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# **SUPPLEMENT FIGURES**

## Supplement Figure 1

```
>sp|P56817| BACE2_HUMAN (Beta-secretase2) Homo sapiens
MAQALPWL LLLWMGAGVLP AHGTQH GIRLPLRSGLGGAPLGLRLPRETDEEPEEPGRRGSFV
EMVDNLRGKSGQGYYVEMTVGSPPTLNILVDTGSSNFAVGAAPHFLHRYYQRQLSSTYR
DLRKGVYVPYTQGWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFINGSNWE GILGLA
YAEIARPDDSLEPFDFSLVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGGSMIIGGIDHSL
YTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRRLPKKVFEAA
VKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRTITLPQQY
LRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFVVFDRARKRIGFAVSACHVHDEFR
TAAVEGPFVTLDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCCLRCLRQ
QHDDFADDISLLK

>sp|Q9Y5Z0| BACE_HUMAN (Betasecretase1) Homo
sapiensMGALARALLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPTGGPGTPAE
RHADGLALALEPALAS PAGAANFLAMVDNLQGD SGRGYLEMLIGTTPPQKLQILVDTGSSN
FAVAGTPHSYIDTYFDTERSSTYRSKGF DVTVKYTQGSWTGFVGEDLVTIPKGFNTSFLVN
IATIFESENFFLPGIKWNGILGLAYATLAKPSSSLETF FDSLVTQANIPNVFSMQMCGAGL
PVAGSGTNGGSLVLGGIEPSLYKGDIIWYTPIKEEWYQIEILKLEIGGQSLNLD CREYNAD
KAIVDSGTLLRLRPQKVFDAVVEAVARASLIPEFSDGFWTGSQLACWTNSETPWSYFPKIS
IYLRDENSRSFRITILPQLYIQPMMGAGLNYECYRFGISPSTNALVIGATVMEGFYVIFD
RAQKRVGFAASPCAIEIAGAAVSEISGPFSTEDVASNCVPAQSLSEPI LWIVSYALMSVCGA
ILLVLIIVLLLLPFRCQRRPRDPEVVNDESSLVRHRWK
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**Supplement Figure 1** Human's BACE1 and BACE2 sequences (query sequences for the analysis)

## Supplement Figure 2

```
>sp|Q2HJ40|Cattle
MAQALPWLLLWMGSGVLP AHGSQP GIRLPLRSGLGGAPLGLRLPRETDEESEEPGRRGSFVEMVDNLRGKSGQ
GYVEMTLGSPPTLNILVDTGSSNF AVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTGKWEDELGTDLV
SIPHGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEIARPDDSLEPFDFSLVKQTHVFNLFSLQLCGAG
FPLNQSEALASVGGSMI IGGIDHSLYMGSLWYTP IRREWYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
TNLRLPKKVF EAAVKSIK AASSTEKFPDGFWLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSFRTITILPQQ
YLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTP
DMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK

>sp|P56819|Rat
MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRSGLAGPPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGS
PPQTLNIVLDTGSSNF AVGAAPHPFLHRYRQLSSTYRDLRKSVYVPYTGKWEDELGTDLV SIPHGPNVTVRANIAAITES
DKFF INGSNWEGILGLAYAEIARPDDSLEPFDFSLVKQTHIPNIFSLQLCGAGFPLNQTEALASVGGSMI IGGIDHSLYTGS
LWYTP IRREWYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGTNLRLPKKVF EAAVKSIK AASSTEKFPDGFWLGEQLVCWQ
AGTTPWNI FPVISLYLMGEVTNQSFRTITILPQQYLRPVEDVATSQDDCYKFAVSQSSTGTVMGAVIMEGFYVVFDRARKRIGF
AVSACHVHDEFRTAAVEGPFVTADMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDIS
LLK

>sp|P56818|Mouse
MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRSGLAGPPLGLRLPRETDEESEEPGRRGSFVEMVDNLRGKSGQ
GYVEMTVGSPPTLNILVDTGSSNF AVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTGKWEDELGTDLV
SIPHGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEIARPDDSLEPFDFSLVKQTHIPNIFSLQLCGAG
FPLNQTEALASVGGSMI IGGIDHSLYTGSWYTP IRREWYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
TNLRLPKKVF EAAVKSIK AASSTEKFPDGFWLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSFRTITILPQQ
YLRPVEDVATSQDDCYKFAVSQSSTGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTA
DMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK

>tr|G3IAK4|ChineseHamster
MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRSGPAGPPLGLRLPRETDEESEEPGRRGSFVEMVDNLRGKSGQ
GYVEMTVGSPPTLNILVDTGSSNF AVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTGKWEDELGTDLV
SIPHGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEIARPDDSLEPFDFSLVKQTHIANVFLSLQLCGAG
FPLNQTEALASVGGSMI IGGIDHSLYTGSWYTP IRREWYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
TNLRLPKKVF EAAVKSIK AASSTEKFPDGFWLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSFRTITILPQQ
YLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTP
DMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK

>sp|Q1KLR6|GuineaPig
MAPALPWLLLWVGSGVLPVHGTQDGIRLPLRSGLAGAPLGLRLPRETDEEPGRRGSFVEMVDNLRGKSGQGY
VEMTVGSPPTLNILVDTGSSNF AVGAAPHPFLHRYRQRSSSTYRDLRKGVYVPYTGKWEDELGTDLV SIP
HGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEIARLQAGFPLNQSEAVASVGGSMI IGGIDHSLYTG
NLWYTP IRREWYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGTNLRLPKKVF EAAVKSIK AASSTEKFPD
GFWLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSFRTITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTV
MGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTATVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAIC
ALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK
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Supplement Figure2 List of BACE1 Sequences

>tr | G5BHK2 | DesertRat  
YVEMTVGSPPTLNILVDTGSSNFVGAAPHPFLHRYRQRSSSTYRDLRKGVYVPYTQGWEGELGTDLVSIP  
HGNPNTVRANIAAITESSDKFFINGSNWEGILGLAYAEIARPDDSLPFFDSLQKTHVPLNLSLQCGAGFPLN  
QSEAVASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLR  
PKKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRTITILPQQYLRPVE  
DVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRQAQRIGFAVSACHVHDEFRTAAVEGPFVTLDMEDCGY  
NIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK

>tr | Q0P4T5 | WesternFrog  
MELVVYARTGSILLVLLPCFLPVTGQVAIKLPLKNCPCGTCSPMAYRAKRSAEKGMELDTNFDLMDNLRGKSGQ  
GYVEMRVGTPPQTLNIVDTGSSNFVGAAPHPFLKRYRHRQSRTYRDRRGGVYVPYTQGWEGELGTDLVT  
IPHGPNVTVTANIAAITDSKFFINGSNWEGILGLAYAEIARPDDELEPFFDSLQKTRVPLNLSLQCGTGFH  
FNESDTSASVGGSMVIGGIDPSLYIGSIWYTPIRKEWYVEVIIVKIEINGQDLHMDCKEYNYDKSIVDSGTTNLR  
RLPKRVFDAAVKSIIKAASSTEKFPDGFWLGEQLVCWQEGTTPWHIFPVISLYLMGEVANQSFRTITILPQQYLRP  
VEDIATAQEDCYKFAVSQSSTGTVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHDYFRTASVEGPFVTFASDLEDC  
GYNTPLQDESALMTTAYVMAGVLCALFMLPLCLMLFQWRCFRCLRARDLADDISLLK

>tr | Q5QHS1 | Chicken  
YVEMTVGSPPKLNILVDTGSSNFVGAAPHPFLRRYRQRQLSSTYRDLRKGVYVPYTQGWEGELGTDLVTIP  
HGNPNTVRANIAAITESSDKFFINGSNWEGILGLAYAEIARPDDSLPFFDSLQKQVPLNLSLQCGAGFSPN  
ETETLASVGGSMIIGGIDRSLYVGDWYTPIRKEWYVEVIIVKLEVNQDLNMDCKEYNYDKSIVDSGTTNLR  
PKKVFEAAVKSIIKTASSTEKFPDGFWLGEQLVCWQVGPWHIFPVISLYLMGEATNQSFRTITILPQQYLGQRN  
VATLKDDELPTGSTTLRPPTATVMGCCIQEGSTVALTGP

>gi | 345799894 | Dog  
MWDAPERSSTYRDLRKGVYVPYTQGWEGELGTDLVSIPHGPNVTVRANIAAITESSDKFFINGSNWEGILGLA  
YAEIARPDDSLPFFDSLQKTHVPLNLSLQCGAGFPLNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRRE  
WYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRPKKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCW  
QAGTTPWNIFPVISLYLMGEVTNQSFRTITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYV  
FDRARKRIGFAVSACHVHDEFRTAAVEGPFITLDMEDCGYNIPTDESTLMTIAYVMAAICALFMLPLCLMVCQ  
WRCLRCLRHQHDDFADDISLLK

>gi | 45387815 | ZebraFish  
MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQGPLTPHSTPAHRSPHGPRARSRAASGISFINMIDNLRG  
KSGQGYIEMAVGSPAQRNLNIVDTGSSNFVGAAPHPFLHRYRHRSLSSSYRDLGRGVYVPYTQGRWEGELGT  
DVVSVPCCPNVSLRANIAAITQSDRFFINGSNWEGILGLAYAEIARPDDELEPFFDSLQKSTVADVFLSLQCG  
AGYNNHSTVSSSTVGGSMIIGVDPSLYVGEWYTPIRREWYVEVIIVRIEVNGQDLNMDCKEYNYDKSIVDS  
GTTNLRPLPKVFAAVKAIEAASSTEQFSGFWLGEQLVCWQAGTTPWHIFPVISLYLMSENQSFRTISILPQ  
QYLRPVEDVASAQEDCYKFAVSQSSTGTVMGAVIMEGFYVVFDRSRKIGFAVSTCHVHDEFRTAAVEGPFHGL  
DLEDCGYNVPQTDESTLMTIAYIMAGICALFMLPLCVMVCQWRFTCCCLQPADGSDDISLLK

>gi | 344293150 | Elephant  
MALVALSWLLLVGSGVLPACHTPHGIRLPLRSLGGAPLGLRPLRDTDEELEDPSRRGSFVEMVDNLRGKSGQ  
GYVEMTVGSPPTLNILVDTGSSNFVGAAPHPFLHRYRQRQLSSTYRDLRKGVYVPYTQGWEGELGTDLVS  
IPHGPNVTVRANIAAITESSDKFFINGSNWEGILGLAYAEIARPDDSLPFFDSLQKTHIPNLSLQCGAGFP  
LNQSEVLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLR  
RLPKKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRTITILPQQYLRP  
VEDVATSQDDCYKFAISQSSTGTVMGAVIMEGFYVVFDRSRKIGFAVSACHVHDEFRTAAVEGPFVTPDMEDC  
GYNIPTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK

## Supplement Figure2 List of BACE1 Sequences



```
>gi | 291383811 |Rabbit
MAPALPWL LLMWGSMLPAQGTQH GIRLPLR SGLGGAPLGLRLPRETEEDPEEPGRRGNFVEMVDNLRGKSGQ
GYYVEMTVGSP PQTLN ILVDTGSSNF AVGAAPHPFLHRY YQRQLSSTYRDLRKG VYVPYTQ GKWEGELGTDLV
SIPHGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEI ARPDDSLEPF FDSL VKQTHV PNLFSLQLCGAG
FPLNQSEVLASVGGSMI IGGIDHSLYTGSLWYTP IRREWY YEVI IVRVE INGQDLKMDCKEYNYDKSIVDSGT
TNLRLPKKVFEAAVKS IKAASSTEKFPDGF WLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSF RITILPQQ
YLRPVEDVATSQDDCYKFAISQSSTGTVMGAV IMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTP
DMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHDDFADDISLLK
>gi | 296216280 |Marmoset

MAQALPWLXLWMGAGVLP AHGTQH GIRLPLR SGLGGAPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQ
GYYVEMTVGSP PQTLN ILVDTGSSNF AVGAAPHPFLHRY YQRQLSSTYRDLRKG VYVPYTQ GKWEGELGTDLV
SIPHGPNVTVRANIAAITESDKFF INGSNWEGILGLAYAEI ARPDDSLEPF FDSL VKQTHV PNLFSLQLCGAG
FPLNQSEVLASVGGSMI IGGIDHSLYTGSLWYTP IRREWY YEVI IVRVE INGQDLKMDCKEYNYDKSIVDSGT
TNLRLPKKVFEAAVKS IKAASSTEKFPDGF WLGEQLVCWQAGTTPWNI FPVISLYLMGEVTNQSF RITILPQQ
YLRPVEDVATSQDDCYKFAISQSSTGTVMGAV IMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTP
DMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQHDDFADDISLLK
```

**Supplement Figure 2** List of BACE1 Sequences

### Supplement Figure 3

```
>sp | Q9Y5Z0 | Human
MGALARALLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPTTPGPGTPAERHADGLALALEPALASPAG
AANFLAMVDNLQGDSDRGYYLEMLIGTPPQKLQILVDTGSSNFAVAGTPHYSYIDTYFDTERSSTYRSKGFVDV
VKYTGQSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFFLPGIKWNGILGLAYATLAKPSSSLETFFDSL
TQANIPNVFMSQMCGAGLPVAGSGTNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEIILKLEIGGQSLNLD
REYNADKAIVDSGTTLRLRPQKVFDAVVEAVARASLIPEFSDGFWTGSQLACWTNSETPWSYFPKISIIYLR
NSSRSFRITILPQLYIQPMMGAGLNYECYRFGISSTNALVIGATVMEGFYVIFDRAQKRVGFAASPCAEIAG
AAVSEISGPFSTEDVASNCVPAQSLSEPIILWIVSYALMSVCGAIIILLVLIIVLILLPLFRQRRPRDPEV
VNDLVRHRWK

>sp | Q6IE75 | Rat
MGALLRALLLPLLAQWLLRAVPVLAPAPFTLPLQVAGANHRASVPLGTPPELPRADGLALALEPARATANF
LAMVDNLQGDSDRGYYLEMLIGTPPQKVRILVDTGSSNFAVAGAPHSYIDTYFDSESSSTYHSGKGFVTV
KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGILGLAYAALAKPSSSLETFFDSL
VAQAKIPDIFSMQMCAGLPVAGSGTNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEIILKLEIGGQSLN
LDCREYNADKAIVDSGTTLRLRPQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWTNSETPWAYFPKIS
IIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRFGISSTNALVIGATVMEGFYVVFDRARRVGF
AVSPCAEIAAGTTVSEISGPFSTEDIASNCVPAQALNEPIILWIVSYALMSVCGAIIILLVLIIVLILL
PLHCRHAPRDPEVNDLVRHRWK

>sp | Q9JL18 | Mouse
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ANFLAMVDNLQGDSDRGYYLEMLIGTPPQKQILVDTGSSNFAVAGAPHSYIDTYFDSESSSTYHSGKGF
VDVTKYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGILGLAYAALAKPSSSLET
FFDSLVAQAKIPDIFSMQMCAGLPVAGSGTNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEIILKLEI
GGQNLNLDCREYNADKAIVDSGTTLRLRPQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWTNSET
PWAYFPKISIIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRFGISSTNALVIGATVMEGFYV
VFDRARRVGFVAVSPCAEIEGTTVSEISGPFSTEDIASNCVPAQALNEPIILWIVSYALMSVCGAII
ILLVLIIVLILLPLHCRHAPRDPEVNDLVRHRWK

>tr | G5C5D1 | DesertRat
QKLQILVDTGSSNFAVAGAPHSYVDSYFDSERSSTYQSKGFVDVTKYTGQSWTGLVGDVVTIPKAFNS
FLVNIAAIFESENFFLPGIKWNGILGLAYASLAKPSSSLETFFDSLVTQAKIPDVFSMQMCAGWPV
ARSGTNGGLVLGGIEPNLYKGDWYTPIKEEWYQIEIILKLEIGGQSLNLDCREYNADKAIVDSGTTL
RLRPQKVFDAVVDVAVARTSLIPEFSDGFWTGAQLACWTNSETPWAYFPKISIIYLRDENASRSFR
ITILPQLYIQPMMGAGLNYECYRFGISSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAEIAGAP
VSEVSGPFSTDGIASNCVPAAPGEPPLWFVSYALLSACGLIILLVLIIVLILLPLCRRRPPRDPEV
INDESSLVRHRWK

>tr | Q5QHS0 | Chicken
HLLNTELSSTYQSQGIEVTVKYSQGSWTGVLGTDVVTIPKIDGRYTIINIATILESENFFLPGVKWH
GILGLAYDTLAKPSSSVETFFDSLVKQAKIPNIFSLQMCAGLPVSGSGTNGGSLVLGGIEPSLYKGN
IWTPIKEEWYQVEIILKLEVGGQNLNLDCREYNADKAIVDSGTTLRLRPQKVFVAVVQAIARTSLI
QEFSSGFWGSQLACWDKTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGENLQCYR
FGISSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEGPFSTTDVASNCVSS
ITFHEPVLWIASYALMSLCGILLIILLIILLIIPRCQHRVTDNDVNDLVRHRWK

>gi | 329663206 | Cattle
MGALARALLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPTTPGPGPPAEPRADGLALALEPAG
GAANFLAMVDNLQGDSDRGYYLEMQIGTPPQKLQILVDTGSSNFAVAGAPHPYIDSYFDAERSSTYR
PKGFVDVTKYTQGSWTGFVGEDVVTIPKGFNSFLVNIATIFESENFFLPGIRWNGILGLAYATLAK
PSSSLETFFDSLVAQAKIPNIFSMQMCAGLPVAGSGTNGGSLVLGGIEPTLYKGDWYTPIKEEWYQ
IEIILKLEIGGQSLNLDCREYNADKAIVDSGTTLRLRPQKVFDAVVEAVARTSLIPEFSEGFWTG
SQLACWTNSETPWSYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRFGISSTNAL
VIGATVMEGFYVVFDRARRVGFVAVSPCAEIAAGPVS EISGPFSTEDIASNCVPAALPLNEPVL
WIVSYTLMSVCGVILLVLIIVLILLPVRCRHHRPRDPEVNDLVRHRWK
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Supplement Figure3 List of all BACE2 Sequences

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>gi | 348508416 | CichlidFish
MAHSTFVSGAFALSIFYGVSYCYFSIPLKIYPGKYNVSSDVNLTSLRRVALKSDGSGLSLASDPTGTVNFLD
MVNNLQGDSDGRGYIEMSIGTPGQKLNILVDTGSSNFVAAAAHQFITHYFNALSSTYSSTGRVAVRYTQG
NWEGLGIDRVSIPRGPNGTITINIAAILSSDGFLLPGINWQIGILGLAYPVLARPDSSVEPFNSVVKQLGIP
DIFSLQMCAGLSASSTDDTTGGSLIMGGAEPFLYRGSVWYTPIIEEWYQVEVLKLEVGDNLNLDCREYNM
DKAIVDSGTTLLRRLPVNVFNALVEAITRSSLIEEFSSGFWEGTKLACWMMGENPWRFFPKLSIYLRAINTSES
FRITILPQLYIQPITDVGTLDCFRFGVSSSTNGMVI GATVMEGFYVVFDRDTRQLGFALSSCAVSDGVALSE
IEGFFSAADVAADCSSGGLKEPLVWVISYALMAVCALALLILLMLILPCRRCGNRNGEITDESSLVRHRK

>gi | 296232194 | Marmoset
LLAQWLLARRPELAPAPFTLPLRVATATNRAAPTSGPGTPAERRADGLALALEPALESAAGSANFLAMVDNL
QGDSGRGYILEMLIGTPPQKLQILVDTGSSNFVAVAGAPHSYIDTYFDMERSSTYRSKGFVDVTVKYTQGSWTGF
VGEDLVITPKGFNSFLVNIATIFESENFFLPGIKWNGILGLAYATLAKPSSSLETFFDLSVKQANIPNVFSM
QMCAGLPVAGSGTNGGSLVLGGIEPSLYKGNIWYTPIKEEWYQIEILKLEIGGQSLNLDCREYNADKAI V
SGTTLLRRLPQKVFDAVVEAVARASLIPEFSDGFWTGSQACWANSERPWSYFPKISIYLRDENSSRSFRLTIL
PQLYIQPMMGAGLNYECYRFGISPSSTNALVIGATVMEGFYVIFDRARKRVGFAASPCAGEQFSHRMGIPDESP
LCECADLEAIPDGT

>gi | 345795292 | Dog
MEDLCAPRQLSSSRLSPVQKQGLDHGHP LDKWTQTYGSQ LSSRRRLQILVDTGSSNFVAVAGAPHSYTD SYFDA
DRSSTYRSKGFVDVTVKYTQGSWTGFVGEDFVTIPKGFNSFLVNIATIFESENFFLPGIKWNGILGLAYAALA
KPSLSLETFFDLSVAQAKIPNVFSMQMCAGLPVAGSGTNGGSLVLGGIEPSLYKGD I WYTPIKEEWYQIEI
LKLEIGGQSLNLDCREYNADKAI VDSGTTLLRRLPQKVFNAVVEAVARTSLIPEFSDGFWTGSQACWNTSETP
WSYFPKISIYLRDENSSQSFRITILPQLYIQPMMGAGLNYECYRFGISPSSTNALVIGATVMEGFYVVFDRARK
RVGFAASPCAEIAGAPVSEISGPFSTDDIASNCVPALPLNEPILWIVSYTLMVCGIILLIILVLLLLLPFRCR
HLPRDPEVVNDESSLVRHRWK

>gi | 213982845 | WesternFrog
MKVPLLAVLLLGAACASANFIFPLKVSPAEMKGAVPVAPATPKGAPGLLLASDPGGQINFFSMVNNLEGDSGR
GYLELLIGTPPQKMNILVDTGSSNFVAVAGALNPDI TFFDLSKSTSYEPLNTQVTVRYTQGSWTGLLGK DVI
SMPKGVNGTFLINIASIFQSENFFLPNINWQIGILGLAYSTLAKPSSSVEPFDFSLVQQENIPNIFSMQMCAG
QPSPGIGINAGSLVLGGIEPSLYQGD I WYTPITEEWYQVEVLKFEVGGQNLNLDCTVYNSDKAIVDSGTTLL
RLPDKVFNAMVD AIVQTSLIQNFAEFWAGLQLACWDKTQDPWNYFPDISIYLRDNTSSRSFRLTLK PQLYIQ
SVLTFQESLNCFRFGISQSASALVIGATVMEGFYVIFDRAEKRVGFAVSSCAEVSGITVSEIAGPFGTSDVSS
NCIARNPLREPI MWIISYSLMSLCCGMILLV L V I L L L L L P N R H R R D D M E T V N D E S S L V Q H R W K

>gi | 348556383 | Guineapig
MGALARALLLPXVAQWLLLRAATAPAPFTLXPXVAIATARPASPTPVPGTPALPRADGLALALEPAGAAANFL
AMVDNLQGDSDGRGYILEMLIGTPPQKLQILVDTGSSNFVAVAGAPHPYVDSYFDVERSSTYRSKGFVDVTVKYTQ
GSWTGFVGEDLVITIPRAFNSFLANVATIFESENFFLPGIKWNGILGLAYATLAKPSSSLETFFDLSLVTQAKI
PDIFSMQMCAGLPVRSRGTNGGSLVLGGIEPSLYKGD I WYTPIKEEWYQIEILKLEIGGQSLNLDCREYNA
DKAIVDSGTTLLRRLPQKVFDAVDAVARTSLIPEFSDGFWTGAQLACWANSERPWAYFPKISIYLRDENSSRS
FRITILPQLYIQPMMGAGLSYECYRFGISPSSTNALVIGATVMEGFYVVFDRARRRVGFAVSPCAETAGVPLSE
VSGPFSTDGIASNCVPSPLNEPVLWVVS YALMSSCGLILLV L I V L L L L P C R C R H A P R D P E V I N D E S S L V R H R
W K

>gi | 54400484 | ZebraFish
MRLYGLLLLSTLFWKSHSVFKIPLNIFAGKFNASVQLDLRPLQKNEAAAKSGLSLASDPAGIVNFLDMINNLK
GDSGRGYMQMIIGTPGQTLN I L V D T G S S N F V A V A A A H P Y I T H Y F N R A L S S T Y Q S T E R A V A V K Y T Q G E W E G E L
G T D L I T I P E G P S G A I T I N I A A I L T S E G F F L P G I N W Q I G I L G L A Y P L L A R P D P S V E P F F N S V V R Q T G I P D V F S L Q
M C G A G V P A S T T G D P A G G S L I M G V E P T L H R G P I W Y T P V L E E W Y Y Q V E V L K L E V G D Q N L N L D C K E Y N S D K A I V D
S G T T L L R L P A N V F T A V V D T I M Q T S L I D D F S A G F F D G T K L A C W M R G E S P W R F F P K V S I Y L R G T N T S Q S F R I T I L
P Q V R I V P

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**Supplement Figure 3** List of all BACE2 Sequences

>gi | 147903717 | AfricanFrog  
MKVPLVRLLLCAAACASNKFIVPLNVSPAIEIKGTLPVAPATPKDKPGLLLASDPGGTINFFSMVDNLAGDSG  
RGYYLELLIGSPPQKVNILVDTGSSNFAVAGSPNPDVNTFFDSKLSYSTYQSLNTEVTVRYTQGSWTGLLGKDV  
VSIKGVNGTFLINIASIFQSESFFLPNINWQGILGLAYSTLAKPSSSVEPFDFSLVQQENIPDVFMSQMCGA  
GQSSPGNGINAGSLVLGGVEPSLYKGNIWYTPITEEWYQVEVLKFEVGGQRLNLDCTVYNSDKAIVDSGTTL  
LRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQLACWDKTPQPNWYFPDISIYLRDNTSRSFRLTLKPLQYI  
QSVLTFQESLNCFRFGISQASATLVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAGPFGTSDVS  
SNCIARNPLREPIMWIISYSLMSLCGMILLVLIILLLSNRQRHDDMETINDESSLVQHRWK

>gi | 326913352 | WildTurkey  
EYENHLSFLLFRQLNILVDTGSSNFAVAGVDPDVTSYFNTELSSTYKSGQIEVTVKYQGSWTGVLGTDVIT  
IPKIDGYSYTNIIATILESENFPLPGVKGWHGILGLAYDTLAKPSSSVETFFDSLVRQAKIPNIFSLQMCAGL  
PVSGSGTNGGSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLDCREYNADKAIVDSGTTLLR  
LPQKVFQAVVQAIARTSLIQEFSSGFWSGSQLACWDKTERPWSLFPKLSIYMRDENSSSLHLYIQPIILGIGEN  
LQCYRFGISSSTNALVIGATVMEGFYVIFDRAQRVGFVAVSPCAEVDGSPVSEIEGPFPTTDDVASNCVSSITF  
HEPVLWIASYALMSLCGILLILIIILLIIPRCQHRVTDNDVVNDESSLVRHRWK

>gi | 345323454 | Platypus  
MAIWQQFPFSQIKMHILVDTGSSNFAVAGSPHSDISSYFDAERSSTYSSKNFDVTVKYTQGSWTGSGVTDVIT  
IPKGFNGSFVNNIATIFESENFPLPGIQWNGILGLAYAALAKPSSSLETFDFSLVKQAKIPNIFSMQMCAGL  
PVAGTGINGGSLVMGGIESSLYTGDIWYTPIKEEWYQIEILKLEVGGQNLNLDREYNANKAIVDSGTTLLR  
LPQKVFQAVVETITSTSSIQDFAEGFWTGSQACWSNSDKPWSLFPKISIYLRDENSSRSFRITILPQLYIQP  
MMGVASNYECYRFGISSSTNALVIGATVMEGFYVIFDRAQRVGFVAVSLCAEVAGSPVSEISGPFPTDDVASN  
CVTTLPFNEPILWIVSYTLMSICGIIILLVLIILLLLPHRCQRRPRDPDTVNDDESSLVRHRWK

>gi | 344294632 | Elephant  
MTSSTYQSKGFDVTVKYTQGSWTGLMGEDLVTIPKGFNSFLVNVATIFESENFPLPGIKWNGILGLAYATLA  
KPSSSLETFDFSLVMQAKIANVFSMQMCAGLPVAGSGTNGGSLVLGGIQPSLYKGDWYTPIKEEWYQIEI  
LKLEIGGQSLNLDREYNADKAIVDSGTTLLRPLQKVFDAVVEAVAHASLIPEFSDGFWTGSQACWNTSETP  
WSYFPKISIYLRDENSSRSFRITILPQLYIQPMIGAGLNYECYRFGISSSTNALVIGATVMEGFYVIFDRARK  
RVGFAMSPCAASPCHEVNDDESSLVRHRWK

>tr | G3HFD5 | ChineseHamster  
MGLMSGKLQILVDTGSSNFAVAGAPHSYVDSYFDSERSSTYHPKGFVTVKYTQGSWTGIVGEDIVTIPKGFN  
SSFLVNIATIFESENFPLPGIKWNGILGLAYAALAKVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQ  
SLNLDREYNADKAIVDSGTTLLRPLQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWNTSETPWAYFPKIS  
IYLRDENSSRSFRITILPQLYIQPMGAGLNYECYRFGISSSTNALVIGATVMEGFYVIFDRARKRVGFVAVSP  
CAEIEGTTVSEISGPFSTEDVASNCVPAPALNEPILWIVSYALMSVCGAILLVLIIILLLLPVRCRHAPRDPEV  
VNDDESSLVRHRWK

**Supplement Figure 3** List of all BACE2 Sequences

## Supplement Figure 4

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CLUSTAL 2.0.11 multiple sequence alignment

tr|Q0P4T5|WesternFrog      MELVVYARTGSILLVLLPCFLPVTG-QVAIKLPLKNCPGT---CSPMAYR
tr|Q5QHS1|Chicken         -----
sp|P56817|Human           ----MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSGLGG---APLGLRL
gi|296216280|Marmoset    ----MAQALPWLLLWMGAGVLP AHGTQH GIRLPLRSGLGG---APLGLRL
sp|P56819|Rat            ----MAPALRWLLLWVSGM LPAQGTHL GIRLPLRSGLAG---PPLGLRL
sp|P56818|Mouse          ----MAPALHWLLLWVSGM LPAQGTHL GIRLPLRSGLAG---PPLGLRL
tr|G3IAK4|ChineseHamster ----MAPALRWLLLWVSGM LPAQGTHL GIRLPLRSGLAG---PPLGLRL
sp|Q1KLR6|GuineaPig     ----MAPALPWLLLWVSGV LPVHGTQD GIRLPLRSGLAG---APLGLRL
sp|Q2HJ40|Cattle         ----MAQALPWLLLWVSGV LP AHGSQP GIRLPLRSGLGG---APLGLRL
gi|291383811|Rabbit      ----MAPALPWLLLWVSGM LPAQGTQH GIRLPLRSGLGG---APLGLRL
gi|344293150|Elephant    ----MALVALSWLLLWVSGV LP AHCTPH GIRLPLRSGLGG---APLGLRL
gi|345799894|Dog        -----
tr|G5BHK2|DesertRat     -----
gi|45387815|ZebraFish    --MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQGPLTPHSTPAAHRS

tr|Q0P4T5|WesternFrog      AKRSAEKGMELDTN--FLDMIDNLRGKSGQGYVEMRVGTPPQTLNILVD
tr|Q5QHS1|Chicken         -----YVEMTVGSP PQKLNILVD
sp|P56817|Human           PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
gi|296216280|Marmoset    PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
sp|P56819|Rat            PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
sp|P56818|Mouse          PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
tr|G3IAK4|ChineseHamster PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
sp|Q1KLR6|GuineaPig     PRETDEE---PGRG SFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
sp|Q2HJ40|Cattle         PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
gi|291383811|Rabbit      PRETDEEPEEPGRRGNFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
gi|344293150|Elephant    PRDTDEELEDPSRRGSFVEMVDNLRGKSGQGYVEMTVGSP PQTLNILVD
gi|345799894|Dog        -----MWD APEIR-----
tr|G5BHK2|DesertRat     -----YVEMTVGSP PQTLNILVD
gi|45387815|ZebraFish    PHGPRARSRAASGISFINMIDNLRGKSGQGYIEMAVGSPAQRN ILVD

tr|Q0P4T5|WesternFrog      TGSSNFVAVGAAPHPFLKRYHRQHSRTYRDVRRGVVYPYTQGWEGELGT
tr|Q5QHS1|Chicken         TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
sp|P56817|Human           TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
gi|296216280|Marmoset    TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
sp|P56819|Rat            TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
sp|P56818|Mouse          TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
tr|G3IAK4|ChineseHamster TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
sp|Q1KLR6|GuineaPig     TGSSNFVAVGAAPHPFLRYYRQRSSSTYRDLRKGVVYPYTQGWEGELGT
sp|Q2HJ40|Cattle         TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
gi|291383811|Rabbit      TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
gi|344293150|Elephant    TGSSNFVAVGAAPHPFLRYYRQLSSTYRDLRKGVVYPYTQGWEGELGT
gi|345799894|Dog        -----SSTYRDLRKGVVYPYTQGWEGELGT
tr|G5BHK2|DesertRat     TGSSNFVAVGAAPHPFLRYYRQRSSSTYRDLRKGVVYPYTQGWEGELGT
gi|45387815|ZebraFish    TGSSNFVAVGAAHPFLRYYHRSLSSSYRDLGRGVVYPYTQGRWEGELGT
                                * :***: :.*****:*****

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**Supplement Figure 4** Multiple sequence alignment resulting of BACE1 sequences from ClustalX.

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tr|Q0P4T5|WesternFrog      DLVTIPHGPNVTVTANIAAAITDSKFFINGSNWEGILGLAYAEIARPDDT
tr|Q5QHS1|Chicken         DLVTIPHGPNVTVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
sp|P56817|Human           DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
gi|296216280|Marmoset    DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
sp|P56819|Rat             DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
sp|P56818|Mouse          DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
tr|G3IAK4|ChineseHamster DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
sp|Q1KLR6|GuineaPig     DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIAR
sp|Q2HJ40|Cattle         DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
gi|291383811|Rabbit      DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
gi|344293150|Elephant    DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
gi|345799894|Dog        DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
tr|G5BHK2|DesertRat     DLVSIIPHGPNTVVRANIAAAITESDKFFINGSNWEGILGLAYAEIARPDDS
gi|45387815|ZebraFish   DVVSVPCGPNVSLRANIAAAITQSDRFFINGSNWEGILGLAYAEIARPDET
*:*:* *:*:* *:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*

tr|Q0P4T5|WesternFrog      LEPFFDSLQKQTRVFNIFSLQLCGTGFHFNED-TSASVGGSMVIGGIDP
tr|Q5QHS1|Chicken         LEPFFDSLQKQTVPNIFSLQLCGAGFSPNETE-TLASVGGSMIIGGIDR
sp|P56817|Human           LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|296216280|Marmoset    LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
sp|P56819|Rat             LEPFFDSLQKQTHIPNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
sp|P56818|Mouse          LEPFFDSLQKQTHIPNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
tr|G3IAK4|ChineseHamster LEPFFDSLQKQTHIANVFNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
sp|Q1KLR6|GuineaPig     -----LCGAGFPLNQSE-AVASVGGSMIIGGIDH
sp|Q2HJ40|Cattle         LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-ALASVGGSMIIGGIDH
gi|291383811|Rabbit      LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|344293150|Elephant    LEPFFDSLQKQTHIPNIFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|345799894|Dog        LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
tr|G5BHK2|DesertRat     LEPFFDSLQKQTHVFNIFSLQLCGAGFPLNQSE-AVASVGGSMIIGGIDH
gi|45387815|ZebraFish   LEPFFDSLRLRQSTVADVFNIFSLQLCGAGYHNHYSTGSSSTVGGSMIIGGVDP
*:*:* *:* *:*:*:*:*:*:*

tr|Q0P4T5|WesternFrog      SLYIGSIWYTPIRKEWYVEVIIVKIEINGQDLHMDCKEYNYDKSIVDSGT
tr|Q5QHS1|Chicken         SLYVVDIYWYTPIRKEWYVEVIIVKLEVNGQDLNMDCKEYNYDKSIVDSGT
sp|P56817|Human           SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|296216280|Marmoset    SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|P56819|Rat             SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|P56818|Mouse          SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
tr|G3IAK4|ChineseHamster SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|Q1KLR6|GuineaPig     SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|Q2HJ40|Cattle         SLYMGSWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|291383811|Rabbit      SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|344293150|Elephant    SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|345799894|Dog        SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
tr|G5BHK2|DesertRat     SLYTGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|45387815|ZebraFish   SLYVVELWYTPIRREWYVEVIIVRIEVNGQDLNMDCKEYNYDKSIVDSGT
*** *:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*

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**Supplement Figure4** Multiple sequence alignment resulting of BACE1 sequences from ClustalX, continued.

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tr|Q0P4T5|WesternFrog      TNLRLPKRVFDDAAVKS IKAASSTEKFPDGFWLGEQLVCWQEGTTPWHIFP
tr|Q5QHS1|Chicken         TNLRLPKKVFEAAVKS IKTASSTEKFPDGFWLGEQLVCWQVVG-PPWHIFP
sp|P56817|Human          TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
gi|296216280|Marmoset    TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
sp|P56819|Rat            TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
sp|P56818|Mouse          TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
tr|G3IAK4|ChineseHamster TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
sp|Q1KLR6|GuineaPig     TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
sp|Q2HJ40|Cattle         TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
gi|291383811|Rabbit      TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
gi|344293150|Elephant    TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
gi|345799894|Dog        TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
tr|G5BHK2|DesertRat     TNLRLPKKVFEAAVKS IKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP
gi|45387815|ZebraFish   TNLRLPRKVQAAVKA IEAASSTEQFPSPGFWLGEQLVCWQAGTTPWHIFP
*****::**:*:*:*:*:*:*:*:*:*:*:*:*:*:*:* * .**:*:*

tr|Q0P4T5|WesternFrog      VISLYLMGEVANQSFKITILPQQYLRPVEDIATAQEDCYKFAVSQS-TTG
tr|Q5QHS1|Chicken         VLSLYLMGEATNQSFRITILPQQYLGQWRNVATLKDDLPTGSTTLRPPTA
sp|P56817|Human          VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
gi|296216280|Marmoset    VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
sp|P56819|Rat            VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG
sp|P56818|Mouse          VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG
tr|G3IAK4|ChineseHamster VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
sp|Q1KLR6|GuineaPig     VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
sp|Q2HJ40|Cattle         VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
gi|291383811|Rabbit      VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
gi|344293150|Elephant    VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
gi|345799894|Dog        VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
tr|G5BHK2|DesertRat     VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG
gi|45387815|ZebraFish   VISLYLMSENRNQSFRISILPQQYLRPVEDVASAQEDCYKFAVSQS-STG
*:*:*:*:* * *:*:*:*:*:* * .:*:*:*

tr|Q0P4T5|WesternFrog      TVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHDYFRITASVEGPFASDLE
tr|Q5QHS1|Chicken         TVMGCCIQEG-----STVALTGP-----
sp|P56817|Human          TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTLDME
gi|296216280|Marmoset    TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
sp|P56819|Rat            TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTADME
sp|P56818|Mouse          TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
tr|G3IAK4|ChineseHamster TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
sp|Q1KLR6|GuineaPig     TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTATVEGPFVTPDME
sp|Q2HJ40|Cattle         TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
gi|291383811|Rabbit      TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
gi|344293150|Elephant    TVMGAVIMEGFYVVFDRSRKRIGFAVSACHVHDEFRTAAVEGPFVTPDME
gi|345799894|Dog        TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFITLDME
tr|G5BHK2|DesertRat     TVMGAVIMEGFYVVFDRQKRIGFAVSACHVHDEFRTAAVEGPFVTLDME
gi|45387815|ZebraFish   TVMGAVIMEGFYVVFERQHKRIGFAVSTCHVHDEFRTAAVEGPFHGLDLE
**** . * ** * .:*:*

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**Supplement Figure 4** Multiple sequence alignment resulting of BACE1 sequences from ClustalX, continued.

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tr|Q0P4T5|WesternFrog      DCGYNTFQLDESALMTTAYVMAGVLCALFMLPLCLMLFQWRCFRCLKRARD
tr|Q5QHS1|Chicken          -----
sp|P56817|Human            DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRQQHD
gi|296216280|Marmoset     DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRQQHD
sp|P56819|Rat              DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
sp|P56818|Mouse            DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
tr|G3IAK4|ChineseHamster  DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
sp|Q1KLR6|GuineaPig      DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
sp|Q2HJ40|Cattle           DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
gi|291383811|Rabbit       DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
gi|344293150|Elephant     DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
gi|345799894|Dog          DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
tr|G5BHK2|DesertRat      DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCLRCLRHQHD
gi|45387815|ZebraFish    DCGYNVPTDESTLMTIAYVMAGICALFMLPLCLMVCQWRFCTCLQPADG

tr|Q0P4T5|WesternFrog      DLADDISLLK
tr|Q5QHS1|Chicken          -----
sp|P56817|Human            DFADDISLLK
gi|296216280|Marmoset     DFADDISLLK
sp|P56819|Rat              DFADDISLLK
sp|P56818|Mouse            DFADDISLLK
tr|G3IAK4|ChineseHamster  DFADDISLLK
sp|Q1KLR6|GuineaPig      DFADDISLLK
sp|Q2HJ40|Cattle           DFADDISLLK
gi|291383811|Rabbit       DFADDISLLK
gi|344293150|Elephant     DFADDISLLK
gi|345799894|Dog          DFADDISLLK
tr|G5BHK2|DesertRat      DFADDISLLK
gi|45387815|ZebraFish    --SDDISLLK

