0031-6997/05/5702-279–288$7.00
PHARMACOLOGICAL REVIEWS
Vol. 57, No. 2
50203/3035332
Pharmacol Rev 57:279–288, 2005
Printed in U.S.A

International Union of Pharmacology. XLVI. G Protein-Coupled Receptor List

STEVEN M. FOORD, TOM I. BONNER,[1] RICHARD R. NEUBIG, EDWARD M. ROSSER, JEAN-PHILLIPE PIN, ANTHONY P. DAVENPORT, MICHAEL SPEDDING, AND ANTHONY J. HARMAR

GlaxoSmithKline Research and Development, Stevenage, Hertfordshire, United Kingdom (S.M.F.); Laboratory of Genetics, National Institute of Mental Health, Bethesda, Maryland (T.I.B.); Department of Pharmacology, University of Michigan, Ann Arbor, Michigan (R.R.N.); Division of Neuroscience and Centre for Neuroscience Research, University of Edinburgh, Edinburgh, United Kingdom (E.M.R., A.J.H.); Centre National de la Recherche Scientifique, Montpellier, France (J.-P.P.); Clinical Pharmacology Unit, University of Cambridge, Cambridge, United Kingdom (A.P.D); and Institut de Recherches Servier (I.d.R.S.), Suresnes, France (M.S.)

***Abstract*——NC-IUPHAR (International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification) and its subcommittees provide authoritative reports on the nomenclature and pharmacology of G protein-coupled receptors (GPCRs) that summarize their structure, pharmacology, and roles in physiology and pathology. These reports are published in Pharmacological Reviews (http://www.iuphar.org/nci-uphar_arti.html) and through the International Union of Pharmacology (IUPHAR) Receptor Database web site (http://www.iuphar-db.org/iuphar-rd). The essentially complete sequencing of the human genome has allowed the cataloging of all of the human gene sequences potentially encoding GPCRs. The IUPHAR Receptor List (http://www.iuphar-db.org/iuphar-rd/list/index.htm) presents this catalog giving IUPHAR-approved nomenclature (where available), known ligands, and gene names for all of these potential receptors (excluding sensory receptors and pseudogenes) together with links to curated sequence, descriptive information, and additional links in the Entrez Gene database (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene). This list is a major new initiative of NC-IUPHAR that, through continuing curation, defines the target of our ongoing receptor classification and invites further input from the scientific community.**

I. Introduction

Although NC-IUPHAR[2] has well advanced projects to cover nuclear receptors, voltage-gated ion channels, and ligand-gated ion channels, its efforts have focused on GPCRs primarily because they represent a very large family of proteins that control many major physiological processes and are the targets of many effective drugs. The recent completion of the human genome sequence at 99% coverage (International Human Genome Sequencing Consortium, 2004) allows the identification of essentially all the GPCR genes that should be included in the IUPHAR receptor classification. Many of these genes are potential GPCRs in the sense that their sequences look like known GPCRs, but their activating ligands and signaling mechanisms are unknown. The characterization of these orphan receptors will be a major focus of pharmacology in the near future, and a well curated public list should be a very valuable resource.

The characteristic feature of all known GPCR proteins is that they have seven α-helical transmembrane domains. There are also extensive amino acid sequence similarities that divide them into several classes, each with characteristic highly conserved residues distributed throughout the molecule, which define identifying motifs, such as the DRY motif at the cytoplasmic end of the third transmembrane domain and prolines at specific positions in helices 5, 6, and 7

Address correspondence to: Steven M. Foord, GlaxoSmithKline Research and Development, Stevenage, Hertfordshire, UK. E-mail: smf3746@ggr.co.uk

[1] This article was written in a personal capacity and does not represent the opinions of the National Institutes of Health, Department of Health and Human Services, or the Federal Government.

Article, publication date, and citation information can be found at http://pharmrev.aspetjournals.org.
doi:10.1124/pr.57.2.5.

[2] Abbreviations: NC-IUPHAR, International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification; GPCR, G protein-coupled receptor; HUGO, The Human Genome Organization; NCBI, National Centre for Biotechnology Information; 7TM, seven transmembrane.

TABLE 1

Class 1 G protein-coupled receptors

Family represents the classification of orphan receptors adapted from Vassilatis et al. (2003). The IUPHAR Receptor Code is described in Humphrey and Barnard (1998). A representative, but not necessarily complete list of putative endogenous ligands is given. Provisional nomenclature is given in square brackets. NC-IUPHAR does not normally allocate names to receptors where there is only a single publication identifying the putative endogenous ligand. Gene symbol is approved by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/nomenclature/). Gene IDs are from Entrez Gene (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene).

