

Supplementary information

Evolutionary conservation of 3-iodothyronamine as agonist at the trace amine-associated receptor 1

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Running title: 3-iodothyronamine as agonist at Taar1

Keywords: trace amine-associated receptor 1, TAAR, 3-iodothyronamine

Abbreviations: GPCR: G protein-coupled receptor, T1AM: 3-iodothyronamine, Taar: trace amine-associated receptor, ADRA2A: α 2A-adrenergic receptor, ADBR2: β 2-adrenergic receptor, DRD4: dopamine receptor D4, HRH2: histamine receptor H2, HTR1F: 5-hydroxytryptamine (serotonin) receptor 1F, RHO: rhodopsin, MC4R: melanocortin receptor 4, β -PEA: β -phenylethylamine, *p*-Tyr: *p*-tyramine

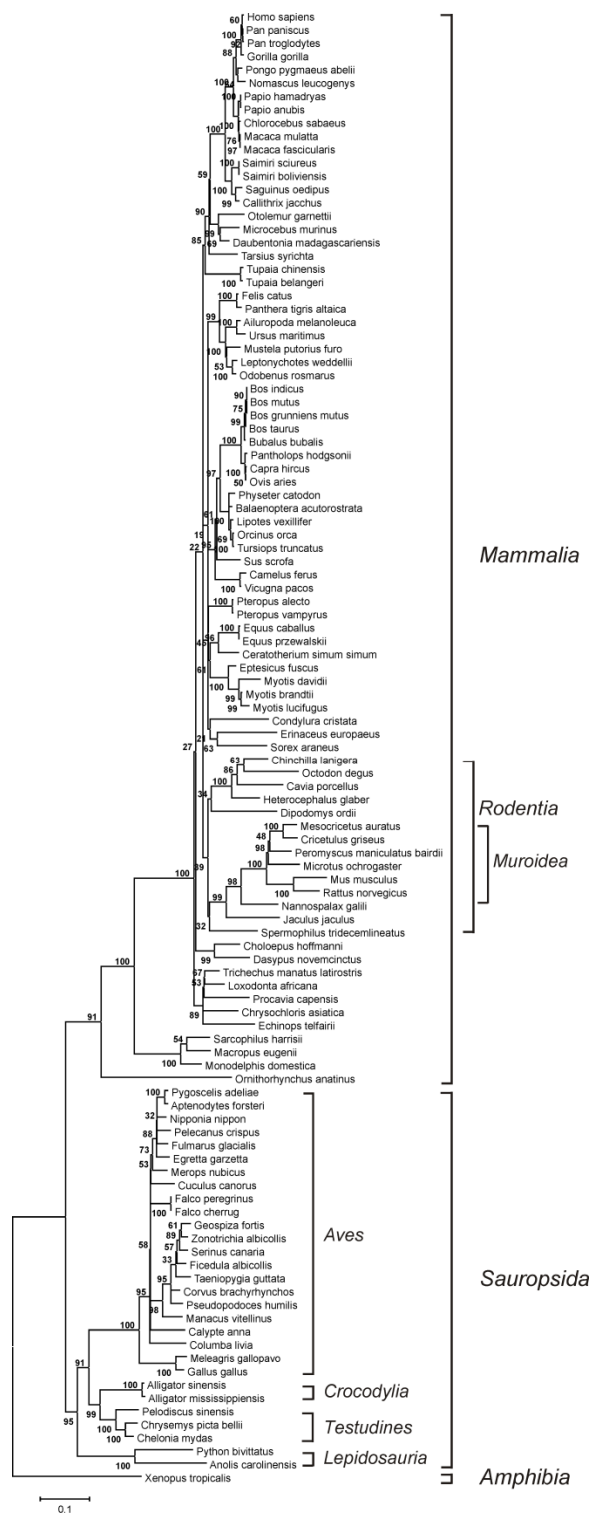


Figure S1 Molecular phylogenetic analysis of vertebrate Taar1 nucleotide sequences using the Maximum Likelihood method. The evolutionary relation was inferred by the Maximum Likelihood method based on the Kimura 2-parameter model [1]. The tree with the highest log likelihood (-24586.1018) is shown. The bootstrap consensus tree inferred from 1,000 replicates is taken to represent the evolutionary history of the taxa analyzed [2]. Initial tree(s) for the heuristic search were obtained by applying the Neighbor-Joining method to a matrix of pairwise distances estimated using the Maximum Composite Likelihood (MCL) approach. A discrete Gamma distribution was used to model evolutionary rate differences among sites (5 categories (+G, parameter = 1.1785)). The rate variation model allowed for some sites to be evolutionarily invariable ([+I], 22.4525% sites). The tree is drawn to scale, with branch lengths measured in the number of substitutions per site. The analysis involved 111 nucleotide sequences. All positions with less than 95% site coverage were eliminated. That is, fewer than 5% alignment gaps, missing data, and ambiguous bases were allowed at any position. There was a total of 984 positions in the final dataset. Evolutionary analyses were conducted in MEGA6 [3].

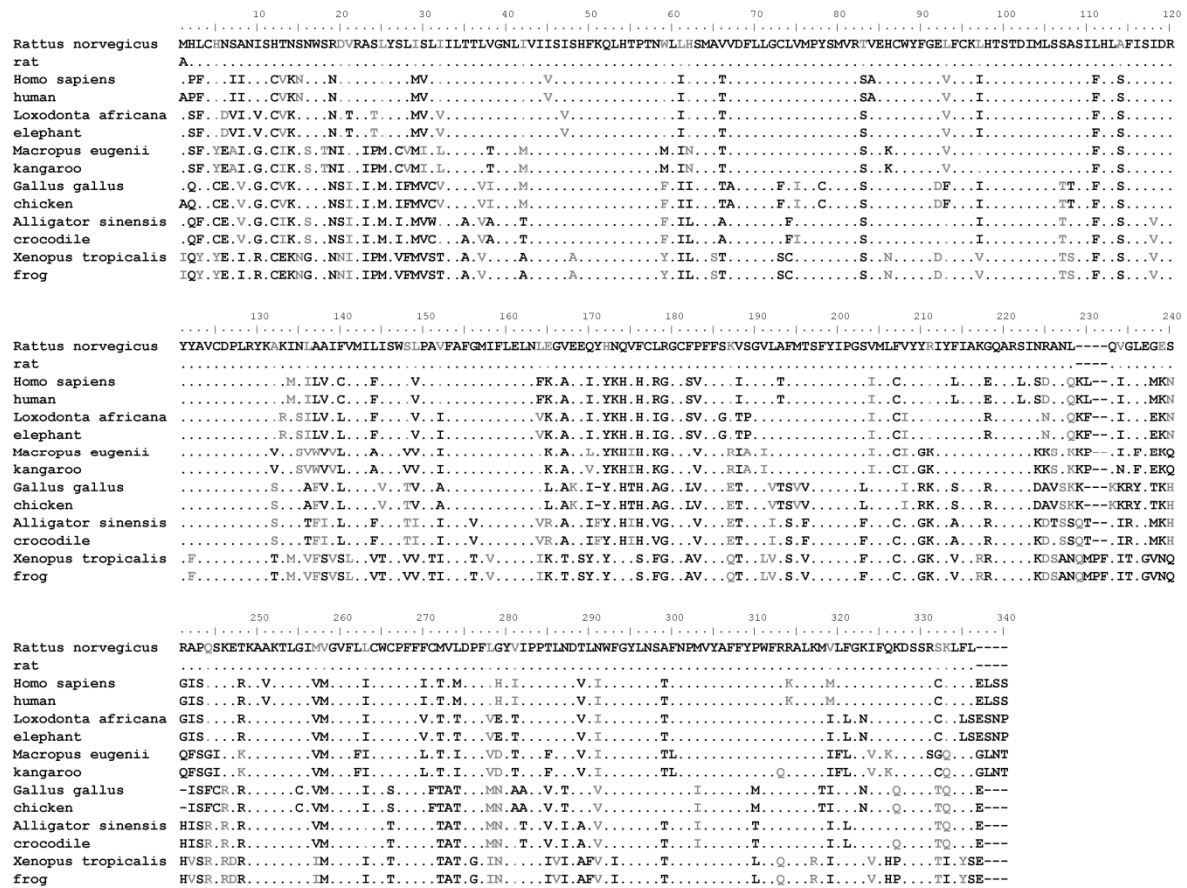


Figure S2 Alignment of cloned protein Taar1 sequences versus database protein Taar1 sequences. The alignment shows a complete alignment of all cloned protein Taar1 sequences (name stated in English) versus Taar1 database sequences: *Rattus norvegicus* (NP_599155.1), *Homo sapiens* (NP_612200.1), *Loxodonta africana* (XP_003404057.1), *Macropus eugenii* (protein sequence derived from assembled and translated NCBI trace archive files: ti:1649014544, ti:1643994001, ti:1616200502, ti:1560294893, ti:1275352077), *Gallus gallus* (XP_004935797.1), *Alligator sinensis* (XP_006034292.1), *Xenopus tropicalis* (XP_002935857.1)

