Figure S1.

A. Multiple alignment of P2X7 sequences from representative vertebrate species. Exon limits in human P2X7 are boxed and highlighted in red, the TM regions are highlighted in yellow and underlined. **Sequences: Mammals**: Human, Homo sapiens (hosa) ; Mouse, Mus musculus (mumu) ; Rat, Rattus norvegicus (rano). **Reptiles and birds** : Carolina anole, Anolis caroninensis (anca) ; Chicken, Gallus gallus (gaga). **Amphibians** : Clawed frog, Xenopus laevis (xela) ; Xenopus tropicalis (xetr1 : ENSXETG00000001030, xetr2 : ENSXETG00000001030) **Crossopterygians** : Coelacanth, Latimeria chalumnae (lach). **Bony fishes** : Spotted gar, Lepisosteus ocelatus (leoc); Rainbow trout Oncorhynchus mykiss (Onmy ; XP_021461359); Zebrafish, Danio rerio (dare) ; Barramundi perch, Lates calcarifer (laca); Makobe Island cichlid, Pundamilia nyererei, (puny); Sunfish, Mola mola (Momo).

B. **Multiple alignment of human P2X sequences.**

The P2X conserved motif (IPR001429 https://www.ebi.ac.uk/interpro/beta/entry/InterPro/IPR001429/) is underlined, and the exon limits highlighted in green. In the p2X7 sequence, the 2nd transmembrane region is highlighted in yellow.

A.

```
                |  exon1                                  |  exon2
hosa            MPACCSCSDVFQYETNKVTRIQSMNYGTIKWFFHVIIFSYVCFALVSDKLYQRKEPVISS 60
mumu            MPACCSWNDVLQYETNKVTRIQSTNYGTVKWVLHMIVFSYISFALVSDKLYQRKEPVISS 60
rano            ---MLPVRHLCSYNSAKVLHIHSTRLGALKNFFLLAICIYICFALMSDKLYQRKEPLISS 57
anca            MAACSSLKNICEYETNKVVRFQSIFYGSLKWAIHTVVFTYVSVVLIADKRYQKKDNVISS 60
gaga            MVAWGWMKDVFNYESPKLIRFPSVGLVCVKWFIYGVIAVYICYTLIVHKRYQEKEELTSS 60
xela            --MTLTLADCFDYSTKKEVRIQSVPLGILKQCITFGVIVFVCFSLITQKRYQKKDSIISS 58
xetr1           --MAPTFADCFDYSTKKEVRIQSVPLGVLKCCITFGVIVFVCFSLITQKSYQKKDSVISS 58
xetr2           --MAPTFADCFDYSTKKEIRIQSVPLGVLKFLITFGVILFVCFSLITQKSYQKKVSVISS 58
lach            MASVCNWKDCCGYETPRVVHIKSVQLGCLKWTLNGVIFIVIALMLFWNKYYQEYDSIISS 60
leoc            --MPCSLLNFCEYETNKLVRIKSIPIGSLKWSINGLILGFICIMLFWNKEYQEYDQVVSS 58
onmy            --MPCKLLNLCEYETHKLVRIQSARLGSLKWTFNGVILMFICIVMFWNKEYQEHDYVVSS 58
dare            --MPCVLLNLCEYDTQKLVKIKSVKLGSLKWTLNGVILMFICIMMLWNKEYQEYDFVVSS 58
laca            -MARCGLLGLCRYETNKLVRIQSVRLGSLKWILNATILLFICIMMLWNREYQEFDLVVSS 59
puny            -MPCCRLRALCQYETNKLVRIQSVRLGSLKWSLNGAILLFICIMMLWNRKYQEFDLVVSS 59
momo            -MACSWFRSLCQYETNKLVRIQSVRLGSMKWGLNGFILLFICIMMLWNREYQEFDLVVSS 59

                                                     |  exon3
hosa            VHTKVKGIAEVKEEIVENGVKKLVHSVFDTADYTFPLQ-G-NSFFVMTNFLKTEGQEQRL 118
