

# **Correlated evolution of GnRH and GnIH and their receptors in mammals**

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**Supplementary Table 1: Accession numbers of the gene sequences used in the study. All sequences are collected from the Ensembl database except AVP of monkey which is collected from the NCBI Reference sequence.**

| <b>Species</b> | <b><i>GnRH</i></b>     | <b><i>GnIH</i></b>     | <b><i>GAL</i></b>      | <b><i>GHRL</i></b>     | <b><i>IAPP</i></b>     | <b><i>SST</i></b>      | <b><i>AVP</i></b>      |
|----------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Human          | ENSG<br>00000147437    | ENSG<br>00000105954    | ENSG<br>00000069482    | ENSG<br>00000157017    | ENSG<br>00000121351    | ENSG<br>00000157005    | ENSG<br>00000101200    |
| Chimpanzee     | ENSPTRG<br>00000020091 | ENSPTRG<br>00000018998 | ENSPTRG<br>00000003985 | ENSPTRG<br>00000014618 | ENSPTRG<br>00000004756 | ENSPTRG<br>00000015727 | ENSPTRG<br>00000013190 |
| Monkey         | ENSMMUG<br>00000029018 | ENSMMUG<br>00000008369 | ENSMMUG<br>00000023496 | ENSMMUG<br>00000019935 | ENSMMUG<br>00000032087 | ENSMMUG<br>00000000850 | XM<br>001115061.1      |
| Cow            | ENSBTAG<br>00000000164 | ENSBTAG<br>00000019447 | ENSBTAG<br>00000009393 | ENSBTAG<br>00000012328 | ENSBTAG<br>00000010530 | ENSBTAG<br>00000017312 | ENSBTAG<br>00000008027 |
| Elephant       | ENSLAFG<br>00000003526 | ENSLAFG<br>00000008838 | ENSLAFG<br>00000013266 | ENSLAFG<br>00000014068 | ENSLAFG<br>00000012562 | ENSLAFG<br>00000012303 | ENSLAFG<br>00000007073 |
| Horse          | ENSECAG<br>00000010664 | ENSECAG<br>00000021063 | ENSECAG<br>00000016579 | ENSECAG<br>00000025073 | ENSECAG<br>00000023618 | ENSECAG<br>00000023368 | ENSECAG<br>00000024857 |
| Dog            | ENSCAFG<br>00000008985 | ENSCAFG<br>00000002863 | ENSCAFG<br>00000010772 | ENSCAFG<br>00000005129 | ENSCAFG<br>00000012365 | ENSCAFG<br>00000013891 | ENSCAFG<br>00000006432 |
| Guinea Pig     | ENSCPOG<br>00000015538 | ENSCPOG<br>00000013784 | ENSCPOG<br>00000004337 | ENSCPOG<br>00000020910 | ENSCPOG<br>00000009711 | ENSCPOG<br>00000009662 | ENSCPOG<br>00000023592 |
| Mouse          | ENSMUSG<br>00000015812 | ENSMUSG<br>00000029831 | ENSMUSG<br>00000024907 | ENSMUSG<br>00000064177 | ENSMUSG<br>00000041681 | ENSMUSG<br>00000004366 | ENSMUSG<br>00000037727 |
| Rat            | ENSRNOG<br>00000013441 | ENSRNOG<br>00000010806 | ENSRNOG<br>00000015156 | ENSRNOG<br>00000010349 | ENSRNOG<br>00000012417 | ENSRNOG<br>00000001837 | ENSRNOG<br>00000021229 |
| Opossum        | ENSMODG<br>00000016713 | ENSMODG<br>00000000610 | ENSMODG<br>00000012764 | ENSMODG<br>00000005491 | ENSMODG<br>00000017812 | ENSMODG<br>00000008503 | ENSMODG<br>00000005433 |

**Supplementary Table 1 Continued**

| <b>Species</b> | <b><i>GnRHR</i></b>    | <b><i>GnIHR</i><br/>(<i>NPFRI</i>)</b> |  |  |  |  |  |
|----------------|------------------------|--|--|--|--|--|--|
| Human          | ENSG<br>00000109163    | ENSG<br>00000148734                    |  |  |  |  |  |
| Chimpanzee     | ENSPTRG<br>00000016100 | ENSPTRG<br>00000002586                 |  |  |  |  |  |
| Monkey         | ENSMMUG<br>00000003779 | ENSMMUG<br>00000005367                 |  |  |  |  |  |
| Cow            | ENSBTAG<br>00000000438 | ENSBTAG<br>00000010930                 |  |  |  |  |  |
| Elephant       | ENSLAFG<br>00000005648 | ENSLAFG<br>00000004049                 |  |  |  |  |  |
| Horse          | ENSECAG<br>00000005763 | ENSECAG<br>00000010498                 |  |  |  |  |  |
| Dog            | ENSCAFG<br>00000002785 | ENSCAFG<br>00000014038                 |  |  |  |  |  |
| Guinea Pig     | ENSCPOG<br>00000014609 | ENSCPOG<br>00000019374                 |  |  |  |  |  |
| Mouse          | ENSMUSG<br>00000029255 | ENSMUSG<br>00000020090                 |  |  |  |  |  |
| Rat            | ENSRNOG<br>00000002011 | ENSRNOG<br>00000000559                 |  |  |  |  |  |
| Opossum        | ENSMODG<br>00000020742 | ENSMODG<br>00000012172                 |  |  |  |  |  |

