Coffill and Lee et al. Supplemental Information

Molecular dynamics

Initial structures for molecular dynamics (MD) simulations were taken from the Protein Data Bank (PDB). Human p53 transactivation domain peptide (residues 17-29) and nutlin-3a were extracted from the PDB structures 1YCR (Kussie et al. 1996) and 4J3E (Vu et al. 2013) respectively and modeled onto the human HDM2^{Nterm} structure (residues 17-112) taken from the PDB structure 3JZR (Phan et al. 2010). Using PyMOL (DeLano 2002), the human p53 peptide was extended by one residue at its N-terminus and then capped by acetyl and amide groups, while HDM2^{Nterm} was capped at its N- and C-termini by acetyl and N-methyl groups respectively. Complexes of HDM2^{Nterm} with lamprey p53, lamprey p53 G22L mutant and human p53 triple alanine mutant (F19A, W23A, L26A) peptides were generated by mutating the human p53 peptide to the appropriate sequence. The mutations were performed by keeping the peptide backbone fixed and using the tleap module of AMBER 12 (Case et al. 2012) to add the side chains of the mutated residues. Residue protonation states were determined by PDB 2PQR (Dolinsky et al. 2004). The LEaP program in the AMBER 12 package was then used to solvate each system with TIP3P (Jorgensen et al. 1983) water molecules in a periodic truncated octahedron box, such that its walls were at least 10 Å (12 Å and 15 Å for the unbound peptides and for nutlin-3a, respectively) away from the HDM2^{Nterm} complex and for neutralization of charges with either sodium or chloride ions.

Three independent explicit-solvent MD simulations were carried out on each of the complexes of HDM2^{Nterm} with human p53, human p53 triple alanine mutant, lamprey p53, lamprey p53 G22L mutant and nutlin-3a, as well as the unbound forms of HDM2^{Nterm}, p53 peptides and nutlin-3a. Energy minimizations and MD simulations were carried out by the

PMEMD module of AMBER 12, using the ff99SB force field (Hornak et al. 2006) for the protein and peptides and the generalized AMBER force field (Wang et al. 2004) for nutlin-3a. All bonds involving hydrogen atoms were constrained by the SHAKE algorithm (Ryckaert et al. 1977), allowing for a time step of 2 fs. Nonbonded interactions were truncated at 9 Å while electrostatic interactions were treated by the particle mesh Ewald method (Darden et al. 1993). Energy minimization was carried out using the steepest descent algorithm for 500 steps, followed by the conjugate gradient algorithm for another 500 steps. Each system was then heated gradually to 300 K over 50 ps at constant volume before equilibration at a constant pressure (1atm) for another 50 ps. Weak harmonic positional restraints with a force constant of 2.0 kcal mol⁻¹ Å⁻² were imposed on the heavy atoms of the solute during the minimization and these two equilibration steps. Subsequent unrestrained equilibration (2 ns) and production (100 ns) runs were carried out at 300 K and 1 atm. The temperature was maintained using a Langevin thermostat (Izaguirre et al. 2001) with a collision frequency of 2 ps⁻¹ while the pressure was maintained by a Berendsen barostat (Berendsen et al. 1984) with a pressure relaxation time of 2 ps.

Binding free energy calculations

Binding free energies for HDM2^{Nterm} complexes were calculated with the molecular mechanics/generalized Born surface area (MM/GBSA) method (Srinivasan et al. 1998). All programs used for MM/GBSA calculations are from AMBER 12. 200 equally-spaced snapshot structures were extracted from the last 10-30 ns of each of the trajectories, depending on when equilibration of the systems occurred (determined from their root mean square deviation plots), and their molecular mechanical energies calculated with the sander module. The polar contribution to the solvation free energy was calculated by the pbsa (Luo et al. 2002) program using the modified generalized Born (GB) model described by Onufriev

et al. (Onufriev et al. 2004) while the nonpolar contribution was estimated from the solvent accessible surface area (SASA) using the molsurf (Connolly 1983) program with $\gamma = 0.0072$ kcal Å⁻² and β set to zero. The nmode program was used to estimate entropies (Brooks et al. 1995). Due to its computational expense, only 50 equally-spaced snapshots from the equilibrated portion of the trajectories were used for entropic analysis. Replica exchange MD simulations were carried out on the free peptides using standard protocols (Lama et al. 2013).

Binding free energy decomposition

The contribution of each peptide residue to the binding free energy was computed using the free energy decomposition method (Gohlke et al. 2003) on the same 200 snapshot structures used for MM/GBSA analysis. Similar to the MM/GBSA calculations, the molecular mechanical energies and polar contribution to solvation free energy were computed by the sander module and pbsa program using the modified GB model described by Onufriev *et al.* (Onufriev et al. 2004) respectively. The nonpolar contribution to solvation free energy was estimated from the SASA using the ICOSA method (Rarey et al. 1996).

Bio-layer Interferometry (BLI) assay

The affinity of HDM2^{Nterm} binding to the Lamprey peptides was determined using the BLItz (ForteBio, USA) system. The purified HDM2^{Nterm} proteins were buffer exchanged into the kinetics buffer (PBS + 0.05% Tween-20) prior to the experiment. Biotinylated human and lamprey peptides were immobilized at a concentration of 2.5μ M on the streptavidin biosensors (ForteBio) which were pre-hydrated in PBS + 5% DMSO for at least 10 minutes. The unbound biotinylated peptides were washed off in the same buffer. The loaded sensors were equilibrated in the kinetics buffer before immersing them into the various titrations of HDM2^{Nterm} (3x serial dilutions from 250µM) over 120 seconds and then immersed into the

kinetics buffer for dissociation. A blank uncoated sensor reference (without biotinylated peptide) was carried out in 250μ M HDM2^{Nterm} to ensure no/low binding of HDM2^{Nterm} to the uncoated sensor and a coated sample reference (peptide but without HDM2^{Nterm} protein) was measured as a background binding control. Data analysis was performed using a global fit in the BLItz Pro software to calculate the K_D value.

Amino acid sequence similarity (Table 1)

The amino acid sequence similarities between human and lamprey proteins were determined using pairwise sequence alignment tools (<u>http://www.ebi.ac.uk/Tools/psa/emboss_needle/</u>) (Rice et al. 2000; Li et al. 2015).

Ligand	Peptide sequence, if applicable	$\Delta \mathbf{H}_{\mathrm{bind}}$	$T\Delta S_{bind}$	ΔG_{bind}
nutlin-3a	N.A.	-82.36	-24.08	-58.29
Hp53 ¹⁶⁻²⁹	Ac-QETFSDLWKLLPEN-NH ₂	-80.39	-37.21	-43.18
Hp53 ^{16-29(AAA)}	Ac-QETASDLAKLAPEN-NH ₂	-79.30	-40.37	-38.92
Lp53 ¹²⁻²⁵	Ac-VDDFDRVWQGGVGL-NH ₂	-80.61	-40.81	-39.80
Lp53 ^{12-25(G22L)}	Ac-VDDFDRVWQGLVGL-NH ₂	-85.63	-37.48	-48.15

Table S1. Computed binding free energies (kcal/mol) of HDM2^{Nterm} complexes.

Table S2. Experimental determination of binding affinities for peptide and HDM2^{Nterm} complexes

Peptide	Sequence	$K_{D}\left(\mu M ight)^{A}$	$K_{D}\left(\mu M\right)^{B}$
Hp53 ¹⁶⁻²⁹	QETFSDLWKLLPEN	2.7 ± 0.5	1.3
Hp53 ^{16-29(AAA)}	QETASDLAKLAPEN	nd	nd
Lp53 ¹²⁻²⁵	VDDFDRVWQGGVGL	nd	nd
Lp53 ^{12-25(G22L)}	VDDFDRVWQGLVGL	41 ± 3	33

^A determined by Fluorescence Anisotropy. Data are averages of at least four replicates \pm SEM.

^B determined by Bio-layer Interferometry (BLI) assay. nd = not determined due difficulty fitting curve to weak binding data

Peptide	Sequence	Organism	Reference sequence	Literature reference
FAM-12.1	5(6)-FAM-RFMDYWEGL- NH_2	Human	-	(Bottger et al. 1997)
Hs-p53 ¹⁶⁻²⁹	$Ac-QETFSDLWKLLPEN-NH_2$		NP_000537.3	
	Biotin-SGSG- QETFSDLWKLLPEN-NH ₂			
Hs-p53 ^{16-29(AAA)}	$Ac-QETASDLAKLAPEN-NH_2$			
	Biotin-SGSG- QETASDLAKLAPEN-NH ₂			
Lj-p53 ¹²⁻²⁵	$Ac-VDDFDRVWQGGVGL-NH_2$	Lamprey	KT960978	
	Biotin-SGSG- VDDFDRVWQGGVGL-NH ₂			
Lj-p53 ^{12-25(G22L)}	$Ac-VDDFDRVWQGLVGL-NH_2$			
	Biotin-SGSG- VDDFDRVWQGLVGL-NH ₂			

Table S3. Peptides synthesized for Fluorescence Anisotropy and Bio-layer Interferometry

 (BLI) assay

5(6)FAM = mixed isomers 5-(and 6-)carboxyfluoresceine; Ac = acetyl; NH₂ = amide

Plasmid	Amino Acids	Tag	Vector	N'/C'	Organism	Reference sequence	Literature reference
Hs-p53	1-393	-	pcDNA3	-	Human	NP_000537.3	
Hs-p53	1-393	3xFLAG 6xHIS	pCI-neo	N'			(Coffill et al. 2012)
Hs-p53∆	1-355	-	pcDNA3	-			
HDM2	1-491	-	pCMV	-		Q00987	
HDM2 ^{Nterm}	1-125	HA	pcDNA3	C'			
GST-HDM2 _{Nterm}	1-125 or 6-125	GST- precision	pGEX- 6P-1	N'			(Bottger et al. 1997; Brown et al. 2013; Chee et al. 2014)
Hs-RPL11	1-178	FLAG	pcDNA3	N'		NP_000966.2	
Hs-RPL5	1-297	FLAG	pcDNA3	N'		NP_000960.2	
Lj-p53	1-428	3xFLAG 6xHIS	pCI-neo	N'	Lamprey	KT960978	
Lj-p53	1-428	FLAG	pcDNA3	N'			
Lj-p53(G22L)	1-428 (G22L)	FLAG	pcDNA3	N'			
Lj-p53∆	1-390	FLAG	pcDNA3	N'			
Lj-Mdm2	1-603	HA	pXJ40	N'		KT960981	
Lj- Mdm2(C464A) (human #)	1-603(C576A)	HA	pXJ40	N'			
Lj-Mdm2	1-603	HA	pCMV	C'			
Lj-Mdm2	1-603	HA	pcDNA3	C'			
Lj-Mdm2 ^{Nterm}	1-106	HA	pcDNA3	C'			
Lj-Mdm4	1-280	myc	pCMV	N'		KT960982	

Table S4. Details	of pl	lasmids	used	in	this	study
-------------------	-------	---------	------	----	------	-------

Coffill and Lee et al. Supplemental Figure Legends

Figure S1. Alignment of p53

Alignment of p53 protein sequences from lamprey (GenBank accession number KT960978); elephant shark (Eshark) (G9J1L8); zebrafish (P79734); *Xenopus laevis* (frog) (P07193); chicken (P10360); mouse (NP_035770.2) and human (P04637). Alignments were carried out using Clustal Omega (Goujon et al. 2010; Sievers et al. 2011) and Jalview (Waterhouse et al. 2009).

Figure S2. Isoforms of p53

Alignment of p53 isoform protein sequences from human (Hs), zebrafish (Dr) and lamprey (Lj): Hs-p53 (P04637); Hs- Δ 40p53 (NP_001119590.1); Hs- Δ 133p53 (NP_001119587.1); Hs- Δ 160p53 (NP_001263626.1); Dr-p53 (P79734); Dr- Δ 18p53 (see (Davidson et al. 2010)); Dr- Δ 113p53 (see (Marcel et al. 2011)); Lj-p53 (KT960978); Lj- Δ 27p53; Lj- Δ 30p53; Lj- Δ 108p53.

Figure S3. Synteny of Tp53, Tp63 and Tp73 genes

Tp53, Tp63 and Tp73 gene loci in human, coelacanth and lamprey. Genes that are colored indicate genes that show conserved synteny. The orientation of the pentagons (genes) denotes the direction of transcription and circles represent end of scaffold.

Figure S4. Intron positions of Lj-p53, Lj-p63 and Lj-p73

Alignment of Lj-p53, Lj-p63 and Lj-p73 proteins indicating the positions of introns. The alignment was generated using Clustal Omega. The phase of each intron is indicated by color: yellow (phase 0), green (phase 1), red (phase 2).

Figure S5. Alignment of p63

Alignment of p63 protein sequences from lamprey (GenBank accession number KT960979); elephant shark (Eshark) (G9J1L9); zebrafish (A7YYJ7); *Xenopus tropicalis* (frog) (F6ZGN7); chicken (F1N8Z7); mouse (O88898) and human (Q9H3D4).

Figure S6. Alignment of p73

Alignment of p73 protein sequences from lamprey (GenBank accession number KT960980) elephant shark (Eshark) (G9J1M0); zebrafish (B0S576); *Xenopus tropicalis* (frog) (F6TKT0); chicken (XP_417545.3); mouse (Q9JJP2) and human (O15350).

Figure S7. Gene structure of *Tp63* and *Tp73*

Gene structure and isoforms of Lj-Tp63 (A) and Lj-Tp73 (B). Coding exons are designated by open boxes and non-coding exons by shaded boxes. The transcription start site is indicated by an arrow. The sizes of 5' introns are labelled in (A). The longest isoform of Tp63 has an alternative 5' splice site at the first intron compared with the other two shorter isoforms. The figure is not drawn to scale.

Figure S8. Isoforms of p63

Alignment of p63 isoform protein sequences from human (Hs) and lamprey (Lj): Hs-TAp63α (NP_003713.3); Hs-TAp63β (NP_001108450.1); Hs-TAp63γ (NP_001108451.1); Hs-ΔNp63α (NP_001108452.1); Hs-ΔNp63β (NP_001108453.1); Hs-ΔNp63γ (NP_001108454.1); Lj-p63_A (KT960979); Lj-p63_B and Lj-p63_C.

Figure S9. Alignment of Mdm2

Alignment of Mdm2 protein sequences from lamprey (GenBank accession number KT960981) elephant shark (Eshark) (G9J1M1); zebrafish (Q561Z0); *Xenopus laevis* (frog) (P56273); chicken (F1NGX6); mouse (P23804) and human (Q00987).

Figure S10. Alignment of Mdm RING

Alignment of Mdm2 and Mdm4 protein sequences with HMD2 (Q00987); HDM4 (O15151); Lj-Mdm2 (KT960981) and Lj-Mdm4 (KT960982). Arrows denote the amino acid residues required for either p53 ubiquitination and/or degradation (Fang et al. 2000; Dolezelova et al. 2012).

Figure S11. Alignment of Mdm4

Alignment of Mdm4 protein sequences from lamprey (GenBank accession number KT960982) elephant shark (Eshark) (G9J1M2); zebrafish (Q7ZUW7); *Xenopus tropicalis* (frog) (B5DFR1); chicken (E1C4B0); mouse (O35618) and human (O15151).

Figure S12. Synteny of *Mdm2* and *Mdm4* genes

Mdm2 and *Mdm4* gene loci in human, coelacanth, elephant shark and lamprey. Genes that are colored indicate genes that show conserved synteny. The orientation of the pentagons (genes) denotes the direction of transcription and circles represent end of scaffold.

