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Revisiting the evolution of the somatostatin family: already five genes in the gnathostome ancestor

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Abstract

The somatostatin (SST) family members are a group of neuropeptides that are best known for their role in the regulation of growth, development and metabolism. The occurrence of six paralogous SST genes named *SST1*, *SST2*, *SST3*, *SST4*, *SST5* and *SST6* has been reported in vertebrates. It has been proposed that *SST1*, *SST2* and *SST5* arose in 2R from a common ancestral gene. *SST3* and *SST6* would have been subsequently generated by tandem duplications of the *SST1* and *SST2* genes respectively, at the base of the actinopterygian lineage. *SST4* is thought to have appeared more recently from *SST1*, in teleost-specific 3R.

In order to gain more insights into the *SST* gene family in vertebrates, we sought to identify which paralogs of this family are present in cartilaginous fish. For this purpose, we first searched the recently available genome and transcriptome databases from the catshark *Scyliorhinus canicula*. In a previous study, three *S. canicula* *SST* genes, called at that time *SSTa*, *SSTb* and *SSTc*, were identified and proposed to correspond to *SST1*, *SST5* and *SST2* respectively. In the present work, two additional *SST* genes, called *SSTd* and *SSTE*, were found in *S. canicula* plus two other chondrichyan species, elephant shark (*Callorhinus milii*) and whale shark (*Rhincodon typus*). Phylogeny and synteny analyses were then carried out in order to reveal the evolutionary relationships of *SSTd* and *SSTE* with other vertebrates *SSTs*. We showed that *SSTd* and *SSTE* correspond to *SST2* and *SST3* respectively, while *SSTc* corresponds to *SST6* and not to *SST2* as initially proposed. Our investigations in other vertebrate species also led us to find that the so-called *SST2* gene in chicken, lungfish, sturgeons and teleosts actually corresponds to *SST6*. Conversely, the so-called *SST6* gene in actinopterygians corresponds to *SST2*.

Taken together, our results suggest that: *i*) *SST3* and *SST6* were already present in the gnathostome ancestor, much earlier than previously thought; *ii*) *SST6* was also present in the tetrapod ancestor and still occurs in living birds; with this respect, it is likely that *SST6* was independently lost several times during evolution: in euteleosts, amphibians, squamates and mammals; *iii*) *SST2*, *SST3* and *SST5* were probably lost in euteleosts, sarcopterygians and tetrapods, respectively.

Introduction

Somatostatin (currently known as somatostatin 1 or SST1) was originally isolated from ovine hypothalamus and found to inhibit the release of growth hormone from the rat pituitary (Brazeau *et al.* 1973). It has been subsequently shown that SST1 is widely distributed in the central nervous system and in various peripheral organs where it plays important roles in the regulation of growth, development and metabolism (Günther *et al.* 2018). The occurrence of SST1 was reported in all vertebrate species investigated so far. Moreover, most species were shown to possess additional SST forms. In gnathostomes (jawed vertebrates), it was demonstrated that all these SST variants are the products of at least six paralogous genes named *SST1*, *SST2* (also known as *Cortistatin* in mammals) *SST3*, *SST4*, *SST5* and *SST6* (de Lecea *et al.* 1996, Liu *et al.* 2010, Tostivint *et al.* 1996, 2008, 2013, 2014). SST-related peptides are thought to act through at least six SST receptor subtypes (Ocampo Daza *et al.* 2012). In lampreys, three *SST* genes have characterized but their phylogenetic status is still unclear (Tostivint *et al.*, 2016), while in the hagfish *Myxine glutinosa*, the occurrence of only one *SST* gene, encoding a SST1-like peptide, is attested to date (Conlon *et al.*, 1988).

It is currently well accepted that the evolution of the *SST* gene family, as that of many other neuropeptides (Elphick *et al.* 2018), was strongly shaped by the different rounds of whole-genome duplications that took place in the vertebrate history, especially the two basal rounds of vertebrate genome doubling (2R) and the teleost fish-specific genome doubling (3R) (Dehal & Boore 2005, Putnam *et al.* 2008, Sacerdot *et al.* 2018). Thus, *SST1*, *SST2* and *SST5* seem to have been generated during 2R from a common ancestral gene, while *SST4* is likely to have appeared during 3R from *SST1*. Impact of 2R on the early evolution of *SST* gene family is notably supported by synteny analysis showing that *SST* genes are located on a same tetraparalogon that contains paralogous genes of at least ten other families (Liu *et al.* 2010, Tostivint *et al.*, 2013, 2014). For their part, *SST3* and *SST6* would have been independently generated by tandem duplications of *SST1* and *SST2* respectively, at the base of the actinopterygian lineage (Liu *et al.* 2010, Tostivint *et al.* 2004, 2008). Some of these genes could have been subsequently lost explaining their absence in some lineages. For example, *SST5* is believed to have been lost in tetrapods.

Cartilaginous fish (chondrichthyans) are of particular interest in evolutionary studies because of their key phylogenetic position at the base of the gnathostome lineage. They consist of two major groups: elasmobranchii (sharks and skates/rays) and holocephali (chimaeras). Until 2013, SST-related peptides were characterized in only a very few species of cartilaginous fish: SST1 from the ray *Torpedo marmorata* (Conlon *et al.* 1985), a SST1-like peptide exhibiting a serine residue at position 5 from the ratfish *Hydrolagus colliei* (Conlon 1990), a SST2-like sequence from the elephant shark *Callorhinus milii* (Tostivint *et al.* 2008) and finally a totally atypical SST-related sequence from both the little skate *Leucoraja erinacea* and *C. milii* (Liu *et al.* 2010). In 2013, three *SST* genes, called *SSTa*, *SSTb* and *SSTc*, were identified in the common dogfish (today referred to as small-spotted catshark, *Scyliorhinus canicula*) and proposed to correspond to *SST1*, *SST5* and *SST2*, respectively (Quan *et al.* 2013). Surprisingly, none of these genes appeared as the apparent ortholog of the atypical *SST*-like gene found in *C. milii* and *L. erinacea*. Nevertheless, these findings were regarded as in good agreement with the model described above since they support the existence of these three *SST* genes in the gnathostome ancestor (Liu *et al.* 2010, Tostivint *et al.* 2013, 2014). However, due to the lack of a fully sequenced and assembled *S. canicula* genome, this view could not be confirmed (Quan *et al.* 2013).

The first goal of the present study was to determine the complete repertoire of the *SST* gene family in cartilaginous fish. For this purpose, we searched the newly available *S. canicula* genome and transcriptome databases (unpublished data). We also took the opportunity to explore or reexplore the genome and transcriptome databases from two additional species, the

whale shark, *Rhincodon typus* (Read *et al.* 2017) and the elephant shark, *C. milii* (Venkatesh *et al.* 2014). We found two novel *S. canicula* SST genes that we propose to provisionally call *SSTd* and *SSTE* (according to the nomenclature initially proposed in Quan *et al.* 2013). *S. canicula* *SSTd* was shown to be the ortholog of the *L. erinacea* and *C. milii* atypical SST-like gene above-mentioned, while *S. canicula* *SSTE* appeared as a totally new SST gene. In both *R. typus* and *C. milii*, four SST genes were found that correspond *SSTA*, *SSTc*, *SSTd* and *SSTE*.

Taking advantage of the genome assembly of various representative species from other vertebrate groups, we then carried out phylogeny and synteny analyses in order to reveal the evolutionary relationships of chondrichthyan *SSTd* and *SSTE* with other vertebrates SSTs. From our investigations, it appeared that *SSTd* and *SSTE* correspond to *SST2* and *SST3*, respectively, while *SSTc* corresponds to *SST6* but not to *SST2* as initially proposed (Quan *et al.* 2013).

The major implication of these results is that the repertoire of the SST gene family in the gnathostome ancestor was already composed of five paralogs namely *SST1*, *SST2*, *SST3*, *SST5* and *SST6*. Our observations also led us to revisit the phylogenetic status of *SST2* and *SST6*. As a result, the nomenclature of these genes had to be corrected in some species.

Material and methods

Nomenclature

In this article, *S. canicula* SSTs, as well as their counterparts from other chondrichthyans, will be first described as *SSTA-SSTE*, according to the provisionnal nomenclature proposed by Quan *et al.* (2013), without prejudice to their evolutionary relationships with other vertebrates SSTs. Thereafter, in the light of the phylogeny and synteny data, they will be renamed according to the phylogenetic nomenclature, *SST1-SST6*, initially introduced by Tostivint *et al.* (2008) then extended by Liu *et al.* (2010). Nevertheless, the correspondence bewteen the two nomenclatures will be regularly reminded throughout the article as follows: *SSTA* = *SST1*; *SSTb* = *SST5*; *SSTc* = *SST6*; *SSTd* = *SST2* and *SSTE* = *SST3*. Note that in Quan *et al.* (2013) *SSTc* was initially but mistakenly referred to as *SST2*.

Identification of *SSTd* and *SSTE* sequences from cartilaginous fish

S. canicula *SSTd* and *SSTE* genes were sought by TBLASTN (Altschul *et al.* 1990) using the *C. milii* and *L. erinacea* *SST2*-like sequences (AGCKLFFWKTFSHC and APCKLFFWKTFSHC) as queries against the *S. canicula* genome draft assembly (version 1, unpublished). *S. canicula* full-length *SSTd* cDNA (but not *SSTE* cDNA) was also retrieved from *S. canicula* Illumina transcriptome (version 1, unpublished).

The SST repertoire of SST genes in *R. typus* and *C. milii* was sought by TBLASTN using the *S. canicula* SST cDNA sequences as queries against the *R. typus* and *C. milii* genome assembly databases (Read *et al.* 2017; Venkatesh *et al.* 2014).

Protein sequences were predicted by using consensus splice donor and acceptor site and by sequence identity comparison with related SST genes. The signal peptide cleavage site was determined using SignalP (<http://www.cbs.dtu.dk/services/SignalP/>) (Petersen *et al.* 2011).

Molecular cloning of the coding sequence of *S. canicula* *SSTE* cDNA

5'RACE-ready cDNAs used for this procedure were constructed as previously described (Gaillard *et al.* 2018). The coding sequence of the *S. canicula* *SSTE* cDNA was amplified by nested PCR using the Advantage 2 PCR kit (Clontech). Nested PCR was carried out in a MyCycler thermal cycler (Bio-Rad, Marne la Coquette, France) with the following primers, csSSTE Rev x Universal Primer A Mix (UPM) then csSSTE Rev Nest x Nested Universal Primer A Mix (NUP) (see **Table S1**) using the manufacturer's procedure. PCR amplifications were carried out for 35 cycles (denaturation 94°C, 30 sec; annealing between 57 and 60°C depending on the Tm of the primers, 30 sec; and extension 72°C, 30 sec) and a final extension

of 72°C for 7 min. The product of the nested PCR was subcloned into the pGEM-T vector (Promega, Charbonnières-les-Bains, France) and sequenced (Value Read Sequencing at MWG Biotech, Ebersberg, Germany).

Synteny analysis

To generate synteny maps, genes flanking *C. milii* and *R. typus* *SST* genes were obtained from the NCBI database. Non-protein coding genes and genes coding unknown proteins were excluded from further analysis. Note that *SSTb* was not included in the study since it is absent in both *C. milii* and *R. typus*, while in *S. canicula*, it is located on a very short scaffold that did not contain any other genes. Genes flanking the *SST* genes in eight additional osteichthyan species, namely human, chicken (*G. gallus*), green anole lizard (*A. carolinensis*), Western clawed frog (*X. tropicalis*), coelacanth (*L. chalumnae*), spotted gar (*L. oculatus*), zebrafish (*Danio rerio*) and medaka (*Oryzias latipes*), were obtained from Genomicus (version 92.01) (Muffato *et al.* 2010).

Phylogeny analysis

A set of 147 vertebrate *SST* precursor sequences was primarily collected from Yun *et al.* (2015) and Tostivint *et al.* (2016) and supplemented by the chondrichthyan sequences characterized in the present study. All these sequences were aligned using the Muscle algorithm (Edgar 2004) then manually adjusted. The phylogeny of *SST* precursors was inferred by Maximum Likelihood using PhyML (Guindon & Gascuel 2003) with the LG model of substitution combined to the neighbor-joining interchange (NNI) method on Seaview browser (Gouy *et al.* 2010). The robustness of the tree was assessed by the approximate likelihood test (aLRT) SH-like branch support and by bootstrapping procedure from 500 data set replicates. The Genbank accession numbers for all sequences used in the analysis are listed in **Figure S1**. The alignment is presented in **Figure S2**.

Tissue expression of *S. canicula SSTd* and *SSTe* genes by reverse transcriptase-polymerase chain reaction (RT-PCR) amplification

The expression profiles of *S. canicula SSTd* and *SSTe* genes were examined by RT-PCR, as previously described (Quan *et al.* 2013, Gaillard *et al.* 2018). Total RNA was extracted from various tissues, including telencephalon, diencephalon, mesencephalon, cerebellum, brain stem, spinal cord, skeletal muscles, heart, spleen, gills, stomach, duodenum, valvular intestine, pancreas, liver, kidney, ovary and testis and purified by using RNAeasy Plus Mini kit (Qiagen, Courtabœuf, France). For each tissue, ~330 ng of total RNA were reverse transcribed using ImProm-II Reverse Transcription System (Promega, Charbonnières, France). Gene-specific primers of *S. canicula SSTd* and *SSTe* were designed according to the predicted sequences (**Table S1**). PCR amplifications were carried out for 35 cycles (denaturation 94°C, 30 sec; annealing between 57 and 60°C depending on the Tm of the primers, 30 sec; and extension 72°C, 30 sec) and a final extension of 72°C for 7 min. The *S. canicula Egf1* gene was amplified in parallel with specific primers (**Table S1**) to verify the quality and quantity of all cDNAs samples. Negative controls were performed without cDNA template. All PCR products were electrophoresed through 2.0% agarose gel and stained with ethidium bromide and then detected under UV light with the ChemiDoc Touch Imaging System (BioRad). Three independent PCR amplifications were performed to check the consistency of amplification.

Results

Structure of *S. canicula SSTd* (*SST2*) and *SSTe* (*SST3*) precursor cDNAs and genes

The nucleotide and deduced amino acid sequences of *S. canicula* SSTs including *SSTd* and *SSTE* are shown in **Figure S3**. The coding region of the *SSTd* cDNA consists of 315 nucleotides (nt) that encode a 105-amino acid (aa) protein (PSSTd) including a 20-residue potential signal sequence (Petersen *et al.* 2011). The primary structure of PSSTd contains a monobasic processing site at position 91 (Lys) potentially yielding the mature 14-aa peptide *SSTd* (*SST2*), TPCKLFFWKTFSHC, plus one dibasic and one monobasic processing sites at positions 87-88 (Arg-Arg) and 79 (Arg) respectively, potentially yielding 17- and 26-aa NH₂-extended forms of *SSTd*.

The coding region of the *SSTE* cDNA consists of 321 nt that encode a 106-aa protein with a 18-residue potential signal sequence. The *SSTE* sequence is flanked by a pair of basic residues (Arg-Lys) at position 92-93 potentially yielding the mature 14-aa peptide *SSTE* (*SST3*), NCKNFFWKTY TLC, plus two monobasic processing sites at positions 85 (Arg) and 90 (Arg) respectively, potentially yielding 17- and 22-aa NH₂-extended forms of *SSTE*.

Comparison of the cDNAs with genomic sequences revealed that *SSTd* and *SSTE* genes are each composed of two exons and one intron (**Figure S4**). For each gene, exon 1 encodes the 5' UTR, the signal peptide and the N-terminus of the prepro-peptide while exon 2 encodes the C-terminus of the precursor, including the putative mature peptide.

Repertoire of SST cDNAs and/or genes in cartilaginous fish

The entire repertoire of SST cDNAs and/or genes found from *S. canicula*, *R. typus* and *C. milii* databases is shown in **Figures S3-S8**. *S. canicula* SST family appears as the richest with no less than five SST genes: the three genes previously reported in Quan *et al.* (2013), namely *SSTA*, *SSTb* and *SSTc*, plus two additional genes characterized in the present study, *SSTd* and *SSTE*. All these genes, with the exception of *SSTb*, were retrieved from *R. typus* and *C. milii*. Only a partial sequence of the *SSTd* gene could be detected from *L. erinacea* (already reported in Liu *et al.* 2010).

General organization of the chondrichthyan SST genes and SST precursors

The molecular organization of the SST precursors is the same in all species examined, with a signal peptide followed by a long central segment, a conserved pair of basic residues and, finally, the SST sequence at their C-terminus (**Figure 1**). All putative SST possess a cyclic conformation ensured by the presence of two Cys residues, and their cyclic region encompasses the Phe-Trp-Lys motif. The structure of the corresponding genes is also very well conserved with two exons and one intron (**Figures S4, S5, S7**). Note that the first exon of *S. canicula* *SSTd* and that of *S. canicula* *SSTA* (*SST1*) exhibit almost the same nucleotide sequence (**Figure S4**). This sequence identity was also found in the corresponding cDNA identified by RT-PCR ruling out an artefact of genome assembly (**Figure S3**).

Structural features of the chondrichthyan putative SST tetradecapeptides

- *SSTA* (*SST1*)

The primary structure of *SSTA* is AGCKNFFWKTFTSC both in *S. canicula* and *R. typus*. In *C. milii*, it exhibits one substitution, Ser vs Asn, at position 5, as previously reported in the ratfish *H. colliei* (Conlon 1990) (**Table S2**). It is to note that the genomic *SSTA* sequence encodes for a Leu in place of Phe at position 6 that was not retrieved in the cDNAs (**Figures S3 and S4**). Chondrichthyan prepro-*SSTA* exhibit high sequence identity (ranging from 66.3 to 74.1% between one another) (**Table S3**).

- *SSTb* (*SST5*)

As mentioned above, the *SSTb* sequence could only be found in *S. canicula* (see Quan 2013 for a complete description of the precursor). Just as a reminder, *S. canicula* *SSTb* exhibits the same primary structure as *SSTA* (*SST1*) (**Table S2**).

- SSTc (SST6)

SSTc exhibits two substitutions at positions 1 and 2 when compared to SSTa (**Table S2**). The residue at position 2 is a Pro, except in *R. typus*. The residue at position 1 is more variable. Chondrichthyan prepro-SSTc exhibit high sequence identity (ranging from 53.8 to 86.7% between one another) (**Table S3**).

- SSTd (SST2)

When compared to that of SSTa, the primary structure of SSTd can be distinguished by the Ser-His-Cys (SHC) motif at its C-terminus (**Table S2**). Variable residues are present at position 1 and 2. However, the residue at position 2 is generally a Pro, except in *C. milii*. Chondrichthyan prepro-SSTd exhibit high sequence identity (ranging from 51.9 to 76% between one another) (**Table S3**).

- SSTe (SST3)

In all species examined, the primary structure of SSTe exhibits the unique Tyr-Thr-Leu-Cys (YTLC) motif at its C-terminus (**Table S2**). Only the residue at position 1 is different depending on the species. *S. canicula* and *C. milii* prepro-SSTe exhibit only 38.1% identity (**Table S3**).

Synteny analysis of SST genomic regions

In both *R. typus* and *C. milii*, SSTe (SST3) and SSTa (SST1) are tandemly arranged on the same scaffold (**Figure 2, Table S4**). However, this scaffold is very short and does not contain any other genes. On the basis of our previous results suggesting that SSTa probably corresponds to SST1 (Quan *et al.* 2013), we aligned the chondrichthyan SSTa-SSTe scaffold with the SST1 locus from the other species analyzed. In teleosts, SST3 is localized in tandem with SST1, as SSTe and SSTa in cartilaginous fish.

In spotted gar, the SST1-SST3 locus bears a third SST gene, here called SST4, surrounded by *Nyap2* and *Irs1* (**Figure 2, Table S4**). In teleosts, the SST known as SST4 is located on a different chromosome than that bearing SST1 and SST3. Its closest neighbors are *Nyap2b* and *Fgf12a* (**Figure 2, Table S4**). The co-orthologs of these two latter genes, *Nyap2a* and *Fgf12b*, are present in the vicinity of both SST1 and SST3. Thus, the teleost SST4 can be viewed as either an ortholog to gar SST4 (as this is what its name implies) or a 3R duplicate of either SST1 or SST3. These three possibilities are illustrated in **Figure 2**.

R. typus and *C. milii* SSTd (named SST2 in **Figure 3**) were found in a genomic region containing several genes, *Kif1b*, *Pgb*, *Cenps* and *Dffa*, that are also present in the vicinity of the human SST2 gene (**Figure 3, Table S4**). It is to note that the gar and zebrafish SST genes present in the syntenic region correspond to genes previously known as SST6.

The neighborhood of the *R. typus* and *C. milii* SSTc (named SST6 in **Figure 3**) is composed of several genes, *Tardbp*, *Masp2* and *Srm*, that, in the other species examined, were present in the vicinity of SST genes previously known as SST2, notably in chicken, spotted gar, zebrafish and medaka (**Figure 3, Table S4**).

Phylogeny analysis of SST precursors

Figure 4 displays an unrooted tree constructed from 147 selected vertebrates SST precursor sequences using maximum likelihood phylogeny analysis. In the resulting tree, osteichthyan SST sequences cluster into six main clades, SST1-SST6. Bootstrap support values for these six groups were 53, 10, 94, 29, 68 and 75%, respectively. The only discrepancy of this patterning is the presence of the gar SST4 sequence into the SST3 clade. It is to note that the actinopterygian SST sequences belonging to the SST2 clade were previously known as SST6. Likewise, chicken, lungfish, sturgeon and teleost SST sequences included in the SST6 clade were previously known as SST2.

Chondrichthyan SSTb, SSTc and SSTd branch at the base of the SST5, SST6 and SST2 clades, respectively. Gnathostome SST2-SSTd and SST6-SSTc appeared as two sister groups as well

as osteichthyan SST1 and SST3. For their part, chondrichthyan SSTa and SSTe formed a monophyletic group that branch at the base of the osteichthyan SST1-SST3 clade.

As previously reported (Tostivint *et al.* 2016), lamprey SST sequences did not group to any of the gnathostome SST clades.

Tissue-specific expression of *S. canicula SSTd (SST2) and SSTe (SST3) genes*

The distribution of *S. canicula SSTd* and *SSTe* mRNAs in various tissues was examined by RT-PCR. **Figure 5** shows the results of one representative experiment out of three performed with identical results. *SSTd* mRNA was detected primarily in the brain (notably in the diencephalon, mesencephalon and brainstem) and spinal cord. In contrast, *SSTe* mRNA appeared particularly abundant in the central nervous system (in all subdivisions examined except in the cerebellum) as well as in the intestinal tract and pancreas. Note that traces of *SSTd* mRNA were also seen in the spleen, gills, pancreas and gonads.

Discussion

The main aim of the present study was to determine the repertoire of the *SST* gene family in cartilaginous fish. For this purpose, the genome and/or transcriptome databases from three representative chondrichthyan species were examined, namely the small-spotted catshark *S. canicula* (unpublished, see Gaillard *et al.* 2018 for more details), the whale shark, *R. typus* (Read *et al.* 2017) and the elephant shark *C. milii* (Venkatesh *et al.* 2014). In *S. canicula*, two new *SST* genes, named *SSTd* and *SSTe* were found, in addition to the three *SST* genes, *SSTa*, *SSTb* and *SSTc*, previously identified (Quan *et al.* 2013). All these genes, with the exception of *SSTb*, were retrieved from *R. typus* and *C. milii*. It is noteworthy that the occurrence of partial sequences of the *SSTc* (Tostivint *et al.* 2008) and *SSTd* genes (Liu *et al.* 2010) were already reported in both *L. erinacea* and/or *C. milii*. In contrast, *SSTe* appeared as a totally novel gene. The nomenclature used above (*SSTa-SSTe*) was initially (and provisionally) proposed to designate the *S. canicula SSTs* without prejudice to their evolutionary relationships with other vertebrate *SSTs* (Quan *et al.* 2013). Synteny comparisons and phylogeny analysis were subsequently carried out in order to reveal the phylogenetic status of all these genes.

Synteny comparisons suggest that *SSTd* is the chondrichthyan counterpart of *SST2* since both *S. canicula* and *C. milii SSTd* reside in the same chromosomal environment as that of human *SST2*. For the same reasons, *SSTc* can be legitimately viewed as the chondrichthyan counterpart of *SST6*. These conclusions are quite consistent with our phylogeny analysis because *SSTd* and *SSTc* precursor sequences branch at the base of the *SST2* and *SST6* clades, respectively, although the bootstrap support values of the new clades are extremely weak (4% and 37% respectively).

Our investigations on the chondrichthyan *SSTc* and *SSTe* also led us to redefine the relationships between *SST2* and *SST6*. The *SST2* gene was first characterized in frog (Tostivint *et al.* 1996) and mammals (de Lecea *et al.* 1996, 1997a), then in most other vertebrates, including chicken (Trabucchi *et al.* 2003), lungfish (Trabucchi *et al.* 1999) and sturgeons (Trabucchi *et al.* 2002, Li *et al.* 2009) (see Tostivint *et al.* 2008 for review). All peptides encoded by *SST2* possessed a Pro residue at position 2 and most of them exhibited the APCKNNFWKTFTSC sequence (Quan *et al.* 2013), except in mammals and some other species such as frog (Vaudry *et al.* 1992; Tostivint *et al.* 2008 for review) (**Table S2**). As for, the *SST6* gene was initially characterized in only one teleost species, the zebrafish (Liu 2010), then in spotted gar (Tostivint *et al.* 2013) and coelacanth (Yun *et al.* 2015) (**Table S2**). In the present study, we found an ortholog of this gene in several other teleost species belonging to various groups (particularly from otocephala) but not from euteleosts. Peptides encoded by *SST6* also shared a Pro at position 2, suggesting a common origin with *SST2*. In support of this latter view, in both zebrafish and gar, *SST2* and *SST6* are closely linked on the same chromosome, indicating that

they most likely arose by tandem duplication. Our phylogeny and synteny analyses showed that most of the non-mammalian *SST* sequences previously referred as to *SST2* are not orthologous to *cortistatin* (the other name of the mammalian *SST2*) but actually correspond to *SST6*. Such is notably the case for birds (chicken) and fish (lungfish, sturgeons, bony and cartilaginous fish), but not for reptiles (lizard) and amphibians (marsh frog). Conversely, all *SST* sequences previously referred to as *SST6* appeared to correspond to *SST2*. As a result, all the *SST* genes concerned with these observations were renamed accordingly. It is to note that the nomenclature adopted in the present article was already proposed in Yun *et al.* (2015) but without explicit justification.

In *R. typus* and *C. milii*, *SSTe* and *SSta* are tandemly arranged suggesting that both genes arose by local duplication of a common ancestral gene. Synteny analysis of the *SSta-SSTe* locus was inhibited by the fact that *SSta* and *SSTe* were the only genes present on their scaffold. However, based on previous results showing that *SSta* probably corresponds to *SST1* (Quan *et al.* 2013), the most credible assumption is that *SSTe* corresponds to *SST3* because in all species possessing both *SST1* and *SST3*, these genes are systematically localized in tandem (Tostivint *et al.* 2004, 2008, 2013, 2014). Phylogeny analysis is in agreement with close evolutionary relationships between *SSta* and *SSTe*, on the one hand, and *SST1* and *SST3*, on the other hand. However, it does not fully support the orthology between *SST1* and *SSta*, on one hand, and *SST3* and *SSTe*, on the other hand, since chondrichthyan *SSta* and *SSTe* sequences did not strictly group with osteichthyan *SST1* and *SST3*, respectively. One explanation to reconcile these contradictory results would be that *SST1/SSta* and *SST3/SSTe* genes were subjected to concerted evolution, a genetic process that leads to homogenize repetitive DNA sequences over time (Liao 1999). Indeed, the major hallmark of concerted evolution is that paralogous genes within species are more similar to one another than they are to their orthologous counterparts in closely related species (Liao 1999). DNA recombination mechanisms, especially unequal crossover and gene conversion, are responsible for concerted evolution (Liao 1999). Interestingly, we have shown that nucleotide sequences of the first exon of *S. canicula SSta* and *S. canicula SSTe* are almost identical (93.5% of identity), while those of the second exon are much more divergent (only 61% of identity). Such level of similarity may be a good indicator of a recent recombination event occurring between the two genes.

