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HsITPR3   1 -MSEMSSFLHIGDIVSLYAEGSVNGFISTGLVDDRCVVEPAAGDLDNPPKKFRDCLFKVCPMNRYSAQKQYWKAKQTKQDKEKIADVVLLQKLQHAAQMEQKQNDTENKKVHGDVVKYGSVIQLLHMKSNKYLTVNKRLPALLEKNAMRVTLDATGNEG 159
HsITPR2   1 MTEKMSSFLYIGDIVSLYAEGSVNGFISTGLVDDRCVVHPEAGDLANPPKKFRDCLFKVCPMNRYSAQKQYWKAKQAKQGN--HTEAALLKKLQHAAELEQKQNESNKKLLGEIVKYSNVIQLLHIKSNKYLTVNKRLPALLEKNAMRVSLDAAGNEG 158
HsITPR1   1 MSDKMSSFLHIGDICSLYAEGSTNGFISTGLVDDRCVVQPETGDLNNPPKKFRDCLFKLCPMNRYSAQKQFWKAAKPGANS--TTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQYGNVIQLLHLKSNKYLTVNKRLPALLEKNAMRVTLDEAGNEG 158
RmITPR1   1 MSDKMSSFLHIGDICSLYAEGSTNGFISTGLVDDRCVVQPEAGDLANPPKKFRDCLFKLCPMNRYSAQKQFWKAAKPGANS--TTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQYGNVIQLLHLKSNKYLTVNKRLPALLEKNAMRVTLDEAGNEG 158
RnITPR1   1 MSDKMSSFLHIGDICSLYAEGSTNGFISTGLVDDRCVVQPEAGDLANPPKKFRDCLFKLCPMNRYSAQKQFWKAAKPGANS--TTDAVLLNKLHHAADLEKKQNETENRKLLGTVIQYGNVIQLLHLKSNKYLTVNKRLPALLEKNAMRVTLDEAGNEG 158
              β1        β2        β3          β4      α5        α6              β7      β8        β9

HsITPR3 160 SWLFIQPFWKLRSNGDNVVVGDKVILNPVNAGQPLHASNYELSDNAGCKEVNSVNCNTSWKINLFMQFRDHLEEVLKGGDVVRLFHAEQEKFLTCDEYKGKLQYVLRTTLRQSATSATSSNALWEVEVVHHDPCRGGAGHWNGLYRFKHLATGNYLAAEE 319
HsITPR2 159 SWFYIHPFWKLRSEGDNIVVGDKVLVNPVNAGQPLHASSLLDNPGCKEVNSVNCNTSWKITLFMKYSSYREDVLKGGDVVRLFHAEQEKFLTCDEYKEKQHIFLRTTLRQSATSATSSKALWEVEVVQHDPCRGGAGWNSLFRFKHLATGNYLAAEL 318
HsITPR1 159 SWFYIQPFYKLRSIGDSVVIGDKVLVNPVNAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILKGGDVVRLFHAEQEKFLTCDEHRKQHVFLRTTGRQSATSATSSKALWEVEVVQHDPCRGGAGYWNSLFRFKHLATGHYLAAEV 318
RmITPR1 159 SWFYIQPFYKLRSIGDSVVIGDKVLVNPVNAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILKGGDVVRLFHAEQEKFLTCDEHRKQHVFLRTTGRQSATSATSSKALWEVEVVQHDPCRGGAGYWNSLFRFKHLATGHYLAAEV 318
RnITPR1 159 SWFYIQPFYKLRSIGDSVVIGDKVLVNPVNAGQPLHASSHQLVDNPGCNEVNSVNCNTSWKIVLFMKWSDNKDDILKGGDVVRLFHAEQEKFLTCDEHRKQHVFLRTTGRQSATSATSSKALWEVEVVQHDPCRGGAGYWNSLFRFKHLATGHYLAAEV 318
              β10      β11      β12      β13        β14            β15    β16    β17          β18      β19    β20    β21