mumu            VHTKVKGIAEVTENVTEGGVTKLGHSIFDTADYTFPLQ-G-NSFFVMTNYVKSEGQVQTL 118
rano            VHTKVKGVAEVTENVTEGGVTKLVHGIFDTADYTLPLQ-G-NSFFVMTNYLKSEGQEQKL 115
anca            VHTKVKGVSQT------------DMRIWDTAEYTIPMQ-GINSFFVVTNIIMTESQTQGV 107
gaga            VRVTLKGVAHV-------------DRIWDAAEYTIPTQ-TRDSFFVMTNIIRTENQIQKT 106
xela            VHTKVKGFADA------------HSRIWDTAEYTVPSP-GGDSFFVITNIVKTEGQMQSN 105
xetr1           VHTKVKGFANA------------YSRIWDTAEYTVPSP-GGDSFFVVTNIVKTENQRQDN 105
xetr2           VHTKVKGIADA------------YSRIWDTAEYTVPSP-GGDSFFVVTNIVKTEDQRQSN 105
lach            VTTKVKGVALTN-------NNELDERIWDVADYIFPAQ-GKNTFFVMTNMIITKNQQQRH 112
leoc            VTAKVKGVAVTN-------ITDVGEILWDAADYSGLSQ-GKNSFFVMTNAIVTNKQRQGK 110
onmy            VTAKVKGVAMTS-------LPDVGDIVWDVVDYSGPSQ-GKNSFFVVTNVIVTKNQRQGK 110
dare            VTTKVKGVAKIT-------LPEVGDVVWDVVDYSGPSQ-GKNSFFVATNAIVTKNQKQGN 110
laca            VTAKVKGVAQTH-------LTGIGDLVWDVVDYSGPSQVGKNSFFVVTNVIVTKNQKQGK 112
puny            VTTKVKGVAQAP-------LHEVGNMVWDEVDYSGPWK-GKNTFFVVTNAIVTQNQKQGK 111
momo            VTTKVKGVAQTH-------LPGIGDTVWDVVDYSGASQT-RNSFFVVTNVIVTKNQRQGK 111

                   |  exon4                 |  exon5                         |
hosa            CPEYPTRRTLCSSDRGCKKGWMDPQSKGIQTGRCVVYEGNQKTCEVSAWCPIEAVEEAPR 178
mumu            CPEYPRRGAQCSSDRRCKKGWMDPQSKGIQTGRCVPYDKTRKTCEVSAWCPTEEEKEAPR 178
rano            CPEYPSRGKQCHSDQGCIKGWMDPQSKGIQTGRCIPYDQKRKTCEIFAWCPAEEGKEAPR 175
anca            CPEFPIAKAICSTDRSCMKGGVDPLSNGIQTGKCVQYNATLKTCEVKAWCPVESMKSAPE 167
gaga            CPEYPTAKAICSSDKSCAKGIVDVHSNGVQTGKCVHYNITHKTCEIKAWCPVQGEERPPV 166
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xela          CSELPSQKTICSRDDICKKGLADPQSNGIQTGRCINFNNTLKTCEVSAWCPVESQ-TTPV 164
xetr1         CSELPSQKTICSRDDVCKKGLADPQSNGIQTGRCINFNSTLKTCEVSAWCPVESQ-TTPV 164
xetr2         CPELPRQKTICSRDDVCKKGLADPQSNGIQTGRCINFNSTLKTCEVSAWCPVESQ-TTPV 164
lach          CPEYPSPLTKCSSQRKCEKGRTALHSNGVQTGRCVNYDAFNKSCEVFAWCPVEAIRAAPV 172
leoc          CAEVPGSGKICYRDQDCTKGYSDQHSHGVQTGSCVKYDTTRKTCQVVAWCPIESKNKPPK 170
onmy          CPEVPPYGKVCWTDKDCVKGFWEQNSHGVQTGACVKFDVKQKTCEVSTWCPIETKKTPPK 170
dare          CAEILPNGKLCRTDKDCEKGFSDQHSHGVQTGACVKLEILKKTCEVTAWCPIENKKN-PR 169
laca          CPEAPRNGRLCRTDKDCEKGAWGQQNHGIQTGSCVKFDVLKKTCEIFAWCPVETKTNPPR 172
puny          CAQVPLKGRFCHTDKDCEKGAWDQQKHGIQTGSCVKFDLSKKTCEVSAWCPIETRSTPPR 171
momo          CPEVPQKGRWCRTDKDCEKGAWDQQSHGIQTGSCVKFDVLKKTCEVSAWCPVESKTNPPR 171

               exon 6                   |  exon7