The phylogenetic status of the *S. canicula SSTd* and *SSTe* genes suggested by synteny and phylogeny analyses is consistent with their tissue expression pattern since *SSTd*, as *SST2*, is primarily expressed in the central nervous system (SNC) (de Lecea *et al.* 1997b, Lin *et al.* 1999, Trabucchi *et al.* 1999, 2003), while *SSTe*, as *SST3*, is expressed both in the SNC and the gastrointestinal tract (Moore *et al.* 1995, Xing *et al.* 2005). Further studies at the cellular level will be needed to speculate about the functions of the corresponding peptides.

In contrast to the other *SST* genes found in cartilaginous fish, *SSTb* was detected only in *S. canicula* and not in *R. typus* and *C. milii*. Phylogeny analysis showed that *SSTb* grouped into the *SST5* clade, as previously reported (Quan *et al.* 2013). However, the orthology relationships between *SSTb* and osteichthyan *SST5* could not be confirmed by synteny analysis since the *S. canicula SSTb*-bearing scaffold was too short.

Among the six *SST* paralogs characterized so far in gnathostomes, *SST4* is the only one not to exist in cartilaginous fish. Up to now, the *SST4* gene was considered as a *SST1* paralog generated by 3R (Liu *et al.* 2010), in agreement with the fact that it was found only in teleosts (**Figure S9A**). Recently, however, Yun *et al.* (2015) reported the occurrence of a so-called *SST4* ortholog in spotted gar. This finding is clearly in conflict with the Liu's view since the gar lineage is known to have diverged from teleosts before the 3R (**Figure S9B**) (Braasch *et al.* 2016). In the present study, synteny analysis showed that teleost *SST4* can be equally viewed as orthologous to the gar *SST4*, or co-orthologous to either teleost *SST1* or teleost *SST3*, without

the possibility to decide between these three conceptions. Indeed, in both zebrafish and medaka, the *SST4*-bearing chromosome block contains only very few paralogs of the neighboring genes of *SST1* and *SST3* (such as *Fgf12* and *Nyap2*), making it impossible to precisely place the teleost *SST4* in relation to gar *SSTs*. Examination of other teleost species whose genome is available in Ensembl failed to resolve the problem (data not shown). What is clear, however, is that phylogeny analysis absolutely does not support the orthology of gar *SST4* and teleost *SST4* since gar *SST4* groups within the gnathostome *SST3* clade, thus without any obvious relationships with the teleost *SST4* clade. Rather, the very high level of sequence similarity between gar *SST3* and gar *SST4* (91 % nucleotide identity) strongly suggests that gar *SST4* arose very recently by tandem duplication of *SST3*. It therefore appears unlikely that gar *SST4* and teleost *SST4* are orthologous unless gar *SST4* and *SST3* were subjected to concerted evolution, as shown above for *S. canicula SST1/SSTa* and *SST3/SSTe*.

Concluding remarks

Over the past few years, significant advances have been made in the understanding of the evolution of the *SST* family. One of the most important results has been the demonstration that the current diversity of the family was initially caused by 2R (Liu *et al.* 2010, Tostivint *et al.* 2013, 2014). According to this view, the last common ancestor of vertebrates possessed four *SST* genes, three of which, *SST1*, *SST2* and *SST5*, are still present in all extant vertebrate species. A fourth *SST* gene (referred to as *SST?* in **Figure 6**) is likely to have been generated by 2R but since this gene has never been found in extant vertebrate species, it is assumed to have been lost very early after 2R. Conversely, the rest of the diversity of the family, represented by *SST3*, *SST4* and *SST6*, was considered restricted to only some groups of bony fish (Tostivint *et al.* 2013, 2014): actinopterygians for *SST3* and *SST6* and teleosts for *SST4*.

The principal result of the present study is the demonstration of an unexpected diversity of *SST* genes in cartilaginous fish. Thus, in *S. canicula*, not less than five *SST* genes, *SST1*, *SST2*, *SST3*, *SST5* and *SST6*, have been identified, while only three of them were characterized so far (Quan *et al.* 2013). Therefore, contrary to what was previously thought, it is likely that all these five genes were already present in the gnathostome ancestor (**Figure 6**).

It is to note that our study did not provide any new data supporting the impact of 2R in the evolution of the *SST* gene family due to the small size of the scaffolds from the three chondrichthyan species examined. Thus, within the regions containing *SST* genes, *Masp 1* and *Masp 2* were the only genes indicating that *SST1* and *SST3*, on the one hand and *SST2* and *SST6*, on the other hand, belong to the same paragon. In contrast, our study confirm the idea that *SST3* and *SST6* likely arose by tandem duplications from *SST1* and *SST2*, respectively (**Figure 6**). In strict logic, however, we must admit that it is currently impossible to know which of *SST1* and *SST3*, on the one hand and *SST2* and *SST6*, on the other hand are the ancestral genes. The uncertainty on this matter will remain as long as the phylogenetic status of lamprey *SSTs* is unsolved (Tostivint *et al.* 2016) because the lamprey *SST* sequences are the only ones that could be currently used as outgroups. Thus, in **Figure 6**, *SST1* and *SST2* are displayed as ancestral genes in a totally arbitrary manner.

Another important result of the present study was the finding that *SST6* was not totally lost in sarcopterygians, as previously thought, because it is still present in coelacanth and birds (**Figure 6**). In this context, it is noteworthy that chicken *SST6* was initially but mistakenly reported as *SST2* (Trabucchi *et al.* 2002), now refuted by synteny and phylogeny analysis. In a general way and for the same reasons, all teleost genes previously known as *SST6* had to be renamed *SST2*, and *vice versa*. Notably, the true *SST2* is also present in amphibians (but not in *Xenopus*), sauropsids (but not in birds) and mammals (**Figure 6**). Taken together, our result show that *SST2* and *SST6* have been lost independently and repeatedly during evolution: in euteleosts, birds and some amphibians for *SST2* and amphibians and mammals for *SST6* (**Figure 6**). After

their appearance, *SST3* and *SST5* were also secondarily lost in sarcopterygians and tetrapods, respectively.

Finally, the present work was unable to precisely determine the phylogenetic status of teleost *SST4*. In particular, whether teleost *SST4* and gar *SST4* are truly orthologous or not remains to be investigated. Further studies in other species than those examined here will be needed to address this issue.

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Legends to figures

Figure 1. Alignment of the amino acid sequences of prepro-SST1 (PSSTA), -SST2 (PSSTD), -SST3 (PSSTD) and -SST6 (PSSTC) characterized from cartilaginous fish. (*) denotes conserved residues. SST peptide sequences are in red. Potential cleavage sites are in bold. Signal peptides are in grey. (p), partial sequences. Sequences of *S. canicula* SST2 (*SSTd*) and SST3 (*SSTE*) cDNAs have been deposited in the GenBank database under the accession numbers MK491629 and MK491630, respectively.

Figure 2. Synteny of genes in the *SST1-SST3* locus in *R. typus* and *C. milii* plus eight selected bony vertebrate species (human, chicken, anole lizard, western clawed frog, coelacanth, spotted gar, zebrafish and medaka). Genes are represented by block arrows. Genes with conserved synteny are coloured. For the teleost *SST4* gene, three possible positions are proposed with respect to the gar SSTs (see the text for more details). Position of the genes (in megabases -Mb) is displayed below each box, according to the Ensembl database. Empty circles indicate the end of scaffolds. Letters inside the boxes refer to the specific and provisional nomenclature of *S. canicula* SSTs initially proposed in Quan (2013). The detailed chromosomal locations of genes displayed in this map are included in **Table S4**.

Figure 3. Synteny of genes in the *SST2-SST6* locus in *R. typus* and *C. milii* plus eight selected bony vertebrate species (human, chicken, anole lizard, western clawed frog, coelacanth, spotted gar, zebrafish and medaka). Letters inside the boxes refer to the nomenclature of *S. canicula* SSTs proposed in Quan (2013), while numerals refer to the previous nomenclature of vertebrate SST genes (Tostivint 2013, 2014). Legends are the same as in the **Figure 3**.

Figure 4. Phylogenetic tree of vertebrate SST precursor sequences. Phylogenetic analysis of 147 vertebrate SST amino acid sequences was performed using Maximal Likelihood, with 500 bootstrap replicates. The number shown at each branch node indicates in percentage the bootstrap value. Sequence references and alignment are given in **Figure S1** and **Figure S2**, respectively

Figure 5. Tissue distribution of *S. canicula* SST2 (*SSTd*) and SST3 (*SSTE*) mRNAs using RT-PCR. Parallel amplification of dogfish *Egfl* mRNA served as internal control. NC, non-template control.

Figure 6. A proposed evolutionary scheme for the evolution of the SST gene family in gnathostomes with special emphasis on chondrichthyan species (in red). The names of the different paralogous genes are given in the boxes. Note the unresolved status of the teleost *SST4*. Gar *SST4* is shown here to have arisen independently of teleost *SST4*. Boxes connected by a vertical line represent linked genes. Crossed-out boxes represent lost genes. Double-headed arrows represent local duplications. R, rounds of whole genome duplication.

Supplementary data

Table S1. Sequences of the oligonucleotides used for PCR amplifications.

Table S2. Primary structure of SST-related peptides from different vertebrate species. Peptides from chondrichthyan species are in red. Conserved residues are in bold.

Table S3. Pair-wise comparison of full-length SST protein sequences from *S. canicula*, *R. typus*, *L. erinacea* and *C. milii*. Values represent percentage of amino acid identity.

Table S4. Chromosomal locations of gene orthologs in the synteny analysis of the *SST* loci. All human gene names in the table are approved HGNC symbols and the genes from other species have been given the name of their human orthologs. Chromosomal locations of genes are expressed in bp. Blanks represent genes that have not been found in the current genome databases. Non-syntenic genes are in grey.

Figure S1. Protein sequences of prepro-SSTs used for phylogenetic analysis and their accession numbers. Chondrichthyan sequences are in red.

Figure S2. Amino acid sequence alignment of the SST family used for the phylogenetic analysis. The alignment was made using Muscle and then manually optimized. Conserved residues between all orthologs are in black bold. Characteristic residues of each ortholog are colored.

Figure S3. Nucleotide sequence and deduced amino acid sequence of *S. canicula* cDNAs. Nucleotides are numbered 5' to 3' and amino acids N-terminal to C-terminal from the putative starting methionine. Signal peptides are in grey. SST peptide sequences are in red. Potential cleavage sites are in bold. Polyadenylation signals, when detected, are underlined. Nucleotide sequence (almost) identical between *SST1* and *SST3* is in red.

Figure S4. Sequence of *S. canicula* *SST* genes, inferred from the cDNA sequences given in **Figure S3**. Exons are indicated by colored boxed. The exon/intron boundary consensus sequences (GT/AG) are highlighted in red. Initiation (ATG) and stop codons are boxed. Polyadenylation signals are underlined. The identity of the scaffolds containing the sequences is indicated. Nucleotide sequence (almost) identical between *SST1* and *SST3* is in red.

Figure S5. Predicted sequence of *R. typus* *SST* genes, inferred from the *SST* cDNA sequences given in **Figure S6**. Legends are the same as in the **Figure S4**.

Figure S6. Nucleotide and deduced amino acid sequences of *R. typus* *SST* cDNAs. Legends are the same as in the **Figure S3**.

Figure S7. Predicted sequence of *C. milii* *SST* genes, inferred from the *SST* cDNA sequences given in **Figure S8**. Legends are the same as in the **Figure S4**.

Figure S8. Nucleotide and deduced amino acid sequences of *C. milii* *SST* cDNAs. Legends are the same as in the **Figure S3**.

Figure S9. Two alternative conceptions regarding the phylogenetic status of the teleost *SST4* gene. **A.** Conception from Liu *et al.*, (2010). **B.** Conception from Yun *et al.* (2015).

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Figure 1

PSST1 (PSSTA)

C. mili
S. canicula
R. typus

MSCGRVQCALALLSIALTVLSVTSAAPAHDRYREILQRSLAAAGARSKEPELKYSLAQLLA
 MWCSRQLQLSALLSIALAVLSVSSAPTDNRYREILQRAMAATGSGGKAELTKYSLAQLLS
 MWCSRQCALALLSIALAVLSAGAAAPTADRYRELLQTSMAGAEPRSKAELIKYNLVQLLA
 * * * * ***** * *** * * * * * * * * * * * * * * *

C. mili
S. canicula
R. typus

ELANAENEALEAEDMARATAQDEVRLERANSANPNLAQRERK**AGCKSFFWKTFTSC**
 ELENAENEALETDAM---GGRNEVRELELERSINPNLANRERK**AGCKNFFWKTFTSC**
 ELANAENEVLGEDLPRMAKQDEVRVDLERSANPNSPQRERK**AGCKNFFWKTFTSC**
 *** *

PSST2 (PSSTD)

C. mili
L. erinacea (p)
S. canicula
R. typus

MQWQAFASVVCLLFIVTVQGVEPQEERMGLQLNREMVKDKKRILIAKLLLAGL LDVDDNLLE
 -----MEDRT---TLQELTKNRKSILKLLAGL LDVDDHLGE
 MKWLMTVSLMSLLYLLRVEGTDLLEERMKLQVNREMTKSRSRKNLIVKLLAGL LETDDNLLE
 ----MTVCLMSLLLLSVEADPLEERMKLQVNREVTKSRSRKYIMLKLLSGLDPDDNLLE
 *

C. mili
L. erinacea (p)
S. canicula
R. typus

SVIAPLGLSKEEGTDFEERSAAGEIPPRKPK**AGCKLFFWKTFSHC**
 SGYTYSNTSEEAGERSLEE~~RAVVAVI~~PRREQK**APCKLFFWKTFSHC**
 NGFAPLKPEEAEGTLFEERSVNAGIPRREQK**TPCKLFFWKTFSHC**
 NDFTSLSPGEEES-SLEERSVNAGIPRRPQK**APCKLFFWKTFSHC**
 *** * * * * * * * * * * * * * * * *

PSST3 (PSSTE)

C. mili
S. canicula
R. typus (p)

-MQARCTLTAL--LSIAALGLSALPTHLRDQLVLQGSPAMELRDGVVRELIQAVADAES
 MWCSRQLQLSALLSIALAVLSVSSAPTDNRYREILQRALDQELLKDTMMKLLPLVTDVDT
 -----DFLKDTIIQLHVVADADK
 * * *

C. mili
S. canicula
R. typus

KPQSEEEAADF-APDEKAE---LRLALAPRWRK**DCKNFFWKTFTLC**
 EAGTLVDVSNAAETSEENNTPMKFQHRQLGMRMRK**NCKNFFWKTFTLC**
 DAVEVNASQVETPPXNK1PMKFQQRQLGTRMRK**NCKNFFWKTFTLC**
 * * * * * * * * * * * * * * * *

PSST6 (PSSTC)

C. mili
S. canicula
R. typus

MQIL--VALISTLFLVSGVTTTASLDDRFLNLQSSREMNQERKEMILKLLSGL LDNAAVS
 MQLLGTASILLSMILLIV-SSVRATAPLEDRLSLRANQELNKERKEVILKLLSGL LDSS--S
 MQLLGSASXVSILLIV-SSVKATAPLEDRLSLRANQELNKERKEVVLKLLSALLDSS--S
 *

C. mili
S. canicula
R. typus

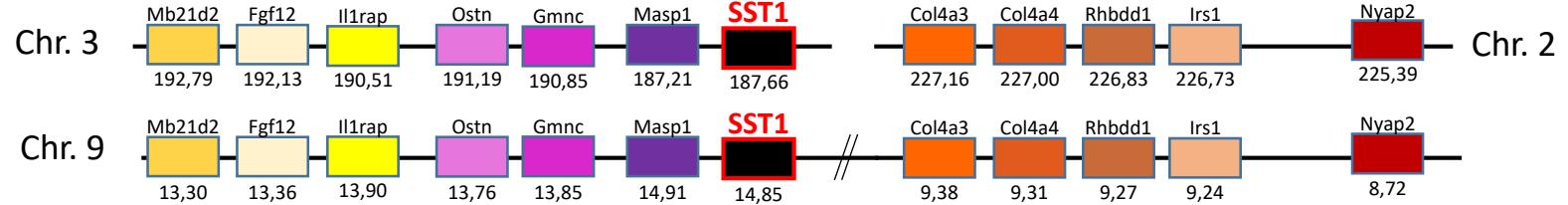
GQTGSEAGYYPEPADGGPVMLEERSRYSQLPQRSRK**VPCKNFFWKTFTSC**
 NQIAIENTFPDPEDVEEMKVEERSRFSQLPQRERK**APCKNFFWKTFTSC**
 NQMGIENTFPDQEDMEEMKVEDRSRFSQLPQRERK**TSCKNFFWKTFTSC**
 *

Whale shark (*R. typus*)

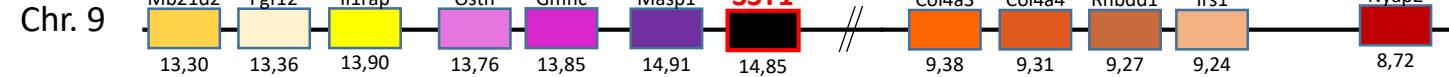
Figure 2

Elephant shark (*C. milii*)

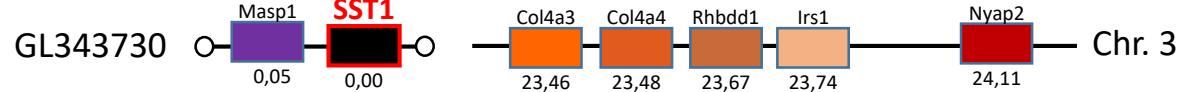
Human (*H. sapiens*)



Chicken (*G. gallus*)



Anolis (*A. carolinensis*)



Xenopus (*X. laevis*)



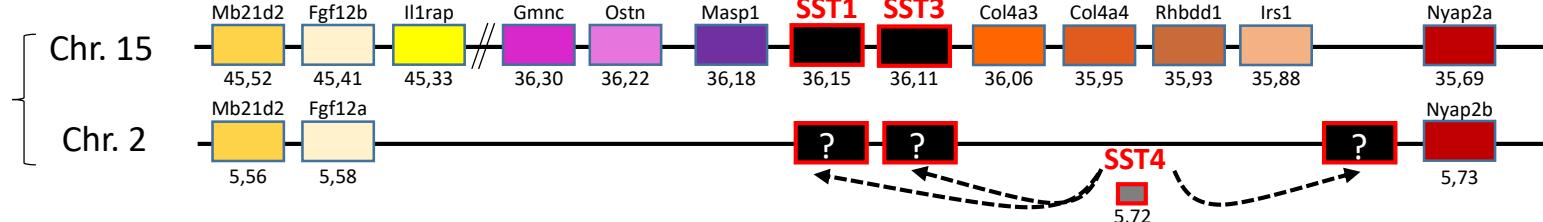
Coelacanth (*L. chalumnae*)



Spotted gar (*L. occulatus*)



Zebrafish (*D. rerio*)



Medaka (*O. latipes*)

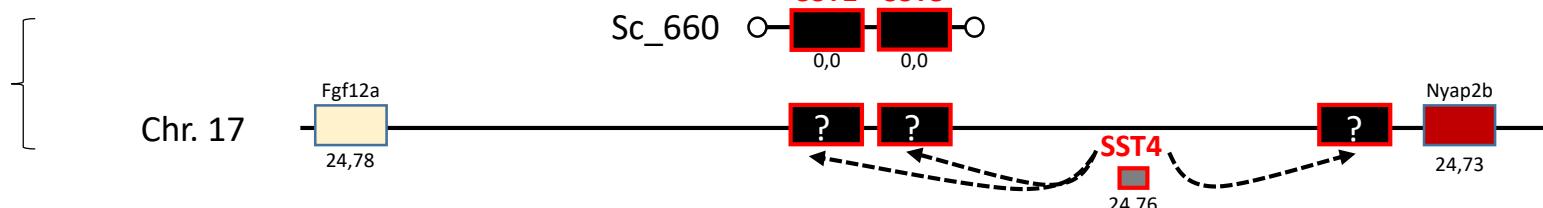


Figure 3

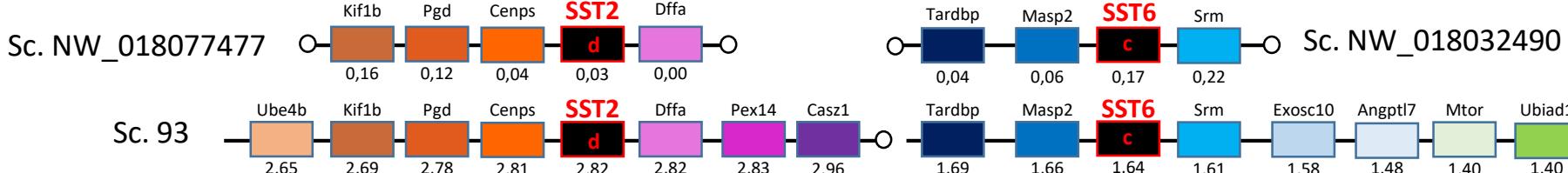
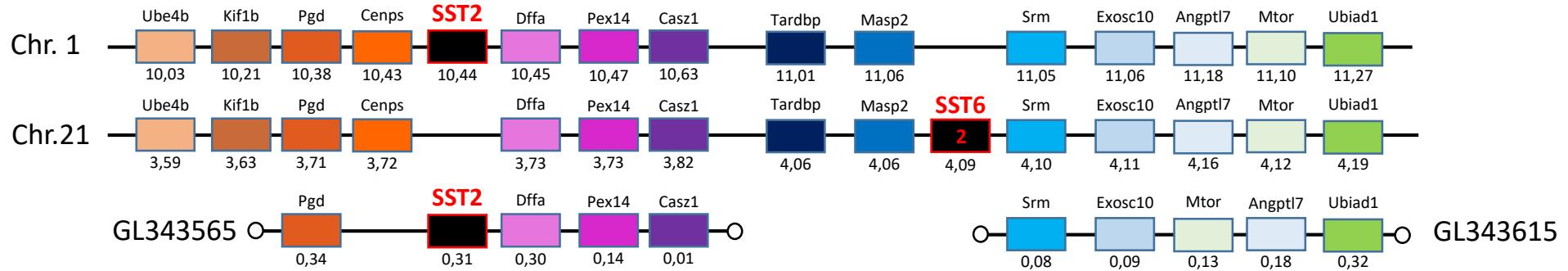
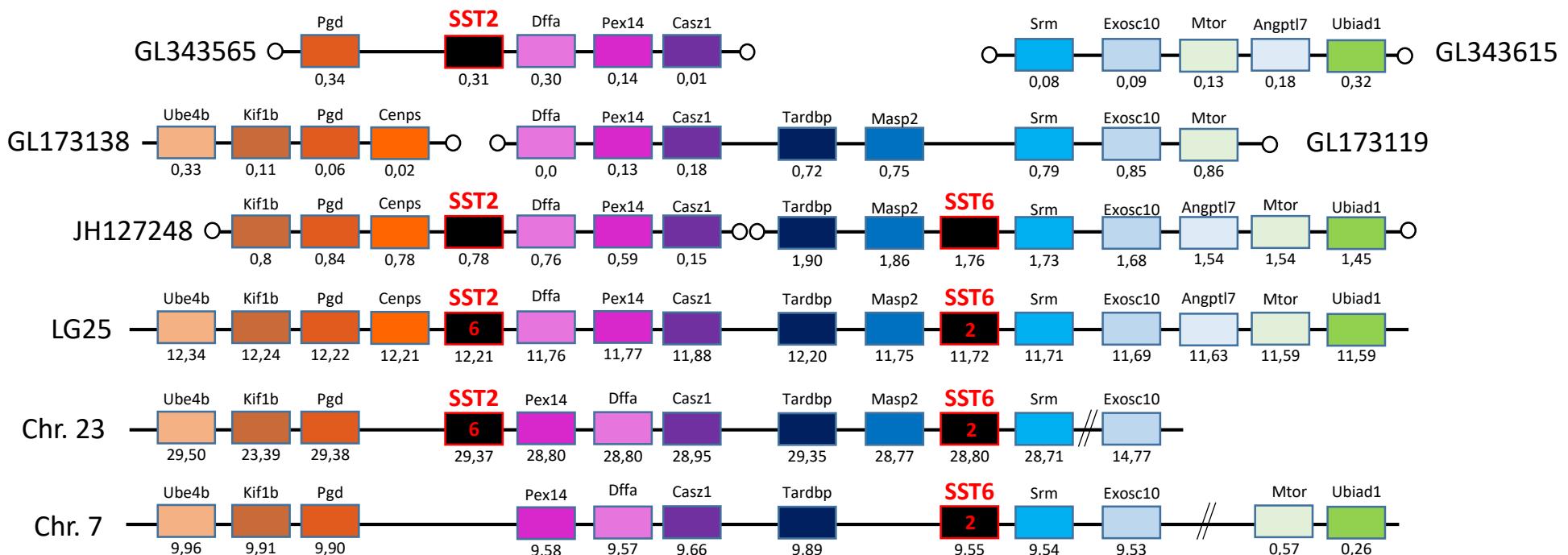
Whale shark (*R. typus*)Human (*H. sapiens*)Chicken (*G. gallus*)Anolis (*A. carolinensis*)Xenopus (*X. tropicalis*)Coelacanth (*L. chalumnae*)Spotted gar (*L. occulatus*)Zebrafish (*D. rerio*)Medaka (*O. latipes*)