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
5-Hydroxytryptamine	2.1:5HT:1:5HT1A:	5-Hydroxytryptamine	5-HT_{1A}	HTR1A	3350	15550	24473
5-Hydroxytryptamine	2.1:5HT:2:5HT1B:	5-Hydroxytryptamine	5-HT_{1B}	HTR1B	3351	15551	25075
5-Hydroxytryptamine	2.1:5HT:3:5HT1D:	5-Hydroxytryptamine	5-HT_{1D}	HTR1D	3352	15552	25323
5-Hydroxytryptamine	2.1:5HT:4:5HT1E:	5-Hydroxytryptamine	5-HT_{1e}	HTR1E	3354		
5-Hydroxytryptamine	2.1:5HT:5:5HT1F:	5-Hydroxytryptamine	5-HT_{1F}	HTR1F	3355	15557	60448
5-Hydroxytryptamine	2.1:5HT:6:5HT2A:	5-Hydroxytryptamine	5-HT_{2A}	HTR2A	3356	15558	29595
5-Hydroxytryptamine	2.1:5HT:7:5HT2B:	5-Hydroxytryptamine	5-HT_{2B}	HTR2B	3357	15559	29581
5-Hydroxytryptamine	2.1:5HT:8:5HT2C:	5-Hydroxytryptamine	5-HT_{2C}	HTR2C	3358	15560	25187
5-Hydroxytryptamine	2.1:5HT:9:5HT4:	5-Hydroxytryptamine	5-HT_{4}	HTR4	3360	15562	25324
5-Hydroxytryptamine		5-Hydroxytryptamine	5-HT_{5A}	HTR5A	3361	15563	25689
5-Hydroxytryptamine	2.1:5HT:10:5HT6:	5-Hydroxytryptamine	5-HT_{6}	HTR6	3362	15565	64354
5-Hydroxytryptamine	2.1:5HT:11:5HT7:	5-Hydroxytryptamine	5-HT_{7}	HTR7	3363	15566	65032
Acetylcholine (muscarinic)	2.1:ACH:1:M1A:	Acetylcholine	M_1	CHRM1	1128	12669	25229
Acetylcholine (muscarinic)	2.1:ACH:2:M2A:	Acetylcholine	M_2	CHRM2	1129	107850	81645
Acetylcholine (muscarinic)	2.1:ACH:4:M2B:	Acetylcholine	M_3	CHRM4	1132	12672	25111
Acetylcholine (muscarinic)	2.1:ACH:3:M1B:	Acetylcholine	M_4	CHRM3	1131	12671	24260
Acetylcholine (muscarinic)	2.1:ACH:5:M1C:	Acetylcholine	M_5	CHRM5	1133	12673	53949
Adenosine	2.1:ADO:1:A1:	Adenosine	A_1	ADORA1	134	11539	29290
Adenosine	2.1:ADO:2:A2A:	Adenosine	A_{2A}	ADORA2A	135	11540	25369
Adenosine	2.1:ADO:3:A2B:	Adenosine	A_{2B}	ADORA2B	136	11541	29316
Adenosine	2.1:ADO:4:A3:	Adenosine	A_3	ADORA3	140	11542	25370
Adrenoceptors	2.1:ADR:1:A1A:	Noradrenaline	α_{1A}	ADRA1A	148	11549	29412
Adrenoceptors	2.1:ADR:2:A1B:	Adrenaline	α_{1B}	ADRA1B	147	11548	24173
Adrenoceptors	2.1:ADR:3:A1D:	Adrenaline	α_{1D}	ADRA1D	146	11550	29413
Adrenoceptors	2.1:ADR:4:A2A:	Adrenaline	α_{2A}	ADRA2A	150	11551	25083
Adrenoceptors	2.1:ADR:5:A2B:	Adrenaline	α_{2B}	ADRA2B	151	11552	24174
Adrenoceptors	2.1:ADR:6:A2C:	Adrenaline	α_{2c}	ADRA2C	152	11553	24175
Adrenoceptors	2.1:ADR:7:B1:	Noradrenaline	β_1	ADRB1	153	11554	24925
Adrenoceptors	2.1:ADR:8:B2:	Adrenaline	β_2	ADRB2	154	11555	24176
Adrenoceptors	2.1:ADR:9:B3:	Adrenaline	β_3	ADRB3	155	11556	25645
Anaphylatoxin		Anaphylatoxin C5a, C5a des Arg[74]		GPR77	27202	319430	445269
Anaphylatoxin		Anaphylatoxin C5a		C5R1	728	12273	113959
Anaphylatoxin		Anaphylatoxin C3a		C3AR1	719	12267	84007
Angiotensin	2.1:ANG:1:AT1:	Angiotensin	AT_1	AGTR1	185	11607	81638
Angiotensin	2.1:ANG:2:AT2:	Angiotensin	AT_2	AGTR2	186	11609	24182
Apelin	2.1:APJ:1:APJ:	Apelin		AGTRL1	187	23796	83518
Bombesin	2.1:BB:1:BB1:	Neuromedin B	BB_1	NMBR	4829	18101	25264
Bombesin	2.1:BB:2:BB2:	Gastrin-releasing peptide	BB_2	GRPR	2925	14829	24938
Bombesin	2.1:BB:3:BB3:		BB_3	BRS3	680	12209	260319
Bradykinin	2.1:BK:1:B1:	Bradykinin	B_1	BDKRB1	623	12061	81509
Bradykinin	2.1:BK:2:B2:	Bradykinin	B_2	BDKRB2	624	12062	25245
Cannabinoid	2.1:CB:1:CB1:	Cannabinoid	CB_1	CNR1	1268	12801	25248
Cannabinoid	2.1:CB:2:CB2:	Cannabinoid	CB_2	CNR2	1269	12802	57302
Chemokine	2.1:CHK:1:CXC1:	CXCL8	CXCR1	IL8RA	3577	227288	54258
Chemokine	2.1:CHK:2:CXC2:	CXCL1–3, CXCL5–8	CXCR2	IL8RB	3579	12765	29385
Chemokine	2.1:CHK:3:CXC3:	CXCL9–11	CXCR3	CXCR3	2833	12766	84475
Chemokine	2.1:CHK:4:CXC4:	CXCL12	CXCR4	CXCR4	7852	12767	60628
Chemokine	2.1:CHK:5:CXC5:	CXCL13	CXCR5	BLR1	643	12145	29363
Chemokine	2.1:CHK:6:CC1:	CCL3, CCL5, CCL7, CCL8, CCL13–16, CCL23	CCR1	CCR1	1230	12768	57301
Chemokine	2.1:CHK:7:CC2:	CCL2, CCL7, CCL8, CCL13	CCR2	CCR2	1231	12772	60463
Chemokine	2.1:CHK:8:CC3:	CCL11 (eotaxin); CCL5, CCL7, CCL8, CCL13, CCL15, CCL24, CCL26	CCR3	CCR3	1232	12771	117027
Chemokine	2.1:CHK:9:CC4:	CCL17, CCL22	CCR4	CCR4	1233	12773	171054
Chemokine	2.1:CHK:10:CC5:	CCL3, CCL4, CCL5, CCL8, CCL14	CCR5	CCR5	1234	12774	117029
Chemokine	2.1:CHK:11:CC6:	CCL20	CCR6	CCR6	1235	12458	
Chemokine	2.1:CHK:12:CC7:	CCL19, CCL21	CCR7	CCR7	1236	12775	287673
Chemokine	2.1:CHK:13:CC8:	CCL1, CCL4, CCL17	CCR8	CCR8	1237	12776	
Chemokine	2.1:CHK:14:CC9:	CCL25	CCR9	CCR9	10803	12769	282832
Chemokine	2.1:CHK:15:CC10:	CCL26–28	CCR10	CCR10	2826	12777	363682
Chemokine	2.1:CHK:17:CX3C1:	CX3CL1	CX_3CR1	CX3CR1	1524	13051	171056
Chemokine	2.1:CHK:18:XC1:	XCL1, XCL2	XCR1	XCR1	2829	23832	301086