HsITPR3 320 NPSYKGDASDPKAAGMGAQGRTG-R-RNAGEKIKYCLVAVPHGNDIASLFELDPTTLQKTDSFVPRNSYVRLRHLCTNTWIQSTNVPIDIEEERPIRLMLGTCPTKEDKEAFAISVPVSEIRDLDFANDASSMLASAVEKLNEGFISQNDRRFVIQLLE 477
HsITPR2 319 NPDYRDAQNEGKNVRDGVPPTSK-KKRQAGEKIMYTLVSVPHGNDIASLFELDATTLQRADCLVPRNSYVRLRHLCTNTWVTSTSIPIDTDEERPVMLKIGTCQTKEDKEAFAISVPLSVRDLDFANDANKVLATTVKKLENGTITQNERRFVTKLLE 478
HsITPR1 319 DPDFEEECLEFQPSVDPDQDASRSRLRNAQEKMVYSLVSVPEGNDISSIFELDPTTLRGGDSLVPRNSYVRLRHLCTNTWVHSTNIPIDKEEEKPVMLKIGTSPVKEDKEAFAIVPVSPAEVRDLDFANDASKVLGSIAGKLEKGTITQNERRSVTKLLE 478
RmITPR1 319 DPDFEEECLEFQPSVDPDQDASRSRLRNAQEKMVYSLVSVPEGNDISSIFELDPTTLRGGDSLVPRNSYVRLRHLCTNTWVHSTNIPIDKEEEKPVMLKIGTSPLKEDKEAFAIVPVSPAEVRDLDFANDASKVLGSIAGKLEKGTITQNERRSVTKLLE 478
RnITPR1 319 DPDFEEECLEFQPSVDPDQDASRSRLRNAQEKMVYSLVSVPEGNDISSIFELDPTTLRGGDSLVPRNSYVRLRHLCTNTWVHSTNIPIDKEEEKPVMLKIGTSPLKEDKEAFAIVPVSPAEVRDLDFANDASKVLGSIAGKLEKGTITQNERRSVTKLLE 478
              β22          β23      β24    β25        β26        α28            α29

HsITPR3 478 DLVFFVSDVPNNGQNVLDIMVTKPNRERQKLMREQNILKQVFGILKAPFREKGGEGPLVRLEELSDQKNAPYQHMFRLCYRVLRHSQDYRKNQEHIAKQFGMMQSQIGYDILAEDTITALLHNNRKLLEKHITKTEVETFVSLVRKNREPRFLDYLSDL 637
HsITPR2 478 DLIFFVADVPNNGQEVLDIVITKPNRERQKLMREQNILAQVFGILKKFEKAGEGSMLRLEDLGDQRAYPAPYKMLRLCYRVLRHSQQDYRKNQEYIAKNFCVMQSQIGYDILAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRRNRERPRFLDYLSDL 637
HsITPR1 479 DLVYFVTGGTNSGQDVLEVVFSKPNRERQKLMREQNILKQIFKLLQAPFTDCG-DGPMLRLEELGDQRHAPFRHICRLCYRVLRHSQQDYRKNQEYIAKQFGFMQKQIGYDILAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNRERPRFLDYLSDL 637
RmITPR1 479 DLVYFVTGGTNSGQDVLEVVFSKPNRERQKLMREQNILKQIFKLLQAPFTDCG-DGPMLRLEELGDQRHAPFRHICRLCYRVLRHSQQDYRKNQEYIAKQFGFMQKQIGYDILAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNRERPRFLDYLSDL 637
RnITPR1 479 DLVYFVTGGTNSGQDVLEVVFSKPNRERQKLMREQNILKQIFKLLQAPFTDCG-DGPMLRLEELGDQRHAPFRHICRLCYRVLRHSQQDYRKNQEYIAKQFGFMQKQIGYDILAEDTITALLHNNRKLLEKHITAAEIDTFVSLVRKNRERPRFLDYLSDL 637
              α30      α31              α32          α33              α34      α35    α36      α37