Figure 4

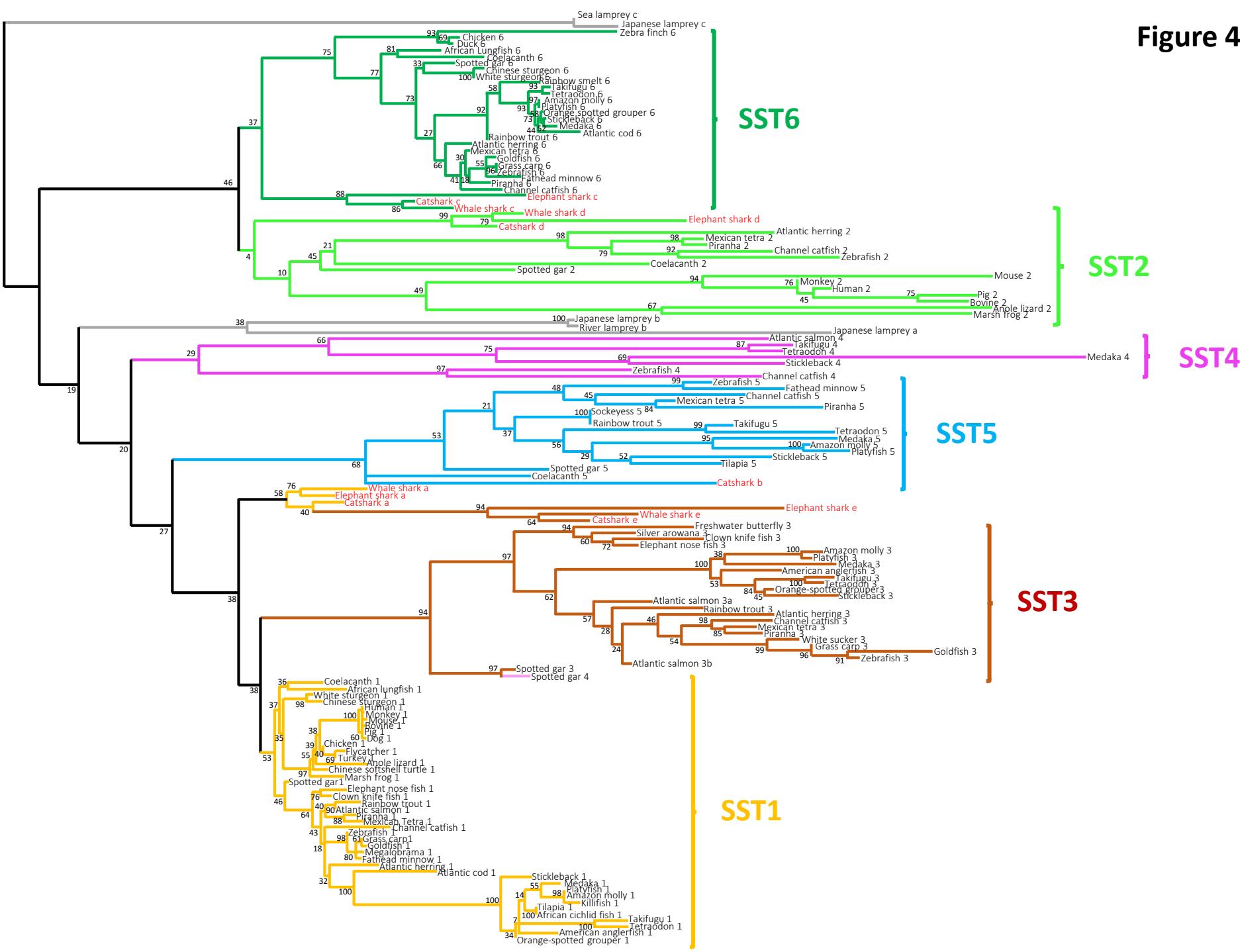
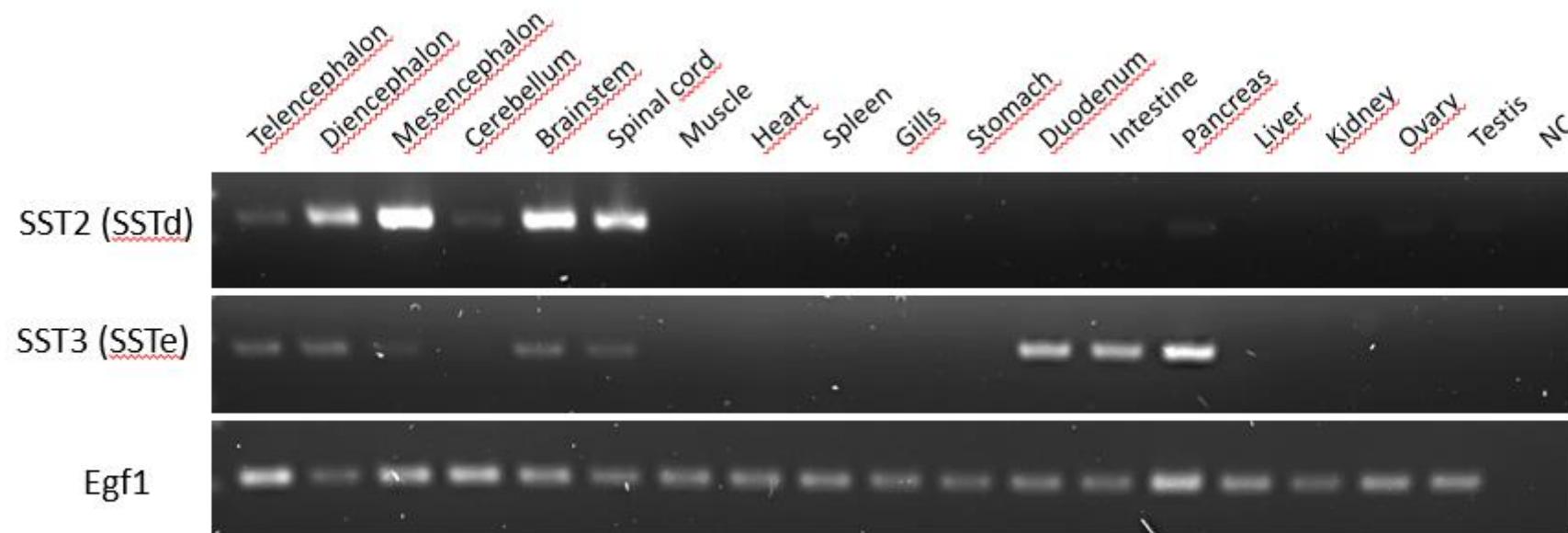


Figure 5



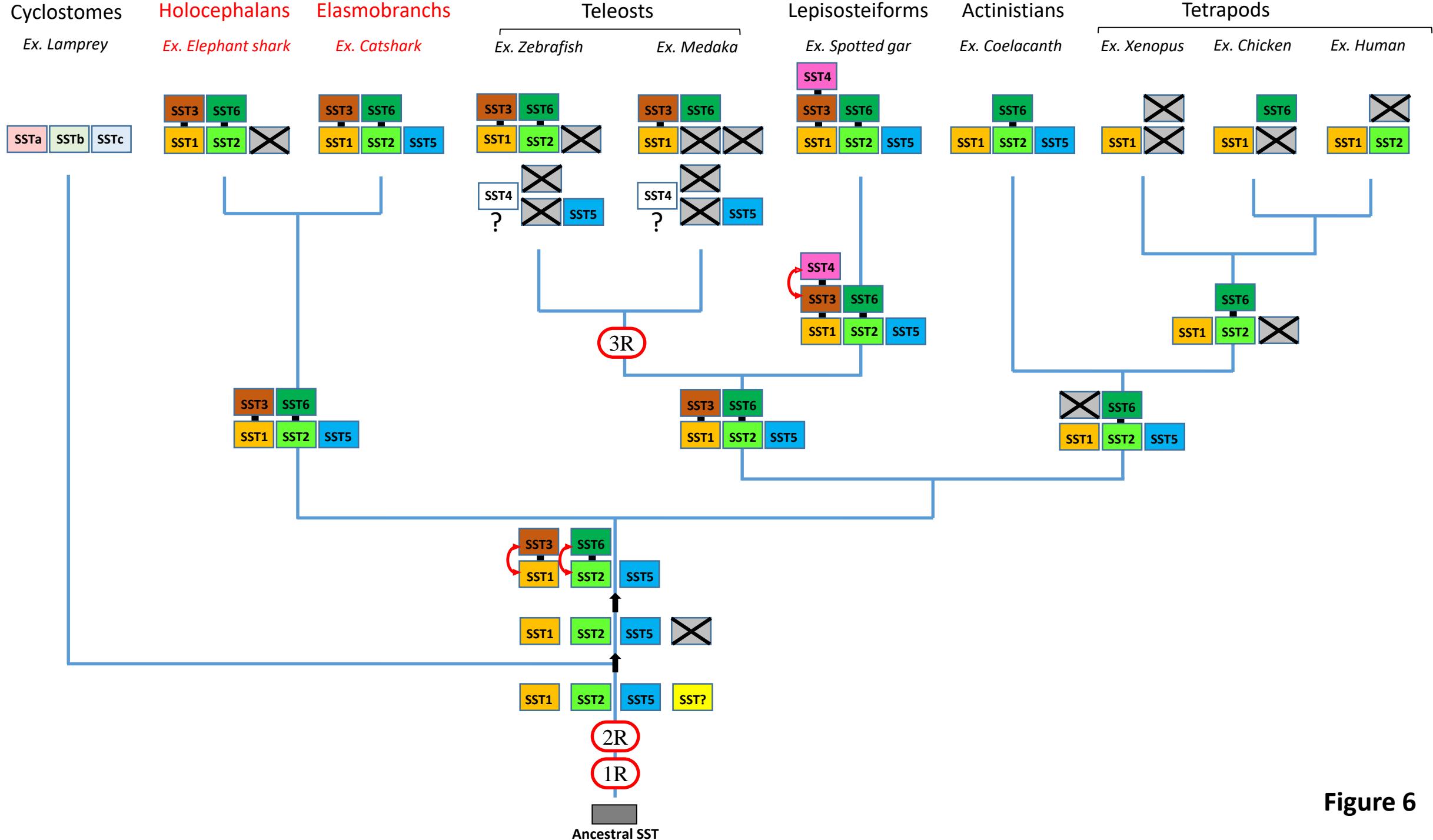


Figure 6

Figure S1

Somatostatin 1

Primates

>Human (*Homo sapiens*) SST1 (BC032625)

MLSCRLQCALAALSVLALGCVTGPASDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPN
QTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

>Monkey (*Macaca fascicularis*) SST1 (XP_005545499)

MLSCRLQCALAALSVLALGGVTGPASDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPN
QTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

Other mammals

>Bovine (*Bos taurus*) SST1 (NP_776385.1)

MLSCRLQCALAALSVLALGGVTGPASDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPN
QTEIDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

>Dog (*Canis lupus familiaris*) SST1 (NP_001003307.1)

MLSCRLQCALAALSVLALGGVTCAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPN
QTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

>Mouse (*Mus musculus*) SST1 (NP_033241.1)

MLSCRLQCALAALCIVLALGGVTGPASDPRLRQFLQKSLAAATGKQELAKYFLAELLSEPN
QTENDALEPEDLPQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

>Pig SS1 (*Sus scrofa*) SST1 (AAT02532.1)

MLSCRLQCALAALSVLALGGVTGPASDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPN
QTENDALEPEDLSQAAEQDEMRLELQRSANSNPAMAPRERKAGCKNFFWKTFTSC

Birds

>Flycatcher (*Ficedula albicollis*) SST1 (ENSFALT00000007767.1)

MLSCRLQCALALLSIALALGTVSAAPSDPRLRQFLQKSLGGGGGGELAKYFLAELLSEPSQ
TENEALESEDLSRGAEQDEVRLELERSANSNPALAPRERKAGCKNFFWKTFTSC

>Chicken (*Gallus gallus*) SST1 (CN210817.1)

MLSCRLQCALALLSIALAVGTVAAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLSEPSQ
TENEALESEDLSRGAEQDEVRLELERSANSNPALAPRERKAGCKNFFWKTFTSC

>Turkey (*Meleagris gallopavo*) SST1 (ENSMGAT00000008507.2)

KELAKYFLAELLSEPSQTENEALESEDLSRGAEQDEVRLELERSANSNPALAPRERKAGCKN
FFWKTFTSC

Reptiles

>Anole lizard (*Anolis carolinensis*) SST1 (XP_003228868)

MLPCRLPCALALLSLALALGSGAAAPADPRLRQFLQKSLAAAAGKQELAKYFLAELLSEP
GQAENEALEPEELSRGGAEQDEVRLELERSASLNPALEPRVRKAGCKNFFWKTFTSC

>Chinese softshell turtle (*Pelodiscus sinensis*) SST1 (ENSPSIT00000016437.1)

MLSCRLQCALALLSLALAVSSVSGAPSDPRLRQFLQKSLAAAAGKQELAKYFLAELLAEPS
QPENEALEPEDLSRGPEQDEVRLERSANPNPALAPRERKAGCKNFFWKTFTSC

Amphibians

>Marsh frog (*Pelophylax ridibundus*) SST1 (P87384.1)

MQSCRVQCALTLLSLALAINSISAAPTDPRLRQFLQKSLASAGKQELAKYFLAELLSEPSQTD
NEALESDDLPRGAEQDEVRLELERSANSSPALAPRERKAGCKNFFWKTFTSC

Lobe-finned fish

>Coelacanth (*Latimeria chalumnae*) SST1 (XP_005992512.1)

MLSSRLQCAFAFLSLALVVSNISAAPSDLRLRQLLQKSLAAAAGKQEVSKEYSLAELAELAQ
AENEALESDDFSKTSDQDEVRLERSANGNPALAPRERKAGCKNFFWKTFTSC

>African lungfish (*Protopterus annectens*) SST1 (AAD39138.1)

MLSCRFCALVLLSLAVVFSKVSAAPSDLRLRQLLQRSLAAAAGKQELTKYSLAELLSEL
QSENDALDSSDLSRGADQDEVRLELDRSANSSPLAARERKAGCKNFFWKTFTSC

Euteleosts

>Orange-spotted grouper (*Epinephelus coioides*) SST1 (AAU93565.1)
MKMVSSSRLCLLLLLTLTASISCSSAAQRDSKLRLLLHRTPLLGSKQDMRSRASLAELLSD
LLQVENEALEEENFPLAEGEPEDVHVDLERAAGSGPLLAPRERKAGCKNFFWKTFTSC
>Killifish (*Fundulus heteroclitus*) SST1 (EV461374.1)
MKMFSSLRCLLLLCLSASISCSAAAQRDSKLRLLLHRTPLLSSQQDVSRSSLAELLSD
LLQMENEALEEDGFTLPEGEPEPEDIRVDLERAASSGPLLAPRERKAGCKNFFWKTFTSC
>Atlantic cod (*Gadus morhua*) SST1 (AAZ85702.1)
MMSVRSTLLLSCAAMLSGSSAAPSDTKLRLQLLQRSLLAPMPGQEETVRYTLAQLLSELAQ
AENEALGTDDQDDERMDLERAAGPMMAPRERKAGCKNFFWKTFTSC
>Stickleback (*Gasterosteus aculeatus*) SST1 (KT235748)
MVSSRLRCLLTLTASISCSSTAQRDGKLHLLLHRTPLLSSKQDMRSASLVELLSDLLQ
VQNEALEEENLAPAGGEPEEVHLDLERAADAGPLLGPRERKAGCKNFFWKTFTSC
>African cichlidfish (*Haplochromis burtoni*) SST1 (AAS97964.1)
MNSSSRCLLVLVSLTASISCTSAAQRDSKLRLLLHRTPLLGSKQDMRSRSSLAELLSDLL
QVENEALEEENFPLADGEPEDIRVDLERAAGSGPLLAPRERKAGCKNFFWKTFTSC
>American anglerfish (*Lophius americanus*) SST1 (P01169.1)
MKMVSSSRLRCLLVLLSLTASISCSFAGQRDSKLRLLLHRYPLQGSQDMTRSLAELLSD
DLLQGENEALEEENFPLAEGGPEDAHDLERAASGGPLLAPRERKAGCKNFFWKTFTSC
>Rainbow trout (*Oncorhynchus mykiss*) SST1 (CA364601.1)
MLSTRVQCALALLSLALAIISSVSAAPSDAKLRQLLQRSLLMAPAGKQELARNTLVELLSELAH
VENEAIELDDMSHGVEQEDVDLELERAPGPVLAPRERKAGCKNFFWKTFTSC
>Tilapia (*Oreochromis niloticus*) SST1 (ENSONIT00000001338.1)
MNSSSRCLLVLVSLTASISCTSAAQRDSKLRLLLHRTPLLGSKQDMRSRSSLAELLSDLL
QVENEALEEENFPLADGEPEDIRVDLERAAGSGPLLAPRERKAGCKNFFWKTFTSC
>Medaka (*Oryzias latipes*) SST1 (XP_004084505.1)
MMSSSSRCLLVLVSLTASISCSSAAQRDSKLRLLLQRTPLLGSKQDMRSRSSLAELLSDLLQM
ENEVLEEDGFPLSDGEPEDVVDLERAASGPLLAPRDRKAGCKNFFWKTFTSC
>Amazon molly (*Poecilia formosa*) SST1 (ENSPFOT00000005658.1)
MKMLSSSLRCLLVLVSLTASISCSSAAQRDSKLRLLLHRTPLLGSKQDMRSRSSLAELLSDL
LQMENEALEEDGFGPEGEPEDIRVDLERAASSGPLLAPRERKAGCKNFFWKTFTSC
>Atlantic salmon (*Salmo salar*) SST1 (CB509644.1)
MLSTRVQCALALLSLALAIISSVSAAPSDAKLRQLLQRSLLMAPAGKQELARYTLAELLSELAQ
AENEAIIESDDLSRGVEQEDVRLELERAAAGPVLAAPRERKAGCKNFFWKTFTSC
>Takifugu (*Takifugu rubripes*) SST1 (ENSTRUG00000010048)
MFSSNSMCLLMLLSSASFSCSSAAHRDFKLPLLLQSNALMGNQEMTRSSLANLLSDLL
QVGNEALEEENLALAEGEPEEVHIDMERAAGIGPFLTPRERKAGCKNFFWKTFTSC
>Tetraodon (*Tetraodon nigroviridis*) SST1 (KT235747)
MKMFSNSCCLLMLLSSASFSCSSAAQRDSKLALMLPPNPLLGHQRQEMSRSSLADLLSDL
LQVENQALDENFPLVEGEPEEVHDMERAADAGIGPFLTPRERKAGCKNFFWKTFTSC
>Platyfish (*Xiphophorus maculatus*) SST1 (ENSXMAT00000014478.1)
MKMLSSSLRCLLVLVSLTASISCSSAAQRDSKLRLLLHRTPLLGSKQDMRSRSSLAELLSDL
LQMENEALEEDGFPEGEPEDIRVDLERAASSGPLLPRERKASCKNFFWKTFTSC

Other teleosts

>Mexican tetra (*Astyanax mexicanus*) SST1 (ENSAMXT00000006698.1)
MLSTRVQCALALLSIALAVGSVSGAPSADAKLRQFLQRSLIGSAGKQELARYTLAELLSELAQ
AENEALEDDVPRGAEQEDVRMELERAAGPVLAAPRERKAGCKNFFWKTFTSC

>Goldfish (*Carassius auratus*) SST1 (Q9YGH5.1)
MLSTRIQCALALLSLALAVCSVSAAPTDAKLRQLLQRSLLNPAGKQELARYTLADLLSELVQ
AENEALEPEDLSRAVEKDEVRLERAGPMLAPRERKAGCKNFFWKTFTSC

>Clown knife fish (*Chitala chitala*) SST1 (AAK97070.2)
MLSTRIQCALALLSLALAVSSVYAAPSDLKLRQLLQRSIIAPASKQELARYTLAELLSELAQV
ENEALESDDLRGADQEEVRLELERAAGPPLAPRERKAGCKNFFWKTFTSC

>Atlantic herring (*Clupea harengus*) SST1 (XP_012673158.1)
MLSLRLQCALALLSIVLAISCISAAPTDVKLRQLLQRSLLFAPGGKQELARLT LAELLSELAQA
ENEALESEDMSRGAEGEDVRYELERSAGSMILAPRERKAGCKNFFWKTFTSC

>Grass carp (*Ctenopharyngodon idella*) SST1 (ACB69423.1)
MLSTRIQCALALLSLALAVCSVSAAPTDAKLRQLLQRSLLNPAGKQELARYTLADLLSDLV
QAENEALEPEDLSRAVEKDDVRLELERAAGPMLAPRERKAGCKNFFWKTFTSC

>Zebrafish (*Danio rerio*) SST1 (AAH76254.1)
MLSTRIQCALALLSLALAVSSVSAAPSDAKLRQLLQRSLLSPAGKQELARYTLADLLSDLVQ
AENEALEPEDLSRGAEKDDVRLELERAAGPMLAPRERKAGCKNFFWKTFTSC

>Elephant nose fish (*Gnathonemus petersii*) SST1 (AF292652)
MLSSRIQCALALLSLALAVSSVSAAPSDLKLRQLLQRSLLAPASKQDLARNPLELLSEMVR
VENEALEPDDLSRGADQEEVRLELERAAGPALAPRERKAGCKNFFWKTFTSC

>Channel catfish (*Ictalurus punctatus*) SST1 (CAA23877.1)
MPSTRIQCALALLVALSVCSVSGAPSADAKLRQFLQRSILAPSVKQELTRYTLAELLAELAQ
AENEVLDSDVSRAAESEGARLEMERAAGPMLAPRERKAGCKNFFWKTFTSC

>Megalobrama (*Megalobrama pellegrini*) SST1 (AAO92644.1)
MLSTRIQCALALLSLALAVSSVSAAPSDAKLRQLLQRSLLNPAGKQELARYTLTDLLSDLVQ
AENEVLEPEDLSRAVEKDEVRLERAGPMLAPRERKAGCKNFFWKTFTSC

>Fathead minnow (*Pimephales promelas*) SST1 (DT100930)
MLSTRIQCALALLSLALAISSVSAAPSDAKLRQLLQRSLLNPAGKQELARYTLADLLSELVQ
AENEALEPEDLSRAVEKDDVRLELERAAGPMLAPRERKAGCKNFFWKTFTSC

>Red-bellied piranha (*Pygocentrus nattereri*) SST1 (XP_017539070.1)
MLSTRVQCALALLSLALALSSVSGAPSADAKLRQFLQRSLIGPSGKQELARYTLAELLSELAQ
AENEALEAEDMPRGAEQEDVRMELERAAGPVLAPRERKAGCKNFFWKTFTSC

Other ray-finned fish

>White sturgeon (*Acipenser transmontanus*) SST1 (AAL13248.1)
MLSSRLQCALALFLSLALAVSSVSAAPSDPRLRQLLQRTLAASAGKQELLKYSIAELLSELAQS
ENDALASDELSRAAEQNDVRLELERSANGNPAMAPRERKAGCKNFFWKTFTSC

>Chinese sturgeon (*Acipenser sinensis*) SST1 (FJ792687.1)
MLSSRLQCALALLSLALAVSSVSAATSEPRIRQLLQRALVASAGKQDLLKYSIAELLSELAQ
SENDALASDELSRAAEQNDVRLELERSANGNPAMAPRERKAGCKNFFWKTFTSC

>Spotted gar (*Lepisosteus oculatus*) SST1 (XP_006637937.1)
MLSSRVQCALALLCLALAVSSVSAAPSDLRLRQLLQRSLAASAGKQELARYTLAELLSELA
QSENEALESDDLSRAAEQDEVRLERANSANPALAPRERKAGCKNFFWKTFTSC

Cartilaginous fish

>Elephant shark (*Callorhinichus milii*) SSTa (XP_007910586.1)
MSCGRVQCALALLSIALTVSVTSAPAHDYREILQRSLAAAGARSKELT KYS LAQLLAEL
ANAENEALEAEDMARATAQDEVRLER SANPNLAQRERKAGCKSFFWKTFTSC

>Whale shark (*Rhincodon typus*) SSTa (XP_020365362.1)
MWCSRVCALALLSIALAVLSAGAAAPTADRYRELLQTSMAGAEPRSKAELIKYNLVQLLAE
LANAENEVLDGEDLPRMAKQDEVRLERSANPNSPQRERKAGCKNFFWKTFTSC

>Catshark (*Scylorhinus canicula*) SSTa (JX964750)
MWCSRQLSLALLSIALAVLSVSSAPTDNRYREILQRAMAATGSGGKAELTKYS LAQLLSEL
ENAENEALETDAMGGRNEVRLELERSINPNLANRERKAGCKNFFWKTFTSC

Somatostatin 2

Primates

>Human (*H. sapiens*) SST2 (AAB66895.1)

MPLSPGLLLLLSGATATAALPLEGGPTGRDSEHMQEAGIRKSSLLTFLAWWFEWTSQAS
AGPLIGEEAREVARRQEGAPPQQSARRDRMPCRNFFWKTFSACK

> Monkey (*M. fascicularis*) SST2 (XP_015298230)

MPLPPGLLLLLSGATATAALPLEGSPTGPDSEHMQEAGIRKSSLLTFLAWWFEWTSQASA
GPLIGEEAREVARRQEGAPPQQSARRDRTPCKNFFWKTFSACK

Other mammals

> Bovine (*B. taurus*) SST2 (NP_001191825)

MLPLCLLPLLLPSGATTALSPEGGLAGHESGHMQEVAEIKTNSSLTFLAWWYEWASQAR
AVPFVGGEAREVSKRQEGAPLHQSTRQDKTPCKNFFWKTFSACK

> Mouse (*M. musculus*) SST2 (AAD51127.1)

MMGGRGTGGKWPSAFGLLLWGVAASALPLESGPTGQDSVQEATEGRSGLLTFLAWWHE
WASQASSSTPVGGGTPGLSKSQERPPPQQPPHLDKKPCKNFFWKTFSACK

> Pig (*S. scrofa*) SST2 (NP_001191865)

MLPPLCLLLLLPPLGATTALPLEGGLTSHDRDSGHMQEVAEIKKNSLLTFLAWWHEWMS
QAREVPFVGGETREMPKKQEGLPRQQASRGDRTPCGNFFWKTFSACK

Reptiles

> Anole lizard (*A. carolinensis*) SST2 (XP_008119733.1)

MAFLVHPPPSAPFLLALLSFSLRMLGAAPAAVLPIPGGLAWKHNEGSADLGRDELLAFLGLV
DRASRRHGMPLSKQEKKVVRSPREERVPFHRHPVREKAPCKNFFWKTFSACK

Amphibians

> Marsh Frog (*P. ridibundus*) SST2 (AAC60094.1)

MLGSAGTLLLLLAWGARALSQPDDNRITTGRNQDLNAIQQDLLLKLLSGWTDSRESNLVE
VERNVPDPPEPKIPPSVKFPRSLRERKAPCKNFFWKTFTMC

Lobe-finned fish

> Coelacanth (*L. chalumnae*) SST2 (NW_005819697)

MQPLILLVPLVLMAWNLGVAAVPKEERLMLYDKVNRETTGFGEERKQFLSNMLDALIGLN
TLENDTPLLGTEQEEHNLERSAFKYSSLKAPCRNFFWKTFSACK

Teleosts

> Mexican tetra (*A. mexicanum*) SST2 (ENSAMXT00000013558.1)

MALSGGGDTCGAADGGMFIMRMLLSLVPLLIAWSGTNTDALPIDNKLPSKEVLTKEQKD
LLIKIMSDLAELNMTLKDLGALDLEQLLNGKLGERSVEKSPCTNFFWKTFSAC

> Atlantic herring (*C. harengus*) SST2 (XP_012681486.1)

MGVALARVDPCSVAQSARITMRVLTSLVPLILIVWSGSQTGALPVREKPLRNESLADEERILL
KILAGLTEKNLTEENLTGHDLEGLLNGTLKGGSVPTPQERSPCKNFFWKTFSACK

> Zebrafish (*D. rerio*) SST2 (ENSDART00000146411.2)

MFLMRVLLSLFPLVFVIWNGEALPIQDKQSQTNEILSKEEDGLKMITYVAELNLTSKELADL
DAELLNGKLWEKSDKPSKDKSPCKLFFWKTFSACK

> Channel catfish (*I. punctatus*) SST2 (XP_017341959.1)

MALGGRINLYQAVDSPMFTMRVLLSLIPLLFVAWSANNADALPVQDKLPNSNEVLTKEQK
DFMTQFLANLAELNMTIKDLETMDHEQLSKLSERAAGLPPAREKSQCNCFFWKTFSACK

> Red-bellied piranha (*P. nattereri*) SST2 (XM_017706353.1)