Figure S13. Averaged binding free energy contributions of peptide residues in the complexes of HDM2^{Nterm} with Hs-p53¹⁶⁻²⁹ (blue), Lj-p53¹²⁻²⁵ (red) and Lj-p53^{12-25(G22L)} mutant (black).

Figure S14. Snapshots of free peptides from Replica exchange molecular dynamics simulations.

Figure S15.

(A) Western blot showing *in vitro* translation (IVT) and immunoprecipitation (IP) of lamprey p53 (top panel) by Lj-Mdm2, which were used as bait. Input levels can be seen in the lower panel. (B) Western blot of Lj-p53 levels following co-transfection with various Lj-Mdm2 expressing constructs. Lanes: (1) Lj-p53; (2) Lj-p53 with MG132; (3) Lj-p53 + HA-Lj-Mdm2; (4) Lj-p53 + HA-Lj-Mdm2 with MG132; (5) Lj-p53 + Lj-Mdm2-HA; (6) Lj-p53 + Lj-Mdm2-HA with MG132; (7) Lj-p53 + Lj-Mdm2-HA + myc-Lj-Mdm4; (8) Lj-p53 + Lj-Mdm2-HA + myc-Lj-Mdm4 with MG132; (9) Lj-p53 9 + myc-Lj-Mdm4; (10) Lj-p53 + myc-Lj-Mdm4 with MG132. Lj-Mdm2 levels can be seen in the upper panel and the loading control can be found in the lower panel.

Figure S16.

(A) A surface presentation (pink) of the human crystal structure of $HDM2^{Nterm}$ (residues 25–109) in complex with Nutlin (B) A surface presentation (green) of a homology model of the p53-binding region of Lj-Mdm2^{Nterm}, in complex with Nutlin. Models were generated based on the $HDM2^{Nterm}$ structure (residues 17-112) from the PDB structure 3JZR (Phan et al. 2010).

Supplemental References

- Berendsen HJC, Postma JPM, Vangunsteren WF, Dinola A, Haak JR. 1984. Molecular dynamics with coupling to an external bath. *J Chem Phys* **81**: 3684-3690.
- Bottger A, Bottger V, Sparks A, Liu WL, Howard SF, Lane DP. 1997. Design of a synthetic Mdm2-binding mini protein that activates the p53 response in vivo. *Curr Biol* **7**: 860-869.
- Brooks BR, Janezic D, Karplus M. 1995. Harmonic analysis of large systems. I. Methodology. *J Comput Chem* 16: 1522-1542.
- Brown CJ, Quah ST, Jong J, Goh AM, Chiam PC, Khoo KH, Choong ML, Lee MA, Yurlova L, Zolghadr K et al. 2013. Stapled peptides with improved potency and specificity that activate p53. *ACS Chem Biol* **8**: 506-512.
- Case DA, Darden TA, Cheatham TE, Simmerling CL, Wang J, Duke RE, Luo R, Walker RC, Zhang W, Merz KM et al. 2012. AMBER 12. University of California, San Francisco.
- Chee SM, Wongsantichon J, Soo Tng Q, Robinson R, Joseph TL, Verma C, Lane DP, Brown CJ, Ghadessy FJ. 2014. Structure of a stapled peptide antagonist bound to nutlin-resistant Mdm2. *PLoS One* **9**: e104914.
- Coffill CR, Muller PA, Oh HK, Neo SP, Hogue KA, Cheok CF, Vousden KH, Lane DP, Blackstock WP, Gunaratne J. 2012. Mutant p53 interactome identifies nardilysin as a p53R273H-specific binding partner that promotes invasion. *EMBO Rep* **13**: 638-644.
- Connolly ML. 1983. Analytical molecular surface calculation. J Appl Crystallogr 16: 548-558.
- Darden T, York D, Pedersen L. 1993. Particle mesh Ewald: an N•log(N) method for Ewald sums in large systems. *J Chem Phys* **98**: 10089-10092.
- Davidson WR, Kari C, Ren Q, Daroczi B, Dicker AP, Rodeck U. 2010. Differential regulation of p53 function by the N-terminal DeltaNp53 and Delta113p53 isoforms in zebrafish embryos. *BMC Dev Biol* **10**: 102.
- DeLano WL. 2002. The PyMOL Molecular Graphics System. DeLano Scientific, San Carlos, CA, USA.
- Dolezelova P, Cetkovska K, Vousden KH, Uldrijan S. 2012. Mutational analysis of Mdm2 Cterminal tail suggests an evolutionarily conserved role of its length in Mdm2 activity toward p53 and indicates structural differences between Mdm2 homodimers and Mdm2/MdmX heterodimers. *Cell Cycle* **11**: 953-962.
- Dolinsky TJ, Nielsen JE, McCammon JA, Baker NA. 2004. PDB2PQR: an automated pipeline for the setup of Poisson-Boltzmann electrostatics calculations. *Nucleic Acids Res* **32**: W665-W667.
- Fang S, Jensen JP, Ludwig RL, Vousden KH, Weissman AM. 2000. Mdm2 is a RING fingerdependent ubiquitin protein ligase for itself and p53. *J Biol Chem* **275**: 8945-8951.
- Gohlke H, Kiel C, Case DA. 2003. Insights into protein-protein binding by binding free energy calculation and free energy decomposition for the Ras-Raf and Ras-RaIGDS complexes. *J Mol Biol* **330**: 891-913.
- Goujon M, McWilliam H, Li W, Valentin F, Squizzato S, Paern J, Lopez R. 2010. A new bioinformatics analysis tools framework at EMBL-EBI. *Nucleic Acids Res* **38**: W695-699.
- Hornak V, Abel R, Okur A, Strockbine B, Roitberg A, Simmerling C. 2006. Comparison of multiple Amber force fields and development of improved protein backbone parameters. *Proteins: Struct Funct Bioinform* 65: 712-725.
- Izaguirre JA, Catarello DP, Wozniak JM, Skeel RD. 2001. Langevin stabilization of molecular dynamics. *J Chem Phys* **114**: 2090-2098.

- Jorgensen WL, Chandrasekhar J, Madura JD, Impey RW, Klein ML. 1983. Comparison of simple potential functions for simulating liquid water. *J Chem Phys* **79**: 926-935.
- Kussie PH, Gorina S, Marechal V, Elenbaas B, Moreau J, Levine AJ, Pavletich NP. 1996. Structure of the MDM2 oncoprotein bound to the p53 tumor suppressor transactivation domain. *Science* **274**: 948-953.
- Lama D, Quah ST, Verma CS, Lakshminarayanan R, Beuerman RW, Lane DP, Brown CJ. 2013. Rational optimization of conformational effects induced by hydrocarbon staples in peptides and their binding interfaces. *Sci Rep* **3**: 3451.
- Li W, Cowley A, Uludag M, Gur T, McWilliam H, Squizzato S, Park YM, Buso N, Lopez R. 2015. The EMBL-EBI bioinformatics web and programmatic tools framework. *Nucleic Acids Res* **43**: W580-584.
- Luo R, David L, Gilson MK. 2002. Accelerated Poisson-Boltzmann calculations for static and dynamic systems. *J Comput Chem* 23: 1244-1253.
- Marcel V, Dichtel-Danjoy ML, Sagne C, Hafsi H, Ma D, Ortiz-Cuaran S, Olivier M, Hall J, Mollereau B, Hainaut P et al. 2011. Biological functions of p53 isoforms through evolution: lessons from animal and cellular models. *Cell Death Differ* 18: 1815-1824.
- Onufriev A, Bashford D, Case DA. 2004. Exploring protein native states and large-scale conformational changes with a modified generalized Born model. *Proteins: Struct Funct Bioinform* **55**: 383-394.
- Phan J, Li Z, Kasprzak A, Li B, Sebti S, Guida W, Schoenbrunn E, Chen J. 2010. Structurebased design of high affinity peptides inhibiting the interaction of p53 with MDM2 and MDMX. *J Biol Chem* **285**: 2174-2183.
- Rarey M, Kramer B, Lengauer T, Klebe G. 1996. A fast flexible docking method using an incremental construction algorithm. *J Mol Biol* **261**: 470-489.
- Rice P, Longden I, Bleasby A. 2000. EMBOSS: the European Molecular Biology Open Software Suite. *Trends Genet* **16**: 276-277.
- Ryckaert JP, Ciccotti G, Berendsen HJC. 1977. Numerical integration of the Cartesian equations of motion of a system with constraints: molecular dynamics of n-alkanes. *J Comput Phys* **23**: 327-341.
- Sievers F, Wilm A, Dineen D, Gibson TJ, Karplus K, Li W, Lopez R, McWilliam H, Remmert M, Soding J et al. 2011. Fast, scalable generation of high-quality protein multiple sequence alignments using Clustal Omega. *Mol Syst Biol* 7: 539.
- Srinivasan J, Cheatham TE, Cieplak P, Kollman PA, Case DA. 1998. Continuum solvent studies of the stability of DNA, RNA, and phosphoramidate–DNA helices. *J Am Chem Soc* **120**: 9401-9409.
- Vu B, Wovkulich P, Pizzolato G, Lovey A, Ding Q, Jiang N, Liu J-J, Zhao C, Glenn K, Wen Y et al. 2013. Discovery of RG7112: a small-molecule MDM2 inhibitor in clinical development. ACS Med Chem Lett 4: 466-469.
- Wang JM, Wolf RM, Caldwell JW, Kollman PA, Case DA. 2004. Development and testing of a general amber force field. *J Comput Chem* **25**: 1157-1174.
- Waterhouse AM, Procter JB, Martin DM, Clamp M, Barton GJ. 2009. Jalview Version 2--a multiple sequence alignment editor and analysis workbench. *Bioinformatics* 25: 1189-1191.

Lamprey	1	-ME <mark>GTA<mark>PG</mark>N<mark>MG</mark>CVDDFD</mark>	R <mark>VWQ<mark>GGVG</mark>LLDM</mark>	IMDMYNM <mark>IN</mark> PDL	E-SS <mark>P</mark> F <mark>DNLP</mark> MPD:	SESA <mark>L</mark> L <mark>D</mark> -58
E shark	1	-ME <mark>D</mark> EL <mark>LE</mark> E <mark>PL<mark>SQET</mark>FG</mark>	<mark>DLW</mark> NQ <mark>L</mark> DF	<mark>PP</mark> I	RAEETLPWPN	VD <mark>PG<mark>W</mark>GD</mark> S45
Zebrafish	1	MAQNDS <mark>Q</mark> EFA	<mark>elw</mark> ekn <mark>l</mark> iiQ	G	<mark>GG</mark>	sc <mark>w</mark> dII31
Frog	1M <mark>E</mark> I	SSET <mark>GMDPP</mark> L <mark>SQET</mark> FE?	<mark>dlw</mark> sl <mark>lp</mark> d	<mark>PL</mark> Q	TVTCRLDNLS	EF <mark>P</mark> D <mark>YP</mark> LA48
Chicken	1MA <mark>e</mark> -	EME <mark>PLLE</mark> PTEVFM	DLWSMLPYSM	QQ	<mark>LP</mark> L <mark>P</mark> E	DHSN <mark>W</mark> Q <mark>E</mark> L41
Mouse	1 MTAME <mark>E</mark> S	SQS <mark>DISLELPLSQET</mark> FS	GLWKLLPPED	ILPSP	HCMDD-LLLPQ	DVEEFF <mark>E</mark> -55
Human	1ME <mark>E</mark>	QS <mark>DP</mark> SVEPPL <mark>SQET</mark> FS	DLWKLLPENN	VLSPL	PSQAMDDLMLSPD	DIEQ <mark>W</mark> FTE56
Lamprey	59	LQ <mark>PP</mark>	CEL <mark>PAC</mark> PT-FNA	PIAGPSIP <mark>ST</mark> D	DYPGSLSFHLSWQ	2CSIA <mark>KS</mark> A105
E shark	46 ALEELNE	RVWLVTGETSGGY <mark>T</mark> EPL	GPAQ <mark>V</mark> QPPAEPP	VLTTSAVPSIT	DYAGPHNFQLLFQ	OFS <mark>TAKS</mark> V112
Zebrafish	32 NDEE	YL <mark>PG</mark> SFD <mark>P</mark> NFFENV	LEEQ <mark>P</mark> OPST	LPPTSTVPETS	DYPGDHGFRLRFP	os <mark>gtaks</mark> v90
Froq	49 AD	MTVLOE <mark>G</mark>	LMGNAVP	TVTSCAVPSTD	DYAGKYGLOLDFO	ONGTAKSV96
Chicken	42 S <mark>P</mark> LE <mark>P</mark> S-	-D <mark>PPPPPPPPPPPLPLAAA</mark>	APPPLNPPTPPR	AA <mark>PSP</mark> VVPSTE	DYGGDFDFRVGFV	EAGTAKSV107
Mouse	56 <mark>GP</mark> SE-	-ALRVSGAPAAODPVTE	T <mark>PGPVAPAPAT</mark> P	WPLSSFVPSOK	TYOGNYGFHLGFL	OS <mark>GTAKS</mark> V119
Human	57 D <mark>PGP</mark> DE-	-APRMPEAAPPVAPAPA	APTPAAPAPAPS	WPLSSSVPSOK	TYOGSYGFRLGFL	HSGTAKSV122
				~	~	
Lamprey	106 <mark>TWTYSP</mark> I	DL <mark>NK</mark> LYCQIG <mark>KT</mark> CPVQL	RVA <mark>TPVP</mark> S <mark>G</mark> CAV	RAMPVYKKADH	LTEVVKRCPNHEI:	SK <mark>E</mark> FND <mark>G</mark> N172
E shark	113 TNTYSTS	SLT <mark>K</mark> LF <mark>CQIA<mark>KTCPIQ</mark>V</mark>	KVS <mark>SPPPPGS</mark> VI	RATAVY <mark>KK</mark> SEH	VAEVV <mark>KRCPHHER</mark>	C <mark>PD</mark> FND177
Zebrafish	91 TCTYSPI	DL <mark>NK</mark> LF <mark>COLAKTCPVO</mark> M	vvdvappo <mark>gs</mark> vv	RATAIY <mark>KKSE</mark> H	VAEVVRRCPHHER'	r <mark>PD-GD</mark> 154
Froa	97 TCTYSPE	LNKLFCOLAKTCPLLV	RVESPPPRGSIL	RATAVYKKSEH	VAEVVKRCPHHER	SVEPG - E161
Chicken			RVGVAPPPGSSL	RAVAVYKKSEH	VAEVVRRCPHHER	CGGGT - D172
Mouse			WVSATPPAGSRV	BAMATYKKSOH	MTEVVBRCPHHER	2500 0183
Human		I.NKMFCOLAKTCPVOL	WVDSTIIII00IV	RAMATYKOSOH		2500 - 0186
naman						
Lamprev	173 n <mark>lapp</mark> se	ILI <mark>RVEG</mark> SVOAD <mark>YVDD</mark> O	N <mark>TGR</mark> OSVRLPYE	PPOVGTDFSTV	LL <mark>N</mark> FM <mark>CNSSC</mark> VGG	MNRRPISV239
E shark	178 GLAPPSE	ILTRVEANSLARYHDDE	HSKROSVVLPYE	EPOVGSECSTV		MNRRPTLT 244
Zebrafish	155 NLAPAGE	ILTRVEGNORANYREDN	TTIRHSVEVPYE	APOLGAEWTTV	LLNYMCNSSCMGG	
Eroa			NSCRHSVCVPVF	CPOVCTE CTTV		
Chicken		ILTRVECNDOARVHDDE				
Mourco						
House Human						
numan						
Lamprev	240 II <mark>TLE</mark> AS	SDGOVLGRRSFEARICA	CPGRDRKSDEEN	LRKOEREOERE	00 GPARVT PPPPP	PPLAVNGG 306
E shark	245 TTTLETE		CPGRDRRYEEEN	ORKOCEKUTVK	RS	TKE 295
Zebrafish	222 TTTLETC	EGOLLGERSFEVENCA	CPGRDRKTEESN	FKKDOETKTMA	кт	TTG272
Frog	229 TTTLETE	OGLILGERCEEVEVCA	CPGRDRRTEEDN	YTKKRGLKPS-	- <mark>G</mark>	KRE277
Chicken		CGOLLGRRCFEVRVCA	CPGBDBKTEEEN	FRKRGGAG	–	GV284
Mouse		SCNLLCRDSFEVRVCA	CPCRDRRTEEEN	FRKKEVI.CPEI.		CS 300
Human		S CNLLCRNSFEVRVCA	CPCRDRRTEEEN	LBKKCEPHHEL		<mark>6</mark> 5303
numun						<mark>0</mark> 0000
Lamprev	307 I <mark>R</mark> SSLVI	PASGOITLSSDSEGPS	vrvft <mark>g</mark> krlrka	HYLAT <mark>KR</mark> SRPD	EKEELFLIPVRGR	EN <mark>YE</mark> LLLH373
E shark	296VS) PT VSTE P -		-SKRKLS	SDTEVETLOVTGR	ERYETLKO 332
Zebrafish	273 TKRSLVP	KESSSATIRP-		-ECSKKAKCSS	SDEETETLOVEGE	
Frog	278 T.AF	IPPSSEPP-				SRVEMTKK 318
Chicken	285 AKRAMSI				PDNFIFYLOVRCB	BRYEMLKE 326
Mourso						
Human				-3DODKKK-D		
numan						
Lamprev	374 LKESLEN	KOLVPOOAMETYROOO	LHO	000LV <mark>P</mark> RIM-K	ALV <mark>K</mark> KEHMDKKEDI	KS <mark>PP</mark> EK 428
E shark	333 INESLET	OELVPASVVO-ACROO	- HKLRIKAAHKKE	SSASEPKKGRK		387
Zebrafish	320 LNDSLEI	SDVVPASDAEK-YROK	FMTKNKKEN	RESSEPKOGKK	LMVKDEGRSDSD-	373
Frog	319 T.NDAT.FT	OESLDOOKVTIKCR	KC	RDETKPKKCKK		363
Chicken		AEGGSAPRPSKCRR	WK	VEGPOPSCCKK		367
Mouse			HCCVI Ku	KKCUCucbukk		307
Human				KKCOGudbhkk		303 230
numan			CATTICOTI	TTTON DUTIN		595

