYPHFTCAVDTENIKRVFNDCRDIIQRMHLRQYELL (0)
       5. SSE PGEDTEVVRAKYFIRDEFLRISTASGDGRHYCYPHFTCAVDTENIRRVFDDCRDIIQRMHLRQYELL (0)
       6. LAEYRHENSEVVRARFFFRDEFLKVTSNNNGGRHYCYPHLTCAVDTENIRRVFNDCRDIIQRMHLRQYELL (0)
consensus           V RA  F RD FL        G HYCYPH TCAVDTENI RVF DCRDIIQRMHL QYELL
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Appendix C12(b)

K^+ channel

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       1. ( 33) RVVINISGLRFETQLKTLAQFPETLLGDP (10) RNEYFFDRNRPSFDAILYYYQSGGRLRRPVNVPLDIFSEEIRFYELGE ( 5) FREDEGY ( 7) LPENEFQRQ
       2. ( 33) RVVINISGLRFETQLKTLSQFPETLLGDP (10) RNEYFFDRNRPSFDAILYFYQSGGRLRRPVNVPLDIFSEEIRFYELGE ( 5) FREDEGF ( 7) LPDNEFQKQ
       3. ( 37) RVVINISGLRFETQLKTLAQFPNTLLGNP (10) RNEYFFDRNRPSFDAILYYYQSGGRLRRPVNVPLDMFSEEIKFYELGE ( 5) FREDEGF ( 7) LPEKEYQRQ
       4. ( 52) RVVINISGLRFETQLKTLCQFPETLLGDP (10) RNEYFFDRNRPSFDAILYYYQSGGRIRRPVNVPIDIFSEEIRFYQLGE ( 5) FREDEGF ( 7) LPRRDFQRQ
       5. (176) RVVINVSGLRFETQMKTLAQFPETLLGDP (10) RNEYFFDRNRPSFDAILYYYQSGGRLKRPVNVPFDIFTEEVKFYQLGE ( 5) FREDEGF ( 8) LPENEFKKQ
       6. ( 41) RLVINISGLRFETQLRTLSLFPDTLLGDP (10) RNEYFFDRNRPSFDAILYYYQSGGRLRRPVNVPLDIFLEEIRFYQLGD ( 5) FREDEGC (10) LPSQPFQRQ
       7. (120) RVHINISGLRFETQLGTQAQFPNTLLGDP (10) RNEYFFDRNRPSFDGILYYYQSGGRLRRPVNVSLDVFADEIRFYQLGD ( 5) FGEDEGF ( 7) LVRNEFQRQ
       8. ( 97) RVVINVSGLRFETQLRTLNQFPDTLLGDP (10) RNEYFFDRSRPSFDAILYYYQSGGRLRRPVNVPLDVFSEEIKFYELGD ( 5) FREDEGF ( 7) LPDNEKQRK
       9. ( 85) RVVINVSGLRFETQLRTLNQFPDTLLGDP (10) RNEYFFDRSRPSFDAILYYYQSGGRLRRPVNVPLDVFSEEIKFYELGD ( 5) FREDEGF ( 7) LPDNEKQRK
      10. ( 66) RVVINVSGLRFETQLKTLNQFPDTLLGNP (10) RNEYFFDRNRPSFDAILYFYQSGGRLRRPVNVPLDVFSEEIKFYELGE ( 5) YREDEGF ( 7) LPQNEFQRR
      11. ( 27) RVRLNVGGLAHEVLWRTLDRLPRTRLGKL (19) DNEYFFDRHPGAFTSILNFYRTG RLHMMEEMCALSFSQELDYWGIDE (22) KREAETL (10) TCCAEKRKK
consensus       R   N  GL  E    T    P T LG        NEYFFDR    F  IL  Y  G R           F  E                E E
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       1. VWLLFEYPESSGPARIIAIVSVMVILISIVSFCLETLPIF (36) VETLCIIWFSFEFLVRFFACPSKAGFFTNIMNIIDIVAIIPYFITL (21) ILRVIRLVRVFRIFKLSRH
       2. VWLLFEYPESSGPARIIAIISVTVILISIVSFCLETLPVF (36) VETLCMIWFSFEFLVLVLACPSKAVFFTNLMNIIDIVAIIPYFITL (21) ILRVIRLVRVFRIFKLSRH
       3. VWLLFEYPESSGPARVIAIVSVMVILISIVIFCLETLPEL (31) VETLCIIWFSFELVVRFFACPSKTDFFKNIMNFIDIVAIIPYFITL (20) ILRVIRLVRVFRIFKLSRH
       4. VWLLFEYPESSGPARGIAIVSVLVILISIVIFCLETLPEF (38) VETLCIIWFSFELLVRFFACPSKATFSRNIMNLIDIVAIIPYFITL (18) ILRVIRLVRVFRIFKLSRH
       5. IWLLFEYPESSDPARGIAIVSVLVILISIVIFCLETLPEF (41) VETVCIVWFSFEFVVRCFACPSQALFFKNIMNIIDIVSILPYFITL (22) ILRIIRLVRVFRIFKLSRH
       6. VWLLFEYPESSGPARGIAIVSVLVILISIVIFCLETLPQF (66) VETLCIVWFTFELLVRFSACPSKPAFFRNIMNIIDLVAIFPYFITL (28) ILRVIRLVRVFRIFKLSRH
       7. VWLIFEYPESSGSARAIAIVSVLVILISIITFCLETLPEF (51) VETTCVIWFTFELLVRFFACPSKAGFSRNIMNIIDVVAIFPYFITL (25) ILRVIRLVRVFRIFKLSRH
       8. VWLLFEYPESSQAARVVAIISVFVILLSIVIFCLETLPEF (29) IETLCIIWFTFELTVRFLACPNKLNFCRDVMNVIDIIAIIPYFITL (32) ILRVIRLVRVFRIFKLSRH
       9. VWLLFEYPESSQAARVVAIISVFVILLSIVIFCLETLPEF (29) IETLCIIWFTFELTVRFLACPNKLNFCRDVMNVIDIIAIIPYFITL (32) ILRVIRLVRVFRIFKLSRH
      10. VWLLFEYPESSAAARLCAIFSVVIILLSIVIFCLETLPQF (31) IETCCIIWFTFELLVRFASCPEKLGFFKNIMNCIDIVAIIPYFITL (18) ILRVIRLVRVFRIFKLSRH
      11. LWDLLEKPNSSVAAKILAIISIMFIVLSTIALSLNTLPEL (17) VEAVCIAWFTMEYLLRFLSSPKKWKFFKGPLNAIDLLAILPYYVTI (17) VVQIFRIMRILRILKLARH
consensus  W   E P SS  A   AI S   I  S     L TLP         E  C  WF  E        P    F     N ID   I PY  T           R  R  RI KL RH
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       1. SKGLQILGQTLKASMRELGLLIFFLFIGVILFSSAVYFAEADERDSQFPSIPDAFWWAVVSMTTVGYGDMVPTTIGGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 79)
       2. SKGLQILGQTLNASMRELGLLIFFLFIGVILFSSAVFFAEADERDSQFPSIPDAFWWAVVSMTTVGYGDMVPTTIGGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 79)
       3. SKGLQILGQTLKASMRELGLLIFFLFIGVILFSSAVYFAEAEEAESHFSSIPDAFWWAVVSMTTVGYGDMYPVTIGGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 77)
       4. SKGLQILGQSLKASMRELGLLIFFLFIGVILFSSAVYFAEADDPTSGFSSIPDAFWWAVVTMTTVGYGDMHPVTIGGKIVGSLCAIAGVLSIALPVPVIVSNFNYFYHRE ( 85)
       5. SKGLQILGHTLRASMRELGLLIFFLFIGVILFSSAVYFAEADEPTTHFQSIPDAFWWAVVTMTTVGYGDMKPITVGGKIVGVLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 83)
       6. SKGLQILGKTLQASMRELGLLIFFLFIGVILFSSAVYFAEADDDDSLFPSIPDAFWWAVVTMTTVGYGDMYPMTVGGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 61)
       7. SKGLQILGKTLQASMRELGLLIFFLFIGVILFSSAVYFAEADNQGTHFSSIPDAFWWAVVTMTTVGYGDMRPITVGGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 87)
       8. SKGLQILGRTLKASMRELGLLIFFLFIGVVLFSSAVYFAEAGSENSFFKSIPDAFWWAVVTMTTVGYGDMTPVGFWGKIVGSLCVVAGVLTIALPVPVIVSNFNYFYHRE (128)
       9. SKGLQILGRTLKASMRELGLLIFFLFIGVVLFSSAVYFAEAGSENSFFKSIPDAFWWAVVTMTTVGYGDMTPVGVWGKIVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE (167)
      10. SKGLQILGQTLKASMRELGLLIFFLFIGVILFSSAVYFAEADADQTHFKSIPDAFWWAVVTMTTVGYGDMRPIGVWGKLVGSLCAIAGVLTIALPVPVIVSNFNYFYHRE ( 70)
      11. STGLQSLGFTLRRSYNELGLLILFLAMGIMIFSSLVFFAEKDEDDTKFKSIPASFWWATITMTTVGYGDIYPKTLLGKIVGGLCCIAGVLVIALPIPIIVNNFSEFYKEQ (434)
consensus S GLQ LG  L  S  ELGLLI FL  G   FSS V FAE       F SIP  FWWA   MTTVGYGD  P    GK VG LC  AGVL IALP P IV NF  FY
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Appendix C13(b)

Na^+ channel (1)