hosa          PALLNSAENFTVLIKNNIDFPGHNYTTRNILPGLNI----TCTFHKTQNPQCPIFRLGDI 234
mumu          PALLRSAENFTVLIKNNIHFPGHNYTTRNILPTMNG----SCTFHKTWDPQCSIFRLGDI 234
rano          PALLRSAENFTVLIKNNIDFPGHNYTTRNILPGMNI----SCTFHKTWNPQCPIFRLGDI 231
anca          PAILRSAENFTVLIKNNIHFPKFNYTTRNISPEFNT----SCTYNERTASSCPIFRLGDI 223
gaga          PAVLRSSEDFTVFIKNNIHFPTFNYTVQNISPKLNT----SCKFNKVTAPLCPIFRLGDI 222
xela          PAVLESAENFTVLIKNNIHFAAFNFTKKNILPNYNV----SCIYDRVKAPLCPIFRLGDI 220
xetr1         PAVLESAENFTVLIKNNIHFAAFNFTKKNILPKYNV----SCIYDRVKAPLCPIFRLGDI 220
xetr2         PAVLESAENFTVLIKNNIHFAAFNFTKKNILPKYNV----SCIYDRVKAPLCPIFRLGDI 220
lach          PALLRGAEKFSVLIKNNIRFPEFNYTKRNILPHVNETYLKTCTFNRTRDPHCPVFILGNI 232
leoc          PALLESAENFTVLIKNNIRFPAFNYIKRNILPHMNDTYLKSCMFSRRMDPLCPILRLGDI 230
onmy          PALLASAENFTVLIKNNIRFPNFNFIRRNILPEMTDSYLKHCQFNRRTDPWCPIFRLGDI 230
dare          PALLAAAENFTVMIKNNIRFPAFNYIRRNILSEMKDTDFKGCIYHRYKNPYCPIFRLGDI 229
laca          PALLAAAENFTVLIKNNIRFPAFNYFRRNILPEMNDAYLKSCN--RANDSLCPIFRLGDM 230
puny          PALLAAAENFTVLIKNNIRFPAFNYIRRNILPEMNDAYLRNCH--RGNDSLCPIFRLGDI 229
momo          PALLAAAENFTVLIKNNIRFPAFNFIRRNILPEMTDAYLKSCH--RRNDSLCPIFRLGDI 229

                                                   | exon8
hosa          FRETGDNFSDVAI------------------------QGGIMGIEIYWDCNLDRWFHHCR 270
mumu          FQEAGENFTEVAV------------------------QGGIMGIEIYWDCNLDSWSHHCR 270
rano          FQEIGENFTEVAVQLLKLFLRELRQKAEKALDAVPWIRGGIMGIEIYWDCNLDSWSHRCQ 291
anca          LQAIGENFSEVAV------------------------QGGIMGIEINWDCNLDKWRHRCG 259
gaga          LQEAKENFSEMAV------------------------KGGIIAIEIKWDCDLDSWSYYCS 258
xela          LREAGENFSQVAV------------------------LGGVIGIEINWDCDLDPLRYKCE 256
xetr1         LREAGENFSQVAV------------------------LGGVIGIEINWDCDLDSLRYKCE 256
xetr2         LREAGENFSQVAV------------------------LGGVIGIEINWDCDLDSLRYKCE 256
lach          FQEAGENFSEVAI------------------------QGGVMGIQINWDCNLDNWNHKCV 268
leoc          VQEARENFSQMAV------------------------EGGVIGIQINWHCNLDRFFHKCL 266
onmy          VQEARENFSEMAV------------------------EGGVIGIQIKWDCNLDGFLRNCL 266
dare          VAEAKEKFSEMAV------------------------EGGVIGIQINWDCDLNRFFHSCL 265
laca          VRDAGEKFSEMAI------------------------EGGVIGILIKWDCNLDRLMQRCL 266
puny          VREAGERFSEMSV------------------------EGGVIGILIKWDCNLDRLMQRCL 265
momo          VQEAGDKFPEIAI------------------------EGGVISIQIKWDCNLDPLMWRCL 265

                                     |  exon 9                      | exon 10
hosa          PKYSFRRLDDKTTNVSLYPGYNFRYAKYYKEN-NVEKRTLIKVFGIRFDILVFGTGGKFD 329