Suppl. Table S1

NCBI database accession numbers and sequence description

<i>Latin species name</i>	<i>English species name</i>	<i>NCBI or ENSEMBL accession number / trace identifiers of NCBI trace archive</i>
<i>Ailuropoda melanoleuca</i>	Giant panda	XM_002923036
<i>Alligator mississippiensis</i>	American alligator	XM_006270537.1
<i>Alligator sinensis</i>	Chinese alligator	XM_006034230.1 (Taar1) XM_006021091.1(ADRB2) XM_006022834.1 (ADRA2A) XM_006018899.1 (HTR1F) XM_006037826.1 (HRH2) XM_006019200.1 (DRD4) NM_001287282.1 (RHO)
<i>Anolis carolinensis</i>	Carolina anole	XM_008114566.1 (Taar1) XM_003226749.2 (MC4R)
<i>Aptenodytes forsteri</i>	Emperor penguin	XM_009281516.1
<i>Balaenoptera acutorostrata scammoni</i>	Minke whale	XM_007191107.1
<i>Bos grunniens mutus</i>	Yak	AGSK01008363
<i>Bos indicus</i>	Zebu	AGFL01087224
<i>Bos mutus</i>	Yak	XM_005887750.1
<i>Bos taurus</i>	Cattle	ti:1082339058, ti:385077944, ti:501173553, ti:624956688, ti:510541075, ti:511691226, ti:986805404, ti:592468958
<i>Bubalus bubalis</i>	Water buffalo	XM_006059307.1
<i>Callithrix jacchus</i>	Common marmoset	GQ892033.1
<i>Callorhynchus milii</i>	Elephant shark	XM_007899229.1
<i>Calypte anna</i>	Anna's hummingbird	XM_008494030.1
<i>Camelus ferus</i>	Wild Bactrian camel	XM_006188447.1
<i>Capra hircus</i>	Goat	XM_005684836.1
<i>Cavia porcellus</i>	Guinea pig	BK006910.1
<i>Ceratotherium simum simum</i>	Southern white rhinoceros	XM_004422329.1
<i>Chelonia mydas</i>	Green sea turtle	XM_007062247.1
<i>Chinchilla lanigera</i>	Long-tailed chinchilla	XM_005389216.1
<i>Chlorocebus sabaeus</i>	Green monkey	XM_008007010.1
<i>Choloepus hoffmanni</i>	Hoffmann's two-toed sloth	ti:1294731600, ti:1294731595, ti:1322469933, ti:1294039915, ti:1338691040, ti:1293674405
<i>Chrysemys picta bellii</i>	Painted turtle	XM_005280289.2
<i>Chrysochloris asiatica</i>	Cape golden mole	XM_006834656.1
<i>Columba livia</i>	Rock pigeon	XM_005515994.1
<i>Condylura cristata</i>	Star-nosed mole	XM_004674118.1
<i>Corvus brachyrhynchos</i>	American crow	XM_008637837.1
<i>Cricetulus griseus</i>	Chinese hamster	XM_003510913

<i>Cuculus canorus</i> +A2	Common cuckoo	XM_009559699.1
<i>Cynoglossus semilaevis</i>	Tongue sole	XM_008328158.1
<i>Danio rerio</i>	Zebra fish	NM_001082904.1
<i>Dasypus novemcinctus</i>	Nine-banded armadillo	XM_004483646.1
<i>Daubentonia madagascariensis</i>	Aye-aye	AGTM011608778
<i>Dipodomys ordii</i>	Ord's kangaroo rat	ti:1535262597, ti:1543429769, ti:1577335924, ti:1585058989
<i>Echinops telfairii</i>	Lesser hedgehog tenrec	XM_004702164.1
<i>Egretta garzetta</i>	Little egret	XM_009644359.1
<i>Eptesicus fuscus</i>	Big brown bat	XM_008162400.1
<i>Equus caballus</i>	Horse	ti:1400434870, ti:1326918636, ti:1268381169, ti:1297706693, ti:1257074521, ti:1278989508, ti:1423364663, ti:1310830425, ti:1312258914, ti:1319412555, ti:1204860944, ti:1298977282, ti:1305892823, ti:1331817236, ti:1331675852
<i>Equus przewalskii</i>	Przewalski's horse	XM_008529439.1
<i>Erinaceus europaeus</i>	European hedgehog	XM_007535381.1
<i>Falco cherrug</i>	Saker falcon	XM_005432837.1
<i>Falco peregrinus</i>	peregrine falcon	XM_005230130.1
<i>Felis catus</i>	Cat	XM_003986568.2
<i>Ficedula albicollis</i>	Collared flycatcher	XM_005043866.1
<i>Fulmarus glacialis</i>	Northern fulmar	XM_009578017.1
<i>Gallus gallus</i>	Red junglefowl	XM_004935740.1 (Taar1) XM_004950587.1 (ADRB2) XM_004942276.1 (ADRA2A) XM_004938334.1 (HTR1F) XM_004944905.1 (HRH2) AB699034.1 (DRD4) NM_001031514.1 (MC4R) NM_001030606.1 (RHO)
<i>Geospiza fortis</i>	Medium ground finch	XM_005425666.1
<i>Gorilla gorilla</i>	Western gorilla	XM_004044694.1
<i>Haplochromis burtoni</i>	Burton's mouthbrooder	XM_005952049.1
<i>Heterocephalus glaber</i>	Naked mole rat	XM_004882033.1
<i>Homo sapiens</i>	Human	NM_138327.1
<i>Jaculus jaculus</i>	Lesser Egyptian jerboa	XM_004651333.1
<i>Latimeria chalumnae</i>	West Indian ocean coelacanth	XM_006010896.1
<i>Lepisosteus oculatus</i>	Spotted gar	XM_006626475.1
<i>Leptonychotes weddellii</i>	Weddell seal	XM_006740285.1
<i>Leucoraja erinacea</i>	Skate	AESE010037337
<i>Lipotes vexillifer</i>	Yangtze River dolphin	XM_007456533.1

<i>Loxodonta africana</i>	African bush elephant	XM_003404009.1 (Taar1) ENSLAFE00000421629 (ADRB2) ENSLAFG00000002225 (ADRA2A) ENSLAFG00000010266 (HTR1F) ENSLAFG00000004764 (HRH2) ENSLAFG00000023284 (DRD4) XM_003406273.1 (MC4R) NM_001280858.1 (RHO)
<i>Macaca fascicularis</i>	Crab-eating macaque	XM_005551857.1
<i>Macaca mulatta</i>	Rhesus macaque	NM_001080765.1
<i>Macropus eugenii</i>	Tammar wallaby	ti:1649014544, ti:1643994001, ti:1616200502, ti:1560294893, ti:1275352077 (Taar1) ENSMEUE00000097510 (ADRB2) ENSMEUG00000008696 (HTR1F)
<i>Manacus vitellinus</i>	golden-collared manakin	XM_008923845.1
<i>Maylandia zebra</i>	zebra mbuna	XM_004566322.1
<i>Meleagris gallopavo</i>	Wild turkey	XM_003204201.1
<i>Merops nubicus</i>	Carmine bee-eater	XM_008938006.1
<i>Mesocricetus auratus</i>	Golden hamster	XM_005065723.1
<i>Microcebus murinus</i>	Gray mouse lemur	ti:1576501568, ti:1567541053, ti:1580865666, ti:1567540397, ti:1550799367, ti:1560314056, ti:1554531623
<i>Microtus ochrogaster</i>	Prairie vole	XM_005360928.1
<i>Monodelphis domestica</i>	Gray short-tailed opossum	XM_007484578.1 (Taar1) XM_007479023.1 (ADRA2A) XM_007474099.1 (HRH2) XM_007506747.1 (DRD4) NM_001111024.1 (MC4R) XM_001366188.2 (RHO)
<i>Mus musculus</i>	House mouse	NM_053205.1
<i>Mustela putorius furo</i>	Ferret	AEYP01006926
<i>Myotis brandtii</i>	Brandt's bat	XM_005859015.1
<i>Myotis davidii</i>	David's myotis	XM_006778490.1
<i>Myotis lucifugus</i>	Little brown bat	ti:994582862, ti:1874379801, ti:1903020267, ti:1902888670, ti:1887388540, ti:1904203664, ti:1889154466, ti:1894302362, ti:2034915255, ti:942092802, ti:1908647976, ti:957991557, ti:2039424342, ti:997802693,