MALAVGGTSCGGADGGMFIMRMLLSLVPLLIAWSGTSTDALPVENKLPSNEVLTKEQK
DLLIKIMSDLAELNMTVKDLGALDLEQLLSGKLGERSVFGPAQEKSQCNCFFWKTFSACQ
H

Other ray-finned fish

>Spotted gar (*L. oculatus*) SST2 (NC_023203.1)

MHLLSSLVPLALLVWSLKAAA VPSEERRALQSNGGLAKERKDVLKVLSGLLVSNLLRKE
QSAVDSEQLKSSLMGERSVFGPSVRERTPCKNFFWKTFS

Cartilaginous fish

>Elephant shark (*C. milii*) SSTd (XP_007900347.1)

MQWQAFASVVCLLFIVTVQGV_EERMLQLNREMVKDKKRLIAKLLAGLLDVDDNLLE
SVIAPLGLSKEEGTD_EERSAAGEIPPRKP_KAGCKLFFWKTFSHC

>Whale shark (*R. typus*) SSTd (XP_020390988.1)

MTVCLMSLLLLSVEAADP_EERMKLQVNREVT_ERSRKYLMKLLSGLDPDDNLLENDFTS
LSPGEEESSLEERSVNAGIPRRPQ_KAPCKLFFWKTFSHC

>Catshark (*S. canicula*) SSTd (MK491629)

MKWLM_TVSLMSLLYLLRVEGTDLLEERMKLQVNREMT_ERSRKNLIVKLLAGLLETDDNLLE
NGFAPLKPEEAEGTLFEERSVNAGIPRREQKTPCKLFFWKTFSHC

Somatostatin 3

Euteleosts

>Orange-spotted grouper (*E. coioides*) SST3 (AAU93566.1)

MQCIRCP_TILVLVALVLCSPGVFSQPD_DRDQDQYQNQDLDLERHHRLQRARSAGLLSQEW
SKRAVEDLLAQMSLPEADTQREAEV_VSMATGGRMNLERSVDPPNNLPPRERKAGCKNFYWK
KGFTSC

>Stickleback (*G. aculeatus*) SST3 (KT235756)

MQYTRCPAILVLVGLVLC_GPGVSSQRNRDQDQDQYQNQDLDPRPHLLLQRARGAGLLSQD
WSKRAVEDLLAQMSLPEADSQ_LGAEV_VSAATGGRLHLERSVDPPNNLPPRERKAGCKNFYWK
KGFTSC

>American anglerfish (*L. Americanus*) SST3 (P01170.2)

MQCIRCPAILALLVLCGPSVSSQLDREQSDNQDLDLERQHWLLERARSAGLLSQEW_WK
RAVEELLAQMSLPEADVQREAEDASMATGGRMNLERSVDSTNNLPPRERKAGCKNFYWK
GFTSC

>Rainbow trout (*O. mykiss*) SST3 (Q91194.1)

MKVCR_IHCALALLGLALAICSQGAASQPD_DDLRSR_RLLQRARA_AAWPHRSGV_SERWRTFYP
NCPLCLR_PR_KV_KCPAGAKEDLRVELERSVGNPNNLPPRERKAGCKNFYWK_GF_TSC

>Medaka (*O. latipes*) SST3 (AU168379.1)

MQHARGPAFVVLAALALSSLGVSSQSDRDQDQFQNHDLDLERHHRLQRARSAGLLSQD
WSKRAIENMLARMPDPEAEAEREAEVGRNNMERSVDANPPRN_RKDGCKNFYWK_GF_TSC

>Amazon molly (*P. formosa*) SST3 (ENSPFOT00000005672.2)

MHHARCPTILVLAALAALSLGVSSQADRDQDPYQNQNLDLDLERHHRLQRARSAGLLS
QDW_SKRAVEDLLAQMSRSAVEAQQDDPEAASKGTDSRLNLERSVETTARERKAGCKNFYWK_GF_TSC

>Atlantic salmon (*S. salar*) SST3a (DW531645.1)

MKF_SQIHCALALLGLALAICSQGAASQPD_DDLRSR_RLLQRARAASIATQEWSKRV_MEDVLS
KLSLPDVEAQKSVG_TADAKEDLERSVDNSNNLPPRERKAGCKNFYWK_GF_TSC

>Atlantic salmon (*S. salar*) SST3b (CB505007.1)

MKVCRIHCALALLGLALAICSQGAASQPDLRLSRRLLQRARAAGIATQEWSKRAVEDILS
QLSWPEAQESEVSPAGAKEDLRVELERSVGNPNLPPRERKAGCKNFYWKGFTSC
>Takifugu (*T. rubripes*) SST3 (ENSTRUT00000025350.1)
MQRIHSSTILMLTTLVLCIQGVSSQPDRLNQNQDLEMEVRHHRLLQHVHGAGLLSQEWSK
RAVEDLIAQMSMPEGTGQRDTEVVSMATGGRMNLERSVDTNNLSPPERKAGCKNFYWK
GPTSC
>Tetraodon (*T. nigroviridis*) SST3 (ENSTNIT00000001563.1)
MPGVRSSTILVLTALVLSIQAVSSQPDRLDQNQDLDQEVRHHRLLQRAHGAGLLSQDW
SKRAVEDLIAQMSLPEGTGQRDTEVVSMATGGRMNLERSVDTNNLPPRKAGCKNFYWK
GFTSC
>Platyfish (*X. maculatus*) SST3
MHHARYPAILVLAALAALSLGVSSQADRDQDPYQNQNLDLDLELRHHRLLQRARSAGLLS
QDW SKRAVEDLLAQMSRSEVEAQQDGPEAASRGTSRLNLERSVETTARERKAGCKNFY
WKGLTSC
Other teleosts
>Mexican tetra (*A. mexicanum*) SST3 (ENSAMXT00000006711.1)
MKCVLQCGLVLLGLALVLCSSGASSQPDLDLDDVDLRHRRLLQRARALGIAAQEWKKR
EMEDLLSQLTLPESEFQESEISTLGSKQDVREMDRSAENPNSLPPRERKAGCKNFYWK
GFTSC
>Goldfish (*C. auratus*) SST3 (AAF15306.1)
MRLCELHCYLALLGLSLVLCGRCANSQLEPDLDFRHHRLLQRASATGQATRWDFTKRDVE
KLLSLLSIPMEMREKGLSMAGESEDLRLEQERSAESSNQLPTRVRKEGCKNFYWK
GFTSC
>White sucker (*Catostomus commersonii*) SST3 (AAK97071.2)
MRLCELHCYLALLGLSLVLCDRGADSQLEPDMDFRHRRLLQRARAIGLATQDW
TKKDIEELLSQLSLPEIEARENGVSTTGGNDDLHLELERSAENTNQLYPRERKAGCKNFYWK
GFTSC
>Clown knife fish (*C. chitala*) SST3 (AAV48555.1)
MKNCQAQCILALMGLFLGLCWPSDASQPDLRYRSLLQRAHSAPASPQDWTRRTVEDLL
LPPPEGEFTPVEDVPAADEGEEVRVELERSVDPNNLPPRERKAGCKNFYWK
GFTSC
>Atlantic herring (*C. harengus*) SST3 (XP_012693360.1)
MMRFSGIHCSLALLGLSLVLCHSASSQPDLDLDDLRHHRLLQRARAAGMSTQEWSKRAV
EDLLSQLSLPEEETQDREVSTVGAAKDDLHMERSAETNNIPPDRKSGCKNFFWK
GRTSC
>Grass carp (*C. idella*) SST3 (ACB69424.1)
MRLCELHCYLALLGLSLVLCGRSANSQLEPDLDFRHHRLLQRARAIGQATQDW
TKKDVEELLSLLSMPMEMRENDISTVDENEDLRVELERSAESSNHIPARERKAGCKNFYWK
GFTSC
>Zebrafish (*D. rerio*) SST3 (XP_694143.1)
MRLCELHCYLALLGLSLVLCGRSANSQLEPEMDFRHHRLLQRARAIGQAQEWT
KKDVEELLSLLSMPMEMQMRESDLSTTDENEDLRVELERSAESSNHIPARERKAGCKNFYWK
GFTSC
>Channel catfish (*I. punctatus*) SST3 (CK424149.1)
MRTCVLQCCCLLGLSLVLCNGVSSQPDLDLRHRRLLQRVQALGVAQEWT
KNDLKAILAQLTMPSEFQESDVSTLGTKQDLTVELERSAEDPNSLPPRERKAGCKNFYWK
GFTSC
>Elephant nose fish (*G. petersii*) SST3 (AAV48556.1)
MKTCQVHCVLVLLGLVGLCYP
SAASQPDLRYRSFMQRAHTAAMSPQDW
SKQAVEELLSRL
LAPPEDDTPQSEMSTAEEGEETR
VELERSVEPNNLPPRERKAGCKNFYWK
GFTSC
>Silver arowana (*Osteoglossum bicirrhosum*) SST3 (AAK97067.1)
MKICQIHCTLVLLGLVGLCYP
SAASQPDLRYRSFLQRAHAAAMSPQDW
SKQAVEELLSRL
APAQGEVPQGA
VSAADEEEDVR
VDLERSLE
NNLPPRERKAGCKNFYWK
GFTSC
>Freshwater butterfly fish (*Pantodon buchholzi*) SST3 (AAK97068.2)
MKLCQVHC
ILALLGLV
LGMC
GSSSATQL
DSRYRSL
VQRARA
ASMGP
QQDW
WGKLS
VEDLS
LAATEAD
MPFG
DM
SAA
EESEGA
HLD
LERS
VEPG
NVPP
RERKAG
CKNFYWK
GFTSC

> Red-bellied piranha (*P. nattereri*) SST3 (XP_017539071.1)

MRVCVLQCCLALLGLSLVLCNGASSQPDLMDVDVLDPRYHRLLQRARALGMAAQD
WRKREMEDLLSQLTLPESFKESEITSLGAKHDVRVELERSAENPNNLPPRERKAGCKNFY
WKGFTSC

Other ray-finned fish

>Spotted gar (*L. oculatus*) SST3 (ENSLOCT00000011545.1)

MLSYRVHCTLALFGLVLAFCVSAVSHSDLRFRRFLQKAKAAGLNKQDSSKYAIEDLISQL
VQSDSEALENEMSVDENSARLELERSTEIGKEIPPRERKAGCRNFYWKTFTSC

Cartilaginous fish

>Elephant shark (*C. milii*) SSTe (XP_007910587.1)

MQARCTLTALLSLAALGLSALPTHLRDQLVLQGSPAMELRDGVVRELIQAVADAESKPQS
EEAAEDFAPDEKAELRLALAPRWRKDCKNFFWKTYTLC

>Whale shark (partial) (*R. typus*) SSTe (XP_020365363.1)

DFLKDTIQLLHVADADKDAVEVNASQVETPPXNKIPMKFQQRQLGTRMRKNCKNFFWK
TYTLC

>Catshark (*S. canicula*) SSTe (MK491630)

MWCSRQLQLSALLSIALAVLSVSSAPTDNRHREILQRALDQELLKDTMMKLLPLVTDVDTE
AGTLDVSNATSEENTTPMKFQHRQLGMRMRKNCKNFFWKTYTLC

Somatostatin 4

Euteleosts

>Stickleback (*G. aculeatus*) SST4 (KT235754)

MAHILCVFALLCFAFCAAQDGETQRGFKDNRLQRDSLWLDKLQDEQDSTKKLNLIIEWLYS
FYKFDNGNIVKGPTDAEEPEKNRRGLGKTTTFFGCRVFFWKSWS

>Medaka (*O. latipes*) SST4 (KT235752)

MANVLCVLAFLCFAVCVVQNTEIMVESEDLPAGQGLLSSFDRISDFQQSVETGILMNLLYKL
SRPDSAITLEQQVRDSEKQEKNRRGVEIATQRPCRVFYWKSWS

>Atlantic salmon (*S. salar*) SST4 (CA039604.1)

MALTGIWCAFVLVCVTLQMGMKVDSFVNEDKPTWLETLQDKQVSAADDKYNLVWLLYKL
SQSHHDNTFKINFPPHPGPESVGKPESRRETIPQDSVRKEGCKVFFWKSWTAC

>Takifugu (*T. rubripes*) SST4 (NC_018911.1)

MARALCILVLLCFAPCCAENSKTEHRFNDLQVQEDLLSWLPQEKWEPSKRQTLEDLLYKL
TNYKSENRLPQQPGDTENQEKNRRLDNLRVQQRQFGCRMFFWKSWTAC

>Tetraodon (*T. nigroviridis*) SST4 (KT235753)

MARALCFLVLLCFASRCAGNSKTEHRLKDLQVEEDVLPWLNSQEKEPSKGQNLEDLLYKL
LTNYRSENRIVSQQPSDTNQEKNRRGLDNLKVQQRQAGCRIFFWKSWTAC

Other teleosts

>Zebrafish (*D. rerio*) SST4 (NP_571802.1)

MASSQLHTATLLCLAMMAGIICGRSHMILLNSALQASRGTSADEEIPERYSLSELEWLLSNS
DPAVFQPDSSLGSLHSGLELMRRDTKEERKTGCKNYFWKSRTAC

>Channel catfish (*I. punctatus*) SST4 (P01172.1)

MSSSPLRLALALMCLVSAVGVISCRPHVVLNSALEEARNVPFGEVPERLTLPELQWMLS
NNELTPVQVEEAPRSRLELVRRDNTVTSKPLNCMNYFWKSRTAC

Other ray-finned fish

>Spotted gar (*L. oculatus*) SST4 (ENSLOCT00000011651.1)

MLSYRVHCTLALFGLVFAFCVSAVNSDLRFRRFLQKAKAASLSTRDSSKYALEDLISQIA
QSDNEALENEMSVDENSARLELERSADMGKVIPPRERKAGCRNYYWKTITSC

Somatostatin 5

Lobe-finned fish

>Coelacanth (*L. chalumnae*) SST5 (XP_005999859.1)

MMCSHVQSLLAVLSASLLLGVGGLPKGEVLTDLFQGQGAEGKEDFSRMLMLKMVSNLL
KSENDVLVPSAEDTASQDELTRRLAPSRRERKAGCKNFFWKTFTSC

Euteleosts

>Stickleback (*G. aculeatus*) SST5 (ALD51533.1)

MQVLLVALFSSVLLVQVSGAPRGDMPTQRGDPADNKDLAYSMLKFVSELTAARGGETLL
VPEQEEEAEGGRQEVMRRLPLTQRERKAGCRNFFWKTFTSC

>Rainbow trout (*O. mykiss*) SST5 (BX909872.3)

MLCSQLQVLLVALSASVFLARVSAAPHRDMAELLRADSTKGNEDELSRTLLLKMMSDLMS
AAVGENEVLPDLEEALGVREEVRQLPLSHRERKAGCRNFFWKTFTSC

>Sockeyess (*Oncorhynchus nerka*) SST5 (EV380196.1)

MLCSQLQVLLVALSASVFLARVSAAPHRDMAELLRADTTKGNEDELSRTLLLKMMSDLMS
TAVGENEVLPDLEEALGVREEVVRQLPLSHRERKAGCRNFFWKTFTSC

>Tilapia (*O. niloticus*) SST5 (XP_005464163.1)

MLRSQVLLVALGLSVLLRVSTAPYSDMLTETLRADLTNDKDLTHWLLLKFMAELMAARG
DETRRGREEVTRRHLSLSQRERKAGCRNFFWKTFTSC

>Medaka (*O. latipes*) SST5 (XP_020567335.1)

MLLAALGLSLLMACVSGAPQRNPLTHTKQLQLLKSEVDPTRLLLKLVLELVALRRQEML
QELEEEELGGGRERLMKRHIRFTQRERKAGCRNFFWKTFTSC

>Amazon molly (*P. formosa*) SST5 (XP_007551472.1)

MLCSQMVKVLVALCSSMLALHVSSAPQMDELTELQAEELISDKDLTGLLLRFMSELMASR
GEEMLREKQEEEEELGGGRQRLMRRHIRFSHRERKAGCRNFFWKTFTSC

>Takifugu (*T. rubripes*) SST5 (N.D.)

MLSQVQLLVTFSFSSMALLMEVSSAPRKHMPSLELPADPLKDSDLAILILLRIISEVMAAEREM
LLLPQEGEREAGVREGEVMMRQVPFSQRDRKAGCRNFFWKTFTSC

>Tetraodon (*T. nigroviridis*) SST5 (ALD51532.1)

MTRSQLLAASFSSLMEAGGTPRKHKFLPADSVKDSDLALVTSLKFAFEGTAAQREMLL
LLQEDEEDAGVREMMMMRQIPFSQRERKAGCRNFFWKSYTSC

>Platyfish (*X. maculatus*) SST5 (XP_005804860.3)

MLCSQMVKVVVALCSSMLALHVSSAPQMDELTELQAEELISDKDLTGLLLRLMSELTASR
GEEMLREQEEEEDELGGGRQRLMRRHIRFTHRERKAGCRNFFWKTFTSC

Other teleosts

> Mexican tetra (*A. mexicanum*) SST5 (XP_007243346.1)

MCSQLQVVLVALSVLVLVSRAAPRGDVLTQLLQNEADTKENEDISRMLMLKLLSELEVA
GENEVLSGADVRNDVVRQLPFSQRERKAGCRNFFWKTFTSC

>Zebrafish (*D. rerio*) SST5 (XP_001333082.1)

MFSRLQVVVTLWVSLLCRVSSAPRGDLLFQLRSQVDPKENELQDLSRLLLKQLSESVT
PEEKDALDSIDEELDVRNEVVRQIPVSQRERKAGCRNFYWKTFTSC

> Channel catfish (*I. punctatus*) SST5 (XP_017327476.1)

MSSQMIVVLAWSLLVLSRVTAAPRTDLLAHMLQNEADGKEDLSRILLKLISELKIPDEN
DTLSDDDMELNRILRHLPLTTRERKAGCRNFFWKTFTSC

>Fathead minnow (*P. promelas*) SST5 (DT105503.1)

MFSPLQMVVATLSLSSLLCSVSSAPGGDMLIQLLRSEVEPKEIELQDFRLLLKQLSESAAP
EEKQPRESIDDDPEVHNEVVRQIPLSHRERKAGCRNFYWKTFTSC

> Red-bellied piranha (*P. nattereri*) SST5 (XP_017578562.1)

MNFEVKSSLLSRAAGRSASTPVIQTFFEFYFKSICLLNHLITRVSAAPRGDILAQLQADPKG
NEELSRMLILKLLSDLEIPGDNEVLSGTDVRSDMVRQLFPQRERKAGCRNFFWKTFTSC

Other ray-finned fish

>Spotted gar (*L. oculatus*) SST5 (XP_006627411.2)

MSTGQPSLPPAPAPNQGFQQHKLQVLLVALSVSLLARVSGVPQRDRLADLLRAEVPEGKE
DLSRMLLKIFSDLLRAENEIPPGSAEDAGIRSDVPRQLPLAQRERKAGCRNFFWKTFTSC

Cartilaginous fish

>Catshark (*S. canicula*) SSTb (JX964751)

MPRSQTQVLLTVALLLRGSSTARVQGLPDILQERNDEGTEELSRTMVLNLLSELLHAG
DKGLPSTERRGLPQAEIVRRWNSPRDRKAGCKNFFWKTFTSC

Somatostatin 6

Birds

>Duck (*Anas platyrhynchos*) SST6

MQLVASLVSVLLLWWSVRATALPGEERLALQNSREQTKLRKDAILKMLAGLLESVDVASPD
LEEEGKLEERATLGRLAQLSQRDRKAPCKNFFWKTFTSC

>Chicken (*G. gallus*) SST6 (DQ279789)

MQLVASLVSVLLLWWSVRATALPGEERLALQNSREQTKLRRDALLKMLAGLLESSDVASP
DLEEGKLEERAALGRLAQLSQRDRKAPCKNFFWKTFTSC

>Zebra finch (*Taeniopygia guttata*) SST6

MQLVASLASVLLLLWSVRATALPGQEGLQSTREQSTARKDVILKMLAGLLGSVDAGAEVA
FPAGQEKARLEEDQAALGRLAQLSQRDRKAPCKNFFWKTFTSC

Lobe-finned fish

>Coelacanth (*L. chalumnae*) SST6 (XP_005994063.1)

MQLLTSVSVFLLVVWSVRATALPIEKLMSHNNVELTKERKELMLKMIAGLLEGIDSPPMG
GEVGSMMDLEEPVEPKLEERAAFNRLPQLPQRDRKAPCKNFFWKTFTSC

>African lungfish (*P. annectens*) SST6 (Q9W7E9.1)

MQFLASLVSVFLLVVWSVKATALPVEDRLSVHSNRDLTREREEMILKMISGLLDGSDNSLFG
GEVTSMDIEEPLENKLEERAAYNALPQLPQRDRKAPCKNFFWKTFTSC

Euteleosts

>Orange-spotted grouper (*E. coioides*) SST6 (AAU93567.1)

MQLVVLAALMGVLFSVRAAAVLPVEDRSSIHVNRELSKERKELILKLVSGLLDGALDTNM
LPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Atlantic cod (*G. morhua*) SST6

MQLMVVLAAALMGVLFSVRAAALLPVEDRSNFSSRELSKERKELILKLVSGLLEGSPDSNM
LPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Stickleback (*G. aculeatus*) SST6 (ENSGACG00000007077)

MQLVVVLATLMGVLF SVRAAAVLPMEDRSSINVNRELSKERKELILKLVSGLLGAADAN
MLPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Rainbow trout (*O. mykiss*) SST6 (CX153272.1)

MQLLVILASLMGVLYSVRAAAVLPVEERSPLLNR ELSKERKELILKLVSGLLDGATDTNMLP
GEGVSPVDLEEPLESRLEERA AYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Medaka (*O. latipes*) SST6 (BJ885293.1)

MQLVVLAALMGVLFSVRAAAVLPVEDRSSIHVNRELSKERKELILKLVSGLLDGSLDTNM
LPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Rainbow smelt (*Osmerus mordax*) SST6 (EL519905.1)

MQLVVLAALMGVLYSARA AAVLPVEERSPIQANRELSTERKQLILKLVSGLLDGASDSNM
LPGDVSPLDLEEPLESRLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Amazon molly (*P. formosa*) SST6

MQLVVLAALMGVLFSVRAAAVLPLEDRSPIHANRELSKERKELILKLVSGLLDGALDTNM
LPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Takifugu (*T. rubripes*) SST6 (ENSTRUG00000012370)

MQLVVLAALTGVLLSIRAAA VLPVEERSPVHLNRELSKERKELILKLVSGLLDGALDTNML
PMETVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Tetraodon (*T. nigroviridis*) SST6 (ENSTNIG00000015178)

MQLLVVLAALTGVLLSVRAAAVLPVEERIPLHNLRELSKERKELMLKLVSGLLDGALDTNM
LPMEAVIDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

>Platyfish (*X. maculatus*) SST6

MQLLVVLAALMGVLFSVRAAAVLPLEDRSPIHANRELSKERKELILKLVSGLLDGALDTNM
LPGEAAPVDLEEPLESRLEERA VYNRLSLPQRDRKAPCKNFFWKTFTSC

Other teleosts

> Mexican tetra (*Astyanax mexicanus*) SST6 (ENSAMXT00000013526.1)

MQILASLVSLLVLYSVRAAAVLPVEERSPAHTRELSKERKELILKLVSGLLDGVDSVLGG
DLVPMEAEPEPLESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Goldfish (*C. auratus*) SST6 (AAD09631.1)

MQLLSSLVSLLVLYSVRAAAVLPVEERNPAQSRELSKERKELILKLISGLLDGVDSVLGD
EIAPVPFDAEPEPLESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

> Atlantic herring (*Clupea harengus*) SST6 (XP_012681579.1)

MQLLASLVSLMLVLYSIRAAA VLPVDERSPAHA RELSKERKELILKLVSGLDGVESNMLPG
DEAPLDLEEPLESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Grass carp (*C. idella*) SST6 (ACB69425.1)

MQLLASLVSLLVLYSVRAAAVLPVEERNLAQSRELSKERKELILKLISGLLDGVDNVLAG
EIAPVPLDVEEPELESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Zebrafish (*D. rerio*) SST6 (BG307388)

MQLLASLVSLLVLYSVRAAAVLPLEERNPAQSRELSKERKELILKLISGLLDGVDSVLAG
EIAPVPLDVEEPELESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

> Channel catfish (*I. punctatus*) SST6

MQLLASLVSLLVLYSVRAAVVLPAAERSPAHTREPSKERKEMILKMVSSLLDGVDNNMLA
GDLLPLEEEEPIDSRLLEERA VYNRLAQLPQRDRKAPCKNFFWKTFTSC

>Fathead minnow (*P. promelas*) SST6 (DT250237.1)

MQLLASLVSLMLVLYSVRAAALLPVEERNLAQSRELSKDRKELILKLISGLLDGVDSVLAG
EIAQVPMDAEPEPLESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

Other ray-finned fish

>White sturgeon (*A. transmontanus*) SST6 (AAL13249.1)

MQLRARLVSMLVVYSLRVVA VLPGEERLSVHSNRELSKERKEGFLKLLSGLLDRVDSSVV
LGEDVSPMDLEEPLDSRLEERA IYNRLSQLPLRARKAPCKNFFWKTFTSC

>Chinese sturgeon (*A. sinensis*) SST6 (FJ792688.1)

MQLRASLVSLMLVVYSLRVVA VLPGEERLSVHSNRELSKERKEGFLKLLSGLLDGVDSSVV
LGEDVSPMDLEEPLDSRLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

>Spotted gar (*L. oculatus*) SST6 (XP_006642047.1)

MQLLASLASLMLVVY SVRAAAVLPGEERATLHTKELS KDRKELILKLISGLLDGADSMLA
GDVASVDLEEPLESRLLEERA VYNRLSQLPQRDRKAPCKNFFWKTFTSC

Cartilaginous fish

>Elephant shark (*C. milii*) SSTc (XP_007895974.1)

MQILVALISTLFLVSGVSTTTASLDDRFNLQSSREMNRQERKEMILKLLSGLLDNAAVSGQTG
SEAGYPEPADGGPVMLEERSRYSQLPQRERKTSCKNFFWKTFTSC

>Whale shark (*R. typus*) SSTc (XP_020368528.1)