TABLE 1
Continued

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Chemokine	2.1:CHK:19:CXC6:	CXCL16		CXCR6	10663	80901	
Cholecystokinin	2.1:CCK:1:CCK1:	Cholecystokinin	CCK_1	CCKAR	886	12425	24889
Cholecystokinin	2.1:CCK:2:CCK2:	Cholecystokinin, gastrin	CCK_2	CCKBR	887	12426	25706
Dopamine	2.1:DA:1:D1A:	Dopamine	D_1	DRD1	1812	13488	25678
Dopamine	2.1:DA:2:D2A:	Dopamine	D_2	DRD2	1813	13489	24318
Dopamine	2.1:DA:3:D2B:	Dopamine	D_3	DRD3	1814	13490	29238
Dopamine	2.1:DA:4:D2C:	Dopamine	D_4	DRD4	1815	13491	25432
Dopamine	2.1:DA:5:D1B:	Dopamine	D_5	DRD5	1816	13492	25195
Endothelin	2.1:ET:1:ETA:	Endothelin 1, endothelin 2	ET_A	EDNRA	1909	13617	24326
Endothelin	2.1:ET:2:ETB:	Endothelins 1, 2 and 3	ET_B	EDNRB	1910	13618	50672
Free fatty acid	2.1:FFA:3:FFA3	Acetate		GPR43	2867	233079	292794
Free fatty acid	2.1:FFA:2:FFA2	Carboxylic acids		GPR41	2865		365228
Free fatty acid				GPR42[a]	2866		
Free fatty acid	2.1:FFA:1:FFA1	Long chain carboxylic acids		GPR40	2864	233081	266607
G protein-coupled bile acid	2.1:BA:1:BA	Bile acids		GPBAR1	151306	227289	
Galanin	2.1:GAL:1:GAL1:	Galanin	GAL_1	GALR1	2587	14427	50577
Galanin	2.1:GAL:2:GAL2:	Galanin	GAL_2	GALR2	8811	14428	29234
Galanin	2.1:GAL:3:GAL3:	Galanin	GAL_3	GALR3	8484	14429	29235
Motilin	2.1:MTLN:1:MTLN	Motilin	Motilin	MLNR	2862		
Ghrelin	2.1:GRLN:1:GRLN	Ghrelin	Ghrelin	GHSR	2693	208188	84022
Glycoprotein hormone	2.1:GLYC:3:FSH:	Follicle-stimulating hormone		FSHR	2492	14309	25449
Glycoprotein hormone	2.1:GLYC:2:LHCG:	Luteinizing hormone, chorionic gonadotropin		LHCGR	3973	16867	25477
Glycoprotein hormone	2.1:GLYC:1:TSH:	Thyroid-stimulating hormone		TSHR	7253	22095	25360
GnRH	2.1:GNRH:1:GNRH1:	Gonadotrophin-releasing hormone		GNRHR	2798	14715	81668
GnRH		Gonadotrophin-releasing hormone		GNRHR2	114814		
Histamine	2.1:HIST:1:H1:	Histamine	H_1	HRH1	3269	15465	24448
Histamine	2.1:HIST:2:H2:	Histamine	H_2	HRH2	3274	15466	25461
Histamine	2.1:HIST:3:H3:	Histamine	H_3	HRH3	11255	99296	85268
Histamine	2.1:HIST:4:H4:	Histamine	H_4	HRH4	59340	225192	170704
KiSS1-derived peptide	2.1:KISS:1:KISS	KiSS-1 gene product		GPR54	84634	114229	78976
Leukotriene and lipoxin	2.1:LT:1:CLT1:	Leukotriene D_4	$CysLT_1$	CYSLTR1	10800	58861	114099
Leukotriene and lipoxin	2.1:LT:2:CLT2:	Leukotriene C_4	$CysLT_2$	CYSLTR2	57105	70086	170926
Leukotriene and lipoxin	2.1:LT:3:BLT1:	Leukotriene B_4	BLT_1	LTB4R	1241	16995	59264
Leukotriene and lipoxin	2.1:LT:4:BLT2:	Leukotriene B_4	BLT_2	LTB4R2	56413	57260	114098
Leukotriene and lipoxin	2.1:LT:5:OXE:	5-Oxo-6,8,11,14-eicosatetraenoic acid	OXE	OXER1	165140		
Leukotriene and lipoxin	2.1:LT:6:ALX:	Lipoxin A[b]	ALX	FPRL1	2358	14294	171328
Lysophospholipid	2.1:LPL:LPA1:	Lysophosphatidic acid	LPA_1	EDG2	1902	14745	116744
Lysophospholipid	2.1:LPL:LPA2:	Lysophosphatidic acid	LPA_2	EDG4	9170	53978	
Lysophospholipid	2.1:LPL:LPA3:	Lysophosphatidic acid	LPA_3	EDG7	23566	65086	66025
Lysophospholipid	2.1:LPL:SIP1:	Sphingosine 1-phosphate	$S1P_1$	EDG1	1901	13609	29733
Lysophospholipid	2.1:LPL:SIP2:	Sphingosine 1-phosphate	$S1P_2$	EDG5	9294	14739	29415
Lysophospholipid	2.1:LPL:S1P3:	Sphingosine 1-phosphate	$S1P_3$	EDG3	1903	13610	29736
Lysophospholipid	2.1:LPL:SIP4:	Sphingosine 1-phosphate	$S1P_4$	EDG6	8698	13611	314649
Lysophospholipid	2.1:LPL:SIP5:	Sphingosine 1-phosphate	$S1P_5$	EDG8	53637	94226	60399
Melanin-concentrating hormone	2.1:MCH:1:MCH1:	Melanin-concentrating hormone	MCH_1	GPR24	2847	207911	83567
Melanin-concentrating hormone	2.1:MCH:2:MCH2:	Melanin-concentrating hormone	MCH_2	GPR145	84539		
Melanocortin	2.1:MC:1:MC1:	α-Melanocyte stimulating hormone	MC_1	MC1R	4157	17199	292083
Melanocortin	2.1:MC:2:MC2:	Adrenocorticotropic hormone	MC_2	MC2R	4158	17200	282839
Melanocortin	2.1:MC:3:MC3:	γ-Melanocyte stimulating hormone	MC_3	MC3R	4159	17201	29310
Melanocortin	2.1:MC:4:MC4:	β-Melanocyte stimulating hormone	MC_4	MC4R	4160	17202	25635
Melanocortin	2.1:MC:5:MC5:	α-Melanocyte stimulating hormone	MC_5	MC5R	4161	17203	25726
Melatonin	2.1:MLT:1:MT1:	Melatonin	$[MT_1]$	MTNR1A	4543	17773	114211
Melatonin	2.1:MLT:1:MT2:	Melatonin	$[MT_2]$	MTNR1B	4544	244701	192646
Neuromedin U	2.1:NMU:2:NMU2	Neuromedin U	NMU2	NMUR2	56923	216749	64042
Neuromedin U	2.1:NMU:1:NMU1	Neuromedin U	NMU1	NMUR1	10316	14767	65276
Neuropeptide FF/neuropeptide AF		Neuropeptide FF		GPR147	64106		64107
Neuropeptide FF/neuropeptide AF		Neuropeptide FF		GPR74	10886	104443	78964

