Liver fibrosis is characterized by an increased deposition of extracellular matrix proteins, including collagen type I, by activated hepatic stellate cells (HSCs). Previous studies have shown that this increase is mediated primarily by a post-transcriptional mechanism. In particular, the RNA-binding protein αCP binds to the α1(I) collagen 3′-untranslated region (UTR) and stabilizes this RNA in activated, but not quiescent, HSCs. This study examines the role of αCP in the decay of transcripts containing the collagen 3′-UTR in extracts obtained from NIH fibroblasts and quiescent and activated HSCs. Using an in vitro decay system, αCP binding activity was competed out with the addition of wild type oligonucleotides, but not with mutant oligonucleotides. Competition of αCP binding activity increased the rate of decay of wild type transcripts containing the αCP 3′-UTR binding site, but not of transcripts containing a mutated binding site. Quiescent HSC extracts contain no αCP binding activity and have no difference in the rate of decay of transcripts with wild type and mutant binding sites for αCP. The addition of recombinant αCP was sufficient to increase the half-life of the wild type transcript, whereas that of the mutant transcript was minimally changed. In vitro decay assays performed with αCP-containing HSC extracts that contain αCP binding activity demonstrate a markedly reduced decay rate of wild type compared with mutant transcripts. In vivo small interfering RNA experiments targeting αCP showed a reduction of the binding activity of αCP and a concomitant reduction in intracellular levels of α1(I) collagen messenger RNA. In conclusion, this study demonstrates the direct role of αCP in the stabilization of α1(I) collagen messenger RNA by blocking RNA degradation in activated HSCs.

Regulated RNA decay can be analyzed in vitro by following a radiolabeled RNA containing the sequence of interest over time in cytoplasmic extracts (26–29). Polyadenylated reporter RNAs incubated with cell extracts of interest have been utilized to show the dependence of α-globin mRNA stability to a region in the 3′-UTR of the message (26, 30). To elucidate the role of the 3′-UTR in regulating α1(I) collagen mRNA stability, we measured relative stabilities of RNA transcripts containing wild type (WT) and mutated (MUT) α1(I) collagen 3′-UTRs using both activated and quiescent HSCs extracts.

The use of small interfering double-stranded RNAs (siRNAs) is a newly described method for assessing gene function in cell culture models (31, 32). siRNAs cause a sequence-specific degradation of messages targeted by the siRNA, effectively down-
regulating endogenous gene expression (33–35). To confirm that the in vitro decay assay had in vivo relevance, we used siRNAs to selectively inhibit αCP levels in activated HSCs and observed what effects this had on collagen α(I) mRNA.

This study utilized lysates from quiescent and activated HSCs to demonstrate that the stability of the α(I) collagen mRNA is directly mediated by binding of αCP to its cognate binding site in the 3′-UTR. Furthermore, selectively inhibiting expression of αCP in rat HSCs resulted in decreased α(I) collagen mRNA steady state levels, demonstrating a direct role for αCP in the stabilization of α(I) collagen message in activated HSCs.