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       1. ( 96) KAIFRFSATSALYILTPFNPLRKIAIKILVHSLFSMLIMCTILTNCVFMTM ( 7) KNVEYTFTGIYTFESLIKIIARGFCLEDFTFLRDPWNWLDFT
       2. ( 97) KAISRFSATSALYILTPFNPIRKLAIKILVHSLFNVLIMCTILTNCVFMTM ( 7) KNVEYTFTGIYTFESLIKILARGFCLEDFTFLRNPWNWLDFT
       3. ( 96) KAIFRFSATSALYILTPLNPVRKIAIKILVHSLFSMLIMCTILTNCVFMTL ( 7) KNVEYTFTGIYTFESLIKILARGFCLEDFTFLRDPWNWLDFS
       4. ( 99) KAIFRFSATPALYLLSPFSVVRRGAIKVLIHALFSMFIMITILTNCVFMTM ( 7) KNVEYTFTGIYTFESLIKILARGFCVDDFTFLRDPWNWLDFS
       5. ( 99) KTIFRFSATNALYVLSPFHPVRRAAVKILVHSLFNMLIMCTILTNCVFMAQ ( 7) KYVEYTFTAIYTFESLVKILARAFCLHAFTFLRDPWNWLDFS
       6. ( 90) NIINRFNAERALYIFSPFNPIRRGAIRVFVNSAFNFFIMFTIFSNCIFMTI ( 7) KIVEYTFTGIYTFEVIVKVLSRGFCIGHFTFLRDPWNWLDFS
       7. ( 86) RTIFRFNAASILCTLSPFNCIRRTTIKVLVHPFFQLFILISVLIDCVFMSL ( 7) PVLENTLLGIYTFEILVKLFARGVWAGSFSFLGDPWNWLDFS
       8. (121) KDIFRFSASKAMWMLDPFNPIRRVAIYILVHPLFSLFIITTILVNCILMIM ( 6) ESTEVIFTGIYTFESAVKVMARGFILCPFTYLRDAWNWLDFV
       9. ( 23) NIIHRFSAKRSLFLFTPRNPIRRLAVCIATNVCFDYFLMFTIMINCVFLAM ( 4) EFAEYIFLGIYTMEMAIKLVAGGFFIDKYTYLRDAWNCLDFT
      10. ( 90) NYIHRFTGTKSLFLFYPWSPARRVCVYIATNQFFDYCVMATILFNCIFLAM ( 4) EEAEYIFLAIYSIEMVIKIIAKGFLLNKYTYLRNPWNWLDFV
      11. ( 63) VKQNCFTVNRSLFVFSEDNVVRKYAKRITEWPPFEYMILATIIANCIVLAL (16) DDTEPYFIGIFCFEAGIKIIALGFVFHKGSYLRNGWNVMDFV
consensus            F               R           F           C              E     I   E   K             L   WN  DF
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       1. VITFAYV ( 7) NVSALRTFRVLRALKTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCVQ (56) CGNSSDAGQCPEGYMCV
       2. VITFAYV ( 7) NVSALRTFRVLRALKTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCLQ (57) CGNSSDAGQCPEGYICV
       3. VIVMAYV ( 7) NVSALRTFRVLRALKTISVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALIGLQLFMGNLRNKCSQ (57) CGNGSDAGQCPEGYICV
       4. VIMMAYL ( 7) NISALRTFRVLRALKTITVIPGLKTIVGALIQSVKKLSDVMILTVFCLSVFALVGLQLFMGNLRQKCVR (77) CGNSSDAGHCPKGYECI
       5. VIIMAYT ( 7) NVSALRTFRVLRALKTISVISGLKTIVGALIQSVKKLADVMVLTVFCLSVFALIGLQLFMGNLRHKCVR (43) CGNSSDAGTCPEGYRCL
       6. VVTMTYI ( 7) NVSALRTFRVLRALKTITIFPGLKTIVRALIESMKQMGDVVILTVFSLAVFTLAGMQLFMGNLRHKCIR (41) CGNNSDAGKCPEGYTCM
       7. VTVFEVI ( 7) FIPTLQTARTLRILKIIPLNQGLKSLVGVLIHCLKQLIGVIILTLFFLSIFSLIGMGLFMGNLKHKCFR (37) CGNRTDAGQCPEGYVCV
       8. VIALAYV ( 7) NLAALRTFRVLRALKTVAIVPGLKTIVGAVIESVKNLRDVIILTMFSLSVFALMGLQIYMGVLTEKCIK (37) CGNISGAGQCDDDYVCL
       9. VIMISYI (13) DITGLRTFRVLRALRTLSIIPGLKTMVNALLRALRMLISVLILILFCLWIFSQAGVQLFGGALRHKCVL (36) CGNATGAGPCPTNYTCL
      10. VITMRYA ( 7) NLAGLRTFRVLRALKTVSIMPGLKTIIRPLLHSVAQLAEVMTLTIFCVMVFALFALQVYMGELRNKCVR (34) CGNLTGARHCPFEYVCL
      11. VVLTGIL ( 7) DLRTLRAVRVLRPLKLVSGIPSLQVVLKSIMKAMVPLLQIGLLLFFAILMFAIIGLEFYMGKFHKACFP (12) CGKEAPARLCEGDTECR
consensus V                L   R LR L        L                   L  F    F         G     C        CG    A  C     C
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       1. KA GRNPNYGYTSFDTFSWAFLSLFRLMTQDFWEN LYQLTLRAAGKTYMIFFVLVIFLGSFYLINLILAVVAMAYEEQNQ (346) IVLNTLFMAMEHYPMTE
       2. KA GRNPNYGYTSFDTFSWAFLSLFRLMTQDFWEN LYQLTLRAAGKTYMIFFVLVIFLGSFYLINLILAVVAMAYEEQNQ (335) IVLNTLFMAMEHYPMTE
       3. KA GRNPNYGYTSFDTFSWAFLSLFRLMTQDYWEN LYQLTLRAAGKTYMIFFVLVIFLGSFYLVNLILAVVAMAYEEQNQ (288) IVLNTLFMAMEHYPMTQ
       4. KT GRNPNYGYTSYDTFSWAFLALFRLMTQDYWEN LFQLTLRAAGKTYMIFFVVIIFLGSFYLINLILAVVAMAYAEQNE (132) IVLNTLFMAMEHYPMTE
       5. KA GENPDHGYTSFDSFAWAFLALFRLMTQDCWER LYQQTLRSAGKIYMIFFMLVIFLGSFYLVNLILAVVAMAYEEQNQ (305) IVLNTLFMALEHYNMTS
       6. KA GRNPNYGYTNYDNFAWTFLCLFRLMLQDYWEN LYQMTLRAAGKSYMVFFIMVIFLGSFYLINLILAVVAMAYEEQNQ (165) IILNTLFMSIEHHPMNE
       7. KA GINPDQGFTNFDSFGWALFALFRLMAQDYPEV LYHLILYASGKVYMIFFVVVSFLFSFYMASLFLGILAMAYEEEKQ (112) IILNVCFLTLEHYPMSK
       8. QGFGPNPNYGYTSFDSFGWAFLSAFRLMTQDFWED LYQLVLRAAGPWHMLFFIVIIFLGSFYLVNLILAIVAMSYDELQR (369) IVVNTMFMAMDHHDMNK
       9. PDIGENPNYGYTNFDSIGWSMLISFQLLTQDYWED VYNKVIRAHSPWTVIYFIVINFFGSLYLMNLMLAVVATAYELEVK ( 78) IVLNTVFLAMEHHGMSM
      10. CV GENPNHGYTNFDNFMWSMLTTFQLITLDYWEN VYNMVLATCGPMSVSFFTVVVFFGSFYLINLMLAVVALSYEEEAE (175) IVLNTAFLAMEHHGMSE
      11. EY WPGPNFGITNFDNILFAILTVFQCITMEGWTDILYNTNDAAGNTWNWLYFIPLIIIGSFFMLNLVLGVLSGEFAKERE (127) VALNTLCVAMVHYNQPR
consensus       P  G T  D         F                           F       S     L L                       N       H
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       1. HFNHVLTVGNLVFTGIFTAEMFLKIIAMDPYYYFQEGWNIFDGFIVTLSLVELGLANVE     GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLT
       2. QFSSVLSVGNLVFTGIFTAEMFLKIIAMDPYYYFQEGWNIFDGFIVSLSLMELGLANVE     GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLT
       3. QFSSVLTVGNLVFTGIFTAEMVLKIIAMDPYYYFQEGWNIFDGIIVSLSLMELGLANVE     GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLT
       4. HFDNVLTVGNLVFTGIFTAEMVLKLIAMDPYEYFQQGWNIFDSIIVTLSLVELGLANVQ     GLSVLRSFRLLRVFKLAKSWPTLNMLIKIIGNSVGALGNLT
       5. EFEEMLQVGNLVFTGIFTAEMTFKIIALDPYYYFQQGWNIFDSIIVILSLMELGLSRMS     NLSVLRSFRLLRVFKLAKSWPTLNTLIKIIGNSVGALGNLT
       6. SFQSLLSAGNLVFTTIFAAEMVLKIIALDPYYYFQQTWNIFDSIIVSLSLLELGLSNMQ     GMSVLRSLRLLRIFKLAKSWPTLNILIKIICNSVGALGNLT
       7. QTNTLLNIGNLVFIGIFTAEMIFKIIAMHPYGYFQVGWNIFDSMIVFHGLIELCLANVA     GMALLRLFRMLRIFKLGKYWPTFQILMWSLSNSWVALKDLV
       8. EMERVLKSGNYFFTATFAIEATMKLMAMSPKYYFQEGWNIFDFIIVALSLLELGLEGVQ     GLSVLRSFRLLRVFKLAKSWPTLNLLISIMGRTMGALGNLT
       9. ELKNVLKVANYVFTTVFVLEAILKLLAFN KQYFKSGWNICDLVVVVASLIDLGVEGLK     GVSVFRSFRLLRVFHLAQSWTTMRLLLCIILNTLGSLGYLT
      10. SFRNALDVGNKVFTSIFTFECIVKLMALS KDFFLCGWNIFDLLIVTASLLDIIFELVD     GLSVLRGLRLLRALKLAKSWTTMKVLLSIIISTIGALGNLR
      11. RLTTTLYFAEFVFLGLFLTEMSLKMYGLGPRSYFRSSFNCFDFGVIVGSVFEVVWAAIKPGSSFGISVLRALRLLRIFKVTKYWSSLRNLVVSLLNSMKSIISLL
consensus      L      F   F  E   K         F    N  D                           R  R LR       W     L             L
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       1. LVLAIIVFIFAVVGMQLFGKSYK (11) LPRWHMNDFFHSFLIVFRVLCGE WIETMWDCME ( 9) VFMMVMVIRNLVVLNLFLALLLSSFS ADNLAATDD
       2. LVLAIIVFIFAVVGMQLFGKSYK (11) LPRWHMHHFFHSFLIVFRVLCGE WIETMWDCME ( 9) VFMMVMVIGNLVVLNLFLALLLSSFS SDNLAATDD
       3. LVLAIIVFIFAVVGMQLFGKSYK (11) LPRWHMNDFFHSFLIVFRVLCGE WIETMWDCME ( 9) VFMLVMVIGNLVVLNLFLALLLSSFS SDNLAATDD
       4. LVLAIIVFIFAVVGMQLFGKSYK (11) LPRWHMHDFFHSFLIVFRILCGE WIETMWDCME ( 9) VFLMVMVIGNLVVLNLFLALLLSSFS ADSLAASDE
       5. LVLAIIVFIFAVVGMQLFGKNYS ( 9) LPRWHMMDFFHAFLIIFRILCGE WIETMWDCME ( 9) VFLLVMVIGNLVVLNLFLALLLSSFS ADNLTAPDE
       6. IVLAIIVFIFALVGFQLFGKNYK (11) LPRWHMNDFFHSFLIVFRALCGE WIETMWDCME ( 9) VYMMVIIIGNLVMLNLFLALLLSSFS SDNLSSIEE
       7. LLLFTFIFFSAAFGMKLFGKNYE (11) LPRWHMHDFFHSFLNVFRILCGE WVETLWDCME ( 9) FYLMVILIGNLLVLYLFLALV SSFS SCKDVTAEE
       8. FVLCIIIFIFAVMGMQLFGKNYH (10) LPRWNFTDFMHSFMIVFRVLCGE WIESMWDCMY ( 8) FFLATVVIGNLVVLNLFLALLLSNFG SSSLSAPTA
       9. IILIIVIYIFAVTGLQLFHTEYT ( 8) VPRWNFNDFLHSFMMVFRILCGE WIEPMYDCMR ( 8) IFIPVTVFGKTLFF LFIGLVLGAFG SDTVEQEVE
      10. LILVIVIYIFAVIGMQLFSKDYT (18) LNRWNFNDFFHSFMMIFRILCGE WIEPLWDCNA (12) IFLPTLVMGNFMVLNLFLALLLNSFN SEELKSKKE
      11. FLLFLFIVVFALLGMQLFGGQFN ( 4) TPTTNFDTFPAAILTVFQILTGEDWNAVMYHGIE (13) YFIVLTLFGNYTLLNVFLAIAVDNLANAQELTKDEE
consensus   L       A  G  LF            F       F  L GE W               F
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Appendix C14(b)

Na$^+$ channel (2)

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 1. D (201) RRTCFRIVEHNWFETFIVFMILLSSGALAFEDIYIDQRKTIKTMLEYADKVFTYIFILEMLLKWVAYG YQ   TYFTNAWCWLDFLIVDVSLVSLT
 2. D (200) RKTCYKIVEHNWFETFIVFMILLSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLKWVAYG FQ   MYFTNAWCWLDFLIVDVSLVSLT
 3. D (197) RKTCYSIVEHNWFETFIVFMILLSSGALAFEDIYIEQRKTIKTMLEYADKVFTYIFILEMLLKWVAYG FQ   TYFTNAWCWLDFLIVDVSLVSLV
 4. D (204) RRACFKIVEHNWFETFIVFMILLSSGALAFEDIYIEQRRVIRTILEYADKVFTYIFIMEMLLKWVAYG FK   VYFTNAWCWLDFLIVDVSIISLV
 5. D (241) RKTCYHIVEHSWFETFIIFMILLSSGALAFEDIYLEERKTIKVLLEYADKMFTYVFVLEMLLKWVAYG FK   KYFTNAWCWLDFLIVDVSLVSLV
 6. D (185) RRTCYTIVEHDYFETFIIFMILLSSGVLAFEDIYIWRRRVIKVILEYADKVFTYVFIVEMLLKWVAYG FK   RYFTDAWCWLDFVIVGASIMGIT
 7. N (181) RKTCCKIVENNWFKCFIGLVTLLSTGTLAFEDIYIDQRKTIKILLEYADMIFTYIFILEMLLKWMAYG FK   AYFSNGWYRLDFVVVIVFCLSLI
 8. D (213) RLKTFRLIEDKYFETAVITMILMSSLALALEDVHLPQRPILQDILYYMDRIFTVIFFLEMLIKWLALG FK   VYLTNAWCWLDFVIVMVSLINFV
 9. V (128) RRQLMMVCENKYFETGVLVIIFASSILLAFEDIYLNEKPRLKLAIFYLDITFCLLFFLEMVLKLVALG FV   HYYTHFWTILDFTIVIITVISLA
10. A (177) RTAVLTVVDTPAFEWFVLVLIFASSITLCFEDINLDKNKTLKRVLYWINFSFCLIFVVEMILKWLALG FS   KYFTSFWTILDFIIVFVSVFSLL
11. E (415) RRFCHYIVTMRYFEVVILVVIALSSIALAAEDP VRTDSPRNNALKYLDYIFTGVFTFEMVIKMIDLGLLLHPGAYFRDLWNILDFIVVSGALVAFA
consensus   R           F          S   L  ED                   F   F  EM  K    G       Y    W  LDF  V

