

a1 domain

Multiple sequence alignment for the a1 domain of MHC class I. It shows amino acid sequences for various species including Hs, Rm, Gg, and Sc. The alignment is approximately 450 amino acids long. Conserved residues are indicated by asterisks, and gaps are shown as dashes. A double underline indicates a bridge between Hs and Gg. A light shaded area at the bottom indicates a conserved region.

a2 domain

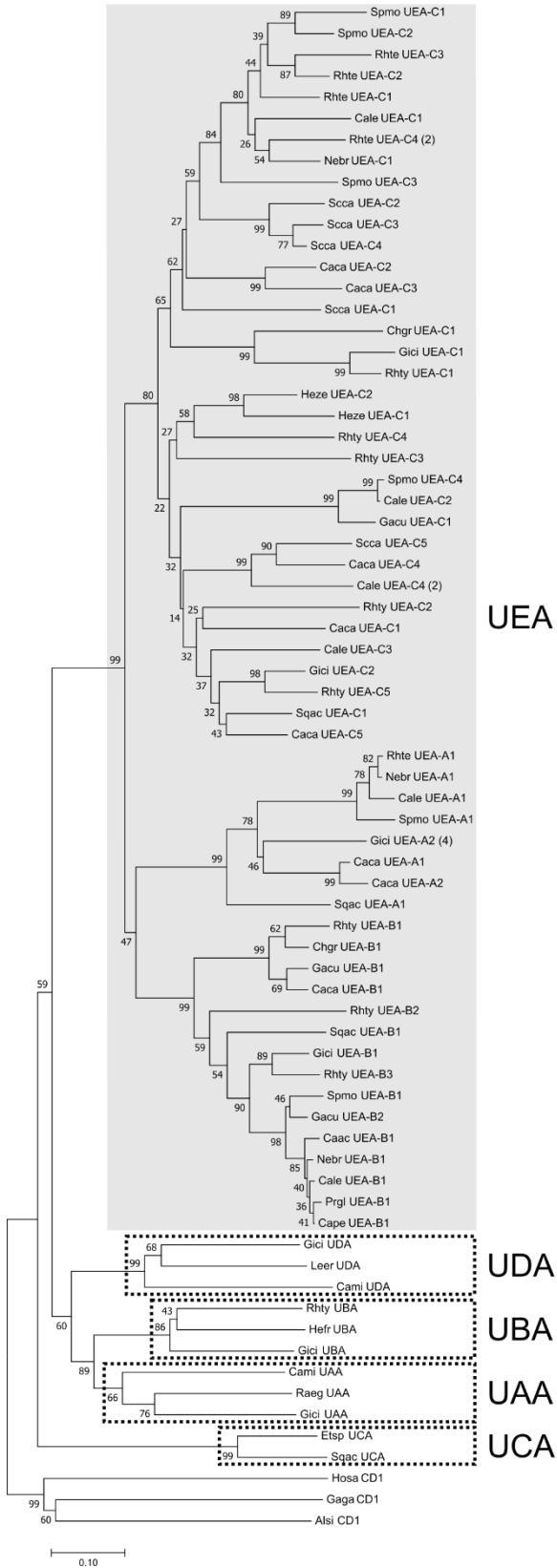
Multiple sequence alignment for the a2 domain of MHC class I. It shows amino acid sequences for various species including Hs, Rm, Gg, and Sc. The alignment is approximately 450 amino acids long. Conserved residues are indicated by asterisks, and gaps are shown as dashes. A double underline indicates a bridge between Hs and Gg. A light shaded area at the bottom indicates a conserved region.