EXPERIMENTAL PROCEDURES

Cell Culture—NIH 3T3 cells were cultured in Dulbecco’s modified Eagle’s medium (Invitrogen) supplemented with 10% calf serum (HyClone). Rat HSCs were isolated as previously described (36). Lysates—Confluent dishes of cells, either NIH 3T3 or HSCs, were washed one time in 5 ml of phosphate-buffered saline and scraped off the dish. The cells were pelleted at 10,000 × g and incubated in a hypotonic buffer (10 mM Tris, pH 7.6, 1 mM potassium acetate, 1.5 mM magnesium acetate, 2 mM dithiothreitol, 0.5 mM Pefabloc, 2 μg/ml aprotinin, 0.5 μg/ml leupeptin, 50 μM Nα-VO4) on ice and cells lysed with 0.5 ml of lysis buffer containing a 1.5-ml pestle (Nalgene 749521–1000). Cellular debris was removed by centrifugation at 16,000 × g and the supernatant collected as cytoplasmic lysates. S100 lysates were generated from the cytoplasmic lysates by centrifugation in a TLS-55 rotor at 100,000 × g and the samples stored at −80 °C. Plasmids and Sequences—The wild type collagen α(I) 3′-UTR (WT 3′-UTR) (GenBank™ accession number 278279) was cloned into pBlueScript using HindIII and Sall to allow in vitro transcription with the T3 promoter. The mutant 3′-UTR (10) that lacks αCP binding capability was cloned into the same site to generate the MUT3′-UTR transcript. The addition of 50 adenosines to the end of the 3′-UTR was performed essentially as previously described (27). The oligonucleotide containing the poly(A) sequence was ligated into the digested pBlueScript-3′-UTR vector at the Sall and a blunted Xhol site and the plasmid DNA transformed into competent DH5α Escherichia coli.

Transcription and Probes—To generate capped and radiolabeled probes from WT 3′-UTR and MUT 3′-UTR, mCAP analog (Stratagene) was added to an in vivo transcription reaction containing 1 μg of NSI linearized plasmid, 50 units of RNasin (Promega), 250 mM dithiothreitol, 1 mM ATP, 1 mM CTP, 0.3 mM GTP, 0.25 mM UTP with 0.06 μCi of [32P]UTP and 20 units of T3 RNA polymerase. Probes were purified in a 4% acrylamide gel containing 7 M urea and radiolabeled bands from the gel and extracted in stop solution (400 mM NaCl, 2.5 mM Tris, pH 7.6, 0.1% SDS). Oligonucleotides were radiolabeled using 3 μl of γ-[32P]ATP (10 mCi/ml) and 10 units of T4 polynucleotide kinase with standard protocols (37).

In Vitro Decay Assay—In vivo decay assays were performed essentially as previously described (27). Briefly, the decay reaction was performed in a 40-μl reaction volume containing 1 μg/ml S100 lysate and 40,000 cpm radiolabeled probe and 20,000 cpm of a radiolabeled 87-mer oligonucleotide as a control for loading and pipetting. Time points were taken at the indicated times and immediately added to a 300-μl stop solution (see above), and 5 μg of yeast RNA was added. The reaction mixture was layered on top of 300 μl of water-equilibrated slurry of glutathione-Sepharose beads. The beads were washed three times with ice-cold phosphate-buffered saline and recombinant protein eluted using 50 mM reduced glutathione in 100 mM Tris, pH 7.8, 100 mM NaCl.

Quantitation of Results—The amount of radioactive probe at the different time points was quantitated using the PhosphorImager software, ImageQuant 5.2. The zero time point was defined as 100% of the probe, and lanes were standardized for loading and/or precipitation variation by normalizing to the amount of the radiolabeled 87-mer oligonucleotide in the reaction. All experiments were repeated at least three times.

RNA Isolation—Total cellular RNA from HSCs was isolated as previously described (36).

siRNA—siRNAs (Table I) were synthesized using the Ambion Silencer siRNA kit according to the manufacturer’s recommendations. Cy3-Luc siRNA was purchased from Pharmacia (Lafayette, CO). HSCs were transfected with 100 pmol siRNA/well in 6-well dishes with 2 μl of LipofectAMINE in a total volume of 1 ml following the manufacturer’s recommended protocol. Cells were analyzed 72 h later after harvesting RNA or cellular extracts as described above.

Electrophoretic Mobility Shift Assays—Electrophoretic mobility shift assays were performed as previously described (39). Briefly, 10 μg of cytoplastic lysates were incubated in a binding buffer (12.5 mM HEPES, pH 7.9, 15 mM KCl, 0.25 mM EDTA, 5 μM MgCl2, 1 mM dithiothreitol, 0.2 mg/ml tRNA, 50 units/ml RNasin, 10% glycerol) with 10,000 cpm of probe for 30 min on ice. Binding reactions were electrophoresed in 6% native gels at 250 V, gels dried, and signals quantitated by PhosphorImager analysis using ImageQuant 5.2 software (Amer sham Biosciences). Mixing EMSAs included 10 μg of activated HSC extracts incubated with either 10 μg of quiescent extracts or 10 μg bovine serum albumin as a negative control.