mumu          PRYSFRRLDDKNTDESFVPGYNFRYAKYYKEN-NVEKRTLIKAFGIRFDILVFGTGGKFD 329
rano          PKYSFRRLDDKYTNESLFPGYNFRYAKYYKEN-GMEKRTLIKAFGVRFDILVFGTGGKFD 350
anca          PKYGFRRLDDKKTSEALYPGYNFRYARYYKQASGREERTLIKAYGIRFDILVFGMAGQFD 319
gaga          PEYSFRRLDDKTR--TQYPGFSIRFARHYKLPDGTEQRTLFKAYGIRFDVLVFGMGGQFK 316
xela          PHYGFRRLDDTVVDESLYPGLNFRFARYYKNAHGTETRTLIKAYGIRFDIQVYGTGGQFN 316
xetr1         PHYSFRRLNNKVVDERLYPGLNFRFARHYKTSDGKDTRTLIKAYGIRFDIQVYGTGGKFS 316
xetr2         PHYSFRRLDDKVVDERLYPGLNFRFARYYKTSDGKETRTLIKAYGIRFDIQVYGMGGKFN 316
lach          PEYTFRRLDNKNANETLSPGYNFRFAQFYKFPNGTEERTLIKAYGIRFDVMVFGTAGRFS 328
leoc          PEYSFRRLDEKESNKTLYPGLNFRFARY-NMNNGIEERMLFKAFGIRFDVMVFGKAGRFS 325
onmy          PKYSFRRLDEKESNRTLSPGLNLRFARY-QTEKGVGERTLFKAFGIRFDVMVFGKAGKFS 325
dare          PKYSFRRLDEKESNRTLYPGLNFRFARY-STVNGVEQRTLFKMYGIRFDVMVFGKAGKFS 324
laca          PRYSFRRLDEKESNRTLYPGINFRYAKY-NTVSGVEERTLYKVFGIRFDVMVFGQAGKFS 325
puny          PRYSFKRLDEKESNKTLYPGLNFRFAKY-NTVNGVEERTLYKAFGIRFDVMVFGQAGKFS 324
momo          PKYSFRRLDEKESNKTLYPGLNFRYAKY-NTVNGVEERTLYKVFGIRFDVMVFGQAGKFS 324

                              |  exon11     <  C-Cyst anchor >
hosa          IIQLVVYIGSTLSYFGLAAVFIDFLIDTYSSNCCRSHIYPWCKCCQPCVVNEYYYRKKCE 389
mumu          IIQLVVYIGSTLSYFGLATVCIDLLINTYSSAFCRSGVYPYCKCCEPCTVNEYYYRKKCE 389
rano          IIQLVVYIGSTLSYFGLATVCIDLIINTYASTCCRSRVYPSCKCCEPCAVNEYYYRKKCE 410
anca          FFELLVYIGSALSYFGLAQLTVDFLITSYSYSCCK-----------YDPVKEYYYKKKCE 368
gaga          LIELFTFIGSTIAYFGLAVTIIEMCFHLYNCSSC----------C-KIQVCENVIRKKYE 365
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xela       LLELALFIGSCLSYFGCASFAIDFIIGRYNSCCCN-----------AKSVLKYYDDRKYE 365
xetr1      LFELAIFIGSCLSYFGCASLAIDFIIGLYKPCCCN-----------AKSVLKYYNDRKYE 365
xetr2      LFELAIFIGSCLSYFGCASLAIDFIIGLYKPCCCN-----------AKSVLKYYDDRKYE 365
lach       FVALILYIGSTLSYYGLTALLIDLLITTYFCPSCP-----------SKEIKDYYLKKIYK 377
leoc       IIQLVIYIGSTLSYYALTTVFIDWFITTYLYPRCC-----------ARATKNNYSEKKYE 374
onmy       IIQLIIYIGSTLSYYALTTLFIDWLIGTS----CF-----------SKEARQNYSEKKVE 370
dare       IIQLIIYIGSTLSYYAITTIFLDWLIGTG----CY-----------SKEAKQNYTERKFE 369
laca       FIQLVIYIGSTLSYYALTSIVLDWLIGTS----CY-----------SAEVGQNYSEKKVE 370
puny       FIQLIIYIGSTLSYYALTTILIDWLIVTS----CY-----------SAEVGQNYSERKVE 369
momo       FIHLIIYIGSTLSYYALTTILIDWLIGTS----CY-----------SAEVGQNYSDRKVE 369



                 |  exon 12                             |  exon13
hosa       SIVEPKP-------TLKYVSFVDESHIRMVNQQLLGRSLQDVKGQEVPRPAMDFTDLS-R 441