TABLE 1
Continued

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Neuropeptide S		Neuropeptide S		GPR154	387129	319239	
Neuropeptide W/ neuropeptide B		Neuropeptide W, neuropeptide B		GPR8	2832		
Neuropeptide W/ neuropeptide B		Neuropeptide W, neuropeptide B		GPR7	2831	14769	297795
Neuropeptide Y	2.1:NPY:1:Y1:	Neuropeptide Y	Y_1	NPY1R	4886	18166	29358
Neuropeptide Y	2.1:NPY:2:Y2:	Neuropeptide Y	Y_2	NPY2R	4887	18167	66024
Neuropeptide Y	2.1:NPY:3:Y4:	Pancreatic polypeptide	Y_4	PPYR1	5540	19065	29471
Neuropeptide Y	2.1:NPY:4:Y5:	Neuropeptide Y	Y_5	NPY5R	4889	18168	25340
Neurotensin	2.1:NTSN:1:NTS1:	Neurotensin	NTS_1	NTSR1	4923	18216	366274
Neurotensin	2.1:NTSN:2:NTS2:	Neurotensin	NTS_2	NTSR2	23620	18217	64636
N-Formylpeptide family				FPRL2	2359		
N-Formylpeptide family		*N*-Formyl-L-Met-L-Leu-L-Phe (fMLP)		FPR1	2357	14293	
Nicotinic acid				GPR81	27198	243270	
Nicotinic acid		Nicotinic acid (low affinity)		GPR109B	8843		
Nicotinic acid		Nicotinic acid (high affinity)		GPR109A	338442	80885	353250
Opioid	2.1:OP:2:DELTA:	β-Endorphin	δ	OPRD1	4985	18386	24613
Opioid	2.1:OP:3:KAPPA:	Dynorphin A	κ	OPRK1	4986	18387	29335
Opioid	2.1:OP:1:MU:	β-Endorphin	μ	OPRM1	4988	18390	25601
Opioid	2.1:OP:4:NOCIC:	Nociceptin/orphanin FQ	NOP	OPRL1	4987	18389	29256
Opsin-like				OPN3	23596	13603	
Orexin (hypocretin)		Orexin A, orexin B	OX_1	HCRTR1	3061	230777	25593
Orexin (hypocretin)		Orexin A, orexin B	OX_2	HCRTR2	3062	387285	25605
P2Y	2.1:NUCT:1:P2Y1:	ADP	$P2Y_1$	P2RY1	5028	18441	25265
P2Y	2.1:NUCT:2:P2Y2:	UTP, ATP	$P2Y_2$	P2RY2	5029	18442	29597
P2Y	2.1:NUCT:3:P2Y4:	UTP	$P2Y_4$	P2RY4	5030	57385	63843
P2Y	2.1:NUCT:4:P2Y6:	UDP	$P2Y_6$	P2RY6	5031	233571	117264
P2Y	2.1:NUCT:5:P2Y11:	ATP	$P2Y_{11}$	P2RY11	5032		
P2Y	2.1:NUCT:6:P2Y12:	ADP	$[P2Y_{12}]$	P2RY12	64805	70839	64803
P2Y	2.1:NUCT:7:P2Y13:	ADP	$[P2Y_{13}]$	P2RY13	53829	74191	310444
P2Y		UDP-Glucose		P2RY14	9934	140795	171108
Peptide P518		RF-Amide P518 gene product[c]		GPR103	84109	243407	
Platelet-activating factor	2.1:PAF:1:PAF	Platelet-activating factor	PAF	PTAFR	5724	19204	58949
Prokineticin	2.1:PROK:1:PK1	Prokineticins 1 and 2	PK_1	GPR73	10887	58182	192648
Prokineticin	2.1:PROK:2:PK2	Prokineticins 1 and 2	PK_2	GPR73L1	128674	246313	192649
Prolactin-releasing peptide	2.1:PRP:1:PRP	Prolactin-releasing peptide	PRP	GPR10	2834	226278	246075
Prostanoid	2.1:PG:1:DP:	Prostaglandin D_2	DP	PTGDR	5729	19214	63889
Prostanoid	2.1:PG:2:EP1:	Prostaglandin E_2	EP_1	PTGER1	5731	19216	25637
Prostanoid	2.1:PG:3:EP2:	Prostaglandin E_2	EP_2	PTGER2	5732	19217	81752
Prostanoid	2.1:PG:4:EP3:	Prostaglandin E_2	EP_3	PTGER3	5733	19218	24929
Prostanoid	2.1:PG:5:EP4:	Prostaglandin E_2	EP_4	PTGER4	5734	19219	84023
Prostanoid	2.1:PG:6:FP:	Prostaglandin F_{2a}	FP	PTGFR	5737	19220	25652
Prostanoid	2.1:PG:7:IP:	Prostacyclin	IP_1	PTGIR	5739	19222	292661
Prostanoid	2.1:PG:8:TP:	Thromboxane A_2	TP	TBXA2R	6915	21390	24816
Prostanoid		11-Dehydro-thromboxane B_2[c]		GPR44	11251	14764	29406
Protease-activated	2.1:PAR:1:PAR1	Thrombin	PAR1	F2R	2149	14062	25439
Protease-activated	2:1:PAR:2:PAR2	Serine proteases	PAR2	F2RL1	2150	14063	116677
Protease-activated	2.1:PAR:3:PAR3	Thrombin	PAR3	F2RL2	2151	14064	29636
Protease-activated	2.1:PAR:4:PAR4	Serine proteases	PAR4	F2RL3	9002	14065	116498
Relaxin		Relaxin		LGR7	59350	381489	
Relaxin		Relaxin		LGR8	122042	170458	171158
Relaxin		Relaxin-3		RLN3R1	51289	239336	294807
Relaxin		INSL5, relaxin-3		RLN3R2	339403	242093	
Somatostatin	2.1:SRIF:1:SRIF1A:	Somatostatin	sst_2	SSTR2	6752	20606	54305
Somatostatin	2.1:SRIF:2:SRIF1B:	Somatostatin	sst_5	SSTR5	6755	20609	25354
Somatostatin	2.1:SRIF:3:SRIF1C:	Somatostatin	sst_3	SSTR3	6753	20607	171044
Somatostatin	2.1:SRIF:4:SRIF2A:	Somatostatin	sst_1	SSTR1	6751	20605	25033
Somatostatin	2.1:SRIF:5:SRIF2B:	Somatostatin	sst_4	SSTR4	6754	20608	25555
SPC/LPC		(lyso)Phospholipid mediators[d]		GPR65	8477	14744	299242
SPC/LPC		(lyso)Phospholipid mediators[d]		GPR4	2828	319197	308408
SPC/LPC		(lyso)Phospholipid mediators[d]		GPR68	8111	238377	
SPC/LPC		(lyso)Phospholipid mediators[d]		GPR132	29933	56696	314480
Tachykinin	2.1:TAC:1:NK1:	Substance P	NK_1	TACR1	6869	21336	24807
Tachykinin	2.1:TAC:2:NK2:	Neurokinin A	$[NK_2]$	TACR2	6865	21337	25007