```

**Supplement Figure 4** Multiple sequence alignment resulting of BACE1 sequences from ClustalX, continued.



## Supplement Figure 5

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CLUSTAL 2.0.11 multiple sequence alignment

tr|Q5QHS0|Chicken          -----
gi|326913352|WildTurkey   -----
tr|G3HFD5|ChineseHamster  -----
gi|345795292|Dog          -----MEDLCAPRQLSSSR---L
sp|Q6IE75|Rat             MGALLRALLLPLLAQWLLRAVPVLAPAPFTLPLQVAGAANHRASTV---P
sp|Q9JL18|Mouse          MGALLRALLLVLQAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P
sp|Q9Y5Z0|Human          MGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPT---P
gi|296232194|Marmoset    -----LLAQWLLARRPELAPAPFTLPLRVATATNRAAAPT---S
gi|344294632|Elephant    -----
gi|329663206|Cattle      MGALARALLLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P
tr|G5C5D1|DesertRat      -----
gi|348556383|Guineapig   MGALARALLLPLXVAQWLLLR-AATAPAPFTLPLXHVAIATARPASPT---P
gi|345323454|Platypus   -----
gi|213982845|WesternFrog -----MKVPLLAVLLLG-AACASANFIFPLKVSPEAMKGAVPV---A
gi|147903717|AfricanFrog -----MKVPLVRLLLLCAAACASNKFI VPLNVSPAEEKGTLPV---A
gi|348508416|CichlidFish -----MAHSTFVSFGAFALSIFYGVSYCYFISPLKIYPGKYNVSSDYNLTS
gi|54400484|ZebraFish    -----MRLYGLLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP

tr|Q5QHS0|Chicken          -----
gi|326913352|WildTurkey   -----EYENHLSFL-----
tr|G3HFD5|ChineseHamster  -----MGLMSG-----
gi|345795292|Dog          SPVQKQQLDHG-----HPLDKWTQTYGSQLSSRR-----
sp|Q6IE75|Rat             GLGTPELPRADGLALALEP---ARATANFLAMVDNLQGDSSGRGYYLEML
sp|Q9JL18|Mouse          GLGTPELPRADGLALALEP---VRATANFLAMVDNLQGDSSGRGYYLEML
sp|Q9Y5Z0|Human          GPGTPAERHADGLALALEPALASPAGANFLAMVDNLQGDSSGRGYYLEML
gi|296232194|Marmoset    GPGTPAERRADGLALALEPALESAAGSANFLAMVDNLQGDSSGRGYYLEML
gi|344294632|Elephant    GPGPPAEPRADGLALALEP---AGGAANFLAMVDNLQGDSSGRGYYLEMQ
gi|329663206|Cattle      -----
tr|G5C5D1|DesertRat      -----
gi|348556383|Guineapig   VPGTPALPRADGLALALEP---AGAAANFLAMVDNLQGDSSGRGYYLEML
gi|345323454|Platypus   -----MAIWQQFP-----
gi|213982845|WesternFrog PATPKGA---PGLLLASDP----GGQINFFSMVNNLEGDSSGRGYYLELL
gi|147903717|AfricanFrog PATPKDK---PGLLLASDP----GGTINFFSMVDNLAGDSSGRGYYLELL
gi|348508416|CichlidFish LRRVALKSDGSLASDP----TGTVNFDMVNNLQGDSSGRGYIEMS
gi|54400484|ZebraFish    LQKNEAAK-SGLSLASDP----AGIVNFLDMINNLKGDSSGRGYMQMI
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Supplement Figure 5 Multiple sequence alignment resulting of BACE2 sequences from ClustalX.

```

tr|Q5QHS0|Chicken          -----HLLNTELSSTYQSQGIEVTV
gi|326913352|WildTurkey   ---LFRQLNILVDTGSSNFVAVAGVDPDVTSYFNTELSSTYKYSQGIEVTV
tr|G3HFD5|ChineseHamster  -----KLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYHPKGFDTV
gi|345795292|Dog           -----RLQILVDTGSSNFVAVAGAPHSYDTSYFDADRSSTYRSKGFDTV
sp|Q6IE75|Rat              IGTPPQKVRILVDTGSSNFVAVAGAPHSYIDTYFDESSTYHSKGFVTV
sp|Q9JL18|Mouse            IGTPPQKVLVDTGSSNFVAVAGAPHSYIDTYFDESSTYHSKGFDTV
sp|Q9Y5Z0|Human            IGTPPQKQLILVDTGSSNFVAVAGTPHSYIDTYFDESSTYRSKGFDTV
gi|296232194|Marmoset     IGTPPQKQLILVDTGSSNFVAVAGAPHSYIDTYFDMERSSTYRSKGFDTV
gi|344294632|Elephant     -----MTSSTYQSKGFDTV
gi|329663206|Cattle       IGTPPQKQLILVDTGSSNFVAVAGAPHSYIDTYFDMERSSTYRYPKGFDTV
tr|G5C5D1|DesertRat       -----QKLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYQSKGFDTV
gi|348556383|Guineapig   IGTPPQKQLILVDTGSSNFVAVAGAPHSYVDSYFDMERSSTYRSKGFDTV
gi|345323454|Platypus    --FSQIKMHILVDTGSSNFVAVAGSPHSDISSYFDMERSSTYSSKNFDTV
gi|213982845|WesternFrog IGTPPQKMNILVDTGSSNFVAVAGALNPDIITFFDSKLSSTSYEPLNTQVTV
gi|147903717|AfricanFrog IGSPQKVNILVDTGSSNFVAVAGSPNPVNTFFDSKLSSTYSQSLNTEVTV
gi|348508416|CichlidFish IGTPGQKLNILVDTGSSNFVAVAAAHPYIITHYFNALSSSTYSSTGRTVAV
gi|54400484|ZebraFish    IGTPGQTLNILVDTGSSNFVAVAAAHPYIITHYFNALSSSTYQSTERAVAV
                                *:* * . *:*

tr|Q5QHS0|Chicken          KYSQGSWTGVLGTDVVTIPKIDGRYTIINIATILESENFFLPVKWHGIL
gi|326913352|WildTurkey   KYSQGSWTGVLGTDVITIPKIDGSYTIINIATILESENFFLPVKWHGIL
tr|G3HFD5|ChineseHamster  KYTQGSWTGIVGEDIVTIPKGFNSSFLVNIATIFESENFFLPKIKWNGIL
gi|345795292|Dog           KYTQGSWTGFVGEDVFTIPKGFNSSFLVNIATIFESENFFLPKIKWNGIL
sp|Q6IE75|Rat              KYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFFLPKIKWNGIL
sp|Q9JL18|Mouse            KYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFFLPKIKWNGIL
sp|Q9Y5Z0|Human            KYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFFLPKIKWNGIL
gi|296232194|Marmoset     KYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFFLPKIKWNGIL
gi|344294632|Elephant     KYTQGSWTGLMGEDLVTIPKGFNSSFLVNVATIFESENFFLPKIKWNGIL
gi|329663206|Cattle       KYTQGSWTGFVGEDVVTIPKGFNSSFLVNIATIFESENFFLPKIRWNGIL
tr|G5C5D1|DesertRat       KYTQGSWTGLVQGDVVTIPKAFNSSFLVNIAAIFESENFFLPKIKWNGIL
gi|348556383|Guineapig   KYTQGSWTGFVGEDLVTIPRAFNSSFLANVATIFESENFFLPKIKWNGIL
gi|345323454|Platypus    KYTQGSWTGSVGTDVITIPKGFNGSFVNIATIFESENFFLPKIQWNGIL
gi|213982845|WesternFrog RYTQGSWTGLGKDVISMVPGVNGTFLINIASIFQSENFFLPNINWQGIL
gi|147903717|AfricanFrog RYTQGSWTGLGKDVVSIKGVNGTFLINIASIFQSEFFLPNINWQGIL
gi|348508416|CichlidFish RYTQGNWEGELGIDRVSIPRGPNGTITINIAAILSSDGFPLPINWQGIL
gi|54400484|ZebraFish    KYTQGEWEGELGTDLITIEGPGSAITINIAAILTSEGFFLPINWQGIL
                                :*:* * * * * :*: * . *:*

tr|Q5QHS0|Chicken          GLAYDTLAKPSSSVETFFDSLQAKIPNIFSLQMCAGLPVSGSG-TNG
gi|326913352|WildTurkey   GLAYDTLAKPSSSVETFFDSLVRQAKIPNIFSLQMCAGLPVSGSG-TNG
tr|G3HFD5|ChineseHamster  GLAYAALAK-----
gi|345795292|Dog           GLAYAALAKPSSSLETFFFDSLVAQAKIPNVFSMQMCGAGLPVAGSG-TNG
sp|Q6IE75|Rat              GLAYAALAKPSSSLETFFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG
sp|Q9JL18|Mouse            GLAYAALAKPSSSLETFFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG
sp|Q9Y5Z0|Human            GLAYATLAKPSSSLETFFFDSLVTQANI PNVFSMQMCGAGLPVAGSG-TNG
gi|296232194|Marmoset     GLAYATLAKPSSSLETFFFDSLQAKIPNIVFSMQMCGAGLPVAGSG-TNG
gi|344294632|Elephant     GLAYATLAKPSSSLETFFFDSLVMQAKIANVFSMQMCGAGLPVAGSG-TNG
gi|329663206|Cattle       GLAYATLAKPSSSLETFFFDSLVAQAKIPNIFSMQMCAGLPVAGSG-TNG
tr|G5C5D1|DesertRat       GLAYASLAKPSSSLETFFFDSLVTQAKIPDVFMSQMCAGWPVARS-G-TNG
gi|348556383|Guineapig   GLAYATLAKPSSSLETFFFDSLVTQAKIPDIFSMQMCAGLPVRS-G-TNG
gi|345323454|Platypus    GLAYAALAKPSSSLETFFFDSLQAKIPNIFSMQMCAGLPVAGTG-ING
gi|213982845|WesternFrog GLAYSTLAKPSSSVEPFFDSLQENIPNIFSMQMCAGQSPGIG-INA
gi|147903717|AfricanFrog GLAYSTLAKPSSSVEPFFDSLQENIPDVFMSQMCAGQSPGNG-INA
gi|348508416|CichlidFish GLAYPVLARLPDSSVEPFFNSVVKQLGIPDIFSLQMCAGLSASSTTDTTG
gi|54400484|ZebraFish    GLAYPLLARLPDSSVEPFFNSVVRQTGIPDVFSLQMCAGVPASTTGDPA
                                **** *:*

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**Supplement Figure 5** Multiple sequence alignment resulting of BACE2 sequences from ClustalX, continued.

```

tr |Q5QHS0 |Chicken          GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLLELDCREYN
gi |326913352 |WildTurkey    GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLLELDCREYN
tr |G3HFD5 |ChineseHamster    ---VLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |345795292 |Dog              GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
sp |Q6IE75 |Rat                GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
sp |Q9JL18 |Mouse             GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
sp |Q9Y5Z0 |Human            GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |296232194 |Marmoset         GSLVLGGIEPSLYKGNIWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |344294632 |Elephant        GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |329663206 |Cattle          GSLVLGGIEPTLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
tr |G5C5D1 |DesertRat        GSLVLGGIEPNLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |348556383 |Guineapig       GSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSNLNDCREYN
gi |345323454 |Platypus        GSLVMGGIESSLYTGDWYTPIKEEWYQIEILKLEVGGQNLNDCREYN
gi |213982845 |WesternFrog     GSLVLGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLNDCTVYN
gi |147903717 |AfricanFrog     GSLVLGGVEPSLYKGNIWYTPITEEWYQVEVLKFEVGGQNLNDCTVYN
gi |348508416 |CichlidFish     GSLIMGGAETPLYRGSVWYTPITEEWYQVEVLKLEVGDQNLNDCREYN
gi |54400484 |ZebraFish       GSLIMGGVEPTLHRGPIWYTPVLEEYQVEVLKLEVGDQNLNDCREYN
      ::* . : . * :**** :*****:***:*. * :**** **

tr |Q5QHS0 |Chicken          ADKAIVDSGTTLLRRLPQKVFDAVVAIARTSLIQEFSSGFWSGSQACWD
gi |326913352 |WildTurkey    ADKAIVDSGTTLLRRLPQKVFDAVVAIARTSLIQEFSSGFWSGSQACWD
tr |G3HFD5 |ChineseHamster    ADKAIVDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWT
gi |345795292 |Dog              ADKAIVDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTGSQACWT
sp |Q6IE75 |Rat                ADKAIVDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWT
sp |Q9JL18 |Mouse             ADKAIVDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTGAQLACWT
sp |Q9Y5Z0 |Human            ADKAIVDSGTTLLRRLPQKVFDAVVEAVARASLIPEFSDGFWTGSQACWT
gi |296232194 |Marmoset         ADKAIVDSGTTLLRRLPQKVFDAVVEAVARASLIPEFSDGFWTGSQACWA
gi |344294632 |Elephant        ADKAIVDSGTTLLRRLPQKVFDAVVEAVAHASLIPEFSDGFWTGSQACWT
gi |329663206 |Cattle          ADKAIVDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSEGFWTGSQACWT
tr |G5C5D1 |DesertRat        ADKAIVDSGTTLLRRLPQKVFDAVDAVARTSLIPEFSDGFWTGAQLACWT
gi |348556383 |Guineapig       ANKAIVDSGTTLLRRLPQKVFDAVVEAVETITSTSIQDFAEGFWTGSQACWS
gi |345323454 |Platypus        SDKAIVDSGTTLLRRLPDKVFAMVDAIVQTSLIQNFNAEFWAGLQACWD
gi |213982845 |WesternFrog     SDKAIVDSGTTLLRRLPDKVFAMVDAIVQTSLIQNFNAEFWAGLQACWD
gi |147903717 |AfricanFrog     MDKAIVDSGTTLLRRLPVNVFNALVEAITRSSLIEEFSSGFWEGTKLACWM
gi |348508416 |CichlidFish     SDKAIVDSGTTLLRRLPANVFTAVVDTIMQTSLIDDFAGFFDGTKLACWM
gi |54400484 |ZebraFish       :***** :** *:***: :* * :* * :* :****

tr |Q5QHS0 |Chicken          KTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGENLQCYRF
gi |326913352 |WildTurkey    KTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGENLQCYRF
tr |G3HFD5 |ChineseHamster    NSETPWAYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF
gi |345795292 |Dog              NSETPWSYFPKISIYLRDENSSQSFRITILPQLYIQPMMGAGLNIECYRF
sp |Q6IE75 |Rat                NSETPWAYFPKISIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF
sp |Q9JL18 |Mouse             NSETPWAYFPKISIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF
sp |Q9Y5Z0 |Human            NSETPWSYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF
gi |296232194 |Marmoset         NSETPWSYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF
gi |344294632 |Elephant        NSETPWSYFPKISIYLRDENSSRSFRITILPQLYIQPMIGAGLNIECYRF
gi |329663206 |Cattle          NSETPWSYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF
tr |G5C5D1 |DesertRat        NSETPWAYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF
gi |348556383 |Guineapig       NSETPWAYFPKISIYLRDENSSRSFRITILPQLYIQPMMGAGLSYIECYRF
gi |345323454 |Platypus        NSDKPWSLFPKISIYLRDENSSRSFRITILPQLYIQPMMGVASNYIECYRF
gi |213982845 |WesternFrog     KTQDPWNYFPDISIYLRDNTSSRSFRITLTKPQLYIQSVLTFQESLNCFRF
gi |147903717 |AfricanFrog     KTQDPWNYFPDISIYLRDNTSRSFRITLTKPQLYIQSVLTFQESLNCFRF
gi |348508416 |CichlidFish     KGENPWRFFPKLSIYLRATNTSEFRITILPQLYIQPITDVGDTLDCFRF
gi |54400484 |ZebraFish       RGENPWRFFPKVSIYLRGTNTSQSFRITILPQVRIVP-----
      . : ** ** :**** * :*          : : * .

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**Supplement Figure 5** Multiple sequence alignment resulting of BACE2 sequences from ClustalX, continued.

|    |           |                |  |
|----|-----------|----------------|--|
| tr | Q5QHS0    | Chicken        | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG  |
| gi | 326913352 | WildTurkey     | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG  |
| tr | G3HFD5    | ChineseHamster | GISSSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEGTTVSEISG    |
| gi | 345795292 | Dog            | GISPSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEGAPVSEISG    |
| sp | Q6IE75    | Rat            | GISSSTNALVIGATVMEGFYVVFDRQRRVGFVAVSPCAIEGTTVSEISG    |
| sp | Q9JL18    | Mouse          | GISSSTNALVIGATVMEGFYVVFDRQRRVGFVAVSPCAIEGTTVSEISG    |
| sp | Q9Y5Z0    | Human          | GISPSTNALVIGATVMEGFYVIFDRAQKRVGFAASPCAIEAGAAVSEISG   |
| gi | 296232194 | Marmoset       | GISPSTNALVIGATVMEGFYVIFDRARKRVGFAASPC---AGEQFSHRMG   |
| gi | 344294632 | Elephant       | GISPSSNALVIGATVMEGFYVVFDRARKRVGFAMSPC----AASCPHPE    |
| gi | 329663206 | Cattle         | GISPSTNALVIGATVMEGFYVVFDRQKRVGFAASPCAIEGAPVSEISG     |
| tr | G5C5D1    | DesertRat      | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAIEGAPVSEVSG    |
| gi | 348556383 | Guineapig      | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAETAGVPLSEVSG   |
| gi | 345323454 | Platypus       | GISSSTNALVIGATVMEGFYVVFDRQKRVGFVAVSLCAEVAGSPVSEISG   |
| gi | 213982845 | WesternFrog    | GISQSASALVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG  |
| gi | 147903717 | AfricanFrog    | GISQSASTLVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG  |
| gi | 348508416 | CichlidFish    | GVSSSTNGMVIATVMEGFYVVFDRDRTQQLGFGALSSCAVSDGVALSEIEG  |
| gi | 54400484  | ZebraFish      | -----  |
| tr | Q5QHS0    | Chicken        | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGIILLILILLIIPPRC    |
| gi | 326913352 | WildTurkey     | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGIILLILILLIIPPRC    |
| tr | G3HFD5    | ChineseHamster | PFSTEDVASNCVPAPALNEPILWIVSYALMSVCGAILLVILLIIPVRC     |
| gi | 345795292 | Dog            | PFSTDDIASNCVPALPLNEPILWIVSYTLMSVCGIILLILIVLILLPFRC   |
| sp | Q6IE75    | Rat            | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVILLIIPVRC     |
| sp | Q9JL18    | Mouse          | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVILLIIPVRC     |
| sp | Q9Y5Z0    | Human          | PFSTEDVASNCVPAQSLSEPILWIVSYALMSVCGAILLVIVLILLPFRC    |
| gi | 296232194 | Marmoset       | -IPDESPLCECADLEAIPDGT-----                           |
| gi | 344294632 | Elephant       | VVNDESSLVRHRWK-----                                  |
| gi | 329663206 | Cattle         | PFSTEDIASNCVPALPLNEPVLWIVSYTLMSVCGVILLVITLILLIIPVRC  |
| tr | G5C5D1    | DesertRat      | PFSTDGIASNCVPAPAPGEPVLLWVSYALLSACGLILLVILLIIPVRC     |
| gi | 348556383 | Guineapig      | PFSTDGIASNCVPSPLNEPVLWVSYALMSVCGIILLVIVLILLIIPVRC    |
| gi | 345323454 | Platypus       | PFSTDDVASNCVTTLPFNEPILWIVSYTLMSVCGIILLVILLIIPVRC     |
| gi | 213982845 | WesternFrog    | PFGTSDVSSNCIARNPLREPIMWIIISYSLMSLCGMILLVIVLILLIIPVRC |
| gi | 147903717 | AfricanFrog    | PFGTSDVSSNCIARNPLREPIMWIIISYSLMSLCGMILLVIVLILLIIPVRC |
| gi | 348508416 | CichlidFish    | PFSAADVAADCSGG-PLKEPLVWMIISYALMAVCALALLIILLIIPVRC    |
| gi | 54400484  | ZebraFish      | -----  |
| tr | Q5QHS0    | Chicken        | QHRYTDNDVVNDESSLVRHRWK                               |
| gi | 326913352 | WildTurkey     | QHRYTDNDVVNDESSLVRHRWK                               |
| tr | G3HFD5    | ChineseHamster | RHAPRDPEVVNDESSLVRHRWK                               |
| gi | 345795292 | Dog            | RHAPRDPEVVNDESSLVRHRWK                               |
| sp | Q6IE75    | Rat            | RHAPRDPEVVNDESSLVRHRWK                               |
| sp | Q9JL18    | Mouse          | RHAPRDPEVVNDESSLVRHRWK                               |
| sp | Q9Y5Z0    | Human          | QRRPRDPEVVNDESSLVRHRWK                               |
| gi | 296232194 | Marmoset       | -----  |
| gi | 344294632 | Elephant       | -----  |
| gi | 329663206 | Cattle         | RHHPRDPEVVNDESSLVRHRWK                               |
| tr | G5C5D1    | DesertRat      | RRPPRDPEVINDESSLVRHRWK                               |
| gi | 348556383 | Guineapig      | RHAPRDPEVINDESSLVRHRWK                               |
| gi | 345323454 | Platypus       | QRRPRDPEVINDESSLVRHRWK                               |
| gi | 213982845 | WesternFrog    | -HRRDDMETVNDESSLVQHRWK                               |
| gi | 147903717 | AfricanFrog    | -QRHDDMETVNDESSLVQHRWK                               |
| gi | 348508416 | CichlidFish    | GNNRGE---ITDESSLVRHRWK                               |
| gi | 54400484  | ZebraFish      | -----  |