**Supplementary Table 2: Correlation between ML distances of background control peptides.**

| <b>Neuropeptide pairs</b> | <b>Correlation coefficient before subtracting speciation</b> | <b>Correlation coefficient after subtracting speciation</b> |
|---------------------------|--|---|
| GAL-GHRL                  | 0.75   | 0.91  |
| GAL-IAPP                  | 0.73   | 0.93  |
| GAL-SST                   | 0.59   | 0.64  |
| GAL-AVP                   | 0.72   | 0.91  |
| GHRL-IAPP                 | 0.83   | 0.92  |
| GHRL-SST                  | 0.54   | 0.82  |
| GHRL-AVP                  | 0.64   | 0.94  |
| IAPP-SST                  | 0.73   | 0.67  |
| IAPP-AVP                  | 0.81   | 0.92  |
| SST-AVP                   | 0.87   | 0.84  |

**Supplementary Table 3: Correlation between similarity indices and patristic distances of background control peptides.**

| <b>Neuropeptide pairs</b> | <b>Correlation coefficient between similarity indices</b> | <b>Correlation coefficient between patristic distances</b> |
|---------------------------|---|--|
| GAL-GHRL                  | 0.82  | 0.49   |
| GAL-IAPP                  | 0.85  | 0.39   |
| GAL-SST                   | 0.35  | 0.30   |
| GAL-AVP                   | 0.66  | 0.39   |
| GHRL-IAPP                 | 0.78  | 0.54   |
| GHRL-SST                  | 0.68  | 0.80   |
| GHRL-AVP                  | 0.77  | 0.70   |
| IAPP-SST                  | 0.47  | 0.39   |
| IAPP-AVP                  | 0.82  | 0.66   |
| SST-AVP                   | 0.82  | 0.84   |

Supplementary Figure 1: Multiple sequence alignment of Gonadotropin-releasing hormone (GnRH)

|            |  |
|------------|--|
| Human      | MIQKLLAGLILLTWCVEGCSSQHWSYGLRPGGKRDAENLIDSFQEIVKEVGQLAETQRFE |
| Chimpanzee | MIQKLLAGLILLTWCVEGCSSQHWSYGLRPGGKRDAENLIDSFQEIVKEAGQLAETQRFE |
| Monkey     | MIPKLLAGLILLTLCVEGCSSQHWSYGLRPGGKRDAENLMSDFQEIVKEVGQLAETQHFE |
| Cow        | MTPKLLAGLILLIICVVGCSGQHWSYGLRPGGKRNAENVIDSFQEIAKEVDQPVEPKCCG |
| Dog        | MIPKLVAGLILLTFCVVGCSGQHWSYGLRPGGKRNAEHLIDSFQEMAKELDQPAEPQHLE |
| Guineapig  | MIPKLLAGLVLLTLCVENGGQYWSYGLRPGGKRNIPLVDSFQEMAKEIDQLAEPQHFE   |
| Mouse      | MILKLMAGILLTVCLEGCSSQHWSYGLRPGGKRNEHLVESFQEMGKEVDQMAEPQHFE   |
| Rat        | MIPKLMAAVLLTVCLEGCSSQHWSYGLRPGGKRNEHLVDSFQEMGKEEDQMAEPQNFE   |
| Horse      | MIPKLLAGLILLTLCVVGCSGQHWSYGLRPGGKRNADNLIDSFQEIAKEVNQPAEPQRFE |
| Elephant   | MVPKLLAGLILLTLCVVGCSGQHWSYGLRPGGKRNADNLIDSFQEIAKEVDQPAEPQRFE |
| Opossum    | MTVKLLTGCLLLTLCVMISSGQHWSYGLRPGGKRADTLIDSFQEVCEVNMSEPQRFE    |
|            | * **:.: .:** *: *.:****.*****: : :.:*****: * .* *.:          |

|            |                                |
|------------|--------------------------------|
| Human      | CTTHQPRSPLRDLKGALESLEEETGQKKI  |
| Chimpanzee | CTMHQPRSPLRDLKGALESLEEETGQKKI  |
| Monkey     | CTMHQPRSPLQDLKGALESLEEETGQKKI  |
| Cow        | CIVHQSHSPLRDLKAALESLEEETGQRKI  |
| Dog        | CTIHKPRPPLRDLRGALESLEEETGQKRI  |
| Guineapig  | CTLHQPRSPLRDLKGAESLMEEETGQKKI  |
| Mouse      | CTVHWPRSPLRDLRGALESLEEERQKKM   |
| Rat        | CTVHWPRSPLRDLRGALESLIEEEAGQKKM |
| Horse      | CTVHQPRSPLRDLKGALESLEEETGQKKI  |
| Elephant   | CTIHQLRSPLRDLKGALESLEEETGQKKI  |
| Opossum    | CTIHQPHSPLRDLKALASLIEGEAGRKKA  |
|            | * * :.***:*.:** *:* *: :.:     |