		ti:1882286647, ti:1905993612, ti:1900791033, ti:1876483354, ti:1896280337, ti:2157629374, ti:1895607303, ti:1899705724
<i>Nannospalax galili</i>	Upper Galilee mountains blind mole rat	XM_008822106.1
<i>Neolamprologus brichardi</i>	Brichard's Lamprologus	XM_006794303.1
<i>Nipponia nippon</i>	crested ibis	XM_009460750.1
<i>Nomascus leucogenys</i>	White-cheeked gibbon	XM_003255724.2
<i>Octodon degus</i>	Degu	XM_004630323.1
<i>Odobenus rosmarus</i>	Pacific walrus	XM_004401171.1
<i>Orcinus orca</i>	killer whale	XM_004263817.1
<i>Oreochromis niloticus</i>	Nile tilapia	XM_003449563.1
<i>Ornithorhynchus anatinus</i>	Platypus	XM_001506403.2
<i>Oryzias latipes</i>	Japanese medaka	XM_004081645.1
<i>Otolemur garnettii</i>	Garnett's greater galago	XM_003781684.1
<i>Ovis aries</i>	Sheep	XM_004011515.1
<i>Pan paniscus</i>	Bonobo	XM_003827665.2
<i>Pan troglodytes</i>	Chimpanzee	NM_001009145.1
<i>Panthera tigris altaica</i>	Amur tiger	XM_007078611.1
<i>Pantholops hodgsonii</i>	Chiru	XM_005967536.1
<i>Papio anubis</i>	Olive baboon	XM_009206074.1
<i>Papio hamadryas</i>	Hamadryas baboon	GAAH01027701.1
<i>Pelecanus crispus</i>	Dalmatian pelican	XM_009485654.1
<i>Pelodiscus sinensis</i>	Chinese softshell turtle	XM_006136250.1
<i>Peromyscus maniculatus bairdii</i>	Prairie deer mouse	XM_006986682.1
<i>Physeter catodon</i>	Sperm whale	XM_007100317.1
<i>Poecilia reticulata</i>	Guppy	XM_008398121.1
<i>Pongo pygmaeus abelii</i>	Sumatran orangutan	BK006907.1
<i>Procavia capensis</i>	Rock hyrax	ti:1303042942, ti:1206111770, ti:1204555238, ti:1256247671
<i>Pseudopodoces humilis</i>	Tibetan ground-tit	XM_005518354.1
<i>Pteropus alecto</i>	Black flying fox	XM_006915408
<i>Pteropus vampyrus</i>	Large flying fox	ti:1320431729, ti:1345684017, ti:1329216416, ti:1366134537, ti:1387479080, ti:1391810654, ti:1322746350
<i>Pundamilia nyererei</i>	Flame Back Cichlid	XM_005751011.1
<i>Pygoscelis adeliae</i>	Adelie penguin	XM_009319055.1
<i>Python bivittatus</i>	Burmese python	XM_007425936.1
<i>Rattus norvegicus</i>	Norway rat	NM_134328.1 (Taarl) NM_012492.2 (ADRB2) NM_012739.3 (ADRA2A) NM_021857.3 (HTR1F) NM_012965.3 (HRH2) NM_012944.1 (DRD4)

		NM_013099.2 (MC4R) NM_033441.1 (RHO)
<i>Saguinus oedipus</i>	Cottontop tamarin	GQ892034.1
<i>Saimiri boliviensis</i>	Black-capped squirrel monkey	XM_003932446.1
<i>Saimiri sciureus</i>	Common squirrel monkey	EF549698.1
<i>Sarcophilus harrisi</i>	Tasmanian devil	XM_003769449.1
<i>Serinus canaria</i>	Common canary	XM_009095226.1
<i>Sorex araneus</i>	Common shrew	XM_004609089.1
<i>Spermophilus tridecemlineatus</i>	thirteen-lined ground squirrel	XM_005329819.1
<i>Stegastes partitus</i>	bicolor damselfish	XM_008295005.1
<i>Strongylocentrotus purpuratus</i>	purple sea urchin	XM_001199619.1
<i>Sus scrofa</i>	Wild boar	XM_001924824.2
<i>Taeniopygia guttata</i>	Zebra finch	XM_002191981.1
<i>Takifugu rubripes</i>	Fugu rubripes	XM_003966556.1
<i>Tarsius syrichta</i>	Philippine tarsier	XM_008058602.1
<i>Trichechus manatus latirostris</i>	Florida manatee	XM_004368913.1
<i>Tupaia belangeri</i>	Northern treeshrew	ti:1044829742, ti:1058512920, ti:1058654161, ti:1052948645, ti:1044380426, ti:1044753695
<i>Tupaia chinensis</i>	Chinese treeshrew	XM_006144373.1
<i>Tursiops truncatus</i>	Common bottlenose dolphin	XM_004332388.1
<i>Ursus maritimus</i>	polar bear	XM_008691080.1
<i>Vicugna pacos</i>	Alpaca	XM_006200063.1
<i>Xenopus tropicalis</i>	Western clawed frog	XM_002935811.2 (Taarl) NM_001123425.2 (ADRB2) NM_001079375.1 (ADRA2A) XM_002931771.2 (HTR1F) XM_002938065.2 (HRH2) XM_002937489.2 (DRD4) XM_004915313.1 (MC4R) NM_001097334.1 (RHO)
<i>Xiphophorus maculatus</i>	southern platyfish	XM_005803810.1

Suppl. Table S2

Primers used for Taar1 ortholog amplification, sequencing and introduction of epitope tags or mutations.

