

**Evolutionary history of DNA methylation related genes in chordates: new insights from multiple whole genome duplications**

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**Supplementary Information**

**Supplemental Table S1.** Percentage Identity Matrix between tetrapod and lamprey/ciona dnmt3 proteins

	ciona savignyi (ENSCSAVP00000200)	ciona savignyi (ENSCSAVG0000031)	chicken dnmt3b	human dnmt3b	mouse dnmt3b	lamprey (ENSPMA T0000000 8525)	lamprey (ENSPMAT 00000007 628)	lamprey (gi 1304 463388  )	chicken dnmt3a	human dnmt3a	mouse dnmt3a
ciona savignyi (ENSCSAVP00000200)	100.00										
ciona savignyi (ENSCSAVG0000031)	48.89	100.00									
chicken dnmt3b	41.19	52.43	100.00								
human dnmt3b	41.48	52.06	62.77	100.00							
mouse dnmt3b	42.36	50.94	60.88	84.07	100.00						
lamprey (ENSPMAT00000008525)	40.07	51.24	55.22	55.94	55.25	100.00					
lamprey (ENSPMAT00000007628)	45.91	56.10	61.39	63.61	61.93	67.20	100.00				
lamprey (gi 1304463388 )	49.50	53.56	66.14	70.58	69.58	68.56	72.06	100.00			
chicken dnmt3a	42.58	52.26	47.66	51.71	51.28	64.27	71.94	75.15	100.00		
human dnmt3a	42.83	53.56	48.01	49.82	49.52	64.69	72.49	75.75	83.37	100.00	
mouse dnmt3a	42.67	53.56	47.94	50.12	49.94	64.69	72.49	75.75	84.06	96.15	100.00

**Supplemental Table S2.** Annotation, location, primer sequences and accession number of DNA methylation toolkit in rainbow trout

Gene	Scaffold No. in Genomicus	Chromosome No. in NCBI	Forward Primer(5'-3')	Reverse Primer (5'-3')	NCBI Accession No.
<i>dnmt1a</i>	scaffold_644	chr.12	AACCGTTTCACAGAGGACACG	GCAGGGGGTGACGATGATC	XM_021557911.1
<i>dnmt1b</i>	scaffold_1433	chr.13	ATACCTCCTGTCTCTGCCG	CTGCTGAGCTGGTCCTGG	XM_021625236.1
<i>dnmt3aa</i>	scaffold_4646	chr.8	AATTTGAGGCAGCCAGGTTG	CGATCCCCACGGTGATAGAA	XM_021614345.1
<i>dnmt3ab1</i>	scaffold_7288	chr.25	TGGCACCAGAAGAGAAATCCT	CATGACTCCATTCTGCACCTG	XM_021585300.1
<i>dnmt3ab2</i>	scaffold_64	chr.19	GTGTGCGAGGACTCCGTC	CCTAGCCGGGTTGACAATAGAG	XM_021573815.1
<i>dnmt3ba1</i>	scaffold_5272	chr.16	CAAGGGTTTTGGCATTGGAGA	ACCTCAGAGAACTTGCCATCA	XM_021566506.1
<i>dnmt3ba2</i>	scaffold_78452	chr.9	ACAAGGGTTTTGGTATTGGGGA	AGCAGACACCTCAGAGAACTT	XM_021615717.1
<i>dnmt3bba1</i>	scaffold_3846	chr.16	GGCGATGGAACCTTTGACAAG	TGGGCAGGAATGGAGGGATA	XM_021567210.1
<i>dnmt3bba2</i>	scaffold_384	chr.9	GGCGATGGAACCTTTAAGCAA	CGAGGGCACTGTTGTTGATG	XM_021616487.1
<i>dnmt3bbb</i>	scaffold_1281	chr.16	AGGACCATCACCAACCAACC	TCTGCTGGCGATTCATGTTCT	XM_021566510.1
<i>tet1a</i>	scaffold_18888 & 2097	chr.1	CAGTGGCCAGACAAGCTCA	GCCTTCGCCCTGTTATGT	XM_021614130.1
<i>tet1b</i>	scaffold_189 & 12473	chr.23	GGCTGACAAACAAGCTGCAA	CACCCACATTCCTGGTCTGT	XM_021580846.1
<i>tet2a/b-glob</i>	scaffold_1163	chr.19	GCTCCATCCTCATCGAGTGT	TCCTTCTCCCGTTGCTTCTC	XM_021573348.1 &XM_021573351.1
<i>tet2c</i>	/	chr.10	AAGAAGCTGAAATCCCCTGGG	CTGCTGCTGTGTCTCCATGAT	XM_021617281.1
<i>tet3a</i>	scaffold_21498 & 36080	chr.6	CAGCACTGCCCTATAGCTACT	GAGTAGGAGTGAGCCAGCC	XM_021606330.1
<i>tet3b</i>	scaffold_605	chr.11	GGCAGGTACACAGTCTCAA	GGGCACACTCGATCAGGATA	XM_021621924.1
<i>tdgaa</i>	scaffold2682	chr.4	GCAGCCACACAAGATACCTG	ACTCCTGAATGTCGTCCGTT	XM_021598712.1
<i>tdgab</i>	scaffold_82	chr.2	GTCAAGAAGAAAAGGGACCGC	GAATCCGGACAAGAACAGGC	XM_021566210.1
<i>tdgba</i>	scaffold_2682	chr.4	CGTTTGACAGACCAGATACCG	ATGGGCCATTTCTCCTCCAT	XM_021598711.1
<i>tdgbb</i>	scaffold_82	chr.2	CATAACACAGGTCATATGGGC	CTCTCTTCTCTCCCTGGCA	XM_021566172.1

**Supplemental Table S3.** Primer sequences of reference genes

Reference gene	Forward Primer(5'-3')	Reverse Primer (5'-3')
<i>luciferase</i>	CATTCTTCGCCAAAAGCACTCTG	AGCCCATATCCTTGTCGTATCCC
<i><math>\beta</math>-actin</i>	GATGGGCCAGAAAGACAGCTA	TCGTCCCAGTTGGTGACGAT
<i>ef1a</i>	TCCTCTTGGTCGTTTCGCTG	ACCCGAGGGACATCCTGTG
<i>18s rRNA</i>	CGGAGGTTCGAAGACGATCA	TCGCTAGTTGGCATCGTTTAT
<i>rps16</i>	TTTCAGGTGGCGAAACATGC	GGGGTCTGCCATTCACCTTG
<i>rpl27</i>	CACAACCATGGGCAAGAAGA	TCAGGGCAGGGTCTCTGAAG

**Supplemental Table S4.** The mRNA levels of DNA methylation genes during oogenesis in trout

Gene	Oogenesis								p value
	Feb.		May		Sep.		Nov.		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
<i>dnmt1a</i>	2.81	2.04	1.19	1.42	0.35	0.43	3.54	4.70	0.109
<i>dnmt1b</i>	1.86 <sup>b</sup>	0.19	1.65 <sup>b</sup>	0.35	0.79 <sup>a</sup>	0.23	4.21 <sup>c</sup>	0.75	< 0.001
<i>dnmt3aa</i>	1.24	0.77	1.51	0.47	1.05	0.29	0.88	0.48	0.173
<i>dnmt3ab1</i>	0.55	0.18	0.62	0.22	0.88	0.25	1.97	4.46	0.043
<i>dnmt3ab2</i>	1.27	0.39	1.12	0.23	0.83	0.15	1.30	0.93	0.093
<i>dnmt3ba1</i>	1.42 <sup>b</sup>	0.33	1.38 <sup>b</sup>	0.13	0.63 <sup>a</sup>	0.16	4.60 <sup>c</sup>	1.48	< 0.001
<i>dnmt3ba2</i>	0.76 <sup>b</sup>	0.14	0.96 <sup>b</sup>	0.16	0.40 <sup>a</sup>	0.09	0.29 <sup>a</sup>	0.14	< 0.001
<i>dnmt3bba1</i>	0.60	0.31	0.52	0.33	0.52	0.33	0.84	0.71	0.749
<i>dnmt3bba2</i>	2.09 <sup>b</sup>	0.06	1.72 <sup>b</sup>	0.30	0.74 <sup>a</sup>	0.24	3.39 <sup>c</sup>	0.50	< 0.001
<i>dnmt3bbb</i>	1.87 <sup>b</sup>	0.32	1.77 <sup>b</sup>	0.43	0.67 <sup>a</sup>	0.20	5.54 <sup>b</sup>	1.78	< 0.001
<i>tet1a</i>	0.56	0.14	0.61	0.13	0.72	0.11	0.56	0.21	0.139
<i>tet1b</i>	0.85	0.27	0.70	0.20	0.98	0.27	0.54	0.55	0.108
<i>tet2a&amp;b</i>	0.83 <sup>a</sup>	0.14	1.47 <sup>b</sup>	0.44	1.74 <sup>b</sup>	0.28	1.70 <sup>ab</sup>	2.87	0.010
<i>tet2c</i>	0.40	0.47	0.55	0.62	1.12	1.32	4.38	6.69	0.609
<i>tet3a</i>	0.70 <sup>ab</sup>	0.14	0.82 <sup>bc</sup>	0.17	1.52 <sup>c</sup>	0.38	0.27 <sup>a</sup>	0.18	< 0.001
<i>tet3b</i>	0.92	0.15	1.16	0.24	0.81	0.12	1.77	0.72	0.004
<i>tdgaa</i>	1.69 <sup>b</sup>	0.26	1.46 <sup>b</sup>	0.28	0.65 <sup>a</sup>	0.12	6.55 <sup>c</sup>	0.90	< 0.001
<i>tdgab</i>	1.51 <sup>ab</sup>	0.51	1.22 <sup>b</sup>	0.21	0.77 <sup>a</sup>	0.13	5.75 <sup>c</sup>	2.00	< 0.001
<i>tdgba</i>	1.24 <sup>b</sup>	0.16	1.43 <sup>b</sup>	0.43	0.66 <sup>a</sup>	0.17	7.16 <sup>c</sup>	2.33	< 0.001
<i>tdgbb</i>	1.88 <sup>b</sup>	0.44	1.76 <sup>b</sup>	0.21	0.74 <sup>a</sup>	0.15	10.65 <sup>c</sup>	2.98	< 0.001

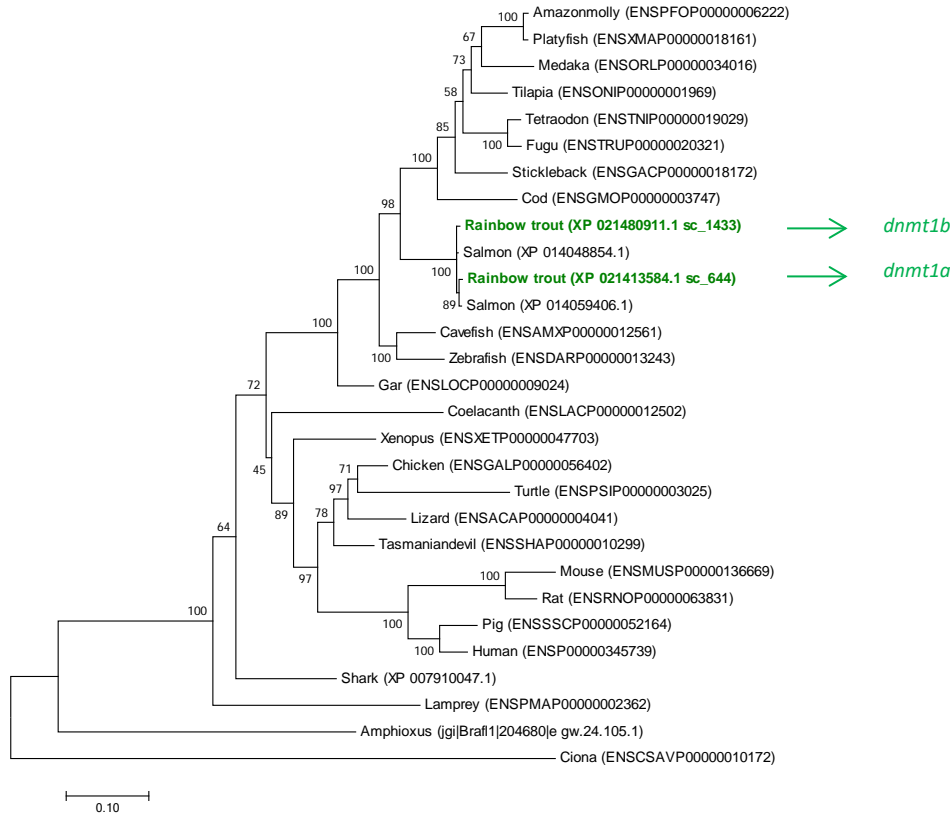
**Supplemental Table S5.** The mRNA levels of DNA methylation genes during spermatogenesis in trout

Gene	Feb.		May		Sep.		Nov.		<i>p</i> value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
<i>dnmt1a</i>	0.39	0.61	0.07	0.10	1.23	1.46	0.18	0.19	0.354
<i>dnmt1b</i>	0.76 <sup>ab</sup>	0.86	0.16 <sup>a</sup>	0.03	1.04 <sup>b</sup>	0.39	0.26 <sup>a</sup>	0.07	0.007
<i>dnmt3aa</i>	0.68	0.29	0.69	0.48	0.50	0.22	0.54	0.22	0.594
<i>dnmt3ab1</i>	1.87 <sup>ab</sup>	1.47	2.71 <sup>b</sup>	1.17	0.50 <sup>a</sup>	0.16	2.13 <sup>b</sup>	0.95	0.010
<i>dnmt3ab2</i>	0.60	0.26	0.58	0.34	0.42	0.13	0.80	0.23	0.053
<i>dnmt3ba1</i>	0.69	0.52	0.61	0.24	0.41	0.35	1.53	0.73	0.005
<i>dnmt3ba2</i>	1.46	1.26	0.71	0.42	0.87	0.71	2.54	1.17	0.033
<i>dnmt3bba1</i>	1.86 <sup>ab</sup>	1.61	1.36 <sup>ab</sup>	1.15	0.28 <sup>a</sup>	0.25	2.81 <sup>b</sup>	0.59	0.007
<i>dnmt3bba2</i>	0.15	0.07	0.24	0.08	0.24	0.04	0.30	0.14	0.059
<i>dnmt3bbb</i>	0.01	0.01	0.01	0.00	0.00	0.00	0.01	0.00	0.030
<i>tet1a</i>	1.04 <sup>ab</sup>	0.46	1.63 <sup>ab</sup>	0.99	0.75 <sup>a</sup>	0.10	2.20 <sup>b</sup>	0.72	0.013
<i>tet1b</i>	1.12 <sup>ab</sup>	0.79	1.35 <sup>ab</sup>	0.66	0.37 <sup>a</sup>	0.20	1.67 <sup>b</sup>	0.46	0.018
<i>tet2a&amp;b</i>	0.76	0.64	0.98	0.69	0.28	0.13	0.82	0.27	0.101
<i>tet2c</i>	1.92	3.30	0.82	1.15	0.26	0.20	0.67	0.58	0.604
<i>tet3a</i>	0.64	0.33	1.48	1.21	0.34	0.15	1.42	0.59	0.018
<i>tet3b</i>	0.24	0.13	0.49	0.39	0.10	0.06	0.38	0.20	0.040
<i>tdgaa</i>	0.16 <sup>ab</sup>	0.11	0.10 <sup>ab</sup>	0.10	0.38 <sup>b</sup>	0.13	0.06 <sup>a</sup>	0.02	0.006
<i>tdgab</i>	0.81 <sup>ab</sup>	0.64	0.31 <sup>a</sup>	0.14	1.48 <sup>b</sup>	0.41	0.31 <sup>a</sup>	0.08	0.009
<i>tdgba</i>	0.20	0.11	0.16	0.04	0.33	0.12	0.20	0.09	0.102
<i>tdgbb</i>	0.12	0.03	0.09	0.03	0.15	0.05	0.17	0.04	0.013

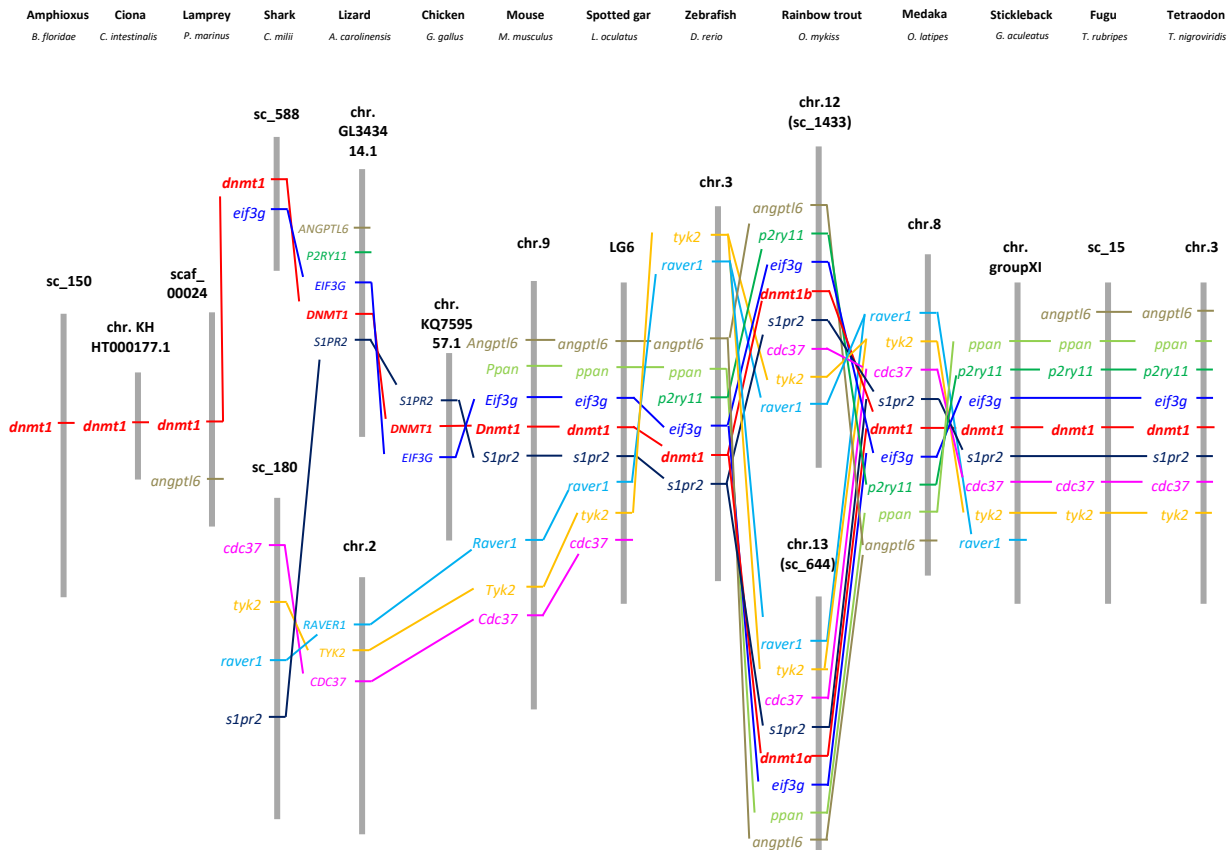
**Supplemental Table S6.** The mRNA levels of DNA methylation genes during ontogenesis in trout

Gene	oocyte		stage5		stage6		stage7		stage8		stage10		stage12		stage15		stage22		stage23		stage31		p value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
<i>dnmt1a</i>	1.28 <sup>abc</sup>	2.22	0.15 <sup>a</sup>	0.16	0.46 <sup>ab</sup>	0.50	0.40 <sup>ab</sup>	0.59	0.13 <sup>a</sup>	0.12	0.38 <sup>ab</sup>	0.48	0.89 <sup>bc</sup>	0.58	1.59 <sup>c</sup>	0.31	17.82 <sup>de</sup>	5.50	23.12 <sup>e</sup>	4.97	4.56 <sup>abcd</sup>	5.68	3.9E-09
<i>dnmt1b</i>	2.00 <sup>b</sup>	0.80	3.51 <sup>c</sup>	0.22	2.24 <sup>bc</sup>	1.42	1.58 <sup>ab</sup>	0.93	1.31 <sup>ab</sup>	1.24	0.49 <sup>a</sup>	0.25	1.10 <sup>ab</sup>	1.06	1.83 <sup>ab</sup>	0.92	12.34 <sup>de</sup>	7.57	19.02 <sup>e</sup>	4.84	2.85 <sup>bcd</sup>	2.19	1.2E-09
<i>dnmt3aa</i>	0.04 <sup>ab</sup>	0.02	0.04 <sup>ab</sup>	0.04	0.02 <sup>ab</sup>	0.02	0.01 <sup>a</sup>	0.01	0.03 <sup>ab</sup>	0.05	0.02 <sup>a</sup>	0.01	0.04 <sup>ab</sup>	0.05	0.08 <sup>b</sup>	0.05	1.70 <sup>c</sup>	1.11	2.84 <sup>c</sup>	0.77	2.81 <sup>c</sup>	2.08	4.5E-05
<i>dnmt3ab1</i>	0.31 <sup>a</sup>	0.04	0.27 <sup>a</sup>	0.09	0.14 <sup>a</sup>	0.05	0.17 <sup>a</sup>	0.08	0.17 <sup>b</sup>	0.15	0.18 <sup>b</sup>	0.07	1.06 <sup>c</sup>	0.99	2.00 <sup>c</sup>	0.97	10.49 <sup>d</sup>	7.12	16.41 <sup>d</sup>	4.92	7.77 <sup>cd</sup>	6.40	2.3E-05
<i>dnmt3ab2</i>	0.03 <sup>ab</sup>	0.01	0.15 <sup>b</sup>	0.07	0.06 <sup>ab</sup>	0.08	0.04 <sup>a</sup>	0.03	0.08 <sup>ab</sup>	0.09	0.10 <sup>ab</sup>	0.02	0.75 <sup>bc</sup>	0.72	1.55 <sup>c</sup>	0.68	12.52 <sup>d</sup>	8.61	22.46 <sup>d</sup>	5.83	8.55 <sup>d</sup>	6.91	1.0E-05
<i>dnmt3ba1</i>	0.18 <sup>b</sup>	0.03	0.28 <sup>c</sup>	0.05	0.22 <sup>abcd</sup>	0.18	0.08 <sup>a</sup>	0.05	0.18 <sup>abcd</sup>	0.20	0.09 <sup>ab</sup>	0.05	0.25 <sup>bc</sup>	0.13	0.61 <sup>de</sup>	0.22	6.11 <sup>f</sup>	4.69	8.90 <sup>f</sup>	1.97	2.68 <sup>ef</sup>	2.29	1.5E-05
<i>dnmt3ba2</i>	0.01 <sup>a</sup>	0.01	0.00 <sup>a</sup>	0.00	0.00 <sup>a</sup>	0.01	0.00 <sup>a</sup>	0.00	0.02 <sup>a</sup>	0.01	0.04 <sup>b</sup>	0.01	0.51 <sup>c</sup>	0.48	1.80 <sup>c</sup>	1.10	12.73 <sup>de</sup>	9.44	18.62 <sup>e</sup>	1.55	2.96 <sup>cd</sup>	2.49	1.4E-05
<i>dnmt3bba1</i>	0.03 <sup>ab</sup>	0.02	0.06 <sup>b</sup>	0.01	0.02 <sup>a</sup>	0.02	0.03 <sup>ab</sup>	0.03	0.02 <sup>a</sup>	0.01	0.03 <sup>a</sup>	0.01	0.92 <sup>c</sup>	0.78	2.46 <sup>c</sup>	1.38	20.49 <sup>d</sup>	15.13	26.99 <sup>d</sup>	7.90	3.12 <sup>c</sup>	2.23	1.4E-05
<i>dnmt3bba2</i>	0.84 <sup>ab</sup>	0.38	1.25 <sup>b</sup>	0.26	0.63 <sup>ab</sup>	0.45	0.55 <sup>a</sup>	0.35	0.77 <sup>ab</sup>	0.73	0.78 <sup>ab</sup>	0.33	5.46 <sup>bc</sup>	5.18	5.60 <sup>c</sup>	2.92	16.00 <sup>cd</sup>	10.87	20.80 <sup>d</sup>	3.96	3.15 <sup>bc</sup>	2.39	3.7E-04
<i>dnmt3bbb</i>	4.08 <sup>ab</sup>	2.87	7.28 <sup>bc</sup>	1.83	3.29 <sup>ab</sup>	2.52	3.20 <sup>ab</sup>	2.44	4.76 <sup>abc</sup>	4.83	2.90 <sup>a</sup>	1.52	5.17 <sup>abc</sup>	5.51	4.40 <sup>ab</sup>	2.59	14.60 <sup>cd</sup>	10.13	19.31 <sup>d</sup>	4.01	2.15 <sup>a</sup>	1.59	1.5E-02
<i>tet1a</i>	0.02 <sup>a</sup>	0.01	0.02 <sup>a</sup>	0.01	0.01 <sup>a</sup>	0.01	0.01 <sup>a</sup>	0.01	0.02 <sup>a</sup>	0.02	0.03 <sup>a</sup>	0.01	0.16 <sup>b</sup>	0.13	0.37 <sup>b</sup>	0.14	5.34 <sup>cd</sup>	3.31	7.98 <sup>d</sup>	1.80	2.26 <sup>c</sup>	1.74	7.6E-06
<i>tet1b</i>	0.02 <sup>ab</sup>	0.01	0.02 <sup>ab</sup>	0.01	0.01 <sup>a</sup>	0.01	0.01 <sup>ab</sup>	0.01	0.02 <sup>ab</sup>	0.01	0.02 <sup>b</sup>	0.00	0.10 <sup>c</sup>	0.09	0.30 <sup>c</sup>	0.17	5.07 <sup>d</sup>	3.10	8.40 <sup>d</sup>	1.96	2.66 <sup>d</sup>	2.05	8.2E-06
<i>tet2a&amp;b</i>	0.01 <sup>ab</sup>	0.02	0.00 <sup>a</sup>	0.00	0.00 <sup>a</sup>	0.01	0.01 <sup>ab</sup>	0.01	0.02 <sup>b</sup>	0.00	0.05 <sup>c</sup>	0.01	0.24 <sup>d</sup>	0.09	0.48 <sup>d</sup>	0.15	6.59 <sup>ef</sup>	4.88	11.28 <sup>f</sup>	2.75	2.88 <sup>e</sup>	2.21	5.9E-06
<i>tet2c</i>	0.02 <sup>abc</sup>	0.03	0.00 <sup>a</sup>	0.00	0.00 <sup>a</sup>	0.00	0.01 <sup>ab</sup>	0.02	0.01 <sup>ab</sup>	0.02	0.08 <sup>abc</sup>	0.05	0.11 <sup>abc</sup>	0.12	0.54 <sup>c</sup>	0.57	10.14 <sup>d</sup>	9.69	5.97 <sup>d</sup>	6.05	4.08 <sup>bcd</sup>	6.08	1.9E-02
<i>tet3a</i>	0.01 <sup>a</sup>	0.00	0.01 <sup>a</sup>	0.01	0.01 <sup>a</sup>	0.01	0.01 <sup>a</sup>	0.01	0.02 <sup>ab</sup>	0.03	0.01 <sup>a</sup>	0.01	0.08 <sup>b</sup>	0.03	0.20 <sup>c</sup>	0.08	6.63 <sup>d</sup>	4.73	10.00 <sup>d</sup>	2.68	3.02 <sup>d</sup>	2.40	1.2E-05
<i>tet3b</i>	0.17 <sup>a</sup>	0.09	0.21 <sup>a</sup>	0.04	0.19 <sup>a</sup>	0.15	0.11 <sup>a</sup>	0.09	0.38 <sup>ab</sup>	0.30	0.17 <sup>a</sup>	0.10	0.83 <sup>bc</sup>	0.27	1.64 <sup>d</sup>	0.57	9.68 <sup>ef</sup>	6.34	16.48 <sup>f</sup>	6.22	3.99 <sup>ede</sup>	3.17	1.9E-05
<i>tdgaa</i>	0.79 <sup>bc</sup>	0.23	1.13 <sup>c</sup>	0.14	0.71 <sup>abc</sup>	0.67	0.54 <sup>ab</sup>	0.32	0.80 <sup>abc</sup>	0.91	0.35 <sup>a</sup>	0.07	0.61 <sup>abc</sup>	0.64	1.32 <sup>bc</sup>	0.72	11.03 <sup>de</sup>	7.63	15.22 <sup>e</sup>	2.71	2.58 <sup>bcd</sup>	2.00	1.2E-03
<i>tdgab</i>	0.32 <sup>bc</sup>	0.13	0.41 <sup>c</sup>	0.02	0.27 <sup>abc</sup>	0.24	0.20 <sup>ab</sup>	0.12	0.25 <sup>abc</sup>	0.24	0.11 <sup>a</sup>	0.01	0.74 <sup>bcd</sup>	0.66	1.83 <sup>d</sup>	1.04	14.45 <sup>ef</sup>	8.98	18.14 <sup>f</sup>	2.59	2.71 <sup>de</sup>	2.18	2.6E-05
<i>tdgba</i>	1.12 <sup>b</sup>	0.56	1.31 <sup>b</sup>	0.51	0.90 <sup>ab</sup>	0.68	0.31 <sup>a</sup>	0.15	0.77 <sup>ab</sup>	0.86	0.39 <sup>a</sup>	0.02	0.45 <sup>ab</sup>	0.34	1.65 <sup>bc</sup>	1.04	4.50 <sup>cd</sup>	3.10	5.39 <sup>d</sup>	2.83	1.15 <sup>abc</sup>	0.90	1.6E-02
<i>tdgbb</i>	1.82 <sup>bc</sup>	0.70	2.27 <sup>c</sup>	0.37	1.43 <sup>abc</sup>	1.14	1.07 <sup>ab</sup>	0.63	1.38 <sup>abc</sup>	1.40	0.57 <sup>a</sup>	0.02	0.89 <sup>ab</sup>	0.80	1.21 <sup>abc</sup>	0.71	6.73 <sup>de</sup>	4.57	10.19 <sup>e</sup>	2.58	2.19 <sup>abcd</sup>	1.72	1.9E-02

**A**



**B**



**Supplementary Fig. S1 *In silico* analysis of *dnmt1* in chrodates.** (A) Phylogenetic of *dnmt1* genes. The phylogenetic trees were built using the Maximum Likelihood method based on the JTT matrix-based model in MEGA7. The tree with the highest log likelihood (-17912.17) is shown. A discrete Gamma distribution was used to model evolutionary rate differences among sites (5 categories (+G, parameter = 0.6612)). The reliability of the inferred trees was estimated by the bootstrap method with 500 replications. All accession numbers are specified in parentheses. (B) Syntenic analysis of *dnmt1* genes. Conserved synteny around the *dnmt1* loci in chrodates. Data were collected with Genomicus software version 01.01, and *dnmt1* genes in rainbow trout were annotated by ourselves according to our phylogenetic analysis following ZFIN nomenclature guidelines. chr., chromosome; sc., scaffold.



10      20      30      40      50      60      70      80

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

```
Tetraodon(ENSTNIP00000019029) -----
Fugu(ENSTRUP00000020321) -----
Tilapia(ENSONIP00000001969) -----MPTRTSLSL
Medaka(ENSORLP00000034016) -----MPSRTLSL
Amazon molly(ENSPFOP0000000622) -----MPSKTSLSL
Platyfish(ENSXMAP00000018161 ) -----MPSKTSLSL
Stickleback(ENSGACP00000018172) -----PFVMPKTSLSL
Cod(ENSGMOP00000003747) -----LFTMPKTSLSL
Salmonlb (XP_014048854.1) -----MPANTLSL
Salmonla(XP_014059406.1) -----MPANTLSL
Troutlb(XP_021480911.1) -----MPANTLSL
Troutla(XP_021413584.1) -----MPANTLSL
Cavefish(ENSAMXP00000012561) -----MPAKTSLSL
Zebrafish(ENSDARP00000013243) -----MPTKTSLSL
Gar(ENSLOCP00000009024) -----MPAKTSLSL
Shark(XP_007910047.1) -----MGDEVKKMPAQTVVVKMEWSGPEGKTLIQPTPCSPQHVFPASSHSPSTTNPYLHHSPTSAPPTCPYRSPFALYLTHITLPT
Coelacanth(ENSLACP00000012502) -----
Xenopus(ENSXETP00000047703) -----LTESVSPLLYTAMPAQSASLAL
Chicken(ENSGALP00000056402) -----
Turtle(ENSPSIP00000003025) -----LPAXMAGGS
Lizard(ENSACAP0000004041) -----MVPSSAGPAPPSSPSPRCARNCSRPPSRSLPTAASLPVCLAGPEMPARAAPLT
Tasmanian devil(ENSSHAP0000001) -----LPATRPQLNPYFTRFSL
Mouse(ENSMUSP000000136669) -----MADSNRPSRSR
Rat(ENSRNOP00000063831) -----MPARTAPARVPALASPAG
Pig(ENSSSCP00000052164) -----MAASRRRRRLG
Human(ENSP000000345739) -----MPARTAPARVPTLAVPAI
Lamprey(ENSPMAP0000002362) -----GHSTWVKL
Ciona(ENSCSAVP00000010172) -----
Amphioxus(jgi|Braf11|204680|e_ -----
```

90      100      110      120      130      140      150      160

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Tetraodon(ENSTNIP00000019029) -----
Fugu(ENSTRUP00000020321) -----
Tilapia(ENSONIP00000001969) -----
Medaka(ENSORLP00000034016) -----
Amazon molly(ENSPFOP0000000622) -----
Platyfish(ENSXMAP00000018161 ) -----
Stickleback(ENSGACP00000018172) -----
Cod(ENSGMOP00000003747) -----
Salmonlb (XP_014048854.1) -----
Salmonla(XP_014059406.1) -----
Troutlb(XP_021480911.1) -----
Troutla(XP_021413584.1) -----
Cavefish(ENSAMXP00000012561) -----
Zebrafish(ENSDARP00000013243) -----
Gar(ENSLOCP00000009024) -----
Shark(XP_007910047.1) -----LVPHCSSTSPASPSPHSPFPAPPPTQLVLLLYLNPPFATPVCLPPVPACSVLSPHTLPPPTLPLQPTCTALPHPLPQ
Coelacanth(ENSLACP00000012502) -----
Xenopus(ENSXETP00000047703) -----
Chicken(ENSGALP00000056402) -----
Turtle(ENSPSIP00000003025) -----
Lizard(ENSACAP0000004041) -----
Tasmanian devil(ENSSHAP0000001) -----
Mouse(ENSMUSP000000136669) -----
Rat(ENSRNOP00000063831) -----SL
Pig(ENSSSCP00000052164) -----
Human(ENSP000000345739) -----SL
Lamprey(ENSPMAP0000002362) -----
Ciona(ENSCSAVP00000010172) -----
Amphioxus(jgi|Braf11|204680|e_ -----
```

**DMAP domain**

170      180      190      200      210      220      230      240

.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|

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Tetraodon(ENSTNIP00000019029) -----
Fugu(ENSTRUP00000020321) -----PED
Tilapia(ENSONIP00000001969) -----PDD
Medaka(ENSORLP00000034016) -----PDD
Amazon molly(ENSPFOP0000000622) -----PDD
Platyfish(ENSXMAP00000018161 ) -----PDD
Stickleback(ENSGACP00000018172) -----PED
Cod(ENSGMOP00000003747) -----PED
Salmonlb (XP_014048854.1) -----PVD
Salmonla(XP_014059406.1) -----PVD
Troutlb(XP_021480911.1) -----PVD
Troutla(XP_021413584.1) -----PVD
Cavefish(ENSAMXP00000012561) -----PED
Zebrafish(ENSDARP00000013243) -----PED
Gar(ENSLOCP00000009024) -----PED
Shark(XP_007910047.1) -----LYPRECLSPASTCSHSQNLNFSWGRGGSQAIVSQAIPLQSGLFKDRVWVSLIFLVAVSGLLCLCALYVKCLFQTTFFYTV
Coelacanth(ENSLACP00000012502) -----
Xenopus(ENSXETP00000047703) -----PAD
Chicken(ENSGALP00000056402) -----
Turtle(ENSPSIP00000003025) -----SADKPRFS
Lizard(ENSACAP0000004041) -----PEE
Tasmanian devil(ENSSHAP0000001) -----NLDLN
```



410 420 430 440 450 460 470 480  
Tetraodon(ENSTNIP00000019029) ...TIFQKL-IKRRKSEDLNGDS--TN---  
Fugu(ENSTRUP00000020321) GRRSKANS DTK--KSPASTRVTRN--SGKOPTIMSMFSKVK-QKRRKSEDLNGDS--TN---  
Tilapia(ENSONIP00000001969) GRRSKANS DTK--KSPASTRVTRN--SGKOPTILSMFISKVK-QKRRKSEDLNGEA--VN---  
Medaka(ENSORLP00000034016) GRRSKSNGDSK--KSPASARVTRN--SGKOPTILSMFISKVK-QKRRKSEEMSEES--VN---  
Amazon molly(ENSPFOP0000000622) GRRSKANSETK--KSPTSTRVTRN--SGKOPTILSLFISKVK-QKRRKSEDLNGEA--VN---  
Platyfish(ENSXMAP00000018161) GRRSKANSETK--KSPTSTRVTRN--SGKOPTILSMFISKVK-QKRRKSEDLNGEA--VN---  
Stickleback(ENSGACP00000018172) GRKSKTNSDNT--KSPASTRVTRN--AKGQPTIMSMFSKVSQKRRKSEDLNGDA--AN---  
Cod(ENSGMOP00000003747) GRKSKSDSD---SPASARVTRN--SGKOPTIMSMFSPKVRQKRRKSEVNGEDSIAN---  
Salmonlb (XP\_014048854.1) GRKSKSDFEPK--KSPGSRVTRNSVSGKOPTILSMFISKVK-QKRRKSEVNGEV--TN---  
Salmonla(XP\_014059406.1) GRKSKSDSEPK--KSPGSRVTRNSVSGKOPTILSMFISNV-QKRRKSEVNGEV--TN---  
Troutlb(XP\_021480911.1) GRKIKSDSEPK--KSPGSRVTRNSVSGKOPTILSMFISKVK-QKRRKSEVNGEV--TN---  
Troutla(XP\_021413584.1) GRKSKSDSEPK--KSPGSRVTRNSVSGKOPTILSMFISKVK-QKRRKSEVNGEV--TN---  
Cavefish(ENSAMXP00000012561) GRRSKADSEPK--KSPGSSRVTRN--SGKOPTILSMFSRV-QKRRKSEVNGET--TN---  
Zebrafish(ENS DARP00000013243) GRRSKADSEPK--KSPASSRVTRN--TEKQPTIVSMFSRV-QKRRKSEVNGET--AN---  
Gar(ENSLOCP0000009024) GRRSKTEGDTK--KSFSSRVTRN--SVKQPTILSMFAKSSKRRKSEVNGET--VA---  
Shark(XP\_007910047.1) KRQSKSNGDNR--RTSGSPRITRNS-MKQCATITSMFAKAAANKRRKSEELNDEE---  
Coelacanth(ENSLACP00000012502) -----  
Xenopus(ENSXETP00000047703) TRKSKTNGENKT-ESPARARSRST-TGKQATILSMFSKGSDDLAMHOHSCNITFDNLITS DGI RRRC SIP FQHIMLEYQ  
Chicken(ENSGALP00000056402) ARRSRSNGESK--KSPASSRVTRNS--SGKOPTILSVFSKGS T KRRKSEVNCAVVKPEV  
Turtle(ENSPSIP0000003025) BRRARHAGPRS--QXPASSRVTRNS--SGKOPTILALFAKGS NKRRKSEVNGEV--KQ---  
Lizard(ENSACAP0000004041) GRKSKSNS ESR--KTPSSSRVTRNS--SGKOPTIVAMFSKGS NKRRKSEVNGK LKQET  
Tasmanian devil(ENSSHAP0000001 Mouse(ENSMUSP000000136669) ARPE THLDEDE--DCKKDKR S SR PRSQPRDPA A-----KRRPKEAEPEQVAPE  
Rat(ENSRNOP00000063831) PRRSKSDSEMTI-EASSSSVATR--TTROTITISHF-KGPAKRRKPKEDSEK G--NA  
Pig(ENSSSCP00000052164) PRRSKSDGEAKS AEVSSSPRITRQ--TTROTITISHFIRGPKRRKPEEDTAKAKPDS  
Human(ENSP000000345739) PRRSKSDGEAKP-EPSSPRITRK--STRQITITISHFAKGA KRRKPQEESERA--KS  
Lamprey(ENSPMAP0000002362) GQRGRKSVGAA-----GGSQPTIASMFSKGS VKRRKSEANGKV  
Ciona(ENSCSAVP00000010172) -----  
Amphioxus(jgi|Braf11|204680|e\_

490 500 510 520 530 540 550 560  
Tetraodon(ENSTNIP00000019029) -----G-----QNE DKKEEDNT EE  
Fugu(ENSTRUP00000020321) -----G-----QNE DKKEEDNV EE  
Tilapia(ENSONIP00000001969) -----G-----QNE PKKDDV VEE  
Medaka(ENSORLP00000034016) -----G-----KDEVKKEED VEE  
Amazon molly(ENSPFOP0000000622) -----G-----INEAQKEDD AEE  
Platyfish(ENSXMAP00000018161) -----G-----INEAQKEDY TEE  
Stickleback(ENSGACP00000018172) -----G-----ENEGKKEEDDA EA  
Cod(ENSGMOP00000003747) -----G-----EKEVKKEEEEEEED  
Salmonlb (XP\_014048854.1) -----GNV-----EKGGEVERDTKEE  
Salmonla(XP\_014059406.1) -----GEVTNR--EVEEKVERDTEEE  
Troutlb(XP\_021480911.1) -----GKV-----EEQEKIERDMEE  
Troutla(XP\_021413584.1) -----GEVTNREVEEKEKVDRT EE  
Cavefish(ENSAMXP00000012561) -----GET-----AMETKT EADV EE  
Zebrafish(ENS DARP00000013243) -----G-----DTEIKT EETT EE  
Gar(ENSLOCP0000009024) -----P-----VTEEGVTDD EEK  
Shark(XP\_007910047.1) -----P-----QVPVKKEEESEEQ  
Coelacanth(ENSLACP00000012502) -----  
Xenopus(ENSXETP00000047703) FQVDKRRPTSSVKFQWSLALTSNSTESSVLSILKASPFYTTITSGLLRSNKRKSSDEEKD TDVSA  
Chicken(ENSGALP00000056402) -----SAEKDEEEEEELEEK  
Turtle(ENSPSIP0000003025) -----E-----TNSEKKEEELEEK  
Lizard(ENSACAP0000004041) -----NLENEEEEEEQFGEK  
Tasmanian devil(ENSSHAP0000001 Mouse(ENSMUSP000000136669) -----E-----MNIKKEEKKIIEASTHQNTLWLKPASEGL  
Rat(ENSRNOP00000063831) -----NESAAEERDQKRRRVAGTESRASRAGESVEKPERVR  
Pig(ENSSSCP00000052164) -----PV-----EEEKQDEKRRKVTSRD SVAGLLPTEEP  
Human(ENSP000000345739) -----DES I KEDKDQDEKRRRVTSRERVARPLPAEEPERAK  
Lamprey(ENSPMAP0000002362) -----KEDIQDSQTKEE  
Ciona(ENSCSAVP00000010172) -----  
Amphioxus(jgi|Braf11|204680|e\_

570 580 590 600 610 620 630 640  
Tetraodon(ENSTNIP00000019029) -----REFEKRL-----KVESN  
Fugu(ENSTRUP00000020321) -----AREFEKRL-----KVESN  
Tilapia(ENSONIP00000001969) -----SREFEKRL-----KVESD  
Medaka(ENSORLP00000034016) -----SQEFKRL-----KVESD  
Amazon molly(ENSPFOP0000000622) -----TQEFKRL-----KADS  
Platyfish(ENSXMAP00000018161) -----TQVEKRL-----RVSD  
Stickleback(ENSGACP00000018172) -----TREFEKRL-----KVESD  
Cod(ENSGMOP00000003747) -----SREFEKRL-----KVDSD  
Salmonlb (XP\_014048854.1) -----TQEFKRF-----KVEPD  
Salmonla(XP\_014059406.1) -----TQKFKRF-----KVEPD  
Troutlb(XP\_021480911.1) -----TPFEKRF-----KVEPD  
Troutla(XP\_021413584.1) -----TQEFKRF-----KVEPD  
Cavefish(ENSAMXP00000012561) -----ASAFH-----LVPDI  
Zebrafish(ENS DARP00000013243) -----VREFEKRL-----KTEDE  
Gar(ENSLOCP0000009024) -----AQDFE KRL-----KVESE  
Shark(XP\_007910047.1) -----EEQDFE KRL-----KVES  
Coelacanth(ENSLACP00000012502) -----  
Xenopus(ENSXETP00000047703) -----DADQPEEKEKEEKRL-----KIEVN  
Chicken(ENSGALP00000056402) -----EQDFE KRL-----KIETK  
Turtle(ENSPSIP0000003025) -----EHDFE KRL-----KIETK  
Lizard(ENSACAP0000004041) -----EPDVKRF-----KTETK  
Tasmanian devil(ENSSHAP0000001 Mouse(ENSMUSP000000136669) KCGCTIRRKL VNEQGEKLM-----KFE LK EGS  
Rat(ENSRNOP00000063831) -----RRKTRK-----KLESH  
Pig(ENSSSCP00000052164) PGTQLCQEEQGEEDDRP RRQTR ELASRRKSR EDP REARP GTHL DV DDDDEKDKR SSR PRS QP RDLATKR RPKEE VE  
RRVRPGTHMEEDDKB EKR LRS QTKELTPKQKIKEELDSTRPG--GAQ PETNEEDKDEKRRHS QPKDLAKRRP EEKEPE