Supplementary Figure 2: Multiple sequence alignment of Gonadotropin-inhibiting hormone (GnIH)

|            |   |
|------------|---|
| Human      | MEIISSKLFILLTLATSSLLTSNIFCADELVISNLHSKENYDKYSEPRGYPKGERSLNFE  |
| Chimpanzee | MEIISSKLFVLLTLATSSLLTSNIFCADELMMSNLHSKENYDKYSEPRGYPKGERSLNFE  |
| Monkey     | MEIISSKLFILLTLATSSLLTSNISCADLMSSNLHSKENYDKYSEPRGYPKRERSLNFE   |
| Cow        | MEIISLKRIFILLMLATSSLLTSNIFCTDESMPNLYSKKNYDKYSEPRGDLGWERSLTFE  |
| Dog        | MKIISSKRFILLILATSSLLTSNVFCTDELMMSNLHSKENYDKYSEHEGDPKGERSLNFE  |
| Guineapig  | MEIISSKRFILLTLATSILLTSNIFYADELTMGHLHSKENYDKCSEPQGTGPKGERSFTFQ |
| Mouse      | MEIISLKRIFILLTVATSSFLTSNTFCTDEFMMPHFHSKEGDGKYSQLRGIPKGVRSVSFQ |
| Rat        | MEIISSKRFILLTLATSSFLTSNTLCSDELMMPHFHSKEGYGKYYQLRGIPKGVRSVTFQ  |
| Horse      | MDFISAKRLILLTLATSSLLTSNIFCGDELMMSNLYSKDNYDKYSKPRGDPKGERSLNFE  |
| Elephant   | MEIILSRQFILLTLATSSLLTSNIFCADNLRMSNLHSKENYDKFCEPRGDSKGVRSVTFQ  |
| Opossum    | MEIISSKRFVILTATSILLASESVCADESVMNLCNWEHYNEYLKPDRHPKEKKSPLPE    |
|            | *.:* : :.:* :*** :*:* *: : : . . .: : .. :*.: :               |

|            |  |
|------------|--|
| Human      | ELKDWGPKIKMTPAVNKMPHSFANLPLRFGRNVQEERSAGANMEVSLVRRVPLNPQRFGR |
| Chimpanzee | ELKDWGPKIKMTPAVNKMPHSFANLPLRFGRNVQEERSAGANMEVSLVRRVPLNPQRFGR |
| Monkey     | ELKDWGPKIKMTPAVNKMPHSVTNPLPLRFGRNTEERSAGANMEVSLVRRVPLNPQRFGR |

|            |  |
|------------|--|
| Cow        | EVKDWAPKIKMKPVVNMPPSAANLPLRFGRNMEEERSTRANREDSLSRWVNLQRFGR    |
| Dog        | ELNDWGPRIKMAPTVNKMPSHAANLPLRFGRMEEKRSTGANIKESILRHIPNLQRFGR   |
| Guineapig  | ELKDWGPKMKMTPAVNKTPHAAAANLPLRFGRMKEERNPRGNMEAGISRHLNLPQRFGR  |
| Mouse      | ELKDWGAKIKMPAPANKVPHSAANLPLRFGRIDEKRSPAANMEAGTRSHFPSLPQRFGR  |
| Rat        | ELKDWGAKIKMPAPANKVPHSAANLPLRFGRNIEDRRSPRANMEAGTMSHFPSLPQRFGR |
| Horse      | EWKDWGPKTKITPAVNKMPSHAANLPLRFGRMEEERGPANTEESISRRIPNLQRFGR    |
| Elephant   | ELKDWGPKIKMTHTVNKMPPSVNNLPLRFGRMEE-RSPGPNMGGSILRRVNLQRFGR    |
| Opossum    | EHQHWGSNYKVNLKLNKIPQLMPHPPLRFGRSFEETERSIESNLDGGISRRIPNLQRFGR |
|            | * :.*... *: ** * : *****. .: * . * . .*****                  |
| Human      | TT   |
| Chimpanzee | TT   |
| Monkey     | TT   |
| Cow        | TT   |
| Dog        | TT   |
| Guineapig  | MT   |
| Mouse      | TT   |
| Rat        | TT   |
| Horse      | TT   |
| Elephant   | TA   |
| Opossum    | AA   |
|            | :  |