Western Blotting—Cell lysates were prepared as described above. Lysates were supplemented with SDS loading buffer, separated by 10% SDS-PAGE, and electrotransferred onto nitrocellulose. Blots were incubated with 5% BLOTTO (TBST + 5% nonfat dry milk) and incubated with anti-αCP antibodies. αCP antibodies were a generous gift from M. Kiledjian.

RESULTS

Validation of RNA in Vitro Decay Assay (IVDA) in NIH Cells—To study the factors involved in α(I) collagen mRNA degradation, we utilized radiolabeled 7mG-capped and polyadenylated transcripts as RNA substrate and cytosolic S100 protein extracts in reaction mixtures (40, 41). Our initial studies to investigate a regulated decay of the collagen 3′-UTR (WT 3′-UTR) utilized extracts from NIH 3T3 cells that express type I collagen and exhibit the same binding activity seen in activated HSCs (Fig. 1, lane 5). Extracts from NIH 3T3 cells (Fig. 1, lane 2) and activated HSCs (lanes 4 and 5) HSC, but not quiescent HSCs (lane 3), have binding activity for the collagen 3′-UTR. This binding activity has previously been identified as αCP using supershift assays with αCP-specific antibodies (39).
To examine whether RNA decay occurred via a regulated, poly(A)-dependent process in NIH 3T3 extracts, an in vitro decay assay containing increasing amounts of unlabeled poly(A) homopolymers was performed. The addition of excess cold poly(A) homopolymers to the reactions will increase the decay rate if decay occurs by a poly(A)-dependent process (26, 30). The addition of increasing amounts of poly(A) homopolymers increased the rate of decay of the WT probe (Fig. 2A, lanes 3–5), whereas addition of other poly(U) had little effect on the rate of decay (Fig. 2A, lane 6), thus confirming a poly(A)-dependent process.

Having established that the decay reactions occurred via a poly(A)-dependent process, we investigated whether the ability of the RNA probe to be bound by αCP had any effect on the rate of decay in the NIH extracts. The decay rates of the WT probe, which αCP binds, and the MUT probe, which αCP fails to bind when using NIH 3T3 extracts, demonstrated an 11-fold increase in stability at 60 min of the WT probe compared with the MUT probe (Fig. 2B). Thus, αCP, either alone or in a complex, is capable of stabilizing the transcript in NIH extracts. Our data for the α1(I) collagen 3′-UTR is consistent with that described for the α-globin mRNA and provides the first evidence that αCP can directly stabilize the α1(I) collagen 3′-UTR.

Competition of αCP Binding Decreases WT Transcript Stability—To confirm that αCP binding to the α1(I) collagen 3′-UTR RNA probe inhibits the decay of the mRNA, competition studies were performed using an unlabeled consensus binding sequence oligonucleotide (WT-oligo) for αCP. By conducting the IVDA under conditions where αCP binding is abolished by the addition of unlabeled WT-oligo, we observed an increase in the decay rate of the WT 3′-UTR transcript (Fig. 2C and D). The addition of a mutant oligonucleotide (MUT-oligo) of the same size incapable of binding αCP had no effect on the decay rate of the WT 3′-UTR (lanes 9–12). The WT-oligo competed with αCP binding (lanes 13–16).
oligo competitor (Fig. 2C). This may reflect αCP sequestering PABP from the transcript because of a direct interaction of PABP with αCP (26, 30). Together these data confirm that αCP binding to the α1(1) collagen 3'-UTR transcript confers stability in a sequence-specific manner.

