

Supporting Information

for

Ca²⁺-Saturated calmodulin binds tightly to the N-terminal domain of A-type fibroblast growth factor homologous factors

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Running Title: (Ca²⁺)₄-CaM Tightly Binds the NTD of A-Type FGFs

Keywords: Molecular recognition, Ca²⁺-dependent interaction, voltage-gated sodium channel, protein-protein interaction, NMR, FRET, FHF, Biosensor, Thermodynamics, Allostery, Affinity

References

Supporting Information – Figure Legends

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(Unique to Supporting Information, Figure S1)

2. Gautier, R., Douguet, D., Antonny, B., and Drin, G. (2008) HELIQUEST: a web server to screen sequences with specific alpha-helical properties. *Bioinformatics (Oxford, England)* **24**, 2101-2102
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3. Shen, Y., and Bax, A. (2010) SPARTA+: a modest improvement in empirical NMR chemical shift prediction by means of an artificial neural network. *J Biomol NMR* **48**, 13-22
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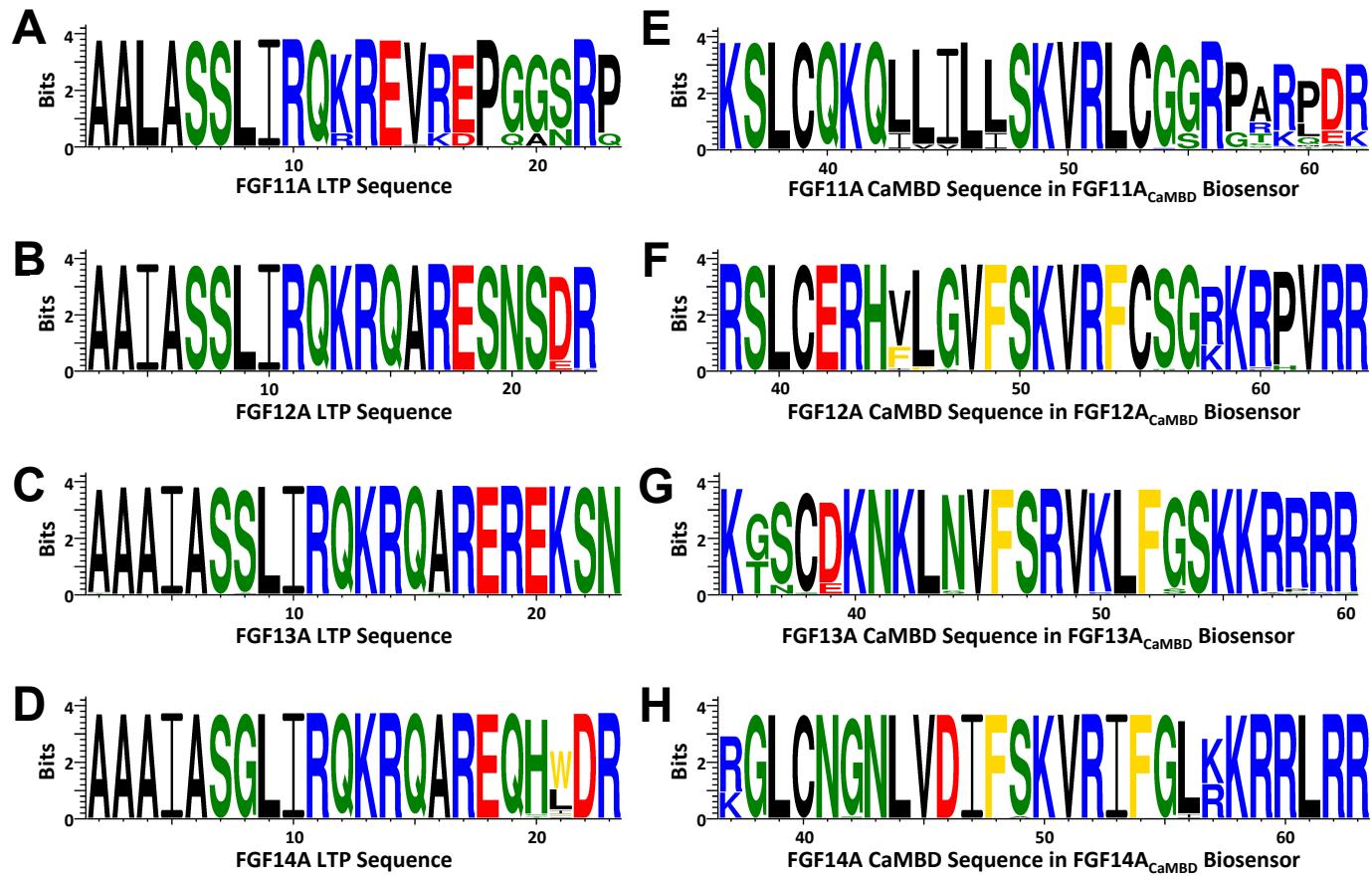


Figure S1 (Related to Fig. 2)
Comparison of A-Type FGF LTP and CaMBD Sequences Contained in Biosensors

A-D: Weblogo [1] comparison of the FGF11A (**A**, a.a. 2 – 23, 60 species), FGF12A (**B**, a.a. 3 – 23, 56 species), FGF13A (**C**, a.a. 2 – 23, 63 species), and FGF14A (**D**, a.a. 2 – 23, 48 species) LTP sequences across species.

E-H: Weblogo [1] comparison of the FGF11A (**E**, a.a. 36 – 62, 60 species), FGF12A (**F**, a.a. 38 – 64, 56 species), FGF13A (**G**, a.a. 35 – 60, 53 species) and FGF14A (**G**, a.a. 37 – 63, 48 species) sequences used in the CaMBD biosensors across species.

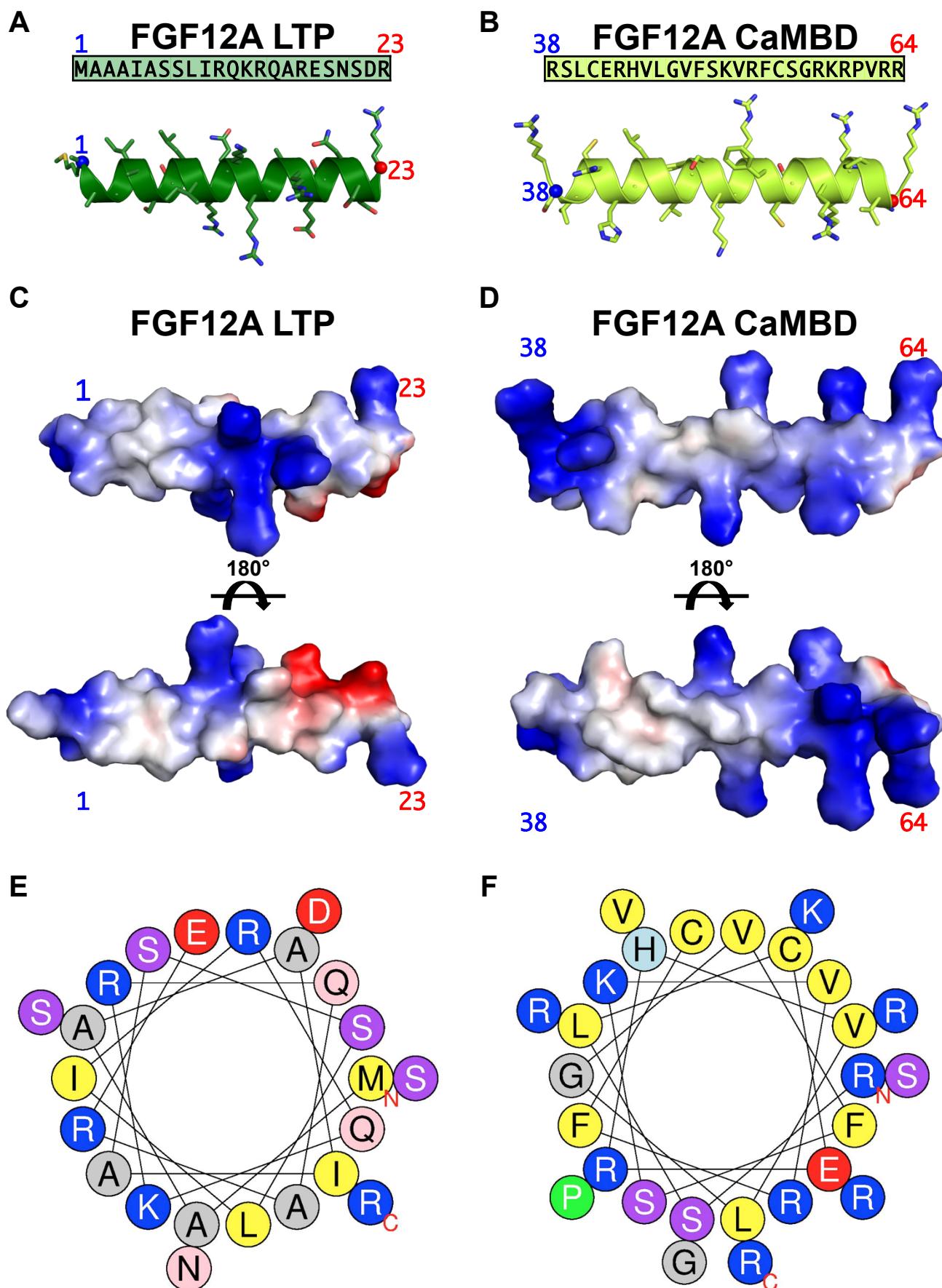


Figure S2 (Related to Fig. 2)**Models of FGF12A LTP and CaMBD**

A: Top: Human FGF12A LTP (a.a. 1-23) sequence. Bottom: FGF12A LTP sequences depicted as sticks on a modeled α -helix. C α of residues 1 (blue) and 23 (red) are spheres.