HsITPR3 638 CVSNHIAIPVTQELICKCVLDPKNSDLIIRTELRPVKEM-AQSH----EYLSIEYSEEEVVWLTWTDKNNEHHEKSVRQLAQEARAGNAHDKNLSYYRYQLKLFARMCLDRQYLAIDEISQQLGVDLIFLCMADEMLHFDLRASFCHLMLHVHVDRDPQE 792
HsITPR2 638 CVSNTTAIPVTQELICKFMLSPGNADILIQTKVVSMQADNPMES-----SILSDDIDDEEVVWLYWIDSNKEPHGKAIRHLAQEAKEGTKADLEVLTYYRYQLNLFARMCLDRQYLAINQISTQLSVDLILRCVSDESLPFDLRASFCHLMLHMHVDRDPQE 793
HsITPR1 638 CVSMNKSIPVTQELICKAVLNPTNADILIETKLVLSRFEFEGVSSTGENALEAGEDEEEVVMLFWRDSNKEIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAINEISGQLDVDLILRCMSDENLPYDLRASFCRLMLHMHVDRDPQE 797
RmITPR1 638 CVSMNKSIPVTQELICKAVLNPTNADILIETKLVLSRFEFEGVS-TGENALEAGEDEEEVVMLFWRDSNKEIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAINEISGQLDVDLILRCMSDENLPYDLRASFCRLMLHMHVDRDPQE 796
RnITPR1 638 CVSMNKSIPVTQELICKAVLNPTNADILIETKLVLSRFEFEGVS-TGENALEAGEDEEEVVMLFWRDSNKEIRSKSVRELAQDAKEGQKEDRDVLSYYRYQLNLFARMCLDRQYLAINEISGQLDVDLILRCMSDENLPYDLRASFCRLMLHMHVDRDPQE 796
              α38        β39              α40        β41  α42      α43          α44    α45      α46

HsITPR3 793 LVTPVKFARLWTEIPTAITIKDYDSNLNASRDDKNKFANTMEFVEDYLNNVVSEAVPFANEEKNKLTFEVVSLARNLIYFGFYSFSELLRTRTLLIIDCVQGPPAMLQA---YEDPGDK----------NVRRSIQGVGHMMSTMVLSRKQSVFSAP 939
HsITPR2 794 SVVPVRYARLWTEIPTKITIHEYDSITDSSRNDMKRKFALTMEFVEEYLKEVVNQPFPFGDKEKNKLTFEVVSLARNLIYFGFYSFSELLRTRTLLAILDIVQAPMSSYFERLSKFQDGGN-------NVMRTIHGVGEMMTQMVLSR--GSIFPM 941
HsITPR1 798 QVTPVKYARLWSEIPSEIAIDDYDSGSGASKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLTFEVVSLARNLIYFGFYNFSDLLRLTKILLAILDCVHVTTIFPISKMAKGEENKGNNDVEKLKSSNVMRSIHGVGELMTQVVLRGGFL 952
RmITPR1 797 QVTPVKYARLWSEIPSEIAIDDYDS-SGTSKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLTFEVVSLARNLIYFGFYNFSDLLRLTKILLAILDCVHVTTIFPISKMTKGEENKG--------SNVMRSIHGVGELMTQVVLRGG---GFL 942
RnITPR1 797 QVTPVKYARLWSEIPSEIAIDDYDS-SGTSKDEIKERFAQTMEFVEEYLRDVVCQRFPFSDKEKNKLTFEVVSLARNLIYFGFYNFSDLLRLTKILLAILDCVHVTTIFPISKMTKGEENKG--------SNVMRSIHGVGELMTQVVLRGG---GFL 942
              α47                  α48          α49

HsITPR3 940 SLSAGASAAEPLDRSKFEENEDIVVMETKLKIILEILQFLNVRLDYRISYLLSVFKKEFVEVFPMQDSGADGTAPAFDSTTAN--MNLDRIGEQAEAMFGVGKTSSMLEVDDEGGRMFLRVLIHLTMHDYAPLVSGALQLLFKHFSQRQEAMHTFKQVQL 1097
HsITPR2 942 SVPDVPPSIHPSKQGSPTEHEDVTVMDTKLKIILEILQFLNVRLDYRISYMLSIYKKEFGEDNDNAETSASGSPDTLLPSAIV--PDIDEIAAAETMFAGRKEKNPVQLDDEGGRTFLRVLIHLTMHDYPPLLSGALQLLFRHFSQRQEAVQAFKQVQL 1099
HsITPR1 953 PMTPMAAAPEGNVKQAEPEKEDIMVMDTKLKIILEILQFLNVRLDYRISCLLCIFKREFDESNSQSSETSSGNSSQEGPSNVPGALDFEHIEEQAEGIFGGSEENTPLDLDDHGGRTFLRVLIHLTMHDYPPLVSGALQLLFRHFSQRVEQLQAFKQVQL 1112
RmITPR1 943 PMTPMAAAPEGNVKQAEPEKEDIMVMDTKLKIILEILQFLNVRLDYRISCLLCIFKREFDESNSQSSETSSGNSSQEGPSNVPGALDFEHIEEQAEGIFGGSEENTPLDLDDHGGRTFLRVLIHLTMHDYPPLVSGALQLLFRHFSQRVEQLQAFKQVQL 1102
RnITPR1 943 PMTPMAAAPEGNVKQAEPEKEDIMVMDTKLKIILEILQFLNVRLDYRISCLLCIFKREFDESNSQSSETSSGNSSQEGPSNVPGALDFEHIEEQAEGIFGGSEENTPLDLDDHGGRTFLRVLIHLTMHDYPPLVSGALQLLFRHFSQRVEQLQAFKQVQL 1102
              α50                α51                  α52    α53      α54