TABLE 1
Continued

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Tachykinin	2.1:TAC:3:NK3:	Neurokinin B	NK_3	TACR3	6870	21338	24808
Trace Amine		β-Phenylethylamine, tyramine[c]	[TA_1]	TRAR1	134864	111174	113914
TRH	2.1:TRH:1:TRH:	Thyrotropin-releasing hormone	TRH	TRHR	7201	22045	25570
Urotensin	2.1:UT:1:UT1:	Urotensin II	UT	UTS2R	2837	217369	57305
Vasopressin/oxytocin	2.1:OXY:1:OT:	Oxytocin	OT	OXTR	5021	18430	25342
Vasopressin/oxytocin	2.1:VASO:1:V1A:	Vasopressin	V_{1A}	AVPR1A	552	54140	25107
Vasopressin/oxytocin	2.1:VASO:2:V2:	Vasopressin	V_2	AVPR2	554	12000	25108
Vasopressin/oxytocin	2.1:VASO:3:V1B:	Vasopressin	V_{1B}	AVPR1B	553	26361	29462
OrphanA1		Sphingosine 1-phosphate[c]		GPR3	2827	14748	266769
OrphanA1		Sphingosine 1-phosphate[c]		GPR12	2835	14738	80840
OrphanA1		Sphingosine 1-phosphate[c]		GPR6	2830	140741	83683
OrphanA2				GPR52	9293		
OrphanA2				GPR21	2844	338346	
OrphanA3				GPR78	27201		
OrphanA3				GPR26	2849	233919	192153
OrphanA4				GPR37	2861	14763	117549
OrphanA4				GPR37L1	9283	171469	252939
OrphanA6				GPR63	81491	81006	297952
OrphanA6				GPR45	11250	93690	301372
OrphanA7				GPR83	10888	14608	140595
OrphanA9				GRCA[e]	27239	14788	362436
OrphanA9				GPR153	387509	100129	
OrphanA12		Lysophosphatidic acid[c]		GPR23	2846	78134	302378
OrphanA12				P2RY5	10161	67168	
OrphanA13				P2RY10	27334	78826	317219
OrphanA13				GPR174	84636		
OrphanA14				GPR142	350383	217302	303661
OrphanA14				GPR139	124274		293545
OrphanA15				ADMR	11318	11536	29307
OrphanA15				CMKOR1	57007	12778	84348
OrphanLGR				LGR4	55366	107515	286994
OrphanLGR				LGR5	8549	14160	299802
OrphanLGR				LGR6	59352		
OrphanSREB				GPR85	54329	64450	64020
OrphanSREB				GPR27	2850	14761	65275
OrphanSREB				GPR173	54328	70771	64021
Orphan		Succinate[c]		SUCNR1	56670	84112	408199
Orphan		α-Ketoglutarate[c]		OXGR1	27199	239283	290493
Orphan (chemokine receptor-like)				CCRL2	9034	54199	
Orphan (Mas-related)				MAS1	4142	17171	25153
Orphan (Mas-related)				MAS1L	116511		
Orphan (Mas-related)		β-Alanine[c]		MRGPRD	116512		
Orphan (Mas-related)				MRGPRE	116534		
Orphan (Mas-related)				MRGPRF	116535		
Orphan (Mas-related)				MRGPRG	386746		
Orphan (Mas-related)		BAM8–22[c]		MRGX1[e]	259249		282547
Orphan (Mas-related)		Cortistatin[c]		MRGX2[e]	117194		
Orphan (Mas-related)				MRGX3[e]	117195		
Orphan (Mas-related)				MRGX4[e]	117196		
Orphan (melatonin-like)				GPR50	9248	14765	117097
Orphan (P2Y-like)				GPR87	53836	84111	
Orphan (trace amine-like)			[TA_3]	TRAR3[f]	134860		319107
Orphan (trace amine-like)			[TA_4]	TRAR4	319100		294124
Orphan (trace amine-like)			[TA_5]	TRAR5	83551		
Orphan (trace amine-like)				PNR[e]	9038		294123
Orphan (trace amine-like)				GPR57[g]	9288		
Orphan (trace amine-like)				GPR58	9287		294121
Other orphan genes		RARRES2[c]		CMKLR1	1240	14747	60669
Other orphan genes				EBI2	1880	321019	306193
Other orphan genes				GPR160	26996	71862	
Other orphan genes				GPR[e]	11245		117257
Other orphan genes				GPR1	2825	241070	25457
Other orphan genes				GPR101	83550		317608
Other orphan genes				GPR119	139760	236781	
Other orphan genes				GPR120	338557	107221	294075
Other orphan genes				GPR135	64582		314213
Other orphan genes				OPN5	221391	353344	316259
Other orphan genes				GPR141	353345	353346	291179
Other orphan genes				GPR146	115330	80290	
Other orphan genes				GPR148	344561		
Other orphan genes				GPR149	344758	229357	192251

TABLE 1
Continued

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Other orphan genes				GPR15	2838		288181
Other orphan genes				GPR150	285601	238725	
Other orphan genes				GPR152	390212	269053	
Other orphan genes				GPR161	23432		289180
Other orphan genes				GPR17	2840		
Other orphan genes				GPR171	29909	229323	
Other orphan genes				GPR18	2841	110168	306191
Other orphan genes				GPR19	2842	14760	140664
Other orphan genes				GPR20	2843	239530	60667
Other orphan genes				GPR22	2845	73010	
Other orphan genes				GPR25	2848		363993
Other orphan genes				GPR30	2852	76854	171104
Other orphan genes				GPR31	2853	107431	292310
Other orphan genes				GPR32	2854		
Other orphan genes				GPR33	2856	14762	299007
Other orphan genes				GPR34	2857	23890	
Other orphan genes				GPR35	2859	64095	
Other orphan genes				GPR39	2863	71111	
Other orphan genes				GPR55	9290		
Other orphan genes				GPR61	83873	229714	310780
Other orphan genes				GPR62	118442		
Other orphan genes				GPR75	10936	237716	
Other orphan genes				GPR79[h]	27200		
Other orphan genes				GPR82	27197	319200	
Other orphan genes				GPR84	53831	80910	367000
Other orphan genes				GPR88	54112	64378	64443
Other orphan genes				GPR92	57121		
Other orphan genes				P2RY8	286530		
Other orphan genes				GPR151	134391	240239	307475

BAM8–22, 15 amino acid C-terminal fragment of bovine adrenal medulla peptide 22.
[a] Very closely related to GPR41. May be a pseudogene.
[b] Under review by IUPHAR.
[c] Proposed ligand(s) supported by a single publication.
[d] Sphingosine-1-phosphate, lysophosphatidic acid, sphingosylphosphorylcholine, and phosphatidic acid.
[e] Interim gene symbol. The official symbol and name have not been established.
[f] A polymorphism introduces a stop codon in some individuals.
[g] May be a pseudogene.
[h] Probable pseudogene.

of the very large class related to rhodopsin. Analysis of the human genome sequence using a variety of techniques ranging from simple BLAST searches for genes with sequences similar to known GPCRs to the use of various gene prediction algorithms which are then filtered for the presence of GPCR motifs have generated well over 1000 candidate genes. A critical but not uniformly successful step in the analysis is to remove the false positives, i.e., the nonfunctional or incomplete genes known as pseudogenes. In some cases in the literature, these predictions are based on inaccurate early versions of the genomic sequence, whereas in others, the predictions do not encode full seven transmembrane domain proteins but retain enough of a GPCR motif for the prediction to be labeled a GPCR.