ID	sequence (5' - 3')	purpose
789	gtgcaaatcaaagaactgtcctc	pcDps forward (amplification/sequencing)
790	cctgggttttccgcctcagaag	pcDps reverse (amplification/sequencing)
2291	cgccgactagttcacttategtcatcgtccttatagtc	FLAG-uni- <i>Spe I</i> AS
2285	cggaattccccaccatgtaccctacgacgtccccgactacgcc	HA-uni-Kozak- <i>Eco RI</i> S
2289	cgccccggggccaccatgtaccctacgacgtccccgactacgcc	HA-uni-Kozak- <i>Xma I</i> S
012	atfttagcacaatgtccagctccaa	rat Taar1 amplification S
013	taaaagcccatgaaatcagtgctca	rat Taar1 amplification AS
010	cccgactacgccatctttgccacaatag	rat Taar1 HA adaptor S
009	catcgtccttatagtcacaaaatagcttagacc	rat Taar1 FLAG adaptor AS
011	tccattgaccgctactatgctgtg	rat Taar1 sequencing S
014	cgcccaccatgatccctaag	ratt Taar1 sequencing AS
2187	gtgcaaatggaggagactgaa	elephant Taar1 amplification S
2189	actcaragaacygacaaaagacc	elephant Taar1 amplification AS
2328	tccccgactacgccatgtcctttgccacgatg	elephant Taar1 HA adaptor S
2329	catcgtccttatagctcgttgattgattctgaaagtaattg	elephant Taar1 FLAG adaptor AS
2217	gctcagcatccattttccac	elephant Taar1 sequencing S
2218	tgaaggacaagtggaaaatgg	elephant Taar1 sequencing AS
2219	aaagaacggaaagctgcaaa	elephant Taar1 sequencing S
2220	gctttccgtctttgctttg	elephant Taar1 sequencing AS
2181	gaaaacacccaaagtacaacaaca	frog Taar1 amplification S
2182	aagccactgtataacccttgagttg	frog Taar1 amplification AS
2204	tccccgactacgccagatacaataactgct	frog Taar1 HA adaptor S
2205	catcgtccttatagctcctctgaatataaaatgggt	frog Taar1 FLAG adaptor AS
2225	tccacctctcttcatttctgt	frog Taar1 sequencing S
2226	acagaaatgaaggagaggtgga	frog Taar1 sequencing AS
2227	tgtcccgaagcagagatagg	frog Taar1 sequencing S
2228	cctatctctgctcgggaca	frog Taar1 sequencing AS
2179	gcagcttcttcacaacaaaaag	chicken Taar1 amplification S
2180	tagtcaactatctgcttgaaacaa	chicken Taar1 amplification AS
2334	tccccgactacgccagctgtgctgtgaatcg	chicken Taar1 HA adaptor S
2335	catcgtccttatagctcctctaaaaataactgagttcttgatga	chicken Taar1 FLAG adaptor AS
2213	tctgcaagatccacacaagc	chicken Taar1 sequencing S
2214	ggaagatggaagctgtgctc	chicken Taar1 sequencing AS
2215	gcaagatccattgatgcagtt	chicken Taar1 sequencing S
2216	gcagaatgaaatgtgcttcg	chicken Taar1 sequencing AS
2185	aaagtgaaacaattctactctga	kangaroo Taar1 amplification S
2186	aattacacatgtttctaagtatttagtyct	kangaroo Taar1 amplification AS
2338	tccccgactacgcctcattttgtatgaagccataatg	kangaroo Taar1 HA adaptor S
2339	catcgtccttatagctcagttatagctcctaaaaataattggca	kangaroo Taar1 FLAG adaptor AS
2229	aagctcagcatcaattttcca	kangaroo Taar1 sequencing S
2230	cggtcaatggaaatgaaga	kangaroo Taar1 sequencing AS
2231	gtcaaaacaagaagccccaaa	kangaroo Taar1 sequencing S
2232	tggggcttctgtttgactt	kangaroo Taar1 sequencing AS
2194	ggctggatgcacagcaga	crocodile Taar1 amplification S
2195	tacctgaacagatttgacaagtggag	crocodile Taar1 amplification AS
2336	tccccgactacgccagtttggctgtgaatctgtaaatg	crocodile Taar1 HA adaptor S
2337	catcgtccttatagctcctctaaaaataattgagttctggaaga	crocodile Taar1 FLAG adaptor AS
2330	cagtggtgcacacacagcat	crocodile Taar1 sequencing AS
2331	cttgctgcctctttgctat	crocodile Taar1 sequencing AS
2332	catgctgagtacagctcca	crocodile Taar1 sequencing S
2333	atagcaaagaggcaggcaag	crocodile Taar1 sequencing S
301	cgttcttttctgcacggctctggaccctttc	rat-Taar1-M268T-788-S
302	aaaggtccaggaccgtgcagaaaaagacgg	rat-Taar1-M268T-818-AS

303	gaatgacacactgattgggtcgggtacc	rat-Taarl-N287I-846-S
304	ggtaccgaaccaaaccagtggtcattc	rat-Taarl-N287I-874-AS
305	ctgaatgacacactggttgggtcgggtacc	rat-Taarl-N287V-844-S
306	ggtaccgaaccaaaccagtggtcattcag	rat-Taarl-N287V-874-AS
307	tccattttttctgtatggccaccgatcccttatg	crocodile-Taarl-T268M-792-S
308	ataaagggatcgggtggccatacagaaaaaaatggag	crocodile-Taarl-T268M-827-AS
309	ccagttctcatagatgcattaaattggttgggtacttgaattc	crocodile-Taarl-V287N-844-S
310	gaattcaagtaaccaaccaatttaatgcatctatgagaactgg	crocodile-Taarl-V287N-887-AS

Suppl. Table S4

Relative evolutionary rate are shown for each site next to the site number.

These rates are scaled such that the average evolutionary rate across all sites is 1. This means that sites showing a rate < 1 are evolving slower than average, and those with a rate > 1 are evolving faster than average. These relative rate were estimated under the Jones-Taylor-Thornton (1992) model (+G) [4]. A discrete Gamma (+G) distribution was used to model evolutionary rate differences among sites (5 categories). The probability of classification of a site in each discrete rate category in Gamma is shown. Mean relative evolutionary rates in discrete Gamma categories are shown in the column headers. The ML estimate of the gamma shape parameter is 0.7626. The maximum Log likelihood for this computation was -12129.054. The analysis involved 111 amino acid sequences. The coding data was translated assuming a Standard genetic code table. There were a total of 332 positions in the final dataset. Evolutionary analyses were conducted in MEGA6 [3].

amino acid	Site No.	Rel. Rate	Gamma Categories				
			#1	#2	#3	#4	#5
			0.064433166	0.277876363	0.619770907	1.195688611	2.842230953
H	1	1.29508622	2.01552E-10	0.000115745	0.040626335	0.781616875	0.177641045
L	2	2.508593467	4.72295E-19	1.55568E-10	3.02865E-06	0.003115069	0.996881902
C	3	1.352495879	9.64992E-06	0.007341963	0.137857424	0.599673734	0.255117229
H	4	2.465629322	1.80599E-16	1.26754E-08	9.17569E-05	0.032505807	0.967402423
N	5	2.311149761	3.20267E-15	1.64149E-07	0.000756619	0.137714596	0.86152862
S	6	2.492794993	5.27105E-21	8.34204E-11	7.84127E-06	0.013959975	0.986032184
A	7	2.469149973	2.10441E-18	2.00724E-09	4.56926E-05	0.030149793	0.969804513
N	8	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
I	9	2.428768653	5.63831E-16	3.48828E-08	0.000211335	0.057662633	0.942125997
S	10	0.26047684	0.208387337	0.62055782	0.166355994	0.004698818	3.10457E-08
H	11	0.562476721	0.033623499	0.296106682	0.445112226	0.221149281	0.004008312
T	12	1.853332713	3.2711E-13	3.53176E-06	0.006219554	0.444793639	0.548983276
N	13	1.674228661	5.9629E-11	4.0375E-05	0.018438214	0.551263941	0.43025747
S	14	1.263384565	2.52863E-13	7.93652E-06	0.016776208	0.835751782	0.147464073
N	15	2.12667411	1.00687E-16	6.95357E-08	0.000946734	0.264167801	0.734885395
W	16	1.359525672	0.000615509	0.033173845	0.194600532	0.4770017	0.294608414
S	17	0.559923722	0.000825909	0.204991499	0.648344725	0.145820466	1.74007E-05
R	18	1.291410419	1.90124E-11	4.29819E-05	0.028765053	0.800265023	0.170926942

