

A

	TM1	TM2	
cdgl (<i>E. coli</i>)	YNENTNVKLIPOMNILMVVVALFFLNAVIFLFMLMKYFTN----	KQILPTLILSLAFISGLIYLVEITVI	141
CELSR3 (<i>H. sapiens</i>)	RERLEGGDLELLAVFTHVVVAVSVAALVLTAAIILS---	LASLKS--NVRGIHANVAALGVAELLFLLGI	2593
CELSR1 (<i>H. sapiens</i>)	SRRENGEVLPLKIVTYAAVSLSLAALLVAFVLLSL---	VRMLRS--NLHSIHKHLAVALFLSLQVLFVIGI	2522
CELSR2 (<i>H. sapiens</i>)	SRRENGEILPLKTLTYVALGVTIAALLTFFFLT---	LAILRS--NQHGIRRNLTAAALGLAQLVFLFGI	2430
GPR157 (<i>H. sapiens</i>)	SPPPETELVPSERAVVLLSCALSALGSGLLVATHAL---	WEDLRS--RARRLLEFLSLADLLSAASYFYGV	68
	TM3	TM4	
cdgl (<i>E. coli</i>)	IHKPINGSTLIQ--TKSNDVSIFYIFRQLSFICITLSALFCYGDNILD-----	NNKKKTGILL	198
CELSR3 (<i>H. sapiens</i>)	HRT-----HNQLVCTAVAILLHYFFLSTFAWLFVQGLHLYRMQVEPRNVD--	RGAMRFYHALGWG	2651
CELSR1 (<i>H. sapiens</i>)	NQT-----ENPFCLCTVVAILLHYIYMSTFAWTLVESHVYRMLTEVRNID--	TGPMRFYYVVGWG	2580
CELSR2 (<i>H. sapiens</i>)	NQA-----DLPFACTVIAILLHFLYLCITFSWALLEALHLYRALTEVRDYN--	TGPMRFYYMLGWG	2488
GPR157 (<i>H. sapiens</i>)	LQNF-----AGPSWDQVLCQALSTFANTSSFFWTVAIALYLYLSTVRAARGPRTDRLLWAFHVVS	SWG	130
	TM4	TM5	
cdgl (<i>E. coli</i>)	LALIPFLVFPFLAHNLSYNADYS-----	LYVVDYCPDNHTATWGINYTKILVCLWAFLLFFI	256
CELSR3 (<i>H. sapiens</i>)	VPAVILGLAVGLDPEG--YGNPDFCWISVH-----	EPLIWSFAGPVVLVIVMNGTMFLLAAR	2706
CELSR1 (<i>H. sapiens</i>)	IPAVVTGLAVGLDPOG--YGNPDFCWLSLQ-----	DTLIWSFAGPIGAVIIINTVTSVLSAK	2635
CELSR2 (<i>H. sapiens</i>)	VPAFITGLAVGLDPEG--YGNPDFCWLSIY-----	DTLIWSFAGPVAFVAVSMSVFLYILAAR	2543
GPR157 (<i>H. sapiens</i>)	VPLVITVAVALKKIG--YDASDVSVGWCWIDLEAK-----	DHVLWMLLTGKLWEMLAYVLLPLLYLL	191
	TM6		
cdgl (<i>E. coli</i>)	IMRTRLAS-----	ELWPLIALLCCLASTCCNLLLLTLDEYNY-----	292
CELSR3 (<i>H. sapiens</i>)	TSCSTGQ-R-----	EAKKTSALTIRSSFLLLLLVSAWLFGLL-----	2745
CELSR1 (<i>H. sapiens</i>)	VSCQRKH-HY-----	YGKKGIVSLRLTAFLLLLSATWLLGLL-----	2675
CELSR2 (<i>H. sapiens</i>)	ASCAAQR-QG-----	FEKKGPSVGLQPSFAVLLLSATWLLALL-----	2583
GPR157 (<i>H. sapiens</i>)	VRKHINR-AHTALSEYRPIILSQEHRLRLRHSMAKKLVLIPLIFTGLRVWST-----	VRFVLTLCGSP	253
	TM7		
cdgl (<i>E. coli</i>)	---TIWYISRGIEVSSKLFVVSFLIYNIFQ-ELQLSSKLAVHD		331
CELSR3 (<i>H. sapiens</i>)	NHSILAFHYLHAGLCGLQGLAVLLLCVNLADARAAMWPACLG		2788
CELSR1 (<i>H. sapiens</i>)	NRDALSFHYLFAITSGLOGPFVLLFHCVLNQEVKRLKGLVGG		2718
CELSR2 (<i>H. sapiens</i>)	NSDTLLFHYLFATNCIQGPFIFLSYVVLSSKEVRKALKLACSR		2626
GPR157 (<i>H. sapiens</i>)	AVQTPVLVLHGIGNTFQGGANCIMFVLCTRAVTRLFLSCLCC		296