Human (ENSP00000345739) S G T R T E K E E E R D E K E E K R L R S Q T K E P T P K Q K L K E E P D R E A R A G V Q A D E D E D G D E - K D E K K H R S Q P K D L A A K R P E E K E P E  
Lamprey (ENSPMAP0000002362) G L E D K R R K V E L V  
Ciona (ENSCSAVP00000010172) Q D E K R V K L A T D  
Amphioxus (jgi|Braf11|204680|e

650 660 670 680 690 700 710 720

Tetraodon (ENSTNIP00000019029) E L T S A E E I K P E I - K - P V A P A K K  
Fugu (ENSTRUP00000020321) E N E S T E E I K P E T - K - P V - P T A K  
Tilapia (ENSONIP00000001969) E N A A P E S K S D I A K - P V - S A V K  
Medaka (ENSORLP00000034016) E N S A A E D C K N D T T K - P V - S A A K  
Amazon molly (ENSPFOP0000000622) E K L A P E E S K S K I T K - P G - P A A K  
Platyfish (ENSMAP00000018161) E K L A P E E S K S K I T K - P G - P A A K  
Stickleback (ENSGACP00000018172) E T A A P E K S E S E I T K - P V - S A A K  
Cod (ENSGMOP00000003747) E - S V P E K A T S E V K N T P V - T A A K  
Salmonlb (XP\_014048854.1) N K P V A E D A T S E K M K - P V - A A A K  
Salmonla (XP\_014059406.1) N K P V A E D A T S E K M K - A V - P A A K  
Troutlb (XP\_021480911.1) N K P V A E D A T S E K M K - Q V - A A A K  
Troutla (XP\_021413584.1) N K P V A E D A T S E K M K - A V - A A A K  
Cavefish (ENSAMXP00000012561) E T A N A E K T K - P V - S T A K  
Zebrafish (ENSADAR00000013243) K P E A E N A A N L K - P V - S T A K  
Gar (ENSLQCP00000009024) E K T - - D T K A S V Q K N P V - P P A K  
Shark (XP\_007910047.1) E E T L P E G A E T N A D R K P K A D Q T E K  
Coelacanth (ENSLACP00000012502)  
Xenopus (ENSXETP00000047703) E S E N E N R S T A E E S K - K V K P V L P P K  
Chicken (ENSGALP00000056402) E G S E I K D E I T Q V K T S T P A K  
Turtle (ENSPTIP00000003025) E G P E I K D E A T P I K T A P P A K  
Lizard (ENSACAP00000004041) E G L E R K E E A T Q I K T G T P V K  
Tasmanian devil (ENSSHAP0000001) S C V L K A F Y Y S G E G S K E R S Q L G P S S L T C A V F P C R K T K Q I F F L S V P P I K K T R I K K K T H Q K T V L H Y R S E I K V V Q G K A V L P V K  
Mouse (ENSMUSP00000136669) T V P V Q S R R E R K A A Q S K S - V I P K  
Rat (ENSRNOP00000063831) Q I T P E P P E G K D E D E K E E K R R - K T T R K K P E P L S I P V Q S - R V E R K A S Q G K A S A I P K  
Pig (ENSSSCP00000052164) R I K P Q V S D E K D E D E K E E K R R - R T T Y K E P T E K - K L A R T K T A V V S K  
Human (ENSP00000345739) K V N P Q I S D E K D E D E K E E K R R K T T P K E P T E K - K M A R A K T V M N S K  
Lamprey (ENSPMAP0000002362) - A E K S L L L S D A P E S S P A K F K - P A R  
Ciona (ENSCSAVP00000010172) - A S D K E N E I P - K V E A T K P K V S -  
Amphioxus (jgi|Braf11|204680|e



730 740 750 760 770 780 790 800

Tetraodon (ENSTNIP00000019029) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Fugu (ENSTRUP00000020321) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Tilapia (ENSONIP00000001969) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Medaka (ENSORLP00000034016) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H R I T N F S V Y D K R G H L C P F D S G  
Amazon molly (ENSPFOP0000000622) T P P P K C P D C R Q M L D D P D L K M F Q G D P D N A L E E P E M L T E S L S L F E - A N E D G F F S Y D L P Q H R I T N F S V Y D K R G H L C P F D S G  
Platyfish (ENSMAP00000018161) T P P P K C P D C R Q M L D D P D L K M F Q G D P D N A L E E P E M L T E S L S L F E - A N E D G F F S Y D L P Q H R I T N F S V Y D K R G H L C P F D S G  
Stickleback (ENSGACP00000018172) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D T A L D E P E M L T D E R L S L F D - S N E D G F F S Y D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Cod (ENSGMOP00000003747) T P P P K C P D C R Q M L D D A D L K F F Q G D P D T A L D E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Salmonlb (XP\_014048854.1) T P P P K C P D C R Q M L D D S D L K L F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F N Y E E L P Q H K I T N F S V Y D K R G H L C P F D S G  
Salmonla (XP\_014059406.1) T P P P K C P D C R Q M L D D S D L K L F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F N Y E E L P Q H K I T N F S V Y D K R G H L C P F D S G  
Troutlb (XP\_021480911.1) T P P P K C P D C R Q M L D D S D L K L F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F N Y E E L P Q H K I T N F S V Y D K R G H L C P F D S G  
Troutla (XP\_021413584.1) T P P P K C P D C R Q M L D D S D L K L F Q G D P D N A L D E P E M L T D E R L S L F D - S N E D G F F N Y E E L P Q H K I T N F S V Y D K R G H L C P F D S G  
Cavefish (ENSAMXP00000012561) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D A L E E P E M L T D E R L S L F D - S N E D G F F S Y D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Zebrafish (ENSADAR00000013243) T P P P K C P D C R Q M L D D S D L K L F F Q G D P D A L E E P E M L T D E R L S L F D - S N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Gar (ENSLQCP00000009024) T P P P K C P D C R Q M L D D P D L K F F Q G D P D A L D E P E M L T D E R L S L F D - A N E D G F F S Y E D L P Q H K I T N F S I Y D K R G H L C P F D S G  
Shark (XP\_007910047.1) T P P P K C P D C R Q M L D D P D L K F F Q G D P D A L E E P E M L T D E R L S L F E G T H D E G F F S Y D L P Q H K I T S F S I Y D K R G H L C P F D S G  
Coelacanth (ENSLACP00000012502) S P P P K C P D C R Q M L D D P D L K F F Q G D P D A L E E P E M L T D E R L S L F D - A N E D G F F S Y E D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Xenopus (ENSXETP00000047703) T P P P K C P D C R Q M L D D P D L K F F Q G D P D A L D E P E M L T D E R L S L F E - A N E D G F F S Y D L P Q H K I T N F S V Y D K R G H L C P F D S G  
Chicken (ENSGALP00000056402) T P P P K C P D C R Q M L D D P D L K F F Q G D P D A L E E P E M L T D E R L S L F D - A N E D G F F S Y E D L P Q H K I T S F S V Y D K R G H L C P F D S G  
Turtle (ENSPTIP00000003025) T P P P K C P D C R Q M L D D P D L K F F Q G D P D A L E E P E M L T D E R L S L F D - A N E D G F F S Y E D L P Q H K I T S F S V Y D K R G H L C P F D S G  
Lizard (ENSACAP00000004041) T P P P K A E C R Q M L D D P D L K F F Q G D P D N A L D E P E M L T D E R L S L F D - A N E D G F F S Y D L P Q H K I T S F S V Y D K R G H L C P F D S G  
Tasmanian devil (ENSSHAP0000001) S T P P K C P D C R Q M L D D P D L K F F Q G D P D A L D E P E M L T D E R L S L F D - A N E D G F F S Y D L P Q H R V T S F S V Y D K R G H L C P F D S G  
Mouse (ENSMUSP00000136669) I N S P K C P E C Q L D D P D L K - Y Q H P E D A V D E P O M L T N E R L S L Y D - S T S T W F D Y E D S P M H R T S F S V Y C S R G H L C P V D T G  
Rat (ENSRNOP00000063831) I N P P C P E C Q L D D P D L K - Y Q H P E D A V D E P O M L T N E R L S V F D - S N S S W F E T Y D S S P M H K T S F S V Y C S R G H L C P V D T G  
Pig (ENSSSCP00000052164) A D P I K C V C G Q L D D A E L K - Y E Q H P E D A V E E I O L L T N E R L S L F D - A N E S G F F S Y E A L P Q H K I T C F S V Y C K R G H L C P I D T G  
Human (ENSP00000345739) T H P P K I C Q G Q L D D P D L K - Y Q H P E D A V D E P O M L T N E R L S L F D - A N E S G F F S Y E A L P Q H K I T C F S V Y C K R G H L C P I D T G  
Lamprey (ENSPMAP0000002362) T P P P K C T E C K Q L D D R D L K L F F Q G D P D A L D E P E M L T D E R L S V F E - S N S D A M E S Y D L P Q H K I T N F S V Y D K R G H L C P F D T G  
Ciona (ENSCSAVP00000010172) - - T K R E C R Q M L N D V E I L - F E G D Q A G A E E E T V L T H E S L S L F V G N E E E G - - - - R P Q H K I T D F T V Y D K S T H I C S F D A G  
Amphioxus (jgi|Braf11|204680|e - - P V K C K E C R Q L D D P D L R M F P G D Q E A V D E V E M L T D E R L S L L E - - E D Q E Y G T Y D D R P Q H K I T N F S V Y D K N H L C P F D A G



810 820 830 840 850 860 870 880

Tetraodon (ENSTNIP00000019029) L I E K N V E L Y F S C V V K P I Y D D N P C L D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y A F I F A L M Q E  
Fugu (ENSTRUP00000020321) L I E K N V E L Y F S C V V K P I Y D D N P C L D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y A F I F A L M Q E  
Tilapia (ENSONIP00000001969) L I E K N V E L Y F S C V V K P I Y D D N P C M D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y A F I F A L M Q E  
Medaka (ENSORLP00000034016) L I E K N V E L Y F S C V V K P I Y D D N P C L D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y A F I F A L M Q E  
Amazon molly (ENSPFOP0000000622) L I E K N V E L Y F S C V V K P I Y D D S P C L T S G V F A R K L G P I N A W W I T - G F D G G E K A L I G F T T S F A D Y I L M Q S S E E Y A F I F A L M Q E  
Platyfish (ENSMAP00000018161) L I E K N V E L Y F S C V V K P I Y D D S P C L T S G V F A R K L G P I N A W W I T - G F D G G E K A L I G F T T S F A D Y I L M Q S S E E Y A F I F A L M Q E  
Stickleback (ENSGACP00000018172) L I E K N V E L Y F S C V V K P I Y D D N P C L D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y A F I F A V M Q E  
Cod (ENSGMOP00000003747) L I E K N V E L Y F S C V V K P I Y D D N P C L D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M Q S S E E Y S V I F A L M Q E  
Salmonlb (XP\_014048854.1) L I E K N V E L Y F S C A V K P I Y D D N P C M D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M P R E E Y A S I F A V M Q E  
Salmonla (XP\_014059406.1) L I E K N V E L Y F S C A V K P I Y D D N P C M D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M P R E E Y A F I F A V M Q E  
Troutlb (XP\_021480911.1) L I E K N V E L Y F S C A V K P I Y D D N P C M D G G V F A K K L G P I N A W W I T - G F D G G E K A L I G F T T A F A D Y I L M P R E E Y A F I F A V M Q E

Troutla (XP\_021413584.1)  
Cavefish (ENSMAMP00000012561)  
Zebrafish (ENSADARP00000013243)  
Gar (ENSLOCP0000009024)  
Shark (XP\_007910047.1)  
Coelacanth (ENSLACP00000012502)  
Xenopus (ENSXETP00000047703)  
Chicken (ENSGALP00000056402)  
Turtle (ENSPSP00000003025)  
Lizard (ENSACAP00000004041)  
Tasmanian devil (ENSSHAP0000001)  
Mouse (ENSMUSP000000136669)  
Rat (ENSRNOP000000063831)  
Pig (ENSSSCP00000052164)  
Human (ENSP000000345739)  
Lamprey (ENSMPAP00000002362)  
Ciona (ENSCSAVP00000010172)  
Amphioxus (jgi|Braf11|204680|e\_



Tetraodon (ENSTNIP00000019029)  
Fugu (ENSTRUP00000020321)  
Tilapia (ENSONIP0000001969)  
Medaka (ENSORLP00000034016)  
Amazon molly (ENSFP0P0000000622)  
Platyfish (ENSXMAP00000018161)  
Stickleback (ENSACAP00000018172)  
Cod (ENSGMOP00000003747)  
Salmonlb (XP\_014048854.1)  
Salmonla (XP\_014059406.1)  
Troutlb (XP\_021480911.1)  
Troutla (XP\_021413584.1)  
Cavefish (ENSMAMP00000012561)  
Zebrafish (ENSADARP00000013243)  
Gar (ENSLOCP0000009024)  
Shark (XP\_007910047.1)  
Coelacanth (ENSLACP00000012502)  
Xenopus (ENSXETP00000047703)  
Chicken (ENSGALP00000056402)  
Turtle (ENSPSP00000003025)  
Lizard (ENSACAP00000004041)  
Tasmanian devil (ENSSHAP0000001)  
Mouse (ENSMUSP000000136669)  
Rat (ENSRNOP000000063831)  
Pig (ENSSSCP00000052164)  
Human (ENSP000000345739)  
Lamprey (ENSMPAP00000002362)  
Ciona (ENSCSAVP00000010172)  
Amphioxus (jgi|Braf11|204680|e\_

zf-CXXC domain

Tetraodon (ENSTNIP00000019029)  
Fugu (ENSTRUP00000020321)  
Tilapia (ENSONIP0000001969)  
Medaka (ENSORLP00000034016)  
Amazon molly (ENSFP0P0000000622)  
Platyfish (ENSXMAP00000018161)  
Stickleback (ENSACAP00000018172)  
Cod (ENSGMOP00000003747)  
Salmonlb (XP\_014048854.1)  
Salmonla (XP\_014059406.1)  
Troutlb (XP\_021480911.1)  
Troutla (XP\_021413584.1)  
Cavefish (ENSMAMP00000012561)  
Zebrafish (ENSADARP00000013243)  
Gar (ENSLOCP0000009024)  
Shark (XP\_007910047.1)  
Coelacanth (ENSLACP00000012502)  
Xenopus (ENSXETP00000047703)  
Chicken (ENSGALP00000056402)  
Turtle (ENSPSP00000003025)  
Lizard (ENSACAP00000004041)  
Tasmanian devil (ENSSHAP0000001)  
Mouse (ENSMUSP000000136669)  
Rat (ENSRNOP000000063831)  
Pig (ENSSSCP00000052164)  
Human (ENSP000000345739)  
Lamprey (ENSMPAP00000002362)  
Ciona (ENSCSAVP00000010172)  
Amphioxus (jgi|Braf11|204680|e\_

zf-CXXC domain

Multiple sequence alignment of the zf-CXXC domain (residues 1050-1120) across various species including Tetraodon, Fugu, Tilapia, Medaka, Amazon molly, Platyfish, Stickleback, Cod, Salmonlb, Troutlb, Cavefish, Zebrafish, Gar, Shark, Coelacanth, Xenopus, Chicken, Turtle, Lizard, Tasmanian devil, Mouse, Rat, Pig, Human, Lamprey, Ciona, and Amphioxus. Conserved motifs like -KQACQRR- and -CPNLAVKEAEDDENVEED- are highlighted.

BAH domain

Multiple sequence alignment of the BAH domain (residues 1130-1200) across the same species. Conserved motifs like -AHGK-MFHAHWFRLG and -KQYVMKQVMDNEVLEVGDCVSVSSEDDPSILYLARITSLWED- are highlighted.

BAH1 domain

Multiple sequence alignment of the BAH1 domain (residues 1210-1280) across the same species. Conserved motifs like -DVKVLEDD- and -DVKVIDDD- are highlighted.

Trout1b(XP\_021480911.1) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-VE--DIKVIDDDGKNFFYQLWYEGDCARF  
Trout1a(XP\_021413584.1) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-VE--DIKVIDDDGKNFFYQLWYEGDCARF  
Cavefish(ENSMAMP00000012561) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-ID--DIKVIDDDGKSFYQLWYEGDARF  
Zebrafish(ENSDARP00000013243) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DE--DIKVIDDDGKSFYQLWYEGDCARF  
Gar(ENSLACP00000009024) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DS--EIKVIDDDGKSFYQLWYEGDARF  
Shark(XP\_007910047.1) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-EGEP-ENHFLKVVDDGKTYFYQMWYDPEYARF  
Coelacanth(ENSLACP00000012502) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DD--DIKVIDDDGKTYFYQMWYDPEYARF  
Xenopus(ENSXETP00000047703) TDTVLGESSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGT-HT--DIKVIDDDGKTYFYQMWYDPEYARF  
Chicken(ENSGALP00000056402) SDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-DM--EIKVIDDDGRTYFYQMWYDPEYARF  
Turtle(ENSPSIP00000003025) MDTVLGGKSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-DM--EIKVIDDDGRTYFYQMWYDPEYARF  
Lizard(ENSACAP00000004041) TDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-DV--EIKVIDDDGRTYFYQMWYDPEYARF  
Tasmanian devil(ENSSHAP000000001) IDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGL-DM--EIKVIDDDGRTYFYQMWYDPEYARF  
Mouse(ENSMUSP00000136669) TDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGT-DP--EITLPGAEDGKTYFYQMWYDPEYARF  
Rat(ENSRNOP00000063831) TDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DP--EITLPGAEDGKTYFYQMWYDPEYARF  
Pig(ENSSSCP00000052164) IDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DP--EITLPGAEDGKTYFYQMWYDPEYARF  
Human(ENSP00000345739) TDTVLGAISDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-DP--EITLPGAEDGKTYFYQMWYDPEYARF  
Lamprey(ENSPMAP0000002362) PDTVLGETSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-ETE-EKTSKDDGKSFYQLWYDPEYARF  
Ciona(ENSCSAVP00000010172) SDSLHLETAQDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-QD--NRQLPTDGSVSYFYQMWYDPEYARF  
Amphioxus(jgi|Braf11|204680|e\_ SDTVLGETSDPLELELVDECEMDMLSYVGGKVNVMYKAPS~~DNWFM~~EGGM-QD--NRQLPTDGSVSYFYQMWYDPEYARF



1290 1300 1310 1320 1330 1340 1350 1360

Tetraodon(ENSTNIP00000019029) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Fugu(ENSTRUP00000020321) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Tilapia(ENSONIP0000001969) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Medaka(ENSORLP00000034016) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Amazon molly(ENSPFOP0000000622) ETTPPKTEQSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Platyfish(ENSMAMP00000018161) ETTPPKTEQSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Stickleback(ENSGACP00000018172) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Cod(ENSGMOP00000003747) ETTPPSSP-DASKHKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Salmon1b(XP\_014048854.1) ETTPPTFTPEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Salmon1a(XP\_014059406.1) ETTPPTFTPEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Trout1b(XP\_021480911.1) ETTPPTFTPEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Trout1a(XP\_021413584.1) ETTPPTFTPEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Cavefish(ENSMAMP00000012561) ETTPPEVVPDEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Zebrafish(ENSDARP00000013243) ETTPPKTTPSEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Gar(ENSLACP00000009024) ETTPPNVSPAEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Shark(XP\_007910047.1) QMPSPCEPNEENKHKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Coelacanth(ENSLACP00000012502) ESPPSCVSAEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Xenopus(ENSXETP00000047703) ETTPPTPOPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Chicken(ENSGALP00000056402) ETTPPRAQPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Turtle(ENSPSIP00000003025) ESPPKIIPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Lizard(ENSACAP00000004041) ETTPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Tasmanian devil(ENSSHAP000000001) ESPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Mouse(ENSMUSP00000136669) ESPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Rat(ENSRNOP00000063831) ESPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Pig(ENSSSCP00000052164) ESPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Human(ENSP00000345739) ESPPKIOPPTEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Lamprey(ENSPMAP0000002362) ESPPKEVTPAEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Ciona(ENSCSAVP00000010172) LDPPEVVPDEDCKKFKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~  
Amphioxus(jgi|Braf11|204680|e\_ EDPPVLE-EGSGHKFCSCVRITLROKQCEIHPHVEPELL-DE-DS~~SKALFALACFK~~GEQFRVGD~~HSVYL~~PPDARNF~~SVKPA~~



1370 1380 1390 1400 1410 1420 1430 1440

Tetraodon(ENSTNIP00000019029) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Fugu(ENSTRUP00000020321) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Tilapia(ENSONIP0000001969) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Medaka(ENSORLP00000034016) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Amazon molly(ENSPFOP0000000622) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Platyfish(ENSMAMP00000018161) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Stickleback(ENSGACP00000018172) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Cod(ENSGMOP00000003747) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Salmon1b(XP\_014048854.1) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Salmon1a(XP\_014059406.1) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Trout1b(XP\_021480911.1) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Trout1a(XP\_021413584.1) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Cavefish(ENSMAMP00000012561) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Zebrafish(ENSDARP00000013243) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Gar(ENSLACP00000009024) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Shark(XP\_007910047.1) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Coelacanth(ENSLACP00000012502) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Xenopus(ENSXETP00000047703) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Chicken(ENSGALP00000056402) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Turtle(ENSPSIP00000003025) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Lizard(ENSACAP00000004041) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Tasmanian devil(ENSSHAP000000001) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Mouse(ENSMUSP00000136669) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Rat(ENSRNOP00000063831) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Pig(ENSSSCP00000052164) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Human(ENSP00000345739) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Lamprey(ENSPMAP0000002362) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Ciona(ENSCSAVP00000010172) SPVKKRSHRK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~  
Amphioxus(jgi|Braf11|204680|e\_ NSTKKAASK--DDVDEELYPEYRKS~~SDYIKGSNLDAP~~EPRI~~GR~~IKET~~IFC~~KRRSNGK~~PD~~TS~~EV~~KLRL~~VK~~FYRPENTHK~~G~~

BAH2 domain

Multiple sequence alignment of the BAH2 domain (residues 1450-1520) across various species including Tetraodon, Fugu, Tilapia, Medaka, Amazon molly, Platyfish, Stickleback, Cod, Salmon, Trout, Cavefish, Zebrafish, Shark, Coelacanth, Chicken, Turtle, Lizard, Tasmanian devil, Mouse, Rat, Pig, Human, Lamprey, Ciona, and Amphioxus. Conserved residues are highlighted in yellow.

Dcm domain

Multiple sequence alignment of the Dcm domain (residues 1530-1600) across various species including Tetraodon, Fugu, Tilapia, Medaka, Amazon molly, Platyfish, Stickleback, Cod, Salmon, Trout, Cavefish, Zebrafish, Shark, Coelacanth, Xenopus, Chicken, Turtle, Lizard, Tasmanian devil, Mouse, Rat, Pig, Human, Lamprey, Ciona, and Amphioxus. Conserved residues are highlighted in yellow.

Motif I

Multiple sequence alignment of Motif I (residues 1610-1680) across various species including Tetraodon, Fugu, Tilapia, Medaka, Amazon molly, Platyfish, Stickleback, and Cod. Conserved residues are highlighted in yellow.



Salmonlb (XP\_014048854.1) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Salmonla (XP\_014059406.1) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Troutlb (XP\_021480911.1) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Troutla (XP\_021413584.1) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Cavefish (ENSAMXP00000012561) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Zebrafish (ENSADARP00000013243) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Gar (ENSLOCP0000009024) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Shark (XP\_007910047.1) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Coelacanth (ENSLACP00000012502) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Xenopus (ENSXETP00000047703) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Chicken (ENSNGALP00000056402) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Turtle (ENSFSP00000003025) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Lizard (ENSACAP0000004041) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Tasmanian devil (ENSSHAP0000001) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Mouse (ENSMUSP000000136669) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Rat (ENSRNOP00000063831) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Pig (ENSSSCP00000052164) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Human (ENSP00000345739) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Lamprey (ENSMPAP0000002362) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Ciona (ENSCSAPV00000010172) IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS

Amphioxus (jgi|Braf11|204680|e\_... IEMWDPAQAFLRNPNP...TVFTEDCNVLLKLVMSGEKTNLSLQRLPQKGDVEMLCGGPPCQGFSGMNRFRNSRTYSKFKNS



Dcm domain

1690 1700 1710 1720 1730 1740 1750 1760

Tetraodon (ENSTNIP00000019029) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Fugu (ENSTRUP00000020321) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Tilapia (ENSONIP0000001969) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Medaka (ENSORLP00000034016) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Amazon molly (ENSFPPOP0000000622) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Platyfish (ENSXMAP00000018161) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Stickleback (ENSGACP00000018172) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Cod (ENSGMOP00000003747) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Salmonlb (XP\_014048854.1) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Salmonla (XP\_014059406.1) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Troutlb (XP\_021480911.1) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Troutla (XP\_021413584.1) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Cavefish (ENSAMXP00000012561) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Zebrafish (ENSADARP00000013243) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Gar (ENSLOCP0000009024) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Shark (XP\_007910047.1) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Coelacanth (ENSLACP00000012502) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Xenopus (ENSXETP00000047703) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Chicken (ENSNGALP00000056402) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Turtle (ENSFSP00000003025) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Lizard (ENSACAP0000004041) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Tasmanian devil (ENSSHAP0000001) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Mouse (ENSMUSP000000136669) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Rat (ENSRNOP00000063831) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Pig (ENSSSCP00000052164) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Human (ENSP00000345739) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Lamprey (ENSMPAP0000002362) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

Ciona (ENSCSAPV00000010172) LVVSMLSYCDYYRPF...FFLLENVRFVSPKSMVLKLTLRCLVRMGYQCTFGVLQAGQYVGAQTRRRRAITLAAAPGEKLP

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Dcm domain

1770 1780 1790 1800 1810 1820 1830 1840

Tetraodon (ENSTNIP00000019029) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Fugu (ENSTRUP00000020321) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Tilapia (ENSONIP0000001969) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Medaka (ENSORLP00000034016) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Amazon molly (ENSFPPOP0000000622) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Platyfish (ENSXMAP00000018161) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Stickleback (ENSGACP00000018172) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

Cod (ENSGMOP00000003747) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

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Troutlb (XP\_021480911.1) YPEPLHVFAPRACSLNVVDDKPKYSNVITRNNGGIYRTITVRDMSDLPEIRNGASALDEISYNGEPQSWFQRQIRGTQY

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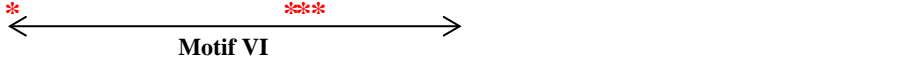
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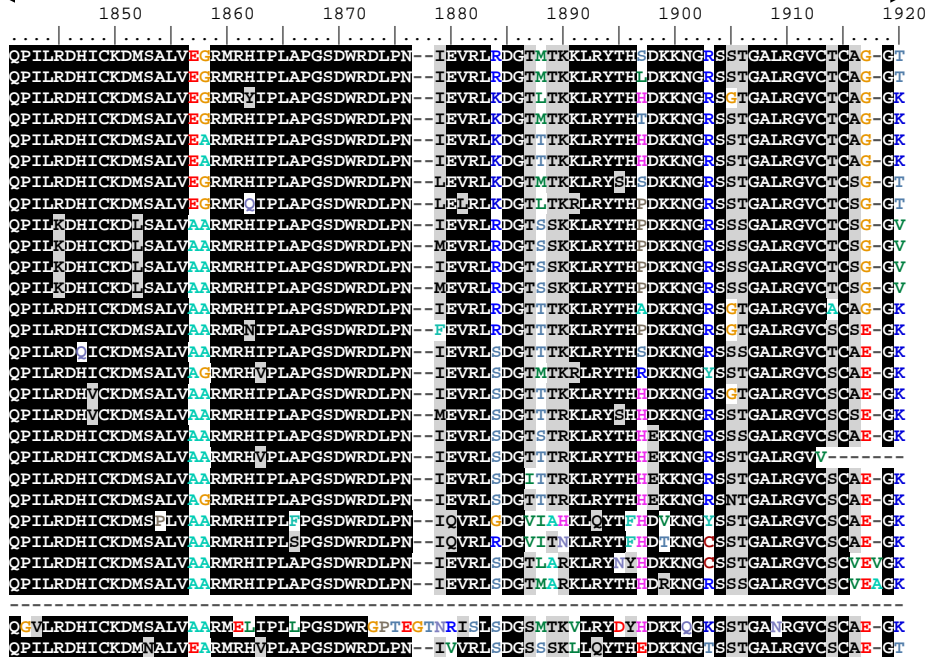
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 Xenopus (ENSXETP00000047703)  
 Chicken (ENSNGALP00000056402)  
 Turtle (ENSFPSIP0000003025)  
 Lizard (ENSACAP0000000401)  
 Tasmanian devil (ENSSHAP0000001)  
 Mouse (ENSMUSP00000136669)  
 Rat (ENSRNOP00000063831)  
 Pig (ENSSSCP00000052164)  
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 Ciona (ENSCSASP00000010172)  
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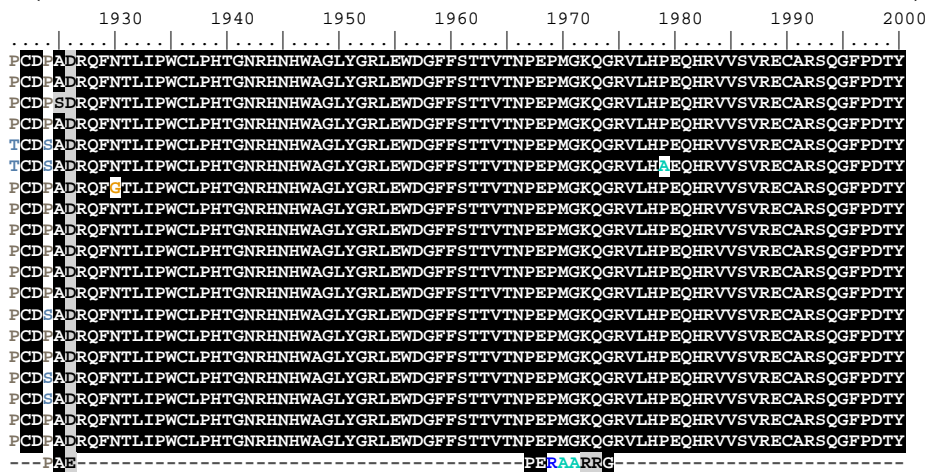
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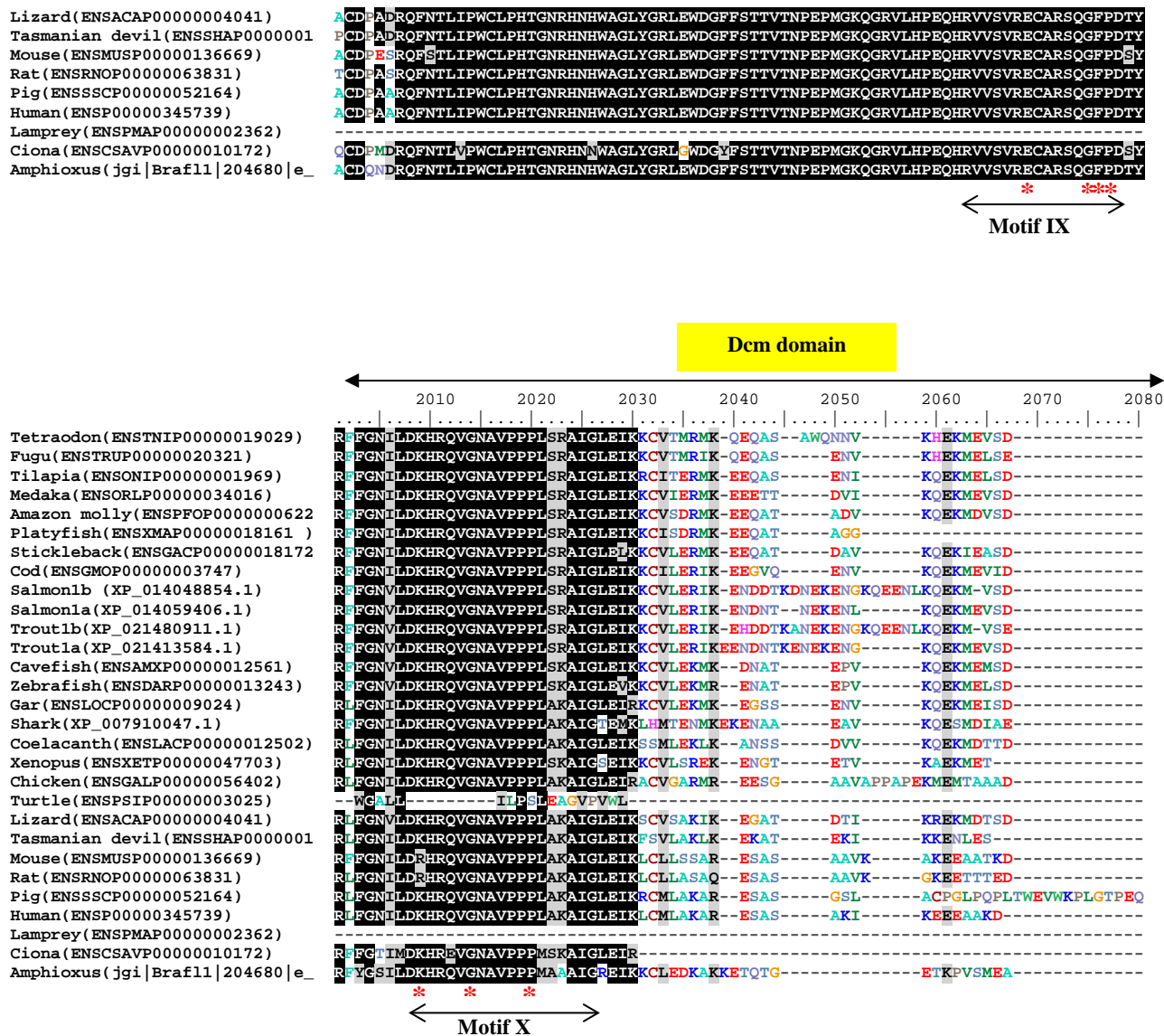


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 Platyfish (ENSXMAP00000018161)  
 Stickleback (ENSACAP00000018172)  
 Cod (ENSGMOP00000003747)  
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 Salmonla (XP\_014059406.1)  
 Troutlb (XP\_021480911.1)  
 Troutla (XP\_021413584.1)  
 Cavefish (ENSAMXP00000012561)  
 Zebrafish (ENSADARP00000013243)  
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 Xenopus (ENSXETP00000047703)  
 Chicken (ENSNGALP00000056402)  
 Turtle (ENSFPSIP0000003025)  
 Lizard (ENSACAP0000000401)  
 Tasmanian devil (ENSSHAP0000001)  
 Mouse (ENSMUSP00000136669)  
 Rat (ENSRNOP00000063831)  
 Pig (ENSSSCP00000052164)  
 Human (ENSP00000345739)  
 Lamprey (ENSMPAP00000002362)  
 Ciona (ENSCSASP00000010172)  
 Amphioxus (jgi|Braf11|204680|e\_



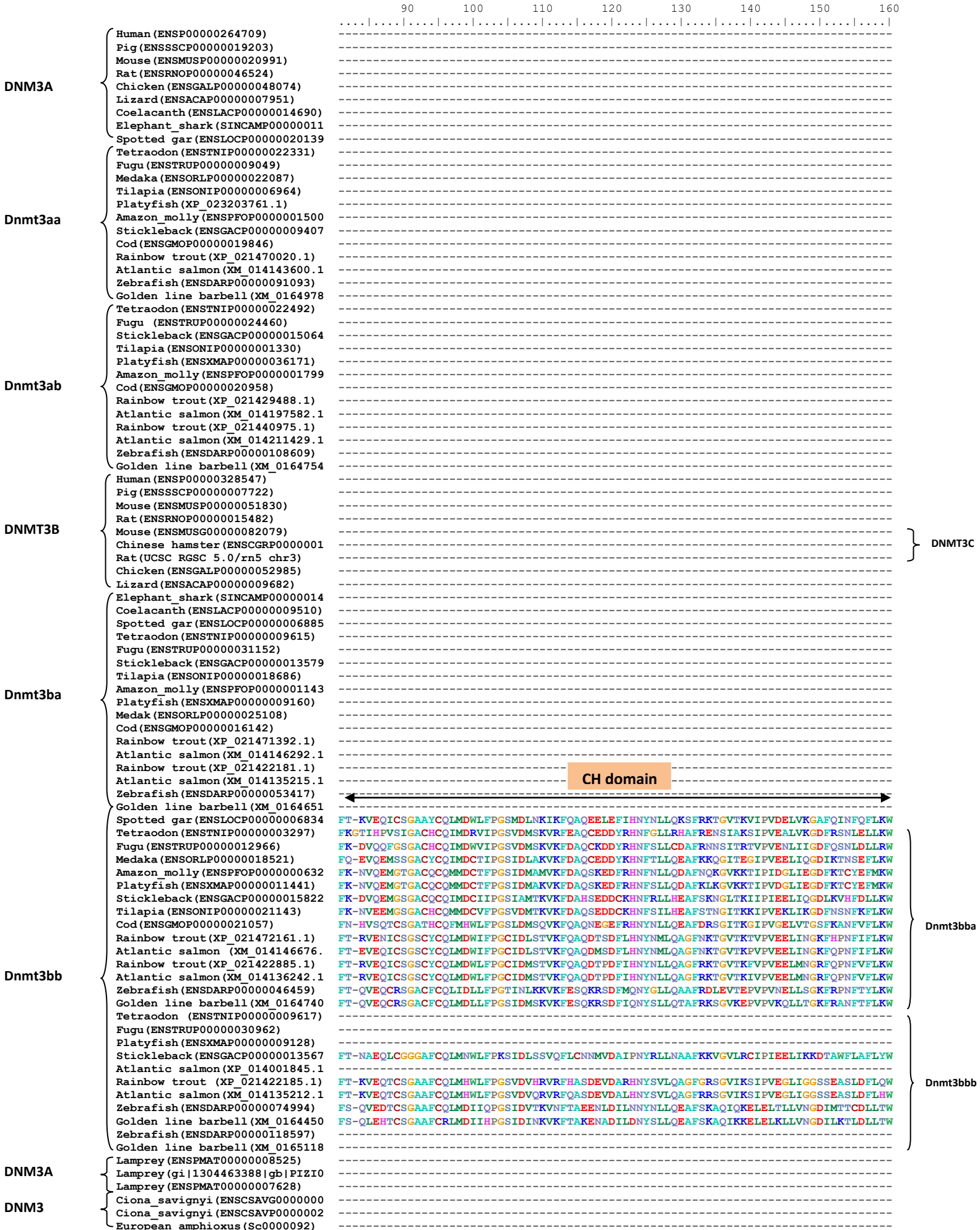
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 Platyfish (ENSXMAP00000018161)  
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 Troutlb (XP\_021480911.1)  
 Troutla (XP\_021413584.1)  
 Cavefish (ENSAMXP00000012561)  
 Zebrafish (ENSADARP00000013243)  
 Gar (ENSLOCP00000009024)  
 Shark (XP\_007910047.1)  
 Coelacanth (ENSLACP00000012502)  
 Xenopus (ENSXETP00000047703)  
 Chicken (ENSNGALP00000056402)  
 Turtle (ENSFPSIP0000003025)





**Supplemental Fig. S2 Dnmt1 protein sequences alignment.** All the protein sequences were aligned with the MUSCLE method in MEGA software. Conserved domains were noted above. Conserved motifs were marked with an asterisk (\*).









.....|.....330.....|.....340.....|.....350.....|.....360.....|.....370.....|.....380.....|.....390.....|.....400.....|.....|.....