B: Top: Human FGF12A CaMBD (a.a. 38-64) sequence. Bottom: FGF12A CaMBD sequence depicted as sticks on a modeled α -helix. C α of residues 38 (blue) and 64 (red) are spheres.

C-D: Calculated vacuum electrostatic surface (positive/blue, negative/red, neutral/white) of the FGF12A LTP (**C**) and FGF12A CaMBD (**D**).

E-F: Helical wheels of FGF12A LTP (**E**) and FGF12A CaMBD (**F**). Helical wheels were generated with HeliQuest (<https://heliquest.ipmc.cnrs.fr/>) [2].

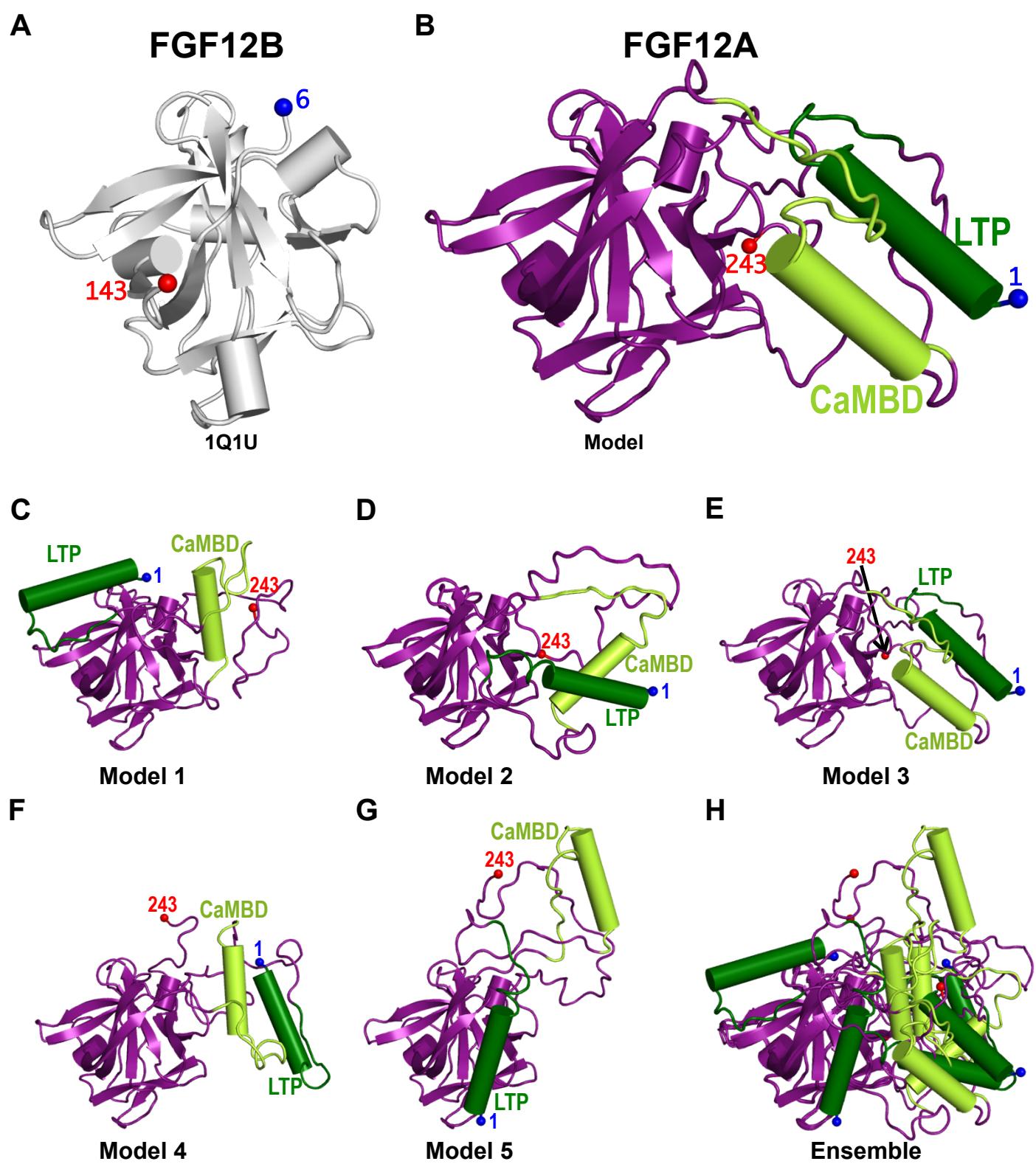


Figure S3 (Related to Fig. 2) Ensemble of FGF12A Models

A-B: Alignment of FGF12B (**B**, 1Q1U, gray) and model 3 of FGF12A (**C**, purple, LTP/green, CaMBD/limon). The FGF12A model was aligned with FGF12B a.a. 6-143. C α of FGF12B residues 6 (blue) and 143 (red) and FGF12A residues 1 (blue) and 243 (red) are shown as spheres.

C-G: Orientations of the LTP (green) and CaMBD (limon) in the models of FGF12A (purple). C α of FGF12A residues 1 (blue) and 243 (red) are shown as spheres.

H: Ensemble of FGF12A aligned with FGF12A (purple) a.a. 69-207. The FGF12A LTP is green and CaMBD is limon. C α of FGF12A residues 1 (blue) and 243 (red) are shown as spheres.

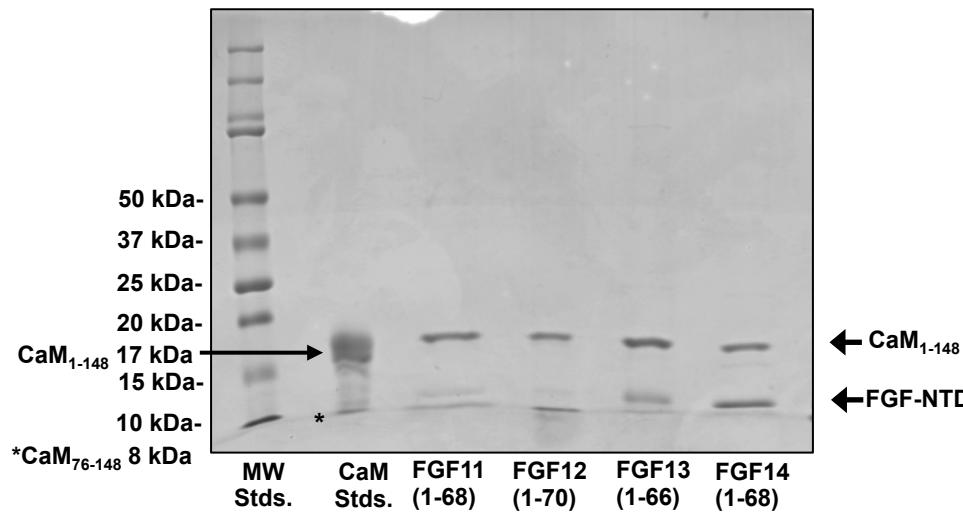
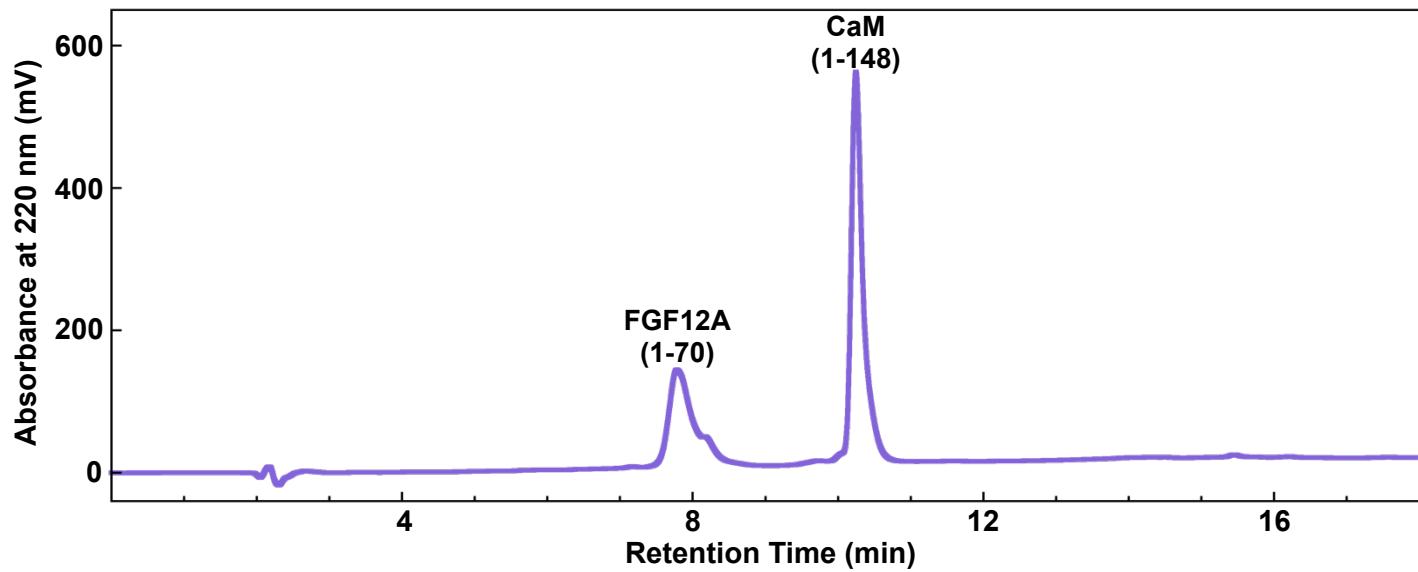
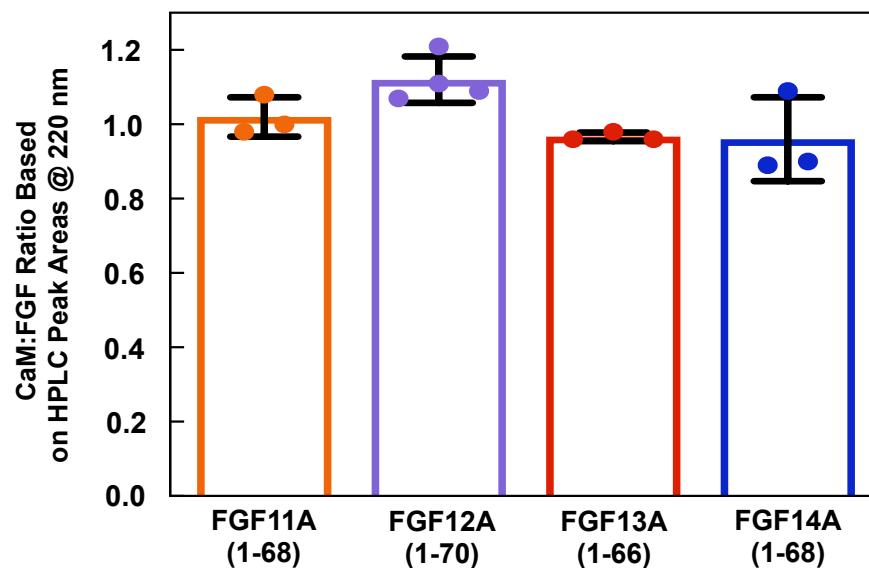
A**B****C**

