

AaegGPCRAL1 MTSSITL 6
 CquiGPCRAL1 MSSTITL 6
 AgamGPCRAL1 MALSTITL 6
 DmelCG32843 MSDQI GNPNTATFSGSGSGGTN - VASIAES 29
 PcorGPCRAL1 0
 NviGPCRAL1 0
 HsapCALCRL MEKKKCTLYFVLLPFFMVTAELEESP...-EDS-IQ 33
 RnorCALCRL MMDKKCTLCFLFLLLNALIAAESEEG...-ANC-ID 33
 GgalCALCRL MTKNW TFLFFFSVTLFATAI PSEGHQNMITESS-GQ 37
 XlaeCALCRL METLQMLLSRSALFKYIIIFLI MINTRGVVASQEQEAKTS - VPEE-RQ 48
 DrerCALCRLA MTASCWTICLFLGSVTEFIVLASPEVNESQQQHPQNVYHD 41
 PolICGRPR MDV/RWTFLLLSFSDQLVASSAEAEH...-QENAKH 34
 CgCTR MYM AVLTLTPM VSYTWADLDI YRGLCRSHLYGHENVQDFRQYSCAWCFRFFVHLKYRPLVNSTGTPVYVI FHNGGRVRFESMDFRNQSVKAVCDV 100

AaegGPCRAL1 TDAIDSEFDORKLQCLEMLNATTEFTTTRS----GPFGRGTWOGWLCMPDTAAGSALLPQDFMDGDFDRFRAKQDDEGEMFRHPLNTRWTSNYITL 101
 CquiGPCRAL1 TEASVDVSELKRLKLEALKNESVESASDSD---QIFGRGTWOGWLCMPDTAAGRIANAPQPEVVFQDITTRFAKADDEGEMFRHPLNTRWTSNYITL 101
 AgamGPCRAL1 TDAVDDEAKQKRLKLELNETVDTTISG---GLFGRGTWOGWLCMPDTAAGSALLPQDFMDGDFDRFRAKQDDEGEMFRHPLNTRWTSNYITL 100
 DmelCG32843 VAESGPDFDALRAACETRLNASGQLAGSGGPGAEGTCHAGTFDGLWLCMPDTAVGTSANELCPDFITGDFDRYAKKQDDEGEMFRHPLNTRWTSNYITL 129
 PcorGPCRAL1 MPANFVLCG...LYCEGTFDGSWCMPTDPAGITANVSPGCVTGEDD...KQDSSKGSIVKQDDEGEMFRHPLNTRWTSNYITL 68
 NviGPCRAL1 MALR...DSWSVATE...PYCPAIFDGSWCMPTDPAGITANVSPGCVTGEDD...KQDSSKGSIVKQDDEGEMFRHPLNTRWTSNYITL 79
 HsapCALCRL LGVITRNKI MTAQYCYCYCKI MDP-PIQQAE...GVYCNRTWOGWLCVNDVAAAGHESMOCQDVFQDFDPSEKVIKIQDQDGNMFRHPLNTRWTSNYITL 126
 RnorCALCRL LGVITRNKI MTAQYCYCYCKI MDP-PIQQAE...GVYCNRTWOGWLCVNDVAAAGHESMOCQDVFQDFDPSEKVIKIQDQDGNMFRHPLNTRWTSNYITL 126
 GgalCALCRL LGVITRNKI MTAQYCYCYCKI MDP-PIHRKE...GPYCNRTWOGWLCVSDVAAAGVSVCHQDVFQDFDPSEKVIKIQDSSGNMFRHPLNTRWTSNYITL 130
 XlaeCALCRL VGVITONKI MTAQYCYCYCKI MDP-PAHGKE...GQF CNRTWOGWLCVSDVAAAGI I SECRQDVFQDFDPSEKVIKIQEGKNGMFRHPLNTRWTSNYITL 141
 DrerCALCRLA IGVITRNKI MTAQYCYCYCKI MDP-NSQDRR...GPV CNRTWOGWLCVDDTEAGI TSECHQDVFQDFDPSEKVIKIQEGKNGMFRHPLNTRWTSNYITL 134
 PolICGRPR GI HSNQI...RAQYCF...MRESHSSKAK...GLTANATWOGWLCVSRITKAGRTKCNQDVFQDFDPSEKVIKIQEGKNGMFRHPLNTRWTSNYITL 128
 CgCTR LITSDECHQWTSCCSAERCCQRQLSVKKG...TNSSCGRVWOGWLCVDAEPGTRSRVGSQPLMPFFITSRCAFRTQOTNGEVI TR-----IDVNP 189

