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## Supplementary Materials

### Supplementary Text

#### 1. Full-length cDNA and bioinformatics of *LcHif-1 $\alpha$*

The full-length cDNA of *LcHif-1 $\alpha$*  (GenBank accession number: MZ197829) was 3 647 bp, including a 272 bp 5' non-coding region, 1 091 bp 3' non-coding region, and 2 256 bp open reading frame (ORF), encoding a total of 751 amino acids (aa) (Figure S1). The predicted molecular weight of the *LcHif-1 $\alpha$*  protein was 84.19 kDa. The *LcHif-1 $\alpha$*  protein contained a basic helix-loop-helix domain (bHLH, 12–82 aa), PAS domain (88–151 aa), PAS\_3 domain (251–338 aa), Hif-1 domain (548–578 aa), and carboxy-terminal transcription activation domain (C-TAD, 714–750 aa) (Figure S2).

Multiple sequence comparison of *LcHif-1 $\alpha$*  with Hif-1 $\alpha$  proteins from other species is shown in Figure S3. *LcHif-1 $\alpha$*  shared 99.3%, 72.4%, 50.8%, 59.8%, 53.9%, 51.5%, 51.4%, 50.2%, and 50.2% homology with the Hif-1 $\alpha$  of *Collichthys lucidus*, *Oryzias latipes*, *Mustelus canis*, *Danio rerio*, *Gallus gallus*, *Homo sapiens*, *Sus scrofa*, *Mus musculus*, and *Xenopus tropicalis*, respectively. The homology of the functional bHLH, PAS, PAS-3, Hif-1, and C-TAD domains among the Hif-1 $\alpha$  proteins of the above species was extremely high, suggesting that the Hif-1 $\alpha$  protein is relatively conserved among species.

The phylogenetic tree of *LcHif-1 $\alpha$*  with homologous Hif-1 $\alpha$  proteins from other species is shown in Figure S4. *LcHif-1 $\alpha$*  was evolutionarily closer to the Hif-1 $\alpha$  protein of bony fish, such as *C. lucidus*, *Micropogonias undulatus*, *Epinephelus coioides*, *Oryzias latipes*, and *Danio rerio*, and more evolutionarily distant from the Hif-1 $\alpha$  protein of cartilaginous fish, mollusks, amphibians, and mammals.

#### 2. Full-length cDNA and bioinformatics of *LcHsp70*

The full-length cDNA of *LcHsp70* (GenBank accession number: MZ197830) was 2 205 bp, including a 142 bp 5' non-coding region, 146 bp 3' non-coding region, and 1 917 bp ORF, encoding a total of 638 aa (Figure S5). The predicted molecular weight of the *LcHsp70* protein was 70.29 kDa. The *LcHsp70* protein contained a DNA binding domain (NBD, 3–387 aa), substrate binding domain (SBD, 395–510 aa), and carboxy-terminal (C-terminal) variable region (VH, 511–634 aa). The nuclear localization signal (NLS, 247–274 aa) was located within the NBD. In addition, 4 aa at the C-terminus (EEVD) were cytoplasm-specific regulatory motifs (Figure S6).

Multiple sequence alignment of *LcHsp70* with homologous Hsp70 proteins from other species is shown in Figure S7. *LcHsp70* shared 99.7%, 70.8%, 89.5%, 84.7%, 85.0%, 85.0%, 83.4%, 82.4%, and 79.1% homology with the Hsp70 of *Drosophila melanogaster*, *Danio rerio*, *H. sapiens*, *X. tropicalis*, *G. gallus*, *Pelodiscus sinensis*, *Procambarus clarkii*, and *Octopus tankahkeei*, respectively, suggesting that the Hsp70 protein is highly conserved among species.

The phylogenetic tree of *LcHsp70* with s Hsp70 proteins from other species is shown in Figure S8. *LcHsp70* was evolutionarily closer to the Hsp70 protein of bony fish, such as *Miichthys miiuy*, *Micropterus salmoides*, *O. mykiss*, and *D. rerio*, and relatively evolutionarily distant from the Hsp70 protein of invertebrates, such as *D. melanogaster* and *Bombyx mori*.

