

Fig. S1. NJ phylogenetic tree for 216 non-OR rhodopsin-like GPCR genes from humans, 31 amphioxus OR genes, 49 Type 2 genes, and 28 Type 1 genes. This tree contains almost all non-OR rhodopsin-like GPCR genes in the human genome (Fredriksson et al. 2003). All genes belonging to groups θ 1, θ 2, κ , and λ in Figure 1B were used. As for the other groups of OR genes (groups α - η), only representative genes were used. Human and zebrafish OR genes were classified into subgroups with a threshold value of a 45% amino acid sequence identity, and a representative gene was chosen from each subgroup. Bootstrap values obtained from 500 replications are shown only for major clades. The number of amino acid sites used was 163. The following genes were used as non-OR rhodopsin-like GPCR genes (from the top of the tree): G-protein coupled purinergic receptor P2Y5 (NP_005758.2), GPCR 23 (NP_005287.1), EBV-induced GPCR 2 (NP_004942.1), GPCR 18 (NP_005283.1), putative GPCR 92 (NP_065133.1), coagulation factor II (thrombin) receptor-like 1 precursor (NP_005233.3), coagulation factor II receptor precursor (NP_001983.1), coagulation factor II (thrombin) receptor-like 3 (NP_003941.1), coagulation factor II (thrombin) receptor-like 2 precursor (NP_004092.1), GPCR 68 (NP_003476.2), GPCR 4 (NP_005273.1), GPCR 65 (NP_003599.2), GPCR G2A (NP_037477.1), purinergic receptor P2Y2 (NP_002555.2), pyrimidinergic receptor P2Y4 (NP_002556.1), pyrimidinergic receptor P2Y6 (NP_004145.1), purinergic receptor P2Y1 (NP_002554.1), purinergic receptor P2Y11 (NP_002557.2), GPCR 17 (NP_005282.1), purinergic receptor P2Y12 (NP_073625.1), purinergic receptor P2Y, G-protein coupled, 13 (NP_076403.2), GPCR 87 (NP_076404.2), purinergic receptor P2Y, G-protein coupled, 14 (NP_055694.2), GPCR 171 (NP_037440.2), putative purinergic receptor FKSG79 (NP_115942.1), G-protein coupled purinergic receptor P2Y10 (NP_055314.1), platelet-activating factor receptor (NP_000943.1), GPCR 35 (NP_005292.2), GPCR 55 (NP_005674.2), GPCR 81 (NP_115943.1), GPCR 109B (NP_006009.1), cysteinyl leukotriene receptor 2 (NP_065110.1), cysteinyl leukotriene receptor 1 (NP_006630.1), succinate receptor 1 (NP_149039.2), adrenomedullin receptor (NP_009195.1), bradykinin receptor B2 (NP_000614.1), bradykinin receptor B1 (NP_000701.2), chemokine (C-C motif) receptor 5 (NP_000570.1), chemokine (C-C motif) receptor 2 isoform B (NP_000639.1), chemokine (C-C motif) receptor 1 (NP_001286.1), CC chemokine receptor 3 (NP_001828.1), chemokine (C-C motif) receptor-like 2 (NP_003956.2), chemokine (C-C motif) receptor 4 (NP_005499.1), chemokine (C-C motif) receptor 8 (NP_005192.1), chemokine (C-X3-C motif) receptor 1 (NP_001328.1), chemokine binding protein 2 (NP_001287.2), XC chemokine receptor 1 (NP_005274.1), chemokine (C-C motif) receptor 7 precursor (NP_001829.1), chemokine (C-C motif) receptor 6 (NP_004358.2), chemokine (C-C motif) receptor-like 1 (NP_057641.1), chemokine (C-C motif) receptor 9 isoform B (NP_006632.2), GPCR TYMSTR (NP_006555.1), interleukin 8 receptor beta (NP_001548.1), interleukin 8 receptor alpha