Decay of WT and MUT Transcripts Are Identical in Quiescent HSC Extracts—Having determined that the in vitro decay reactions recapitulate in vivo RNA poly(A)-dependent decay, the stability of WT and MUT transcripts was investigated in lysates from quiescent HSC extracts. These extracts lack detectable αCP binding activity (Fig. 1) despite expression of αCP protein (10). If αCP binding activity is required to stabilize the collagen mRNA via the 3'-UTR, then the decay rates of the WT and MUT 3'-UTR transcripts should be similar in these extracts. As predicted, the WT 3'-UTR (Fig. 3A, lanes 1–6) and the MUT 3'-UTR (lanes 7–12) displayed almost identical decay rates using these extracts. This demonstrates the requirement that αCP bind to the WT 3'-UTR to stabilize the transcript, as observed in NIH extracts (Fig. 2B).

WT Transcripts Are Stabilized in Activated HSCs—To examine whether a difference exists in decay rates between the WT and MUT 3'-UTR transcripts in activated HSCs, IVDAs were performed using extracts obtained from day 14 culture-activated HSCs. A significant increase in the stability of the WT transcript was observed compared with the MUT transcript (Fig. 3B, lanes 1–6 and 7–12).

Recombinant αCP Increases Stability of WT Transcripts—To determine whether αCP specifically increases the stability of the WT 3'-UTR transcripts, recombinant αCP was added to the IVDA reactions using quiescent HSC extracts that do not contain an endogenous αCP binding activity (Fig. 1). Recombinant αCP stabilized the WT 3'-UTR transcript but failed to affect the stability of the WT 3'-UTR transcript (Fig. 4). The substantial increase in the WT but not MUT transcript indicates a direct role for the binding of αCP in stabilizing the α1(1) collagen 3'-UTR.

Inhibition of Endogenous αCP Expression Decreases α1(1) Collagen mRNA Levels—To investigate the role of αCP in vivo,
siRNAs targeting the rat aCP mRNA (Table I) were transiently transfected into Rat1 fibroblasts, cells that express a1(I) collagen and possess aCP binding activity. Binding of the aCP protein, as assessed by EMSA, was inhibited ∼30% by addition of siRNA against aCP compared with a control siRNA (Fig. 5A). Because the siRNA decreases the binding activity of aCP, we wanted to assess the effects of inhibiting aCP binding activity on the steady state levels of the a1(I) collagen mRNA. Steady state levels of a1(I) collagen mRNA were reduced ∼60% in cells transiently transfected with aCP siRNA compared with control siRNA as determined by RNase protection assay (Fig. 5B). There was no change in glyceraldehyde-3-phosphate dehydrogenase mRNA levels. These data corroborate the role of aCP in stabilizing the a1(I) collagen mRNA. To examine the effects of inhibiting aCP expression in HSCs, we transfected siRNAs against aCP into culture-activated HSCs and assessed aCP binding by EMSA. A decrease of 30–40% in aCP binding activity was observed in HSCs transfected with siRNAs targeting aCP compared with control siRNAs (Fig. 5C). We again examined the steady state levels of a1(I) collagen mRNA in HSCs transfected with siRNAs targeting aCP compared with control siRNAs (Fig. 5D). Together, these experiments demonstrate that aCP interaction with the a1(I) collagen mRNA 3′-UTR increases stability of the mRNA molecule in activated HSCs.

Endogenous Regulation of aCP in HSCs—To investigate the mechanism of aCP binding regulation during HSC activation, we examined the cellular distribution of aCP protein in quiescent and activated HSCs. In quiescent HSC lysates, aCP was located primarily in the nuclear fraction with very low aCP protein levels observed in the cytoplasmic fraction. However, in the activated HSC extracts the total amount of aCP protein expression increased and exhibited a relocalization of aCP to the cytoplasmic fraction (Fig. 6A). Thus, activated HSCs contain higher aCP protein levels, and the aCP protein demonstrates a markedly different distribution. For comparison, the binding activity of PABP was similar in extracts from quiescent and activated HSCs (data not shown).