HsITPR3 1098 LISAQDVENYKVIKSELDRLRTMVEKSELWWDKKGSGKGEEVEAGAAKDKKERPTDEEGFLHPPG--------EKSSENYQIVKGILERLNKMCGVG----EQMRKKQQRILKNMDAHKVMLDLLQIPYDKGDA-KMMEILRYTHQFLQKFCAGNPGNQA 1244
HsITPR2 1100 LVSNQDDVNYKQIKADLDQLRLTVEKSELWWEKSSNYENGEIGESQVKGGEEPIEESNILSPAVGGGTKKPQIDSNKSNNYRVVKEILIRLSKLCVQG----KKCRNQHQRLLKNMGAHSVVLDLLQIPYEKNDE-KMNEVMNLAHTFLQNFCRGNPQNQV 1254
HsITPR1 1113 LVTSQDVDNYKQIKQDLDQLRSIVEKSELWWYKGQGPDETMDGASGENEHKKTEEGNNKPQKHES---------TSSYNYRVVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMGAHAVVLELLQIPYEKAEDTKMQEIMRLAHEFLQNFCAGNQQNQA 1263
RmITPR1 1103 LVTSQDVDNYKQIKQDLDQLRSIVEKSELWWYKGQGPDEPMDGASGENEHKKTEEGTSKPLKHES---------TSSYNYRVVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMGAHAVVLELLQIPYEKAEDTKMQEIMRLAHEFLQNFCAGNQQNQA 1253
RnITPR1 1103 LVTSQDVDNYKQIKQDLDQLRSIVEKSELWWYKGQGPDEPMDGASGENEHKKTEEGTSKPLKHES---------TSSYNYRVVKEILIRLSKLCVQESASVRKSRKQQQRLLRNMGAHAVVLELLQIPYEKAEDTKMQEIMRLAHEFLQNFCAGNQQNQA 1253
              α55                α56          α57      α58      α59      α60

HsITPR3 1245 LLHKHLHLFLTPGLLEAETMQHIFLNNYQLCSEISEPVLQHFVHLLATHGRHVQYLDFLHTVIKAEGKYVKKCQDMIMTELTNAGDDVVVFYNDKASLAHLLDMMKAARDGVEDHSP-LMYHISLVDLLAACAEGKNVYTEIKCTSLLPLEDVVSVVTHE 1403
HsITPR2 1255 LLHKHLNLFLTPGLLEAETMRHIFMNNYHLCNEISERVQHFVHCIETHGRHVEYLRFLQTIVKAEDGVVNDKPVKDDKGENPQLIDQGGRTFIRDLLLLLSIALATHGRHVDKLRFLLQTIVKAEDGVVN 1413
HsITPR1 1264 LLHKHLNLFLNPGILEAVTMQHIFMNNFQLCSEIENRVQHFVHCIETHGRNVQYIKFLQTILKAEGGQDKKCQDMIMAELVNSGEDVLVFYNDRASFQTILQMMRSERDRMDENSP-LMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRVVTHE 1422
RmITPR1 1254 LLHKHLNLFLNPGILEAVTMQHIFMNNFQLCSEIENRVQHFVHCIETHGRNVQYIKFLQTILKAEGGQDKKCQDMIMAELVNSGEDVLVFYNDRASFQTILQMMRSERDRMDENSP-LMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRVVTHE 1412
RnITPR1 1254 LLHKHLNLFLNPGILEAVTMQHIFMNNFQLCSEIENRVQHFVHCIETHGRNVQYIKFLQTILKAEGGQDKKCQDMIMAELVNSGEDVLVFYNDRASFQTILQMMRSERDRMDENSP-LMYHIHLVELLAVCTEGKNVYTEIKCNSLLPLDDIVRVVTHE 1413
              α61    α62      α63        α64      α65          α66      α67      α68      α69