Pseudogenes are genes that, in the absence of selective pressure to maintain the gene on an evolutionary time scale, have accumulated disabling mutations (Harrison and Gerstein, 2002; Harrison et al., 2002). Most arise from a continuing evolutionary process of gene duplication in which a small fraction of the duplicated genes find new functions and are maintained while the vast majority decay through accumulated mutations. Severely disabled genes are easy to recognize since they have accumulated multiple disruptions of the coding sequence. At the other end of the spectrum are genes where only a single nucleotide creates a frameshift or in-frame termination codon leading to a truncated protein. In the latter cases, one must be concerned whether the reference human genomic sequence is truly representative of the human population or represents a polymorphism or sequencing error. A known example of such a polymorphism is the trace amine family receptor TRAR3, which has a polymorphic premature stop codon with an allele frequency of about 20% (Vanti et al., 2003). It is inevitable that some pseudogenes will not be excluded because their disabling mutations are too subtle to be easily recognized. In addition, we have chosen to include some pseudogenes with appropriate annotation when their omission could cause confusion. Some pseudogenes are included because their DNA sequence is so close to that of a functional GPCR that they might confound assays of mRNA expression. More commonly, confusion could arise as to whether a

TABLE 2

Class 2 G protein-coupled receptors

Family represents the classification of orphan receptors adapted from Vassilatis et al. (2003). The IUPHAR Receptor Code is described in Humphrey and Barnard (1998). A representative, but not necessarily complete list of putative endogenous ligands is given. Provisional nomenclature is given in square brackets. Gene symbol approved by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/nomenclature/). Gene IDs from Entrez Gene (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene). For definition of LNBTM7 receptors see Stacey et al., 2000.

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Calcitonin receptor family	2.2.CALC:1:CT:	Calcitonin	CT	CALCR	799	12311	116506
Calcitonin receptor family	2.2.CALC:2:AMY1:	Amylin, CGRP	AMY_1[a]	CALCR	799	12311	116506
				RAMP1	10267	51801	58965
Calcitonin receptor family	2.2.CALC:3:AMY2:	Amylin	AMY_2[a]	CALCR	799	12311	116506
				RAMP2	10266	54409	58966
Calcitonin receptor family	2.2.CALC:4:AMY3:	Amylin, CGRP	AMY_3[a]	CALCR	799	12311	116506
				RAMP3	10268	56089	56820
Calcitonin receptor family				CALCRL	10203	54598	25029
Calcitonin receptor family	2.2.CALCL:1: CGRP1:	CGRP, adrenomedullin	$CGRP_1$[a]	CALCRL	10203	54598	25029
				RAMP1	10267	51801	58965
Calcitonin receptor family	2.2.CALCL:1:AM1:	Adrenomedullin, CGRP	AM_1[a]	CALCRL	10203	54598	25029
				RAMP2	10266	54409	58966
Calcitonin receptor family	2.2.CALCL:1:AM2:	Adrenomedullin, CGRP	AM_2[a]	CALCRL	10203	54598	25029
				RAMP3	10268	56089	56820
CRF receptor family	2.2:CRF:1:CRF1:	Corticotropin releasing factor, urocortins	CRF_1	CRHR1	1394	12921	58959
CRF receptor family	2.2:CRF:2:CRF2:	Urocortins	CRF_2	CRHR2	1395	12922	64680
Glucagon receptor family	2.2:GHRH:1:GHRH:	Growth hormone-releasing hormone	GHRH	GHRHR	2692	14602	25321
Glucagon receptor family	2.2:GIP:1:GIP:	Gastric inhibitory polypeptide	GIP	GIPR	2696	107830	25024
Glucagon receptor family	2.2:GLP1:1:GLP1:	Glucagon-like peptide 1	GLP-1	GLP1R	2740	14652	25051
Glucagon receptor family	2.2:GLP2:1:GLP2:	Glucagon-like peptide 2	GLP-2	GLP2R	9340	93896	60432
Glucagon receptor family	2.2:GCG:1:GCG:	Glucagon	Glucagon	GCGR	2642	14527	24953
Glucagon receptor family	2.2:SEC:1:SEC:	Secretin	Secretin	SCTR	6344	319229	81779
PTH receptor family	2.2:PTH:2:PTH2:	TIP-39	[PTH2]	PTHR2	5746	213527	81753
PTH receptor family	2.2:PTH:1:PTH1:	Parathyroid hormone	[PTH1]	PTHR1	5745	19228	56813
VIP/PACAP	2.2:VPAC:1:VPAC1:	VIP, PACAP	$VPAC_1$	VIPR1	7433	22354	24875
VIP/PACAP	2.2:VPAC:2:PAC1:	PACAP	PAC_1	ADCYAP1R1	117	11517	24167
VIP/PACAP	2.2:VPAC:3:VPAC2:	VIP, PACAP	$VPAC_2$	VIPR2	7434	22355	29555
LNB7TM				GPR64	10149	237175	
LNB7TM				GPR56	9289	14766	
LNB7TM				GPR115	221393		
LNB7TM				GPR114	221188		
LNB7TM:Brain specific angiogenesis inhibitor				BAI1	575	107831	
LNB7TM:Brain specific angiogenesis inhibitor				BAI2	576	230775	
LNB7TM:Brain specific angiogenesis inhibitor				BAI3	577	210933	
LNB7TM:Proto-cadherin				CELSR1	9620	12614	300128
LNB7TM:Proto-cadherin				CELSR2	1952	53883	83465
LNB7TM:Proto-cadherin				CELSR3	1951	107934	
LNB7TM:EGF, mucin-like receptor				EMR1	2015	13733	
LNB7TM:EGF, mucin-like receptor				EMR2	30817	Absent	Absent
LNB7TM				GPR97	222487	54672	
LNB7TM				GPR110	266977		
LNB7TM				GPR111	222611		

TABLE 2
Continued

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
LNB7TM				GPR112	139378		
LNB7TM				GPR113	165082		
LNB7TM				GPR116	221395		
LNB7TM				MASS1	84059	110789	
LNB7TM				ELTD1	64123		64124
LNB7TM				GPR123	84435		
LNB7TM				GPR124	25960	78560	
LNB7TM				GPR125	166647		
LNB7TM				GPR126	57211		
LNB7TM				GPR128	84873		
LNB7TM				GPR144	347088		
LNB7TM:EGF, mucin-like receptor				EMR3	84658	Absent	Absent
LNB7TM:EGF, mucin-like receptor				EMR4[b]	326342	52614	
LNB7TM				CD97	976	26364	
LNB7TM:Latrophilin substrate				LPHN2	23266	99633	
LNB7TM:Latrophilin substrate				LPHN3	23284	319387	
LNB7TM:Latrophilin substrate				LPHN1	22859	330814	
Unclassified				GPR157	80045		

CGRP, calcitonin gene-related peptide; PACAP, pituitary adenylate cyclase activating polypeptide; TIP-39, tuberoinfundibular peptide of 39 residues; VIP, vasoactive intestinal peptide.
[a] Functional receptor is a dimer of 7TM and RAMP.
[b] Probable pseudogene.

gene is functional or a pseudogene, if the basis for calling it a pseudogene, is relatively subtle. We hope to document these issues for each of these pseudogenes in the IUPHAR receptor database as it progresses.