 1. A (11) KSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYH CVNTT (26) RWKNVKVNFDNVGFGYLSLLQVA
 2. A (11) KSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYH CINYT (26) RWKNVKVNFDNVGLGYLSLLQVA
 3. A (11) KSLRTLRALRPLRALSRFEGMRVVVNALVGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYH CVNTT (23) RWKNVKVNFDNVGAGYLALLQVA
 4. A (11) KSLRTLRALRPLRALSRFEGMRVVVNALLGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFYY CINTT (25) RWLNVKVNYDNVGLGYLSLLQVA
 5. A (11) KSLRTLRALRPLRALSRFEGMRVVVNALVGAIPSIMNVLLVCLIFWLIFSIMGVNLFAGKFGR CINQT (26) YWTKVKVNFDNVGAGYLALLQVA
 6. S (11) KNLRTIRALRPLRALSRFEGMKVVVRALLGAIPSIMNVLLVCLMFWLIFSIMGVNLFAGKFYR CINTT (25) RWVNLKVNYDNAGMGYLSLLQVS
 7. G ( 6) KPLISMKFLRPLRVLSQFERMKVVVRALIKTTLPTLNVFLVCLMIWLIFSIMGVDLFAGRFYE CIDPT (25) LWENAKMNFDNVGNGFLSLLQVA
 8. A (11) KTMRTLRALRPLRAMSRMQGMRVVVNALVQAIPSIFNVLLVCLIFWLIFAIMGVQLFAGKYFK CEDMN (20) TWVNSAMNFDHVGNAYLCLFQVA
 9. A (11) RSLRTLRALRPLRAVSRWQGMKIIVNALMLSIPSIFNVLLVCVVFWLIFAIMGVQLFAGKFYK CVNET (20) TWVNSNVNFDNVGGAFLALFQVA
10. I ( 9) RSLRTLRALRPLRAISRWQGMRIVVNALMYAIPSIFNVLLVCLVFWLIFSIMGVQFFGGKFLSALINII (19) TWINSKITFDHVGMGYLALLQVA
11. F (11) KSLRVLRVLRPLKTIKRLPKLKAVFDCVVNSLKNVLNILIVYMLFMFIFAVIAVQLFKGKFFY CTDES (24) QWKKYDFHYDNVLWALLTLFTVS
consensus          LRPL                        N   V      IF    V  F G                 W       D      L L  V

       1. TFKGWMDIMYAAVDSRNVELQPKYEESLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKK (37) FQGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQ
       2. TFKGWMDIMYAAVDSRNVELQPKYEDNLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKK (37) FQGMVFDFVTKQVFDISIMILICLNMVTMMVETDDQ
       3. TFKGWMDIMYAAVDSRDVKLQPIYEENLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKK (37) FQGMVFDFVTRQVFDISIMILICLNMVTMMVETDDQ
       4. TFKGWMDIMYAAVDSREKEEQPQYEVNLYMYLYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKK (37) IQGMVYDLVTKQAFDITIMILICLNMVTMMVETDDQ
       5. TFKGWMDIMYAAVDSRGYEEQPQWEYNLYMYIYFVIFIIFGSFFTLNLFIGVIIDNFNQQKKK (37) YQGFIFDIVTKQAFDVTIMFLICLNMVTMMVETDDQ
       6. TFKGWMDIMYAAVDSREVEDQPIYEINVYMYLYFVIFIVFGAFFTLNLFIGVIIDNFNRQKQK (37) VQGVVYDIVTQPFTDIFIMALICINMVAMMVESEDQ
       7. TFNGWITIMNSAIDSVAVNIQPHFEVNIYMYCYFINFIIFGVFLPLSMLITVIIDNFNKHKIK (37) LQGFIFDVVTSQAFNVIVMVLICFQAIAMMIDTDVQ
       8. TFKGWIQIMNDAIDSREVDKQPIRETNIYMYLYFVFFIIFGSFFTLNLFIGVIIDNFNEQKKK (38) PQAIVFEIVTDKKFDIIIMLFIGLNMFTMTLDRYDA
       9. TFEGWMEIMADAVDVTEVDEQPKFEATVYYYFYFVLFIIFGSFFVLNLVIGVIIDKFSFLKKK (39) CQAVVYDLVMSNQFEIFITTIIITNMIFMAFEHYNQ
      10. TFEGWNEVMADAVDARGVDLQPRREANLYAYIYFVIFIVCGSFFTLNLFIGVIIDNFNMLRRS (39) FLAMFYDLSNSRRFEIAIFVLIFLNMLTMGIEHYDQ
      11. TGEGWPMVLKHSVDATYEEQGPSPGYRMELSIFYVVYFVVFPFFFVNIFVALIIITFQEQGDK (34) FQYKTWTFVVSPPFEYFIMAMIALNTVVLMMKFYDA
consensus T  GW        D       P                    F         II  F                                 I

       1. SDYVTSILSRINLVFIVLFTGECVLKLISLR HYYFTIGWNIFDFVVVILSIVGMFLAELIEK (7) FRVIRLARIGRILRLIKGAKGIRTLLFALMMSLPALF
       2. SQEMTNILYWINLVFIVLFTGECVLKLISLR HYYFTIGWNIFDFVVVILSIVGMFLAELIEK (7) FRVIRLARIGRILRLIKGAKGIRTLLFALMMSLPALF
       3. SKYMTLVLSRINLVFIVLFTGEFLLKLISLR YYYFTIGWNIFDFVVVILSIVGMFLAELIEK (7) FRVIRLARIGRILRLIKGAKGIRTLLFALMMSLPALF
       4. SQLKVDILYNINMIFIIIFTGECVLKMLALR QYYFTVGWNIFDFVVVILSIVGLALSDLIQK (7) FRVIRLARIGRVLRLIRGAKGIRTLLFALMMSLPALF
       5. SPEKINILAKINLLFVAIFTGECIVKLAALR HYYFTNSWNIFDFVVVILSIVGTVLSDIIQK (7) FRVIRLARIGRILRLIRGAKGIRTLLFALMMSLPALF
       6. SQVKKDILSQINVIFVIIFTVECLLKLLALR QYFFTVGWNVFDFAVVVISIIGLLLSDIIEK (7) FRVIRLARIARVLRLIRAAKGIRTLLFALMMSLPALF
       7. SLQMSIALYWINSIFVMLYTMECILKLIAFR CFYFTIAWNIFDFMVVIFSITGLCLPMTVGS (7) VQLILLSRIIHMLRLGKGPKVFHNLMLPLMLSLPALL
       8. SDTYNAVLDYLNAIFVVIFSSECLLKIFALR YHYFIEPWNLFDVVVVILSILGLVLSDIIEK (7) LRVVRVAKVGRVLRLVKGAKGIRTLLFALAMSLPALF
       9. SEVVTEVLATANIAFTILYAVEAIIKIIGLR IHYLRNLWNVFDFLVVTLSVMDAFLNDIFGD (8) LRVARMFRIGRIIRLIKWAKGMRKLLFALVISLPALF
      10. PHAVFFILEVSNAFFTTVFGLEAIVKIVGLR YHYFTVPWNSVDFLLVLASIFGILMEDIMID (7) LRVVRVFRIGRILRLIKAAKGIRKLLFALVVSLPALF
      11. PYEYELMLKCLNIVFTSMFSMECVLKIIAFGVLNYFRDAWNVFDFVTVLGSITDILVTEIAET (5) LSFLRLFRAARLIKLLRQGYTIRILLWTFVQSFKALP
consensus        L   N  F      E   K             WN  D   V  S                               L         L      S  AL

       1. NIGLLLFLVMFIYAIFGMSNFAYVKRE  VGIDDMFNFETFGNSMICLFQITTSAGWDGLLAPIL (25) SVGIFFFVSYIIISFLVVVNMYIAVILE (222)
       2. NIGLLLFLVMFIYAIFGMSNFAYVKRE  VGIDDMFNFETFGNSMICLFQITTSAGWDGLLAPIL (25) SVGIFFFVSYIIISFLVVVNMYIAVILE (228)
       3. NIGLLLFLVMFIYAIFGMSNFAYVKKE  AGIDDMFNFETFGNSMICLFQITTSAGWDGLLAPIL (25) SVGIFFFVSYIIISFLVVVNMYIAVILE (228)
       4. NIGLLLFLVMFIYSIFGMSNFAYVKKE  SGIDDMFNFETFGNSIICLFEITTSAGWDGLLNPIL (25) SIGICFFCSYIIISFLIVVNMYIAIILE (237)
       5. NIGLLLFLVMFIYSIFGMANFAYVKWE  AGIDDMFNFQTFANSMLCLFQITTSAGWDGLLSPIL (24) AVGILFFTTYIIISFLIVVNMYIAIILE (243)
       6. NIGLLLFLIMFIFSIFGMSNFAYVKKQ  GGVDDIFNFETFGNSMICLFEITTSAGWDGLLLPTL (25) GKGITFFCSYIILSFLVVVNMYIAIILE (252)
       7. NIILLIFLVMFIYAVFGMYNFAYVKKE  AGINDVSNFETFGNSMLCLFQVAIFAGWDGMLDAIF (25) SVGIFYFVSYILISWLIIVNMYIVVVME (185)
       8. NICLLLFLVMFIFAIFGMSFFMHVKEK  SGINDVYNFKTFGQSMILLFQMSTSAGWDGVLDAII (21) TVGITFLLSYLVISFLIVINMYIAVILE (  3)
       9. NIGALLMLVMFIYTIIGMSSFGQIKLS  GALNDQVNFQTFGKTFLLLVRLATSAGWNDILGPLL (29) WLAISYMVSYIIIVFMIVFNMYIAVILE (170)
      10. NIGALLGLITFIYAILGMSLFGNVKLQ  GALDDMVNFQTFGRSMQLLFQLMTSAGWNDVLESLM (21) LLAITYFTSFIIISYMIVINMYIAIILE ( 62)
      11. YVCLLIAMLFFIYAIIGMQVFGNIALDDDTSINRHNNFRTFLQALMLLFRSATGEAWHEIMLSCL (16) DFAYFYFVSFIFLCSFLMLNLFVAVIMD (630)
consensus     L     FI    GM  F               NF TF      L        W                                 N
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Appendix C14(b) (Continued)

SERCA (1)

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   1. (22) GLTPDQVKRHLEKYGPNELPAEEGKSLWELVVEQFEDLLVRILLLAACISFVLA (10) AFVEPFVILLILIANAIVGVWQERNAENAIEALKEYEPEMGKVYRA
   2. (22) GLSGEQVRRALEKYGHNELPAEEGKTIWELVVEQFEDLLVRILLLAACISFVLA (10) AFVEPFVILLILIANAVVGVWQERNAENAIEALKEYEPEMGKVYRA
   3. (22) GLSLDQVKKNFDKFGPNELPAEEGKSLWELVAEQFEDLLVRILLLAAIISFVLA (10) AFVEPFVILLILIANAVVGVWQERNAEDAIEALKEYEPEMGKVYRS
   4. (22) GLSLEQVKKLKERWGSNELPAEEGKTLLELVIEQFEDLLVRILLLAACISFVLA (10) AFVEPFVILLILVANAIVGVWQERNAENAIEALKEYEPEMGKVYRQ
   5. (22) GLSLEQVKKLKEKWGSNELPAEEGKTLLELVIEQFEDLLVRILLLAACISFVLA (10) AFVEPFVILLILVANAIVGVWQERNAENAIEALKEYEPEMGKVYRQ
   6. (22) GLTLEQVTDARERYGPNELPTEEGKSLWELVVEQFEDLLVRILLLAALVSFVLA (10) AFVEPLVIMLILVANAIVGVWQERNAESAIEALKEYEPEMGKVIRS
   7. (22) GLTLDQIKANQKKYGPNELPTEEGKSIWQLVLEQFDDLLVKILLLAAIISFVLA (10) AFVEPLVILLILIANAVVGVWQERNAESAIEALKEYEPEMGKVVRQ
   8. (22) GLALEQVKKNQEKYGPNELPAEEGKSLLTLILEQFDDLLVKILLLAAIISLVLA (13) AYVEPFVILLILIANAVVGVWQEKNAESAIEALKEYEPEMGKVIRA
   9. (26) GLSTYEVDKRRERYGLNELEKEKGKPLWRLVLEQFDDTLVKILLGAAFISFVLA (13) AYVEPLVILWILVLNAIVGVWQESNAEKALEALKEMQGESAKVLR
consensus  GL            G NEL  E GK    L  EQF D LV ILL AA  S VLA      A VEP VI  IL  NA VGVWQE NAE A EALKE   E  KV R

       1. DRKSVQRIKARDIVPGDIVEVAVGDKVPADIRILSIKSTTLRVDQSILTGESVSVIKHTDPVPDPRAVNQDKKNMLFSGTNIAAGKAVGIVATTGVSTEIGKIRDQM  AA
       2. DRKAVQRIKARDLVPGDIAEVAVGDKVPADIRIISIKSTTLRVDQSILTGESVSVIKHTEPVPDPRAVNQDKKNMLFSGTNIGAGKAVGIVVATGVNTEIGKIRDEM  AA
       3. DRKSVQRIKARELVPGDIVEVAVGDKVPADIRLISIKSTTLRIDQSILTGESVSVIKHTEVVPDTRAVNQDKKNMLFSGTNVGAGKAVGVVIATGPNTEIGKIRDEM  AA
       4. DRKSVQRIKAKDIVPGDIVEIAVGDKVPADIRLTSIKSTTLRVDQSILTGESVSVIKHTDPVPDPRAVNQDKKNMLFSGTNIAAGKAMGVVVATGVNTEIGKIRDEM  VA
       5. DRKSVQRIKARDIVPGDIVEVAVGDKVPADIRITSIKSTTLRVDQSILTGESVSVIKHTDPVPDPRAVNQDKKNMLFSGTNIAAGKAMGVVIATGVNTEIGKIRDEM  VA
       6. DRKGVQRIRARDIVPGDIVEVAVGDKVPADLRLIEIKSTTLRVDQSILTGESVSVTKHTDAIPDPRAVNQDKKNMLFSGTNIASGKALGVAVATGLHTELGKIRSQM  AA
       7. DKSGIQKVRAKEIVPGDLVEVSVGDKIPADIRITHIYSTTLRIDQSILTGESVSVIKHTDAIPDPRAVNQDKKNILFSGTNVAAGKARGVVIGTGLSTAIGKIRTEM  SE
       8. DKTGIQKIKARDLVPGDIVEISVGDKIPADLRLISILSTTLRIDQSILTGESVSVIKHTDPVPDPRAVNQDKKNMLFSGTNVSAGKARGVVMGTGLNTAIGSIRTQM  FE
       9. DGYLVPDFPAKELVPGDIVELRVGDKVPADMRVATLKSSTLRVEQSSLTGESMPVTKSTDFLATDDCELQAKENMVFAGTTVVNGSCICIVVNTGMCTEIGKIQRQIHDAS
consensus D        A   VPGD  E  VGDK PAD R     S TLR  QS LTGES  V K T          Q K N  F GT    G        TG  T  G I

