**Supplementary Table 2.** The amino acid sequences of SEPP1 (aka SEPP1a) in vertebrate species included in this study and closely related species (fish). The total Sec (**U**) and the Sec content upstream and including the APOER2 binding site (E-CQC----A; shaded in yellow) within the C-terminal domain (SEPP1←APOER2), and the region downstream of the APOER2 binding site (SEPP1APOER2→) are also shown.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Se requirements | Species | Amino acid sequence | TotalSec | SEPP1 ←APOER2 | SEPP1APOER2→ |
| Known Se requirements | Human | MWRSLGLALALCLLPSGGTESQDQSSLCKQPPAWSIRDQDPMLNSNGSVTVVALLQAS**U**YLCILQASKLEDLRVKLKKEGYSNISYIVVNHQGISSRLKYTHLKNKVSEHIPVYQQEENQ  TDVWTLLNGSKDDFLIYDRCGRLVYHLGLPFSFLTFPYVEEAIKIAYCEKKCGNCSLTTL  KDEDFCKRVSLATVDKTVETPSPHYHHEHHHNHGHQHLGSSELSENQQPGAPNAPTHPAP  PGLHHHHKHKGQHRQGHPENRDMPASEDLQDLQKKLCRKRCINQLLCKLPTDSELAPRS**U**  CCHCRHLIFEKTGSAIT**U**QCKENLPSLCS**U**QGLRAEENITESCQ**U**RLPPAA**U**QISQQLIP  TEASAS**U**R**U**KNQAKK**U**E**U**PSN | 10 | 4 | 5 |
| Mouse | MWRSLGLALALCLLPYGGAESQGQSSACYKAPEWYIGDQNPMLNSEGKVTVVALLQAS**U**Y  LCLLQASRLEDLRIKLESQGYFNISYIVVNHQGSPSQLKHSHLKKQVSEHIAVYRQEEDG  IDVWTLLNGNKDDFLIYDRCGRLVYHLGLPYSFLTFPYVEEAIKIAYCEERCGNCNLTSL  EDEDFCKTVTSATANKTAEPSEAHSHHKHHNKHGQEHLGSSKPSENQQPGPSETTLPPSG  LHHHHRHRGQHRQGHLES**U**DTTASEGLHLSLAQRKL**U**RRGCINQLLCKLSKESEAAPSSC  CCHCRHLIFEKSGSAIA**U**QCAENLPSLCS**U**QGLFAEEKVTESCQCRSPPAA**U**QNQPMNPM  EANPN**U**S**U**DNQTRK**U**K**U**HSN | 10 | 4 | 5 |
| Rat | MWRSLGLALALCLLPYGGAESQGQSPACKQAPPWNIGDQNPMLNSXGTVTVVALQAS**U**YL  CLLQASRLEDLRIKLENQGYFNISYIVVNHQGSPSQLKHAHLKKQVSDHIAVYRQDEHQT  DVWTLLNGNKDDFLIYDRCGRLVYHLGLPYSFLTFPYVEEAIKIAYCEKRCGNCSFTSLE  DEAFCKNVSSATASKTTEPSEEHNHHKHHDKHGHEHLGSSKPSENQQPGALDVETSLPPS  GLHHHHHHHKHKGQHRQGHLES**U**DMGASEGLQLSLAQRKL**U**RRGCINQLLCKLSEESGAA  TSSCCCHCRHLIFEKSGSAIT**U**QCAENLPSLCS**U**QGLFAEEKVIESCQCRSPPAA**U**HSQH  VSPTEASPN**U**S**U**NNKTKK**U**K**U**NLN | 10 | 4 | 5 |
