

**Kokumi taste perception is functional in a model carnivore, the domestic cat (*Felis catus*) – Supplementary Data**

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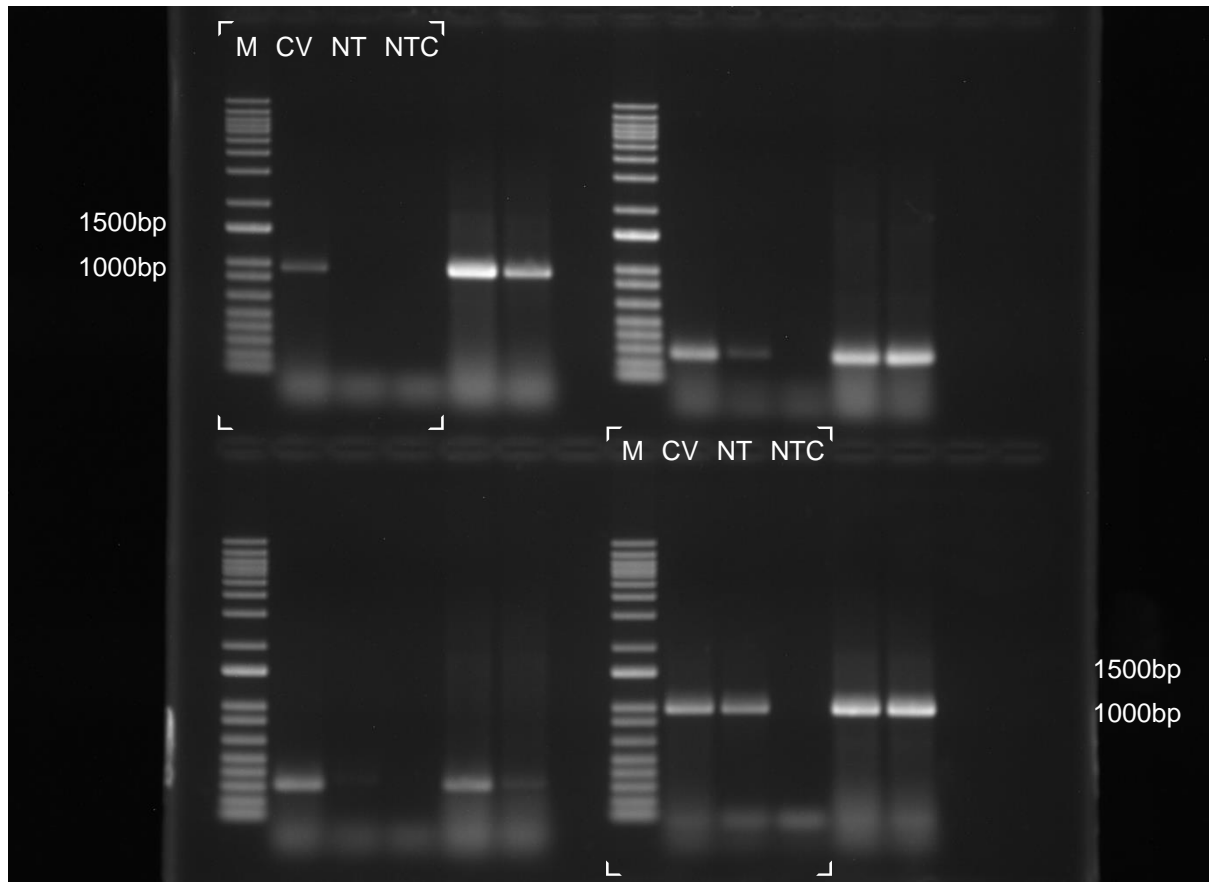
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*CaSR expression in cat circumvallate papillae RT-PCR gels*



**Supplementary Figure 1:** Full gel corresponding to Figure 1 in the manuscript, with *CaSR* expression (white brackets upper left-hand corner) and *GAPDH* expression (white brackets lower right-hand corner). Other samples shown are not relevant to the work presented in the paper. CV- circumvallate papilla, NT-non-taste epithelial tissue, NTC- no-template controls, M - molecular size marker.



# Mammalian CaSR Sequence alignment

CLUSTAL O (1.2.4) multiple sequence alignment

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QQQSQQQPRCKQKQVIFGSGTVTFSLFDEPQKNAMA-----HRNSTHONSLEAOKS- 1013

ENSCANP00000040262\_Capa/1-1088 QQQSQQQPRCKQKQVIFGSGVTVTFSLSFDEPQKNAMA-----HRNSTHQNSLEAQKS- 1013  
ENSPTEP00000016080\_Ptep/1-1088 QQQSQQQPRCKQKQVIFGSGVTVTFSLSFDEPQKNAMA-----HRNSTHQNSLEAQKS- 1013  
ENSRBIP00000006831\_Rbie/1-1078 QQQSQQQPRCKQKQVIFGSGVTVTFSLSFDEPQKNAMA-----HRNSTHQNSLEAQKS- 1003  
ENSRROP00000007818\_Rrox/1-1088 QQQSQQQPRCKQKQVIFGSGVTVTFSLSFDEPQKNAMA-----HRNSTHQNSLEAQKS- 1013  
ENSOGAP00000002850\_Ogar/1-1077 QPPPQQPQRCKQKQVIFGSGVTVTFSLSFDEPQKNAPA-----HRNSAHQNSLEAQKS- 1002  
ENSMICP00000005654\_Mmur/1-1075 LQQPQQPQRCKQKQVIFGSGVTVTFSLSFDEPQKNATA-----HRNSTPRNSLEAQKS- 1000  
ENSPCOP00000009624\_Pcoq/1-1076 QQQPQQPQRCKQKQVIFGSGVTVTFSLSFDEPQKNATA-----HRNSTPQNSLEAQKT- 1001  
ENSPSPM00000007909\_Psim/1-1084 TLQPQQPQRCKQKQVIFGSGVTVTFSLSFDEPQKNATA-----HRNSTPQNSLEAQKG- 1009