**Supplement Figure 5** Multiple sequence alignment resulting of BACE2 sequences from ClustalX, continued.

## Supplement Figure 6

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CLUSTAL 2.0.11 multiple sequence alignment

tr|Q5QHS0|Chicken-----
gi|326913352|WildTurkey-----
tr|G3HFD5|ChineseHamster-----
gi|345795292|Dog-----MEDLCAPRQLSSSR---L
sp|Q6IE75|RatMGALLRALLLPLLAQWLLRAVPVLAPAPFTLPLQVAGAANHRASTV---P
sp|Q9JL18|MouseMGALLRALLLVLQAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P
sp|Q9Y5Z0|HumanMGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAATNRRVVAPT---P
gi|296232194|Marmoset-----LLAQWLLARRPELAPAPFTLPLRVATATNRAAAPT---S
gi|344294632|Elephant-----
gi|329663206|CattleMGALARALLLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P
tr|G5C5D1|DesertRat-----
gi|348556383|GuineapigMGALARALLLPXVAQWLLLR-AATAPAPFTLPLXHVAIATARPASPT---P
gi|345323454|Platypus-----
gi|213982845|WesternFrog-----MKVPLLAVLLLG-AACASANFIFPLKVSPAEMKGAVPV---A
gi|147903717|AfricanFrog-----MKVPLVRLLLCAACASNKFIPLNVSPAIEIKGTLPV---A
gi|348508416|CichlidFish----MAHSTFVSFGAFALSLYFGVSYCYFSIPLKIYPGKYNVSSDVNLT
gi|54400484|ZebraFish-----MRLYGLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP

tr|Q5QHS0|Chicken-----
gi|326913352|WildTurkey-----EYENHLSFL-----
tr|G3HFD5|ChineseHamster-----MGLMSG-----
gi|345795292|DogSPVQKQQLDHG-----HPLDKWTQTYGSQLSSRR-----
sp|Q6IE75|RatGLGTPPELPRADGLALALEP---ARATANFLAMVDNLQGDSDGRGYYLEML
sp|Q9JL18|MouseGLGTPPELPRADGLALALEP---VRATANFLAMVDNLQGDSDGRGYYLEML
sp|Q9Y5Z0|HumanGPGTPAERHADGLALALEPALASPAGAAANFLAMVDNLQGDSDGRGYYLEML
gi|296232194|MarmosetGPGTPAERRADGLALALEPALESAAGSANFLAMVDNLQGDSDGRGYYLEML
gi|344294632|Elephant-----
gi|329663206|CattleGPGPPAEPRADGLALALEP---AGGAANFLAMVDNLQGDSDGRGYYLEMQ
tr|G5C5D1|DesertRat-----
gi|348556383|GuineapigVPGTPALPRADGLALALEP---AGAAANFLAMVDNLQGDSDGRGYYLEML
gi|345323454|Platypus-----MAIWQQFP-----
gi|213982845|WesternFrogPATPKGA---PGLLLASDP-----GGQINFFSMVNNLEGDSDGRGYYLELL
gi|147903717|AfricanFrogPATPKDK---PGLLLASDP-----GGTINFFSMVDNLQGDSDGRGYYLELL
gi|348508416|CichlidFishLRRVALKSDGSLASDP-----TGTVNFLDMVNNLQGDSDGRGYIEMS
gi|54400484|ZebraFishLQKNEAAK-SGLSLASDP-----AGIVNFLDMINNLKGDSDGRGYMQMI

```

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX.

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CLUSTAL 2.0.11 multiple sequence alignment

tr|Q0P4T5|WesternFrog1      -----MELVVYARTGSILLVLLPCFLPVTG-QVAIKLPLKN---C
tr|Q5QHS1|Chicken1         -----
sp|P56817|Human1           -----MAQALPWLLLWVGAGVLPAGHTQHGIRLPLRS---G
gi|296216280|Marmoset1     -----MAQALPWLLXWVGAGVLPAGHTQHGIRLPLRS---G
sp|P56819|Rat1             -----MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRS---G
sp|P56818|Mouse1          -----MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRS---G
tr|G3IAK4|ChineseHamster1  -----MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRS---G
sp|Q1KLR6|GuineaPig1      -----MAPALPWLLLWVGSGVLPVHGTQDGIPLRS---G
sp|Q2HJ40|Cattle1         -----MAQALPWLLLWVGSGVLPAGHSQPGIRLPLRS---G
gi|291383811|Rabbit1      -----MAPALPWLLLWVGSGMLPAQGTQHGIRLPLRS---G
gi|345799894|Dog1         -----
gi|344293150|Elephant1    -----MALVALSWLLLWVGSGVLPAGCTPHGIRLPLRS---G
tr|G5BHK2|DesertRat1      -----
gi|45387815|ZebraFish1    -----MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQ---G
sp|Q9Y5Z0|Human2          MGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVAVPT---P
gi|296232194|Marmoset2    -----LLAQWLLARRPELAPAPFTLPLRVATATNRAAPT---S
sp|Q6IE75|Rat2            MGALLRALLLPLLAQWLLRAVPVLPAPFTLPLQVAGAAANHRASV---P
sp|Q9JL18|Mouse2          MGALLRALLLVLVAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P
tr|G3HFD5|ChineseHamster2 -----
gi|329663206|Cattle2      MGALARALLLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P
tr|G5C5D1|DesertRat2     -----
gi|348556383|Guineapig2   MGALARALLLPXVAQWLLRA-ATAPAPFTLPLXHVAIATARPASPT---P
gi|345795292|Dog2        -----M---E
gi|344294632|Elephant2   -----
tr|Q5QHS0|Chicken2       -----
gi|326913352|WildTurkey2 -----
gi|345323454|Platypus2   -----
gi|213982845|WesternFrog2 -----MKVPLLAVLLLG-AACASANFIFPLKVSPAEMKGAVPV---A
gi|147903717|AfricanFrog2 -----MKVPLVRLLLCAAACASNKFIPLNVSPAIEIKGTLPV---A
gi|348508416|CichlidFish2 -----MAHSTFVSGAFALSLYFGVSYCYFSIPLKIYPGKYNVSSDVNLTSS
gi|54400484|ZebraFish2   -----MRLYGLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP

tr|Q0P4T5|WesternFrog1      PG--TCSPMAYR---AKRSAEKGMELDTNFLDMIDNLRGKSGQGYVEMR
tr|Q5QHS1|Chicken1         -----YVEMT
sp|P56817|Human1          LGGAPLGLRLRPR---ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT
gi|296216280|Marmoset1    LGGAPLGLRLRPR---ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT
sp|P56819|Rat1            LAGPPLGLRLRPR---ETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT
sp|P56818|Mouse1          LAGPPLGLRLRPR---ETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMT
tr|G3IAK4|ChineseHamster1  PAGPPLGLRLRPR---ETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMT
sp|Q1KLR6|GuineaPig1      LAGAPLGLRLRPR---ETDEE---PGRRGSFVEMVDNLRGKSGQGYVEMT
sp|Q2HJ40|Cattle1         LGGAPLGLRLRPR---ETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMT
gi|291383811|Rabbit1     LGGAPLGLRLRPR---ETEEDPEEPGRRGNFVEMVDNLRGKSGQGYVEMT
gi|345799894|Dog1        -----MWDAPEIR
gi|344293150|Elephant1    LGGAPLGLRLRPR---DTDEELEDPSRRGSFVEMVDNLRGKSGQGYVEMT
tr|G5BHK2|DesertRat1      -----YVEMT
gi|345795292|Dog2        DLCAPRQLSSSRLSPVQKQQLD----HGHPDKWTQTYGS-----
gi|344294632|Elephant2   -----
tr|Q5QHS0|Chicken2       -----

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

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gi|326913352|WildTurkey2 -----EYENHL
gi|345323454|Platypus2 -----MAIWQQF
gi|213982845|WesternFrog2 PATPKGA---PGLLLASDPGGQ-----INFFSMVNNLEGDSSGRGYYLELL
gi|147903717|AfricanFrog2 PATPKDK---PGLLLASDPGGT-----INFFSMVDNLAGDSSGRGYYLELL
gi|348508416|CichlidFish2 LRRVALKSDGSGLSLASDPTGT-----VNFLDMVNNLQGDSSGRGYYLEMS
gi|54400484|ZebraFish2 LQKNEAAAK-SGLSLASDPAGI-----VNFLDMINNLKGDSSGRGYMQMI

tr|Q0P4T5|WesternFrog1 VGTPPQTLNIIIVDTGSSNFVAVGAAPHPFLKRYHRQHSRTYRDVRRGVVY
tr|Q5QHS1|Chicken1 VGSPQKLNIIIVDTGSSNFVAVGAAPHPFLRRYYQRQLSSTYRDLRKGVVY
sp|P56817|Human1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
gi|296216280|Marmoset1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
sp|P56819|Rat1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKSIVY
sp|P56818|Mouse1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
tr|G3IAK4|ChineseHamster1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
sp|Q1KLR6|GuineaPig1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
sp|Q2HJ40|Cattle1 LGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
gi|291383811|Rabbit1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
gi|345799894|Dog1 -----SSTYRDLRKGVVY
gi|344293150|Elephant1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
tr|G5BHK2|DesertRat1 VGSPQTLNIIIVDTGSSNFVAVGAAPHPFLHRYQRQLSSTYRDLRKGVVY
gi|45387815|ZebraFish1 VGSPAQRNLIIIVDTGSSNFVAVGAAHPFLHRYHRSLSSSYRDLGRGVVY
sp|Q9Y5Z0|Human2 IGTTPQKLQIILVDTGSSNFVAVAGTPHYSIDTYFDTERSSSTYRSGKFDVTV
gi|296232194|Marmoset2 IGTTPQKLQIILVDTGSSNFVAVAGAPHSYIDTYFDMERSSTYRSGKFDVTV
sp|Q6IE75|Rat2 IGTTPQKVRILVDTGSSNFVAVAGAPHSYIDTYFDSESSTYHSGKFEVTV
sp|Q9JL18|Mouse2 IGTTPQKQVILVDTGSSNFVAVAGAPHSYIDTYFDSESSTYHSGKFDVTV
tr|G3HFD5|ChineseHamster2 MGLMSGKLQIILVDTGSSNFVAVAGAPHSYVDSYFDERSSTYRSGKFDVTV
gi|329663206|Cattle2 IGTTPQKLQIILVDTGSSNFVAVAGAPHSYIDSYFDAERSSTYRSGKFDVTV
tr|G5C5D1|DesertRat2 -----QKLQIILVDTGSSNFVAVAGAPHSYVDSYFDERSSTYRSGKFDVTV
gi|348556383|Guineapig2 IGTTPQKLQIILVDTGSSNFVAVAGAPHSYVDSYFDERSSTYRSGKFDVTV
gi|345795292|Dog2 QLSSRRRLQIILVDTGSSNFVAVAGAPHSYVDSYFDADRSSTYRSGKFDVTV
gi|344294632|Elephant2 -----MTSSTYRSGKFDVTV
tr|Q5QHS0|Chicken2 -----HLLLNTELSSTYRSGKFEVTV
gi|326913352|WildTurkey2 SFLLFRQLNIIIVDTGSSNFVAVAGVDPDPVTSYFNTELSSTYRSGKFEVTV
gi|345323454|Platypus2 PFSQIK-MHILVDTGSSNFVAVAGSPHSDISSYFDAERSSTYRSGKFDVTV
gi|213982845|WesternFrog2 IGTTPQKMNIIIVDTGSSNFVAVAGALNPDITTFDSKLSSTYRSGKFDVTV
gi|147903717|AfricanFrog2 IGSPQKVNIIIVDTGSSNFVAVAGSPNPDVNTFFDSKLSSTYRSGKFEVTV
gi|348508416|CichlidFish2 IGTTPGQKLNIIIVDTGSSNFVAVAAAHQFITHYFNALSSTYRSGKFEVTV
gi|54400484|ZebraFish2 IGTTPGQTLNIIIVDTGSSNFVAVAAAHPYITHYFNALSSSTYRSGKFEVTV

* : * * *

tr|Q0P4T5|WesternFrog1 PYTQGWEGELGTDLVTIPHGPNVTVTANIAAITSDKFFINGSNWEGIL
tr|Q5QHS1|Chicken1 PYTQGWEGELGTDLVTIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
sp|P56817|Human1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
gi|296216280|Marmoset1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
sp|P56819|Rat1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
sp|P56818|Mouse1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
tr|G3IAK4|ChineseHamster1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
sp|Q1KLR6|GuineaPig1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
sp|Q2HJ40|Cattle1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
gi|291383811|Rabbit1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL
gi|345799894|Dog1 PYTQGWEGELGTDLVSIPHGPNVTVRANIAAITSDKFFINGSNWEGIL

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2

sequences from ClustalX, continued.

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gi|344293150|Elephant1      PYTQGWEGELGTDLVSIHPGPNVTVRANIAAITE$DKFFINGSNWEGIL
tr|G5BHK2|DesertRat1      PYTQGWEGELGTDLVSIHPGPNVTVRANIAAITE$DKFFINGSNWEGIL
gi|45387815|ZebraFish1    PYTQGRWEGELGTDVVSVP$CPGNVSLRANIAAITQ$DRFFINGSNWEGIL
sp|Q9Y5Z0|Human2          KYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFFLPGIKWNGIL
gi|296232194|Marmoset2    KYTQGSWTGFVGEDLVTIPKGFNS$FLVNIATIFESENFFLPGIKWNGIL
sp|Q6IE75|Rat2           KYTQGSWTGFVGEDLVTIPKGFNS$FLVNIATIFESENFFLPGIKWNGIL
sp|Q9JL18|Mouse2         KYTQGSWTGFVGEDLVTIPKGFNS$FLVNIATIFESENFFLPGIKWNGIL
tr|G3HFD5|ChineseHamster2  KYTQGSWTGFVGEDLVTIPKGFNS$FLVNIATIFESENFFLPGIKWNGIL
gi|329663206|Cattle2     KYTQGSWTGFVGEDVVTIPKGFNS$FLVNIATIFESENFFLPGIRWNGIL
tr|G5C5D1|DesertRat2     KYTQGSWTGLVGDVVTIPKAFNS$FLVNIAAIFESENFFLPGIKWNGIL
gi|348556383|Guineapig2  KYTQGSWTGFVGEDLVTIPRAFNS$FLANVATIFESENFFLPGIKWNGIL
gi|345795292|Dog2        KYTQGSWTGFVGEDFVTIPKGFNS$FLVNIATIFESENFFLPGIKWNGIL
gi|344294632|Elephant2   KYTQGSWTGLMGEDLVTIPKGFNS$FLVNVATIFESENFFLPGIKWNGIL
tr|Q5QHS0|Chicken2       KYSQGSWTGLGTDVVTIPKIDGRY$TINIATILESENFFLPGIKWNGIL
gi|326913352|WildTurkey2 KYSQGSWTGVLGTDVITIPKIDG$SYTINIATILESENFFLPGV$KWHGIL
gi|345323454|Platypus2   KYTQGSWTG$VGTDVITIPKGFNG$FVVNIATIFESENFFLPGIQWNGIL
gi|213982845|WesternFrog2 RYTQGSWTGLL$GKDVI$SMPKGVN$GTF$LINIASIFQ$SENF$FLPNINWQ$GIL
gi|147903717|AfricanFrog2 RYTQGSWTGLL$GKD$VVS$IPKGVN$GTF$LINIASIFQ$SENF$FLPNINWQ$GIL
gi|348508416|CichlidFish2 RYTQGNWEGELGIDRV$SIPR$GPN$GTTINIAAIL$SSDG$FFLPGINWQ$GIL
gi|54400484|ZebraFish2   KYTQGEWEGELGTDLTIPE$G$PSG$AITINIAAILT$SEG$FFLPGINWQ$GIL
                          *** ** ** ** * : : * * . .   * : * : * * : * : * . . * : * : * : * : * : * : * : * :

tr|Q0P4T5|WesternFrog1    GLAYAEIARPDDTLE$FFFD$SLVKQTRV$PNIFSLQ$LCGTGFHFNESD-TSA
tr|Q5QHS1|Chicken1       GLAYAEIARPDD$SLE$FFFD$SLVKQTQV$PNIFSLQ$LCGAGFSPNETE-TLA
sp|P56817|Human1         GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-VLA
gi|296216280|Marmoset1   GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-VLA
sp|P56819|Rat1          GLAYAEIARPDD$SLE$FFFD$SLVKQTHI$PNIFSLQ$LCGAGFPLNQTE-ALA
sp|P56818|Mouse1        GLAYAEIARPDD$SLE$FFFD$SLVKQTHI$PNIFSLQ$LCGAGFPLNQTE-ALA
tr|G3IAK4|ChineseHamster1  GLAYAEIARPDD$SLE$FFFD$SLVKQTHI$ANV$FSLQ$LCGAGFPLNQSE-ALA
sp|Q1KLR6|GuineaPig1     GLAYAEIAR-----LCGAGFPLNQSE-AVA
sp|Q2HJ40|Cattle1       GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-ALA
gi|291383811|Rabbit1     GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-VLA
gi|345799894|Dog1       GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-VLA
gi|344293150|Elephant1   GLAYAEIARPDD$SLE$FFFD$SLVKQTHI$PNL$FSLQ$LCGAGFPLNQSE-VLA
tr|G5BHK2|DesertRat1     GLAYAEIARPDD$SLE$FFFD$SLVKQTHV$PNL$FSLQ$LCGAGFPLNQSE-AVA
gi|45387815|ZebraFish1   GLAYAEIARPDETLE$FFFD$SLRQ$STVADV$FSLQ$LCGAGY$NHNY$STG$SS
sp|Q9Y5Z0|Human2         GLAYATLAKP$SSSLE$TFFFD$SLV$TQANI$PNV$F$SMQ$MCGAGL$PVAG$SG----
gi|296232194|Marmoset2   GLAYATLAKP$SSSLE$TFFFD$SLV$QANI$PNV$F$SMQ$MCGAGL$PVAG$SG----
sp|Q6IE75|Rat2          GLAYAALAKP$SSSLE$TFFFD$SLV$AQAKI$PDI$F$SMQ$MCGAGL$PVAG$SG----
sp|Q9JL18|Mouse2        GLAYAALAKP$SSSLE$TFFFD$SLV$AQAKI$PDI$F$SMQ$MCGAGL$PVAG$SG----
tr|G3HFD5|ChineseHamster2  GLAYAALAK-----
gi|329663206|Cattle2     GLAYATLAKP$SSSLE$TFFFD$SLV$AQAKI$PNIF$SMQ$MCGAGL$PVAG$SG----
tr|G5C5D1|DesertRat2     GLAYASLAKP$SSSLE$TFFFD$SLV$TQAKI$PDV$F$SMQ$MCGAGL$PVARS$SG----
gi|348556383|Guineapig2  GLAYATLAKP$SSSLE$TFFFD$SLV$TQAKI$PDI$F$SMQ$MCGAGL$PVSRS$SG----
gi|345795292|Dog2       GLAYAALAKP$SSSLE$TFFFD$SLV$AQAKI$PNV$F$SMQ$MCGAGL$PVAG$SG----
gi|344294632|Elephant2   GLAYATLAKP$SSSLE$TFFFD$SLV$MQAKI$ANV$F$SMQ$MCGAGL$PVAG$SG----
tr|Q5QHS0|Chicken2      GLAYDTLAKP$SSSVE$TFFFD$SLV$QAKI$PNIF$SLQ$MCGAGL$PVS$GSG----
gi|326913352|WildTurkey2 GLAYDTLAKP$SSSVE$TFFFD$SLV$RQAKI$PNIF$SLQ$MCGAGL$PVS$GSG----
gi|345323454|Platypus2   GLAYAALAKP$SSSLE$TFFFD$SLV$QAKI$PNIF$SMQ$MCGAGL$PVAGT$G----
gi|213982845|WesternFrog2 GLAYSTLAKP$SSSVE$FFFD$SLV$Q$ENI$PNIF$SMQ$MCGAGQ$P$SPIG----
gi|147903717|AfricanFrog2 GLAYSTLAKP$SSSVE$FFFD$SLV$Q$ENI$PNIF$SMQ$MCGAGQ$S$SPNG----
gi|348508416|CichlidFish2 GLAYPVLARPD$SSV$E$FFFD$SVV$KQL$GIPDI$F$SLQ$MCGAGL$SAS$T---D
gi|54400484|ZebraFish2   GLAYPLLARPD$PSV$E$FFFD$SVR$QTGI$PDV$F$SLQ$MCGAGL$V$PAST$G---D
                          ***** **

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.



|    |           |                 |   |
|----|-----------|-----------------|---|
| tr | Q0P4T5    | WesternFrog1    | SVGGSMVIGGIDPSLYIGSIWYTPIRKEWYVEVIIVKIEINGQDLHMDCK    |
| tr | Q5QHS1    | Chicken1        | SVGGSMIIGGIDRSLYVGDWYTPIRKEWYVEVIIVKLEVNGQDLNMDCK     |
| sp | P56817    | Human1          | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| gi | 296216280 | Marmoset1       | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| sp | P56819    | Rat1            | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| sp | P56818    | Mouse1          | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| tr | G3IAK4    | ChineseHamster1 | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| sp | Q1KLR6    | GuineaPig1      | SVGGSMIIGGIDHSLYTGNLWYTPIRREWYVEVIIVRVEINGQDLKMDCK    |
| sp | Q2HJ40    | Cattle1         | SVGGSMIIGGIDHSLYMGSLWYTPIRREWYVEVIIVRVEINGQDLKMDCK    |
| gi | 291383811 | Rabbit1         | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| gi | 345799894 | Dog1            | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| gi | 344293150 | Elephant1       | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| tr | G5BHK2    | DesertRat1      | SVGGSMIIGGIDHSLYTGSWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| gi | 45387815  | ZebraFish1      | TVGGSMIIGGIDHSLYVGDWYTPIRREWYVEVIIVRVEINGQDLKMDCK     |
| sp | Q9Y5Z0    | Human2          | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| gi | 296232194 | Marmoset2       | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| sp | Q6IE75    | Rat2            | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| sp | Q9JL18    | Mouse2          | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| tr | G3HFD5    | ChineseHamster2 | -----VLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| gi | 329663206 | Cattle2         | TNGGSLVGGIEPTLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| tr | G5C5D1    | DesertRat2      | TNGGSLVGGIEPNLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| gi | 348556383 | GuineaPig2      | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| gi | 345795292 | Dog2            | TNGGSLVGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| gi | 344294632 | Elephant2       | TNGGSLVGGIQPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLNLDCL       |
| tr | Q5QHS0    | Chicken2        | TNGGSLVGGIEPSLYKGNWYTPIKEEWYQVEILKLEVGGQNLCLDCL       |
| gi | 326913352 | WildTurkey2     | TNGGSLVGGIEPSLYKGNWYTPIKEEWYQVEILKLEVGGQNLCLDCL       |
| gi | 345323454 | Platypus2       | INGGSLVMGGIESSLYTGDIWYTPIKEEWYQIEILKLEVGGQNLCLDCL     |
| gi | 213982845 | WesternFrog2    | INAGSLVGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLCLDCL       |
| gi | 147903717 | AfricanFrog2    | INAGSLVGGIEPSLYKGNWYTPITEEWYQVEVLKFEVGGQNLCLDCL       |
| gi | 348508416 | CichlidFish2    | TTGGSLIMGGAEPTLYRGSVWYTPITEEWYQVEVLKLEVGDQNLCLDCL     |
| gi | 54400484  | ZebraFish2      | PAGGSLIMGGVEPTLHRGPWYTPVLEEWYQVEVLKLEVGDQNLCLDCL      |
|    |           |                 | ::** : .* : * :**** : ***** : ::.* : . * : **         |
|    |           |                 |   |
| tr | Q0P4T5    | WesternFrog1    | EYNYDKSIVDSGTTNLRPLPKRVFDAAVKSIIKAASSTEFKPDGFWLGEQLV  |
| tr | Q5QHS1    | Chicken1        | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKTASSTEFKPDGFWLGEQLV |
| sp | P56817    | Human1          | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| gi | 296216280 | Marmoset1       | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| sp | P56819    | Rat1            | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| sp | P56818    | Mouse1          | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| tr | G3IAK4    | ChineseHamster1 | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| sp | Q1KLR6    | GuineaPig1      | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| sp | Q2HJ40    | Cattle1         | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| gi | 291383811 | Rabbit1         | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| gi | 345799894 | Dog1            | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| gi | 344293150 | Elephant1       | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| tr | G5BHK2    | DesertRat1      | EYNYDKSIVDSGTTNLRPLPKRVFEEAAVKSIIKAASSTEFKPDGFWLGEQLV |
| gi | 45387815  | ZebraFish1      | EYNYDKSIVDSGTTNLRPLPKRVFQAAVKAIEAASSTEQPFGFWLGEQLV    |
| sp | Q9Y5Z0    | Human2          | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARASLIEFSDGFWTGSQLA  |
| gi | 296232194 | Marmoset2       | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARASLIEFSDGFWTGSQLA  |
| sp | Q6IE75    | Rat2            | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARTSLIEFSDGFWTGAQLA  |
| sp | Q9JL18    | Mouse2          | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARTSLIEFSDGFWTGAQLA  |
| tr | G3HFD5    | ChineseHamster2 | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARTSLIEFSDGFWTGAQLA  |
| gi | 329663206 | Cattle2         | EYNADKAIIVDSGTTLLRPLPKRVFDDAVVEAVARTSLIEFSEGFWTGSQLA  |

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

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tr | G5C5D1 | DesertRat2          EYNADKAIVDSGTTLLRRLPQKVFDAVVDVAVARTSLIPEFSDGFWTGAQLA
gi | 348556383 | Guineapig2      EYNADKAIVDSGTTLLRRLPQKVFDAVVDVAVARTSLIPEFSDGFWTGAQLA
gi | 345795292 | Dog2                EYNADKAIVDSGTTLLRRLPQKVFNAVVEAVARTSLIPEFSDGFWTGSQLA
gi | 344294632 | Elephant2          EYNADKAIVDSGTTLLRRLPQKVFDAVVEAVAHASL IPEFSDGFWTGSQLA
tr | Q5QHS0 | Chicken2          EYNADKAIVDSGTTLLRRLPQKVFQAVVQAIARTSLIQEFSSGFWSGSQLA
gi | 326913352 | WildTurkey2       EYNADKAIVDSGTTLLRRLPQKVFQAVVQAIARTSLIQEFSSGFWSGSQLA
gi | 345323454 | Platypus2         EYNANKAIVDSGTTLLRRLPQKVFQAVVETITSTSSIQDFAEGFWTGSQLA
gi | 213982845 | WesternFrog2      VYNSDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQLA
gi | 147903717 | AfricanFrog2     VYNSDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQLA
gi | 348508416 | CichlidFish2     EYNMDKAIVDSGTTLLRRLPVNFNALVEAITMQLSLIEEFSSGFWSGKLA
gi | 54400484 | ZebraFish2       EYNSDKAIVDSGTTLLRRLPANVFTAVVDEITMQLSLIDDFAGFFDGTKLA
** :*:***** ***** .** * *.: :* . * *: * :.

tr | Q0P4T5 | WesternFrog1      CWQEGTTPWHIFPVISLYLMGEVANQSFKITILPQQYLRPVEDIATAQED
tr | Q5QHS1 | Chicken1          CWQVG-PPWHIFPVLISLYLMGEATNQSFRITILPQQYLGQWRNVATLKDD
sp | P56817 | Human1            CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
gi | 296216280 | Marmoset1        CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
sp | P56819 | Rat1              CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
sp | P56818 | Mouse1           CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
tr | G3IAK4 | ChineseHamster1  CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
sp | Q1KLR6 | GuineaPig1       CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
sp | Q2HJ40 | Cattle1         CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
gi | 291383811 | Rabbit1          CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
gi | 345799894 | Dog1             CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
gi | 344293150 | Elephant1        CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
tr | G5BHK2 | DesertRat1      CWQAGTTPWNIFFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDD
gi | 45387815 | ZebraFish1      CWQAGTTPWHIFPVISLYLMSENRNQSFRISILPQQYLRPVEDVASAQED
sp | Q9Y5Z0 | Human2          CWTNSETPWSYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
gi | 296232194 | Marmoset2       CWANSETPWSYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
sp | Q6IE75 | Rat2           CWTNSETPWAYFPPKIS IYLRDENASRSFRITILPQLYIQPMMGAGFN-YE
sp | Q9JL18 | Mouse2          CWTNSETPWAYFPPKIS IYLRDENASRSFRITILPQLYIQPMMGAGFN-YE
tr | G3HFD5 | ChineseHamster2 CWTNSETPWAYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
gi | 329663206 | Cattle2         CWTNSETPWSYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
tr | G5C5D1 | DesertRat2      CWTNSETPWAYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
gi | 348556383 | Guineapig2     CWANSETPWAYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLS-YE
gi | 345795292 | Dog2           CWTNSETPWSYFPPKIS IYLRDENSSRSFRITILPQLYIQPMMGAGLN-YE
gi | 344294632 | Elephant2      CWTNSETPWSYFPPKIS IYLRDENSSRSFRITILPQLYIQPMIGAGLN-YE
tr | Q5QHS0 | Chicken2          CWDKTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGEN-LQ
gi | 326913352 | WildTurkey2   CWDKTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGEN-LQ
gi | 345323454 | Platypus2     CWSNSDKPWSLFPKLSIYLRDENSSRSFRITILPQLYIQPMMGVASN-YE
gi | 213982845 | WesternFrog2  CWDKTQDPWNYFPDISIYLRDTNNSRSFRILTLKPQLYIQSVLTFQES-LN
gi | 147903717 | AfricanFrog2  CWDKTQDPWNYFPDISIYLRDTNTSRSFRILTLKPQLYIQSVLTFQES-LN
gi | 348508416 | CichlidFish2  CWMKGENPWRFFPKLSIYLRATNTSESFRITILPQLYIQPITDVDGT-LD
gi | 54400484 | ZebraFish2    CWMRGESPWRFFPKVSIYLRGTNTSRSFRITILPQVRIVP-----
**      **      ** :*:*: . : :

tr | Q0P4T5 | WesternFrog1      CYKFAVSQS-TTGTVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHDYFRT
tr | Q5QHS1 | Chicken1          LPTGSTTLRPPTATVMGCCIQEG-----ST
sp | P56817 | Human1            CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
gi | 296216280 | Marmoset1        CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
sp | P56819 | Rat1              CYKFAVSQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
sp | P56818 | Mouse1           CYKFAVSQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
tr | G3IAK4 | ChineseHamster1  CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

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sp|Q1KLR6|GuineaPig1      CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
sp|Q2HJ40|Cattle1        CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
gi|291383811|Rabbit1     CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
gi|345799894|Dog1       CYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRT
gi|344293150|Elephant1  CYKFAISQS-STGTVMGAVIMEGFYVVFDRSRKRIGFAVSACHVHDEFRT
tr|G5BHK2|DesertRat1    CYKFAISQS-STGTVMGAVIMEGFYVVFDRQKRIGFAVSACHVHDEFRT
gi|45387815|ZebraFish1  CYKFAISQS-STGTVMGAVIMEGFYVVFDRQKRIGFAVSTCHVHDEFRT
sp|Q9Y5Z0|Human2        CYRFGISPS-TNALVIGATVMEGFYVIFDRAQKRVGFAASPCAEIAGAAV
gi|296232194|Marmoset2  CYRFGISPS-TNALVIGATVMEGFYVIFDRAQKRVGFAASPCAEIAGAAV
sp|Q6IE75|Rat2          CYRFGISSS-TNALVIGATVMEGFYVVFDRQRRVGFVSPCAEIAIGTTV
sp|Q9JL18|Mouse2        CYRFGISSS-TNALVIGATVMEGFYVVFDRQRRVGFVSPCAEIEGTTV
tr|G3HFD5|ChineseHamster2 CYRFGISSS-TNALVIGATVMEGFYVVFDRARKRVGFAASPCAEIEGTTV
gi|329663206|Cattle2    CYRFGISPS-TNALVIGATVMEGFYVVFDRQKRVGFAASPCAEIAGAPV
tr|G5C5D1|DesertRat2    CYRFGISPS-TNALVIGATVMEGFYVVFDRARRRVGFAASPCAEIAGAPV
gi|348556383|Guineapig2 CYRFGISPS-TNALVIGATVMEGFYVVFDRARRRVGFAVSPCAETAGVPL
sp|Q9Y5Z0|Human2        CYRFGISPS-TNALVIGATVMEGFYVVFDRARKRVGFAASPCAEIAGAPV
gi|344294632|Elephant2  CYRFGISPS-SNALVIGATVMEGFYVVFDRARKRVGFAMSPCAAS-----
tr|Q5QHS0|Chicken2     CYRFGISSS-TNALVIGATVMEGFYVIFDRAQRRVGFVSPCAEIVDGSPP
gi|326913352|WildTurkey2 CYRFGISSS-TNALVIGATVMEGFYVIFDRAQRRVGFVSPCAEIVDGSPP
gi|345323454|Platypus2  CYRFGISSS-TNALVIGATVMEGFYVVFDRQKRVGFAVSLCAEIVGSPV
tr|G3HFD5|ChineseHamster2 CFRFGISQS-ASALVIGATVMEGFYVIFDRAEKRVGFVSSCAEIVSGITV
gi|213982845|WesternFrog2 CFRFGISQS-ASTLVIGATVMEGFYVIFDRAEKRVGFVSSCAEIVSGITV
gi|147903717|AfricanFrog2 CFRFGISQS-ASTLVIGATVMEGFYVIFDRAEKRVGFVSSCAEIVSGITV
gi|348508416|CichlidFish2 CFRFGVSSS-TNGMVIGATVMEGFYVVFDRDQQLRGLFALSSCAVSDGVAL
gi|54400484|ZebraFish2  -----

tr|Q0P4T5|WesternFrog1  ASVEGPFASDLEDCGYNTPQLDESALMTTAYVMAGVLCALFMLPLCLMLF
tr|Q5QHS1|Chicken1      VALTGP-----
sp|P56817|Human1        AAVEGPFVTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
gi|296216280|Marmoset1  AAVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
sp|P56819|Rat1          AAVEGPFVTADMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
sp|P56818|Mouse1        AAVEGPFVTADMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
tr|G3IAK4|ChineseHamster1 AAVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
sp|Q1KLR6|GuineaPig1    ATVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
sp|Q2HJ40|Cattle1        AAVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
gi|291383811|Rabbit1     AAVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
gi|345799894|Dog1       AAVEGPFITLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
gi|344293150|Elephant1  AAVEGPFVTPDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
tr|G5BHK2|DesertRat1    AAVEGPFVTLDMEDCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVC
gi|45387815|ZebraFish1  AAVEGPFHGLDLEDCGYNVPQTDESTLMTIAYIMAGICALFMLPLCLMVC
sp|Q9Y5Z0|Human2        SEISGPFSTEDVASNCVPAQSLSEPIILWIVSYALMSVCGAILLVLIIVLLL
gi|296232194|Marmoset2  SHRMG-IPDESPLCECADLEAIPDGT-----
sp|Q6IE75|Rat2          SEISGPFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIIVLLL
sp|Q9JL18|Mouse2        SEISGPFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIIVLLL
tr|G3HFD5|ChineseHamster2 SEISGPFSTEDVASNCVPAPALNEPILWIVSYALMSVCGAILLVLIIVLLL
gi|329663206|Cattle2    SEISGPFSTEDIASNCVPALPLNEPVLWIVSYTLMSVCGVILLVLIIVLLL
tr|G5C5D1|DesertRat2    SEVSGPFSTDDGIASNCVPAPAPGEPPLWVFSYALLSACGLIILLVLIIVLLL
gi|348556383|Guineapig2 SEVSGPFSTDDGIASNCVSPSLNEPVLWVFSYALMSVCGVILLVLIIVLLL
gi|345795292|Dog2       SEISGPFSTDDIASNCVPALPLNEPILWIVSYTLMSVCGIILLVLIIVLLL
gi|344294632|Elephant2  -----
tr|Q5QHS0|Chicken2     SEIEGPFSTDDVASNCVSSITFHEPVLWIASYALMSLCGIILLVLIIVLLL
gi|326913352|WildTurkey2 SEIEGPFSTDDVASNCVSSITFHEPVLWIASYALMSLCGIILLVLIIVLLL
gi|345323454|Platypus2 SEISGPFPTDDVASNCVTTLPFNEPILWIVSYTLMSICGIILLVLIIVLLL

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

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gi|213982845|WesternFrog2      SEIAGPFGTSDVSSNCIARNPLREPIMWIIISYLSMLCGMILLVLVILL
gi|147903717|AfricanFrog2     SEIAGPFGTSDVSSNCIARNPLREPIMWIIISYLSMLCGMILLVLVILL
gi|348508416|CichlidFish2     SEIEGPFSAADVAADC-SGGPLKEPLVWMISYALMAVCALALLLILLML
gi|54400484|ZebraFish2       -----
-

tr|Q0P4T5|WesternFrog1       QWRCFRCLKRARDLADDISLLK----
tr|Q5QHS1|Chicken1           -----
sp|P56817|Human1             QWCCLRCLRQHQHDDFADDISLLK----
gi|296216280|Marmoset1       QWRCLRCLRQHQHDDFADDISLLK----
sp|P56819|Rat1               QWRCLRCLRHQHDDFADDISLLK----
sp|P56818|Mouse1            QWRCLRCLRHQHDDFADDISLLK----
tr|G3IAK4|ChineseHamster1    QWRCLRCLRHQHDDFADDISLLK----
sp|Q1KLR6|GuineaPig1        QWRCLRCLRHQHDDFADDISLLK----
sp|Q2HJ40|Cattle1           QWRCLRCLRHQHDDFADDISLLK----
gi|291383811|Rabbit1        QWRCLRCLRHQHDDFADDISLLK----
gi|345799894|Dog1           QWRCLRCLRHQHDDFADDISLLK----
gi|344293150|Elephant1      QWRCLRCLRHQHDDFADDISLLK----
tr|G5BHK2|DesertRat1        QWRCLRCLRHQHDDFADDISLLK----
gi|45387815|ZebraFish1     QWRFTCCLQPADG--SDDISLLK----
sp|Q9Y5Z0|Human2            LPPFCQRRPRDPEVVNDESSLVRRHWK
gi|296232194|Marmoset2     -----
sp|Q6IE75|Rat2              FPLHCRHAPRDPEVVNDESSLVRRHWK
sp|Q9JL18|Mouse2            LPLHCRHAPRDPEVVNDESSLVRRHWK
tr|G3HFD5|ChineseHamster2    LPVRCRHAPRDPEVVNDESSLVRRHWK
gi|329663206|Cattle2        LPVRCRHAPRDPEVVNDESSLVRRHWK
tr|G5C5D1|DesertRat2        LPCR-RRPPRDPEVINDESSLVRRHWK
gi|348556383|Guineapig2     LPCRHRHAPRDPEVINDESSLVRRHWK

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**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

## Supplement Figure 7

|               |           |                |   |
|---------------|-----------|----------------|---|
| tr            | Q0P4T5    | WesternFrog    | MELVVYARTGSILLVLLPCFLPVTG-QVAIKLPLKNCPGT---CSPMAYR  |
| tr            | Q5QHS1    | Chicken        | -----   |
| sp            | P56819    | Rat            | ----MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRSGLAG---PPLGLRL  |
| sp            | P56818    | Mouse          | ----MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRSGLAG---PPLGLRL  |
| tr            | G3IAK4    | ChineseHamster | ----MAPALRWLLLWVGSGMLPAQGTHLGIRLPLRSGLAG---PPLGLRL  |
| sp            | Q1KLR6    | GuineaPig      | ----MAPALPWLLLWVGSGVLPVHGTQDGIRLPLRSGLAG---APLGLRL  |
| gi            | 291383811 | Rabbit         | ----MAPALPWLLLWVGSGMLPAQGTQHGIRLPLRSGLGG---APLGLRL  |
| gi            | 344293150 | Elephant       | ----MALVALSWLLLWVGSGVLPVHGTQDGIRLPLRSGLGG---APLGLRL |
| gi            | 345799894 | Dog            | -----   |
| tr            | G5BHK2    | DesertRat      | -----   |
| gi            | 45387815  | ZebraFish      | --MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQGPLTPHSTPAAHR   |
| <b>Group1</b> |           |                | -----   |
|               |           |                |   |
| sp            | P56817    | Human          | ----MAQALPWLLLWVGAGVLPVHGTQHGIRLPLRSGLGG---APLGLRL  |
| gi            | 296216280 | Marmoset       | ----MAQALPWLLLWVGAGVLPVHGTQHGIRLPLRSGLGG---APLGLRL  |
| sp            | Q2HJ40    | Cattle         | ----MAQALPWLLLWVGSGVLPVHGTQHGIRLPLRSGLGG---APLGLRL  |
| <b>Group2</b> |           |                | ----MAQALPWL-LWVG-GVLPVHGTQHGIRLPLRSGLGG---APLGLRL  |
| <b>P1</b>     |           |                | -----   |
|               |           |                |   |
| tr            | Q0P4T5    | WesternFrog    | AKRSAEKGMELDTN--FLDMIDNLRGKSGQGYVEMRVGTPPQTLNII     |
| tr            | Q5QHS1    | Chicken        | -----YVEMTVGSPQKLNII                                |
| sp            | P56819    | Rat            | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| sp            | P56818    | Mouse          | PRETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| tr            | G3IAK4    | ChineseHamster | PRETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| sp            | Q1KLR6    | GuineaPig      | PRETDEE---PGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| gi            | 291383811 | Rabbit         | PRETDEEPEEPGRRGNFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| gi            | 344293150 | Elephant       | PRDTDEELEDPSRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| gi            | 345799894 | Dog            | -----MWDAPVIR-----                                  |
| tr            | G5BHK2    | DesertRat      | -----YVEMTVGSPQKLNII                                |
| gi            | 45387815  | ZebraFish      | PHGPRARSRAASGISFINMIDNLRGKSGQGYIEMAVGSPAQRNII       |
| <b>Group1</b> |           |                | -----   |
|               |           |                |   |
| sp            | P56817    | Human          | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| gi            | 296216280 | Marmoset       | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| sp            | Q2HJ40    | Cattle         | PRETDEESEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII      |
| <b>Group2</b> |           |                | PRETDEE-EEPGRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNII       |
| <b>P1</b>     |           |                | -----   |

Supplement Figure 7 The result of p1 partition and extracting the sequences of BACE.

|    |               |                |   |
|----|---------------|----------------|---|
| tr | Q0P4T5        | WesternFrog    | TGSSNFVAVGAAPHPFLKRYHRQHSRTYRDVRRGVYVPYTQGKWEWELGT        |
| tr | Q5QHS1        | Chicken        | TGSSNFVAVGAAPHPFLRRYYQRQLSSTYRDLRKGVYVPYTQGKWEWELGT       |
| sp | P56819        | Rat            | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKSIVYVPYTQGKWEWELGT        |
| sp | P56818        | Mouse          | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| tr | G3IAK4        | ChineseHamster | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| sp | Q1KLR6        | GuineaPig      | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| gi | 291383811     | Rabbit         | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| gi | 344293150     | Elephant       | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| gi | 345799894     | Dog            | -----SSTYRDLRKGVYVPYTQGKWEWELGT                           |
| tr | G5BHK2        | DesertRat      | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| gi | 45387815      | ZebraFish      | TGSSNFVAVGAAHPFLHRYHRSLSSSYRDLGRGVYVPYTQGRWEWELGT         |
|    | <b>Group1</b> |                | -----S--YRD---GVYVPYTQG--WEGELGT                          |
|    |               |                |   |
| sp | P56817        | Human          | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| gi | 296216280     | Marmoset       | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
| sp | Q2HJ40        | Cattle         | TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT         |
|    | <b>Group2</b> |                | <b>TGSSNFVAVGAAPHPFLHRYRQLSSTYRDLRKGVYVPYTQGKWEWELGT</b>  |
|    | <b>P1</b>     |                | -----S--YRD---GVYVPYTQG--WEGELGT                          |
|    |               |                |   |
| tr | Q0P4T5        | WesternFrog    | DLVTIPHGPNVTVRANIAAITSDKFFINGSNWEGILGLAYAEIARPDST         |
| tr | Q5QHS1        | Chicken        | DLVTIPHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD        |
| sp | P56819        | Rat            | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| sp | P56818        | Mouse          | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| tr | G3IAK4        | ChineseHamster | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| sp | Q1KLR6        | GuineaPig      | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIAR----         |
| gi | 291383811     | Rabbit         | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| gi | 344293150     | Elephant       | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| gi | 345799894     | Dog            | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| tr | G5BHK2        | DesertRat      | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| gi | 45387815      | ZebraFish      | DVSVPCGPNVSLRANIAAITQSDRFFINGSNWEGILGLAYAEIARPDST         |
|    | <b>Group1</b> |                | <b>D-V--P-GPNV---ANIAAIT-SDKFFINGSNWEGILGLAYAEIAR----</b> |
|    |               |                |   |
| sp | P56817        | Human          | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| gi | 296216280     | Marmoset       | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
| sp | Q2HJ40        | Cattle         | DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD         |
|    | <b>Group1</b> |                | <b>DLVSIHGPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDSD</b>  |
|    | <b>P1</b>     |                | <b>D-V--P-GPNV---ANIAAIT-SDKFFINGSNWEGILGLAYAEIAR----</b> |

**Supplement Figure 7** The result of p1 partition and extracting the sequences of BACE1, continued.