<b>DNMT3A</b>	Human (ENSP00000264709)	PRGK-----EERQEPSTTARKVGRP-GRKRKHPPVESGDTPKDPAVISKSPSMAQDSGASELLPNGDLKRSRSE--
	Pig (ENSSSCP00000019203)	-----EERQEPSTATARKVGRP-GRKRKHPPVESSDTPKDPVTTKSPMAQDSGPSDLLPNGDLKRSRSE--
	Mouse (ENSMUSP00000020991)	NRGK-----EERQEPSTATARKVGRP-GRKRKHPPVESSDTPKDPVTTKSPMAQDSGPSDLLPNGDLKRSRSE--
	Rat (ENSRNOP00000046524)	NRGK-----EERQEPSTATARKVGRP-GRKRKHPPVESSDTPKDPVTTKSPMAQDSGPSDLLPNGDLKRSRSE--
	Chicken (ENSGALP00000048074)	LIFLTRLNPQRRASVSPPAAPPAGRPSELGTQRRGATGTRC-
	Lizard (ENSACAP00000007951)	SAPKCPPASAHSSSSSEMEQVPNGDVVEAGSPEKATTAATAAEPKGR-
	Coelacanth (ENSLACP00000014690)	-----
	Elephant_shark (SINCAMP00000011)	-----
<b>Dnmt3aa</b>	Spotted gar (ENSLQCP00000020139)	DQEQ---DR---GKEPGNSVPLRRVGRP-GRKRKQLPVSNCETSKEDVGSKCHASVESQSSEQVHNGDVIDSHPGDTIAAS
	Tetraodon (ENSTNIP00000022331)	-----
	Fugu (ENSTRUP00000009049)	-----
	Medaka (ENSRPLP00000022087)	-----
	Tilapia (ENSONIP0000006964)	-----DQDSPEEGTPASPFRNRKRVRGSRKRKQLLEPMATSE-
	Platyfish (XP_023203761.1)	-----DQDSPEEGTPASPFRNRKRVRGSRKRKQLLEPMATSE-
	Amazon_molly (ENSPFOP0000001500)	-----
	Stickleback (ENSGACP00000009407)	-----
<b>Dnmt3ab</b>	Cod (ENSGMOP00000019846)	-----
	Rainbow trout (XP_021470020.1)	EGSLASPPALCRVDRPNRQHMT-
	Atlantic salmon (XM_014143600.1)	-----
	Zebrafish (ENSDARF00000091093)	QMSDTMDHQSASVGSQEDEPAMILPTPIPIGGRSDKAGKGF-
	Golden line barbell (XM_0164978)	VTDT---PT---RRVGRP-ARKRKTPEGEDICGRVIEGVTCKMQAGCNGEAESRVSQKMLEQN-
	Tetraodon (ENSTNIP00000022492)	-----
	Fugu (ENSTRUP00000024460)	GESTIMDVLDLMTEDKSASA--SYKGSKP-GRKRKHFPGESCGPKDVGGGHSHYPG--MGRLSQVYNGDADGHRERMSDA
	Stickleback (ENSGACP00000015064)	-----
<b>Dnmt3ab</b>	Tilapia (ENSONIP0000001330)	GERTILDSDLMEEK-----SPKSSKP-GRKRKQFSVESRGLKDSASVGHSHY---TMAMAQVFNQDGGIRDRMPDA
	Platyfish (ENSMAP00000036171)	GESVLLDVGOMKEPRSTFSSASFKVKGPE-GRKRKQFPVESCISITGCASVCNSYLELCRPSISQVYNGETDRSGDKTTPDA
	Amazon_molly (ENSPFOP0000001799)	-----
	Cod (ENSGMOP00000020958)	-----
	Rainbow trout (XP_021429488.1)	SESTILDKEPASEEKPAKSNTSCKVVRPAGRRKRKPIPVEGVS SVKESVVGCGGNSRGTGLAAERERQSVSVAQVHNGVVSS
	Atlantic salmon (XM_014197582.1)	SESTILDKELAPEEKPAKSNTSYKVVVRPAGRRKRKQIPVEGVS SVKESVVGCGGNSRGTGLAAERERQSVSVAQVHNGVVSS
	Rainbow trout (XP_021440975.1)	RESTITLDKELAPEEKSSKSNTSCKEGRPAGRKHQIAAEGSVSVKDSVPGGGNSLGTGVAERER--VSVAQVQVNGVMWG
	Atlantic salmon (XM_014211429.1)	-----
<b>DNMT3B</b>	Zebrafish (ENSDARF000000108609)	-----
	Golden line barbell (XM_0164754)	NSRT---DTVVIDEMPSSLCTPVRKVRGPR-GRKRKHLPEVICYGPDQLVGVAQKHGVEIQSSLQSQNGDVERHENKSCSCEG
	Human (ENSP00000328547)	QSSDSPPILEAIRTPETIRGRSSSR-----
	Pig (ENSSSCP00000007722)	KPPILEAISTPETIRGRSSSR-----
	Mouse (ENSMUSP00000051830)	QSSDTKDAPSPPPVLEAICTEPCVCTPETRGRSSSR-----
	Rat (ENSRNOP00000015482)	QSSDTKDAPSPPPVLEAICTEPCVCTPETRGRSSSR-----
	Mouse (ENSMUSG00000082079)	QS-----
	Chinese hamster (ENSCGRP000000001)	QSSDAKDVTLT-----
<b>Dnmt3ba</b>	Rat (UCSC RGSC 5.0/rn5 chr3)	RS-----
	Chicken (ENSGALP00000052985)	AWSSLGEEGPAAMKKEKSHGRDEADCRAELILFDGDCT-
	Lizard (ENSACAP00000009682)	-----
	Elephant_shark (SINCAMP000000014)	EQAT-----
	Coelacanth (ENSLACP00000009510)	-----
	Spotted gar (ENSLQCP00000006885)	ATAAVNSDVAMDGLSEKDSGLELTNHL-
	Tetraodon (ENSTNIP00000009615)	-----
	Fugu (ENSTRUP00000031152)	-----
<b>Dnmt3bb</b>	Stickleback (ENSGACP00000013579)	NGDVPPAKGLAESDSGV-
	Tilapia (ENSONIP00000018686)	NMTATAAVNGDTPPAEGLSEENDSGV-
	Amazon_molly (ENSPFOP0000001143)	IAEGLSEENDSGV-
	Platyfish (ENSMAP00000009160)	VTATAAVNGDTPPLIAEGLSEENDSGV-
	Medak (ENSRPLP00000025108)	ATAAVNRNCTGTEGLSEENDSGV-
	Cod (ENSGMOP00000016142)	-----
	Rainbow trout (XP_021471392.1)	AADDSGM-
	Atlantic salmon (XM_014146292.1)	AADDSGM-
<b>Dnmt3bb</b>	Rainbow trout (XP_021422181.1)	AAEGPSENDSCA-
	Atlantic salmon (XM_014135215.1)	AAEGPSENDSCA-
	Zebrafish (ENSDARF00000053417)	ATAAMNRDTSVGDGLSEENDSGL-
	Golden line barbell (XM_0164651)	VGEGLSEENDSGL-
	Spotted gar (ENSLQCP00000006834)	IKKYCTSLKSFKVRDGSRSVNCRARILGLKHPKDIASICSQTPYCIYLHRNV---DVGDGEQADVVLVGFFDEKAGQ
	Tetraodon (ENSTNIP0000003297)	ALCFVREYGE-PASAPQQTASAGSARQELGSERRSGVQSALRRAPYCVIYGGVILES-LKEDGTVSVVLVGYFDVDAGG
	Fugu (ENSTRUP00000012966)	AIWFIGEYCEPAPGAEVSAHLARSKL-GRYPRDIESACQRPYCVIYAGVTLKLS-SREGGTIAVVLVGYFDVGANR
	Medaka (ENSRPLP00000018521)	ALRFIRSRNFAPMNEGKPSKHF-LYRTFLGRYPKDIASVCRHTPYCVYVVEESVVK---DQHSVMLVGYFDLQTTAA
<b>DNMT3C</b>	Amazon_molly (ENSPFOP0000000632)	AVRFIFNRCTYGSAGGQVSRHFARCKL-GSKYPKDLVAVSNRTPYCVYVDTLA---AGNDETVAVILGFFDESSESSG
	Platyfish (ENSMAP00000011441)	AVRFIFNRCTYGSAGGQVSRHFARCKL-GLKYPKDLVAVSNRTPYCVYVDTLA---AGNDETVAVILGFFDESSESSG
	Stickleback (ENSGACP00000015822)	YNRVCPKTNPSKPRPSSDAISRHFARSKLGLQNSNMFPVQHPTPYCVYVGGTGLM----DTVSVVLVGYFDVKITSR
	Tilapia (ENSONIP00000021143)	ALQFIYNHCYTSAGGQVSRHFARCKL-GSQYPKDIIISACENTPYCLYIYGGVPLEG---DEAVSVVLVGYFDVEASS
	Cod (ENSGMOP00000021057)	AKKPNWNCFKNLPDCAAVSSGFPARYMLGLEFFPDLVLSICKQTPYCLYVYGGVLEE---AATVSVVLVGYFDIESAT
	Rainbow trout (XP_021472161.1)	VIRFIQANCVSGPSAAEDQVSNRYGQYVVLGLQYPKDIVSACQKTPYCIYMYGGVVLGQ---TDMASVVLVGYFDVKEAR
	Atlantic salmon (XM_014146676)	VIRFIQANCVSGPSAAEDQVSNRYGQYVVLGLQYPKDIVSACQKTPYCIYMYGGVVLGQ---TDMASVVLVGYFDVKEAR
	Rainbow trout (XP_021422185.1)	VLCFPI--NCVSGPSAAGDQVSNRYGQYVVLGLQYPKDIVSACQKTPYCIYMYGGVVLG---AGIASVVLVGYFDVKEAR
<b>Dnmt3bbb</b>	Atlantic salmon (XM_014136242.1)	VLCFPIQVNCVSGPSAAGDQVSNRYGQYVVLGLQYPKDIVSACQKTPYCIYMYGGVVLG---AGIASVVLVGYFDVKEAR
	Zebrafish (ENSDARF00000046459)	MLLFTIQSHCLSSLPVSRIRVSRQRTARCLILGLKYPNDIVSACKLNPYCIYIYGGVPLDVKTDKNCBHVLLAGFFDEEQRAR
	Golden line barbell (XM_0164740)	MLLFTIQSHCLSSLPVSRIRVSRQRTASYLGLNYPNDIVSACKLNPYCIYIYGGVPLDVAENIKRSSCHAVLVGFFPEEKRSR
	Tetraodon (ENSTNIP00000009617)	-----
	Fugu (ENSTRUP00000030962)	VVRA-----CDSFPSYSLYLVGVHLDE---GQRTSVMLLGYFDLSSGL
	Platyfish (ENSMAP00000009128)	HLCQSVVLLHTLQMSDTSADPRQPMDDAMARVADSADW
	Stickleback (ENSGACP00000013567)	SGRSDDTLLRFRVKRYRHTSDGSDQVSGPILSNHPTDVMASCRVPSYSLYLVGVLEGG---GQNTSVVLVGYFDQSSGV
	Atlantic salmon (XP_014001845.1)	-----
<b>DNMT3A</b>	Rainbow trout (XP_021422185.1)	LLQLIQKHWPSPAKHGTELTQDQVARHVLGQYKYPQDITAAACSQTPYCLYLYRGVE-LGGDQRETRASVLLVGYFDQRSGV
	Atlantic salmon (XM_014135212.1)	LLQLIQKHWPSPAKRGTELTQDQVARHVLGQYKYPQDITAAACSQTPYCLYLYRGVELEGG-DGDOERASVLLMGYFDQRSGV
	Zebrafish (ENSDARF00000074994)	LTSFIRKYGSSTLDDSENNVNSDKCP--GQKSGDITPFRQTPYCYLYLYHGVELED---DKKASVLLGFFDKEVTEGE
	Golden line barbell (XM_0164450)	TMCFIRKYSSSTSDAGSNFASSDSLVLDGKQCRDITAFCSQTPYCYLYLYHGVELED---ENKASVLLGFFDKEVTEGE
	Zebrafish (ENSDARF00000118597)	TMCFIRKYASSTSDCGSVSKNPA---LDQKYWEDITAICRQTPYCYLYLYHGVEIEN---DKKASVLLGFFDEDTEGK
	Golden line barbell (XM_0165118)	TMCFIRKYG---SPDAGSNFASGKDSLVLDGQYKYPQDITAFCSQTPYCYLYLYHGVEIE---DKKASVLLGFFDKEVTEGE
	Lamprey (ENSPMAT00000008525)	-----
	Lamprey (gi 1304463388 gb PIZ10)	-----
<b>DNMT3</b>	Lamprey (ENSPMAT00000007628)	-----
	Ciona savignyi (ENSCSAVG00000000)	-----
<b>DNMT3</b>	Ciona savignyi (ENSCSAVP00000002)	-----
	European amphioxus (Sc00000992)	-----





	490	500	510	520	530	540	550	560
DNM3A	Human (ENSP00000264709)	.....	.....	.....	.....	.....	.....	.....
	Pig (ENSSSCP00000019203)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSP00000020991)	.....	.....	.....	.....	.....	.....	.....
	Rat (ENSRNOP00000046524)	.....	.....	.....	.....	.....	.....	.....
	Chicken (ENSGALP00000048074)	.....	.....	.....	.....	.....	.....	.....
	Lizard (ENSACAP00000007951)	.....	.....	.....	.....	.....	.....	.....
	Coelacanth (ENSLACP00000014690)	.....	.....	.....	.....	.....	.....	.....
	Elephant shark (SINCCAMP00000011)	.....	.....	.....	.....	.....	.....	.....
	Spotted gar (ENSLGPC00000020139)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000022331)	.....	.....	.....	.....	.....	.....	.....
Dnmt3aa	Fugu (ENSTRUP00000009049)	.....	.....	.....	.....	.....	.....	.....
	Medaka (ENSORLP00000022087)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000006964)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (XP_023203761.1)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSPFOP0000001500)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000009407)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000019846)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021470020.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014143600.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000091093)	.....	.....	.....	.....	.....	.....	.....
Dnmt3ab	Golden line barbell (XM_0164978)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000022492)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP00000024460)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000015064)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000001330)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP00000036171)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSPFOP0000001799)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000002958)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021429488.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014197582.1)	.....	.....	.....	.....	.....	.....	.....
DNMT3B	Rainbow trout (XP_021440975.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014211429.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000108609)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164754)	.....	.....	.....	.....	.....	.....	.....
	Human (ENSP00000328547)	.....	.....	.....	.....	.....	.....	.....
	Pig (ENSSSCP00000007722)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSP00000051830)	.....	.....	.....	.....	.....	.....	.....
	Rat (ENSRNOP00000015482)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSG000000082079)	.....	.....	.....	.....	.....	.....	.....
	Chinese hamster (ENSCGRP0000001)	.....	.....	.....	.....	.....	.....	.....
Dnmt3ba	Rat (UCSC RGSC 5.0/rn5 chr3)	.....	.....	.....	.....	.....	.....	.....
	Chicken (ENSGALP000000052985)	.....	.....	.....	.....	.....	.....	.....
	Lizard (ENSACAP00000009682)	.....	.....	.....	.....	.....	.....	.....
	Elephant shark (SINCCAMP000000014)	.....	.....	.....	.....	.....	.....	.....
	Coelacanth (ENSLACP00000009510)	.....	.....	.....	.....	.....	.....	.....
	Spotted gar (ENSLGPC000000006885)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000009615)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP000000031152)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP000000013579)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000018686)	.....	.....	.....	.....	.....	.....	.....
Dnmt3bb	Amazon molly (ENSPFOP00000001143)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP000000009160)	.....	.....	.....	.....	.....	.....	.....
	Medak (ENSORLP00000025108)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000016142)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021471392.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014146292.1)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021422181.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014135215.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000053417)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164651)	.....	.....	.....	.....	.....	.....	.....
Dnmt3bbb	Spotted gar (ENSLGPC000000006834)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP000000003297)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP00000012966)	.....	.....	.....	.....	.....	.....	.....
	Medaka (ENSORLP00000018521)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSPFOP00000000632)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP00000011441)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000015822)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000021143)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000021057)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021472161.1)	.....	.....	.....	.....	.....	.....	.....
DNM3A	Atlantic salmon (XM_014146676.1)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021422885.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014136242.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000046459)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164740)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000009617)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP000000030962)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP000000009128)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000013567)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XP_014001845.1)	.....	.....	.....	.....	.....	.....	.....
DNM3	Rainbow trout (XP_021422185.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014135212.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000074994)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164450)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSDARP00000118597)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0165118)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (ENSPMAT00000008525)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (gi 1304463388 gb PIZ10)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (ENSPMAT00000007628)	.....	.....	.....	.....	.....	.....	.....
	Ciona savignyi (ENSCSAVG00000000)	.....	.....	.....	.....	.....	.....	.....
European amphioxus (Sc0000092)	.....	.....	.....	.....	.....	.....	.....	

DNMT3C

Dnmt3baa

Dnmt3bbb





		730	740	750	760	770	780	790	800		
DNM3A	Human (ENSP00000264709)	..... ..... ..... ..... ..... ..... ..... ..... ..... .....									
	Pig (ENSSSCP00000019203)	-----MNAMEENQGSTESQKVEE-----									
	Mouse (ENSMUSP00000020991)	-----									
	Rat (ENSRNOP00000046524)	-----									
	Chicken (ENSGALP00000048074)	-----									
	Lizard (ENSACAP00000007951)	-----									
	Coelacanth (ENSLACP00000014690)	-----									
	Elephant_shark (SINCAMP00000011)	-----									
	Spotted gar (ENSLLOCP00000020139)	-----									
	Tetraodon (ENSTNIP00000022331)	-----									
Dnmt3aa	Fugu (ENSTRUP00000009049)	-----									
	Medaka (ENSORLP00000022087)	-----									
	Tilapia (ENSONIP00000006964)	-----									
	Platyfish (XP_023203761.1)	-----									
	Amazon molly (ENSFPFOP0000001500)	-----									
	Stickleback (ENSGACP00000009407)	-----									
	Cod (ENSGMOP00000019846)	-----									
	Rainbow trout (XP_021470020.1)	-----									
	Atlantic salmon (XM_014143600.1)	-----									
	Zebrafish (ENSDARP00000091093)	-----									
Dnmt3ab	Golden line barbell (XM_0164978)	-----									
	Tetraodon (ENSTNIP00000022492)	-----									
	Fugu (ENSTRUP00000024460)	-----									
	Stickleback (ENSGACP00000015064)	-----									
	Tilapia (ENSONIP00000001330)	-----									
	Platyfish (ENSXMAP00000036171)	-----									
	Amazon molly (ENSFPFOP0000001799)	-----									
	Cod (ENSGMOP00000020958)	-----									
	Rainbow trout (XP_021429488.1)	-----									
	Atlantic salmon (XM_014197582.1)	-----									
DNMT3B	Rainbow trout (XP_021440975.1)	-----									
	Atlantic salmon (XM_014211429.1)	-----									
	Zebrafish (ENSDARP00000108609)	-----									
	Golden line barbell (XM_0164754)	-----									
	Human (ENSP00000328547)	-----									
	Pig (ENSSSCP00000007722)	-----CGRHHVDESPVEFSATRS LR-----									
	Mouse (ENSMUSP00000051830)	-----									
	Rat (ENSRNOP00000015482)	-----									
	Mouse (ENSMUSG000000082079)	-----									
	Chinese hamster (ENSCGRP00000001)	-----									} DNMT3C
Rat (UCSC RGSC 5.0/rn5 chr3)	-----										
Dnmt3ba	Chicken (ENSGALP00000052985)	-----									
	Lizard (ENSACAP00000009682)	-----									
	Elephant_shark (SINCAMP000000014)	-----									
	Coelacanth (ENSLACP00000009510)	-----									
	Spotted gar (ENSLLOCP00000006885)	-----									
	Tetraodon (ENSTNIP00000009615)	-----									
	Fugu (ENSTRUP000000031152)	-----									
	Stickleback (ENSGACP000000013579)	-----									
	Tilapia (ENSONIP00000018686)	-----									
	Amazon molly (ENSFPFOP0000001143)	-----									
Dnmt3bb	Platyfish (ENSXMAP00000009160)	-----									
	Medak (ENSORLP00000025108)	-----									
	Cod (ENSGMOP00000016142)	-----									
	Rainbow trout (XP_021471392.1)	-----									
	Atlantic salmon (XM_014146292.1)	-----									
	Rainbow trout (XP_021422181.1)	-----									
	Atlantic salmon (XM_014135215.1)	-----									
	Zebrafish (ENSDARP00000053417)	-----									
	Golden line barbell (XM_0164651)	-----									
	Spotted gar (ENSLLOCP00000006834)	TAQIMQNLPL--LNDTLLRNISILLNPSCKLK--ITGKVVADLATHLGLCKRPEETTQLIDEFLEYQLLENDEAQVLP--									
Tetraodon (ENSTNIP00000003297)	TRCVAETLPL--LSERTRQSVAHLLNPRGWLH--LAGKAVGRLGGELGVCSSAEDAARLTQEFLLQHRGEGEEVEG--										
Fugu (ENSTRUP00000012966)	TRCITEKLP--LGEGLVKSIAQLLSPHRWLK--VAGKAVGELGTQLGICSSAEDATQLTDEFLLQHRLLLE--										
Medaka (ENSORLP00000018521)	TGCTAEELP--LSVKALRSIAQLLSPQSWLK--VTSAQVKELGTQLGVCNSTDEIRQLTEEFLECKPRTREVGPAGTTV										
Amazon molly (ENSFPFOP0000000632)	TCCIAEELP--LSDTVLRNVAQLLNPESSLK--VTDVAVEDLGRKLGVCSS--PEEVRQLKQEFSEYQQAEEERSDQGEN										
Platyfish (ENSXMAP00000011441)	TCCIAEELP--LSDTVLRNVAQLLNPESSLK--VTDVAVEDLGRKLGVCSS--PEEVRQLKQEFSEYQQAEEERSDQGEN										
Stickleback (ENSGACP00000015822)	TGCTAEELP--LSDQVLSGIAQLLNPDQRSLK--LSGKEVEKLGTSKVCSS--PEEVEQLTREFLEYQQAERGDKEPSGV										
Tilapia (ENSONIP00000021143)	TGCTAEELP--LSDVLSKIAQLLNPDQRSLK--VTEETVGEELGTQLGICNSPEEVRQLTNEFLEYQQAERKEAE--										
Cod (ENSGMOP00000021057)	TGLIAKEVP--LSDRILKSMAQLLNPEETKLE--VTDFAVEELGKRLGVCSTEGEVNQLTKELLEYQQRREEEEEDGEH										
Rainbow trout (XP_021472161.1)	TARVAEGLP--LSDGVLRSMAQLLSPQGRLE--VTGKAVGELGAKLGLCSS--PEEISQLNKEFLEYQLAEEGEGDDGEN										
Atlantic salmon (XM_014146676)	TASVAEGLP--LSDGVLRSMAQLLSPQGRLE--VTGKAVGELGAKLGLCSS--PEEISQLNKEFLEYQLAEEGEGDEGEN										
Rainbow trout (XP_021422885.1)	TASVAEGLP--LSDGVLRSMAQLLSPQGRLE--VTGKAVGELGAKLGLCSS--PEEISQLNKEFLEYQLAEEGEGDEGEN										
Atlantic salmon (XM_014136242.1)	TASVAEGLP--LSDGVLRSMAQLLSPQGRLE--VTGKAVGELGAKLGLCSS--PEEISQLNKEFLEYQLAEEGEGDEGEN										
Zebrafish (ENSDARP00000046459)	TTSIAASLP--LSDSVLRAISQLLSPAGRLK--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLAEEENLSST--										
Golden line barbell (XM_0164740)	TTSIADSLP--LSDSVLRGISQLLSPAGRLK--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLAEEEDTTSST--										
Tetraodon (ENSTNIP00000009617)	LETLVQNIIPKRLGNAAALMTVITKVLKHPEDLCVINVLIKSGVQLGVCCKDSAESRQMASDYLSALQAIKEEQ--										
Fugu (ENSTRUP00000030962)	LQSLVEICIPGLGDVTLRNIGLMLKHPESITKEHFPWEVLSVMAVQLGLCAAGPEVELEERSCCDFRKLIQEQSS--										
Platyfish (ENSXMAP000000009128)	LECLVESLPRHLGEEVVLTNITVTLKHSIRGNTLSRNVLVELGFLFKCGLSEKHQLAYDYHKLKLT--										
Stickleback (ENSGACP00000013567)	-----										
Atlantic salmon (XP_014001845.1)	-----										
Rainbow trout (XP_021422185.1)	TWSLMKSLP--LPNVALKNIPILLRPAGRLE--VTSRVVAELGSLMGLCGV--PGDMALLTDEFLEYMISEGKEPTADSP										
Atlantic salmon (XM_014135212.1)	TWSLMESLP--LPNVALKNIPILLRPAGRLE--VTRGVVAELGSLMGLCGV--PGDMALLTDEFLEYMISEGKEPTADSPS										
Zebrafish (ENSDARP00000074994)	TVNIVKRLP--LPDSTLRNLSLVLSPGKLE--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLIDGGDTGSVD--										
Golden line barbell (XM_0164450)	TVNIIERLP--FSDSILRNLSLVLSPGKLE--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLIDGGDTQLAD										
Zebrafish (ENSDARP00000118597)	TVNIVKRLP--LPDSTLRNLSLVLSPGKLE--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLIDGGDTQPAD										
Golden line barbell (XM_0165118)	TVNIVECLP--FSDSTMRNLSLVLSPGKLE--VTGKIVDLDLAVRFGVCSG--PENVSLLNDEFLEYQLIDGGDTHPAD										
DNM3A	Lamprey (ENSPMAT00000008525)	-----									
	Lamprey (gi 1304463388 gb PIZIO)	-----									
DNM3	Lamprey (ENSPMAT00000007628)	-----									
	Ciona savignyi (ENSCSAVG00000000)	-----									
	Ciona savignyi (ENSCSAVP00000002)	-----									
	European amphioxus (Sc00000092)	-----									





	970	980	990	1000	1010	1020	1030	1040
DNM3A	Human (ENSP00000264709)	.....	.....	.....	.....	.....	.....	.....
	Pig (ENSSSCP00000019203)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSP00000020991)	.....	.....	.....	.....	.....	.....	.....
	Rat (ENSRNOP00000046524)	.....	.....	.....	.....	.....	.....	.....
	Chicken (ENSGALP00000048074)	.....	.....	.....	.....	.....	.....	.....
	Lizard (ENSACAP00000007951)	.....	.....	.....	.....	.....	.....	.....
	Coelacanth (ENSLACP00000014690)	.....	.....	.....	.....	.....	.....	.....
	Elephant shark (SINCAMP00000011)	.....	.....	.....	.....	.....	.....	.....
	Spotted gar (ENSLACP00000020139)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000022331)	.....	.....	.....	.....	.....	.....	.....
Dnmt3aa	Fugu (ENSTRUP00000009049)	.....	.....	.....	.....	.....	.....	.....
	Medaka (ENSORLP00000022087)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000006964)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (XP_023203761.1)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSFPFOP0000001500)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000009407)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000019846)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021470020.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014143600.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000091093)	.....	.....	.....	.....	.....	.....	.....
Dnmt3ab	Golden line barbell (XM_0164978)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000022492)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP00000024460)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000015064)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000001330)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP00000036171)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSFPFOP0000001799)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000020958)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021429488.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014197582.1)	.....	.....	.....	.....	.....	.....	.....
DNMT3B	Rainbow trout (XP_021440975.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014211429.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000108609)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164754)	.....	.....	.....	.....	.....	.....	.....
	Human (ENSP00000328547)	.....	.....	.....	.....	.....	.....	.....
	Pig (ENSSSCP00000007722)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSP00000051830)	.....	.....	.....	.....	.....	.....	.....
	Rat (ENSRNOP00000015482)	.....	.....	.....	.....	.....	.....	.....
	Mouse (ENSMUSG000000082079)	.....	.....	.....	.....	.....	.....	.....
	Chinese hamster (ENSCGRP0000001)	.....	.....	.....	.....	.....	.....	.....
Dnmt3ba	Rat (UCSC RGSC 5.0/rn5 chr3)	.....	.....	.....	.....	.....	.....	.....
	Chicken (ENSGALP000000052985)	.....	.....	.....	.....	.....	.....	.....
	Lizard (ENSACAP00000009682)	.....	.....	.....	.....	.....	.....	.....
	Elephant shark (SINCAMP000000014)	.....	.....	.....	.....	.....	.....	.....
	Coelacanth (ENSLACP00000009510)	.....	.....	.....	.....	.....	.....	.....
	Spotted gar (ENSLACP00000006885)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000009615)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP000000031152)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP000000013579)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000018686)	.....	.....	.....	.....	.....	.....	.....
Dnmt3bb	Amazon molly (ENSFPFOP0000001143)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP00000009160)	.....	.....	.....	.....	.....	.....	.....
	Medak (ENSORLP00000025108)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000016142)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021471392.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014146292.1)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021422181.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014135215.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000053417)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164651)	.....	.....	.....	.....	.....	.....	.....
Dnmt3bbb	Spotted gar (ENSLACP000000006834)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000003297)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP00000012966)	.....	.....	.....	.....	.....	.....	.....
	Medaka (ENSORLP00000018521)	.....	.....	.....	.....	.....	.....	.....
	Amazon molly (ENSFPFOP00000006632)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP00000011441)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP000000015822)	.....	.....	.....	.....	.....	.....	.....
	Tilapia (ENSONIP00000021143)	.....	.....	.....	.....	.....	.....	.....
	Cod (ENSGMOP00000021057)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021472161.1)	.....	.....	.....	.....	.....	.....	.....
DNM3A	Atlantic salmon (XM_014146676)	.....	.....	.....	.....	.....	.....	.....
	Rainbow trout (XP_021422885.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014136242.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000046459)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164740)	.....	.....	.....	.....	.....	.....	.....
	Tetraodon (ENSTNIP00000009617)	.....	.....	.....	.....	.....	.....	.....
	Fugu (ENSTRUP000000030962)	.....	.....	.....	.....	.....	.....	.....
	Platyfish (ENSXMAP000000009128)	.....	.....	.....	.....	.....	.....	.....
	Stickleback (ENSGACP00000013567)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XP_014001845.1)	.....	.....	.....	.....	.....	.....	.....
DNM3	Rainbow trout (XP_021422185.1)	.....	.....	.....	.....	.....	.....	.....
	Atlantic salmon (XM_014135212.1)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000074994)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0164450)	.....	.....	.....	.....	.....	.....	.....
	Zebrafish (ENSADARP000000118597)	.....	.....	.....	.....	.....	.....	.....
	Golden line barbell (XM_0165118)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (ENSPMAT00000008525)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (gi 1304463388 gb PIZIO)	.....	.....	.....	.....	.....	.....	.....
	Lamprey (ENSPMAT00000007628)	.....	.....	.....	.....	.....	.....	.....
	Ciona savignyi (ENSCSAVG00000000)	.....	.....	.....	.....	.....	.....	.....
Ciona savignyi (ENSCSAVP00000002)	.....	.....	.....	.....	.....	.....	.....	
European amphioxus (Sc00000092)	.....	.....	.....	.....	.....	.....	.....	

DNMT3C

Dnmt3ba

Dnmt3bbb







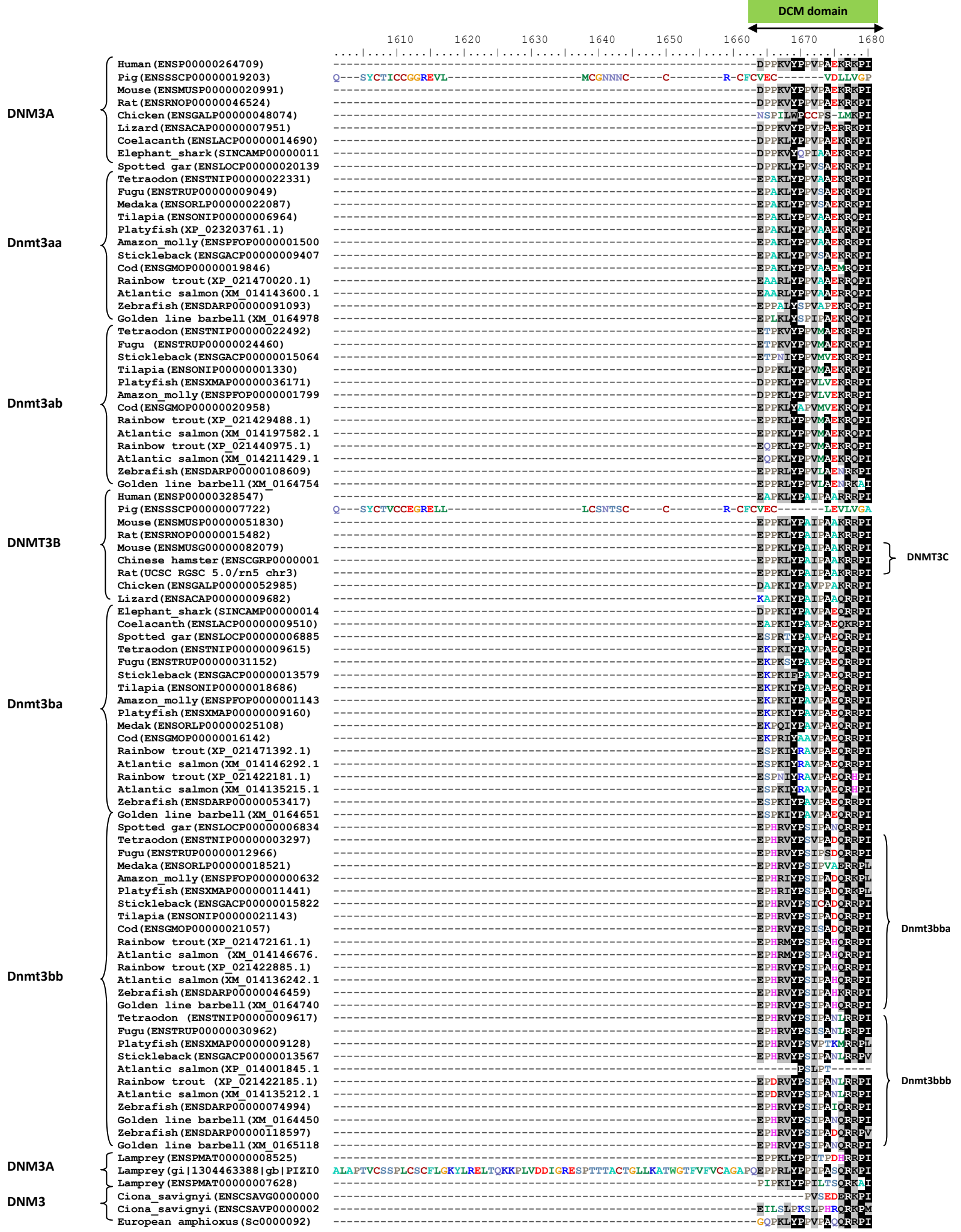














DCM domain

1690 1700 1710 1720 1730 1740 1750 1760

- DNM3A: Human (ENSP00000264709), Pig (ENSSSCP00000019203), Mouse (ENSMUSP00000020991), Rat (ENSRNOP00000046524), Chicken (ENSGALP00000048074), Lizard (ENSACAP0000007951), Coelacanth (ENSLACP00000014690), Elephant\_shark (SINCAMP00000011), Spotted gar (ENSLOCP00000020139), Tetraodon (ENSTNIP00000022331), Fugu (ENSTRUP0000009049), Medaka (ENSORLP00000022087), Tilapia (ENSONIP0000006964), Platyfish (XP\_023203761.1), Amazon\_molly (ENSFP0P0000001500), Stickleback (ENSGACP00000009407), Cod (ENSGMOP00000019846), Rainbow\_trout (XP\_021470200.1), Atlantic\_salmon (XM\_014143600.1), Zebrafish (ENSADARP00000091093), Golden\_line\_barbell (XM\_0164978), Tetraodon (ENSTNIP00000022492), Fugu (ENSTRUP00000024460), Stickleback (ENSGACP00000015064), Tilapia (ENSONIP0000001330), Platyfish (ENSXMAP00000036171), Amazon\_molly (ENSFP0P0000001799), Cod (ENSGMOP00000020958), Rainbow\_trout (XP\_021429488.1), Atlantic\_salmon (XM\_014197582.1), Rainbow\_trout (XP\_021440975.1), Atlantic\_salmon (XM\_014211429.1), Zebrafish (ENSADARP00000108609), Golden\_line\_barbell (XM\_0164754), Human (ENSP00000328547), Pig (ENSSSCP00000007722), Mouse (ENSMUSP00000051830), Rat (ENSRNOP00000015482), Mouse (ENSMUSG00000082079), Chinese\_hamster (ENSCGRP0000001), Rat (UCSC RGSC 5.0/rn5 chr3), Chicken (ENSGALP00000052985), Lizard (ENSACAP00000009682), Elephant\_shark (SINCAMP000000014), Coelacanth (ENSLACP00000009510), Spotted gar (ENSLOCP00000006885), Tetraodon (ENSTNIP00000009615), Fugu (ENSTRUP000000031152), Stickleback (ENSGACP000000013579), Tilapia (ENSONIP00000018686), Amazon\_molly (ENSFP0P00000001143), Platyfish (ENSXMAP00000009160), Medak (ENSORLP00000025108), Cod (ENSGMOP000000016142), Rainbow\_trout (XP\_021471392.1), Atlantic\_salmon (XM\_014146629.1), Rainbow\_trout (XP\_021422181.1), Atlantic\_salmon (XM\_014135215.1), Zebrafish (ENSADARP00000053417), Golden\_line\_barbell (XM\_0164651), Spotted gar (ENSLOCP000000006834), Tetraodon (ENSTNIP000000003297), Fugu (ENSTRUP00000012966), Medaka (ENSORLP00000018521), Amazon\_molly (ENSFP0P00000000632), Platyfish (ENSXMAP00000011441), Stickleback (ENSGACP000000015822), Tilapia (ENSONIP00000021143), Cod (ENSGMOP00000021057), Rainbow\_trout (XP\_021472161.1), Atlantic\_salmon (XM\_014146676), Rainbow\_trout (XP\_021422885.1), Atlantic\_salmon (XM\_014136242.1), Zebrafish (ENSADARP00000046459), Golden\_line\_barbell (XM\_0164740), Tetraodon (ENSTNIP00000009617), Fugu (ENSTRUP000000030962), Platyfish (ENSXMAP000000009128), Stickleback (ENSGACP00000013567), Atlantic\_salmon (XP\_014001845.1), Rainbow\_trout (XP\_021422185.1), Atlantic\_salmon (XM\_014135212.1), Zebrafish (ENSADARP00000074994), Golden\_line\_barbell (XM\_0164450), Zebrafish (ENSADARP00000118597), Golden\_line\_barbell (XM\_0165118), Lamprey (ENSPMAT00000008525), Lamprey (gi|1304463388|gb|PIZIO), Lamprey (ENSPMAT00000007628), Ciona\_savignyi (ENSCSAVG000000000), Ciona\_savignyi (ENSCSAVP00000002), European\_amphioxus (Sc0000092)

Sequence alignment of DCM domain across various species. Conserved motifs are highlighted in red. Motif I and Motif IV are indicated at the bottom.

conserved motif

DNMT3C

Dnmt3bba

Dnmt3bbb

Motif I Motif IV

DCM domain

1770 1780 1790 1800 1810 1820 1830 1840

DNM3A	Human (ENSP00000264709)	NDLSIVNPKRGLY	
	Pig (ENSSSCP00000019203)	PSRLQMFAN-NHDQEF	
	Mouse (ENSMUSP00000020991)	NDLSIVNPKRGLY	
	Rat (ENSRNOP00000046524)	NDLSIVNPKRGLY	
	Chicken (ENSGALP00000048074)	NDLSIVNPKRGLY	
	Lizard (ENSACAP00000007951)	NDLSIVNPKRGLY	
	Coelacanth (ENSLACP00000014690)	NDLSIVNPKRGLF	
	Elephant_shark (SINCAMP00000011)	NDLSIVNPKRGLF	
	Spotted gar (ENSLOCP00000020139)	NDLSIVNPKRGLY	
	Tetraodon (ENSTNIP00000022331)	NDLSIVNPKRGLY	
Dnmt3aa	Fugu (ENSTRUP00000009049)	NDLSIVNPKRGLY	
	Medaka (ENSORLP00000022087)	NDLSIVNPKRGLY	
	Tilapia (ENSONIP00000006964)	NDLSIVNPKRGLY	
	Platyfish (XP_023203761.1)	NDLSIVNPKRGLF	
	Amazon molly (ENSFFOP0000001500)	NDLSIVNPKRGLF	
	Stickleback (ENSGACP00000009407)	NDLSIVNPKRGLF	
	Cod (ENSGMOP00000019846)	NDLSIVNPKRGLY	
	Rainbow trout (XP_021470020.1)	NDLSIVNPKRGLF	
	Atlantic salmon (XM_014143600.1)	NDLSIVNPKRGLF	
	Zebrafish (ENSDARP00000091093)	NDLSIVNPKRGLF	
Dnmt3ab	Golden line barbell (XM_0164978)	NDLSIVNPKRGLY	
	Tetraodon (ENSTNIP00000022492)	NDLSIVNPKRGLY	
	Fugu (ENSTRUP00000024460)	NDLSIVNPKRGLY	
	Stickleback (ENSGACP00000015064)	NDLSIVNPKRGLF	
	Tilapia (ENSONIP00000001330)	NDLSIVNPKRGLY	
	Platyfish (ENSXMAP00000036171)	NDLSIVNPKRGLY	GMFTQLLFLHSPVVFYKSFCSRCEQDYSSMCFCP
	Amazon molly (ENSFFOP0000001799)	NDLSIVNPKRGLY	
	Cod (ENSGMOP000000020958)	NDLSIVNPKRGLF	
	Rainbow trout (XP_021429488.1)	NDLSIVNPKRGLY	
	Atlantic salmon (XM_014197582.1)	NDLSIVNPKRGLY	
DNMT3B	Rainbow trout (XP_021440975.1)	NDLSIVNPKRGLY	
	Atlantic salmon (XM_014211429.1)	NDLSIVNPKRGLY	
	Zebrafish (ENSDARP00000108609)	NDLSIVNPKRGLY	
	Golden line barbell (XM_0164754)	NDLSIVNPKRGLY	
	Human (ENSP00000328547)	NDLSIVNPKRGLY	
	Pig (ENSSSCP00000007722)	SVRLQAFFTS-DPGLY	
	Mouse (ENSMUSP00000051830)	NDLSIVNPKRGLY	
	Rat (ENSRNOP00000015482)	NDLSIVNPKRGLY	
	Mouse (ENSMUSG00000082079)	NDLSIVNPKRGLY	
	Chinese hamster (ENSCGRP00000001)	NDLSIVNPKRGLY	
Dnmt3ba	Rat (UCSC RGSC 5.0/rn5 chr3)	NDLSIVNPKRGLY	
	Chicken (ENSGALP000000052985)	NDLSIVNPKRGLY	
	Lizard (ENSACAP00000009682)	NDLSIVNPKRGLY	
	Elephant_shark (SINCAMP000000014)	NDLSIVNPKRGLY	
	Coelacanth (ENSLACP00000009510)	QPLVSTLKGKGRIS	
	Spotted gar (ENSLOCP00000006885)	NDLSIVNPKRGLY	
	Tetraodon (ENSTNIP00000009615)	NDLSIVNPKRGLY	
	Fugu (ENSTRUP000000031152)	NDLSIVNPKRGLY	
	Stickleback (ENSGACP000000013579)	NDLSIVNPKRGLY	
	Tilapia (ENSONIP00000018686)	NDLSIVNPKRGLY	
Dnmt3bb	Amazon molly (ENSFFOP0000001143)	NDLSIVNPKRGLF	
	Platyfish (ENSXMAP000000009160)	NDLSIVNPKRGLF	
	Medak (ENSORLP00000025108)	NDLSIVNPKRGLY	
	Cod (ENSGMOP00000016142)	NDLSIVNPKRGLY	
	Rainbow trout (XP_021471392.1)	NDLSIVNPKRGLY	
	Atlantic salmon (XM_014146292.1)	NDLSIVNPKRGLY	
	Rainbow trout (XP_021422181.1)	NDLSIVNPKRGLY	
	Atlantic salmon (XM_014135215.1)	NDLSIVNPKRGLY	
	Zebrafish (ENSDARP000000053417)	NDLSIVNPKRGLY	
	Golden line barbell (XM_0164651)	NDLSIVNPKRGLY	
Dnmt3bbb	Spotted gar (ENSLOCP00000006834)	NDLSIVNPKRGLF	
	Tetraodon (ENSTNIP00000003297)	NDLSIVNPKRGLF	
	Fugu (ENSTRUP00000012966)	NDLSIVNPKRGLF	
	Medaka (ENSORLP00000018521)	NDLSIVNPKRGLY	
	Amazon molly (ENSFFOP0000000632)	NDLSIVNPKRGLF	
	Platyfish (ENSXMAP00000011441)	NDLSIVNPKRGLF	
	Stickleback (ENSGACP00000015822)	NDLSIVNPKRGLF	
	Tilapia (ENSONIP00000021143)	NDLSIVNPKRGLF	
	Cod (ENSGMOP00000021057)	NDLSIVNPKRGLF	
	Rainbow trout (XP_021472161.1)	NDLACVNPARKGLF	
DNM3A	Atlantic salmon (XM_014146676)	NDLACVNPARKGLF	
	Rainbow trout (XP_021422885.1)	NDLACVNPARKGLF	
	Atlantic salmon (XM_014136242.1)	NDLACVNPARKGLF	
	Zebrafish (ENSDARP00000046459)	NDLSIVNPKRGLF	
	Golden line barbell (XM_0164740)	NDLSIVNPKRGLF	
	Tetraodon (ENSTNIP00000009617)	NDLSIVNPKRGLY	
	Fugu (ENSTRUP000000030962)	NDLSIVNPKRGLY	
	Platyfish (ENSXMAP000000009128)	NDLSIVNPKRGLY	
	Stickleback (ENSGACP00000013567)	NDLSIVNPKRGLY	
	Atlantic salmon (XP_014001845.1)	VDSRFSSHCLMCLA	
DNM3	Rainbow trout (XP_021422185.1)	NDLAVNPKRGLF	
	Atlantic salmon (XM_014135212.1)	NDLSIVNPKRGLF	
	Zebrafish (ENSDARP00000074994)	NDLSIVNPKRGLY	
	Golden line barbell (XM_0164450)	NDLSIVNPKRGLF	
	Zebrafish (ENSDARP00000118597)	NDLCTVNPCKRGLF	
	Golden line barbell (XM_0165118)	NDLCTVNPCKRGLF	
	Lamprey (ENSPMAT00000008525)	SDLSIVNPKRGLY	
	Lamprey (gi 1304463388 gb PIZIO)	NDLSIVNPKRGLY	
	Lamprey (ENSPMAT00000007628)	NDLSIVNPKRGLY	
	Ciona savignyi (ENSCSAVG00000000)	NDLSIVNPKRGLL	D
Ciona savignyi (ENSCSAVP00000002)	NDLSIVNPKRGLI	S	
European amphioxus (Sc00000092)	NDLSIVNPKRGLY	FTDLLCSPP	