ENSMEUP00000013310\_Neug/1-956 --GDSLRRQAL----- 956  
ENSTBEP00000002487\_Tbel/1-914 --SDALTRHQALLPQCENDESEPATQ-----DTGLQGP-VGGDHPPEME---DPEEMS 887  
ENSPCAP00000000755\_Pcap/1-1085 --NEMLTRHQALLPQCETEPGSELTRQ-----ETDLQGS-PGGDYQVEME---GPEKRA 1059  
ENSCHOP00000011907\_Chof/1-954 ----- 954  
ENSVAP00000001982\_Vpac/1-1087 --NDALTRHQALLPQCCEADSELSTQ-----ETGLQGP-VGRDHQPEME---DPEEMS 1060  
ENSEEUP00000009670\_Eeur/1-946 --GDPLPRHQALLPQCCTDSDPIFP-----ETGLQGP-VGGDCQAEQ---DPEEMS 919  
ENSOANP00000001352\_Oana/1-1083 GGGDGPVRPRRALLPLRDGNPDSGSDPGS--REACLPE-----SGGEEPRDPEEGP 1054  
ENSOPRP00000000261\_Opri/1-1082 --NETLTRHQALLPQCGETEAEALMMGQ-----EESMHG-PVGGDCRDPDT---EAEPEEMS 1055  
ENSJJAP00000004721\_Jjac/1-1084 --NDTLRRHQALLPQCCTDSETTIP-----DAGLQRPIMVGDHQPMPQLEEEEEEMS 1051  
ENSPCIP000000034747\_Pcin/1-1018 --GDSLARRQALLPQSSSEAGSLGSG-----VLGSEE-SVVGDSQPDT--QIP-EEMS 991  
ENSMODP000000022810\_Mdom/1-1069 --GDSLARRQALLPQSSSEAGSLGSG-----DSGSNE-SVVGDSQSES---QIP-EEMS 1042  
ENSVURP00010007344\_Vurs/1-1070 --GDSLARRQALLPQSSSEAGSLGSG-----VLGSNE-SVVGDSQPET--QIP-EEMS 1043  
ENSSHAP000000014890\_Shar/1-1072 --GDSLARRQALLPQSSSEAGSLDLSG-----DLSNE-SVVGDSQPET--QIP-EEMS 1045  
ENSMAUP00000005394\_Maur/1-954 --SDTVTTSFHLRLCYSLDY-DPQPHI-----KRLV 940  
ENSOCUP000000025672\_Ocun/1-1063 --NDTLTRHQALLPQRGETDSETDGPDRPARAYGWGP-PARD-----QG 1062  
ENSPVAP000000011981\_Pvam/1-1085 --NDMTTRHQALLPQCGETDSELSTQ-----ETGLQG-PVGGDCQPET---EDP-EELS 1058  
ENSETEP00000011160\_Etel/1-1024 --SETLVRHQALLPQCAEMGSELAVP-----ETDLQG-SAGDRQPEM---EDP-EELT 997  
ENSFADP00000010532\_Fdam/1-1108 --SDGLSRHQALLPQYRDTDAGLATQ-----ETGLQG-LVAGDHQPEV---EE-TEEGS 1080  
ENSODEP000000013257\_Odeg/1-1070 --NDSLTKHQALLPQCCTDSDSLSTQ-----DTGLQG-LGAGDHQPEM---EAP-EEMA 1051  
ENSHGLP00000002019\_Hgfe/1-1108 --NDGLSRHQALLPQYRDTDGLTQ-----ETGQQG-MVAGDHQPEL---EDP-EEMS 1081  
ENSLAP000000021334\_Clan/1-1114 --NDGLTRHQALLPQGRDTSDLTQ-----ETGMQG-SVAGDHQPEV---EDP-EEMS 1087  
ENSCAPP000000014352\_Cape/1-1068 --NDGLTRHQ-----EKG-----QFEM---EDPEEMS 1041  
ENSCPOP00000011705\_Cpor/1-1071 --NDGLTRHQ-----LQCRDADSDPSTQ-----EKG-----QFEM---EDPEEMS 1044  
ENSSARP00000006151\_Sara/1-1085 --NDALTRHQALLPQGEADLELSPQ-----EAGLPG-PV-GGEHQPE---MEGREEMS 1058  
ENSLAFP000000018459\_Lafr/1-1090 --NEALTKHQALLPQCCTEPGSELTMQ-----DTDLQG-SA-GGDHQP-----TEGPEERA 1063  
ENSDNOP000000011819\_Dnov/1-1075 --NDTLGRQPAPLPQCCEAGSELAVQ-----ETGSPG-PV-AGDHQPE---TEDPEEMS 1048  
ENSSSCP000000041077\_Sscr/1-1089 --NDALTRHQALLPQCCEADAELTAQ-----ETGLQG-SV-GGDHHP---MEDPEEMS 1062  
ENSTTRP00000001326\_Ttrur/1-1091 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHQP---MEDPEEMS 1064  
ENSBEBP00000002858\_Bbbi/1-1068 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1041  
ENSOARP000000021602\_Oari/1-1032 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1005  
ENSHIP000000033853\_Chir/1-1085 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-SEDHQP---MEDPEEMS 1058  
ENSBTAP000000059078\_Btau/1-1085 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1058  
ENSBIXP000000038534\_Bthy/1-1085 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1058  
ENSBMUP000000019115\_Bmut/1-1081 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1054  
ENSBIXP00000005030570\_Bihy/1-1085 --NDALTKHQALLPQCGETDSELSTQ-----ETGLQG-PV-GEDHQP---MEDPEEMS 1058  
ENSMUGP000000006365\_Mung/1-1080 --NDALSRHQALLPQCADTDSEMTIQ-----ETGLQG-PM-LGDHQP---MESPEEMS 1053  
ENSRNOP000000069629\_Rnor/1-1079 --NDTLGRHQALLPQCADSDSEMTIQ-----ETGLQG-PM-VGDHQP---MESPEEMS 1052  
MGP\_PahariEij\_P0043347\_Mpah/1-1003 --NDALNRHQALLPQCAEADSEMTIQ-----ETGLQG-PM-VGDHQP---MESADEMS 976  
MGP\_SPRETEiJ\_P0043347\_Mspr/1-1079 --NDTLNRHQALLPQCAEADSEMTIQ-----ETGLQG-PM-VGDHQP---IESPDEMS 1052  
ENSMUP000000069080\_Mmus/1-1079 --NDTLNRHQALLPQCAEADSEMTIQ-----ETGLQG-PM-VGDHQP---IESPDEMS 1052  