a3 domain

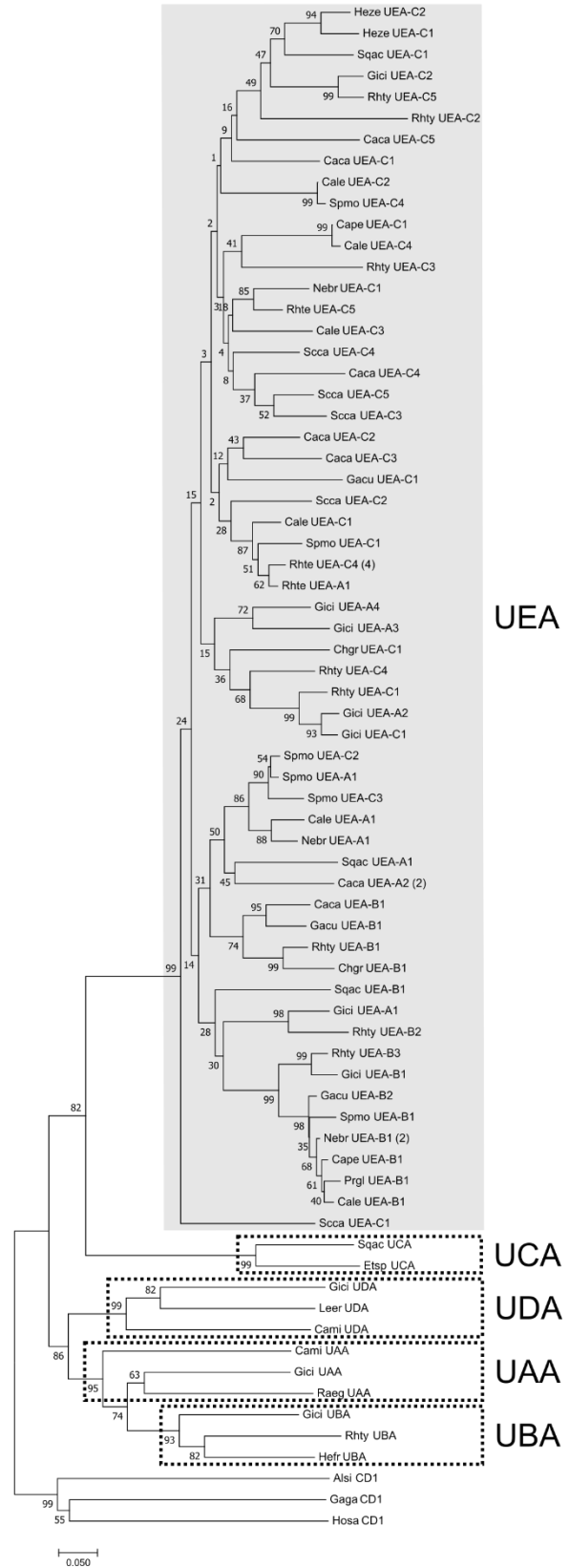
Multiple sequence alignment for the a3 domain of MHC class I. It shows amino acid sequences for various species including Hs, Rm, Gg, and Sc. The alignment is approximately 450 amino acids long. Conserved residues are indicated by asterisks, and gaps are shown as dashes. A double underline indicates a bridge between Hs and Gg. A light shaded area at the bottom indicates a conserved region.

Supplemental Figure 1. Amino acid alignment of the representative a1-3 domains of MHC class I in cartilaginous fish. The UAA, UBA, UCA, LEA and the new multiplex lineage LEA. GenBank accession numbers are listed in Supplemental Table 1. Dashes indicate gaps, and asterisks indicate the stop codons. s and h indicate the positions and residues, and the line connecting the two Cys in the a2 domain indicates the class I conserved disulfide bridge. Note that the a2 domain cysteines are not present in UCA and LEA. The double underline between the amino acids Hs and Gg indicates the possible salt bridge, while s, h and T indicate the residues that are potential binding sites for CD8 $\alpha$ -microglobulin and T cell receptor, respectively. P marks the invariant residues that are part of the P and C' elements of the bound peptide in the classical class I molecules and p indicates the other 28 potential conserved peptide binding residues. The asterisk marks the Acceptor-Terminator glycosylation site. Arginine indicates the typical Aspartic acid and Glutamic acid residues found in the connecting peptide (Conn; light shade). The potential Asn in the a3 domain perhaps rotting a glycosylation site from some LEA sequences is also underlined. Due to the high diversity in the cytoplasmic tail, the alignment would be mostly speculative. The numbering of amino acid positions is based on human HLA-A2.