D	19	2.416991292	9.12831E-18	7.55871E-09	0.000138991	0.065849769	0.934011233
V	20	2.33154093	3.00621E-17	2.23171E-08	0.000345832	0.124263328	0.875390818
R	21	0.743467219	0.000178904	0.072776101	0.50512077	0.420077195	0.001847032
A	22	1.360144164	1.55976E-11	3.61166E-05	0.025183206	0.757899669	0.216881009
S	23	0.897807996	3.20849E-07	0.0072388	0.308576416	0.681726788	0.002457676
L	24	0.255084769	0.325964789	0.471498558	0.183572389	0.018952829	1.14348E-05
Y	25	0.159246755	0.627064961	0.283604718	0.079802481	0.00950489	2.29503E-05
S	26	1.034323607	1.17357E-09	0.000490657	0.104190169	0.874344599	0.020974573
L	27	2.231277375	5.9263E-11	1.32453E-05	0.004753186	0.187161221	0.808072347
I	28	0.191703967	0.453222277	0.448355855	0.094917075	0.003504683	1.10437E-07
S	29	2.299198705	3.7303E-16	7.19785E-08	0.000595725	0.146140659	0.853263544
L	30	1.398869867	1.03387E-06	0.002987011	0.102481248	0.622367972	0.272162735
I	31	1.260042756	2.58949E-11	5.45905E-05	0.033182504	0.815829699	0.150933206
I	32	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
L	33	0.510236712	0.043703385	0.346205501	0.440968244	0.167594435	0.001528435
T	34	1.0635896	7.92664E-10	0.000358336	0.08598983	0.879015268	0.034636564
T	35	0.091029241	0.836394919	0.153272641	0.010222343	0.000110097	3.26006E-10
L	36	1.232657451	2.10129E-07	0.002084296	0.111391881	0.72591324	0.160610373
V	37	2.506817184	8.49127E-24	2.20027E-12	8.55173E-07	0.004338068	0.995661077
G	38	0.338066229	0.224588315	0.437816749	0.274406363	0.062834265	0.000354308
N	39	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
L	40	0.507518367	0.044305755	0.348977749	0.440447136	0.16483117	0.00143819
I	41	2.431609682	6.87082E-19	2.23028E-09	7.8613E-05	0.055890429	0.944030956
V	42	0.096955854	0.812648681	0.172460565	0.014649099	0.000241652	2.75746E-09
I	43	0.292436871	0.163169094	0.599591258	0.225830071	0.011409158	4.18489E-07
I	44	0.400646459	0.031910941	0.504633247	0.422499721	0.040952575	3.51543E-06
S	45	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
I	46	0.401990358	0.031564411	0.502169506	0.424468316	0.04179403	3.73717E-06
S	47	1.495382952	1.10826E-14	1.50279E-06	0.007111056	0.68945625	0.303431191
H	48	0.101867596	0.793616131	0.187370059	0.018628192	0.000385612	6.40049E-09
F	49	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
K	50	0.822403125	9.49079E-05	0.045554505	0.411947038	0.534159555	0.008243994

Q	51	0.842808741	1.5478E-05	0.026456823	0.391619275	0.577458636	0.004449789
L	52	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
H	53	0.101867596	0.793616131	0.187370059	0.018628192	0.000385612	6.40049E-09
T	54	0.167002779	0.522094025	0.41449292	0.062106715	0.001306331	9.5195E-09
P	55	0.298071461	0.266720133	0.459014397	0.235630704	0.038551561	8.3205E-05
T	56	0.386529743	0.035603429	0.53064312	0.401511557	0.032240465	1.42828E-06
N	57	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
W	58	2.141785217	8.99165E-08	0.000342637	0.018246127	0.229904583	0.751506563
L	59	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
L	60	0.785613336	2.76253E-05	0.040487115	0.473524167	0.484319479	0.001641613
H	61	1.248603176	2.14307E-09	0.000318845	0.059684352	0.78750407	0.152492731
S	62	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
M	63	0.320380834	0.132455039	0.571958825	0.275326097	0.020258376	1.66276E-06
A	64	0.522544255	0.0039775	0.287251161	0.584507359	0.124231527	3.24525E-05
V	65	1.581205342	7.61432E-14	2.86628E-06	0.008031101	0.62926397	0.362702062
V	66	0.863181524	2.59669E-06	0.015439746	0.365705506	0.615622961	0.00322919
D	67	0.106366332	0.777373975	0.199247319	0.022769606	0.000609076	2.45298E-08
F	68	0.333506266	0.228959661	0.440480608	0.270398817	0.059852204	0.000308711
L	69	0.508437604	0.044100525	0.348037196	0.440629313	0.165764948	0.001468018
L	70	0.317596649	0.24522903	0.449216319	0.255416273	0.049950615	0.000187763
G	71	0.540008811	0.037570198	0.316765412	0.444866505	0.198080794	0.002717092
C	72	2.49265607	6.04671E-15	2.90171E-08	6.51173E-05	0.013978042	0.985956812
L	73	2.384272143	1.18476E-11	3.17947E-06	0.001486979	0.086498952	0.912010889
V	74	0.970080081	1.38267E-07	0.003686065	0.208544567	0.772639489	0.01512974
M	75	0.100195107	0.799911279	0.182574313	0.017189916	0.000324488	4.12918E-09
P	76	0.300394941	0.263919243	0.458010875	0.238189933	0.039789408	9.05413E-05
Y	77	0.549193575	0.035961688	0.308345364	0.444950655	0.207485696	0.003256597
S	78	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
M	79	0.191374729	0.454048439	0.448032308	0.09445642	0.003462726	1.06741E-07
V	80	0.307938922	0.145772119	0.584659992	0.25335778	0.016208945	1.1632E-06
R	81	0.10904722	0.767811151	0.206155112	0.0252804	0.000753299	3.83171E-08
T	82	0.362052812	0.044094492	0.578129905	0.357218683	0.020556545	3.74866E-07

V	83	0.418501133	0.027722918	0.472724178	0.446529276	0.053015533	8.0952E-06
E	84	0.115309756	0.746742676	0.220464513	0.031562608	0.001230061	1.41688E-07
H	85	2.332309019	2.32422E-16	4.80495E-08	0.000439212	0.123609674	0.875951066
C	86	1.662729824	4.76588E-07	0.001534191	0.06233582	0.49758293	0.438546582
W	87	0.259513657	0.464404987	0.311856157	0.164810854	0.056309144	0.002618857
Y	88	1.395647693	1.01308E-06	0.002946952	0.102009799	0.625279942	0.269762294
F	89	0.333025719	0.229417333	0.440762588	0.269979843	0.059536519	0.000303718
G	90	0.159171431	0.62719081	0.283588335	0.079728059	0.009470282	2.25142E-05
E	91	0.783908827	0.000129652	0.057411437	0.457155234	0.481054239	0.004249438
L	92	2.502731333	2.03646E-20	8.70937E-11	4.77487E-06	0.0071392	0.992856025
F	93	0.333115066	0.22933423	0.4407092	0.270055643	0.059596182	0.000304745
C	94	0.174970428	0.593466611	0.295226491	0.096530765	0.01470757	6.85622E-05
K	95	0.245659301	0.341766053	0.471615502	0.170845551	0.015765558	7.3352E-06
L	96	0.953876528	1.59904E-07	0.004166848	0.225556522	0.760058016	0.010218455
H	97	0.101867596	0.793616131	0.187370059	0.018628192	0.000385612	6.40049E-09
T	98	0.59627244	0.000599073	0.167326849	0.63753314	0.194489324	5.16138E-05
S	99	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
T	100	2.318233619	3.1145E-18	8.96777E-09	0.000260633	0.13351866	0.866220698
D	101	0.106366332	0.777373975	0.199247319	0.022769606	0.000609076	2.45298E-08
I	102	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
M	103	0.318059143	0.134631374	0.57457513	0.271440306	0.019351739	1.45215E-06
L	104	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
S	105	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
S	106	0.374094033	0.039606709	0.554563717	0.379945432	0.025883403	7.38234E-07
A	107	0.41198663	0.028974579	0.483770543	0.439250967	0.047998763	5.14877E-06
S	108	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
I	109	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
L	110	0.714940541	0.004175322	0.149543004	0.457383926	0.377804782	0.011092965
H	111	0.196010226	0.442552382	0.452405937	0.100964966	0.004076549	1.66088E-07
L	112	0.510559384	0.043636085	0.345884626	0.441013832	0.167924544	0.001540913
A	113	0.153539832	0.565180365	0.387962654	0.046191353	0.000665627	1.76945E-09
F	114	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05