MQLLGSASXVSILLIVSSVKATAPLEDRLSLRANQELNKERKEVVLKLLSALLDSSSNQMGIE
NTFPDQEDMEEMKVVEDRSRFSQLPQRERKTSCKNFFWKTFTSC

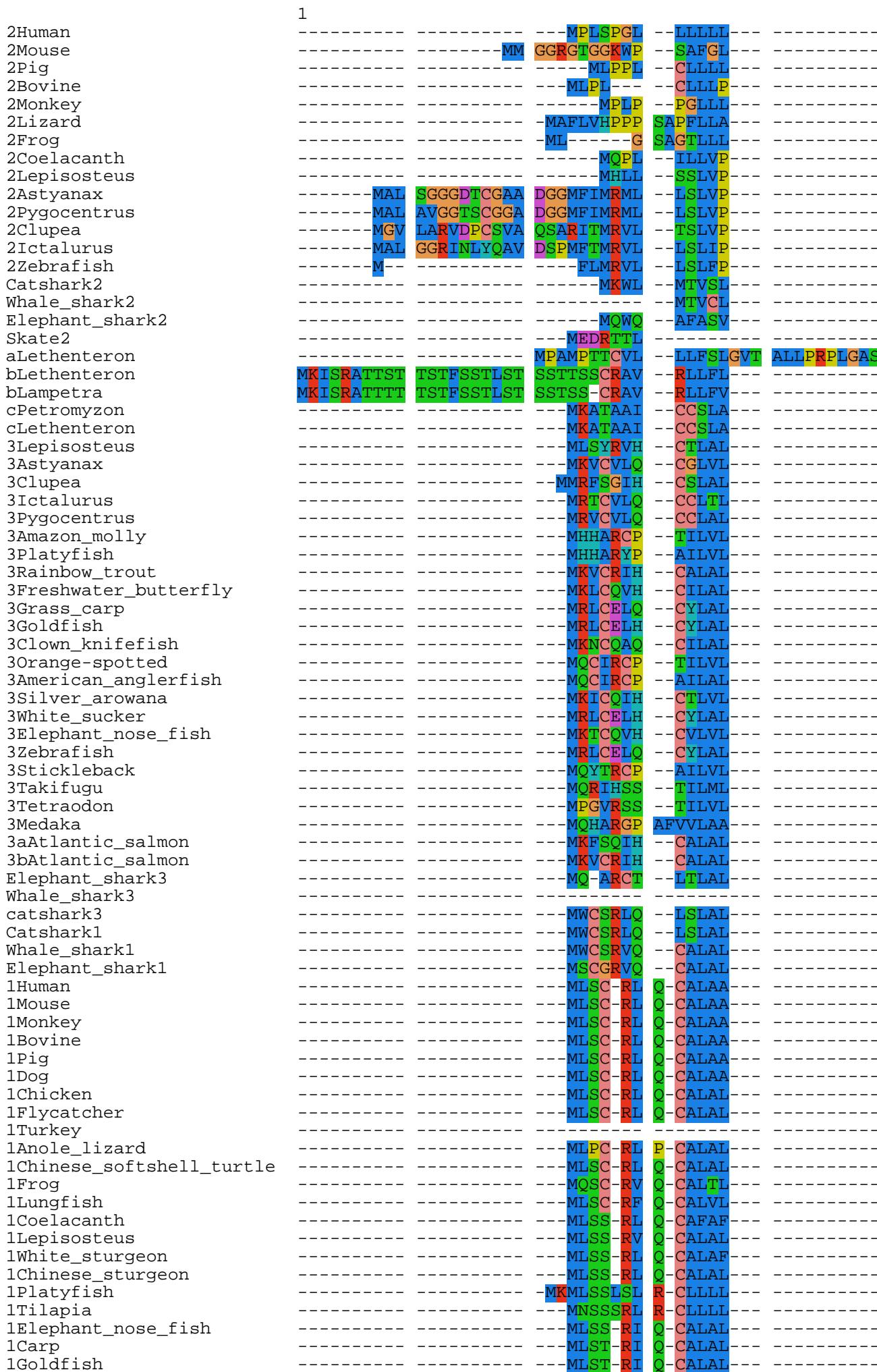
> Catshark (*S. canicula*) SSTc (JX964752) = SST6

MQLLGTASLLSMLLIVSSVRATAPLEDRLSLRANQELNKERKEVILKLLSGLLDSSSNQIAIE
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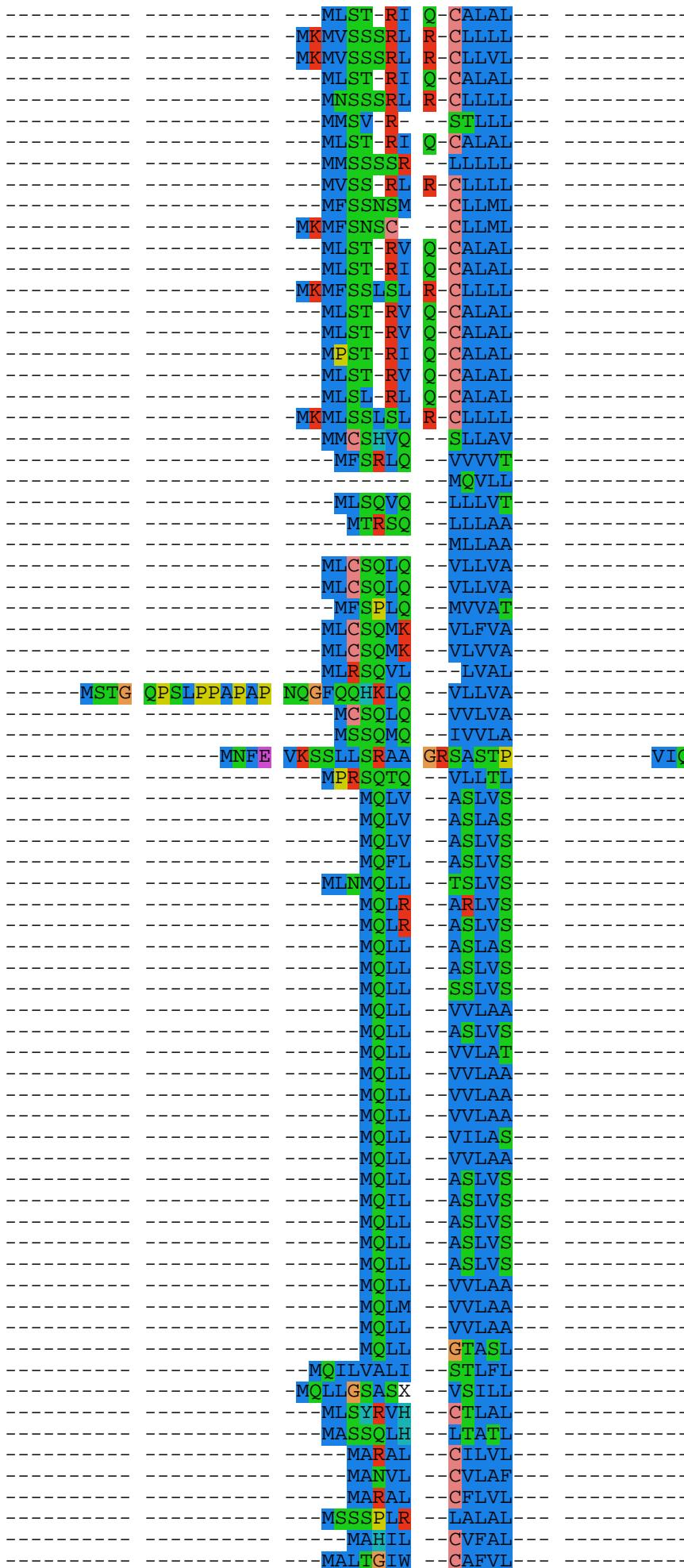
Other somatostatins

Lampreys

>Japanese lamprey (*Lethenteron japonicum*) SSTa (KU522234)
MPAMPTTCVLLLFSLGVTALLPRPLGASPFRPAEGSSLAGLGAWALGPGAGXGGAGLIID
RLQQRVEAVLTQELSREERALVGRLLAELAAGGAGLGGALPPLGWGPSSSDEEGGEEGEG
AGGDGGRGERALSARVRKAGCKNFFWKTFTSC
>River lamprey (*Lampetra fluviatilis*) SSTb (KX345282)
MKISRATTTTSTFSSTLSTSSTSSCRAVRLFVLPMLSVVLGSVTADVRPLHVRMALERVM
DGPBMENLDQDQKQFLVRLLAAIDSSADETNELNHSED GSLPEVLVARALAAAAPGAAG
GAQLPLGNRERKAGCKNFFWKTFTSSC
>Japanese lamprey (*Lethenteron japonicum*) SSTb (KU522235)
MKISRATTSTFSSTLSTSSTSSCRAVRLFLLSVLSVVLGSVTADVRPLHARMALERVM
DGLGMENLDQDQKFLVRLLAAIDSSADETNELNHSED GSLPEALVARALAAAAPGAAG
GAQLPLGNRERKAGCKNFFWKTFTSSC
>Japanese lamprey (*Lethenteron japonicum*) SSTc (KU522236)
MKATAAACSLALVLVATGGRRGGGLHAASIGRSAILRAPASYRQLEAHPDLMQGDQDDSQ
MLLN MIVEAMRMRDAGPETDGPGEGEAARVVDGLPEFPREEVRALGPNERPFVPGALSPRDRK
RKANCRMFYWKTMAAC
>Sea lamprey (*Petromyzon marinus*) SSTc (KU529940)
MKATAAACSLALVLVASGGRRSGLHAASIGRSAILRAPASFRQLEAHPDLMQGDQDDSQL
LN MIVEAMRMRDAGPETDGPGEGEATRVVDGLPEFPREEARALVPNERPFVPGALSPRDRK
ANC CRMFYWKTMAAC



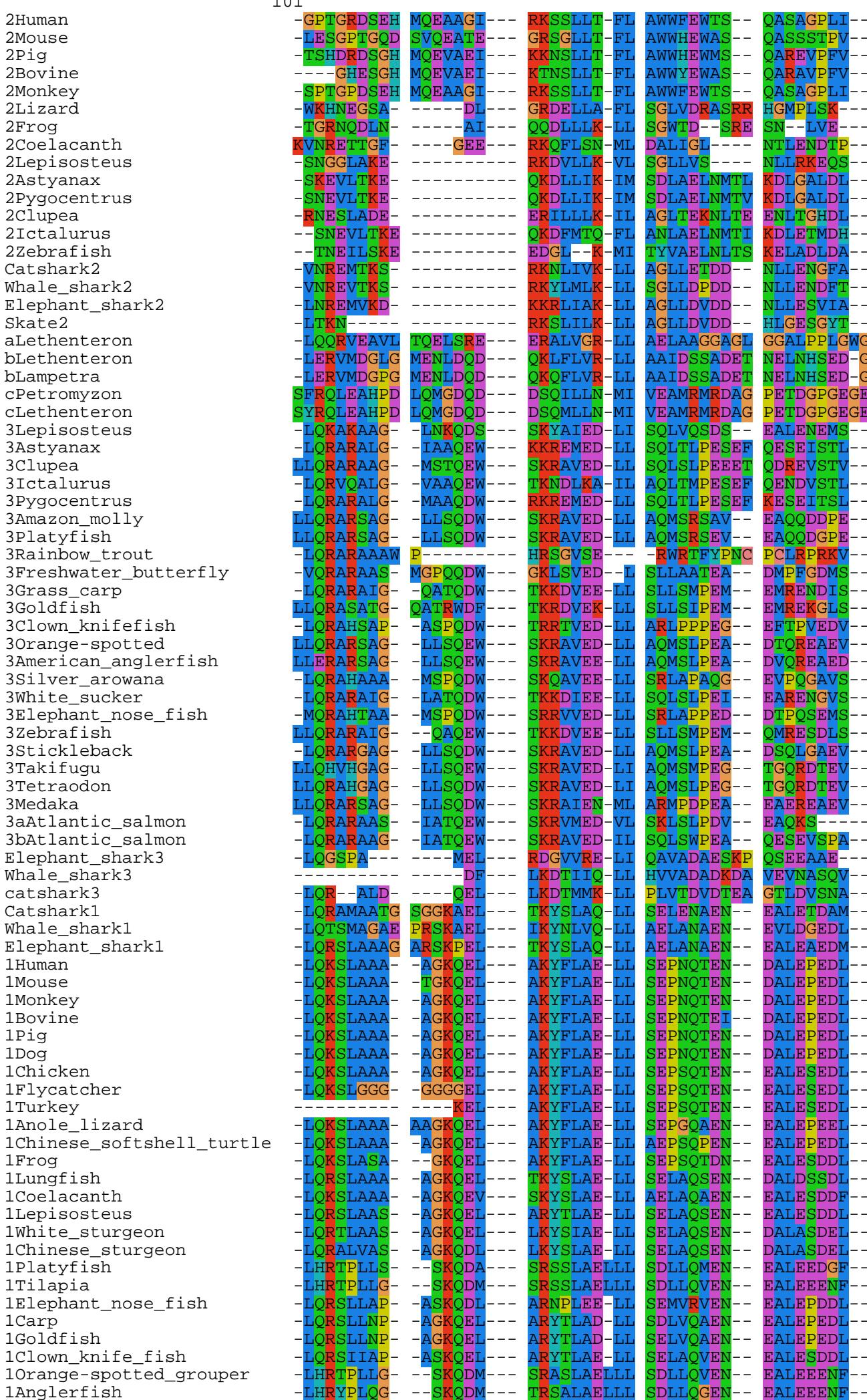
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 1Medaka
 1Stickleback
 1Takifugu
 1Tetraodon
 1Trout
 1Fathead_minnow
 1Killifish
 1Salmon
 1Pygocentrus
 1Ictalurus
 1Astyanax
 1Clupea
 1Amazon_molly
 5Coelacanth
 5Zebrafish
 5Stickleback
 5Takifugu
 5Tetraodon
 5Medaka
 5Sockeyess
 5Trout
 5Fathead_minnow
 5Amazon_molly
 5Platyfish
 5Tilapia
 5Lepisosteus
 5Astyanax
 5Ictalurus
 5Pygocentrus
 Catshark5
 6Chicken
 6Zebra Finch
 6Duck
 6Lungfish
 6Coelacanth
 6White_sturgeon
 6Chinese_sturgeon
 6Lepisosteus
 6Carp
 6Goldfish
 6Orange-spotted_grouper
 6Zebrafish
 6Stickleback
 6Takifugu
 6Tetraodon
 6Rainbow_smelt
 6Trout
 6Medaka
 6Fathead_minnow
 6Astyanax
 6Pygocentrus
 6Clupea
 6Ictalurus
 6Amazon_molly
 6Cod
 6Platyfish
 Catshark6
 Elephant_shark6
 whale_shark6
 4Lepisosteus
 4Zebrafish
 4Takifugu
 4Medaka
 4Tetraodon
 4Channel_catfish
 4Stickleback
 4Atlantic



2Human
 2Mouse
 2Pig
 2Bovine
 2Monkey
 2Lizard
 2Frog
 2Coelacanth
 2Lepisosteus
 2Astyanax
 2Pygocentrus
 2Clupea
 2Ictalurus
 2Zebrafish
 Catshark2
 Whale_shark2
 Elephant_shark2
 Skate2
 aLethenteron
 bLethenteron
 bLampetra
 cPetromyzon
 cLethenteron
 3Lepisosteus
 3Astyanax
 3Clupea
 3Ictalurus
 3Pygocentrus
 3Amazon_molly
 3Platyfish
 3Rainbow_trout
 3Freshwater_butterfly
 3Grass_carp
 3Goldfish
 3Clown_knifefish
 3Orange-spotted
 3American_anglerfish
 3Silver_arowana
 3White_sucker
 3Elephant_nose_fish
 3Zebrafish
 3Stickleback
 3Takifugu
 3Tetraodon
 3Medaka
 3aAtlantic_salmon
 3bAtlantic_salmon
 Elephant_shark3
 Whale_shark3
 catshark3
 Catshark1
 Whale_shark1
 Elephant_shark1
 1Human
 1Mouse
 1Monkey
 1Bovine
 1Pig
 1Dog
 1Chicken
 1Flycatcher
 1Turkey
 1Anole_lizard
 1Chinese_softshell_turtle
 1Frog
 1Lungfish
 1Coelacanth
 1Lepisosteus
 1White_sturgeon
 1Chinese_sturgeon
 1Platyfish
 1Tilapia
 1Elephant_nose_fish
 1Carp
 1Goldfish
 1Clown_knife_fish
 1Orange-spotted_grouper
 1Anglerfish



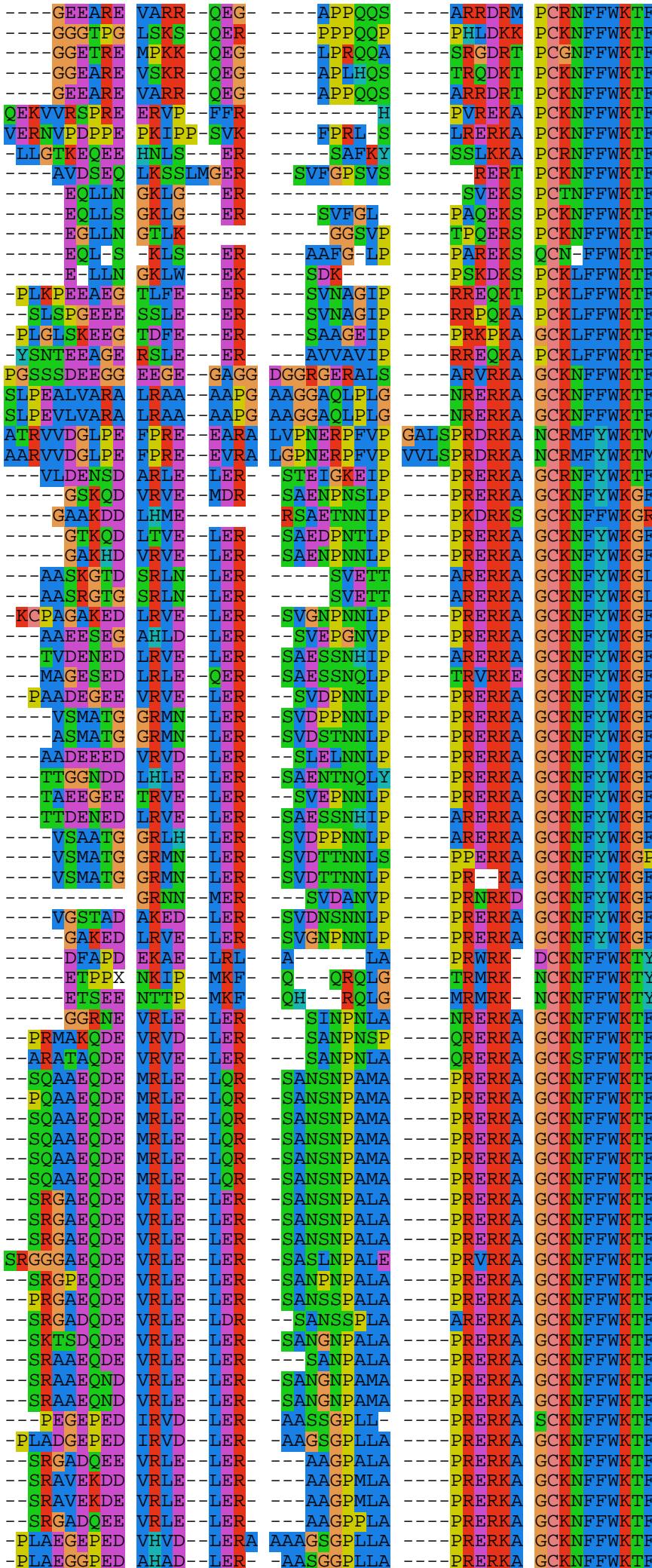
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1African_cichlid_fish
1Cod
1Zebrafish
1Medaka
1Stickleback
1Takifugu
1Tetraodon
1Trout
1Fathead_minnow
1Killifish
1Salmon
1Pygocentrus
1Ictalurus
1Astyanax
1Clupea
1Amazon_molly
5Coelacanth
5Zebrafish
5Stickleback
5Takifugu
5Tetraodon
5Medaka
5Sockeyess
5Trout
5Fathead_minnow
5Amazon_molly
5Platyfish
5Tilapia
5Lepisosteus
5Astyanax
5Ictalurus
5Pygocentrus
Catshark5
6Chicken
6Zebra Finch
6Duck
6Lungfish
6Coelacanth
6White_sturgeon
6Chinese_sturgeon
6Lepisosteus
6Carp
6Goldfish
6Orange-spotted_grouper
6Zebrafish
6Stickleback
6Takifugu
6Tetraodon
6Rainbow_smelt
6Trout
6Medaka
6Fathead_minnow
6Astyanax
6Pygocentrus
6Clupea
6Ictalurus
6Amazon_molly
6Cod
6Platyfish
Catshark6
Elephant_shark6
whale_shark6
4Lepisosteus
4Zebrafish
4Takifugu
4Medaka
4Tetraodon
4Channel_catfish
4Stickleback
4Atlantic



1Megalobrama
 1African_cichlid_fish
 1Cod
 1Zebrafish
 1Medaka
 1Stickleback
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 1Trout
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 1Pygocentrus
 1Ictalurus
 1Astyanax
 1Clupea
 1Amazon_molly
 5Coelacanth
 5Zebrafish
 5Stickleback
 5Takifugu
 5Tetraodon
 5Medaka
 5Sockeyess
 5Trout
 5Fathead_minnow
 5Amazon_molly
 5Platyfish
 5Tilapia
 5Lepisosteus
 5Astyanax
 5Ictalurus
 5Pygocentrus
 Catshark5
 6Chicken
 6Zebra Finch
 6Duck
 6Lungfish
 6Coelacanth
 6White_sturgeon
 6Chinese_sturgeon
 6Lepisosteus
 6Carp
 6Goldfish
 6Orange-spotted_grouper
 6Zebrafish
 6Stickleback
 6Takifugu
 6Tetraodon
 6Rainbow_smelt
 6Trout
 6Medaka
 6Fathead_minnow
 6Astyanax
 6Pygocentrus
 6Clupea
 6Ictalurus
 6Amazon_molly
 6Cod
 6Platyfish
 Catshark6
 Elephant_shark6
 whale_shark6
 4Lepisosteus
 4Zebrafish
 4Takifugu
 4Medaka
 4Tetraodon
 4Channel_catfish
 4Stickleback
 4Atlantic

-LQRSLNP-	-AGKQEL-	-ARYTLTD-	-LL	-SDLVQAEN-	-EVLEPEDL-
-LHRTPLLG-	-SKQDM-	-SRSSLAEL-	-LL	-SDLLQVEN-	-EALEEENF-
-LQRSLAP-	-MPGQEET-	-VRYTLAQ-	-LL	-SELAQAEN-	-EALGTDDQ-
-LQRSLSP-	-AGKQEL-	-ARYTLAD-	-LL	-SDLVQAEN-	-EALEPEDL-
-LQRTPLLG-	-SKQDM-	-SRSSLVELL-	-LL	-SDLLQVEN-	-EVLEEDGF-
-LQSNALMG-	-NKQEM-	-TRSSLANLLL-	-	-SDLLQVGN-	-EALEENLA-
-LPPNPLLG-	-HRQEM-	-SRSSLADLLL-	-	-SDLLQVEN-	-QALDENFP-
-LQRSLMAP-	-AGKQEL-	-ARNTLVE-	-LL	-SELAHVEN-	-EAIELDDM-
-LQRSLNP-	-AGKQEL-	-ARYTLAD-	-LL	-SELVQAEN-	-EALEPEDL-
-LHRTPLLS-	-SQQDV-	-SRSSLAELLL-	-	-SDLLQMEN-	-EALEEDGF-
-LQRSLMAP-	-AGKQEL-	-ARYTLAE-	-LL	-SELAQAEN-	-EAIEESDDL-
-LQRSLIGP-	-SGKQEL-	-ARYTLAE-	-LL	-SELAQAEN-	-EALEEAEDM-
-LQRSLILAP-	-SVKQEL-	-TRYTLAE-	-LL	-AELAQAE-	-EVLDSDDEV-
-LQRSLIGS-	-AGKQEL-	-ARYTLAE-	-LL	-SELAQAEN-	-EALEDDDPV-
-LQRSLFAP-	-GGKQEL-	-ARLTAAE-	-LL	-SELAQAEN-	-EALESEDMD-
-LHRTPLLS-	-SKQDA-	-SRSSLAELLL-	-	-SDLLQVGN-	-EALEEDGF-
-FQGQGAEG-	-KEDE-	-SRMLMLK-	-MV	-SNLLKSEN-	-DVLVPSAE-
QLLRSQVDPK-	ENELQDD-	SRLLLK-	QL	SESVTPEEK-	DALDSIDE-
-MPTQORGDP-	-ADNKDL-	-AYSMMLK-	FV	SELTAAARGGE-	TLLVPEQE-
-MPSELLPAD-	PLKDKDL-	AILILLR-	II	SEVMAAER-	EMLLLIPQE-
--KFLIPAD-	SVKDKDL-	ALVTSLK-	FA	FEGTAAQR-	EMLLLLIQE-
-LTHTKQLQL-	LKSEVDP-	TRLLLMK-	LV	LELVALRR-	QEMIQLQEL-
-LRADFTTKG-	-NEDL-	SRTLLLK-	MM	SDLMSTAVGE-	NEVLPDLE-
-LRADSTKG-	-NEDL-	SRTLLLK-	MM	SDLMSAAVGE-	NEVLPDLE-
-LLRSEVEPK-	EIELQDF-	FRLLLLK-	QL	SESAAPE-	EKQPRESI-
-LTETLQAE-	LISDKDL-	TGLLLLR-	FM	SELMASRG-	EEMLREKQ-
-LTETLQAE-	LISDKDL-	TGLLLLR-	LM	SELTASRGE-	MLREQEEE-
-LRADLTND-	-KDL-	THWLLLK-	FM	AELMAAR-	-
-LRAEVPEG-	-KEDL-	SRMILLK-	IF	SDLLRAEN-	-EIPPG-
-LQNEADTK-	-ENEDI-	SRMLMLK-	LL	SELEVAGEN-	EVLSGADV-
-LLAHMLQNE-	ADGKEDL-	SRILLK-	LI	SELKIPDEN-	DTLSDDDM-
--QAD-	PKGNEEL-	SRMLILK-	LL	SDLEIPGD-N	EVLSGTIDV-
-LQERNDEG-	-TEEL-	SRTMVNL-	LL	SELLHAGD-	-
-NSREQTKL-	-	RRDALLK-	ML	AGLLESSD-	-VASPDL-
-LQSTREQS-	-TA-	RKDVLK-	ML	AGLLGSVD-	AGAEVAFP-
-NSREQTKL-	-	RKDAILK-	ML	AGLLESVD-	-VASPDL-
-SNRDLTRE-	-	REEMILK-	MI	SGLLDGSD-	NSLFGGGEV-
-SHNNVELT-	-KE-	RKELMLK-	MI	AGLLEGID-	SPPMGGEV-
-SNRELSKE-	-	RKEGFLK-	LL	SGLLDREVDS-	SVVLGEDV-
-SNRELSKE-	-	RKEGFLK-	LL	SGLLDGVD-	SVVLGEDV-
--TKELSKD-	-	RKELILK-	LI	SGLLDGAD-	SAMLAGDV-
-SRELSKE-	-	RKELILK-	LI	SGLLDGVD-	NNVLAGEIAP
--SRELSKE-	-	RKELILK-	LI	SGLLDGVD-	NSVLGEIAP
-VNRELSKE-	-	RKELILK-	LV	SGLLDGALDT-	NMLPGEAA-
--SRELSKE-	-	RKELILK-	LI	SGLLDGVD-	NSVLAGEIAP
-VNRELSKE-	-	RKELILK-	LV	SGLLDGVD-	NMLPGEAA-
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-ANRELSTE-	-	RKOLIK-	LV	SGLLDGASDS-	NMLPGDVS-
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-VNRELSKE-	-	RKELILK-	LV	SGLLDGSLDT-	NMLPGEAA-
-LAQSRELS-	-KD-	RKELILK-	LI	SGLLDGVD-	NSVLAGEIAQ
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-SSRELSKE-	-	RKELILK-	LV	SGLLEGSPDS-	NMLPGELS-
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-SSREMNQE-	-	RKEMILK-	LL	SGLLDNAAVS-	GQTGSEAG-
-ANQELNKE-	-	RKEVVLK-	LL	SALLDSSS-	NQMGIENT-
-LQAKAAS-	-LSTRDS-	SKYALED-	LI	SQIAQSDN-	EALENEMS-
-LNSALQASR-	GTSADEEIP-	ERYSLSE-	LL	EWLLSNSD-	PAVFQPDSSS
-QVQEDLLSW-	IKPQEKWEPS-	KRQTLLED-	LL	YKLTNYKSEN-	RILPQQPG-
GLLSSFDRI-	SDFQQSV-	ETGILMN-	LL	YKLSRPDSAI-	TLQQVRDS-
-QVEEDVLPW-	LNSQEKEWPS-	KGQNLED-	LL	YKLTNYRSEN-	RIVSQQPS-
ALEEARNVP-	-FGEVEP-	ERLTLPE-	LL	QWMLSN-	NELTPOVQ-
-LQRDSLWPL-	DKLODECDST-	KKLNLIE-	WL	YSFYKFDFNG-	NIVKGPID-
TLQDKQVSA-	-AD-	DKYNLVW-	LL	YKLSQSHHD-	NTFKINFPFH