Figure S4 (Related to Fig. 4) (Ca^{2+})₄-CaM Co-Purifies with A-Type FGF NTDs at a 1:1 Ratio

A: 17% SDS-PAGE gel of the (Ca^{2+})₄-CaM+FGF11A_{NTD}, FGF12A_{NTD}, FGF13A_{NTD}, or FGF14A_{NTD} complexes following co-purification.

B: rpHPLC chromatogram of the co-purified (Ca^{2+})₄-CaM+FGF12A_{NTD} complex.

C: Molar ratio of (Ca^{2+})₄-CaM to FGF11A_{NTD} (orange), FGF12A_{NTD} (purple), FGF13A_{NTD} (red) or FGF14A_{NTD} (blue) in the copurified complexes. The molar ratio was determined by comparing the area of the peak at 220 nm for CaM to that of FGF NTD construct in rpHPLC chromatograms. Error bars show the standard deviation of ≥ 3 experiments.

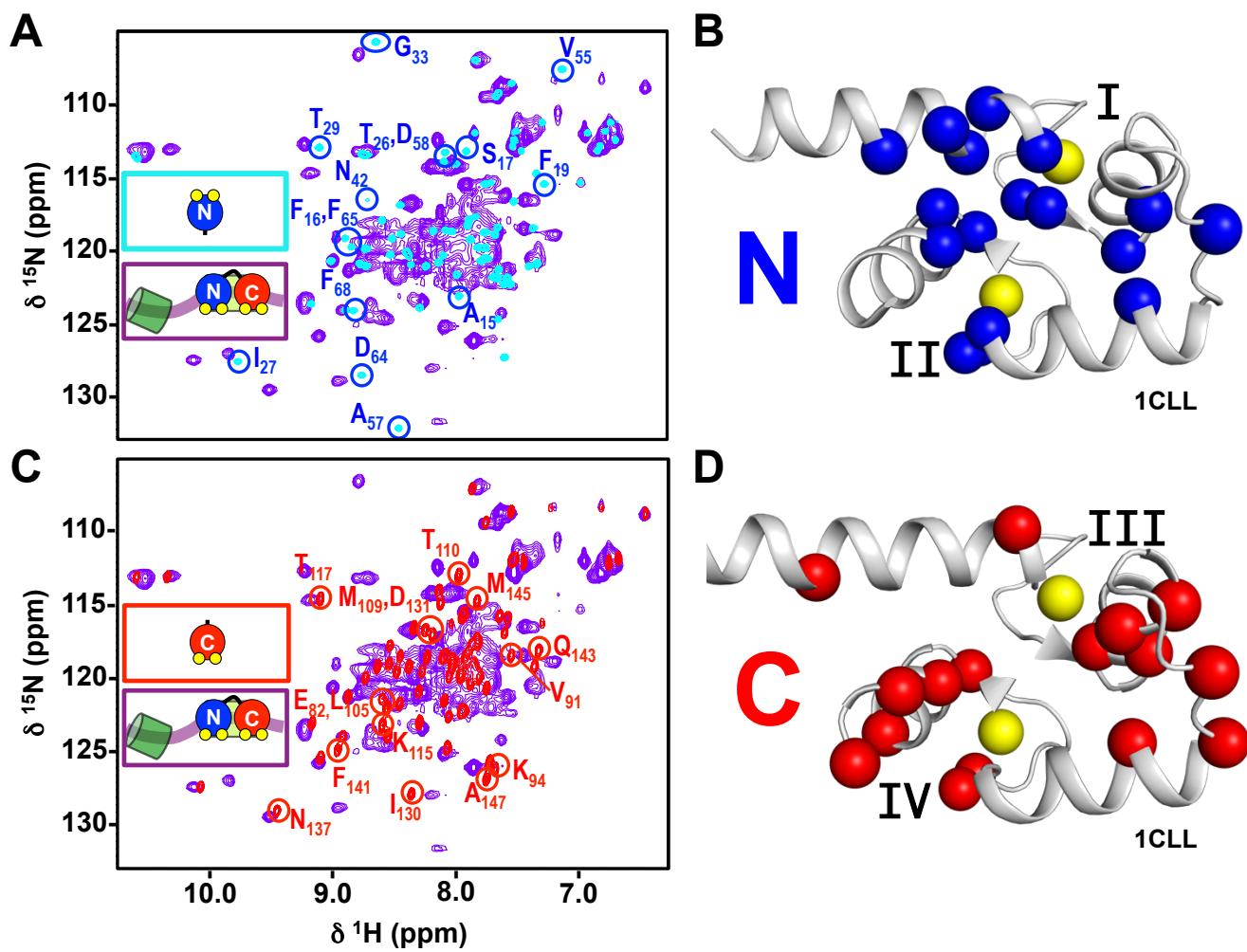


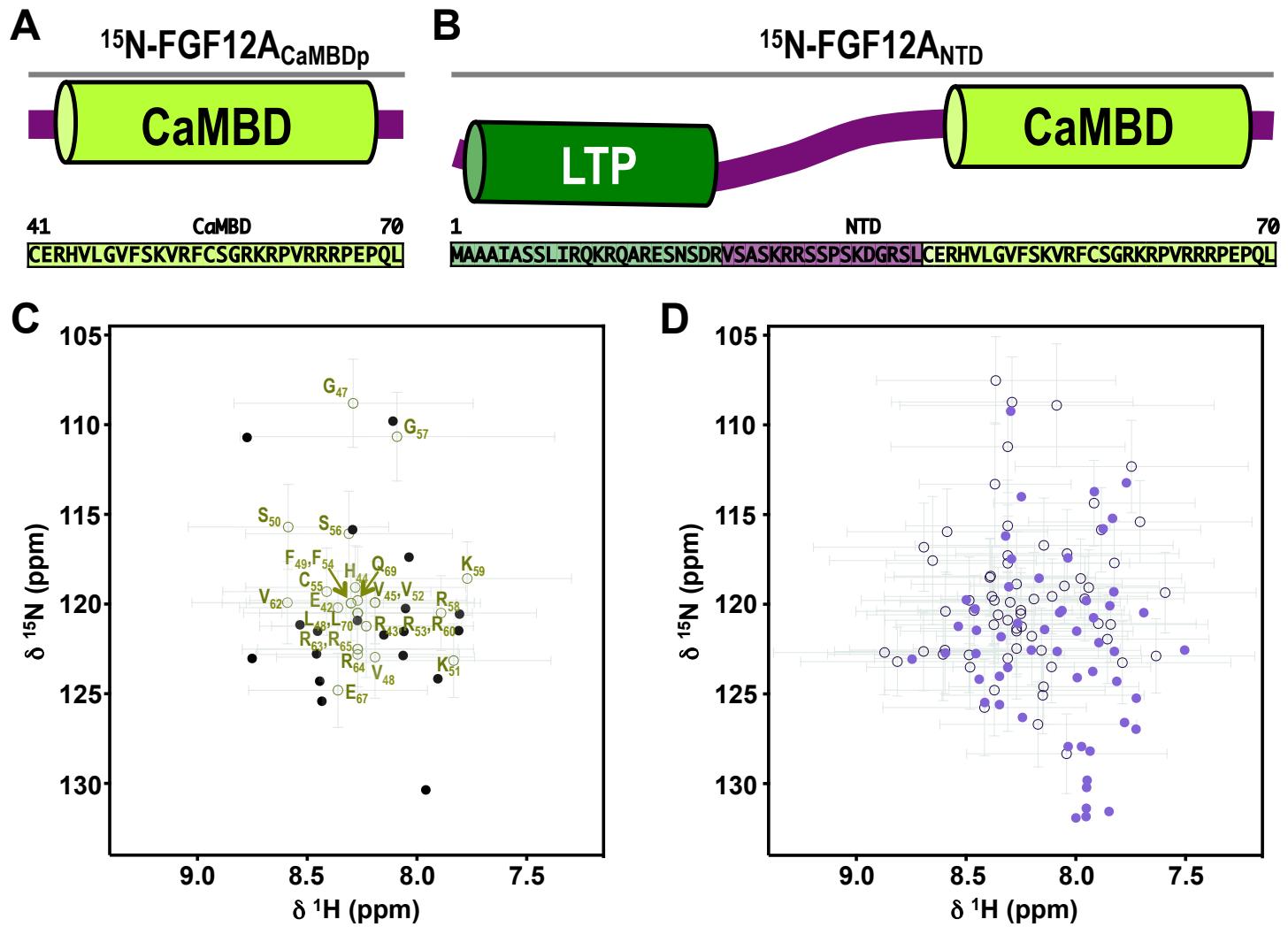
Figure S5 (Related to Fig. 4) FGF12A_{NTD} Binding Perturbs Residues in Both CaM Domains