Coffill and Lee et al. Fig S1

Hs-p53	1 MEE <mark>P</mark> QSD <mark>P</mark> SVE <mark>PP</mark> LSQETFSDLWKLL <mark>P</mark> ENNVLS <mark>P</mark> L <mark>P</mark> SQAMDDLMLSPDDIEQWFTED <mark>PGP</mark> 60
Hs-∆40p53	1MDDLMLSPDDIEQWFTED <mark>PGP</mark> 21
Hs-∆133p53	
$Hs - \Delta 160p53$ Dr - p53 $Dr - \Delta 18p53$ $Dr - \Delta 113p53$	1MAQNDSQEFAELWEKNLI- <mark>IQPPGGG</mark> SCWDIIND 33 1MHLSNVLFIWSSLYELQQINTNFSLFLFNCLRS-IQPPGGGSCWDIIND 48
LI=Δ113 _{D33} Lj=p53 Lj=Δ27p53 Lj=Δ30p53 Lj=Δ108p53	1 ME <mark>G</mark> TA <mark>PG</mark> NM <mark>G</mark> CVDDFDRVWQ <mark>GG</mark> V <mark>G</mark> LLDMMDMYNMI-NPDLESSPFDNLPMP 50 1MMDMYNMI-NPDLESSPFDNLPMP 23 1MYNMI-NPDLESSPFDNLPMP 20
Hs-p53	61 DEA <mark>PRMPEAAPPVAPAPAAPTPAAPAPAP</mark> APSW <mark>PL</mark> SS <mark>SVP</mark> SQKTYQGSYGFRLGFLHSGTAKSVTC 124
Hs-∆40p53	22 DEA <mark>PRMPEAAPPVAPAPAAPTPAAPAPAPSWPLSSSVP</mark> SQKTYQGSYGFRLGFLHSGTAKSVTC 85
Hs-∆133p53	
$Hs - \Delta 160p53$ Dr - p53 $Dr - \Delta 18p53$ $Dr - \Delta 113p53$	34EEY <mark>LPG</mark> SFD <mark>PNFFENVLEEQPQP</mark> STL <mark>PP</mark> TS TVP ETSD <mark>YPG</mark> DHGFRLRFPQSGTA <mark>KS</mark> VTC 92 49EEYLPGSFDPNFFENVLEEQPQPSTLPPTSTVPETSD <mark>YPG</mark> DHGFRLRFPQSGTA <mark>KS</mark> VTC 107
Lj -p53	51 DSESALLDLQP-PCELPACPTFNAPIAGPSIPSTDDYPGSLSFHLSWQQCSIAKSATW 107
Lj-Δ27p53	24 DSESALLDLQP-PCELPACPTFNAPIAGPSIPSTDDYPGSLSFHLSWQQCSIAKSATW 80
Lj-Δ30p53	21 DSESALLDLSP-PCELPACPTFNAPIAGPSIPSTDDYPGSLSFHLSWQQCSIAKSATW 77
Lj-Δ108p53	1MGGDLCFYLF 10
Hs-p53	125 TYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHERCSDS 185
Hs-Δ40p53	86 TYSPALNKMFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHERCSDS 146
Hs-Δ133p53	1MFCQLAKTCPVQLWVDSTPPPGTRVRAMAIYKQSQHMTEVVRRCPHHERCSDS 53
Hs-Δ160p53	1MAIYKQSQHMTEVVRRCPHHERCSDS 26
Dr-p53	93 TYSPDLNKLFCQLAKTCPVQMVVDVAPPQGSVVRATAIYKKSEHVAEVVRRCPHHERTPDG 153
Dr-Δ18p53	108 TYSPDLNKLFCQLAKTCPVQMVVDVAPPQGSVVRATAIYKKSEHVAEVVRRCPHHERTPDG 168
Dr-Δ113p53	1MVVDVAPPQGSVVRATAIYKKSEHVAEVVRRCPHHERTPDG 41
Lj-p53	108 TYSPDLNKLYCQIGKTCPVQLRVATPVPSGCAVRAMPVYKKADHLTEVVKRCPNHEISKEFNDG 171
Lj-Δ27p53	81 TYSPDLNKLYCQIGKTCPVQLRVATPVPSGCAVRAMPVYKKADHLTEVVKRCPNHEISKEFNDG 144
Lj-Δ30p53	78 TYSPDLNKLYCQIGKTCPVQLRVATPVPSGCAVRAMPVYKKADHLTEVVKRCPNHEISKEFNDG 141
Lj-Δ108p53	11 QYSPDLNKLYCQIGKTCPVQLRVATPVPSGCAVRAMPVYKKADHLTEVVKRCPNHEISKEFNDG 74

Coffill and Lee et al. Fig S2



Coffill and Lee et al. Fig S3

Lamprey_p53	MEGTAPGNMGCVDDFDRVWQG
Lamprey_p63	MDSSPPIEDLLSQDTMQLIYND <mark>I</mark> TSGNSMLSIDNVDLRFDESPGSKLQINMEVLQMEN <mark>KN</mark>
Lamprey_p73	MLYVSNTSQAQYG <mark>GP</mark>
	: .
Temperature E 2	
Lamprey_p53	
Lamprey_p63	HCEAFSDIPENVSQQPVSTFPTIMQQQQQQPD5GIAQQQINEHQIFGDESWCENQGLSCI
Lamprey_p/3	QYTTL
Lamprey_p53	YNMINPDLESSPFDNLPMPDSESALLDLQPPCELPACPTFNAPIAGP
Lamprey p63	-APMVANSTAGFCPSTEPILCGPMVSPSLPLEMPGQLYGS
Lamprey p73	LGPVSAAGVQGAPRMERGGSPFGSEPGGPLASPSPY-AQPSSTYEAASPAA
—	.**
τ	
Lamprey_p53	SIPSTDDYPGSLSFHLSWQQCSIAKSATWTYSPDLNKLYCQIGKTCPVQLRVATPVPS
Lamprey_p63	TIPSNTDIKGPFNFTVNFSPSSTAKSATWIFSTKLKKLYCQMSKICPAEIRTSTLPPQ
Lamprey_p/3	AIPSITDYPGPHGFDVSFQQSSTAKSATW <mark>TY</mark> SPDLKKLYCQIAKTCPIQFKVLSVPPPPA
	:*** ** ** :* ******:**:********
Lamprev p53	GCAVRAMPVYKKADHLTEVVKRCPNHEISKEFNDGNNLAPPSHLIRVEGSVOADYVDDON
Lamprev p63	GTIIRIMAMFKKSEHISEVVRRCPTHOOSPELNHG-SIAPVTHLIRVEGNRNVRYEEHPV
Lamprev p73	GCVLRAMPVYKKAEHVTEVVKRCPNHELGRDENE <mark>A</mark> GOTAPPSHLTRVEGNNHAOYAEDAV
Lampio1_p + o	* :* *.::**::*::*::*:*::*: ::*:. ::*:
Lamprey_p53	TGRQSVRLPYEPP <mark>QV</mark> GTDFSTVLLNFMCNSSCVGGMNRRPISVIITLEAS <mark>D</mark> GQVLGRRSF
Lamprey_p63	TGRQSVVMLFEFP <mark>QV</mark> GTDFTKVMFCFMCNTSCLGSMNRRPIYTILTMETL <mark>N</mark> GQVLGRFCC
Lamprey_p73	SGRQSVVVPYDSP <mark>QV</mark> GTEFTTVLYNFMCNSSCVGGMNRRPVLIIITLETR <mark>D</mark> AQVLGRRCF
	•***** • •• *****•*• *• ****•**********
Lamprey n53	EARTCACPERDRKSDEENLRKOEREOEREOOGPARVTPPPPPPPLAVNGGT
Lamprey_p55	
Lamprov p73	
Tambrey_b/2	LAKICACFGNDRADEENFHRQQQFLDFAGGGA
Lamprev p53	RSS-LVLPASGOITLSSDSEGPSVR
Lamprev p63	
Lamprev p73	SAV-GGLGGPGKRPMKOGSPGL-
	· · · · · · · · · · · · · · · · · · ·
Lamprey_p53	VFTGKR <mark>L</mark> RKAHYLATKRSRPDEKEE-LFLI <mark>PV</mark> RGRENYELLLHLKESLEMKQLVPQQAME
Lamprey_p63	KVVHDMLM-IS-SNVGNKRPSDQEDIFPLL <mark>VV</mark> QGRENFEILKKIKESLELMRMLPKDTVN
Lamprey_p73	HTSSGTKKRRLGDDD-VYYV <mark>PV</mark> HGRENYEVLMKIKESLELSQFVPSGAVE
	··* ··· · * *·******* ··**************
Lamprov p53	
Lamprov p63	
Lamprey_p03	
rambrey_b/2	* * *
Lamprey p53	
Lamprey p63	LTVVEANGSNGPPRSPDGDSPPAWPETLPDSSKPQNTIS <mark>N</mark> FLKQMDCFEFLENFTS
Lamprev p73	TPMLNGHTGLHGDLNGVSSTOLHLPTPTHCTPPPYSPESVASFLTRLGCVACVDFFTS
Lamprey_p53	
Lamprey_p63	RGLLSLQQLKNFTL <mark>QD</mark> LDKLGVPEAKRQLLLSGIQEHRVSTTIFSKTTLKRSPSEETVHL
Lamprey_p73	QGLQYANEVAQLSP <mark>QD</mark> LEMLKIPEQYRAAIFKGILELRSPLHDYGTPSHPPPPHPLQQHQ
Lamprey p53	
Lamprey p63	SPEDDDNGIDTKDGIRAKVFPALQASGSNLSSVSNHSHNSGISKYIFRVH
Lamprey p73	QQHQQQQQQHQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ
· · ·	
Lamprey_p53	
Lamprey_p63	ARQTIYLPRSGSWGGSSSLEVPRSKMRKLSSCSDTEEEERLE
Lamprey_p73	LKQTVQMPRHHDWVEYG-FDLPDGAKRCKQQQQQQIKEEYKEVH