2Human
 2Mouse
 2Pig
 2Bovine
 2Monkey
 2Lizard
 2Frog
 2Coelacanth
 2Lepisosteus
 2Astyanax
 2Pygocentrus
 2Clupea
 2Ictalurus
 2Zebrafish
 Catshark2
 Whale_shark2
 Elephant_shark2
 Skate2
 aLethenteron
 bLethenteron
 bLampetra
 cPetromyzon
 cLethenteron
 3Lepisosteus
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 3Silver_arowana
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 3aAtlantic_salmon
 3bAtlantic_salmon
 Elephant_shark3
 Whale_shark3
 catshark3
 Catshark1
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 Elephant_shark1
 1Human
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 1Coelacanth
 1Lepisosteus
 1White_sturgeon
 1Chinese_sturgeon
 1Platyfish
 1Tilapia
 1Elephant_nose_fish
 1Carp
 1Goldfish
 1Clown_knife_fish
 1Orange-spotted_grouper
 1Anglerfish



1Megalobrama
 1African_cichlid_fish
 1Cod
 1Zebrafish
 1Medaka
 1Stickleback
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 1Tetraodon
 1Trout
 1Fathead_minnow
 1Killifish
 1Salmon
 1Pygocentrus
 1Ictalurus
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 1Clupea
 1Amazon_molly
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 5Stickleback
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 5Medaka
 5Sockeyess
 5Trout
 5Fathead_minnow
 5Amazon_molly
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 5Astyanax
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 5Pygocentrus
 Catshark5
 6Chicken
 6Zebra Finch
 6Duck
 6Lungfish
 6Coelacanth
 6White_sturgeon
 6Chinese_sturgeon
 6Lepisosteus
 6Carp
 6Goldfish
 6Orange-spotted_grouper
 6Zebrafish
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 6Tetraodon
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 6Pygocentrus
 6Clupea
 6Ictalurus
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 Catshark6
 Elephant_shark6
 whale_shark6
 4Lepisosteus
 4Zebrafish
 4Takifugu
 4Medaka
 4Tetraodon
 4Channel_catfish
 4Stickleback
 4Atlantic

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-PLADGEPE	IRVD	-LER-	-AGSGPLLA	--PRERKA	GCKNFFWKT
--DD	ERMD	-LER-	--AAGPMMA	--PRERKA	GCKNFFWKT
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-PLSDGEPE	VRVD	-LER-	AAAASGPLLA	--PRDRKA	GCKNFFWKT
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--LVEGEPEE	VHVD	-MERA	ADAGIGPFLT	--PRERKA	GCKNFFWKT
--SHGVEQED	VDLE	-LER-	--APGPVLA	--PRERKA	GCKNFFWKT
--SRAVEKDD	VRLE	-LER-	--AAGPMLA	--PRERKA	GCKNFFWKT
-TLPGEPEPED	IRVD	-LER-	-AASSGPLLA	--PRERKA	GCKNFFWKT
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-GLEGEPEPED	IRVD	-LER-	AASSGPLLA	--PRERKA	GCKNFFWKT
--DTASQDE	LTRR	-LAP-		--SRERKA	GCKNFFWKT
--LD	VRNE	--VV	-QIPVS	--QERKA	GCRNFYWK
--EEEAEQ	GROE	--VMR	RHLPLT	--QERKA	GCRNFFWKT
--GEEEAQ	VREGEVMMR		ROVPFS	--QRDRKA	GCRNFFWKT
--DEEDAG	VREMMMMMR		ROIPFS	--QERKA	GCRNFWKSY
--EEELG	GRER	-LMK-	RHIFT	--QERKA	GCRNFFWKT
--EALG	VREE	-VVR-	QLPLS	--HRERKA	GCRNFFWKT
--EALG	VREE	-VVR-	VRQLPLS	--HRERKA	GCRNFFWKT
--DDDPE	VHNE	-VVR-	QIPLS	--HRERKT	GCRNFYWK
--EEEEELG	GRQR	-LMR-	RHIFES	--HRERKA	GCRNFFWKT
--EEDELG	GRQR	-LMR-	RHIFT	--HRERKA	GCRNFFWKT
--GDETRR	GREE	-VTR-	RHLSLS	--QERKA	GCRNFFWKT
--SAEDAG	IRSD	-VPR-	QLPLA	--QERKA	GCRNFFWKT
--RND	VND	-VVR-	QLPFS	--QERKT	GCRNFFWKT
--E	LNR	-ILR	RHLPLT	--TRERKA	GCRNFFWKT
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--KGLPST	ERRG	-LPQ-	AEIVRRWNS	--PRDRKA	GCKNFFWKT
--EEE	GKLE	-EER-	AALGRLAQSL	--QRDRKA	PCKNFFWKT
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GSMDLEEPVE	PKLE	--ER	AAFNRLPOLP	--QRDRKA	PCKNFFWKT
SPMDLEEPPLD	SRLE	--ER	AIYNRLSQLP	--LRARKA	PCKNFFWKT
SPMDLEEPPLD	SRLE	--ER	AVYNRLSQLP	--QRARKA	PCKNFFWKT
ASVDLEEPLE	SRLE	--ER	AVYNRLSQLP	--QRDRKA	PCKNFFWKT
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VNMEEVEE	SRLE	--ER	AVYNRLSQLP	--QRDRKA	PCKNFFWKT
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-YPEPADGGP	VMLE	--ER	SRYSQLP	--QRERKA	PCKNFFWKT
-FPDQEDMEE	MKVE	-DR-	SRFSQLP	--QRERKT	SCKNFFWKT
--VLDENSD	ARLE	-LER-	SADMGKV1P	--PRERKA	GCRNYYWKT
LGSLHSGLEL	MRRD		J	--KEERKT	GCKNYFWKS
--DTENQEK	NRRD	-LDN-	LR	--VQQRQE	GCRMFFWKS
--EKQEK	NRRG	-VEI-		--ATQR-	PCRVFYWKS
--DTNQEK	NRRG	-LDN-	LK	--VQQRQA	GCRIFFWKS
--EEAPR	SRLE	-LVRR-	DNTVTSKPLN		-CMNYFWKS
--AEEPEK	NRRG			--KTRRF	GCRVFFWKS
GPESVGKPE	RRET	-IPO-		--SRVRKE	GCKVFFWKS

	201
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2Mouse	SSCK--
2Pig	SSCK--
2Bovine	SSCK--
2Monkey	SSCK--
2Lizard	SSC--
2Frog	TMC--
2Coelacanth	SSC--
2Lepisosteus	SSC--
2Astyanax	SAC--
2Pygocentrus	SACQH
2Clupea	SSC--
2Ictalurus	SSC--
2Zebrafish	SSC--
Catshark2	SHC--
Whale_shark2	SHC--
Elephant_shark2	SHC--
Skate2	SHC--
aLethenteron	TSC--
bLethenteron	SSC--
bLampetra	SSCX-
cPetromyzon	AAC--
cLethenteron	AAC--
3Lepisosteus	TSC--
3Astyanax	TSC--
3Clupea	TSC--
3Ictalurus	TSC--
3Pygocentrus	TSC--
3Amazon_molly	TSC--
3Platyfish	TSC--
3Rainbow_trout	TSC--
3Freshwater_butterfly	TSC--
3Grass_carp	TSC--
3Goldfish	TSC--
3Clown_knifefish	TSC--
3Orange-spotted	TSC--
3American_anglerfish	TSC--
3Silver_arowana	TSC--
3White_sucker	TSC--
3Elephant_nose_fish	TSC--
3Zebrafish	TSC--
3Stickleback	TSC--
3Takifugu	TSC--
3Tetraodon	TSC--
3Medaka	TSC--
3aAtlantic_salmon	TSC--
3bAtlantic_salmon	TSC--
Elephant_shark3	TLC--
Whale_shark3	TLC--
catshark3	TLC--
Catshark1	TSC--
Whale_shark1	TSC--
Elephant_shark1	TSC--
1Human	TSC--
1Mouse	TSC--
1Monkey	TSC--
1Bovine	TSC--
1Pig	TSC--
1Dog	TSC--
1Chicken	TSC--
1Flycatcher	TSC--
1Turkey	TSC--
1Anole_lizard	TSC--
1Chinese_softshell_turtle	TSC--
1Frog	TSC--
1Lungfish	TSC--
1Coelacanth	TSC--
1Lepisosteus	TSC--
1White_sturgeon	TSC--
1Chinese_sturgeon	TSC--
1Platyfish	TSC--
1Tilapia	TSC--
1Elephant_nose_fish	TSC--
1Carp	TSC--
1Goldfish	TSC--
1Clown_knife_fish	TSC--
1Orange-spotted_grouper	TSC--
1Anglerfish	TSC--

1Megalobrama	TSC--
1African_cichlid_fish	TSC--
1Cod	TSC--
1Zebrafish	TSC--
1Medaka	TSC--
1Stickleback	TSC--
1Takifugu	TSC--
1Tetraodon	TSC--
1Trout	TSC--
1Fathead_minnow	TSC--
1Killifish	TSC--
1Salmon	TSC--
1Pygocentrus	TSC--
1Ictalurus	TSC--
1Astyanax	TSC--
1Clupea	TSC--
1Amazon_molly	TSC--
5Coelacanth	TSC--
5Zebrafish	TSC--
5Stickleback	TSC--
5Takifugu	TSC--
5Tetraodon	TSC--
5Medaka	TSC--
5Sockeyess	TSC--
5Trout	TSC--
5Fathead_minnow	TSC--
5Amazon_molly	TSC--
5Platyfish	TSC--
5Tilapia	TSC--
5Lepisosteus	TSC--
5Astyanax	TSC--
5Ictalurus	TSC--
5Pygocentrus	TSC--
Catshark5	TSC--
6Chicken	TSC--
6Zebra Finch	TSC--
6Duck	TSC--
6Lungfish	TSC--
6Coelacanth	TSC--
6White_sturgeon	TSC--
6Chinese_sturgeon	TSC--
6Lepisosteus	TSC--
6Carp	TSC--
6Goldfish	TSC--
6Orange-spotted_grouper	TSC--
6Zebrafish	TSC--
6Stickleback	TSC--
6Takifugu	TSC--
6Tetraodon	TSC--
6Rainbow_smelt	TSC--
6Trout	TSC--
6Medaka	TSC--
6Fathead_minnow	TSC--
6Astyanax	TSC--
6Pygocentrus	TSC--
6Clupea	TSC--
6Ictalurus	TSC--
6Amazon_molly	TSC--
6Cod	TSC--
6Platyfish	TSC--
Catshark6	TSC--
Elephant_shark6	TSC--
whale_shark6	TSC--
4Lepisosteus	TSC--
4Zebrafish	TAC--
4Takifugu	TYC--
4Medaka	AKC--
4Tetraodon	TSC--
4Channel_catfish	TAC--
4Stickleback	SPC--
4Atlantic	TAC--

Figure S3

A. Catshark SST1 (SST_a)

gctgtccacagagccagtgctgaaaccaccgccaattcaaagcgttgtaaa
atgtggtgccgcgccttcagttgagcctggctccatgcgcctggcagtaactg
M W C S R L Q L S L A L L S I A L A V L
agtgtcagctcagcacccacagacaacaggatcgcgaaatcctgcagagagccatggca
S V S S A P T D N R Y R E I L Q R A M A
gccccacaggaaagcgagggaaagcgagttgacgaaatattccctcgcccaactgctctcc
A T G S G G K A E L T K Y S L A Q L L S
gaactggaaaacgcggagaatgaagctctggaaacggatgcaatggcggacgcaacgag
E L E N A E N E A L E T D A M G G R N E
gtgcggctcgaactggagagatcgataaattccaaacctggcgaacaggagcgaaaagcg
V R L E L E R S I N P N L A N R E **R K A**
ggatgtaaagaacttctttggaaaacccatccacatcctgttaactctccgaattctccata
G C K N F F W K T F T S C -
gcaaccccacacactcagaatgtggcattcagataactaaataatcatgtgtgaatgat
tctatttgaattatgtaaagagaagacaattggttgaattgtccatagcaggccagtt
gaatggtgactggatagagtcgctatttcattaatctgttgcataaaaatctctgttt
gaaatttg

B. Catshark SST2 (SST_d)

ttagcattttgtccaggagtgcgcgaagattcagc
atgaagtggctaataatgcacagtggcattcagataactaaataatcatgtgtgaatgat
M K W L M T V S L M S L L Y L L R V E G
actgacctacttggaaagaaagaatgaaacttcaggtaaacagagaaaatgacaaaaaggcagg
T D L L E E R M K L Q V N R E M T K S R
aagaatctgattgtaaagactggctggcttggagactgtgataatcttggag
K N L I V K L L A G L L E T D D N L L E
aatggctttgcacccatggaaaccagaagaggcagaaggacttgcgaagagaggcgc
N G F A P L K P E E A E G T L F E E **R S**
gttaacgcgttgcacccatggaaaccagaagaggcagaaggacttgcgaagagaggcgc
V N A G I P **R R E Q K T P C K L F F W K**
acctttccactgttaataaccgttagcggattttctaaagcagtggagatgatggaaa
T F S H C -
aaaaatgggtgtaaaggcttaacttaaaactatcgaaaatacactgcataatgttt
tctctatccaaatattaattcaaatttacaggaaatgcgcaataaattaacctga
aagttacacccatggaaacatgtgaaattttgtgtttaaatgagatgacatccagg
aaactttctcagttttctatcatgcctgttattccctgtttccagcattgttt
cttctctcagttccgccttgcgttgcgtttagccccctcttccacagaatgct
cctgggattccgtactctccctcgcttaccccttgcgttagacgaaatgttt
ctgaaagatgcacccctgacacagccggctggacttcttgcgttagacgaaatgttt
tgcgcagacacaatttggatatttctgagttaaagcctatataatgttgcacgtgacc
tttccttgcgttagatctgagcatattgttaatgtttgaccaggct
atctgcataacaatgtacatacttatctgcataatcctgtgagtaatgctaaataaa
agaca

C. Catshark SST3 (SST_e)

acatgg
ggagagacagtgcgtgaaacgcgcctccactttccgtcggttccgcctgtgcagag
atgtggtgccgcgccttcagttgagcctggctccatgcgcctggcagtaactg
M W C S R L Q L S L A L L S I A L A V L
agtgtcagctcagccccacagacaacaggatcgcgaaatcctgcagagagccatggat
S V S S A P T D N R H R E I L Q R A L D
caggaacttctgaaggacacaatgtgaaactgttgccttggactgtatgttagacact
Q E L L K D T M M K L L P L V T D V D T
gaggccggaaacactggatgttcaatgcgtgagacttcagaagaaaacacaacccatg
E A G T L D V S N A E T S E E N T T P M
aaattccagcatcgtcagttggaaatgagaatgcggaaaaactgcgaagaacttctttgg
K F Q H R Q L G M **R M R K N C K N F F W**

aaaacctacacttatgctaattccactgtacccagttagcccttcactggaccctgct
K T Y T L C -
gtaccccac

D. Catshark SST5 (SSTb)

tcgaccctcgctccggagcagttacacagagaagctcgctctcgcccacactgccga
cgagacagttgccaatcgccccatctccactccgcagaagaaaatcagagctcgag
atgccgagatcgccagactcaagtccctcactctggcactgtcgctctgttactg
M P R S Q T Q V L L T L V T V A L L L L
cggggatcgagttacaggccagactgcagggctgcccgcataatcttacaggagaggaacgac
R G S S T A R V Q G L P D I L Q E R N D
gaggggactgaggagctgtccaggaccatggctgaacctcctccgcagctgctccat
E G T E E L S R T M V L N L L S E L L H
gctggggacaaggggttgccagcaccgcagagacggagctcccccaggctgagatcgtc
A G D K G L P S T E R R E L P Q A E I V
cgccgggtggaaactcacccggggaccgcaaagcaggctgcaagaacttctttggaaaacc
R R W N S P R D R K A G C K N F F W K T
ttcacctctgttaacgtgcggagagagagagggaaagagaaagtgagccggcgaaaaacc
F T S C -
gagatataaagagaattccctccctccaaaaccatcttcagtcctgaagggaggca
aaaaaaaaatcaattgcctctaacttgttagatttaagattcacaaatcccaaccaccc
gtccctcgaaagattgcctccccccttggctgcctccgcgtgaggattctgtgtc
ttatccaagggtttgtaaatgattgactgtttgtttctgtgactggacttg
ctctcacatcataaaatatcttatttcagcaaaaaaaaaaaaaaaa

E. Catshark SST6 (SSTc)

tcgaccctcgctccggccaagggtcgaggcaca
ttgagaagatctcgccaggctccgcttcattccaaacttcacaagatcgagactgtca
atgcagttgcggaaacggcgaggccctgtccatgcgtcatcggtccaggctgtgagg
M Q L L G T A S L L S M L L I V S S V R
gccacggcaccttggaaagatcggtgagttctgcggcaaatcaggagctgaacaaagaa
A T A P L E D R L S L R A N Q E L N K E
agaaagaggtcatttgaagctgttatccggactgctgactcccgacgcaatcaa
R K E V I L K L L S G L L D S S S N Q I
gcgattgagaacacttccggatccaggatgtggaggatgaaagtggaggagagg
A I E N T F P D P E D V E E M K V E E R
tcccgcttccagccaggtaaccgcagagagagcgcaaggctccctgcaaaaacttctttgg
S R F S Q L P Q R E R K A P C K N F F W
aaaacctcacctctgtgacgacagacaatgccacccggctgccaactaaagccgccc
K T F T S C -
agaaaggaactgathtagactgtacataagctgttttatttattcatctgtgagg
gtgggtggagggtgggggggggttaatatttctgtcgtgcacaagaaaaataaaaagagc
atgattgtgtgatttcaccgcacccgtatgtatttatttcttcccgatataatgttgc
gcgctcaacctgcccaggcaataagtggatcccgagataaaaaaaaaaaaaaaa

Figure S4

A. Catshark SST1 = SSa (scaffold122178)

AACAGAAGTAAAATGATACCTGGTCCCAGTGTGAAATCTGTAACAGCCCCATTCTGGCATTCAAT
 GAAAAGCTAGTTAACCTGACGAATACAGTGGAGTTATTGAGATGAACACATTGCAGATTGGCACATGT
 GGGCCACAAAGAGAACACGCTGTTAAATCACAAACTACACACAATTATTCAAGATGGCAGCGAGTCTTC
 CCCAGGAAACATTCTTATTCTGCTCACTCAGTCTAACTTGTACATTCACTGGGATTACC
 CAACCCATTCCCCACTGATCCAGTGTGTTCAATGCTCAAGGAAGATTGAGATTATGGATGAGGGTGT
 ACTGGGATTGATGTTCACTTTCCACGGATTCTAGTTGAAGACTTGGCTGCATTCTTGATC
 GACACGAACCAATACAATCGTAGGGCAGCTGCCAACACGCGATAGGGTGTCCACATTGAGACTCCATGG
 ATCTATCTCAATCTCCTCATGGTAATGGGTTGGTGGAGATGTGACTGGGTTGTGCGTAAATACTCGT
 CATCTCCTGGGACCCCTCCCAACGTGTGAGCTGGTGTGAAGGCCGTTAAAAGGAGCTTCCCGATT
 GCAGGGACAGAAGGAGCGGAGCTGTCCACAGAGCCAGTGCTGAAACCACCAGCCAATTCAAAGCGTTGG
 AAACTGCTCTCCTCTCGCTGTCTCCCGTTGA**TCTTCGCTGTGCAGAG****ATG****TGGTGCAGCCGCCTT**
 M W C S R L
CAGTTGAGCCTGGCTCTCCTCTCCATCGCCCTGGCAGTACTGAGTGTCA**GCTCAGCACCCACAGACAACA**
 Q L S L A L L S I A L A V L S V S S A P T D N
GGTATCGCGAAATCCTGCAGAGAGCCATGGCAGCCACAGGAAGCGGAGGGAAAGCGGTA**AAGGACCCAGCA**
 R Y R E I L Q R A M A A T G S G G K A
 AAAAGTCACATTCAATAGAAATGGTAGTTGTGTTCATCCGTTCACCTCGAATAGAAACAGGGACTGGG
 AAATAACTGGTCAATTCTGATCTAGTGAGAAGACCCACTTTAACAGGACTATAATTGAGAGTGAAT
 TGGCTTGTAGTGTGGGATCATTCATTGGTTAGAAAGGTTCTGAGCGCGTTGATCAAATTAC
 TGAGTTCTCGTCATCGAGTAAATCTGTCCTCTCAATCCATAGCCACTCTGCACAAAGAGTAACAG
 ACAAGAAGTAGACATCGTCCACAATCCCAGAGAACTTACTGCTCTCTCTCCAAACTGCCTCTCC
 CATCTTAACCCCAACCCCTCTCTCCCCAAATCCGCTCTCCATCCAAACCCCAACCCCTCTCTCCC
 CAAATCCCTCTCCGTCCAACCCCAACCCCTCTCTCCCCAAGCTCCAAACCCCTCTCCATCC
 CAACCCCAATCCCCTCTCCCCAAACCCCTCTCCCCACCCAAACCCCAACCCCTCTCTCCCCAAACC
 CCTCTCTCCCCACCCAAACCCCTCTCTCCCCACCCAAACCCCTCTCTCCCCACCCCTGGGACTTCTGACCAGGCTCAT
 TTGGTCTGTATTATCATTGAAGACGAGCACCTGAGTCTCTCTCAGTCACCTCCAATAACCATCTAGAAT
 GGGGCAGCTGAATCAAATCTGCAACCAAGTCATTCAAGTTGAAAGAAATTATTCAATTACAAATTATGTTT
 CAATTGCCTCATGTTGAAAAGAAACTCCGAGCACGGGATTGGTCTTCAGAGATTTCCTCGCTCTT
 TCCAATGTCCACCTCCCTTGAAAGGTTCAAGATTGTGGATGGAATGGAGTTGGGGGGAGTGGGA
 GGGGGTTGGGCAAGTCTCAGGTCTATTGCGAATTGGGATCTTCCGGGGTTGCAATGGAGAAAT
 GAAGATAAAATGAAGATAATTTCACAAAGTTGAATTAAATTCTAGTTGAGATTATTGCGGGAGTTGCAA
 CTTCGTTGCAAAACAAACGTAATATAGCGTCAATTGGCGGAAATTCTCCCTAAATCTATTCTGT
 TGGTCTCAGGGAG**TTGACGAAATATTCCCTGCCCAACTGCTCTCGA****ACTGGAAAACGCCGAGAATGAAG**
 E L T K Y S L A Q L L S E L E N A E N
CTCTGGAAACGGATGCAATGGGCGGACGCAACGAGGTGCGGCTCGAACCGGAGAGATCGAGAAATCCAA
 E A L E T D A M G G R N E V R L E P E R S N P N
CCTGCCGAACAGGGAGCGAAAAGCGGGATGTAAGAACATTATTGGAAAACCTTCACATCCTGT**TAA****CTC**
 L P N R E R K A G C K N L F W K T F T S C -
 TCCGAATTCTCCATAGCAACCCACACACTCAGAATGTGGCATTCAAGATAACT**AATAAA****T****CATGTGGTGA**
 ATGATTCTATTGAATTATGTAAGAGAACAGAACATTGGTTGAATTGTCAATAGCAGGCCAGTTGAATG
 GTGACTGGATAGAGTCGCTATTTCATTATCTGTTGCAATAAAATCTGTTGAAAGTGGACCAATT
 GTGGATTCTGTTCTGGGAGATGGGCAATATAACAAAGGGACAGAATTAACTCGGCTAGTTCAACA
 CCAGTCTGTCCTGCAAAGGTACAGAGCGAGGGAGTCATTCCACAGTTGACTTTGAAATCAGCTCT
 GGGTGAATCGCTCTGGGTCACTGTCATCTGGAAATGTGGTGTGAAAGTCCCTCGCGTATTCA
 AACTCAGAGGAGACAATGAATGGACGGATATTAAAGGGGTTCTGCTCTGTCACAGCAACCGTGCTCTG
 TGAGTGCTGTAATCTGAGGAGAGCAAACATTACACCTGCATCACACTGGTAAAGCCGGTTCCATTCTAA
 ATGAAAGCATCAATCCACAAATCACAAACCTGCTTCCAGCCTCCCTGTAAGAGCCGGTTCCATTCTAA
 CCTAGCGGCACGGTAGCACAGTGGTTAGCACTGCTACTTCACAGCGGCAGGGTCCGGGGTTGATCTCCCA
 CTGGGTCACTGTCATGCCAGTGTGACCTGTCACGTTCTCCCGTGTGCGTGGGGTTCTCCGGGTGCTCCG
 GTTCCCTCCACAAGTCCCAGACAGTGTGTTGGGTAATTGGACATTGGAATTCTCCCTCTGT
 CCCGGACAGGCACCAGAACATGTGGCAGTAGGGGTTTCACAGTGGAAATGTCAGTGGAGGTTCTGTACA
 ATACCAATGTTCCGTACAGGTGTGAAATTGTTCTACACAGGAAATTGCCCTCATCATCCCCTATTAT
 GTCTAGAAACATAGAAAATAGGGCAGGAGGAGTCATTGGCCCTTGAGCCTGTTGCCATTCA
 TGATCATGGCTGATCATCCAGCTCAATAGCCTCTCCAGCAGTCCCGCATATCCTTGATCTCCTCACC
 ATAAGTGCTATATCTAAGTGTGTTCTGAAATTATATTGAGAGGGATTCTCATCCTGCCACACCAGGAGC
 TGGATTCTCTGCCGTGCGATTCTCTATTGCGAGAACGACGGGGTTCCCAACAGCGTAGGGTGGCC
 CCACAAGGAGAAACCCCGTTGACCAAGCTGGGAAACGGAGAATCCCGATGGCATATGGGGACAGAGAA

ACCCGCCAGATTCGATGCGCATGTCGTCGGATTCTCCATTGCCACTGGTCAATGGGTTTC
CCATCATGGGCAGCCCCATGTCGTCGGAAACCCCTGGCTGGGTAAAATGGAAAATCATGATGGC...

