

Supplemental Table 1. Summary of known and predicted homologues of clc chloride channel family. Gene loci organization in the genomic region are collected from NCBI and Release 79 (March 2015) of Ensembl Genome Browser.

| CLC-1 orthologs | | | |
|-------------------------|------------------------------|-----------------------------------|-------------------------------------|
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Human CLC-1 | <i>Homo sapiens</i> | Ch.7: 143.01m | NP_000074 |
| Rat CLC-1 | <i>Rattus norvegicus</i> | Ch.4: 136.48m | ENSRNOG000000016917 |
| Zebrafish CLC-1a | <i>Danio rerio</i> | Ch.19: 10.23m | ENSDARG000000062084 |
| Zebrafish CLC-1b | <i>Danio rerio</i> | Ch.16: 19.54m | ENSDARG000000012269 |
| Tilapia CLC-1a | <i>Oreochromis niloticus</i> | Scaffold GL831254.1: 0.67m | ENSONIG000000007006 |
| Tilapia CLC-1b | <i>Oreochromis niloticus</i> | Scaffold GL831225.1: 0.85m | ENSONIG000000012880 |
| Cave fish CLC-1a | <i>Astyanax mexicanus</i> | Scaffold KB882251.1: 1.14m | ENSAMXG000000009534 |
| Cave fish CLC-1b | <i>Astyanax mexicanus</i> | Scaffold KB882127.1: 2.86m | ENSAMXG000000019025 |
| Spotted gar CLC-1 | <i>Lepisosteus oculatus</i> | Ch.LG26: 13.68m | ENSLOCG000000008392 |
| CLC-2 orthologs | | | |
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Human CLC-2 | <i>Homo sapiens</i> | Ch.3: 184.06m | NP_004357 |
| Rat CLC-2 | <i>Rattus norvegicus</i> | Ch.11: 86.96m | ENSRNOG000000001742 |
| Zebrafish CLC-2a | <i>Danio rerio</i> | Ch.2: 16.73m | ENSDARG000000062427 |
| Zebrafish CLC-2b | <i>Danio rerio</i> | Scaffold Zv9_NA428: 31,423 | ENSDARG000000074681 |
| Zebrafish CLC-2c | <i>Danio rerio</i> | Ch.15: 46.08m | ENSDARG000000060439 |
| Tilapia CLC-2a | <i>Oreochromis niloticus</i> | Scaffold GL831134.1: 6.10m | ENSONIG000000009832 |
| Tilapia CLC-2b | <i>Oreochromis niloticus</i> | Scaffold GL831338.1: 0.15m | ENSONIG000000010801 |
| Tilapia 19823 | <i>Oreochromis niloticus</i> | Scaffold GL831632.1: 0.11m | ENSONIG000000019823 |
| Cave fish CLC-2a | <i>Astyanax mexicanus</i> | Scaffold KB882241.1: 1.54m | ENSAMXG000000019335 |
| Cave fish CLC-2b | <i>Astyanax mexicanus</i> | Scaffold KB882110.1: 1.46m | ENSAMXG000000011765 |
| Cave fish CLC-2c | <i>Astyanax mexicanus</i> | Scaffold KB882110.1: 1.62m | ENSAMXG000000011800 |
| Spotted gar CLC-2 | <i>Lepisosteus oculatus</i> | Ch.LG14: 17.69m | ENSLOCG000000008814 |
| CLC-K orthologs | | | |
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Human CLC-Ka | <i>Homo sapiens</i> | Ch.1: 16.35m | NP_004061 |
| Human CLC-Kb | <i>Homo sapiens</i> | Ch.1: 16.37m | NP_000076 |
| Rat CLC-Ka | <i>Rattus norvegicus</i> | Ch.5: 163.64m | ENSRNOG000000009680 |
| Rat CLC-Kb | <i>Rattus norvegicus</i> | Ch.5: 163.67m | ENSRNOG000000009897 |
| Zebrafish CLC-K | <i>Danio rerio</i> | Ch.23: 24.56m | ENSDARG000000022560 |
| Tilapia CLC-K | <i>Oreochromis niloticus</i> | Scaffold GL831308.1: 0.28m | ENSONIG000000006556 |
| Cave fish CLC-K | <i>Astyanax mexicanus</i> | Scaffold KB882098.1: 0.50m | ENSAMXG000000012509 |
| Spotted gar CLC-K | <i>Lepisosteus oculatus</i> | Ch.LG25: 14.22m | ENSLOCG000000007948 |

Supplemental Table 2. Summary of known and predicted homologues of clc chloride channel family. Gene loci organization in the genomic region are collected from NCBI and Release 79 (March 2015) of Ensembl Genome Browser.