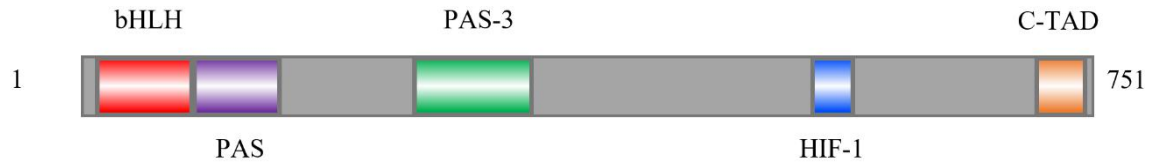
## Supplementary Figures

1 AGCGTGGCACTGTCTTTGAAGAAGAGGAAGAGTACAGACGAGTGGGCTGTGCGTGTGTTTTTTTGTAGCGGATTAAGGCTCGGCTTTTCTTTTCTT  
100 TTCTTTGTTTTTTGGCGAAATATACACCGTGAGAACTCGTATGCACTCGTATTTTTTTAAAAACAGGATTCATAAAAAAATCGTGGGATTTTTTTGG  
199 TTCATTTCCCTCGACGGGCCCCGATACAGCTCGATAACCCAGAGAGAGACTCAACTCAGGTCCTTTTCGTCTGACATGGACACAGGAATGTACCAGAAA  
1 M D T G I V P E  
298 AGAAAAGGGTGTAGTTCGGAGCGGAGAAAGGAGAAGTCCAGGGATGCAGCACGATGCCGGCTGGGAAGGAGTTCGAGGTTCTACGAGCTGGCCAGG  
9 K K R V S S E R R K E K S R D A A R C R R G K E S E V F Y E L A Q  
397 AGCTGCCCTGCCCCACAGCGTCCAGCTCCAGCCTGGACAAGGCCTCAATAATAGGGCTCACAATCAGCTACCTGCGCATGAGGAACTGCACGACTG  
42 E L P L P H S V S S S L D K A S I M R L T I S Y L R M R K L L S T  
496 ATGAGCCAATCGCAGAGGAGGACAGATCTTGATTTCCAGCTCAATGGCTCTACCTAAAGGCTCTGGACGGCTTTTTCATGGTGTGTCTGAAGACG  
75 D E P I A E E E T D L D F Q L N G S Y L K A L D G F F M V L S E D  
595 GAGATATGATCTATCTGTGCGGAGAATCAACAAGTCCGCGGCTGGCAGCAGTTTGATCTGACCGGACACAGCGTGTGACTTCACGCATCCCTGTG  
108 G D M I Y L S E N I N K C L G L A Q F D L T G H S V F D F T H P C  
694 ACCACGAGGAGTTCGAGGAGATGCTGATCCACAAAACAGGCTCCAAAAAGGCCAAGGAACCAACACAGAGCGCAACTTCTTCATCCGGATGAAGTGCA  
141 D H E E L R E M L I H K T G S K K A K E P N T E R N F F I R M K C  
793 CTCTCACAAGCCGGCCGACCCGTCATATGTCAAATCAGCTACATGGAAGGTGCTCCACTGCTCAGGTCATGTCGGTGTGACTGACAACCCGACCCGAC  
174 T L T S R G R T V N V K S A T T W K V L H C S G H V R V S D N R T E  
892 AGACAAAAGGGCAAAGGAACCCCGTCCCTACCTGGTTTTTAACTCTGATCCCATCCACACCCCTCCAACATCGAGGTCCTCTGGACACCAAGA  
207 Q T N G Q K E P P V P Y L V L I C D P I P H P S N I E V P L D T K  
991 CCTTCTCAGCCGCATACAAATGGACATGAAGTTCACATATTTGACGAGAGGATCACCAGGCTCATGGGTTATGATCCAGATGACCTGTTGAATCGTT  
240 T F L S R H T M D M K F T Y C D E R I T E L M G Y D P D D L L N R  
1090 CTGTGTACGAGTACTATCAGCTCAGGACTCAGACCATCTACCAAGACTCACCACAACCTGTTTGCAAAAGGGCCAGGTCGACACAGGCCAGTACAGGA  
273 S V Y E Y Y H A Q D S D H L T K T H H N L F A K G Q V C T G Q Y R  
1189 TGTGGCAAGAGAGGAGGCTTTGTGTGGTGGAAACCAAGCCACTGTCTACTACAACAAGAATCTCAGCCACAGTGTGCTGTGTGTCAACT  
306 M L A K R G G F V W V E T Q A T V I Y N N K N S Q P Q C V V C V N  
1288 TTGTGCTCAGTGGCATCCAGGATGAGAAGCTGATCTGTCTCTGGAGCAGACAGAGGATGTAACCAGTGAAGGAGGAGTGCAGTGGAGGAAGAAG  
339 F V L S G I Q D E K L I L S L E Q T E D V K P V K E E L Q L E E E  
1387 AGGCTGTAGTGGAGAGCAGCCAGCCGAGATGTCTCAGTCTGCCGAAGGAGGAGTGGAGGAGAAGTCTCAAAAAGCGATGTATCAAACTGTTC  
372 E A V V E S S Q P E M S P V L P K E E V E E K V S K S D V I K L F  
1486 CTCGGCAATAGAGAGCGAGACTGGTCAAGCTGTACGACCAACTGAAGGAAGAGCCGAGGCTCTCACCCTGTGGCCCTGCTCCCGGAGACACCA  
405 T R A I E S E T L V S L Y D Q L K E E P E A L T L L A P A P G D T  
1585 TCGTCCCTGGACTTCAGTCTGATCCAGAGATCCAGTCCCTCTTACAAAAGATGTAATGCTCCCTCCACCGAGTGAAGCTGGCTGCTGCTGCTC  
438 I V P L D F S C S D P E I Q L P L Y K D V M L P S T S D K L A L P  
1684 TTTCCCTCTGCCACCCAGCGAGCTCTCCAGTACCAGTCCACTTCTGAGGATACAAAACTGAGCGCTATGATCCATCCCTTCCACTACAACAG  
471 L S P L P P S E P L H V T T A T S E D T K T E R Y D P S P S T T T  
1783 CTAGTCCCTCAGAGGCTGACAGTCCACTGGACTTTTGTTCCCCATGGACTCAGATATGAGTTCAGATTCAAACTCGACTTGTGGAGAGGCTGTTT  
504 A S S S E A D S P L D F C F P M D S D M S S D F K L D L V E K L F  
1882 CCATCGATACAGAGCCCAAGACTCCTTCACTACAGGCAAGTGGAGACTGGATCTGGAGATGTAGCTCCCTACATCCCATGGACGAGCAGTCC  
537 A I D T E P K T P F T T Q A V E D L D L E M L A P I P M D D D F  
1981 AGCTACGAGTCTGCCCAAGAAGAGCTCTATCTTGTGGACAGTCAAACTCCCTTGACAGTCTCCAGTCTGTGCTACTAAGGACATCCAGAGCTATC  
570 Q L R S L P Q E E P L S C G P V K S L D S S P V C V T K D I Q S Y  
2080 CCAGTCCCATTCAGCTCACCAGGACGCGCAGCGCTCCCGCAGCACCAGGAGCAGTTAACACCTCTCATCTGCCACCATCCTTGTATGAGGA  
603 P S S P F S S P G S R T A S P A P P E P V N T S H L A T I L A M R  
2179 CCACACAGTGGGCAACGAAGTCTCGCTTCGGACTTTGGCAGCGCAGAACTCGCAGCGCAAAAAGAAAATTATGTGACATAAAGAGATGATTGGACAG  
636 T T Q L G N E V S L R T L A A Q N S Q R K R K L C D I K E M I G Q  
2278 GAACTTGGCCAGGAAGAGTGGAAAGGCAAAAGCTGAAGCTCAGAGTCCAGGAACAACGACCACTGTGCTGCTCAGATTGGCGAGTGC  
669 G T C L R Q E E L E Q G K K L K A S E S G T T T I L L L P S D L A S  
2377 GTCTGCTGGGAAGCAGTCCAGAGAACCAGTCCCTCTTCACTGCGCAGCTCACCAGGAGTGGAGGTCACCGCCCTTGCAGGGTCGTC  
702 R L L G S T S E N T S S L F T L P Q L T R D D C E V N A P L Q G R  
2476 AGTACCTGCTCCAGGGGAGGAGTGTGCGCGCTTGGACCAGTCAATTTGAGTTCATTGCTTACCTGCTACTGCTGAACTAGACTGGACACTACAA  
735 Q Y L L Q G E E L L R A L D H V I \*  
2575 TTTCTCCCTCATATTTGCTGCTCCCTTCCCTCACCCCCACCCAGGCTGCCCCATTTTATGTATCTGAATGAGTTCGACTATAAATTTGGCTGCC  
2674 GTTTGTGCACATCAAGTGATATCTGCAGCATTCCACCGTGACAAACGCATAGCAGCATCTGGGTTTTTTTTTGGTGAAGGATTCAGGCATCATGAG  
2773 ATGTCCCAATTGTCATTTTTCTCGTTGTTGTTTTTCTCCCTCTCTCCGGGGAGTCTCTCAGCACACAGCGCTCGACAGATGACCCCTTTCC  
2872 AGCAGTCCACACAGAACCTGGCGTACTGCCAGCAGTGTATTGTAAGCTTCAGTCCGACAATTTATATTTTCTTAAAAAGAAAAATATTACCAGCAAT  
2971 ATATATTAAGCCTTTTTAGAGTCGTTTTAATGGGATTTGAACAATTTTTTCTCCCATACTTGTATGTTGACTGCTACCTAACAAAGATGCTCT  
3070 TAGTCCAGAAATATGAACACATGTTTAAACCTTGGTGGTTTGAATGTTATCTCCATTAATAGCTATCAGTCTTGGAGGTAATACATTTAATTTGTT  
3169 AGCAGTCCAGTACAGGTCACCTTTACTTTACTGTAAGTGTGTGTTACTGTACATATACCAGGGAATAAATTTACTCAGTATGGCTTCACGG  
3268 CTTAACTCTCAAAATGAAATGAGTCTTTACTCTTTTTTCTGATTACTTCTCATCATGGAGGATGGCATTCCCTCAACATGAAGTACTTTCATGTT  
3367 TCTTTTTTTTTGTTGTTTACTGTGCTACTTACTCAAAAGAGTCAAGTTAAAAAAGTGGGTCGCAACAACAAATTCATATTTAATCGTGTGATCA  
3466 GTCATCAATAGTATCATTTCGTGAGTTGTCAAACTGTTGCTCAATTAATGAGTGGGTTAATACCATGTTGGGTCATGCTTCTGTTGCTGTC  
3565 TAACATTAATGGCTTTAATAAAGTGTGATAAAAAAAAAAAAAAAAAAAAAAAAAA