Motif IV





DCM domain

2010 2020 2030 2040 2050 2060 2070 2080

Species	Accession	Sequence	Group
Human	ENSPP00000264709	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	DNM3A
Pig	ENSSSCP00000019203	Q---KHIQ--EWGPFDLVIGGSPCNDLSIVNPAKGLY---	
Mouse	ENSMSUSP00000020991	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Rat	ENSRNOP00000046524	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Chicken	ENSALP00000048074	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Lizard	ENSACAP0000007951	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Coelacanth	ENSLACP00000014690	EKEDILWCTEME...R	
Elephant shark	SINCAMP00000011	RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Spotted gar	ENSLOCP00000020139	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Tetraodon	ENSTNIP00000022331	RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Fugu	ENSTRUP0000009049	SKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Medaka	ENSORLP00000022087	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Tilapia	ENSONIP0000006964	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Platyfish	XP_023203761.1	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Amazon molly	ENSFPFOP0000001500	NKEDILWCTEMESDEDEGKAEKKKKEKESGGTGENRVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Stickleback	ENSACAP0000009407	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Cod	ENSNGMOP00000019846	SKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Rainbow trout	XP_021472020.1	SKEDILWCTEME...SRLLGRORLLGRSWSVPPVIRHLEFAPLKE YFA	
Atlantic salmon	XM_014143600.1	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Zebrafish	ENSADARP00000091093	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Golden line barbell	XM_0164978	NKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Tetraodon	ENSTNIP00000022492	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Fugu	ENSTRUP00000024460	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Stickleback	ENSACAP00000015064	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Tilapia	ENSONIP0000001330	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Platyfish	ENSXMAP00000036171	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Amazon molly	ENSFPFOP0000001799	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Cod	ENSNGMOP00000020958	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Rainbow trout	XP_021429488.1	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Atlantic salmon	XM_014197582.1	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Rainbow trout	XP_021440975.1	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Atlantic salmon	XM_014211429.1	EKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Zebrafish	ENSADARP00000108609	DKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Golden line barbell	XM_0164754	DKEDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Human	ENSPP00000328547	GKEDVLWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
Pig	ENSSSCP00000007722	K---KNIE--EWGPFDLVIGGSPCNDLSNVNPAKGLY---	
Mouse	ENSMSUSP00000051830	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Mouse	ENSMSUG000000082079	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
Chinese hamster	ENSRCRPO000001	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
Rat	UCSC RGSC 5.0/rn5 chr3	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
Chicken	ENSALP000000052985	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
Lizard	ENSACAP00000009682	GKDDVLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Tetraodon	ENSTNIP00000009615	GKEDILWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Zebrafish	ENSADARP00000053417	GKEDILWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Platyfish	ENSXMAP00000011441	GKDDILWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Golden line barbell	XM_0164740	GKDDILWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Fugu	ENSTRUP000000030962	GRDDILWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Rainbow trout	XP_021422185.1	GVDDNLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Zebrafish	ENSADARP00000118597	GKDDSLWCTEME...RVFCFPVHYTDVSNMGRGAROKLLGRSWSVPPVIRHLEFAPLKE YFA	
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Lamprey	(gi 1304463388 gb PIZIO	GKDDILWCTEME...RVFCFPVHYTDVSNMSRLARORLLGRSWSVPPVIRHLEFAPLKE YFA	
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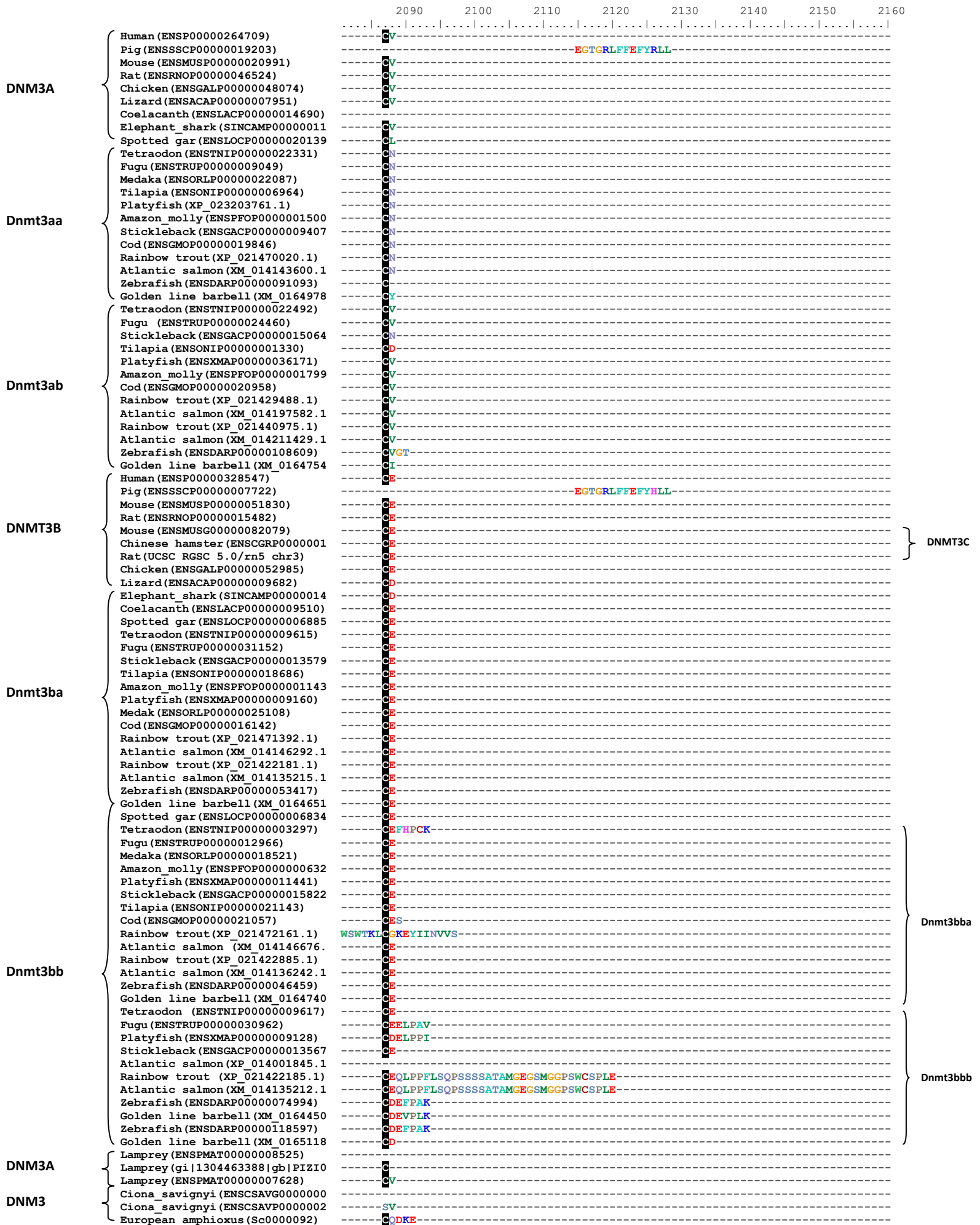
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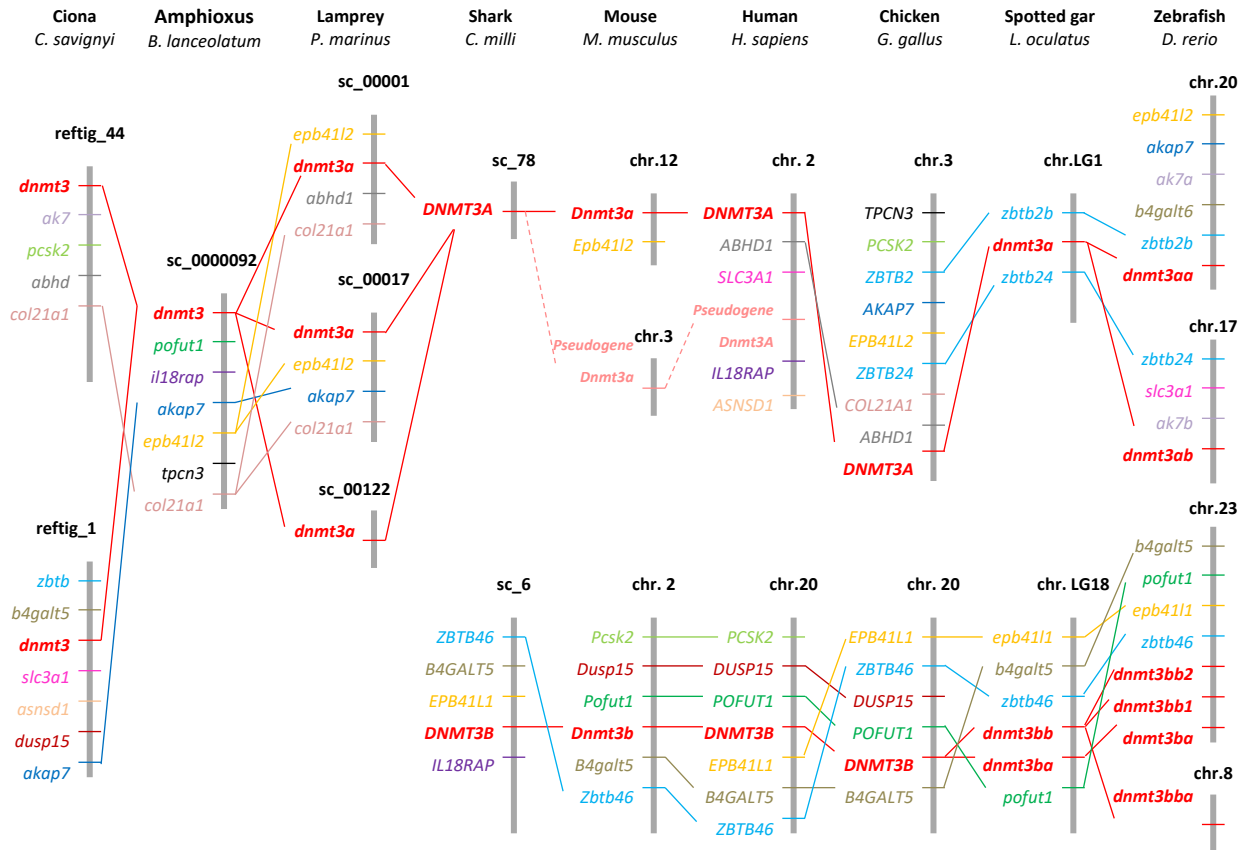
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Motif IX Motif X

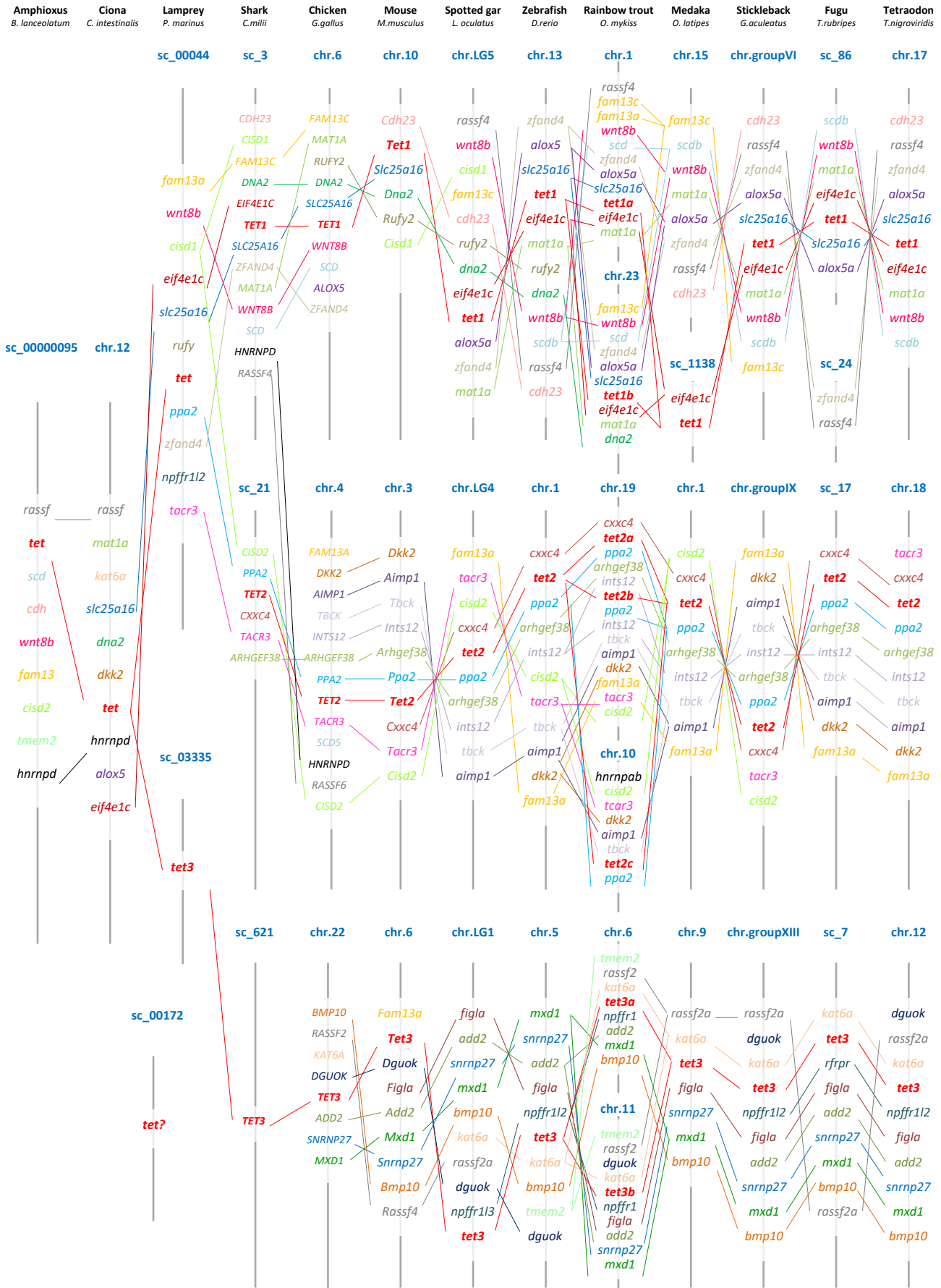


**Supplemental Fig.S3 Dnmt3 protein sequences alignment.** All the protein sequences were aligned with the MUSCLE method in MEGA software. Conserved domains were noted above. Chromatin binding sites were marked with an asterisk (\*); Conserved motifs were marked with a triangle (Δ); Zn binding sites were marked with a number sign (#).

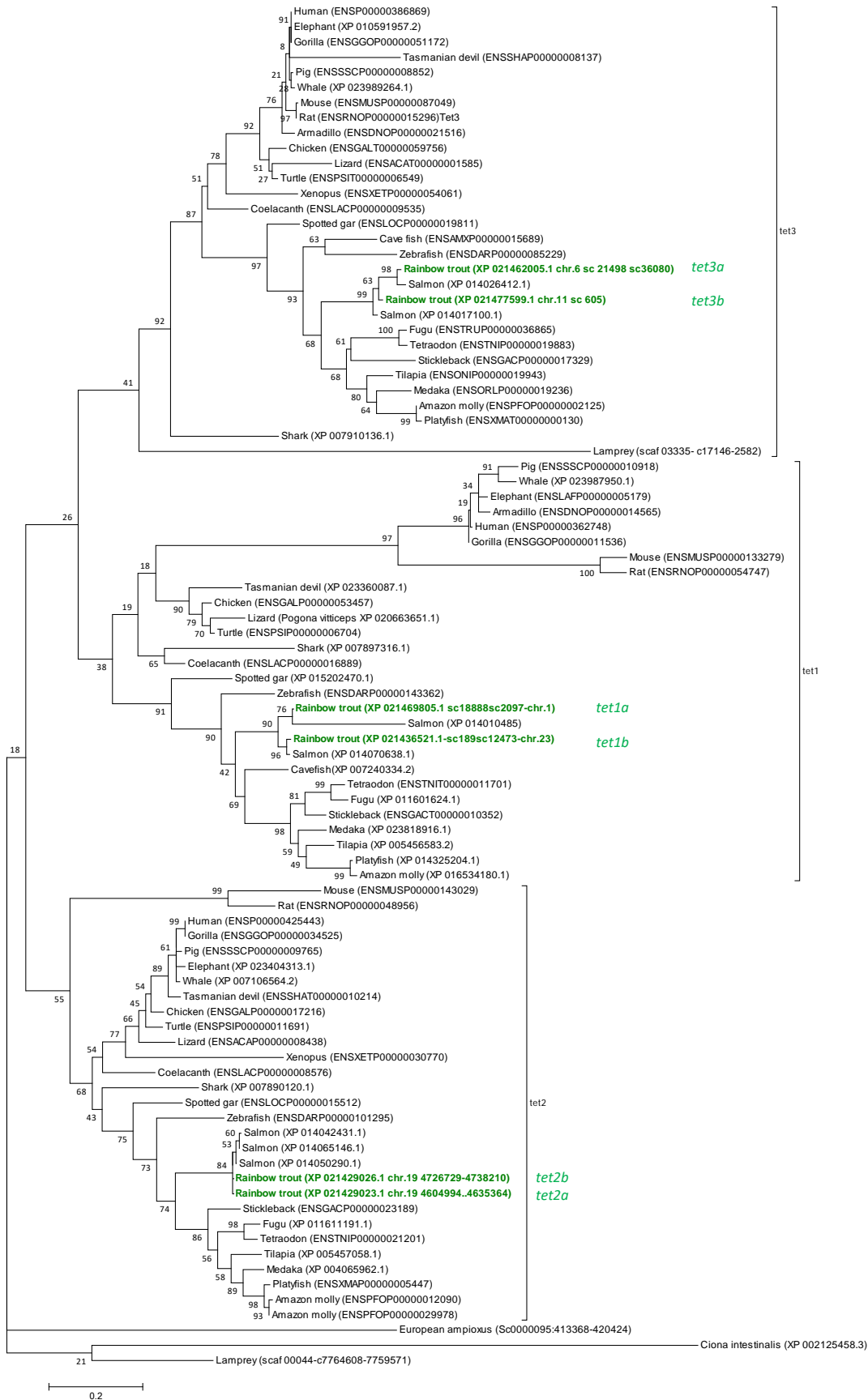


**Supplementary Fig. S4 Conserved synteny around the *dnmt3* loci in chordates.** Data were collected with Genomicus software version 01.01. chr., chromosome; sc., scaffold.





Supplementary Fig. S5 Conserved synteny around the *tet* loci in chrodates. Data were collected with Genomicus software version 01.01. chr., chromosome; sc., scaffold.



**Supplementary Fig. S6: Phylogenetic of tet family genes.** The phylogenetic trees were built using the Maximum Likelihood method based on the JTT matrix-based model in MEGAX software. The tree with the highest log likelihood (-14106.84) is shown. A discrete Gamma distribution was used to model evolutionary rate differences among sites (5 categories (+G, parameter = 0.5234)). The reliability of the inferred trees was estimated by the bootstrap method with 500 replications. All accession numbers are specified in parentheses.



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Salmon (XP\_014026412.1) MHRAKGGPGPPPFQDIYEFSDGDDETTQIFLFRGPRAMEGPGPELSPHSEYIQTEHQGGGLFSLRPPAHGVPHAPQGGKRRRCVCGCAP  
Salmon (XP\_014017100.1) MHRAKGGPGPPPHIQDIYEFSLDGDDETTQIFLFRGPKAMEGPGPLPSPHHYKYIQTEHQGGVIFSLGPPTHGEALAAPQGGKRRRCVCGCP  
  
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Ciona intestinalis (XP\_0021254) -----  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) -----  
Lizard (XP\_020663651.1) -----  
Chicken (ENSGALP00000053457) -----  
Turtle (ENSPSIP00000006704) -----  
Human (ENSP00000362748) -----  
Gorilla (ENSGGOP00000011536) -----  
Mouse (ENSMUSP00000133279) -----  
Rat (ENSRNOP00000054747) -----  
Pig (ENSSSCP00000010918) -----  
Whale (XP\_023987950.1) -----  
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Armadillo (ENSDNOP00000014565) -----  
Tasmanian devil (XP\_023360087) -----  
Coelacanth (ENSLACP00000016889) -----  
Cavefish (XP\_007240334.2) -----  
Platyfish (XP\_014325204.1) -----  
Tilapia (XP\_005456583.2) -----  
Spotted gar (XP\_015202470.1) -----  
Stickleback (ENSGACT0000001035) -----  
Tetraodon (ENSTNIT00000011701) -----  
Fugu (XP\_011601624.1) -----  
Zebrafish (ENSDARP00000143362) -----  
Amazon\_molly (XP\_016534180.1) -----  
Medaka (XP\_023818916.1) -----  
Rainbow\_trout (XP\_021469805.1) -----  
Rainbow trout (XP\_021436521.1) -----  
Salmon (XP\_014010485) -----  
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Shark (XP\_007890120.1) -----  
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Pig (ENSSSCP00000009765) -----  
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Stickleback (ENSGACP00000002318) -----  
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Salmon (XP\_014042431.1) -----  
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Rainbow trout (XP\_021429026.1) -----  
Rainbow trout (XP\_021429023.1) -----  
Shark (XP\_007910136.1) -----  
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Mouse (ENSMUSP00000087049) -----  
Rat (ENSRNOP00000015296) Tet3 -----  
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Elephant (XP\_010591957.2) -----  
Whale (XP\_023989264.1) -----  
Tasmanian devil (ENSSHAP000000) -----  
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Salmon (XP_014026412.1) -----
Salmon (XP_014017100.1) -----
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Ciona intestinalis (XP_0021254) -----
Lamprey (scaf_00044) -----
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-----SEAGMENRLEVF-----
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MW-----DKKDSGDIMDDPELTKPGEF-----
MW-----DKKDDGIMDDPELTKPGEF-----
-----
MW-----DKKDDGIMDDPELTKPGEF-----
-----
VPGQMDSPVYHGD SRQLSA--SGVPVNGAREPAGPSLLGTGGPWRVD-----
VPGQMDSPVYHGD SRQLSA--SGVPVNGAREPAGPSLLGTGGPWRVD-----
VPGPMDSPVYHGASRQLSA--SGAPVNGAREPAGPGLLAGGPPWRAD-----
-----MDSGPVYHGD SRQLST--SGAPVNGAREPAGPGLLAGGPPWRVD-----
VPGQMDSPVYHGD SRQLST--SGAPVNGAREPAGPSLLGAAGPWRVD-----
-----MDSGPVYHGD SRQLSA--PGAPVNGAREPAGPSLLGTGGPWRAD-----
VPGQMDSPVYHGD SRQLSS--SGVPVNGAREPAGPSLLGAGPWRVD-----
VPGQMDSPVYDGD SRQLSA--SGAPVNGAREPAGPGLLTGGPWRAD-----
-----MDPGPVYHGBERRLKT--PRAPVNGAREPAGPGLLVGGVWQVN-----
LTPLLSPRSQTGPGGDPV DGRGPMEEGLLDYGGERTLS EGG--RLG-----
BERRLSGLLTNGGGGGRMDG--RGGREGG--GGGSAMLS DGSWLGGLC-----
LNSDPPASLVSDP-----MALEQLLG-----
KTDQMEAGPVNHVQEGRLKQECDSTLPSKGCEDLANQLLMEANSWLSNTA-----
KTGQMEBGINHVVEESRLRLESEPSVNGARERDETSALMEESDWLE-----

```

Spotted\_gar (ENSLOC0000001981)  
Amazon\_molly (ENSPFOP000000021)  
Cave\_fish (ENSAMXP00000015689)  
Fugu (ENSTRUP00000036865)  
Medaka (ENSORLP00000019236)  
Platyfish (ENSXMAT0000000130)  
Stickleback (ENSGACP0000001732)  
Tetraodon (ENSTNIP00000019883)  
Tilapia (ENSONIP00000019943)  
Zebrafish (ENSDARP00000085229)  
Rainbow\_trout (XP\_021462005.1)  
Rainbow\_trout (XP\_021477599.1)  
Salmon (XP\_014026412.1)  
Salmon (XP\_014017100.1)

N-----LGLVNGASRQPSSEEEGR-----

-----IGAS-----

SLKVAN-----GVNNYPSGDGTSIETEQQRTGSVPPRPVWS-----

LSLEPTNGVIRQPSDTNEGGAGLDTQREPHRSGSVSPGQGWVPQGKAP-----

LSLEPTNGVSRHRPDTHEEGGAGLEPQREPORSSSVSPGQCVPGHFKAT-----

LSLEPTNGVSRQPSDTHHEGGAGLDTQREPHRSGSVSPGQGWVPQGKAP-----

LSLEPIINGVSRHRPDTHEEGGAGLGPQREPORSRVSPGQCVPGHFKAT-----

280 290 300 310 320 330 340 350 360  
.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....|.....

European\_ampoioxus (Sc00000095)  
Ciona\_intestinalis (XP\_0021254)  
Lamprey (scaf\_00044)  
Lamprey (scaf\_03335)  
Shark (XP\_007897316.1)  
Lizard (XP\_020663651.1)  
Chicken (ENSGALP00000053457)  
Turtle (ENSPSIP00000006704)  
Human (ENSP00000362748)  
Gorilla (ENSGGOP00000011536)  
Mouse (ENSMUSP000000133279)  
Rat (ENSRNOP00000054747)  
Pig (ENSSSCP00000010918)  
Whale (XP\_023987950.1)  
Elephant (ENSLAFP00000005179)  
Armadillo (ENSDNOP00000014565)  
Tasmanian\_devil (XP\_023360087)  
Coelacanth (ENSLACP00000016889)  
Cavefish (XP\_007240334.2)  
Platyfish (XP\_014325204.1)  
Tilapia (XP\_005456583.2)  
Spotted\_gar (XP\_015202470.1)  
Stickleback (ENSGACT0000001035)  
Tetraodon (ENSTNIT00000011701)  
Fugu (XP\_011601624.1)  
Zebrafish (ENSDARP000000143362)  
Amazon\_molly (XP\_016534180.1)  
Medaka (XP\_023818916.1)  
Rainbow\_trout (XP\_021469805.1)  
Rainbow\_trout (XP\_021436521.1)  
Salmon (XP\_014010485)  
Salmon (XP\_014070638.1)  
Shark (XP\_007890120.1)  
Human (ENSP00000425443)  
Gorilla (ENSGGOP00000034525)  
Mouse (ENSMUSP000000143029)  
Rat (ENSRNOP00000048956)  
Pig (ENSSSCP00000009765)  
Tasmanian\_devil (ENSSHAT000000)  
Whale (XP\_007106564.2)  
Elephant (XP\_023404313.1)  
Lizard (ENSACAP00000008438)  
Chicken (ENSGALP00000017216)  
Turtle (ENSPSIP00000011691)  
Xenopus (ENSXETP00000030770)  
Coelacanth (ENSLACP00000008576)  
Amazon\_molly (ENSPFOP0000000120)  
Amazon\_molly (ENSPFOP0000000299)  
Fugu (XP\_011611191.1)  
Medaka (XP\_004065962.1)  
Platyfish (ENSXMAP00000005447)  
Spotted\_gar (ENSLOC0000000155)  
Stickleback (ENSGACP00000002318)  
Tilapia (XP\_005457058.1)  
Tetraodon (ENSTNIP000000021201)  
Zebrafish (ENSDARP000000101295)  
Salmon (XP\_014042431.1)  
Salmon (XP\_014065146.1)  
Salmon (XP\_014050290.1)  
Rainbow\_trout (XP\_021429026.1)  
Rainbow\_trout (XP\_021429023.1)  
Shark (XP\_007910136.1)  
Human (ENSP00000386869)  
Gorilla (ENSGGOP00000051172)  
Armadillo (ENSDNOP00000021516)  
Mouse (ENSMUSP000000087049)  
Rat (ENSRNOP00000015296)Tet3  
Pig (ENSSSCP00000008852)  
Elephant (XP\_010591957.2)  
Whale (XP\_023989264.1)  
Tasmanian\_devil (ENSSHAP000000)

-----IVNPS ECDRQAEKGE SSSP-----EKSISPSISDIPN

-----CAGQEEEGEETPE-----TKNSVPSY

-----NPSLLK-GKSQETTQFWS-----QREVDSKINIPTHSGPA

-----NPSLLK-GKSQETTQFWS-----QREVDSKINIPTHSGPA

-----NRCLVE-GESQEIITQSCPVEERIEDTQSCISASGNLE

-----NMCLVE-GESQEIITQSC-----SQTVEDS QS CIS EYGNLE

-----NTSLIK-DEGQETTQSWP-----QSV E E E V N H S T H S G P V

-----NASLIK-DESQETTQSWP-----QSVENSKINRSIHS GPA

-----NSSLIK G E S Q E I T Q S W S-----QRI E D A K I N I P T H S D P A

-----NVSLIK-GEQETTQSWP-----QREVDSRINIPTHSGPV

-----RHTCNSLSQHDPADLRSRTRSF

-----ETDTRGGD-----VQHS CDGLITEDE- TSF S N N S E G D

-----KADSP LC NN T L E D C V Q N S C D G P I T Q Q E K I T D S H K S I G D

-----NSRCRLPARPSPPEHRSTGA

-----KADSPPCADTLDDCGGQCSHDSATSQRDNNAVSRDASGD

-----RHTTSSLNQNGLLLECNCGKSKSP

-----ETDTRRGD-----LQHS CD S L I T E D E - K S F S N N S E G D

-----KVPSPEGT D M L D D S L P L G C D R H A A H Q D Q K T V I S D G D S D

LDDTSCVDQQEPGVSHDSEKPNORTELDHSCIDQQEPGVGHGEGKPLNLR TDD SAS DDKHEELVAHN GDAVGTDPHDKPFSHSGEGK

-----SLRTD D L A S D D K Q E E L V A H N G E T V G T D S Y D K P V S H S G E G N

LDDP-----SCIDQL E P G V G H D G E G K P L N L R T D D S A S D G K H E E L V A H N G D V V G T D P H N K P F S H S G D G N

-----NLRTD D L A S D D K Q E E L V A H N G E T V G A D S H D K T V S H S G E G N







Shark (XP\_007910136.1)
Human (ENSP00000386869)
Gorilla (ENSGGOP0000051172)
Armadillo (ENSDNOP0000021516)
Mouse (ENSMUSP0000087049)
Rat (ENSRNOP0000015296)Tet3
Pig (ENSSSCP0000008852)
Elephant (XP\_010591957.2)
Whale (XP\_023989264.1)
Tasmanian devil (ENSSHAP000000)
Chicken (ENSGALT0000059756)
Lizard (ENSACAT0000001585)
Turtle (ENSPSIT0000006549)
Xenopus (ENSXETP0000054061)
Coelacanth (ENSLACP0000009535)
Spotted\_gar (ENSLGCP0000001981)
Amazon\_molly (ENSPFOP00000021)
Cave\_fish (ENSAMXP0000015689)
Fugu (ENSTRUP00000036865)
Medaka (ENSORLP00000019236)
Platyfish (ENSXMAT0000000130)
Stickleback (ENSGACP0000001732)
Tetraodon (ENSTNIP00000019883)
Tilapia (ENSONIP00000019943)
Zebrafish (ENSDDAR00000085229)
Rainbow\_trout (XP\_021462005.1)
Rainbow\_trout (XP\_021477599.1)
Salmon (XP\_014026412.1)
Salmon (XP\_014017100.1)

--REMSREAGN-NSRGPRPGECSAGS--EDLDTLQT
--REMSREAGN-NSRGPRPGECSAGS--EDLDTLQT
--REMSGEAGD-ASRGPRPGECPVGS--EDLDTLQT
--REMSREAGS-NGRGPR--PESCSBGS--EDLDTLQT
--REMSREAGN-NGRAPR--PESCSBGG--EDLDTLQT
--REMSREAGDDNSRGPQSGEPCPAGS--EDLDTLQT
--REMSREAGN-NSREPRPGECSAGS--EDLDTLQT
--REMSREAGN-NSRGPRSGPECSAGS--EDLDTLQT
--REMSREGGG-NLSGPQSGPESYSAGG--EDLDTLQT
--YKRFDEMS--RGG--LAPRDGVPRG--EDLHALKA
RLYEKFNAEMK--AGESPSGSAASDGP--EDLSALQA
--LKEAGSS--HPKLASSQLLQ--EADFHKKT
QLYEKFNYETN--RDNSGHLEGNAPSCP--EDLNTLKA
QLYKFFLEMSRSPALDSSLPLPESSSGT--EDLSTLRN
HLYEKFNQEMNTGGVRGKTEAKGGSVGTGHCCTEDLNTLQM
KLYEKFQTQETCADGAH--SRVSAGAPETSCEPLEDLDTLQT
QLYEKFIQEMG-GRGDDAKQKGSWGDGKKNCTP--EDLNTLQT
QLYERFSQEMGSNQAQ--ARLSAGTSEGAQPPEDLKTTLQT

550 560 570 580 590 600 610 620 630
...|...|...|...|...|...|...|...|...|...|...|...|...|...|...|...|...

European ampioxus (Sc0000095)
Ciona intestinalis (XP\_0021254)
Lamprey (scaf\_00044)
Lamprey (scaf\_03335)
Shark (XP\_007897316.1)
Lizard (XP\_020663651.1)
Chicken (ENSGALP00000053457)
Turtle (ENSPSIP0000006704)
Human (ENSP00000362748)
Gorilla (ENSGGOP00000011536)
Mouse (ENSMUSP00000133279)
Rat (ENSRNOP00000054747)
Pig (ENSSSCP00000010918)
Whale (XP\_023987950.1)
Elephant (ENSLAFP00000005179)
Armadillo (ENSDNOP00000014565)
Tasmanian devil (XP\_023360087)
Coelacanth (ENSLACP00000016889)
Cavefish(XP\_007240334.2)
Platyfish (XP\_014325204.1)
Tilapia (XP\_005456583.2)
Spotted\_gar (XP\_015202470.1)
Stickleback (ENSGACT0000001035)
Tetraodon (ENSTNIP00000011701)
Fugu (XP\_011601624.1)
Zebrafish (ENSDDAR00000143362)
Amazon\_molly (XP\_016534180.1)
Medaka (XP\_023818916.1)
Rainbow\_trout (XP\_021469805.1)
Rainbow trout (XP\_021436521.1)
Salmon (XP\_014010485)
Salmon (XP\_014070638.1)
Shark (XP\_007890120.1)
Human (ENSP00000425443)
Gorilla (ENSGGOP00000034525)
Mouse (ENSMUSP00000143029)
Rat (ENSRNOP00000048956)
Pig (ENSSSCP00000009765)
Tasmanian devil (ENSSHAT000000)
Whale (XP\_007106564.2)
Elephant (XP\_023404313.1)
Lizard (ENSACAP00000008438)
Chicken (ENSGALP00000017216)
Turtle (ENSPSIP00000011691)
Xenopus (ENSXETP00000030770)
Coelacanth (ENSLACP00000008576)
Amazon\_molly (ENSPFOP0000000120)
Amazon\_molly (ENSPFOP0000000299)
Fugu (XP\_011611191.1)
Medaka (XP\_004065962.1)
Platyfish (ENSXMAP00000005447)
Spotted\_gar (ENSLGCP000000155)
Stickleback (ENSGACP0000002318)
Tilapia (XP\_005457058.1)
Tetraodon (ENSTNIP000000021201)
Zebrafish (ENSDDAR00000101295)

QPGLH--SLTESGNGLKDPVPCMESYLPKIVLELPGNKAL
VHLAA--TGSNSSLHVESVSSLVESNM-KLVDFVPVHKEL
WELPG--ADPVHGEALGETPDLPEIPGAIPVQGEVFGTIL
WELPG--ADPVHGEALGETPDLPEIPGAIPVQGEVFGTIL
WGFSG--ANLVQVEALGKGSDEDLGAI--TML
WGFPG--ANLVHSETLKGSVSPEDLGA--TML
WEVPG--ANPVHGEPLGETPNPPEIPGAIPVQGEVFGAIL
WEVPG--ANPVHGEPLGETPGPEIPGAIPVQGEVFGALL
WKVPG--VNPVCGEALGETSSLEVPVGAIAVQGEVFGAIL
WEVPG--ANPFYGEALGETPDPPEIPGTILAQEVEFGATQ
--TEQPSTTNESEDDAFVKEHDPVAVKVDVVCET
NTPTC--QIPDPHTHN-PLTAQSESP--VRVFSN--AATSYPFKALSNSDLCELEVVNQAKTDLQPTV
GTPAC--QTPDPPHSNKGLTAQSESP--CVLLVSN--TATSNPTKAPSTSESLGKVLK--KIDIQPAT
--SADSATSVDLPLKNAEDNNVVAESQREVSSSL
NTPGP--RTPDPSDANRRWTVQSEPPVVRVPPVSN--TATSNTTKAPCTSEVLDPPELLSQKTDMDQPPP
QPNTVFVDQDDPLK-HNPVNNVDFAYNN
NTPTC--QNPDPHICN-PLTAQSESP--VRVFSN--AATSYPFKALSNSDLCELEVVNQAKTDLQPTV
SLPAR--QTPHPLSSNNQLAAQSDLPAPALLFSN--QTSSSPTKVLCSTSE--EDLSQHKTDVIPVT
AEPATSDLVSPPLPHPHPTFTLHPTMSHDIKVLNQGAKLIQPTQVVEIHKPLKVPTTFHETSQTTSVHPVLSLSVAFLSEPHKSLCVIP
SEPATSDLASPPLHLP--SPPHPTVSHGKMLVKKVGVKPIQPTQVVEIHKPLKVPTTFHETSQSASPMPVLSLSVAFLSEPHKSLCVIP
SEPATSDLASPPLPHPHPTSPHPTMSHDIKVLNQGAKLIQPTQVVEIHKSLKVPTTFHETSQTTSVHPVLSLSVAFLSEPHKSLCVIP
SEPATSDLASPPLRLP--SPPHPTVSHGKMLVNVGVKPIQPTQVVEIHKPLKVPTTFHETSQVSPMPVLSLSVAFLSEPHKSLCVIP



Spotted\_gar (ENSLOCP000000155)
Stickleback (ENSGACP0000002318)
Tilapia (XP\_005457058.1)
Tetraodon (ENSTNIP00000021201)
Zebrafish (ENSXDAR000000101295)
Salmon (XP\_014042431.1)
Salmon (XP\_014065146.1)
Salmon (XP\_014050290.1)
Rainbow\_trout (XP\_021429026.1)
Rainbow\_trout (XP\_021429023.1)
Shark (XP\_007910136.1)
Human (ENSP00000386869)
Gorilla (ENSGGOP00000051172)
Armadillo (ENSDNOP00000021516)
Mouse (ENSMUSP00000087049)
Rat (ENSRNOP00000015296)Tet3
Pig (ENSSSCP00000008852)
Elephant (XP\_010591957.2)
Whale (XP\_023989264.1)
Tasmanian\_devil (ENSSHAP000000)
Chicken (ENSGALP00000059756)
Lizard (ENSACAT0000001585)
Turtle (ENSPSIT00000006549)
Xenopus (ENSXETP00000054061)
Coelacanth (ENSLACP00000009535)
Spotted\_gar (ENSLOCP0000001981)
Amazon\_molly (ENSPFOP000000021)
Cave\_fish (ENSAMXP00000015689)
Fugu (ENSTRUP00000036865)
Medaka (ENSORLP00000019236)
Platyfish (ENSXMAT0000000130)
Stickleback (ENSGACP0000001732)
Tetraodon (ENSTNIP00000019883)
Tilapia (ENSONIP00000019943)
Zebrafish (ENSXDAR000000085229)
Rainbow\_trout (XP\_021462005.1)
Rainbow\_trout (XP\_021477599.1)
Salmon (XP\_014026412.1)
Salmon (XP\_014017100.1)

730 740 750 760 770 780 790 800 810

European\_ampoixus (Sc00000095)
Ciona\_intestinalis (XP\_0021254)
Lamprey (scaf\_00044)
Lamprey (scaf\_03335)
Shark (XP\_007897316.1)
Lizard (XP\_020663651.1)
Chicken (ENSGALP00000053457)
Turtle (ENSPSIP00000006704)
Human (ENSP00000362748)
Gorilla (ENSGGOP00000011536)
Mouse (ENSMUSP00000133279)
Rat (ENSRNOP000000054747)
Pig (ENSSSCP0000001918)
Whale (XP\_023987950.1)
Elephant (ENSLAFP00000005179)
Armadillo (ENSDNOP00000014565)
Tasmanian\_devil (XP\_023360087)
Coelacanth (ENSLACP00000016889)
Cavefish(XP\_007240334.2)
Platyfish (XP\_014325204.1)
Tilapia (XP\_005456583.2)
Spotted\_gar (XP\_015202470.1)
Stickleback (ENSGACT0000001035)
Tetraodon (ENSTNIT00000011701)
Fugu (XP\_011601624.1)
Zebrafish (ENSXDAR000000143362)
Amazon\_molly (XP\_016534180.1)
Medaka (XP\_023818916.1)
Rainbow\_trout (XP\_021469805.1)
Rainbow\_trout (XP\_021436521.1)
Salmon (XP\_014010485)
Salmon (XP\_014070638.1)
Shark (XP\_007890120.1)
Human (ENSP00000425443)
Gorilla (ENSGGOP00000034525)
Mouse (ENSMUSP00000143029)
Rat (ENSRNOP00000048956)
Pig (ENSSSCP00000009765)
Tasmanian\_devil (ENSSHAT000000)
Whale (XP\_007106564.2)
Elephant (XP\_023404313.1)
Lizard (ENSACAP00000008438)
Chicken (ENSGALP00000017216)
Turtle (ENSPSIP00000011691)
Xenopus (ENSXETP00000030770)
Coelacanth (ENSLACP00000008576)

-----GHQQYNQYEHMSSFNGPNQPH
-----MEEGISNQDEEHGLEQSTRPPFGHRLHTEEEVTTAE-RDECTEG--QIQSL
-----SFALGDLERTLENIIVPEFHVPA--VPVMPLNPEESTSDCVLVSSSQAIKES--WPSKGATLELPSDTAGGAEAG-ILT
-----NIEVEDIEQLVKCIDAEITLILNSGYVPALSSDIEKRAVDNISSESSREFSEG--FVSELPSSTEI--SVLALKA-INA
-----ETLVLDSDYVIPISSNTEKNTVALVSR-TTTFQENSAHCSGEGSTSSNIGSSTLISVSG-KNV
-----APSKWPEPQSTVSYGLAVQGAIQILPLG-SGHTPQSSSNSEKNSLPPVMAISNVENEKQVHISFLPANTQGFPLAPERG
-----APSKWPEPQSTVSYGLAVQGAIQILPLG-SGHTPQSSSNSEKNSLPPVMAISNVENEKQVHISFLPANTQGFPLAPERG
-----SPLLGPEPHSSTSGLLEVOGATPILTLG-SGHTPQLPPNPESSSVPLVIAANGTRAERKQFGTSLFPAVPQGFVAAENE
-----CLLSGPEPHSSTASCGLEVOGATPILTLG-SGHTPQPPQNSSELSSVPLVIAANGTRAERKQFGANLFPANIQGFITIAPENE
-----PLPEWPEPLSTVSSGLVQGMQILPLG-SDHTPQSSSNEISSVPPVMAINSIENEKQVHISFLPANTQGFITIAPERG
-----AFPPEWPEPQSTVSSGLLEVOGATPILTLG-SGHTPQSSSNEISSVPPVMAINSIENEKQVHISFLPANTQGFITIAPERG
-----VPEWPEPQSTVSSGLLEVOGATPILTLG-SGHTPQSSSNEISSVPPVMAINSIENEKQVHISFLPVYSQRFITLVEKE
-----ALPEWP-----VSYGLEAQGGTQVPLPLG-SGHTPQSSN-----SVPPAKTISNKEKEQAHVSFLPVSTQGFISTPERG
-----ILQADLEKKAFFNGSKSEHMEGIPNGAETHSLKLNITPPLNGLHNEQETMTVLGETKWKVQDGHQDFSI
TDVKY-----AENGELDSTDDDLTKDENDNDNDEFASKNEG-----ALSLSLSLSTGAYSGFLSTLDCGPSTT
TPVAG-----LEKQACTPGETKD-EGEYIYKAEQKESFPFMLLTEANTKP--PTG-----KHEPNFVVDGTQATMPEDDVPVKIS
PHQPQSQEVLNPNQGESLACTPAESQTKDSEISIQEPLHKSQKAVPLGSSALLSQ--LAAP-----STLELNLSEVQVAMPEQDSVPKIS
VLLVS-----GPPCKEDTKECARSPPEQELIAASKTP-----VPHCNIIADISESATALDSGFRTD
-----ESLFSRGGRRVCTPAETQTKDTESEGREPSKHLIKETLLMSSPPFSQLSVDVAA-----EFKPSPSKGGVLLVVGPEQDPAPKIS
T-----ELRSTADVDTKDESID--AEMLMKKEG-----ALSLSLSLAAIYNTTLCMGGHQAT
TPVAG-----VEKQACTPGTKD-EGEYIYKAEQKESFPFMLLTEANTKP--STG-----KHEPNFVVDGTRAAMPEDDVPVKIS
SFQFQ-----RSVIVPQQGERGTRSTAETKDLDFQHQGFSCQKEAFPPP--FPQP-----GVAPSEPTDTEFAGMPEQDLVVKTS
EPPSS--SSLPYTKKDVFTTGSPEPKDIVSVSDCLDLSGPMTHNKYNQDEPQPSLPTDTRSEPTDTEFAGMPEQDLVVKTS
EPPSS--SSLPYTKIDLFTTGSAPDKDTCVSVSLGVSVEKTHNKNNQDEPQPSLPTDTRSEPTDTEFAGMPEQDLVVKTS
EPPSS--SSLPYTKKDVFTTGSPEPKDIVSVSDCLDLSGPMTHNKYNQDEPQPSLPTDTRSEPTDTEFAGMPEQDLVVKTS
APPSS--SSLPYTKIDLFTTGSAPDKDTCVSVSLGVSVEKTHNKNNQDEPQPSLPTDTRSEPTDTEFAGMPEQDLVVKTS
-----TQPPHSTGLTVSTWTS
-----CEITHPSHTSGQINSAPQTS
-----CEITHPSHTSGQINSAPQTS
-----HEIPQPSLTAQINFSQTS
-----REITQPSLTAQINFSQTS
-----CEITHPSHTSGQINFPQTS
-----YEVTHPSHTSGQINSPQTS
-----CEITHPSHTSGQINFPQTS
-----CEITHPSHTSGQINFPQTS
-----HETTHSSHTSGQITSPQTS
-----YMTTHSSHTSGQITSPQTS
-----TLATHPSHTSGQITSPQTS
-----HGTHSSHTSGLTNSPQTS

```

Amazon_molly (ENSPFOP00000120) -----GAQPPAVTSGLP-----
Amazon_molly (ENSPFOP00000299) -----GAQPPAVTSGLP-----
Fugu (XP_011611191.1) -----NAKSHSSTSGSPGSAQIP
Medaka (XP_004065962.1) -----GAQPPALASGLLPSGQMP
Platyfish (ENSXMAP0000005447) -----GAQPPAVTSGLS-----
Spotted_gar (ENSLQCP000000155) -----ARNSPSPVSGLPISFPQIP
Stickleback (ENSGACP0000002318) -----
Tilapia (XP_005457058.1) -----GAQLPPMTSGLPNSAQMP
Tetraodon (ENSTNIP00000021201) -----
Zebrafish (ENSDARP00000101295) -----PSFTSGFPISQIS
Salmon (XP_014042431.1) -----
Salmon (XP_014065146.1) -----Q-----ATTQSPTSLTSGFPPIISAQM
Salmon (XP_014050290.1) -----Q-----ATTQSPTSLTSGFPPIISAQM
Rainbow_trout (XP_021429026.1) -----
Rainbow_trout (XP_021429023.1) -----Q-----VTQSPTSLTSGFPPIISAQM
Shark (XP_007910136.1) -----
Human (ENSP00000386869) -----ALALARHGKMPNPNCDGFPEC
Gorilla (ENSGGOP00000051172) -----ALALARHGKMPNPNCDGFPEC
Armadillo (ENSDNOP00000021516) -----ALALARHGKMPNPNCDGFPEC
Mouse (ENSMUSP00000087049) -----ALALARHGKMPNPNCDGFPEC
Rat (ENSRNOP00000015296)Tet3 -----ALALARHGKMPNPNCDGFPEC
Pig (ENSSSCP00000008852) -----ALALARHGKMPNPNCDGFPEC
Elephant (XP_010591957.2) -----ALALARHGKMPNPNCDGFPEC
Whale (XP_023989264.1) -----ALALARHGKMPNPNCDGFPEC
Tasmanian_devil (ENSSHP000000) -----ALALARHGKMPNPNCDGFPEC
Chicken (ENSGALT00000059756) -----ALALARHGKMPNPNCDGFPEC
Lizard (ENSACAT0000001585) -----ALALARHGKMPNPNCDGFPEC
Turtle (ENSPSIT00000006549) -----QMVLLQHLHKKRNLFDQSLA
Xenopus (ENSXETP00000054061) -----ALALARHGKMPNPNCDGFPEC
Coelacanth (ENSLACP00000009535) -----ALTLARQGGKMPNPNCDGFPEC
Spotted_gar (ENSLQCP0000001981) -----ALKLAKHGKMPNPNCDGFPEC
Amazon_molly (ENSPFOP0000000021) -----ALRQAKHGKMPNPNCDGFPEC
Cave_fish (ENSAMXP00000015689) -----ALNQARHGKMPNPNCDGFPEC
Fugu (ENSTRUP00000036865) -----ALSQAKHGKMPNPNCDGFPEC
Medaka (ENSORLP00000019236) -----
Platyfish (ENSXMAT00000000130) -----
Stickleback (ENSGACP0000001732) -----
Tetraodon (ENSTNIP00000019883) -----
Tilapia (ENSONIP00000019943) -----ALSQAKHGKMPNPNCDGFPEC
Zebrafish (ENSDARP000000085229) -----
Rainbow_trout (XP_021462005.1) -----ALSQARHGKMPNPNCDGFPEC
Rainbow_trout (XP_021477599.1) -----ALSQARHGKMPNPNCDGFPEC
Salmon (XP_014026412.1) -----ALSQARHGKMPNPNCDGFPEC
Salmon (XP_014017100.1) -----ALSQARHGKMPNPNCDGFPEC