```

tr|Q0P4T5|WesternFrog      LEPFFDSLQTRVNIIFSLQLCGTGFHFNESD-TSASVGGSMVIGGIDP
tr|Q5QHS1|Chicken         LEPFFDSLQVQVNIIFSLQLCGAGFSPNETE-TLASVGGSMIIGGIDR
sp|P56819|Rat             LEPFFDSLQTHIPNIIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
sp|P56818|Mouse          LEPFFDSLQTHIPNIIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
tr|G3IAK4|ChineseHamster LEPFFDSLQTHIANVFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH
sp|Q1KLR6|GuineaPig      -----LCGAGFPLNQSE-AVASVGGSMIIGGIDH
gi|291383811|Rabbit      LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|344293150|Elephant    LEPFFDSLQTHIPNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|345799894|Dog        LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
tr|G5BHK2|DesertRat     LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-AVASVGGSMIIGGIDH
gi|45387815|ZebraFish   LEPFFDSLRLRQSTVADVFSLQLCGAGYNHNYSTGSSSTVGGSMIIGGVDP
Group1                   -----LCG-G---N-----VGGSM-IGG-D-

sp|P56817|Human          LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
gi|296216280|Marmoset   LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH
sp|Q2HJ40|Cattle        LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-ALASVGGSMIIGGIDH
Group2                   LEPFFDSLQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH

P1                       -----LCG-G---N-----VGGSM-IGG-D-

tr|Q0P4T5|WesternFrog      SLYIGSIWYTPIRKEWYVEVIVKIEINGQDLHMDCKEYNYDKSIVDSGT
tr|Q5QHS1|Chicken         SLYVGDWYTPIRKEWYVEVIVKLEVNGQDLNMDCKEYNYDKSIVDSGT
gi|296216280|Marmoset     SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|P56819|Rat             SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|P56818|Mouse          SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
tr|G3IAK4|ChineseHamster SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|Q1KLR6|GuineaPig      SLYTGNLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|291383811|Rabbit      SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|344293150|Elephant    SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|345799894|Dog        SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
tr|G5BHK2|DesertRat     SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|45387815|ZebraFish   SLYVGEWYTPIRREWYVEVIVRVEINGQDLNMDCKEYNYDKSIVDSGT
Group1                   SLY-G--WYTPIR-EWYVEVIV--E-NGQDL-MDCKEYNYDKSIVDSGT

sp|P56817|Human          SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
gi|296216280|Marmoset   SLYTGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
sp|Q2HJ40|Cattle        SLYMGSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT
Group2                   SLY-GSLWYTPIRREWYVEVIVRVEINGQDLKMDCKEYNYDKSIVDSGT

P1                       SLY-G--WYTPIR-EWYVEVIV--E-NGQDL-MDCKEYNYDKSIVDSGT

```

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

|               |           |                |   |
|---------------|-----------|----------------|---|
| tr            | Q0P4T5    | WesternFrog    | TNLRLPKRVFDAAVKSIKAASSTEKFPDGFWLGEQLVCWQEGTTPWHIFP          |
| tr            | Q5QHS1    | Chicken        | TNLRLPKVKVFEAAVKSIKTASSTEKFPDGFWLGEQLVCWQVG--PPWHIFP        |
| sp            | P56819    | Rat            | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| sp            | P56818    | Mouse          | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| tr            | G3IAK4    | ChineseHamster | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| sp            | Q1KLR6    | GuineaPig      | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| gi            | 291383811 | Rabbit         | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| gi            | 344293150 | Elephant       | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| gi            | 345799894 | Dog            | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| tr            | G5BHK2    | DesertRat      | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| gi            | 45387815  | ZebraFish      | TNLRLPKRVFQAAVKAIKAASSTEKFPDGFWLGEQLVCWQAGTTPWHIFP          |
| <b>Group1</b> |           |                | <b>TNLRLP--VF-AAVK-I--ASSTE-FP-GFWLGEQLVCWQ-G--PW-IFP</b>   |
|               |           |                |   |
| sp            | P56817    | Human          | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| gi            | 296216280 | Marmoset       | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| sp            | Q2HJ40    | Cattle         | TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP        |
| <b>Group2</b> |           |                | <b>TNLRLPKVKVFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPWNIFP</b> |
| <b>P1</b>     |           |                | <b>TNLRLP--VF-AAVK-I--ASSTE-FP-GFWLGEQLVCWQ-G--PW-IFP</b>   |
|               |           |                |   |
| tr            | Q0P4T5    | WesternFrog    | VISLYLMGEVANQSFKITILPQQYLRPVEDIATAQEDCYKFAVSQS-TTG          |
| tr            | Q5QHS1    | Chicken        | VLSLYLMGEATNQSFRITILPQQYLGQWRNVATLKDDLPTGSTTLRPPTA          |
| sp            | P56819    | Rat            | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG          |
| sp            | P56818    | Mouse          | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG          |
| tr            | G3IAK4    | ChineseHamster | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| sp            | Q1KLR6    | GuineaPig      | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| gi            | 291383811 | Rabbit         | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| gi            | 344293150 | Elephant       | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| gi            | 345799894 | Dog            | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| tr            | G5BHK2    | DesertRat      | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| gi            | 45387815  | ZebraFish      | VISLYLMSENRNQSFRISILPQQYLRPVEDVASAQEDCYKFAVSQS-STG          |
| <b>Group1</b> |           |                | <b>VISLYLM-E--NQSF-I-ILPQQYL-----A----D-----T-</b>          |
|               |           |                |   |
| sp            | P56817    | Human          | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| gi            | 296216280 | Marmoset       | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| sp            | Q2HJ40    | Cattle         | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG          |
| <b>Group2</b> |           |                | <b>VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG</b>   |
| <b>P1</b>     |           |                | <b>VISLYLM-E--NQSF-I-ILPQQYL-----A----D-----T-</b>          |

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.



```

tr|Q0P4T5|WesternFrog      TVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHDYFRTASVEGPFPPASDLE
tr|Q5QHS1|Chicken         TVMGCCIQEG-----STVALTGP-----
sp|P56819|Rat             TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
sp|P56818|Mouse          TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
tr|G3IAK4|ChineseHamster TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
sp|Q1KLR6|GuineaPig     TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
gi|291383811|Rabbit      TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
gi|344293150|Elephant   TVMGAVIMEGFYVVFDRSRKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
gi|345799894|Dog        TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
tr|G5BHK2|DesertRat     TVMGAVIMEGFYVVFDRARQKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
gi|45387815|ZebraFish   TVMGAVIMEGFYVVFERQHKRIGFAVSTCHVHDEFRTAAVEGPFPHGLDLE
Group1                   TVMG--I-EG-----T---GP-----

sp|P56817|Human          TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
gi|296216280|Marmoset   TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
sp|Q2HJ40|Cattle         TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME
Group2                   TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTTADME

P1                       TVMG--I-EG-----T---GP-----

tr|Q0P4T5|WesternFrog    DCGYNTPQLDESALMTTAYVMAGVLCALFMLPLCLMLFQWRCFRCLKRARD
tr|Q5QHS1|Chicken       -----
sp|P56819|Rat           DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
sp|P56818|Mouse        DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
tr|G3IAK4|ChineseHamster DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
sp|Q1KLR6|GuineaPig    DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
gi|291383811|Rabbit     DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
gi|344293150|Elephant  DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
gi|345799894|Dog       DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
tr|G5BHK2|DesertRat    DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD
gi|45387815|ZebraFish  DCGYNVPQTDESTLMTIAYIMAGICALFMLPLCLMVCQWRFTCCCLQPADG
Group1                   -----

sp|P56817|Human          DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCCCLRCLRQQHD
gi|296216280|Marmoset   DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHD
sp|Q2HJ40|Cattle         DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHD
Group2                   DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCCCLRCLRQQHD

P1                       -----

```

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

```

tr|Q0P4T5|WesternFrog      DLADDISLLK
tr|Q5QHS1|Chicken         -----
sp|P56819|Rat             DFADDISLLK
sp|P56818|Mouse           DFADDISLLK
tr|G3IAK4|ChineseHamster  DFADDISLLK
sp|Q1KLR6|GuineaPig      DFADDISLLK
gi|291383811|Rabbit       DFADDISLLK
gi|344293150|Elephant     DFADDISLLK
gi|345799894|Dog          DFADDISLLK
tr|G5BHK2|DesertRat       DFADDISLLK
gi|45387815|ZebraFish    --SDDISLLK
Group1                    -----

sp|P56817|Human           DFADDISLLK
gi|296216280|Marmoset     DFADDISLLK
sp|Q2HJ40|Cattle          DFADDISLLK
Group2                    DFADDISLLK

P1                          -----

```

**Supplement Figure 6** Multiple sequence alignment resulting of BACE1 & BACE2 sequences from ClustalX, continued.

## Supplement Figure 8

|                              |  |
|------------------------------|--|
| tr   Q0P4T5   WesternFrog    | MELVVYARTGSILLVLLPCFLPVTG-QVAIKLPLKNCPGT---CSPMAYR |
| tr   Q5QHS1   Chicken        | -----  |
| sp   P56819   Rat            | ----MAPALRWLLLWVSGMLPAQGTHLGIRLPLRSGLAG---PPLGLRL  |
| sp   P56818   Mouse          | ----MAPALHWLLLWVSGMLPAQGTHLGIRLPLRSGLAG---PPLGLRL  |
| tr   G3IAK4   ChineseHamster | ----MAPALRWLLLWVSGMLPAQGTHLGIRLPLRSGPAG---PPLGLRL  |
| sp   Q1KLR6   GuineaPig      | ----MAPALPWLLLWVSGVLPVHGTQDQGIRLPLRSGLAG---APLGLRL |
| gi   344293150   Elephant    | ---MALVALSWLLLWVSGVLPVHGTQDQGIRLPLRSGLAG---APLGLRL |
| gi   345799894   Dog         | -----  |
| tr   G5BHK2   DesertRat      | -----  |
| gi   45387815   ZebraFish    | --MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQGPLTPHSTPAAHRS |
| <b>Group1</b>                | -----  |
| <br>                         |  |
| sp   P56817   Human          | ----MAQALPWLLLWWMGAGVLPAGHTQHGIPLRSGLGG---APLGLRL  |
| gi   296216280   Marmoset    | ----MAQALPWLXLWWMGAGVLPAGHTQHGIPLRSGLGG---APLGLRL  |
| <b>Group2</b>                | ----MAQALPWL-LWMGAGVLPAGHTQHGIPLRSGLGG---APLGLRL   |
| <b>P2</b>                    | -----  |
| <br>                         |  |
| tr   Q0P4T5   WesternFrog    | AKRSAEKGMELDTN--FLDMIDNLRGKSGQGYVEMRVGTPPQTLNIVD   |
| tr   Q5QHS1   Chicken        | -----YVEMTVGSPQKLNILVD                             |
| sp   P56819   Rat            | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| sp   P56818   Mouse          | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| tr   G3IAK4   ChineseHamster | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| sp   Q1KLR6   GuineaPig      | PRETDEE---PGRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD     |
| gi   344293150   Elephant    | PRDTDEELEDPSRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| gi   345799894   Dog         | -----MWDAPFIR-----                                 |
| tr   G5BHK2   DesertRat      | -----YVEMTVGSPQTLNIVD                              |
| gi   45387815   ZebraFish    | PHGPRARSRAASGISFINMIDNLRGKSGQGYIEMAVGSPAQRNIVD     |
| <b>Group1</b>                | -----  |
| <br>                         |  |
| sp   P56817   Human          | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| gi   296216280   Marmoset    | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| <b>Group2</b>                | PRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMTVGSPQTLNIVD    |
| <b>P2</b>                    | -----  |

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1.

|                              |  |
|------------------------------|--|
| tr   Q0P4T5   WesternFrog    | TGSSNFVAVGAAPHPFLKRYYHRQHSRTYRDVRRGVVVPYTQGWEGELGT           |
| tr   Q5QHS1   Chicken        | TGSSNFVAVGAAPHPFLRRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| sp   P56819   Rat            | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKSIVYVVPYTQGWEGELGT         |
| sp   P56818   Mouse          | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| tr   G3IAK4   ChineseHamster | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| sp   Q1KLR6   GuineaPig      | TGSSNFVAVGAAPHPFLHRYYQRQRSSTYRDLRKGVYVVPYTQGWEGELGT          |
| gi   344293150   Elephant    | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| gi   345799894   Dog         | -----SSTYRDLRKGVYVVPYTQGWEGELGT                              |
| tr   G5BHK2   DesertRat      | TGSSNFVAVGAAPHPFLHRYYQRQRSSTYRDLRKGVYVVPYTQGWEGELGT          |
| gi   45387815   ZebraFish    | TGSSNFVAVGAAHPFLHRYYHRSLSSSYRDLGRGVYVVPYTQGRWEGELGT          |
| <b>Group1</b>                | -----S--YRD---VYVPYTG-WEGELGT                                |
|                              |  |
| sp   P56817   Human          | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| gi   296216280   Marmoset    | TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT          |
| <b>Group2</b>                | <b>TGSSNFVAVGAAPHPFLHRYYQRQLSSTYRDLRKGVYVVPYTQGWEGELGT</b>   |
| <b>P2</b>                    | <b>-----S--YRD---VYVPYTG-WEGELGT</b>                         |
|                              |  |
| tr   Q0P4T5   WesternFrog    | DLVTIPHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDT         |
| tr   Q5QHS1   Chicken        | DLVTIPHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS         |
| sp   P56819   Rat            | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| sp   P56818   Mouse          | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| tr   G3IAK4   ChineseHamster | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| sp   Q1KLR6   GuineaPig      | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIAR----        |
| gi   344293150   Elephant    | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| gi   345799894   Dog         | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| tr   G5BHK2   DesertRat      | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| gi   45387815   ZebraFish    | DVSVPCGPNVSLRANIAAITE SDRFF INGSNWEGILGLAYAEIARDET           |
| <b>Group1</b>                | <b>D-V--P-GPNV---ANIAAIT-SDKFF INGSNWEGILGLAYAEIAR----</b>   |
|                              |  |
| sp   P56817   Human          | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| gi   296216280   Marmoset    | DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS        |
| <b>Group2</b>                | <b>DLVSI PHGPNTVTRANIAAITE SDKFF INGSNWEGILGLAYAEIARPDDS</b> |
| <b>P2</b>                    | <b>D-V--P-GPNV---ANIAAIT-SDKFF INGSNWEGILGLAYAEIAR----</b>   |

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1, continued.

|    |           |                |  |
|----|-----------|----------------|--|
| tr | Q0P4T5    | WesternFrog    | LEPFFDSLVKQTRVFNIFSLQLCGTGFHFNED-TSASVGGSMVIGGIDP      |
| tr | Q5QHS1    | Chicken        | LEPFFDSLVKQTQVFNIFSLQLCGAGFSPNETE-TLASVGGSMIIGGIDR     |
| sp | P56819    | Rat            | LEPFFDSLVKQTHIPNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH     |
| sp | P56818    | Mouse          | LEPFFDSLVKQTHIPNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH     |
| tr | G3IAK4    | ChineseHamster | LEPFFDSLVKQTHIANVFNIFSLQLCGAGFPLNQTE-ALASVGGSMIIGGIDH  |
| sp | Q1KLR6    | GuineaPig      | -----LCGAGFPLNQSE-AVASVGGSMIIGGIDH                     |
| gi | 344293150 | Elephant       | LEPFFDSLVKQTHIPNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH     |
| gi | 345799894 | Dog            | LEPFFDSLVKQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH     |
| tr | G5BHK2    | DesertRat      | LEPFFDSLVKQTHVFNLFSLQLCGAGFPLNQSE-AVASVGGSMIIGGIDH     |
| gi | 45387815  | ZebraFish      | LEPFFDSSLRQSTVADVFNLFSLQLCGAGYHNHNYSTGSSSTVGGSMIIGGVDP |
|    |           | <b>Group1</b>  | -----LCG-G--N-----VGGSM-IGG-D-                         |
|    |           |                |  |
| sp | P56817    | Human          | LEPFFDSLVKQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH     |
| gi | 296216280 | Marmoset       | LEPFFDSLVKQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH     |
|    |           | <b>Group2</b>  | LEPFFDSLVKQTHVFNLFSLQLCGAGFPLNQSE-VLASVGGSMIIGGIDH     |
|    |           | <b>P2</b>      | -----LCG-G--N-----VGGSM-IGG-D-                         |
|    |           |                |  |
| tr | Q0P4T5    | WesternFrog    | SLYIGSIWYTPIRKEWYEVIIVKIEINGQDLHMDCKEYNYDKSIVDSGT      |
| tr | Q5QHS1    | Chicken        | SLYVGDWYTPIRKEWYEVIIVKLEVNGQDLNMDCKEYNYDKSIVDSGT       |
| sp | P56819    | Rat            | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| sp | P56818    | Mouse          | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| tr | G3IAK4    | ChineseHamster | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| sp | Q1KLR6    | GuineaPig      | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| gi | 344293150 | Elephant       | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| gi | 345799894 | Dog            | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| tr | G5BHK2    | DesertRat      | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| gi | 45387815  | ZebraFish      | SLYVGLWYTPIRREWYEVIIVRVEINGQDLNMDCKEYNYDKSIVDSGT       |
|    |           | <b>Group1</b>  | SLY-G--WYTPIR-EWYEVIIV--E-NGQDL-MDCKEYNYDKSIVDSGT      |
|    |           |                |  |
| sp | P56817    | Human          | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
| gi | 296216280 | Marmoset       | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
|    |           | <b>Group2</b>  | SLYTGSLWYTPIRREWYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGT      |
|    |           | <b>P2</b>      | SLY-G--WYTPIR-EWYEVIIV--E-NGQDL-MDCKEYNYDKSIVDSGT      |

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1, continued.

|                              |   |
|------------------------------|---|
| tr   Q0P4T5   WesternFrog    | TNLRRLPKRVFDAAVKSIKAASSTEKFPDGFVLGQELVLCWQEGTTPWHIFP  |
| tr   Q5QHS1   Chicken        | TNLRRLPKKVFEAAVKSIKTASSTEKFPDGFVLGQELVLCWQVG-PPWHIFP  |
| sp   P56819   Rat            | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| sp   P56818   Mouse          | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| tr   G3IAK4   ChineseHamster | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| sp   Q1KLR6   GuineaPig      | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| gi   344293150   Elephant    | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| gi   345799894   Dog         | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| tr   G5BHK2   DesertRat      | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| gi   45387815   ZebraFish    | TNLRRLPKRVQAAVKAIEAASSTEQFPDGFVLGQELVLCWQAGTTPWHIFP   |
| Group1                       | TNLRRLPK-VF-AAVK-I--ASSTE-FP-GFVLGQELVLCWQ-G--PW-IFP  |
| sp   P56817   Human          | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| gi   296216280   Marmoset    | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| Group2                       | TNLRRLPKKVFEAAVKSIIKAASSTEKFPDGFVLGQELVLCWQAGTTPWNIFP |
| P2                           | TNLRRLPK-VF-AAVK-I--ASSTE-FP-GFVLGQELVLCWQ-G--PW-IFP  |
| tr   Q0P4T5   WesternFrog    | VISLYLMGEVANQSFKITILPQQYLRPVEDIATAQEDCYKFAVSQS-TTG    |
| tr   Q5QHS1   Chicken        | VLSLYLMGEATNQSFRITILPQQYLGQWRNVATLKDDLPTGSTTLRPPTA    |
| sp   P56819   Rat            | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG    |
| sp   P56818   Mouse          | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQS-STG    |
| tr   G3IAK4   ChineseHamster | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| sp   Q1KLR6   GuineaPig      | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| gi   344293150   Elephant    | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| gi   345799894   Dog         | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| tr   G5BHK2   DesertRat      | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| gi   45387815   ZebraFish    | VISLYLMSENRNQSFRIISILPQQYLRPVEDVASAQEDCYKFAVSQS-STG   |
| Group1                       | VISLYLMGE--NQSF-I-ILPQQYL-----A----D-----T-           |
| sp   P56817   Human          | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| gi   296216280   Marmoset    | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| Group2                       | VISLYLMGEVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQS-STG    |
| P2                           | VISLYLMGE--NQSF-I-ILPQQYL-----A----D-----T-           |

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1, continued.

|    |           |                |   |
|----|-----------|----------------|---|
| tr | Q0P4T5    | WesternFrog    | TVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHDYFRTASVEGPFASDLE         |
| tr | Q5QHS1    | Chicken        | TVMGCCIQEG-----STVALTGP-----                              |
| sp | P56819    | Rat            | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPADME       |
| sp | P56818    | Mouse          | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPADME       |
| tr | G3IAK4    | ChineseHamster | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME        |
| sp | Q1KLR6    | GuineaPig      | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTATVEGPFVTPDME        |
| gi | 344293150 | Elephant       | TVMGAVIMEGFYVVFDRSRKRIGFAVSACHVHDEFRTAAVEGPFVTPDME        |
| gi | 345799894 | Dog            | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFITLDME        |
| tr | G5BHK2    | DesertRat      | TVMGAVIMEGFYVVFDRQAQKRIGFAVSACHVHDEFRTAAVEGPFVTPDME       |
| gi | 45387815  | ZebraFish      | TVMGAVIMEGFYVFERQHKRIGFAVSTCHVHDEFRTAAVEGPFHGLDLE         |
|    |           | <b>Group1</b>  | <b>TVMG--I-EG-----T---GP-----</b>                         |
|    |           |                |   |
| sp | P56817    | Human          | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME        |
| gi | 296216280 | Marmoset       | TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME        |
|    |           | <b>Group1</b>  | <b>TVMGAVIMEGFYVVFDRARKRIGFAVSACHVHDEFRTAAVEGPFVTPDME</b> |
|    |           | <b>P2</b>      | <b>TVMG--I-EG-----T---GP-----</b>                         |
|    |           |                |   |
| tr | Q0P4T5    | WesternFrog    | DCGYNTPQLDESALMTTAYVMAGVCALFMLPLCLMLFQWRFCRCLKRARD        |
| tr | Q5QHS1    | Chicken        | -----   |
| sp | P56819    | Rat            | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| sp | P56818    | Mouse          | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| tr | G3IAK4    | ChineseHamster | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| sp | Q1KLR6    | GuineaPig      | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| gi | 344293150 | Elephant       | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| gi | 345799894 | Dog            | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| tr | G5BHK2    | DesertRat      | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQHD        |
| gi | 45387815  | ZebraFish      | DCGYNVPQTDESTLMTIAYIMAGICALFMLPLCMVCQWRFTCCCLQPADG        |
|    |           | <b>Group1</b>  | <b>-----</b>  |
|    |           |                |   |
| sp | P56817    | Human          | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWCCCLRCLRQQHD       |
| gi | 296216280 | Marmoset       | DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHD        |
|    |           | <b>Group2</b>  | <b>DCGYNIPQTDESTLMTIAYVMAAICALFMLPLCLMVCQW-CLRCLRQQHD</b> |
|    |           | <b>P2</b>      | <b>-----</b>  |

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1, continued.