### A $\alpha 1$ domain



### B $\alpha 2$ domain



**Supplemental Figure 2.** Phylogenetic trees of cartilaginous fish class I lineages with the  $\alpha 1$  domains (A) and  $\alpha 2$  domains (B). These trees were constructed using the neighbor-joining (NJ) method and rooted with CD1. Bootstrap support values are shown as percentages on the branches. GeneBank accession numbers for all the sequences are listed in Supplemental Table II, and the corresponding alignment is found in Supplemental Figure 1. Common names are shown followed by the abbreviation of the scientific name (two letters of the genus and two letters of species). The sublineages are represented by the letters A, B and C, followed by the number corresponding to a specific sequence. The scale bar indicates the number of amino acid differences per sequence.

Supplemental Table I. Genomic resource used in bioinformatic searches of MHC class I in Chondrichthyan Fish.

Project	Group	Order	Family	Species	No. specimens	Tissue type	Bioproject	Reference (doi)	
SRA	Holocephali	Chimaeriformes	Callorhynchidae	<i>Callorhynchus milii</i>	1	thymus, testis, spleen, ovary, liver, muscle, kidney, intestine, heart, gills, brain	PRJNA168475	10.1038/nature12826	
	Holocephali	Chimaeriformes	Callorhynchidae	<i>Callorhynchus milii</i>	32	embryos	PRJNA135005	10.1126/science.1210912 10.12688/f1000research.4996.1	
	Batoidea	Myliobatiformes	Dasyatidae	<i>Neotrygon kuhlii</i>	1	eyes (retine)	PRJNA135005 PRJNA292033	10.1126/science.1210912 10.12688/f1000research.4996.1	
	Batoidea	Myliobatiformes	Dasyatidae	<i>Neotrygon kuhlii</i>	Multiisolate	venom gland	PRJNA240112	—	
	Batoidea	Myliobatiformes	Potamotrygonidae	<i>Potamotrygon amandae</i>	Multispecies	venom gland	PRJNA284840	—	
	Batoidea	Myliobatiformes	Potamotrygonidae	<i>Potamotrygon falkneri</i>	nd	nd	PRJNA284840	—	
	Batoidea	Myliobatiformes	Urotrygonidae	<i>Urobatis jamaicensis</i>	1	heart	PRJNA313962	—	
	Batoidea	Rajiformes	Rajidae	<i>Amblyraja radiata</i>	1	testis	PRJNA516733	—	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	3	embryos	PRJNA288370	10.1093/database/bar064	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	20–29	embryos	PRJNA135005	10.1126/science.1210912 10.12688/f1000research.4996.1	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	4	ampullary receptor cells	PRJNA361222	10.1038/nature21401	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	6	pectoral fin	PRJNA414974	10.1016/j.cell.2018.01.013	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	2	axial skeleton	PRJNA497994	10.3389/fevo.2019.00012	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	1	ampullae of Lorenzini	PRJNA550453	—	
	Batoidea	Rajiformes	Rajidae	<i>Okamejei kenojei</i>	1	embryo	PRJNA438719	10.1038/sdata.2018.200	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Carcharhinus acronotus</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Carcharhinus leucas</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Carcharhinus leucas</i>	4	kidney	PRJDB8034	—	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Carcharhinus perezi</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Galeocerdo cuvier</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Negaprion brevirostris</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Prionace glauca</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Prionace glauca</i>	1	kidney, spleen	PRJNA414891	10.1016/j.margen.2017.11.009	