Supplementary Figure S1 Full-length *LcHif-1a* cDNA and predicted *LcHif-1a* protein. Green letters represent corresponding amino acid sequences. Bold red letters

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show start and stop codons. Bold black letters show polyadenylate tail (Poly A) signals.



**Supplementary Figure S2 Predicted structural domains of *LcHif-1 $\alpha$*  protein.** Red module shows basic helix-loop-helix (bHLH, 12–82 aa), purple module shows PAS domain (88~151 aa), green module shows PAS\_3 domain (251–338 aa), blue module shows Hif-1 $\alpha$  domain (548–578 aa) and orange module shows C terminal transactivation domain (C-TAD, 714–750 aa).

**Larimichthys crocea** (1) **bHLH** (70) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Collichthys lucidus** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
*Oryzias latipes* (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Danio rerio** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Gallus gallus** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Homo sapiens** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
*Sus scrofa* (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Mus musculus** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
*Xenopus tropicalis* (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Mustelus canis** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR  
**Consensus** (1) MDTGIVPEKRRSSERRRKEKSRDAARCRGKSESEVYFELAQELPLPHVSSSLDKASIMRLTISYLMRR

**Larimichthys crocea** (70) **bHLH** (71) **PAS** (140) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Collichthys lucidus** (70) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
*Oryzias latipes* (70) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Danio rerio** (70) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Gallus gallus** (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Homo sapiens** (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
*Sus scrofa* (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Mus musculus** (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
*Xenopus tropicalis* (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Mustelus canis** (70) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP  
**Consensus** (71) KLLSTDEPIAEETLDFQLNGSYLKALDGFVVLSEDDGMIIYSENINRCKGLAQFDLGHVDFDTHP

**Larimichthys crocea** (140) **PAS** (210) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Collichthys lucidus** (140) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
*Oryzias latipes* (140) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Danio rerio** (140) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Gallus gallus** (139) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Homo sapiens** (139) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
*Sus scrofa* (139) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Mus musculus** (139) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
*Xenopus tropicalis* (139) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Mustelus canis** (138) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE  
**Consensus** (141) CDHEELREMLIRHGTGSKRAKPNTRNPFIRMKCTLTSRGRVNIKSAATKWLHCGHRRVSNRTELE

**Larimichthys crocea** (209) **PAS-3** (280) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Collichthys lucidus** (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
*Oryzias latipes* (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Danio rerio** (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Gallus gallus** (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Homo sapiens** (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
*Sus scrofa* (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Mus musculus** (209) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
*Xenopus tropicalis* (208) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Mustelus canis** (208) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY  
**Consensus** (211) HCGKRPMTCLVLCDFPIPHPSNIEVPLDSKTFLSRHSLSLDMKESYCDERITELMGVPEELLGRSVVEY

**Larimichthys crocea** (278) **PAS-3** (350) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Collichthys lucidus** (278) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
*Oryzias latipes* (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Danio rerio** (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Gallus gallus** (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Homo sapiens** (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
*Sus scrofa* (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Mus musculus** (279) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
*Xenopus tropicalis* (278) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Mustelus canis** (278) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE  
**Consensus** (281) YHALDSHLTKTHHNLFRGQVCTGGYRMLAKRGGYVWVETQATVLYNKNKSNOPQVVCVNVLSGQVGE

**Larimichthys crocea** (348) **PAS-3** (420) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Collichthys lucidus** (348) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
*Oryzias latipes* (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Danio rerio** (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Gallus gallus** (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Homo sapiens** (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
*Sus scrofa* (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Mus musculus** (349) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
*Xenopus tropicalis* (348) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Mustelus canis** (348) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS  
**Consensus** (351) KLLSLEQTHDVPKVEELQLEEEAAVSSQPEMSPILPKEVEEKVSSDMLKLFTRHII--SEFLVS

**Larimichthys crocea** (416) **PAS-3** (490) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Collichthys lucidus** (416) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
*Oryzias latipes* (409) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Danio rerio** (398) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Gallus gallus** (386) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Homo sapiens** (386) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
*Mus musculus* (386) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
*Xenopus tropicalis* (386) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Mustelus canis** (386) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP  
**Consensus** (421) LYLQKKEPEALTLAFAPGDTIPLDFSS--CSBPETOL--FLYKDVMLPSGSS--KIALPLSPLFP

**Larimichthys crocea** (477) **HIF-1** (860) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Collichthys lucidus** (477) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
*Oryzias latipes* (476) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Danio rerio** (463) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Gallus gallus** (454) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Homo sapiens** (456) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
*Sus scrofa* (456) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Mus musculus** (455) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
*Xenopus tropicalis* (451) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Mustelus canis** (449) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP  
**Consensus** (491) SEPLHVTITSEITKTERYDF-----PSTTASS--ADAPLDFGFP

**Larimichthys crocea** (519) **HIF-1** (860) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Collichthys lucidus** (519) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
*Oryzias latipes* (519) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Danio rerio** (515) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Gallus gallus** (521) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Homo sapiens** (523) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
*Sus scrofa* (524) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Mus musculus** (522) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
*Xenopus tropicalis* (517) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Mustelus canis** (516) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS  
**Consensus** (561) VDSMSSEFKLDLVEKFAIDTEAKPFSTQTDLDLLEMLAPYIPMDDDFQLRSFDQLSPLSSSS