To determine whether the lack of binding activity observed in quiescent HSCs is solely because of low levels of protein expression in the cytoplasm or whether there is active repression of aCP binding in the quiescent HSCs, we examined binding activity in mixed extracts. Incubation of activated HSC extracts with equal amounts of bovine serum albumin had no effect on the observed binding activity. However, the addition of equal amounts of quiescent HSC extracts reduced the binding activity of the activated HSC extracts by 50% in the cytoplasmic extracts. (Fig. 6B.) In the nuclear fractions, the binding activity was not affected significantly.

DISCUSSION

Culture-induced activation of HSCs is accompanied by an ∼50-fold increase in the steady state levels of a1(I) collagen mRNA (10, 42). This dramatic increase results primarily from an increase in the half-life of the a1(I) collagen mRNA from 1.5 to >24 h. The increased half-life of the a1(I) collagen mRNA correlates with increased binding activity of aCP to the a1(I) collagen 3′-UTR following HSC activation (10). This study demonstrates that aCP plays a direct role in stabilizing of the a1(I) collagen mRNA in activated, but not quiescent, HSCs.

Utilizing IVDAs, proteins can be assessed for their role in mRNA degradation or stabilization. RNAs that only differ in their aCP binding sites display different decay rates with NIH 3T3 cell extracts, supporting a role for aCP in mRNA decay. Competition of aCP binding using an unlabeled WT-oligo results in a rapid decay of transcripts containing a WT aCP binding site, confirming a direct role of aCP in mRNA decay. We investigated the role of aCP in the differential regulation of a1(I) collagen mRNA expression in quiescent and activated HSCs. Quiescent HSCs express only trace amounts of type I collagen, the a1(I) collagen mRNA has a short half-life, and the cells contain no detectable aCP binding activity (2, 5, 36, 39). The decay rates with quiescent extracts for WT and MUT 3′-UTR RNA are nearly identical, as expected in extract that lack aCP binding activity. However, when WT and MUT 3′-UTR RNAs were incubated with lysates from activated HSCs, which produce collagen, have a long half-life of the a1(I) collagen mRNA, and contain aCP binding activity, a significant decrease in the decay rate was observed. This suggests that aCP binding activity is responsible for stabilizing the a1(I) mRNA.
collagen mRNA by the 3′-UTR in activated HSCs. Although different extracts cannot be directly compared, the relative rate of decay of different transcripts in the same extract provides comparison of the specificity and rate of decay because preparation variables are not a factor. Therefore, binding activity of αCP present in activated, but not quiescent HSCs, contributes to the dramatic increase of the collagen mRNA half-life.

As a further approach to assess the role of αCP binding in stabilizing the α1(I) collagen mRNA, siRNA technology was utilized. αCP binding activity was decreased by ~40% in activated HSCs transfected with siRNA, whereas a control siRNA had no effect on αCP binding activity. This reduction of αCP binding activity resulted in decreased steady state mRNA levels of α1(I) collagen, whereas cells treated with control siRNAs did not. These data demonstrate that the increased αCP binding activity in activated HSCs is responsible for increasing α1(I) collagen mRNA stability resulting in elevated steady state levels of α1(I) collagen as a probe alone (lane 1) or incubated with 10 µg of extracts from Rat1 fibroblasts transiently transfected with 100 pmol of siRNA against either luciferase (Luc, lane 2) or αCP (siA1, siA2, siA3, and siA4, lanes 3–6, respectively). Binding activity compared with control Luc-transfected extracts is shown and is expressed as a percentage of binding activity in the Luc control reactions. B, steady state α1(I) collagen mRNA levels were analyzed in Rat1 fibroblasts transiently transfected with siRNAs against either luciferase or αCP as assessed by RNase protection assays. Results shown are representative of three independent experiments. C, EMSA performed with probe alone (lane 1) or with 10-µg extracts from activated HSCs transiently transfected with siRNAs targeting αCP (siA1, siA2, siA3, and siA4, lanes 3–6, respectively) or a control siRNA against luciferase (Luc, lane 2). D, steady state levels of α1(I) collagen mRNA in siRNA-transfected HSCs examined by RNase protection assays. Results shown are the average of three independent experiments.