HsITPR3 1404 DCITEVKMAYVNFVNHCYVDTEVEMKEIYTSNHCYVDTEVEMKEIYTSNIIWKLFENFLVDMARVCNTTTDRKHADIFLEKCVTESIMNIVSGFFNSPFSDNSTSLQTHQPVFIQLLQSAFRIYNCTWPNPAQKASVESCIRTLAEVAKNRGIAIPVDLDSQVNTLFMKSHSNMVQR 1573
HsITPR2 1414 DCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNTTTDRKHADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPSQKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHN-IVQK 1572
HsITPR1 1423 DCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNTTSDRKHADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPSQKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHS-IVQK 1581
RmITPR1 1413 DCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNTTSDRKHADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPSQKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHN-IVQK 1571
RnITPR1 1414 DCIPEVKIAYINFLNHCYVDTEVEMKEIYTSNHMWKLFENFLVDICRACNTTSDRKHADSILEKYVTEIVMSIVTTFFSSPFSDQSTTLQTRQPVFVQLLQGVFRVYHCNWLMPSQKASVESCIRVLSDVAKSRAIAIPVDLDSQVNNLFLKSHN-IVQK 1572
              α70        α71          α72          α73        α74        α75

HsITPR3 1563 QRNASSYKATTRAFPRVTPTANQWDYKNIIEKLQDIITALEERLKPLVQAELSVLVDVLHWPELLFLEGSEAYQRCESGGFLSKLIQHTKDLME-SEEKLCIKVLRTLQQMLLKKTKYGD--------------------------------------- 1681
HsITPR2 1574 AAMGWRLSARSGPRRFKEALGGPAWDYRNIIEKLQDVVASLEHQFSPMMQAEFSVLVDVLYSPELLFPEGSDARIRC--GAFMSKLINHTKKLME-KEEKLCIKILQTLREMLEKKDSFVE--------------------------------------- 1690
HsITPR1 1582 TAMNWRLSARN-AARRDSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKCESGGFICKLIKHTKQLLEENEEKLCIKVLQTLREMMTKDRGYGEKQISIDELDNAELPPAPDSEN-ATEELEPSPPLRQLEDHK 1739
RmITPR1 1572 TALNWRLSARN-AARRDSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKCESGGFICKLIKHTKQLLEENEEKLCIKVLQTLREMMTKDRGYGEKQISIDESENAELPQAPEAENSTEQELEPSPPLRQLEDHK 1730
RnITPR1 1573 TAMNWRLSARN-AARRDSVLAASRDYRNIIERLQDIVSALEDRLRPLVQAELSVLVDVLHRPELLFPENTDARRKCESGGFICKLIKHTKQLLEENEEKLCIKVLQTLREMMTKDRGYGEKQISIDELNAELPQPPEAENSTEQELEPSPPLRQLEDHK 1731
              α76            α77    α78      α79

HsITPR3 1682 RGNQLRKMLLQNYLQNRKSTSRGDLPD-------------------------------PIGTGLDPDWSAIAATQCRLDKEGATKLVCDLITSTKNEKIFQESIGLAIHLLDGGNTEIQKSFHNLMMSDKKSERFFKVLHDRMKRAQQETKSTVAVNMNDLGSQPHEDRE 1820
HsITPR2 1691 EGNTLRKIKNRYFKGDYSIGVNGHLSGA--------YSKTAQVGGSFSGGDSDKMGISMSDIQCLLDKEGASELVIDVIVTKNDRIFSEGILGIALLEGGNTQTQYSFYQQLHEQKKSEKFFKVLYDRMKAAQKEIRSTVTVNTIDLGNKKKDDEV 1841
HsITPR1 1740 RGEALRQVLVNRYYGNVRPSGRRESLTSFGNGPLSAGGPGKPGGGGGGSGSSSMRGEMSLAEVQCHLDKEGASNLVIDLIMNASSDRVFHESILLAIALLEGGNTTIQHSFFCRLTEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDLGNKKKDDEV 1899
RmITPR1 1731 RGEALRQILVNRYYGNVRPSGRRESLTSFGNGPLSPGGPSKPGGGGGGPGSGSTSRGEMSLAEVQCHLDKEGASNLVIDLIMNASSDRVFHESILLAIALLEGGNTTIQHSFFCRLTEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDLGNKKKDDEV 1890
RnITPR1 1732 RGEALRQILVNRYYGNVRPSGRRESLTSFGNGPLSPGGPSKPGGGGGGPGSGSTSRGEMSLAEVQCHLDKEGASNLVIDLIMNASSDRVFHESILLAIALLEGGNTTIQHSFFCRLTEDKKSEKFFKVFYDRMKVAQQEIKATVTVNTSDLGNKKKDDEV 1732
              α80              α82      α83          α84      α85