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                820          830          840          850          860          870          880          890          900
    ... |... |... |... |... |... |... |... |... |... |... |... |... |... |... |
European ampioxus (Sc0000095) -----
Ciona intestinalis (XP_0021254) INQPKDISPRVPSRQHSSDKQWNFQAPPLIATNHSSVSNLTSPEHLQORS-----AYPHGRRPSNTPGECFPVAVPPRHLS
Lamprey (scaf_00044) -----
Lamprey (scaf_03335) -----
Shark (XP_007897316.1) -----
Lizard (XP_020663651.1) -----
Chicken (ENSGALP00000053457) -----
Turtle (ENSPSIP00000006704) -----
Human (ENSP00000362748) -----
Gorilla (ENSGGOP00000011536) -----
Mouse (ENSMUSP000000133279) -----
Rat (ENSRNOP00000054747) -----
Pig (ENSSSCP00000010918) -----
Whale (XP_023987950.1) -----
Elephant (ENSLAFP00000005179) -----
Armadillo (ENSDNOP00000014565) -----
Tasmanian_devil (XP_023360087) -----
Coelacanth (ENSLACP000000016889) -----MSDLFFIVPFRSLPFAET-----GFENSFRLQVQGG
Cavefish(XP_007240334.2) -----HLNGDINRTVA-----ETKNLKVIGEDNKVSFFHDSVEP-----QKLFAQTFMNGFKPEVVDLTDASVP-----LKKVLEESTDSFKSNQ
Platyfish (XP_014325204.1) -----ASLDSSK-----VSSSTDSTRSFDTESEAGSLELALEHRAA-GASPLLDVDIRORLLQAQVRKERKRRRCGACGPCLLKYSYG
TSSVDSSTLS-----CCSESTRSSSFDTESETGCGNASFSALP--GSWGTGEGTSRACTPTLTSERKGRKRRRCGACGCEPCLRKINCG
Tilapia (XP_005456583.2) -----TPSLDSSSTFS-----CSSESTRSSSFDTESEAGYGEPSLSVQP--GSWAQEGACSLAWTASKLQKQKRRRCGACGCEPCLRKINCG
Spotted_gar (XP_015202470.1) -----VSTDKS-----LYSSSENPPFDMGELQCLDQTPGVVS--TSRPSSEVGSQVVSDDQEKDKKRRRCGACGCEPCLRKINCG
Stickleback (ENSGACT0000001035) -----
Tetraodon (ENSTNIT00000011701) -----
Fugu (XP_011601624.1) -----
Zebrafish (ENSDARP00000143362) -----IPSLDSSSTFS-----FSSSEARSSSFLDADSDVGYAEPGLSAPS--GSCSPEAASFSSRDAQPKQKRRKRRRCGACGCEPCLRKINCG
Amazon_molly (XP_016534180.1) -----ALLSS-----STESTQSSSFDSESE-----LVLEHRTS--GKSIPQVEDIQLRLLQDQRRREQNKRGHGCVAPCQCKVNCG
Medaka (XP_023818916.1) -----TSSVDSSTLS-----CCSESTRSSSFDTESETGCGDASFSALP--GSWGTGEGTSLTPTLTSERKGRKRRRCGACGCEPCLRKINCG
Rainbow_trout (XP_021469805.1) -----AP-LDSSSTFS-----CSSESTRSSSFDTESESGYEPTPSTLS--ERWQEEAGLLFSSSPKLRKRRKRRRCGACGCEPCLRKINCG
Rainbow_trout (XP_021436521.1) -----CIPNQESSSSKFSFSSFCSSSESTQSSSFDTESETGYGELSPGHPSLDLGHLDGATSLPRTPIIRRRERKRRRCGACGCEPCLRKINCG
Salmon (XP_014010485) -----SIPNQESSTSK-----FSCSSESTQSSSFDTESEBQYVGPSPGHPSLGRPLBEGTSLPRTPIIRRRERKRRRCGACGCEPCLRKINCG
Salmon (XP_014070638.1) -----SIPNQESCTSK-----FSCSSESTQSSSFDTESEBQYVGPSPGHPSLGRPLBEGTSLPRTPIIRRRERKRRRCGACGCEPCLRKINCG
Shark (XP_007890120.1) -----TSAQPQVPTMETVRLVTQ-----NYSVSPAFKTIHTFKTEGQLQPPQHNLHSAPVNNKQEPQSYAGQVPSQRYSAVMNCLQIPNSIPTM
Human (ENSP00000425443) -----NSELPPKPAVAVSEACDADDADNASKLAAMLN--TCSFQKP-EQLQOQKSVFEICPS-PAEN-NIQGTTKLASGEEPCSGSSSNLQAPGG
Gorilla (ENSGGOP00000034525) -----NSELPPKPAVAVTEACDADDADNASKPAIVGN--TCSFQKP-EQLQOQKSVFEICPS-PAEN-NIQGTTKLASGEEPCSGSSSNLQAPGG
Mouse (ENSMUSP00000143029) -----SLQLPEPAAMVTKACDAD--NASKPAAMVFN--TCPFQKAHQHQQ--KVALDIGPS-RAENKTIQSMTEFLA-EEYYPSSDRNLQASHG
Rat (ENSRNOP00000048956) -----SAQLPEPAAMVTKACDLD--SASKPAGVLG--TCAFQKAHQHQQ--KSVLIGIPSSCAENINIQGNTKPPA-EEYYPSSDRNLQASHG

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Medaka (XP\_023818916.1) LCSCCLNRRRTCHQICKLRKCKELKRRRPSSSPFGSAKEV-----IPESGSVNGKSKAQMEDTHMAAEEDEEGEETHIPH

1000 1010 1020 1030 1040 1050 1060 1070 1080

European ampioxus (Sc0000095) SQVSMPLHASSPITSNVAAPQIPHSGSNPFGSGSS-----

Stickleback (ENSACT0000001035) -----  
Tetraodon (ENSTNIT00000011701) -----  
Fugu (XP\_011601624.1) -----  
Zebrafish (ENSDARP000000143362) -----  
Amazon\_molly (XP\_016534180.1) -----  
Medaka (XP\_023818916.1) -----  
Rainbow\_trout (XP\_021469805.1) -----  
Rainbow\_trout (XP\_021436521.1) -----  
Salmon (XP\_014010485) -----  
Salmon (XP\_014070638.1) -----  
Shark (XP\_007890120.1) -----  
Human (ENSP00000425443) -----  
Gorilla (ENSGGOP00000034525) -----  
Mouse (ENSMUSP00000143029) -----  
Rat (ENSRNOP00000048956) -----  
Pig (ENSSSCP00000009765) -----  
Tasmanian\_devil (ENSSHAT000000) -----  
Whale (XP\_007106564.2) -----  
Elephant (XP\_023404313.1) -----  
Lizard (ENSACAP00000008438) -----  
Chicken (ENSGALP00000017216) -----  
Turtle (ENSPSIP000000011691) -----  
Xenopus (ENSXETP00000030770) -----  
Coelacanth (ENSLACP00000008576) -----  
Amazon\_molly (ENSPPOP0000000120) -----  
Amazon\_molly (ENSPPOP00000029) -----  
Fugu (XP\_011611191.1) -----  
Medaka (XP\_004065962.1) -----  
Platyfish (ENSXMAP00000005447) -----  
Spotted\_gar (ENSLOCP000000155) -----  
Stickleback (ENSACAP00000002318) -----  
Tilapia (XP\_005457058.1) -----  
Tetraodon (ENSTNIP000000021201) -----  
Zebrafish (ENSDARP000000101295) -----  
Salmon (XP\_014042431.1) -----  
Salmon (XP\_014065146.1) -----  
Salmon (XP\_014050290.1) -----  
Rainbow\_trout (XP\_021429026.1) -----  
Rainbow\_trout (XP\_021429023.1) -----  
Shark (XP\_007910136.1) -----  
Human (ENSP00000386869) -----  
Gorilla (ENSGGOP00000051172) -----  
Armadillo (ENSDNOP000000021516) -----  
Mouse (ENSMUSP000000087049) -----  
Rat (ENSRNOP000000015296) Tet3 -----  
Pig (ENSSSCP000000008852) -----  
Elephant (XP\_010591957.2) -----  
Whale (XP\_023989264.1) -----  
Tasmanian\_devil (ENSSHAP000000) -----  
Chicken (ENSGALT00000059756) -----  
Lizard (ENSACAT00000001585) -----  
Turtle (ENSPSIT00000006549) -----  
Xenopus (ENSXETP000000054061) -----  
Coelacanth (ENSLACP00000009535) -----  
Spotted\_gar (ENSLOCP00000001981) -----  
Amazon\_molly (ENSPPOP0000000021) -----  
Cave\_fish (ENSAMXP00000015689) -----  
Fugu (ENSTRUP00000036865) -----  
Medaka (ENSORLP00000019236) -----  
Platyfish (ENSXMAT00000000130) -----  
Stickleback (ENSACAP0000001732) -----  
Tetraodon (ENSTNIP000000019883) -----  
Tilapia (ENSONIP00000019943) -----  
Zebrafish (ENSDARP000000085229) -----  
Rainbow\_trout (XP\_021462005.1) -----  
Rainbow\_trout (XP\_021477599.1) -----  
Salmon (XP\_014026412.1) -----  
Salmon (XP\_014017100.1) -----

1090 1100 1110 1120 1130 1140 1150 1160 1170

European ampioxus (Sc0000095) -----  
Ciona intestinalis (XP\_0021254) -----  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) -----  
Lizard (XP\_020663651.1) -----  
Chicken (ENSGALP00000053457) -----  
Turtle (ENSPSIP00000006704) -----  
Human (ENSP00000362748) -----  
Gorilla (ENSGGOP000000011536) -----  
Mouse (ENSMUSP00000133279) -----  
Rat (ENSRNOP000000054747) -----  
Pig (ENSSSCP00000010918) -----  
Whale (XP\_023987950.1) -----  
Elephant (ENSLAPP00000005179) -----  
Armadillo (ENSDNOP00000014565) -----  
Tasmanian\_devil (XP\_023360087) -----





Pig (ENSSSCP00000010918) FQKPGFNCKS----FPDPANCLNSR---TSVHNESDQPKSLENIITNRE-PKEGATLQPSLLSLMKDRRLTLEQVVAIEALTQLSSEAP  
Whale (XP\_023987950.1) IQKPGFNCKS----FPDPANCLNSH---PSIHNESDQPKSLEIITNRE-LKEGSTLQPSLLSLMKDRRLTLEQVVAIEALTQLSSEAP  
Elephant (ENSLAFP00000005179) FHKPGFNCKS----VPDPTNFNLNH---TGTHNESDQPKTPEAPIKKE-PKDGSPVQSLFSLVKDRRLTLEQVVAIEALTQLSSEAP  
Armadillo (ENSDNOP00000014565) FQKPGFNCKS----IPDSAKLSNSH---TSPHNESDQPKTPEIIPSKKE-PKDGSPVQPSLLSLMKDRRLTLEQVVAIEALTQLSSEAP  
Tasmanian devil (XP\_023360087) IQKTDPICHS---AQDPTDVLKSNIDAQENPHIITWGKGEAPESKHISELKYNSPVQPCLLSLMRDRRLTLEQVVAIEALTQLSSEAP  
Coelacanth (ENSLACP00000016889) SQQSEQQPESQ----WSLLHQQLPSQ---PVPVSGSLTNTSTWENSPETS-----NVLLHACSSAALVSDH---VNSHHTVENSQA  
Cavefish (XP\_007240334.2) GPQTSNACNIKTER-----EPEPYQSHSQER-TSNSPAGADNSHPK---DPVPLTNNVQSLVEHRNHSIDQAIATIEALTQLAATP  
Platyfish (XP\_014325204.1) GTRSSILCSIKTEPPDLHFVKTEK---DELKKS-TPANLQRTPPQIKS--EPPQSVLLPSVQSLVERNLSFDQAIATIEALTQLAATP  
Tilapia (XP\_005456583.2) SSRASILHSIKAEAPDLHFVKTEK---DLYLKS-TPVNLQSTPPPIKS--EPLPVLPSVQSLAERLNLSVDQAIATIEALTQLAATP  
Spotted gar (XP\_015202470.1) KPISPFNRNETCK-----LEETEVTDDACSTSGATNGATSLENIDASFRCNLSLVSHPSLQSLVEKRNHSIEQAIATIEALTLESEIP  
Stickleback (ENSGACT0000001035) -----  
Tetraodon (ENSTNIT00000011701) -----  
Fugu (XP\_011601624.1) SRRASILRSIKTEPPDLHLVKEEPEEFKNNSCQKS-TPLGQRPSPHGKVS--EPPPSLLLPSVQSLAEKRNLSFDQAIATIEALTQLAATP  
Zebrafish (ENSDARP00000143362) GSQTSQDVC-LKTEP-----KEEYPQCQLNQEE-PPQN-----DYIALSLPTVQSLVQHRNLSVDQAIATIEALTQLAATP  
Amazon molly (XP\_016534180.1) GTRSSILCSIKTEPPDLHFVKTEK---DELKKN-TPANLQRTPPQIKS--EPPQSVLLPSVQSLAERLNLSFDQAIATIEALTQLAATP  
Medaka (XP\_023818916.1) SRRSSILRSIKTEPPDLHFVKKEENYLNDDWCPSK-TPLNTRKTPHTIKC--EPSPSVLLPSVQSLAERLNLSFDQAIATIEALTQLAATP  
Rainbow trout (XP\_021469805.1) SRRSPVLRSEFK-----TEPEDFKVDICLKS-APISPRKTFDIIVKREQSPDLSQPSIQSLVEERNISNDQAIATIEALTLLAAIP  
Rainbow trout (XP\_021436521.1) SRRSPVLRSEFK-----TEPEDFKVDICLKS-APISPRKALDIIVKREQSPDLSQPSIQSLVEERNISNDQAIATIEALTLLASIP  
Salmon (XP\_014010485) SRRSPVLRSEFK-----TEPEDFKVDICLKS-APISPRKALDIIVKREQSPDLSQPSIQSLVEERNISNDQAIATIEALTLLAAIP  
Salmon (XP\_014070638.1) SRRSPVLRSEFK-----LKTTEPEDFKVDICLKS-TPISPRKGLDIIVKREQSPDLSQPSIQSLVEERNISNDQAIATIEALTLLASIP  
Shark (XP\_007890120.1) YLTKHEEITSKLCSN-----SQTDDAEPRGVQLQQKQKSSQTQQEEAQSQTQPKSQMQMVHQYRPP  
Human (ENSP00000425443) QYQPNLSNQMTSK-----QYTGNSNMPGGLPRQAYTQKTTQLEHKSQMYQVEMNQGSQGTVD  
Gorilla (ENSGGOP00000034525) QYQPNLSNQMTSK-----QYTGNSNMPGGLPRQAYTQKTTQLEHKSQMYQVEMNQGSQGTVD  
Mouse (ENSMUSP00000143029) HSQTPGNVQMSK-----QSTGNVNMPPGGQRLPYLQKTAQPEQAQMYQVQVNMQGSQGTVD  
Rat (ENSRNOP00000048956) RYQTSPTNIGSI-----QSTGNSNMTGEFQRPPYIQTAKQPEHKSQMYQVEMNQGSQGTVD  
Pig (ENSSSCP00000009765) QYQSNPNHMTSK-----QYTGNSNMPGGLPRQAYIQTMTQDQRPQRYHVEMNQGSQGTVD  
Tasmanian devil (ENSSHAT000000) QYQSNKIDQMTSK-----QYSRGNISKGTQGGTYIQKMYQDQMPQYQVEMNAQVQFQALMD  
Whale (XP\_007106564.2) QYQSKPSHQVTSK-----QYTGNSNMPGGLPRQAYTQKIMQPEQRPRYQAEEMNQGSQGTVD  
Elephant (XP\_023404313.1) LYESHPSNQMTSR-----RYTGYSNVRGGLPRQAYVQKLMQLEQRSQMYQAEELNQGSQGTVD  
Lizard (ENSACAP00000008438) QYQSNSSSQTHPE-----QYSENPDRSKGHTEQAQYQNTQCCQIPALYKNEVTQLPHLITAN  
Chicken (ENSGALP00000017216) QYQANTSKAAYMK-----QYAGSDPDLKGGSPGQEQIPQYKQESSQMQHPHTAD  
Turtle (ENSPSIP00000011691) QYQANPMEQVHSD-----QYQGNPDALKGSPGQPHSEKTIQPEMPQLYKSEAPQRLPHPIAE  
Xenopus (ENSXETP00000030770) QSQTN--NKKLR-----QYQKQGLAN-----RKNSQDSEBHLQ  
Coelacanth (ENSLACP00000008576) QYQHQNEIQCCQK-----QYVLDSPNVSNGFQLQNFQ---DQLCLLNYNELAHGQQSRAE  
Amazon molly (ENSPPOP000000120) R---AKPQSEQQTT-----SPQVQNIQLEPN---QAQRFRRETQQTGLFTDAGRSGNSLQKQP  
Amazon molly (ENSPPOP000000299) R---AKPQSEQQTT-----SPQVQNIQLEPN---QAQRFRRETQQTGLFTDAGRSGNSLQKQP  
Fugu (XP\_011611191.1) REFPSKLSQDQIV-----NPQVHNQISEPK---PTQRF---QTRQSFSDSNQSSNSFQQQK  
Medaka (XP\_004065962.1) RALPPK-PNVERTA-----SPQRDTQIMEFG---PVQRF---QIQRSALDMSPGSNTSQKLP  
Platyfish (ENSXMAP00000005447) R---AKPQSEQQTT-----SPVQVNIQLEPN---QVQRYSETQQTGLFTDTSRGSNSLQKQP  
Spotted gar (ENSLQCP0000000155) RLWKDFNLRQQQM-----SNQSQEKILDSDNMQGFQIQGFSSSMQQQKQLSDVYKPNVEQDQ  
Stickleback (ENSGACP00000002318) -----  
Tilapia (XP\_005457058.1) RNFSIKSMSEQQA-----NPPVHGQMFEPN---PTQRF---QYQVFSVSDGSGSNF-QKKQ  
Tetraodon (ENSTNIP000000021201) -----  
Zebrafish (ENSDARP00000101295) Q-SQSQCINSLPPN-----NFQSHNFSNSFF---PSHEIEAQENKNMLPPTRFPHSAAPESQ  
Salmon (XP\_014042431.1) -----  
Salmon (XP\_014065146.1) ANSKGPPSHMQQC-----NLPPQQPHTQH---MHQQCNLPPPPQQQQGGENCFRAMPQPEH  
Salmon (XP\_014050290.1) ADSKGPPSHMQQC-----NLLPQQPHTQH---MHQQCNLPPPPQQQQGGENCFRAMPQPEH  
Rainbow trout (XP\_021429026.1) -----  
Rainbow trout (XP\_021429023.1) ADSKGPPSHMQQC-----NLPPQQPHTQH---MHQQCNLPPPPQQQQGGENCFRAMPQPEH  
Shark (XP\_007910136.1) -----  
Human (ENSP00000386869) PAPAPSPVLQREAP-----TPSSEPDTHQKAQTALQOHLHKKRSLFLEQVHDSFPP-APSEPS  
Gorilla (ENSGGOP00000051172) PAPAPSPVLQREAP-----TPSSEPDTHQKAQTALQOHLHKKRSLFLEQVHDSFPP-APSEPS  
Armadillo (ENSDNOP00000021516) PAPAPSPAPQREAP-----EPDAHQAQTALQOHLHKKRGLFLEQARDAFSP-APLEPP  
Mouse (ENSMUSP000000087049) PAPVPSPIQREAP-----LLSSEPDTHQKAQTALQOHLHKKRSLFLEQADASFPP-TSTEPQ  
Rat (ENSRNOP00000015296) Tet3 PAPAPSPISQREAP-----LPSSSEPDTHQKAQTALQOHLHKKRSLFLEQADASFPP-TSTEPQ  
Pig (ENSSSCP00000008852) PSPSPT--LQREAP-----TPSSEPDTHQKAQTALQOHLHKKRSLFLEQARDAFPP-HPSEPP  
Elephant (XP\_010591957.2) -----  
Whale (XP\_023989264.1) PSPSPPILQREAP-----TPSSEPDTHQKAQTALQOHLHKKRSLFLEQADASFPP-PPSEPP  
Tasmanian devil (ENSSHAP000000) PPAPTSPKRKEAP-----TPSSDPDTHRQVQSTLQOHLHKKRSLFLEQNGGCGPRASSVPP  
Chicken (ENSGALP00000059756) ---RTPGKEAASSP-----RVLQEPDLHRKTQLVLQOHLHKKRSLFLEQNLSS---APSEPP  
Lizard (ENSACAT00000001585) AGYRRPSACSPHLS-----QLLQEPNPHKKTRTALQOHLHKKRSLFLEQKATPTATPPPGQPP  
Turtle (ENSPSIT00000006549) -----AAQSPQLQQLDDRSQAPNTQEMC  
Xenopus (ENSXETP00000054061) STEFLKMSPDQQLS-----QLLQTNFHRNTQALQOHLHKKRSLFLEQDNAMEACTQEQQN--  
Coelacanth (ENSLACP00000009535) GARYYGTTCRQQLS-----QPTBQTGLQQTQKALQOHLHKKRSLFLEQGGQTQASQPMQPN--  
Spotted gar (ENSLQCP0000001981) GASVARIKQEPFSE-----GDFPGSAIHHKTQVALQOHLHKKRSLFLEQDQSDQ---TSALPSS  
Amazon molly (ENSPPOP0000000021) ---RIKQEPDSGNP-----MSPGQAIRHSTQALQOHLHKKRSLFLEQGGVPSRAPMT  
Cave fish (ENSAMXP00000015689) -----IRHSTQALQOHLHKKRSLFSSPPP---FSPQSPMA  
Fugu (ENSTRUP00000036865) APARIKQEPDLANC-----QQQQTSTISHSTQALQOHLHYKRNLSFNHSPSPGAPGRASLA  
Medaka (ENSORLP00000019236) -----  
Platyfish (ENSXMAT00000000130) -----  
Stickleback (ENSGACP0000001732) -----  
Tetraodon (ENSTNIP00000019883) -----  
Tilapia (ENSONIP00000019943) NPALHQGHYPGTP-----LSPGQAASHSTQALQOHLHYKRNLSFNHSPSGGGVGRGPLA  
Zebrafish (ENSDARP00000085229) -----LSKHASNEENVCDNE--  
Rainbow trout (XP\_021462005.1) LMNGQQQPGYPGPP-----LSAGSTAIHYSTQALQOHLHKKRSLFLEQGGVPSRAPMT  
Rainbow trout (XP\_021477599.1) LMNGQQQPRYPGPP-----LSLGSASIRHSTQALQOHLHKKRSLFNSPGLPLGLCPLRPAKA  
Salmon (XP\_014026412.1) RMNGQQQPGYPGPP-----LSAGSTAIHYSTQALQOHLHKKRSLFNSPGLPLGLCPLRPTQA  
Salmon (XP\_014017100.1) LMNGQQQPRYPGPP-----LSPGSAIRHSTQALQOHLHKKRSLFNSPGLPLGLCPLRPAKA

1270 1280 1290 1300 1310 1320 1330 1340 1350  
European ampioxus (Sc0000095) SDPAKPNPLLEIKTASSPTDQPS-----TISPGESEYDSADLISTVDSQR  
Ciona intestinalis (XP\_0021254) -----  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) NGNCQFFPNLSSDLPNINYSTLTQSL-----EFSRENCVDEKGVSKCLITG-----VRNKAEBEAAQTLQLAATIES  
Lizard (XP\_020663651.1) AGASSPAKTERVQCTDEQISHSLSNYSKDNACSLTSSALKAIKGTCPQKQDLFVSHVSPRRILP-KSLYNGQGAISEFPKSSGSSSL  
Chicken (ENSGALP00000053457) LGTSSPAKADNTECTEERTSNLLHSYKRDISSSTSTLKEIKDLYLEKEBQLTHCAHSQKQLPNKPVLYNGQSSISELDRKPPNLASE



Lamprey (scaf\_00044) Lamprey (scaf\_03335) Shark (XP\_007897316.1) Lizard (XP\_020663651.1) Chicken (ENSGALP00000053457) Turtle (ENSPSIP0000006704) Human (ENSP00000362748) Gorilla (ENSGG0P00000011536) Mouse (ENSMUSP00000133279) Rat (ENSRNOP00000054747) Pig (ENSSSCP00000010918) Whale (XP\_023987950.1) Elephant (ENSLAFP00000005179) Armadillo (ENSDNOP00000014565) Tasmanian devil (XP\_023360087) Coelacanth (ENSLACP00000016889) Cavefish (XP\_007240334.2) Platyfish (XP\_014325204.1) Tilapia (XP\_005456583.1) Spotted gar (XP\_015202470.1) Stickleback (ENSGACT0000001035) Tetraodon (ENSTNIT00000011701) Fugu (XP\_011601624.1) Zebrafish (ENSDARP000000143362) Amazon molly (XP\_016534180.1) Medaka (XP\_023818916.1) Rainbow trout (XP\_021469805.1) Rainbow trout (XP\_021436521.1) Salmon (XP\_014010485) Salmon (XP\_014070638.1) Shark (XP\_007890120.1) Human (ENSP00000425443) Gorilla (ENSGG0P00000034525) Mouse (ENSMUSP00000143029) Rat (ENSRNOP00000048956) Pig (ENSSSCP00000009765) Tasmanian devil (ENSSHAT000000) Whale (XP\_007106564.2) Elephant (XP\_023404313.1) Lizard (ENSCAP00000008438) Chicken (ENSGALP00000017216) Turtle (ENSPSIP00000011691) Xenopus (ENSXETP00000030770) Coelacanth (ENSLACP00000008576) Amazon molly (ENSPFOP000000120) Amazon molly (ENSPFOP0000000299) Fugu (XP\_011611191.1) Medaka (XP\_004065962.1) Platyfish (ENSMXAP00000005447) Spotted gar (ENSLACP0000000155) Stickleback (ENSGACP0000002318) Tilapia (XP\_005457058.1) Tetraodon (ENSTNIP00000021201) Zebrafish (ENSDARP000000101295) Salmon (XP\_014042431.1) Salmon (XP\_014065146.1) Salmon (XP\_014050290.1) Rainbow trout (XP\_021429026.1) Rainbow trout (XP\_021429023.1) Shark (XP\_007910136.1) Human (ENSP00000386869) Gorilla (ENSGG0P00000051172) Armadillo (ENSDNOP00000021516) Mouse (ENSMUSP00000087049) Rat (ENSRNOP00000015296) Tet3 Pig (ENSSSCP00000008852) Elephant (XP\_010591957.2) Whale (XP\_023989264.1) Tasmanian devil (ENSSHAP000000) Chicken (ENSGALP00000059756) Lizard (ENSCAT00000001585) Turtle (ENSPSIT00000006549) Xenopus (ENSXETP00000054061) Coelacanth (ENSLACP00000009535) Spotted gar (ENSLACP0000000021) Cave fish (ENSMXCP00000015689) Fugu (ENSTRUP000000036865) Medaka (ENSORLP00000019236) Platyfish (ENSMAT00000000130) Stickleback (ENSGACP0000001732) Tetraodon (ENSTNIP00000019883) Tilapia (ENSONIP00000019943) Zebrafish (ENSDARP00000085229) Rainbow trout (XP\_021462005.1) Rainbow trout (XP\_021477599.1) Salmon (XP\_014026412.1) Salmon (XP\_014017100.1)

1450 1460 1470 1480 1490 1500 1510 1520 1530  
European ampioxus (Sc0000095) SRCSTSSIIISNEARSHNLPQLQATTCCNGGPIHTSLRRAFTAPNFSSRRSPVSRSHSADCCTPDSDTGLDSTLETTKKKVLLRRYSSQGIG  
Ciona intestinalis (XP\_0021254) -----  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) QGHQLTQQPNQATSFRQQEQCLGHLHQ-----QONQLEKFRKYSVDVQCCQQIQDANLNQETHQQIQPESSEMQSYSNPPQMSQEKG  
Lizard (XP\_020663651.1) DEEEVATQLTQLAAIIESSKTSPPDQK----ASLFSRIPSDMQSKHKQDQCLLQKKQSVFIRNNYSSLLVQQRQPSRKNDAKAVPRAKRLKK  
Chicken (ENSGALP0000053457) DEEDVATQLTQLAAIIESSNRRANPAQKNDIKTSLNLLISHERQAKHNQD--LLQRKESVFFFRNNYSSLLVQQRQPSRKNDAKAVPRAKRLKK  
Turtle (ENSPSIP0000006704) DEEDVATQLTQLAAIIESSNQTSPBQKNDVKTSLLSLSSHETQPKHNQDQCLLKKQSVFIRNNYSSLLVQQRQPSRKNDAKAVPRAKRLKK  
Human (ENSP00000362748) IEEVDATQLTQLASIIKINIKPEDEKVV-ESTPTSLVTCNVVQKYQNEKGTIQQKPPSSVHNNHGSSLTQKQKNTQKTKKSTPSRDRRKK  
Gorilla (ENSGGOP00000011536) IEEVDATQLTQLASIIKINIKPEDEKVV-ENTPTSLVTCNVVQKYQNEKGTIQQKPPSSVHNNHGSSLTQKQKNTQKTKKSTPSRDRRKK  
Mouse (ENSMUSP0000013279) IEEVDAAQLTQLASTI--NHINAEVRNA-ESTPESLVAKNTKQKHSQEKRMVHQKPPSSVTQTKPSVSAKPKK-AQKKARATPHANKRKK  
Rat (ENSRNOP00000054747) IEEVDAAQLTQLASTI--NHINAEVRNA-ESTPESLVAKNTKQKHSQEKRMVHQKPPSSVTQTKPSVSAKPKK-AQKKARATPHANKRKK  
Pig (ENSSSCP00000010918) IEEVDATQLTQLASIIKFNFKYIKPEDEKVV-ESTPN-LTAYNVQYQYQK--TIQKPPSSVQNNHGSSVTQTKQKNTQKTKKSTPSRDRRKK  
Whale (XP\_023987950.1) IEEVDAAQLTQLASIIKFNFKYIKPEDEKVV-ESTPTSLVAYNVQYQYQK--TIQKPPSSVQNNHGSSVTQTKQKNTQKTKKSTPSRDRRKK  
Elephant (ENSLAFP00000005179) IEEVDATQLTQLASIIKFNFKYIKPEDEKVV-ESTPTSLVAYNVQYQYQK--TIQKPPSSVQNNHGSSVTQTKQKNTQKTKKSTPSRDRRKK  
Armadillo (ENSDNOP00000014565) IEEVDATQLTQLASIIKFNFKYIKPEDEKVV-ENTPTSLVAHALQKQYRQEKGMIPQKPPSSVQNNHGSSVTQTKQKNTQKTKKSTPSRDRRKK  
Tasmanian devil (XP\_023360087) IEEVDAAQLTQLASIIENNAKREKEG-AKMFPSELECHNAQKSKQEQSSFEKPPVPIQNNHSSLLAKQKSSSHRKGSAWQRLKK  
Coelacanth (ENSLACP00000016889) VAFQELSNQKKPKYKIQN-IWIQQLNK-----FSQFLQDLKSTKIKKPKTKVQKVLPRKKPHLFLPQIQFHKYLPKPTQENI  
Cavefish (XP\_007240334.2) DEEEVAAQLVQLAFIIQSRTPMSS-----ENSPKGMPPVQTIKYN-----HHVVQGVNKKRQKQKNTQKTKKSTPSRDRRKK  
Platyfish (XP\_014325204.1) DEEEVAAQLADLAFIIQARHNQ-----SDNDPPKGTVPVSAIKYN--YKSQSPSQKPPKIKITPSKPRKK--SDGL  
Tilapia (XP\_005456583.2) DEEEVAAQLANLAFIIQSQHNQ-----SENNPLKGAIPVSAIKYN--YKSQSPSQKTPVRKKTKATPSKPRKK--TDGI  
Spotted gar (XP\_015202470.1) DEEDVAAQLAQLAFIIESSHKKQVNSSSGVDSTQAQLAPHTPQGFPLQPKNN-----HSSLQGLSTSLPKKNTTPSPKQRTKKAQLQK  
Stickleback (ENSGACT0000001035) -----  
Tetraodon (ENSTNIT00000011701) -----  
Fugu (XP\_011601624.1) DEEVAAQLADLAFIIQSRHSQH-----SENPSPKGTVPVSAIKYN--YNSQLTASQKNNAKTKATPSKPRKK--SDGL  
Zebrafish (ENSDARP00000143362) DEEEVAAQLVQLAFMIESRQAQVS-----ENSPNMGATQSLKYN-----QNYLQGLLKKQRKPKMTPSNFRMSKKKVAE  
Amazon molly (XP\_016534180.1) DEEEVAAQLAELAFIIQARHNQ-----SDNGPPKGTVPVSAIKYN--YKSQSPSQKPPKIKITPSKPRKK--SDGL  
Medaka (XP\_023818916.1) DEEEVAAQLADLAFIIQSRHNQ-----SENNPPKGTVPVSAIKYN--YNSQAPNNHKKLQQLSLOKPNLARKQKSTPSRDRRKK--SDGL  
Rainbow trout (XP\_021469805.1) DEEEVAAQLAELAFIIQSRHKQ--GFDP-----SQHSENNPPRGTPVSAIKYN--YNSQAPNNHKKTPVKKPRTTSLKPRKKGTBGL  
Rainbow trout (XP\_021436521.1) DEEEVAAQLAELAFIIQSRHKQ--GFDP-----SQHSENNPPRGTPVSAIKYN--YNSQAPNNHKKTPVKKPRTTSLKPRKKGTBGL  
Salmon (XP\_014010485) DEEEVAAQLAELAFIIQSRHKQ--GFHP-----SQHSENNPPRGTPVSAIKYN--YNSQAPNNHKKTPVKKPRTTSLKPRKKGTBGL  
Salmon (XP\_014070638.1) DEEEVAAQLAELAFIIQSRHKQ--GFQP-----SQHSENNPPRGTPVSAIKYN--YNSQAPNNHKKTPVKKPRTTSLKPRKKGTBGL  
Shark (XP\_007890120.1) QPYGIFANSSIHRRRIETQFSKLVPAVCHNIETIPEKADTFYRESENTITQDLHKPNNDLHQVPNDQDQSVQSQSQEQVQQLQQAHHMSV  
Human (ENSP00000425443) EVQINRRNSPYSQTMKSSACKIQVSCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDILLHRCFQEQEQKQQAS-  
Gorilla (ENSGGOP00000034525) EVQINRRNSPYSQTMKSSACKIQVSCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDILLHRCFQEQEQKQQAS-  
Mouse (ENSMUSP00000143029) QVQNVNR--SFYAKIETPNSSSKVQLCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDILLHRCFQEQEQKQQAS-  
Rat (ENSRNOP00000048956) QVQNMNRKSPYQQLKSNQSKVQISCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDILLHRCFQEQEQKQQAS-  
Pig (ENSSSCP00000009765) QVHNISSKNSSYGQMLKSN--INTQLSCQNNIYLASERKENTNNEFFIGNTKQDLQHIQYFPNNVTP--KQDVSHRCFQEQEQKQQAS-  
Tasmanian devil (ENSSHAT000000) QVQNMNSINSFYDQILKSNQSKVQISCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDVSHRCFQEQEQKQQAS-  
Whale (XP\_007106564.2) QVQNMNSINSFYDQILKSNQSKVQISCSNTHLVSSENKEQTIHPPELFAKNQTLNHHMQYFPNNVIP--KQDVSHRCFQEQEQKQQAS-  
Elephant (XP\_023404313.1) HGSQINN---HAFKVTNI---EKHSYPNMHLIPEKREKLMNTELFENMTHDLQHMQYYSNSMTP--KQDTSQ--CFQDQKQPSPLGSA  
Lizard (ENSACAP00000008438) QVQNMNNTPLYSQKSTG---LQHPCPNVMHLMSEKTEANAANLEHFPAGANKRDLQHVQYFPNNVTP--KQDVSHRCFQEQEQKQQAS-  
Chicken (ENSGALP00000017216) QEQSINNKTSLYQILKTN---THLQRPVGHVHLVSEKENTISAELLGLKKRQDLQYQYPSMAP--KQDVQH--RFQEQEQHTQQAASA  
Turtle (ENSPSIP00000011691) -----  
Xenopus (ENXSXETP00000030770) -----  
Coelacanth (ENSLACP00000008576) -----  
Amazon molly (ENSPFOP000000120) -----  
Amazon molly (ENSPFOP0000000299) -----  
Fugu (XP\_011611191.1) -----  
Medaka (XP\_004065962.1) -----  
Platyfish (ENSMAP00000005447) -----  
Spotted gar (ENSLQCP000000155) -----  
Stickleback (ENSGACP00000002318) -----  
Tilapia (XP\_005457058.1) -----  
Tetraodon (ENSTNIP00000021201) -----  
Zebrafish (ENSDARP00000101295) -----  
Salmon (XP\_014042431.1) -----  
Salmon (XP\_014065146.1) -----  
Salmon (XP\_014050290.1) -----  
Rainbow trout (XP\_021429026.1) -----  
Rainbow trout (XP\_021429023.1) -----  
Shark (XP\_007910136.1) -----  
Human (ENSP00000386869) -----  
Gorilla (ENSGGOP00000051172) -----  
Armadillo (ENSDNOP00000021516) -----  
Chicken (ENSMUSP00000087049) -----  
Rat (ENSRNOP00000015296) Tet3 -----  
Pig (ENSSSCP00000008852) -----  
Elephant (XP\_010591957.2) -----  
Whale (XP\_023989264.1) -----  
Tasmanian devil (ENSSHAP000000) -----  
Chicken (ENSGALP00000059756) -----  
Lizard (ENSACAT0000001585) -----  
Turtle (ENSPSIT00000006549) -----  
Xenopus (ENXSXETP00000054061) -----  
Coelacanth (ENSLACP00000009535) -----  
Spotted gar (ENSLQCP0000001981) -----  
Amazon molly (ENSPFOP0000000021) -----  
Cavefish (ENSAMXP00000015689) -----  
Fugu (ENSTRUP00000036865) -----  
Medaka (ENSORLP00000019236) -----  
Platyfish (ENSMAT0000000130) -----  
Stickleback (ENSGACP0000001732) -----  
Tetraodon (ENSTNIP00000019883) -----  
Tilapia (ENSONIP00000019943) -----  
AAAAAG-LPAPAQSLG-----PILPPVGLAAHNKSEEMGS-LASSNTSTMTPTSTSS

Zebrafish (ENSDARP0000085229) -NDVDMEDAQTILVAFS-----VGSLLPPTYNHQPSPTP-----TA  
Rainbow\_trout (XP\_021462005.1) PTQAAAAGLPTPAQSQVSIILNSSIARSVTAPA-----FSVNSPFAVSTPLPLPAAPDAPASSGEAGAT-----QTS  
Rainbow\_trout (XP\_021477599.1) PTQAAAAGLPAQSQVSIILNSSIARSVAA-----LSVNTFDDVSTPQPLVALDIPASSAEASAT-----QTS  
Salmon (XP\_014026412.1) PTQAAAAGLPTPAQSQVSIILNSSIARSVTAPA-----FSVNSPFAVSTPLPLPAAPDAPASSGEAGAT-----QTS  
Salmon (XP\_014017100.1) PTQAAAAGLPAQSQVSIILNSSIAPPVAAST-----LSVNTFDDVLTPOPLTVALNIPASSAEAIATQA-----STPQTS