A: Overlay of the ^{15}N -HSQC spectra of $^{15}\text{N}-(\text{Ca}^{2+})_2\text{-CaM}_N$ (blue) and $^{15}\text{N}-(\text{Ca}^{2+})_4\text{-CaM} + ^{14}\text{N}\text{-FGF12A}_{\text{NTD}}$ (purple). Peaks labeled in $^{15}\text{N}-(\text{Ca}^{2+})_2\text{-CaM}_N$ spectrum are shifted in the $^{15}\text{N}-(\text{Ca}^{2+})_4\text{-CaM} + ^{14}\text{N}\text{-FGF12A}_{\text{NTD}}$ spectrum.

B: $\text{C}\alpha$ of CaM_N residues (blue spheres) labeled in panel **A** on a structure of $(\text{Ca}^{2+})_4\text{-CaM}$ (1CLL, gray helices). For clarity of residues 1-75 of 1CLL are shown.

C: Overlay of the ^{15}N -HSQC spectra of $^{15}\text{N}-(\text{Ca}^{2+})_2\text{-CaM}_C$ (red) and $^{15}\text{N}-(\text{Ca}^{2+})_4\text{-CaM} + ^{14}\text{N}\text{-FGF12A}_{\text{NTD}}$ (purple). Peaks labeled in $^{15}\text{N}-(\text{Ca}^{2+})_2\text{-CaM}_C$ spectrum are shifted in the $^{15}\text{N}-(\text{Ca}^{2+})_4\text{-CaM} + ^{14}\text{N}\text{-FGF12A}_{\text{NTD}}$ spectrum.

D: $\text{C}\alpha$ of CaM_C residues (red spheres) labeled in panel **C** on a structure of $(\text{Ca}^{2+})_4\text{-CaM}$ (1CLL, gray helices). For clarity of residues 76-148 of 1CLL are shown.

**Figure S6 (Related to Fig. 4)****Predicted ^{15}N -HSQC Spectra of ^{15}N -FGF12A_{CaMBDp} and ^{15}N -FGF12A LTP**

A-B: Schematic depictions and sequences of the FGF12A_{CaMBDp} (**A**, limon cylinder) and FGF12A_{NTD} (**B**, LTP/green cylinder, CaMBD/limon green cylinder). The sequences have been shaded to match the schematics.

C: Peaks observed in the ^{15}N -HSQC spectrum of ^{15}N -FGF12A_{CaMBDp}+ ^{14}N -(Ca²⁺)₄-CaM (closed, black) are compared to peak positions predicted by SPARTA+ [3] for residues 41 – 70 (FGF12A_{CaMBDp}/open, olive) of the energetically most favorable Robetta model (model 1, Fig. 8A) of full-length FGF12A (olive).

D: Peaks observed in the ^{15}N -HSQC spectrum of ^{15}N -FGF12A_{NTD}+ ^{14}N -(Ca²⁺)₄-CaM (closed, purple) are compared to peak positions predicted by SPARTA+ [55] for residues 1 – 70 (FGF12A_{NTD}/open, dark purple) of the energetically most favorable Robetta model (model 1, Fig. 8A) of full-length FGF12A.

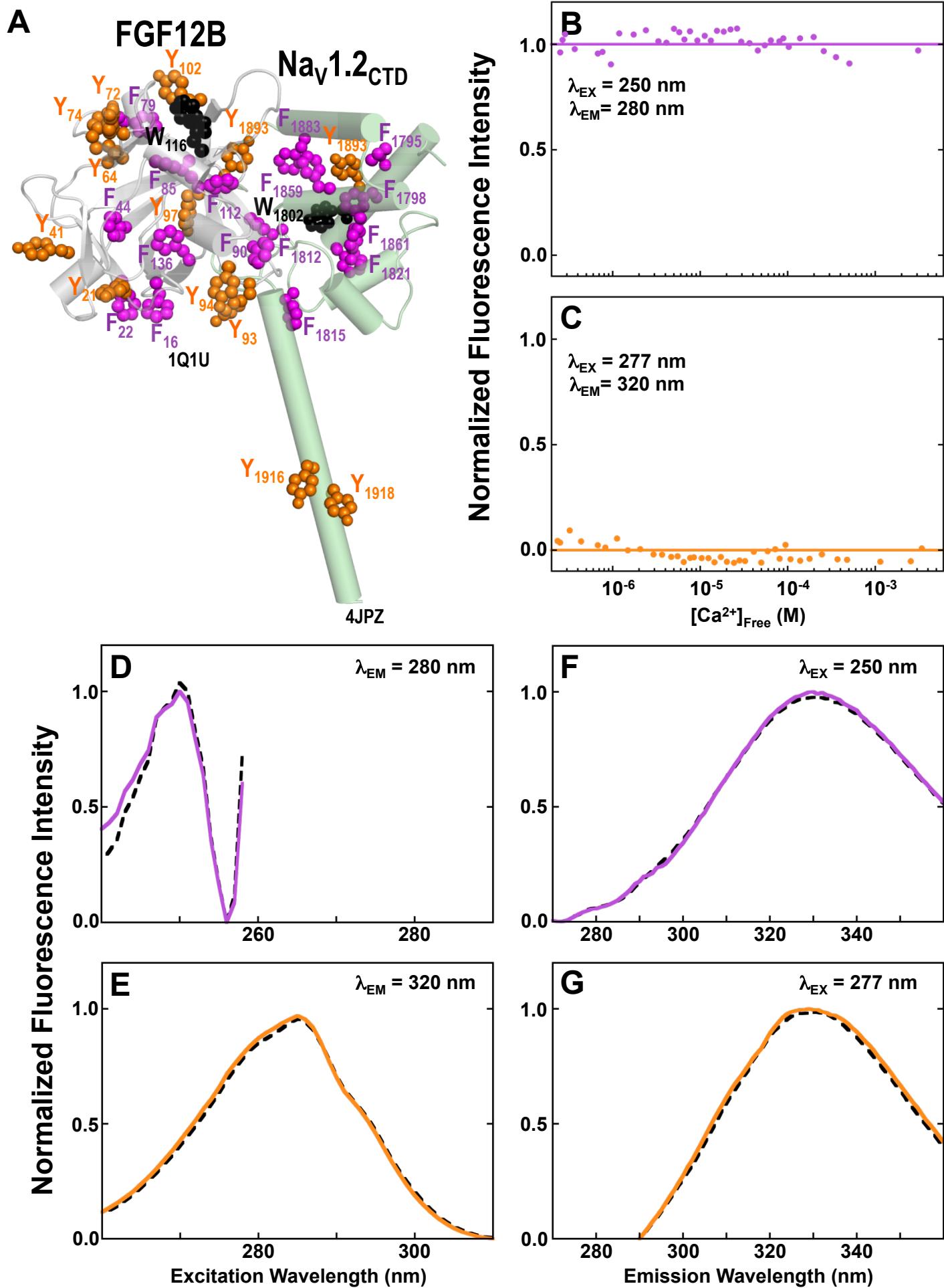


Figure S7 (Related to Fig. 6)**Equilibrium Ca²⁺ Titrations of the FGF12B+Na_v1.2_{CTD} Complex**

A: Position of Phe (magenta, ball-and-stick), Tyr (orange, ball-and-stick) and Trp (black, ball-and-stick) residues in a model of FGF12B (1Q1U, gray) bound to Na_v1.2_{CTD} (4JPZ, forest green). The model is a composite of FGF12B from 1Q1U aligned with FGF13U from 4JPZ via FGF13U residues 11-158. FGF13U and CaM in 4JPZ are not shown.

B-C: Equilibrium Ca²⁺ titrations of the FGF12B+Na_v1.2_{CTD} complex. The average Phe (**B**) or Tyr (**C**) fluorescence intensity of FGF12B+Na_v1.2_{CTD} in each titration was normalized to the average net change in intensity in Ca²⁺ titrations of CaM+FGF12B+Na_v1.2_{CTD}. The solid lines at 1 (**B**) and 0 (**C**) are for reference.