	Selachii	Carcharhiniformes	Carcharhinidae	<i>Rhizoprionodon terraenovae</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Carcharhiniformes	Scyliorhinidae	<i>Scyliorhinus canicula</i>	4	liver, brain, pancreas	PRJNA255185	10.1186/1471-2164-15-1074	
	Selachii	Carcharhiniformes	Scyliorhinidae	<i>Scyliorhinus canicula</i>	at least 2	ovary, testis	PRJNA504730	—	
	Selachii	Carcharhiniformes	Scyliorhinidae	<i>Scyliorhinus canicula</i>	24–30	embryos	PRJNA135005	10.1126/science.1210912 10.12688/f1000research.4996.1	
	Selachii	Carcharhiniformes	Sphyrnidae	<i>Sphyrna mokarran</i>	1	heart	PRJNA313962	10.1186/s12864-016-3411-x	
	Selachii	Carcharhiniformes	Triakidae	<i>Mustelus canis</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Lamniformes	Cetorhinidae	<i>Cetorhinus maximus</i>	nd	white muscle	PRJNA305977	—	
	Selachii	Lamniformes	Lamnidae	<i>Carcharodon carcharias</i>	1	heart	PRJNA313962	10.1186/s12864-016-3411-x	
	Selachii	Lamniformes	Lamnidae	<i>Carcharodon carcharias</i>	3	muscle, subdermis, epidermis, blood	PRJNA485795 PRJNA177971	—	
	Selachii	Lamniformes	Lamnidae	<i>Isurus oxyrinchus</i>	1	heart	PRJNA313962	10.1186/s12864-016-3411-x	
	Selachii	Lamniformes	Odontaspidae	<i>Carcharias taurus</i>	1	white muscle	PRJNA274450	10.1186/s12862-016-0696-y	
	Selachii	Orectolobiformes	Ginglymostomidae	<i>Ginglymostoma cirratum</i>	1	spleen, thymus	PRJNA183979	10.1038/nature12826	
	Selachii	Orectolobiformes	Hemiscyllidae	<i>Chiloscyllium griseum</i>	2	spleen, thymus	PRJEB4999	10.1371/journal.pone.0100018	
	Selachii	Orectolobiformes	Rhincodontidae	<i>Rhincodon typus</i>	3	blood cells	PRJDB6260	10.1038/s41559-018-0673-5	
	Selachii	Squaliformes	Etmopteridae	<i>Etmopterus spinax</i>	1	ventral skin, eye	PRJNA369748	10.1371/journal.pone.0209767	
	TSA	Batoidea	Rajiformes	Rajidae	<i>Leucoraja ocellata</i>	4	muscle, liver	PRJNA319888	10.1098/rsos.160299
		Batoidea	Torpediniformes	Torpedinidae	<i>Tetronarce californica</i>	1	pre-synaptic electric organ	PRJNA322346	10.1186/s12864-017-3890-4
		Selachii	Carcharhiniformes	Carcharhinidae	<i>Prionace glauca</i>	1	spleen, thymus	PRJNA414891	10.1016/j.margen.2017.11.009
		Selachii	Heterodontiformes	Heterodontidae	<i>Heterodontus zebra</i>	1	embryo	PRJNA431332	10.1038/sdata.2018.197
Selachii	Squaliformes	Squalidae	<i>Squalus acanthias</i>	1	liver, ovary, lidney, brain	PRJEB14721	10.1371/journal.pone.0182756		
WGS	Holocephali	Chimaeriformes	Callorhynchidae	<i>Callorhynchus milii</i>	1	testis	PRJNA18361	10.1038/nature12826	
	Batoidea	Rajiformes	Rajidae	<i>Leucoraja erinacea</i>	1	embryo	PRJNA60893	10.1093/database/bar064	
	Selachii	Carcharhiniformes	Scyliorhinidae	<i>Scyliorhinus torazame</i>	1	nd	PRJDB6260	10.1038/s41559-018-0673-5	
	Selachii	Lamniformes	Lamnidae	<i>Carcharodon carcharias</i>	1	heart	PRJNA269969	10.1073/pnas.1819778116	
	Selachii	Orectolobiformes	Hemiscyllidae	<i>Chiloscyllium plagiosum</i>	nd	blood	PRJNA478295	—	
	Selachii	Orectolobiformes	Hemiscyllidae	<i>Chiloscyllium punctatum</i>	1	nd	PRJDB6260	10.1038/s41559-018-0673-5	
	Selachii	Orectolobiformes	Rhincodontidae	<i>Rhincodon typus</i>	1	spleen, liver	PRJNA255419	10.1186/s12864-017-3926-9	

nd: No data available.