II. The Scope of the International Union of Pharmacology Receptor List

Based on a number of phylogenetic analyses, the GPCRs are divided into three main classes based on protein sequence similarity, i.e., classes 1, 2, and 3 whose prototypes are rhodopsin, the secretin receptor, and the metabotropic glutamate receptors, respectively (Bockaert and Pin, 1999; Josefsson, 1999; Graul and Sadee, 2001; Joost and Methner, 2002; Fredriksson et al., 2003). About half of class 1 are presumed to be involved in the detection of odor, taste, or light (Adler et al., 2000; Zozulya et al., 2001; Niimura and Nei, 2003; Zhang et al., 2003). Relatively few of these "sensory receptors" have been shown experimentally to respond to sensory stimuli or to be expressed in sensory organs. The vast majority have been classified as sensory solely because they share significant sequence identity to known sensory receptors. In our first iteration of the list, we have included only "nonsensory" GPCRs. This list omits 7 opsin-like receptors, 39 members of the taste receptor family, and roughly 400 potentially functional olfactory receptors. We expect to add to the next version of the list the opsins, the taste receptors, and those olfactory family receptors with well documented expression in nonolfactory tissues.

After extensive curation, our current list includes 276 functional genes from class 1, 53 from class 2, and 19 from class 3 (Tables 1–3). We have also listed 11 frizzled and smoothened receptors as a separate class (Table 4). The frizzled receptors have been extensively studied, and G protein coupling appears to be a feature of some, but not all, family members (Winklbauer et al., 2001). They most closely resemble class 2. In each table, receptors are listed alphabetically, in families, according to the descriptions of their ligands in common usage or, in the case of orphans, according to the phylogenetic clustering of Vassilatis et al. (2003). From left to right are listed the IUPHAR receptor code (Humphrey and Barnard, 1998); the endogenous ligands associated with each receptor; the official or proposed IUPHAR receptor nomenclature; the human gene symbol assigned by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/nomenclature/); and the unique identifiers (GeneIDs) assigned to the human, mouse, and rat genes in the Entrez Gene (formerly LocusLink) database (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene) where more detailed information about each gene can be found.

A regularly updated, hyperlinked version of the receptor list can be found at http://www.iuphar-db.org/iuphar-rd/list/index.htm. The receptor list is also available for download either as tab-delimited text files or as an Excel spreadsheet from http://www.iuphar-db.org/iuphar-rd/list/downloads.htm. In addition to the information displayed on the Web, these files also include the human

TABLE 3
Class 3 G protein-coupled receptors
Family represents the classification of orphan receptors adapted from Vassilatis et al. (2003). The IUPHAR Receptor Code is described in Humphrey and Barnard (1998). A representative, but not necessarily complete list of putative endogenous ligands is given. Provisional nomenclature is given in square brackets. NC-IUPHAR does not normally allocate names to receptors where there is only a single publication identifying the putative endogenous ligand. Gene symbol approved by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/nomenclature/). Gene IDs from Entrez Gene (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene).

Family	IUPHAR Receptor Code	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
$GABA_B$	2.3:GABA:1:GABAB1:	GABA[a]	$GABA_{B1}$	GABBR1	2550	54393	81657
$GABA_B$	2.3:GABA:2:GABAB2:	None	$GABA_{B2}$	GPR51	9568	242425	83633
$GABA_B$			[GABABL]	GPR156	165829		260430
Metabotropic glutamate	2.3:GLU:1:MGLU1:	Glutamate	$mGlu_1$	GRM1	2911	14816	24414
Metabotropic glutamate	2.3:GLU:2:MGLU2:	Glutamate	$mGlu_2$	GRM2	2912	108068	24415
Metabotropic glutamate	2.3:GLU:3:MGLU3:	Glutamate	$mGlu_3$	GRM3	2913	108069	24416
Metabotropic glutamate	2.3:GLU:4:MGLU4:	Glutamate	$mGlu_4$	GRM4	2914	108070	24417
Metabotropic glutamate	2.3:GLU:5:MGLU5:	Glutamate	$mGlu_5$	GRM5	2915	108071	24418
Metabotropic glutamate	2.3:GLU:6:MGLU6:	Glutamate	$mGlu_6$	GRM6	2916	108072	24419
Metabotropic glutamate	2.3:GLU:7:MGLU7:	Glutamate	$mGlu_7$	GRM7	2917	108073	81672
Metabotropic glutamate	2.3:GLU:8:MGLU8:	Glutamate	$mGlu_8$	GRM8	2918	14823	60590
Calcium sensor	2.3:CASN:1:CAS:	Calcium	CaS	CASR	846	12374	24247
Calcium sensor				GPRC6A	222545	210198	
GPRC5			[RAIG1]	GPRC5A	9052		
GPRC5			[RAIG2]	GPRC5B	51704	64297	
GPRC5			[RAIG3]	GPRC5C	55890	70355	
GPRC5				GPRC5D	55507	93746	
Unclassified				GPR158	57512	241263	291352
Unclassified				GPR158L1	342663		287657

[a] Functional GABA receptors contain both $GABA_{B1}$ and $GABA_{B2}$ subunits.

chromosomal location and two sequence standards. The RefSeq identifier supplied and curated by the National Centre for Biotechnology Information (NCBI: http://www.ncbi.nih.gov/RefSeq/) represents the nucleotide sequence, and the SwissProt identifier (http://www.ebi.ac.uk/swissprot/index.html) represents the protein sequence. The SwissProt Protein Knowledgebase is a highly curated and annotated protein sequence database established in 1986. It is maintained collaboratively by the Swiss Institute for Bioinformatics and the European Bioinformatics Institute.

There are a number of caveats with regard to this list. First, it is complete only to the extent that the human genomic sequence is complete and adequately annotated. The current version, NCBI build 35, dates from July 2004, and much of the sequence analysis predates its release which filled quite a few gaps, including one which contained the well known vasopressin V_{1B} receptor. Thus, there may be some genes in the new regions that have not been incorporated in the list. Furthermore, the newest version still contains 308 gaps containing 28 Mb of euchromatic sequence that could easily contain a number of relatively compact GPCR genes. Second, the receptor list is human-centric, partially reflecting a bias in favor of human pharmacology, but also reflecting the incomplete sequencing of other mammalian genomes. There are quite a few examples where the mouse or rat genomes contain genes without a functional human counterpart (Vassilatis et al., 2003). Many of the genes are missing in human, due to recent expansions in the rodent lineage of clustered gene families such as the trace amine receptor family. Many of the remainder are cases where the human ortholog is a pseudogene. Neither of these categories are listed unless the human pseudogene is potentially confusing. At the time of writing, the gaps in the mouse and rat lists have more to do with the completeness of the genomic sequences than a lack of mouse and rat orthologs for

TABLE 4
Frizzled family receptors
A representative, but not necessarily complete list of putative endogenous ligands is given. Provisional nomenclature is given in square brackets. Gene symbol approved by the HUGO Gene Nomenclature Committee (http://www.gene.ucl.ac.uk/nomenclature/). Gene IDs from Entrez Gene (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene).