D: Steady-state excitation spectra ($\lambda_{EM} = 280$ nm) of the FGF12B+Na_v1.2_{CTD} complex in Ca²⁺-depleted conditions (black, dashed) and in the presence or 10 mM Ca²⁺ (pink, solid).

E: Steady-state excitation spectra ($\lambda_{EM} = 320$ nm) of the FGF12B+Na_v1.2_{CTD} complex in Ca²⁺-depleted conditions (black, dashed) and in the presence of 10 mM Ca²⁺ (orange, solid).

F: Steady-state emission spectra ($\lambda_{EX} = 250$ nm) of the FGF12B+Na_v1.2_{CTD} complex in Ca²⁺-depleted conditions (black, dashed) and in the presence of 10 mM Ca²⁺ (pink, solid).

G: Steady-state emission spectra ($\lambda_{EX} = 277$ nm) of the FGF12B+Na_v1.2_{CTD} complex in Ca²⁺-depleted conditions (black, dashed) and in the presence of 10 mM Ca²⁺ (orange, solid).

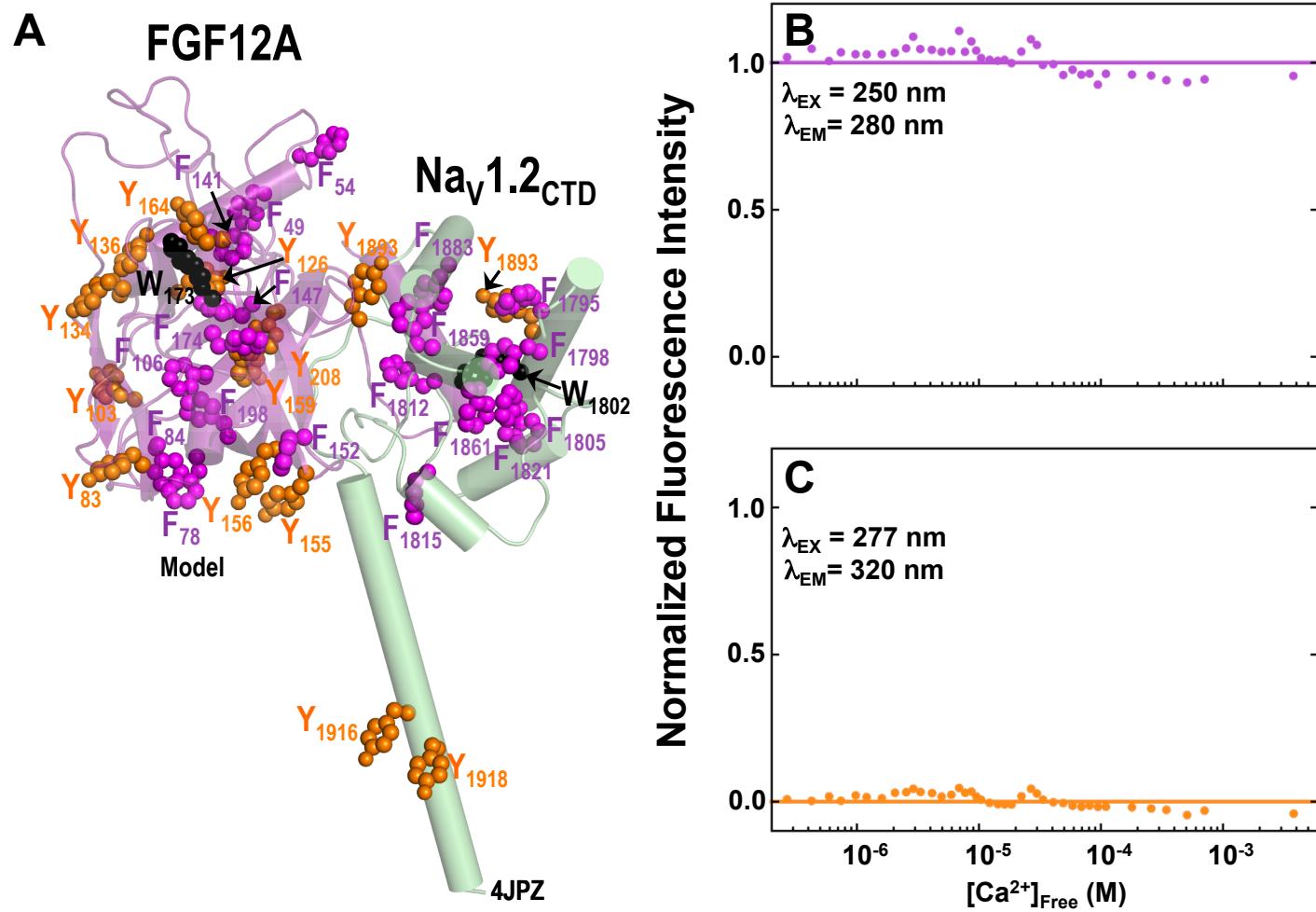


Figure S8 (Related to Fig. 6)
Equilibrium Ca²⁺ Titrations of the FGF12A+Na_v1.2_{CTD} Complex

A: Position of Phe (magenta, ball-and-stick), Tyr (orange, ball-and-sticks), and Trp (black, ball-and-stick) residues in a model of FGF12A (model, purple) bound to Na_v1.2_{CTD} (4JPZ, forest green). The model is a composite of the FGF12A aligned with FGF13U from 4JPZ via FGF13U residues 11–158. FGF13U and CaM in 4JPZ are not shown.

B-C: Equilibrium Ca²⁺ titrations of the FGF12A+Na_v1.2_{CTD} complex. The average Phe (**B**) or Tyr (**C**) fluorescence intensity of FGF12A+Na_v1.2_{CTD} in each titration was normalized to the average net change in intensity in Ca²⁺ titrations of CaM+FGF12A+Na_v1.2_{CTD}. The solid lines at 1 (**B**) and 0 (**C**) are for reference.

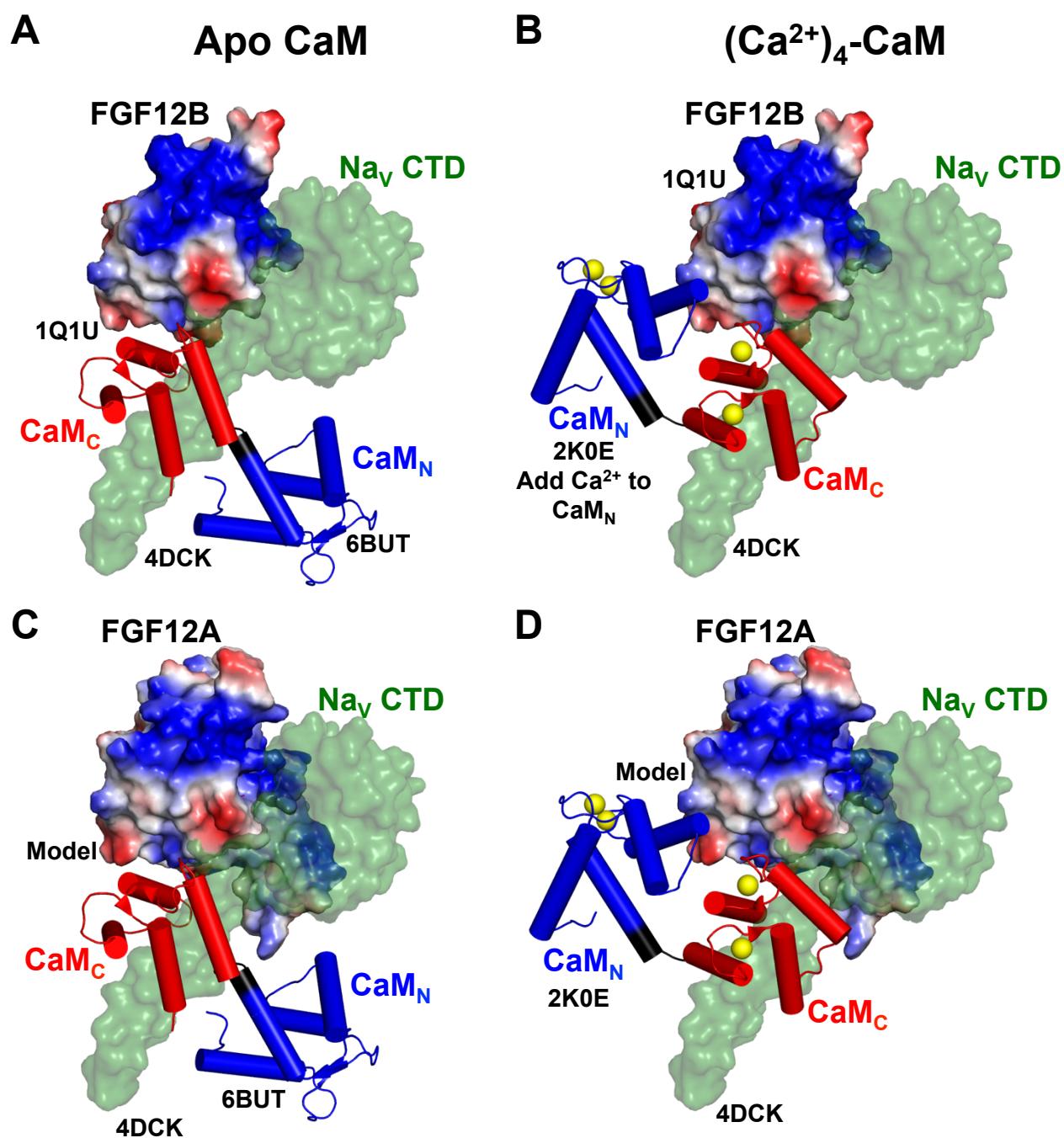


Figure S9 (Related to Fig. 9)**Models of CaM and FGF12B or FGF12A Bound to an Na_v CTD**

In all models the Na_v CTD (4DCK) is shown as a transparent surface (green), FGF12B (1Q1U) and FGF12A are shown as a vacuum electrostatic surface (basic/blue, acidic/red, neutral/white), CaM residues 1-75 are blue, 76-80 are black, and 81-148 are red. Ca²⁺ are shown as yellow spheres where appropriate.