ENSMOCP000000010340\_Moch/1-1076 --NDTLRRHQALLPQCADTDSEMTQ-----ETGLQG-PM-VGDHQP---MESTEMS 1049  
ENSPMP000000029995\_Pmba/1-1076 --NDTLGRHQALLPQCADTDSEMTIQ-----E---TG-PM-VGDHQP---MESPEEMS 1049  
ENSCGRP00015024036\_Cgpi/1-1081 --NDTLRRHQALLPQCADTDSEMTIQ-----ETGLQG-PM-VGDHQP---MESPEEMS 1054  
ENSCGRP000000116053\_Cgch/1-1081 --NDTLRRHQALLPQCADTDSEMTIQ-----ETGLQG-PM-VGDHQP---MESPEEMS 1054  
ENSCGRP000000017369\_Cgcr/1-1081 --NDTLRRHQALLPQCADTDSEMTIQ-----ETGLQG-PM-VGDHQP---MESPEEMS 1054  
ENSDORP00000002959\_Dord/1-1078 --HEALTRHQALLPLPCEDTSELSTQ-----EPGKGG-GFAGGDCQPE---MEDPEEMS 1051  
ENSTSP00000002643\_Csyr/1-1015 --NDTLRRHQALLPQCGETDSELSTQ-----DPGLQG-PV-GGDHQP---MEDPEEMS 988  
ENSMLUP000000008249\_Mluc/1-1075 --NDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHQP---AEDPEEMS 1048  
ENSECAP000000022285\_Ecab/1-1084 --NDTLTRHQALLPQRGEIDSELSTQ-----ETGLQG-PA-VGDRQPE---RRNPEEMS 1057  
ENSEASP00000002676\_Eaas/1-1094 --NDTLTRHQALLPQRGEIDSELSTQ-----ETGLQG-PA-VGDRQPE---RRNPEEMS 1067  
ENSCAFP000000017381\_Cfam/1-1075 --PEPPARPQALLPQGGDDAELPAQ-----EPGLQG-PG-GADRRPE---MRDPEELS 1048  
ENSCAFP000000020007154\_Cldi/1-1075 --PEPPARPQALLPQGGDDAELPAQ-----EPGLQG-PG-GADRRPE---MRDPEELS 1048  
ENSVVUP000000030826\_Vvul/1-1075 --PEPPARPQALLPQGGDDAELPAQ-----EPGLQG-PG-GADRRPE---MRDPEELS 1048  
ENSFACAP000000008080\_Fvac/1-1081 --NETLTRHQALLPQCGETDSELSTQ-----ERGLQG-PV-DGDFRPE---MEDPEEMS 1054  
ENSPRP000000023800\_Ppar/1-1081 --NETLTRHQALLPQCGETDSELSTQ-----ERGLQG-PV-DGDFRPE---MEDPEEMS 1054  
ENSPPTIP00000015042\_Ptal/1-1081 --NETLTRHQALLPQCGETDSELSTQ-----ERGLQG-PV-DGDFRPE---MEDPEEMS 1054  
ENSMUP000000004759\_Mpfu/1-1082 --NETLSRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---TEDPEEMS 1055  
ENSNVIP00000018564\_Nvis/1-1092 --NETLSRHQALLPQCGETDSELSTQ-----EAGLQG-PG-GGDHRPE---TEDPEEMS 1065  
ENSUMAP000000035085\_Umar/1-1071 ----TLTRHQALLPQCREIDSLTQ-----ETGLQG-PV-GGDHRPE---TEDPEEMS 1044  
ENSUAMP000000035930\_Uame/1-1079 --NETLTRHQALLPQCCEIDSLTQ-----ETGLQG-PV-GGDHRPE---TEDPEEMS 1052  
ENSAMEP00000015060\_Amel/1-1089 --NETLTRHQALLPQCCEIDSLTQ-----ETGLQG-PV-GGDHRPE---TEDPEEMS 1062  
ENSSDAP000000007437\_Sdau/1-1079 --SDALTRHQALLPQCGETDSELSTQ-----ETGLQG-PM-AGAHQPE---MEDPEEMS 1052  
ENSSTOP000000003945\_Itri/1-1070 --SDALTRHQALLPQCGETDSELSTQ-----ETGLQG-PM-AGAHQPE---MEDPEEMS 1043  
ENSMMP00000015298\_Mmma/1-1083 --SDALTRHQALLPQCGETDSELSTQ-----ETGLQG-PM-AGAHQPE---MEDPEEMS 1056  
ENSUPAP00010025947\_Upar/1-1086 --SDALTRHQALLPQCGETDSELSTQ-----ETGLQG-PM-AGAHQPE---MEDPEEMS 1059  
ENSSBOP000000036416\_Sbbo/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-SV-GADHRPE---VEDPEELS 1051  
ENSANAP000000028404\_Anan/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSCCAP000000024327\_Ccap/1-1077 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1050  
ENSCJAP000000062854\_Cjac/1-1089 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1062  
ENSNLEP000000003336\_Nleu/1-1088 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1061  
ENSPYP000000015087\_Pabe/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSP000000420194\_Hsap/1-1088 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1061  
ENSGGQP000000020287\_Ggor/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSPFAP000000026371\_Ppan/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSPTRP000000043346\_Ptro/1-1078 --SDTLTRHQALLPQCGETDSELSTQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSCSAP000000003635\_Csab/1-882 --SDTLTRHQALLPQCCEADSLSVQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 855  
ENSMMP000000061002\_Mmul/1-1078 --SDTLARHQALLPQCCEADSLSVQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1051  
ENSPANP0000000004316\_Panu/1-1081 --SDTLARHQALLPQCCEADSLSVQ-----ETGLQG-PV-GGDHRPE---VEDPEELS 1054