Phase 0 intron Phase 1 intron Phase 2 intron

Lamprey Eshark Zebrafish	1 MNS <mark>G</mark> HVEC	SALLTDE <mark>P</mark> TCS]	C <mark>GG</mark> ECQRCE <mark>P</mark>	LA <mark>P</mark> RW <mark>P</mark> RI <mark>P</mark> S	LLVFRLA <mark>DPPG</mark> I	R <mark>gs</mark> wl <mark>es</mark> cch <mark>s</mark> t	-M1 :M64
Chicken	1					HESWKESVYRS	M20
Mouse	1		-MNFETSRCATI	LOYC <mark>P</mark> E	PYIORFIETPA	HESWKESYYRSA	M40
Human	1		-MNFETSRCAT	LQYC <mark>P</mark> D	PYIQRFVETPAN	HF <mark>S</mark> WK <mark>ES</mark> YYR <mark>S</mark> I	M 40
Lamprey	2 DS <mark>SPP</mark> IE <mark>D</mark>	LL <mark>S</mark> Q <mark>D</mark> TM <mark>Q</mark> LIY	IDITS <mark>G</mark> NSML <mark>S</mark>	IDN <mark>VD</mark> LRF	DESPGSKL	ZINMEVLQMENK	KN 60
Eshark	65 <mark>SQ<mark>G</mark>SQ</mark> SS <mark>D</mark>	LLNQ <mark>D</mark> WFNQLF <mark>I</mark>	LAAQPVLN	V <mark>QP</mark> ISLSFS <mark>D</mark>	ELR <mark>EG</mark> F <mark>PG</mark> T <mark>RI</mark>	EISMDGVRMQDS	<mark>e</mark> 126
Zebrafish	1					MLYL <mark>E</mark> TN	IA 8
Frog	1					MAYLDAI	DS 8
Chicken	21 SQSSQPRE	FL <mark>SPE</mark> VIQHIWI	FLEQPICS	VQPIDLNFID	DPSENGPTNKI	EISMDCVRLQDI	E82
Mouse Human	41 SQSTQTSE 41 SQSTQTNE	FLSPEVFQHIWI FL <mark>SPE</mark> VFQHIWI)FLEQPICS)FLEQPICS	VQPIELNFVD V <mark>QPIE</mark> LNFVD	EPSENGATNKI EPSED <mark>G</mark> ATN <mark>K</mark> II	EISMDCIRMQDS EI <mark>SMD</mark> CIRMQDS	D102 D102
Lamprou							0110
Lampiey	127 DDD	<u>Р</u> ЕМVSQQ <mark>Р</mark> VS I I			IAQQQINERQI CCTCDVNE_UT	GDF2MCFUQGT	162
Zehrafish	$9 \mathbf{p} \mathbf{q} \mathbf{q} \mathbf{v} \mathbf{v} \mathbf{v} \mathbf{v} \mathbf{v} \mathbf{v} \mathbf{v} v$	S F		SMDONCCS			
Frog		T.					- 45
Chicken		کلیے MN	POYTNI,GLUNS		SSTSPYNTEHA-		-119
Mouse		MV	POYTNIGLIN		SSTSPYNTDHA-		-139
Human	103 L <mark>SDP</mark>	MV	PQYTNLGLLN:	SM <mark>D</mark> QQIQN <mark>G</mark> S	SSTSPYNTDHA-		
Lamprey	119 CIA <mark>P</mark> MVA <mark>N</mark>	STAGFCPSTEP1	LC <mark>GPMV</mark> S <mark>PS</mark> L	PLEM <mark>PG</mark> QL <mark>Y</mark> G	STIPSNTDYKGI	PENETVNESPSS	<mark>ст</mark> 182
Eshark	163S <mark>N</mark>	NV <mark>T</mark> A	PSPYAQPSS	IFDTLSPS	PAIPSNTDYPG	HGFDVSFQQSS	<mark>ст</mark> 209
Zebrafish	44 <mark>Q</mark> N	NV <mark>T</mark> A	<mark>pspyaqpss</mark>	IF <mark>E</mark> AL <mark>SP</mark> S	PAIPSNTDYAG	PHTFDVSFQQSS	<mark>зт</mark> 90
Frog	46QN	sv <mark>t</mark> a	<mark>pspyaqpss</mark>	IFDAL <mark>SP</mark> S	PAIPSNTDYPGI	PHSFDVSFQQSS	<mark>зт</mark> 92
Chicken	120QN	sv <mark>t</mark> a	<mark>pspyaqpss</mark>	IFDAL <mark>SP</mark> S	PAIPSNTDYPGI	PHSFDVSFQQSS	<mark>ст</mark> 166
Mouse	140 <mark>QN</mark>	SV <mark>T</mark> A	<mark>PSPYAQP</mark> SS	F <mark>D</mark> AL <mark>SP</mark> S	PAI <mark>PSNT</mark> DYPGI	PHSFDVSFQQSS	<mark>ст</mark> 186
Human	140 <mark>QN</mark>	SV <mark>T</mark> A	<mark>PSPYAQP</mark> SS	IF <mark>D</mark> AL <mark>SP</mark> S	PAI <mark>PSNTDY</mark> PGI	PHSFDVSFQQSS	ST <mark>186</mark>
Lamprey	183 A <mark>ksatwtf</mark>	STKL <mark>KK</mark> LYCQMS	KICPAEIRTS	TLPP <mark>Q</mark> G <mark>T</mark> IIR	IMAMF <mark>KKSEH</mark> I	SEVV <mark>RRCP</mark> T <mark>HQ</mark> Ç	2 <mark>8</mark> 246
Eshark	210 A <mark>K</mark> SATWTY	S <mark>P</mark> EL <mark>KK</mark> LYCQI <i>I</i>	A <mark>KTCPIQI</mark> KVM	IQPPAGAVV <mark>R</mark>	AM <mark>PVY</mark> KKAEHV.	<mark>levvkrcpnhe</mark> i	<mark>s</mark> 273
Zebrafish	91 A <mark>K</mark> SATWTY	STEL <mark>KK</mark> LYCQIA	A <mark>KTCPIQ</mark> I <mark>K</mark> VL	I <mark>NPPQ</mark> GAVI	AM <mark>PVYKKAEH</mark> V.	IEVV <mark>KRCPNHE</mark> I	<mark>S</mark> 154
Frog	93 A <mark>K</mark> SATWTY	STDL <mark>KK</mark> LYCQI <i>I</i>	A <mark>KT</mark> CPIQV <mark>K</mark> VM	<mark>TPPPQ</mark> GAVV <mark>R</mark>	AMPVYKKAEHV.	TEVVKRCPNHEI	<mark>.s</mark> 156
Chicken	167 AKSATWTY	STELKKLYCQI <i>I</i>	AKTCPIQIKVM	IPPPQGAVIR	AMPVYKKAEHV.	TEVVKRCPNHEI	S 230
Mouse Human	187 AKSATWTY 187 AKSATWTY	STELKKLYCQIA STELKKLYCOIA	AKTCPIQIKVM AKTCPIQIKVM	IPPPQGAVIR IPPPOGAVIR	AMPVYKKAEHV Ampvykkaehv	IEVVKRCPNHEI IEVVKRCPNHEI	S250 S250
Lamprey	247 PELNHGSI	APVTHLIR	/EGN RNVRYI	EEHPVTGRQS	VVMLFEFPQVG:	IDFTKVMFCFMC	N 305
Eshark	274 REFNDGQV	APPSHLIR	EGNSHAQY	VEDPITGRQS	VMVPYEPPQVG	FEFTTILYNFMC	N 332
Zebraiish	155 REFNDGQL	APPSHLI <mark>R</mark> \	EGNSHAQY	VEDSITGRQS	VLVPYEPPQVG'	LEF.L.LTTTTTANE.WC	N213
Frog	15/ REFNEGMS		IVKFCHGQILY	VNNTVCRYRK	GTLPYQLAQVG'	LEF.L.LTTTTANE.WC	
Chicken	231 REFNEGQL	APPSHLIR	EGNSHAQY	VEDPITGRQS	VLVPYEPPQVG'	LEF.L.LATAFMC	N 289
Mouse	251 REFNEGQL	APPSHLIR	EGNSHAQY	VEDPITGRQS	VLVPIEPPQVG.		N 309
Human	221 KELNEGÖT	APPSHLI <mark>K</mark> /	EGNSHAQY	VEDP11G <mark>R</mark> QS	VLV <mark>PIEPPQ</mark> VG.	Ľ₽₽ĨŢŢŲĿ <u>¥</u> Ŋ₽M <mark>C</mark>	N 309
Lamprey	306 TSCLGSMN	RRPI <mark>YT</mark> IL <mark>T</mark> MET	L <mark>NGQ</mark> VLGRFC	C <mark>ETR</mark> VCA <mark>S</mark> PG	RDKKMDEQRM <mark>Q</mark> I	KDDQERQQQQ <mark>P</mark> I	s369
Eshark	333 SSCVGGMN	RRPILIIVTLEN	IRDGQVLGRRCI	FEARICACPG	RORKADEDSIR	KQQVTEGT	391
Zebrafish	214 SSCVGGMN		RDGQVLGRRCI	FEARICACPG	RDRKADEDSIR	QHVTDGT	272
Frog	221 SSCVGGMN	RRPILIIVTLE	RDGQVLGRRCI	FEARICACPG	RURKADEDSIR	KQQVSDST	279
Chicken	290 SSCVGGMN	RRPILIIVTLE		FEARICACPG	RURKADEDSIR	QQVSDST	348
MOUSE	310 SSCVGGMN	KRPILIIVTLEI		TEARICACPG	RORKADEDSIR		368
нuman	310 <mark>SSCVGGMN</mark>	KK ^P ILIIV <mark>I</mark> L <mark>E</mark> J		E EARICACPG	RDRKADED <mark>S</mark> IRI	VQVSDST	368

Coffill and Lee et al. Fig S5, Panel A

Lamprey	370 <mark>p</mark> tt <mark>on</mark> si	PT <mark>T</mark> QNS <mark>P</mark> TTQNS <mark>P</mark> TTQN <mark>AP</mark> Q	SVQQ <mark>YP</mark> TLAEAETQTSÇ	Q <mark>P</mark> TNQ <mark>PP</mark> QA <mark>Q</mark> PVEHT <mark>P</mark> QV	PKSS433
Eshark	392 <mark>KN</mark> GI	DA <mark>T</mark> KRL	R	HV	403
Zebrafish	273 <mark>K</mark> SSI	<u>A</u>	<mark>F</mark>	<mark>RQ</mark>	280
Frog	280 <mark>KN</mark> GI	<mark></mark> <mark>A</mark>	<mark>F</mark>	<mark>RQ</mark>	287
Chicken	349 <mark>KN</mark> GI	<mark>DGT</mark> KR <mark>P</mark>	<mark>F</mark>	<mark>RQ</mark>	360
Mouse	369 <mark>KN</mark> GI	DGTKR <mark>P</mark>	<mark>F</mark>	<mark>RQ</mark>	380
Human	369 <mark>KN</mark> GI	DG <mark>T</mark> KR <mark>P</mark>	<mark>F</mark>	<mark>RQ</mark>	380
Lamprey	434 S <mark>G</mark> SSQ <mark>P</mark> I	PS <mark>GEP</mark> TSDTSSQ <mark>G</mark> CKKVV <mark>H</mark> D	MLMIS <mark>S</mark> NV <mark>G</mark> NKRP <mark>S</mark> DQE	DIF <mark>P</mark> LLVV <mark>QGRE</mark> NFEII	.K <mark>KIK</mark> 497
Eshark	404	Q <mark>GI</mark> Q	e <mark>VA</mark> SI <mark>TS</mark> KKRRPG-E	EELF <mark>Y</mark> LPV <mark>RGRE</mark> TYEVI	L <mark>KIK</mark> 442.
Zebrafish	281	S <mark>SH</mark> L	<mark>SQ</mark> LN <mark>S</mark> I <mark>KKRR</mark> ST-I	DEEVFCL <mark>PIKGREIYE</mark> II	V <mark>KIK</mark> 319
Frog	288	S <mark>TH</mark> G	IQM <mark>TS</mark> I <mark>KKRR</mark> SP-I	DEVL <mark>Y</mark> LPV <mark>KGREIYE</mark> MI	L <mark>KIK</mark> 325
Chicken	361	<mark>GTH</mark> G	IQM <mark>TS</mark> I <mark>KKRR</mark> SP-I	DELL <mark>Y</mark> LPV <mark>RGRETYE</mark> MI	L <mark>KIK</mark> 398
Mouse	381	NTHG	IQM <mark>TS</mark> IKKRRSP-I	DELL <mark>YL</mark> PV <mark>RGRETYE</mark> MI	L <mark>KIK</mark> 418
Human	381	N <mark>TH</mark> G	I <mark>Q</mark> MTSIKKRRSP-I	DELL <mark>Y</mark> LPV <mark>RGRETYE</mark> MI	L <mark>KIK</mark> 418
Lamprey	498 <mark>ES</mark> LELM	RMLPKDTVNVLRNLQQKRYM	MEL <mark>RGR</mark> PA <mark>S</mark> LSR <mark>HO</mark>	SEC	<mark>S</mark> Q <mark>E</mark> 543
Eshark	443 ESLELM	OLLPOHTIESYROOOO	HLLOKO-SSLOSOOSFO	TSPPPMNKMPSMGNKLE	svso501
Zebrafish	320 ESLELM	OFLPOOTIESYBOOHO	NLLOKO-SSLPPOPAFO	SSSPTLGKNKLE	svso373
Frog			HLLOKO-SSLPGOSSFC	STSPPLGKMNNM-NKLF	SVS0383
Chicken				SNSPPI.SKMNSM-NKLE	SVSO460
Mouse				NSSDDI NKMNSM-NKI I	
Uuman					
пишап			TTTÄVÄ-191Å9516		
Lamprey	544 <mark>VL<mark>NG</mark>S<mark>Q</mark></mark>	GS <mark>SS</mark> AGVG <mark>SS</mark> SGVAQ <mark>NG</mark> LTV	'VE <mark>A</mark> N <mark>GS</mark> N <mark>C</mark>	<mark>PPRSP</mark> DGD	<mark>S</mark> 586
Eshark	502 LIS <mark>PQ</mark> -I	RNPITHSGMPGNL	V <mark>P</mark> QMM <mark>G</mark> N <mark>P</mark> M	IQMN <mark>GDLN</mark> GL <mark>SPTQ</mark> GLPF	<mark>М</mark> 546
Zebrafish	374 LI <mark>NPQQ</mark> I	RNALTPSGMPGGLTDSLLQS	Q <mark>PFPL</mark> PSVT <mark>PPMMGGP</mark> V	/ <mark>P</mark> MNT <mark>D</mark> LSSL <mark>SP</mark> NN <mark>P</mark> LQ <mark>S</mark>	QLQM437
Frog	384 LMNPQQ	RNSL <mark>TP</mark> NAMSDGMGA <mark>N</mark> ILIM	IIF <mark>P</mark> FLV <mark>P</mark> MMS <mark>TH</mark> M	1 <mark>PMTSDLNGLSPSQ</mark> TLPE	SL <mark>S</mark> L443
Chicken	461 LINPOO	RNALTPTTIPDGMGTNI	<mark>P</mark> MM <mark>GT</mark> HM	1AMT <mark>GDMNGLSPTQ</mark> ALPE	PLSM 511
Mouse	481 LINPOO	RNALTPTTMPEGMGANI	<mark>P</mark> MM <mark>GT</mark> HM	IPMAGDMNGLSPTOALPE	PL <mark>S</mark> M531
Human	481 LI <mark>NPQQ</mark> I	RNALTPTTIPDGMGANI	PMMGTHN	1 <mark>PMAGDMNGLSPTQ</mark> ALPE	PL <mark>SM</mark> 531
Lamprey	587 <mark>pp</mark> aw <mark>p</mark> e	ILPDSSKPONTISNFLKOMD	CFEFLENF <mark>TSRG</mark> LL <mark>S</mark> LQ	QLKNFTLQDLDKLGVPE	AK <mark>R</mark> Q650
Eshark	547 PTTSHC	IPPPPYPSDNSISSFLARVG	CAVCLEYFTTOGLINIY	OIEHFTMDDLMSLKIPE	OFRH 610
Zebrafish	438 VPSSHC	TPPPPYPMDNSISSFLLRLG	CSACLDYFTAOGLTNIY	OIENYNLEDLSRLKIPI	EFOH 501
Frog	444 PSTSHC	PPPPYPSDCSTASFLARLG	CSSCLDYFTTOGLNTI	OTENYSTEDLASLKTPD	OFRH 507
Chicken	512 PSTSHC	PPPPYPTDCSTVSFLABLG	CSSCVDYFTTOGL TTIN		OFRH 575
Mouse	532 PSTSHC	PPPPYPTDCSTVSFLARLG	CSSCI.DYFTTOGI.TTI	OTEHYSMDDLASLKIPF	
Human	532 PSTSHC	IPPPPYPTDCSIVSFLARLG	CSSCLDYFTTQGLTTI	QIEHYSMDDLASLKIPE	QFRH 595
Lamprev	651 LLLS <mark>G</mark> T	DEHRVSTTIFSKTTLK <mark>RSP</mark> S	EE-TVHLSPEDDDNGT	TKDGIRAKVF <mark>P</mark> ALOASC	SNLS713
Eshark	611 ATWKGT	VEHROSLEYAGTPOLL PNTS	SASSGSLASOSETRCE	V	654
Zehrafish	502 TTWKGT	VEYROTMEFSPPPHTI.RTSS	CTSTUSV-CSTEARCEE		544
Frog		VEHROMHDETS POHLL RTTS	SASTUSV-CONEPRCEE		550
Chicken			CASTUSU-CSSETRCEL	W	618
Mource	506 ATWRCT			V V	010
Human	506 ATWRGT				دعم دعم
Hullian	596 AIW <mark>K</mark> GI	DUKÄTHEL22521TTKI.52	SASIVSV-GSSEIRGEF	v	638
Lamprey	714 SVSNHS	HNS <mark>G</mark> ISKYIF <mark>R</mark> VHA <mark>RQT</mark> IYL	PRSGSWGG <mark>S</mark> SSLEVPRS	KMR <mark>K</mark> LSSCSDTEEEERI	JE 774
Eshark	655	IDAVRFTLRQTISF	'PPRDDWNDFGFDVDC	GRRN-K <mark>QRIKEEGE</mark>	- 695
Zebrafish	545	IDAVRFTLRQTISF	PPRDDWTDFSFDLAPDS	S <mark>RRNKQQRI</mark> KEEGE	- 588
Frog	551	IDAVRFTLRQTISF	PPRDDWNDFNFDLD	RRN <mark>KQQ</mark> RIKEEGE	- 592
Chicken	619	IDAVRFTLRQTISF	'PPRDEWNDFNFDMDA	A <mark>RRNKQQR</mark> IKEEGE	660
Mouse	639	IDAVRFTLRQTISF	'PPRDEWNDFNFDMDS	SRRN <mark>KQQ</mark> RIKEEGE	680
Human	639	I <mark>D</mark> AV <mark>R</mark> F T L <mark>RQT</mark> ISF	'PPRDEW <mark>ND</mark> F <mark>N</mark> FDMDA	A <mark>RR<mark>NKQQ</mark>RIKEEGE</mark>	- 680