I	115	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
S	116	0.152480403	0.568741018	0.385619074	0.045012571	0.000627336	1.51563E-09
I	117	0.755963984	3.55156E-05	0.04898071	0.515740115	0.434461172	0.000782487
D	118	0.106366332	0.777373975	0.199247319	0.022769606	0.000609076	2.45298E-08
R	119	0.356260847	0.10443533	0.528459236	0.329258181	0.03783523	1.20229E-05
Y	120	0.159246755	0.627064961	0.283604718	0.079802481	0.00950489	2.29503E-05
Y	121	2.312217344	3.16071E-11	7.47599E-06	0.002934827	0.134029836	0.863027861
A	122	0.178707399	0.488167435	0.432374234	0.077266262	0.002192031	3.81939E-08
V	123	0.184244322	0.473493261	0.438897461	0.084821557	0.00278764	8.20037E-08
C	124	0.791540989	0.002875391	0.114199275	0.411285178	0.444651596	0.02698856
D	125	0.480918645	0.017486182	0.373377181	0.50258096	0.106480762	7.49144E-05
P	126	0.1422213	0.668036421	0.26588703	0.060940407	0.005131577	4.56466E-06
L	127	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
R	128	0.10904722	0.767811151	0.206155112	0.0252804	0.000753299	3.83171E-08
Y	129	0.336564919	0.226070949	0.438672613	0.273041349	0.061873707	0.000341383
K	130	0.40081646	0.079441229	0.47216766	0.380744744	0.067572149	7.42178E-05
A	131	2.432318474	4.03928E-19	1.56475E-09	6.63526E-05	0.055420135	0.944513511
K	132	1.223549291	2.36565E-08	0.000890509	0.086457619	0.767684463	0.144967385
I	133	0.521439356	0.004036118	0.289259091	0.583366216	0.123304651	3.39244E-05
N	134	1.819459805	3.75177E-15	5.83209E-07	0.003422353	0.471839898	0.524737166
L	135	2.331943818	3.61695E-17	2.27154E-08	0.00034437	0.123988571	0.875667036
A	136	2.511763624	6.01361E-21	8.95592E-12	4.19122E-07	0.000941125	0.999058456
A	137	0.917312117	1.34416E-06	0.009418607	0.284995323	0.69676266	0.008822066
I	138	0.978703008	7.62875E-08	0.00261279	0.185750426	0.799155292	0.012481415
F	139	2.512477511	1.69151E-22	1.06959E-12	1.08834E-07	0.000451201	0.99954869
V	140	1.188828724	3.41943E-10	0.000179039	0.054479087	0.835804656	0.109537218
M	141	0.100195107	0.799911279	0.182574313	0.017189916	0.000324488	4.12918E-09
I	142	0.292880311	0.162641766	0.599191301	0.226632517	0.011533983	4.32519E-07
L	143	2.51085269	1.35016E-19	4.97681E-11	1.15337E-06	0.001565821	0.998433025
I	144	1.389958617	1.15383E-11	2.88837E-05	0.022160599	0.741512297	0.23629822
S	145	0.658708838	8.58419E-05	0.09128974	0.637169202	0.271382653	7.25629E-05
W	146	0.259513657	0.464404987	0.311856157	0.164810854	0.056309144	0.002618857

S	147	1.46538626	1.12598E-13	4.01177E-06	0.010324267	0.70571888	0.283952841
L	148	2.462217216	3.28039E-19	1.11602E-09	4.25609E-05	0.034915882	0.965041556
P	149	0.1422213	0.668036421	0.26588703	0.060940407	0.005131577	4.56466E-06
A	150	0.412040617	0.028958801	0.483666978	0.439340986	0.048028087	5.14814E-06
V	151	2.511224562	1.10707E-23	8.78968E-13	2.38516E-07	0.001311631	0.99868813
F	152	0.532165571	0.039059237	0.324246951	0.444337997	0.190017434	0.002338381
A	153	0.301352544	0.152429296	0.591665861	0.242048863	0.013855324	6.56587E-07
F	154	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
G	155	0.58145665	0.029782018	0.277442294	0.4473397	0.240655085	0.004780902
M	156	0.439652059	0.023255105	0.435781917	0.472660565	0.068288349	1.40628E-05
I	157	0.404069345	0.030987662	0.498278361	0.42772031	0.043009734	3.93262E-06
F	158	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
L	159	0.84915139	0.000419126	0.061257416	0.383086202	0.529739777	0.02549748
E	160	1.032843821	5.05803E-07	0.004306373	0.179756022	0.767420672	0.048516428
L	161	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
N	162	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
L	163	2.513127982	5.84828E-31	5.87504E-18	3.61352E-11	4.56217E-06	0.999995438
E	164	2.39213611	2.39553E-14	2.13382E-07	0.000541361	0.082378467	0.917079958
G	165	0.159171431	0.62719081	0.283588335	0.079728059	0.009470282	2.25142E-05
V	166	1.800334796	2.22211E-13	2.84144E-06	0.00593652	0.481579103	0.512481536
E	167	0.382065697	0.089113079	0.49583817	0.360745772	0.054263701	3.92777E-05
E	168	2.34874411	2.14442E-14	2.98728E-07	0.000791215	0.111845488	0.887362999
Q	169	2.513054922	3.9412E-30	1.09533E-16	7.38896E-10	5.47438E-05	0.999945255
Y	170	0.646154707	0.023409464	0.233750051	0.429511195	0.299078672	0.014250618
H	171	2.418160416	7.73947E-13	8.03916E-07	0.000718496	0.064263299	0.935017402
N	172	2.507700614	6.20687E-22	1.13305E-11	1.35659E-06	0.003730595	0.996268049
Q	173	1.849777966	3.15644E-13	3.42742E-06	0.006114427	0.447377326	0.546504819
V	174	2.513073934	2.93611E-31	3.10923E-17	3.87696E-10	4.16854E-05	0.999958314
F	175	2.463407485	2.50402E-18	2.36254E-09	5.29777E-05	0.034084266	0.965862753
C	176	0.607795276	0.027347315	0.259485359	0.439140291	0.265705299	0.008321736
L	177	2.513132253	1.00243E-35	2.49542E-20	2.23932E-12	1.62917E-06	0.999998371
R	178	0.72467098	0.003968807	0.144244291	0.451546195	0.387601627	0.012639081

G	179	2.501375298	2.22493E-16	4.47317E-09	2.13042E-05	0.008048294	0.991930397
C	180	0.174970428	0.593466611	0.295226491	0.096530765	0.01470757	6.85622E-05
F	181	2.481215076	9.77246E-19	1.03693E-09	2.73157E-05	0.021887515	0.978085168
P	182	1.188884275	3.50604E-10	0.000182376	0.055002285	0.835055104	0.109760235
F	183	0.846520268	0.000421835	0.061625378	0.384703395	0.528786512	0.02446288
F	184	0.332692224	0.22974069	0.440955494	0.269683051	0.05932023	0.000300534
S	185	0.652488004	9.08157E-05	0.094875878	0.643627395	0.261344913	6.09989E-05
K	186	0.847399086	7.76409E-05	0.039222323	0.383878986	0.564767242	0.012053808
V	187	1.00120147	1.30529E-08	0.001384004	0.151752954	0.831504655	0.015358374
S	188	0.662123887	8.32661E-05	0.089392422	0.633512997	0.276931293	8.00225E-05
G	189	0.537556015	0.038029936	0.319090842	0.444724727	0.195559633	0.002594862
V	190	1.061804361	6.93453E-09	0.000829174	0.110494913	0.84643186	0.042244046
L	191	1.274351693	1.78443E-07	0.001821343	0.10172852	0.710727903	0.185722056
A	192	0.760330248	3.43273E-05	0.047680295	0.509458562	0.441968115	0.000858701
F	193	0.412797285	0.074023847	0.457229283	0.391773345	0.07686152	0.000112005
M	194	2.214820866	6.20027E-16	1.16187E-07	0.000914692	0.20366615	0.795419041
T	195	1.112407168	4.90601E-10	0.000243958	0.067702949	0.870345536	0.061707558
S	196	0.361583814	0.044298881	0.579060564	0.356255037	0.020385147	3.70551E-07
F	197	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
Y	198	0.541749861	0.037282567	0.315211271	0.444813832	0.19986172	0.00283061
I	199	0.629710997	0.000458235	0.139811327	0.616271111	0.24331129	0.000148038
P	200	0.1422213	0.668036421	0.26588703	0.060940407	0.005131577	4.56466E-06
G	201	1.111721699	2.00242E-05	0.013484084	0.208697314	0.65985164	0.117946939
S	202	0.789876055	2.59782E-05	0.038889934	0.467556778	0.491936455	0.001590855
V	203	1.140451643	4.346E-10	0.000219045	0.06256331	0.858058948	0.079158697
M	204	0.100195107	0.799911279	0.182574313	0.017189916	0.000324488	4.12918E-09
L	205	0.866120748	0.000384826	0.057372224	0.370496008	0.541186787	0.030560156
F	206	2.488157001	8.32664E-15	3.90904E-08	8.46086E-05	0.017041965	0.982873387
V	207	1.310108547	2.19039E-11	4.72443E-05	0.029836236	0.785969459	0.18414706
Y	208	0.336564919	0.226070949	0.438672613	0.273041349	0.061873707	0.000341383
Y	209	2.386366204	1.35401E-12	1.32857E-06	0.001090291	0.085598939	0.913309441
R	210	0.226520672	0.376456454	0.469057998	0.14434864	0.010134727	2.18122E-06