       1. TEQDKTPLQQKLDEFGEQLSKVISLICVAVWLINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       2. TEQDKTPLQQKLDEFGEQLSKVISLICVAVWLINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       3. TEQEKTPLQQKLDEFGEQLSKVISLICVAVWLINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       4. TEQERTPLQQKLDEFGEQLSKVISLICIAVWIINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       5. TEQERTPLQQKLDEFGEQLSKVISLICIAVWIINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       6. VEPERTPLQRKLDEFGRQLSHAISVICVAVWVINIGHF (12) AVYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMARKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       7. TEEIKTPLQQKLDEFGEQLSKVISVICVAVWAINIGHF (12) AIYYFKIAVAVAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       8. TEEMKTPLQQKLDEFGEQLSKVISVICVAVWAINIGHF (12) AIYYFKIAVALAVAAIPEGLPAVITTCLALGTRRMAKKNAIVRSLPSVETLGCTSVICSDKTGTLTT
       9. MEESDTPLKKKLDEFGNRLTFAIGVVCLVVWAINYKYF (19) CAYYFKIAVALAVAAIPEGLPSVITTCLALGTRKMAQKNAIVRKLQSVETLGCTTVICSDKTGTLTT
consensus  E   TPL  KLDEFG  L   I   C  VW IN   F        YYFKIAVA AVAAIPEGLP VITTCLALGTR MA KNAIVR L SVETLGCT VICSDKTGTLTT

       1. NQMSVCKMF (14) FSITGSTYAP (17) GLVELATICALCNDSSLDFNETKGVYEKVGEATETALTTLVEKMN (31) LEFSRDRKSMSVYC (12) KMFVKGAPE
       2. NQMSVCKMF (14) FSITGSTYAP (17) GLVELATICALCNDSSLDYNEAKGIYEKVGEATETALTCLVEKMN (31) LEFSRDRKSMSVYC (12) KMFVKGAPE
       3. NQMSVCRMF (14) FTITGSTYAP (17) GLVELATICALCNDSSLDFNESKGVFEKVGEATETALTTLVEKMN (31) LEFSRDRKSMSVYC (12) KMFVKGAPE
       4. NQMSVCRMF (14) FTITGSTYAP (17) GLVELATICALCNDSALDYNEAKGVYEKVGEATETALTCLVEKMN (31) LEFSRDRKSMSVYC (11) KMFVKGAPE
       5. NQMSVCRMF (14) FTVTGSTYAP (17) GLVELATICALCNDSSLDYNEAKGVYEKVGEATETALTCLVEKMN (31) LEFSRDRKSMSVYC (11) KMFVKGAPE
       6. NQMSVCRMF (14) FTISGTTYTP (17) GLVELATICALCNDSALDYNEAKGVYEKVGEATETALTCLVEKMN (31) LEFSRDRKSMSVYC (12) KMFVKGAPE
       7. NQMSVSRMF (14) FEMTGSTYEP (17) TLQELSTICIMCNDSAIDYNEFKQAFEKVGEATETALIVLAEKLN (31) LEFSRDRKSMSSYC (12) KLFVKGAPE
       8. NQMSVSRMF (15) FELTGSTYEP (17) AVKEITTICMMCNDSAIDFNEYKQAFEKVGEATETALIVLGEKLN (31) LEFSRDRKSMSSYC (12) KMFVKGAPE
       9. NQMSVSEFF (11) FGVEGTTYDP (15) NLLLMAEICAICNDAGV FCDGR LFKATGLPTEAALKVLVEKMG (43) LEFDRVRKSMGVIV ( 7) RLLVKGAFE
consensus NQMSV   F      F   G TY P             IC  CND               G  TE AL  L EK         LEF R RKSM                VKGA E
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Appendix C15(b)

SERCA (2)

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       1. GVIDRCNYVRV (25) RDTLRCLALATRDTP ( 7) LDDSAKFMEYEMDLTFVGVVGMLDPPRKEVTGSIQLCRDAGIRVIMITGDNKGTAIAICRRIGIFSENEEVAD
       2. GVIDRCNYVRV (25) RDTLRCLALATRDTP ( 7) LVDSTKFAEYETDLTFVGCVGMLDPPRKEVMGSIRLCRDAGIRVIMITGDNKGTAIAICRRIGIFTEDEEVSG
       3. GVIDRCNYVRV (25) RDTLRCLALATRDTP ( 7) LDEATRFIEYETDLTFVGCVGMLDPPRKEVMGSIQLCREAGIRVIMITGDNKGTAIAICRRIGIFGEDDDVSG
       4. GVIDRCTHIRV (25) SDTLRCLALATHDNP ( 7) LEDSANFIKYETNLTFVGCVGMLDPPRIEVASSVKLCRQAGIRVIMITGDNKGTAVAICRRIGIFGQDEDVTS
       5. GVIDRCTHVRV (25) RDTLRCLALATHDNP ( 7) LEDSSNFINYETNLTFVGCVGMLDPPRIEVASSIKLCKQAGIRVIMITGDNKGTAVAICRRIGIFVEDEDVST
       6. SVIERCSSVRV (25) SHTLRCLALATRDTP ( 7) LDDCSQFVQYETGLTFVGCVGMLDPPRPEVAACITRCSRAGIRVVMITGDNKGTAVAICRRLGIFGDTEDVLG
       7. GVLERCTHARV (25) RDTLRCLALAVADSP ( 7) LGDSTKFYQYEVNLTFVGVVGMLDPPRKEVFDSIVRCRAAGIRVIVITGDNKATAEAICRRIGVFAEDEDTTG
       8. GVLDRCTHVRV (25) RDTLRCLALATIDDP ( 7) IIDSTKFVKYEQNCTFVGVVGMLDPPRKEVLDAIERCRAAGIRVIVITGDNKATAEAICRRIGVFGEDENTEG
       9. SLLERSTYVQL (24) SKGLRCLGLAYKDDL (16) LLDPSCYSSIESDLVFVGVVGLRDPPREEVHRAVNDCRRAGIKIMVITGDNKSTAEAVCREIQLFSNGENLRG
consensus     R                 LRCL LA  D              E    FVG VG  DPPR EV      C  AGI    ITGDNK TA A CR    F
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       1. RAYTGREFDDLPLAEQREACRRA  CCFARVEPSHKSKIVEYLQSYDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMK
       2. RAYTGREFDDLPPAEQREACRRA  CCFARVEPTHKSKIVEFLQSFDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMK
       3. RAFTGREFDDLPPAEQREACKRA  SCFARVEPAHKSKIVEFLQSFDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMK
       4. KAFTGREFDELNPSAQRDACLNA  RCFARVEPSHKSKIVEFLQSFDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMK
       5. KAFTGREFDELSLAAQRDACHHA  RCFARVEPSHKSKIVEFLQSFDEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKTASEMVLADDNFSTIVAAVEEGRAIYNNMK
       6. KAYTGREFDDLSPEQQRQACRTA  RCFARVEPAHKSRIVENLQSFNEITAMTGDGVNDAPALKKAEIGIAMG SGTAVAKSAAEMVLSDDNFASIVAAVEEGRAIYNNMK
       7. KSYSGREFDDLSPTEQKAAVARS  RLFSRVEPQHKSKIVEFLQSMNEISAMTGDGVNDAPALKKAEIGIAMG SGTAVAKSAAEMVLADDNFSSIVSAVEEGRAIYNNMK
       8. MAYTGREFDDLSVEGQRDAVARS  RLFARVEPFHKSKIVEYLQGMGEISAMTGDGVNDAPALKKAEIGIAMG SGTAVAKSAAEMVLADDNFSTIVAAVEEGRAIYNNMK
       9. SSFTGKEFMAFSSQQQIEILSQDGGKVFSRAEPRHKQEIVRMLKEMGEIVAMTGDGVNDAPALKLADIGIAMGITGTEVAKEASDMVLADDNFSTIVSAVAEGRSIYNNMK
consensus     G EF       Q           F R EP HK  IV  L    EI AMTGDGVNDAPALK A IGIAMG  GT VAK A  MVL DDNF  IV AV EGR IYNNMK
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       1. QFIRYLISSNVGEVVCIFLTAALGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMDRPPRSPKEPLISGWLFFRYMAIGGYVGAATVGAAAWWFL ( 5) PHVSYH
       2. QFIRYLISSNVGEVVCIFLTAALGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMDKPPRSPKEPLISGWLFFRYLAIGGYVGAATVGAAAWWFL ( 5) PSLTYH
       3. QFIRYLISSNVGEVVCIFLTAALGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMDRPPRSPKEPLISGWLFFRYMAIGGYVGAATVGAAAWWFM ( 5) PNVTFY
       4. QFIRYLISSNVGEVVCIFLTAALGFPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMNKPPRNPKEPLISGWLFFRYLAIGCYVGAATVGAAAWWFI ( 5) PRVSFY
       5. QFIRYLISSNVGEVVCIFLTAALGFPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMNKPPRNPKEPLISGWLFFRYLAIGCYVGAATVGAAAWWFI ( 5) PRVTFY
       6. QFIRYLISSNVGEVVCIFLTAILGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMEKLPRNPREALISGWLFFRYLAIGVYVGLATVAAATWWFL ( 5) PQVTFH
       7. QFIRYLISSNIGEVVSIFLTAALGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMEKPPRKADEGLISGWLFFRYMAIGFYVGAATVGAAAWWFV ( 5) PKLSYW
       8. QFIRYLISSNIGEVVSIFLTAALGLPEALIPVQLLWVNLVTDGLPATALGFNPPDLDIMNKPPRRADEGLITGWLFFRYMAIGTYVGAATVGAAAHWFM ( 5) PGLNFY
       9. AFIRYMISSNVGEVISIFLTAVLGIPECLIPVQLLWVNLVTDGPPATALGFNPADVDIMQKPPRKNTDALINSWVFFRYMVIGSYVGIATVGIFIVWYT (14) TLVELS
consensus  FIRY ISSN GEV  IFLTA LG PE LIPVQLLWVNLVTDG PATALGFNP D DIM   PR     LI  W FFRY  IG YVG ATV     W
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       1. QLTHFMQC (19) PMTMALSVLVTIEMCNALNSLSENQSLLRMPPWVNIWLLGSICLSMSLHFLILYVDPLPMIFKLRALDFTQWLMVLKISLPVIGLDELLKFIAR ( 5)
       2. QLTHFMQC (19) PMTMALSVLVTIEMCNALNSLSENQSLLRMPPWVNIWLVGSICLSMSLHFVILYVDPLPMIFKLTHLDLAHWLVVLRISFPVILLDEALKFVAR ( 5)
       3. QLSHFMQC (19) PMTMALSVLVTIEMCNALNSLSENQSLIRMPPWSNFWLLGSICLSMSLHFLILYVEPLPMIFKLTPLNVEQWFIVLKMSFPVILLDELLKFVAR ( 5)
       4. QLSHFLQC (19) PMTMALSVLVTIEMCNALNSLSENQSLLRMPPWENIWLVGSICLSMSLHFLILYVEPLPLIFQITPLNVTQWLMVLKISLPVILMDETLKFVAR (54)
       5. QLSHFLQC (19) PMTMALSVLVTIEMCNALNSLSENQSLMRMPPWENIWLVGAICLSMSLHFLILYVEPLPIIFQITPLNVTQWLMVLKISLPVILLDETLKYVAR ( 9)
       6. QLRNFLKC (19) PTTMALSVLVTIEMCNALNSVSENQSLLRMPPWLNPWLLGAVVMSMALHFLILLVPPLPLIFQVTPLSGRQWGVVLQMSLPVILLDEALKYLSR (10)
       7. QLTHHLSC (19) AMTMALSVLVTIEMLNAMNSLSENQSLITMPPWCNLWLIGSMALSFTLHFVILYVDVLSTVFQVTPLSAEEWITVMKFSIPVVLLDETLKFVAR (13)
       8. QLSHHLQC (19) PMTMALSVLVTIEMLNAINSLSENQSLLVMPPWSNIWLISAICLSMTLHFVILYVEILSTVFQICPLTLTEWIVVLKISFPVLLLDEVLKFVAR (10)
       9. QLRNWGEC (33) AMTLSLSVLVAIEMFNSLNALSEDNSLIKMPPWRNPWLLVAMSLSFALHSVILYVPFLADIFGIVPLSLYEWLLVILLSAPVILIDEVLKFVGR (10)
consensus QL     C        T  LSVLV IEM N  N  SE  SL  MPPW N WL      S  LH  IL V  L   F    L    W  V   S PV   DE LK   R
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Appendix C15(b) (Continued)