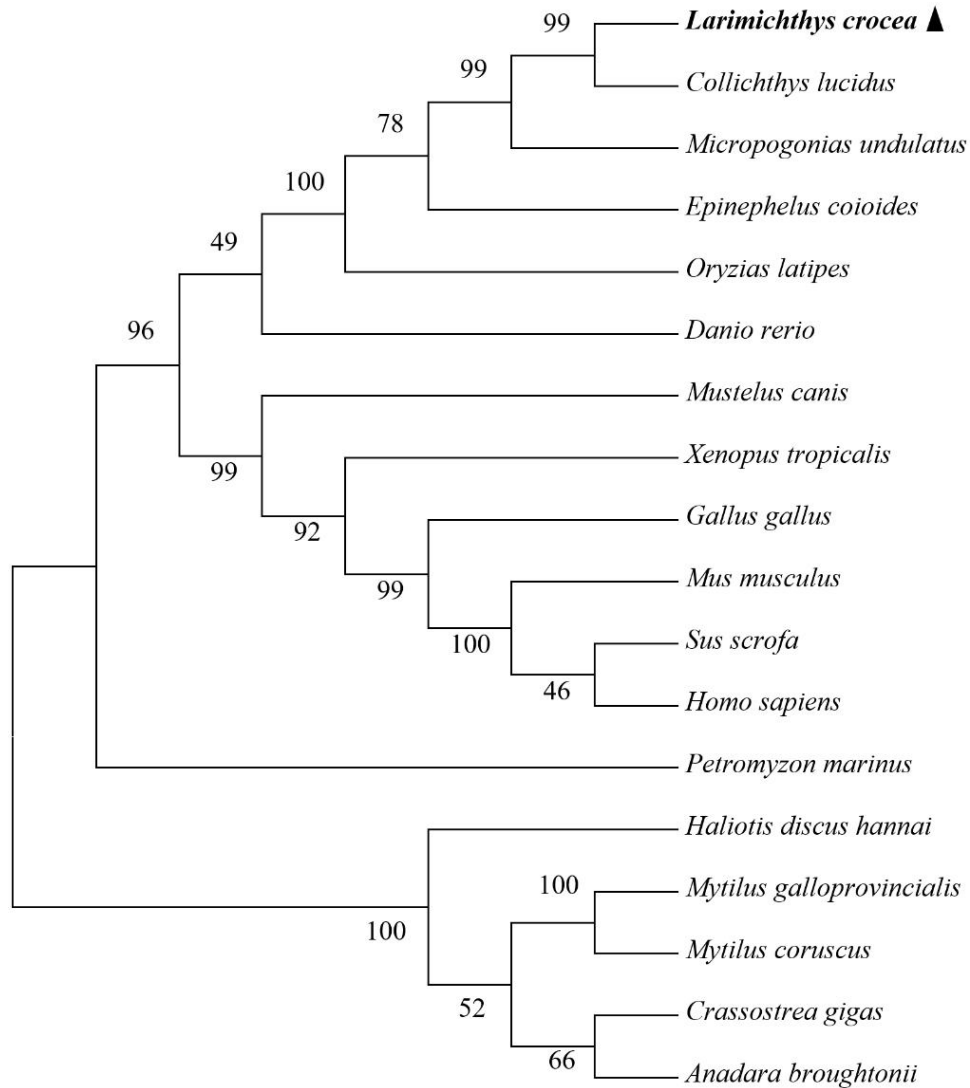
**Larimichthys crocea** (581) **HIF-1** (860) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Collichthys lucidus** (581) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
*Oryzias latipes* (580) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Danio rerio** (585) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Gallus gallus** (590) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Homo sapiens** (592) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
*Sus scrofa* (593) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Mus musculus** (591) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
*Xenopus tropicalis* (586) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Mustelus canis** (586) -----SCGPKRSLSDFP--VCTKDIQYVPSH  
**Consensus** (631) -----SCGPKRSLSDFP--VCTKDIQYVPSH

**Larimichthys crocea** (607) **HIF-1** (860) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Collichthys lucidus** (607) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
*Oryzias latipes* (606) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Danio rerio** (620) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Gallus gallus** (644) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Homo sapiens** (659) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
*Sus scrofa* (657) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Mus musculus** (656) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
*Xenopus tropicalis* (630) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Mustelus canis** (647) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR  
**Consensus** (701) VNTSHLAILLARTIQGN-----EYSLTILAAQNSQRKR

**Larimichthys crocea** (658) **HIF-1** (860) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Collichthys lucidus** (658) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
*Oryzias latipes* (657) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Danio rerio** (674) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Gallus gallus** (706) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Homo sapiens** (721) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
*Sus scrofa* (719) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Mus musculus** (717) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
*Xenopus tropicalis* (691) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Mustelus canis** (717) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE  
**Consensus** (771) -----LEQGKRLRASES-----TTT-TILLPSDLASRLLSGSMSE

**Larimichthys crocea** (711) **CTAD** (881) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Collichthys lucidus** (711) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
*Oryzias latipes* (710) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Danio rerio** (740) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Gallus gallus** (775) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Homo sapiens** (790) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
*Sus scrofa* (788) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Mus musculus** (786) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
*Xenopus tropicalis* (760) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Mustelus canis** (783) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI  
**Consensus** (841) SSELFTLPQTRDCEVNAFQGRYLLQGEELRALDHI

**Supplementary Figure S3 Multiple sequence comparisons of homologous Hif-1 $\alpha$  proteins.** Red boxes show functional domains of bHLH, PAS, PAS\_3, Hif-1, and C-TAD shared by Hif-1 $\alpha$  protein. Homology of *LcHif-1 $\alpha$*  to Hif-1 $\alpha$  of *Collichthys lucidus*, *Oryzias latipes*, *Mustelus canis*, *Danio rerio*, *Gallus gallus*, *Homo sapiens*, *Sus scrofa*, *Mus musculus*, and *Xenopus tropicalis* (99.3%, 72.4%, 50.8%, 59.8%, 53.9%, 51.5%, 51.4%, 50.2% and 52.2%, respectively).



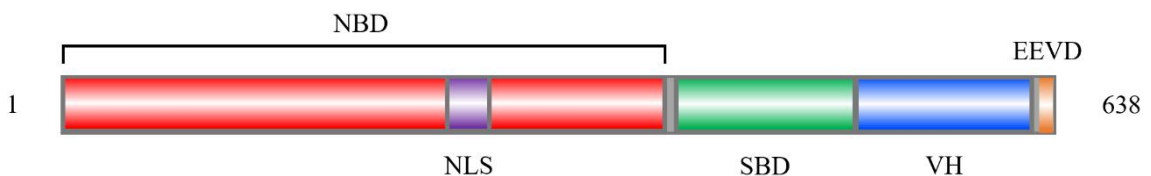
**Supplementary Figure S4 Phylogenetic tree of homologous Hif-1 $\alpha$  proteins.** Constructed using MEGA v5.1 software and neighbor-joining method. Same below.