I	211	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
Y	212	0.539892168	0.037618689	0.316941186	0.444754109	0.19795706	0.002728956
F	213	2.500146308	2.7315E-18	7.88965E-10	1.24249E-05	0.008904434	0.99108314
I	214	0.510640337	0.004416775	0.304652816	0.579266556	0.111639071	2.47816E-05
A	215	0.095453674	0.818462909	0.167910222	0.013429952	0.000196915	1.43147E-09
K	216	2.298145172	3.71194E-14	4.87053E-07	0.001180521	0.146074305	0.852744687
G	217	2.239171256	5.8296E-12	4.98571E-06	0.00330288	0.183709649	0.812982486
Q	218	0.477408382	0.017761822	0.377670573	0.502041538	0.10246831	5.77573E-05
A	219	0.095453674	0.818462909	0.167910222	0.013429952	0.000196915	1.43147E-09
R	220	0.856254596	1.38097E-05	0.024192936	0.373547117	0.596145123	0.006101014
S	221	0.261032299	0.207473134	0.620346047	0.167398453	0.004782332	3.27129E-08
I	222	0.093636931	0.825820633	0.161908367	0.0121099	0.0001611	9.89601E-10
N	223	2.493438577	5.72166E-19	5.94605E-10	1.56802E-05	0.013507339	0.98647698
R	224	2.501445531	2.38332E-20	1.01458E-10	5.5042E-06	0.008021387	0.991973109
A	225	2.512570247	1.10366E-27	6.18304E-15	1.48879E-08	0.00038763	0.999612355
N	226	2.480349309	1.07301E-20	1.64546E-10	1.44847E-05	0.022499499	0.977486016
-	227	1.915114938	2.75229E-12	7.79203E-06	0.00755117	0.400553641	0.591887397
-	228	2.493565627	5.71162E-17	4.0326E-09	3.10429E-05	0.013399331	0.986569622
L	229	2.513129283	4.32079E-32	1.68237E-18	1.95721E-11	3.66911E-06	0.999996331
Q	230	1.075884142	4.56705E-08	0.001544521	0.125598873	0.815259873	0.057596687
V	231	2.511227198	8.33106E-25	2.75705E-13	1.52867E-07	0.001309936	0.998689911
G	232	2.325181812	2.75322E-12	2.54182E-06	0.001893202	0.126538653	0.871565603
L	233	2.247679965	5.33275E-11	1.20189E-05	0.00437307	0.176409855	0.819205056
E	234	0.807497643	0.000107277	0.049882674	0.429318662	0.514188192	0.006503195
G	235	2.491856742	6.60237E-19	6.77091E-10	1.74942E-05	0.014591395	0.98539111
E	236	1.577627813	7.87598E-10	0.000133928	0.03117474	0.600278445	0.368412886
S	237	2.510977169	1.14843E-25	1.37469E-13	1.31661E-07	0.001481701	0.998518168
R	238	2.507834144	5.7742E-20	7.25418E-11	2.58094E-06	0.003637225	0.996360194
A	239	2.411903802	8.89085E-18	7.58279E-09	0.00014371	0.069337812	0.93051847
P	240	0.813759136	4.33077E-06	0.022838912	0.444530947	0.531646366	0.000979444
Q	241	2.466958931	2.4124E-17	5.859E-09	6.99976E-05	0.031621928	0.968308069
S	242	1.946582767	2.54467E-15	4.08591E-07	0.002531943	0.385725846	0.611741803

K	243	2.322498505	2.87679E-14	3.88488E-07	0.000982741	0.12961399	0.86940288
E	244	0.900437551	9.35937E-06	0.017902214	0.318733382	0.64958839	0.013766654
T	245	2.329340822	2.79796E-15	1.44273E-07	0.000672484	0.125333407	0.873993965
K	246	0.121163771	0.7279604	0.232562183	0.037681367	0.0017957	3.48854E-07
A	247	0.095453674	0.818462909	0.167910222	0.013429952	0.000196915	1.43147E-09
A	248	1.110443483	5.1693E-10	0.000253234	0.069001163	0.869927575	0.060818027
K	249	0.39113672	0.084163953	0.484350202	0.370999184	0.060434339	5.23213E-05
T	250	0.091029241	0.836394919	0.153272641	0.010222343	0.000110097	3.26006E-10
L	251	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
G	252	0.341800676	0.221118558	0.435583214	0.277570952	0.065329925	0.000397351
I	253	0.51151652	0.00439014	0.303490849	0.579453313	0.112639776	2.59221E-05
M	254	0.77368659	3.0845E-05	0.043913738	0.490414981	0.464370634	0.001269802
V	255	1.241251004	2.36838E-10	0.000133277	0.045166023	0.812439486	0.142261215
G	256	0.339876063	0.222907948	0.436733716	0.275938783	0.06404433	0.000375223
V	257	0.419154984	0.027598137	0.471621863	0.447248069	0.053523495	8.43592E-06
F	258	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
L	259	0.860431343	0.000395755	0.058622935	0.374639603	0.537535398	0.028806308
L	260	2.334383686	2.62555E-17	2.01402E-08	0.000325319	0.122338434	0.877336228
C	261	0.174970428	0.593466611	0.295226491	0.096530765	0.01470757	6.85622E-05
W	262	0.259513657	0.464404987	0.311856157	0.164810854	0.056309144	0.002618857
C	263	1.952541473	2.2391E-10	4.42058E-05	0.01301139	0.36741993	0.619524474
P	264	0.1422213	0.668036421	0.26588703	0.060940407	0.005131577	4.56466E-06
F	265	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
F	266	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
F	267	1.96322327	2.28678E-11	1.71743E-05	0.009254635	0.365195859	0.625532332
C	268	0.970013753	0.000239609	0.039787548	0.304420502	0.586645109	0.068907233
M	269	1.150056076	4.21325E-11	8.24833E-05	0.044349163	0.876259675	0.079308679
V	270	0.975402462	1.17908E-07	0.003299137	0.198448478	0.78321382	0.015038447
L	271	2.509702062	1.3754E-23	1.33703E-12	4.2088E-07	0.002357135	0.997642444
D	272	0.729993165	0.00020107	0.079024963	0.520437057	0.398889023	0.001447886
P	273	0.322984076	0.237256868	0.447846424	0.262629961	0.052096266	0.000170481
F	274	0.332636863	0.229793977	0.440987705	0.269634197	0.059284136	0.000299986