Regulation of α1(I) Collagen mRNA

Based on our previous (10, 39, 43–46) and current studies, our current model (Fig. 7) of α1(I) collagen mRNA regulation in activated and quiescent HSCs involves αCP as a key component in a multilayered regulation process. The role of PABP on general mRNA turnover is well established, and evidence exists that PABP interacts with αCP, increasing the affinity of both proteins for RNA (30). In activated HSCs, αCP binds and together with PABP stabilizes the 3′-UTR complex and prevents loading of the degradosome, a protein complex that degrades cellular RNAs, onto the α1(I) collagen mRNA. We have also shown that a conserved 5′-stem loop structure in the α1(I) collagen mRNA interacts with an unidentified binding activity in activated HSCs (43, 44). This 5′-stem loop inhibits mRNA stability and translation, while its inhibition is diminished by the αCP binding (45, 46). We speculate that the 5′-binding protein can interact with either αCP or PABP to facilitate circularizing the mRNA and increasing translation efficiency as well as protecting the mRNA from degradation machinery. In this model, αCP binding would stabilize the mRNA in a dual manner: αCP increases binding of PABP to the poly(A) tail and also interacts with the 5′-stem loop protein(s). Quiescent HSCs do not have αCP binding activity. Therefore, PABP is not stabilized, there is no interaction with the 5′-stem loop, and the mRNA molecule is rapidly degraded. Upon HSC activation, however, αCP binds to the 3′-UTR and interacts with PABP...
and/or proteins binding to the 5'-stem loop, resulting in an increase in mRNA half-life, thus allowing for efficient translation (Fig. 7).

There are many similarities between the regulation of α1(I) collagen mRNA in activated HSCs and the regulation of α-globin and lipooxygenase mRNAs in erythroid cells and the tyrosine hydroxylase mRNA in response to hypoxia (17, 47–49). These mRNAs form a class of molecules post-translationally regulated via 3'-UTR interactions with protein(s). There are three predominant classes of mRNAs that are regulated by interactions at the 3'-UTR: transcripts containing an AU-rich element (ARE), transcripts containing iron-responsive elements, and transcripts containing poly(pyrimidine)-rich regions in the 3'-UTR. These three classes of mRNAs are regulated by interactions between cis-acting regions in the UTR and trans-acting proteins via different mechanisms.

Many cell cycle mRNAs contain AREs in their 3'-UTRs and have very short half-lives (17). ARE-containing transcripts interact with two types of proteins that regulate message stability. AUF-1 can bind to the ARE, resulting in a rapid degradation of the transcript (50, 51). This prevents message accumulation and keeps the protein levels low. Alternatively, the ELAV family of proteins can bind to ARE-containing transcripts, resulting in stabilization of the transcript, effectively allowing for a rapid increase in the cellular protein levels (28, 52).

Gene regulation in response to levels of metabolites allows for subtle changes at the post-transcriptional level to alter gene expression. Genes containing iron-responsive elements are bound by a family of proteins called iron-responsive proteins (IRPs) that recognize the iron-responsive element site under low intracellular iron concentrations. This interaction stabilizes the mRNA and allows for production of the transferrin receptor to transport iron into the cell. As the cellular iron levels increase, the IRPs lose their binding capability and dissociate from the transcript, allowing the transcript to be targeted by degradation machinery. In this manner the cell is able to tightly regulate the amount of gene product in response to the availability of cellular factors (51).