mumu       SIMEPKP-------TLKYVSFVDEPHIRMVDQQLLGKSLQVVKGQEVPRPQMDFSDLS-R 441
rano       PIVEPKP-------TLKYVSFVDEPHIWMVDQQLLGKSLQDVKGQEVPRPQTDFLELS-R 462
anca       SVPGPRW-------TVLYVTYVDEPHIFMIDK-LLKTSLQNIKGKIVHRQTGNFKLGP-K 419
gaga       TVLMPEQ--------VILVSYVDKPHITLIKM-PLRTSLQNAEGSIFEDHPVKSYDP--R 414
xela       TIPGPSVSLAHLKAHLKFVSFVDKEDILMVDQ-KLKGSLQLASGPYIQRERFADTKA--- 421
xetr1      MVPGPA-S------QLKFVSFADEEDILMVDN-NLKDSLQFASGRYIQRERFAYTEA--- 414
xetr2      KVPGPTVS------QLKFVSFVDKEDILMVDI-NSRGSLQFASGQHIQRERFEYTEA--- 415
lach       SVDRPTS-------TLLYVSFVDEQNIFVVKG-PLKVRLQDAKSDIVLEHKVKL-----Q 424
leoc       TVEELNQ-------IPLCISFVDEDQIIVVKR-PLKKSLQETKPSSSQHRKPEHSFGRTR 426
onmy       SVQDRQQ-------CILCVSFVDENHIRVVKR-SHRKSLQQVKPMSVHPFKDDIRH--LS 420
dare       AVQDREE-------CFLCVSFVDEDNLRVVKK-SRKKRLQETKPLSLHQRKNELAS--MK 419
laca       SVQDKQK-------CVLCVSYVDENNIRLLKK-SLKKSLQDVKPMSVQPRKEDTGH--LR 420
puny       SIQDQVK-------CILCVSYIDENNLRLIKR-SQKKSLQVIKPMSVQPRKEDPGH--LR 419
momo       SVQDKEK-------CILCVSYVDVEDIHLVKR-SHKKSLQDIKPMSVQPRKDDTGH--LR 419

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hosa       LPLALH--DTPPI-PGQPEE----------------IQLLRKE-ATPRSRDSPVWCQCGS 481
mumu       LSLSLH--DSPLT-PGQSEE----------------IQLLHEE-VAPKSGDSPSWCQCGN 481
rano       LSLSLH--HSPPI-PGQPEE----------------MQLLQIE-AVPRSRDSPDWCQCGN 502
anca       LLLKPP--KEARS-PGAPHE----------------LQPLQNERVASPSRERPPWCSCRE 460
gaga       TC-CSH--KSNEKHGAAQSE----------------LRPLT---QSSSSTNCPKWCCCGR 452
xela       KC--------KDSHKQDENE----------------MRLIKG----RSAMLPPAWCKCNK 453
xetr1      NC--------KDSHKQNESE----------------MRLIKG----SSTTLPPAWCKCNK 446
xetr2      KC--------KDSHKKNQTE----------------MRLIKG----SSTTLPPAWCKCNK 447
lach       EHIALLQPNIEMVCV------------------------RRTCQSSSEHIIPPWCQCGN 459
leoc       VLVNLLQSPSRNA----------------------DTEIQEMQPPKGRGRSAPAWCQCGR 464
onmy       AMAGVLQKGHSI--------D------------K--------QPQALPRPSCPAWCLCGC 452
dare       TLLSVLQCGQSRSEPVQNGQSGGLIVDENLSSRHNGRQNPDTPLLETIQSSSPTWCQCGS 479
laca       AALSLLQPGVDVDHDAQPLLN------------H--------KPEPKPKVERPSWCKCDC 460
puny       AILCLLQPSDDTNDDVQPSLG------------K--------KTDPNAKPHRPAWCMCDS 459
momo       AVLSLLPPCAGSE----RPLI------------H--------KPSPNPKPHLPAWCKCNC 455

           ---- Ballast domain ----------------------------------------
hosa       CLPSQLPESHRCLEELCCRKKPGACITTSELFRKLVLSRHVLQFLLLYQEPLLALDVD-S 540
mumu       CLPSRLPEQRRALEELCCRRKPGRCITTSKLFHKLVLSRDTLQLLLLYQDPLLVLGEE-A 540
rano       CLPSQLPENRRALEELCCRRKPGQCITTSELFSKIVLSREALQLLLLYQEPLLALEGE-A 561
anca       CRPT-----ERYWEQLCCRRKDGDCIAGSALFDQLVLSRPRLEFILLYADPLLDLKAD-D 514