Supplementary Figure 3: Multiple sequence alignment of Galanine (GAL)

|            |  |
|------------|--|
| Human      | AKEKRGWTLNSAGYLLGPHAVGNHRFS SDKNGLTSKREL RPEDDMKPGSFDRSIPENNIM   |
| Chimpanzee | AKEKRGWTLNSAGYLLGPHAVGNHRFS SDKNGLTSKREL RPEDDMKPGSFDRSIPENNIM   |
| Monkey     | AKEKRGWTLNSAGYLLGPHAVGNHRFS SDKNGLTSKREL QPQDDVKPGSFDRSPENNIM    |
| Cow        | VKEKRGWTLNSAGYLLGPHALDSHRFSQDKHGLAGKRELEPEDEARPGSFDRPLAENNVV     |
| Dog        | VKEKRGWTLNSAGYLLGPHAIDNHRFSFHEKPGLTGKREL PPEDEGRSGFAGLSLSENAAV   |
| Guineapig  | AKEKRGWTLNSAGYLLGYPY AIDNHRFS SDKHGLAGKREL QPDGDVQTGSSDRLLPESSIV |
| Mouse      | AKEKRGWTLNSAGYLLGPHAIDNHRFS SDKHGLTGKREL QLEEEERRPGSVDVPLPESNIV  |
| Rat        | TKEKRGWTLNSAGYLLGPHAIDNHRFS SDKHGLTGKREL PLEEEGRLGSAVAVPLPESNIV  |
| Horse      | VKEKRGWTLNSAGYLLGPHAIDNHRFS HDKHGLAGKREL QPEDEARPGSYDRPLPENNVV   |
| Elephant   | AKEKRGWTLNSAGYLLGPHAIDNHRFS FHEKHGLAGKREL QPDDET KPGSYDRLLPESSVV |
| Opossum    | AKEKRGWTLNSAGYLLGPHAVDNHRFS FNDKHGLAGKREL QPEDGMKSGNFARPTTDDNIV  |
|            | .*****:*.**** :* **:.**** : : * . . . :                          |
| Human      | RTIIEFLSFLHLKEAGALDDL PAAASSEDIERS                               |
| Chimpanzee | RTIIEFLSFLHLKEAGALDDL PAAASSEIEQS                                |
| Monkey     | RTIIEFLSFLHLKEAGAFDDL PAGASSEMERS                                |
| Cow        | RTIIEFLTFLHLKDAGALES LPTAESAE DAERS                              |
| Dog        | RMLIEFLTFLRLKEAGALPDLPSAVSAEDMEQP                                |
| Guineapig  | RTVIEFLTFLHLKEAGLLGGIPLAGSPEDMEQS                                |
| Mouse      | RTIMEFLSFLHLKEAGALDGIPLATSSLEDLEKS                               |
| Rat        | RTIMEFLSFLHLKEAGALDGIPLATSSLEDLEQS                               |
| Horse      | RTIIEFLNFLHLKEAGALEDLLPVASTEDTEQA                                |
| Elephant   | RTIIEFLT YLQLKEAGALEDLPSALSSLEDTEQT                              |
| Opossum    | RTVLEFLTFLHLKEAGALDSLPLAISSEETNQP                                |
|            | * :.***.:.***.*** : .: *.*: :..                                  |

Supplementary Figure 4: Multiple sequence alignment of Appetite regulating



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Mouse      NVGSNTYGKRNAAGDPNRESLDFLL
Rat        NVGSNTYGKRNVAEDPNRESLDFLL
Horse      SVGSNTYGKRNTVEIFNREPLNYLP
Elephant   NVGSNTYGKRNTAEVLNRPAPLNYLL
Opossum    NVGSNTYGKREIAGILSREPLNQFP
.:*****:      . * * :

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Supplementary Figure 6: Multiple sequence alignment of Somatostatin (SST)

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Human      MLSCRLQCALAALSIVLALGCVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Chimpanzee MLSCRLQCALAALSIVLALGGVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Monkey     MLSCRLQCALAALSIVLALGGVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Cow        MLSCRLQCALAALSIVLALGGVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Dog        MLSCRLQCALAALSIVLALGGVTCAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Guineapig MLSCRLQCALAALSIVLALGVSAGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Mouse      MLSCRLQCALAALCIVLALGGVTGAPSDPRLRQFLQKSLAAATGKQELAKYFLAELLSEP
Rat        MLSCRLQCALAALCIVLALGGVTGAPSDPRLRQFLQKSLAAATGKQELAKYFLAELLSEP
Horse      MLSCRLQCALAALSIVLALGGVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Elephant   MLSCRLQCALAALSIVLALGGVTGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
Opossum    MLSCRLQCALALLSITLAVSSVSAAPSDPRLRQFLQKSLAATAGKQELAKYFLAELLSEP
***** * : . * * : * : ***** : * : *****

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Human      NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Chimpanzee NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Monkey     NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Cow        NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Dog        NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Guineapig NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Mouse      NQTENDALEPEDLPQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Rat        NQTENDALEPEDLPQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Horse      NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Elephant   NQTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC
Opossum    SQTENEALEPEELTQDVEPEEMRME LQRSANSNPAMTTREKAGCKNFFWKTFTSC
.***.***. * * * :***.*****. *****