HsITPR3 1821 PVDPTTKGRVASFSIPGSSSRYS---------------------------LGPSLRRGHEVSERVQSSEMGTSVLIMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCETLQFLDIMCGSTTGGLGLLGLYINEDNVGLVIQTLETLTEYCQGPCH 1953
HsITPR2 1842 ELMTSGPRMRVRDSTLHLKEGMKGQLTEHEDVTVMDTKLKIILEILQFLNIMCGPEAGNTEEKSAEEVTMSPAIAIMQPILRFLQLLCENHNRELQNFLRCQNNKTNYNLVCETLQFLDCICGSTTGGLGLLGLYINEKNVALVNQNLESLTEYCQGPCH 2001
HsITPR1 1900 DRDAPS-RKKAKEPTTQITEEVRDQLLEASAATRKAFTTFRREADPD-DHYQPGEGTQATADKAKDDLEMSAVITMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCETLQFLDCICGSTTGGLGLLGLYINEKNVALINQTLESLTEYCQGPCH 2057
RmITPR1 1891 DRDAPS-RKKAKEPTTQITEEVRDQLLEASAATRKAFTTFRREADPD-DHYQSGEGTQATTDKAKDDLEMSAVITMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCETLQFLDCICGSTTGGLGLLGLYINEKNVALINQTLESLTEYCQGPCH 2048
RnITPR1 1892 DRDAPS-RKKAKEPTTQITEEVRDQLLEASAATRKAFTTFRREADPD-DHYQSGEGTQATTDKAKDDLEMSAVITMQPILRFLQLLCENHNRDLQNFLRCQNNKTNYNLVCETLQFLDCICGSTTGGLGLLGLYINEKNVALINQTLESLTEYCQGPCH 2049
              α86        α87          α88        α89      α90      α91

HsITPR3 1954 ENQTCIVTHESNGIDIITALILNDISPLCKYRMDLVLQLKDNASKLLLALMESRHDSENAERILISLRPQELVDVIKKAYLQ-------EEERENSEVSPREVGHNIYILALQLSRHNKQLHLLKPVKRIQEEEAEGISSMLSLNNKLQSMLKSSAPA 2106
HsITPR2 2002 ENQTCIATHESNGIDIIITALILNDINPLGKKRMDLVLQLKNNASKLLLAIMESRHDSENAERILFNMRPRELVDVMKNAYNQGLECDHGDDEGGDDGVSPKDVGHNIYILAHQLARHNKQLLQQMLKPG------------------------------SD 2131
HsITPR1 2058 ENQNCIATHESNGIDIIITALILNDINPLGKKRMDLVLQLKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVIKKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQSMLKPG-------------------------------G 2176
RmITPR1 2049 ENQNCIATHESNGIDIIITALILNDINPLGKKRMDLVLELKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVIKKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQTMLKPG-------------------------------G 2177
RnITPR1 2050 ENQNCIATHESNGIDIIITALILNDINPLGKKRMDLVLELKNNASKLLLAIMESRHDSENAERILYNMRPKELVEVIKKAYMQGEVEFEDGENGEDGAASPRNVGHNIYILAHQLARHNKELQTMLKPG-------------------------------G 2178
              α92    α93    α94          α95    α96        α97        α98