gaga       CQVA-----QKHHEQLCCRKKEGQCITTTYWFAQLVLSRDTLNKALLYEDPFLDLTGH-S 506
xela       CINT-----THLEEQLCCRLEEGECITDTKMFNSLVLNRESLEYAFQYDNPLSKTP---I 505
xetr1      CIDV-----TQPEEQLCCRLGEGQCITDTKIFNYLVLNKEALEYAFQYDNPLSKTP---E 498
xetr2      CIDV-----TQPEEQLCCRLGQGQCITDTEMFKYLVLNKEALEYAFQYDNPLSKTP---E 499
lach       CHES-----SGFQEMLCCRKNSGPCITTSTMFSQFALSQTTLEFILLYNDPLLDLHAN-R 513
leoc       CQPM-----PTPQEQLCCRRSKGQCITTSPAFPRLVLDRHTLESALLYREPLLELPQA-R 518
onmy       CLPS-----THPQEQLCCRMSRGRCITTSSLFEQLVLSRPLLEAVLLYREPLCELTEGEQ 507
dare       CRPA-----ETLQEQLCCRLKKGRCITSSPIFSSLIVSRSVLENALFFVDPLAELHEE-- 532
laca       CAPS-----SLLQEELCCRQSDGACITSSPLFERLVLHRPLLEAVLLYHDPLSAPADR-G 514
puny       CAPS-----SLPEEELCCRRTEGTCITSSPLFGQLVLRRSLLEAVLLYQDPLSPSVKK-L 513
momo       CAPS-----SVPHEEVCCRQSDGACITSSPLFEQLVLCRPLLEAVLLYRDPLSSPPDR-G 509

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hosa       TNSRLRHCAYRCYATWRFGSQ-DMADFAILPSCCRWRIRKEFPKSEGQYSGFKSPY---- 595
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mumu      TNSRLRHRAYRCYATWRFGSQ-DMADFAILPSCCRWRIRKEFPKTEGQYSGFKYPY---- 595
rano      INSKLRHCAYRSYATWRFVSQ-DMADFAILPSCCRWKIRKEFPKTQGQYSGFKYPY---- 616
anca      LNKRLRHCAYEQYIHWRFGE--ELEERAVLPSCCRWKIRDAFPSEKGEYTGFRSQR---- 568
gaga      SNSQLRRIAYKQYIHWRFGSF-ELEDRAIIPSCCRRLIRSTYPKENGNYTGFNLE----- 560
xela      SKEHLRYYAKQKYVEWRFGCRKYMLNFAVIPNCCKTAIETCNLQTEGP------------ 553
xetr1     S-EDLKCYAKQKYIEWRFRCRRYMLDFAVIPSCCKNAIETCNLQTQHPSGALYLPPTHGM 557
xetr2     S-EDLKCYAKQKYIEWRFGCRRYMLDFAVIPSCCKNAIETCNLQTQHPSGALYLPPTHGM 558
lach      DKDMLRHCAYQQYIHWRFGG-LEKENCAVIPSCCIWKIRETYPSLDGQYTGFRGC----- 567
leoc      CHGHLRHCAYSLYIEWRFGR-IQTGTFAAVPSCSVWRIRDEYPSEDGRYSGLCYENMVII 577
onmy      WTTAMRHCAYNQYITWRFGA-PPRESLPVIPSCSVWRIREEYSSQDGEYTGMRPRRTTSP 566
dare      --SQLRHGAYAQFIRWRFGDSTPRDALPVIPSCCIWRIRAEYPSPDGTYRGLRSFQVITS 590
laca      RTAALRHCAYRQYMSWRFGD-PPVDTQPAIPSCCVWRVREEYPSPDGQYSGFKPTRMVSM 573
puny      QTAALRHCAYREYISWRFGV-PPNDTHPAIPSCCVWRIRREYPSPDGQYSGFRPVKMTSM 572
momo      QTAALRHCAYGQYISWRFGV-TPKDSQPVIPSCCTRRVREEYPSPDGQYSGLRPARLASM 568


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hosa      -------- 595
mumu      -------- 595
rano      -------- 616
anca      -------- 568
gaga      -------- 560
xela      -------- 553
xetr1     C------- 558
xetr2     C------- 559
lach      -------- 567
leoc      SSNG---- 581
onmy      QSSPNT-- 572
dare      QTEVNR-- 596
laca      QACANGEV 581
puny      QACENGEL 580
momo      QACKNGEL 576
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B.