1540 1550 1560 1570 1580 1590 1600 1610 1620

European ampioxus (Sc00000095) -----  
Ciona intestinalis (XP\_0021254) ALENIVRAVTPQPSSTNTLPTQRLPLPPNHISRLPNFIPATKCEPFLPTQFPTP-----  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) EVMQS----VSQEQKCFPTDLSLPSNFRTHSPHS- SMSSSQCTAKETDTPKWCAETVLPSCSPNEVNSYNQSIILTK---VKSILKQS  
Lizard (XP\_020663651.1) KPQPI----PDQQ-NQLQOE---CQHSEVQEMQKPKSKLRKLRIVSODSKLTSLGKSSKTKVQKTRKWSLTPSQKPTALFLPKTQI  
Chicken (ENSGALP00000053457) KPQEA----RYQQINRNQLELLSCQHSSELQDIWIS-SKFLKLGQAMPQDSRIALAEKKSFRTRKVKALNQNALTLQEK-PRFLPLPTQTI  
Turtle (ENSPSIP0000006704) KSQVP----DYQQNQIQPQEQQLAYEYSKLDHIWIA-SKFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Human (ENSP00000362748) KPTVV----SYQENDRQKWEKLSYMYGTICDIWIA-SKFNQFQFPHDFPVTFG-KISSSTKIWKPLAQTRSIMQPK--TVFPPLTQI  
Gorilla (ENSGG000000011536) KPTVV----SYQENDRQKWEKLSYMYGTICDIWIA-SKFNQFQFPHDFPVTFG-KISSSTKIWKPLAQTRSIMQPK--TVFPPLTQI  
Mouse (ENSMUSP00000133279) KPPAR----SSQENDQKQEQQLAYEYSKLDHIWIS-SKFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Rat (ENSRNOP00000054747) KAPAH----SSQESDQKQERLAIEYSKLDHIWIS-SQFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Pig (ENSSSCP00000010918) KPAVI----SCQENDQKQEQQLAYEYSKLDHIWIA-SKFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Whale (XP\_023987950.1) KPAIL----SCEEDIRKQEQQLAYEYSKLDHIWIA-SKFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Elephant (ENSLAFP00000005179) KPAVI----SCQENDQKQEQQLAYEYSKLDHIWIA-SKFORFGQFPHDFPILLG-KIPPLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Armadillo (ENSDNOP00000014565) KPPAK----SIQNDQSERERLQAYEYSKLDHIWIS-SKLRRLQYVSSREPHATMIERSPSLTKVWKLPTQSSALEHK--TRFLPLPTQTI  
Tasmanian devil (XP\_023360087) KDLQP----BLDKPDLCSNHLKS-----KTDFF-----EHSRLQGSIVTN---TIPLQPL  
Coelacanth (ENSLACP00000016889) VEG-----GNHRIPLAKRTPNSKPPFKTKAQHVALQEK-PKQPQKWSFPLPQTQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Cavefish(XP\_007240334.2) QEG-----ASRRT-----AQGETPHRSRGQNLPHGK--SSRQPKNNFPLPAQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Platyfish (XP\_014325204.1) QEG-----ASRRT-----AQGETPHRSRGQNLPHGK--SSRQPKNNFPLPAQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Tilapia (XP\_005456583.2) NQR-----TPNR-----ETAYRSRNQNPFGQK-SGLHKKNLFLPAQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Spotted\_gar (XP\_015202470.1) LEDTNGHLWGQSPANVGHVFKRGAANTKAPORTKVQKVFPRQ-MVQNHKSPLFPQTQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Stickleback (ENSGACT0000001035) -----  
Tetraodon (ENSTNIT00000011701) -----  
Fugu (XP\_011601624.1) QEG-----LNCRMSLSKRPNGEVAHKGKKNLTQGR-SGVHQKKNLFLPQTQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Zebrafish (ENSDARP00000143362) IDD-----NHCRIILAKTIPNKTPLKATIQAKAISQHK-MRFQHKRNPFLPAQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Amazon\_molly (XP\_016534180.1) QEG-----ASRRT-----AQGETPHRSRGQNLPHGK--SSRQPKNNFPLPAQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Medaka (XP\_023818916.1) QEP-----HNRRTPLSKRPNGETPHRGKHSKLSQGGK-SGPHLKNLFLPQTQIDLKLYLAQAHEKHLQFLHFS--KRQD  
Rainbow\_trout (XP\_021469805.1) EEEGC-----KPNNTPLPKRIPNKTTPHARVQKVLPPQKTSLSLHRSKRSFLPQAQMDLKRYLEAQEERRQLFYYSN---AHSGV  
Rainbow\_trout (XP\_021436521.1) EEEESY-----NPNNKIPMSKRTIPNKTTPHARVQKVLPPQKTSLSLHRSKRSFLPQAQMDLKRYLEAQEERRQLFYYSN---AHSGV  
Salmon (XP\_014010485) EEEGY-----KLNNTPLPKRIPNKTTPHARVQKVLPPQKTSLSLHRSKRSFLPQAQMDLKRYLEAQEERRQLFYYSN---AHSGV  
Salmon (XP\_014070638.1) EEEGY-----NPNNKIPMSKRTIPNKTTPHARVQKVLPPQKTSLSLHRSKRSFLPQAQMDLKRYLEAQEERRQLFYYSN---AHSGV  
Shark (XP\_007890120.1) IQQTQQLRMHQHHSQIQHGLSQDTSKMKEMQRNAAPHNRHVAVPMKGTFLNRYRYPPSIQNEEFKHAALNSHLLQQQERKMYQQRMQ  
Human (ENSP00000425443) -----VLQGYKRNQDMSGQQAQLAQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Gorilla (ENSGG000000034525) -----VLQGYKRNQDMSGQQAQLAQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Mouse (ENSMUSP00000143029) -----SLQGLKDRSQGESPAPEAAQQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Rat (ENSRNOP00000048956) -----SLQGLKDRSQGESPAPEAAQQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Pig (ENSSSCP00000009765) -----VLQGYKRNQDMSGQQAQLAQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Tasmanian devil (ENSSHAT000000) HQQLPQPQGGYHNKNDLPSKQITQDLQRYSLHGHQPAALALPEQRANHIQSLPQ-----KDFQKHAALRWHLLOKQEQQTQQPQT  
Whale (XP\_007106564.2) -----VLQGYKRNQDMSGQQAQLAQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Elephant (XP\_023404313.1) -----VLQGYKRNQDMSGQQAQLAQRYLHINHANVFPVDPDQGGSHITQTPPQ-----KDIQKHAALRWHLLOKQEQQTQQPQT  
Lizard (ENSAAP00000008438) PQRPFQQTQEXP-NFTSNMCSQQAQTPQPS-YLPHSQQTVAHIDQRECCITSPH-----RDFQKHAALRWHLLOKQEQQTQQPQT  
Chicken (ENSGALP00000017216) IQLPQG-----YGGSLSDQPPQAAAPMPQR-YLPHSQQTVAHIDQRECCITSPH-----RDFQKHAALRWHLLOKQEQQTQQPQT  
Turtle (ENSPSIP00000011691) MQLPLQQPERCGGNLKPQGGQATPQQR-YLPHSQQTVAHIDQRECCITSPH-----RDFQKHAALRWHLLOKQEQQTQQPQT  
Xenopus (ENSXETP00000030770) -----NYEHLDS-----ARIATQHCLPESSSSPHLHDKMGYYSQFENQ-----VDCIPKHAALRWHLLOKQEQQTQQPQT  
Coelacanth (ENSLACP00000008576) -----VLGGLNFKSNSSPQATMQQRLLVAASQPPVQVESQVSNQPTLQN-----KDFQKHAALRWHLLOKQEQQTQQPQT  
Amazon\_molly (ENSPPOP0000000120) QGLFSQQP-----GTRMYPKAEQEQARASCAQFQGRPLPLGPASPH-----ADFQRHAALRWHLLOKQEQQTQQPQT  
Amazon\_molly (ENSPPOP0000000299) QGLFSQQP-----GTRMYPKAEQEQARASCAQFQGRPLPLGPASPH-----ADFQRHAALRWHLLOKQEQQTQQPQT  
Fugu (XP\_011611191.1) -----QNMNQQL-----STQIFPKAEQKQL--SCTQFQRGQPLFLRGTGPH-----GSFQRHTALRTHLLOKQEQQTQQPQT  
Medaka (XP\_004065962.1) QGALNQV-----RNQMHKPAEQPQLKSSCTQFQRGQPLPLGPASPH-----ADFQRHAALRWHLLOKQEQQTQQPQT  
Platyfish (ENSMAP000000005447) QGLFSQQS-----GTRMYPKAEQEQARASCAQFQGRPLPLGPASPH-----ADFQRHAALRWHLLOKQEQQTQQPQT  
Spotted\_gar (ENSLQCP0000000155) -----STQRNPQQGALNQHILGLMTAQMYPKTESQDSCAQAQQGQGNQHP-----GDLQKHAALRWHLLOKQEQQTQQPQT  
Stickleback (ENSGACP00000002318) -----  
Tilapia (XP\_005457058.1) -----QGALSQQV-----TRQMYKAEQQLKTSCTQFQRGQPLPLGPASPH-----ADFQRHAALRWHLLOKQEQQTQQPQT  
Tetraodon (ENSTNIP000000021201) -----  
Zebrafish (ENSDARP00000101295) -----QSQHSQASDGLQIPVTRTLKAEFHESFAQIQRE--SLSSNGAQ-----MDVQRHAALRWHLLOKQEQQTQQPQT  
Salmon (XP\_014042431.1) -----HGALNQVSAQQQQMYPKMEQNQESCAQFQGRGPPPLGHGGPQ-----GDFQRHAALRWHLLOKQEQQTQQPQT  
Salmon (XP\_014065146.1) -----HGALNQVSAQQQQMYPKMEQNQESCAQFQGRGPPPLGHGGPQ-----GDFQRHAALRWHLLOKQEQQTQQPQT  
Salmon (XP\_014050290.1) -----HGALNQVSAQQQQMYPKMEQNQESCAQFQGRGPPPLGHGGPQ-----GDFQRHAALRWHLLOKQEQQTQQPQT  
Rainbow\_trout (XP\_021429026.1) -----HGALNQVSAQQQQMYPKMEQNQESCAQFQGRGPPPLGHGGPQ-----GDFQRHAALRWHLLOKQEQQTQQPQT  
Rainbow\_trout (XP\_021429023.1) -----HGALNQVSAQQQQMYPKMEQNQESCAQFQGRGPPPLGHGGPQ-----GDFQRHAALRWHLLOKQEQQTQQPQT  
Shark (XP\_007910136.1) -----  
Human (ENSP00000386869) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Gorilla (ENSGG0000000051172) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Armadillo (ENSDNOP00000021516) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Mouse (ENSMUSP000000087049) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Rat (ENSRNOP00000015296) Tet3 -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Pig (ENSSSCP00000008852) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Elephant (XP\_010591957.2) -----DKLEELIRQFEAEFGDSFGLPGPPSVPIQDPENQQT-----  
Whale (XP\_023989264.1) -----DKLEELIRQFEAEFGDNFGLPGPQSVPIQDPENQQT-----  
Tasmanian devil (ENSSHAP000000) -----DKLEELFQQFEAEFGDNFGLAAAPPAPACSPQELAS-----  
Chicken (ENSGALP000000059756) -----SGATALPQGGPPAPQVTAAPASAPSAAPGGSALSPG-----  
Lizard (ENSAAT00000001585) -----ENLDELIIQFEAEFGDSFGLPGPQSVPIQDPENQQT-----  
Turtle (ENSPSIT00000006549) -----RGSSTLQVPAEEDGGPPLADAVEVGPKGFSFSPK-----  
Xenopus (ENSXETP00000054061) -----DDKLEELIRQFEAEFGEDFGLPGSAVPSQNGGPPKQTPSGDPQFKLFPSPQLLPEENSTKPATHSNPALSNPVSRE-----  
Coelacanth (ENSLACP000000009535) -----DKFEELIRQFEAEFGDSFGLPGPQSVPIQDPENQQT-----  
Spotted\_gar (ENSLQCP00000001981) -----ISSSAPDGLNSIDDKFEELIRQFEAEFEDRVAVPS-----QTQTQITKAQAVTIRAPVQEQP-----  
Amazon\_molly (ENSPPOP0000000021) -----SNTSPLQKLNIDPKYBELIRQFEAEFGNLAPDSTSPRKEETTPAPT-----LANQFLISPDQLSSANTTSQVSSVPTPQ-----  
Cave\_fish (ENSAMXP00000015689) -----QPTPLLAGLGLSDPKFEDLIRQFEAEFGDPLPSASV-----ADAPGQGPQQHRLIADPFTMS-----  
Fugu (ENSTRUP00000036865) -----TSNSQLPSLVNVDPKYBELIRQFEAEFGESHTPHSKLSKSPTCPNPTPTPNPDPNDQMEVKGDESIGQCBTAPVGGRRNGTQEGSLQVS-----

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Medaka (ENSORLP0000019236) -----
Platyfish (ENSXMAT0000000130) -----MCVCKPYPVLSLS-----
Stickleback (ENSGACP0000001732) -----
Tetraodon (ENSTNIP00000019883) -----
Tilapia (ENSONIP00000019943) -----
Zebrafish (ENSARDP000000085229) -----
Rainbow_trout (XP_021462005.1) -----
Rainbow_trout (XP_021477599.1) -----
Salmon (XP_014026412.1) -----
Salmon (XP_014017100.1) -----

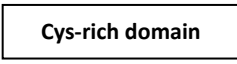
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1630 1640 1650 1660 1670 1680 1690 1700 1710

European ampioxus (Sc0000095) -----
Ciona intestinalis (XP_0021254) -----
Lamprey (scaf_00044) -----
Lamprey (scaf_03335) -----
Shark (XP_007897316.1) -----
Lizard (XP_020663651.1) -----
Chicken (ENSGALP00000053457) -----
Turtle (ENSPSIP00000006704) -----
Human (ENSP00000362748) -----
Gorilla (ENSGGOP00000011536) -----
Mouse (ENSMUSP00000133279) -----
Rat (ENSRNOP00000054747) -----
Pig (ENSSSCP00000010918) -----
Whale (XP_023987950.1) -----
Elephant (ENSLAFP00000005179) -----
Armadillo (ENSNDOP00000014565) -----
Tasmanian devil (XP_023360087) -----
Coelacanth (ENSLACP00000016889) -----
Cavefish (XP_007240334.2) -----
Platyfish (XP_014325204.1) -----
Tilapia (XP_005456583.2) -----
Spotted_gar (XP_015202470.1) -----
Stickleback (ENSGACT0000001035) -----
Tetraodon (ENSTNIT00000011701) -----
Fugu (XP_011601624.1) -----
Zebrafish (ENSARDP00000143362) -----
Amazon_molly (XP_016534180.1) -----
Medaka (XP_023818916.1) -----
Rainbow_trout (XP_021469805.1) -----
Rainbow_trout (XP_021436521.1) -----
Salmon (XP_014010485) -----
Salmon (XP_014070638.1) -----
Shark (XP_007890120.1) -----
Human (ENSP00000425443) -----
Gorilla (ENSGGOP00000034525) -----
Mouse (ENSMUSP00000143029) -----
Rat (ENSRNOP00000048956) -----
Pig (ENSSSCP00000009765) -----
Tasmanian devil (ENSSHAT000000) -----
Whale (XP_007106564.2) -----
Elephant (XP_023404313.1) -----
Lizard (ENSACAP00000008438) -----
Chicken (ENSGALP00000017216) -----
Turtle (ENSPSIP00000011691) -----
Xenopus (ENSXETP00000030770) -----
Coelacanth (ENSLACP00000008576) -----
Amazon_molly (ENSPPOP000000120) -----
Amazon_molly (ENSPPOP000000299) -----
Fugu (XP_011611191.1) -----
Medaka (XP_004065962.1) -----
Platyfish (ENSXMAP00000005447) -----
Spotted_gar (ENSLOCP000000155) -----
Stickleback (ENSGACP0000002318) -----
Tilapia (XP_005457058.1) -----
Tetraodon (ENSTNIP00000021201) -----
Zebrafish (ENSARDP000000101295) -----
Salmon (XP_014042431.1) -----
Salmon (XP_014065146.1) -----
Salmon (XP_014050290.1) -----
Rainbow_trout (XP_021429026.1) -----
Rainbow_trout (XP_021429023.1) -----
Shark (XP_007910136.1) -----
Human (ENSP00000386869) -----
Gorilla (ENSGGOP00000051172) -----
Armadillo (ENSNDOP00000021516) -----
Mouse (ENSMUSP00000087049) -----
Rat (ENSRNOP00000015296)Tet3 -----
Pig (ENSSSCP00000008852) -----
Elephant (XP_010591957.2) -----
Whale (XP_023989264.1) -----
Tasmanian devil (ENSSHAP000000) -----
Chicken (ENSGALP00000059756) -----
Lizard (ENSACAT00000001585) -----
Turtle (ENSPSIT00000006549) -----
Xenopus (ENSXETP00000054061) -----

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Tasmanian\_devil (ENSSHAP000000) -----GRSRKQMKIEASGSVAIVSTTCLAEIEGG--  
 Chicken (ENSGALT00000059756) -----VRSPKQIKIESSGAIIVVSTTCFYSEESQNADEA-  
 Lizard (ENSACAT00000001585) -----PRSPKQIKIESSGAIIVLSTTCFYSDGNQGGDATA-  
 Turtle (ENSPSIT00000006549) -----ARSPKQIKIESSGAIIVVSTTCFYSEENQNDAA-  
 Xenopus (ENSXETP00000054061) -----SKSPKQIKIESSGAIIVVSTTCFYSEENQH-  
 Coelacanth (ENSLACP00000009535) -----ARSPKQIKIESSGAIIVLSTTCFHSBDTQSTDGPS-  
 Spotted\_gar (ENSLLOCP0000001981) -----PNSIKKIKVSESSGAIIVLSTTACFS--TED-  
 Amazon\_molly (ENSPFOP000000021) -----SPLPKRKIKIEASGELAVLSTT--CYSEE-  
 Cave\_fish (ENSAMXP00000015689) -----STPPPKRVKIESSGGVIVLSTTCGFSTVDDL-  
 Fugu (ENSTRUP00000036865) -----SPLPKRMIKIESSGDIIVLSTT--CYSEE-  
 Medaka (ENSORLP00000019236) -----  
 Platyfish (ENSXMAT0000000130) -----  
 Stickleback (ENSGACP0000001732) -----  
 Tetraodon (ENSTNIP00000019883) -----  
 Tilapia (ENSONIP00000019943) -----  
 Zebrafish (ENSDARP000000085229) -----CFSEE-  
 Rainbow\_trout (XP\_021462005.1) ---TQPCTESPMEEQPEGAQLPLSLRQEVHLEQQQHRVLEDPFTVPLSPMSPLPKRMKIEITNGNVAVLSTTGFSEGGED-  
 Rainbow\_trout (XP\_021477599.1) ---TQPSTESPMEEQREATKLPLS-----PSQLPKRMKIEITNGNVAVLSTTGLFSDGGED-  
 Salmon (XP\_014026412.1) ---TQPSTESPMEEQPEGAQLPLSLRQEVHLEQQQHRVLEDPFTVPLSPASPLPKRMKIEITNGNVAVLSTTGFSEGGED-  
 Salmon (XP\_014017100.1) ---TQPSTESPMEEQREATKLPLS-----SSPLPKRMKIEITNGNVAVLSTTGLFSDGGED-



European\_ampioxus (Sc00000095) -----DFVSEKDEEGP--YYTHLGSPTIQAIRLEIM  
 Ciona\_intestinalis (XP\_0021254) -----STKQPTFAPPELLATPKLLSDELGRGRAVYTKGTNGVETKHHIFPRCTIPGSDGLEETPPYYTHLGSASHIQGIRKLF  
 Lamprey (scaf\_00044) -----DQIVKEKDEGP--YYTHLGAETVAARVRLM  
 Lamprey (scaf\_03335) -----  
 Shark (XP\_007897316.1) EDNQSGSFGQTTPTKSNAPSQATLNSFLESFPMKFLDTPPKNLDTPSKKQSEFFPMCDQVEQIIEKDEGP--YYTHLGAETVAARVREMI  
 Lizard (XP\_020663651.1) LETENL---QGRGVLRCSPTNNTLSFLESFPMKFLDTPPKNLDTPSKKQSDDFPSQDVEQIIEKDEGP--YYTHLGTGPSVAARVREIM  
 Chicken (ENSGALP00000053457) LGTDHP---QSTGDSGCSPAKNLSFLESFPMKFLDTPPKNLDTPSKKQSEELPTCDQVEQIIEKDEGP--YYTHLGTGPSVAARVREIM  
 Turtle (ENSPSIP0000006704) SGTETP---QGIDGLGCSPAKNLSFLESFPMKFLDTPPKNLDTPSKKQSEFFVCDQVEQIIEKDEGP--YYTHLGTGPSVAARVREIM  
 Human (ENSP00000362748) EEVCS---SSFSTSEFSTVDSAQKFNNDYAMNFFNTPPKNLSVITKD--SELPTCSCLDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Gorilla (ENSGGOP00000011536) EEVCS---SSFSTSEFSTVDSAQKFNNDYAMNFFNTPPKNLSVITKD--SELPTCSCLDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Mouse (ENSMUSP00000133279) EAQTS---SNG--PLGPTTDSAQSEFKESIMDLLSKPAKNLTAELKE--QEAAPCDQDQ--GTOKEKGP--YYTHLGAETVAARVREIM  
 Rat (ENSRNOP00000054747) EAQTS---SNG--PSDPTTDSAQADFNNGNVMDFLSMPAKKLTAEELKE--QEAATCCQDQ--GPOKDKGP--YYTHLGAETVAARVREIM  
 Pig (ENSSSCP00000010918) EDVCS---SSIGASEFSPIDNAQKFNNDYAMNFFNTPPKNLSVITKD--SELPTCNCLDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Whale (XP\_023987950.1) EDVCS---SSVGADEFSPIDSAQKFNNDYAMNFFNTPPKNLSVITKD--SELPTCNCLDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Elephant (ENSLAFP000000005179) EDVCL---SSAGASEFSPGDSAQKFNNDYAMNFFNTPPKNLSVITKD--SDLPSCSQVDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Armadillo (ENSDNOP00000014565) EDVCS---SNVGTSEFSPVDAQKFNNDYAMNFFNTPPKNLSVITKD--SELPTCNVDRVIOKDKGP--YYTHLGAETVAARVREIM  
 Tasmanian\_devil (XP\_023360087) SGLVTS---QGVGDLGSFPGKNTLSFLESFPMKFLDTPPKNLDTPSKKQSEELPSQDVEQIIEKDEGP--YYTHLGTGPSVAARVREIM  
 Coelacanth (ENSLACP00000016889) EDTHS---EMEPDFTGEGTPTKNTLNSFLESFPMKFLDTPPKNLDTPSKKQSDDFPTCDQVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Cavefish (XP\_007240334.2) ENANT---ESVEENTPTKMLNSFLESFPLKYLDTPIKNLNTPSKK--TPELPSQDVEQIIEKDEGP--YYTHLGSPTVAARVREIM  
 Platyfish (XP\_014325204.1) TDG---AHPAESTPTRNGVNSFLESFPMKFLDTPPKNLDTPSKK--LADLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Tilapia (XP\_005456583.2) TDGVQ---GHSADSTPKKNNINNSFLESFPLKYLDTPIKNLNTPSKK--LADLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Spotted\_gar (XP\_015202470.1) SGVEP---NFNGESTPTKNTLNSFLESFPLNFLDTPPKNLDTPSKK--GSDFFPTCDQVEQIIEKDEGP--YYTHLGSPTVAARVREIM  
 Stickleback (ENSGACT0000001035) -----FMDTPIKNLNTPSKK--LADLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Tetraodon (ENSTNIP00000011701) -----  
 Fugu (XP\_011601624.1) TDGDV---GHSADSTPKKNSISFLESFPMKFLDTPPKNLDTPSKK--VSDLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Zebrafish (ENSDARP00000143362) ENGDM---VYAGEQTPTKHNTNSFLESFPMKFLDTPPKNLDTPSKK--SMEIPLSCDVEQIIEKDEGP--YYTHLGSPTVAARVREIM  
 Amazon\_molly (XP\_016534180.1) TDG---AHPVEPTKRTAGVNSFLESFPMKFLDTPPKNLDTPSKK--LADLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Medaka (XP\_023818916.1) TDGVQ---DHSADSTPKKNNINNSFLESFPLKYLDTPIKNLNTPSKK--LADLPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Rainbow\_trout (XP\_021469805.1) ANGDL---DLSEESTPTKHNNSFLESFPLKYLDTPIKNLNTPSKK--LSEIPLSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Rainbow\_trout (XP\_021436521.1) TDGAL---DLSEELTPTKHNNSFLESFPLIFLDTPIKNLNTPSKK--LSEIPLSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Salmon (XP\_014010485) ANDDL---DLSEESTPTKHNNSFLESFPLKYLDTPIKNLNTPSKK--LSEIPLSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Salmon (XP\_014070638.1) TDGAL---DLSEELTPTKHNNSFLESFPLIFLDTPIKNLNTPSKK--LSEIPLSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Shark (XP\_007890120.1) SST---EATPTKRRPESTLNSFLESFPLKFLDTPPKSLDTPPKI--QYDVPAQSCFEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Human (ENSP00000425443) SSE---KTPTKRTAASVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Gorilla (ENSGGOP00000034525) SSE---KTPTKRTAASVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Mouse (ENSMUSP00000143029) -----TKSTDCSVDLDDVSESDT-----PGEQ--SQNGKQEGCN--PKDDEAP--YYTHLGAETVAARVREIM  
 Rat (ENSRNOP00000048956) LSE---KTPTKRTADSVLTVDSESPS-----DSDT--PVEDISEACKN--AEKDEGP--YYTHLGAETVAARVREIM  
 Pig (ENSSSCP00000009765) PSSS---EKTPKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Tasmanian\_devil (ENSSHAT000000) SSE---KTPTKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Whale (XP\_007106564.2) PSS---EKTPKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Elephant (XP\_023404313.1) PSS---EKTPKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Lizard (ENSACAP00000008438) SSS-----SSSSSSSS-----SSSSCKQIIEKDEGP--YYTHLGAETVAARVREIM  
 Chicken (ENSGALP00000017216) VSA---EKTPKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Turtle (ENSPSIP00000011691) PSA---EKTPKRTAGVNLNNSFLESFPLKFLDTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Xenopus (ENSXETP00000030770) -----PTKRAAGSALHNFIESPSNLLSTPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Coelacanth (ENSLACP00000008576) FER---TPTKQSGSTLSFLESFPLNLFNTPPKNLDTPVKT--QYDFPSCDVEQIIEKDEGP--YYTHLGSPTVAARVREIM  
 Amazon\_molly (ENSPFOP000000120) TAASVL---KNTLDSTPKKEQLLKNFIDSFPMKLLDTPPKNLDTPMKT--QYELASQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Amazon\_molly (ENSPFOP000000299) TAASVL---KNTLDSTPKKEQLLKNFIDSFPMKLLDTPPKNLDTPMKT--QYELASQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Fugu (XP\_011611191.1) -----L---KKAPNLTPKKEHLLQSFLESFPLKFLDTPPKNLDTPVKT--QYDIASQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Medaka (XP\_004065962.1) QST---KKGLESTPKKEQLLQSFLESFPMKLLDTPPKNLDTPVKT--QYDIASQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Platyfish (ENSXMAP00000005447) TAASVL---KNTLFTPKKEQLLKNFIDSFPMKLLDTPPKNLDTPMKT--QYELASQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Spotted\_gar (ENSLLOCP000000155) GAASLK---KKDCTPTKKEANLNSFLESFPMKLLDTPPKNLDTPVKT--QYEFPSQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Stickleback (ENSGACP00000002318) -----EKDEGP--YYTHLGAETVAARVREIM  
 Tilapia (XP\_005457058.1) SSTEVL---KKTPDSTPKKEQLLQSFLESFPMKLLNTPPKNLDTPMKT--QYDIASQDVEQIIEKDEGP--YYTHLGAETVAARVREIM  
 Tetraodon (ENSTNIP00000021201) -----EKDEGP--YYTHLGAETVAARVREIM  
 Zebrafish (ENSDARP00000101295) -KEQCK---QQHFTPPKKEPGLQSFLESFPMKLLNTPPKNLDTPVKT--QYELPSQDVEQIIEKDEGP--YYTHLGSASNTVAARVREIM  
 Salmon (XP\_014042431.1) -----  
 Salmon (XP\_014065146.1) GSNGLK---RPHLDFTPKQEPQLLQSFLESFPMKLLDTPPKNLDTPVKT--QYDIPSQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Salmon (XP\_014050290.1) GSNGLK---RPHLDFTPKQEPQLLQSFLESFPMKLLDTPPKNLDTPVKT--QYDIPSQDVEQIIEKDEGP--YYTHLGSAPTVAARVREIM  
 Rainbow\_trout (XP\_021429026.1) -----



Rainbow trout (XP\_021429023.1) GSNGLK----RSHLDFTPKQEPPLQSEFMNSPMKLLDTPKRNLLDTPPIKT-QYDIPSCQCMESI SEKDEGP-VYTHLGSAPNKAIRDLI  
Shark (XP\_007910136.1) -----CSRSGG-----  
Human (ENSP0000038689) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Gorilla (ENSGGOP00000051172) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Armadillo (ENSDNOP00000021516) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Mouse (ENSMUSP000000087049) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Rat (ENSRNOP00000015296)Tet3 -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Pig (ENSSSCP00000008852) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Elephant (XP\_010591957.2) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Whale (XP\_023989264.1) -----EATPTKAENP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Tasmanian devil (ENSSHAP000000) -----LETPKIQEHT--ATPNLRCFLESPKLYLDTPIKSLDTPSKRAQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Chicken (ENSGALP00000059756) -----EGTPTKDEVP--LTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Lizard (ENSACAT00000001585) -----SVEGTPTKEEVPPPLTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Turtle (ENSPSIP00000006549) -----LDGTPTKNDVP--FTPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTDCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Xenopus (ENSXETP00000054061) -----LDGTPTKSDLP--FNPTLSGFLESPKLYLDTPIKSLDTPAKRAQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Coelacanth (ENSLACP00000009535) -----EGTPTKNECP--LTPTLSGFLESPKLYLDTPIKSLDTPSKRAQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Spotted gar (ENSLOCP0000001981) -----ETPTKNEPP--LTPSLSGFLESPKLYLDTPIKSLDTPAKDAQSEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Amazon molly (ENSPFOP0000000021) -----GTPVKDGLN--SSPSLKGFLDSPKLYLDTPIKSLDTPKIDPQLEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Cave fish (ENSAMXP00000015689) -----DTPTKDALA--SGPSLKGFLDSPKLYLDTPIKSLDTPVKDNQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Fugu (ENSTRUP00000036865) -----DTPTKDSLFP--SSPSLRGFLESPKLYLDTPIKSLDTPSKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Medaka (ENSORLP00000019236) -----I-----I  
Platyfish (ENSXMAT00000000130) -----QEHILEKDEGP-VYNHLGSGPTVASIRSLM  
Stickleback (ENSGACP0000001732) -----I-----I  
Tetraodon (ENSTNIP00000019883) -----I-----I  
Tilapia (ENSONIP00000019943) -----DTPTEKGVSS--SSPSLKGFLDSPKLYLDTPIKSLDTPSKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Zebrafish (ENSZARP000000085229) -----LKECFLESPKLYLDTPIKSLDTPCKDQVDFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Rainbow trout (XP\_021462005.1) -----DTPTKDGFPP--LNPSLKGFLDSPKLYLDTPIKSLDTPAKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Rainbow trout (XP\_021477599.1) -----DTPTKDGFPP--LNPSLKGFLDSPKLYLDTPIKSLDTPAKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Salmon (XP\_014026412.1) -----DTPTKDGFPP--LNPSLKGFLDSPKLYLDTPIKSLDTPAKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM  
Salmon (XP\_014017100.1) -----DTPTKDGFPP--LNPSLKGFLDSPKLYLDTPIKSLDTPAKDLQAEFFPTCCVVEQIVKDEGP-VYTHLGSPTVASIRSLM

Cys-rich domain

1900 1910 1920 1930 1940 1950 1960 1970 1980 #

European ampioxus (Sc0000095) EKR-----IITGKEGKSSQGCPIDAKW---IVRR--SSEEEKLLCLVR  
Ciona intestinalis (XP\_0021254) EER-----CGFTGRALRHEKVCYTGKKGKTSRGCPIDAKW---VLRSSBQEKLLMVCVR  
Lamprey (scaf\_00044) ETR-----S-----VEKVVYTGKKGKSSQGCPIDAKW---VVRASBQEKLLCLVR  
Lamprey (scaf\_03335) -----KVIFTGKEGRSQGCPIDAKWSSR--VLRGGLOEKLLVVVR  
Shark (XP\_007897316.1) EDRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SNDEEKLLCLVR  
Lizard (XP\_020663651.1) EDRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SDDEEKLLCLVR  
Chicken (ENSGALP00000053457) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SDDEEKLLCLVR  
Turtle (ENSPSIP00000006704) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SDDEEKLLCLVR  
Human (ENSP00000362748) ENRY-----GKGNARIEVIVYTGKKGKSSHGCPIDAKW---VIRR--SDDEEKVLCVR  
Gorilla (ENSGGOP00000011536) ENRY-----GKGNARIEVIVYTGKKGKSSHGCPIDAKW---VIRR--SDDEEKVLCVR  
Mouse (ENSMUSP000000133279) ETRF-----GKGNARIEKLIVYTGKKGKSSQGCPIDAKW---VIRR--SGEEEKLLCLVR  
Rat (ENSRNOP000000054747) ENRY-----GKGNARIEKLIVYTGKKGKSSQGCPIDAKW---VIRR--SGEEEKVLCVR  
Pig (ENSSSCP00000010918) ENRY-----GKGNARIEVIVYTGKKGKSSNGCPIDAKW---VIRR--SDDEEKVLCVR  
Whale (XP\_023987950.1) ENRY-----GKGNARIEVIVYTGKKGKSSNGCPIDAKW---VIRR--SDDEEKVLCVR  
Elephant (ENSLAFP00000005179) ENRY-----GKGNARIEVIVYTGKKGKSSHGCPIDAKW---VIRR--SDDEEKVLCVR  
Armadillo (ENSDNOP00000014565) ENRY-----GKGNARIEVIVYTGKKGKSSHGCPIDAKW---VIRR--SDDEEKVLCVR  
Tasmanian devil (XP\_023360087) EARY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SDDEEKLLCLVR  
Coelacanth (ENSLACP00000016889) BSRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SNDEEKLLCLVR  
Cavefish (XP\_007240334.2) BDRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--ASEEEKLLCLVR  
Platyfish (XP\_014325204.1) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Tilapia (XP\_005456583.2) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Spotted gar (XP\_015202470.1) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--ASVEEEKLLCLVR  
Stickleback (ENSGACT0000001035) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Tetraodon (ENSTNIP00000011701) -----W-----VIRR--DSDEEKLLCLVR  
Fugu (XP\_011601624.1) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--DSDEEKLLCLVR  
Zebrafish (ENSZARP00000143362) ETRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Amazon molly (XP\_016534180.1) ENRY-----GKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Medaka (XP\_023818916.1) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Rainbow trout (XP\_021469805.1) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Rainbow trout (XP\_021436521.1) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Salmon (XP\_014010485) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Salmon (XP\_014070638.1) ENRY-----GKGNARIEVIVYTGKGRGSSQGCPIDAKW---VIRR--GSEEEKLLCLVR  
Shark (XP\_007890120.1) ENR-----FGKGNARIEKLIVYTGKKGKSSQGCPIDAKW---VIRR--SGEEEKLLCLVR  
Human (ENSP00000425443) EER-----FGKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SSSEEEKLLCLVR  
Gorilla (ENSGGOP00000034525) -----ELKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SSSEEEKLLCLVR  
Mouse (ENSMUSP000000143029) EER-----YGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VYRR--SSSEEEKLLCLVR  
Rat (ENSRNOP00000048956) EER-----YGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VYRR--SSTEEKLLCLVR  
Pig (ENSSSCP00000009765) EER-----YGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SGSEEEKLLCLVR  
Tasmanian devil (ENSSHAT000000) EER-----FGKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SCNEEEKLLCLVR  
Whale (XP\_007106564.2) EER-----FGKGNARIEVIVYTGKGRGSSQGCPIDAKW---VVRR--SCSEEEKLLCLVR  
Elephant (XP\_023404313.1) ESQQLQVCKYLPEQPQLLQVEDSYERDQCREGLSYRFYGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--GSEEEKLLCLVR  
Lizard (ENSACAP00000008438) EER-----YGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--GSTEEEKLLCLVR  
Chicken (ENSGALP00000017216) EER-----FGKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SSQEEKLLCLVR  
Turtle (ENSPSIP00000011691) EER-----YGEKGNARIEVIVYTGKKGKSSQGCPIDAKW---VVRR--SDDEEKLLCLVR  
Xenopus (ENSXETP00000030770) EER-----FGKGNARIEVIVYTGKKGKSSQGCPIDAKW---VIRR--SGTDEEKLLCLVR  
Coelacanth (ENSLACP00000008576) ENR-----FGKGNARIEKLIVYTGKKGKSSQGCPIDAKWQ---VIRR--SSDEEEKLLCLVR  
Amazon molly (ENSPFOP0000000120) EKR-----SGITGNARIEKLIVYTGKKGKSSQGCPIDAKW---VVRR--SSVEEEKLLCLVR  
Amazon molly (ENSPFOP0000000299) EKR-----SGITGNARIEKLIVYTGKKGKSSQGCPIDAKW---VIRR--SSVEEEKLLCLVR  
Fugu (XP\_011611191.1) EKR-----SGITGNARIEKLIVYTGKKGKSSQGCPIDAKW---VIRR--GSEEEKLLCLVR

Medaka (XP\_004065962.1)  
Platyfish (ENSXMAP00000005447)  
Spotted\_gar (ENSLOCP000000155)  
Stickleback (ENSGACP0000002318)  
Tilapia (XP\_005457058.1)  
Tetraodon (ENSTNIP00000021201)  
Zebrafish (ENSDDAR000000101295)  
Salmon (XP\_014042431.1)  
Salmon (XP\_014065146.1)  
Salmon (XP\_014050290.1)  
Rainbow trout (XP\_021429026.1)  
Rainbow trout (XP\_021429023.1)  
Shark (XP\_007910136.1)  
Human (ENSP00000386869)  
Gorilla (ENSGGOP00000051172)  
Armadillo (ENSNDOP00000021516)  
Mouse (ENSMUSP00000087049)  
Rat (ENSRNOP00000015296)  
Tet3 Pig (ENSSSCP00000008852)  
Elephant (XP\_010591957.2)  
Whale (XP\_023989264.1)  
Tasmanian devil (ENSSHAP000000)  
Chicken (ENSGALP00000059756)  
Lizard (ENSACAT0000001585)  
Turtle (ENSPSIT00000006549)  
Xenopus (ENSKETP00000054061)  
Coelacanth (ENSLACP00000009535)  
Spotted\_gar (ENSLOCP0000001981)  
Amazon molly (ENSPFOP0000000021)  
Cave\_fish (ENSAMXP00000015689)  
Fugu (ENSTRUP00000036865)  
Medaka (ENSORLP00000019236)  
Platyfish (ENSXMAT00000000130)  
Stickleback (ENSGACP0000001732)  
Tetraodon (ENSTNIP00000019883)  
Tilapia (ENSONIP00000019943)  
Zebrafish (ENSDDAR000000085229)  
Rainbow\_trout (XP\_021462005.1)  
Rainbow\_trout (XP\_021477599.1)  
Salmon (XP\_014026412.1)  
Salmon (XP\_014017100.1)

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...SGLTGRAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--SSVEEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--ASVEEKLLVLRV  
...FGTGRAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--SGVEEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--SSVEEKLLVLRV  
...SGLTGRAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--SGVEEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--GSVEEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--ANDEEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--GSVDEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--GSVDEKLLVLRV  
...SGLTGAIRTEKVIYTGKEGKSTQGCPPIAKW---VIRR--GSVDEKLLVLRV  
...REGWERADPLFAVSPGCG  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
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...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RFGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RFGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
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...RYGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
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...RFGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR  
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...RFGKGRADIRTEKVIYTGKEGKSTSRGCPPIAKW---VIRRHTLLEEKLLCLVR
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European ampioxus (Sc0000095) CRPGHCDDSSYIITCIWAWEGIQRDRADLYDYPTSGILSKA-GLPTRRRCVNETKTCACQGVNENSCGASFSGCWSMY  
Ciona intestinalis (XP_0021254 CRPGHRCITAVMVMVILMVEGVSRLADFSYKCTQLIPTN-GIATERRCETNEERTCACQGDDEPKGGASVDFGCSWSMY  
Lamprey (scaf_0044) BRAGHRCENAVVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Lamprey (scaf_03335) BRRGHRCACAVMVMVILAWEGVPSSELADLLYSELAEILIRH-GAFTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Shark (XP_007897316.1) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Lizard (XP_020663651.1) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Chicken (ENSGALP00000053457) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Turtle (ENSPSIT0000006704) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Human (ENSP00000362748) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Gorilla (ENSGGOP00000011536) CRTGHRCPTAVMVMVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Mouse (ENSMUSP00000133279) BRVDHRCSTAVIVVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Rat (ENSRNOP00000054747) BRVDHRCSTAVIVVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Pig (ENSSSCP00000010918) CRAGHRCPTAVMVMVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Whale (XP_023987950.1) CRAGHRCPTAVMVMVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Elephant (ENSLAFP00000005179) CRTGHRCPTAVMVMVILMWDGIPPLMADRLLYTELTELKSYNGHPTDRRCFLNEDRTACQGDDEPKGGASVDFGCSWSMY  
Armadillo (ENSNDOP00000014565) CRTGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Tasmanian devil (XP_023360087. CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Coelacanth (ENSLACP00000016889) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Cavefish (XP_007240334.2) CRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Platyfish (XP_014325204.1) CRPGHRCQTAIVIVLILAWEGIPRAVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Stickleback (ENSGACT0000001035) CRPGHRCQTAIVIVLILAWEGIPRAVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Tilapia (XP_005456583.2) CRPGHRCQTAIVIVLILAWEGIPRAVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Spotted_gar (XP_015202470.1) KRAGHRCQTAIVIVLILAWEGIPRIVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Tetraodon (ENSTNIT00000011701) RRPGHRCQTAIVIVLILAWEGIPRPVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Fugu (XP_011601624.1) RRPGHRCQTAIVIVLILAWEGIPRPVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Zebrafish (ENSDDAR000000143362) CRAGHRCQTAIVIVLILAWEGIPRSVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Amazon molly (XP_016534180.1) CRPGHRCQTAIVIVLILAWEGIPRSVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Medaka (XP_023818916.1) CRPGHRCQTAIVIVLILAWEGIPRSVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Rainbow_trout (XP_021469805.1) HRAGHRCQTAIVIVLILAWEGIPRGVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Rainbow_trout (XP_021436521.1) HRAGHRCQTAIVIVLILAWEGIPRGVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Salmon (XP_014010485) HRAGHRCQTAIVIVLILAWEGIPRGVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Salmon (XP_014070638.1) HRAGHRCQTAIVIVLILAWEGIPRGVADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Shark (XP_007890120.1) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Human (ENSP00000425443) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Gorilla (ENSGGOP00000034525) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Mouse (ENSMUSP00000143029) VRPNHTCQTAIVIVLILAWEGIPKLLASELYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Rat (ENSRNOP00000048956) VRAHRCQTAIVIVLILAWEGIPKLLASELYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Pig (ENSSSCP00000009765) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Tasmanian devil (ENSSHAT000000) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY  
Whale (XP_007106564.2) BRAGHRCQTAIVIVLILAWEGIPRLADKLYOELTQLRKY-GSPTERRCALNEDRTACQGDDEPKGGASVDFGCSWSMY
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Elephant (XP\_023404313.1) BRAGHTCEAAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Lizard (ENSACAP0000008438) BRAGHSCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEEKSSQ-LLI RTCACQGLDDETCGASFSFGCSWSMY

Chicken (ENSGALP00000017216) BRAGHTCEAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Turtle (ENSPSIP00000011691) BRAGHTCEAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Xenopus (ENSXETP00000030770) BRAGHSCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Coelacanth (ENSLACP00000008576) BRAGHSCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GILTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Amazon\_molly (ENSPFOP00000001205) BRAGHRCDTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Amazon\_molly (ENSPFOP000000299) BRAGHRCDTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Fugu (XP\_011611191.1) BRAGHTCNTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Medaka (XP\_004065962.1) BRAGHRCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Platyfish (ENSXMAP00000005447) BRAGHRCDTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Spotted\_gar (ENSLOC000000155) BRAGHSCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Stickleback (ENSGACP0000002318) BRAGHRCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Tilapia (XP\_005457058.1) BRAGHRCATTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Tetraodon (ENSTNIP00000021201) BRAGHTCNTACIIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Zebrafish (ENSDARP000000101295) BRAGHSCETAIVIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Salmon (XP\_014042431.1) -----

Salmon (XP\_014065146.1) BRERHKCEAACTIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Salmon (XP\_014050290.1) BRERHKCEAACTIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Rainbow\_trout (XP\_021429026.1) -----

Rainbow\_trout (XP\_021429023.1) BRERHKCEAACTIVVILVWEGIPQLSLADRLYLELSEITLTKH-GADTNRRCALNEE-----RTCACQGLDDETCGASFSFGCSWSMY

Shark (XP\_007910136.1) -----

Human (ENSP000000386869) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Gorilla (ENSGGOP000000051172) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Armadillo (ENSDNOP000000021516) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Mouse (ENSMUSP000000087049) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Rat (ENSRNOP00000015296) Tet3 BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Pig (ENSSSCP00000008852) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Elephant (XP\_010591957.2) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Whale (XP\_023989264.1) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Tasmanian\_devil (ENSSHAP000000) BRSGHRCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Chicken (ENSGALP00000059756) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Lizard (ENSGALP00000001585) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Turtle (ENSPSIT00000006549) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Xenopus (ENSXETP00000054061) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Coelacanth (ENSLACP00000009535) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Spotted\_gar (ENSLOC00000001981) KRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Amazon\_molly (ENSPFOP0000000021) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Cave\_fish (ENSAMPX000000015689) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Fugu (ENSTRUP000000036865) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Medaka (ENSORLP00000019236) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Platyfish (ENSXMAP00000000130) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Stickleback (ENSGACP00000001732) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Tetraodon (ENSTNIP000000019883) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Tilapia (ENSONIP000000019943) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Zebrafish (ENSDARP000000085229) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Rainbow\_trout (XP\_021462005.1) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Rainbow\_trout (XP\_021477599.1) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Salmon (XP\_014026412.1) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

Salmon (XP\_014017100.1) BRAGHBCQNAVIVVILVWEGIPQLSLADRLYLELSEITLTKYK-GNPTNRRCALNDD-----RTCACQGLDDETCGASFSFGCSWSMY

DSBH-domain

2080 2090 2100 2110 2120 2130 2140 2150 2160

European ampioxus (Sc0000095) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Ciona intestinalis (XP\_0021254) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Lamprey (scaf\_0044) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Lamprey (scaf\_03335) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Shark (XP\_007897316.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Lizard (XP\_020663651.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Chicken (ENSGALP00000053457) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Turtle (ENSPSIP00000006704) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Human (ENSP000000362748) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Gorilla (ENSGGOP00000011536) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Mouse (ENSMUSP000000133279) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Rat (ENSRNOP000000054747) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Pig (ENSSSCP00000010918) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Elephant (XP\_023987950.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Elephant (ENSLAFP000000005179) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Armadillo (ENSDNOP00000014565) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Tasmanian\_devil (XP\_023360087) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Coelacanth (ENSLACP000000016889) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Cavefish (XP\_007240334.2) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Platyfish (XP\_014325204.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Tilapia (XP\_005456583.2) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Spotted\_gar (XP\_015202470.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Stickleback (ENSGACT0000001035) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Tetraodon (ENSTNIP00000011701) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Fugu (XP\_011601624.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Zebrafish (ENSDARP000000143362) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Amazon\_molly (XP\_016534180.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Medaka (XP\_023818916.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Rainbow\_trout (XP\_021469805.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Rainbow\_trout (XP\_021436521.1) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Salmon (XP\_014010485) N-GCKFARSVPRKFRLLGDDPSSE-----EALTEEDHQRLEAGEVGPVMEOLAPDAFRNQTAYS

Salmon (XP\_014070638.1) N-GCKFARSKLPRKFRLLGDDMPQE-----BEKLEENRLLQNLATDLGPPVYQRLAPDAFQNOVDQE

Shark (XP\_007890120.1) N-GCKFARSKLPRKFRLLGDDPK-----BEERLESNLLQNLATLLAPTYKKLAPDAFQNOLEFFE

Human (ENSP00000425443) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Gorilla (ENSGGOP0000034525) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Mouse (ENSMUSP00000143029) N-GCKFARSKLPRKFRLLGAEFK-----BEERLESNLLQNLATVITAPTYKKLAPDAYNQVEFFE

Rat (ENSRNOP00000048956) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYRNQVEFFE

Pig (ENSSSCP00000009765) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Tasmanian\_devil (ENSSHAT000000) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Whale (XP\_007106564.2) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Elephant (XP\_023404313.1) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Lizard (ENSACAP00000008438) N-GCKFARSKLPRKFRLLGDDPK-----BEKLETSLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Chicken (ENSGALP00000017216) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESHLLQNLSTLMAPTYKKLAPDAYNQLEVEE

Turtle (ENSPSIP00000011691) N-GCKFARSKLPRKFRLLGDDPK-----BEKLESNLQNLSTLMAPTYKKLAPDAYNQLEVEE

Xenopus (ENSXETP00000030770) TNCKSGVAKLGLVAIVRTDVKF-----BEKLEANLQNLSTLMAPTYKKLAPDAYNQLEHEE

Coelacanth (ENSLACP00000008576) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEESNLLQNLATLLAPTYKKLAPDAYNQLEVEE

Amazon\_molly (ENSPFOP0000000120) N-GCKFARSKLPRKFRLLGDDVR-----BEKLEKSNLQNLATLLAPTYKKLAPDAYNQVEHEE

Amazon\_molly (ENSPFOP000000029) N-GCKFARSKLPRKFRLLGDDVR-----BEKLEKSNLQNLATLLAPTYKKLAPDAYNQVEHEE

Fugu (XP\_011611191.1) N-GCKFARSKLPRKFRLLGDDMK-----BEERLEQNRLQNLATLLGPIYKSLAPDAYNQVEHEE

Medaka (XP\_004065962.1) N-GCKFARSKLPRKFRLLGDDVR-----BEKVEQRNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Platyfish (ENSXMAP00000005447) N-GCKFARSKLPRKFRLLGDDVR-----BEENLEKSNLQNLATLLAPTYKKLAPDAYNQVEHEE