```

tr|Q0P4T5|WesternFrog      DLADDISLLK
tr|Q5QHS1|Chicken         -----
sp|P56819|Rat             DFADDISLLK
sp|P56818|Mouse           DFADDISLLK
tr|G3IAK4|ChineseHamster  DFADDISLLK
sp|Q1KLR6|GuineaPig      DFADDISLLK
gi|344293150|Elephant     DFADDISLLK
gi|345799894|Dog         DFADDISLLK
tr|G5BHK2|DesertRat      DFADDISLLK
gi|45387815|ZebraFish    --SDDISLLK
Group1                    -----

sp|P56817|Human           DFADDISLLK
gi|296216280|Marmoset    DFADDISLLK
Group1                    DFADDISLLK

P2                          -----

```

**Supplement Figure 8** The result of p2 partition and extracting the sequences of BACE1, continued.



## Supplement Figure 9

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | -----  |
| gi   326913352   WildTurkey  | -----  |
| gi   345795292   Dog         | -----MEDLCAPRQLSSSR---L                            |
| gi   345323454   Platypus    | -----  |
| gi   213982845   WesternFrog | -----MKVPLLAVLLLG-AACASANFIFPLKVSPAEMKGAVPV---A    |
| gi   147903717   AfricanFrog | -----MKVPLVRLLLCAAACASNKFIVPLNVSPAIEKGTLPV---A     |
| gi   348508416   CichlidFish | ----MAHSTFVSGAFALSLYFGVSYCYFSIPLKIYPGKYNVSSDVNLT   |
| gi   54400484   ZebraFish    | -----MRLYGLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP      |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | -----  |
| sp   Q6IE75   Rat            | MGALLRALLLPLLAQWLLRAVPVLAPAPFTLPLQVAGAANHRASTV---P |
| sp   Q9JL18   Mouse          | MGALLRALLLVLQAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P |
| sp   Q9Y5Z0   Human          | MGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPT---P |
| gi   296232194   Marmoset    | -----LLAQWLLARRPELAPAPFTLPLRVATATNRAAAAPT---S      |
| gi   344294632   Elephant    | -----  |
| gi   329663206   Cattle      | MGALARALLLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P |
| tr   G5C5D1   DesertRat      | -----  |
| gi   348556383   Guineapig   | MGALARALLLPXVAQWLLLR-AATAPAPFTLXPXVAIATARPASPT---P |
| <b>Group2</b>                | -----  |
| <b>P1</b>                    | -----  |
| tr   Q5QHS0   Chicken        | -----  |
| gi   326913352   WildTurkey  | -----EYENHLSFL-----                                |
| 45795292   Dog               | SPVQKGQLDHG-----HPLDKWTQTYGSQLSSRR-----            |
| gi   345323454   Platypus    | -----MAIWQQFP-----                                 |
| gi   213982845   WesternFrog | PATPKGA---PGLLLASDP-----GGQINFFSMVNNLEGDSGRGYYLELL |
| gi   147903717   AfricanFrog | PATPKDK---PGLLLASDP-----GGTINFFSMVDNLQDSDGRGYYLELL |
| gi   348508416   CichlidFish | LRRVALKSDGSLASDP-----TGTVNFLDMVNNLQDSDGRGYIEMI     |
| gi   54400484   ZebraFish    | LQKNEAAK-SGLSLASDP-----AGIVNFLDMINNLKGDSDGRGYMOMI  |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | -----MGLMSG-----                                   |
| sp   Q6IE75   Rat            | GLGTPELPRADGLALALEP----ARATANFLAMVDNLQDSDGRGYYLEML |
| sp   Q9JL18   Mouse          | GLGTPELPRADGLALALEP----VRATANFLAMVDNLQDSDGRGYYLEML |
| sp   Q9Y5Z0   Human          | GPGTPAERHADGLALALEPALASPAGANFLAMVDNLQDSDGRGYYLEML  |
| gi   296232194   Marmoset    | GPGTPAERRADGLALALEPALESAAGSANFLAMVDNLQDSDGRGYYLEML |
| gi   344294632   Elephant    | -----  |
| gi   329663206   Cattle      | GPGPPAEPRADGLALALEP----AGGAANFLAMVDNLQDSDGRGYYLEMQ |
| tr   G5C5D1   DesertRat      | -----  |
| gi   348556383   Guineapig   | VPGTPALPRADGLALALEP----AGAAANFLAMVDNLQDSDGRGYYLEML |
| <b>Group2</b>                | -----  |
| <b>P1</b>                    | -----  |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of

BACE2.

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | -----HLLNTELSSTYQSQGIEVTV                            |
| gi   326913352   WildTurkey  | ---LFRQLNILVDTGSSNFVAVAGVPPDPVTSYFNTELSSTYKQSQGIEVTV |
| gi   345795292   Dog         | -----RLQILVDTGSSNFVAVAGAPHSYTDSDADRSTYRSKGFVTV       |
| gi   345323454   Platypus    | --FSQIKMHILVDTGSSNFVAVAGSPHSDISSYFDAERSSTYSKKNFDVTV  |
| gi   213982845   WesternFrog | IGTAPPQKMNILVDTGSSNFVAVAGALNPDITTFDSDLSTSYEPLNTQVTV  |
| gi   147903717   AfricanFrog | IGSPPQKVNILVDTGSSNFVAVAGSPNPDVNTFFDSDLSTSYQSLNTEVTV  |
| gi   348508416   CichlidFish | IGTAPPQKLNILVDTGSSNFVAVAAAHPYITHYFNALSTYSSTGRVAV     |
| gi   54400484   ZebraFish    | IGTAPPQTLNILVDTGSSNFVAVAAAHPYITHYFNALSTYQSTERAVAV    |
| Group1                       | -----S--Y-----V-V                                    |
|                              |  |
| tr   G3HFD5   ChineseHamster | -----KLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYHPKGFVTV    |
| sp   Q9JL18   Mouse          | IGTAPPQKQILVDTGSSNFVAVAGAPHSYIDTYFDSSESSTYHSGKGFVTV  |
| sp   Q9Y5Z0   Human          | IGTAPPQKLQILVDTGSSNFVAVAGTPHSYIDTYFDTERSTYRSKGFVTV   |
| gi   296232194   Marmoset    | IGTAPPQKLQILVDTGSSNFVAVAGAPHSYIDTYFDMERSSTYRSKGFVTV  |
| gi   344294632   Elephant    | -----MTSSTYQSKGFVTV                                  |
| gi   329663206   Cattle      | IGTAPPQKLQILVDTGSSNFVAVAGAPHPYIDSYFDAERSSTYRPKGFVTV  |
| tr   G5C5D1   DesertRat      | -----QKLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYQSKGFVTV   |
| gi   348556383   Guineapig   | IGTAPPQKLQILVDTGSSNFVAVAGAPHPYVDSYFDFVERSSTYRSKGFVTV |
| Group2                       | -----SSTY--KGFVTV                                    |
|                              |  |
| P1                           | -----S--Y-----V-V                                    |
|                              |  |
| tr   Q5QHS0   Chicken        | KYSQGSWTGVLGTDVVTIPKIDGRYTIINIATILESENFFLPGVKWHGIL   |
| gi   326913352   WildTurkey  | KYSQGSWTGVLGTDVITIPKIDGYSYTIINIATILESENFFLPGVKWHGIL  |
| gi   345795292   Dog         | KYTQGSWTGFVGEDFVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL    |
| gi   345323454   Platypus    | KYTQGSWTGSGVTDVITIPKGFNGSFVNIATIFESENFFLPGIQWNGIL    |
| gi   213982845   WesternFrog | RYTQGSWTGLLGDVISMFKGVNGTFLINIASIFQSENFPLPNINWQGIL    |
| gi   147903717   AfricanFrog | RYTQGSWTGLLGDVVSIPKGVNGTFLINIASIFQSENFPLPNINWQGIL    |
| gi   348508416   CichlidFish | RYTQGNWEGELGIDRVSI PRGPNGTITINIAAILSSDGFFLPGINWQGIL  |
| gi   54400484   ZebraFish    | KYTQGEWEGELGTDLITIPKGFNSGAILINIAAILTSEGFFLPGINWQGIL  |
| Group1                       | -Y-QG-W-G--G-D---P-G-----NIA-I--S--FFLP---W-GIL      |
|                              |  |
| tr   G3HFD5   ChineseHamster | KYTQGSWTGIVGEDIVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL    |
| sp   Q6IE75   Rat            | KYTQGSWTGFVGEDLVITIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| sp   Q9JL18   Mouse          | KYTQGSWTGFVGEDLVITIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| sp   Q9Y5Z0   Human          | KYTQGSWTGFVGEDLVITIPKGFNTSFLVNIATIFESENFFLPGIKWNGIL  |
| gi   296232194   Marmoset    | KYTQGSWTGFMGEDLVITIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| gi   344294632   Elephant    | KYTQGSWTGLMGEDLVITIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| gi   329663206   Cattle      | KYTQGSWTGFVGEDVVTIPKGFNSFLVNIATIFESENFFLPGIRWNGIL    |
| tr   G5C5D1   DesertRat      | KYTQGSWTGLVGDVVTIPKAFNSFLVNIATIFESENFFLPGIKWNGIL     |
| gi   348556383   Guineapig   | KYTQGSWTGFVGEDLVITIPRAFNSFLANVATIFESENFFLPGIKWNGIL   |
| Group2                       | KYTQGSWTG--G-D-VTIP--FN-SFL-N-A-IFESENFFLPGI-WNGIL   |
|                              |  |
| P1                           | -Y-QG-W-G--G-D---P-----N-A-I--S--FFLP---W-GIL        |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of

BACE2, continued.

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | GLAYDTLAKPSSSVETFFDSLQAKIPNIFSLQMCAGLPVSGSG-TNG          |
| gi   326913352   WildTurkey  | GLAYDTLAKPSSSVETFFDSLVRQAKIPNIFSLQMCAGLPVSGSG-TNG        |
| gi   345795292   Dog         | GLAYAALAKPSSSLETFDDSLVAQAKIPNVFSMQMCGAGLPVAGSG-TNG       |
| gi   345323454   Platypus    | GLAYAALAKPSSSLETFDDSLVKQAKIPNIFSMQMCAGLPVAGTG-ING        |
| gi   213982845   WesternFrog | GLAYSTLAKPSSSVEPFFDSLQENIPNIFSMQMCAGQSPGIG-INA           |
| gi   147903717   AfricanFrog | GLAYSTLAKPSSSVEPFFDSLQENIPDVFSMQMCGAGQSSPGNG-INA         |
| gi   348508416   CichlidFish | GLAYPVLARPDSSVEPFFNSVVKQLGIPDIFSLQMCAGLSASSTDTTG         |
| gi   54400484   ZebraFish    | GLAYPLLARPDPSVEPFFNSVVRQTGIPDVFSLQMCAGVPASTTGDPAQ        |
| <b>Group1</b>                | <b>GLAY--LA-P--S-E-FF-S-V-Q--IP--FS-QMCGAG-----</b>      |
| tr   G3HFD5   ChineseHamster | GLAYAALAK-----   |
| sp   Q6IE75   Rat            | GLAYAALAKPSSSLETFDDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG        |
| sp   Q9JL18   Mouse          | GLAYAALAKPSSSLETFDDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG        |
| sp   Q9Y5Z0   Human          | GLAYATLAKPSSSLETFDDSLVTQANIPNVFSMQMCGAGLPVAGSG-TNG       |
| gi   296232194   Marmoset    | GLAYATLAKPSSSLETFDDSLVKQANIPNVFSMQMCGAGLPVAGSG-TNG       |
| gi   344294632   Elephant    | GLAYATLAKPSSSLETFDDSLVMQAKIANVFSMQMCGAGLPVAGSG-TNG       |
| gi   329663206   Cattle      | GLAYATLAKPSSSLETFDDSLVAQAKIPNIFSMQMCAGLPVAGSG-TNG        |
| tr   G5C5D1   DesertRat      | GLAYASLAKPSSSLETFDDSLVTQAKIPDVFSMQMCGAGWPVARSQ-TNG       |
| gi   348556383   Guineapig   | GLAYATLAKPSSSLETFDDSLVTQAKIPDIFSMQMCAGLPVRSRQ-TNG        |
| <b>Group2</b>                | <b>GLAYA-LAK-----</b>                                    |
| <b>P1</b>                    | <b>GLAY--LA-----</b>                                     |
| tr   Q5QHS0   Chicken        | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLNLDCREYN        |
| gi   326913352   WildTurkey  | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLNLDCREYN        |
| gi   345795292   Dog         | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| gi   345323454   Platypus    | GSLVMGGIESSLYTGDWYTPIKEEWYQVEILKLEVGGQNLNLDCREYN         |
| gi   213982845   WesternFrog | GSLVLGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLNLDCTVYN         |
| gi   147903717   AfricanFrog | GSLVLGGVEPSLYKGNIWYTPITEEWYQVEVLKFEVGGQRLNLDCTVYN        |
| gi   348508416   CichlidFish | GSLIMGGAEPPLYRGSVWYTPITEEWYQVEVLKLEVGDQNLNLDCREYN        |
| gi   54400484   ZebraFish    | GSLIMGGVEPTLHRGPWYTPVLEEWYQVEVLKLEVGDQNLNLDCKEYN         |
| <b>Group1</b>                | <b>GSL--GG-E--L--G--WYTP--EEWYQ-E-LK-E-G-Q-L-LDC--YN</b> |
| tr   G3HFD5   ChineseHamster | ---VLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| sp   Q6IE75   Rat            | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| sp   Q9JL18   Mouse          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| sp   Q9Y5Z0   Human          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| gi   296232194   Marmoset    | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN        |
| gi   344294632   Elephant    | GSLVLGGIQPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| gi   329663206   Cattle      | GSLVLGGIEPTLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| tr   G5C5D1   DesertRat      | GSLVLGGIEPNLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| gi   348556383   Guineapig   | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDCREYN         |
| <b>Group2</b>                | <b>---VLGGI-P-LYKG-IWYTPIKEEWYQVEILKLEIGGQ-LNLDCREYN</b> |
| <b>P1</b>                    | <b>----GG----L--G--WYTP--EEWYQ-E-LK-E-G-Q-L-LDC--YN</b>  |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of

BACE2, continued

|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | ADKAIVDSGTTLLRRLPQKVFGAVVQAIARTSLIQEFSSGFWSGSQLACWD         |
| gi   326913352   WildTurkey  | ADKAIVDSGTTLLRRLPQKVFTAVVQAIARTSLIQEFSSGFWSGSQLACWD         |
| gi   345795292   Dog         | ADKAIVDSGTTLLRRLPQKVFNNAVVEAVARTSLIPEFSDGFWTGSQLACWT        |
| gi   345323454   Platypus    | ANKAIVDSGTTLLRRLPQKVFEAVVETITSTSSIQDFAEGFWTGSQLACWS         |
| gi   213982845   WesternFrog | SDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQLACWD         |
| gi   147903717   AfricanFrog | SDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQLACWD         |
| gi   348508416   CichlidFish | MDKAIVDSGTTLLRRLPVNVFNALVEAITRSSLIEEFSSGFWEFTKLACWM         |
| gi   54400484   ZebraFish    | SDKAIVDSGTTLLRRLPANVFTAVVDTIMQTSLIDDFSGFFDGTKLACWM          |
| <b>Group1</b>                | <b>-DKAIVDSGTTLLRRLP--VF-A-V-----S-I--F---F--G--LACW-</b>   |
| tr   G3HFD5   ChineseHamster | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT        |
| sp   Q9JL18   Mouse          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT        |
| sp   Q9Y5Z0   Human          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQLACWT        |
| gi   296232194   Marmoset    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQLACWA        |
| gi   344294632   Elephant    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVAHASLIPEFSDGFWTGSQLACWT        |
| gi   329663206   Cattle      | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSEGFWTGSQLACWT        |
| tr   G5C5D1   DesertRat      | ADKAIVDSGTTLLRRLPQKVFDVAVVDAVARTSLIPEFSDGFWTGAQLACWT        |
| gi   348556383   Guineapig   | ADKAIVDSGTTLLRRLPQKVFDVAVVDAVARTSLIPEFSDGFWTGAQLACWA        |
| <b>Group2</b>                | <b>ADKAIVDSGTTLLRRLPQKVFDVAVV-AVA--SLIPEFS-GFWTG-QLACW-</b> |
| <b>P1</b>                    | <b>-DKAIVDSGTTLLRRLP--VF-A-V-----S-I--F---F--G--LACW-</b>   |
| tr   Q5QHS0   Chicken        | KTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGENLQCYRF          |
| gi   326913352   WildTurkey  | KTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGENLQCYRF            |
| gi   345795292   Dog         | NSETPWSYFPKISIIYLRDENSSQSFRITILPQLYIQPMMGAGLNYECYRF         |
| gi   345323454   Platypus    | NSDKPWSLFPKISIIYLRDENSSRSFRITILPQLYIQPMMGVASNYECYRF         |
| gi   213982845   WesternFrog | KTQDPWNYFPDISIYLRDTNSSRSFRRLTLKPKQLYIQSVLTFQESLNCFRF        |
| gi   147903717   AfricanFrog | KTQDPWNYFPDISIYLRDTNTRSFRRLTLKPKQLYIQSVLTFQESLNCFRF         |
| gi   348508416   CichlidFish | KGENPWRFFPKLSIYLRATNTSEFRITILPQLYIQPITDVDGTLDCFRF           |
| gi   54400484   ZebraFish    | RGESPWRFFPKVSIYLRGTNTSRSFRITILPQVRIVP-----                  |
| <b>Group1</b>                | <b>----PW--FP--SIY-R--N-S-----I-----</b>                    |
| tr   G3HFD5   ChineseHamster | NSETPWAYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF         |
| sp   Q6IE75   Rat            | NSETPWAYFPKISIIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF         |
| sp   Q9JL18   Mouse          | NSETPWAYFPKISIIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF         |
| sp   Q9Y5Z0   Human          | NSETPWSYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF         |
| gi   296232194   Marmoset    | NSETPWSYFPKISIIYLRDENSSRSFRRLTILPQLYIQPMMGAGLNYECYRF        |
| gi   344294632   Elephant    | NSETPWSYFPKISIIYLRDENSSRSFRITILPQLYIQPMIGAGLNYECYRF         |
| gi   329663206   Cattle      | NSETPWSYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF         |
| tr   G5C5D1   DesertRat      | NSETPWAYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF         |
| gi   348556383   Guineapig   | NSETPWAYFPKISIIYLRDENSSRSFRITILPQLYIQPMMGAGLSYECYRF         |
| <b>Group2</b>                | <b>NSETPW-YFPKISIIYLRDEN-SRSFRITILPQLYIQPM-GAGL-YECYRF</b>  |
| <b>P1</b>                    | <b>----PW--FP--SIY-R--N-S-----I-----</b>                    |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of BACE2, continued.

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG  |
| gi   326913352   WildTurkey  | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG  |
| gi   345795292   Dog         | GISPSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAEIAGAPVSEISG   |
| gi   345323454   Platypus    | GISSSTNALVIGATVMEGFYVVFDRQKRVGFVAVSLCAEVAGSPVSEISG   |
| gi   213982845   WesternFrog | GISQSASALVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG  |
| gi   147903717   AfricanFrog | GISQSASTLVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG  |
| gi   348508416   CichlidFish | GVSSSTNGMVIGATVMEGFYVVFDRDRTQQRLGFALSSCAVSDGVALSEIEG |
| gi   54400484   ZebraFish    | -----  |
| Group1                       | -----  |
| tr   G3HFD5   ChineseHamster | GISSSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAEIEGTTVSEISG   |
| sp   Q6IE75   Rat            | GISSSTNALVIGATVMEGFYVVFDRQKRVGFVAVSPCAEIAGTTVSEISG   |
| sp   Q9JL18   Mouse          | GISSSTNALVIGATVMEGFYVVFDRQKRVGFVAVSPCAEIEGTTVSEISG   |
| sp   Q9Y5Z0   Human          | GISPSTNALVIGATVMEGFYVIFDRAQKRVGFAASPCAEIAGAAVSEISG   |
| gi   296232194   Marmoset    | GISPSTNALVIGATVMEGFYVIFDRARKRVGFAASPC---AGEQFSHRMG   |
| gi   344294632   Elephant    | GISPSSNALVIGATVMEGFYVVFDRARKRVGFAMSPC----AASPCHPE    |
| gi   329663206   Cattle      | GISPSTNALVIGATVMEGFYVVFDRQKRVGFAASPCAEIAGAPVSEISG    |
| tr   G5C5D1   DesertRat      | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAEIAGAPVSEVSG   |
| gi   348556383   Guineapig   | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAVSPCAETAGVPLSEVSG   |
| gi   345323454   Platypus    | GISSSTNALVIGATVMEGFYVVFDRQKRVGFVAVSLCAEVAGSPVSEISG   |
| Group2                       | GIS-S-NALVIGATVMEGFYV-FDRA--RVGFA-S-C-----           |
| P1                           | -----  |
| tr   Q5QHS0   Chicken        | PFTTTDDVASNCVSSITFHEPVLWIASYALMSLCGIIILLIILLLLIPPRC  |
| gi   326913352   WildTurkey  | PFTTTDDVASNCVSSITFHEPVLWIASYALMSLCGIIILLIILLLLIPPRC  |
| gi   345795292   Dog         | PFSTDDIASNCVPALPLNEPILWIVSYTLMSVCGIILLIIVLLLLPFR     |
| gi   345323454   Platypus    | PFPTDDVASNCVTTLPFNPEPILWIVSYTLMSICGIIILLVLIILLLLPHRC |
| gi   213982845   WesternFrog | PFGTSDVSSNCIARNPLREPIMWIIISYSLMSLCGMILLVIVLLLLPNR-   |
| gi   147903717   AfricanFrog | PFGTSDVSSNCIARNPLREPIMWIIISYSLMSLCGMILLVIVLLLLLSNR-  |
| gi   348508416   CichlidFish | PFSAADVAADCSGG-PLKEPLVMMISYALMAVCALALLIILLMLILPCRC   |
| gi   54400484   ZebraFish    | -----  |
| Group1                       | -----  |
| tr   G3HFD5   ChineseHamster | PFSTEDVASNCVPAPALNEPILWIVSYALMSVCGAILLVLILLLLPLVRC   |
| sp   Q6IE75   Rat            | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLILLLLPLHC    |
| sp   Q9JL18   Mouse          | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLILLLLPLHC    |
| sp   Q9Y5Z0   Human          | PFSTEDVASNCVPAQSLSEPILWIVSYALMSVCGAILLVLIVLLLLPFR    |
| gi   296232194   Marmoset    | -IPDESPLCECADLEAIPDGT-----                           |
| gi   344294632   Elephant    | VVNDESSLVRHRWK-----                                  |
| gi   329663206   Cattle      | PFSTEDIASNCVPALPLNEPVLWIVSYTLMSVCGVILLVITLLLLLPVRC   |
| tr   G5C5D1   DesertRat      | PFSTDGIASNCVPAPAPGEPPLWFVSYALLSACGLIILLVLIILLLLPCR-  |
| gi   348556383   Guineapig   | PFSTDGIASNCVSPSLNEPVLWVVSALMSSCGLILLVIVLLLLLPVRC     |
| Group2                       | -----  |
| P1                           | -----  |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of

BACE2, continued

|    |  |           |  |                |  |                         |
|----|--|-----------|--|----------------|--|-------------------------|
| tr |  | Q5QHS0    |  | Chicken        |  | QHRYTDNDVVNDESSLVRHRWK  |
| gi |  | 326913352 |  | WildTurkey     |  | QHRYTDNDVVNDESSLVRHRWK  |
| gi |  | 345795292 |  | Dog            |  | RHLPRDPEVVNDESSLVRHRWK  |
| gi |  | 345323454 |  | Platypus       |  | QRRPRDPTVNDDESSLVRHRWK  |
| gi |  | 213982845 |  | WesternFrog    |  | -HRRDDMETVNDDESSLVQHRWK |
| gi |  | 147903717 |  | AfricanFrog    |  | -QRHDDMETINDESSLVQHRWK  |
| gi |  | 348508416 |  | CichlidFish    |  | GNNRNGE---ITDESSLVRHRIK |
| gi |  | 54400484  |  | ZebraFish      |  | -----                   |
|    |  |           |  | <b>Group1</b>  |  | -----                   |
| tr |  | G3HFD5    |  | ChineseHamster |  | RHAPRDPEVVNDESSLVRHRWK  |
| sp |  | Q6IE75    |  | Rat            |  | RHAPRDPEVVNDESSLVRHRWK  |
| sp |  | Q9JL18    |  | Mouse          |  | RHAPRDPEVVNDESSLVRHRWK  |
| sp |  | Q9Y5Z0    |  | Human          |  | QRRPRDPEVVNDESSLVRHRWK  |
| gi |  | 296232194 |  | Marmoset       |  | -----                   |
| gi |  | 344294632 |  | Elephant       |  | -----                   |
| gi |  | 329663206 |  | Cattle         |  | RHHPRDPEVVNDESSLVRHRWK  |
| tr |  | G5C5D1    |  | DesertRat      |  | RRPPRDPEVINDESSLVRHRWK  |
| gi |  | 348556383 |  | Guineapig      |  | RHAPRDPEVINDESSLVRHRWK  |
|    |  |           |  | <b>Group2</b>  |  | -----                   |
|    |  |           |  | <b>P1</b>      |  | -----                   |

**Supplement Figure 9** The result of P1 partition and extracting the sequences of

BACE2, continued

## Supplement Figure 10

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | -----  |
| gi   326913352   WildTurkey  | -----  |
| gi   345323454   Platypus    | -----  |
| gi   213982845   WesternFrog | -----MKVPLLAVLLG--AACASANFIFPLKVSPAEMKGAVPV---A    |
| gi   147903717   AfricanFrog | -----MKVPLVRLLLLCAAACASNKFIVPLNVSPAIEKGTLPV---A    |
| gi   348508416   CichlidFish | -----MAHSTFVSGAFALSIFYGVSYCYFSIPLKIYPGKYNVSSDVNLT  |
| gi   54400484   ZebraFish    | -----MRLYGLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP      |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | -----  |
| sp   Q6IE75   Rat            | MGALLRALLPLLAQWLLRAVPVLAPAPFTLPLQVAGAANHRASV---P   |
| sp   Q9JL18   Mouse          | MGALLRALLLVLAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P  |
| tr   G5C5D1   DesertRat      | -----  |
| gi   348556383   Guineapig   | MGALARALLLPXVAQWLLLR--AATAAPFTLXPXVAIATARPASPT---P |
| <b>Group2</b>                | -----  |
| sp   Q9Y5Z0   Human          | MGALARALLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPT---P  |
| gi   296232194   Marmoset    | -----LLAQWLLARRPELAPAPFTLPLRVATATNRAAAP---S        |
| gi   344294632   Elephant    | -----  |
| gi   329663206   Cattle      | MGALARALLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P  |
| <b>Group3</b>                | -----  |
| <b>P2</b>                    | -----  |
| tr   Q5QHS0   Chicken        | -----  |
| gi   326913352   WildTurkey  | -----EYENHLSFL-----                                |
| gi   345323454   Platypus    | -----MAIWQQFP-----                                 |
| gi   213982845   WesternFrog | PATPKGA---PGLLLASDP----GGQINFFSMVNNLEGDSGRGYYLELL  |
| gi   147903717   AfricanFrog | PATPKDK---PGLLLASDP----GGTINFFSMVDNLQDSDGRGYYLELL  |
| gi   348508416   CichlidFish | LRRVALKSDGSGLSLASDP----TGTVNFLDMVNNLQDSDGRGYIEMS   |
| gi   54400484   ZebraFish    | LQKNEAAAK-SGLSLASDP----AGIVNFLDMINNLKGDSDGRGYMQMI  |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | -----MGLMSG-----                                   |
| sp   Q6IE75   Rat            | GLGTPELPRADGLALALEP---ARATANFLAMVDNLQDSDGRGYYLEML  |
| sp   Q9JL18   Mouse          | GLGTPELPRADGLALALEP---VRATANFLAMVDNLQDSDGRGYYLEML  |
| tr   G5C5D1   DesertRat      | -----  |
| gi   348556383   Guineapig   | VPGTPALPRADGLALALEP---AGAAANFLAMVDNLQDSDGRGYYLEML  |
| <b>Group2</b>                | -----  |
| sp   Q9Y5Z0   Human          | GPGTPAERHADGLALALEPALASPAGANFLAMVDNLQDSDGRGYYLEML  |
| gi   296232194   Marmoset    | GPGTPAERRADGLALALEPALESAAGSANFLAMVDNLQDSDGRGYYLEML |
| gi   344294632   Elephant    | -----  |
| gi   329663206   Cattle      | GPGPPAEPRADGLALALEP---AGGAANFLAMVDNLQDSDGRGYYLEMQ  |
| <b>Group3</b>                | -----  |
| <b>P2</b>                    | -----  |

**Supplement Figure 10** The result of P2 partition and extracting the sequences of BACE2.