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Supplementary Figure 7: Multiple sequence alignment of Vasopressin (AVP)

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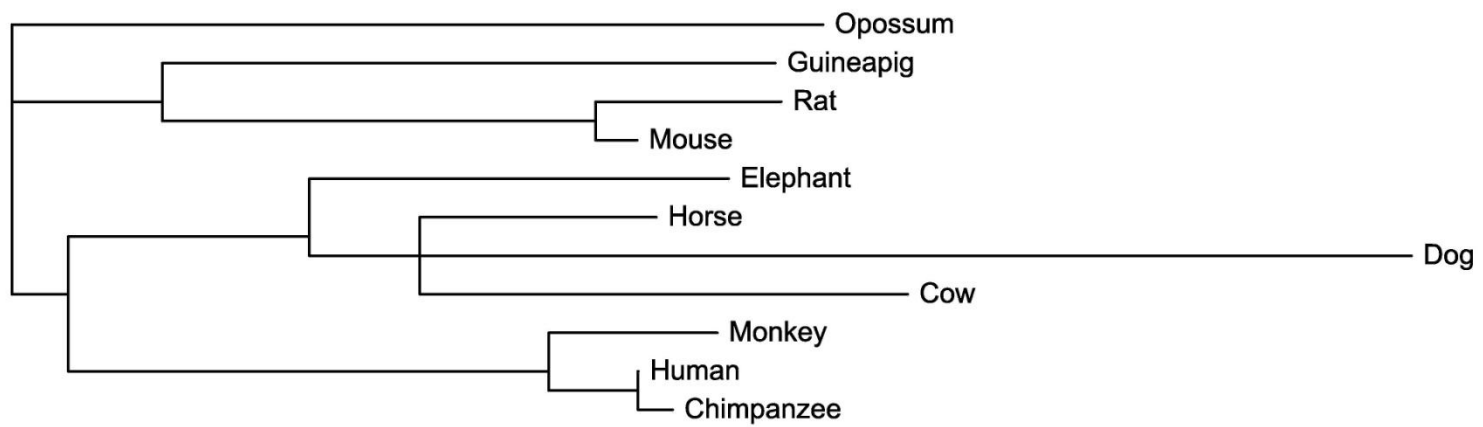
Human      PACFLGLLAFSSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCGSPICCADELGCFVGT
Chimpanzee PACFLGLVALSSGWYFQNCPRGGKRAVSDLELRQCGPGGKGRFCGSPICCADELGCFVGT
Monkey     PACFLGLLAFSSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCGSPICCADELGCFVGT
Cow        PACFLSLLAFTSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCRPSICCEDELGCFVGT
Dog        PACFLGLLAFTSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCGSPICCGDELGCFVGT
Guineapig PACLLGLLAFTSACYFQNCPRGGKRALSDELQCGPGGQGRFCGSPICCADALGCFVGT
Mouse      SACFLSLLAFSSACYFQNCPRGGKRAISDMELRQCGPGGKGRFCGSPICCADELGCFVGT
Rat        SACFLSLLALTSACYFQNCPRGGKRATSDMELRQCGPGGKGRFCGSPICCADELGCFVGT
Horse      PACFLGLLAFTSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCGSPICCGDELGCFVGT
Elephant   PACFLGLLAFTSACYFQNCPRGGKRAMSDLELRQCGPGGKGRFCGSPICCGEELGCFVGT
Opossum    PACFFLLAFTSACYFQNCPRGGKRLADTELQCGPGSKGRFCGSPICCGEELGCFVGT
.*.: *.:*.* ***** . * ***** . ***** : *.:**

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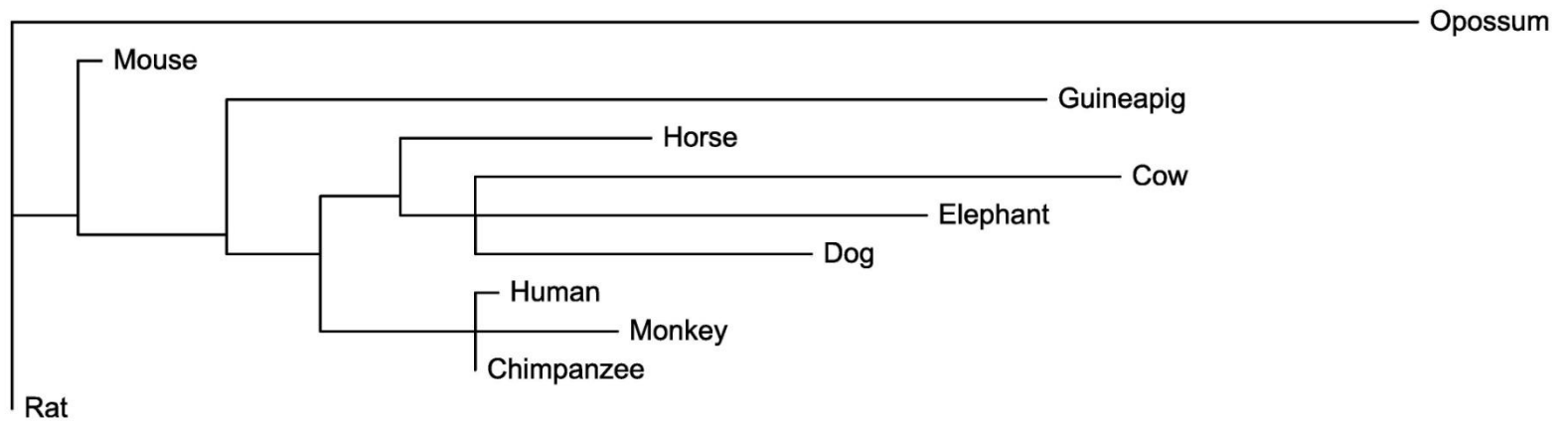