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1   GAAGCATTAGTTCAAGAGGAACACACAGAGGCAAAGCTCAAGACAAAGGGAATTACTCGAGGAGACTCTCGGGAGATCCTTCAACAATCTTTGAGAA
100 ACAGAGAGATTATCATAGAAAAGAACTCTAAAACAACAAGCAAGATGTCAGCTAAAGGAATATCTATTGGCATTGATCTGGGCCACCCTATTCTTGTGT
1   M S A K G I S I G I D L G T T Y S C V
199 CGGGTTTTCCAGCATGGCAAAGTGGAGATCATCGCCAACGACCAGGAAAACAGAACCCTCCAGCTATGTGGCCTTACTGACACAGAGAGGCTCAT
20   G V F Q H G K V E I I A N D Q G N R T T P S Y V A F T D T E R L I
298 TGGAGATGCTGCCAAGAATCAGGTTGCCATGAACCCGCCAACACAATCTTTGATGCCAAGCGGCTCATCGGGAGAAAGTTACCGACCCTGTTGTCCA
53   G D A A K N Q V A M N P A N T I F D A K R L I G R K F T D P V V Q
397 GTCTGACATGAAGCTCTGGCCCTTCAAAGTGATCAGTGATAGCGGAAAACCAAAGTCCAGGTTGAGTATAAAGGGGAGACCAAAGCCTTCTACCCAGA
86   S D M K L W P F K V I S D S G K P K V Q V E Y K G E T K A F Y P E
496 AGAAATCTCCTCTATGGTCTGGTAAAAATGAAGGAGATCGCTGAAGCCTACCTGGGACAAAAAGTGCAAAACGCAGTCATCACAGTCCGGCGTATTT
119  E I S S M V L V K M K E I A E A Y L G Q K V S N A V I T V P A Y F
595 TAAGGACTCCCAGAGGCAAGCCACCAAGGACGCTGGGGTGATCTCTGGACTGAATGTTCTGAGGATCATCAATGAACCCACAGCAGCAGCCATCGCCTA
152  N D S Q R Q A T K D A G V I S G L N V L R I N E P T A A A I A Y
694 CGGCCTGGATAAAGGTAAGAGAGGGGAGCGCAACGTCATCTTTGATCTCGGTGGAGGCACCTTTGATGTGCCATCTGACCATTGAAGAGCGGCAT
185  G L D K G K R G E R N V L I F D L G G G T F D V S I L T I E D G I
793 CTTTGAAGTAAATCCACTGCAGGCGACACACATCTTGGTGGGGAGGACTTTGACAACCGGATGGTCAACCCTTTGTAGAGAAATTTAAAAGAAAAACA
218  F E V K S T A G D T H L G G E D F D N R M V N H F V E E F K R K H
892 CAAGAAGGACATCAGCCAAAATAAGAGAGCAGTGAGGAGGCTGCGCACTGCTTGTGAAAGAGCAAAGAGGACCTGTCTCCAGCACCAGGCTAGCCT
251  K K D I S Q N K R A V R R L R T A C E R A K R T L S S S T Q A S L
991 TGAGATTGACTCTCTGTTGAGGATCGACTTCTACACTCAATCACAAGGCGACGCTTTGAGGAGCTCAACTCAGAGCTTTCAGGGGAACACTGGA
284  E I D S L F E G I D F Y T S I T R A R F E E L N S E L F R G T L D
1090 TCCAGTTGAGAAGTCTCGCAAGATGCCAAGCTGGATAAAGTCCAAGATCCATGAAATGTCTGGTGGTGGCTCCACAAGAATCCCAAAATCCAGAA
317  P V E K S L Q D A K L D K S K I H E I V L V G G S T R I P K I Q K
1189 GCTCTGCAGGACTTTTTAATGGCAGAGAATTGAACAAGAGCATCAACCCGGATGAAGCTGTGGCCTATGGTGCAGCAGTCCAGGCTGCTATCCTGAT
350  L L Q D F F N G R E L N K S I N P D E A V A Y G A A V Q A A I L M
1288 GGGTGACACTTCAGAAAATGTCCAAGATTGCTACTGCTGGATGTGGCTCCTCTGCTCTGGGCATTGAGACTGCGGGTGGAGTTATGACACCTTAAAT
383  G D T S E N V Q D L L L L D V A P L S L G I E T A G G V M T P L I
1387 CAAACGAAACACCACCATCCCACCAAGCAGACCCAGATCTTCTACATATTCAGATAACCAGCCAGGTGTGCTGATTGAGGTTGATGAGGGTGAGAG
416  K R N T T I P T K Q T Q I F S T Y S D N Q P G V L I Q V Y E G E R
1486 AGCCATGACCAAGGACAACAACCTCCTTGGCAAGTTTGAGCTCACAGGTATCCCTCCTGCTCCCGAGGTGCCACAGGTGGAGGTAACCTTCGACAT
449  A M T K D N N L L G K F E L T G I P P A P R G V P Q V E V T F D I
1585 TGATGCCAATGGAATCTAAATGTGTCGCTGTCGACAAAAGCACTGGCAAGAAAACAAAATCACCATCACCATGACAAGGGCCGACTTAGCAAAGA
482  D A N G I L N V S A V D K S T G K E N K I T I T N D K G R L S K E
1684 GGAGATAGAGCGCATGGTACAGGACTCTGAAAAGTACAAGGCTGATGATGACATACAGAGGGAGAAGATTGCGGCAAGAACTCACTGGAGTCATACGC
515  E I E R M V Q D S E K Y K A D D D I Q R E K I A A K N S L E S Y A
1783 CTACCACATGAAGAGCAGCGTTGAGGATGAGAACATGAAAGGAAAGATTAGCGAGGAGGATAAAAAGGTGGTCATTGACAAGTGAAGCAGACAATCTC
548  Y H M K S S V E D E N M K G K I S E E D K K V V I D K C K Q T I S
1882 CTGGCTGGAGAACAACAGCTGGCAGAGAAGGAGGATGAACATCAACAGAATGAACTAGAGAAGGTGCAAGCCGATTGTGACCAAGTTGTACCA
581  W L E N N Q L A E K E E Y E H Q Q N E L E K V C K P I V T K L Y Q
1981 GGGAGGAGCACCATCAGGAGGATGTGGCAGCCAGGAGGAGCAGCTCCAAGGCCCCACTATTGAGGAAGTTGACTAAACAGAGGCATCAGCATT
614  G G A P S G G C G S Q A G G S S K G P T I E E V D *
2080 TGTTTACAGAAATACTCGACCGTATCGCTGTTGTTGATACAAAAATAAAGTAATTTGACTGTTTCTTCTCCGATGTCTTAATAAAAAATCTTTGA
2179 AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**Supplementary Figure S5 Full-length *LcHsp70* cDNA and predicted *LcHsp70* protein.**



**Supplementary Figure S6 Predicted structural domains of *LcHsp70* protein.** Red module shows DNA binding domain (NBD, 3–387 aa), green module shows substrate binding domain (SBD, 395–510 aa), blue module shows carboxy-terminal variable region (VH, 511–634 aa), purple module shows nuclear localization signal (NLS, 247–274 aa), and orange module shows EEVD cytoplasm-specific regulatory motifs.