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hP2RX1     ------------MARRFQEELAAFLFEYDTPRMVLVRNKKVGVIFRLIQLVVLVYVIG--46
hP2RX2     MAAAQPKYPAGATARRLARGCWSALWDYETPKVIVVRNRRLGVLYRAVQLLILLYFVW--58
hP2RX3     ------------------MNCISDFFTYETTKSVVVKSWTIGIINRVVQLLIISYFVG--40
hP2RX4     -------------MAGCCAALAAFLFEYDTPRIVLIRSRKVGLMNRAVQLLILAYVIGCY47
hP2RX5     ------------MGQAGCKGLCLSLFDYKTEKYVIAKNKKVGLLYRLLQASILAYLVV--46
hP2RX6     ---MCPQLAGAGSMGSPGATTGWGLLDYKTEKYVMTRNWRVGALQRLLQFGIVVYVVG--55
hP2RX7     -------------MPACC--SCSDVFQYETNKVTRIQSMNYGTIKWFFHVIIFSYVC---42

hP2RX1     --------------WVFLYEKGYQTSSGLI-SSVSVKLKGLAVT-------QLPGLGPQV84
hP2RX2     --------------YVFIVQKSYQESETGPESSIITKVKGITTS------------EHKV92
hP2RX3     --------------WVFLHEKAYQVRDTAIESSVVTKVKGSGL------------YANRV74
hP2RX4     HPHLAEVEMESPRRWVFVWEKGYQETDSVV-SSVTTKVKGVAVT-------NTSKLGFRI99
hP2RX5     --------------WVFLIKKGYQDVDTSLQSAVITKVKGVAFT-------NTSDLGQRI85
hP2RX6     --------------WALLAKKGYQERDLEPQFSIITKLKGVSVT-------QIKELGNRL94
hP2RX7     --------------FALVSDKLYQRKEPVI-SSVHTKVKGIAEVKEEIVENGVKKLVHSV87

hP2RX1     WDVADYVFPAQGDNSFVVMTNFIVTPKQTQGYCAEHPEG--GICKEDSGCTPGKAKRKAQ142
hP2RX2     WDVEEYVKPPEGGSVFSIITRVEATHSQTQGTCPESIRVHNATCLSDADCVAGELDMLGN152
hP2RX3     MDVSDYVTPPQGTSVFVIITKMIVTENQMQGFCPESEEK--YRCVSDSQCGPER--LPGG130
hP2RX4     WDVADYVIPAQEENSLFVMTNVILTMNQTQGLCPEIPDAT-TVCKSDASCTAGSAGTHSN158
hP2RX5     WDVADYVIPAQGENVFFVVTNLIVTPNQRQNVCAENEGIPDGACSKDSDCHAGEAVTAGN145
hP2RX6     WDVADFVKPPQGENVFFLVTNFLVTPAQVQGRCPEHPSVPLANCWVDEDCPEGEGGTHSH154
hP2RX7     FDTADYTFPLQG-NSFFVMTNFLKTEGQEQRLCPEYPTRR-TLCSSDRGCKKGWMDPQSK145

hP2RX1     GIRTGKCVAF-NDTVKTCEIFGWCPVEVDDDIPRPALLREAENFTLFIKNSISFPRFKVN201
hP2RX2     GLRTGRCVPYYQGPSKTCEVFGWCPVEDGASVS-QFLGTMAPNFTILIKNSIHYPKFHFS211
hP2RX3     GILTGRCVNY-SSVLRTCEIQGWCPTEVDTV--ETPIMMEAENFTIFIKNSIRFPLFNFE187
hP2RX4     GVSTGRCVAF-NGSVKTCEVAAWCPVEDDTHVPQPAFLKAAENFTLLVKNNIWYPKFNFS217
hP2RX5     GVKTGRCLRRENLARGTCEIFAWCPLETS-SRPEEPFLKEAEDFTIFIKNHIRFPKFNFS204
hP2RX6     GVKTGQCVVF-NGTHRTCEIWSWCPVESG-VVPSRPLLAQAQNFTLFIKNTVTFSKFNFS212
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hP2RX7      GIQTGRCVVY-EGNQKTCEVSAWCPIEAVEEAPRPALLNSAENFTVLIKNNIDFPGHNYT204

hP2RX1      RRNLVEEVNAAHMKTCLFHKTLHPLCPVFQLGYVVQESGQNFSTLAEKGGVVGITIDWHC261
hP2RX2      KGNIADR-TDGYLKRCTFHEASDLYCPIFKLGFIVEKAGESFTELAHKGGVIGVIINWDC270
hP2RX3      KGNLLPNLTARDMKTCRFHPDKDPFCPILRVGDVVKFAGQDFAKLARTGGVLGIKIGWVC247
hP2RX4      KRNILPNITTTYLKSCIYDAKTDPFCPIFRLGKIVENAGHSFQDMAVEGGIMGIQVNWDC277
hP2RX5      N-NVMDVKDRSFLKSCHFGPK-NHYCPIFRLGSVIRWAGSDFQDIALEGGVIGINIEWNC262
hP2RX6      KSNALETWDPTYFKHCRYEPQFSPYCPVFRIGDLVAKAGGTFEDLALLGGSVGIRVHWDC272
hP2RX7      TRNILPGLNI----TCTFHKTQNPQCPIFRLGDIFRETGDNFSDVAIQGGIMGIEIYWDC260