|            |  |
|------------|--|
| Human      | AEALRCQEENYLSPCQSGQKACGSGGRCAAFGVCCNDESCVTEPECREGFHRRRASDR   |
| Chimpanzee | AEALRCQEENYLSPCQSGQKACGSGGRCAAFGVCCNDESCTTEPECREGFQRRRASDR   |
| Monkey     | AEALRCQEENYLSPCQSGQKACGSGGRCAAFGICCNDSCMTEPDCREGFHRRRASDR    |
| Cow        | AEALRCQEENYLSPCQSGQKPCGSGGRCAAAGICCNDSCVTEPECREGFPRRVRANDR   |
| Dog        | AEALRCQEENYLSPCQSGRTPCGSGGRCAAAGICCNDSCVTEPECREGLHRGARASDR   |
| Guineapig  | AEALRCQEENYLSPCQSGQKPCGSGGRCAANGVCCNDESCVIEPECREEFHRPVRAGDR  |
| Mouse      | AEALRCQEENYLSPCQSGQKPCGSGGRCAAVGICCSDESCVAEPECHDGF FRLTRAREP |
| Rat        | AEALRCQEENYLSPCQSGQKPCGSGGRCAAAGICCSDESCVAEPECREGF FRLTRAREQ |
| Horse      | AEALRCQEENYLSPCQSGQKPCGSGGRCAAAGICCNDSCVTEPRIAEGIHRRTRASDR   |
| Elephant   | AEALRCQEENYLSPCQSGQKPCGSGGRCAAAGICCYEESC VTEPECREGIHRRTRASDR |
| Opossum    | AESLRCQEESYLSPCQSGQKPCGNNGRCAAPGICCNDENCMMEPACRDESRRRARASEK  |
|            | ** :***** .*****:..** .***** *:* ** :*.* ** : * .** :        |

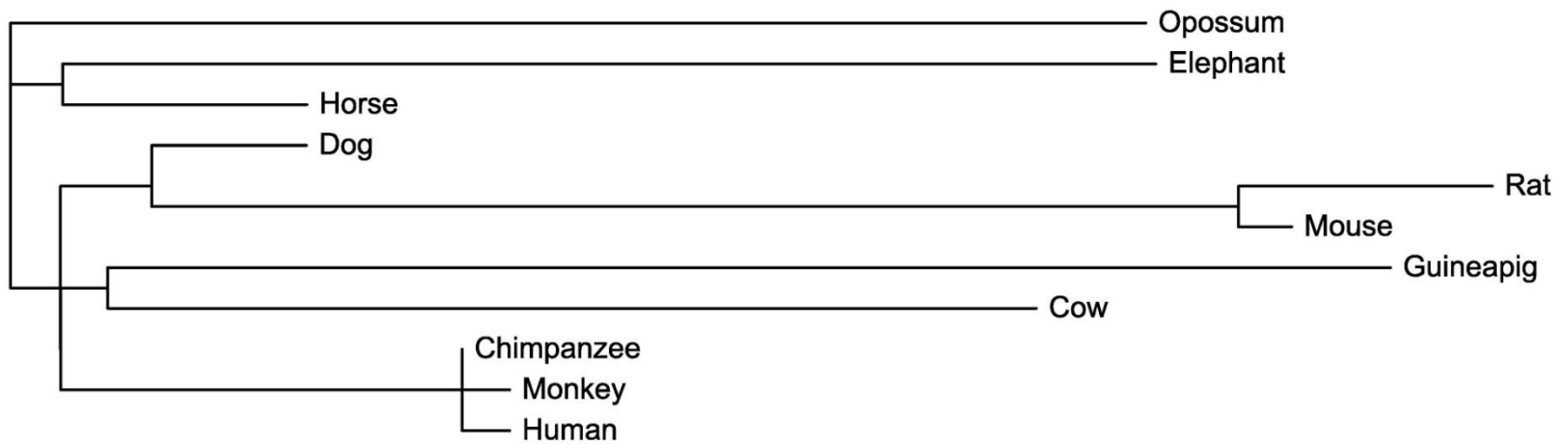
|            |                                  |
|------------|----------------------------------|
| Human      | SNATQLDGPAGALLRLVQLAGAPEPFEPAPD  |
| Chimpanzee | SNATQLDGPAGALLRLVQLAGAPEPFEPSTS  |
| Monkey     | SNATQLDGPAGALLRLVQLAGAPEPFEPAPG  |
| Cow        | SNATLLDGPAGALLRLVQLAGAPEPAEPAPG  |
| Dog        | SNATQLDGPTGALLRLVQLAGAPEPAEPAPG  |
| Guineapig  | SNVTQLDGPAGALLRLMQLATKPRPQNPEPA  |
| Mouse      | SNATQLDGPAGALLRLVQLAGTRESVDSAPR  |
| Rat        | SNATQLDGPARELLRLVQLAGTQESVDSAPR  |
| Horse      | SNATQLDGPAGALLRLVQLAGAPEPEEPSAS  |
| Elephant   | SNATQLDGPAGALLRLVQLAGAPEPEEPSAS  |
| Opossum    | SNETQLDGPASAFLLRLVQLAGQQMSELQSPQ |
|            | ** * ****: :****:*** . .         |