| Guinea pig | MWRSLGLALALCLLPGGGTQSQSKSSYCEQPPPWSIGDQNPMQNATGTVTVVALLDAS**U**Y  VCILQASRFEDLRVKLKLEGYSNISYIIVNGPGADARSQYLYLKKHVSDHISVYQQEQHQ  PDIWSRLKGNKDDILIYDRCGRLAYHLRMPYSFLSFPYVEQAIKIVYCVEKCGNCSLKNL  EDDDFCKNVSLAAVTTEAPQKHHHRQIHPPKRGHPYLGSREPEAPDNPVQSLPLGLHNLH  RGQPRQVHSPS**U**DMVPGEGFQPSPQLRKLCPKGCKTQVLCKPPKNSHSAPSSCCCHCRHL  VFEQPGSSVTCQCAENLPSLCSCEGLFGEEKVIESCQCRLPLAP**U**QVSPQQKPTETNPN**U**  S**U**KNMAQK**U**K**U**PSN | 7 | 1 | 5 |
| Pig | MWRGLGLALALCLLSWGGTESQGKSSFCEQPPGWSIKDQDPMLNSYGSVTVVALLQAS**U**Y  LCILQASRLEDLRVKLEKEGYSNISYIVVNHQGIASQLKYVYLKSKVSEHIPVYQQEENQ  TDVWTLLNGNKDDFLIYDRCGLLVYHLGLPYSFLTFPYVEEAIKTVYCENKCGNCSLKTL  KDEDFCKNVYLATEEKTTEAPQPHHHHDHHHHRHHHHHHGHQHLGNGHLSEHPKPEAPDT  PEQPPPSGLHHHHGHKGHQRQGHSEN**U**DMPAGSESLQLSLPQKKL**U**RRGCISQLLCKFPK  NSESALRS**U**C**U**HCRHLIFEKTESAVT**U**QCGENLPSLCS**U**QGLLAEENVIES**U**Q**U**RLPPAA  **U**QASQQLNPAEASTK**U**S**U**KNKAGR**U**K**U**PSN | 14 | 8 | 5 |
| Cow | MWRGLGLALALCLLLTGGTESQGQSSYCKQPPPWSIKDQDPMLNSYGSVTVVALLQAS**U**Y  LCILQASRLEDLRVKLEKEGYSNISYVVVNHQGISSRLKYVHLKNKVSEHIPVYQQEENQ  PDVWTLLNGNKDDFLIYDRCGRLVYHLGLPYSFLTFTYVEDSIKTVYCEDKCGNCSLKAL  EDEDVCKNVFLATKEKTAEASQRHHHPHPHSHPHPHPHPHPHPHPHPHHGHQLHENAHLS  ESPKPDTPDTPENPPPSGLHHHHHRHKGPQRQGHSDNCDTPVGSESLQPSLPQKKL**U**RKR  CINQLL**U**QFPKDSESALSSCCCHCRHLVFEKTGSAIT**U**QCTEKLPSLCS**U**QGLLAEENVI  ES**U**Q**U**RLPPAA**U**QAAGQQLNPTEASTK**U**S**U**KNKAKM**U**K**U**PSN | 12 | 6 | 5 |
| Dog | MWRSLGLALALCLLPWGGAESQGQSSFCKQPPAWSIRDQNPMLNSSGSVTVVALLQAS**U**Y  LCILQASRLEDLRVKLEKEGFLNISYVVVNHQGLSSQLKYMYLKNKVSEHIPVYQQEENQ  TDVWTLLNGKKDDFLIYDRCGRLVYHLGLPYSFLTFPYVEEAIKRAYCEEKCGNCSLTVL  EDEEVCKMVSSGTVESTTEAPQPHPHDHHLHHHHHHHHKHWHRLMPHGNDELSENQQPEE  PDVSEHPAPQGLHRHHKHKDHQRQGHPDN**U**DMPAGSESLQLSVPQNQL**U**RKGCRNQLLCK  LPRDSGLAPSS**U**C**U**H**U**RHLIFEKTGSAIT**U**QCKETLPSLCS**U**QGLWAEENVIES**U**Q**U**RWP  PAA**U**QASQQLRPTEASTN**U**S**U**KYKTKM**U**K**U**LTY | 15 | 9 | 5 |
| Horse | MWRSLGLALALCLLPWGGTESQGQSSFCKQPPAWSIRDQDPMLNSYGSVTVVALLQAS**U**Y  LCLLQASRLEDLRVKLEKEGYSNISYVVVNHQEISARLKYIHLKNKVSEYIAVYQQEENQ  TDIWTLLNGSKDDFLIYDRCGRLVYHLGLPYSFLTFPYVEEAIKIAYCEKKCGNCSLMTL  EDEDFCKTLSLATVEKTTEDSQPHHHHHHQHHHKHGHQHVGNSQLSENQQPEATGAPEHP  PPPGLHHHHKHKGQQRRGHPEN**U**DMPGGESLQLSLPQKKL**U**QKGCINQLLCKMPKDSKLA  PSS**U**C**U**HCRHLIFENTRSAIT**U**QCTENLPSLCS**U**QGLWAEENVIESCQ**U**RLPPAA**U**QPSQ  QLKPTEASTN**U**S**U**KYKAAM**U**K**U**PSN | 13 | 7 | 5 |