TM1 TM2

AaegGPCRAL1 CVN--DKLWMEQVRTI YETGYSI SLIALI LSLG LSYFRSLKCAR...ITLHMNLFASFAISNNTWLLWYRMVLAD-----PEVUKHNGASQITLH 190
 CquiGPCRAL1 CVN--IDPFTWSROI NTI YETGYSI SLIALI LSLG LSYFRSLKCAR...ITLHMNLFASFAISNNTWLLWYRMVLAD-----PEVUSHNGSPQITLH 190
 AgamGPCRAL1 CVN--IDDFWVRKQVNL I YETGYAI SLIALI LSLG LSYFRSLKCAR...ITLHMNLFVSAQANNSWLLWYRLVLTQ-----LDLTKESGAGQITLH 189
 DmelCG32843 CVN--LEDLNWRHTVNL I SEVGYGSLAL ILSUA LSYFRSLKCAR...ITLHMNLFASFAANNSWLLWYLLMPPN-----SELLHQSPROVALITL 218
 PcorGPCRAL1 CVD--QEDLSAR...TI NOI YETGYLI SLIALIASUA IYTFKSLRCSR...ITLHLLVSVFAVNNALWLLWYRFILGD-----PNVIKENGVAQRI FHV 157
 NviGPCRAL1 CVN--LVBL SWOQCLNLYETGYVITSLVALLVSLGLTYFRSLKCAR...ITLHMNLFASFAANNSWLLWYGSVAVN-----AQQLNNGMCRFLFHV 168
 HsapCALCRL CNVNTHEKVTALNLYLTI LGHLSI ASLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITILHTAVANN-----CALVATNPVSKVVSQF 217
 RnorCALCRL CNMSTHEKVTALNLYLTI LGHLSI ASLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITILHTAVANN-----CALVATNPVSKVVSQF 217
 GgalCALCRL CNI YTHEKVTALNLYLTI LGHLSI TSLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITILHTAVANN-----CKLVATNPVSKVAMF 221
 XlaeCALCRL CNTFTHEKVTALNLYLTI LGHLSI ASLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITILHTAVANN-----CALVATNPVSKVVSQF 232
 DrerCALCRLA CNLHTTGRRTAMNLYLTI LGHLSI TSLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITILHTAVANN-----CBVQONPVSKVVSQF 225
 PolICGRPR CORNTTHNEMVAMSHFVLMGQGLSLVSLLSLG FFFYKSLSCOR...ITLHKNLFFSFVNSIVITLVMNNTLKDCK-----PGHNNDSVSKLVI 219
 CgCTR CIK-----KLELETTLFI GLGCSI ASLVALVPALELKYRSLRCHRRLHNLSELLKEVMDILVMDLTYDKVSTTTFVETTMONGVQGLSSE 284

TM3 TM4 TM5

AaegGPCRAL1 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--ESVYDNVFKA PVGIM SMLNLLVFCNII 289
 CquiGPCRAL1 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--ESVYDNVFKA PVGIM SMLNLLVFCNII 289
 AgamGPCRAL1 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--DSFNKVFVPGVIM SMLNLLVFCNII 288
 DmelCG32843 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--CTNYQNLVMPVGI SMLNLLVFCNII 317
 PcorGPCRAL1 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--ETKYTNVNLVVPVIM SMLNLLVFCNII 255
 NviGPCRAL1 VLHYFLI TNYAMMLCEGFYLHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--BGNMVMVLLI YPVVCSITLNLVFCNII 267
 HsapCALCRL LHLYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 313
 RnorCALCRL LHLYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 313
 GgalCALCRL LYQYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 317
 XlaeCALCRL LHLYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 328
 DrerCALCRLA LHLYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 321
 PolICGRPR LHYL MGNFYFWM LCEG IYHTLVLSAFVSEKKLVNVLVGLWTTGPIVIMAYGFLRCYAGTPEDTI ECWMN--NDNCWSSDTHLHYI HGPI CAALLVNLFFLLNVL 314
 CgCTR LKI YKRCQTYTVMFCGFYLRMSNAHSP- RSLKVMYFVWAAAPLSSSTLYGI LRGVNLN--NESCAWTSPTSLHYI HGPI CAALLVNLFFLLNVL 379

TM6 TM7

AaegGPCRAL1 RVVLLKLRAPAGPQG-TGPSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 372
 CquiGPCRAL1 RVVLLKMRAPAGPQG-SGPSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 372
 AgamGPCRAL1 RVVLLKLRAPAGPQG-AGPSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 371
 DmelCG32843 RVVLLKLRAPASI QSGGPSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 401
 PcorGPCRAL1 RVVMTLKRAGPHVCS-QRPSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 354
 NviGPCRAL1 RVVMTLKRAGPAIS-Q-PSRSRTI LCAFRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 349
 HsapCALCRL RVVITKLRVTHQAES-----NLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 396
 RnorCALCRL RVVITKLRVTHQAES-----NLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 396
 GgalCALCRL RVVITKLRVTHQAES-----NLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 400
 XlaeCALCRL RVVITKLRVTHQAES-----NLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 411
 DrerCALCRLA RVVITKLRVTHQAES-----SLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 404
 PolICGRPR RVVITKLRVTHQAES-----SLYMKAVRATLLVPLLIGQYI LTPFRDPGHPYERTYELISAFTASFOGLFVAVLFOFFNGEV----- 397
 CgCTR RI LLLQMQTHNEPQG-----NFRRAVKAFTLILPLFGHRRFFTLRYRPI SQEGHEYEKVSITISEHOGFLVSMFCFLNGEVI SNI KR----- 463