B

	TM1	TM2	
dgcT (<i>E. coli</i>)	WFNQPQ--VEEVVPRSTYLMVMIALFFIDTVAFIFMQLYFIYDR-----	RQFSNCVLSLAFLISCLIFYVI	90
RXFP1 (<i>H. sapiens</i>)	NTDITSSLENLLASIIQRFVFWVVSATCFGNIFVICMRFYIRSE---	NKLYAMSIISLCCADCLMGIIYL	458
VN1R5 (<i>H. sapiens</i>)	CENFPSKMIKLPGFITTIQIFFYPOASFGISANTLLLFHIFTFVESHRSKSIDMIISHLSLHILLETO		98
VN1R1 (<i>H. sapiens</i>)	NQHPIDDFEAMAGKVKSGISFLIQTGVGILGNSFLLCFYNLILFTGHKLRPTDLILSQLALANSVMVLEFFK		101
VN1R3 (<i>H. sapiens</i>)	-----MASKDFAIGMILLSOIMVGFLGNFFLLYHYSLFCFTRGMLOSTDILKHLTIANSVLILSK		61
VN1R2 (<i>H. sapiens</i>)	LHSLVSAHGEKPTKPVGLDPTLFQVVGILGNFSLLYYMFYFRGYKPRSTDILRLHLTADSLVILSK		142
VN1R4 (<i>H. sapiens</i>)	-----MASRYVAVGMILSQTVVGVLGSESVLLHLYSFYCTGCRLRSTDILIVKHLIVANFLAIRCK		60
	TM2	TM3	
dgcT (<i>E. coli</i>)	TVIIIQQTIEERLTSS-----	VVQNDIAIYYLFRMSLCILIFLALVNKVSSEN-----	138
RXFP1 (<i>H. sapiens</i>)	FVIGGFDLKF-RGEYNKHAQLWMESTHCQLVGSALISTEVSVLLLTFLTLEKYICIVYPFR-----	CVR	522
VN1R5 (<i>H. sapiens</i>)	AIIIVSLDFFG-SQNTQ-----	DDLRYKVIVFLKVMRGLSICTPCLLSVLQAIISPSIFSLAK--LKH	158
VN1R1 (<i>H. sapiens</i>)	GIPQTMAAFQ-LKYLL-----	NDTGCKFFVYHRVGTTRVSLSTICLNGFQAIKNPSICKWME--IKI	162
VN1R3 (<i>H. sapiens</i>)	GIPQTMAAFQ-LKDSL-----	SDIGCKFFVYVHRVGRVAVCVGNACLLSVFQVITISPSEFRWAEIKLH	123
VN1R2 (<i>H. sapiens</i>)	RIPETMATFG-LKHFD-----	NYFGCKFLLYAHRVGRGVSIGSTCLLSVFQVITINPRNSRWAE--MKV	203
VN1R4 (<i>H. sapiens</i>)	GVPQTMAAFQ-VRYFL-----	NALGCKLVFYLHRVGRGVSIGTCLLSVFQVITVSSRKSRLWAK--LKE	121
	TM4		
dgcT (<i>E. coli</i>)	-TKQRNLFSSKMTLCISLFFVFGGPIVAHILSHSYESYN-----	LHIAELTNENGQVVKAS	194
RXFP1 (<i>H. sapiens</i>)	PGKCRITIVLILWIITGFIVAFIPLSNKEFFK-NYYGTNGVCFPLHSED-TESIGAQIYSVAIFLGINLA		590
VN1R5 (<i>H. sapiens</i>)	PSASHILGFFFLSWVLNMFIVIFCCTLRLLP-LVKRGQSSVCHT-----	ALFLFAHELHPQETVFHTND	221
VN1R1 (<i>H. sapiens</i>)	RSRPRIDFCCLLCWAPHVLMNASVLLLVNGLPL--SKNSSAKNNYGCYSY-KASKRFSSLHAVIYFSPDFM		230
VN1R3 (<i>H. sapiens</i>)	AHKYIRSFILVLCWILNTLVNITVLLHVTGKW--NSINSTNDYGYCSGGSRSRIPHSILHVLSSLDVL		192
VN1R2 (<i>H. sapiens</i>)	KAPTYYIGLSNLCWAFHMLVNAIFPIYTTGKW--SNNNITKKGDLYGCSAPLSDEVTKSVYAALTSTFHDVL		272
VN1R4 (<i>H. sapiens</i>)	KAPKHVGSVLLCWIVCMLVNIIFPMYVTGKW--NYTNITVNEDLYGCSGGGNKIAQTLRAMLLSFDPVL		190