| Sheep\*\* | MWRGLGLALALCLLLTGGTESQGQSSYCKQPPAWSIKDQDPMLNSYGSVTVVALLQAS**U**YLCILQASRLEDLRVKLEKEGYSNISYVVVNHQEISSRLKYAHLKNKVSEHIPVYQQEEDQPDVWTLLNGNKDDFLIYDRCGRLVYHLGLPYSFLTFTYVEDSIKTVYCEDKCGNCSLKTQEDEDFCKNVSLATRRKQLRLHSDITITWTPAGTGPEFPGRPTRPHHHHHRHKGHQRQGHSDNCDTPVGSENLQLSLPQKKL**U**RKRCINQLL**U**QFPKDSESALSSCCCHCRHLVFEKTGSAIT**U**QCTENLPSLCS**U**QGLLAEENVIES**U**Q**U**RLPPAA**U**QAAGQQLNPTEASTK**U**S**U**KNKAKM**U**K**U**PSN | 12 | 6 | 5 |
| Zebrafish | MWKALSLTLALCLLVGCSAESETEGARCKLPPEWKVGDVEPMKNALGQVTVVAYLQAS**U**L  FCLEQASKLNDLLLKLEKQGYPNIAYMVVNNREERSQRLHHLLQERLLNITLYAQDLSQP  DAWQAVNAEKDDILVYDRCGRLTYHLSLPYTILIHPHVEEAIKHTYCDRICGECSLESSA  QLEECKKATEEVNKPVEEEPRQDHGHHEQGHHEHQGEAERHRHGHHHPHHHHHHHRGQQQ  VDVDQQVLSQVDFGQVAVETPMMKRP**U**AKHSR**U**KVQYS**U**QQGADSPVAS**U**C**U**H**U**RQLFGG  EGNGRVAGL**U**HCDEPLPAS**U**P**U**QGLKEQDNHIKET**U**Q**U**RPAPPAE**U**ELSQPT**U**V**U**PAGDA  T**U**G**U**RKK | 17 | 11 | 5 |
| Rainbow trout\* | MMWVGLSLLLALCLLPGGGTESEGEGTRCKQPPGWSIGEVEPMKEVMGQVTVVALLQAS**U**  LFCLVQASLLDGLRLKLEGQGLENVTYMVVNHQGEQAQRLHTLLRQKLSENITLYKQQPK  QEDVWQTLAGEKDDFLIYDRCGRLTYHISLPYSILGTPYVENAIKETYCTRVCGDCTYES  KEIPAECNRTVEAKPEGEEKPVTGRETTHGGHGHHHHGHGHNGNRHGHNGNRHGHDHHGE  RGMGRGHGRDHGAERQHQHDTEGLQHGQAHGQLHVGQEHMGQQAVQLGQMPQEGQRGHIM  QNP**U**VKGKSR**U**KAEHS**U**QWKEGSDLSPSSKAS**U**C**U**H**U**RRLFGDGVSNEPIGL**U**HCDEALP  AS**U**Q**U**QGLIGLRET**U**Q**U**RSSLAD**U**QQPQPVM**U**A**U**PLGVES**U**G**U**GLL | 17 | 11 | 5 |
| Channel catfish\*\* | MWRSLSLTLLAALVVGCRGESETDGARCKPAAVWKIGDVEPLKDSLGRVTVVSFLQAS**U**WFCLSQATRLEELRQKLEDAGFVNITYMVVNSQDENSLRVHSLLKKKLSDNITLYKQNPEEPNVWSMAKAEKDDFQIYDRCGRLTHHLSMPYTILSQPHVEEAIRNAYCAAVCGECELERSDQLEECNKTKEEKTEETPKTEEEDHHHHQHHHHHGHHEGHHHRGHHHGHHPHDGVETRGGSNQQHGHEGQVQVQRSQVDLGQAHVGQIDLGQVGINQQVMRRP**U**ASR**U**KFQFMCQQGALSDPSS**U**C**U**H**U**RRLIGLHLNERPL**U**QCDEPLAASCL**U**QGLLTDQNNMET**U**Q**U**RPAHLGD**U**QPAQPI**U**A**U**PAGISQ**U**E**U**QVI | 15 | 8 | 5 |