B. Catshark SST2

(scaffold 83887)

..CACTCTTCTCAAAAAGCAGTGACCGACTCTAAATATGTTCAAGACAGAGGTAGATAGATTCTTGAA
AGGTAATGGGGTGCAAGGTTGGGGTAGGCGGGAGATTACAGTCCGATGGCCATGATCTTATTGAA
TGGCAGATCAGGCTGAAGGGCCAGTGGCTACACGTGCTCTAGTCCTATGTCTGTAACATCCGACA
CTTGGAGAAGAATATTTGATTGTCAGGAATCCAGCCCTCCAGAATTTCAGGGTGTAAATAAT
CAGTTTACTTAGATTCTAGTCAACCTACAGGTTAGATTCTTCTTACAGTGCATTGGAGGG
TCAGTTGTAACAGCATCCATCCAATTCCACTTTATAACTCTAAAAATATAATTGTTAAATGGC
TGAACATTCTGGATTGGAGGCTATAAAGCTTTAATGGCTGCTTATTCAAATTGAACTGCAATT
AACTGTCCACATTACAGATCCTTCATCTACTTGCCATAAATTACAGAACGAAAAGTGTAAATAATC
AGTCAGGTATGTTCTTCTGAATTAAATATTCTCCATTACGATAACGCAAACCTGTTACTCCTTATATA
CATATTGTTTCAGGCTGTATTGGTTAATGATGCACACTGGCTATTAGGCTTGATTGTATCATTAAAT
TTGTGCGTCAGAGTTGCTCTGCTATAAAAGAGCTGGAAACACTTCGAAAAAATAGATTGAGG
AGTTCACAAACATTTAGCATTGTCAGGAGTGCTCGAACGATTAGCAGTGAAAGTGGCTAATGACAGTG
M K W L M T V
AGCCTGATGTCCTGCTGTACCTCTGAGAGTCGAGGGTACTGACCTACTGGAAGAAAATGAAACTTC
S L M S L L Y L R V E G T D L L E E R M K L
AGTAACAGACT GAGTAGAAAGATCATTACTAAATGCACAGAGGTGGCGGAGTGTGGTGAAGGGGTG
Q V N R
GGAGGGACGAAATCCACAGCCATAAGGAGAGAATTGACGTAAAATATTGGAAAATTATGTAGAGAGAT
GAGAGACAATGGGATTGTTCTCTAAATGCTAGGAGATTAAGGGAAAGACTTAATAGAGGTGTTCAAATA
ATGAGAAAGCGTTCCACAGGCAGATGGGCCGGTGACCACGAGGAGAACATTAAACTAATTGATAAAA
GAGCAAGAGGGAGCGATGAGGAAAATTGTTTACATCGTAATCATTATAATCTGAAACGTGTTGCCT
GAAAGTTGATGGAAGCAGATTCAATAGTAACCTTCAAAGGACTTAGATATATACTTGAAGGTTGGAAA
CTGCGAAACTATCAGGAAGAGGGAGGGAGCACTATAATTCTGCACTGTAATTCTATGATTACGTTA
AGGCAGGAAAATGGAAGTAATTGAGTAGCTCTTACAAAGGGCTGGTATAGATGTGATGGATGAATGGC
CTTTTGCTGAAAGTCCATGAAAGCCAACATCAGCAATAATCAGACTTCAGATTCCAGCATCCAC
ACTATTTGTTAAATCAGCATTAATATATCATCAAGGGACTGGTAGTGGTAGTTGTCTTACTGGACA
AGATTAATAATCACGAGAATTGAGTTCAAAAACCACATGGCAGTTGAGAACCTGAAATTGTTGAA
AATAAAATCTGAAACAAGAAACTGGTTCACTCAAAGACGTAACACTGTCGATTGTCATAAACCTCAA
CTGGTTCGTCAATACCTTTAAATATAAGTTAGAGTTCCAATTAAATTGTTCAATTAGGGCA
ATTAGCGTGGCCAATCCACCAACCCTGCACATCTTGGGTTGGGGTAGACCCACGCAGACACGG
GGAGAATGTCGAAACTCCACACGGACAGTGACCCGGGGCTGGGATCGAACCTGGGCCCTGGCGCTGTGA
GGCAGCAGTCTAACCCACTGCGCCACCGTGTGCCCTGGCAATACCTCTAAGGAAGGAAACTGATCT
GCCAGGTATCCTGGGCATAGCAATCTGTTGGCTGTTAACAGATTCTTAGTGACCTAACGAGCCACAC
AGTTTAACCAGGATGCAATAATGTCGCACTGGACTTGTGAAAAGATCAGAAAACCCGGC
GCAGACTGTTCTCGGGAAAATTGCTGATTAAGTTGGGATTACTTAAACTAGTGGAACATTAT
TGAAGGACTGTTGACCTGAACAGCTGACACTCATTTGCTTAAATCTAATGTCCTCAGGGAAAT
GAAATCTGCGTCCTTACCTGGCTGCTACATGTGACTCCAGATCCACAGCAATGTTGGACTCTT
AACTGCCCTCAAGGGCAATTAGATATGGCAATAATGTCGCCAGCCTGCGACGCCATGTCCTTG
AGCGAATAAAATAATCAGGCCAAGTACAAAATATTGAGGGAAACAGAAAGATTAGGTTAGGGAT
GTTGAGTTGGCAAGATATGCAAGAGGTAGCAACGAGTAAACTGTAACAAACTGGTCAATGGTGGAA
TAATGGTTGAAATAAGTGTAAAGACAACATAAAAGAGCTGAGCTAGATCTGAGTGAGTGAATTGTT
TGGCATCAACAAACAGTGCCTGCAATGAAATGAAAACGAAAGCTTCTATTCTGTGTTATCCACA
GAAATGACAAAAGCAGGAAGAATCTGATTGTAAGCTACTGGCTGGCTGTTGGAGACTGATGATAATC
E M T K S R K N L I V K L L A G L L E T D D L
TCTGGAGAATGGCTTGCACCTTGAAACCGGAAGAGGGCAGAAGGGACTTGTGCAAGAGAGGTGGT
D L L E N G F A P L K P E E A E G T L F E E R S
TAACGCTGGAATTCCACGCGAGGGAGCAAAACCCATGCAAACGTGTTCTGGAAACCTTTCCCAC
V N A G I P R R E Q K T P C K L F F W K T F S
TGTAA TAACCGTGTAGCGGATTCTAAACGAGTGGAGTATGAAAGAAAATGGGTGAAAGGCTTA
H C -
ACTTAAAACCGAAAATACACTGCAATCATGTTCTAGGCCAAATATTAAATTCAAATTACAGG
AAATGCTTGC**AATAAA** GTTAACCTGAAAGTTACACCTTTAAGACATGTGAAATTATTGTTAAATG
AGATAGCAATCCAGTTAAACTTCTCAGTTGTTCTATCATGCTGTTATTCCCTGTTCCAGCAT
TGTGTTCTCTCGAGTCCTCGCTTGGCATGTTAGCCCCCTCTTCCCACAGAATGCTCCTG
GGATTCCGTACTCTCCCCCTCGCTTACCTTCCCTTCCCTAGACGAATGTTCTGAAAGATTGCA
CCTGCCCTGACACAGCCGGCTGGACTTCTGGAAGCAGTGAATTGCAAGACACAATTGGGATATT

TTCTGAGTAAAGCCTATATATGTTGACAGTGACCTTCCTCTGATCGTAGAGATCTGAGCATATTGT
AATGGTGTAAATTGTTTGACCAGTCTATCTGCATACAATGTACATACTTATCTGAAATATCCTGTGA...

C. Catshark SST3 (scaffold121269)

TTAGATCCTGGCTTGGGTCACTGTCGTGCGGAGTCTGCACGTTCTCCCGTGTGCGTGCGGGTTCCCT
CCGGGTGCTCCGGTTCTCCCACAGTCAAAGATGTCAGGTTAGGGATTGCCATGCTAAATTGTC
CTCAGTGTCAAATTGCCCTAGTGTGGGTGGGTTACTGAGTTATGGGATAAGGTGGAGGTGTTGAC
CTTNNN
NN
NN
TATAAAAGTAATAATTTAAGCAGAGCAGTCTGACTGAGGAACAAGGAAGGGCTGAAGCACACCAGG
TGAACCAGTTTTGAAGATATTCACTGCGAATCTGAAGGGCTCTAATAGGAGTGTAAATATTCTGTTG
AAGCAATTTCACACTGTCATGCTGATTGTAAGATGGATAAGAGCTGTATGTTATTCTGTTGTTG
TTCATGGGAATTGAGTAGTTGCTTTAAGGGTAATTGTAACACTGTTCTCGGATGTGAAGTAAAG
AGATAATATTGATTCAATAAGGTTTGTGAGAAATACCAAACCCCTTATTACGCAATCGTT
CCTGAAGTGAAGTCATTCTCTGCATAGCTGTACAACAAACTAAAATATTAGGGTTTGGTCCAGTATCC
TGTGTTGGTCTGGTCTGGGATCACAATATGCAATACATCTCAAATTACTACATTCACTCAGGTCAATTGA
TGAAGCAGCTGAAGATGGTTGACTGAGGAACACTACCCCTGAGGAACCTGCAGTGATGGCTGGAGCTG
ACATGATTGACCTCAACACCACAAACCATCTCCCTTGTGCCGGGTATGACTCCAACCAGCGGAGAGTT
TCCCCCTGATTCCATTGACTCTGTTGCTCGGGTGCCTAATGTTACAAATCTGGATCAGACCGC
AACATTGCTAAGATAACGACAGAACGACAATATTATTAAATTGTAAGACTGTGAGGAAGGAA
TACTTCACTCCAGGAGTGATGACGAGAATTAGGGATTGGTTGTTAAAACAAACTTATTACTAAC
AGTAATAATAACTGTGACATCATATAACATATAAGCTTCAATTACAGTTAAATGCTTATCAGTAC
AATGACACAATAACCCCTCAACTGCTATTTCACCTCAAACACACCCATCTCAAACCAAATCCAC
TTTAAACACAATGAGCAGTCTCAGGAATCCATGCTGAAAGAACATCCTGGATAAAACAAACTTGATA
AAGCAATATTCTCAGCTTAGGCTCGGTGATTGGNNNNNNNNNNNCTAGTGTCCAAAATGTTAAGT
GGGGTTAGTGGTTACAGAGATAGGGTAGATATGTTGGCTCAGTCGGGTGCTCTTGTAAAGGCTGGT
GTAGACTTGATGGCGAATAACCTCCATCTGCACGGTAAATTCTATGGTTATATGGTTCTATTCTGTGG
TCTCAACTTACTGTTGAACTCCCTCTCTGTTCATAGGCAAATCATTAATGCATTGCCTGAGATCAGC
TGCTCTGGTCTGCCCCAGTCAGATATTAACTGAACTGTTGGAAAGTTCTCTAGTCTGTCTACAG
GCACATTTAACTGAACTGATTGAGAGCAGCTTTATAAAATCCCCACATGGCAGAAGGAAGCCAT
TCAGCCATTGCGTTCGCGACCCATGAAAGACCAACCCATCTGAACAAATTCCCCACCCATTCTCC
AAGCCCAACCTGAGGGCAATTGATCTTGATCAATTCCATCAACTGCAACATGTTGGACTGTGGAAGGAA
CTGGAGGAAACCCATGCAAGCATGGGAGAATGTGCAAACACTCACACAGACAGTGACCAGAGGTTGGAAT
CAAACCTGGGCCCCCTGCCGTGTGAGGCAGCAGTGTAAACTACTGTACCAACCATGTTCCCTGACTCTGT
GAGGCAGTAGTGCTAACACTGTGAAACTCTGCCACCCATTGTCTCCCTGTTCACACCCAACTAAAAC
TAAACTGAAACCTAACATCTGACTGTTCATCCCTGGCTCCTCCATTAACTACATCATCTCATTAAG
CTGAACACGCTGCTCTAAATTCTATTCCAGGAAACCCCTCTCAATATAAAAGTCATACCCCA
ACTTGTAGGATGCTTAATTGACACTCTGTAGCCGCAAAACCTGGCTGTCTGCAAACACTAGAATTAA
AAAACGCTACTGCAACAGTCACACACACTAACCCAGGATTAAACCTTACGGCACCGGTACATACAGT
ACAATATATCTGAAATCCCTACATTCACTCACAGATAACCACACTCGGTCAAATATTCTGTGTCAG
GCAGTCACTCTCACCTCACCTCTGAAATTCAACTCTGGGCCATATTGTGGAGCAGAATGGTTCTT
ATTCTACATGGAAACAATAGTTGAAGATTGCTTTAGACATGAGTTACATGGATGAGAAACTGGGT
AATCACTCACATGTACTCACAGAGAGTATAAGCATGTCAGAAATCAGGGATGTAAGAAATTGAAAATC
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(scaffold 604248)

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 E L L K D
 CACAATGATGAAACTGTTGCCCTGGTTACTGATGTAGACACTGAGGCCGAACACTGGATGTTCCAAT
 T M M K L L P L V T D V D T E A G T L D V S N
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 K N C K N F F W K T Y T L C -
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D. Catshark SST5 = SsB

(scaffold 888145)

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M P R S Q T Q V
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L L T L V T V A L L L R G S S T A R V Q G L P
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D I L Q E R N D E G T E
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(scaffolds 316000)

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E L S R T M V L N L L S E L L L H A G
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D K G L P S T E R R E L P Q A E I V R R W N S
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P R D R K A G C K N F F W K T F T S C -
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E. Catshark SST6 = SSc

(scaffold 66610)

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M Q L L G T A S L L S M L L I V S S V R A
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E L N K E R K E V I L K L L S G
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K V E E R S R F S Q L P Q R E R K A P C K N F
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Figure S5

A. Whale shark SST1/3 (NW_018029766.1)

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B. Whale shark SST2 (NW_018077477.1)

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C. Whale shark SST6 (NW_018032490.1)

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L E D R L S L R A N Q

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CAGTAAGAGAGTGGCATGTTAAAATGGGAGGGAAACAAGTGCATGAGACAGAAAAAAACAAAAACGAA
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GTTGTAAACCCCTCAAAACTTCAGCGACAAGCCAGGCTCTGGAATAAGACAACCAGAATTAAATAGTC
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TCTACACCTGTTATCTTAATAGTGCACAAATACCATGTTCACATGAGCAGTTCTCAGAACATTGACTTA
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CAAGTACAGTTCTAGTTTATAGTGTATTCCACATTAATTTCCTTGCTGTTATCTCTAACAGG
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CAAGTGCAGGACTCTCCCTGTTGCTGAGTTGAAGGGAACAGTCCCTGGCAGATGTTACAACCTTGATTG
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CAAACCTATTCTGTCAGAGGGCAGGAAACAGCAAGGGAGTTCGGTGAGGGCTGGGGTGGGGGTG
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 AAATAACGTGCTGAGATTATATCCACTGGCTAAAGGCTAAATGTTCATAGATACCACTGAACAATC
 CCCCTTCAGACTAAAACACTGATCATTCTGGTTGTTATAATATGCAGAATTTCAGTTGGCATG
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 GGGTCAGTGGTTAACACTGTCCTCACAAATGCCATGGGGCTGGGTTGATTTCACCGTTGAGCAGTG
 TCAGTGTGGAGTTGCATATTCTCCCGTGTCTGCTTGGGTTCTCTGGCTCCAGTTCTCCAC
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 CCATGAGATATGCAGGATTACAGGAATAAGTAGGGGTTGGGTTGGGTTGCTCTGGAGGGCCA
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 AATATCTGATCATGTAAGTATAGGTCTAGAGAGGGGATAATTACCAATTGAACTGTTATCTTATTCGC
 CTGGAGTTCACAGCTTAATTTTAGTGGAAATGTAATAGACACCCCTGGTCATTGCAG
 CTGGACTGTTGTTGAGGTCACTAAAGCATTGGAGACTGTGTGGCTCAGGACACAGCAGAAGGA
 GTGTCTGATGATTGATTTGATATGTGCCATCAGCTCTTTAGGCCCAATACCTGATTCTGTT
 GCTCTATAAGAAAGTGTGGATTGTTCATATTTACTGAGCTGTTATTCAGCTAACTCCAGGCTCAA
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 TTGTCAGGAGTGGACGGGGATTGGGTAATGGGACAGAAAACATGTGACACTCAGCACTGTCA
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 AGGATGTGCTGTTGAGGCATCTTCCAAGACAAGATGTCAAACAGAGGCCCTGCCAGATGA
 GTAGACTATCCCACATCAAGTCAGAAATTGCTGGAGAATCTCAGCAGGTCTGGCAGTGTCAAGAGAG
 AGAACAGAGTTAACGTTCAAGTCAGCTTCTCAGAACAGTAAACTATCCGTGTTCTG
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 TCTGAAAAAAAWTCTTAATTGGGATTAAAGTGTCTAGAAGAGCAAGATGCAACATAATTGCAAGTTA
 TTTCTTAAACGGTATGTGTACAAAGGCTCAGGTTGGGAAAAAAATTACTCTTACACATGGCAGGC
 CACCCATCACGTGTACAAATAAACCTCCACCTCAGCAAATAATGGGCTCAATCCTCAGAGTGC
 TTTGGCACAGGTTTACAGAGGGCAAACACGAATAGTCTGAGGAAGCATCACTGGACCTGAAACGTT
 TACTCTGATTCTTACCATAGATAATACCAGACCTTCCAGCAATTCTGTTCTGTTCCGATTACA
 ACTTCCACAGTTCTTCGGTTTGTGAATGAGTTCTGTTGTTAACAGGCTGAATAAGAAA

E L N K E

GGAAAGAGGTTGTTCTCAAGCTGTTATCTGCACTGCTTGACTCCAGCAGCAATCAAATGGGATTGAGAA
 R K E V V L K L L S A L L D S S S N Q M G I E N
 CACGTTCCCAGATCAGGAGGACATGGAAGAGATGAAAGTGGAGACAGGTCCGCTTCAGTCACTTACCA
 T F P D Q E D M E E M K V E D R S R F S Q L P

CAACGAGAGCGGAAGACATCCTGCAAAAACCTTCTGGAAAACCTTCACCTCCTGC
 Q R E R K T S C K N F F W K T F T S C -
 TGACATGTCGCTAGGAACGTGATTAGCACTGTCATAAGCTGGTGTGTTATTCTTCTGTTCTGGG
 GGTTACATTCTTCTGCAAAAGAAAATTAAAAAGCATGAAATGTGTGTAATTGCTGCAACT
 TGATGTATTCTTCCAGCAATGTGGTGGCGCTGTTCTGTTAGAGC
 TCAAATTGATTGATCGTTACTGACTTGGCCTTCAAGCTGTTGAGATCTGTTCAGGGATTG

TAA

C

CGTCAGACGA

ATGTCTTAAGTGAGAGAGGGAAAGTCATAGTCAAAGCTACAGGGAGGCAATGGCCTGGTGGTATTATCRG
TGGGCTGTTAACAGAGATCCAGGTAATATTTGGGACCCGGTTGAATCCTGCCATGGCAGATGGT
GGAATTGAAATTCACTATAAAGAAAATCTAGCTGGTGCTCTGGTTCTCCCACAGCCCCAAGATGTGC
AGGCTAGGTGGATTGCCATGCTAAATTGCCTATAGTGGTAGATTAGGTGGTTATAG...

Figure S6

A. Whale shark SST1 (SSTa)

atgtggtgccgcggaggttcagtgcgcctcgccctgctctccatcgctctggcagtgctg
M W C S R V Q C A L A L L S I A L A V L
agtgcgggcgcgcgtcccaccgcgcacaggatcgcgaactcctccagacatcaatggct
S A G A A P T A D R Y R E L L Q T S M A
ggcgcagagccccggagtaaagcggagctgatcaaatacatctcgccaattgctcg
G A E P R S K A E L I K Y N L V Q L L A
gagctggcaaacgcgcgagaacgaaactttggatggggaggattggccggatggc
E L A N A E N E V L D G E D L P R M A K
caggatgaggtacgggtgatctggaaacgatccgcaccccaattcgccccagagg
Q D E V R V D L E R S A N P N S P Q R E
cgaaagcgggctgaaaaacttcttctggaaaaccttcacatcctgttaa
R K A G C K N F F W K T F T S C -

B. Whale shark SST2 (SSTd)

gaagtggcaa
atgacagtgtgcctgatgtccctgctgcttcttaagtgttggaggcagcagaccactg
M T V C L M S L L L L S V E A A D P L
gaggaacgaatgaaactccaggtaaatagggaaagttacaaaagcaggaaagtatctgatg
E E R M K L Q V N R E V T K S R K Y L M
ttaaaaactgctgtctggctgttggatcctgatgataatctcttggaaaatgacttcacg
L K L L S G L L D P D D N L L E N D F T
tctttgagcccaggagagaaagagatgtcgcttgaagagaggtcggttaacgctggcatc
S L S P G E E S S L E E R S V N A G I
cctcgttagaccgcagaaggcaccgtgtaaattgttcttctggaaaacatttcgcactgt
P R R P Q **K A P C K L F F W K T F S H C**
taattat
-

C. Whale shark SST3 (SSTe) (exon 2 only)

gactttctgaaggcacacaattatccaacttctacatgtggtcgcggatgcagacaaggat
D F L K D T I I Q L L H V V V A D A D K D
gctgtggaaagtgaatgctctcaagttgagactccaccagwtacaagattccaatgaaa
A V E V N A S Q V E T P P X N K I P M K
ttccagcagcgtcaattggaaacaagaatgcggaaaaactgcaagaatttcttctggaaa
F Q Q R Q L G T R M **R K N C K N F F W K**
acatacacttatgttaa
T Y T L C -

D. Whale shark SST6 (SSTc)

aaccacacagagacttcaagggtcgaggcacattg
caaagatctcgaaaaggcaccacttcaatccaattccaagcgactgagagaagaggcagc
atgcagctactgggtcagcgagcttkgtgtctatactgctatgtgtccagtgtaag
M Q L L G S A S X V S I L L I V S S V K
gccacagcaccttggaaagacagactgagttcgccaaatcaggagactgaataaagaa
A T A P L E D R L S L R A N Q E L N K E
agaaaagagttgttcaagctgttatctgcactgcttgcactccaggcagcaatcaaatg
R K E V V L K L L S A L L D S S S N Q M
gggattgagaacacgttcccagatcaggaggacatggaaagagatgaaagtggaaagacagg
G I E N T F P D Q E D M E E M K V E D R
tcccgcttcaagtcaattaccacaacgagagcggaaagacatcctgcaaaaacttcttctgg
S R F S Q L P Q R E **R K T S C K N F F W**
aaaaccttccacccctgctaactgcagatgcacatgtcgcttaggaactgatggacac
K T F T S C -

tgtacataagctggtgttatttccttgttctgggggtacattcttcatgc
acaagaaaa

Figure S7

A. Elephant shark SST1 (Sc_821)

...TTTAGTGGATGGTATGTTGTGGATGCTGTATAGGGATTGTGTAAATGGATTGTGTAAAGGGATGGT
GTGTAGTGGTTGGTGTAGAGGATAGTGTAGTGGATGGTGTGGTGGTGGTTGGTTAGAGGATAGT
GTATAGTGGACGGTGTGGTGGTGGTGGCATGGTGTGCGGAGGATGGTGTGCGATGGTGT
GTAGAAGACTGTTGTAGAGGATGCTGTCAAGTGAAGGGTGTGTTGGGATGGTATGTAGTGAATGGTGT
GTAATGGATAGTGTAAAGGGATGGTGTATGGATGGTGTAGAGGATGGTGTGTTGGGATGGTGT
TTCAGGATGTCCTCTAAATATTGCACTACAGTATTAGAATTGAAAAGTTGCCTCTGTTGCT
GTATTTAAATCCATAGAATTAAAGAAAAAAATGTAATATTAAAGAGGAGTGGACGTGGTACAATC
TCTGCCCTAATCTTAAAGCCTCGTCAGGCCGGATGGTGGGGTGGGAGAGTCAACGTATCGGAGGCG
ATAACATCCCCAAGTGGCAGGTTATGGACATTATCTCAATACTCGTCACGTGGTTATTATTTGTC
ATGATGTGACTAAATTGAGCATAAATTGCTAAATCTGAGGACATTGCTTGTACGTCAAAGGTGG
CGTGAGGCGGCTTATAAGGCGAGTCTATGGACACCAGGACCAGAACGATCCAGACGAGGAGCGTCCA
GAGAGGCCGGTGCTGAACCACGAGCGTCCCTCCGTCCTCTCGCTCCCTTGTACAGTTGGTGCCT
CGCCCGAGATGTCGTGCCGCCAGTGCAGTGCGCCCTGGCGTTGCTCTCCATGCCCTGACAGTGCTGA
M S C G R V Q C A L A L L S I A L T V L
GTGTCACCTCGCGCCAGCACACGACAGGTACCGCGAAATCCTGCAGCGATCACTGCCCGCGCGGGAGC
S V T S A P A H D R Y R E I L Q R S L A A A G A
CAGGAGTAACCGGTAAAGACAGCCGATTCCACACTGGTAATTAAATATCTGACAAGGTTGCTAAATACAC
R S K P
ATATTTACAACATTGACCTGTATTCTAAAGTACATTCAATTGGGATTTGACTGGAGCTAATTATCCG
ACCGTCAGATTTATTCTCATTCTGTAAATTCTGAATTAGCGCATTTCAGATGTCAGTCTATAACTG
TAAAGGAGATATCACGTAACTCGTCTCTAATTGCAAGAGGAGATGCGCACCTGCCAGGATGCCGA
TGGCCCAGAGACACACCCCGATCTGGAGCCCGGTACCGCGCTCTGGGCTCTGAGGATAACATTCCA
AACCATCAGATTACCGCACTCTCAGTCTCAGGCCACTGCTCAGTGCCTCCGAGGACCCATAGCTCCGA
GCGCTCCGTGTCAGTCGTAGTGGAACCGTTGACACCTTGAGAGGCCATTGCTCTAAACCAAGTT
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AACTGAACCTCCCCAAATCTCTCCGACAATTGTCCCCATAAACAGAAACCTCCGAACACAGCACAA
GAACCAAGTAAACAGTACAGATTGTAAGTAGCTGTAAAACAACCGCTAACTAGTAACACTAGTCCGGT
TGGTGCATTCTGGCACAATAGAGAGGACTCCAGACTCCAGGCTGAAAACCTTACATCTTCTTACATT
TACTAAACATTGATATCTCTAAGCTGAGAGAGCACATCCGTGTTACCCCCCACCCCCCACCC
CGGAGCGCTGGCTCTCATGTAGCCAATGGCTTAGAACCTATTCTCCGGAAAGTGAATGCTCGTGA
TACATTCCGGTTCTGAATTGAGTGATTTCAGACATTCTGCTTAGTGAGTAGTTGGACTGAGGAG
GAGTTTGACGTATATAGGAGGTTGGAGTCAGTGAGCCATAAACAGACAAACACGCTGATTTCCTGATCT
TCACACAAACAGCCAAGCTGGAGAGGAAACTGCGCAAACGATACATTGTGAATGTAGTCATTAAAT
CCGGGTTGAGTAATGCCATCAGCTGCTGCCATGTACATGTGCTCACTGATTACTGTTCTTGT
GTTACTGTTCTCAGGAGCTGACCAAGTACAGCCTGGCTCAGCTGTTGGCGGAATTGCCAACGCGGAGAA
E L T K Y S L A Q L L A E L A N A E N
CGAGGCCTGGAGGCGGAGGACATGGCCCGAGCACCGCAAGGACGAAGTAAGGGTTGAATTGGAGAGA
E A L E A E D M A R A T A Q D E V R V E L E R
TCGGCCAACCCCAACCTGGCGCAGAGAGAGAGCGCAAAGCGGCTGAAAAGCTTCTTGTGAAAACCTTCA
S A N P N L A Q R E R K A G C K S F F W K T F
CTTCCTGC[TAA]CTCTGAGCAGCCCCACCACCCCTCTCACACACACTCATACACACACTTCCCTGACCC
T S C -
CCACCCCTCCATCCCCACCCCTACACACAAAGTTCCGATCCCCGCCACACACACACACACAT
TGTATTGCTTACGCTACG TGGTCTGTTCTGATTAAACATACTGTAAATAAAACACATGGTGTGATA
ATTCAACCTAAATTATGTGACAGAACCTTAGATGGGTTGTGACTGTATAGTTACCCACTCTTCTGG
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GCTTTCAAGCGATGGAGTCTGTAGCTCAGTGGTAGAGGACTCGCTTGCAAGTGAAGAGACCTGAG
TTCAATCCCCGGGGGTCAAGGCCAAACCTCGGGCAAGTTCTTACTCCACACAGAGCCTAATAATAAT
CCTCCAAAACCAAAACAATAATAAAATTGGTCATTCAATCTACGACTGTTGTGGACATTGCTGTG
GCAATTGGCTGCCGCTCGCCACAAATACAGTCAATTCACTTACAGTGTGTTGTGAAGTGCT
TGGGACATCTCCGACGTGAAAAGCGCTATACAAATGCAAGGATTATTATTATTATGGCTCAGAC
AGATCTGCCATAGTCTTCACTGTGTGATTGACATTGCGCTCTCATTCACCAACTCCAGAACAGCTCA
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CTCTGTTCTGCTCTCACTCTCGCACTCCTCAACCATTCCATCACCAGATGGTTATCTCATACTC...