Coffill and Lee et al. Fig S5, Panel B

Lamprey	
Eshark	1MAQSSPADEGHTFENLWSSLEPDSTYFDIPQTNL <mark>SG</mark> NNEAVPNL <mark>PQNRTE</mark> VCMDVFQMR 59
Zebrafish	1M <mark>SQSSTADEGPTFEHLWSTLEPDSTYFELPQAG</mark> H <mark>SG</mark> DRA- <mark>S</mark> SSL <mark>PGN</mark> RA <mark>E</mark> VCM <mark>DVY</mark> HMR 58
Frog	1 LKM <mark>SQSSGADEGTTFEHLWSTLEPDSTYFEL</mark> PQSSH <mark>S</mark> NNT <mark>E-ASNRTD</mark> VNMDVYQMR 56
Chicken	1M <mark>SQSSP</mark> ADESTTFEHLWSTLAPDSTYFDLSPSSH <mark>TG</mark> SNE-VS <mark>N</mark> RTEVTMDVFQMR 54
Mouse	1MAQ <mark>T</mark> S <mark>SSSSSTFEHLWSSLEPDSTYFDLPQPS</mark> Q- <mark>G</mark> TS <mark>E-AS</mark> GSEESNMDVFHLQ 52
Human	1 MAQ <mark>S</mark> TA <mark>T</mark> S <mark>PDGGTTFEHLW<mark>SS</mark>LEPDSTYFDLPQSS</mark> R- <mark>G</mark> NN <mark>E</mark> -VV <mark>GGTD</mark> SSMDVFHLE 55
Lamprey	1 -MLY <mark>V</mark> SN <mark>TS</mark> QAQY <mark>GGP<mark>QY</mark>T<mark>T</mark>LL<mark>GP</mark>V<mark>S</mark>AA<mark>GVQGAP</mark>RMER<mark>GGSP</mark>F<mark>GSEPGGPLASPSPYAQPS</mark> 60</mark>
Eshark	60DM <mark>NES</mark> VMSQFNLLNSTMDQSISNRASSGSPYNSEHTSNVPTPSPYSQPS 108
Zebrafish	59 DMRDM <mark>ND</mark> NVM <mark>SQY</mark> SLLSSSMDQGLGNRAASTSPYSSETTSNVPTPSPYSQPN 110
Frog	57TM <mark>NES</mark> IMSQFNLLNNTMDQSIGSRAASTSPYNPDHTSNVPTHSPYSQPS 105
Chicken	55 <mark>GMNDS</mark> VMSQFNLLNNSMDQSIGSRAASTSPYSSEHTSNVPTHSPYSQPS 103
Mouse	53 <mark>G</mark> MAQFNLLSSAMDQ-MGSRAAPASPYTPEHAASAPTHSPYAQPS 95
Human	56 <mark>G</mark> MTT <mark>SVM</mark> AQFNLLSSTMDQ-MS <mark>SR</mark> AASASPYTPEHAASVPTHSPYAQPS 103
Lamprey	61 <mark>stye</mark> aa <mark>sp</mark> aaai <mark>psitdypgphg</mark> fdv <mark>sfqqsstaksatwtysp</mark> dl <mark>kklycq</mark> ia <mark>ktcpiqfk</mark> 121
Eshark	109 STFDTMSPAPAIPSNTDYPGPHLFEVTFQQSSTAKSATWTYSPLLKKLYCQIAKTCPIQAK 169
Zebrafish	111 STFEAMSPAPAIPSNTDYPGPHNFEVTFQQSSTA <mark>K</mark> SATWTYSPLL <mark>KK</mark> LYCQIAKTCPIQIK 171
Frog	106 STFDAMSPAPVIPSNTDYPGTHNFEVTFQQSSTAKSATWTYSPLLKKLYCQIAKTCPIQIK 166
Chicken	104 <mark>STFD</mark> AM <mark>SPAP</mark> VI <mark>PSNTDYPGPHHFEVTFQQSSTA</mark> KSATWTYSPLLKKLYCQIAKTCPIQIK 164
Mouse	96 <mark>STFD</mark> TM <mark>SPAP</mark> VI <mark>PSNTDYPGPHHFEVTFQQSSTA</mark> KSATWTYSPLLKKLYCQIAKTCPIQIK 156
Human	104 <mark>STFD</mark> TM <mark>SPAPVIPSNTDYPGPH</mark> HFEV <mark>T</mark> FQQSSTA <mark>K</mark> SATWTYSPLL <mark>KK</mark> LYCQIAKTCPIQIK 164
Lamprey	122 VL <mark>S</mark> VPPPPAGCVLRAMPVYKKAEHVTEVVKRCPNHELGRDF <mark>NEAGQT</mark> APPSHLIRVEGNNH 182
Eshark	170 V TSL^{PPSGSVVR} AM <mark>PVYKK</mark> AEHVTEVVKRCPNHELGRDFND-GQSAPASHLIRVEGNNL 227
Zebrafish	172 LA <mark>SSPPNGSVIRAMPIYKKAEHVTEVVKRCPNHELGRDFNE-SQT</mark> APASHLIRVEGNNL 229
Frog	167 L <mark>SNPPPPGSVIRAMPVFKKAEHVTEVVKRCPNHELGRDFND-GQAAPASHLIRVEGNN</mark> L 224
Chicken	165 V <mark>SSPPPPGTIIR</mark> AM <mark>PVYKKAEHVTEVVKRCPNHELGRDFND-GQSAPASHLIR</mark> VEGNNL 222
Mouse	157 V <mark>STPPPPGTAIR</mark> AM <mark>PVYKK</mark> AEHVTDIVKRCPNHELGRDFNE-GQSAPASHLIRVEGNNL 214
Human	165 V <mark>STPPPPGTAIR</mark> AMPVYKKAEHVTDVVKRCPNHELGRDFNE-GQSAPASHLIRVEGNNL 222
Lamprey	183 A <mark>qyaedavsgrqsvvvpydspqvgte</mark> f <mark>ttvlynfmcnsscvggmnrrp</mark> vliiitletrdaq 243
Eshark	228 AQYVDDPVTGRQSVMVPYEPPQVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLETRDGQ 288
Zebrafish	230 CQYVDDPVTGRQSVLVPYESPQVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLETRDGQ 290
Frog	225 SQYVDDPVTGRQSVMVPYEPPQVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLETRDGQ 285
Chicken	223 SQYVDDPVTGRQSVMVPYEPPQVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLETRDGQ 283
Mouse	215 AQYVDDPVTGRQSVVVPYEPPQVGTEFTTILYNFMCNSSCVGGMNRRPILVIITLETRDGQ 275
Human	223 SQYVDDPVTGRQSVVVPYEPPQVGTEFTTILYNFMCNSSCVGGMNRRPILIIITLEMRDGQ 283
Lamprey	244 <mark>VLGRRCFEARICACPGRDRKADEENF</mark> HR <mark>QQ</mark> Q <mark>PLDPAGGG</mark> K <mark>GG</mark> TSAV <mark>GGLGGPGKRPMKQGS</mark> 304
Eshark	289 VLGRRSFEGRICACPGRDRKADEDHYREQQAINENAAKNANGSKRPFKQTP 339
Zebrafish	291 VL <mark>GRRSFEGRICACPGRDRKADEDHFREQQ</mark> ALNESVAKNGNANKRNFKQTP 341
Frog	286 VL <mark>GRRSFEGRICACPGRDRKADEDHFREQ</mark> AALNETAAKNGNANKRTFKQSP 336
Chicken	284 VL <mark>GRRS</mark> FEGRICACPGRDRKADEDHYREQQALNENAAKNGNANKRTFKQSP 334
Mouse	276 VL <mark>GRRS</mark> FEGRICACPGRDRKADEDHYREQQALNESTTKNGAASKRAFKQSP 326
Human	284 VL <mark>GRRS</mark> FEGRICACPGRDRKADEDHYREQQALNESSAKNGAASKRAFKQSP 334

Coffill and Lee et al. Fig S6, Panel A

Lamprey	305 <mark>pglh-t</mark> ss <mark>gtkkrrlgdddvyyvp</mark> vh <mark>grenye</mark> vlm <mark>kikeslelso</mark> fv <mark>psgaveayrooooo</mark> 3	64
Eshark	340 PGAQGPTAGIKKRRHGDEEFFYVPVRGRENFEILMKIKESLELMELVPQQLIDSYRQQQQQ 4	00
Zebrafish	342 TNITGPSINIKKRRHGEEEMYYIPVRGRENFDILMKIKDSLELVEFVPQQLVDSYRQQQQQ 4	02
Frog	337 PSVPSMGSNI <mark>KKRR</mark> HGEDEIFYIPVRGRENFEILMKIKESLELVELVPQQLVDSYRQQQQQ 3	97
Chicken	335 QAIPALGPGVKKRRHGEEEMYYVPVRGRENFEILMKIKESLELVELVPQQLVDSYRQQQQQ 3	95
Mouse	327 PAIPALCTNVKKRRHGDEDMFYMHVRGRENFEILMKVKESLELMELVPQPLVDSYRQQQQQ 3	87
Human	335 <mark>pavp</mark> al <mark>gagvkkrr</mark> hgdedtyylqv <mark>rgrenfe</mark> ilm <mark>klkesle</mark> lmelvpqplvdsyrqqq 3	93
Lamprey	365 LFQQQPCDLFPPSLPRPCLQSQLPYPGPPLPMGPKLPSVSQFVGHGAMG 4	13
Eshark	401 QLLQRQQ-QA <mark>SSAYGA-VNPPMNKIPNVNK</mark> LPSVNQLVGQPSQHSPSTSVNLGPMG 4	54
Zebrafish	403 LLQRQNHVAS <mark>PSSYGTLNNMNKIHGPISKLPSVNQLVTQQTQQS</mark> AGPSASLSHMG 4	57
Frog	398 LLQRQTHLQS <mark>TSSYGP-VLSPMNKLHGGINK</mark> LPSVNQLVGQPNQHNSNAGPNMGPMG 4	53
Chicken	396 LLQRQNQLQT <mark>PSSYGP-VLSPMNK</mark> AHGGGINKLPSVNQLVGQPAQHSSGSAPSLGPMG 4	52
Mouse	388 QLLQR <mark>P</mark> SHLQ <mark>PPSYGP-VLSPMNK</mark> VHGGVNKLPSVNQLVGQPPPHSSAAGPNLGPMG 4	43
Human	394 QLL <mark>Q</mark> R <mark>P</mark> SHLQ <mark>PPSYGP-VLSP</mark> MNKVHGGMNKLPSVNQLVGQPPPHSSAAT <mark>PNLGP</mark> VG 4	49
Lamprey	414 TPMLNGHTGLHGDLNGVSSTQL-HLPTPTHCTPPP-YSP-ESVASFLTRLGCVAC 4	65
Eshark	455 PTLMNNHHHHHHYMPPNGNMNGGNPSQSTAMGPTSHCTPPPPYNADPALVSFLTGLGCPNC 5	15
Zebrafish	458 ANML <mark>GGHHMQSNGDVNG</mark> AHQSQSIVSTSHCTPPPPYNPDPSLVSFLTSLGCQNC 5	11
Frog	454 PSMLNSHPLQTNGEMNGAHSSQSMVSGSHCTPPPPYNADPSLVSFLTGLGCPNC 5	07
Chicken	453 <mark>PGMLN</mark> SHPMQPNGEMNGGHSSQSMVSGSHCTPPPPYNPDPSLVSFLTGLGCPNC 5	06
Mouse	444 <mark>SGMLN</mark> SHGH <mark>S</mark> MPANGEMNGGHSSQTMVSGSHCTPPPPYHADPSLV <mark>S</mark> FLTGLGCPNC 4	99
Human	450 <mark>pgmln</mark> n <mark>hg</mark> hav <mark>p</mark> angemssshsa <mark>qs</mark> mv <mark>sgshCtppppy</mark> hadpslv <mark>s</mark> fltglgcpnc 5	05
Lamprey	466 VDFFTSQGLQYANEVAQLSPQDLEMLKIPEQYRAAIFKGILELESPLHDYGTPSHPPPPHP 5	26
Eshark	516 LEYFTSQGLQTMYHLQNLSMEDLGALKIPEQYRLLIWRGLQEFKP-GHDYNSPQL 5	69
Zebrafish	512 IDYFTSQGLQSVYHLQTLTMEDLGALKIPEQFRLAIWRGLQEMKQ-GHDYGQ-QL 5	64
Frog	508 IEYFTSQ <mark>GLQNIYHLQNLTMEDLGALKIPEHYKS</mark> MIW <mark>RGIQE</mark> LNK-S <mark>HEYG</mark> AQQL 5	61
Chicken	507 IDYFTSQGLQNIYHLQNLSIEDLGALKIPEQYRMIIWRGLQELKQ-SHDYGAQQL 5	60
Mouse	500 IECFTSQGLQSIYHLQNLTIEDLGALKVPDQYRMTIWRGLQDLKQ-SHDCGQ-QL 5	52
Human	506 IEYFTSQGLQSIYHLQNLTIEDLGALKIPEQYRMTIWRGLQDLKQ-GHDYSTAQQ 5	59
Lamprey	527 LQQHQQQHQQQQQQQQQQQQQQQQQQQQQQQQQQQQQQ	87
Eshark	570NNNPSVGGELQRQRVMEA 5	91
Zebrafish	565SNMATMAIGPSGELQRQRVMEA 5	90
Frog	562SNAS <mark>TISIG</mark> SSGELQRQRVMEA 5	87
Chicken	561SNAS <mark>TISIGSSGELQRQR</mark> VMEA 5	86
Mouse	553SNAATISIGGSGELQRQRVMEA 5	78
Human	560SNAATISIGGSGEL <mark>QRQR</mark> VMEA 5	85
Lamprey	588 <mark>VHFTL<mark>R</mark>QTV<mark>Q</mark>MPRHHDWVEYGFDLPDGAKR</mark> CKQQQ <mark>QQQIKEEY</mark> KEVH 6	34
Eshark	592 VHFRVRHTITIPNRGDDWGDFGFDVPDCKTRKQPIKEEFTENELN 6	36
Zebrafish	591 VHFRVRHTITIPNRGPANGPEEWPDFGFDMPDCRLHKHSIKEEFAEGDVH 6	40
Frog	588 VHFRVRHTITIPNRGGADEWADFGFDLPDCKSRKQSIKEEYENSDIN 6	34
Chicken	587 VHFRVRHTITIPNRGAADEWADFGFDLPDCKSRKQSIKEEFTEGEIN 6	33
Mouse	579 VHFRVRHTITIPNRGGAGAVTGPDEWADFGFDLPDCKSRKQPIKEEFTETESH 6	31
Human	586 VHFRVRHTITIPNRGGPGGGPDEWADFGFDLPDCKARKOPIKEEFTEAEIH 6	36