| Unknown Se requirements | Medaka (*Oryzias latipes*) | MLRLCSALPALLWASLSVLSAEGDSNASKICKPAPYWDIEGHVPMQEHLGNVVVVALLKAT**U**EFCLTQASKIGNLRDKLNRNNITEVSFMIVNELEALSQTMHWKLKKKAPTGVPVYQQSSLQKDVWEILDGDKDDFLIYDRCGLLTFHIVLPNSFLQNADVENAITATYTQDICNCSGNSTLSGGGNNFTRNSSQSHSGSPAGEEHQHQHPHHGHHGHNHGDNHGLHPRGFGHGHDHRHGHHHRHHHGRAETRLQEHQHHASSDQMQHAVQLEQIGQEVVGAPVRP**U**VQETAR**U**KTKFT**U**HMVAGSENEAS**U**C**U**H**U**RRLFGHAGSEQPLGL**U**HCQEELPAS**U**QCRGLTGELANTVIES**U**Q**U**RSPPAA**U**QQPQPAQ**U**A**U**APGAAS**U**A**U**EQL | 16 | 10 | 5 |
| Atlantic salmon (*Salmo salar*) | MKAGLSLLLALCLLPGGGAESEGEGTRCKPPAGWSIGEVEPMKGVMGQVTVVALLQAS**U**LFCLVQASLLDELRLKLEGQGLDNVTYMVVNHQGDQAQHLHTLLSQKLSENIILYKQEPKQADVWQALAGKKDDFLIYDRCGRLTHHIFLPFSILGTPYVENAIKETYCQSICGDCTYESTEIPAECNRMVEVKPEGEEKPVTGGDTPHGGRGHHHHGNGHGHHSKSHGHGHHGESEVGRDHGRGHGVEQQQHQHGAEGLHHGQAHGQLHVGQEEGHIMQRP**U**VKGRAR**U**KAELS**U**HLKEGSDISPSSKVS**U**C**U**H**U**RGLFGNGVSNEPIGL**U**HCDEALPAS**U**Q**U**QGLMGDSTNHIRET**U**Q**U**RSPPAD**U**QQPPPVM**U**A**U**PLVES**U**G**U**GQL | 17 | 11 | 5 |
| Tilapia\* (*Oreochromis niloticus*) | MWAGLSLLLTLCLLHGGGAESEGGGPRCQLPSDWRIGDVEPMKGSVGRVTVVALLQAS**U**L  FCLVQASSRLDGLQQKLERQGLKNVVYMVVNHQGEQSRHLHPLLEAKLSKNIILYKQDGH  QPDVWQTLAGEKDDFFIYDRCGRLTYRISLPYSIIGEGHIEKAIKDTYCKRLCGDCTHES  AEIPEECKDNAGVQPDVPAEQDDTRHDHHHGHGHGHHHGHGHHHGHGHGHHGDNQDVHPH  GHGSDHNNGHHHRNHDGADQTQHGVRPHGHFHEGDMPQTQHHFDLGQIPQEVHNQQVAQE  AHAVIERP**U**LSRKNR**U**KLKYN**U**QGLTGSDNEIKSS**U**C**U**H**U**RRLFGEAGSEQPVGL**U**HCDE  ALPTS**U**R**U**HGLIGDAVNDVRET**U**Q**U**RLPHAA**U**QEPQPAQ**U**A**U**PPGVVS**U**G**U**EQL | 17 | 11 | 5 |
| Common carp\*\*  (Cyprinus carpio) | MWKALSLTLALCLLVGCSAESETDGARCKLPPVWKIGEEEPMKNALGHVTVVAYLQAS**U**LFCLEQASKLNDLLLKFENQGYVNINYMVVNNRDERSQQLHHLLKERLMNITLYAQDLSQPDVWQAVNVEKDDILVYDRCGRLTYHLSLPYTILSHPHVMLAQVDFGQAAIEPPVMKRP**U**AKHTR**U**KVQYS**U**QQGADASATS**U**C**U**H**U**RQLFDDSNGHVAGL**U**HCEGALPAS**U**R**U**QGLKEDNHIRET**U**Q**U**RPAPPAE**U**ELSQKT**U**A**U**PAGDAS**U**V**U**KEK | 17 | 11 | 5 |
| Tetraodon\*\* (*Tetraodon nigroviridis*) | MRACLGLLLTLCMLHGGGAESDGDGPRCQLPPTWKIGDLEPMTGAMGRVTVVALLDAS**U**LFCLVQASRMDSLRQKLENQGLRDVVYMVVNHQGAQARGLHAMLAQRLSEHISLHRQDEALADVWQTLGGNKDDFFIYDRCGRLTHRISLPYAVIGHGHVEKAVKDTYCSSLCGECTHETTETQQECTPKTDTQPQEDTRHECHHRHHQGHQHHGDGHRDHGDNQCTHTQGSGPGHGHGHHGGQGHHQGHDQAGGVAQRPDHLELGQAQHDAAAAKP**U**ESKR**U**KFQFS**U**QWTEASDPDASPKAS**U**C**U**H**U**RRLFGSVGSERPAGL**U**RCSEALPAS**U**Q**U**HGPMADRADARET**U**Q**U**RSPLAV**U**QQPQPAP**U**A**U**PQGAN**U**G**U**EQV | 17 | 11 | 5 |