ENSCATP00000028615\_Caty/1-1078 --SDTLARHQALLPQCGEADSDLSVQ-----ETGLQG-FV-GGDHRPE--VEVPEELS 1051
ENSMFAP00000042132\_Mfas/1-1078 --SDTLARHQALLPQCGEADSDLSVQ-----ETGLQG-FV-GGDHRPE--VEVPEELS 1051
ENSMNEP00000024602\_Mnem/1-1078 --SDTLARHQALLPQCGEADSDLSVQ-----ETGLQG-FV-GGDHRPE--VEVPEELS 1051
ENSMLEP00000008744\_Mleu/1-1088 --SDTLARHQALLPQCGEADSDLSVQ-----ETGLQG-FV-GGDHRPE--VEVPEELS 1061
ENSTGEP00000008766\_Tgel/1-1088 --SDTLARHQALLPQCGEADSDLSVQ-----ETGLQG-FV-GGDHRPE--VEVPEELS 1061
ENSCANP00000040262\_Capa/1-1088 --SDTLTRHQALLPQCCEVSDSDLSVQ-----ETGLQG-FV-GGDHRPE--MEDPEELS 1061
ENSPTEP00000016080\_Ptep/1-1088 --SDTLTRHQALLPQCCEVSDSDLSVQ-----ETGLQG-FV-GGDHRPE--VEDPEELS 1061
ENSRBIP00000006831\_Rbie/1-1078 --SDTLTRHQALLPQCCEVSDSDLSVQ-----ETGLQG-FV-GGDHRPE--VEDPEELS 1051
ENSRROP00000007818\_Rrox/1-1088 --SDTLTRHQALLPQCCEVSDSDLSVQ-----ETGLQG-FV-GGDHRPE--VEDPEELS 1061
ENSOGAP00000002850\_Ogar/1-1077 --NDTLTRHQALLPQCGETDSELTIQ-----ETGLQG-PG-GGDHQR--REDPEEMS 1050
ENSMICP000000050654\_Mmur/1-1075 --SDTLSRHQALLPQCGETDPDPTAQ-----DAGLQG-PG-GGDLPE--MEGPEEMS 1048
ENSPCOP00000009624\_Pcoq/1-1076 --NDALSRHQALLPQCGETDSELMIQ-----DTGLQG-PG-GGDHPPE--MEDPEEMS 1049
ENSPSPM00000007909\_Psim/1-1084 --SDPLGRHQALLPQCGETDSELTVP-----DTGLQG-PG-GGDHPPE--MEDPEEMS 1057