Coffill and Lee et al. Fig S6, Panel B



Coffill and Lee et al. Fig S7

Hs-TAp63α Hs-TAp63β Hs-TAp63γ Hs-ΔNp63α Hs-ΔNp63β	1 MNFETSRCATLQYC <mark>P</mark> DPYIQRFVET <mark>P</mark> AHFSWKESYYRST <mark>MSQS</mark> TQTN <mark>EFLSPEVFQHIW</mark> 1 MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQSTQTNEFLSPEVFQHIW 1 MNFETSRCATLQYCPDPYIQRFVETPAHFSWKESYYRSTMSQ <mark>S</mark> TQTNEFLSPEVFQHIW) 60 D 60 D 60
Hs-ΔNp63γ Lj-p63 Lj-p63B Lj-p63C	1MDS <mark>SPP</mark> IEDLLSQDTMQLIY 1MDS <mark>SPP</mark> IEDLLSQDTMQLIY 1MDS <mark>SPP</mark> IEDLLSQDTMQLIY 1MDS <mark>SPP</mark> IEDLLSQDTMQLIY	- N 21 N 21 N 21
Hs-TAp63α Hs-TAp63β Hs-TAp63γ Hs-ΔNp63α Hs-ΔNp63β Hs-ΔNp63γ Lj-p63 Lj-p63B Lj-p63C	61 FLEQPICSVQPIDLNFVDEPSEDGATNKIEISMDCIRMQDSDLS 61 FLEQPICSVQPIDLNFVDEPSEDGATNKIEISMDCIRMQDSDLS 61 FLEQPICSVQPIDLNFVDEPSEDGATNKIEISMDCIRMQDSDLS 1	- 104 - 104 - 10 - 10 - 10 - 10 P 76 P 76 P 76 P 76
Hs-TAp63α Hs-TAp63β Hs-TAp63γ Hs-ΔNp63α Hs-ΔNp63β Hs-ΔNp63γ Lj-p63 Lj-p63B Lj-p63C	105DPMWPQYTNLGLLNSMDQQIQNGSSSTS 105DPMWPQYTNLGLLNSMDQQIQNGSSSTS 105DPMWPQYTNLGLLNSMDQQIQNGSSSTS 11QFSEPQYTNLGLLNSMDQQIQNGSSSTS 11QFSEPQYTNLGLLNSMDQQIQNGSSSTS 11QFSEPQYTNLGLLNSMDQQIQNGSSSTS 77 VSTFPTYMQQQQQPDSGIAQQQYNEHQYFGDESWCENQGLSCIAPMVANSTAGFC 77 VSTFPTYMQQQQQPDSGIAQQQYNEHQYFGDESWCENQGLSCIAPMVANSTAGFC 77 VSTFPTYMQQQQQPDSGIAQQQYNEHQYFGDESWCENQGLSCIAPMVANSTAGFC	2 133 2 133 2 133 2 39 2 39 2 39 2 39 2 39 2 39 2 133 P 133 P 133
Hs-TAp63α Hs-TAp63β Hs-TAp63γ Hs-ΔNp63α Hs-ΔNp63β Hs-ΔNp63γ Lj-p63 Lj-p63B Lj-p63C	 134 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 134 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 134 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 YNTDHAQNSVTAPSPYAQPSSTFDALSPSPAIPSNTDYPGPHSFDVSFQQSSTAKSA 40 STEPILCGPMVSPSLPLEMPGQLYGSTIPSNTDYKGPFNFTVNFSPSSTAKSA 134 STEPILCGPMVSPSLPLEMPGQLYGSTIPSNTDYKGPFNFTVNFSPSSTAKSA 	F 191 F 191 F 191 F 97 F 97 F 97 F 187 F 187 F 187
Hs-TAp63α Hs-TAp63β Hs-TAp63γ Hs-ΔNp63α Hs-ΔNp63β Hs-ΔNp63γ Lj-p63 Lj-p63 Lj-p638 Lj-p63C	192 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 192 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 192 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 98 WTYSTELKKLYCQIAKTCPIQIKVMTPPPQGAVIRAMPVYKKAEHVTEVVKRCPNHELS 188 WTFSTKLKKLYCQMSKICPAEIRTSTLPPQGTIIRIMAMFKKSEHISEVVRRCPTHQQS 188 WTFSTKLKKLYCQMSKICPAEIRTSTLPPQGTIIRIMAMFKKSEHISEVVRRCPTHQQS	251 251 251 157 157 157 157 247 247 247 247

Hs-TAp63 $lpha$	252 <mark>e</mark>	EF <mark>NEGQIAPPSH</mark> LI	I <mark>R</mark> VEGNSHAQYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	311
Hs-TAp63β	252 <mark>e</mark>	EF <mark>NEG</mark> QIA <mark>PPSH</mark> LI	I <mark>R</mark> VEGNSHAQYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	311
Hs-TAp63y	252 <mark>e</mark>	EF <mark>NEG</mark> QIA <mark>PPSH</mark> LI	I <mark>RVEGNSHA</mark> QYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	311
Hs- $\Delta Np63\alpha$	158 <mark>8</mark>	EF <mark>NEG</mark> QIA <mark>PPSH</mark> LI	I <mark>R</mark> VEGNSHAQYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	217
$Hs - \Delta Np 63\beta$	158 <mark>B</mark>	EF <mark>NEG</mark> QIA <mark>PPSH</mark> LI	I <mark>R</mark> VEGNSHAQYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	217
$Hs - \Delta Np 63\gamma$	158 <mark>B</mark>	EF <mark>NEG</mark> QIA <mark>PPSH</mark> LI	I <mark>R</mark> VEGNSHAQYVED	PITGRQS	VLV <mark>PYEPPQ</mark>	V <mark>GTE</mark> FTTV	'L <mark>YN</mark> FM <mark>CNSS</mark>	217
Lj-p63	248 <mark>b</mark>	EL <mark>NHG</mark> SIAPVTHL	I <mark>RVEGN</mark> RNVR <mark>Y</mark> EEH	PVTGRQS	VVMLF <mark>efp</mark> q	V <mark>GTD</mark> F <mark>T</mark> KV	MFCFM <mark>CNTS</mark>	307
Lj-p63B	248 <mark>b</mark>	EL <mark>NHG</mark> SIAPV <mark>TH</mark> L	I <mark>RVEGN</mark> RNVR <mark>Y</mark> EEH	PVTGRQS	VVMLF <mark>efp</mark> q	V <mark>GTD</mark> F <mark>T</mark> KV	MFCFM <mark>CNTS</mark>	307
Lj-p63C	248 <mark>b</mark>	EL <mark>N</mark> HGSIAPV <mark>T</mark> HL	I <mark>RVEGN</mark> RNVR <mark>Y</mark> EEH	PVT <mark>GR</mark> QS	VVMLF <mark>E</mark> F <mark>PQ</mark>	V <mark>GTD</mark> F <mark>T</mark> KV	MFCFM <mark>CNTS</mark>	307
Hs-TAp63 $lpha$	312 0	CV <mark>GG</mark> M <mark>NRRP</mark> ILII	V <mark>TLETRDGQ</mark> VLGRR	CFEARIC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> IRKQ	QV <mark>SD</mark> ST <mark>K</mark>	369
Hs-TAp63 β	312 0	CV <mark>GG</mark> M <mark>NRRP</mark> ILII	V <mark>TLETRDGQ</mark> VLGRR	CFEARIC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> IRKQ	QV <mark>SD</mark> ST <mark>K</mark>	369
<i>Нs−ТАр63</i> γ	312 (CV <mark>GG</mark> M <mark>NRRP</mark> ILIIY	V <mark>TLETRDGQ</mark> VL <mark>G</mark> RR	CFEA <mark>R</mark> IC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> IRK <mark>Q</mark>	QVSDST <mark>K</mark>	369
Hs- $\Delta Np63lpha$	218 (CV <mark>GG</mark> M <mark>NRRP</mark> ILII	V <mark>TLETRDGQ</mark> VL <mark>GRR</mark>	CF <mark>EAR</mark> IC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> I <mark>RK</mark> Q	QVSDST <mark>K</mark>	275
Hs- $\Delta Np63eta$	218 (CV <mark>GG</mark> M <mark>NRRP</mark> ILII	V <mark>TLETRDGQ</mark> VL <mark>GRR</mark>	CF <mark>EAR</mark> IC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> I <mark>RK</mark> Q	QVSDST <mark>K</mark>	275
Hs- $\Delta Np63\gamma$	218 (CV <mark>GG</mark> M <mark>NRRP</mark> ILII	V <mark>TLETRDGQ</mark> VL <mark>GRR</mark>	CFEA <mark>R</mark> IC.	AC <mark>PGRDRK</mark> A	.DED <mark>S</mark> I <mark>RK</mark> Q	QVSDST <mark>K</mark>	275
Lj-p63	308 0	CLGSM <mark>NRRPIYT</mark> I:	L <mark>TMET</mark> LN <mark>GQ</mark> VL <mark>GR</mark> F	'CC <mark>ETR</mark> VC.	A <mark>SPGRDKK</mark> M	DEQRM <mark>Q</mark> KD	DQERQQ <mark>Q</mark> Q <mark>P</mark>	367
Lj-p63B	308 0	CLGSM <mark>NRRPIYT</mark> I	L <mark>TMET</mark> LN <mark>GQ</mark> VL <mark>GR</mark> F	CC <mark>ETR</mark> VC.	A <mark>SPGRDKK</mark> M	DEQRM <mark>Q</mark> KD	DQERQQ <mark>Q</mark> Q <mark>P</mark>	367
Lj-p63C	308	CLGSMNRRPIYTI	L <mark>TMET</mark> LN <mark>GQVLGR</mark> F	CCE <mark>TR</mark> VC.	A <mark>S</mark> PG <mark>RD</mark> KKM	DEQRM <mark>QK</mark> D	DQERQQ <mark>Q</mark> Q <mark>P</mark>	367
	270							270
HS - TAp 630	370 -	NGD						372
HS-TAP63p	370 -	NGD						372
$HS - TAp 63\gamma$	370 -	NGD						372
$HS - \Delta Np 63\alpha$	276 -	NGD						278
$HS - \Delta Np 63\beta$	276 -	NGD						278
$HS - \Delta Np 63\gamma$	2/6 -							278
Lj-p63	368	PSPTTQNSPTTQN:	SPTTQNSPTTQNAP	QSVQQYP	TLAEAETQT	SQPTNQPP	QAQPVEHTP	427
<i>Lj-р63В</i>	368	PSPTTQNS	PTTQNAP	QSVQQYP	TLAEAETQT	SQPTNQPP	QAQPVEHTP	415
<i>Lj-р63С</i>	368	PSPITIQ <mark>N</mark> S	PTTQNAP	QSVQQY <mark>P</mark>	TLAEAETQT	SQPTNQPP	QAQ <mark>P</mark> VEHT <mark>P</mark>	415
Hs-TAp63 α	373 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNT <mark>HG</mark> IQI	M <mark>TSI</mark> K	KRR <mark>SP</mark> DDE	LL <mark>Y</mark> LPV <mark>RGR</mark>	408
Hs-TAp63β	373 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNT <mark>H</mark> GIQI	M <mark>TS</mark> I <mark>K</mark>	KRR <mark>S</mark> PDDE	LL <mark>Y</mark> LPV <mark>RGR</mark>	408
Hs-TAp63y	373 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNTHGIQ	M <mark>TSIK</mark>	KRR <mark>SP</mark> DDE	LL <mark>Y</mark> LPVRGR	408
$Hs - \Delta Np 63\alpha$	279 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNTHGIQ	M <mark>TSIK</mark>	KRR <mark>SP</mark> DDE	LL <mark>Y</mark> LPVRGR	314
$Hs - \Delta Np 63\beta$	279 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNT <mark>H</mark> GIQI	M <mark>TS</mark> I <mark>K</mark>	KRR <mark>S</mark> PDDE	LL <mark>Y</mark> LPV <mark>RGR</mark>	314
$Hs - \Delta Np 63\gamma$	279 -	G <mark>T</mark> KRP	F <mark>R</mark>	QNTHGIQ	M <mark>TSIK</mark>	KRR <mark>SP</mark> DDE	LL <mark>Y</mark> LPVRGR	314
Lj-p63	428 Ç	QV <mark>P</mark> KSSS <mark>GS</mark> SQPP	S <mark>GE</mark> PTSDTSSQ <mark>GC</mark> K	KVV <mark>H</mark> DML	MI <mark>S</mark> SNV <mark>G</mark> NK	RPSDQEDI	F <mark>P</mark> LLVV <mark>QGR</mark>	487
Lj-p63B	416 🤇	QV <mark>P</mark> KSSS <mark>GS</mark> SQPP	S <mark>GE</mark> PTSDTSSQ <mark>GC</mark> K	KVV <mark>H</mark> DML	MI <mark>S</mark> SNVGN <mark>K</mark>	RPSDQEDI	F <mark>P</mark> LL-V <mark>QGR</mark>	474
Lj-p63C	416 ç	QV <mark>P</mark> KSSS <mark>GS</mark> SQPP:	S <mark>GE</mark> PTSDTSSQ <mark>GC</mark> K	KVVHDML	MI <mark>S</mark> SNVGNK	RPSDQEDI	F <mark>P</mark> LL-V <mark>Q</mark> GR	474
	400					atoan		450
HS - TAp 630	4091	ETYEMLLKIKESLI Inventionalise	ELMQYLPQHTIETY		HQHLLQKQT	SIQSP		456
HS-TAP63p	4091	ETYEMLLKIKESLI Inventionalise	ELMQYLPQHTIETY		HQHLLQKQT	SIQSP		456
$HS - TAP63\gamma$	409 H	STIEMLLKIKESLI	T MONT DOMETRICA		HÖHTTÖKHT	LSACERNE	TAR <mark>B</mark> KKEI. <mark>B</mark>	468
$HS - \Delta Np 63\alpha$	315 F	STYEMLLKIKESLI	SLMQYLPQHTIETY		HQHLLQKQT	SIQSP		362
$HS - \Delta Np 63\beta$	315 E	ETYEMLLKIKESL	ILMQYLPQHTIETY	RQQQQQQ	HQHLLQKQT	SIQSP		362
HS-ΔNp63γ	315 E	ETYEMLLKIKESLI	ILMQYLPQHTIETY	RQQQQQQ	HQHLLQKHL	LSACERNE	LVE <mark>P</mark> RRET <mark>P</mark>	374
<i>цр63</i>	488	INFEILKKIKESL	LMRMLPKDTVNVL		YMMELRGRP	ASLS		534
<i>Lj-р63В</i>	475 E	INFEILKKIKESL	ELMRMLPKDTVNVL	RNLQQKR	YMMELRGRP	ASLS		521
Lj-p63C	475 <mark>E</mark>	ENFEILK <mark>kikes</mark> li	<u>-</u> LMRML <mark>P</mark> KD <mark>T</mark> VNVL	I <mark>R</mark> NL <mark>QQ</mark> KR	YMMELRGRP	A <mark>S</mark> L <mark>S</mark>		521

