Sequence of *Xenopus laevis* ferritin mRNA

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Submitted March 12, 1990 EMBL accession no. X51395

Intracellular iron stores are dependent on the relative levels of transferrin receptor and ferritin, the expression of each controlled by the relative amount of ferrous ion itself. The mRNAs for each protein contain a palindromic stem-loop sequence, the iron response element (IRE) (1) which is recognized by a specific IRE-binding protein (IRE-BP) whose activity is modulatted by the concentration of intracellular iron (2). Low levels of intracellular iron activate IRE-BP resulting in the stabilization of transferrin receptor mRNA and inhibited translation of ferritin mRNA (3, 4). We have isolated a cDNA encoding the complete sequence of ferritin mRNA from a library prepared from male *Xenopus laevis* liver, the sequence of which is presented below. *Xenopus* ferritin mRNA is larger than those in *Rana* and human by approximately 200 nt; the difference is primarily in the length of the 5′ UTR. A palindromic sequence (underlined) in the 5′ UTR bears a high degree of similarity to the IRE present in human ferritins, suggesting that regulation of its translation by iron is highly conserved between amphibians and mammals.

In mammals ferritin is found in two forms (H and L), and three forms (H, M, L) have been identified in *Rana*. Because of the high degree of similarity between the ferritin isoforms in mammals and amphibia it is not possible to definitively assign the cloned *Xenopus* ferritin as H, L or M. However the presence of this mRNA in both liver and erythrocytes suggests it is analogous to the H or M forms of the *Rana* homologue. The aligned peptide sequences of the amphibian and human ferritins is shown beneath the cDNA sequence [Xelfer = *Xenopus* ferritin, Ranferh = *Rana* ferritin H chain, Ranferm = *Rana* ferritin M chain, Humferh = human ferritin H chain]. *Xenopus* ferritin shares 84.6% amino acid identity with *Rana* ferritin H chain, and 82.9% amino acid identity with *Rana* ferritin M chain. The overall similarities between the *Xenopus* and *Rana* proteins (H and M) are 95 and 92% respectively. Comparison of the translated *Xenopus* ferritin sequence with human ferritin H chain revealed 68% amino acid identity, and overall similarity of 84.6%. The degree of conservation of ferritin sequence between the divergent amphibians is striking. Furthermore, the amino acid identity between the *Xenopus* and human ferritins is much greater than that which we have found (39%) upon comparison between the mammalian and amphibian albumins (5), suggesting a strong evolutionary pressure to maintain the ferritin peptide structure.

ACKNOWLEDGEMENTS

Supported by grants GM38277 from the NIH and C07577 from the USUHS.

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  1 GGGTCAGAGC TGTCCTCCAA TCCCCACCCT GTCGGTCCCT AGTTCTATGG GTCCCTTGGG CTGCAGTACT ACCGGCCCTT GTTCCCTATT AAATGGTATT TCGTTGATGG
111 TCTAAGCCCG ACAGACAGTG CTTGTTGCAC ACACTCATAC ATTCTTGTTT TTGAGAGTTC TTGCTTCAAC AGTGTTTGAA CGGAACCTCT CTGAGTCTTT TTTTAGACCA
221 AACTCTCTCT CTCGCATTAC TCTCTTGCTT TTTGTGACTC TTTTGCGCCA CCAGCAAACA CCGAAGCGCC ATCA ATG CAA TCC CAG GTG CTC CAG AAC TTC
                                                                                    M  Q  S  Q  V  L  Q  N  F
322 AAC AGC GAC TGC GAG ATC GCC ATC AAC CGG ATG GTG AAC CTG GAG ATG TAT GCC TCC TAT GTC TAC CTG TCC ATG TCT TAC TAC TTC GAT
    N  S  D  C  E  I  A  I  N  R  M  V  N  L  E  M  Y  A  S  Y  V  Y  L  S  M  S  Y  Y  F  D
412 CGT GAT GAC GTG GCA CTC CAT CAT GTG GCC AAG TTC TTC AAG GAG CAG AGT CAC GAG GAA AGG GAG CAC GCC GAA CAA AAC AAA CGT GGG
    R  D  D  V  A  L  H  H  V  A  K  F  F  K  E  Q  S  H  E  E  R  E  H  A  E  Q  N  K  R  G
502 GGC CGT GTC GTC CTT CAG GAT ATC AAG AAA CCA GAG AAG TTC CTC AAA TAC CGT GAC GAA TGG AGT AAC ACC CTG GAA GCC ATG CAG GCC
    G  R  V  V  L  Q  D  I  K  K  P  E  K  F  L  K  Y  R  D  E  W  S  N  T  L  E  A  M  Q  A
592 GCT CTG CAA TTG GAG AAG ACC GTG AAC CAG GCC TTG CTG GAT CTG CAC AAG CTG GCA TCC GAC AAG GTT GAT CCT CAG CTC TGT GAC TTC
    A  L  Q  L  E  K  T  V  N  Q  A  L  L  D  L  H  K  L  A  S  D  K  V  D  P  Q  L  C  D  F
682 CTT GAA TCT GAG TAC TTG GAG GAA CAG GTG AAG GCC ATG AAG GAG CTT GGA GAC TAC ATC ACC AAC CTG AAG CGC CTT GGG GCG CAG AAT
    L  E  S  E  Y  L  E  E  Q  V  K  A  M  K  E  L  G  D  Y  I  T  N  L  K  R  L  G  A  Q  N
772 GGC ATG GGC GAG TAC CTG TTC GAC AAG CAC ACC CTG GGG GAG AGT AGC T AAGCGCGCTC TCAGGGTAGA AACAACCAGT CAGCTCTCTG TTTCAAAATA
    G  M  G  E  Y  L  F  D  K  H  T  L  G  E  S  S
871 CTGTCTCTTA ATATCTGTGT GGTATATACC ATAGCTCCCA TGCCCATGTT CAGACCTTTT CATTTTGAGG ACGATGGGAA TATATCTGTG CTCTTAATCA TGCAGAAGCT
981 GCTGTGCTTG TCAACATGTT TTCAATAAAG TTTTTTCAGC ATTCCAAAAA AAAAAA
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      1                                                                                                   100
Xelfer     MQSQVL QNFNSDCEIA INRMVNLEMY ASYVYLSMSY YFDRDDVALH HVAKFFKEQS HEEREHAEKF LKYQNKRGGR VVLQDIKKPE RDEWSNTLEA
Ranferh     .D...R ...HRD..A. ......M.L. ...T....AF ......I... N......... .........L M.D..... I....V.... ....G.....
Ranferm     .V...R ..YH....A. V...L....L. ...T.S..YA F......... N..E....N. .......... M......... .......... ....G.....
Humferh  NTTAST...R ..YHQ.S.A. ...QI...L. .......... .........K NF..Y.LN.. .........L M.L..Q.... IF.......D C.D.ESG.NA

      101                                                                                                 183
Xelfer  MQAALQLEKT VNQALLDLHK LASDKVDPQL CDFLESEYLE EQVKAMKELG DYITNLKRLG  AQNGMGEYL FDKHTLGESS
Ranferh .......... .......... VG......H. ......T.... ....SI.Q.. .......... LP........ .....M....
Ranferm .......... .......... ..T.....H. .......... ....DI.RI. .F........ LPE....... ....SVK...
Humferh .EC..H...N ...S..E... ..T..N..H. ...I.TH..N .....I.... .HV...RKM. APES.LA... .......D.D NES
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