```

tr | Q5QHS0 | Chicken -----HLLLNTELSSTYQSQGIEVTV
gi | 326913352 | WildTurkey ---LFRQLNILVDTGSSNFVAVAGVDPDVTSYFNTELSSTYKSGQIEVTV
gi | 345323454 | Platypus --FSQIKMHILVDTGSSNFVAVAGSPHSDISSYFDAERSSTYSSKNFDVTV
gi | 213982845 | WesternFrog IGTTPQKMNILVDTGSSNFVAVAGALNPDITTFDSDLSTSYEPLNTQVTV
gi | 147903717 | AfricanFrog IGSPPQKVNILVDTGSSNFVAVAGSPNDVNTFFDSDLSTSYQSLNTEVTV
gi | 348508416 | CichlidFish IGTGPKQLNILVDTGSSNFVAVAAAHPYI THYFNALSSSTYSSTGRTVAV
gi | 54400484 | ZebraFish IGTGPKQLNILVDTGSSNFVAVAAAHPYI THYFNALSSSTYQSTERAVAV
Group1 -----S--Y-----V-V

tr | G3HFD5 | ChineseHamster -----KLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYHPKGFDTV
sp | Q6IE75 | Rat IGTTPQKVRILVDTGSSNFVAVAGAPHSYIDTYFDSESSSTYHSGKGFDTV
sp | Q9JL18 | Mouse IGTTPQKVVQILVDTGSSNFVAVAGAPHSYIDTYFDSESSSTYHSGKGFDTV
tr | G5C5D1 | DesertRat -----QKLQILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYQSKGFDTV
gi | 348556383 | Guineapig IGTTPQKQLILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYRSGKGFDTV
Group2 -----ILVDTGSSNFVAVAGAPHSYVDSYFDSERSSTYRSGKGFDTV

sp | Q9Y5Z0 | Human IGTTPQKQLQILVDTGSSNFVAVAGTPHSYIDTYFDTERSSTYRSGKGFDTV
gi | 296232194 | Marmoset IGTTPQKQLQILVDTGSSNFVAVAGTPHSYIDTYFDMERSSTYRSGKGFDTV
gi | 344294632 | Elephant -----MTSSTYQSKGFDTV
gi | 329663206 | Cattle IGTTPQKQLQILVDTGSSNFVAVAGAPHSYIDSYFDAERSSTYRSGKGFDTV
Group3 -----SSTY-KGFDTV
P2 -----S--Y-----V-V

tr | Q5QHS0 | Chicken KYSQGSWTGVLGTDVVTIPKIDGRYTINIATILESENFFLPGVKWHGIL
gi | 326913352 | WildTurkey KYSQGSWTGVLGTDVITIPKIDGYSYINIATILESENFFLPGVKWHGIL
gi | 345323454 | Platypus KYTQGSWTGVSVDVITIPKGFNGSFVNIATIFESENFFLPGIQWNGIL
gi | 213982845 | WesternFrog RYTQGSWTGLGKDVISMFKGVNGTFLINIASIFQSENFFLPINWQNGIL
gi | 147903717 | AfricanFrog RYTQGSWTGLGKDVVSIKGVNGTFLINIASIFQSEFFLPINWQNGIL
gi | 348508416 | CichlidFish RYTQGNWEGELGIDRVSIKGVNGTITINIAAILSSDGFLLPGINWQNGIL
gi | 54400484 | ZebraFish KYTQGEWEGELGTDLITIPKGFNGSFVNIATIFESENFFLPGIQWNGIL
Group1 -Y-QG-W-G--G-D---P-G--G---NIA-I--S--FFLP---W-GIL

tr | G3HFD5 | ChineseHamster KYTQGSWTGIVGEDIVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL
sp | Q6IE75 | Rat KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL
sp | Q9JL18 | Mouse KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL
tr | G5C5D1 | DesertRat KYTQGSWTGLVGDVVTIPKAFNSFLVNIATIFESENFFLPGIKWNGIL
gi | 348556383 | Guineapig KYTQGSWTGFVGEDLVTIPRAFNSFLANVATIFESENFFLPGIKWNGIL
Group2 KYTQGSWTG-VG-D-VTIP--FNSSFL-N-A-IFESENFFLPGIKWNGIL