Нѕ-ТАрб3α Нѕ-ТАрб3β Нѕ-ТАрб3γ	457SSYGNSSPPLNKMNSMNKLPSVSQLINPQQRNALTPTTIPDGMGANIPMMGTHM 5 457SSYGNSSPPLNKMNSMNKLPSVSQLINPQQRNALTPTTIPDGMGANIPMMGTHM 5 469 KOSDVFFRHSKPPNRSVYP	510 510 487
Hs- $\Delta Np63\alpha$ Hs- $\Delta Np63\beta$	363SSYGNSSPPLNKMNSMNKLPSVSQLINPQQRNALTPTTIPDGMGANIPMMGTHM 4 363SSYGNSSPPLNKMNSMNKLPSVSQLINPQQRNALTPTTIPDGMGANIPMMGTHM 4 275 KOSDVEEPHCKPPNCSVXP	416 416
Lj-p63 Lj-p63B	575 KQSDVFTKHGKFFNKSVTF 535RHGSECSQEVLNGSQGSSSAGVGSSSGVAQNGLTV 5 522RHGSECSQEVLNGSQGSSSAGVGSSSGVAQNGLTV 5	569 569 556
<i>р63С</i>	522RH <mark>GSEC</mark> SQEVLNGSQGSSSAGVGSSSGVAQNGLTV	226
Hs-TAp63α Hs-TAp63β Hs-TAp63γ	511 PMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVSFLARLGCSSCLDYFTTQ 5 511 PMAGDMNGLSPTQALPPPLSMPSTSHCTPPPPYPTDCSIVRIWQV5	568 555
Hs-ΔNp63α Hs-ΔNp63β	417 <mark>PMAG</mark> DM <mark>NGLSP</mark> TQAL <mark>PPP</mark> LSM <mark>P</mark> STSHC <mark>TPPPP</mark> YPTDC <mark>S</mark> IVSFLARL <mark>G</mark> CSSCLDYF TT Q 4 417 <mark>PMAG</mark> DM <mark>NGLSP</mark> TQALPPPLSMPSTSHCTPPPPYPTDC <mark>S</mark> IVRIWQV4	474 461
Hs-∆Np63γ Lj-p63 Lj-p63B	570 VEANGSNGPPRSPDGDSPPAWPETLPDSSKPQNTISNFLKQMDCFEFLENFTSR (557 VEANGSNGPPRSPDGDSPPAWPETLPDSSKPQNTISNFLKQMDCFEFLENFTSR (523 610
Lj-p63C	557 <mark>VEANG</mark> SNGPPR <mark>SP</mark> DGDSPPAWPETLPDSSKPQNTISNFLKQMDCFEFLENFTSR (510
Hs-TAp63α Hs-TAp63β Hs-TAp63γ	569 <mark>G</mark> LT <mark>T</mark> IY <mark>Q</mark> IEHY <mark>S</mark> MDDLASLKI <mark>P</mark> EQFRHAIWK <mark>G</mark> ILDHRQLHEFSS <mark>P</mark> SHLLRT <mark>P</mark> SSASTVSV (528
Hs $-\Delta Np63\alpha$ Hs $-\Delta Np63\beta$ Hs $-\Delta Np63\gamma$	475 <mark>G</mark> LT <mark>T</mark> IYQIEHY <mark>S</mark> MDDLASLKIPEQFRHAIWK <mark>G</mark> ILDHRQLHEFSSPSHLLRTPSSASTVSV 5	534
Lj-p63 Lj-p63B Lj-p63C	624 <mark>GLLSLQQ</mark> LKNFTLQDLDKL <mark>GVP</mark> EAKRQLLLS <mark>G</mark> IQEHRVSTTIFSKTTLKRS <mark>P</mark> SEETVHLS (611 GLLSLQQLKNFTLQDLDKLGVPEAKRQLLLSGIQEHRVSTTIFSKTTLKRSPSEETVHLS (611 GLLSLQQLKNFTLQVSS-FGRFHANYVFFFTYTGLGFIFKL (583 570 650
Hs-TAp63α Hs-TAp63β	629 GSSETRGERVIDAVRFTLRQTISFPPRD 6	656
$HS = TAP 63\gamma$ $HS = \Delta NP 63\alpha$ $HS = \Delta NP 63\gamma$	535 GSSETRGERVIDAVRFTLRQTISFPPRD 5	562
Lj-p63 Lj-p63B Lj-p63C	684 <mark>P</mark> EDDDNGIDTKDGIRAKVF <mark>P</mark> ALQASGSNLSSVSNHSHNSGISKYIFRVHARQTIYLPRSG 671 <mark>P</mark> EDDDNGIDTKDGIRAKVF <mark>P</mark> ALQASGSNLSSVSNHSHNSGISKYIFRVHARQTIYLPRSG 	743 730
Hs-TAp63α Hs-TAp63β	657 EWNDFNFDMDARRNKQQRIKEE <mark>G</mark> E	580
$Hs - TAp63\gamma$ $Hs - \Delta Np63\alpha$ $Hs - \Delta Np63\beta$	563 EWNDFNFDMDARRNKQQRIKEEGE	586
<i>Hs-</i> ΔNp63γ Lj-p63 Lj-p63B Lj-p63C	744 SW <mark>GG</mark> SSSL-EV <mark>P</mark> RSKMRKLSSCSDTEEEERLE 731 SW <mark>GG</mark> SSSL-EV <mark>P</mark> RSKMRKLSSCSDTEEEERLE	774 761

Coffill and Lee et al. Fig S8, Panel C

Lamprey	1MSAS <mark>PS</mark> ASS <mark>SSG</mark> VRKEDLV <mark>R</mark> PVPLLL <mark>R</mark> LLQ <mark>SVG</mark> AKSDTFTVQQVIHHLGQYIKTKQL5	57
Eshark	1 MARN- <mark>GP</mark> TACFST <mark>S</mark> NEQ <mark>Q</mark> LLA <mark>SEQ</mark> ESQV <mark>RPKP</mark> LLL <mark>K</mark> LLQFAGAQNEIFTIKEVMYYLGQYIMAKHL6	5
Zebrafish	1MATESCLSSSQISKVDNEKLVRPKVQLKSLLEDAGADKDVFTMKEVMFYLGKYIMSKEL5	9
Frog	1MNL-TS <mark>T</mark> TNCLENNHI <mark>STSDQE</mark> KLV <mark>QPTP</mark> LLLSLLK <mark>SAGAQ</mark> KETFTM <mark>KEVIYHLGQY</mark> IMA <mark>K</mark> QL6	52
Chicken	1 MCNTEMTSL <mark>TDG</mark> S <mark>PVS</mark> A <mark>SEQ</mark> EALV <mark>KPK</mark> PLLL <mark>K</mark> LLKLAGAEKDTFTMKEVIFYLGQYIM <mark>SK</mark> QL6	52
Mouse	1 MCNTNMSVS <mark>TEG</mark> AAST <mark>SQIPASEQE</mark> TLV <mark>RPKP</mark> LLL <mark>K</mark> LLK <mark>SVGAQ</mark> NDTYTMKEIIFYIGQYIMTKRL6	6
Human	1 MCNTNMSV <mark>PTDG</mark> AV <mark>T</mark> T <mark>SQIPASEQE</mark> TLV <mark>RPKP</mark> LLL <mark>K</mark> LLK <mark>SVG</mark> AQK <mark>DTYTMKE</mark> VLFYLGQYIMTKRL6	6
Lamprey	58 YDK <mark>QRQHIVHCKGDPLGEVFGVES</mark> F <mark>SLKEP</mark> SS <mark>SSGS</mark> VGALLAKAL <mark>SIA</mark> ATD-KRKD <mark>HTGVGDG</mark> AVK1	.22
Eshark	66 YDEKQQHVVHCSDNPLGRLFGVQSFSIKEPRTLYTMLSKNLIPLNPEDSASHLPLMKEI1	.24
Zebrafish	60 YDKQQQHIVHCGEDPLGAVLGVKSFSVKEPRALFALINRNLVTVKNPESQSTFSEP1	.15
Frog	63 YDEKQQHIVHCSNDPLGELFGVQEFSVKEPRRLYAMISRNLVSANVKESSEDIFGNV1	19
Chicken	63 YDEKEQHIVHCANDLLGDLFGVTSFSVKEHRRIYSMISRNLIAINQQDSTLAVPPEDDA1	21
Mouse	67 YDEKQQHIVYCSNDLLGDVFGVPSFSVKEHRKIYAMIYRNLVAVSQQDSGTSLSES1	.22
Human	67 <mark>YDEKQQHIVYCSND</mark> LL <mark>GD</mark> LF <mark>GVPS</mark> F <mark>S</mark> V <mark>KEHR</mark> KIYTMIY <mark>RN</mark> LVVVNQQESSDS <mark>G</mark> TSVSEN1	25
Lamprey	123 ESSLAAADGDNKQVALV <mark>V</mark> DS <mark>VRQGDPPHGG</mark> ST <mark>S</mark> T <mark>PMTG</mark> ATTVAA <mark>KR</mark> R-RD <mark>SE</mark> CGSGVVAA <mark>GS</mark> PEEE1	.87
Eshark	125NCE-LESEDYLRVR-SNEGTECTSCDVSPLHTSGRKSTYYDSD-NDVPSVEQ-1	.73
Zebrafish	116RSQSEPDRGPGDTDSDSRSSTSQQQRRRRRSSD-PESSSAED-1	.56
Frog	120CCF-PDKQSSQ <mark>KEK-LQELPD</mark> KLIAP-ASD <mark>S</mark> KPCNLSQRKSSNET-EEISSVDH-1	.69
Chicken	122KFR-LEKENVLKES-MQELEEKQ-TSSNATSQP-TTSRRRTHSES-EENSSDD-1	.69
Mouse	123RRQ- <mark>PEGG</mark> SDL <mark>KDP-LQ</mark> A <mark>PPE</mark> EK <mark>P</mark> SS <mark>S</mark> DLI <mark>S</mark> RLS <mark>TS</mark> <mark>S</mark> R <mark>RRS</mark> I <mark>SET</mark> -EENTDEL-1	.72
Human	126R <mark>C</mark> H- <mark>legg</mark> sdq <mark>kd</mark> l- <mark>vqelqe</mark> ek <mark>p</mark> ss <mark>s</mark> hlv <mark>s</mark> rps <mark>is</mark> <mark>s</mark> r <mark>rr</mark> ai <mark>sei-ee</mark> n <mark>s</mark> del-1	.75
Lamprey	188 DSGAK <mark>RPRAPSPAPPC</mark> WNDD <mark>DQGVPWWFLRSLP</mark> HTLDRVS <mark>T</mark> AS <mark>STD</mark> IC <mark>S</mark> RR <mark>GYE</mark> TAVVTDSSD2	:50
Eshark	174 PYTGR <mark>RKR</mark> H <mark>R</mark> SDSISLHWDD-LSLYLISKLRREHENCDSSSDSCSNADVDAGT2	25
Zebrafish	157 ESRER <mark>RKR</mark> H <mark>K</mark> S <mark>DSFSLTFDDSLSWCVIGGLH</mark> RERGN <mark>SESS</mark> DAN <mark>SN</mark> SDVGISR <mark>S</mark> EGS2	12
Frog	170 PAEQQ <mark>RKR</mark> H <mark>K</mark> SDSFSLTFDESLSWWVISGLRCDRNS <mark>SEST</mark> DS <mark>S</mark> SNSDPERHST2	22
Chicken	170 <u>LH</u> SDR <mark>RKR</mark> H <mark>K</mark> SDSISLTFDESLSWCVVSGLCRDRSNSSDSTDSVSIPDLDASSLSEN2	26
Mouse	173 <mark>PG</mark> ERH <mark>RKR</mark> RRSLSFDPSLGLCELREMCSGGSSSSSSSSSSSSSSESTETPSHQDLDDGVSEHS2	30
Human	176 S <mark>G</mark> ERQ <mark>RKRHKSDSISLSFDES</mark> LALCVIREICCERSSS <mark>SESTGTPSNPDLD</mark> AGV <mark>S</mark> EHS2	32
Lamprey	251 DLWFLD <mark>ES</mark> N <mark>SDQFS</mark> VEFEVESIHSEDYDGEGEDGESG-EHSSDDEVYDVTVIYSDSQS <mark>SY</mark> NESS3	:13
Eshark	226DGEDSSDKFSVEFEVESIHSEDYSEHSQELSDEEVYEVTIYEAAGSDEDSYNDDI2	80
Zebrafish	213 EESEDSDSDSDNFSVEFEVESINSDAYSENDVDSVPGENEIYEVTIFAEDEDSFDE2	68
Frog	223NDNSEHD <mark>SDQFS</mark> VEFEVESVC <mark>SDDYSP</mark> SGDEHGVSEEEEINDEVYQVTIYETEESETDSFDV2	84
Chicken	227 SDWFDH <mark>GSVSDQFSVEFEVESIYSEDYS</mark> HNEEGQELTDEDDEVYQLTIYQDEDSDSDSFNE2	87
Mouse	231 <mark>GDCLDQDSVSDQFSVEFEVES</mark> LD <mark>SEDYS</mark> LS <mark>DEG</mark> HEL <mark>SDEDDEVYRVTVYQ</mark> T <mark>GESDTDS</mark> FEG2	91
Human	233 GDWLDQDSVSDQFSVEFEVESLDSEDYSLSEEGQELSDEDDEVYQVTVYQAGESDTDSFEE2	93