ENSMEUP00000013310\_Neug/1-956 ----- 956
ENSTBEP00000002487\_Tbel/1-914 PALVVSNSRSFVVISGGSTGTENILHS----- 914
ENSPCAP00000000755\_Pcap/1-1085 PALVVSQSFSFVISGGGTGQRNVNS----- 1085
ENSCPOP00000011907\_Chof/1-954 ----- 954
ENSVAP000000001982\_Vpac/1-1087 PALVVSNSRSFVVISGGSTVTENMLHS----- 1087
ENSEEUP00000009670\_Eeur/1-946 PALVVSNAHSFVISRGGSTITENILHL----- 946
ENSOANP00000015961\_Oana/1-1083 PALLVFNARSFVISGXXXXXXXXXXXXXXXXX---- 1083
ENSOPRP00000000261\_Opri/1-1082 PGLVVSNSRSFVVISGGGSAVAENRLHS----- 1082
ENSJJAP00000004721\_Jjac/1-1084 PALVMSKSGSFVISGGGSAVTEVDLRSQSQKSS 1084
ENSPCIP000000034747\_Pcin/1-1018 PGLVVSNSRGFVISGGGSAITEKKIHS----- 1018
ENSMODP000000022810\_Mdom/1-1069 PALVVSNSRGFVISGGGSAITEKKLHS----- 1069
ENSVURP00010007344\_Vurs/1-1070 PALVVSNSRGFVISGGGSAVTEKKIHS----- 1070
ENSSHAP00000014890\_Shar/1-1072 PALVVSNSRGFVISGGGSAVTEKKIHS----- 1072
ENSMAP000000005394\_Maur/1-954 PCMVLE-----GHGAFSK----- 954
ENSOCUP000000025672\_Ocun/1-1063 P----- 1063
ENSPVAP00000011981\_Pvam/1-1085 PALVVSNSRSFVVISGGSTVTENILHS----- 1085
ENSETEP000000011160\_Etel/1-1024 PTLVVSTRSLVISGGGSAARENPNPS----- 1024
ENSFDAP00000010532\_Fdam/1-1108 PTLVMAKRSFVISGGASTAKESSPHSQ----- 1108
ENSODEP00000013257\_Odeg/1-1070 QAFVVSQSQGFVVIKNIWHS----- 1070
ENSHGLP000000002019\_Hgfe/1-1108 PALVMSKRSFVISGGGSTVTENILHS----- 1108
ENSCLAP000000021334\_Clan/1-1114 PAFVVSQSQGFVISGGGSAVTENILHT----- 1114
ENSCAPP00000014352\_Cape/1-1068 PAFVMSKSQGFVFSGGGSTVTENILHS----- 1068
ENSCPOP000000011705\_Cpor/1-1071 PAFVMSKSQGFVFSGGGSTVTENILHS----- 1071
ENSSARP00000006151\_Sara/1-1085 PALVVSNSRSFVISGAGSTVTENIMHS----- 1085
ENSLAFP00000018459\_Lafr/1-1090 PALVVSNSRSFVISGGGSTVTENIPNS----- 1090
ENSDNOP000000011819\_Dnov/1-1075 PALMVNSRSGFVISGGGSTVTENMLRS----- 1075
ENSSSCP000000041077\_Sscr/1-1089 PALVMSNSRSFVISGGGSTVTENMLHS----- 1089
ENSTTRP00000001326\_Ttru/1-1091 PALVVSNSRSFVISGGGSTVTENMLRS----- 1091
ENSBEP000000002858\_Bbbi/1-1068 PALVVSNSRSFVISGGGSTVTENMLRS----- 1068
ENSOARP000000021602\_Oari/1-1032 PALVVSNSRSFVISGGGSTVTENMLRS----- 1032
ENSCHIP000000033385\_Chir/1-1085 PALVVSNSRSFVISGGGSTVTENMLRS----- 1085
ENSBTAP000000059078\_Btau/1-1085 PALVVSNSRSFVISGGGSTVTENMLRS----- 1085
ENSBIXP000000038534\_Bthy/1-1085 PALVVSNSRSFVISGGGSTVTENMLRS----- 1085
ENSBMUP000000019115\_Bmut/1-1081 PALVVSNSRSFVISGGGSTVTENMLRS----- 1081
ENSBIXP00000005030570\_Bihy/1-1085 PALVVSNSRSFVISGGGSTVTENMLRS----- 1085
ENSMUGP000000006365\_Mung/1-1080 PALVVSTRSFSFVISGGSSVTENILHS----- 1080
ENSRNOP000000069629\_Nrong/1-1079 PALVMSTRSFSFVISGGSSVTENVLHS----- 1079
MGP\_PahariEiJ\_P0028852\_Mpah/1-1003 PALVMSTRSFSFVISGGSSMSENILHS----- 1003
MGP\_SPRETEiJ\_P0043347\_Mspr/1-1079 PALVMSTRSFSFVISGGSSVTENILHS----- 1079
ENSMUSP000000069080\_Mmus/1-1079 PALVMSTRSFSFVISGGSSVTENILHS----- 1079
ENSMOCP00000010340\_Moch/1-1076 PALVMSTRSFSFVISGGSSVTENILHS----- 1076
ENSPEMP000000029995\_Pmba/1-1076 PALVVSTRSFSFVISGGSSVTENILHS----- 1076
ENSCGRP00015024036\_Cgpi/1-1081 PALVVSTRSFSFVISGGSSVTENILHS----- 1081
ENSCGRP00001016053\_Cgch/1-1081 PALVVSTRSFSFVISGGSSVTENILHS----- 1081
ENSCGRP00000017369\_Cgcr/1-1081 PALVVSTRSFSFVISGGSSVTENILHS----- 1081
ENSDORP000000002959\_Dord/1-1078 PALVMSKRSFVISGGGSTVTENILHS----- 1078
ENSTSY000000002643\_Csyr/1-1015 PARVVSNSRSFVISGGGSTVTENILHS----- 1015
ENSMMLUP000000008249\_Mluc/1-1075 PALVVSNSRSFVISGGGSTVTENILHS----- 1075
ENSECAP000000022285\_Ecab/1-1084 PTLVVSNSRSFVISGGGSTVTENILHS----- 1084
ENSEASP000000022676\_Eaas/1-1094 PTLVVSNSRSFVISGGGSTVTENILHS----- 1094
ENSCAFP00000017381\_Cfam/1-1075 PALVVSNSRSFVISGGGSTVTENILHS----- 1075
ENSCAFP000200007154\_Cldi/1-1075 PALVVSNSRSFVISGGGSTVTENILHS----- 1075
ENSVVUP000000030826\_Vvul/1-1075 PALVVSNSRSFVISGGGSTVTENILHS----- 1075
ENSFAP000000008080\_Fcat/1-1081 PALVVSNSRSFVISGGGSTVTENILHS----- 1081
ENSPRP0000000023800\_Ppar/1-1081 PALVVSNSRSFVISGGGSTVTENILHS----- 1081
ENSPPIP00000015042\_Ptal/1-1081 PALVVSNSRSFVISGGGSTVTENILHS----- 1081
ENSMUP000000004759\_Mpfu/1-1082 PALVVSNSRSFVISGGGSTVTENILHS----- 1082
ENSNVIP000000018564\_Nvis/1-1092 PALVVSNSRSFVISGGGSTVTENILHS----- 1092
ENSUMAP000000035085\_Umar/1-1071 PALVVSNSRSFVISGGGSTVTENILHS----- 1071
ENSUAMP000000035930\_Uame/1-1079 PALVVSNSRSFVISGGGSTVTENILHS----- 1079
ENSAMEP000000015060\_Amel/1-1089 PALVVSNSRSFVISGGGSTVTENILHS----- 1089
ENSSDAP000000007437\_Sdau/1-1079 PALVVSNSRSFVISGGGSTVTENILHS----- 1079
ENSSTOP000000003945\_Itri/1-1070 PALVVSNSRSFVISGGGSTVTENILHS----- 1070
ENSMMP000000015298\_Mmma/1-1083 PALVVSNSRSFVISGGGSTVTENILHS----- 1083
ENSUPAP00010025947\_Upar/1-1086 PALVVSNSRSFVISGGGSTVTENILHS----- 1086
ENSSBOP000000036416\_Sbbo/1-1078 PALVVSNSRSFVISGGGSTVTENVLHS----- 1078
ENSANAP000000028404\_Anan/1-1078 PALVVSNSRSFVISGGGSTVTENVLHS----- 1078
ENSCCAP000000024327\_Ccap/1-1077 PALVVSNSRSFVISGGGSTVTENVLHS----- 1077
ENSCJAP000000062854\_Cjac/1-1089 PALVVSNSRSFVISGGGSTVTENVLHS----- 1089
ENSNLEP000000000336\_Nleu/1-1088 PALVVSNSRSFVISGGGSTVTENVLNS----- 1088
ENSPYP00000015087\_Pabe/1-1078 PALVVSNSRSFVISGGGSTVTENVLNS----- 1078
ENSP00000420194\_Hsap/1-1088 PALVVSNSRSFVISGGGSTVTENVVNS----- 1088
ENSGOP000000020287\_Ggor/1-1078 PALVVSNSRSFVISGGGSTVTENVLNS----- 1078