**Supplemental Table II:** List of sequences used for the studied of MHC class I in cartilaginous fish

Sample	Common Name	Specie	Nucleotide Accession Number	Protein Accession Number
Gici UAA	nurse shark	Gingimostoma cirratum	AF220063	AAF66110
Raeg UAA	clearnose skate	Raja eglanteria	KC335152	AGH32767
Camu UAA	elephant shark	Callorhynchus milii	JW872001	AFP04519
Hefr UBA	horn shark	Heterodontus francisci	AF028558	AA060348
Rhty UBA	whale shark	Rhincodon typus	XM_020536967	XP_020392556
Gici UBA	nurse shark	Gingimostoma cirratum	AF028557	AA060347
Xela UAA	african clawed frog	Xenopus laevis	L20733	AAA16064
Gaga BF1	chicken	Gallus gallus	NM_001044683	NP_001038148
Mumu H2D	mouse	Mus musculus	M23444	AAA39567
Hosa HLA-A	human	Homo sapiens	U18930	AAA87076
Lach U	coelacanth	Latimeria chalumnae	XM_014491396	XP_014346882
Leoc U	spotted gar	Lepisosteus oculatus	XM_015339735	XP_015196221
Acisi U	chinese sturgeon	Acipenser sinensis	GQ485578	ACV87433
Leer UDA	little skate	Leucoraja erinacea	LS-transcriptB2-ctg40765*	nd
Gici UDA	nurse shark	Gingimostoma cirratum	MN339476	nd
Camu UDA	elephant shark	Callorhynchus milii	JW870817	AFP03335
Leoc Z	spotted gar	Lepisosteus oculatus	GFM101040660	nd
Teni Z	tetraodon	Tetraodon nigroviridis	nd	CAF90807
Dare Z	zebra fish	Danio rerio	KC607850	AHA37389
Sqac UCA	spiny dogfish	Squalus acanthias	AF515705	AAAN78091
Etsp UCA	velvet belly	Etmopterus spinax	NODE_21300_length_1311	nd
Sqac UEA-C1	spiny dogfish	Squalus acanthias	HAGW01116852	nd
Sqac UEA-B1	spiny dogfish	Squalus acanthias	HAGU01093266	nd
Sqac UEA-A1	spiny dogfish	Squalus acanthias	HAGT01097031	nd
Heze UEA-C1	zebra bullhead shark	Heterodontus zebra	GGL01273748	nd
Heze UEA-C2	zebra bullhead shark	Heterodontus zebra	GGL01273734	nd
Gici UEA-A1	nurse shark	Gingimostoma cirratum	epigonal.TR369523_c3_g7_i20	nd
Gici UEA-A2	nurse shark	Gingimostoma cirratum	spleen.comp334747_c4_seq45	nd
Gici UEA-A3	nurse shark	Gingimostoma cirratum	NODE_26056_length_1453	nd
Gici UEA-A4	nurse shark	Gingimostoma cirratum	spleen.comp334747_c4_seq43	nd
Gici UEA-B1	nurse shark	Gingimostoma cirratum	epigonal.TR369523_c3_g7_i17	nd
Gici UEA-C1	nurse shark	Gingimostoma cirratum	epigonal.TR369523_c3_g7_i16	nd
Gici UEA-C2	nurse shark	Gingimostoma cirratum	thymus.comp349191_c5_seq12	nd
Chgr UEA-B1	grey bamboo shark	Chiloscyllium griseum	NODE_37004_length_984	nd
Chgr UEA-C1	grey bamboo shark	Chiloscyllium griseum	NODE_16046_length_2065	nd
Rhty UEA-B1	whale shark	Rhincodon typus	XM_020522040	XP_020377629
Rhty UEA-B2	whale shark	Rhincodon typus	NODE_17269_length_1605	nd
Rhty UEA-B3	whale shark	Rhincodon typus	XM_020522039	XP_020377628