| NCC orthologs | | | |
|-------------------------|-------------------------------|-----------------------------|-------------------------------------|
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Human NCC | <i>Homo sapiens</i> | Ch.16: 56.90m | ENSG00000070915 |
| Rat NCC | <i>Rattus norvegicus</i> | Ch.19: 11.08m | ENSRNOG00000018607 |
| Dog NCC | <i>Canis lupus familiaris</i> | Ch.2: 59.41m | ENSCAFG00000009034 |
| Zebrafish NCC | <i>Danio rerio</i> | Ch.18: 17.24m | ENSDARG00000013855 |
| Tetraodon NCC | <i>Tetraodon nigroviridis</i> | Ch.13: 0.78m | ENSTNIG00000005238 |
| Medaka NCC | <i>Oryzias latipes</i> | Ch.6: 0.46m | XP_004069408 |
| Tilapia NCC | <i>Oreochromis niloticus</i> | Scaffold GL831139.1: 1.40m | ENSONIG00000010663 |
| Stickleback NCC | <i>Gasterosteus aculeatus</i> | group XIX: 1.04m | ENSGACG00000002419 |
| Cave fish NCC | <i>Astyanax mexicanus</i> | Scaffold KB882123.1: 1.90m | ENSAMXG00000003658 |
| Lamprey NCCa | <i>Petromyzon marinus</i> | Scaffold GL478333: 5,880 | ENSPMAG00000002656 |
| Lamprey NCCb | <i>Petromyzon marinus</i> | Scaffold GL481265: 678 | ENSPMAG00000007638 |
| Spotted gar NCC | <i>Lepisosteus oculatus</i> | Ch.LG23: 16.11m | ENSLOCG00000007841 |
| Platyfish NCC | <i>Xiphophorus maculatus</i> | Scaffold JH556669.1: 1.43m | ENSXMAG00000015658 |
| NCC2 orthologs | | | |
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Zebrafish NCC2a1 | <i>Danio rerio</i> | Ch.7: 4.60m | ENSDARG00000055313 |
| Zebrafish NCC2a2 | <i>Danio rerio</i> | Ch.7: 5.46m | ENSDARG00000013743 |
| Zebrafish NCC2b | <i>Danio rerio</i> | Ch.7: 4.50m | ENSDARG00000071173 |
| Zebrafish NCC2c1 | <i>Danio rerio</i> | Ch.7: 4.56m | ENSDARG00000055253 |
| Zebrafish NCC2c2 | <i>Danio rerio</i> | Ch.7: 5.44m | ENSDARG00000055424 |
| Medaka NCC2a | <i>Oryzias latipes</i> | Scaffold474: 0.12m | AIE58038 |
| Medaka NCC2b | <i>Oryzias latipes</i> | Scaffold1284: 17,354 | AIE58039 |
| Tilapia NCC2a | <i>Oreochromis niloticus</i> | Scaffold GL831294.1: 1.65m | ENSONIG00000007875 |
| Tilapia NCC2b | <i>Oreochromis niloticus</i> | Scaffold GL831294.1: 1.71m | ENSONIG00000007896 |
| Stickleback NCC2a1 | <i>Gasterosteus aculeatus</i> | groupVII: 1.81m | ENSGACG00000018949 |
| Stickleback NCC2a2 | <i>Gasterosteus aculeatus</i> | groupVII: 1.83m | ENSGACG00000018955 |
| Cave fish NCC2a | <i>Astyanax mexicanus</i> | Scaffold KB882169.1: 0.89m | ENSAMXG00000009214 |
| Cod NCC2a | <i>Gadus morhua</i> | GeneScaffold_3889: 66,754 | ENSGMOG00000013213 |
| Spotted gar NCC2 | <i>Lepisosteus oculatus</i> | Scaffold JH591451.1:0.22m | ENSLOCG00000000965 |
| Platyfish NCC2a | <i>Xiphophorus maculatus</i> | Scaffold JH556911.1: 906 | ENSXMAG00000000941 |
| Platyfish NCC2b | <i>Xiphophorus maculatus</i> | Scaffold JH556911.1: 40,835 | ENSXMAG00000000951 |
| NCC paralogs | | | |
| Protein name | Species | Gene loci | Accession/Prediction Numbers |
| Ciona NKCC1 | <i>Ciona intestinalis</i> | Ch.8: 0.16m | ENSCING00000023743 |
| Ciona KCC | <i>Ciona intestinalis</i> | Scaffold HT000119.1: 0.26m | ENSCING00000003302 |

Supplemental Table 3. The identities of human and zebrafish CLC-1 and -2.