Na^+-K^+ pump (1)

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      1. (30) DMDELKKEVSMDDHKLSLDELHRKYGTDLSRGLTSARAAEILARDGPNALTPPPTTPEWIKFCRQLFGGFSMLLWIGAILCFLAYSIQAAT EEEP
      2. (28) DMDELKKEISMDDHKLSLDELHRKYGTDLSRGLTTARAAEILARDGPNTLTPPPTTPEWVKFCRQLFGGFSLLLWIGSLLCFLAYGITSVM EGEP
      3. (32) DMDELKKEVTMEDHKLSLDELHRKFGTDMQRGLTTARAAEILARDGPNALTPPPTTPEWVKFCRQLFGGFSMLLWIGAILCFLAYGIQAAM EEEP
      4. (30) DMEELKKEVTMEDHKMTLEELHRKYGTDLTRGLTTARAAEILARDGPNALTPPPTTPEWVKFCRQLFGGFSMLLWIGAILCFLAYGIRKAS DLEP
      5. (33) DMDELKKEVDLDDHKLSLEELHHKYGTDLSKGLSNSRAEEILARDGPNALTPPPTTPEWVKFCKQMFGGFSMLLWTGAVLCFLAYGILAAM EDEP
      6. (28) ELDELKKEVAMDDHKLSLDELGRKYQVDLSKGLTNQRAQDVLARDGPNALTPPPTTPEWVKFCRQLFGGFSILLWIGAILCFLAYGIQAAM EDEP
      7. (25) ELDELKKEVNLDDHKLSLDELGRKYQVDLSRGLSNARAAEVLAQDGPNALTPPPTTPEWVKFCRQLFGGFSILLWIGAILCFLAYGIQAAM EDEP
      8. (18) DLDDLKKEVAMTEHKMSVEEVCRKYNTDCVQGLTHSKAQEILARDGPNALTPPPTTPEWVKFCRQLFGGFSILLWIGAILCFLAYGIQAGT EDDP
      9. (17) DLDDLKKEVAMTEHKMSIEEVCRKYNTDCVQGLTHSKAQEILARDGPNALTPPPTTPEWVKFCRQLFGGFSILLWIGAILCFLAYGIQAGT EDEP
     10. (30) DLDELKKEVSLDDHKLNLDELHQKYGTDLTQGLTPARAKEILARDGPNALTPPPTTPEWIKFCRQLFGGFSILLWTGAILCFLAYGIQVAT VDNP
     11. (48) NLDDLKQELDIDFHKISPEEMYQRFQTHPENGLSHARAKENLERDGPN LTPPKQTPEWVKFCEDLF GVAMLLWIGAILCFVAYSIQAST SEEP
     12. (10) DLNELKKELDIDFHKIPIEECYQRLGSNPETGLTNAQARSNIERDGPNCLTPPKTTPEWIKFCKNLFGGFALLLWTGAILCFLAYGIEASSGNEDM
     13. ( 7) QLSDLKKELELDQHKIPLEELCRRLGTNTETGLTSSQAKSHLEKYGPNALTPPRTTPEWIKFCKQLFGGFQMLLWIGSILCFIAYTMEKYK NPDV
     14. (36) KLEDLKKELEMTEHSMKLESLLSMYETSLEKGLSENIVARNLERDGLNALTPPKQTPEWVKFCKQMFGGFSMLLWIGAILCFFAFGIRAVR DTNP
consensus         LK E     H                 GL            G N LTPP  TPEW KFC   F G   LLW G  LCF A
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       1. QNDNLYLGVVLSAVVIITGCFSYYQEAKSSKIMESFKNMVPQQALVIRNGEKMSINAEEVVVGDLVEVKGGDRIPADLRIISANGCKVDNSSLTGESEPQT
       2. NSDNLYLGVVLAAVVIITGCFSYYQEAKSSKIMESFKNMVPQQALVVRNGEKMSINAEGVVVGDLVEVKGGDRIPADLRIISAHGCKVDNSSLTGESEPQT
       3. QNDNLYLGVVLSAVVIITGCFSYYQEAKSSKIMESFKNMVPQQALVIRSGEKLSINAEEVVLGDLVEVKGGDRIPADLRVISSHGCKVDNSSLTGESEPQT
       4. DNDNLYLGVVLSAVVIITGCFSYYQEAKSSRIMESFKNMVPQQALVIRNGEKLSINAENVVQGDLVEVKGGDRIPADLRIISAHGCKVDNSSLTGESEPQT
       5. ANDNLYLGVVLSAVVIITGCFSYYQDAKSSKIMDSFKNLVPQQALVVRDGEKKQINAEEVVIGDLVEVKGGDRIPADLRIISSHGCKVDNSSLTGESEPQT
       6. SNDNLYLGVVLAAVVIVTGCFSYYQEAKSSKIMDSFKNMVPQQALVIREGEKMQINAEEVVVGDLVEVKGGDRVPADLRIISSHGCKVDNSSLTGESEPQT
       7. SNDNLYLGVVLAAVVIVTGCFSYYQEAKSSKIMDSFKNMVPQQALVIREGEKIQINAENVVVGDLVEVKGGDRVPADMRIISSHGCKVDNSSLTGESEPQT
       8. SGDNLYLGIVLAAVVIITGCFSYYQEAKSSKIMESFKNMVPQQALVIREGEKMQVNAEEVVVGDLVEIKGGDRVPADLRIISAHGCKVDNSSLTGESEPQT
       9. SNDNLYLGIVLAAVVIITGCFSYYQEAKSSKIMESFKNMVPQQALVIREGEKMQLNAEEVVVGDLVEVKGGDRVPADLRIISAHGCKVDNSSLTGESEPQT
      10. ANDNLYLGVVLSTVVIITGCFSYYQEAKSSKIMDSFKNMVPQQALVIRDGEKSSINAEQVVVGDLVEVKGGDRIPADLRIISACSCKVDNSSLTGESEPQS
      11. ADDNLYLGIVLSAVVIVTGVFSYYQESKNSKIMESFKNMVPQFATVIREGEKPSLRAEDLVLGVLVELEFGDLIPLVYRIIEARDFKVDNSSLTGESEPQS
      12. LKDNLYLGIVLATVVIVTGIFSYYQENKSSRIMDSFKNLVPQYALALREGQRVTLKAEELTMGDIVEVKFGDRVPADLRVLEARSFKVDNSSLTGESEPQA
      13. LGDNLYLGLALLFVVIMTGCFAYYQDHNASKIMDSFKNLMPQFAFVIRDGKKIQLKAEEVTVGDLVEVKFGDRIPADIRITSCQSMKVDNSSLTGESEPQS
      14. NMDELYLGIVLSVVVIITGCFSYYQESKSSKIMESFKKMIPQEALVLRDGKKITINAEQCVVGDVVFVKFGDRIPADIRIVECKGLKVDNSSLTGESEPQS
consensus   D LYLG  L  VVI TG F YYQ    S IM SFK   PQ A   R G      AE    G  V    GD  P   R       KVDNSSLTGESEPQ
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       1. RSPDFTNENPLETRNIAFFSTNCVEGTARGIVVYTGDRTVMGRIATLASGLEGGQTPIAAEIEHFIHIITGVAVFLGVSFFILSLILEYTWLEAVIFLIGI
       2. RSPDFSNENPLETRNIAFFSTNCVEGTAVGIVISTGDRTVMGRIASLASGLEGGKTPIAMEIEHFIHLITGVAVFLGVSFFILSLILEYTWLEAVIFLIGI
       3. RSPDFTNENPLETRNIAFFSTNCVEGTARGIVVNTGDRTVMGRIATLASGLDGGRTPIAIEIEHFIHIITGVAVFLGVSFFILSLILQYTWLEAVIFLIGI
       4. RSPDFTNENPLETRNIAFFSTNCVEGTARGIVINTGDRTVMGRIATLASGLEGGQTPIAVEIGHFIHIITGVAVFLGVSFFILSLILHYTWLEAVIFLIGI
       5. RSPDFSNDNPLETKNIAFFSTNCVEGTARGIVISTGDRTVMGRIATLASGLEVGRTPISIEIEHFIHIITGVAVFLGVSFLLLSLVLGYSWLEAVIFLIGI
       6. RSPEFTHENPLETRNICFFSTNCVEGTARGIVIATGDRTVMGRIATLASGLEVGRTPIAMEIEHFIQLITGVAVFLGVSFFVLSLILGYSWLEAVIFLIGI
       7. RSPEFTHENPLETRNICFFSTNCVEGTARGIVISTGDRTVMGRIASLASGLEVGRTPIAMEIEHFIRLITGVAVFLGLSFFILSLILGYTWLEAVIFLIGI
       8. RSPDCTHDNPLETRNITFFSTNCVEGTARGVVVATGDRTVMGRIATLASGLEVGKTPIAIEIEHFIQLITGVAVFLGVSFFILSLILGYTWLEAVIFLIGI
       9. RSPDCTHDNPLETRNITFFSTNCVEGTARGVVIATGDRTVMGRIATLASGLEVGKTPIAVEIEHFIQLITGVAVFLGISFFVLSLILGYTWLEAVIFLIGI
      10. RSPEYSSENPLETKNIAFFSTNCVEGTARGIVINIGDHTVMGRIATLASGLEVGQTPIAAEIEHFIHIITGVAVFLGVSFFILSLILGYTWLEAVIFLIGI
      11. RGAEFTHENPLETKNLAFFSTNAVEALPKGVVISCGDHTVMGRIAALASGLDTG TPIAKEIHHFIHLITGVAVFLGVTFFVIAFILGYHWLDAVIFLIGI
      12. RSPEFTNDNPLETKNLAFFSTNAVEGTMRGIVIGIGDNTVMGRIAGLASGLDTGETPIAKEIAHFIHIITGVAVFLGVTFFIIAFVLGYHWLDAVVFLIGI
      13. RSTECTNDNPLETKNLAFFFTNTLEGTGRGIVINVGDDSVMGRIACLASSLDSGKTPIAREIEHFIHIITAMAVSLAAVFAVISFLYGYTWLEAAIFMIGI
      14. RAVDFTHENPIETKNLAFFSTNAVEGTATGIVVRIGDNTVMGRIANLASGLGSGKTPIALEIEHFIHIVTGVAVFLGVSFLIISLAMGYHWLEAIIFLIGI
consensus R       NP ET N  FF TN  E    G V   GD  VMGRIA LAS L  G TPI  EI HFI   T  AV L   F        Y WL A  F IGI
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       1. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGVSFDKTSATWLALSRIAGLC
       2. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVGTLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGASFDKSSATWLALSRIAGLC
       3. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGASFDKSSPTWTALSRVAGLC
       4. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGASFDKSSPTWTALARIAGLC
       5. IVANVPEGLLATVTVCLTLTAKRMAKKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGTSFDRSSDTWASLARIAGLC
       6. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTEDQSGATFDKRSPTWTALSRIAGLC
       7. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTEDQSGATFDKRSPTWAALSRIAGLC
       8. IVANVPEGLLATVTVCLTVTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTEDQSGTSFDKSSHTWVALSHIAGLC
       9. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTEDQSGTSFDKSSATWVALSHIAGLC
      10. IVANVPEGLLATVTVCLTLTAKRMARKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIHEADTTENQSGISFDKTSLSWNALSRIAALC
      11. IVANVPEGLLATVTVCLTLTAKRMASKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDNQIIEADTTEDQSGVQYDRTSPGFKALSRIATLC
      12. IVANVPEGLLATVTVCLTLTAKRMASKNCLVKNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDGTITEADTTEDQSGAQFDKSSAGWKALVKIAALC
      13. IVAKVPEGLLATVTVCLTLTAKRMAKKNCLVRNLEAVETLGSTSTICSDKTGTLTQNRMTVAHMWFDQKIVTADTTENQSGNQLYRGSKGFPELIRVASLC
      14. IVANVPEGLLATVTVCLTLTAKKMAKKNCLVKHLEAVETLGSTSVICSDKTGTLTQNRMTVAHMWFDKMIVEADTTEDQSGIAHDKGSLTWKSLAKVAALC
consensus IVA VPEGLLATVTVCLT TAK MA KNCLV  LEAV TLGSTS ICSDKTGTLTQNRMTVAHMWFD  I  ADTTE QSG      S     L   A LC
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       1. NRAVFQANQENLPILKRAVAGDASESALLKCIELCCGSVKEMRERYAKIVEIPFNSTNKYQLSIHKNPNT (5) LLVMKGAPERILDRCSSILLHGKEQP
       2. NRAVFQANQENVPILKRAVAGDASESALLKCIELCCGSVKEMRERYPKVVEIPFNSTNKYQLSIHKNANA (5) LLVMKGAPERILDRCDSILIHGKVQP
       3. NRAVFQAGQENTPILKRDVAGDASESALLKCIELCCGSVRDMREKNHKVAEIPFNSTNKYQLSVHKNANP (5) ILVMKGAPERILDRCTSIILQGKEQP
       4. NRAVFPAGQENTPILKRDVVGDASESALLKCIELCCGSVKDMREKNQKVAEIPFNSTNKYQLSVHKNANP (5) LLVMKGAPERILDRCSSILLQGKEQP
       5. NRAVFLAEQIDVPILKRDVAGDASESALLKCIELCCGSVKEMREKFTKVAEIPFNSTNKYQLSVHKIPSG (6) LLVMKGAPERILDRCATIMIQGKEQL
       6. NRAVFKAGQENISVSKRDTAGDASESALLKCIELSCGSVRKMRDRNPKVAEIPFNSTNKYQLSIHEREDS (4) VLVMKGAPERILDRCSTILVQGKEIP
       7. NRAVFKPGQENISISKRDTAGDASESALLKCIQLSCGSVKKMRDKNPKVTEIPFNSTNKYQLSIHEREED (4) ILVMKGAPERILERCSRILLQGQEVP
       8. NRAVFKGGQDNIPVLKRDVAGDASESALLKCIELSSGSVKLMRERNKKVAEIPFNSTNKYQLSIHETEDP (5) LLVMKGAPERILDRCSTILLQGKEQP
       9. NRAVFKGGQENVPILKRDVAGDASESALLKCIELSSGSVKVMRERNKKVAEIPFNSTNKYQLSIHETEDP (5) LLVMKGAPERILDRCSTILLQGKEQP
      10. NRAVFQAGQDSVPILKRSVAGDASESALLKCIELCCGSVSQMRDRNPKIVEIPFNSTNKYQLSIHENDKA (4) LLVMKGAPERILDRCSTILLNGEDKP
      11. NRAEFKGGQDGVPILKKEVSGDASEAALLKCMELALGDVMNIRKRNKKIAEVPFNSTNKYQVSIHETEDT (5) LLVMKGAPERILERCSTIFINGKEKV
      12. SRAEFKPNQSTTPILKREVTGDASEAAILKCVELTTGETEAIRKRNKKICEIPFNSANKFQVSIHENEDK (5) LLVMKGAPERILERCSTIFMNGKEID
      13. SRAEFKTEHAHLPVLKRDVNGDASEAAILKFAEMSTGSVMNIRSKQKKVSEIPFNSANKYQVSVHEREDK (3) FLVMKGAPERILERCSTILIDGTEIP
      14. SRAEFKPNQNDVAVLRKECTGDASETAILKFVELSVGNVMDIRAKNKKVTEIPFNSTNKYQVSVHEQENS (3) LLVMKGAPEKVLERCSTILINGEEQP
consensus  RA F               GDASE A LK      G     R    K  E PFNS NK Q S H           LVMKGAPE  L RC  I   G
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Appendix C16(b)