A: Model of apo CaM and FGF12B bound to an Na_v CTD. Model was generated by aligning the solution structure of apo CaM+Na_v1.2_{IQp} (6BUT) to the crystallographic structure of apo CaM+FGF13B+Na_v1.5 CTD (4DCK) with CaM residues 101-112 and 117-128. The crystallographic structure of FGF12B (1Q1U) was docked using FGF13U residues 11–136.

B: Model of (Ca²⁺)₄-CaM and FGF12B bound to an Na_v CTD. Model was generated by docking the structure of (Ca²⁺)₂-CaM_C+Na_v1.2 IQ motif (2M5E) with the Na_v1.5 IQ motif in the crystallographic structure of apo CaM+FGF13U+Na_v1.5 CTD (4DCK) via Na_v1.2 IQ motif residues 1904-1924. A solution structure of (Ca²⁺)₄-CaM (2K0E) was docked via CaM residues 101-112 and 117-128 of 2M5E. FGF12B (1Q1U) was docked through residues 11–136 of FGF13U.

C: Model of apo CaM and FGF12A bound to an Na_v CTD. Model was generated by aligning the solution structure of apo CaM+Na_v1.2_{IQp} (6BUT) to the crystallographic structure of apo CaM+FGF13U+Na_v1.5 CTD (4DCK) with CaM residues 101-112 and 117-128. The modeled structure of FGF12A was docked using FGF13U residues 11–136.

D: Model of (Ca²⁺)₄-CaM and FGF12A bound to an Na_v CTD. Model was generated by docking the structure of (Ca²⁺)₂-CaM_C+Na_v1.2 IQ motif (2M5E) with the Na_v1.5 IQ motif in the crystallographic structure of apo CaM+FGF13U+Na_v1.5 CTD (4DCK) via Na_v1.2 IQ motif residues 1904-1924. A solution structure of (Ca²⁺)₄-CaM (2K0E) was docked via CaM residues 101-112 and 117-128 of 2M5E. The model structure of FGF12A was docked through residues 11–136 of FGF13U. For clarity, ribbon drawings of CaM and FGF13U of 4DCK, CaM and Na_v1.2 IQ motif of 2M5E and Na_v1.2 IQ motif of 6BUT are not shown.

Table S1
(Related to Fig. 2)
Comparison of FGF11A LTP Sequences From 60 Species

		LTP Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																												
Species	Common Name	Start Residue	R																							End Residue				
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23					
1	Homo sapiens	1	M	A	A	L	A	S	S	L	I	R	Q	K	R	E	V	R	E	P	G	S	R	P	23					
2	Danio rerio	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	P	K	A	N	R	Q	23				
3	Pangasianodon hypophthalmus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
4	Anarrhichthys ocellatus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
5	Myripristis murdjan	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
6	Hippoglossus hippoglossus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
7	Oreochromis aureus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
8	Denticeps clupeoides	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
9	Astyanax mexicanus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
10	Cyprinus carpio	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	V	V	D	Q	Q	A	N	R	Q	23			
11	Clupea harengus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	E	I	K	D	D	P	Q	A	N	R	Q	23	
12	Scophthalmus maximus	1	M	A	A	L	A	S	S	S	L	I	R	Q	R	R	E	E	I	V	R	E	P	P	G	S	R	Q	23	
13	Microcebus murinus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
14	Vicugna pacos	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
15	Macaca mulatta	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
16	Papio anubis	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
17	Trachypithecus francoisi	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
18	Castor canadensis	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
19	Rhinopithecus roxellana	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
20	Tupaia chinensis	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
21	Carlitro syrichta	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
22	Canis lupus familiaris	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
23	Crocuta crocuta	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
24	Canis lupus dingo	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
25	Sapajus apella	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	N	R	P	23
26	Autos nancymaei	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
27	Felis catus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
28	Zalophus californianus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
29	Nomascus leucogenys	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
30	Callirhinus ursinus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
31	Otolemur garnettii	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
32	Pteropus alecto	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
33	Suricata suricatta	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
34	Dasyurus novemcinctus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
35	Bos taurus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
36	Phyllostomus discolor	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
37	Hylobates moloch	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
38	Pongo abelii	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
39	Heterocephalus glaber	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
40	Equus caballus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
41	Ovis aries	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
42	Eptesicus fuscus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
43	Leptonychotes weddellii	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
44	Octodon degu	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
45	Gorilla gorilla gorilla	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
46	Cavia porcellus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
47	Callithrix jacchus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	N	R	P	23
48	Mus musculus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
49	Mirounga leonina	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
50	Ailuropoda melanoleuca	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
51	Grammomys surdaster	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
52	Ursus arctos horribilis	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
53	Grizzly Bear	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
54	Nannospalax galili	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
55	Rattus norvegicus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
56	Desmodus rotundus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
57	Meriones unguiculatus	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
58	Mus caroli	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
59	Uroctellus parryii	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G	S	R	P	23
60	Lontra canadensis	1	M	A	A	L	A	S	S	S	L	I	R	Q	K	R	R	E	V	V	R	E	P	P	G	G				

Table S2
(Related to Fig. 2)
Comparison of FGF12A LTP Sequences From 56 Species

		LTP Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																									
Species	Common Name	Start Residue	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	N	S	22	23	End Residue		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23		
1	Homo sapiens	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	N	S	D	R	23	
2	Danio rerio	1	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	N	N	S	D	R	22	
3	Apteryx rowi	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
4	Castor canadensis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
5	Cavia porcellus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
6	Cricetulus griseus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
7	Cyprinus carpio	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
8	Fukomys damarensis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
9	Gallus gallus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
10	Lynx pardinus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
11	Macaca mulatta	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
12	Mirounga leonina	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
13	Myotis davidi	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
14	Myotis lucifugus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
15	Rattus norvegicus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
16	Spheniscus humboldti	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
17	Thamnophis elegans	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
18	Todus mexicanus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
19	Mus musculus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
20	Arvicathis niloticus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
21	Phocoena sinus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
22	Camelus dromedarius	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
23	Nannospalax galilii	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
24	Camelus ferus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
25	Rhinolophus ferrumequinum	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
26	Trichechus manatus latirostris	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
27	Lonchura striata domestica	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
28	Tupaia chinensis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
29	Dasyurus novemcinctus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
30	Ornithorhynchus anatinus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
31	Camarhynchus parvulus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
32	Dromaius novaehollandiae	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
33	Microcaecilia unicolor	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
34	Podarcis muralis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
35	Geotrypetes seraphini	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
36	Gaboon Caecilian	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
37	Terrapene carolina triunguis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
38	Notechis scutatus	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
39	Xenopus tropicalis	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
40	Gopherus evgoodei	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
41	Chelonoidis abingdonii	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
42	Labeo rohita	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
43	Denticeps clupeoides	1	M	A	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
44	Chanos chanos	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
45	Epinephelus lanceolatus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
46	Paramormyrops kingsleyae	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
47	Betta splendens	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
48	Anabas testudineus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	23
49	Notolabrus celidotus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
50	Oryzias melastigma	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
51	Oryzias latipes	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
52	Fundulus heteroclitus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
53	Boleophthalmus pectinirostris	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
54	Labrus bergylta	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
55	Oreochromis niloticus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22
56	Hippoglossus hippoglossus	1	M	-	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	S	S	N	S	D	R	22