| Fugu\*\*  (*Takifugu rubripes*) | MRACLGLLLALCMLHGGGAESEGDGPRCQLPPVWKIGDLEPMKEAMGRVTVVALLESS**U**LFCVVQASRMDSLRQRLENQGLRDVVYMVVSHQGAHAPGLHAMLAQKLTEHISLYKQDEALPDVWQTLGGNNNDFFIYDRCGRLTHRISLPYSIIGHGHVERAVKDTYCNSLCGECTHETTETLQECTPKTSALPDNGVAPGAEETGHECHHHGRQHHGDGHRDHGDSQCTHTRGSGRGHGHHHGHGGQGQHEGRVHMGDIPQRPDHLDLGQAQQHDAAATRP**U**ESKR**U**KAQFS**U**QWAEASDTGAFPKAS**U**C**U**H**U**RRLFGDVVGEEPVGL**U**HCSEALPAS**U**Q**U**RGPTGDAVNAVRET**U**Q**U**RSPLAV**U**QQPQPAQ**U**A**U**PQGVN**U**G**U**EQV | 17 | 11 | 5 |
| Cave fish\* (*Astyanax mexicanus*) | MWAGLSVALALCVLAGCSAESDGDGARCKPPAVWKIGDVEPLKDSLGQVTVVAFLQAS**U**L  FCLVQAAKLDSLRLKLEKAGYANITYLVVNSQDENSRRLHSLLEQRLSANITLYGQEPDA  QDIWQIANVMKDDFQIYDRCGRLTHHLSLPYTILSGPHVEEAIRNTYCDRTCGECSMEDH  GGQQRGHHDHEGGSHHQHGHQGQVVISQVQRGQVVHRHTDMGQLGLRHIDLGQVAQEAGN  PQVMNQP**U**AKRSRCKIQYT**U**QQGGLSQTTS**U**C**U**H**U**RRLIGSQSEEPAAL**U**HCEEPLAAS**U**  H**U**QGLAAGDNNVRET**U**Q**U**RSASTAD**U**QLPQPS**U**N**U**PAGSSV**U**E**U**QVV | 16 | 10 | 5 |
| Stickleback  (*Gasterosteus aculeatus*) | MWAYLSLLVALCLLRGGGAESVGGGPHCQLPSPWRIGEVEPMQGTMGRVTVVALLQAS**U**L  FCLVQASRMDGLRQKLESQGLKDVAYMVVNQQGEQARRLHPMLAQRLSVNIDLYKQDEQQ  PDVWKTLGGDKDDFLVYDRCGRLTHHIALPYSIIGQGHVESAIKDAYCKRTCGDCVHESA  TTPEECVEKAVAQPDADAPPVVEDNGGGGGHHGHHHHGHGHHRGHHHGHHHGHHHGGDHG  AGQQAVVHQEHERDGGASHGQHNSALDQMQQQAHIPQMPHGAQAAPVRP**U**VEENAK**U**KSK  HS**U**KLTAGSDNEASLKLS**U**CCH**U**RRLFGEVGSEQPLGL**U**HCDEALPAS**U**Q**U**HGL  TDGVPNNVRET**U**QCRSPPAA**U**QQPEPAP**U**A**U**AAGVS**U**G**U**EQL | 15 | 9 | 5 |

\*Sequence obtained at ensemble.org then searched for Sec and SECIS elements using <http://seblastian.crg.es/>

\*\*Sequences obtained from Lobanov et al. (2008).

Abbreviations; SEPP1←APOER2, Sec residues in the C-terminal domain of full length SEPP1in and upstream of the APOER2 binding site (E-CQC----A; in fish may range between E-CQC--A to E-CQC-----A); SEPP1APOER2→, Sec residues in full length SEPP1upstream of the APOER2 binding site.