Na+-K+ pump (2)

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        1. LDEELKDAFQNAYLELGGLGERVLGFCHLFLPDEQFPEGFQFDTDD VNFPIDNLCFVGLISMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        2. LDEEIKDAFQNAYLELGGLGERVLGFCHLALPDDQFPEGFQFDTDE VNFPVEKLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        3. LDEELKDAFQNAYLELGGLGERVLGFCHLALPDDQFPDGFQFDTEE VNFPTENLCFVGLISMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        4. LDEELKDAFQNAYLELGGLGERVLGFCHLLLDDEQFPDGFSFDTED VNFPTEGLCFVGLISMIDPPRAAVPDRVGKCRSAGIKVIMVTGDHPITAKAIAK
        5. LDDEIKESFQNAYLELGGLGERVLGFCHFYLPDEQFPEGFQFDADD VNFPTENLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        6. LDKEMQDAFQNAYMELGGLGERVLGFCQLNLPSGKFPRGFKFDTDE LNFPTEKLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        7. LDEEMKEAFQNAYLELGGLGERVLGFCHLYLPPDKFPRGFRFDADE VNFPTSDLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        8. LDEEMKEAFQNAYLELGGLGERVLGFCHYYLPEEQYPQGFAFDCDD VNFTTDNLCFVPLMSMIGPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
        9. LDEEMKEAFQNAYLELGGLGERVLGFCHFYLPEEQYPKGFAFDCDD VNFATDNLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
       10. LNEEMKEAFQNAYLELGGLGERVLGFCHLKLSTSKFPEGYPFDVEE PNFPITDLCFVGLMSMIDPPRAAVPDAVGKCRSAGIKVIMVTGDHPITAKAIAK
       11. LDEEMKEAFNNAYMELGGLGERVLGFCDFMLPSDKYPNGFKFNTDD INFPIDNLRFVGLMSMIDPPRAAVPDAVAKCRSAGIKVIMVTGDHPITAKAIAK
       12. MTEELKEAFNNAYMELGGLGERVLGFCDYLLPLDKYPHGFAFNADD ANFPLTGLRFAGLMSMIDPPRAAVPDAVAKCRSAGIKVIMVTGDHPITAKAIAK
       13. LDNHMKECFNNAYMELGGMGERVLGFCDFELPSDQYPRGYVFDADE PNFPISGLRFVGLMSMIDPPRAAVPDAVSKCRSAGIKVIMVTGDHPITAKAIAR
       14. LKDDVIEIYNKAYDELGGLGERVLGFCHYYLPVDQYPKGFLFKTEEEQNFPLEGLCFLGLLSMIDPPRAAVPDAVSKCRSAGIKVIMVTGDHPITAKAIAK
consensus            AY ELGG GERVLGFC   L     P G  F       NF    L F  L SMI PPRAAVPD V KCRSAGIKVIMVTGDHPITAKAIA

        1. GVGIISEGNETVEDIAARLNIP   VSQVNPRDAKACVVHGSDLKDMTSEQLDDILKYHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        2. GVGIISDGNETVEDIAARLNIP   VSQVNPRDAKACVVHGSDLKDMTSEQLDDILLHHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        3. GVGIISEGNETVEDIAARLNIP   VNQVNPRDAKACVIHGTDLKDMTEEQIDDILRHHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        4. GVGIISEGNETVEDIAARLNIP   VNQVNPRDAKACVIHGTDLKDMNADQIDDILRHHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        5. GVGIISEGNETVEDIAARLNIP   VNEVNPRDAKACVVHGGDLKDLSCEQLDDILKYHTEIVFARTSPQQKLIIVEGCQRTGAIVAVTGDGVNDSPALKK
        6. GVGIISEGNETVEDIAARLNIP   MSQVNPREAKACVVHGSDLKDMTSEQLDEILKNHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        7. GVGIISEGNETVEDIAARLNIP   VSQVNPREAKACVVHGSDLKDMTAEQLDEILRNHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        8. GVGIISEGNETVEDIAARLNIP   VSQVNPRDAKACVIHGTDLKDFTSEQIDEILQNHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
        9. GVGIISEGNETVEDIAARLNIP   VSQVNPRDAKACVIHGTDLKDMSSEQIDEILQNHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
       10. GVGIISEGNETVEDIAARLNIP   VNQVNPRDAKACVVHGTDLKDLSHENLDDILHYHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
       11. SVGIISEGNETVEDIAQRLNIP   VSEVNPREAKAAVVHGAELRDVSSDQLDEILRYHTEIVFARTSPQQKLIIVEGCQRMGAIVAVTGDGVNDSPALKK
       12. SVGIISEGNETVEDIAARLNIP   VSEVNPRDAKAAVVHGGELRDITPDALDEILRHHPEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
       13. QVGIISEGHETVDDIAARLNIP   VSEVNPRSAQAAVIHGNDLKDMNSDQLDDILRHYREIVFARTSPQQKLIIVEGVQRQGEFVAVTGDGVNDSPALKK
       14. GVGIISEGNECEEDIALRLNIPLEDLSEDQKKSAKACVIHGAKLKDIKNEELDKILCDHTEIVFARTSPQQKLIIVEGCQRQGAIVAVTGDGVNDSPALKK
consensus  VGIIS G E   DIA RLNIP             A A V HG  L D      D IL    EIVFARTSPQQKLIIVEG QR G  VAVTGDGVNDSPALKK

        1. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLIFIIANIPLPLGTVTILCIDLGTDMVPAISLAYEQAE
        2. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLIFIIANIPLPLGTCTILCIDLGTDMVPAISLAYEQAE
        3. ADIGIAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLIFIIANIPLPLGTVTILCIDLGTDMVPAISLAYEQAE
        4. ADIGIAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLIFIIADIPLPLGTVTILCIDLGTDMVPAISLAYEQAE
        5. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLFFIIANIPLPLGTVTILCIDLGTDMLPAISLAYEAAE
        6. ADIGIAMGISGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLLFIIANIPLPLGTVTILCIDLGTDMVPAISLAYEAAE
        7. ADIGIAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLLFIIANIPLPLGTVTILCIDLGTDMVPAISLAYEAAE
        8. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLLFIMANIPLPLGTITILCIDLGTDMVPAISLAYEAAE
        9. ADIGVAMGIRGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLLFIMANIPLPLGTITILCIDLGTDMVPAISLAYEAAE
       10. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEITPFLVFIIANVPLPLGTVTILCIDLGTDMVPAISLAYERAE
       11. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIAYTLTSNIPEISPFLASILCDIPLPLGTVTILCIDLGTDMVPAISLAYDHAE
       12. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIVYTLTSNIPEISPFLLFILFDIPLPLGTVTILCIDLGTDMVPAISLAYEEAE
       13. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNIKKSIAYTLTSKIPELSPFLMYILFDLPLAIGTVTILCIDLGTDVVPAISMAYEGPE
       14. ADIGVAMGIAGSDVSKQAADMILLDDNFASIVTGVEEGRLIFDNLKKSIVYTLTSNIPEISPFLMFILFGIPLPLGTITILCIDLGTDMVPAISLAYEKAE
consensus  ADIG AMGI GSDVSKQAADMILLDDNFASIVTGVEEGRLIFDN KKSI YTLTS IPE  PFL  I    PL  GT TILCIDLGTD  PAIS AY   E

        1. SDIMKRQPRNPKTDKLVNERLISMAYGQIGMIQALGGFFTYFVILAENGFLPIHLLGLRVDWDDRWINDVEDSYGQQWTYEQRKIVEFTCHTAFFVSIVVV
        2. SDIMKRQPRNPKTDKLVNERLISMAYGQIGMIQALGGFFTYFVIMAENGFLPSGLVGIRLQWDDRWINDVEDSYGQQWTFEQRKIVEFTCHTAFFVSIVVV
        3. SDIMKRQPRNPKTDKLVNERLISMAYGQIGMIQALGGFFTYFVILAENGFLPWTLLGIRVNWDDRWTNDVEDSYGQQWTYEQRKIVEFTCHTSFFISIVVV
        4. SDIMKRHARNPKKDKLVNERLISMAYGQIGMIQALGGFFAYFVILAENGFLPSTLLGIRVAWEDRYVNDVEDSYGQQWTYEQRKIVEFTCHTAFFVSIVVV
        5. SDIMKRQPRNPKTDKLVNERLISIAYGQIGMIQALAGFFTYFVILAENGFLPPRLLGIRMNWDDKYINDLEDSYGQQWTYEQRKIVEFTCHTAFFTSIVIV
        6. SDIMKRQPRNSQTDKLVNERLISMAYGQIGMIQALGGFFTYFVILAENGFLPSRLLGIRLDWDDRTMNDLEDSYGQEWTYEQRKVVEFTCHTAFFASIVVV
        7. SDIMKRQPRNPRTDKLVNERLISMAYGQIGMIQALGGFFTYFVILAENGFLPARLLGVRLAWDDRSTNDLEDSYGQEWTYEQRKVVEFTCHTAFFASIVVV
        8. SDIMKRQPRNPRTDKLVNERLISMAYGQIGMIQALGGFFSYFVILAENGFLPGNLVGIRLNWDDRTVNDLEDSYGQQWTYEQRKVVEFTCHTAFFVSIVVV
        9. SDIMKRQPRNPRSDKLVNERLISMAYGQIGMIQALGGFFSYFVILAENGFLPSCLVGIRLSWDDRTINDLEDSYGQQWTYEQRKVVEFTCHTAFFVSIVVV
       10. SDIMKRQPRNPKTDKLVNERLISMAYGQIGMIQALGGFFSYFVILAENGFLPIDLIGIREKWDELWTQDLEDSYGQQWTYEQRKIVEYTCHTSFFVSIVIV
       11. ADIMKRPPRDPFNDKLVNSRLISMAYGQIGMIQAAAGFFVYFVIMAENGFLPKKLFGIRKMWDSKAVNDLTDSYGQEWTYRDRKTLEYTCHTAFFISIVVV
       12. SDIMKRRPRNPVTDKLVNERLISLAYGQIGMIQASAGFFVYFVIMAECGFLPWDLFGLRKHWDSRAVNDLTDSYGQEWTYDARKQLESSCHTAYFVSIVIV
       13. ADP  RKPRDPVKEKLVNERLISMAYGQIGVMQAFGGFFTYFVIMGECGFLPNRLFGLRKWWESKAYNDLTDSYGQEWTWDARKQLEYTCHTAFFISIVIV
       14. SDIMKRHPRNPIRDKLVNERLISLAYGQIGMMQATAGFFTYFIILAENGFLPSYLFGLRSQWDDMSNNNLLDSFGSEWTYFQRKEIELTCQTAFFTTIVVV
consensus   D   R  R     KLVN RLIS AYGQIG  QA   GFF YF  I   E GFLP  L G R  W           DS G  WT    RK  E   C T   F   IV V