sp | Q9Y5Z0 | Human KYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFFLPGIKWNGIL
gi | 296232194 | Marmoset KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL
gi | 344294632 | Elephant KYTQGSWTGLMGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL
gi | 329663206 | Cattle KYTQGSWTGFVGEDVVTIPKGFNSFLVNIATIFESENFFLPGIRWNGIL
Group3 KYTQGSWTGF-GED-VTIPKGFN-SFLVN-ATIFESENFFLPGI-WNGIL
P2 -Y-QG-W-G--G-D---P-----N-A-I--S--FFLP---W-GIL

```

**Supplement Figure 10** The result of P2 partition and extracting the sequences, continued.



|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | GLAYDTLAKPSSSVETFFDSLQKAKIPNIFSLQMCAGLPVSGSG-TNG          |
| gi   326913352   WildTurkey  | GLAYDTLAKPSSSVETFFDSLVRQAKIPNIFSLQMCAGLPVSGSG-TNG         |
| gi   345323454   Platypus    | GLAYAALAKPSSSLETTFFDSLQKAKIPNIFSMQMCAGLPVAGTG-ING         |
| gi   213982845   WesternFrog | GLAYSTLAKPSSSVETFFDSLQKAKIPNIFSMQMCAGQPSPIG-INA           |
| gi   147903717   AfricanFrog | GLAYSTLAKPSSSVETFFDSLQKAKIPNIFSMQMCAGQSSPGNG-INA          |
| gi   348508416   CichlidFish | GLAYPVLARPDSSVEFFNSVVKQLGIPDIFSLQMCAGLSASSTDTTG           |
| gi   54400484   ZebraFish    | GLAYPLLARPDSSVEFFNSVVRQTGIPDVFSLQMCAGVPASTTGDPA           |
| <b>Group1</b>                | <b>GLAY--LA-P--S-ETFF-S-V-Q--IP--FS-QMCGAG-----</b>       |
| tr   G3HFD5   ChineseHamster | GLAYAALAK-----  |
| sp   Q6IE75   Rat            | GLAYAALAKPSSSLETTFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG        |
| sp   Q9JL18   Mouse          | GLAYAALAKPSSSLETTFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG        |
| tr   G5C5D1   DesertRat      | GLAYASLAKPSSSLETTFFDSLVTQAKIPDVFSMQMCAGWPVARSQ-TNG        |
| gi   348556383   Guineapig   | GLAYATLAKPSSSLETTFFDSLVTQAKIPDIFSMQMCAGLPVSRSG-TNG        |
| <b>Group2</b>                | <b>GLAYA-LAK-----</b>                                     |
| sp   Q9Y5Z0   Human          | GLAYATLAKPSSSLETTFFDSLVTQANIPNVFSMQMCAGLPVAGSG-TNG        |
| gi   296232194   Marmoset    | GLAYATLAKPSSSLETTFFDSLQKAKIPNIFSMQMCAGLPVAGSG-TNG         |
| gi   344294632   Elephant    | GLAYATLAKPSSSLETTFFDSLVMQAKIANVFSMQMCAGLPVAGSG-TNG        |
| gi   329663206   Cattle      | GLAYATLAKPSSSLETTFFDSLVAQAKIPNIFSMQMCAGLPVAGSG-TNG        |
| <b>Group3</b>                | <b>GLAYATLAKPSSSLETTFFDSLQ-QA-I-N-FSMQMCAGLPVAGSG-TNG</b> |
| <b>P2</b>                    | <b>GLAY--LA-----</b>                                      |
| tr   Q5QHS0   Chicken        | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLNLDREYN          |
| gi   326913352   WildTurkey  | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLNLDREYN          |
| gi   345323454   Platypus    | GSLVMGGIESSLYTGDWYTPIKEEWYQVEILKLEVGGQNLNLDREYN           |
| gi   213982845   WesternFrog | GSLVLGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLNLDCTVYN          |
| gi   147903717   AfricanFrog | GSLVLGGIEPSLYKGNIWYTPITEEWYQVEVLKFEVGGQRLNLDCTVYN         |
| gi   348508416   CichlidFish | GSLIMGGAETPLYRGSVWYTPITEEWYQVEVLKLEVGDQNLNLDREYN          |
| gi   54400484   ZebraFish    | GSLIMGGVEPTLHRGPIWYTPVLEEWYQVEVLKLEVGDQNLNLDCKEYN         |
| <b>Group1</b>                | <b>GSL--GG-E--L--G--WYTP--EEWYQ-E-LK-EVG-Q-L-LDC--YN</b>  |
| tr   G3HFD5   ChineseHamster | ---VLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| sp   Q6IE75   Rat            | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| sp   Q9JL18   Mouse          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQNLNLDREYN           |
| tr   G5C5D1   DesertRat      | GSLVLGGIEPNLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| gi   348556383   Guineapig   | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| <b>Group2</b>                | <b>---VLGGIEP-LYKGDWYTPIKEEWYQVEILKLEIGGQ-LNLDREYN</b>    |
| sp   Q9Y5Z0   Human          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| gi   296232194   Marmoset    | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEIGGQSLNLDREYN          |
| gi   344294632   Elephant    | GSLVLGGIQPSLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| gi   329663206   Cattle      | GSLVLGGIEPTLYKGDWYTPIKEEWYQVEILKLEIGGQSLNLDREYN           |
| <b>Group3</b>                | <b>GSLVLGGI-PSLYKG-IWYTPIKEEWYQVEILKLEIGGQSLNLDREYN</b>   |
| <b>P2</b>                    | <b>-----GG-----L--G--WYTP--EEWYQ-E-LK-EXG-Q-L-LDC--YN</b> |

**Supplement Figure 10** The result of P2 partition and extracting the sequences, continued.

|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | ADKAIVDSGTTLLRRLPQKVFGAVVQAIARTSLIQEFSSGFWSGSQACWD                   |
| gi   326913352   WildTurkey  | ADKAIVDSGTTLLRRLPQKVFTAVVQAIARTSLIQEFSSGFWSGSQACWD                   |
| gi   345323454   Platypus    | ANKAIVDSGTTLLRRLPQKVFEAVVETITSTSSIQDFAEGFWTGSQACWS                   |
| gi   213982845   WesternFrog | SDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQACWD                   |
| gi   147903717   AfricanFrog | SDKAIVDSGTTLLRRLPDKVFNAMVDAIVQTSLIQNFNAEFWAGLQACWD                   |
| gi   348508416   CichlidFish | MDKAIVDSGTTLLRRLPVNVFNALVEAITRSSLIIEFFSSGFWEGTKLACWM                 |
| gi   54400484   ZebraFish    | SDKAIVDSGTTLLRRLPANVFTAVVDTIMQTSLIDDFSSAGFFDGTKLACWM                 |
| <a href="#">Group1</a>       | <a href="#">-DKAIVDSGTTLLRRLP--VF-A-V--I---S-I--F---F--G--LACW-</a>  |
| tr   G3HFD5   ChineseHamster | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT                 |
| sp   Q6IE75   Rat            | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT                 |
| sp   Q9JL18   Mouse          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT                 |
| tr   G5C5D1   DesertRat      | ADKAIVDSGTTLLRRLPQKVFDVAVVAVARTSLIPEFSDGFWTGAQLACWT                  |
| gi   348556383   Guineapig   | ADKAIVDSGTTLLRRLPQKVFDVAVVAVARTSLIPEFSDGFWTGAQLACWA                  |
| <a href="#">Group2</a>       | <a href="#">ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACW-</a> |
| sp   Q9Y5Z0   Human          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQACWT                  |
| gi   296232194   Marmoset    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQACWA                  |
| gi   344294632   Elephant    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVAHASLIPEFSDGFWTGSQACWT                  |
| gi   329663206   Cattle      | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSEGFWTGSQACWT                  |
| <a href="#">Group3</a>       | <a href="#">ADKAIVDSGTTLLRRLPQKVFDVAVVEAVA--SLIPEFS-GFWTGSQACW-</a>  |
| <b>P2</b>                    | <b>-DKAIVDSGTTLLRRLP--VF-A-V--X---S-I--F---F--G--LACW-</b>           |
| tr   Q5QHS0   Chicken        | KTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGENLQCYRF                   |
| gi   326913352   WildTurkey  | KTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGENLQCYRF                     |
| gi   345323454   Platypus    | NSDKPWSLFPKLSIYLRDENSSRSFRITILPQLYIQPMMGVASNYECYRF                   |
| gi   213982845   WesternFrog | KTQDPWNYFPDISIYLRDTNNSRSFRITLTKPQLYIQSVLTFQESLNCFRF                  |
| gi   147903717   AfricanFrog | KTQDPWNYFPDISIYLRDTNNSRSFRITLTKPQLYIQSVLTFQESLNCFRF                  |
| gi   348508416   CichlidFish | KGENPWRFFPKLSIYLRATNTSESFRITILPQLYIQPITDVGDTLDCFRF                   |
| gi   54400484   ZebraFish    | RGESPWRFPPKLSIYLRGTNTSQSFRITILPQVRIVP-----                           |
| <a href="#">Group1</a>       | <a href="#">----PW--FP--SIY-R--N-S-----I-----</a>                    |
| tr   G3HFD5   ChineseHamster | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| sp   Q6IE75   Rat            | NSETPWAYFPKLSIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF                   |
| sp   Q9JL18   Mouse          | NSETPWAYFPKLSIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF                   |
| tr   G5C5D1   DesertRat      | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| gi   348556383   Guineapig   | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLSYECYRF                   |
| <a href="#">Group2</a>       | <a href="#">NSETPWAYFPKLSIYLRDEN-SRSFRITILPQLYIQPMMGAGL-YECYRF</a>   |
| sp   Q9Y5Z0   Human          | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| gi   296232194   Marmoset    | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| gi   344294632   Elephant    | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| gi   329663206   Cattle      | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNYECYRF                   |
| <a href="#">Group3</a>       | <a href="#">NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPM-GAGLNYECYRF</a>   |
| <b>P2</b>                    | <b>----PW--FP--SIY-R--N-S-----I-----</b>                             |

**Supplement Figure 10** The result of P2 partition and extracting the sequences,

Continued.

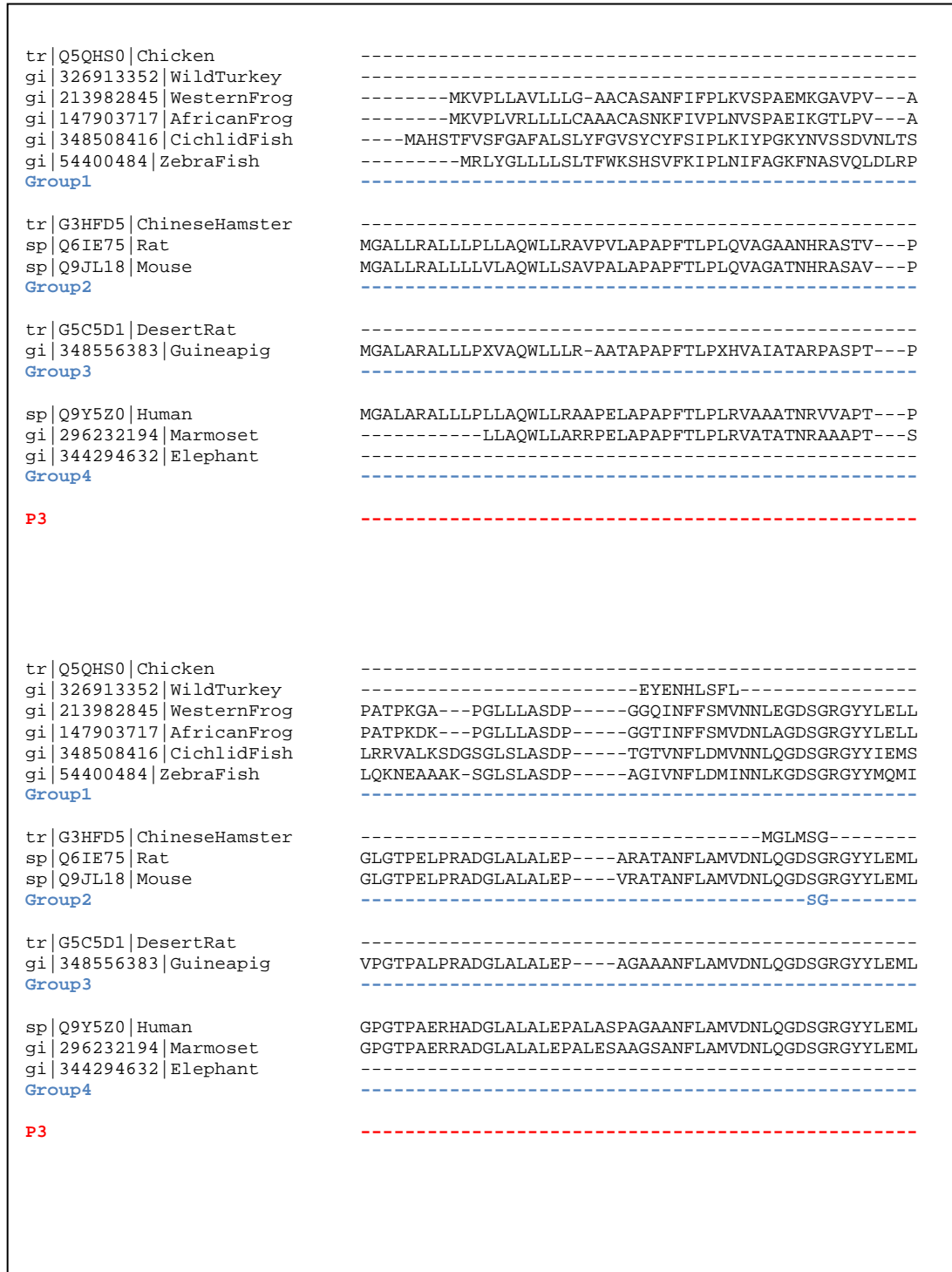
|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG                       |
| gi   326913352   WildTurkey  | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG                       |
| gi   345323454   Platypus    | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSLCAEVAGSPVSEISG                       |
| gi   213982845   WesternFrog | GISQSASALVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG                       |
| gi   147903717   AfricanFrog | GISQSASTLVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG                       |
| gi   348508416   CichlidFish | GVSSSTNGMVIGATVMEGFYVVFDRDRTQQRLGFALSSCAVSDGVALSEIEG                      |
| gi   54400484   ZebraFish    | -----   |
| Group1                       | -----   |
| tr   G3HFD5   ChineseHamster | GISSSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEGTTVSEISG                         |
| sp   Q6IE75   Rat            | GISSSTNALVIGATVMEGFYVVFDRQRRVGFVAVSPCAIEIAGTTVSEISG                       |
| sp   Q9JL18   Mouse          | GISSSTNALVIGATVMEGFYVVFDRQRRVGFVAVSPCAIEGTTVSEISG                         |
| tr   G5C5D1   DesertRat      | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAIEIAGAPVSEVSG                       |
| gi   348556383   Guineapig   | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAVSPCAETAGVPLSEVSG                        |
| Group2                       | GIS - STNALVIGATVMEGFYVVFDR - KRVGFAASPCAIE - G -- VSE - SG               |
| sp   Q9Y5Z0   Human          | GISPSTNALVIGATVMEGFYVIFDRAQKRVGFAASPCAIEIAGAAVSEISG                       |
| gi   296232194   Marmoset    | GISPSTNALVIGATVMEGFYVIFDRARKRVGFAASPC --- AGEQFSHRMG                      |
| gi   344294632   Elephant    | GISPSSNALVIGATVMEGFYVVFDRARKRVGFAMSPC --- AASPCHPE                        |
| gi   329663206   Cattle      | GISPSTNALVIGATVMEGFYVVFDRQKRVGFAASPCAIEIAGAPVSEISG                        |
| Group3                       | GISPS - NALVIGATVMEGFYV - FDRA - KRVGFA - SPC ---                         |
| P2                           | -----   |
| tr   Q5QHS0   Chicken        | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGILLILLIILLIIPRC                         |
| gi   326913352   WildTurkey  | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGILLILLIILLIIPRC                         |
| gi   345323454   Platypus    | PFPTDDVASNCVTTLPFNPEILWIVSYTLMSICGILLVLIILLIIPRC                          |
| gi   213982845   WesternFrog | PFGTSDVSSNCIARNPLREPIMWII SYSLMSLCGMILLVLIILLIIPRC                        |
| gi   147903717   AfricanFrog | PFGTSDVSSNCIARNPLREPIMWII SYSLMSLCGMILLVLIILLIIPRC                        |
| gi   348508416   CichlidFish | PFSAADVAADCSSG - PLKEPLVWMI SYALMAVCALALLIILLIIPRC                        |
| gi   54400484   ZebraFish    | -----   |
| Group1                       | -----   |
| tr   G3HFD5   ChineseHamster | PFSTEDVASNCVPALNEPILWIVSYALMSVCGAILLVLIILLIIPRC                           |
| sp   Q6IE75   Rat            | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIILLIIPRC                         |
| sp   Q9JL18   Mouse          | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIILLIIPRC                         |
| tr   G5C5D1   DesertRat      | PFSTDGIASNCVPAPAPGEP LLWFVSYALLSACGLILLVLIILLIIPRC                        |
| gi   348556383   Guineapig   | PFSTDGIASNCVPSLNEPVLWVSYALMSSCGILLVLIILLIIPRC                             |
| Group2                       | PFST - D - ASNCVP - P --- EP - LW - VSYAL - S - CG - ILLVLI - LLL - P --- |
| sp   Q9Y5Z0   Human          | PFSTEDVASNCVPAQSLSEPI LWIVSYALMSVCGAILLVLIILLIIPRC                        |
| gi   296232194   Marmoset    | - IPDESPLCECADLEAIPDGT - - - - -  |
| gi   344294632   Elephant    | VVNDESSLVRHRWK - - - - -  |
| gi   329663206   Cattle      | PFSTEDIASNCVPALPLNEPVLWIVSYTLMSVCGIILLVLIILLIIPRC                         |
| Group1                       | --- E ---   |
| P2                           | -----   |

**Supplement Figure 10** The result of P2 partition and extracting the sequences, continued.

|    |           |                |                               |
|----|-----------|----------------|-------------------------------|
| tr | Q5QHS0    | Chicken        | QHRYTDNDVVNDESSLVRHRWK        |
| gi | 326913352 | WildTurkey     | QHRYTDNDVVNDESSLVRHRWK        |
| gi | 345323454 | Platypus       | QRRPRDPDTVNDESSLVRHRWK        |
| gi | 213982845 | WesternFrog    | -HRRDDMETVNDESSLVQHRWK        |
| gi | 147903717 | AfricanFrog    | -QRHDDMETINDESSLVQHRWK        |
| gi | 348508416 | CichlidFish    | GNRNGE---ITDESSLVRHRIK        |
| gi | 54400484  | ZebraFish      | -----                         |
|    |           | <b>Group1</b>  | -----                         |
| tr | G3HFD5    | ChineseHamster | RHAPRDPEVVNDESSLVRHRWK        |
| sp | Q6IE75    | Rat            | RHAPRDPEVVNDESSLVRHRWK        |
| sp | Q9JL18    | Mouse          | RHAPRDPEVVNDESSLVRHRWK        |
| tr | G5C5D1    | DesertRat      | RRPPRDPEVINDESSLVRHRWK        |
| gi | 348556383 | Guineapig      | RHAPRDPEVINDESSLVRHRWK        |
|    |           | <b>Group2</b>  | <b>RH-PRDPEV-NDESSLVRHRWK</b> |
| sp | Q9Y5Z0    | Human          | QRRPRDPEVVNDESSLVRHRWK        |
| gi | 296232194 | Marmoset       | -----                         |
| gi | 344294632 | Elephant       | -----                         |
| gi | 329663206 | Cattle         | RHHPRDPEVVNDESSLVRHRWK        |
|    |           | <b>Group1</b>  | -----                         |
|    |           | <b>P2</b>      | -----                         |

**Supplement Figure 10** The result of P2 partition and extracting the sequences, continued.

## Supplement Figure 11



**Supplement Figure 11** The result of P3 partition and extracting the sequences of

BACE2.

|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | -----HLLNTELSSTYQSQGIEVTV                           |
| gi   326913352   WildTurkey  | ---LFRQLNILVDTGSSNFAVAGVDPDPVTSYFNTELSSTYKSKGIEVTV  |
| gi   213982845   WesternFrog | IGTPPQKMNILVDTGSSNFAVAGALNPDITTFDSDLSTSYEPLNTQVTV   |
| gi   147903717   AfricanFrog | IGSPPQKVNILVDTGSSNFAVAGSPNPDVNTFFDSDLSTSYQSLNTEVTV  |
| gi   348508416   CichlidFish | IGTPGQKLNILVDTGSSNFAVAAAAHQFITHYFNALSSSTYSSTGRVAV   |
| gi   54400484   ZebraFish    | IGTPGQTLNILVDTGSSNFAVAAAAHPYITHYFNALSSSTYQSTERAVAV  |
| Group1                       | -----LS--Y-----V-V                                  |
| tr   G3HFD5   ChineseHamster | -----KLQILVDTGSSNFAVAGAPHSYVDSYFDSERSSTYHPKGFDTV    |
| sp   Q6IE75   Rat            | IGTPPQKVRILVDTGSSNFAVAGAPHSYIDTYFDESSTYHSGKGFVTV    |
| sp   Q9JL18   Mouse          | IGTPPQKLQILVDTGSSNFAVAGAPHSYIDTYFDESSTYHSGKGFDTV    |
| Group2                       | -----K--ILVDTGSSNFAVAGAPHSY-D-YFDSE-SSTYH-KGF-VTV   |
| tr   G5C5D1   DesertRat      | -----QKLQILVDTGSSNFAVAGAPHSYVDSYFDSERSSTYQSKGFDTV   |
| gi   348556383   Guineapig   | IGTPPQKLQILVDTGSSNFAVAGAPHPYVDSYFDVERSSTYRSGKGFDTV  |
| Group3                       | -----QKLQILVDTGSSNFAVAGAPH-YVDSYFD-ERSSTY-SKGFDTV   |
| sp   Q9Y5Z0   Human          | IGTPPQKLQILVDTGSSNFAVAGTPHSYIDTYFDTERSSTYRSGKGFDTV  |
| gi   296232194   Marmoset    | IGTPPQKLQILVDTGSSNFAVAGAPHSYIDTYFDMERSSTYRSGKGFDTV  |
| gi   344294632   Elephant    | -----MTSSTYQSKGFDTV                                 |
| Group4                       | -----SSTY-SKGFDTV                                   |
| P3                           | -----S--Y-----V-V                                   |
| tr   Q5QHS0   Chicken        | KYSQGSWTGVLGTDVVTIPKIDGRYTINIATILESENFFLPGVKWHGIL   |
| gi   326913352   WildTurkey  | KYSQGSWTGVLGTDVITIPKIDGYSYINIATILESENFFLPGVKWHGIL   |
| gi   213982845   WesternFrog | RYTQGSWTGLLGKDVISMVPGVNGTFLINIASIFQSENFFLPNINWQGIL  |
| gi   147903717   AfricanFrog | RYTQGSWTGLLGKDVVSIIPKGVNGTFLINIASIFQSESFFLPNINWQGIL |
| gi   348508416   CichlidFish | RYTQGNWEGELGIDRVSIIPRGPNGTITINIAAILSSDGFPLPGINWQGIL |
| gi   54400484   ZebraFish    | KYTQGEWEGELGTDLITIPGPGSAGITINIAAILTSEGFFLPGINWQGIL  |
| Group1                       | -Y-QG-W-G-LG-D---P-G--G---INIA-I--S--FFLP---W-GIL   |
| tr   G3HFD5   ChineseHamster | KYTQGSWTGIVGEDIVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| sp   Q6IE75   Rat            | KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| sp   Q9JL18   Mouse          | KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| Group2                       | KYTQGSWTGIVGEDIVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| tr   G5C5D1   DesertRat      | KYTQGSWTGLVGQDVVTIPKAFNSFLVNIAAIFESENFFLPGIKWNGIL   |
| gi   348556383   Guineapig   | KYTQGSWTGFVGEDLVTIPRAFNSFLANVATIFESENFFLPGIKWNGIL   |
| Group3                       | KYTQGSWTG-VG-DVVTIPKAFNSFL-N-AAIFESENFFLPGIKWNGIL   |
| sp   Q9Y5Z0   Human          | KYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFFLPGIKWNGIL  |
| gi   296232194   Marmoset    | KYTQGSWTGFVGEDLVTIPKGFNSFLVNIATIFESENFFLPGIKWNGIL   |
| gi   344294632   Elephant    | KYTQGSWTGLMGEDLVTIPKGFNSFLVNVATIFESENFFLPGIKWNGIL   |
| Group4                       | KYTQGSWTGF-GEDLVTIPKGFN-SFLVN-ATIFESENFFLPGIKWNGIL  |
| P3                           | -Y-QG-W-G-XG-D---P-X-X---XN-A-I--S--FFLP---W-GIL    |

**Supplement Figure 11** The result of P3 partition and extracting the sequences of BACE2, continued.

|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | GLAYDTLAKPSSSVETFFDSLQAKIPNIFSLQMCAGLPVSGSG-TNG     |
| gi   326913352   WildTurkey  | GLAYDTLAKPSSSVETFFDSLVRQAKIPNIFSLQMCAGLPVSGSG-TNG   |
| gi   213982845   WesternFrog | GLAYSTLAKPSSSVETFFDSLQVENIPNIFSMQMCAGQPSPGIG-INA    |
| gi   147903717   AfricanFrog | GLAYSTLAKPSSSVETFFDSLQVENIPDVFSMQMCAGQSSPGNG-INA    |
| gi   348508416   CichlidFish | GLAYPVLARPDSSVEPFNSVVKQLGIPDIFSLQMCAGLSASSTDTTG     |
| gi   54400484   ZebraFish    | GLAYPLLARPDSSVEPFNSVVRQTGIPDVFSLQMCAGVPASTTGDPA     |
| Group1                       | GLAY--LA-P--SVE-FF-S-V-Q--IP--FS-QMCGAG-----        |
| tr   G3HFD5   ChineseHamster | GLAYAALAK-----                                      |
| sp   Q6IE75   Rat            | GLAYAALAKPSSSLETFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG   |
| sp   Q9JL18   Mouse          | GLAYAALAKPSSSLETFFDSLVAQAKIPDIFSMQMCAGLPVAGSG-TNG   |
| Group2                       | GLAYAALAK-----                                      |
| tr   G5C5D1   DesertRat      | GLAYASLAKPSSSLETFFDSLVTQAKIPDVFSMQMCAGWPVARS-G-TNG  |
| gi   348556383   Guineapig   | GLAYATLAKPSSSLETFFDSLVTQAKIPDIFSMQMCAGLPVRSR-G-TNG  |
| Group3                       | GLAYA-LAKPSSSLETFFDSLVTQAKIPD-FSMQMCAG-PV-RSG-TNG   |
| sp   Q9Y5Z0   Human          | GLAYATLAKPSSSLETFFDSLVTQANIPNVFSMQMCAGLPVAGSG-TNG   |
| gi   296232194   Marmoset    | GLAYATLAKPSSSLETFFDSLQANIPNVFSMQMCAGLPVAGSG-TNG     |
| gi   344294632   Elephant    | GLAYATLAKPSSSLETFFDSLVMQAKIANVFSMQMCAGLPVAGSG-TNG   |
| Group4                       | GLAYATLAKPSSSLETFFDSLQ-VQANI-NVFSMQMCAGLPVAGSG-TNG  |
| P3                           | GLAY--LA-----                                       |
| tr   Q5QHS0   Chicken        | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLDCREYN     |
| gi   326913352   WildTurkey  | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEVGGQNLDCREYN     |
| gi   213982845   WesternFrog | GSLVLGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLNLDCTVYN    |
| gi   147903717   AfricanFrog | GSLVLGGVPEPSLYKGNIWYTPITEEWYQVEVLKFEVGGQRLNLDCTVYN  |
| gi   348508416   CichlidFish | GSLIMGGAEP TLYRGSVWYTP IIEEWYQVEVLKLEVGDQNLNLDCKEYN |
| gi   54400484   ZebraFish    | GSLIMGGVEPTLHRGPIWYTPVLEEWYQVEVLKLEVGDQNLNLDCKEYN   |
| Group1                       | GSL--GG-EP-L--G--WYTP--EEWYQVE-LK-EVG-Q-L-LDC--YN   |
| tr   G3HFD5   ChineseHamster | ---VLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| sp   Q6IE75   Rat            | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| sp   Q9JL18   Mouse          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| Group2                       | ---VLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQ-LNLDCKEYN    |
| tr   G5C5D1   DesertRat      | GSLVLGGIEPNLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| gi   348556383   Guineapig   | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| Group3                       | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| sp   Q9Y5Z0   Human          | GSLVLGGIEPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| gi   296232194   Marmoset    | GSLVLGGIEPSLYKGNIWYTPIKEEWYQVEILKLEIGGQSNLDCREYN    |
| gi   344294632   Elephant    | GSLVLGGIQPSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| Group4                       | GSLVLGGI-PSLYKGDWYTPIKEEWYQVEILKLEIGGQSNLDCREYN     |
| P3                           | -----GG--P-L--G--WYTP--EEWYQVE-LK-EXG-Q-L-LDC--YN   |

**Supplement Figure 11** The result of P3 partition and extracting the sequences of BACE2, continued.

|                              |   |
|------------------------------|---|
| tr   Q5QHS0   Chicken        | ADKAIVDSGTTLLRRLPQKVFGAVVQAIARTSLIQEFSSGFWSGSQACWD          |
| gi   326913352   WildTurkey  | ADKAIVDSGTTLLRRLPQKVFTAVVQAIARTSLIQEFSSGFWSGSQACWD          |
| gi   213982845   WesternFrog | SDKAIVDSGTTLLRRLPKVFNAMVDAIVQTSLIQNFNAEFWAGLQLACWD          |
| gi   147903717   AfricanFrog | SDKAIVDSGTTLLRRLPKVFNAMVDAIVQTSLIQNFNAEFWAGLQLACWD          |
| gi   348508416   CichlidFish | MDKAIVDSGTTLLRRLPVNVFNALVEAITRSSLIEEFSSGFWEGTKLACWM         |
| gi   54400484   ZebraFish    | SDKAIVDSGTTLLRRLPANVFTAVVDTIMQTSLLIDDFSAGFFDGTKLACWM        |
| <b>Group1</b>                | <b>-DKAIVDSGTTLLRRLP--VF-A-V--I---SLI--F---F--G--LACW-</b>  |
| tr   G3HFD5   ChineseHamster | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT        |
| sp   Q6IE75   Rat            | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT        |
| sp   Q9JL18   Mouse          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT        |
| <b>Group2</b>                | <b>ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARTSLIPEFSDGFWTGAQLACWT</b> |
| tr   G5C5D1   DesertRat      | ADKAIVDSGTTLLRRLPQKVFDVAVDAVARTSLIPEFSDGFWTGAQLACWT         |
| gi   348556383   Guineapig   | ADKAIVDSGTTLLRRLPQKVFDVAVDAVARTSLIPEFSDGFWTGAQLACWA         |
| <b>Group3</b>                | <b>ADKAIVDSGTTLLRRLPQKVFDVAVDAVARTSLIPEFSDGFWTGAQLACW-</b>  |
| sp   Q9Y5Z0   Human          | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQACWT         |
| gi   296232194   Marmoset    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVARASLIPEFSDGFWTGSQACWA         |
| gi   344294632   Elephant    | ADKAIVDSGTTLLRRLPQKVFDVAVVEAVAHASLIPEFSDGFWTGSQACWT         |
| <b>Group4</b>                | <b>ADKAIVDSGTTLLRRLPQKVFDVAVVEAVA-ASLIPEFSDGFWTGSQACW-</b>  |
| <b>P3</b>                    | <b>-DKAIVDSGTTLLRRLP--VF-A-V--X---SLI--F---F--G--LACW-</b>  |
| tr   Q5QHS0   Chicken        | KTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGENLQCYRF          |
| gi   326913352   WildTurkey  | KTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGENLQCYRF            |
| gi   213982845   WesternFrog | KTQDPWNYFPDISIYLRDTNSSRSFRILTLPKQLYIQSVLTFQESLNCFRF         |
| gi   147903717   AfricanFrog | KTQDPWNYFPDISIYLRDTNTRSRFRILTLPKQLYIQSVLTFQESLNCFRF         |
| gi   348508416   CichlidFish | KGENPWRFFPKLSIYLRATNTSESFRITILPQLYIQPITDVGDTLDCFRF          |
| gi   54400484   ZebraFish    | RGESPWRFFPKVSIYLRGTNTSQSFRITILPQVRIVP-----                  |
| <b>Group1</b>                | <b>----PW--FP--SIY-R--N-S-----I-----</b>                    |
| tr   G3HFD5   ChineseHamster | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF          |
| sp   Q6IE75   Rat            | NSETPWAYFPKLSIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF          |
| sp   Q9JL18   Mouse          | NSETPWAYFPKLSIYLRDENASRSFRITILPQLYIQPMMGAGFNIECYRF          |
| <b>Group2</b>                | <b>NSETPWAYFPKLSIYLRDENASRSFRITILPQLYIQPMMGAG-NIECYRF</b>   |
| tr   G5C5D1   DesertRat      | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF          |
| gi   348556383   Guineapig   | NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLSYIECYRF         |
| <b>Group3</b>                | <b>NSETPWAYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGL-YIECYRF</b>  |
| sp   Q9Y5Z0   Human          | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMMGAGLNIECYRF          |
| gi   296232194   Marmoset    | NSETPWSYFPKLSIYLRDENSSRSFRILTILPQLYIQPMMGAGLNIECYRF         |
| gi   344294632   Elephant    | NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPMIGAGLNIECYRF          |
| <b>Group4</b>                | <b>NSETPWSYFPKLSIYLRDENSSRSFRITILPQLYIQPM-GAGLNIECYRF</b>   |
| <b>P3</b>                    | <b>----PW--FP--SIY-R--N-S-----I-----</b>                    |

**Supplement Figure 11** The result of P3 partition and extracting the sequences of BACE2, continued.



|                              |  |
|------------------------------|--|
| tr   Q5QHS0   Chicken        | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG          |
| gi   326913352   WildTurkey  | GISSSTNALVIGATVMEGFYVIFDRAQRRVGFVAVSPCAEVDGSPVSEIEG          |
| gi   213982845   WesternFrog | GISQSASALVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG          |
| gi   147903717   AfricanFrog | GISQSASTLVIGATVMEGFYVIFDRAEKRVGFVAVSSCAEVSGITVSEIAG          |
| gi   348508416   CichlidFish | GVSSSTNGMVIGATVMEGFYVVFDRDRTQQRQLGFALSSCAVSDGVALSEIEG        |
| gi   54400484   ZebraFish    | -----  |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | GISSSTNALVIGATVMEGFYVVFDRARKRVGFAASPCAEIEGTTVSEISG           |
| sp   Q6IE75   Rat            | GISSSTNALVIGATVMEGFYVVFDRARVGFVAVSPCAEIEGTTVSEISG            |
| sp   Q9JL18   Mouse          | GISSSTNALVIGATVMEGFYVVFDRARVGFVAVSPCAEIEGTTVSEISG            |
| <b>Group2</b>                | <b>GISSSTNALVIGATVMEGFYVVFDRARVGFVAVSPCAEIEGTTVSEISG</b>     |
| tr   G5C5D1   DesertRat      | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAASPCAEIAGAPVSEVSG           |
| gi   348556383   Guineapig   | GISPSTNALVIGATVMEGFYVVFDRARRRVGFAVSPCAETAGVPLSEVSG           |
| <b>Group3</b>                | <b>GISPSTNALVIGATVMEGFYVVFDRARRRVGFA-SPCAETAG-P-SEVSG</b>    |
| sp   Q9Y5Z0   Human          | GISPSTNALVIGATVMEGFYVIFDRAQKRVGFAASPCAEIAGAAVSEISG           |
| gi   296232194   Marmoset    | GISPSTNALVIGATVMEGFYVIFDRARKRVGFAASPC---AGEQFSHRMG           |
| gi   344294632   Elephant    | GISPSSNALVIGATVMEGFYVVFDRARKRVGFAMSPC-----AASPCHE            |
| <b>Group4</b>                | <b>GISPSTNALVIGATVMEGFYV-FDRA-KRVGFA-SPC-----</b>            |
| <b>P3</b>                    | -----  |
| tr   Q5QHS0   Chicken        | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGIIILLIILLIIPRC             |
| gi   326913352   WildTurkey  | PFTTTDVASNCVSSITFHEPVLWIASYALMSLCGIIILLIILLIIPRC             |
| gi   213982845   WesternFrog | PFGTSDVSSNCIARNPLREPIMWIIISYLSMLCGMILLVVLVILLPLNR-           |
| gi   147903717   AfricanFrog | PFGTSDVSSNCIARNPLREPIMWIIISYLSMLCGMILLVVLVILLPLNR-           |
| gi   348508416   CichlidFish | PFSAADVAADCSGG-PLKEPLVWMIISYALMAVCALALLIILLMLILPCRC          |
| gi   54400484   ZebraFish    | -----  |
| <b>Group1</b>                | -----  |
| tr   G3HFD5   ChineseHamster | PFSTEDVASNCVPAPALNEPILWIVSYALMSVCGAILLVLIILLIIPVRC           |
| sp   Q6IE75   Rat            | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIILLIIPVRC           |
| sp   Q9JL18   Mouse          | PFSTEDIASNCVPAQALNEPILWIVSYALMSVCGAILLVLIILLIIPVRC           |
| <b>Group2</b>                | <b>PFSTED-ASNCVPA-ALNEPILWIVSYALMSVCGAILLVLIILLIIPVRC</b>    |
| tr   G5C5D1   DesertRat      | PFSTDGIASNCVPAPAPGEPILLWVFSYALMSVCGAILLVLIILLIIPVRC-         |
| gi   348556383   Guineapig   | PFSTDGIASNCVPSLNEPVLWVFSYALMSVCGAILLVLIILLIIPVRC-            |
| <b>Group3</b>                | <b>PFSTDGIASNCVP-P-P-EPLLW-VSYAL-S-CGLIILLVLI-ILLIIPVRC-</b> |
| sp   Q9Y5Z0   Human          | PFSTEDVASNCVPAQSLSEPILWIVSYALMSVCGAILLVLIILLIIPVRC-          |
| gi   296232194   Marmoset    | -IPDESPLCECADLEAIPDGT-----                                   |
| gi   344294632   Elephant    | VVNDESSLVRHRWK-----  |
| <b>Group4</b>                | -----  |
| <b>P3</b>                    | -----  |

**Supplement Figure 11** The result of P3 partition and extracting the sequences of.

BACE2, continued.

|                          |                               |
|--------------------------|-------------------------------|
| tr Q5QHS0 Chicken        | QHRYTDNDVVNDESSLVRHRWK        |
| gi 326913352 WildTurkey  | QHRYTDNDVVNDESSLVRHRWK        |
| gi 213982845 WesternFrog | -HRRDDMETVNDDESSLVQHRWK       |
| gi 147903717 AfricanFrog | -QRHDDMETINDESSLVQHRWK        |
| gi 348508416 CichlidFish | GNRNGE---ITDESSLVRHRWK        |
| gi 54400484 ZebraFish    | -----                         |
| <b>Group1</b>            | -----                         |
| tr G3HFD5 ChineseHamster | RHAPRDPEVVNDESSLVRHRWK        |
| sp Q6IE75 Rat            | RHAPRDPEVVNDESSLVRHRWK        |
| sp Q9JL18 Mouse          | RHAPRDPEVVNDESSLVRHRWK        |
| <b>Group2</b>            | <b>RHAPRDPEVVNDESSLVRHRWK</b> |
| tr G5C5D1 DesertRat      | RRPPRDPEVINDESSLVRHRWK        |
| gi 348556383 Guineapig   | RHAPRDPEVINDESSLVRHRWK        |
| <b>Group3</b>            | <b>RRPPRDPEVINDESSLVRHRWK</b> |
| sp Q9Y5Z0 Human          | QRRPRDPEVVNDESSLVRHRWK        |
| gi 296232194 Marmoset    | -----                         |
| gi 344294632 Elephant    | -----                         |
| <b>Group4</b>            | -----                         |
| <b>P3</b>                | -----                         |

**Supplement Figure 11** The result of P3 partition and extracting the sequences of BACE2, continued.

## Supplement Figure 12

|               |           |                 |  |
|---------------|-----------|-----------------|--|
| tr            | Q0P4T5    | WesternFrog1    | -----MELVVYARTGSILLVLLPCFLPVTG-QVAIKLPLKN----      |
| tr            | Q5QHS1    | Chicken1        | -----  |
| sp            | P56817    | Human1          | -----MAQALPWLLLWMGAGVLP AHGTQHGIRLPLRS----         |
| gi            | 296216280 | Marmoset1       | -----MAQALPWLLXLMGAGVLP AHGTQHGIRLPLRS----         |
| sp            | P56819    | Rat1            | -----MAPALRWLLLWVSGMPLPAQGTHLGIRLPLRS----          |
| sp            | P56818    | Mouse1          | -----MAPALHWLLLWVSGMPLPAQGTHLGIRLPLRS----          |
| tr            | G3IAK4    | ChineseHamster1 | -----MAPALRWLLLWVSGMPLPAQGTHLGIRLPLRS----          |
| sp            | Q1KLR6    | GuineaPig1      | -----MAPALPWLLLWVSGVLPVHGTQDGIRLPLRS----           |
| sp            | Q2HJ40    | Cattle1         | -----MAQALPWLLLWMGSGVLP AHGSQPGIRLPLRS----         |
| gi            | 291383811 | Rabbit1         | -----MAPALPWLLLWMGSGMPLPAQGTQHGIRLPLRS----         |
| gi            | 345799894 | Dog1            | -----  |
| gi            | 344293150 | Elephant1       | -----MALVALSWLLLWVSGVLP AHCTPHGIRLPLRS----         |
| tr            | G5BHK2    | DesertRat1      | -----  |
| gi            | 45387815  | ZebraFish1      | -----MRAARLLLLCGVAVCVARLCASSGPALLRVPLRQG----       |
| <b>Group1</b> |           |                 | -----  |
|               |           |                 |  |
| sp            | Q9Y5Z0    | Human2          | MGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPT---P |
| gi            | 329663206 | Cattle2         | MGALARALLLPLLAQWLLRAAPALASAPFTLPLRVASATSRGAVPT---P |
| sp            | Q6IE75    | Rat2            | MGALLRALLLPLLAQWLLRAVPVLAPAPFTLPLQVAGAANHRASTV---P |
| sp            | Q9JL18    | Mouse2          | MGALLRALLLVLVAQWLLSAVPALAPAPFTLPLQVAGATNHRASAV---P |
| tr            | G3HFD5    | ChineseHamster2 | -----  |
| tr            | G5C5D1    | DesertRat2      | -----  |
| gi            | 348556383 | Guineapig2      | MGALARALLLXPVAQWLLRA-ATAPAPFTLXPXVAIATARPASPT---P  |
| gi            | 345795292 | Dog2            | -----MEDLCAPRQLSSSR---L                            |
| gi            | 344294632 | Elephant2       | -----  |
| gi            | 345323454 | Platypus2       | -----  |
| tr            | Q5QHS0    | Chicken2        | -----  |
| gi            | 326913352 | WildTurkey2     | -----  |
| gi            | 213982845 | WesternFrog2    | -----MKVPLLAVLLG-AACASANFIFPLKVSPAEMKGAVPV---A     |
| gi            | 147903717 | AfricanFrog2    | -----MKVPLVRLLLCAAACASNKFIVPLNVSPAIEIKGTLPV---A    |
| gi            | 296232194 | Marmoset2       | -----LLAQWLLARRPELAPAPFTLPLRVATATNRAAAPT---S       |
| gi            | 348508416 | CichlidFish2    | ----MAHSTFVSFGAFALSIFYGVSYCYFSIPLKIYPGKYNVSSDVNLTS |
| gi            | 54400484  | ZebraFish2      | -----MRLYGLLLLSLTFWKSHSVFKIPLNIFAGKFNASVQLDLRP     |
| <b>Group2</b> |           |                 | -----  |
|               |           |                 |  |
| <b>P1</b>     |           |                 | -----  |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2.

|               |           |                 |  |
|---------------|-----------|-----------------|--|
| tr            | Q0P4T5    | WesternFrog1    | --CPG--TCSPMAYRAKRSAEKGMELDTNFLDMIDNLRGKSGQGYVEMR    |
| tr            | Q5QHS1    | Chicken1        | -----YVEMT   |
| sp            | P56817    | Human1          | --GLGGAPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| gi            | 296216280 | Marmoset1       | --GLGGAPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| sp            | P56819    | Rat1            | --GLAGPPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| sp            | P56818    | Mouse1          | --GLAGPPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| tr            | G3IAK4    | ChineseHamster1 | --GPAGPPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| sp            | Q1KLR6    | GuineaPig1      | --GLAGAPLGLRLPRETDEE---PGRRSFVEMVDNLRGKSGQGYVEMT     |
| sp            | Q2HJ40    | Cattle1         | --GLGGAPLGLRLPRETDEEPEEPGRRGSFVEMVDNLRGKSGQGYVEMT    |
| gi            | 291383811 | Rabbit1         | --GLGGAPLGLRLPRETEEDPEEPGRRGNFVEMVDNLRGKSGQGYVEMT    |
| gi            | 345799894 | Dog1            | -----MWDAPAIR-----                                   |
| gi            | 344293150 | Elephant1       | --GLGGAPLGLRLPRDTDEELEDPSRRGSFVEMVDNLRGKSGQGYVEMT    |
| tr            | G5BHK2    | DesertRat1      | -----YVEMT   |
| gi            | 45387815  | ZebraFish1      | PLTPHSTPAAHRSPHGPRARSRAASGISFINMIDNLRGKSGQGYIEMA     |