	TM5	TM6	
dgcT (<i>E. coli</i>)	YVTIMIFMWLTLLSVNLYENG-----	LYRDIWNGVTVIAFCVLYNLSLLFMSRY	244
RXFP1 (<i>H. sapiens</i>)	AFIIIVFSYGSMEFYSVHQSAITATE-----	RNOVKKEMILAKRFFIFIVFDALCWEIFVVKFL	650
VN1R5 (<i>H. sapiens</i>)	FEGCHLYRVHGPIKRLHGDYFIQTIRGYLSAFTQPA--CPRVSPVKRASQAILLLVSFVFTYVWDFTSFSG		291
VN1R1 (<i>H. sapiens</i>)	SLGFMVWASGSMVFLLYRHKQOVQHNSNRL-----	SCRPSQEARATHIMVLVSVFVYFVSHSFTITW	295
VN1R3 (<i>H. sapiens</i>)	CLGLMLTLAGSGMVFILHRHKQOVQHIHGT-----	NLSARSSPESRVITQSILVLVSLCYFTRSPPSLH	255
VN1R2 (<i>H. sapiens</i>)	CLGLMLWASSSIVLVLYRHKQOVQHIHGRNNI-----	YPNSSPGNRAIQSILALVSTFALCYALSFTIYVY	337
VN1R4 (<i>H. sapiens</i>)	CLGLMLWVSSSMVCILHRHKQOVQHIHGRSDI-----	SPRASPENRATQSILILVSTFVSSYTLSCLEQVC	255
	TM7		
dgcT (<i>E. coli</i>)	SVS-----TWYISRTIEVVSKLTVMVIFMCHIFSALRVTKNIAH--DP		286
RXFP1 (<i>H. sapiens</i>)	SLLQVEIPGTITTSWVVIFILPINSALNPILYTLTRPFEKEMIHFRWFYNYR		700
VN1R5 (<i>H. sapiens</i>)	GVT--WINDSLLVWLOVIVANSYAAISPLMLIYADNQIFKTLQMLWFXYL		339
VN1R1 (<i>H. sapiens</i>)	TTIV-VANPGQWIVTNSVLVASCFFPARSPFVILMSDTHISOFCFACRTRKT		344
VN1R3 (<i>H. sapiens</i>)	MSL--FPNPSWWLLNTSALITACFPMVSPFVLMRHRPRLGSAACCGRNP		304
VN1R2 (<i>H. sapiens</i>)	LAL--FDNSSWWLVNTAALIIACFPPTISPFVLMCRDPSRRLCSICCRNNR		386
VN1R4 (<i>H. sapiens</i>)	MAL-LDNPNSSLVNTSALMSVCFPTLSPFVLMSCDPSVYRFFCFWAKR---		301

Supplemental Figure S4. Sequence alignment between *E. coli* cdgI and dgcT with human GPCR proteins

The 7TM domains of cdgI (A) and dgcT (B) of *E. coli* were aligned with a collection of human GPCRs. The sequence alignment was performed by incorporating the cdgI and dgcT sequences to the existing alignment result of 846 human GPCR proteins using ClustalX2. (PLoS Comput. Biol. **2016**, 12(3), e1004805) The established alignment of human GPCR proteins was generated using a structure-guided sequence alignment method. The figure displays the human GPCR proteins that align best to cdgI and dgcT within the multiple sequence alignment file. The color indicates residue groups (blue, hydrophobic; red, positive charge; magenta, negative charge; green, polar).