hP2RX1      DLDWHVRHCRPIYEFHGLY---EEKNLSPGFNFRFARHFVEN-GTNYRHLFKVFGIRFDI317
hP2RX2      DLDLPASECNPKYSFRRLDPKHV--PASSGYNFRFAKYYKIN-GTTTRTLIKAYGIRIDV327
hP2RX3      DLDKAWDQCIPKYSFTRLDSVSEKSSVSPGYNFRFAKYYKMENGSEYRTLLKAFGIRFDV307
hP2RX4      NLDRAASLCLPRYSFRRLDTRDVEHNVSPGYNFRFAKYYRDLAGNEQRTLIKAYGIRFDI337
hP2RX5      DLDKAASECHPHYSFSRLDNKL-SKSVSSGYNFRFARYYRDAAGVEFRTLMKAYGIRFDV321
hP2RX6      DLDTGDSGCWPHYSFQLQE---------KSYNFRTATHWWEQPGVEARTLLKLYGIRFDI323
hP2RX7      NLDRWFHHCRPKYSFRRLDDKTTNVSLYPGYNFRYAKYYKEN-NVEKRTLIKVFGIRFDI319

hP2RX1      LVDGKAGKFDIIPTMTTIGSGIGIFGV--------------------------ATVLCDL
hP2RX2      IVHGQAGKFSLIPTIINLATALTSVGVVRNPLWGPSGCGGSTRPLHTGLCWPQGSFLCDW
hP2RX3      LVYGNAGKFNIIPTIISSVAAFTSVGV--------------------------GTVLCDI
hP2RX4      IVFGKAGKFDIIPTMINIGSGLALLGM--------------------------ATVLCDI
hP2RX5      MVNGK------------------------------------------------GAFFCDL
hP2RX6      LVTGQAGKFGLIPTAVTLGTGAAWLGV--------------------------VTFFCDL
hP2RX7      LVFGTGGKFDIIQLVVYIGSTLSYFGL--------------------------AAVFIDF
             <             transmembrane2 region


hP2RX1      LLLHILP------------------KRHYYKQKKFKYAEDMGPGAAERDLA-ATSSTLGL
hP2RX2      ILLTFMN------------------KNKVYSHKKFDKVCTPSHPSGSWPVT--LA-----
hP2RX3      ILLNFLK------------------GADQYKAKKFEEVNETTLKIAALTNP-VYPSDQTT
hP2RX4      IVLYCMK------------------KRLYYREKKYKYVEDYEQGLASELDQ---------
hP2RX5      VLIYLIK------------------KREFYRDKKYEEVRGLEDSSQEAEDE---ASGLGL
hP2RX6      LLLYVDR------------------EAHFYWRTKYEEAKAPKATANSVWRELALASQARL
hP2RX7      LIDTYSSNCCRSHIYPWCKCCQPCVVNEYYYRKKCESIVEPKPTLKYVSF--VDESHIRM
             >

hP2RX1      QENMRTS-----------------------------------------------------
hP2RX2      RVLGQAPPEPGHRSEDQHPSPPSGQEGQQGAECGPAFPPLRPCPISAPSEQMVDTPASEP
hP2RX3      AEKQSTDSGAFSIGH---------------------------------------------
hP2RX4      ------------------------------------------------------------
hP2RX5      SEQLTSGPGLLGMPEQQELQEPPEAKRGSSSQKGNGSVCPQLLEPHRLRTPSASPLHQE
hP2RX6      AECLRRSSAPAPTATAAGSQTQTPGWPCPSSDTHLPTHSGSL-----------------
hP2RX7      VNQQLLGRSLQDVKGQEVPRPAMDFTDLSRLPLALHDTPPIPGQPEEIQLLRKEATPRS

hP2RX1      ------------------------------------------------------------
hP2RX2      PAQASTPTDPKGLAQL--------------------------------------------
hP2RX3      ------------------------------------------------------------
hP2RX4      ------------------------------------------------------------
hP2RX5      ------------------------------------------------------------
hP2RX6      ------------------------------------------------------------
hP2RX7      RDSPVWCQCGSCLPSQLPESHRCLEELCCRKKPGACITTSELFRKLVLSRHVLQFLLLYQ

hP2RX7      EPLLALDVDSTNSRLRHCAYRCYATWRFGSQDMADFAILPSCCRWRIRKEFPKSEGQYSG

hP2RX7      FKSPY   595
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