| | CLC-1 | clc-1a | clc-1b | CLC-2 | clc-2a | clc-2b | clc-2c |
|--------------------|--------------|------------------|------------------|--------------|------------------|------------------|------------------|
| | Human | Zebrafish | Zebrafish | Human | Zebrafish | Zebrafish | Zebrafish |
| CLC-1 | | | | | | | |
| Human | - | 53% | 52% | 45% | 44% | 45% | 35% |
| clc-1a | | | | | | | |
| Zebrafish | | - | 60% | 44% | 43% | 45% | 35% |
| clc-1b | | | | | | | |
| Zebrafish | | | - | 47% | 46% | 49% | 39% |
| CLC-2_Human | | | | | | | |
| an | | | | - | 63% | 69% | 44% |
| clc-2a | | | | | | | |
| Zebrafish | | | | | - | 67% | 44% |
| clc-2b | | | | | | | |
| Zebrafish | | | | | | - | 53% |
| clc-2c | | | | | | | |
| Zebrafish | | | | | | | - |

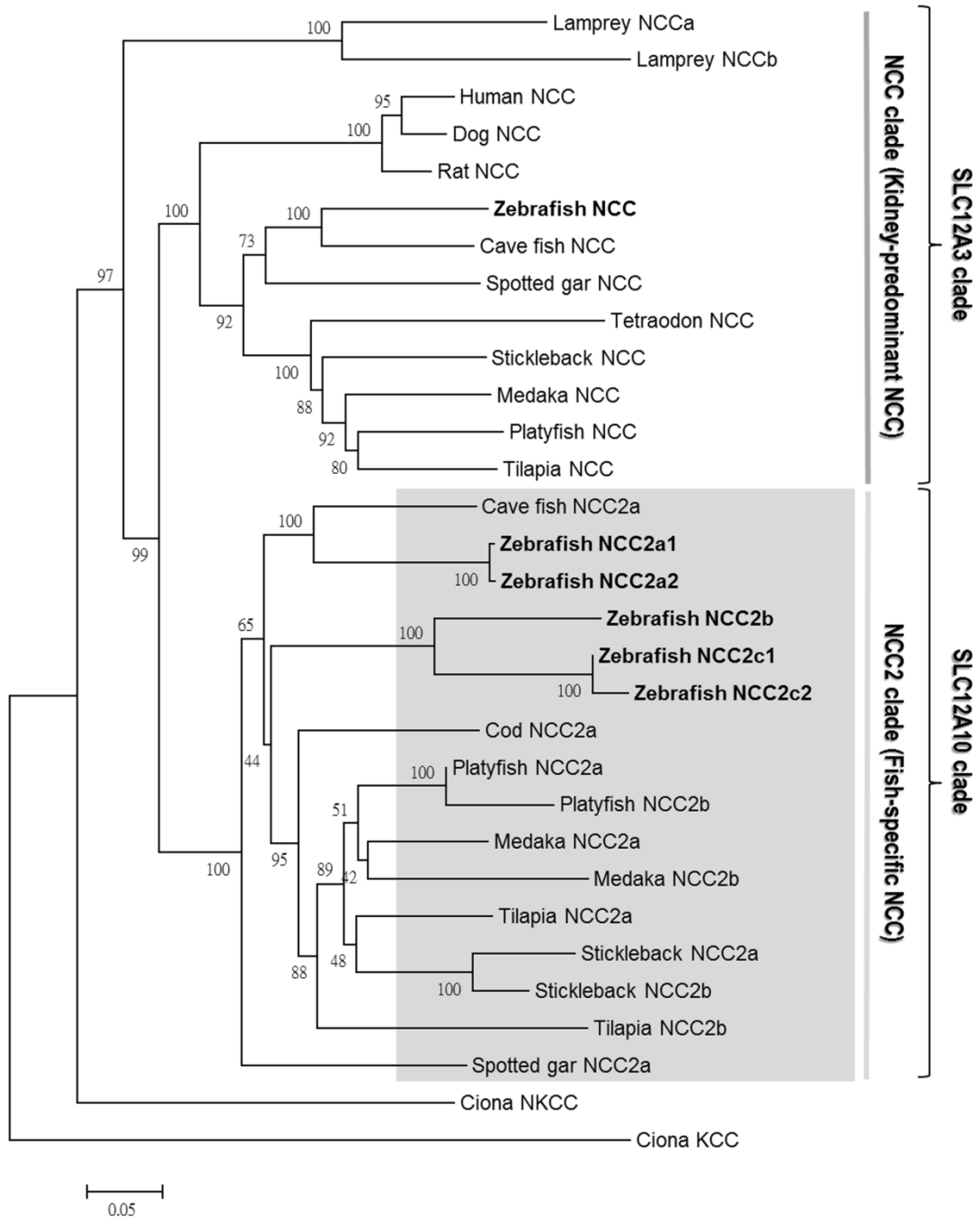
Supplemental Figure Legends

Supplemental Fig 1. A phylogenetic tree of NCC and NCC2s proteins. Zebrafish NCC and NCC2s proteins are shown in bold. The phylogenetic tree was constructed using the neighbor-joining method with ClustalW and MEGA6. Numbers indicate bootstrap values and the scale bar represents a genetic distance of 0.05 amino-acid substitutions per site. The nomenclature of the proteins are renamed according to the paper [52]. The NCBI or Ensembl accession numbers are as listed in Table S2.