Another method to regulate gene expression by mRNA stability occurs when certain genes are up-regulated in a sustained manner when the cell differentiates, such as erythroid cell maturation or HSC activation. Certain genes are up-regulated by binding of nucleic acid-binding proteins to a poly(pyrimidine)-rich region in the 3'-UTR. In the α-globin message, αCP binds to a CU-rich region in the 3'-UTR and increases the mRNA stability, allowing for expression from the mRNA for many hours after synthesis (53). Similarly, HSCs dramatically increase the stability of the α1(I) collagen mRNA as the cells

![Fig. 7. Model for αCP stabilization of the α1(I) collagen mRNA.](image-url)
undergo cellular activation. αCP binding to a CU-rich region in the 3′-UTR of α1(I) collagen is responsible for increased stability of the α1(I) collagen transcript.

During liver fibrosis, quiescent HSCs undergo a phenotypic and genotypic change where they lose vitamin A stores and increase production of extracellular matrix proteins, including α1(I) collagen. Investigating the regulation of type I collagen in this study, we have demonstrated that (i) transcripts are stabilized by the presence of an αCP binding site in activated, but not quiescent HSC extracts; (ii) addition of recombinant αCP restores stability to transcripts containing αCP binding sites in quiescent HSC extracts; (iii) knockdown of endogenous αCP results in decreased αCP binding activity and a corresponding loss of endogenous collagen α1(I) mRNA levels; (iv) the activation of HSCs induces a subcellular redistribution of αCP from primarily nuclear localization in quiescent HSCs to equal cytoplasmic and nuclear distribution in activated HSCs; and (v) there is a soluble, cytoplasmic activity in quiescent HSCs that inhibits the binding activity of endogenously activated αCP.

Taken together, this work demonstrates for the first time that αCP binding activity is required for collagen α1(I) mRNA stabilization during HSC activation and that alteration of this activity is sufficient to alter the endogenous collagen α1(I) mRNA levels. Thus, αCP is a potential target for therapy of liver fibrosis.

Acknowledgment—We thank the Center of Gastrointestinal Biology and Disease core facility for HSC isolations.

REFERENCES

1. Friedman, S. L., Rockey, D. C., McGuire, R. F., Maher, J. J., Boyles, J. K., and Yamasaki, G. (1992) Hepatology 15, 234–243
2. Friedman, S. L. (1999) Alcohol. Clin. Exp. Res. 23, 904–910
3. Schuppan, D. (1990) Semin. Liver Dis. 10, 1–10
4. Aycock, R. S., and Seyer, J. M. (1989) Connect. Tissue Res. 18, 177–183
5. Safadi, R., and Friedman, S. L. (2002) Arch. Biochem. Biophys. 409, 1–10
6. de Leeuw, A. M., Mccarthy, S. P., Geerts, A., and Knook, D. L. (1984) J. Gastroenterol. 23, 403–410
7. Ford, L. P., and Wilusz, J. (1999) Trends Biochem. Sci. 24, 409–411
8. Hendriks, H. F., Verhoofstad, W., Yamasaki, G. (1992) Trends Biochem. Sci. 17, 409–413
9. Holcik, M., and Liebhaber, S. A. (1997) Cell 88, 494–498
10. Krecic, A. M., and Swanson, M. S. (1999) J. Biol. Chem. 274, 3821–3828
11. Kiledjian, M., Wang, X., and Liebhaber, S. A. (1995) J. Biol. Chem. 270, 849–856
Regulation of α1(I) Collagen Messenger RNA Decay by Interactions with αCP at the 3’-Untranslated Region

Jeffrey N. Lindquist, Christopher J. Parsons, Branko Stefanovic and David A. Brenner

J. Biol. Chem. 2004, 279:23822-23829.
doi: 10.1074/jbc.M314060200 originally published online February 17, 2004

Access the most updated version of this article at doi: 10.1074/jbc.M314060200

Alerts:

• When this article is cited
• When a correction for this article is posted

Click here to choose from all of JBC’s e-mail alerts

This article cites 52 references, 23 of which can be accessed free at http://www.jbc.org/content/279/22/23822.full.html#ref-list-1