(NP_000625.1), chemokine (C-X-C motif) receptor 3 (NP_001495.1), Burkitt lymphoma receptor 1 isoform 1 (NP_001707.1), chemokine (C-X-C motif) receptor 4 isoform b (NP_003458.1), relaxin 3 receptor 1 (NP_057652.1), angiotensin II receptor, type 2 (NP_000677.2), GPCR 25 (NP_005289.2), GPCR 15 (NP_005281.1), angiotensin II receptor-like 1 (NP_005152.1), formyl peptide receptor-like 1 (NP_001453.1), formyl peptide receptor-like 2 (NP_002021.3), formyl peptide receptor 1 (NP_002020.1), GPCR 32 (NP_001497.1), chemokine-like receptor 1 (NP_004063.1), GPCR 1 (NP_005270.2), complement component 5 receptor 1 (C5a ligand) (NP_001727.1), GPCR C5L2 (NP_060955.1), complement component 3a receptor 1 (NP_004045.1), GPCR 44 (NP_004769.1), leukotriene B4 receptor 2 (NP_062813.1), opioid receptor, kappa 1 (NP_000903.2), opioid receptor, mu 1 isoform MOR-1 (NP_000905.2), opioid receptor, delta 1 (NP_000902.3), opiate receptor-like 1 (NP_000904.1), somatostatin receptor 3 (NP_001042.1), somatostatin receptor 5 (NP_001044.1), somatostatin receptor 2 (NP_001041.1), somatostatin receptor 4 (NP_001043.1), GPCR 24 (NP_005288.2), GPCR 145 (NP_115892.1), galanin receptor 3 (NP_003605.1), galanin receptor 2 (NP_003848.1), galanin receptor 1 (NP_001471.1), GPCR 54 (NP_115940.2), endothelin receptor type A (NP_001948.1), endothelin receptor type B isoform 1 (NP_000106.1), GPCR 37 like 1 (NP_004758.2), GPCR 37 (NP_005293.1), neuromedin B receptor (NP_002502.1), bombesin-like receptor 3 (NP_001718.1), prostaglandin E receptor 1, subtype EP1 (NP_000946.2), prostaglandin F receptor (NP_000950.1), thromboxane A2 receptor isoform 2 (NP_001051.1), prostaglandin E receptor 3, subtype EP3 isoform 1 (NP_000948.2), prostaglandin I2 (prostacyclin) receptor (IP) (NP_000951.1), prostaglandin E receptor 2 (subtype EP2) (NP_000947.2), prostaglandin E receptor 4, subtype EP4 (NP_000949.1), GPCR 82 (NP_543007.1), GPCR MRGX3 (NP_473372.2), GPCR MRGX4 (NP_473373.1), GPCR MRGX2 (NP_473371.1), MAS1 oncogene (NP_002368.1), mas-related G protein-coupled MRG (NP_443199.1), MAS-related GPR, member F (AAH16964.1), neurotensin receptor 2 (NP_036476.1), neurotensin receptor 1 (NP_002522.1), motilin receptor (NP_001498.1), neuromedin U receptor 2 (NP_064552.2), neuromedin U receptor 1 (NP_006047.2), thyrotropin-releasing hormone receptor (NP_003292.1), cholecystokinin A receptor (NP_000721.1), arginine vasopressin receptor 1B (NP_000698.1), arginine vasopressin receptor 1A (NP_000697.1), oxytocin receptor (NP_000907.2), arginine vasopressin receptor 2 (NP_000045.1), gonadotropin-releasing hormone receptor isoform 1 (NP_000397.1), 5-hydroxytryptamine (serotonin) receptor 1F (NP_000857.1), 5-hydroxytryptamine (serotonin) receptor 1E (NP_000856.1), 5-hydroxytryptamine (serotonin) receptor 1B (NP_000854.1), 5-hydroxytryptamine (serotonin) receptor 1A (NP_000515.2), 5-hydroxytryptamine receptor 7 isoform a (NP_000863.1), 5-hydroxytryptamine (serotonin) receptor 5A (NP_076917.1), dopamine receptor D1 (NP_000785.1), dopamine receptor D5

(NP_000789.1), 5-hydroxytryptamine (serotonin) receptor 4 isoform b (NP_000861.1), 5-hydroxytryptamine (serotonin) receptor 6 (NP_000862.1), beta-1-adrenergic receptor (NP_000675.1), beta-2-adrenergic receptor, surface (NP_000015.1), beta-3-adrenergic receptor (NP_000016.1), histamine receptor H2 (NP_071640.1), GPCR 102 (NP_444508.1), trace amine receptor 4 (AAK71243.1), trace amine receptor 3 (AAK71240.1), putative neurotransmitter receptor (NP_003958.1), trace amine associated receptor 2 (NP_055441.1), trace amine receptor 1 (AAK71236.1), alpha-1A-adrenergic receptor isoform 1 (NP_000671.1), alpha-1B-adrenergic receptor (NP_000670.1), alpha-1D-adrenergic receptor (NP_000669.1), 5-hydroxytryptamine (serotonin) receptor 2C (NP_000859.1), 5-hydroxytryptamine (serotonin) receptor 2A (NP_000612.1), 5-hydroxytryptamine (serotonin) receptor 2B (NP_000858.2), alpha-2C-adrenergic receptor (NP_000674.2), alpha-2A-adrenergic receptor (NP_000672.2), alpha-2B-adrenergic receptor (NP_000673.2), dopamine receptor D2 isoform long (NP_000786.1), dopamine receptor D3 isoform a (NP_000787.1), dopamine receptor D4 (NP_000788.2), cholinergic receptor, muscarinic 3 (NP_000731.1), cholinergic receptor, muscarinic 5 (NP_036257.1), cholinergic receptor, muscarinic 1 (NP_000729.2), cholinergic receptor, muscarinic 4 (NP_000732.2), cholinergic receptor, muscarinic 2 isoform a (NP_000730.1), adenosine A2b receptor (NP_000667.1), adenosine A2a receptor (NP_000666.2), adenosine A3 receptor isoform 2 (NP_000668.1), GPCR 52 (NP_005675.2), GPCR 21 (NP_005285.1), melanocortin 4 receptor (NP_005903.1), melanocortin 5 receptor (NP_005904.1), melanocortin 3 receptor (NP_063941.2), melanocortin 2 receptor (NP_000520.1), melanocortin 1 receptor (NP_002377.3), GPCR 3 (NP_005272.1), GPCR 6 (NP_005275.1), GPCR 12 (NP_005279.1), cannabinoid receptor 2 (macrophage) (NP_001832.1), endothelial differentiation, sphingolipid GPCR, 1 (NP_001391.2), endothelial differentiation, sphingolipid GPCR, 3 (NP_005217.2), endothelial differentiation, sphingolipid GPCR, 5 (NP_004221.2), endothelial differentiation, sphingolipid GPCR, 8 (NP_110387.1), endothelial differentiation, GPCR 6 precursor (NP_003766.1), endothelial differentiation, lysophosphatidic acid GPCR, 4 (NP_004711.2), endothelial differentiation, lysophosphatidic acid GPCR, 2 (NP_001392.2), endothelial differentiation, lysophosphatidic acid GPCR, 7 (NP_036284.1), follicle stimulating hormone receptor isoform 1 precursor (NP_000136.2), luteinizing hormone/choriogonadotropin receptor precursor (NP_000224.1), thyroid stimulating hormone receptor isoform 1 (NP_000360.2), leucine-rich repeat-containing GPCR 5 (NP_003658.1), leucine-rich repeat-containing GPCR 4 (NP_060960.1), leucine-rich repeat-containing GPCR 7 (NP_067647.1), GPCR affecting testicular descent (NP_570718.1), opsin 1 (cone pigments), medium-wave-sensitive (color blindness, deutan) (NP_000504.1), opsin 1 (cone pigments), long-wave-sensitive (color blindness, protan) (NP_064445.1), rhodopsin (NP_000530.1), opsin 1 (cone pigments), short-wave-sensitive (color

blindness, tritan) (NP_001699.1), opsin 3 isoform 1 (NP_055137.2), peropsin (NP_006574.1), pancreatic polypeptide receptor 1 (NP_005963.2), neuropeptide Y receptor Y1 (NP_000900.1), neuropeptide Y receptor Y5 (NP_006165.1), GPCR 83 (NP_057624.2), neuropeptide Y receptor Y2 (NP_000901.1), GPCR 10 (NP_004239.1), tachykinin receptor 1 isoform long (NP_001049.1), tachykinin receptor 3 (NP_001050.1), tachykinin receptor 2 (NP_001048.1), GPCR 74 isoform 1 (NP_004876.1), GPCR 147 (NP_071429.1), orexin receptor 2 (NP_001517.1), orexin receptor 1 (NP_001516.1), melatonin receptor 1B (NP_005950.1), melatonin receptor 1A (NP_005949.1), GPCR 50 (NP_004215.1), GPCR 173 (NP_061842.1), GPCR 85 (NP_061843.2), GPCR 27 (NP_061844.1), GPCR 61 (NP_114142.3), opsin 4 isoform 1 (NP_150598.1), GPCR 161 isoform 1 (NP_031395.1), GPCR 101 (NP_473362.1), GPCR 153 (AAH68275.1), and gene rich cluster, A isoform 2 (NP_062832.1).