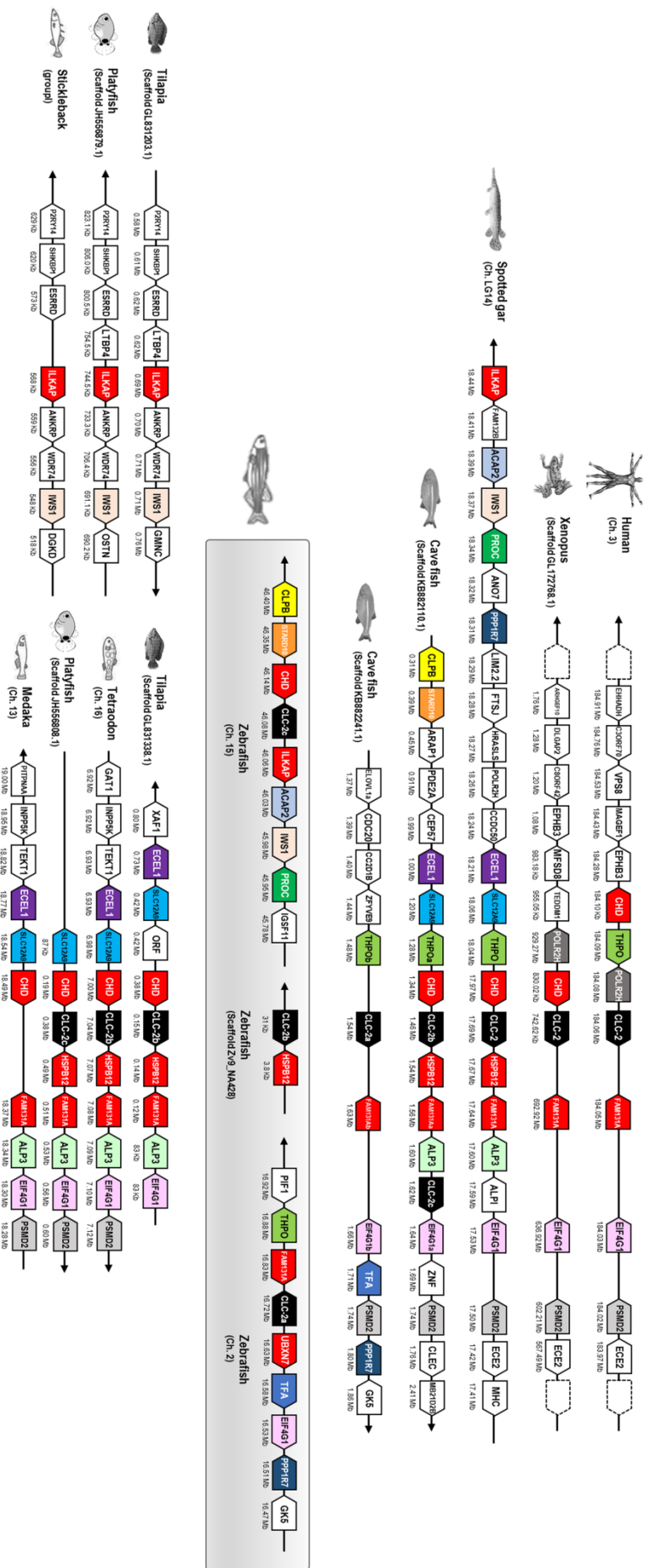
Supplemental Fig 2. Synteny map comparing homologues of the CLC-2 loci and the flanking genes in human (*Homo sapiens*), African clawed frog (*Xenopus laevis*), spotted gar (*Lepisosteus oculatus*), cave fish (*Astyanax mexicanus*), tilapia (*Oreochromis niloticus*), platyfish (*Xiphophorus maculatus*), pufferfish (*Tetraodon nigroviridis*), medaka (*Oryzias latipes*), and zebrafish (*Danio rerio*). The putative annotation of the transcripts neighboring the CLC-2 homologues was determined using both the NCBI and Ensembl genome browser system.

Supplemental Fig 3. Synteny map comparing homologues of the CLC-1 loci and the flanking genes in human (*Homo sapiens*), spotted gar (*Lepisosteus oculatus*), and zebrafish (*Danio rerio*). The putative annotation of the transcripts neighboring the CLC-1 homologues was determined using both the NCBI and Ensembl genome browser system.

Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3