Supplementary Figure 8: Phylogenetic tree of Galanine (GAL)



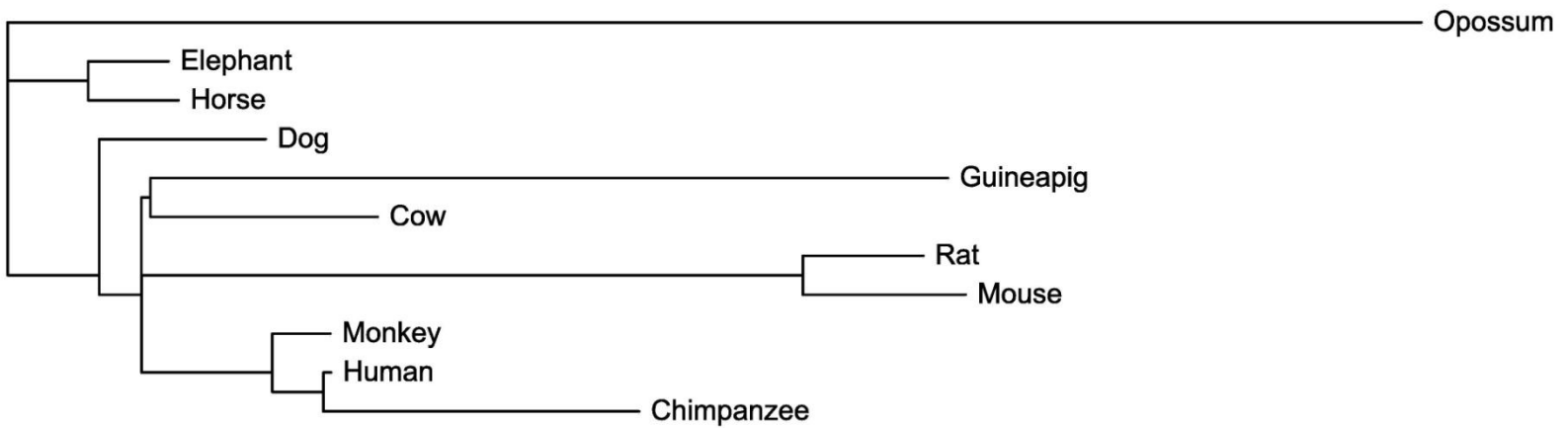
Supplementary Figure 9: Phylogenetic tree of Appetite regulating hormone (GHRH)



Supplementary Figure 10: Phylogenetic tree of Islet amyloid polypeptide (IAPP)



Supplementary Figure 11: Phylogenetic tree of Somatostatin (SST)



Supplementary Figure 12: Phylogenetic tree of Vasopressin (AVP)



|           |  |
|-----------|--|
| Monkey    | VLHQDPHKLQLNQSKNNIPRARLRTLKMTVAFATSFTVCWTPYYVVLGIWYWFDPPEMLNRV |
| Cow       | VLHQDPHKLQLNQSKNNIPRARLRTLKMTVAFATSFTVCWTPYYVVLGIWYWFDPDMVNRV  |
| Horse     | -----  |
| Dog       | VLHQDPHELQLNQSKNNIPRARLRTLKMTVAFATSFTVCWTPYYVVLGIWYWFDPPEMLNRV |
| Guineapig | VLQQDSNKLQLNQSKNNIPRARLRTLKMTVAFASFIVCWTPYYVVLGLWYWFDPGMLHRM   |
| Rat       | VLHQDPRKLQLNQSKNNIPRARLRTLKMTVAFATSFVICWTPYYVVLGIWYWFDPPEMLNRV |
| Mouse     | VLHQDPRKLQLNQSKNNIPRARLRTLKMTVAFATSFVVCWTPYYVVLGIWYWFDPPEMLNRV |
| Elephant  | VLHQDPHKLQLNQSKNNIPRARLRTLKMTVAFATSFTVCWTPYYVVLGIWYWFDPPEMLNRV |
| Opossum   | VLHQDPHKLQLNRSKNNIPRARLRTLKMTVAFATLFTVCWTPYYVVLGIWYWFDPPEMLNRV |