Table S3
(Related to Fig. 2)
Comparison of FGF13A LTP Sequences From 63 Species

	Species	Common Name	LTP Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																							
			M	A	A	I	A	S	L	I	R	Q	K	R	Q	R	E	R	E	R	E	K	S	N	End Residue	
Start Residue	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23			
1	Loxodonta africana	African Bush Elephant	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
2	Vicugna pacos	Alpaca	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
3	Uroctellus parryi	Arctic Ground Squirrel	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
4	Alaudala cheleensis	Asian Short-Toed Lark	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
5	Serinus canaria	Atlantic Canary	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
6	Hirundo rustica	Barn Swallow	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
7	Limosa lapponica baueri	Bar-tailed Godwit	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
8	Rattus rattus	Black Rat	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
9	Myotis brandtii	Brandt's Bat	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
10	Python bivittatus	Burmese Python	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
11	Bos taurus	Cattle	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
12	Alligator sinensis	Chinese Alligator	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
13	Macaca fascicularis	Crab-eating Macaque	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
14	Myotis davidi	David's Myotis	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
15	Gopherus evgoodei	Desert Tortoise	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
16	Canis lupus familiaris	Dog	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
17	Camelus dromedarius	Dromedary	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
18	Pseudonaja textilis	Eastern Brown Snake	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
19	Eriothacus rubecula	European Robin	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
20	Geotrypetes seraphini	Gaboone Caecilian	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
21	Mesocricetus auratus	Golden Hamster	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
22	Acrocephalus arundinaceus	Great Reed Warbler	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
23	Rhinolophus ferrumequinum	Greater Horseshoe Bat	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
24	Chelonia mydas	Green Sea Turtle	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
25	Cavia porcellus	Guinea Pig	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
26	Mus musculus	House Mouse	1	M	T	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23
27	Homo sapiens	Human	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	E	K	S	N	23
28	Cercotrichas coryphoeus	Karoo Scrub Robin	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
29	Phascolarctos cinereus	Koala	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
30	Turnix velox	Little Buttonquail	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
31	Mionectes macconnelli	McConnell's Flycatcher	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
32	Suricata suricatta	Meerkat	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	R	E	K	S	N	23
33	Meriones unguiculatus	Mongolian Gerbil	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
34	Heterocephalus glaber	Naked Mole-rat	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
35	Otolemur garnettii	Northern Greater Galago	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
36	Papio anubis	Olive Baboon	6	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
37	Chloropsis hardwickii	Orange-bellied Leafbird	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
38	Phainopepla nitens	Phainopepla	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
39	Pedionomus torquatus	Plains-wanderer	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
40	Ornithorhynchus anatinus	Platypus	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
41	Protobothrops mucrosquamatus	Pointed Scale Viper	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
42	Todus mexicanus	Puerto Rican Tody	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
43	Gallus gallus	Red Junglefowl	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
44	Malurus elegans	Red-winged Fairywren	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
45	Macaca mulatta	Rhesus Macaque	6	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	G	R	E	E	K	S	N	23	
46	Rhinatremra bivittatum	Rhinatremra bivittatum	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
47	Origma solitaria	Rockwarbler	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
48	Turdus rufiventris	Rufous-bellied Thrush	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
49	Xiphophorus maculatus	Southern Platfish	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
50	Drymodes brunneopygia	Southern Scrub Robin	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
51	Acipenser ruthenus	Sterlet	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
52	Pongo abelii	Sumatran Orangutan	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
53	Cathartes ustulatus	Swainson's Thrush	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
54	Notechis Scutatus	Tiger Snake	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
55	Thalassophryne amazonica	Toadfish	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
56	Tupaia chinensis	Treeshrew	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
57	Podarcis muralis	Wall Lizard	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
58	Xenopus tropicalis	Western Clawed Frog	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
59	Nicator chloris	Western Nicator	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
60	Chrysemys picta bellii	Western Painted Turtle	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
61	Thamnophis elegans	Western Terrestrial Garter Snake	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
62	Sus scrofa	Wild Boar	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	
63	Taeniopygia guttata	Zebra Finch	1	M	A	A	I	A	S	S	L	I	R	Q	K	R	Q	A	R	E	E	K	S	N	23	

Table S4
(Related to Fig. 2)
Comparison of FGF14A LTP Sequences From 48 Species

LTP Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)

Species	Common Name	Start Residue	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	D	R	End Residue		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23		
1	Calypte anna	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
2	Scleropages formosus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	I	D	R	23
3	Monopterus albus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
4	Alectura lathami	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
5	Limosa lapponica baueri	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
6	Pteropus alecto	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
7	Rattus rattus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
8	Felis catus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
9	Cricetulus griseus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
10	Desmodus rotundus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
11	Cottoperca gobio	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
12	Cynoglossus semilaevis	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
13	Denticeps clupeoides	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
14	Canis lupus dingo	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
15	Camelus dromedarius	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
16	Electrophorus electricus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
17	Anguilla anguilla	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	V	D	R	23
18	Geotrypetes seraphini	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
19	Aquila chrysaetos chrysaetos	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
20	Microcebus murinus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
21	Mus musculus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
22	Homo sapiens	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
23	Clarias magur	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
24	Oryzias latipes	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
25	Trichechus manatus latirostris	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
26	Microcaecilia unicolor	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
27	Chanos chanos	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	I	D	R	23
28	Fundulus heteroclitus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
29	Dasyurus novemcinctus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
30	Paramormyrops kingsleyae	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	I	D	R	23
31	Chelonoidis abingdonii	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
32	Microtus ochrogaster	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
33	Takifugu flavidus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
34	Gallus gallus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
35	Erpetoichthys calabaricus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	T	D	R	23
36	Xiphophorus maculatus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
37	Mirounga leonina	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
38	Nannopalax galili	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
39	Mustela erminea	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
40	Thalassophryne amazonica	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	F	D	R	23
41	Amazona aestiva	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
42	Rhinatremabivittatum	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
43	Bubalus bubalis	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
44	Xenopus tropicalis	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23
45	Chrysemys picta bellii	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
46	Zonotrichia albicollis	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
47	Sus scrofa	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	W	D	R	23
48	Mastacembelus armatus	1	M	A	A	A	I	A	S	G	L	I	R	Q	K	R	R	Q	A	R	E	Q	H	L	D	R	23

Table S5
(Related to Fig. 2)
Comparison of FGF11A CaMBD Sequences From 60 Species

	Species	Common Name	CaMBD Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																				End Residue												
			36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62						
1	Homo sapiens	Human	K	S	L	C	Q	K	Q	L	L	I	L	S	K	V	R	L	C	G	G	R	P	A	R	P	D	R	62						
2	Danio rerio	Zebrafish	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	K	V	R	L	C	G	S	R	G	R	K	L	E	K	62				
3	Pangasianodon hypophthalmus	Iridescent shark	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	L	E	K	62			
4	Anarrhichthys ocellatus	Wolf eel	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	L	E	K	62			
5	Myripristis murdjan	Soldierfish	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	M	E	K	62		
6	Hippoglossus hippoglossus	Righteye Founder	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	E	K	62		
7	Oreochromis aureus	Blue Tilapia	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	E	K	62		
8	Dentichaps clupeoides	Denticle Herring	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	E	K	62		
9	Astyanax mexicanus	Mexican Tetra	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	E	K	62		
10	Cyprinus carpio	Carp	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	V	K	62		
11	Clupea harengus	Atlantic Herring	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	L	E	K	62		
12	Scophthalmus maximus	Turbot	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	S	R	G	R	K	K	M	E	R	62		
13	Microcebus murinus	Gray Mouse Lemur	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	P	A	R	P	D	R	62	
14	Vicugna pacos	Alpaca	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
15	Macaca mulatta	Rhesus Macaque	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
16	Papio anubis	Olive Baboon	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
17	Trachypithecus francoisi	Tonkin leaf monkey	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
18	Castor canadensis	North American Beaver	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
19	Rhinopithecus roxellana	Golden snub-nosed monkey	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
20	Titipia chinenesis	Treeshrew	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
21	Carlito syrichta	Philippine Tarsier	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
22	Canis lupus familiaris	Dog	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
23	Crocuta crocuta	Spotted Hyena	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
24	Canis lupus dingo	Dingo	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
25	Sapajus apella	Tufted Capuchin	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
26	Aotus nancymaeae	Night Monkey	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
27	Felis catus	Cat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
28	Zalophus californianus	California Sea Lion	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
29	Nomascus leucogenys	Northern White-Cheeked Gibbon	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
30	Callithrinus ursinus	Northern Fur Seal	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
31	Otolemur garnettii	Northern Greater Galago	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	T	R	D	R	62	
32	Pteropus alecto	Black Flying Fox	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	N	R	62
33	Suricata suricatta	Meerkat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	S	R	P	D	R	62
34	Dasyurus novemcinctus	None-banded Armadillo	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	S	R	P	D	R	62
35	Bos taurus	Cattle	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	T	P	D	R	62
36	Phyllostomus discolor	Pale Spear-nosed Bat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	G	R	P	D	H	62
37	Hylobates moloch	Silvery Gibbon	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
38	Pongo abelii	Sumatran Orangutan	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	L	P	D	R	62
39	Heterocephalus glaber	Naked mole-rat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	A	P	D	R	62
40	Equus caballus	Horse	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	A	P	D	R	62
41	Ovis aries	Sheep	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	T	D	R	62
42	Eptesicus fuscus	Big Brown Bat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
43	Leptonychotes weddelli	Weddell Seal	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
44	Otocodon degus	Common Degu	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
45	Gorilla gorilla gorilla	Gorilla	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
46	Cavia porcellus	Guinea Pig	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	R	62
47	Calithrix jacchus	Common Marmoset	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	R	P	D	G	62
48	Mus pahari	Gardiner's Shrewmouse	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	T	R	Q	D	R	62
49	Mirounga leonina	Southern Elephant Seal	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	T	R	Q	D	R	62
50	Mus musculus	House Mouse	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	T	P	D	R	62
51	Ailuropoda melanoleuca	Giant Panda	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	A	T	P	D	R	62
52	Grammomys surdaster	African Tree Rat	36	K	S	L	C	Q	K	Q	I	L	I	L	I	S	S	K	V	R	L	C	G	G	R	G	R	R	P	T	A	R	P	D	R

Table S6
(Related to Fig. 2)
Comparison of FGF12A CaMBD Sequences From 56 Species