L	275	2.258298954	5.03454E-13	1.67823E-06	0.002108712	0.172188531	0.825701079
G	276	2.461748866	2.92584E-18	2.6781E-09	5.7619E-05	0.035217247	0.964725131
Y	277	0.535823405	0.038371564	0.320772761	0.444557515	0.193779604	0.002518556
V	278	2.509948572	1.89522E-24	5.93556E-13	3.00102E-07	0.002187979	0.997811721
I	279	0.759257735	3.4537E-05	0.047969138	0.511103557	0.440034209	0.000858558
P	280	0.646656392	0.006074605	0.194235909	0.495229856	0.300813533	0.003646096
P	281	2.471861947	1.96985E-15	3.31176E-08	0.000118904	0.028188169	0.971692894
T	282	2.512191235	3.19118E-27	1.583E-14	3.19957E-08	0.000647937	0.999352031
L	283	2.00017999	1.83643E-09	9.61986E-05	0.015747346	0.330924851	0.653231602
N	284	1.763362409	4.34421E-14	1.74594E-06	0.005431456	0.50765753	0.486909268
D	285	0.729139734	0.000203005	0.079524082	0.521330801	0.39748826	0.001453852
T	286	1.49453617	1.04492E-12	9.76338E-06	0.013734552	0.681084787	0.305170898
L	287	0.845929852	0.000426596	0.062078356	0.385582407	0.527292074	0.024620568
N	288	1.282594722	2.30111E-11	4.95852E-05	0.031128743	0.803119475	0.165702196
W	289	0.259513657	0.464404987	0.311856157	0.164810854	0.056309144	0.002618857
F	290	2.319374537	2.95298E-11	7.02889E-06	0.002786693	0.129314462	0.867891816
G	291	0.159171431	0.62719081	0.283588335	0.079728059	0.009470282	2.25142E-05
Y	292	0.159246755	0.627064961	0.283604718	0.079802481	0.00950489	2.29503E-05
L	293	0.319015597	0.243692513	0.44848869	0.256831235	0.050791514	0.000196048
N	294	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
S	295	0.085806603	0.858613312	0.134357741	0.006979159	4.97874E-05	4.88337E-11
A	296	0.605840855	0.000552966	0.158779695	0.632504054	0.208094531	6.87543E-05
F	297	1.366647525	1.10291E-06	0.003167837	0.107480894	0.637470206	0.251879959
N	298	0.092727133	0.829386794	0.15908543	0.011390392	0.000137384	5.3483E-10
P	299	0.1422213	0.668036421	0.26588703	0.060940407	0.005131577	4.56466E-06
M	300	0.894844619	1.74794E-06	0.011486489	0.316207885	0.66684363	0.005460247
V	301	0.883293546	2.07672E-06	0.013012511	0.334950516	0.647102121	0.004932775
Y	302	0.159246755	0.627064961	0.283604718	0.079802481	0.00950489	2.29503E-05
A	303	0.301837599	0.151846402	0.591230488	0.242935164	0.013987279	6.66811E-07
F	304	0.535171701	0.038486171	0.321374709	0.444549871	0.193106721	0.002482528
F	305	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
Y	306	0.339235412	0.223576204	0.437082854	0.275317688	0.063651574	0.00037168

P	307	1.535610677	7.82739E-09	0.000350688	0.044617769	0.61065585	0.344375685
W	308	1.40665862	0.000555761	0.030396071	0.182531912	0.46534464	0.321171616
F	309	0.156796527	0.632619616	0.281447219	0.077129329	0.008785165	1.8671E-05
R	310	0.492622068	0.016059013	0.356585352	0.509234043	0.118021544	0.000100048
R	311	1.558721728	8.20448E-11	5.36478E-05	0.023125594	0.624253912	0.352566847
A	312	0.095453674	0.818462909	0.167910222	0.013429952	0.000196915	1.43147E-09
L	313	0.150445968	0.647701727	0.275075858	0.07010731	0.007103884	1.12209E-05
K	314	0.400260102	0.079659491	0.47285185	0.380311237	0.067105638	7.17832E-05
M	315	1.60720391	7.55233E-13	7.32399E-06	0.010964895	0.60743959	0.381588191
V	316	0.624776273	0.000478576	0.143812027	0.619499578	0.236077993	0.000131826
L	317	1.053204196	2.55083E-05	0.016365777	0.235033172	0.660000492	0.088575051
F	318	2.513128762	5.09639E-31	5.09336E-18	3.13287E-11	4.02681E-06	0.999995973
G	319	0.159171431	0.62719081	0.283588335	0.079728059	0.009470282	2.25142E-05
K	320	0.935184611	6.99429E-06	0.014282351	0.281953514	0.681008028	0.022749112
I	321	0.74495096	4.03168E-05	0.053313062	0.530200809	0.415751569	0.000694242
F	322	0.3331792	0.229272267	0.440672008	0.270112473	0.059637882	0.000305371
Q	323	0.739488996	0.000182998	0.074158225	0.510012195	0.41404792	0.001598661
K	324	2.424364059	7.70014E-16	4.41955E-08	0.000244432	0.060643303	0.939112221
D	325	1.058287145	5.50442E-08	0.001785929	0.13662221	0.812091614	0.049500193
S	326	0.152440106	0.568884827	0.38551723	0.044971529	0.000626412	1.51727E-09
S	327	0.361724271	0.044232379	0.578779558	0.35655767	0.020430023	3.70113E-07
R	328	1.076430329	4.68571E-08	0.001572815	0.126642056	0.813432588	0.058352494
S	329	2.508701069	4.42289E-21	2.16125E-11	1.45809E-06	0.003043281	0.996955261
K	330	2.512875699	2.67743E-26	1.16599E-14	1.00113E-08	0.000177833	0.999822157
L	331	0.526765615	0.039245473	0.32798007	0.447144058	0.183810705	0.001819694
F	332	2.42744008	7.02838E-13	7.23741E-07	0.000643026	0.057991424	0.941364826

Suppl. Table S5

Maximum likelihood estimates of d_N/d_S ratios (ω) for vertebrate Taar1 under different models using PAML.

Likelihood ratio test (LRT) statistics for testing hypotheses concerning positive selection in certain branches.

branch models	ρ	ℓ	κ	Estimates of Parameters	hypothesis	χ^2	P-Value
One ratio: ω_0	222	-23501.7131	3.354	$\omega_0 = 0.223$	ω		
Two ratios: $\omega_0, \omega_{\text{rat/mouse}}$	223	-23500.9579	3.354	$\omega_0 = 0.222, \omega_{\text{rat/mouse}} = 0.278$	$\omega_0 \neq \omega_{\text{rat/mouse}}$	1.510	0.219
Two ratios: $\omega_0, \omega_{\text{rodentia}}$	223	-23490.5815	3.360	$\omega_0 = 0.222, \omega_{\text{rodentia}} = 0.294$	$\omega_0 \neq \omega_{\text{rodentia}}$	22.263	< 0.0001
branch-site models							
<i>vertebrate tree</i>							
model A versus model A' (foreground branch: <i>Muroidea</i>)	225	-23081.312	3.839	$\omega_0 = 0.106, p_0 = 0.589$ $\omega_1 = 1, p_1 = 0.273$ $\omega_{2(\text{Muroidea})} = 1$ $\omega_{2a(\text{other rodents})} = 0.106, p_{2a} = 0.095$ $\omega_{2b(\text{other rodents})} = 1, p_{2b} = 0.044$ H12: 0.934; T35: 0.832; P183: 0.992; A193: 0.896; F266: 0.848; N287: 0.987	$\omega_0 \neq \omega_{\text{muroidea}}$	0	n.s.
Model A' (foreground branch: <i>Muroidea</i> , $\omega_2 = 1$)	224	-23081.312	3.839	$\omega_0 = 0.106, p_0 = 0.589$ $\omega_1 = 1, p_1 = 0.273$ $\omega_{2(\text{Muroidea})} = 1$ $\omega_{2a(\text{other rodents})} = 0.106, p_{2a} = 0.095$ $\omega_{2b(\text{other rodents})} = 1, p_{2b} = 0.044$	positive selected sites?		
<i>rodent tree</i>							
model A versus model A' (foreground branch: <i>Muroidea</i>)	31	-6358.679	3.997	$\omega_0 = 0.108, p_0 = 0.667$ $\omega_1 = 4.863, p_1 = 0.323$ $\omega_{2(\text{Muroidea})} = 4.863$ $\omega_{2a(\text{other rodents})} = 0.108, p_{2a} = 0.007$ $\omega_{2b(\text{other rodents})} = 1, p_{2b} = 0.003$			

Model A'(foreground branch: <i>Muroidea</i> , $\omega_2 = 1$)	30	-6360.076	3.942	F176 0.856; R237 0.780; N287: 0.902 $\omega_0 = 0.102$, $p0 = 0.644$ $\omega_1 = 1$, $p1 = 0.290$ $\omega_{2(Muroidea)} = 1$ $\omega_{2a(other\ rodents)} = 0.102$, $p2a = 0.045$ $\omega_{2b(other\ rodents)} = 1$, $p2b = 0.020$	$\omega_0 \neq \omega_{muroidea}$ positive selected sites?	2.794	0.0946
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p , number of free parameters; ℓ , Log likelihood; κ , transition to transversion rate ratio; ω , d_N/d_S ratio; ω_0 , indicates ω of all other branches (the ones that are not specifically labeled in a model), LRT tests were performed between nested models. $\omega_{other\ rodents}$: ω of all other rodents except *Muroidea* which were labelled as foreground branches in branch-site test of positive selection

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