ENSPPAP00000026371_Ppan/1-1078	PALVVSSSQSFVISGGGSTVTENVLNS-----	1078
ENSPTRP00000043342_Ptro/1-1078	PALVVSSSQSFVISGGGSTVTENVLNS-----	1078
ENSCSAP00000003635_Csab/1-882	PALVVSSSQSFVISGGGSTVTENVLHS-----	882
ENSMMP000000061002_Mmul/1-1078	PALVVSSSQSFVISGGGSTVTENVLHS-----	1078
ENSPANP00000004316_Panu/1-1081	PALVVSSSQSFVISGGGSTVTENVLHS-----	1081
ENSCATP000000028615_Caty/1-1078	PALVVSSSQSFVISGGGSTVTENVLHS-----	1078
ENSMFAP00000042132_Mfas/1-1078	PALVVSSSQSFVISGGGSTVTENVLHS-----	1078
ENSMNEP000000024602_Mnem/1-1078	PALVVSSSQSFVISGGGSTVTENVLHS-----	1078
ENSMLEP000000008744_Mleu/1-1088	PALVVSSSQSFVISGGGSTVTENVLHS-----	1088
ENSTGEP000000008766_Tgel/1-1088	PALVVSSSQSFVISGGGSTVTENVLHS-----	1088
ENSCANP000000040262_Capa/1-1088	PALVVSSSQSFVISGGGSTVTENVLHS-----	1088
ENSPTEP000000016080_Ptep/1-1088	PGLVVSSSQSFVISGGGSTVTENVLHS-----	1088
ENSRBIP000000006831_Rbie/1-1078	PALVVSSSQSFVISGGGSTVTENVLHS-----	1078
ENSRROP000000007818_Rrox/1-1088	PALVVSSSQSFVISGGGSTVTENVLHS-----	1088
ENSOGAP000000002850_Ogar/1-1077	PALVVSNSRSFVISGGGSTVTENVLHL-----	1077
ENSMICP000000050654_Mmur/1-1075	PALVVSSRSFVISGGGSTVTENVLHL-----	1075
ENSPCOP000000009624_Pcoq/1-1076	PALVVSNSRSFVISGGGSTVTENVLHL-----	1076
ENSPSMP000000007909_Psim/1-1084	PALVVPNSRSFVISGGGSTVTENVLHL-----	1084