Coffill and Lee et al. Fig S9, Panel A

Lamprey	314 <mark>daefp</mark> eedo	WRCTECSETNH	MHGYCQRCWCL	RKDWLPDAAKQQ	QQQEQQQQQQQHT	ITTTTSTL <mark>P</mark> 379
Eshark	281 <mark>dpeis</mark> aady	WKCENCGELNPI	PLPRYCH <mark>R</mark> CWFL	RRDWLPDKPKRQ	TC	326
Zebrafish	269 DTEITEADY	W <mark>KCPKCDQFNP</mark> I	PLPR <mark>HC</mark> KS <mark>C</mark> WTV	RADWLPETHSNW	<u>en</u> lsrntrtn <mark>p</mark> ed	I326
Frog	285 DTEISEADY	W <mark>KCPECGEVN</mark> PI	PLPSYCPRCWTV	<mark>R</mark> K DWLPE QRRKE	PP	330
Chicken	288 <mark>DPEIS</mark> LADY	WKCPECSEMNPI	PLPR <mark>HC</mark> HRCWAL	REDWLPDEKSDK	LV	333
Mouse	292 DPEISLADY	WKCTSCNEMNPI	PLPS <mark>HCK</mark> RCWTL	RENWLPDDKGKD	KV	337
Human	294 <mark>DPEIS</mark> LADY	WKCTSCNEMNPI	PLPS <mark>HC</mark> NRCWAL	REN <mark>WLPE</mark> DK <mark>G</mark> KD	K <mark>G</mark>	339
Lamprey	380 TTM <mark>G</mark> S <mark>P</mark> AA <mark>B</mark>	R <mark>G</mark> VFAM <mark>PG</mark> ITT	ALLEEALARN <mark>I</mark> C	SDD <mark>GH</mark> DEIDGRR	SKKTANE <mark>D</mark> DEDDE	Y <mark>E</mark> KAYEKEY 445
Eshark	327		NTD <mark>PLIE</mark>	QDE <mark>GIDVP</mark> DC <mark>KK</mark>	PSLETNESYC <mark>SE</mark> S	Q <mark>E</mark> T361
Zebrafish	327SVTTT <mark>e</mark>	NTTFEK	-KLSK <mark>P</mark> SS <mark>P</mark> L <mark>S</mark> E	TDD <mark>GVDVP</mark> DG <mark>K</mark> C	F <mark>P</mark> S <mark>P</mark> ATTKDELPS	374
Frog	331	<mark>P</mark> S	-KRKLLE <mark>IE</mark>	EDE <mark>GF</mark> DVPDC <mark>KK</mark>	SKLTSSQ <mark>DTNVD</mark> K	К <mark>Е</mark> АЕN 370
Chicken	334	KS	-KLE <mark>G</mark> SFH <mark>LE</mark>	SDEGFD <mark>VP</mark> DC <mark>KK</mark>	VKTNEDK <mark>EP</mark> A <mark>V</mark> EE	N <mark>E</mark> DKA374
Mouse	338	EI	-SEKAKLENS <mark>A</mark> Ç	AEEGLD <mark>VP</mark> DG <mark>KK</mark>	LTENDAK <mark>EP</mark> C <mark>A</mark> EE	DSEEKA381
Human	340	EI	-SEKAKLENS <mark>TÇ</mark>	AEEGFDVPDC <mark>KK</mark>	TIVNDSR <mark>E</mark> SC <mark>VEE</mark>	N <mark>D</mark> DKI 382
Lamprey	446 EKVY <mark>E</mark> K <mark>E</mark> YE	K <mark>ey</mark> ekeeea <mark>g</mark> vi	KR <mark>GPSG</mark> AATHTI	RC <mark>G</mark> SEDEQ <mark>EPE</mark> E	YEYE <mark>E</mark> DVDDD <mark>G</mark> KM	KKSSKSEAL511
Eshark	362 <u>-</u>	<mark>E</mark> S	-SQ <mark>P</mark> SVS-S <mark>S</mark> FI	N <mark>SSQE</mark> TEEN <mark>AE</mark> K	<mark>ge</mark> k	388
Zebrafish	375 - <u>s</u> a <mark>tit</mark> dsç)TT <mark>S</mark>	-SQ <mark>P</mark> STS- <mark>S</mark> GGG	- <mark>SSQEETPEL</mark>		404
Frog	371 I <mark>Q</mark> N <mark>SESQE</mark> T	EDC	-SQ <mark>P</mark> STS- <mark>G</mark> SIA	SC <mark>SQE</mark> VTKED		402
Chicken	375 V <mark>QISE</mark> SQES	ED <mark>Y</mark>	-SQ <mark>P</mark> STS-SSVI	C <mark>SSQED</mark> FR <mark>EPE</mark> K	K <mark>E</mark> M	411
Mouse	382 E <mark>QT</mark> PLSQES	DD <mark>Y</mark>	-SQ <mark>P</mark> STS-SSIV	Y <mark>SSQE</mark> SVK <mark>EL</mark> K-	E <mark>E</mark> T	417
Human	383 T <mark>Q</mark> A <mark>SQSQE</mark> S	EDY	-SQ <mark>P</mark> STS-SSII	Y <mark>SSQED</mark> VK <mark>EFE</mark> R	E <mark>E</mark> T	419
Lamprey	512 q <mark>p</mark> adavsa <i>f</i>	SSAAASSAYENI	DS <mark>R</mark> S <mark>G</mark> AGGANN <mark>A</mark>	C <mark>PLLDMCIICQ</mark> H	EP <mark>R</mark> SC <mark>TIVH</mark> G <mark>K</mark> TG	HLVT <mark>CY</mark> MCA577
Eshark	389	<mark>(</mark>	GESNN	SGPVEPCVICQT	RP <mark>KN</mark> GCIV <mark>H</mark> G <mark>KT</mark> G	HLLA <mark>CYTC</mark> A427
Zebrafish	405		- <mark>er</mark> fn <mark>sle</mark> ac <mark>lf</mark>	ATCLEPCVICQS	RP <mark>KN</mark> GCIV <mark>H</mark> G <mark>RT</mark> G	HLMA <mark>CYTC</mark> A449
Frog	403		-SSKESMESSLF	LTSIDPCVICQT	RP <mark>KN</mark> GCIV <mark>H</mark> GRTG	HLMA <mark>CYTC</mark> A447
Chicken	412	F	KD <mark>K</mark> EEGMESSLF	VS <mark>SIEPC</mark> VI <mark>C</mark> QS	RP <mark>KN</mark> GCIV <mark>H</mark> G <mark>KT</mark> G	HLMS <mark>CFTC</mark> A457
Mouse	418	·(D <mark>dk</mark> desvessfs	LNAIEPCVICQG	RP <mark>KN</mark> GCIV <mark>H</mark> G <mark>KT</mark> G	HLMS <mark>CFTC</mark> A463
Human	420	·(D <mark>KEESVESSL</mark> F	LNAIEPCVICQG	RP <mark>KNGCIVHG</mark> KTG	HLMA <mark>CFTC</mark> A465
Lamprey	578 <mark>KKLKRRN</mark> KI	CPVCRSPIQAV	[K <mark>TY</mark> LL			603
Eshark	428 <mark>KKLKRRN</mark> KI	CPLCREPIQMVV	/L <mark>TY</mark> FS			453
Zebrafish	450 <mark>KKLK</mark> NRNKI	CPVCREPIQSVV	/L <mark>TY</mark> MS			475
Frog	448 <mark>KKL</mark> KKR <mark>N</mark> K	CPVCREPIQMIV	/L <mark>TY</mark> FS			473
Chicken	458 <mark>RKLKKRN</mark> KI	CPVCRQPIQMIV	/L <mark>TY</mark> F <mark>G</mark>			483
Mouse	464 <mark>KKL</mark> KKR <mark>N</mark> K	CPVCRQPIQMIV	/L <mark>TY</mark> FN			489
Human	466 <mark>KKLKKRN</mark> KI	CPVCRQPIQMI	/L <mark>TY</mark> F <mark>P</mark>			491

Coffill and Lee et al. Fig S9, Panel B



Coffill and Lee et al. Fig S10

Lamprey	1 MM <mark>SGSPS</mark> ISMS <mark>S</mark> ASGVCEEALAV <mark>RPVP</mark> LLL <mark>B</mark> LLRSVGATGD T FTLPQV48
Eshark	1 MTTA <mark>STS</mark> NPYPSSDILCGNSTEKIRPKPLLLNLLHEAGASGEIFTLKEV49
Zebrafish	1 MTSLASSSQLPGSCRTLPGEGTQVHPRAPLLQILKVAGAQEEVFTLKEV49
Froq	1 MSTSTTFHLMNEPDSAPMTIONTKESPVRPOPALLKILOTAGASGEIFTLKOV53
Chicken	1 - MTSSSSAO-HPAAENACRTTLGOANOVRPKLPLLKTLOAAGAOGETETLKEV51
Mouse	1 MTSHSTSAO-CSASDSACRISSEOISOVRPKLOLLKILHAAGAOGEVETMKEV52
Uuman	
IIuman	
Lamprev	49 FHHLGGYTKTKOLYDKRRLHTVHCKGDPLGELFGVESFSLKEPSSSPKSLGAL10
Eshark	50 MHYLGOYTMLKOLYDKOOOHTVYCGNDPLGKVFGVESFSVKVPSOLYEMLSRN102
Zehrafich	
FLOG	
Chicken	52 MHYLGQYIMVRQLYDKRQQHMVYCGGDQLGELLGLESFSVKDPSPVYEMLKKN104
Mouse	53 MHYLGQYIMVKQLYDQQEQHMVYCGGDLLGDLLGCQSFSVKDPSPLYDMLRKN10
Human	53 MHYLGQYIMV <mark>KQLYDQQEQHMVYCGGDLLGE</mark> LLGRQSFSVKDPSPLYDMLRKN105
Lamprey	102 LAKALGRAATDRRKGGARPRQDHAAGAVKGS132
Eshark	103 LIALNFHDAAQTR <mark>T</mark> LV <mark>KE</mark> TNCLPLREEHLKCLTGETSEGE142
Zebrafish	103 LVILNNSDAAKNLSVGKDSN-ESPSEDPGQVSSGSINSAQPLIAGSSSTGT152
Frog	107 L <mark>S</mark> RVTCTDA <mark>GH</mark> S <mark>PS</mark> <mark>RD</mark> K <mark>SLASHGLE</mark> LEKSFNNKTEVTEDIKR148
Chicken	105 L <mark>T</mark> SAAMTATDAAQNLA <mark>KEQSVD</mark> K <mark>PSQD</mark> QLKFS <mark>P</mark> KE <mark>G</mark> SDTVIM <mark>G</mark> DESNAS153
Mouse	106 LVTSASINTDAAQTLALAQDHTMDFPSQDRLKHGATEYSNPRKRTEEEDTH156
Human	106 LVTLATATTDAAQ <mark>T</mark> LALA <mark>QD</mark> H <mark>SMD</mark> I <mark>PSQD</mark> QLKQSAEESSTSRKRTT <mark>E</mark> DDI <mark>P</mark> 156
Lamprey	133 <mark>SLA</mark> 135
Eshark	143 TVCIVPNSATSHLKRKNSESDDLDADDOPELOSKRORSESVSDHWDAAGLPWW195
Zebrafish	153 TOSCSORRPRDPDEDSSDGLPRSACKRPKLDVTLEEWDLSGLPWW19
Froa	149 NDCVSDDVCTSLNKSHLKGNERSDYTKOSLDLVFEEWDEAGLPWW193
Chicken	154 AVSTSEHKCENYEDKDLTENLSKSKKPKLDLVFEEWDVAGLPWW19
Mouse	157 TLPTSRHKCRDSRADEDLIEHLSODETSRIDLDEEEWDVAGLPWW201
Нитар	$157 \text{ mLP}_{}$
naman	
Lamprev	13613 ⁻
Fshark	
Zohrafich	
Eroc	
r r og	
Chicken	198 FLGMLKSNYKSKSNGSTDIQTNQUIDTAIVSDTTDDLWFLNESPLDQT24
Mouse	202 FLGNLRNNC1PKSNGSTDLQTNQDIGTAIVSDTTDDLWFLNETVSEQL249
Human	202 FLGNLRSNYTPRSNGSTDLOTNODVGTAIVSDTTDDIWFLNESVSEOL24

Coffill and Lee et al. Fig S11, Panel A

Lamprey	138 DGDKRQEPQRRGGDGHEEEEEGVDDDV16	55
Eshark	244 N <mark>GEIKEGAIHP</mark> KEIRDQEEEK <mark>EE</mark> DKNTD <mark>PK</mark> EVIEVTIYEAGEGLSC <mark>SG</mark> HA <mark>T</mark> 29	94
Zebrafish	251 SVEIKEAVLEQGSDGESPHEDEDTGKDSKDDGKMQEEQEEDSQCLSDDT29)9
Frog	242 NMEVKMEAPGSLSNKVEELGESDSKKVVKLTLYDDDDLDDTQSLSDDT28	39
Chicken	246 NTA <mark>VK</mark> METADCEEVKEGDKKVTEDACLHDFEDSQCLSDDT28	35
Mouse	250 GVGIKVEAANSEQTS-EVGKTSNKKTVEVGKDDDLEDSRSLSDDT29	33
Human	250 GVGIKVEAADTEQTSEEVGKVSDKKVIEVGKNDDLEDSKSLSDDT29	94
Lamprey	166 K <mark>T</mark> K <mark>TSSD</mark> -AVSAAPSA <mark>P</mark> 18	31
Eshark	295 <mark>DPEI-SD</mark> KSWKCTKCGEDNPSQKQYCLQCWALRGGWHLKCPKLTRSTSGPSIA34	16
Zebrafish	300 DTEISTQDAWQCSECRKFNTPLQRYCMRCWALRKDWYKDCPRLVHSISVPDIP35	52
Frog	290 DTEVTSQDCWQCTKCHKLNSPVKRYCYRCWALRKDWYLDYPSLLHSSSTPTLP34	12
Chicken	286 DTEAASEDCWQCTKCKKFNSPGKRYCYRCWALRKDWYSDCPKLTHSLSLSNID33	38
Mouse	294 DVELTSEDEWQCTECKKFNSPSKRYCFRCWALRKDWYSDCSKLTHSLSTSNIT34	16
Human	295 DVEVTSEDEWQCTECKKFNSPSKRYCFRCWALRKDWYSDCSKLTHSLSTSDIT34	17
Lamprey	182 ASSDSS <mark>G</mark> SSS19	€∢
Eshark	347 <mark>IAENEP</mark> YEGIDVPD <mark>SKRSIS</mark> EPVIQI <mark>K</mark> DLKC <mark>K</mark> EMG-IISTPCA38	38
Zebrafish	353 ACSSR <mark>P</mark> ERDEDEEEEDD <mark>DGIDMPDCLRTVS</mark> DPVVLPSHRV <mark>SR</mark> NIPSSSASSSK4()5
Frog	343 <mark>A</mark> KCSSQYSMA <mark>GLDMPDCRRTVS</mark> APIVGV <mark>R</mark> VPEC <mark>K</mark> AQV-PF38	31
Chicken	339 <mark>TM-QNENSDEGIDVPDCRRTIS</mark> APVGPPKDMYVVENK-SHVDPCG38	31
Mouse	347 <mark>AI-P</mark> EKKDNEGIDVPDC <mark>RRTIS</mark> APVVR <mark>PKDG</mark> YL <mark>K</mark> EEK-PRFDPCN38	39
Human	348 <mark>AI-P</mark> <mark>E</mark> K-EN <mark>EG</mark> NDVPDCRRTISAPVVRPKDAYIKKENSKLFDPCN39)0
Lamprey	196 <u>-dss<mark>sdss</mark>s<mark>gs</mark>ss<mark>sg</mark>ss<mark>s</mark>sss<u>d</u>anaa<u></u>cl<mark>ac</mark>lv<mark>c</mark>22</u>	27
Eshark	389 <mark>SSESLDSL</mark> SQ <mark>P</mark> STSSLWRSREDLE <mark>SVG</mark> KEAKTVKRKCEDSLQSRRQRLGPC43	39
Zebrafish	406 <mark>GKGPSQIH</mark> HHFQETSEGDSQDTLDMETEYQPEALLEPC44	łЗ
Frog	382 -L <mark>EPLDLA</mark> AN <mark>S</mark> KALSKSTDTLLTYQAEEA <mark>SL</mark> LSSRPLLEPC42	21
Chicken	382 <mark>SIESLDLA</mark> RECERRDSLL <mark>SFTE</mark> HKKEE <mark>E</mark> I <mark>QSLE</mark> SIKKLLN <mark>PC</mark> 42	23
Mouse	390 <mark>SVGFLDLA</mark> HS <mark>SESQE</mark> IIS <mark>SAREQT</mark> DIF <mark>S</mark> EQKA <mark>E</mark> TE <mark>S</mark> MEDFQNVLK <mark>PC</mark> 43	36
Human	391 <mark>S</mark> VEFLDLAHS <mark>S</mark> ESQETIS <mark>SMGE</mark> QLDNL <mark>S</mark> EQRTDTENMEDCQNLLKPC43	37
Lamprey	228 LVC <mark>Q</mark> H <mark>RPR</mark> SCTLVH <mark>GETGHLVT</mark> CCACAKKLKRRNEPCPACGRPVHAVVRTYLL28	30
Eshark	440 LICGV <mark>RPR</mark> TG <mark>NIIHRKMGHLVACY</mark> TCAKSLYKRKM <mark>PCPVCVQP</mark> IIMVIQTFIG49	92
Zebrafish	444 KLCRV <mark>RPR</mark> NGNIIHGRTAHLITCFPCARKLHKFHAPCPGCGQVIQKVIKTFIA49	96
Frog	422 RLCQRRQRNGNVVHGRTAHLVTCFSCARNLKKNRKGCPVCQKPIQMVVKIYVA47	14
Chicken	424 FLCHH <mark>RPR</mark> DG <mark>NIVHGRT</mark> AHLVACFKCAKMLKKRRSPCPVCRKDIEMVIRIFMG47	16
Mouse	437 SLCEK <mark>RPR</mark> DGNIIHGKTSHLTTCFHCARRLKKSGASCPACKKEIQLVIKVFIA48	39
Human	438 SLCEK <mark>RPR</mark> DGNIIHGRTGHLVTCFHCARRLKKAGASCPICKKEIQLVIKVFIA49)0

Coffill and Lee et al. Fig S11, Panel B

Mdm2 locus





Coffill and Lee et al. Fig S13



В

C¹¹VDDFDRVWQGG²²VGL

э.*1*

А

S¹⁵QETFSDLWKLL²⁶PEN

1

2

3

4

5



2.9



3.2



С

C¹¹VDDFDRVWQGL²²VGL

2.0

Coffill and Lee et al. Fig S14



В



Coffill and Lee et al. Fig S15



Coffill and Lee et al. Fig S16

В