	Species	Common Name	CaMBD Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																						End Residue						
			38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64		
1	Homo sapiens	Human	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	R	K	R	P	V	R	64		
2	Danio rerio	Zebrafish	R	S	L	C	E	R	H	F	L	G	V	F	S	K	V	R	F	C	S	G	K	K	R	P	V	R	63		
3	Apteryx rowi	Kiwi	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	R	K	R	P	V	R	64		
4	Castor canadensis	North American Beaver	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	R	K	R	P	V	R	64		
5	Cavia porcellus	Guinea Pig	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	R	K	R	P	V	R	64		
6	Cricetulus griseus	Chinese Hamster	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	R	K	R	P	V	R	64		
7	Cyprinus carpio	Common Carp	R	S	L	C	E	R	H	F	L	G	V	F	S	K	V	R	F	C	S	G	K	K	I	P	V	R	64		
8	Fukomys damarensis	Damara Land Mole-Rat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	K	K	I	P	V	R	64		
9	Gallus gallus	Red Junglefowl	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
10	Lynx pardalis	Iberian Lynx	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
11	Macaca mulatta	Rhesus Macaque	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
12	Mirounga leonina	Southern Elephant Seal	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
13	Myotis davidi	Vesper Bat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
14	Myotis lucifugus	Little Brown Bat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
15	Rattus norvegicus	Brown Rat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
16	Spheniscus humboldti	Humboldt Penguin	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
17	Thamnophis elegans	Western Terrestrial Garter Snake	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
18	Todus mexicanus	Puerto Rican Tody	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
19	Mus musculus	House Mouse	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
20	Arvicathis niloticus	African grass rat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
21	Phocaena sinus	Porpoise	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
22	Camelus dromedarius	Arabian Camel	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
23	Nannospalax galili	Mole-rat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
24	Camelus ferus	Bactrian Camel	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
25	Rhinolophus ferrumequinum	Horseshoe Bat	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
26	Trichechus manatus latirostris	Florida Manatee	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
27	Lonchura striata domestica	Society Finch	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
28	Tupaia chinensis	Tree Shrew	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
29	Dasyurus novemcinctus	Nine-Banded Armadillo	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
30	Ornithodoros anatinus	Platypus	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
31	Camarhynchus parvulus	Small Tree Finch	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
32	Dromaius novaehollandiae	Emu	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
33	Microcaecilia unicorn	Microcaecilia unicorn	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
34	Podarcis muralis	Wall Lizard	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
35	Geotrypetes seraphini	Gaboon Caecilian	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
36	Chrysemys picta bellii	Western Painted Turtle	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
37	Terrapene carolina triunguis	Three-Toed Box Turtle	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
38	Notechis scutatus	Tiger Snake	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
39	Xenopus tropicalis	Western Clawed Frog	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
40	Gopherus evgoodei	Goode's Thornscurt Tortoise	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
41	Chelonoidis abingdonii	Pinta Island Tortoise	R	S	L	C	E	R	H	V	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
42	Labeo rohita	Rohu	R	S	L	C	E	R	H	I	F	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63	
43	Denticlops clupeoides	Denticle Herring	R	S	L	C	E	R	H	I	F	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63	
44	Chanos chanos	Milkfish	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
45	Epinephelus lanceolatus	Giant Grouper	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
46	Paramormyrops kingsleyae	Paramormyrops kingsleyae	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
47	Betta splendens	Siamese Fighting Fish	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
48	Anabas testudineus	Climbing Perch	R	S	L	C	E	R	H	I	F	S	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	64	
49	Notolabrus celidotus	Spotty	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
50	Oryzias melastigma	Marine Medaka	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
51	Oryzias latipes	Japanese Rice Fish	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
52	Fundulus heteroclitus	Mummichog	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
53	Boleophthalmus pecteniostriatus	Mudskipper	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
54	Labrus bergylta	Ballan Wrasse	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
55	Oreochromis niloticus	Nile Tilapia	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63
56	Hippoglossus hippoglossus	Atlantic Halibut	R	S	L	C	E	R	H	F	F	L	G	V	F	S	K	V	R	F	C	S	G	G	R	K	R	P	V	R	63

Table S7
(Related to Fig. 2)
Comparison of FGF13A CaMBD Sequences From 53 Species

	Species	Common Name	CaMBD Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																						End Residue				
			35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	
1	Homo sapiens	Human	K	T	S	C	D	K	N	L	N	V	F	R	V	K	L	F	G	S	K	R	R	R	R	60			
2	Myotis davidii	David's Myotis	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
3	Meriones unguiculatus	Mongolian Gerbil	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
4	Myotis brandtii	Brandt's Bat	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
5	Tupaia chinensis	Treeshrew	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
6	Camelus dromedarius	Dromedary	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
7	Vicugna pacos	Alpaca	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
8	Rhinolophus ferrumequinum	Greater Horseshoe Bat	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
9	Bos taurus	Cattle	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
10	Suricata suricatta	Meerkat	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
11	Loxodonta africana	African Bush Elephant	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
12	Cavia porcellus	Guinea Pig	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
13	Pongo abelii	Sumatran Orangutan	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
14	Sus scrofa	Wild Boar	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
15	Otolemur garnettii	Northern Greater Galago	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
16	Urocitellus parvii	Arctic Ground Squirrel	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
17	Mesocricetus auratus	Golden Hamster	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
18	Macaca fasciularis	Crab-eating Macaque	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
19	Heterocephalus glaber	Naked Mole-rat	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
20	Mus musculus	House Mouse	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
21	Canis lupus familiaris	Dog	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
22	Rattus rattus	Black Rat	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	A	Q	K	60	
23	Limosa lapponica baueri	Bar-tailed Godwit	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
24	Nicator chloris	Western Nicator	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
25	Malurus elegans	Red-winged Fairywren	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
26	Origma solitaria	Rockwarbler	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
27	Acrocephalus arundinaceus	Great Reed Warbler	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
28	Mionectes macconnelli	McConnell's Flycatcher	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
29	Drymodes brunneopygia	Southern Scrub Robin	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
30	Todus mexicanus	Puerto Rican Tody	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
31	Hirundo rustica	Barn Swallow	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
32	Pedionomus torquatus	Plains-wanderer	K	G	N	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
33	Alligator sinensis	Chinese Alligator	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
34	Erythacus rubecula	European Robin	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
35	Phascolarctos cinereus	Koala	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
36	Alaudala cheleensis	Asian Short-toed Lark	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
37	Chloropsis hardwickii	Orange-bellied Leafbird	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
38	Turnix velox	Little Buttonquail	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
39	Taeniopygia guttata	Zebra Finch	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
40	Catharus ustulatus	Swainson's Thrush	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
41	Serinus canaria	Atlantic Canary	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
42	Gallus gallus	Red Junglefowl	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
43	Ornithorhynchus anatinus	Platypus	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
44	Cercotrichas coryphoeus	Karoo Scrub Robin	K	G	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
45	Turdus rufiventris	Rufous-bellied Thrush	K	G	N	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
46	Xenopus tropicalis	Western Clawed Frog	K	G	N	C	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
47	Rhinatremabivittatum	Rhinatremabivittatum	K	G	N	C	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60	
48	Chelonia mydas	Green Sea Turtle	K	G	N	S	E	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60
49	Geotrypetes seraphini	Gaboon Caecilian	K	G	N	S	E	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	K	K	R	R	R	60
50	Gopherus evgoodei	Desert Tortoise	K	G	N	S	E	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	S	K	K	R	R	60
51	Chrysemys picta bellii	Western Painted Turtle	K	G	N	S	E	E	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	S	K	K	R	R	60
52	Papio anubis	Olive Baboon	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	S	K	K	P	R	60	
53	Macaca mulatta	Rhesus Macaque	K	T	S	C	D	K	N	K	L	N	V	F	S	R	V	K	L	F	G	S	S	K	K	P	R	60	

Table S8
(Related to Fig. 2)
Comparison of FGF14A CaMBD Sequences From 48 Species

CaMBD Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)

Species	Common Name	CaMBD Sequence Table (Completely Conserved Positions Highlighted in Yellow, Positions Conserved in ≥ 90% of Species Highlighted in Green)																																	End Residue
		37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63							
1	Calypte anna	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
2	Scleropages formosus	K	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
3	Monopterus albus	K	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
4	Alectura lathami	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
5	Limosa lapponica baueri	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
6	Pteropus alecto	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
7	Rattus rattus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
8	Felis catus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
9	Cricetulus griseus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
10	Desmodus rotundus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
11	Cottoperca gobio	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
12	Cynoglossus semilaevis	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
13	Denticeps clupeoides	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
14	Canis lupus dingo	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
15	Camelus dromedarius	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
16	Electrophorus electricus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
17	Anguilla anguilla	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
18	Geotrypetes seraphini	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
19	Aquila chrysaetos chrysaetos	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
20	Microcebus murinus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
21	Mus musculus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
22	Homo sapiens	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
23	Clarias magur	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
24	Oryzias latipes	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
25	Trichechus manatus latirostris	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
26	Microcaecilia unicornalis	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
27	Chanos chanos	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
28	Fundulus heteroclitus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
29	Dasyurus novemcinctus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
30	Paramormyrops kingsleyae	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
31	Chelonoidis abingdonii	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
32	Microtus ochrogaster	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
33	Takifugu flavidus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
34	Gallus gallus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
35	Erpetoichthys calabaricus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
36	Xiphophorus maculatus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
37	Mirounga leonina	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
38	Nannospalax galili	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
39	Mustela erminea	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
40	Thalassophryne amazonica	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
41	Amazona aestiva	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
42	Rhinatremabivittatum	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
43	Bubalus bubalis	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
44	Xenopus tropicalis	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
45	Chrysemys picta bellii	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
46	Zonotrichia albicollis	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
47	Sus scrofa	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							
48	Mastacembelus armatus	R	G	L	C	N	G	N	L	V	D	I	S	K	V	R	I	F	G	L	K	K	R	R	L	R	R	63							