HsITPR3 2107 QEEEEDPLAYYENHTSQIEIVRQDRSMEQIVFPVPGICVQLTEETKHRLFTTTEQDEQGSKVNDFFQQTEDLYNEMKWQKKLRSMPLIYWFSRRMTLWGSISFNLAVFINLIIAFFYPYFDDGDEGTLSPLFSVLLWIAVACTSMLFFFSKPVGIRPFL 2265
HsITPR2 2132 PDEGDEALKYYANHTAQIEIVRHDRTMEQIVFPVPNICEYLTRESKCRVFNTTEQDEQGSKVNDFFQQTEDLYNEMKWQKKLRSHLSLWGSISFNLAVFINLIVAFFYPYFGGDGDEGTLSPLFSVLLWIAVACTSMLFFSKPVGIRPFL 2291
HsITPR1 2187 QVDGDEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKESKLRIYYTTERDEQGSKINDFFLRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKG-VRGGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALI 2345
RmITPR1 2178 QVDGDEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKESKLRIYYTTERDEQGSKINDFFLRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKG-VRGGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALI 2336
RnITPR1 2179 QVDGDEALEFYAKHTAQIEIVRLDRTMEQIVFPVPSICEFLTKESKLRIYYTTERDEQGSKINDFFLRSEDLFNEMNWQKKLRAQPVLYWCARNMSFWSSISFNLAVLMNLLVAFFYPFKG-VRGGTLEPHWSGLLWTAMLISLAIVIALPKPHGIRALI 2337
              α99    β100    β101      α102        α103          α104        S1              S1'        S1''

HsITPR3 2266 VALILRSIYYLGIGPTLNILGALNLTNKIVFVSVGNRGTFIRGYKAMVMDMEFLYHVGYILTSVLGLFAVHLFYFSILLFDLVYREETLLNVIKSVTRNGRSIILTALLVYFSIVGFLKDDFTVEILYSISVGLSLPGMPHGAAAFVDTC 2425
HsITPR2 2292 VSIMLRSIYTIGLGPTLILLGAANLCNKIVFLVSFVGNRGTFIRGYKAMVMDFELFYHVAYILVCMLGLFVHEFFYSLLFDLVYREETLLNVIKSVTRNGRSIILTAVLALILIVYLFSIIGFLFLKDDFIEVDRLKNRTPVTGSHQVPTMTLLTMMEA 2451
HsITPR1 2346 ASTILRLIFSVGLQPTLFLLGAFNVCNKIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREETLLNVIKSVTRNGRSIILTAALIALILVYLFSIVGYLFFKDDFIEVDRLPNETAVPETGESLASEFLYSDVC 2505
RmITPR1 2337 ASTILRLIFSVGLQPTLFLLGAFNVCNKIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREETLLNVIKSVTRNGRSIILTAALIALILVYLFSIVGYLFFKDDFILEVDRLPNETAVPETGESLANDFLYSDVC 2496
RnITPR1 2338 ASTILRLIFSVGLQPTLFLLGAFNVCNKIIFLMSFVGNCGTFTRGYRAMVLDVEFLYHLLYLVICAMGLFVHEFFYSLLLFDLVYREETLLNVIKSVTRNGRPIILTAALIALILVYLFSIVGYLFFKDDFILEVDRLPNETAVPETGESLANDFLYSDVC 2497
              S2                    α105    α106    S3          S4        S5              β107

HsITPR3 2426 SGDKMD-CVSGLSVPEVLEEDRELDSTERACDTLLMCIVTVMNHGLRNGGGVGDILRKPSKDESLFPARVVYDLLFFFIVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLERDKFDNKTVSFEEHIKLEHNMWNYLYFIVLVRVKNKTDYT 2584
HsITPR2 2452 CAKEN---CSPTIPASNTADEEYEDGIERTCDTLLMCIVTVLNQGLRNGGGVGDILRRPSKDEPLFAARVVYDLLFFFIVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLERDKFDNKTVSFEEHIKEEHNMWHYLYFIVLVKVKKDTEYT 2588
HsITPR1 2506 RVETGENCTSPAPKEELLPAEETEQDKEHTCETLLMCIVTVLSHGLRSGGGVGDVLRKPSKEEPLFAARVIYDLLFFVIVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLERDKFDNKTVTFEEHIKEEHNMWHYLCFIVLVKVKDSTEYT 2665
RmITPR1 2497 RVETGENCTSPAPKEELLPVEETEQDKEHTCETLLMCIVTVLSHGLRSGGGVGDVLRKPSKEEPLFAARVIYDLLFFVIVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLERDKFDNKTVTFEEHIKEEHNMWHYLCFIVLVKVKDSTEYT 2656
RnITPR1 2498 RVETGENCTSPAPKEELLPVEETEQDKEHTCETLLMCIVTVLSHGLRSGGGVGDVLRKPSKEEPLFAARVIYDLLFFVIVIIIVLNLIFGVIIDTFADLRSEKQKKEEILKTTCFICGLERDKFDNKTVTFEEHIKEEHNMWHYLCFIVLVKVKDSTEYT 2657
              β108          Pore Helix            S6                            α109