Rhty UEA-C1	whale shark	Rhincodon typus	XM_020509571	XP_020365160
Rhty UEA-C2	whale shark	Rhincodon typus	NODE_2223_length_4069	nd
Rhty UEA-C3	whale shark	Rhincodon typus	XM_020510578	XP_020366167
Rhty UEA-C4	whale shark	Rhincodon typus	XM_020528997	XP_020384586
Rhty UEA-C5	whale shark	Rhincodon typus	NODE_15126_length_1815	nd
Cale UEA-A1	bul shark	Carcharhinus leUEAs	003_NODE_22119_length_2064	nd
Cale UEA-B1	bul shark	Carcharhinus leUEAs	003_NODE_3965_length_5162	nd
Cale UEA-C1	bul shark	Carcharhinus leUEAs	NODE_44384_length_1450	nd
Cale UEA-C2	bul shark	Carcharhinus leUEAs	003_NODE_42772_length_1051	nd
Cale UEA-C3	bul shark	Carcharhinus leUEAs	003_NODE_31356_length_1230	nd
Cale UEA-C4	bul shark	Carcharhinus leUEAs	NODE_54089_length_1169	nd
Caca UEA-C1	great white shark	Carcharodon carcharias	021_4_NODE_11670_length_2979	nd
Caca UEA-C2	great white shark	Carcharodon carcharias	021_3_NODE_12626_length_1777	nd
Caca UEA-C3	great white shark	Carcharodon carcharias	021_3_NODE_20018_length_1708	nd
Caca UEA-C4	great white shark	Carcharodon carcharias	021_3_NODE_23139_length_1474	nd
Caca UEA-C5	great white shark	Carcharodon carcharias	021_3_NODE_35710_length_864	nd
Caca UEA-A1	great white shark	Carcharodon carcharias	021_3_NODE_21051_length_1627	nd
Caca UEA-A2	great white shark	Carcharodon carcharias	021_2_NODE_3507_length_1252	nd
Caca UEA-B1	great white shark	Carcharodon carcharias	021_3_NODE_19998_length_1710	nd
Caac UEA-B1	backnose shark	Carcharhinus acronotus	NODE_14517_length_2054	nd
Spmo UEA-A1	great hammerhead	Sphyrna mokarran	NODE_26619_length_1253	nd
Spmo UEA-B1	great hammerhead	Sphyrna mokarran	NODE_24502_length_1385	nd
Spmo UEA-C1	great hammerhead	Sphyrna mokarran	NODE_15205_length_2271	nd
Spmo UEA-C2	great hammerhead	Sphyrna mokarran	NODE_30986_length_1033	nd
Spmo UEA-C3	great hammerhead	Sphyrna mokarran	NODE_26620_length_1253	nd
Spmo UEA-C4	great hammerhead	Sphyrna mokarran	NODE_10788_length_2968	nd
Scca UEA-C1	lesser spotted dogfish	Scyliorhinus canicula	012_NODE_23542_length_1184	nd
Scca UEA-C2	lesser spotted dogfish	Scyliorhinus canicula	012_NODE_17951_length_1595	nd
Scca UEA-C3	lesser spotted dogfish	Scyliorhinus canicula	011_NODE_28234_length_1020	nd
Scca UEA-C5	lesser spotted dogfish	Scyliorhinus canicula	011_NODE_27984_length_1029	nd
Rhte UEA-A1	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_16706_length_1105	nd
Rhte UEA-C1	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_11875_length_1581	nd
Rhte UEA-C2	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_11164_length_1679	nd
Rhte UEA-C3	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_3919_length_3393	nd