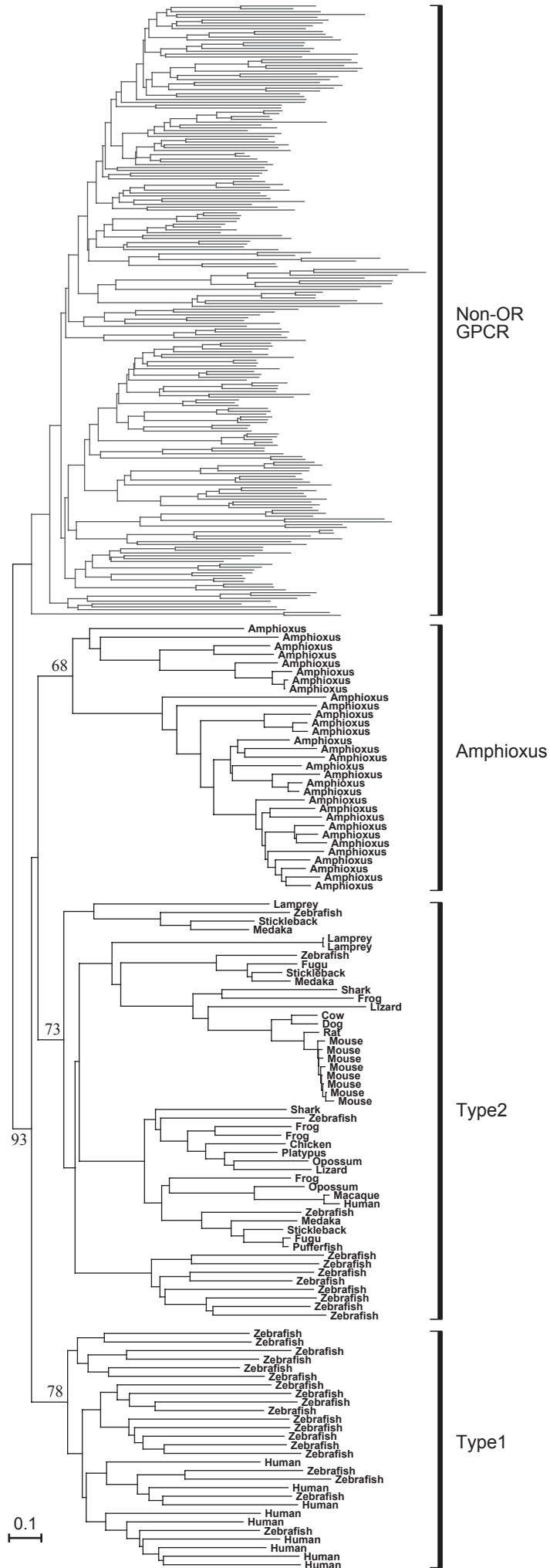


FIG. S1