1 NBD 70  
*Larimichthys crocea* (1) MSARGISIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Miichthys miuy* (1) MSARGISIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Drosophila auraria* (1) ---MPAIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDPAKNOVAMNPRNTVFD  
*Danio rerio* (1) -MARGLSIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Homo sapiens* (1) -MKAASIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Xenopus laevis* (1) MPTKGVAVGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Gallus gallus* (1) MSKGPAAIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Pelodiscus sinensis* (1) MSKGPAAIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Procambarus clarkii* (1) ---MPKAVGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
*Octopus tankahkeei* (1) ---MSKAVGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNPNTVFD  
Consensus (1) MSAKG AIGIDLGTYSVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERLIGDAAKNOVAMNP NTVFD

71 NBD 140  
*Larimichthys crocea* (71) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGQV  
*Miichthys miuy* (71) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGQV  
*Drosophila auraria* (67) AKRLIGRKYDDEKAEEMKHWPFFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGETV  
*Danio rerio* (70) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGHV  
*Homo sapiens* (70) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGPV  
*Xenopus laevis* (71) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGHV  
*Gallus gallus* (71) AKRLIGRKYDDEKAEEMKHWPFFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGGV  
*Pelodiscus sinensis* (71) AKRLIGRKYDDEKAEEMKHWPFFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGRV  
*Procambarus clarkii* (68) AKRLIGRKFNDASVQADMKHWPFFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGSV  
*Octopus tankahkeei* (68) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGRV  
Consensus (71) AKRLIGRKFDPVQVSDMKLWPFKVISDGGKPKVQVEYKGETKAFYPEEISSMVLTKMKEIAEAYLGKV

141 NBD 210  
*Larimichthys crocea* (141) SNAVITVPAYFNDSQRQATKDAGVISGLNVLRIINEPTAAAIAYGLDK--GKRGERNVLI FDLGGGTFDV  
*Miichthys miuy* (141) SNAVITVPAYFNDSQRQATKDAGVISGLNVLRIINEPTAAAIAYGLDK--GKRGERNVLI FDLGGGTFDV  
*Drosophila auraria* (137) TDAVITVPAYFNDSQRQATKDAGRIAGLNVLRIINEPTAAAIAYGLDKNLQ--GERNVLI FDLGGGTFDV  
*Danio rerio* (140) NNAVITVPAYFNDSQRQATKDAGVIAGLNVLRIINEPTAAAIAYGLDK--GRKGERNVLI FDLGGGTFDV  
*Homo sapiens* (140) TNAVITVPAYFNDSQRQATKDAGVIAGLNVLRIINEPTAAAIAYGLDK--TGKGERNVLI FDLGGGTFDV  
*Xenopus laevis* (141) TNAVITVPAYFNDSQRQATKDAGVIAGLNVLRIINEPTAAAIAYGLDK--GARGENVLI FDLGGGTFDV  
*Gallus gallus* (141) QNAVITVPAYFNDSQRQATKDAGTITGLNVLRIINEPTAAAIAYGLDKKGRTRAGENVLI FDLGGGTFDV  
*Pelodiscus sinensis* (141) QNAVITVPAYFNDSQRQATKDAGTITGLNVLRIINEPTAAAIAYGLDKKGSAGAKENVLI FDLGGGTFDV  
*Procambarus clarkii* (138) KDAVITVPAYFNDSQRQATKDAGTISGMNVLRIINEPTAAAIAYGLDKKVG--GERNVLI FDLGGGTFDV  
*Octopus tankahkeei* (138) TNAVITVPAYFNDSQRQATKDAGTITAGLNVLRIINEPTAAAIAYGLDKKVG--GERNVLI FDLGGGTFDV  
Consensus (141) TNAVITVPAYFNDSQRQATKDAGVIAGLNVLRIINEPTAAAIAYGLDK GRGERNVLI FDLGGGTFDV

211 NBD 280  
*Larimichthys crocea* (209) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Miichthys miuy* (209) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Drosophila auraria* (205) SILTIEDGSIFEVKSTAGDTHLGGEDFDNRLVTHLAEFKRHKRDLRSNPRALRRLRRTAERAKRTLSS  
*Danio rerio* (208) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Homo sapiens* (208) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRLVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Xenopus laevis* (209) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRALRRLRRTACERAKRTLSS  
*Gallus gallus* (211) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Pelodiscus sinensis* (211) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Procambarus clarkii* (206) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVTHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
*Octopus tankahkeei* (206) SILTIEDG-IFEVKSTAGDTHLGGEDFDNRMVTHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS  
Consensus (211) SILTIEDG IFEVKSTAGDTHLGGEDFDNRMVNHFEVEFKRHKHDDISONKRAVRLRRTACERAKRTLSS

281 NBD 350  
*Larimichthys crocea* (278) STQASIEIDSLFEGIDFYTSITRARFEELNSELFRGTLDPVEKSLQDAKLDKSKIHEIVLVGGSTRIPKI  
*Miichthys miuy* (278) STQASIEIDSLFEGIDFYTSITRARFEELNSELFRGTLDPVEKSLQDAKLDKSKIHEIVLVGGSTRIPKI  
*Drosophila auraria* (275) STEATIEIDALFEGHDFYTKVSRARFEELCADLFRNTLQVEKALDAMKDGQIHDIVLVGGSTRIPKI  
*Danio rerio* (277) SSQASIEIDSLFEGIDFYTSITRARFEELNSELFRGTLDPVEKALDAMKDSQIQDILVVGSTRIPKI  
*Homo sapiens* (277) STQASIEIDSLFEGIDFYTSITRARFEELNSELFRGTLDPVEKALDAMKDLKSKIHEIVLVGGSTRIPKI  
*Xenopus laevis* (278) SSQASIEIDSLFEGIDFYTAITRARFEELNSELFRGTLDPVEKALDAMKDLKSKIHEIVLVGGSTRIPKI  
*Gallus gallus* (280) STQASIEIDSLFEGIDFYTSITRARFEELNADLFRGTLDPVEKALDAMKDLKQIQEIVLVGGSTRIPKI  
*Pelodiscus sinensis* (280) STQASIEIDSLFEGIDFYTSITRARFEELNADLFRGTLDPVEKALDAMKDLKQIXEIVLVGGSTRIPKI  
*Procambarus clarkii* (275) STQASIEIDSLYEGVDFYTSITRARFEELCADLFRGTLDPVEKSLDAMKDSQINIEIVLVGGSTRIPKI