| <b>Group1</b> |           |                 | -----  |
|               |           |                 |  |
| sp            | Q9Y5Z0    | Human2          | GPGTPAERHADGLALALEPALASPAGAAANFLAMVDNLQGDSDGRGYYLEML |
| gi            | 329663206 | Cattle2         | GPGPAAEPADGLALALEPAG----GAANFLAMVDNLQGDSDGRGYYLEMQ   |
| sp            | Q6IE75    | Rat2            | GLGTPELPRADGLALALEPAR----ATANFLAMVDNLQGDSDGRGYYLEML  |
| sp            | Q9JL18    | Mouse2          | GLGTPELPRADGLALALEPVR----ATANFLAMVDNLQGDSDGRGYYLEML  |
| tr            | G3HFD5    | ChineseHamster2 | -----  |
| tr            | G5C5D1    | DesertRat2      | -----  |
| gi            | 348556383 | Guineapig2      | VPGTPALPRADGLALALEPAG----AAANFLAMVDNLQGDSDGRGYYLEML  |
| gi            | 345795292 | Dog2            | SPVQKQQLDHG-----HPLDKWTQTYG-----S                    |
| gi            | 344294632 | Elephant2       | -----  |
| gi            | 345323454 | Platypus2       | -----MAIWQQFP-----                                   |
| tr            | Q5QHS0    | Chicken2        | -----  |
| gi            | 326913352 | WildTurkey2     | -----EYENHL  |
| gi            | 213982845 | WesternFrog2    | PATPKGA---PGLLLASDPGG----QINFFSMVNNLEGDSDGRGYYLELL   |
| gi            | 147903717 | AfricanFrog2    | PATPKDK---PGLLLASDPGG----TINFFSMVDNLAGDSDGRGYYLELL   |
| gi            | 296232194 | Marmoset2       | GPGTPAERRADGLALALEPALESAAGSANFLAMVDNLQGDSDGRGYYLEML  |
| gi            | 348508416 | CichlidFish2    | LRRVALKSDGSLASDPTG----TVNFLDMVNNLQGDSDGRGYIEMS       |
| gi            | 54400484  | ZebraFish2      | LQKNEAAK-SGLSLASDPAG----IVNFLDMINNLKGDSDGRGYMQMI     |
| <b>Group2</b> |           |                 | -----  |
|               |           |                 |  |
| <b>P1</b>     |           |                 | -----  |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|               |           |                 |            |                |       |            |                   |                  |
|---------------|-----------|-----------------|------------|----------------|-------|------------|-------------------|------------------|
| tr            | Q0P4T5    | WesternFrog1    | VGTPPQTLN  | ILVDTGSSNFAVGA | ----  | APHPFLKRY  | YHRQHSRTYRDVRR    |                  |
| tr            | Q5QHS1    | Chicken1        | VGSPPPQKLN | ILVDTGSSNFAVGA | ----  | APHPFLRRYY | QRQLSSTYRDLRK     |                  |
| sp            | P56817    | Human1          | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| gi            | 296216280 | Marmoset1       | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| sp            | P56819    | Rat1            | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| sp            | P56818    | Mouse1          | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| tr            | G3IAK4    | ChineseHamster1 | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| sp            | Q1KLR6    | GuineaPig1      | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQRSSSTYRDLRK   |                  |
| sp            | Q2HJ40    | Cattle1         | LGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| gi            | 291383811 | Rabbit1         | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| gi            | 345799894 | Dog1            | -----      | -----          | ----- | -----      | -----S--YRD-----  |                  |
| gi            | 344293150 | Elephant1       | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQLSSTYRDLRK    |                  |
| tr            | G5BHK2    | DesertRat1      | VGSPPPQTLN | ILVDTGSSNFAVGA | ----  | APHPFLHRY  | YQRQRSSSTYRDLRK   |                  |
| gi            | 45387815  | ZebraFish1      | VGSPAQRNLN | ILVDTGSSNFAVGA | ----  | AAHPFLHRY  | YHRSLSSTYRDLRG    |                  |
| <b>Group1</b> |           |                 |            |                |       |            |                   | -----S--YRD----- |
|               |           |                 |            |                |       |            |                   |                  |
| sp            | Q9Y5Z0    | Human2          | IGTPPPQKLQ | ILVDTGSSNFAVAG | ----  | TPHSYIDTY  | FDTERSSTYRSKGF    |                  |
| gi            | 329663206 | Cattle2         | IGTPPPQKLQ | ILVDTGSSNFAVAG | ----  | APHPYIDSY  | FDAERSSTYRPKGF    |                  |
| sp            | Q6IE75    | Rat2            | IGTPPPQKVR | ILVDTGSSNFAVAG | ----  | APHSYIDTY  | FDSESSSTYHSGKF    |                  |
| sp            | Q9JL18    | Mouse2          | IGTPPPQKVQ | ILVDTGSSNFAVAG | ----  | APHSYIDTY  | FDSESSSTYHSGKF    |                  |
| tr            | G3HFD5    | ChineseHamster2 | MGLMSGKQL  | ILVDTGSSNFAVAG | ----  | APHSYVDSY  | FDSERSSTYHPKGF    |                  |
| tr            | G5C5D1    | DesertRat2      | -----      | -----          | ----- | -----      | -----             |                  |
| gi            | 348556383 | Guineapig2      | IGTPPPQKLQ | ILVDTGSSNFAVAG | ----  | APHPYVDSY  | FDVERSSTYRSKGF    |                  |
| gi            | 345795292 | Dog2            | QLSSRRRLQ  | ILVDTGSSNFAVAG | ----  | APHSYTDSY  | FADRSSSTYRSKGF    |                  |
| gi            | 344294632 | Elephant2       | -----      | -----          | ----- | -----      | -----             |                  |
| gi            | 345323454 | Platypus2       | --FSQIKMH  | ILVDTGSSNFAVAG | ----  | SPHSDISSY  | FDAERSSTYSSKNF    |                  |
| tr            | Q5QHS0    | Chicken2        | -----      | -----          | ----- | -----      | -----             |                  |
| gi            | 326913352 | WildTurkey2     | SFLLFRQLN  | ILVDTGSSNFAVAG | ----  | VPDPDVT    | SYFNTELSSTYKSGI   |                  |
| gi            | 213982845 | WesternFrog2    | IGTPPPQKMN | ILVDTGSSNFAVAG | ----  | ALNPDIT    | TFFDKSLSTSYEPLNT  |                  |
| gi            | 147903717 | AfricanFrog2    | IGSPPPQKVN | ILVDTGSSNFAVAG | ----  | SPNPDVNT   | FFDSDKSLSTSYQSLNT |                  |
| gi            | 296232194 | Marmoset2       | IGTPPPQKLQ | ILVDTGSSNFAVAG | ----  | APHSYIDTY  | FDMERSSTYRSKGF    |                  |
| gi            | 348508416 | CichlidFish2    | IGTPGQKLN  | ILVDTGSSNFAVAA | ----  | AAHQFITHY  | FNTALSSSTYSSTGR   |                  |
| gi            | 54400484  | ZebraFish2      | IGTPGQTLN  | ILVDTGSSNFAVAA | ----  | AAHPYITHY  | FNALSSSTYQSTER    |                  |
| <b>Group2</b> |           |                 |            |                |       |            |                   | -----S--Y-----   |
| <b>P1</b>     |           |                 |            |                |       |            | -----S--Y-----    |                  |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1 & BACE2, continued.

|    |               |                 |   |
|----|---------------|-----------------|---|
| tr | Q0P4T5        | WesternFrog1    | GYYVPTYQGKWEGELGTDLVTIPHGPNVTVTANIAAAITDSKFFFINGSNW       |
| tr | Q5QHS1        | Chicken1        | GYYVPTYQGKWEGELGTDLVTIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| sp | P56817        | Human1          | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| gi | 296216280     | Marmoset1       | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| sp | P56819        | Rat1            | SVYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| sp | P56818        | Mouse1          | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| tr | G3IAK4        | ChineseHamster1 | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| sp | Q1KLR6        | GuineaPig1      | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| sp | Q2HJ40        | Cattle1         | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| gi | 291383811     | Rabbit1         | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| gi | 345799894     | Dog1            | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| gi | 344293150     | Elephant1       | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| tr | G5BHK2        | DesertRat1      | GYYVPTYQGKWEGELGTDLVSIPHGPNVTVRANIAAITESDKFFFINGSNW       |
| gi | 45387815      | ZebraFish1      | GYYVPTYQGRWEGELGTDVVSVPCGPNVSLRANIAAAITQSDRFFINGSNW       |
|    | <b>Group1</b> |                 | <b>GYYVPTYQG-WEGELGTD-V--P-GPNV---ANIAAIT-SD-FFINGSNW</b> |
|    |               |                 |   |
| sp | Q9Y5Z0        | Human2          | DVTVKYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENFLLPGIKW        |
| gi | 329663206     | Cattle2         | DVTVKYTQGSWTGFVGEDVVTIPKGFNSSFLVNIATIFESENFLLPGIRW        |
| sp | Q6IE75        | Rat2            | EVTVKYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFLLPGIKW        |
| sp | Q9JL18        | Mouse2          | DVTVKYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFLLPGIKW        |
| tr | G3HFD5        | ChineseHamster2 | DVTVKYTQGSWTGIVGEDIVTIPKGFNSSFLVNIATIFESENFLLPGIKW        |
| tr | G5C5D1        | DesertRat2      | DVTVKYTQGSWTGLVGDVVTIPKAFNSSFLVNIAAIFESENFLLPGIKW         |
| gi | 348556383     | Guineapig2      | DVTVKYTQGSWTGFVGEDLVTIPRAFNSSFLANVATIFESENFLLPGIKW        |
| gi | 345795292     | Dog2            | DVTVKYTQGSWTGFVGEDFVTIPKGFNSSFLVNIATIFESENFLLPGIKW        |
| gi | 344294632     | Elephant2       | DVTVKYTQGSWTGLMGEDLVTIPKGFNSSFLVNIVATIFESENFLLPGIKW       |
| gi | 345323454     | Platypus2       | DVTVKYTQGSWTGSGVTDVITIPKGFNGSFVNIATIFESENFLLPGIQW         |
| tr | Q5QHS0        | Chicken2        | EVTVKYSQGSWTGVLGTDVVTIPKIDGRYTINIATILESENFLLPGVKW         |
| gi | 326913352     | WildTurkey2     | EVTVKYSQGSWTGVLGTDVITIPKIDGYSYINIATILESENFLLPGVKW         |
| gi | 213982845     | WesternFrog2    | QVTVRYTQGSWTGLLGKDVISMPKGVNGTFLINIASIFQSENFLLPNINW        |
| gi | 147903717     | AfricanFrog2    | EVTVRYTQGSWTGLLGKDVVSIPKGVNGTFLINIASIFQSENFLLPNINW        |
| gi | 296232194     | Marmoset2       | DVTVKYTQGSWTGFVGEDLVTIPKGFNSSFLVNIATIFESENFLLPGIKW        |
| gi | 348508416     | CichlidFish2    | TVAVRYTQGNWEGELGIDRVSIPRGPNGTITINIAAILSSDGFLLPGINW        |
| gi | 54400484      | ZebraFish2      | AVAVKYTQGEWEGELGTDLITIPGPGSAITINIAAILTSEGFFLLPGINW        |
|    | <b>Group2</b> |                 | <b>-V-V-Y-QG-W-G--G-D---P-----N-A-I--S--FFLP---W</b>      |
|    | <b>P1</b>     |                 | <b>-V-V-Y-QG-W-G--G-D---P-----N-A-I--S--FFXX---W</b>      |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|    |  |               |  |                 |                      |              |              |              |              |                     |
|----|--|---------------|--|-----------------|----------------------|--------------|--------------|--------------|--------------|---------------------|
| tr |  | Q0P4T5        |  | WesternFrog1    | EGILGLAYAEIARPD      | DTLEPFFD     | SLVKQTRV     | PNIFSL       | QLCGTGFH     | FNESD               |
| tr |  | Q5QHS1        |  | Chicken1        | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTQV     | PNIFSL       | QLCGAGF      | SPNETE              |
| sp |  | P56817        |  | Human1          | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| gi |  | 296216280     |  | Marmoset1       | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| sp |  | P56819        |  | Rat1            | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHI     | PNIFSL       | QLCGAGF      | PLNQTE              |
| sp |  | P56818        |  | Mouse1          | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHI     | PNIFSL       | QLCGAGF      | PLNQTE              |
| tr |  | G3IAK4        |  | ChineseHamster1 | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHI     | ANVFSL       | QLCGAGF      | PLNQTE              |
| sp |  | Q1KLR6        |  | GuineaPig1      | EGILGLAYAEIAR        | -----        | -----        | -----        | -----        | LCGAGFPLNQSE        |
| sp |  | Q2HJ40        |  | Cattle1         | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| gi |  | 291383811     |  | Rabbit1         | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| gi |  | 345799894     |  | Dog1            | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| gi |  | 344293150     |  | Elephant1       | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHI     | PNLFSL       | QLCGAGF      | PLNQSE              |
| tr |  | G5BHK2        |  | DesertRat1      | EGILGLAYAEIARPD      | SLEPFFD      | SLVKQTHV     | PNLFSL       | QLCGAGF      | PLNQSE              |
| gi |  | 45387815      |  | ZebraFish1      | EGILGLAYAEIARPD      | ETLEPFFD     | SLLRQSTV     | ADVFSL       | QLCGAGY      | NHNYST              |
|    |  | <b>Group1</b> |  |                 | <b>EGILGLAYAEIAR</b> | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>LCG-G---N---</b> |
| sp |  | Q9Y5Z0        |  | Human2          | NGILGLAYATLAKP       | SSSLETFFD    | SLVTQANI     | PNVFSM       | QMCGAGL      | PVAGSG              |
| gi |  | 329663206     |  | Cattle2         | NGILGLAYATLAKP       | SSSLETFFD    | SLVAQAKI     | PNIFSM       | QMCGAGL      | PVAGSG              |
| sp |  | Q6IE75        |  | Rat2            | NGILGLAYAALAKP       | SSSLETFFD    | SLVAQAKI     | PDIFSM       | QMCGAGL      | PVAGSG              |
| sp |  | Q9JL18        |  | Mouse2          | NGILGLAYAALAKP       | SSSLETFFD    | SLVAQAKI     | PDIFSM       | QMCGAGL      | PVAGSG              |
| tr |  | G3HFD5        |  | ChineseHamster2 | NGILGLAYAALAK        | -----        | -----        | -----        | -----        | -----               |
| tr |  | G5C5D1        |  | DesertRat2      | NGILGLAYAALAKP       | SSSLETFFD    | SLVTQAKI     | PDVFSM       | QMCGAGL      | PVARS               |
| gi |  | 348556383     |  | Guineapig2      | NGILGLAYATLAKP       | SSSLETFFD    | SLVTQAKI     | PDIFSM       | QMCGAGL      | PVSRSG              |
| gi |  | 345795292     |  | Dog2            | NGILGLAYAALAKP       | SSSLETFFD    | SLVAQAKI     | PNVFSM       | QMCGAGL      | PVAGSG              |
| gi |  | 344294632     |  | Elephant2       | NGILGLAYATLAKP       | SSSLETFFD    | SLVMQAKI     | ANVFSM       | QMCGAGL      | PVAGSG              |
| gi |  | 345323454     |  | Platypus2       | NGILGLAYAALAKP       | SSSLETFFD    | SLVKQAKI     | PNIFSM       | QMCGAGL      | PVAGTG              |
| tr |  | Q5QHS0        |  | Chicken2        | HGILGLAYDTLAKP       | SSSVETFFD    | SLVKQAKI     | PNIFSL       | QMCGAGL      | PVSGSG              |
| gi |  | 326913352     |  | WildTurkey2     | HGILGLAYDTLAKP       | SSSVETFFD    | SLVRQAKI     | PNIFSL       | QMCGAGL      | PVSGSG              |
| gi |  | 213982845     |  | WesternFrog2    | QGILGLAYSTLAKP       | SSSVETFFD    | SLVQENI      | PNIFSM       | QMCGAGQ      | PSPGIG              |
| gi |  | 147903717     |  | AfricanFrog2    | QGILGLAYSTLAKP       | SSSVETFFD    | SLVQENI      | PDVFSM       | QMCGAGQ      | SSPGNG              |
| gi |  | 296232194     |  | Marmoset2       | NGILGLAYATLAKP       | SSSLETFFD    | SLVKQANI     | PNVFSM       | QMCGAGL      | PVAGSG              |
| gi |  | 348508416     |  | CichlidFish2    | QGILGLAYPVLARPD      | SVEPFFN      | SVVKQLGI     | PDIFSL       | QMCGAGL      | SASSTT              |
| gi |  | 54400484      |  | ZebraFish2      | QGILGLAYPLLARPD      | SVEPFFN      | SVVVRQTGI    | PDVFSL       | QMCGAGV      | PASTTG              |
|    |  | <b>Group2</b> |  |                 | <b>-GILGLAY--LA</b>  | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>-----</b>        |
|    |  | <b>P1</b>     |  |                 | <b>-GILGLAY--XA</b>  | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>-----</b> | <b>-----</b>        |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|    |           |                 |  |
|----|-----------|-----------------|--|
| tr | Q0P4T5    | WesternFrog1    | -TSASVGGSMVIGGIDPSLYIGSIWYTPIRKEWYVEVIIVKIEINGQDLH |
| tr | Q5QHS1    | Chicken1        | -TLASVGGSMIIGGIDRSLYVGDWYTPIRKEWYVEVIIVKLEVNGQDLN  |
| sp | P56817    | Human1          | -VLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| gi | 296216280 | Marmoset1       | -VLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| sp | P56819    | Rat1            | -ALASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| sp | P56818    | Mouse1          | -ALASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| tr | G3IAK4    | ChineseHamster1 | -ALASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| sp | Q1KLR6    | GuineaPig1      | -AVASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| sp | Q2HJ40    | Cattle1         | -ALASVGGSMIIGGIDHSLYMGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| gi | 291383811 | Rabbit1         | -VLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| gi | 345799894 | Dog1            | -VLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| gi | 344293150 | Elephant1       | -VLASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| tr | G5BHK2    | DesertRat1      | -AVASVGGSMIIGGIDHSLYTGSLWYTPIRREWYVEVIIVRVEINGQDLK |
| gi | 45387815  | ZebraFish1      | GSSSTVGGSMIIGGVDPVSLYVGLWYTPIRREWYVEVIIVRIEVNGQDLN |
|    | Group1    |                 | -----VGGSM-IGG-D-SLY-G--WYTPIR-EWYVEVIIV--E-NGQDL- |
|    |           |                 |  |
| sp | Q9Y5Z0    | Human2          | ----TNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 329663206 | Cattle2         | ----TNGGSLVLGGIEPTLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| sp | Q6IE75    | Rat2            | ----TNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| sp | Q9JL18    | Mouse2          | ----TNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| tr | G3HFD5    | ChineseHamster2 | -----VLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN        |
| tr | G5C5D1    | DesertRat2      | ----TNGGSLVLGGIEPNLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 348556383 | Guineapig2      | ----TNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 345795292 | Dog2            | ----TNGGSLVLGGIEPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 344294632 | Elephant2       | ----TNGGSLVLGGIQPSLYKGDWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 345323454 | Platypus2       | ----INGGSLVMGGIESSLYTGDIWYTPIKEEWYQIEILKLEVGGQNLN  |
| tr | Q5QHS0    | Chicken2        | ----TNGGSLVLGGIEPSLYKGNWYTPIKEEWYQVEILKLEVGGQNLN   |
| gi | 326913352 | WildTurkey2     | ----TNGGSLVLGGIEPSLYKGNWYTPIKEEWYQVEILKLEVGGQNLN   |
| gi | 213982845 | WesternFrog2    | ----INAGSLVLGGIEPSLYQGDWYTPITEEWYQVEVLKFEVGGQNLN   |
| gi | 147903717 | AfricanFrog2    | ----INAGSLVLGGVPEPSLYKGNWYTPITEEWYQVEVLKFEVGGQRLN  |
| gi | 296232194 | Marmoset2       | ----TNGGSLVLGGIEPSLYKGNWYTPIKEEWYQIEILKLEIGGQSLN   |
| gi | 348508416 | CichlidFish2    | ---DTTGGSLIMGGAEPVLYRGSVWYTPIEEWYQVEVLKLEVGDQNLN   |
| gi | 54400484  | ZebraFish2      | ---DPAGGSLIMGGVEPTLHRGPIWYTPVLEEWYQVEVLKLEVGDQNLN  |
|    | Group2    |                 | -----GG-----L--G--WYTP--EEWYQ-E-LK-E-G-Q-L-        |
|    | P1        |                 | -----GG-----L--G--WYTP--EWYX-X-X--E-X-Q-L-         |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.



|                           |   |
|---------------------------|---|
| tr Q0P4T5 WesternFrog1    | MDCKEYNYDKSIVDSGTTNLRRLPKRVFDAAVKSIIKAASSTEKFPDGFWL       |
| tr Q5QHS1 Chicken1        | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKTASSTEKFPDGFWL       |
| sp P56817 Human1          | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| gi 296216280 Marmoset1    | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| sp P56819 Rat1            | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| sp P56818 Mouse1          | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| tr G3IAK4 ChineseHamster1 | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| sp Q1KLR6 GuineaPig1      | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| sp Q2HJ40 Cattle1         | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| gi 291383811 Rabbit1      | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| gi 345799894 Dog1         | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| gi 344293150 Elephant1    | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| tr G5BHK2 DesertRat1      | MDCKEYNYDKSIVDSGTTNLRRLPKKVFEEAVKSIIKAASSTEKFPDGFWL       |
| gi 45387815 ZebraFish1    | MDCKEYNYDKSIVDSGTTNLRRLPKRVFQAAVKAI EAASSTEQFP SGFWL      |
| <b>Group1</b>             | <b>MDCKEYNYDKSIVDSGTTNLRRLP--VF-AAVK-IKAASSTE-FP-GFWL</b> |
|                           |   |
| sp Q9Y5Z0 Human2          | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARASLIPEFSDGFWTG      |
| gi 329663206 Cattle2      | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSEGFWTG      |
| sp Q6IE75 Rat2            | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTG      |
| sp Q9JL18 Mouse2          | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTG      |
| tr G3HFD5 ChineseHamster2 | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTG      |
| tr G5C5D1 DesertRat2      | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVDVAVARTSLIPEFSDGFWTG     |
| gi 348556383 Guineapig2   | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVDVAVARTSLIPEFSDGFWTG     |
| gi 345795292 Dog2         | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARTSLIPEFSDGFWTG      |
| gi 344294632 Elephant2    | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVAHASLIPEFSDGFWTG      |
| gi 345323454 Platypus2    | LDCREYNANKAI VDSGTTLLRRLPQKVFEEAVVETITSTSSIQDFAEGFWTG     |
| tr Q5QHS0 Chicken2        | LDCREYNADKAI VDSGTTLLRRLPQKVFVAVVQAIARTSLIQEFSSGFWSG      |
| gi 326913352 WildTurkey2  | LDCREYNADKAI VDSGTTLLRRLPQKVFVAVVQAIARTSLIQEFSSGFWSG      |
| gi 213982845 WesternFrog2 | LDCTVYNSDKAI VDSGTTLLRRLPDKVFNAMVDIVQTSLIQNFNAEFWAG       |
| gi 147903717 AfricanFrog2 | LDCREYNADKAI VDSGTTLLRRLPDKVFNAMVDIVQTSLIQNFNAEFWAG       |
| gi 296232194 Marmoset2    | LDCREYNADKAI VDSGTTLLRRLPQKVFDAVVEAVARASLIPEFSDGFWTG      |
| gi 348508416 CichlidFish2 | LDCREYNMDKAI VDSGTTLLRRLPVNVFNALVEAITRSSLIIEEFSSGFWE      |
| gi 54400484 ZebraFish2    | LDCREYNMDKAI VDSGTTLLRRLPANVFTAVVDTIMQTSLIDDFSAGFFDG      |
| <b>Group2</b>             | <b>LDC--YN--KAIVDSGTTLLRRLP--VF-A-V-----S-I--F--F--G</b>  |
| <b>P1</b>                 | <b>XDC--YN--KXIVDSGTTXLRLP--VF-A-V-----S-X--F--F--G</b>   |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|               |           |                 |   |
|---------------|-----------|-----------------|---|
| tr            | Q0P4T5    | WesternFrog1    | EQLVCWQEGTTPWHIFPVISLYLMGEVANQSFKITILPQQYLRPVEDIAT      |
| tr            | Q5QHS1    | Chicken1        | EQLVCWQVG-PPWHIFPVLISLYLMGEATNQSFRITILPQQYLGQWRNVAT     |
| sp            | P56817    | Human1          | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| gi            | 296216280 | Marmoset1       | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| sp            | P56819    | Rat1            | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| sp            | P56818    | Mouse1          | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| tr            | G3IAK4    | ChineseHamster1 | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| sp            | Q1KLR6    | GuineaPig1      | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| sp            | Q2HJ40    | Cattle1         | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| gi            | 291383811 | Rabbit1         | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| gi            | 345799894 | Dog1            | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| gi            | 344293150 | Elephant1       | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| tr            | G5BHK2    | DesertRat1      | EQLVCWQAGTTPWNIFPVISLYLMGEVTNQSFRITILPQQYLRPVEDVAT      |
| gi            | 45387815  | ZebraFish1      | EQLVCWQAGTTPWHIFPVISLYLMSENRNQSFRIISILPQQYLRPVEDVAS     |
| <b>Group1</b> |           |                 | <b>EQLVCWQ-G--PW-IFPVISLYLMGE--NQSFI-ILPQQYL-----A-</b> |
|               |           |                 |   |
| sp            | Q9Y5Z0    | Human2          | SQLACWTNSETPWSYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| gi            | 329663206 | Cattle2         | SQLACWTNSETPWSYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| sp            | Q6IE75    | Rat2            | AQLACWTNSETPWAYFPKISYLRDENASRSFRITILPQLYIQPMMGAGF       |
| sp            | Q9JL18    | Mouse2          | AQLACWTNSETPWAYFPKISYLRDENASRSFRITILPQLYIQPMMGAGF       |
| tr            | G3HFD5    | ChineseHamster2 | AQLACWTNSETPWAYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| tr            | G5C5D1    | DesertRat2      | AQLACWTNSETPWAYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| gi            | 348556383 | Guineapig2      | AQLACWANSETPWAYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| gi            | 345795292 | Dog2            | SQLACWTNSETPWSYFPKISYLRDENSSRSFRITILPQLYIQPMMGAGL       |
| gi            | 344294632 | Elephant2       | SQLACWTNSETPWSYFPKISYLRDENSSRSFRITILPQLYIQPMIGAGL       |
| gi            | 345323454 | Platypus2       | SQLACWSNSDKPWSLFPKISYLRDENSSRSFRITILPQLYIQPMMGVAS       |
| tr            | Q5QHS0    | Chicken2        | SQLACWDKTERPWSLFPKLSIYMRDENSSRSFRISILPQLYIQPILGIGE      |
| gi            | 326913352 | WildTurkey2     | SQLACWDKTERPWSLFPKLSIYMRDENSSS-----LHLYIQPILGIGE        |
| gi            | 213982845 | WesternFrog2    | LQLACWDKTQDPWNYFPDISIYLRDTNSSRSFRLTLKPQLYIQSVLTFQE      |
| gi            | 147903717 | AfricanFrog2    | LQLACWDKTQDPWNYFPDISIYLRDTNTRSRFRLTLKPQLYIQSVLTFQE      |
| gi            | 296232194 | Marmoset2       | SQLACWANSETPWSYFPKISYLRDENSSRSFRLTILPQLYIQPMMGAGL       |
| gi            | 348508416 | CichlidFish2    | TKLACWMKGENPWRFPKLSIYLRATNTSEFRITILPQLYIQPITDVDG        |
| gi            | 54400484  | ZebraFish2      | TKLACWMRGESPWRFPKVSILRGNTSFSFRITILPQVRIVP-----          |
| <b>Group2</b> |           |                 | <b>--LACW----PW--FP--SIY-R--N-S-----I-----</b>          |
|               |           |                 |   |
| <b>P1</b>     |           |                 | <b>--LXCW----PW--FP--SXY-X---X-----X-----</b>           |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|    |               |                 |  |
|----|---------------|-----------------|--|
| tr | Q0P4T5        | WesternFrog1    | AQEDCYKFAVSQS-TTGTVMGAVIMEGFYVVFDRANKRIGFAVSTCHVHD |
| tr | Q5QHS1        | Chicken1        | LKDDLPTGSTTLRPPATVMGCCIQEG-----                    |
| sp | P56817        | Human1          | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| gi | 296216280     | Marmoset1       | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| sp | P56819        | Rat1            | SQDDCYKFAVSQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| sp | P56818        | Mouse1          | SQDDCYKFAVSQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| tr | G3IAK4        | ChineseHamster1 | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| sp | Q1KLR6        | GuineaPig1      | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| sp | Q2HJ40        | Cattle1         | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| gi | 291383811     | Rabbit1         | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| gi | 345799894     | Dog1            | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| gi | 344293150     | Elephant1       | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| tr | G5BHK2        | DesertRat1      | SQDDCYKFAISQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSACHVHD |
| gi | 45387815      | ZebraFish1      | AQEDCYKFAVSQS-STGTVMGAVIMEGFYVVFDRARKRIGFAVSTCHVHD |
|    | <b>Group1</b> |                 | -----D-----T-TVMG--I-EG-----                       |

|    |               |                 |   |
|----|---------------|-----------------|---|
| sp | Q9Y5Z0        | Human2          | N-YECYRFGISPS-TNALVIGATVMEGFYVIFDRAQKRVGFAASPCAIEIA |
| gi | 329663206     | Cattle2         | N-YECYRFGISPS-TNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEIA |
| sp | Q6IE75        | Rat2            | N-YECYRFGISSS-TNALVIGATVMEGFYVVFDRARRVGFVSPCAEIA    |
| sp | Q9JL18        | Mouse2          | N-YECYRFGISSS-TNALVIGATVMEGFYVVFDRARRVGFVSPCAEIE    |
| tr | G3HFD5        | ChineseHamster2 | N-YECYRFGISSS-TNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEIE |
| tr | G5C5D1        | DesertRat2      | N-YECYRFGISPS-TNALVIGATVMEGFYVVFDRARRVGFVSPCAEIA    |
| gi | 348556383     | Guineapig2      | S-YECYRFGISPS-TNALVIGATVMEGFYVVFDRARRVGFVSPCAETA    |
| gi | 345795292     | Dog2            | N-YECYRFGISPS-TNALVIGATVMEGFYVVFDRARKRVGFAASPCAIEIA |
| gi | 344294632     | Elephant2       | N-YECYRFGISPS-TNALVIGATVMEGFYVVFDRARKRVGFAMSPCAAS-  |
| gi | 345323454     | Platypus2       | N-YECYRFGISSS-TNALVIGATVMEGFYVVFDRARKRVGFVSLCAEVA   |
| tr | Q5QHS0        | Chicken2        | N-LQCYRFGISSS-TNALVIGATVMEGFYVIFDRAQRRVGFVSPCAEVD   |
| gi | 326913352     | WildTurkey2     | N-LQCYRFGISSS-TNALVIGATVMEGFYVIFDRAQRRVGFVSPCAEVD   |
| gi | 213982845     | WesternFrog2    | S-LNCFRFGISQS-ASALVIGATVMEGFYVIFDRAEKRVGFVSSCAEVS   |
| gi | 147903717     | AfricanFrog2    | S-LNCFRFGISQS-ASTLVIGATVMEGFYVIFDRAEKRVGFVSSCAEVS   |
| gi | 296232194     | Marmoset2       | N-YECYRFGISPS-TNALVIGATVMEGFYVIFDRARKRVGFAASPCAGEQ  |
| gi | 348508416     | CichlidFish2    | T-LDCFRFGVSSS-TNGMVIGATVMEGFYVVFDRQQRLGFALSSCAVSD   |
| gi | 54400484      | ZebraFish2      | -----   |
|    | <b>Group2</b> |                 | -----   |

**P1**

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**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.

|    |               |                 |  |
|----|---------------|-----------------|--|
| tr | Q0P4T5        | WesternFrog1    | YFRTASVEGPPFASDLEDCGYNTPQLDESALMTTAYVMAGVCALFMLPLC   |
| tr | Q5QHS1        | Chicken1        | --STVALTGP-----                                      |
| sp | P56817        | Human1          | EFRTAAVEGPPFVTLDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| gi | 296216280     | Marmoset1       | EFRTAAVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| sp | P56819        | Rat1            | EFRTAAVEGPPFVTADMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| sp | P56818        | Mouse1          | EFRTAAVEGPPFVTADMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| tr | G3IAK4        | ChineseHamster1 | EFRTAAVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| sp | Q1KLR6        | GuineaPig1      | EFRTATVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| sp | Q2HJ40        | Cattle1         | EFRTAAVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| gi | 291383811     | Rabbit1         | EFRTAAVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| gi | 345799894     | Dog1            | EFRTAAVEGPPFITLDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| gi | 344293150     | Elephant1       | EFRTAAVEGPPFVTPDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| tr | G5BHK2        | DesertRat1      | EFRTAAVEGPPFVTLDMEDCGYNI PQTDESTLMTIAYVMAAICALFMLPLC |
| gi | 45387815      | ZebraFish1      | EFRTAAVEGPPFHGLDLEDCGYNVPQTDESTLMTIAYVMAGICALFMLPLC  |
|    | <b>Group1</b> |                 | ---T---GP-----                                       |
|    |               |                 |  |
| sp | Q9Y5Z0        | Human2          | GAAVSEISGPFSTEDVASNCVPAQSLSEPI LWIVSYALMSVCGA ILLVLI |
| gi | 329663206     | Cattle2         | GAPVSEISGPFSTEDIASNCVPALPLNEPVLWIVSYTLMSVCGV ILLVLI  |
| sp | Q6IE75        | Rat2            | GTTVSEISGPFSTEDIASNCVPAQALNEPILWIVSYALMSVCGA ILLVLI  |
| sp | Q9JL18        | Mouse2          | GTTVSEISGPFSTEDIASNCVPAQALNEPILWIVSYALMSVCGA ILLVLI  |
| tr | G3HFD5        | ChineseHamster2 | GTTVSEISGPFSTEDVASNCVPAPALNEPILWIVSYALMSVCGA ILLVLI  |
| tr | G5C5D1        | DesertRat2      | GAPVSEVSGPFSTDGIASNCVPAPAPGEP LLWFVSYALLSACGL ILLVLI |
| gi | 348556383     | Guineapig2      | GVPLSEVSGPFSTDGIASNCVPSPLNEPVLWVVS YALMSSCGL ILLVLI  |
| gi | 345795292     | Dog2            | GAPVSEISGPFSTDDIASNCVPALPLNEPILWIVSYTLMSVCGI ILLILI  |
|    |               |                 | -----  |
| gi | 344294632     | Elephant2       | GSPVSEISGPFPTDDVASNCVTTLPPFNEPILWIVSYTLMSICGI ILLVLI |
| gi | 345323454     | Platypus2       | GSPVSEIEGPFPTTDDVASNCVSSITFHEPVLWIASYALMSLCGI ILLILI |
| tr | Q5QHS0        | Chicken2        | GSPVSEIEGPFPTTDDVASNCVSSITFHEPVLWIASYALMSLCGI ILLILI |
| gi | 326913352     | WildTurkey2     | GSPVSEIEGPFPTTDDVASNCVSSITFHEPVLWIASYALMSLCGI ILLILI |
| gi | 213982845     | WesternFrog2    | GITVSEIAGPFGTSDVSSNCIARNPLREPIMWII SYSLMSLCGM ILLVLI |
| gi | 147903717     | AfricanFrog2    | GITVSEIAGPFGTSDVSSNCIARNPLREPIMWII SYSLMSLCGM ILLVLI |
| gi | 296232194     | Marmoset2       | FSHRMGIPDESPLCECA-----                               |
| gi | 348508416     | CichlidFish2    | GVALSEIEGPFSAADVAADC-SGGPLKEPLVWMISYALMAVCA LALLIL   |
| gi | 54400484      | ZebraFish2      | -----  |
|    | <b>Group2</b> |                 | -----  |
|    | <b>P1</b>     |                 | -----  |

**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1 & BACE2, continued.

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tr|Q0P4T5|WesternFrog1      LMLFQWRCFRCLKRARDDLADDISLLK----
tr|Q5QHS1|Chicken1        -----
sp|P56817|Human1           LMVCQWCCLRCLRQHQHDDFADDISLLK----
gi|296216280|Marmoset1     LMVCQWRCLRCLRQHQHDDFADDISLLK----
sp|P56819|Rat1             LMVCQWRCLRCLRQHQHDDFADDISLLK----
sp|P56818|Mouse1           LMVCQWRCLRCLRQHQHDDFADDISLLK----
tr|G3IAK4|ChineseHamster1  LMVCQWRCLRCLRQHQHDDFADDISLLK----
sp|Q1KLR6|GuineaPig1      LMVCQWRCLRCLRQHQHDDFADDISLLK----
sp|Q2HJ40|Cattle1          LMVCQWRCLRCLRQHQHDDFADDISLLK----
gi|291383811|Rabbit1       LMVCQWRCLRCLRQHQHDDFADDISLLK----
gi|345799894|Dog1          LMVCQWRCLRCLRQHQHDDFADDISLLK----
gi|344293150|Elephant1    LMVCQWRCLRCLRQHQHDDFADDISLLK----
tr|G5BHK2|DesertRat1      LMVCQWRCLRCLRQHQHDDFADDISLLK----
gi|45387815|ZebraFish1    VMVCQWRFTCCLQPADG--SDDISLLK----
Group1                      -----

sp|Q9Y5Z0|Human2           VLLLLPFCRQRRPRDPEVVNDESSLVRHRWK
gi|329663206|Cattle2       TLLLLPVRCRHHPRDPEVVNDESSLVRHRWK
sp|Q6IE75|Rat2             LLLLPLHCRHAPRDPEVVNDESSLVRHRWK
sp|Q9JL18|Mouse2           LLLLPLHCRHAPRDPEVVNDESSLVRHRWK
tr|G3HFD5|ChineseHamster2  LLLLPLVRCRHAPRDPEVVNDESSLVRHRWK
tr|G5C5D1|DesertRat2      ILLLPCP-RRPPRDPEVINDESSLVRHRWK
gi|348556383|Guineapig2   VLLLLPCRCRHAPRDPEVINDESSLVRHRWK
gi|345795292|Dog2          VLLLLPFCRHLPRDPEVVNDESSLVRHRWK
gi|344294632|Elephant2    -----PCHPEVVNDESSLVRHRWK
gi|345323454|Platypus2    ILLLPHRCQRRPRDPTVNDDESSLVRHRWK
tr|Q5QHS0|Chicken2        ILLLIPRCQHRYTDNDVVNDESSLVRHRWK
gi|326913352|WildTurkey2  ILLLIPRCQHRYTDNDVVNDESSLVRHRWK
gi|213982845|WesternFrog2 ILLLIPNR--HRRDDMETVNDDESSLVQHRWK
gi|147903717|AfricanFrog2 ILLLISNR--QRHDDMETINDESSLVQHRWK
gi|296232194|Marmoset2    -----DLEAIPDGT-----
gi|348508416|CichlidFish2 LMLILPCR---CGNRNGEITDESSLVRHRWK
gi|54400484|ZebraFish2    -----
Group2                      -----

P1                          -----

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**Supplement Figure 12** The result of P1 partition and extracting the sequences of BACE1& BACE2, continued.