|            |                              |
|------------|------------------------------|
| Human      | SDPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Chimpanzee | SDPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Monkey     | SDPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Cow        | SDPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Horse      | -----                        |
| Dog        | SDPVNHFFFLFALLNPCFDPLIYGYFSL |
| Guineapig  | SEPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Rat        | SEPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Mouse      | SEPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Elephant   | SDPVNHFFFLFAFLNPCFDPLIYGYFSL |
| Opossum    | SDPVSHFFFLFGLLNPCFDPLIYGYFSL |

Supplementary Figure 14: Multiple sequence alignment of gonadotrophin-inhibitory hormone receptor (GnIHR)

|            |  |
|------------|--|
| Human      | MEGEPSPPNSSWPLSQNGTNTTEATPATNLTFSYYQHTSPVAAMFIVAYALIFLLCMVG    |
| Chimpanzee | MEGEPSPPNSSWPLSQNGTNTTEATPAANLTFSYYQHTSPVAAMFIVAYALIFLLCMVG    |
| Monkey     | VLGEPSPPNSSWPLSQNGTNAEATPAANLTFSYYQHTSPVAAMFIVAYALIFLLCMVG     |
| Cow        | MSGEPAPSNSSWPPSENGSDAQATPAANLTFSYYQHSSPVAAMFIVAYVLIIFLLCMVG    |
| Horse      | -----NLTFSSYYQHSSPVAAMFIVAYVLIIFLLCMVG                         |
| Dog        | LLGEPSPPNSSWPPSQNGSHTKATPTVNLTFSSYYQHSSPVAALFIVAYVLIIFLLCMVG   |
| Guineapig  | VLGVPKSPNGSWPPSQNGSNAEATPAANLTFSYYQHSSPVAAMFIVAYALIFLLCMVG     |
| Rat        | -PAEPSPPNNGSWPLGQNGSDVETSIAATSLTFSSYYQHSSPVAAMFIAAYVLIIFLLCMVG |
| Mouse      | MEAPSPPNNGSWPPLNESDAETAPVASLTFSSYYQHSSPVAAMFIAAYALIFLLCMVG     |
| Elephant   | VLGKPSQPPNASWPRSQNGSSAEADPAANLTFSYYQHSSPVAAMFIVAYVLIIFLLCMVG   |
| Opossum    | LERSPQAGNDSSFASNENSS--QAPSPQNFTFSSYYQHSWPVAAMFIMAYVLIIFLLMCLVG |
|            | .:*****:****:* **.:***:***                                     |

|            |  |
|------------|--|
| Human      | NTLVCFIVLKNRHMHTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Chimpanzee | NTLVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Monkey     | NTLVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Cow        | NTLVCFIVLKNRHMRTVTNMFILNLAISDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Horse      | NALVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Dog        | NALVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Guineapig  | NALVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNITCKMSG |
| Rat        | NTLVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Mouse      | NTLVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Elephant   | NALVCFIVLKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNATCKMSG |
| Opossum    | NSLVCFVVKNRHMRTVTNMFILNLAVSDLLVGFICMPTTLVDNLITGWPFDNITCKISG  |
|            | *:*** *:***.:***:*****:***** *****:***** ***:**              |

|            |  |
|------------|--|
| Human      | LVQGMVSASVFTLVIAIAVERFRCIVHPFREKLTLRKALVTIAVIWALALLIMCPSAVTL   |
| Chimpanzee | LVQGMVSASVFTLVIAIAVERFRCIVHPFREKLTLRKALVTIAVIWALALLIMCPSAVTL   |
| Monkey     | LVQGMVSASVFTLVIAIAVERFRCIVYHPFREKLTLRKALVTIAIWIWALALLIMCPSAVTL |
| Cow        | LVQGMVSASVFTLVIAIAVERFRCIVHPFREKLTLRKALVTIAVIWALALLIMCPSAITL   |





Elephant KEAYSERPSGLLRRRALTDVHRSDSGLPSESGPSSGARRPGRLPLRNGRVAHHGLTPERP  
Opossum RETYTERPRRLLCNRIFVEVQPTES-----GQSGDAQRMGRFPLRNGWVAHRRRLAPDGG

Human GCSHLPLTIPAWDI  
Chimpanzee GCSHLPLTIPAWDI  
Monkey GCSHLPLTIPAWDI  
Cow GCSHLPLTIPAWDI  
Horse -----L  
Dog GCGHLPVTIPAWDI  
Guineapig GCSHLPSTMPAWSI  
Rat GCNHMPLTIPAWNI  
Mouse GCNHMPLTIPAWNI  
Elephant GCSPMPLTTPAWDL  
Opossum GSARVPLRTPAWNI  
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