351 NBD SBD 420  
*Larimichthys crocea* (348) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTPLIKR  
*Miichthys miuy* (348) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTPLIKR  
*Drosophila auraria* (345) EALLQDFNFKGELNKSINPDEAVAYGAAVQAAIILSGDQKCTODVLLMDVAPLSLGIETAGGVMTKLIER  
*Danio rerio* (347) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTALIKR  
*Homo sapiens* (347) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTALIKR  
*Xenopus laevis* (348) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTALIKR  
*Gallus gallus* (350) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVTPLSLGIETAGGVMTALIKR  
*Pelodiscus sinensis* (350) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVTPLSLGIETAGGVMTALIKR  
*Procambarus clarkii* (345) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTALIKR  
*Octopus tankahkeei* (345) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILSGDQKCTODVLLMDVAPLSLGIETAGGVMTPLIKR  
Consensus (351) OKLLQDFNFKGELNKSINPDEAVAYGAAVQAAIILMGDTSENVODLILLDVAPLSLGIETAGGVMTALIKR

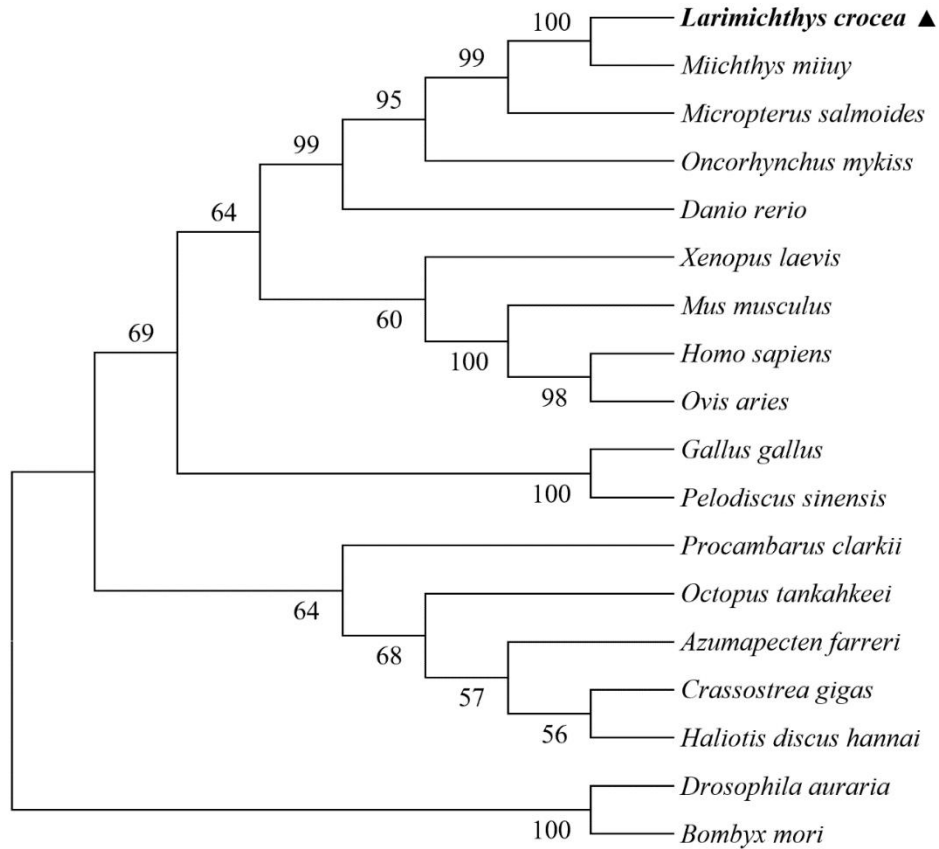
421 SBD 490  
*Larimichthys crocea* (418) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Miichthys miuy* (418) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Drosophila auraria* (415) NCRIPCQKTKIFSTYSDNQPGVSIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Danio rerio* (417) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Homo sapiens* (417) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Xenopus laevis* (418) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Gallus gallus* (420) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Pelodiscus sinensis* (420) NTTIPTKQTQIFSTYSDNQNSVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Procambarus clarkii* (415) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
*Octopus tankahkeei* (415) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL  
Consensus (421) NTTIPTKQTQIFSTYSDNQPGVLIQVYEGERAMTKDNNLLGKFEITGIPPARPGVQIEVTFDIDANGIL

491 NBD SBD 560  
*Larimichthys crocea* (488) NVSAVDKSTGKENKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Miichthys miuy* (488) NVSAVDKSTGKENKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Drosophila auraria* (485) NVSAKDMSTGKANKITITNDKGRLSQAEIIRMVNEAEKYADEDEKRRQRTASRNALESYAFNMKSTVEDE  
*Danio rerio* (487) NVSAADKSTGKENKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Homo sapiens* (487) NVSATDKSTGKANKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Xenopus laevis* (488) NVSAVEKSSGKONKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Gallus gallus* (490) NVSAVDKSTGKENKITITNDKGRLSKDDIDRMVQEAKEYKAEDANRDRVGAKNLSLEYAFNMKSTVEDE  
*Pelodiscus sinensis* (490) NVSATDKSTGKENKITITNDKGRLSKDDIDRMVQEAKEYKAEDANRDRVGAKNLSLEYAFNMKSTVEDE  
*Procambarus clarkii* (485) NVSAADKSTGKENKITITNDKGRLSKEEIERMVQDSEKYEKADDDIQRERIAAKNSLESYAFNMKSTVEDE  
*Octopus tankahkeei* (485) NVSATDKSTGKENKITITNDKGRLSKDDIIRMVNEAEKEYQDEEQRERIAAKNSLESYAFNMKSTVEDE  
Consensus (491) NVSA DKSTGKENKITITNDKGRLSKEDIERMVQEAKEYKAED QRERIAAKNSLESYAFNMKSTVEDE

561 NBD SBD 630  
*Larimichthys crocea* (558) NMKGIISEEDKVVLDKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG-----APSG  
*Miichthys miuy* (558) NMKGIISEEDKVVLDKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG-----APSG  
*Drosophila auraria* (555) GAG-KLDEADKNSVLEKCNFTISWLENSNTAEKEEFDHLELTHCSPIIMTKMHQQGAGAQAQ-GGPG  
*Danio rerio* (557) NLRGKISSEQKKKILDKCTEVVSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG---A---PPAG  
*Homo sapiens* (557) GLKGIISEEDKVVLDKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG-----AG---GPG  
*Xenopus laevis* (558) NMKGIISEEDKVVLDKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQSSVPGG---VPGG  
*Gallus gallus* (560) KLGKISIDQDKQKVLKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG-----APSG  
*Pelodiscus sinensis* (560) KLGKISIDQDKQKVLKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG-----APSG  
*Procambarus clarkii* (555) KFKDKVSTDSKTLDACNEATKWLDSNQAEDFEHQQNELEKVCNPIVTKLYQASSGGAP---GAPGG  
*Octopus tankahkeei* (555) KFKDKVSTDSKTLDKCTEVVSWLENQLAKEEYEHQNELEKVCNPIVTKLYQATGGMP---GGMPGG  
Consensus (561) LKGIISE DKKVLDKCKQTSWLENQLAKEEYEHQNELEKVCNPIVTKLYQG APGG