        1. QWADLVICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMGVALRMYPLKPTWWFCAFPYSLLIFVYDEVRKLIIRRRPGGWVEKETYY (0)
        2. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPTWWFCAFPYSLLIFLYDEIRKLIIRRNPGGWVERETYY (0)
        3. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPTWWFCAFPYSLIIFIYDEVRKLIIRRSPGGWVEKESYY (0)
        4. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPTWWFCAFPYSLLIFIYDEVRKLILRRSPGGWVEKETYY (0)
        5. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPNWWFCAFPYSLLIFIYDEIRKLILRRNPGGWMERETYY (0)
        6. QWADLIICKTRRNSVFQQGMKNKILIFGLLEETALAAFLSYCPGMGVALRMYPLKVTWWFCAFPYSLLIFIYDEVRKLILRRYPGGWVEKETYY (0)
        7. QWADLIICKTRRNSVFQQGMKNKILIFGLLEETALAAFLSYCPGMGVALRMYPLKVTWWFCAFPYSLLIFAYDEVRKLILRRYPGGWVEKETYY (0)
        8. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPSWWFCAFPYSFLIFVYDEIRKLILRRNPGGSVEKETYY (0)
        9. QWADLIICKTRRNSVFQQGMKNKILIFGLFEETALAAFLSYCPGMDVALRMYPLKPSWWFCAFPYSFLIFVYDEIRKLILRRNPGGWVEKETYY (0)
       10. QWADLIICKTRRNSIFQQGMKNKILIFGLFEETALAAFLSYTPGTDIALRMYPLKPSWWFCAFPYSLIIFLYDEARRFILRRNPGGWVEQETYY (0)
       11. QWADLIICKTRRNSIFQQGMRNWALNFGLVFETVLAAFLSYCPGMEKGLRMYPLKLVWWFPAIPFALAIFIYDETRRFYLRRNPGGWLEQETYY (0)
       12. QWADLIISKTRRNSVFQQGMRNNILNFALVFETCLAAFLSYTPGMDKGLRMYPLKINWWFPALPFSFLIFVYDEARKFILRRNPGGWVEQETYY (0)
       13. QWTDLIICKTRRLSLFQQGMKNGTLNFALVFETCVAAFLSYTPGMDKGLRMYPLKIWWWFPPMPFSLLILVYDECRKFLMRRNPGGFLERETYY (0)
       14. QWADLIISKTRRLSLFQQGMTNWFLNFGLFFETALAAFLQYTPGVNTGLRLRPMNFTWWLPGLPFSLLIFVYDEIRRYLLRKNPGGWVEKETYY (0)
consensus  QW DL  I KTRR S FQQGM N   L F L   ET   AAFL  Y PG     LR  P      WW     P      I    YDE R      R  PGG   E E YY
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Appendix C16(b) (Continued)

EF-1α

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    1. (1) GKEKTHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAEMGKGSFKYAWVLDKLKAERERGITIDISLWKFETSKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIVAAGVGEFEAGISKNGQTREHALLAYTLGVKQLIVGVN
    2. (1) GKEKTHIKIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAEMGKGSFKYAWVLDKLKAERERGITIDISLWKFETSKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIVAAGVGEFEAGISKNGQTREHALLAYTLGVKQLIVGIN
    3. (1) GKEKTHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAEMGKGSFKYAWVLDKLKAERERGITIDISLWKFETTKYYITIIDAPGHRDFIKNMITGTSQADCAVLIVAAGVGEFEAGISKNGQTREHALLAYTLGVKQLIVGVN
    4. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAEMGKGSFKYAWVLDKLKAERERGITIDISLWKFETGKYYITIIDAPGHRDFIKNMITGTSQADCAVLIVAGGVGEFEAGISKNGQTREHALLAFTLGVKQLIIGVN
    5. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAEMGKGSFKYAWVLDKLKAERERGITIDISLWKFETGKFYITIIDAPGHRDFIKNMITGTSQADCAVLIVAGGVGEFEAGISKNGQTREHALLAFTLGVKQLIIGVN
    6. (1) GKEKTHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGIQIDIALWKFETPKYYITIIDAPGHRDFIKNMITGTSQADCAVLVVACGTGEFEAGISKNGQTREHALLAQTLGVKQMIVACN
    7. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGITIDIALWKFETAKYYVTIIDAPGHRDFIKNMITGTSQADCAVQIDAAGTGEFEAGISKNDQTREHALLAFTLGVKQLIVGVN
    8. (1) GKEKTHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGITIDIALWKFETSKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIVAAGTGEFEAGISKNGQTREHALLAFTLGVKQLIVGVN
    9. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGITIDIALWKFETSKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIDAAGTGEFEAGISKNGQTREHALLAFTLGVKQLIVGVN
   10. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGITIDIALWKFETAKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIVAAGIGEFEAGISKNGQTREHALLAFTLGVKQLIVGVN
   11. (1) GKEKIHINIVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAQEMGKGSFKYAWVLDKLKAERERGITIDIALWKFETAKYYVTIIDAPGHRDFIKNMITGTSQADCAVLIVAAGVGEFEAGISKNGQTREHALLAYTLGVKQLIVGVN
   12. (1) GKEKSHINVVVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEAAELGKGSFKYAWVLDKLKAERERGITIDIALWKFETPKYQVTVIDAPGHRDFIKNMITGTSQADCAILIIAGGVGEFEAGISKDGQTREHALLAFTLGVRQLIVAVN
consensus      GKEK HI  VVIGHVDSGKSTTTGHLIYKCGGIDKRTIEKFEKEA E GKGSFKYAWVLDKLKAERERGI IDI LWKFET K   T IDAPGHRDFIKNMITGTSQADCA    A G GEFEAGISK  QTREHALLA TLGV Q I   N

    1. KMDSTE (2) YSQKRYEEIVKEVSTYIKKIGYNPDTVAFVPISGWNGDNMLEPSANMPWFKGWKVTRKDGNASGTTLLEALDCILPPTRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGVLKPGMVVTFAPVNVTTEVKSVEMHHEALSEALPGD
    2. KMDSTE (2) YSQKRYEEIVKEVSTYIKKIGYNPDTVAFVPISGWNGDNMLEPSPNMPWFKGWKITRKEGSGSGTTLLEALDCILPPSRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGVIKPGMVVTFAPVNVTTEVKSVEMHHEALTEAVPGD
    3. KMDSTE (2) YSEKRYDEIVKEVSAYIKKIGYNPATVPFVPISGWHGDNMLEPSPNMPWFKGWKVERKEGNASGVSLLEALDTILPPTRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGILRPGMVVTFAPVNITTEVKSVEMHHEALSEALPGD
    4. KMDSTE (2) FSQKRFEEITKEVSAYIKKIGYNPATVPFVPISGWHGDNMLEASTNMPWFKGWKIERKEGNASGITLLEALDCIIPPQRPTNKPLRLPLQDVYKIGGIGTVPVGRVETGVLKPGMIVTFAPSNVTTEVKSVEMHHEALVEALPGD
    5. KMDSTE (2) FSQKRFEEITKEVSAYIKKIGYNPATVPFVPISGWHGDNMLEASTNMPWFKGWKIERKEGNASGVTLLEALDCIIPPQRPTAKPLRLPLQDVYKIGGIGTVPVGRVETGVLKPGMIVTFAPSNVTTEVKSVEMHHEALQEALPGD
    6. KMDSTD (2) FSEARFGEVTTEVSNYIKKIGYNPKSIPFVPISGFNGDNMLEPSANMPWFKGWSVERKEGTMTGKTLLEALDSVVPPQRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGILKPGMIVTFAPQNLTTEVKSVEMHHEALQEALPGD
    7. KMDSSE (2) YSEARYEEIKKEVSSYIKKVGYNPAAVAFVPISGWHGDNMLEPSTNMPWFKGWEVGRKEGNADGKTLVDALDAILPPARPTDKALRLPLQDVYKIGGIGTVPVGRVETGVLKPGTVVVFAPANITTEVKSVEMHHEALQEAVPGD
    8. KMDSTE (2) YSEPRFEEIKKEVSSYIKKIGYNPAAVAFVPISGWHGDNMLEPSTKMPWFKGWQVERKEGKADGKSLIEALDAILPPARPTDKPLRLPLQDVYKIGGIGTVPVGRVETGVLKPGTIVVFAPANITTEVKSVEMHHEALQEAVPGD
    9. KMDSTE (2) YSEARYEEIKKEVSSYIKKIGYNPASVAFVPISGWHGDNMLEPSEKMPWFKGWSVERKEGKAEGKCLIDALDAILPPQRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGLLKPGMVVNFAPVNLVTEVKSVEMHHEALTEAMPGD
   10. KMDMTD (2) YSEARFEEIKKEVSSYIKKIGYNTASVAFVPISGWHGDNMLEPSPKTPWYKGWKVERKDGNADGKTLIEALDAILPPSRPTDKALRLPLQDVYKIGGIGTVPVGRVETGILKPGMLVTFAPAALTTEVKSVEMHHEALTEALPGD
   11. KMDSTE (2) FSEARFEEIKKEVSAYIKKIGYNPAAVAFVPISGWHGDNMLEASDRLPWYKGWNIERKEGKADGKTLLDALDAILPPSRPTEKPLRLPLQDVYKIGGIGTVPVGRVETGIIKPGMIVTFAPANITTEVKSVEMHHESLEQASPGD
   12. KMDSVK (0) WDESRFQEIVKETSNFIKKVGYNPKTVPFVPISGWNGDNMIEATTNAPWYKGWEKETKAGVVKGKTLLEAIDAIEQPSRPTDKPLRLPLQDVYKIGGIGTVPVGRVETGVIKPGMVVTFAPAGVTTEVKSVEMHHEQLEQGVPGD
consensus  KMD              R E   E S  IKK GYN     FVPISG  GDNM E     PW KGW    K G   G L   A D    P RPT K LRLPLQDVYKIGGIGTVPVGRVETG   PG  V FAP     TEVKSVEMHHE L     PGD