**Supplementary Figure 3: Mammalian CaSR multiple sequence alignment including the residue 91 (red arrows). The alignment was generated using the Clustal Omega server [1].**

*In vitro* screening of 159 predicted kokumi-active compounds on cCaSR

Compound ID	CAS number	EC <sub>50</sub> Ago (M)	EC <sub>50</sub> PAM (M)
(1R)-(+)-(1-Amino-2-methylpropyl)phosphonic acid	66254-56-6	-	-
(S)- $\alpha$ -Methylaspartic acid	3227-17-6	-	-
1,4,8,11-tetraazacyclotetradecane	295-37-4	0.000773242	-
1-isopropyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid	436811-11-9	-	-
1s,3s-1-aminocyclobutane-1,3-dicarboxylic acid	73550-55-7	> 0.01	-
2,6-Diaminopimelic acid	583-93-7	-	-
2-Amino-4-phosphonobutyric acid	20263-07-4	> 0.01	-
2-aminododecanedioic acid	3721-90-2	-	-
2-Aminopimelic acid	627-76-9	-	-
2S,4S-g-Hydroxy-L-glutamic acid	3913-68-6	> 0.01	-
3,5-Dimethyl-4-methoxybenzoylacetone nitrile	884504-21-6	-	-
3-Glutathionyl-S-methylindole	101038-93-1	0.003746383	-
3-O-Methyl-D-glucopyranose	13224-94-7	-	-
4-Fluoro-DL-glutamic acid	2708-77-2	> 0.01	-
9H-pyrido[3,4-b]indole-3-carboxylic acid	42438-90-4	-	-
AC-265347	1253901-26-6	-	5.11238E-08
Antibiotic G418	49863-47-0	-	-
BaCl <sub>2</sub>	10361-37-2	0.001172392	-
CaCl <sub>2</sub>	10035-04-8	0.001622123	-
Cadaverine	462-94-2	-	-
Calcium Ionophore	58801-34-6	-	-
Calhex 231	2387505-78-2	-	-
Calindol	729610-18-8	-	2.96569E-07
Cerium(III) carbonate	54451-25-1	-	-
ChemBridge CORE Library - 7126534	N/A	-	3.99941E-06
ChemBridge CORE Library - 7156222	N/A	-	3.68478E-06
Cinacalcet	226256-56-0	-	7.46105E-07
Cystine (disulfide)	56-89-3	-	-
D-(+)-Glucose	2280-44-6	-	-
D-Arginine	157-06-2	-	-
D-Aspartic Acid	1783-96-6	-	-
D-Glutamic acid	6893-26-1	-	-
Dichloromethylenediphosphonic acid	22560-50-5	-	-
DL-Aspartic acid alpha-methyl ester	65414-77-9	> 0.01	-
D-Lysine	923-27-3	-	-
Enamine Screening - Z1362199910	N/A	-	5.88796E-05
Enamine Screening - Z1436888168	N/A	-	4.57134E-05
Enamine Screening - Z1437387381	N/A	-	9.00814E-06
Enamine Screening - Z1532507755	N/A	-	8.68191E-06
Enamine Screening - Z1563602968	N/A	-	-
Enamine Screening - Z1589915397	N/A	-	0.000122222
Enamine Screening - Z1592615858	N/A	-	1.92068E-06

Enamine Screening - Z1627256025	N/A	-	0.000796597
Enamine Screening - Z1857407854	N/A	-	5.5023E-06
Enamine Screening - Z317045236	N/A	-	2.41537E-06
Enamine Screening - Z336933272	N/A	-	1.21254E-05
Gd <sup>3+</sup>	16056-77-2	0.000294595	-
Gentamicin	1403-66-3	0.000989847	-
Glutathione (γ-Glu-Cys-Gly)	70-18-8	0.006396298	-
Glycine	56-40-6	-	-
Hexamethylenetetramine	100-97-0	-	-
Hydroxyproline	51-34-4	-	-
Hygromycin B	31282-04-9	-	-
InterBioScreen Screening - STOCK1N-20329	N/A	-	9.87677E-07
InterBioScreen Screening - STOCK1N-29175	N/A	-	7.13774E-07
InterBioScreen Screening - STOCK1N-29290	N/A	-	4.49052E-06
InterBioScreen Screening - STOCK1N-32683	N/A	-	6.73283E-07
InterBioScreen Screening - STOCK1N-32983	N/A	-	7.51716E-07
InterBioScreen Screening - STOCK2S-09124	N/A	-	1.40781E-06
InterBioScreen Screening - STOCK2S-10026	N/A	-	4.57282E-07
InterBioScreen Screening - STOCK3S-12225	N/A	-	2.25131E-06
InterBioScreen Screening - STOCK3S-57962	N/A	-	1.44874E-06
InterBioScreen Screening - STOCK3S-69159	N/A	-	0.000135294
InterBioScreen Screening - STOCK4S-85937	N/A	-	0.000114962
InterBioScreen Screening - STOCK5S-00071	N/A	-	0.000171864
Kanamycin solution	25389-94-0	-	-
L-(+)-2-Amino-3-phosphonopropionic acid	23052-80-4	> 0.01	-
L-2-Amino-4-phosphonobutyric acid	20263-07-4	-	-
L-2-Aminoadipic acid	1118-90-7	> 0.01	-
L-Alanine	56-41-7	-	-
L-Arginine	74-79-3	-	-
L-Arginine methyl ester	2577-94-8	-	-
L-Asparagine	70-47-3	-	-
L-Aspartic acid	56-84-8	0.004114576	-
L-Aspartic acid β-methyl ester hydrochloride	16856-13-6	> 0.01	-
L-Cysteic acid	498-40-8	0.002339771	-
L-Cysteine	52-90-4	-	-
L-Glutamic acid	56-86-0	0.00915731	-
L-Glutamic Acid 5-Methyl Ester	1499-55-4	-	-
L-Glutamine	56-85-9	-	-
L-Histidine	71-00-1	-	-
L-Homocysteic acid	14857-77-3	> 0.01	-
L-Homoserine	672-15-1	-	-
L-Isoglutamine	636-65-7	> 0.01	-
L-Isoleucine	73-32-5	-	-
L-Leucine	61-90-5	-	-
L-Methionine	63-68-3	-	-
L-Ornithine	70-26-8	-	-