Spotted\_gar (ENSLOCP000000155) N-GCKFARSKLPRKFRLLGDDPK-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEVEE

Stickleback (ENSGACP00000002318) N-GCKFARSKLPRKFRLLGDDMK-----BEKLEQRNRLQNLATLLGPIYKSLAPDAYNQVEHEE

Tilapia (XP\_005457058.1) N-GCKFARSKLPRKFRLLGDDVK-----BEERVEENRLQNLATLLAPTYKKLAPDAYNQVEHEE

Tetraodon (ENSTNIP000000021201) N-GCKFARSKLPRKFRLLGDDMR-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Zebrafish (ENSDARP000000101295) N-GCKFARSKLPRKFRLLGDDPK-----BEKLEQNRLQNLATVITAPTYKKLAPDAYNQVEHEE

Salmon (XP\_014042431.1) -----

Salmon (XP\_014065146.1) N-GCKFARSKLPRKFRLLGDDPK-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Salmon (XP\_014050290.1) N-GCKFARSKLPRKFRLLGDDPK-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Rainbow\_trout (XP\_021429026.1) N-GCKFARSKLPRKFRLLGDDPK-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Rainbow\_trout (XP\_021429023.1) N-GCKFARSKLPRKFRLLGDDPK-----BEERLEQNRLQNLATLLAPTYKKLAPDAYNQVEHEE

Shark (XP\_007910136.1) N-GCKYARSKLPRKFRLLGDDNPKE-----EDDLKERLQNLATLLAPTYKKLAPDAYNQVAQEE

Human (ENSP00000386869) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Gorilla (ENSGGOP00000051172) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Armadillo (ENSDNOP000000021516) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Mouse (ENSMUSP000000087049) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Rat (ENSRNOP00000015296) Tet3 N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Pig (ENSSSCP00000008852) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Elephant (XP\_010591957.2) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Whale (XP\_023989264.1) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Tasmanian\_devil (ENSSHAY000000) N-GCKYARSKLPRKFRLLGDDNPVE-----BEENLRKSNLQNLATVITAPTYKKLAPDAYNQVETNE

Chicken (ENSGALT00000059756) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Lizard (ENSACAT00000001585) N-GCKYARSKLPRKFRLLGDDNPNE-----BDVLRKSNLQNLATVITAPTYKKLAPDAYNQVETNE

Turtle (ENSPSIT00000006549) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATLLAPTYKKLAPDAYNQVETNE

Xenopus (ENSXETP00000054061) N-GCKYARSKLPRKFRLLGDDNPKE-----EDDLKDNRLQNLATVITAPTYKKLAPDAYNQVETNE

Coelacanth (ENSLACP00000009535) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATVITAPTYKKLAPDAYNQVETNE

Spotted\_gar (ENSLOCP0000001981) N-GCKYARSKLPRKFRLLGDDNPKE-----BEVLRKSNLQNLATVITAPTYKKLAPDAYNQVETNE

Amazon\_molly (ENSPFOP0000000021) N-GCKYARSKLPRKFRLLGDDHPEE-----BEKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Cave\_fish (ENSAMXP00000015689) N-GCKYARSKLPRKFRLLGDDHPEE-----BEVLRKSNLQNLATVITAPTYKKLAPDAYNQCAAEE

Fugu (ENSTRUP00000036865) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKVRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Medaka (ENSORLP00000019236) N-GCKYARSKLPRKFRLLGDDHPEE-----BEKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Platyfish (ENSXMAP00000000130) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Stickleback (ENSGACP00000001732) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Tetraodon (ENSTNIP000000019883) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKVRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Tilapia (ENSONIP000000019943) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Zebrafish (ENSDARP000000085229) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

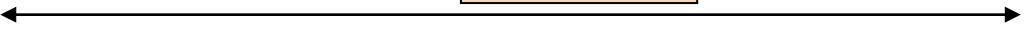
Rainbow\_trout (XP\_021462005.1) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Rainbow\_trout (XP\_021477599.1) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Salmon (XP\_014026412.1) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

Salmon (XP\_014017100.1) N-GCKYARSKLPRKFRLLGDDHPEE-----BDKLRDNRLQNLATVITAPTYKKLAPDAYNQCAAEE

DSBH-domain



2170 2180 2190 2200 2210 2220 2230 2240 2250

European ampioxus (Sc0000095) -----GVASDCLRGFGP-ESTRPFSGVTACVDFCAHAHRTDHNMMNGSTTV-CTLTKCPENRRLGVPPEDEQLHVLPLYKMSPTIDE

Ciona intestinalis (XP\_0021254) CE-----GQECRLGYNPNNEGRPFSGVTCDMDFCAHAHRTDHNMMNGSTTV-LVLTLLKPELRLVIGQKPPDEQLHVLPLYKLDLTINE

Lamprey (scaf\_00044) -----LHAPDCRLGL-ODGRPFSGVTACVDFCAHAHRTDHNMMNGSTTVV-CTLTKEDNRRVIGVVPPEDEQLHVLPLYKLAELDE

Lamprey (scaf\_03335) PLVSAMSPRVAPAGECRLGE-----GEGRPFSGVTACVDFCAHAHRTDHNMMNGCTTVVSCCHSPNGPP-----

Shark (XP\_007897316.1) -----NIASNCRLGL-ESGRPFSGVTACVDFCAHAHRTDHNMMNGSTTVV-CTLTKEDNRRVINSIPPEDEQLHVLPLYKISHADE

Lizard (XP\_020663651.1) -----HLGPDCLRLGI-KEGRPFSGVTACVDFCAHAHRTDHNMMNGSTTVV-CTLTKEDNRRVIGVVPPEDEQLHVLPLYKISQIDE

Chicken (ENSGALP00000053457) -----HMGPDCLRLGS-KDGRPFSGVTACVDFCAHAHRTDHNMMNGSTTVV-CTLTKEDNRRVIGVVPPEDEQLHVLPLYKISQIDE

Turtle (ENSPSIP00000006704) -----HMGPDCLRLGS-KDGRPFSGVTACVDFCAHAHRTDHNMMNGSTTVV-CTLTKEDNRRVIGVVPPEDEQLHVLPLYKISQIDE

Human (ENSP00000362748) -----NVARECRLGS-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Gorilla (ENSGGOP00000011536) -----NVARECRLGS-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Mouse (ENSMUSP000000133279) -----EVAGDCRLGN-EEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Rat (ENSRNOP000000054747) -----DIAGDCRLGN-EEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Pig (ENSSSCP00000010918) -----HVARECRLGK-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Whale (XP\_023998750.1) -----HVARECRLGK-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Elephant (ENSLAFP00000005179) -----HVARECRLGK-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Armadillo (ENSDNOP00000014565) -----HVARECRLGK-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSDTIDE

Tasmanian\_devil (XP\_023360087) -----HLGSDCRLGR-KDGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSQIDE

Coelacanth (ENSLACP00000016889) -----HVAPDCRLGL-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRSLGVIPPEDEQLHVLPLYKLSQIDE

Cavefish (XP\_007240334.2) -----QSQNCRLGR-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRVIRNIPPEDEQLHVLPLYKISDTIDE

Platyfish (XP\_014325204.1) -----AAVDACRLGR-MEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRVIRNIPPEDEQLHVLPLYKISDTIDE

Tilapia (XP\_005456583.2) -----AAGGECRLGK-KEGRPFSGVTACVDFCAHFRHTDHNMMNGSTTVV-CTLTKEDNRRVIRNIPPEDEQLHVLPLYKISDTIDE

Fe binding

Spotted\_gar (XP\_015202470.1) -----HLGIDCRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDDE

Stickleback (ENSACT0000001035) -----AAGGD CRLGV--REGRRPFGSVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDRDE

Tetraodon (ENSTNIT000000011701) -----EAGRD CRLGQ--REGRRPFGSVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDRDE

Fugu (XP\_011601624.1) -----DGGGD CRLGQ--REGRRPFGSVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDRDE

Zebrafish (ENSDARP00000143362) -----QRGQD CRLGC--REGRRPFGSVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDTDE

Amazon\_molly (XP\_016534180.1) -----AAGDA CRLGR--MEGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDKDE

Medaka (XP\_023818916.1) -----VAGSD CRLGR--REGRRPFGSVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISDVDE

Rainbow\_trout (XP\_021469805.1) -----QAGQD CRLGR--RAGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISORDE

Rainbow trout (XP\_021436521.1) -----QAGQD CRLGR--RAGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISORDE

Salmon (XP\_01401120.1) -----QAGQD CRLGR--RAGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CSSHG-----WLFHMHPIRCQNRD

Salmon (XP\_014070638.1) -----QAGQD CRLGR--RAGRPFSGVTACVDFCAHAHRTLNHMNGSTVIV--CTLTKEDNRAVRNIPDEDEQLHVLVLYKISORDE

Shark (XP\_007890120.1) -----QRAPD CRLGK--CEGRPFAGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGQIPDEDEQLHVLVLYKISPTDE

Human (ENSP00000425443) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDVDE

Gorilla (ENSGGOP00000034525) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDVDE

Mouse (ENSMUSP00000143029) -----HQAPD CRLGL--KEGRPFSGVTACVDFSAHSHRTLNHMNGST--VVVTLKEDNRHIGAKIPDEDEQLHVLVLYKISATDE

Rat (ENSRNOP00000048956) -----HRAIE CRLGL--KEGRPFSGVTACVDFSAHSHRTLNHMNGST--VVVTLKEDNRHIGGKIPDEDEQLHVLVLYKISATDE

Pig (ENSSSCP00000009765) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDVDE

Tasmanian\_devil (ENSSHAT000000) -----NRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGRTIPDEDEQLHVLVLYKISNMDE

Whale (XP\_007106564.2) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDVDE

Elephant (XP\_023404313.1) -----DRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDMDE

Lizard (ENSACAP00000008438) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGQIPDEDEQLHVLVLYKISNDDE

Chicken (ENSGALP00000017216) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISDVDE

Turtle (ENSPSIP00000011691) -----HRAPE CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGGKIPDEDEQLHVLVLYKISNVDE

Xenopus (ENSXETP00000030770) -----HRAPD CRLGL--KEGRPFSGVTACVDFCAHSHRTLNHMNGST--LVCTLRKEDNRHNGKIPDEDEQLHVLVLYKISNVDE

Coelacanth (ENSLACP00000008576) -----HRASD CRLGL--KEGRPFSGVTACVDFCAHSHRTLNHMNGST--LVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Amazon\_molly (ENSPFOP0000000120) -----HRAPD CRLGI--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISSTDE

Amazon\_molly (ENSPFOP0000000299) -----HRAPD CRLGI--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISSTDE

Fugu (XP\_011611191.1) -----QRGLD CRLGH--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Medaka (XP\_004065962.1) -----HRAPD CRLGI--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGRTIPDEDEQLHVLVLYKISNTDE

Platyfish (ENSXMAP000000005447) -----HRAPD CRLGI--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISSTDE

Spotted\_gar (ENSLACP0000000155) -----HRAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--LVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISSTDE

Stickleback (ENSACAP00000002318) -----QRAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Tilapia (XP\_005457058.1) -----HRAID CRLGL--KDRPFGSVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Tetraodon (ENSTNIP000000021201) -----QRALD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Zebrafish (ENSDARP00000101295) -----NRAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISSTDE

Salmon (XP\_014042431.1) -----MDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Salmon (XP\_014065146.1) -----QRAPD CRLGK--CEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Salmon (XP\_014050290.1) -----QRAPD CRLGK--CEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Rainbow trout (XP\_021429026.1) -----QRAPD CRLGK--CEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Rainbow trout (XP\_021429023.1) -----QRAPD CRLGK--CEGRPFSGVTACVDFCAHAHRTLNHMNGST--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Shark (XP\_007910136.1) -----QAGPD CRLGL--CEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISPTDE

Human (ENSP00000386869) -----EIAID CRLGL--KEGRPFAGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Gorilla (ENSGGOP000000051172) -----EIAID CRLGL--KEGRPFAGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Armadillo (ENSMNOP000000021516) -----EIAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Mouse (ENSMUSP000000087049) -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Rat (ENSRNOP00000015296) Tet3 -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Pig (ENSSSCP00000008852) -----EIAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Elephant (XP\_010591957.2) -----EIAID CRLGL--KEGRPFAGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Whale (XP\_023989264.1) -----EIAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Tasmanian\_devil (ENSSHAP000000) -----EIAID CRLGL--KEGRPFAGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Chicken (ENSALP000000059756) -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Lizard (ENSACAP00000001585) -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Turtle (ENSPSIT00000006549) -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Xenopus (ENSXETP000000054061) -----DVAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Coelacanth (ENSLACP00000009535) -----HIAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Spotted\_gar (ENSLACP00000001981) -----KSAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Amazon\_molly (ENSPFOP00000000021) -----QRAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Cave\_fish (ENSAMXP00000015689) -----KVASD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Fugu (ENSTRUP000000036865) -----SKAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Medaka (ENSORLP00000019236) -----DKASD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Platyfish (ENSXMAT00000000130) -----QRAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Stickleback (ENSACAP00000001732) -----SKAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Tetraodon (ENSTNIP000000019883) -----SKAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Tilapia (ENSONIP000000019943) -----SKAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Zebrafish (ENSDARP000000085229) -----DVASD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Rainbow\_trout (XP\_021462005.1) -----TKAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Rainbow\_trout (XP\_021477599.1) -----VTAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Salmon (XP\_014026412.1) -----TKAID CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Salmon (XP\_014017100.1) -----VTAPD CRLGL--KEGRPFSGVTACVDFCAHAHRTLNHMNGCT--VVCTLRKEDNRHIGKIPDEDEQLHVLVLYKISNTDE

Fe binding

DSBH-domain

European ampioxus (Sc0000095) FDSBEGQEKIRTGALMLTSYTH-QI

Ciona intestinalis (XP\_0021254) EGTBEGLGAKIKAGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

Lamprey (scaf\_00044) HGDPHSLDERIRTGAIQVKT

Lamprey (scaf\_03335) YGNEDIQEKMKNGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

Shark (XP\_007897316.1) EGTBEGLGAKIKAGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

Lizard (XP\_020663651.1) EGTBEGLGAKIKAGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

Chicken (ENSALP000000053457) EGTBEGLGAKIKAGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

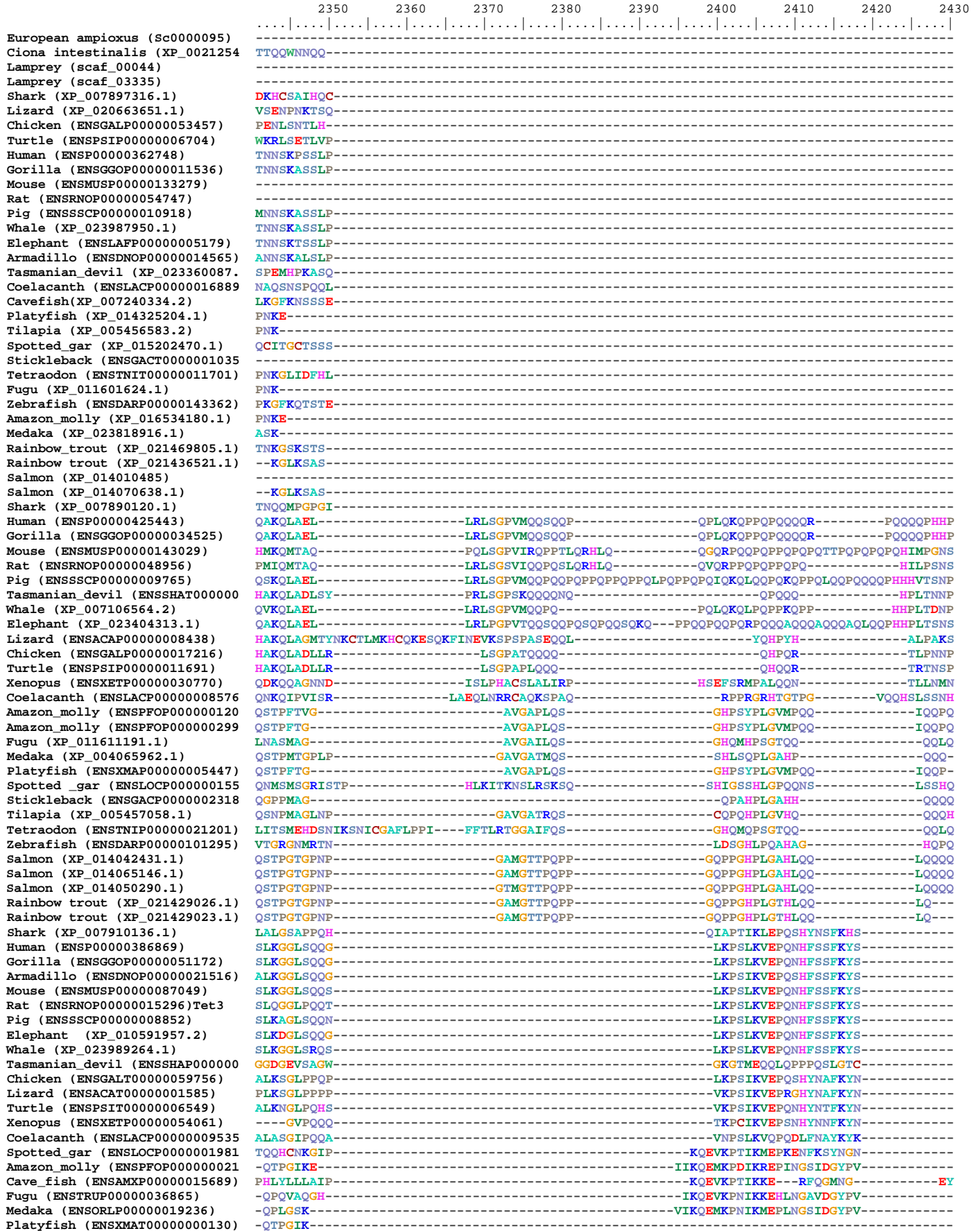
Turtle (ENSPSIP00000006704) EGTBEGLGAKIKAGAIQVLTAFPR--EVRMLAEPL-RATKKKPPDTRTLEKQKQ-----LVDDKYSTPIKLG-----TEA

Human (ENSP000000362748) FGSREGMEAKIKSGAIQVLTAFPR--KRTCTFQPVPRSGKKRAAMTTEVLAHKIR-----AVEKPIPIRKRKNS--TT

Gorilla (ENSGGOP00000011536) FGSREGMEAKIKSGAIQVLTAFPR--KRTCTFQPVPRSGKKRAAMTTEVLAHKIR-----AVEKPIPIRKRKNS--TT

Mouse (ENSMUSP00000133279) FGSVVEGSMKAKIKS GAIQVNGPTRK RRLRFTEPVRPCGKR -----AKMKQNHN-----  
Rat (ENSRNOP0000054747) FGSVVEGSMKAKIQS GAIQVNGPTRK RRLCFSEPVRPCGKR -----AKMKEKDK-----  
Pig (ENSSSCP0000010918) FGSREGTEAKIKS GAIQVLPCHSR RRTRFTEPVRPSGKKRAAMMTEVLAHKIR -----AVEKFFIPRIKRNKN-----SM  
Whale (XP\_023987950.1) FGSRDGMEAKIKS GAIQVLAHPRH RTRTFTEPVRPSGKKRAAMMTEVLAHKIR -----AVEKFFIPRIKRNKN-----SM  
Elephant (ENSLAPP0000005179) FGSREGLEAKIKS GAIQVLPCHSR RRTRFTEPVRPSGKKRAAMMTEVLAHKIR -----AVEKFFIPRIKRNKN-----SV  
Armadillo (ENSDNOP0000014565) FGSREGTEAKIKS GAIQVLPCHSR RRTRFTEPVRPSGKKRAAMMTEVLAHKIR -----AVEKFFIPRIKRNKN-----LT  
Tasmanian devil (XP\_023360087) FGTREGLEAKIKT GAIQVLAHPRH RTRTFTEPVRPSGKKRAAMMTEVLAHKIR -----AVEKFFIPRIKRNKN-----NE  
Coelacanth (ENSLACP0000016889) FGDEAGQEAQIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Cavefish (XP\_007240334.2) FGRVVEGQAKIQT GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Platyfish (XP\_014325204.1) FGQVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tilapia (XP\_005456583.2) FGHAEQMAKIQS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Spotted gar (XP\_015202470.1) FGSVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Stickleback (ENSGACT0000001035) FGHVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tetraodon (ENSTNIT0000011701) FGQVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Fugu (XP\_011601624.1) FGQVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Zebrafish (ENSDARP00000143362) FGKVEGQAKIKT GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Amazon molly (XP\_016534180.1) FGQVEGQAKIKS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Medaka (XP\_023818916.1) FGMVEGQAKIQS GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021469805.1) FGRADGQAKIQT GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021436521.1) FGSANGQAKIQT GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014010485) IDTS-----QIKSKFIG-PVMSLADV-----  
Salmon (XP\_014070638.1) FGSADGQAKIQT GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Shark (XP\_007890120.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Human (ENSP00000425443) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Gorilla (ENSGGOP0000034525) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Mouse (ENSMUSP00000143029) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rat (ENSRNOP00000048956) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Pig (ENSSSCP00000009765) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tasmanian devil (ENSSHAT000000) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Whale (XP\_007106564.2) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Elephant (XP\_023404313.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Lizard (ENSACAP0000008438) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Chicken (ENSGALP00000017216) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Turtle (ENSPSIP00000011691) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Xenopus (ENSKETP00000030770) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Coelacanth (ENSLACP00000008576) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Amazon molly (ENSPPOP000000120) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Amazon molly (ENSPPOP000000299) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Fugu (XP\_011611191.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Medaka (XP\_004065962.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Platyfish (ENSXMAP00000005447) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Spotted gar (ENSLACP0000000155) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Stickleback (ENSGACT0000002318) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tilapia (XP\_005457058.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tetraodon (ENSTNIP00000021201) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Zebrafish (ENSDARP00000101295) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014042431.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014065146.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014050290.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021429026.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021429023.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Shark (XP\_007910136.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Human (ENSP00000386869) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Gorilla (ENSGGOP00000051172) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Armadillo (ENSDNOP00000021516) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Mouse (ENSMUSP00000087049) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tet3 (ENSRNOP00000015296) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Pig (ENSSSCP00000008852) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Elephant (XP\_010591957.2) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Whale (XP\_023989264.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tasmanian devil (ENSSHAP000000) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Chicken (ENSGALP00000059756) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Lizard (ENSACAP00000001585) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Turtle (ENSPSIP00000006549) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Xenopus (ENSKETP00000054061) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Coelacanth (ENSLACP00000009535) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Spotted gar (ENSLACP0000001981) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Amazon molly (ENSPPOP0000000021) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Cave fish (ENSAMXP00000015689) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Fugu (ENSTRUP00000036865) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Medaka (ENSORLP00000019236) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Platyfish (ENSXMAP00000000130) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Stickleback (ENSGACT0000001732) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tetraodon (ENSTNIP00000019883) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Tilapia (ENSONIP00000019943) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Zebrafish (ENSDARP00000085229) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021462005.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Rainbow trout (XP\_021477599.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014026412.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL  
Salmon (XP\_014017100.1) FGSVEAQEAKIKK GAIQVLSAFPR EVRLLLEPVRKSSKKKQDSKRVAADKQN -----NPKDKQSTPTKSKDG-----LL

DSBH-domain



Stickleback (ENSOGAC000001732)  
Tetraodon (ENSTNIP0000019883)  
Tilapia (ENSONIP0000019943)  
Zebrafish (ENSNDARP0000085229)  
Rainbow\_trout (XP\_021462005.1)  
Rainbow\_trout (XP\_021477599.1)  
Salmon (XP\_014026412.1)  
Salmon (XP\_014017100.1)

--QLQDNK-----AIKQEVKPNIKKEPFNGSMDGYRV-----  
--QAQVNOG-----RSMRDTLRRQPTCSTSAH-----  
--PQQGNKVKQT-----AIKQEVKPNIKKDFLNGSIDGYSV-----  
IQQ--GNKAIP-----KQEVKPTIKKEPVDHFQPFNGAI-----HG  
RQN--GNKAIP-----KQEVKPTIKKEPVDORFQPFHG-----  
RQH--GNKVIPT-----KQEVKPTIKKEAVDQ-----  
RQN--GNKAIP-----KQEVKPTIKKEPVDORFQPFHG-----  
RQH--GNKAIP-----KQEVKPTIKKEPMDQ-----

DSBH-domain

European\_ampioxus (Sc0000095)  
Ciona\_intestinalis (XP\_0021254)  
Lamprey (scaf\_00044)  
Lamprey (scaf\_03335)  
Shark (XP\_007897316.1)  
Lizard (XP\_020663651.1)  
Chicken (ENSGALP0000053457)  
Turtle (ENSPSIP00000006704)  
Human (ENSP00000362748)  
Gorilla (ENSGGOP00000011536)  
Mouse (ENSMUSP00000133279)  
Rat (ENSRNOP00000054747)  
Pig (ENSSSCP00000010918)  
Whale (XP\_023987950.1)  
Elephant (ENSLAFP00000005179)  
Armadillo (ENSDNOP0000014565)  
Tasmanian\_devil (XP\_023360087)  
Coelacanth (ENSLACP00000016889)  
Cavefish (XP\_007240334.2)  
Platyfish (XP\_014325204.1)  
Tilapia (XP\_005456583.2)  
Spotted\_gar (XP\_015202470.1)  
Stickleback (ENSGCAT000001035)  
Tetraodon (ENSTNIT0000011701)  
Fugu (XP\_011601624.1)  
Zebrafish (ENSDARP00000143362)  
Amazon\_molly (XP\_016534180.1)  
Medaka (XP\_023818916.1)  
Rainbow\_trout (XP\_021469805.1)  
Rainbow\_trout (XP\_021436521.1)  
Salmon (XP\_014010485)  
Salmon (XP\_014070638.1)  
Shark (XP\_007890120.1)  
Human (ENSP00000425443)  
Gorilla (ENSGGOP00000034525)  
Mouse (ENSMUSP00000143029)  
Rat (ENSRNOP00000048956)  
Pig (ENSSSCP00000009765)  
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Whale (XP\_007106564.2)  
Elephant (XP\_023404313.1)  
Lizard (ENSCAP0000008438)  
Chicken (ENSGALP00000017216)  
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Zebrafish (ENSNDARP00000101295)  
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Salmon (XP\_014065146.1)  
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Human (ENSP00000386869)  
Gorilla (ENSGGOP00000051172)  
Armadillo (ENSDNOP00000021516)  
Mouse (ENSMUSP00000087049)  
Rat (ENSRNOP00000015296)Tet3  
Pig (ENSSSCP0000008852)  
Elephant (XP\_010591957.2)  
Whale (XP\_023989264.1)  
Tasmanian\_devil (ENSSHAP000000)

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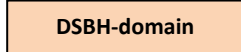




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Stickleback (ENSGACP000002318 AEPG---LQVNGYNAC-----S-MRPGHPARPYGP-----YGPNGASDPQFMDPLSRAPS-AHG-GLDYAAAVSKGNQFG-
Tilapia (XP_005457058.1) GEPG---LQVNGYNAS-----S-IRPVPMRPPYGP-----YTPNSVSDRFMDPLSRASS-AHA-GVDYTTAMSKGNRFG-
Tetraodon (ENSTNIP0000021201) GEAG---LQVNGYNTC-----G-MRPVSPMRPPFP-----YGANGASDERFIDPLSRAPS-THE-GLDYTAANKSNQLG-
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Salmon (XP_014042431.1) GESG---LQINGYSNC-----SSMRSSIHMPSPYGPSS-----YGPSGAPDAQYLDALSRPPS-AHHPGLDYAAAVSKGNQFG-
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Salmon (XP_014050290.1) GEPG---LQINGYSNC-----SSMRSGIHMPSPYGPSS-----YGPSGAPDAQYLDALSRPPS-AHHPGLDYAAAVSKGNQFG-
Rainbow_trout (XP_021429026.1) GEPG---LQINGYSNC-----SSMRSGIHMPSPYGPSS-----YGPSGAPDAQYLDALSRPPS-AHHPGLDYAAAVSKGNQFG-
Rainbow_trout (XP_021429023.1) GEPG---LQINGYSNC-----SSMRSGIHMPSPYGPSS-----YGPSGAPDAQYLDALSRPPS-AHHPGLDYAAAVSKGNQFG-
Shark (XP_007910136.1) --ASAQPRRQALGRLO-----SQREPAVATAARGVRP-----REAVEPVRGVGRLRARAVGVTEGQPEAPAFR
Human (ENSP00000386869) RSIKQEPVDPLTQAEVPRD---AGKMGKTPLESVSQNGGP-----SHLWG-QYSGGPSMSPKRTNGVGGSWGVPSSGESPA---I
Gorilla (ENSGGOP00000051172) RSIKQEPVDPLTQAEVPRD---AGKMGKTPLESVSQNGGP-----SHLWG-QYSGGPSMSPKRTNGVGGSWGVPSSGESPA---I
Armadillo (ENSNDOP0000021516) -----EVEVPRD---PGKVGKTPVEVSVQNGGP-----SHLWG-QYSGGSSVSPKRTNRVGGAWGVLPPEAPSPA---V
Mouse (ENSMUSP00000087049) RSIKQEPIDPLTQAEVPRD---SAKMSRTPLEASQNGGP-----SHLWG-QYSGGPSMSPKRTNSVGGNWGVFPGESPT---I
Rat (ENSRNOP00000015296) RSIKQEPVDPLTQAEVPRD---SGKMSRTPLEASQNGGP-----GHLWG-QYSGGPSMSPKRTNSVGGSWGVPSSGESPT---I
Pig (ENSSSCP00000008852) RSIKQEPVDPLVHVESVRE---PGKIGKTPLEASQNGGP-----NHLWG-QYSGGPSMSPKRTNSVGGSWGVPPEAPSPA---L
Elephant (XP_010591957.2) RSIKQEPVDPLAQAEVPRD---PSKMGKTPLEASQNGGP-----NHLWG-QYAGGPPSIIPKRTNSVGGSWGVPSSGESPA---I
Whale (XP_023989264.1) RSIKQEPVDPLVHVESVRE---PGKMGKMPLEASQNGGP-----NHLWG-QYSGGPSVSPKRTNSVGGSWGVPPEAPSPA---V
Tasmanian_devil (ENSSHAP000000) QVIKQEPCDRLPQAEPLPGV---PGNMKGPPIPEASQNGTK-----EHLWGGAHPGSQSASPKRTNGVGTGAWGLFAPGESP---V
Chicken (ENSGALT00000059756) RTIKQEPDPPPSIEPLNRP---AAAVPTGTLALPA-VVPV-----EQQWSPYKASSRSGSSPEQTGAADSSWSLVLG---AG
Lizard (ENSACAT0000001585) RTIKQEPADPEAVQRPAELS---CQNLN-PEMSQG-GPME-----PPAWSYKP-HRNESPERTSHAENPWSAFPSSGDSM--LGN
Turtle (ENSPSIT0000006549) RAIKQEPVDALSHIESIQRA---AVNVQNSLSLNSA-VPVASQNGEQEQQWSPYKV-NRNGSPDRSNAERSWNTFTPDNNTLPTS
Xenopus (ENSKETP00000054061) KVIKKEP-GSDPLVDSFQR---ANSVHSHSPGNHSLQAS---DLPI SYKA--NGALSSSGRTNAESPSCSMFPND-----KN
Coelacanth (ENSLACP000000015689) RVIKQEPGSEFPLDVSVHGS---ALSTRNGNCSSAATLPASSQTCEQERLWVSHKM--NGTLPSSERTVPGASVNVFGSNESTKLSNMN
Spotted_gar (ENSLOCP0000011981) KMIKQEPIDSPQYTDCCGGAAGDANPPARDITHGSIQGPSGFP---QHEQWPGYKMNGLGSESWSNRRKVSTPHDGTATPLPSP---
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Cave_fish (ENSAMXP00000015689) -VIKQEPTEVELVDNR---TDQVRS CPNTPSVTPQP-----DAWSGHKPNGLSKGWDGNLR-PGVAHSPPTPKQRQLH
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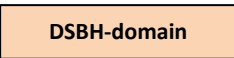
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Tasmanian_devil (ENSSHAT000000) -----HPPPHLVHDI---
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Xenopus (ENSXETP00000030770) -----PLPHSFQGHES-----
Coelacanth (ENSLACP00000008576) -----SQNPYVVQEH-----
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Medaka (XP_004065962.1) -----EYPNTYLHQN-----
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Stickleback (ENSGACP0000002318) -----GYPNPYLSRSP-----
Tilapia (XP_005457058.1) -----ECPNPYLPQNP-----
Tetraodon (ENSTNIP00000021201) -----GYPSSYLSRSP-----
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Salmon (XP_014042431.1) -----GYPNPYLSQST-----
Salmon (XP_014065146.1) -----GYPNPYLSQST-----
Salmon (XP_014050290.1) -----GYPNPYLSQST-----
Rainbow_trout (XP_021429026.1) -----GYPNPYLSQST-----
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Tilapia (ENSONIP00000019943) -----VQPPPHLARDY-----
Zebrafish (ENSDARP00000085229) -----VQPPPHLARDY-----
Rainbow_trout (XP_021462005.1) -----VQPPPHLARDY-----
Rainbow_trout (XP_021477599.1) -----VQPPPHLARDY-----
Salmon (XP_014026412.1) -----VQPPPHLARDY-----
Salmon (XP_014017100.1) -----VQPPPHLARDY-----

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←-----→

2800 2810 2820 2830 2840 2850 2860 2870 2880

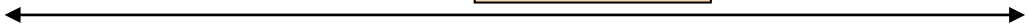
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European_ampioxus (Sc0000095) -----
Ciona_intestinalis (XP_0021254) -----
Lamprey (scaf_00044) -----
Lamprey (scaf_03335) -----
Shark (XP_007897316.1) -----
Lizard (XP_020663651.1) -----
Chicken (ENSGALP00000053457) -----
Turtle (ENSPSIP00000006704) -----
Human (ENSP00000362748) -----
Gorilla (ENSGGOP00000011536) -----
Mouse (ENSMUSP00000133279) -----
Rat (ENSRNOP00000054747) -----
Pig (ENSSSCP00000010918) -----
Whale (XP_023987950.1) -----
Elephant (ENSLAFP00000005179) -----
Armadillo (ENSDNOP00000014565) -----
Tasmanian_devil (XP_023360087) -----
Coelacanth (ENSLACP00000016889) -----
Cavefish(XP_007240334.2) -----
Platyfish (XP_014325204.1) -----
Tilapia (XP_005456583.2) -----
Spotted_gar (XP_015202470.1) -----
Stickleback (ENSGACT0000001035) -----
Tetraodon (ENSTNIT00000011701) -----
Fugu (XP_011601624.1) -----
Zebrafish (ENSDARP00000143362) -----
Amazon_molly (XP_016534180.1) -----
Medaka (XP_023818916.1) -----
Rainbow_trout (XP_021469805.1) -----
Rainbow_trout (XP_021436521.1) -----
Salmon (XP_014010485) -----
Salmon (XP_014070638.1) -----

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Shark (XP\_007890120.1) -----PANSFQIENKENELNMLRANG-----LSRLLPSINFDMA  
Human (ENSP00000425443) SAAPGMFNSSLHALHLQNKENDMLSHANG-----LSKMLPALNHDRT  
Gorilla (ENSGGOP00000034525) SAAPGMFNSSLHALHLQNKENDMLSHANG-----LSKMLPALNHDRT  
Mouse (ENSMUSP00000143029) AAASG--SSSSHAFHNKEND----NIANG-----LSRVLPGFNHDRT  
Rat (ENSRNOP00000048956) TAASGSVSSSSHAFHNKENDN-MVSHANG-----LSRVLPGFNHDRT  
Pig (ENSSSCP00000009765) SAAPGMFNSSLHALHLQNKENDMLSHANG-----FSKMLPGLNHDRT  
Tasmanian devil (ENSSHAT000000) HAVSGIFTSFHSFHLNPKEREMLSHTTNE-----LSKMLPGFNHDRT  
Whale (XP\_007106564.2) SAAPGMFNSSLHALHLNPKENDVLSHANG-----LSKTLPLGLNHDGT  
Elephant (XP\_023404313.1) RAAPGMFNSSLHALPLQNKENDVLSHANG-----LLKMLPLGLNHDGT  
Lizard (ENSACAP00000008438) QSTAGMFSGPPHSLHLQNKD---SQTNG-----LSNMLPLDLNPNRT  
Chicken (ENSGALP00000017216) HSASSMFSGPPNSLHLQNKDSEMITSHAVNG-----LSNTIPGQNHDT  
Turtle (ENSPSIP00000011691) HSASNIFSGPPHSLHLQNKDSEMTSHANG-----LSNMLPGLNHDRT  
Xenopus (ENSXETP00000030770) NMSSSLGGRAGSLPPFGKQSEMHSRTANG-----TSEMLPLGLNHDRT  
Coelacanth (ENSLACP00000008576) QSASGLFSNVNPTSHLQNOEADLNLLTING-----ISRMLPSLNHNRA  
Amazon molly (ENSPPOP000000120) HIP-----GRDSFPMQLNLDVAMPNP-----QMLPAQISSGCLNPEQ  
Amazon molly (ENSPPOP000000299) HIP-----GRDSFPMQLNLDVAMPNP-----QMLPAQISSGCLNPEQ  
Fugu (XP\_011611191.1) QVLP--GQDPFHMQIKTEIGIPHPNS--HPLSSQIGGGCLNSDTK  
Medaka (XP\_004065962.1) HILPS--GLDPLHTQVKTEMGIPDP-----QMLSAQLRGRCLNPDQ  
Platyfish (ENSXMAP00000005447) HIP-----GRDSFPMQLNLDVAIPNP-----QMLPAQISSGCLNPEQ  
Spotted gar (ENSLOCP000000155) SVFSS--VHDSFHMQHKTEVNLHGPNG--IARVLTPLGNECPNLSQL  
Stickleback (ENSGACP0000002318) QIFAP--GQDPFHMQIKTEAGTTPRP-----QVLSAPLGGGCGYNPEAQ  
Tilapia (XP\_005457058.1) QMLHP--GQDPFHLQIKAEIMGMPG-----QMLSAQSGSGLNPEQ  
Tetraodon (ENSTNIP00000021201) QILPP--GQDSFHMQIKTEMGVPH-----LSAQIGGGCLTSDTK  
Zebrafish (ENSDARP000000101295) HMFSP--NLNTLSMQSHKDLGISMHEANGISQGFPPGKBCFNPNQ  
Salmon (XP\_014042431.1) KMFPFGSPQDFPCMQVKTEMLGQS-----PCMTPTQP  
Salmon (XP\_014065146.1) KMFPFGSPQDFPCMQVKTEMLGQS-----PCMTPTQP  
Salmon (XP\_014050290.1) KMFPFGSPQDFPCMQVKTEMLGQS-----PCMTPTQP  
Rainbow trout (XP\_021429026.1) KMFPFGSPQDFPCMQVKTEMLGQS-----PCMTPTQP  
Rainbow trout (XP\_021429023.1) KMFPFGSPQDFPCMQVKTEMLGQSP-----ISCQSNFPCMTPTQP  
Shark (XP\_007910136.1) ARHVVHTSPPPAAAAAAPP--PPAHRP-----QEKPWDLFAFGK  
Human (ENSP00000386869) STS-ALAGPSSLTEKPWAL--GAGDFNSALKGS---PGFQDKLWNPVKGEE  
Gorilla (ENSGGOP00000051172) STS-ALAGPSSLTEKPWAL--GAGDFNSALKGS---PGFQDKLWNPVKGEE  
Armadillo (ENSDNOP00000021516) ATATSLTAPGLTEKPGV--VAGDFNSALKGG---PGFQDKLWNPVKGEE  
Mouse (ENSMUSP000000087049) GTS-ALTGPSLTKPWGM--GTGDFNPALKGG---PGFQDKLWNPVKVEE  
Rat (ENSRNOP00000015296)Tet3 GTS-ALSGPSLTKPWGM--GAGDFNSALKGG---PGFQDKLWNPVKVEE  
Pig (ENSSSCP00000008852) TPT-ALSGPSLTKSWGV--GAGDLTSALKGG---PGFQDKLWSPKGG  
Elephant (XP\_010591957.2) SAS-ALAGPGLTEKPWSI--GAGDFNSALKGS---AGYQDKLWSPKGG  
Whale (XP\_023989264.1) NTS-ALAGPSSLTEKPWAV--GAGDFNSALKGG---PRFQDKLWSPKGG  
Tasmanian devil (ENSSHAP000000) STS-TLNGPSLAEPKPGV--AP-DFGPALKGA---PGYPEKLWGPVKGE  
Chicken (ENSGALT00000059756) ETVLGGAGTTLRDKGWEL--GPLGGSALPEL---PVFSEBPWGSKAAE  
Lizard (ENSACAT0000001585) PNSVFAAPGS-DLQEKRWGF--GQLDLSKGGG---RTLGD-DLWGPVKADS  
Turtle (ENSPSIT00000006549) SPSALPSSANSNLOEKPWHL--PQLNYSSTLKN---SGFQDELWNSVKVDE  
Xenopus (ENSXETP00000054061) SSAALPSSAS--TQDKNNG--RQVSLNQGMKES---ALFQEKLWNSVAASD  
Coelacanth (ENSLACP00000009535) TPSPLPGSANGNLGAPSWNL--ASMMLTAAIKTN---SELQDKLWNSVKINE  
Spotted gar (ENSLOCP0000001981) PGEGCCPSPNPQKSWNS---NGYNANLRA--TPVGGFPDKLWC--KDGE  
Amazon molly (ENSPPOP000000021) RHWASAPSPQPNPWGF--SPAAYSPLKHS-NPAGAYPDKIWS--KTGE  
Cave fish (ENSAMXP00000015689) STPHHWESEVPSPQKAWGP-IGSAGFGPGLRQGTVPVGAFFDKMLS--QTVE  
Fugu (ENSTRUP00000036865) -----RPQNAWAM--GPVAYSPLKHS-NPAGACPDKIWS--KTGE  
Medaka (ENSORLP00000019236) ASLQGSTRHVSPHPGTPLQPTSHRSRLTPQPLQGLPLRHLSPASSPQNAWAM--GPAPCSPGLKHS-NPAGAYPDKIWS--KTGE  
Platyfish (ENSXMAT0000000130) GNLY-----RGAIRHSASYPGTQP-----VTSHSGPLKHS-NPAGAYPDKIWS--KTGE  
Stickleback (ENSGACP0000001732) GTPRHWASAPSPQPNWAM--GPAAYSPLKHS-NPAGAYPDKIWS--KTGE  
Tetraodon (ENSTNIP00000019883) GTLMHWASAPSPQPNWAV--GPLAYSPALKHS-NPAGACPDKIWS--KTGE  
Tilapia (ENSONIP00000019943) GTPRHWSVSPASPPQTGM--GP--YSPGMKHS-NPAGAYPDKIWS--KTGE  
Zebrafish (ENSDARP000000085229) STPRHWASAPSPQKAWGP-YGPMYAGVIRQGNPAGAYPDNMLS--QAGV  
Rainbow trout (XP\_021462005.1) GTPHHWSDSPSPQKAWPMSMVPAGYSP-----SPVGGFPDKMWS--KAGE  
Rainbow trout (XP\_021477599.1) GTPRHWDSPASPPQKAWPMDMVPAGYCP-----SPARGFPDKICS--KAGE  
Salmon (XP\_014026412.1) GTPRHWDSPDSSPQKAWPMGMVPAGYSP-----SPAGGFPDKMWS--KAGE  
Salmon (XP\_014017100.1) GTPRHWDSPASPPQKAWPMGMVPAGYCP-----SPARGFPDKICS--KAGE

DSBH-domain



2890      2900      2910      2920      2930      2940      2950      2960      2970

European ampioxus (Sc0000095)  
Ciona intestinalis (XP\_0021254)  
Lamprey (scaf\_00044)  
Lamprey (scaf\_03335)  
Shark (XP\_007897316.1)  
Lizard (XP\_020663651.1)  
Chicken (ENSGALP00000053457)  
Turtle (ENSPSIP00000006704)  
Human (ENSP00000362748)  
Gorilla (ENSGGOP00000011536)  
Mouse (ENSMUSP00000133279)  
Rat (ENSRNOP00000054747)  
Pig (ENSSSCP00000010918)  
Whale (XP\_023987950.1)  
Elephant (ENSLAFP00000005179)  
Armadillo (ENSDNOP00000014565)  
Tasmanian devil (XP\_023360087)  
Coelacanth (ENSLACP00000016889)  
Cavefish (XP\_007240334.2)  
Platyfish (XP\_014325204.1)  
Tilapia (XP\_005456583.2)  
Spotted gar (XP\_015202470.1)  
Stickleback (ENSGACT0000001035)



Elephant (ENSLAFP00000005179) -----KLPHIDIEWSDSEHIFLDANIGGVAIPAHGSLIECARREIHATTPVEHPPNRRHPPTISLVFYCHQNLNKPQHGF  
Armadillo (ENSNDOP00000014565) -----KLPHIDIEWSDSEHIFLDANIGGVAIPAHGSLIECARREIHATTPVEHPPNRRHPPTISLVFYCHQNLNKPQHGF  
Tasmanian devil (XP\_023360087) -----TESADSEKSEKSEEMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPIRKPNRRHPPTISLVFYCHQNLNKPQHGF  
Coelacanth (ENSLACP00000016889) -----APMGNGTLP-EEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Cavefish (XP\_007240334.2) -----PEEVKAE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Platyfish (XP\_014325204.1) -----PQQAQKE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tilapia (XP\_005456583.2) -----PEEVKQE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPVLPKPNRRHPPTISLVFYCHQNLNKPQHGF  
Spotted gar (XP\_015202470.1) -----APEAKPG--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Stickleback (ENSGACT0000001035) -----AEVVKQE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tetraodon (ENSTNIT00000011701) -----PEGVKQEVVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Fugu (XP\_011601624.1) -----AEGVKQEVVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Zebrafish (ENSDARP00000143362) -----PEVAKAE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Amazon molly (XP\_016534180.1) -----PQQAQKE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Medaka (XP\_023818916.1) -----AELLKQE--EVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021469805.1) -----PEEVKQEQEVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021436521.1) -----PKEVKQEQEVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014010485) -----PKEVKQEQEVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014070638.1) -----PKEVKQEQEVEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Shark (XP\_007890120.1) -----PEIISMPQNNGVGAPEEP0EIIWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Human (ENSP00000425443) -----QEKQPLALVQGVASGAEDNDEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Gorilla (ENSGG0P00000034525) -----QEKQPLALVQGVASGAEDNDEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Mouse (ENSMUSP00000143029) -----EKQPE--VSGQDAAAQVEIEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rat (ENSRNOP00000048956) -----EKQPG--VSGQDASVEDIEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Pig (ENSSSCP00000009765) -----QEKQ--LSAEDNDEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tasmanian devil (ENSSHA000000) -----LEKQLHAPIQGLSTPEK-DDVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Whale (XP\_007106564.2) -----QEKP-----PCAEDNDEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Elephant (XP\_023404313.1) -----QEKQPLVPGQGVASGAEDNDEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Lizard (ENSACAP00000008438) -----LEKQPE--VSGQDAAAQVEIEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Chicken (ENSGALP00000017216) -----EKQPE--VSGQDAAAQVEIEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Turtle (ENSPSIP00000011691) -----EKQPE--VSGQDAAAQVEIEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Xenopus (ENSXETP00000030770) -----KLPYQ-----LPPVPEEPAEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Coelacanth (ENSLACP00000008576) -----QGNVSQLPIQN-HEDAQEPAEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Amazon molly (ENSPFOP000000102) -----IKSEP--GAPQTPTTK-KPEWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Amazon molly (ENSPFOP0000000299) -----IKSEP--GAPQTPTTK-KPEWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Fugu (XP\_011611191.1) -----IKQEP--GMPQTPTTPQ-KPELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Medaka (XP\_004065962.1) -----IKQEP--GMPQTPTTPQ-KPEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Platyfish (ENSXMAP00000005447) -----IKSEP--GTPQTPTTK-KPEWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Spotted gar (ENSLOC0000000155) -----LSEPEPGAQNKESN--EDVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Stickleback (ENSGACP0000002318) -----IKQEP--GTPQTPTTPQ-KPEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tilapia (XP\_005457058.1) -----IKLEP--GTPQTPTTPQ-KPELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tetraodon (ENSTNIP00000021201) -----IKQEP--GMPQTPTTPQ-KPELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Zebrafish (ENSDARP00000101295) -----NPTQLP-----QVSEKKEEDVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014042431.1) -----MIKQEP--GPPMPTTPK-KPPAMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014065146.1) -----MIKQEP--GPPMPTTPK-KPPAMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014050290.1) -----MIKQEP--GPPMPTTPK-KPPAMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021429026.1) -----MIKQEP--GPPMPTTPK-KPPAMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021429023.1) -----MIKQEP--GPPMPTTPK-KPPAMWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Shark (XP\_007910136.1) -----EEEEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Human (ENSP00000386869) -----AEEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Gorilla (ENSGG0P00000051172) -----AEEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Armadillo (ENSNDOP00000021516) -----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Mouse (ENSUSP000000087049) -----VEDEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rat (ENSRNOP00000015296) -----VEDEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tet3 Pig (ENSSSCP00000008852) -----AVEEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Elephant (XP\_010591957.2) -----AEEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Whale (XP\_023989264.1) -----SGVGG-----AEEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tasmanian devil (ENSSHA000000) -----GGGGSGVGPKGNSAVEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Chicken (ENSGALP000000059756) -----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Lizard (ENSACAP00000001585) -----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Turtle (ENSPSIT00000006549) -----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Xenopus (ENSXETP00000054061) -----EDDEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Coelacanth (ENSLACP00000009535) -----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Spotted gar (ENSLOC00000001981) -----MEQQS-----QVKEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Amazon molly (ENSPFOP000000021) -----SFKH-----RE-EEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Cave fish (ENSAMXP00000015689) -----RDA-----EEEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Fugu (ENSTRUP00000036865) -----STKG-----LEDEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Medaka (ENSORLP00000019236) -----SIQH-----REDDEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Platyfish (ENSXMAP0000000130) -----STKG-----KEDEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Stickleback (ENSGCAP00000001732) -----STKG-----REEVDEEELWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tetraodon (ENSTNIP00000019883) -----STKN-----LEDKKEVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Tilapia (ENSXNIP00000019943) -----RDP-----EEDVWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Zebrafish (ENSDARP00000085229) -----RNL-----EEEE-EDWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021462005.1) -----RDLE-----EEEE-EDWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Rainbow trout (XP\_021477599.1) -----HNLE-----DEEE-RWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014026412.1) -----CDL-----DEEE-QWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF  
Salmon (XP\_014017100.1) -----CDL-----DEEE-QWSDSEHNFDDNIGGVAIPAHGSLIECARREIHATTPILKPNRRHPPTISLVFYCHQNLNKPQHGF

Fe binding 2-OG binding 5mC binding

3070 3080 3090 3100 3110 3120 3130 3140 3150

European ampioxus (Sc0000095) .....  
Ciona intestinalis (XP\_0021254) **A**E**V**G**L**K**E**A**K**R**N****O**V**K**A**E**K**A****O**K**E**K**E**R**E**R**E**E**K**R**D**E**E**K**R**V**I**N**E**A**S**L**I**A**R**L**N**P**H****K**A**P**N**O****P**S**T**L**P**Q**H**P**Y**Q**P**D**G**Y**P**Q**M**P**Q**V**K**R**W**P**N**P  
Lamprey (scaf\_00044) .....  
Lamprey (scaf\_03335) .....  
Shark (XP\_007897316.1) **A**L**W**P**A**K**L****T**K**M**A**E**R**A**K**E****K**E**V**N**H**E**H**N**L**T**K**P-----**N**K**F**K**R**A**V**P**Q**P**P**E**L**L**Q**.....