Family	Ligand	Official IUPHAR Nomenclature	Human Gene Symbol	Human Gene ID	Mouse Gene ID	Rat Gene ID
Frizzled	Wnt3A, Wnt3, Wnt1 and to a lesser extent Wnt2	[FZD1]	FZD1	8321	14362	58868
Frizzled	Wnt	[FZD2]	FZD2	2535	57265	64512
Frizzled	Wnt	[FZD3]	FZD3	7976	14365	266715
Frizzled	Wnt, Wnt5a, and NDP	[FZD4]	FZD4	8322	14366	64558
Frizzled	Wnt and Wnt5a	[FZD5]	FZD5	7855	14367	317674
Frizzled	Wnt	[FZD6]	FZD6	8323	14368	282581
Frizzled	Wnt and Wnt5a	[FZD7]	FZD7	8324	14369	
Frizzled	Wnt and Wnt1	[FZD8]	FZD8	8325	14370	
Frizzled	Wnt and Wnt2	[FZD9]	FZD9	8326	14371	266608
Frizzled	Wnt	[FZD10]	FZD10	11211	93897	
Smoothened	Constitutive	[SMO]	SMO	6608	20596	25273

human genes. Third, not all 7TM proteins need be GPCRs, and we have only included 7TM proteins where at least one member of a phylogenetic cluster is known to be G protein-coupled. Fourth, as annotated in the list, some GPCRs are composed of multiple distinct protein subunits not all of which have a 7TM structure (Bockaert and Pin, 1999; Kniazeff et al., 2002; Poyner et al., 2002; Zhang et al., 2003).

III. Maintenance of the List

Over the past 10 years, the ligands for orphan receptors have been discovered at a steady rate of about six per year. Such discoveries are generally supported by other laboratories and become seminal publications in the pharmacological literature. At some point, however, these publications will always be isolated reports. NC-IUPHAR, through the receptor list, will maintain the current consensus as perceived by its members and correspondents, yet also reflect the invaluable efforts of the teams associated with the HUGO, NCBI, and SwissProt nomenclature groups. This will be monitored by an "evolving pharmacology committee" consisting of the authors.

It is in everyone's interest that the receptor list is public, that the names are consistent, and that the entries are displayed in an organized and recognizable way. By definition, this list is a "moving target" and will be modified based on feedback from scientists who may address comments to comments@iupharbb.org. The receptor list will be updated every 6 months.

References

Adler E, Hoon MA, Mueller KL, Chandrashekar J, Ryba NJ, and Zuker CS (2000) A novel family of mammalian taste receptors. *Cell* **100:**693–702.

Bockaert J and Pin JP (1999) Molecular tinkering of G protein-coupled receptors: an evolutionary success. *EMBO (Eur Mol Biol Organ) J* **18:**1723–1729.

Fredriksson R, Lagerstrom MC, Lundin LG, and Schioth HB (2003) The G-protein-coupled receptors in the human genome form five main families. Phylogenetic analysis, paralogon groups and fingerprints. *Mol Pharmacol* **63:**1256–1272.

Graul RC and Sadee W (2001) Evolutionary relationships among G protein-coupled receptors using a clustered database approach. *AAPS PharmSci* **3:**E12.

Harrison PM and Gerstein M (2002) Studying genomes through the aeons: protein families, pseudogenes and proteome evolution. *J Mol Biol* **318:**1155–1174.

Harrison PM, Hegyi H, Balasubramanian S, Luscombe NM, Bertone P, Echols N, Johnson T, and Gerstein M (2002) Molecular fossils in the human genome: identification and analysis of the pseudogenes in chromosomes 21 and 22. *Genome Res* **12:**272–280.

Humphrey PP and Barnard EA (1998) International Union of Pharmacology. XIX. The IUPHAR receptor code: a proposal for an alphanumeric classification system. *Pharmacol Rev* **50:**271–277.

International Human Genome Sequencing Consortium (2004) Finishing the euchromatic sequence of the human genome. *Nature (Lond)* **431:**931–945.

Joost P and Methner A (2002) Phylogenetic analysis of 277 human G-protein-coupled receptors as a tool for the prediction of orphan receptor ligands. *Genome Biol* **3:**RESEARCH0063.

Josefsson LG (1999) Evidence for kinship between diverse G-protein coupled receptors. *Gene* **239:**333–340.

Kniazeff J, Galvez T, Labesse G, and Pin JP (2002) No ligand binding in the GB2 subunit of the $GABA_B$ receptor is required for activation and allosteric interaction between the subunits. *J Neurosci* **22:**7352–7361.

Niimura Y and Nei M (2003) Evolution of olfactory receptor genes in the human genome. *Proc Natl Acad Sci USA* **100:**12235–12240.

Poyner DR, Sexton PM, Marshall I, Smith DM, Quirion R, Born W, Muff R, Fischer JA, and Foord SM (2002) International Union of Pharmacology. XXXII. The mammalian calcitonin gene-related peptides, adrenomedullin, amylin and calcitonin receptors. *Pharmacol Rev* **54:**233–246.

Stacey M, Lin HH, Gordon S, and McKnight AJ (2000) LNB-TM7, a group of seven-transmembrane proteins related to family-B G-protein-coupled receptors. *Trends Biochem Sci* **25:**284–289.

Vanti WB, Muglia P, Nguyen T, Cheng R, Kennedy JL, George SR, and O'Dowd BF (2003) Discovery of a null mutation in a human trace amine receptor gene. *Genomics* **82:**531–536.

Vassilatis DK, Hohmann JG, Zeng H, Li F, Ranchalis JE, Mortrud MT, Brown A, Rodriguez SS, Weller JR, Wright AC, et al. (2003) The G protein-coupled receptor repertoires of human and mouse. *Proc Natl Acad Sci USA* **100:**4903–4908.

Winklbauer R, Medina A, Swain RK, and Steinbeisser H (2001) Frizzled-7 signalling controls tissue separation during Xenopus gastrulation. *Nature (Lond)* **413:**856–860.

Zhang Y, Hoon MA, Chandrashekar J, Mueller KL, Cook B, Wu D, Zuker CS, and Ryba NJ (2003) Coding of sweet, bitter and umami tastes: different receptor cells sharing similar signaling pathways. *Cell* **112:**293–301.

Zozulya S, Echeverri F, and Nguyen T (2001) The human olfactory receptor repertoire. *Genome Biol* **2:**RESEARCH0018.