L-Proline	147-85-3	-	-
L-Selenocystine monohydrate	29621-88-3	-	-
L-Serine	56-45-1	-	-
L-Taurine	107-35-7	-	-
L-Threonine	72-19-5	-	-
L-Tyrosine	60-18-4	-	-
L-Valine	72-18-4	-	-
Methylenediphosphonic acid	1984-15-2	0.001292506	-
Methylphosphonic acid	993-13-5	>0.01	-
Mg <sup>2+</sup>	22537-22-0	0.006293176	-
N,N'-Bis(2-aminoethyl)-1,3-propanediamine	4741-99-5	-	-
Neomycin	119-04-0	0.001868047	-
NG,NG-Dimethylarginine dihydrochloride	220805-22-1	-	-
NG-methyl L Arginine	53308-83-1	-	-
NG-Nitro-L-Arginine Methyl Ester	2149-70-4	-	-
NPS 2143	284035-33-2	-	-
N $\omega$ -Nitro-L-arginine methyl ester hydrochloride	51298-62-5	-	-
O-Phospho-L-tyrosine	21820-51-9	> 0.01	-
Paromomycin sulfate salt	1263-89-4	0.001084496	-
Poly-L-arginine	26982-20-7	1.0135E-06	-
Poly-L-histidine	26062-48-6	-	-
Poly-L-lysine	25988-63-0	> 0.01	-
Poly-L-ornithine	26982-21-8	0.000239862	-
Praseodymium(III) trifluoromethanesulfonate	52093-27-3	0.000397784	-
Ribostamycin sulfate salt	53797-35-6	> 0.01	-
S-(2-Hydroxyethyl)glutathione	28747-20-8	0.002097055	-
S-1,1-dimethyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylic acid	N/A	-	-
S-2,3-diaminopropanoic acid	4033-39-0	-	-
Se-(Methyl)selenocysteine	863394-07-4	0.004468107	-
Sisomicin sulfate salt	53179-09-2	0.000299662	-
S-Lactoylglutathione	25138-66-3	0.006084892	-
S-Methylglutathione	2922-56-7	0.004418495	-
Sodium pyrophosphate tetrabasic decahydrate	13472-36-1	-	-
Spermidine	124-20-9	0.002495307	-
Spermine	71-44-3	0.012240719	-
S-piperazine-2-carboxylic acid	158663-69-5	-	-
Sr <sup>2+</sup>	22537-39-9	>0.01	-
Sucralose	56038-13-2	-	-
Sucrose	57-50-1	-	-
Terbium(III) acetate hydrate	100587-92-6	0.000174627	-
Tobramycin	32986-56-4	-	0.024201762
Triethylenetetramine	112-24-3	-	-
Vitas M Labs Express Pick - STK530456	N/A	-	2.61244E-05
$\beta$ -Asp-Ala	13110-25-3	> 0.01	-
$\beta$ -Asp-Gly	3790-52-1	> 0.01	-

$\beta$ -Asp-Leu	14650-26-1	> 0.01	-
$\beta$ -Asp-Lys	56523-60-5	-	-
$\beta$ -Asp-Phe	13433-10-8	> 0.01	-
$\gamma$ -Carboxy-DL-glutamic acid	56271-99-9	> 0.01	-
$\gamma$ -D-Glu-Trp	66471-20-3	0.004204093	-
$\gamma$ -Glu-Abu	16869-42-4	> 0.01	-
$\gamma$ -Glu-Abu-Gly	495-27-2	0.002658678	-
$\gamma$ -Glu-Ala	5875-41-2	> 0.01	-
$\gamma$ -Glu-Cys	636-58-8	> 0.01	-
$\gamma$ -Glu-Cys-Gly-Oet	92614-59-0	-	-
$\gamma$ -Glu-Gln	10148-81-9	> 0.01	-
$\gamma$ -Glu-Glu	1116-22-9	0.002064774	-
$\gamma$ -Glu-Glu-Gln	211430-99-8	> 0.01	-
$\gamma$ -Glu-Glu-Glu	7446-63-1	0.002345792	-
$\gamma$ -Glu-Gly	1948-29-4	> 0.01	-
$\gamma$ -Glu-Gly-Gly	13640-39-6	-	-
$\gamma$ -Glu-His	37460-15-4	-	-
$\gamma$ -Glu-Leu	2566-39-4	> 0.01	-
$\gamma$ -Glu-Lys	56523-60-5	-	-
$\gamma$ -Glu-Met	17663-87-5	> 0.01	-
$\gamma$ -Glu-Phe	13433-10-8	0.002316942	-
$\gamma$ -Glu-Trp	66471-20-3	> 0.01	-
$\gamma$ -Glu-Tyr	7432-23-7	0.003877693	-
$\gamma$ -Glu-Val	2746-34-1	0.004518862	-
$\gamma$ -Glu-Val-Gly	38837-70-6	0.004222828	-
$\gamma$ -Glu- $\epsilon$ -Lys	17105-15-6	-	-

**Supplementary Table I:** List of all 159 tested compounds on cCaSR using in vitro cellular assays. The table contains the EC<sub>50</sub> values for both agonists (EC<sub>50</sub> Ago(M)) and positive allosteric modulators (EC<sub>50</sub> PAM (M)). All compounds listed here were screened, using the HEK293/ T-REx/ natClytin cell line inducibly expressing cCaSR in an agonist assay. All measurements were repeated over at least three wells on the same assay plate. If the maximal response to a compound was not reached, the EC<sub>50</sub> value could not be determined and is expressed as an estimation at > 0.01 M. -: compounds that showed no activity on cCaSR in the specific testing parameters used.

**References:**

- 1 Sievers, F. *et al.* Fast, scalable generation of high-quality protein multiple sequence alignments using Clustal Omega. *Mol Syst Biol* **7**, 539, doi:10.1038/msb.2011.75 (2011).