Rhte UEA-C4	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_11862_length_1583	nd
Rhte UEA-C5	atlantic sharpnose shark	Rhizoprionodon terraenovae	NODE_11863_length_1583	nd
Prgi UEA-B1	blue shark	Prionace glauca	NODE_8161_length_2072	nd
Nebr UEA-A1	lemon shark	Negaprion brevirostris	NODE_5283_length_2521	nd
Nebr UEA-B1	lemon shark	Negaprion brevirostris	NODE_7370_length_2018	nd
Nebr UEA-C1	lemon shark	Negaprion brevirostris	NODE_6259_length_2264	nd
Gacu UEA-B1	tiger shark	Galeocerdo cuvier	NODE_30512_length_1068	nd
Gacu UEA-B2	tiger shark	Galeocerdo cuvier	NODE_16880_length_2046	nd
Gacu UEA-C1	tiger shark	Galeocerdo cuvier	NODE_30425_length_1072	nd
Cape UEA-B1	caribbean reef shark	Carcharhinus perezi	NODE_13043_length_2062	nd
Cape UEA-C1	caribbean reef shark	Carcharhinus perezi	NODE_20712_length_1239	nd
Icpu S	channel catfish	Ictalurus punctatus	JT320438	nd
Sasa S	atlantic salmon	Salmo salar	ACY30362	nd
Plal S	ayu	Plecoglossus altivelis	JP747954	nd
Leoc L	spotted gar	Lepisosteus oculatus	XM_015339776	XP_015196262
Omi-L	tilapia	Oreochromis niloticus	ENSONIG00000001466	ENSONIT00000001840
Sasa L	atlantic salmon	Salmo salar	XM_014127629	XP_0139631004
Hosa CD1	human	Homo sapiens	M28262	AAA51939
Gaga CD1	chicken	Gallus gallus	AY849319	AAAX49405
Alsi CD1	chinese alligator	Alligator sinensis CD1	KJ191190	AI277408
Xetr 112	western clawed frog	Xenopus tropicalis	XM_002934793	XP_002934839
Alsi 112	chinese alligator	Alligator sinensis	XM_006037891	XP_006037953
Chmy 112	green sea turtle	Chelonia mydas	KB575999.1	EMP26826
Gamo P	atlantic cod	Gadus morhua	P_GW844691.1	nd
Teni P	tetraodon	Tetraodon nigroviridis	nd	nd (TNS_Grimholt et al. 2015)
Leoc P	spotted gar	Lepisosteus oculatus	NM_015339565	XP_015196051
Mumu FcRn	mouse	Mus musculus	NM_010189	NP_034319
Bota FcRn	cow	Bos taurus	XM_005219177	XP_005219234
Hosa FcRn	human	Homo sapiens	NM_001136019	NP_001129491
Leoc H-1	spotted gar	Lepisosteus oculatus	XM_015339736	XP_015196222
Leoc H	spotted gar	Lepisosteus oculatus	XM_015361424	XP_015216910
Xela 18004	african clawed frog	Xenopus laevis	XM_018253839	XP_018109328
Xetr 18004	western clawed frog	Xenopus tropicalis	NM_001278434	NP_001285363
Bota MR1	cow	Bos taurus	NM_001190298	NP_001117727
Mumu MR1	mouse	Mus musculus	NM_006209	NP_032235
Rano MR1	rat	Rattus norvegicus	CH473658	EDM05513
Xela 145	african clawed frog	Xenopus laevis	XM_018231157	XP_018088646
Xetr 145	western clawed frog	Xenopus tropicalis	XM_012969674	XP_012825128

\*The sequences are obtained from skate database (<http://skatebase.org/>). The remaining sequences are obtained from NCBI (<https://www.ncbi.nlm.nih.gov/>); nd meaning no data