    1. NVGFNVKNVSVKDVRRGNVAGDSKNDPPMEAAGFTAQVIILNHPGQISAGYAPVLDCHTAHIACKFAELKEKIDRRSGKKLEDGPKFLKSGDAAIVDMVPGKPMCVESFSDYPPLGRFAVRDMRQTVAVGVIKAVDKKAAGAGKVTKSAQKAQ (3)
    2. NVGFNVKNVSVKDVRRGNVAGDSKIDPPMEAGSFTAQVIILNHPGQIGAGYAPVLDCHTAHIACKFAELKEKIDRRSGKKLEDNPKFLKSGDAAIVDMIPGKPMCVESFSDYPPLGRFAVRDMRQTVALGVIKAVEKKAAGSGKVTKSAQKAA (3)
    3. NVGFNVKNVSVKDIRRGNVCGDSKADPPQEAAQFTSQVIILNHPGQISAGYSPVIDCHTAHIACKFAELKEKIDRRSGKKLEDNPKSLKSGDAAIVEMVPGKPMCVESFSQYPPLGRFAVRDMRQTVAVGVIKNVEKKSGGAGKVTKSAQKAQ (4)
    4. NVGFNVKNISVKDIRRGNVAGDSKNDPPMQAGSFTAQVIILNHPGQISAGYAPVLDCHTAHIACKFAELKQKIDRRSGKKLEDDPKFLKSGDAAIVEMIPGKPMCVETFSDYPPLGRFAVRDMRQTVAVGVIKGVDKKLASSGKVTKSAAKAG (2)
    5. NVGFNVKNISVKDIRRGNVAGDSKNDPPMQAGSFTAQVIILNHPGQISAGYAPVLDCHTAHIACKFAELKQKIDRRSGKKLEDDPKFLKSGDAAIVEMIPGKPMCVESFSDYPPLGRFAVRDMRQTVAVGVIKGVDKKAASSGKVTKSAVKAG (2)
    6. NVGFNVKNISIKDIRRGSVASDSKNDPAKETKMFTAQVIIMNHPGQISAGYTPVLDCHTAHIACKFAELKEKVDRRSGKKVEDNPKSLKSGDAGIIDLIPTKPLCVETFTEYPPLGRFAVRDMRQTVAVGVIKNVDKSEG VGKVQKAAQKAG (6)
    7. NVGFNVKNVSVKELRRGYVAGDSKANPPKGAADFTAQVIVLNHPGQIANGYTPVLDCHTAHIACKFAEILEKVDRRSGKTTEENPKFIKSGDAAIVNLVPSKPLCVEAFQEFPPLGRFAVRDMRQTVAVGVIKAVNFKDASGGKVTKAAEKAT (4)
    8. NVGFNVKNVSVKELRRGYVAGDSKNNPPKGAADFTAQVIVLNHPGQISNGYTPVLDCHTAHIACKFAEIKEKVDRRTGKSTEVNPKSIKSGDAAIVNLVPSKPLCVESFQEFPPLGRFAVRDMRQTVAVGVIKAVNFKEAGGGKVTKAAEKAT (4)
    9. NVGFNVKNVSVKELRRGYVAGDSKNNPPRGAADFTAQVIVLNHPGQIANGYTPVLDCHTAHIACKFSEIKEKYDRRTGGTTEDGPKAIKSGDAAIIVLVPSKPLCVESFQEFPPLGRFAVRDMRQTVAVGVIKSVNFKETTSGKVTKAAEKAQ (3)
   10. NVGFNVKNISVKELRRGYVAGDSKNQPPRGAADFTAQVIVLNHPGQISNGYTPVLDCHTAHIACKFAEIKEKCDRRTGKTTEENPKSIKSGDAAIVMLQPTKPMCVEAFQEFPPLGRFAVRDMRQTVAVGVIKSVTFKDT QGKVTKAAEKAQ (3)
   11. NVGFNVKNVSVKELRRGYVASDSKNNPARGSQDFFAQVIVLNHPGQISNGYTPVLDCHTAHIACKFAEIKEKCDRRTGKTTEAEPKFIKSGDAAMITLVPSKPLCVEAFSDFPPLGRFAVRDMRQTVAVGVIKSVNFKDPTAGKVTKAAEKAG (3)
   12. NVGFNVKNVSVKEIRRGNVCGDAKNDPPKGCASFNATVIVLNHPGQISAGYSPVLDCHTAHIACRFDELLEKNDRRSGKKLEDHPKFLKSGDAALVKFVPSKPMCVEAFSEYPPLGRFAVRDMRQTVAVGVIKSVDKTEK AAKVTKAAQKAA (2)
consensus  NVGFNVKN S K  RRG V  D K  P     F  VI  NHPGQI  GY PV DCHTAHIAC F E   K DRR G   E  PK  KSGDA      P KP CVE F   PPLGRFAVRDMRQTVA GVIK V          KV K A KA
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Appendix C17(b)

aldolase

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       1. (7) LTPEQKKELSDIAHRIVAPGKGILAADESTGSIAKRLQSIGTENTEENRRFYRQLLLTADDRVNPCIGGVILFHETLYQKADDGRPFPQVIKSKGGVVGIKVDKGVVPLAGTNGETTT
       2. (7) LTQEQKKELSEIAQSIVANGKGILAADESVGTMGNRLQRIKVENTEENRRQFREILFSVDSSINQSIGGVILFHETLYQKDSQGKLFRNILKEKGIVVGIKLDQGGAPLAGTNKETTI
       3. (7) LSPEQKKALSDIAQRIVASGKGILAADESVGTMGNRLQRINVENTEENRRAFREILFSSDASISKSIGGVILFHETLYQKDSSGKPFPAIIKEKGMVVGIKLDAGTAPLAGTNGETTI
       4. (7) LSAEQKKELSDIALRIVAPGKGILAADESVGSMAKRLSQIGVENTEENRRLYRQVLFSADDRVKKCIGGVIFFHETLYQKDDNGVPFVRTIQDKGIVVGIKVDKGVVPLAGTDGETTT
       5. (1) LTAEQKKELSDIALAIVAPGKGILAADESVGSMAKRLNQIGVENTEENRRLYRQILFSADSRVKKCIGGVIFFHETIYQKADDGIPFVQMIKDKGIVVGIKVDKGVVPLAGTDGETTT
       6. (7) LSAEQKKELADIAQRIVAPGKGILAADESVGSMDKRLGGIGVDNTEENRRLYRQLLFKGDERMQECIGGVIFFHETMYQQGDCGTDFVKMIKDKGIVVGIKVDKGVVPLAGTNGETTT
       7. (7) PSKELQDELREIAQKIVAPGKGILAADESGPTMGKRLQDIGVENTEDNRRAYRQLLFSTDPKLAENISGVILFHETLYQKADDGTPFAEILKKKGIILGIKVDEGVVPLFGSEDEVTT
       8. (3) YCGKYKDELIKNAAYIGTPGKGILAADESTGTIGKRLSSINVENVEENRRALRELLFCCPG ALQYISGVILFEETLYQKTKDGKPFVDVLKEGGVLPGIKVDKGTIEVVGTDKETTT
consensus             L   A  I   GKGILAADES      RL  I   N E NRR  R L           I GVI F ET YQ    G  F       G   GIK D G     G   E T

       1. QGLDGLSERCAQYKKDGADFAKWRCVLKIGEHTPSALAIMENANVLARYASICQQNGIVPIVEPEILPDGDHDLKRCQYVTEKVLAAVYKALSDHHIYLEGTLLKPNMVTPGHACTQKFSH
       2. QGLDGLSERCAQYKKDGVDFGKWRAVLRIADQCPSSLAIQENANALARYASICQQNGLVPIVEPEVIPDGDHDLEHCQYVTEKVLAAVYKALNDHHVYLEGTLLKPNMVTAGHACTKKYTP
       3. QGLDKLAERCAQYKKDGADFGKWRAVLKISSTTPSQLAIQENANTLARYASICQQNGLVPIVEPEVLPDGDHDLQRCQYVTEKVLAAVYKALNDHHVYLEGTLLKPNMVTAGHSCPKKYTP
       4. QGLDGLSERCAQYKKDGADFAKWRCVLKISERTPSALAILENANVLARYASICQQNGIVPIVEPEILPDGDHDLKRCQYVTEKVLAAVYKALSDHHVYLEGTLLKPNMVTPGHACPIKYTP
       5. QGLDGLSERCAQYKKDGADFAKWRCVLKISDNTPSALAIMENANVLARYASICQQNGIVPIVEPEILPDGDHDLKRCQYVTEKVLAAVYKALSDHHVYLEGTLLKPNMVTPGHSCPTKYSP
       6. QGLDGLSERCAQYKKDGADFAKWRSVLKISETTPSPLAILENANVLARYASICQQNGIVPIVEPEILPDGEHDLKRCQYITEKVLAAVYKALSDHHVYLEGTLLKPNMVTAGHACPTKYSA
       7. QGLDDLAARCAQYKKDGCDFAKWRCVLKIGKNTPSYQSILENANVLARYASICQSQRIVPIVEPEVLPDGDHDLDGAQKVTETVLAAVYKALSDHHVYLEGTLLKPNMVTAGQSAK KNTP
       8. QGHDDLGKRCAKYYEAGARFAKWRAVLKIGPNEPSQLAIDLNAQGLARYAIICQENGLVPIVEPEILVDGPHDIDRCAYVTETVLAACYKALNEHHVLLEGTLLKPNMVTPGSDSK KVTP
consensus QG D L  RCA Y   G  F KWR VL I    PS   I  NA  LARYA ICQ    VPIVEPE   DG HD       TE VLAA YKAL  HH  LEGTLLKPNMVT G     K

       1. EEIAMATVTALRRTVPPAVTGITFLSGGQSEEEASINLNAINKCPLLKPWALTFSYGRALQASALKAWGGKKENLKAAQEEYVKRALANSLACQGKYTPSG (7) ESLFVSNHAY (0)
       2. EQVAMATVTALHRTVPAAVPGICFLSGGMSEEDATLNLNAINLCPLPKPWKLSFSYGRALQAVALAAWGGKAANKEATQEAFMKRAMANCQAAKGQYVHTG (7) QSLFTACYTY (0)
       3. QDVAVATVTTLLRTVPAAVPGICFLSGGQSEEEASLNLNAMNQSPLPKPWKLTFSYGRALQASALAAWLGKSENKKAAQEAFCKRAQINSLACRGQYVTSG (7) QSLFTASYTY (0)
       4. EEIAMATVTALRRTVPPAVPGVTFLSGGQSEEEASFNLNAINRCPLPRPWALTFSYGRALQASALNAWRGQRDNAGAATEEFIKRAEVNGLAAQGKYEGSG (7) QSLYIANHAY (0)
       5. EEIAMATVSPLRRTVPPAVPGVTFLSGGQSEEEASINLNAINTCPLFAPWALTFSYGRPLQASALSAWRGQRDNANAATEEFVKRAEVNWLAALGKYEGSG (7) QSLYVANHAY (0)
       6. EEVAMATVTALRRSVPPAVPGVTFLSGGQSEEEATINLNAINNCPLARPWALTFSYGRALQASALNAWRGKKDNEDAATKVFLTRAEANGLAALGKYEHSG (7) QSLYVANHAY (0)
       7. EEIALTTVQALRRTVPAAVTGVTFLSGGQSEEEATVNLSAINNVPLIRPWALTFSYGRALQASVLRAWAGKKENIAAGQNELLKRAKANGDAAQGKYVAGS (5) GSLFVANHAY (0)
       8. EVIAEYTVRTLQRTVPAAVPAVLFLSGGQSEEEATRNLNAMNKLSTKKPWSLSFSFGRALQASTLKAWAGKVENLEKARAAFLARCKANSEATLGTYKGDA (4) ESLHVKDYKY (0)
consensus    A  TV  L R VP AV    FLSGG SEE A  NL A N      PW L FS GR LQA  L AW G   N          R   N  A  G Y           SL      Y
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Appendix C18(b)

Appendix D Comparison of the evolutionary rates between the first (I) and latter (II) periods in the chordate lineages after the separation from arthropods.

Subfamily gene	evolutionary rate (sites / Myr) v_I	v_{II}	v_I/v_{II}
nAChR			
beta3	1.5 E-3	2.2 E-4	6.8
alpha	1.6 E-3	2.6 E-4	6.2
alpha3	1.2 E-3	2.1 E-4	5.7
beta2 *	9.5 E-4	3.2 E-4	3.1
delta	1.5 E-3	5.5 E-4	2.8
gamma (epsilon) *	1.8 E-3	6.3 E-4	2.6
beta	1.3 E-3	5.4 E-4	2.4
(Average	1.4 E-3	3.9 E-4	3.6)
opsin			
rhodopsin **	6.9 E-3	1.9 E-4	36
opsin Red	3.1 E-3	2.7 E-4	11
opsin Green	3.2 E-3	3.6 E-4	8.9
opsin Blue	3.0 E-3	4.5 E-4	6.7
(Average	4.1 E-3	3.3 E-4	12)
mAChR			
m4 *	7.1 E-4	1.3 E-4	5.5
src			
fyn	6.3 E-4	5.6 E-5	11
yes	6.4 E-4	8.3 E-5	7.7
src	6.9 E-4	1.3 E-4	5.3
(Average	6.5 E-4	9.0 E-5	7.2)
FGFR			
FGFR *	8.1 E-4	1.3 E-4	6.2
raf			
raf *	5.2 E-4	9.4 E-5	5.5
CDK2			
CDK2	5.0 E-4	1.1 E-4	4.5
EGF-R			
EGF-R	8.1 E-4	2.1 E-4	3.9
IR			
IGF1R	4.3 E-4	4.2 E-5	10
IR *	2.5 E-4	1.2 E-4	2.1
(Average	3.4 E-4	8.1 E-5	4.2)

Appendix D (continued)

Subfamily gene	evolutionary rate (sites / Myr) v_I	 v_{II}	v_I/v_{II}
erk			
erk *	2.8 E-4	4.0 E-5	7.0
ras			
ras	2.7 E-4	8.8 E-6	31
*rap*1 (*Krev*)			
*rap*1	2.3 E-4	1.5 E-5	15
Gαi			
i1 *	2.7 E-4	3.0 E-5	9.0
i3 *	2.8 E-4	1.0 E-4	2.8
(Average	2.8 E-4	6.5 E-5	4.3)
Gαs			
Gαs *	5.6 E-4	1.1 E-4	5.1
K^+ channel			
MK2 *	3.3 E-4	7.7 E-5	4.3
Na^+ channel			
Na^+ channel	5.7 E-4	3.1 E-4	1.8
SERCA			
SERCA *	3.4 E-4	1.3 E-4	2.6
Na^+ -K^+ pump			
Na^+ -K^+ pump	3.5 E-4	1.9 E-4	1.8
EF-1α			
EF-1α *	2.3 E-4	6.7 E-5	3.4
aldorase			
aldorase C *	4.7 E-4	2.3 E-4	2.0

Note - *, because no fish data were available, the branching point of fish and amphibian was inferred from that of amphibian and mammals, by assuming 400 million years and 350 million years. **, because lamprey data was used, the branching point of bony fish and amphibian was inferred from that of lamprey and bony fish, by assuming 400 million years and 500 million years.

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