B. Elephant shark SST2 (Sc_58)

...TACTTATTTCACATAATAATAATCCTGCATTGATATAGCGCTTCACGTGGGAGGACA
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 GGAGGGATTATTGTGGTGGCTGTGGTGCCTGTTGTCAGTTAATTAGCTTATCTTGAAAAAGAAA
 CAATGAGGTTTGAATGAAGAAACAATTAACAATCCTGTTGAGACTGAAATCTTCCGACTTGATATGAC
 TTGTTGAGGTTTTACTCTATTCAACCTGCTGTTCAAGTGTATAACTAATCGACCTTC
 TTGCACTTGTGACAGTACCTAATAGTGTGACACCTCACCTCATATAAGAAAAGAACACTTGTAAATTATAGTACC
 TAAACATGTGAAGTGGCTAAATGCTTACGGTATTGAGTGTGCTGAATGAAATAATGATAATAGT
 ACTTGCATTGCACCTTATATTGTCGTTGAGACGTCTCAAAGCAAGCGCTCACAGACTATAATGAAAGT
 GGATTGACTGTAGTTGTGGTAAAAGTATCAGAAATCCTGATAACCGTCTACGACAGATGTATGAACAC
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 GTCCCACATCCCATAAGCTGTAACCCCTATTAGTAAACTGGAGGTCAATCATGTAATACTGTGGAC
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 GGCTCAGCCTCACTGATTCTTATCAGTCTTGAACAAATGACTTCTGAGTTGTGAAAATCTTATGT
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 GGAAAGCTCTTTAATTATCAGTGTCTAACTTTGATGCAAATCGAAATTGAAAATATAAAATAATC
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 ATGGTTCTCATTGTATATTGTCGATTAGCACTAATTGTCACGTCAAGCAGTGTCTATAATTGTG
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 GATCCATTGAAAAGAGAGAAAGTTGAGTCAGCAGTGGCAAGCATTGCAAGTGTGTTGCTG
 ATGCAAGTGTGTTGCTG
 M Q W Q A F A S V V C L
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 L F I V T V Q G V E P Q E E R M G L Q L N R
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 E M V K D K K R L I A K L L A G L L D V D D N
 CTGTTAGAAAGTGTCTCGCCCCATTGGGCTGAGCAAAGAAGAGGGACTGATTGAGGAGAGATCAG
 L L E S V I A P L G L S K E E G T D F E E R S
 CTGCCGGTGAATCCCTCCCAGAAAACCGAAGGCAGGGTGCCTGAAACTGTTCTCTGAAAACCTCTCGCA
 A A G E I P P R K P K A G C K L F F W K T F S H
 CTGT TAG TGAGATTGTCAAAGATAAACATTTTAAAAATCCAGTTGTTCTGTTGATATGTAAA
 C -
 CACTTCCCCCCCCCACTGCCCAATTCCCTGCACCCCTCCTCCACTCCCTCCCCCCCCACCC
 CTTCCATACATCAAACGATTGTAATATTCACTGA**AATAAA**ACTGGAAAATAATAGGTGGCTTCTAA
 AAGGCAGCGTAAATGATTACATTAAATAATGGAAATTCTGCAATTAGAATTACAGTGTCTGTGCGT
 TTTTTAAAGGAAAAGAATCTGAATTATTCCATGTTCCCTTAAATCATCGCTGCGCTAAAGAGATGC
 ACAGGTCCCTGCTCAGCGCATCCCGCGAGTGAAGCTCATATCTTAACTCATACCCACAGCCCACAACT
 TTCTGACTCAGAGGCAAGAGTGAACCAACTGAGCCAGACTGACACCTGTGACTAATAGTAATTCTATT
 CAGACATCTTATCACATCTCAAACATCTCAAAGCGATTACACGATATACTGAAAGCGAGTGA
 TTTCAAGAGTGTATTGTCAGTTGAGGGTTGTCAGCCTGGCTAGTCGGTAATGTTCA...

CACTTCCCCCCCCCACTGCCCAATTCCCTGCACCCCTCCTCCACTCCCTCCCCCCCCACCC
 CTTCCATACATCAAACGATTGTAATATTCACTGA**AATAAA**ACTGGAAAATAATAGGTGGCTTCTAA
 AAGGCAGCGTAAATGATTACATTAAATAATGGAAATTCTGCAATTAGAATTACAGTGTCTGTGCGT
 TTTTTAAAGGAAAAGAATCTGAATTATTCCATGTTCCCTTAAATCATCGCTGCGCTAAAGAGATGC
 ACAGGTCCCTGCTCAGCGCATCCCGCGAGTGAAGCTCATATCTTAACTCATACCCACAGCCCACAACT
 TTCTGACTCAGAGGCAAGAGTGAACCAACTGAGCCAGACTGACACCTGTGACTAATAGTAATTCTATT
 CAGACATCTTATCACATCTCAAACATCTCAAAGCGATTACACGATATACTGAAAGCGAGTGA
 TTTCAAGAGTGTATTGTCAGTTGAGGGTTGTCAGCCTGGCTAGTCGGTAATGTTCA...

C. Elephant shark SST3 (Sc_821)

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M Q A R C T L T L A L L S L A A L G L S
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E	L	R	D	G	V	V	R	E	L	I	Q	A	V	A	D	A	E	S						
A	A	C	C	C	A	G	A	G	G	G	A	G	A	G	G	G	G	G						
K	P	Q	S	E	E	A	A	E	D	F	A	P	D	E	K	A	E	L	R	L	A	L	A	
T	C	C	A	G	G	T	G	C	G	G	A	T	T	G	T	G	C	C	A	T	G	C	A	G

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D. Elephant shark SST6 (Sc_58)

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M Q I L V A L I S T L F L V S G V S T T T
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A S L D D R F N L Q S S R
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A. Elephant shark SST1 (SSTa)

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E L A N A E N E A L E A E D M A R A T A
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gaaatacatgtttgaaactgaaa

B. Elephant shark SST2 (SSTd)

atcaaatgcaaggattattatattatattatgttgcacgtcttcccgatgtgaaaagca
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atgttgcatt
cagttatgtttctcatt
gagtgttgcatt
ggaaaagagtcagtggaaagctgcacagatcatttttttttttttttttttttttt
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M Q W Q A F A S V V C L L F I V T V Q G
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V E P Q E E R M G L Q L N R E M V K D K
aaacgcctgatttgcgaagctgtggcggttttttttttttttttttttttttttt
K R L I A K L L A G L L D V D D N L L E
agtgtcatcgccccatt
S V I A P L G L S K E E G T D F E E R S
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A A G E I P P **R K P K A G C K L F F W K**
accccttcgcactgttagtggatttgcataagataaaacattttttttttttttttt
T F S H C -
gttttctgttatgttaaacacttccccccccact

C. Elephant shark SST3 (SSTe)

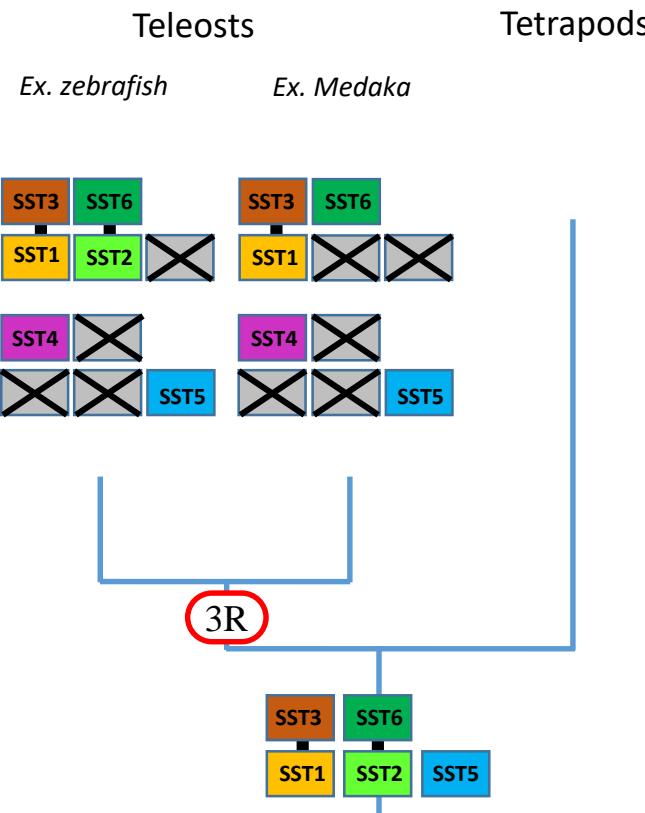
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tcattgtgaattcttaatcaagtgttactgttacg

D. Elephant shark SST6 (SSTc)

cgctctccc
tcactcgccctgtccctgttcctctcgctctcgctcgccctcgctccgctcacacc
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M Q I L V A L I S T L F L V S G V S T T
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T A S L D D R F N L Q S S R E M N Q E R
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K E M I L K L S G L L D N A A V S G Q
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T G S E A G Y P E P A D G G P V M L E E
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R S R Y S Q L P Q R S R K V P C K N F F
tgaaaaacattcacccctgttgcataaacagtagacacccctacaccccccctcc
W K T F T S C -
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Figure S9

A.



B.

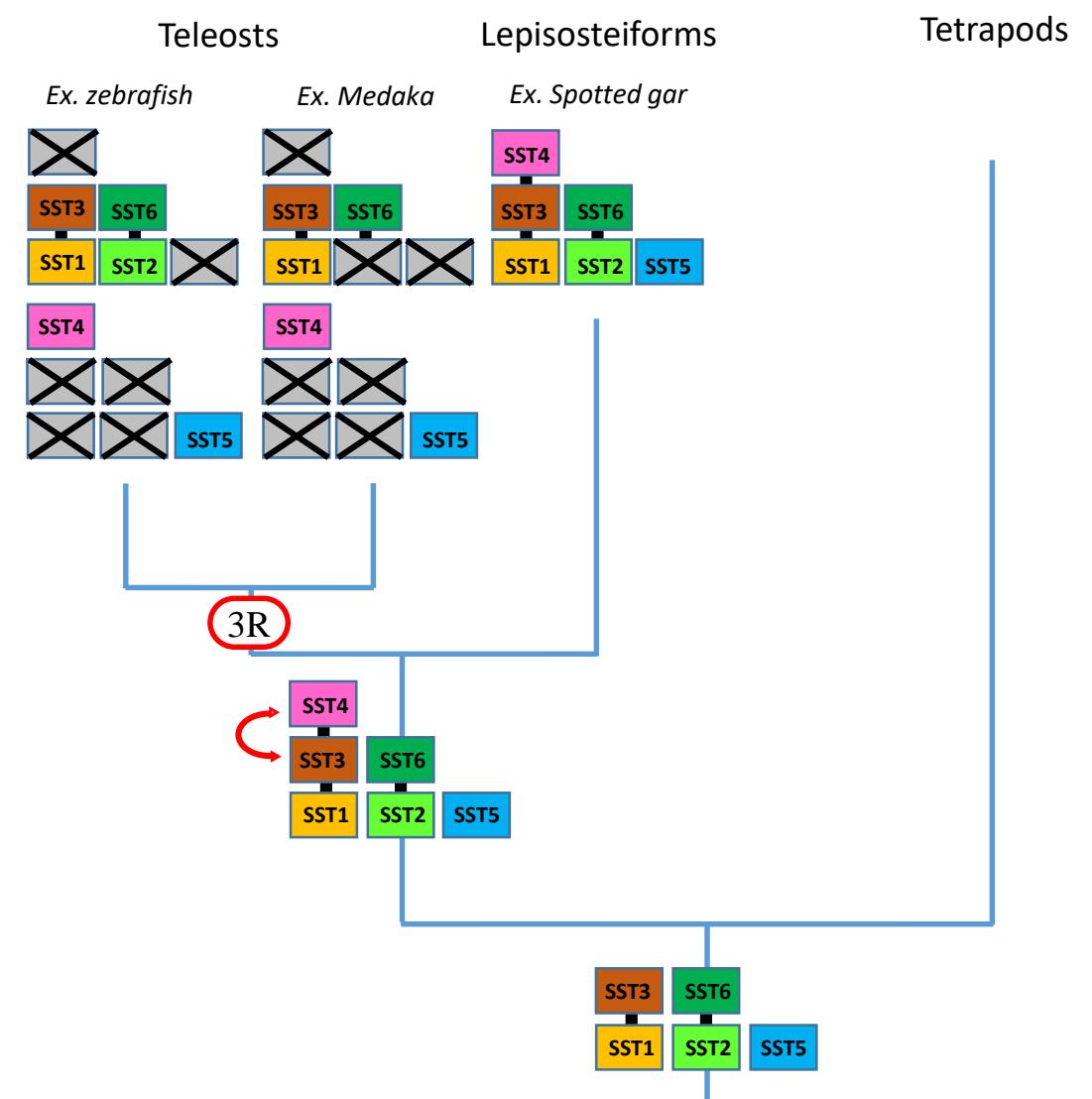


Table S1.

Molecular cloning		
Catshark SST3 (SSTe)	CshSSTe Rev	CAGTGGGATGGAGTCAGTGGGTGCA
	CshSSTe Rev Nest	GGAGTCAGTGGGTGCAGTGGGTAC
Tissue distribution analysis		
Catshark SST2 (SSTd)	CshSSTd For	TTGTCCAGGAGTGCTCGAAGA
	CshSSTd Rev	GTC CTTCTGCCCTTTCTGGT
Catshark SST3 (SSTe)	CshSSTd For	ATGTAGACACTGAGGCCGGAA
	CshSSTd Rev	AGAAGGGCTCACTGGGTACA
Egf1	Egf1 For	CTTCGCTCACCTACCCAAAG
	Egf1 Rev	GGTCAAAC TGCTCCCAGAAG

Table S2

Name	Sequence	Species
SST1	AGCKNFFWK TFTSC	<i>Most vertebrates, including catshark (SSTa)</i>
	AGCKSFFWK TFTSC	<i>Elephant shark, ratfish (SSTa)</i>
SST2 <small>(*previously known as SST6)</small>	MPCRN FFWK TFTSSCK	<i>Human</i>
	PCKN FFWK TFTSSCK	<i>Mouse, rat</i>
	TPCKN FFWK TFTSSCK	<i>Bovine, monkey</i>
	TPCGN FFWK TFTSSCK	<i>Pig</i>
	APCKN FFWK TFTMC	<i>Frog</i>
	APCKN FFWK TFTSSC	<i>Anolis</i>
	APCRN FFWK TFTSSC	<i>Coelacanth</i>
	SPCTN FFWK TFTSAC	<i>Mexican tetra*</i>
	SPCKN FFWK TFTSAC	<i>Piranha*</i>
	TPCKN FFWK TFTSSC	<i>Spotted gar*</i>
	SPCKL FFWK TFTSSC	<i>Zebrafish*</i>
	SPCKN FFWK TFTSSC	<i>Herring*</i>
	APCKL FFWK TFTSHC	<i>Whale shark, skate (SSTd)</i>
	TPCKL FFWK TFTSHC	<i>Catshark (SSTd)</i>
	AGCKL FFWK TFTSHC	<i>Elephant shark (SSTd)</i>
SST3	AGCK NFYWKGF TSC	<i>Most teleosts</i>
	AGCK NFYWKGLT SC	<i>Tilapia</i>
	AGCK NFYWKGP TSC	<i>Takifugu</i>
	DGCK NFYWKGF TSC	<i>Medaka</i>
	AGCRN FYWK TFTSC	<i>Spotted gar</i>
	SGCK NFFWKGR TSC	<i>Herring</i>
	NCK NFWKTY TLC	<i>Whale shark, catshark (SSTE)</i>
	DCK NFFWKTY TLC	<i>Elephant shark (SSTE)</i>
SST4	FGCRVP FWKSWSPC	<i>Stickleback</i>
	PCRVF YWKSWAKC	<i>Medaka</i>
	QFGCRM FFWKSWTYC	<i>Takifugu</i>
	QAGCRIFF WKSRTAC	<i>Tetraodon</i>
	TGCKNYF WKSRTAC	<i>Zebrafish</i>
	PLNCMNYF WKSRTAC	<i>Catfish</i>
SST5	A GCRNF FWKTFTSC	<i>Most actinopterygians</i>
	A GCRNF FWKSYTSC	<i>Tetraodon</i>
	T GCRNF FWKTFTSC	<i>Piranha, mexican tetra*</i>
	A GCRNF YWK TFTSC	<i>Zebrafish</i>
	A GCKNF FWKTFTSC	<i>Coelacanth, catshark (SSTb)</i>
SST6 <small>(*previously known as SST2)</small>	APC KNFFWK TFTSC	<i>Chicken*, lungfish*, coelacanth*, actinopterygians*, catshark (SSTc)*</i>
	TSC KNFFWK TFTSC	<i>Whale shark (SSTc)</i>
	VPC KNFFWK TFTSC	<i>Elephant shark (SSTc)</i>
Others		
SSTa	AGCKNFF WKTFTSC	<i>Lampreys</i>
SSTb	AGCKNFF WKTFTSSC	
SSTc	ANCRM FYWKTMAAC	

Table S3

SST1 (SSTA)	Csh	Wsh	Esh
Catshark		66.37	73.45
Whale shark			74.14
Elephant shark			

SST2 (SSTc)	Csh	Wsh	Sk	Esh
Catshark		76.0	62.03	58.1
Whale shark			62.82	53.0
Skate				51.9
Elephant shark				

SST3 (SSTE)	Csh	Wsh
Catshark		38.14
Elephant shark		

SST6 (SSTc)	Csh	Wsh	Esh
Catshark		86.79	58.65
Whale shark			53.85
Elephant shark			

Table S4

Gene	Designation	Species	Ensembl ID	Chromosome location	Position (Mb)
Mb21d2	Mab-21 domain containing 2	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000180611	3	192,796,815 - 192,918,161
		<i>G. Gallus</i>	ENSGALG0000007218	9	13,300,318 - 13,348,379
		<i>X. tropicalis</i>	ENSXETG0000002143	GL172717.1	276,595 - 277,885
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000017891	JH126687.1	2,299,815 - 2,301,095
		<i>L. ocellatus</i>	ENSLOCG0000009364	LG14	18,861,293 - 18,899,827
		<i>D. rerio</i>	ENSDARG00000072316	15	45,527,281 - 45,538,773
		<i>O. latipes</i>	ENSDARG00000077690	2	5,563,077 - 5,581,772
Fgf12	Fibroblast growth factor 12	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000114279	3	192,139,395 - 192,767,764
		<i>G. Gallus</i>	ENSGALG00000036971	9	13,369,379 - 13,357,972
		<i>X. tropicalis</i>	ENSXETG0000002144	GL172717.1	393,831 - 321,960
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000017275	JH126687.1	2,003,413 - 2,281,293
		<i>L. ocellatus</i>	ENSLOCG0000009371	LG14	18,996,717 - 19,055,669
		<i>D. rerio</i>	ENSDARG00000113525	15	45,414,883 - 45,510,977
Il1rap	Interleukin 1 receptor accessory protein	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000196083	3	190,514,051 - 190,659,750
		<i>G. Gallus</i>	ENSGALG0000007253	9	13,905,510 - 13,926,442
		<i>X. tropicalis</i>	ENSXETG0000015044	GL172717.1	998,488 - 1,097,171
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000016241	JH126687.1	1,498,996 - 1,521,109
		<i>L. ocellatus</i>	ENSLOCG00000093978	LG14	19,120,504 - 19,150,963
		<i>D. rerio</i>	ENSDARG00000114719	15	45,338,623 - 45,356,635
Gmc	Geminin coiled-coil domain containing	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000205835	3	190,852,877 - 190,892,420
		<i>G. Gallus</i>	ENSGALG00000069097	9	13,833,476 - 13,857,367
		<i>X. tropicalis</i>	ENSXETG0000026307	GL172717.1	524,087 - 836,733
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000016600	JH126687.1	1,636,912 - 1,645,473
		<i>L. ocellatus</i>	ENSLOCG00000093976	LG14	19,190,052 - 19,196,340
		<i>D. rerio</i>	ENSDARG0000068719	15	36,309,070 - 36,316,825
Ostn	Osteocrin	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000188729	3	191,199,241 - 191,265,619
		<i>G. Gallus</i>	ENSGALG0000007226	9	13,761,297 - 13,772,476
		<i>X. tropicalis</i>	ENSXETG0000015042	GL172717.1	750,574 - 755,484
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000016886	JH126687.1	1,792,819 - 1,800,129
		<i>L. ocellatus</i>	ENSLOCG0000009421	LG14	19,280,012 - 19,292,855
		<i>D. rerio</i>	ENSDARG0000054055	15	36,228,835 - 36,249,087
Masp1	Mannan binding lectin serine peptidase 1	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000127241	3	187,217,285 - 187,292,022
		<i>G. Gallus</i>	ENSGALG00000074749	9	14,910,364 - 14,937,972
		<i>X. tropicalis</i>	ENSXETG00000197257	GL172717.1	2,406,583 - 2,454,003
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG0000006732	GL343730.1	51,210 - 227,647
		<i>L. ocellatus</i>	ENSLOCG0000003574	JH127453.1	88,278 - 90,189
		<i>D. rerio</i>	ENSDARG00000040799	15	36,156,986 - 36,158,851
SST1	Somatostatin 1	<i>R. typhus</i>	NW_025059721.1	NW_018059766	122,914 - 124,407
		<i>C. mili</i>	NW_007912355.1	Sc_821	1,008 - 5,116
		<i>H. sapiens</i>	ENSG00000157095	3	187,668,906 - 187,620,390
		<i>G. Gallus</i>	ENSGALG00000073651	9	14,852,386 - 14,853,973
		<i>X. tropicalis</i>	ENSXETG0000019777	GL172717.1	2,228,041 - 2,229,578
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG0000006732	GL343730.1	4,342 - 23,375
		<i>L. ocellatus</i>	ENSLOCG0000009439	LG14	19,404,762 - 19,407,399
		<i>D. rerio</i>	ENSDARG00000040799	15	36,156,986 - 36,158,851
SST3	Somatostatin 3	<i>R. typhus</i>	NW_025059741.1	NW_018059766	131,098 - 130,771
		<i>C. mili</i>	NW_007912356.1	Sc_821	1,287 - 22,446
		<i>H. sapiens</i>			
		<i>G. Gallus</i>			
		<i>X. tropicalis</i>			
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLOCG0000009445	LG14	19,441,987 - 19,443,409
		<i>L. ocellatus</i>	ENSDARG0000033161	15	36,115,955 - 36,120,277
		<i>D. rerio</i>	ENSOIRLG0000019158	scaffold660	8,674 - 10,556
Col4a3	Collagen type IV alpha 3 chain	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000169031	2	227,164,565 - 227,314,792
		<i>G. Gallus</i>	ENSGALG0000038612	9	9,384,943 - 9,430,089
		<i>X. tropicalis</i>			
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG0000004217	3	23,464,166 - 23,573,541
		<i>L. ocellatus</i>	ENSLACG00000099918	JH126709.1	458,799 - 567,615
		<i>D. rerio</i>	ENSLOCG0000009454	LG14	19,454,926 - 19,507,683
Col4a4	Collagen type IV alpha 4 chain	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000081052	2	227,002,711 - 227,164,453
		<i>G. Gallus</i>	ENSGALG0000004946	9	9,318,986 - 9,370,173
		<i>X. tropicalis</i>			
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000033770	3	23,583,599 - 23,670,714
		<i>L. ocellatus</i>	ENSLACG00000012078	JH126709.1	673,429 - 787,527
		<i>D. rerio</i>	ENSLOCG00000094945	LG14	19,522,370 - 19,590,210
Rhbdd1	Rhomboid domain containing 1	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000144468	2	226,835,581 - 226,999,215
		<i>G. Gallus</i>	ENSGALG0000004957	9	9,276,974 - 9,300,051
		<i>X. tropicalis</i>	ENSXETG00000020088	GL172898.1	477,735 - 505,838
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG00000038287	3	23,670,816 - 23,710,982
		<i>L. ocellatus</i>	ENSLACG00000013155	JH126709.1	816,263 - 961,971
		<i>D. rerio</i>	ENSLOCG00000095054	LG14	19,592,741 - 19,635,912
Irs1	Insulin receptor substrate 1	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000169047	2	226,731,317 - 226,799,759
		<i>G. Gallus</i>	ENSGALG0000004959	9	9,244,127 - 9,248,424
		<i>X. tropicalis</i>	ENSXETG0000020086	GL172898.1	560,083 - 563,337
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG0000003830	3	23,742,830 - 23,746,420
		<i>L. ocellatus</i>	ENSLACG00000014111	JH126709.1	963,541 - 1,032,531
		<i>D. rerio</i>	ENSLOCG0000004087	LG14	19,644,120 - 19,647,556
SST4	Somatostatin 4	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>			
		<i>G. Gallus</i>			
		<i>X. tropicalis</i>			
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLOCG0000009520	LG14	19,696,596 - 19,698,886
		<i>L. ocellatus</i>	ENSDARG0000014190	2	5,726,381 - 5,728,843
		<i>D. rerio</i>	ENSDARG00000054087	15	35,888,549 - 35,930,070
Nyap2b	Neuronal tyrosine-phosphorylated phosphoinositide-3-kinase adaptor Z	<i>R. typhus</i>			
		<i>C. mili</i>			
		<i>H. sapiens</i>	ENSG00000144460	2	225,399,710 - 225,654,018
		<i>G. Gallus</i>	ENSGALG0000004946	9	8,727,389 - 8,844,775
		<i>X. tropicalis</i>	ENSXETG0000005150	GL172898.1	945,276 - 992,671
		<i>A. carolinensis</i>			
		<i>L. chalumnae</i>	ENSLACG0000003843	2	24,114,255 - 24,276,004
		<i>L. ocellatus</i>	ENSLACG00000029528	JH126709.1	1,040,760 - 1,041,760
		<i>D. rerio</i>	ENSDARG00000079581	LG14	19,921,041 - 19,971,639
		<i>O. latipes</i>	ENSDARG0000003357	2	35,698,508 - 35,895,161
		<i>R. typhus</i>	ENSOIRLG0000001604	17	24,738,491 - 24,749,441