HsITPR3 2585 GPESYVAQMIKNKNLDWFPRMRAMSLVSNEGEGEQNEIRILQDKLNSTMKLVSHLTAQLNELKEQMTEQRKRRQRLGFVDVQNCISR------ 2671
HsITPR2 2609 GPESYVAQMIVNKENLDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRKQRQRIGLLGHHPHMNVPQQPA 2701
HsITPR1 2666 GPESYVAEMIKERNLDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRKQRQRIGLLGHHPHMNVNPQQPA 2758
RmITPR1 2657 GPESYVAEMIRERNLDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRKQRQRIGLLGHHPHN-VNPQQPA 2749
RnITPR1 2658 GPESYVAEMIRERNLDWFPRMRAMSLVSSDSEGEQNELRNLQEKLESTMKLVTNLSGQLSELKDQMTEQRKQRQRIGLLGHHPHN-VNPQQPA 2749
              α110
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Supplementary Note 1

Supplementary Note 1: Secondary structure of hIP$_3$R3. Secondary structural elements of hIP$_3$R3 are matched against the primary sequence and colored by domain with BTF1 in purple, BTF2 in blue, ARM1 in violet, the CLD in cyan, ARM2 in green, ARM3 in yellow, the JD in orange and the TMD in red. Sequence of hIP$_3$R3 is aligned with human IP$_3$R1, human IP$_3$R2, mouse IP$_3$R1 and rat IP$_3$R1. Residues not modeled in the structure are represented by dashed lines. Boxes denote residues that coordinate ligands. Black – IP$_3$, magenta – CD Ca^{2+}, green – JD Ca^{2+} and blue – Zn^{2+}. Jpred4 was used to estimate the approximate start and finish of the unregistered a-helices in ARM2 and the TMD, which are colored in grey.

	hIP$_3$R3 apo CD focus refinement (EMD-7979)	hIP$_3$R3 S1-S4 focus refinement (EMD-7980)	hIP$_3$R3 IP$_3$ class 1 CD focus refinement (EMD-7982)	hIP$_3$R3 IP$_3$ class 2 CD focus refinement (EMD-7985)	hIP$_3$R3 Ca^{2+} TMD focus refinement (EMD-7990)	hIP$_3$R3 Ca^{2+} CD focus refinement (EMD-7989)	hIP$_3$R3 Low IP$_3$-Ca^{2+} TMD Focus Refinement (EMD-7993)	hIP$_3$R3 Low IP$_3$-Ca^{2+} CD focus refinement (EMD-7992)	hIP$_3$R3 High IP$_3$-Ca^{2+} TMD focus refinement (EMD-7995)	hIP$_3$R3 High IP$_3$-Ca^{2+} CD focus refinement (EMD-7996)
Data collection and processing										
Magnification	105,000x	105,000x	22,500x	22,500x	22,500x	22,500x	22,500x	22,500x	22,500x	22,500x
Voltage (kV)	300kV	300kV	300kV	300kV	300kV	300kV	300kV	300kV	300kV	300kV
Electron exposure (e–/Å^2)	60	60	61	61	61	61	61	61	61	61
Defocus range (μm)	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5	-1.0 – 2.5
Pixel size (Å)	1.096	1.096	1.088	1.088	1.088	1.088	1.088	1.088	1.088	1.088
Symmetry imposed	C1	C1	C1	C4	C4	C1	C4	C1	C4	C1
Initial particle images (no.)	211,068	211,068	428,144	185,800	49,060	135,228	74,277	196,348	170,308	657,372
Final particle images (no.)	119,904	81,299	428,144	185,800	33,807	135,228	49,087	158,389	77,871	349,652
Map resolution (Å)	3.76	3.69	3.26	3.94	4.22	4.69	3.80	4.22	3.66	3.78
FSC threshold	0.143	0.143	0.143	0.143	0.143	0.143	0.143	0.143	0.143	0.143
Map resolution range (Å)	300-3.76	300-3.69	300-3.26	300-3.94	300-4.22	300-4.69	300-3.80	300-4.22	300-3.66	300-3.78

Supplementary Table 1: Cryo-EM data collection, refinement and validation statistics for focused refinement reconstructions.