AaegGPCRAL1 --IAQVKKWR-TVFL--RITRNSYTAQVSEI RSE--P----PI PGEKVK 412
 CquiGPCRAL1 --IAQVKKWR-TVFL--RITRNSYTAQVSVK-----F----LI KDARRO 410
 AgamGPCRAL1 --IAQVKKWR-TVFL--RITRNSYTAQVSVST-----LTVLRV 406
 DmelCG32843 --IAQVKKWR-MMCFNRPRTNSYTAQVSEVRCG--P----PI PGEKVK 443
 PcorGPCRAL1 AVISQIKRKYQ-FAI F--RNRANSCTATVSRFRST--P----PIMAGEKVK 396
 NviGPCRAL1 --IAQVKKWEGTAAFA--RKRANSCTATVSRFRST--AG--PIMAGEKVK 391
 HsapCALCRL RNNVQYKI QFENGSSNSSEALRSASVITVSTI SDGPEY--SHDCPS EHLNKGSI HDI ENVLLKPENLYN 461
 RnorCALCRL RNNVQYKI QFENGSSNSSDALRSASVITVSTI SDVQCY--SHDCPT EHLNKGSI HDI ENVALKPEKMYDLVM 464
 GgalCALCRL RHNWQYKI QFESHSSSDAMRTVSVITVSTI SDGPEYNNHDOCTS EHLNKGYHDMT 457
 XlaeCALCRL RHNWQYKI QFESAHSEGRSASVITVSSI SEI QCTTYTHOY-SEHSGNKNCHDMENVFFKTEKQYM 476
 DrerCALCRLA RHNWQYRI QFESTITSDALRSASVITVASSI TEVQCC-YSDGHT EHLNKNYHFDNAI I KPNPFA 470
 PolICGRPR RHWQORNI QFESTITANADFFRSASVITVASSI TEVHRC-YSEHTEHLNKSQYSPDFR----SDSPFV 459
 CgCTR SI RHGRSLSLSTSKRNLQTDQQTLSI RSEYDVGNKEDQYKSLI VPTGKDEMLKEKSTNGSLLNHNGPHGET 536

Figure S2. Amino acid sequence alignment of calcitonin receptor-like receptors. *Aaeg*GPRCAL1 was aligned with those of other arthropods, a mollusk, and vertebrates. The *A. aegypti* GPRCAL1(AEU12191)¹ sequence is 79% identical to *C. quinquefasciatus* GPRCAL1 (CPIJ014419-PA)², 75% identical to *A. gambiae* GPRCAL1 (AGAP009770-PA)³, 64% to sequenced *D. melanogaster* GPRCAL1 (AAN16138)⁴, 55% to *P. humanus corporis* GPRCAL1 (PHUM428070-PA)⁵, 59% to *Nasonia vitripennis* GPRCAL1 (XP_001601649)⁶, 33% to human CALCLR (NP_005786)⁷, 33% to rat *R. norvegicus* CALCRL (NP_036849)⁸, 32% to chicken *G. gallus* CALCRL (NP_001157122)⁹, 32% to frog *X. laevis* CALCRL (NP_001080206)¹⁰, 34% to *D. rerio* CALCRLA (NP_001004010)¹¹, 31% to *P. olivaceus* CGRPR (BAA92817)¹² and 27% to *C. gigas* CTR (CAD82836)¹³. Accession numbers in parenthesis are of putative (2-3 and 5-6) or cloned translated sequences (1, 4 and 7-13) from GenBank or VectorBase. Predicted transmembrane domains (TM) of *Aaeg*GPRCAL1 are indicated by a line above the sequences. Blastp analysis of the *Anopheles* genome with the *Aedes* receptor sequence identified the prediction of the *AgamGPRcal1* ORF, permitting the localization of intron-exon boundaries in the genome by eye gazing because the gene organization is also conserved in *Anopheles*. **Conserved residues between *Aaeg*GPRCAL1 and hCALCRL:** Residues in *Aaeg*GPRCAL1 with demonstrated functional significance in hCALCRL are as follows: receptor coupling with Gs (R146), receptor cell-surface expression (Y209, L210, H211, E371, and V372) [1,2], structural stabilization (P236, P273, P323 and P333) [3], GPCR kinases phosphorylation (S391, S398, T382, T387, T389 and T395) [4]. In hCALCRL, aspartate (D69) in the N-terminus and leucine (L351) in TM6 are important residues associated with RAMP1; these corresponding residues are conserved in *Aaeg*GPRCAL1 (D45 and L331) and *Dmel*GPRCAL1 (D73 and L360) [5,6].

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