631 SBD 660  
*Larimichthys crocea* (620) GCG-----SQAGG-----SSKGPTIEEVD  
*Miichthys miuy* (620) GCG-----SQAGG-----SSKGPTIEEVD  
*Drosophila auraria* (623) NCRQQAGGFGG-----YSGPTIEEVD  
*Danio rerio* (620) GCG-----FQAQP-----ESSQGPTEEVD  
*Homo sapiens* (620) G-G-----FQAQP-----SSKGPTIEEVD  
*Xenopus laevis* (624) MPC-----SSCGQARQGGSSGPTIEEVD  
*Gallus gallus* (617) AGG-----AGAG-----GSGGPTIEEVD  
*Pelodiscus sinensis* (617) GAA-----PGGG-----AGGPTIEEVD  
*Procambarus clarkii* (622) APE-----GAS-----TGGGPTIEEVD

**Supplementary Figure S7 Multiple sequence comparisons of homologous Hsp70 proteins.** Red and black boxes show NBD and SBD functional domains shared by Hsp70 proteins, respectively. Homology of *LcHsp70* to Hsp70 of *Miichthys miiuy*, *Drosophila auraria*, *Danio rerio*, *Xenopus tropicalis*, *Gallus gallus*, *Pelodiscus sinensis*, *Procambarus clarkii*, and *Octopus tankahkei* (99.7%, 70.8%, 89.5%, 84.7%, 85.0%, 85.0%, 83.4%, 83.4%, 83.1%, and 79.1%, respectively).



**Supplementary Figure S8 Phylogenetic tree of homologous Hsp70 proteins.**



**Supplementary Table S1 Primer sequences and siRNA information in this study.**

Names	Sequences (5'-3')	Application
<i>LcHif-1α</i> -R1	AGTGATATCTGCAGCATTCCACCGTG	5' RACE
<i>LcHif-1α</i> -R2	GGTAGTCGGTTTAATACCATTGTTGGG	5' RACE
<i>LcHif-1α</i> -F1	AGTGATATCTGCAGCATTCCACCGTG	3' RACE
<i>LcHif-1α</i> -F2	GGTAGTCGGTTTAATACCATTGTTGGG	3' RACE
<i>LcHsp70</i> -R1	CGCATGGTACAGGACTCTGAA	5' RACE
<i>LcHsp70</i> -R2	GAGAAGGTGTGCAAGCCGATT	5' RACE
<i>LcHsp70</i> -F1	CGCATGGTACAGGACTCTGAA	3' RACE
<i>LcHsp70</i> -F2	GAGAAGGTGTGCAAGCCGATT	3' RACE
<i>LcHif-1α</i> -F3	CCTCTCATCTTGCCACCATCC	RT-qPCR
<i>LcHif-1α</i> -R3	GTTCCCTGTCCAATCATCTCTTTTA	RT-qPCR
<i>LcHsfl</i> -F1	TGATTGGACGGACGCAGGA	RT-qPCR
<i>LcHsfl</i> -R1	GAAAGTGGTGGGGGAAAGGG	RT-qPCR
<i>LcHsp70</i> -F3	CTCTGCGGAGATCCTTCAACA	RT-qPCR
<i>LcHsp70</i> -R3	ACAAGAATAGGTGGTGCCCAG	RT-qPCR
<i>LcBax</i> -F	CGCACTATTCTACTTTGCCTGTCTG	RT-qPCR
<i>LcBax</i> -R	GCGAATGACTATGACAGTGGTGAGA	RT-qPCR
<i>LcBcl-2</i> -F	TCCACCGACTTTAGTCCGCC	RT-qPCR
<i>LcBcl-2</i> -R	AACAGTTCGTCTATCACCTCGGC	RT-qPCR
<i>LcCaspase-3</i> -F	CAGTTCTGAAATAGCATCAAAGGCA	RT-qPCR
<i>LcCaspase-3</i> -R	AAATGAACATAGGTCACTTCTGCCC	RT-qPCR
<i>Lcβ-actin</i> -F	CTGTCCCTGTATGCCTCTGGTC	RT-qPCR
<i>Lcβ-actin</i> -R	CTTGATGTCACGCACGATTTCC	RT-qPCR
<i>LcHsp70</i> -F3	ATGTCAGCTAAAGGAATATCTATTGG	Antibody preparation
<i>LcHsp70</i> -R3	CTGAATCAGCACACCTGGCT	Antibody preparation
<i>siLcHsp70</i>	F: CGGCCUGGAUAAAAGGUAAATT R: UUUACCUUUAUCCAGGCCGTT	RNAi
<i>siLcHif-1α</i>	F: CGCACCGUCAAUGUCAAAUTT R: AUUUGACAUUGACGGUGCGTT	RNAi
<i>siNC</i>	F: UUCUCCGAACGUGUCAGGUTT R: ACGUGACACGUUCGGAGAATT	RNAi
<i>LcHif-1α</i> -F4	CGGGATCCATGGACACAGGAATTGTAC	Overexpression
<i>LcHif-1α</i> -R4	CCGCTCGAGAATGACGTGGTCCAGAG	Overexpression
<i>LcHsp70</i> -F4	CCCAAGCTTATGTCAGCTAAAGGAATATCT ATTGG	Overexpression
<i>LcHsp70</i> -R4	CCGCTCGAGGTCAACTTCTCAATAGTGGG GC	Overexpression
<i>LcHsfl</i> -F2	ACGGAATTCATGGAGTATCCCG	Overexpression
<i>LcHsfl</i> -R2	ACCGCTCGAGTCAGAGGTCAGAGTC	Overexpression
<i>LcHsfl</i> -F3	ACCGCTCGAGAAAGGTCACACGTCACCGCG	Luciferase reporter
<i>LcHsfl</i> -R3	ACCCAAGCTTGAGAGAGACACAAATCAAAC	Luciferase reporter

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	ACTCAA	
<i>LcHsp70-F5</i>	ACGGGGTACCAGACTCTGCGGAGATCCTTC	Luciferase reporter
	AACA	
<i>LcHsp70-R5</i>	ACCGCTCGAGTCAGACACATGTTAGCAGTT	Luciferase reporter
	CAGTTCA	

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