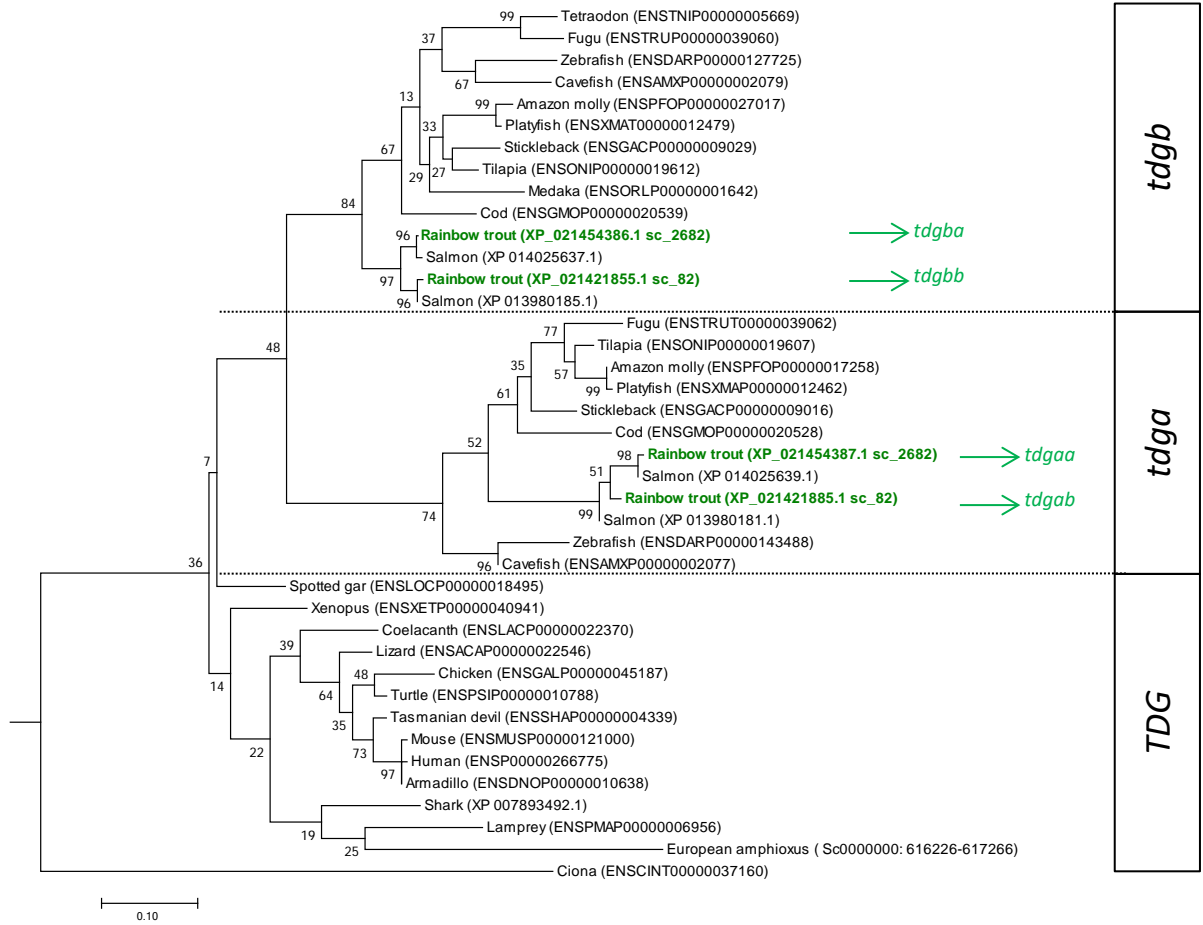


European ampioxus (Sc0000095) -----  
Ciona intestinalis (XP\_0021254) PVSRTFFPIEGELPRVMTSPRNPRLMTSPTNQAPHPTGGIPTSSEYPIPOYCHPMPQRT  
Lamprey (scaf\_00044) -----  
Lamprey (scaf\_03335) -----  
Shark (XP\_007897316.1) -----EDNELVRRVTRKALSTPRDSVITVSSYALTQVITGPPYSRWI  
Lizard (XP\_020663651.1) -----EDNEFNQIPSRRALVTVDNIIITVSTYALTTRVAGPYNHWA  
Chicken (ENSGALP00000053457) -----EDNEFNQIPSRRALVTVDNIIITVSSYALTTRVAGPYNHWA  
Turtle (ENSPSIP00000006704) -----EENEFNQIPSRRALVTVDNIIITVSSYALTTRVAGPYNHWA  
Human (ENSP00000362748) -----EVNELNQIPSHKALTLTHDNVTVSSYALTTRVAGPYNHVV  
Gorilla (ENSGGOP00000011536) -----EVNELNQIPSHKALTLTHDNVTVSSYALTTRVAGPYNHVV  
Mouse (ENSMUSP00000133279) -----EANLSHQIPSRVASTLTRDNVTVSSYSLTTRVAGPYNRWV  
Rat (ENSRNOP00000054747) -----ETNLSYQIPSRVASTLTSNDVTVSSYALTTRVAGPYNRWV  
Pig (ENSSSCP00000010918) -----EINEFSQIPSHKALTLTHDNVTVSSYALTTRVAGPYNHVV  
Whale (XP\_023987950.1) -----EVNEFNQIPSHKALTLTHDNVTVSSYALTTRVAGPYNHVV  
Elephant (ENSLAFP00000005179) -----EVNELNQIPSHKALTLTHDNVTVSSYALTTRVAGPYNRWV  
Armadillo (ENSDNOP00000014565) -----AVNELNQIPSHKALTLTHDNVTVSSYALTTRVAGPYNHVV  
Tasmanian devil (XP\_023360087) -----EQNELNQIPSRKALVTVDNIIITVSSYALTQVAGPYNHVV  
Coelacanth (ENSLACP00000016889) -----KDNELIKIPTRKSLTATRDVITVSSYALTQVITGPPYNRWV  
Cavefish (XP\_007240334.2) -----DEREKLOVETRQSLTATRDGLVTSAPYSLTRVITGPPYNRWV  
Platyfish (XP\_014325204.1) -----ETRRVMNVETRQAFAPTGGAITVSSYALTTRVITGPPYNRWS  
Tilapia (XP\_005456583.2) -----EMR-IMNVETRKAWTLPRDEVITASPYALTQVITGPPYNRWS  
Spotted gar (XP\_015202470.1) -----EERELLOVETRQALAITRDGVITVSSYALTQVITGPPYNRWV  
Stickleback (ENSGACT0000001035) -----TRRIMNVETRQARTLQRDGVVITASPYALTQVITGPPYNRWA  
Tetraodon (ENSTNIT00000011701) -----DE-RTTHVETRQAWTFPRDGVITVSSYALTQVITGPPYNRWT  
Fugu (XP\_011601624.1) -----EERELLOVETRQAWTFPRDGVITVSSYALTQVITGPPYNRWT  
Zebrafish (ENSDARP00000143362) -----DERHKFQVETRQSLTVSRDSLVMSSAPYALTTRVITGPPYNRWT  
Amazon molly (XP\_016534180.1) -----EARRVMNVETRQAFAPTGGVITVSSYALTTRVITGPPYNRWS  
Medaka (XP\_023818916.1) -----ATRRIMNVETRQAWTLPRDGVITVSSYALTQVITGPPYNRWT  
Rainbow trout (XP\_021469805.1) -----EKKGVLVKVEVTRQAVTVARDGVVITVSSYALTQVITGPPYNRWT  
Rainbow trout (XP\_021436521.1) -----EKKGVLTVEVTRKAVTVPRDGVVITVSSYALTQVITGPPYNRWT  
-----  
Salmon (XP\_014010485) -----  
Salmon (XP\_014070638.1) -----EKKGVLTVEVTRKAVTVPRDGVVITVSSYALTQVITGPPYNRWT  
Shark (XP\_007890120.1) -----QLRFIKTLTQRTMT-FTTNSVTTASPYALTTRVITGPPYNRWI  
Human (ENSP00000425443) -----YLRFIKSLAERTMS-VTTDSTVITVSSYALTTRVITGPPYNRYI  
Gorilla (ENSGGOP00000034525) -----YLRFIKSLAERTMS-VTTDSTVITVSSYALTTRVITGPPYNRYI  
Mouse (ENSMUSP00000143029) -----YLRFIQSLAENTGS-VTTDSTVITVSSYALTQVITGPPYNFV  
Rat (ENSRNOP00000048956) -----YLRFIHSLAENTVS-MTTDSTVITVSSYALTQVITGPPYNFV  
Pig (ENSSSCP00000009765) -----YLRFIRSLAERTMS-VTTDSTVITVSSYALTTRVITGPPYNRYV  
Tasmanian devil (ENSSHAT000000) -----YLRFIKSLTQRTMS-ITTNSVITVSSYALTTRVITGPPYNRYV  
Whale (XP\_007106564.2) -----YLRFIKSLAERTMS-VTTDSTVITVSSYALTTRVITGPPYNRYI  
Elephant (XP\_023404313.1) -----YLRFIKSLTERMS-VTTDSTVITVSSYALTTRVITGPPYNRYI  
Lizard (ENSACAP00000008438) -----YMRFIRSLAQRMS-LTTNSVITVSSYALTTRVITGPPYNRYI  
Chicken (ENSGALP00000017216) -----YLRFIKSLAQRMLS-VTTDSTVITVSSYALTTRVITGPPYNRYI  
Turtle (ENSPSIP00000011691) -----YMRFVKSQAQRMS-VTTNSVITVSSYALTTRVITGPPYNRYI  
Xenopus (ENSXETP00000030770) -----YLRFIKSLTQRTMS-ITTDSQVITVSSYALTTRVITGPPYNRYI  
Coelacanth (ENSLACP00000008576) -----YLRFVKSQAQRMS-ITTNSVITVSSYALTTRVITGPPYNRYI  
Amazon molly (ENSPFOP000000120) -----YKRFIRALMEGSSSFTTNTHVMTTPYASTKVTGPPYSQFV  
Amazon molly (ENSPFOP0000000299) -----YKRFIRALMEGSSSFTTNTHVMTTPYASTKVTGPPYSQFV  
Fugu (XP\_011611191.1) -----YKRFIKALAEGLSAS-CTTNTVNTAPYASTKVTGPPYSHFV  
Medaka (XP\_004065962.1) -----YKRFIKALMEGSLSS-CTTNTVNTSEYASTKVTGPPYSRFA  
Platyfish (ENSMAP00000005447) -----YKRFIKALMEGSSSFTTNTHVITTPYASTKVTGPPYSQFV  
Spotted gar (ENSLQCP000000155) -----YKRFIQTLTQRTVS-CTTNSIVNTSEYASTKVTGPPYNRYI  
Stickleback (ENSGACP00000002318) -----YKRFIQALMEGSSS-CTTNSHVNTTPYASTKVTGPPYSQFA  
Tilapia (XP\_005457058.1) -----YKRYIKALMEGSLSS-CTTNTYVSTSEYASTKVTGPPYSQLA  
Tetraodon (ENSTNIP00000021201) -----YKRFIKALAEGLSAS-CTTNTVNTAPYASTKVTGPPYSHFV  
Zebrafish (ENSDARP00000101295) -----YKQFLMLTERTSMS-CTTNTYVSTSEYASTKVTGPPYNNFM  
Salmon (XP\_014042431.1) -----YKRFIQTLMERMS-CTTNTYVNTSEYASTKVTGPPYSRFI  
Salmon (XP\_014065146.1) -----YKRFIQTLMERMS-CTTNTYVNTSEYASTKVTGPPYSRFI  
Salmon (XP\_014050290.1) -----YKRFIQTLMERMS-CTTNTYVNTSEYASTKVTGPPYSRFI  
Rainbow trout (XP\_021429026.1) -----YKRFIQTLMERMS-CTTNTYVNTSEYASTKVTGPPYSRFI  
Rainbow trout (XP\_021429023.1) -----YKRFIQTLMERMS-CTTNTYVNTSEYASTKVTGPPYSRFI  
Shark (XP\_007910136.1) -----REWLKILLQKNKPPWSSTGTEEKRLTNTWQESKALLFQPTPGAQGVKS  
Human (ENSP00000386869) -----KE-KKGVVETRQALAVPTDSAVTVSSYAMTKVTGPPYSRWI  
Gorilla (ENSGGOP00000051172) -----KE-KKGVVETRQALAVPTDSAVTVSSYAMTKVTGPPYSRWI  
Armadillo (ENSDNOP00000021516) -----KE-RRGAVETRQALAVPTDSAVTVSSYAMTKVTGPPYSRWI  
Mouse (ENSMUSP000000087049) -----KE-KKGAPETRQALAMPDTSAVTVSSYAMTKVTGPPYSRWI  
Rat (ENSRNOP00000015296) Tet3 -----KE-KKGAPETRQALAMPDTSAVTVSSYAMTKVTGPPYSRWI  
Pig (ENSSSCP00000008852) -----KE-KKGLVETRQALAMPDTSAVTVSSYAMTKVTGPPYSRWI  
Elephant (XP\_010591957.2) -----KE-KKGAPETRQALAMPDTSAVTVSSYAMTKVTGPPYSRWI  
Whale (XP\_023989264.1) -----KE-KKGLVETRQALAVPTDSAVTVSSYAMTKVTGPPYSRWI  
Tasmanian devil (ENSSHAP000000) -----EE-QKSPIPTR-----HTKVTGPPYSRWI  
Chicken (ENSGALP00000059756) -----KE-RRNAVETRQAVAIPTNSAITVSSYAMTKVTGPPYSRWV  
Lizard (ENSACAT0000001585) -----KE-RRGAVETREALVTPHSAITASAYASTKVTGPPYSRWI  
Turtle (ENSPSIT00000006549) -----KE-KKDSVETRQAVAIPTNSAITVSSYAMTKTN--CWEWL  
Xenopus (ENSXETP00000054061) -----VE-KKDYETPRQAATILTDSATTSFSAATKVTGPPYSRFI  
Coelacanth (ENSLACP00000009535) -----KE-KKDIIPRQALALTTNSVITVSSYAMTKVTGPPYSRWI  
Spotted gar (ENSLQCP0000001981) -----S-ASGQSQSKD-KKEGHTRHAPTHTNSLTVSSYALTQVITGPPYSRWV  
Amazon molly (ENSPFOP0000000021) -----QLKD-KKDGVPVTRLSHFTYTTSMVTVSSYALTTRVITGPPYSHFV  
Cave fish (ENSAMXP00000015689) -----PTKD-RRGVVTRMAPQHTTTMVTLSYASTQVITGPPYSRFM  
Fugu (ENSTRUP00000036865) -----QSKD-KREGVTRLAPVHTTSTVTVSSYALTTRITGPPYSHFV  
Medaka (ENSORLP00000019236) -----  
Platyfish (ENSMAT0000000130) -----QSKD-KKDGVPVTRLSHFTYTTSMVTVSSYALTTRVITGPPYSHFV  
Stickleback (ENSGACP0000001732) -----QSKD-KREGVTRLAPVHTTSTVTVSSYALTTRITGPPYSHFV  
Tetraodon (ENSTNIP00000019883) -----QSKD-KREGVTRLAPVHTTSTVTVSSYALTTRITGPPYSHFV  
Tilapia (ENSONIP00000019943) -----QSKD-KREGVTRLAPVHTTSTVTVSSYALTTRITGPPYSHFV  
Zebrafish (ENSDARP00000085229) -----QTKD-KREGVTRMAPQHTTTMVTLSYASTQVITGPPYSRFV  
Rainbow trout (XP\_021462005.1) -----QTTD-KREGVTRLASTRHHTTSTVTVSSYALTTRITGPPYSHFV  
Rainbow trout (XP\_021477599.1) -----QTTGPGVMGMVTRLASTRHHTTSTVTVSSYALTTRITGPPYSHFV

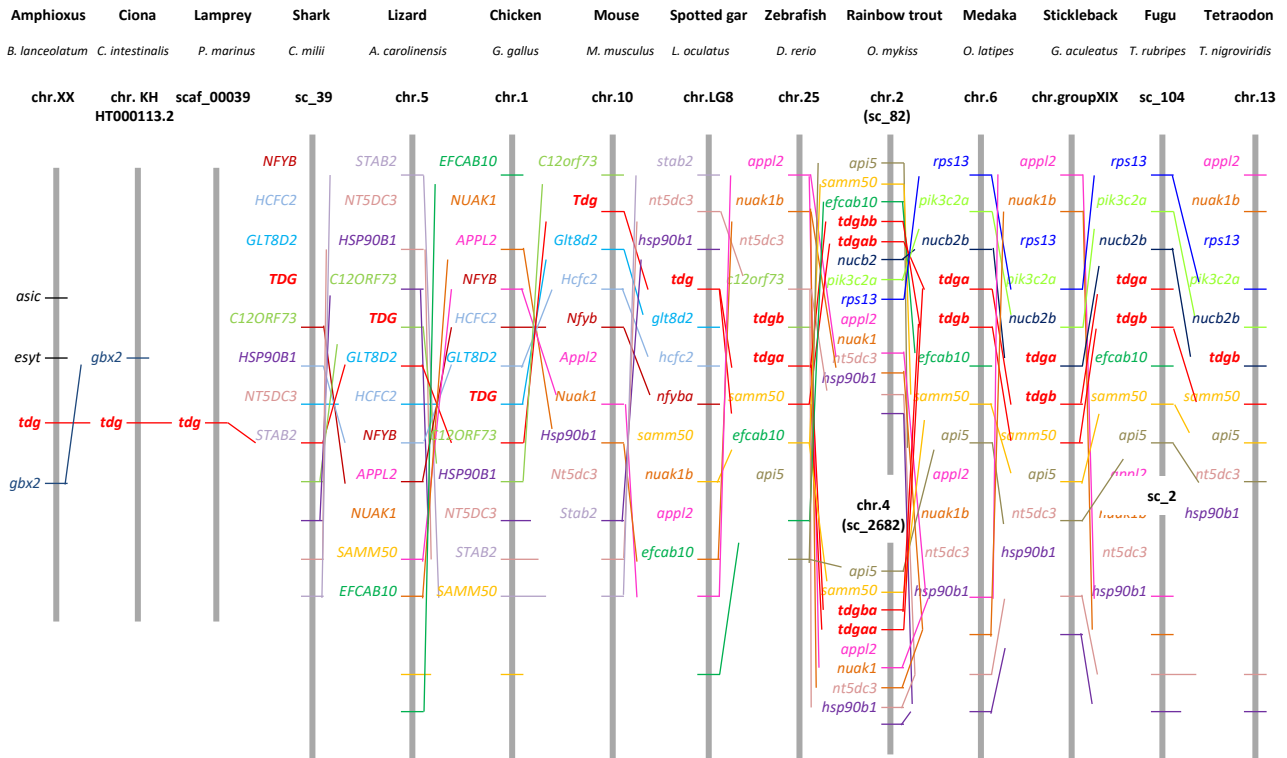
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Salmon (XP_014026412.1) -----QTTD-KREGPVTRLAPTRHHTTSTITVSPYARTTLLTGPYSHFV
Salmon (XP_014017100.1) -----QTTEGPPVMGTVTRLAPTHHTTSTITVSPYARTTLLTGPYSHFV
```

**Supplemental Fig.S7 Tet protein sequences alignment.** All the protein sequences were aligned with the MUSCLE method in MEGA software. Conserved domains were noted above. # Zn binding sites; red box, Fe binding sides; yellow box, 2-OG binding sites; blue box, 5mC binding sites.

**A**



**B**



**Supplementary Fig. S8 *In silico* analysis of *tdg* in chordates.** (A) Phylogenetic of *tdg* genes. The phylogenetic trees were built using the Maximum Likelihood method based on the WAG model in MEGA7. The tree with the highest log likelihood (-5287.94) is shown. A discrete Gamma distribution was used to model evolutionary rate differences among sites (5 categories (+G, parameter = 1.1866)). The reliability of the inferred trees was estimated by the bootstrap method with 500 replications. All accession numbers are specified in parentheses. (B) Syntenic analysis of *dnmt1* genes. Conserved synteny around the *tdg* genes in chordates. Data were collected with Genomicus software version 01.01, and *tdg* genes in rainbow trout were annotated by ourselves according to our phylogenetic analysis following ZFIN nomenclature guidelines. chr., chromosome; sc., scaffold.

MUG domain

European amphioxus\_ (Sc0000000) Lamprey (ENSPMAP0000006956) Ciona (ENSCINT0000037160) Shark (XP\_007893492.1) Coelacanth (ENSLACP0000022370) Human (ENSP0000266775) Mouse (ENSMUSP00000121000) Armadillo (ENSDNOP0000010638) Tasmanian devil (ENSSHAP000000) Lizard (ENSACAP0000022546) Chicken (ENSGALP0000045187) Turtle (ENSPSIP0000010788) Xenopus (ENSXETP0000040941) Spotted gar (ENSLOCP000001849) Fugu (ENSTRUT0000039062) Tilapia (ENSONIP0000019607) Amazon molly (ENSPPOP00000172) Platyfish (ENSXMAP0000012462) Stickleback (ENSGACP000000901) Cod (ENSGMOP0000020528) Cavefish (ENSAMXP000002077) Zebrafish (ENSDARP00000143488) Salmon (XP\_014025639.1) Trout (XP\_021454387.1 sc\_2682) Salmon (XP\_013980181.1) Trout (XP\_021421885.1 sc\_82) Tetraodon (ENSTNIP000005669) Fugu (ENSTRUP0000039060) Stickleback (ENSGACP000000902) Tilapia (ENSONIP0000019612) Platyfish (ENSXMAT0000012479) Amazon molly (ENSPPOP00000270) Cod (ENSGMOP0000020539) Cavefish (ENSAMXP000002079) Medaka (ENSORLP000001642) Zebrafish (ENSDARP0000012725) Salmon (XP\_014025637.1) Trout (XP\_021454386.1 sc\_2682) Salmon (XP\_013980185.1) Trout (XP\_021421855.1 sc\_82)

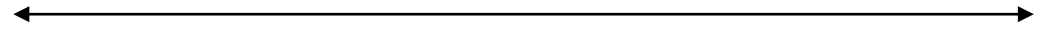
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Trout (XP\_021454386.1 sc\_2682)  
 Salmon (XP\_013980185.1)  
 Trout (XP\_021421855.1 sc\_82)

**EDRV--MTELSVHQELP VHQLDFH**-----**HDQPVDTSQA**  
**EDRV--MTELSVHQELP VHQLDFH**-----**HDQPVDTSQA**  
**EDRV--MTELSVHQELP VHQLDFH**-----**HDQPVDTSQA**

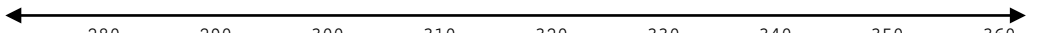
**MUG domain**



	190	200	210	220	230	240	250	260	270	
European amphioxus (Sc0000000)	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
Lamprey (ENSPMAP00000006956)	K	E	E	K	R	P	P	R	G	P
Ciona (ENSCINT00000037160)	S	S	P	V	V	V	K	K	K	R
Shark (XP_007893492.1)	R	G	R	P	P	K	S	Q	K	S
Coelacanth (ENSLACP00000022370)	V	E	P	K	K	P	P	P	P	K
Human (ENSP00000266775)	V	E	P	K	K	P	P	P	P	K
Mouse (ENSMUSP00000121000)	V	E	P	K	K	P	P	P	P	K
Armadillo (ENSDNOP00000010638)	A	E	P	P	K	K	P	P	P	K
Tasmanian devil (ENSSHAP0000000)	V	E	P	K	K	P	P	P	P	K
Lizard (ENSACAP00000022546)	A	A	K	V	P	K	P	P	P	K
Chicken (ENSGALP00000045187)	A	A	K	V	P	K	P	P	P	K
Turtle (ENSPSIP00000010788)	S	T	E	P	K	P	P	P	P	K
Xenopus (ENSXETP00000040941)	S	E	P	K	P	K	P	P	P	K
Spotted gar (ENSLOCP0000001849)	P	G	P	K	P	K	P	P	P	K
Fugu (ENSTRUT00000039062)	P	G	P	K	P	K	P	P	P	K
Tilapia (ENSONIP00000019607)	P	G	P	K	P	K	P	P	P	K
Amazon molly (ENSPPOP000000172)	P	G	P	K	P	K	P	P	P	K
Platyfish (ENSXMAP00000012462)	P	G	P	K	P	K	P	P	P	K
Stickleback (ENSGACP0000000901)	P	G	P	K	P	K	P	P	P	K
Cod (ENSGMOP00000020528)	P	G	P	K	P	K	P	P	P	K
Cavefish (ENSAMXP0000002077)	P	G	P	K	P	K	P	P	P	K
Zebrafish (ENSARP00000143488)	P	G	P	K	P	K	P	P	P	K
Trout (XP_021454386.1 sc_2682)	P	G	P	K	P	K	P	P	P	K
Salmon (XP_013980185.1)	P	G	P	K	P	K	P	P	P	K
Trout (XP_021421855.1 sc_82)	P	G	P	K	P	K	P	P	P	K
Tetraodon (ENSTNIP00000005669)	P	G	P	K	P	K	P	P	P	K
Fugu (ENSTRUP00000039060)	P	G	P	K	P	K	P	P	P	K
Stickleback (ENSGACP0000000902)	P	G	P	K	P	K	P	P	P	K
Tilapia (ENSONIP00000019612)	P	G	P	K	P	K	P	P	P	K
Platyfish (ENSXMAT00000012479)	P	G	P	K	P	K	P	P	P	K
Amazon molly (ENSPPOP0000000270)	P	G	P	K	P	K	P	P	P	K
Cod (ENSGMOP00000020539)	P	G	P	K	P	K	P	P	P	K
Cavefish (ENSAMXP00000002079)	P	G	P	K	P	K	P	P	P	K
Medaka (ENSORLP0000001642)	P	G	P	K	P	K	P	P	P	K
Zebrafish (ENSARP00000012725)	P	G	P	K	P	K	P	P	P	K
Salmon (XP_014025639.1)	P	G	P	K	P	K	P	P	P	K
Trout (XP_021454386.1 sc_2682)	P	G	P	K	P	K	P	P	P	K
Salmon (XP_013980185.1)	P	G	P	K	P	K	P	P	P	K
Trout (XP_021421855.1 sc_82)	P	G	P	K	P	K	P	P	P	K

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**MUG domain**



	280	290	300	310	320	330	340	350	360	
European amphioxus (Sc0000000)	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....	..... ..... ..... ..... ..... ..... ..... ..... ..... .....
Lamprey (ENSPMAP00000006956)	P	G	N	H	F	W	K	C	L	F
Ciona (ENSCINT00000037160)	P	G	N	H	F	W	K	C	L	F
Shark (XP_007893492.1)	P	G	N	H	F	W	K	C	L	F
Coelacanth (ENSLACP00000022370)	P	G	N	H	F	W	K	C	L	F
Human (ENSP00000266775)	P	G	N	H	F	W	K	C	L	F
Mouse (ENSMUSP00000121000)	P	G	N	H	F	W	K	C	L	F
Armadillo (ENSDNOP00000010638)	P	G	N	H	F	W	K	C	L	F
Tasmanian devil (ENSSHAP0000000)	P	G	N	H	F	W	K	C	L	F
Lizard (ENSACAP00000022546)	P	G	N	H	F	W	K	C	L	F
Chicken (ENSGALP00000045187)	P	G	N	H	F	W	K	C	L	F
Turtle (ENSPSIP00000010788)	P	G	N	H	F	W	K	C	L	F
Xenopus (ENSXETP00000040941)	P	G	N	H	F	W	K	C	L	F
Spotted gar (ENSLOCP0000001849)	P	G	N	H	F	W	K	C	L	F
Fugu (ENSTRUT00000039062)	P	G	N	H	F	W	K	C	L	F
Tilapia (ENSONIP00000019607)	P	G	N	H	F	W	K	C	L	F
Amazon molly (ENSPPOP000000172)	P	G	N	H	F	W	K	C	L	F
Platyfish (ENSXMAP00000012462)	P	G	N	H	F	W	K	C	L	F
Stickleback (ENSGACP0000000901)	P	G	N	H	F	W	K	C	L	F
Cod (ENSGMOP00000020528)	P	G	N	H	F	W	K	C	L	F
Cavefish (ENSAMXP0000002077)	P	G	N	H	F	W	K	C	L	F
Zebrafish (ENSARP00000143488)	P	G	N	H	F	W	K	C	L	F
Salmon (XP_014025639.1)	P	G	N	H	F	W	K	C	L	F
Trout (XP_021454386.1 sc_2682)	P	G	N	H	F	W	K	C	L	F
Salmon (XP_013980185.1)	P	G	N	H	F	W	K	C	L	F
Trout (XP_021421855.1 sc_82)	P	G	N	H	F	W	K	C	L	F
Tetraodon (ENSTNIP00000005669)	P	G	N	H	F	W	K	C	L	F
Fugu (ENSTRUP00000039060)	P	G	N	H	F	W	K	C	L	F
Stickleback (ENSGACP0000000902)	P	G	N	H	F	W	K	C	L	F

\* Active site



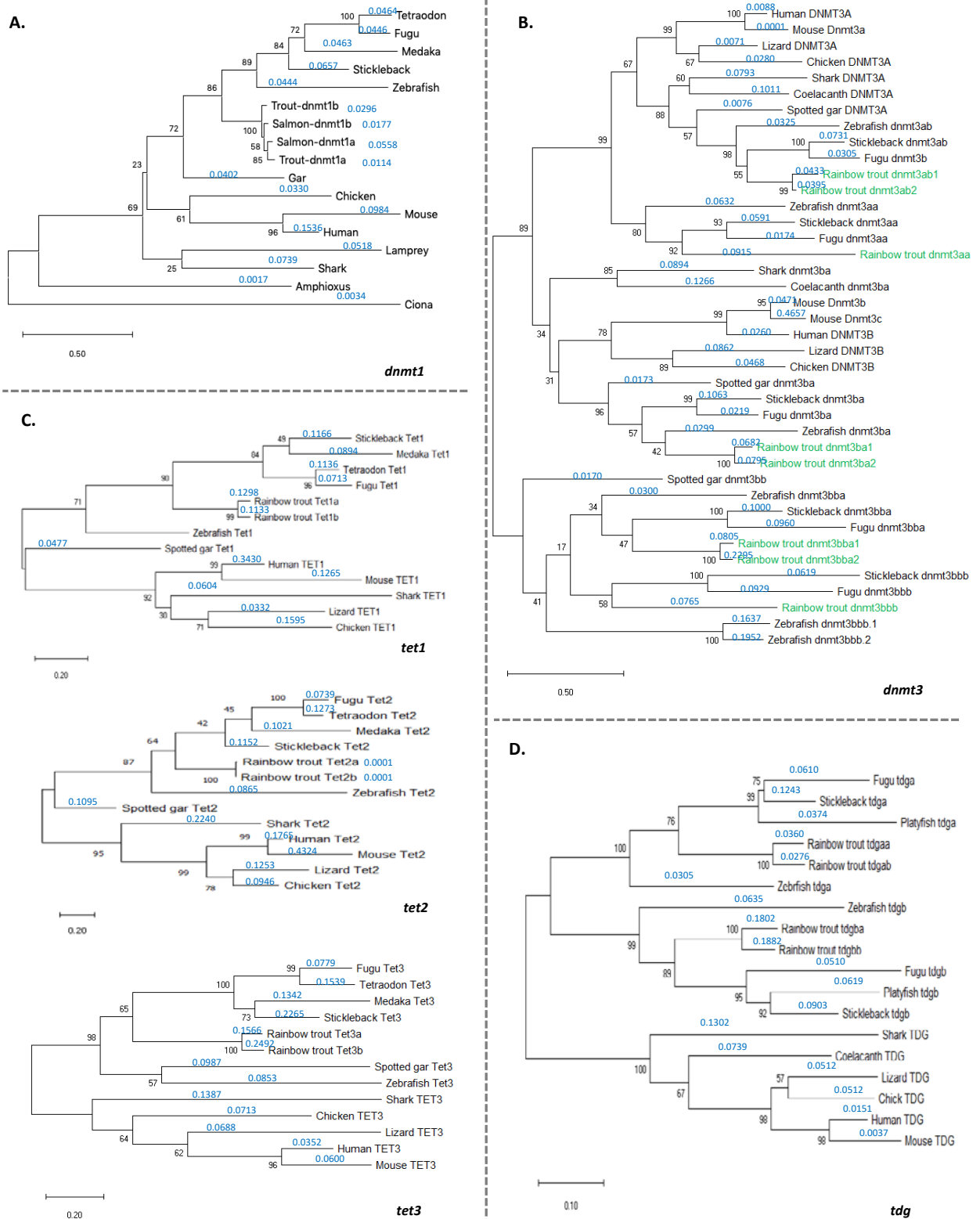
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Trout (XP_021454387.1 sc_2682) EEAYDPEYEA-AFGGAYGEGGPGPEEGQSNNGHHCNFSSAENTVSDAVEKADTSQLPAATAAATEEGQLPDGQWMMQSFADQIPDIGGSKE
Salmon (XP_013980181.1) EEAYDPEYEA-AFGGAYGEGGPG-----PEEGQSNHG-----
Trout (XP_021421885.1 sc_82) EEAYDPEYEA-ALGGAYGEGGPG-----PEEGQSNHG-----
Tetraodon (ENSTNIP0000005669) EEQYDPEYED-EGGARREGQS-----QVNGHCTFSS-----DAPREKDasPA--AEGGVQDGRWMTQSFADQIPDIS----
Fugu (ENSTRUP00000039060) --GKQPSFSPVPVGLTF SRL-----QCCF-----CLQKMARG-WPSKRSRKILSMRAAAGS
Stickleback (ENSGACP0000000902) EEQVDPEYES-CAEVRGDAR-----QSSNSTN-----
Tilapia (ENSONIP00000019612) EEQDPEYES-CSALHEETR-----HSNNSN-----
Platyfish (ENSXMAT00000012479) EEQVDPEYES-CSGLHDGVRQSS-----FLINS-----
Amazon molly (ENSPPOP0000000270) -----FGHRKCSVLQFIY-----
Cod (ENSGMOP00000020539) EEQVDPEYEN-CDRGEREAR-----QGPSHCSI-----
Cavefish (ENSAMXP0000002079) EEQDPEYES-ESSTSGSQA-----CSFYPANER-----DAANSEHSS-----LMDQVRSSQWTVQPFEDQIPDIRCPNT
Medaka (ENSORLP0000001642) EEQVDPEYED-AYGGAYVEKTAEEGQAEQGQSNHGCSFSSAEN-----KEGQLPDGQWMTQSFADHIPPDIS----
Zebrafish (ENSDARP00000012725) EEQNDPEYETCAHGSWGEP-----QQAFGVHPST-----NTDQVMDRRTMPPFAEQIPDIRCSNN
Salmon (XP_014025637.1) EEQVDPEYET-CDGEREAR-----QSTSYCNISSTKET-----AMPSKDQAQAT--PLNHMPYDQWMTQSFADQIPDISCNSS
Trout (XP_021454386.1 sc_2682) EEQVDPEYET-CDGEREAR-----QSTSYCNISSTKET-----AMPSKDQAQAT--PLNHMPYDQWMTQSFADQIPDISCNSS
Salmon (XP_013980185.1) EEQVDPEYEN-CGGARQDAK-----QSTSYCNISSTKET-----AMPSKDQAT--AMSHMPYDQWMTQSFADQIPDISCNSS
Trout (XP_021421855.1 sc_82) EEQVDPEYEN-CGGASQDAK-----QSTSYCNISSTKET-----GMPSKDQAT--AMSHMPYDQWMTQSFADQIPDISCNSS

          550      560      570
.....|.....|.....|.....|.....|.....|.....|..
European amphioxus_(Sc0000000) -----
Lamprey (ENSPMAP00000006956) -----
Ciona (ENSCINT00000037160) -----
Shark (XP_007893492.1) PQAENST-----
Coelacanth (ENSLACP00000022370) QQQG-----
Human (ENSP00000266775) TQEQEESHASHA-----
Mouse (ENSMUSP000000121000) -----
Armadillo (ENSDNOP00000010638) TPEQEESHASHA-----
Tasmanian devil (ENSSHAP000000) TLEQE-----
Lizard (ENSACAP00000022546) QEEGNDA-----
Chicken (ENSGALP00000045187) QEREGSSA-----
Turtle (ENSPSIP00000010788) QEQEESV-----
Xenopus (ENSXETP00000040941) QQQGGSSNA-----
Spotted gar (ENSLOCP0000001849) -----
Fugu (ENSTRUT00000039062) DGGV-----
Tilapia (ENSONIP00000019607) DGSI-----
Amazon molly (ENSPPOP0000000172) ASST-----
Platyfish (ENSXMAP00000012462) ASSVLSLSSTSLEGRIEPGLLLHSRCYELIRCTVTTR
Stickleback (ENSGACP0000000901) EVFEWNI-----
Cod (ENSGMOP00000020528) AVTQI-----
Cavefish (ENSAMXP00000002077) APAGAV-----
Zebrafish (ENSDARP000000143488) AQNWGV-----
Salmon (XP_014025639.1) PQAWAGNV-----
Trout (XP_021454387.1 sc_2682) PQAWAGNV-----
Salmon (XP_013980181.1) -----
Trout (XP_021421885.1 sc_82) -----
Tetraodon (ENSTNIP00000005669) -----
Fugu (ENSTRUP00000039060) SASPPPE-----
Stickleback (ENSGACP0000000902) -----
Tilapia (ENSONIP00000019612) -----
Platyfish (ENSXMAT00000012479) -----
Amazon molly (ENSPPOP0000000270) -----
Cod (ENSGMOP00000020539) -----
Cavefish (ENSAMXP00000002079) NRIS-----
Medaka (ENSORLP0000001642) -----
Zebrafish (ENSDARP00000012725) TRTS-----
Salmon (XP_014025637.1) NVAQPQLGAETF-----
Trout (XP_021454386.1 sc_2682) NVAQPHLGAETF-----
Salmon (XP_013980185.1) NVPQPQLGAETF-----
Trout (XP_021421855.1 sc_82) NVPQPQLGAETF-----

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**Supplemental Fig.S9 Tdg protein sequences alignment.** All the protein sequences were aligned with the MUSCLE method in MEGA software. Conserved domains were noted above. Active sites were marked with an asterisk (\*); SUMO-1 interface (Δ).



**Supplemental Fig. S10 Branch test of dN/ds ratio for dnmt, tet and tdg genes.** The ratios between non-synonymous and synonymous differences (dN/ds) were also calculated with the codeml program in the PAML package version 4.9i. The aligned amino acids sequences of *dnmt1*, *dnmt3*, *tet1*, *tet2*, *tet3* and *tdg* genes in selected representative species were used to guide the alignment of the nucleotides sequences by PAL2NAL to get codon alignments of these genes. We further built phylogenetic trees with their respective codon alignment of these genes using Maximum likelihood method. The codon alignments and phylogenetic trees were used as the input file for codeml program. Branch tests with the free-ratios model (Alternative hypothesis: heterogeneity of dN/ds among branches) and model 0 (Null hypothesis: homogeneous dN/ds across all sites and branches) were performed to calculate the dN/ds for each of the branches of the gene tree. The comparison between two models was conducted using a likelihood ratio test (LRT) followed by a chi-squared test of significance.