Messenger RNA preparations from the livers of normal and acutely inflamed rats were translated in a mRNA-dependent cell-free protein-synthesizing system. Immunoprecipitation of the translation products with a specific antibody prepared against purified rat plasma α₁-acid glycoprotein (α₁-AGP) detected an abundant 23,000 molecular weight peptide induced by inflammation. In order to examine the regulation of this acute phase protein, a double-stranded cDNA to partially purified rat α₁-AGP mRNA was synthesized, inserted into the Pst I site of the plasmid pBR322 by a GC-tailing technique, and used to transform Escherichia coli RR1. A recombinant plasmid containing a 740-base pair insert with a contiguous poly(dA) segment was identified as containing α₁-AGP cDNA sequences by partial DNA sequence analysis, and by specific hybrid selection of mRNA followed by in vitro translation and immunoprecipitation. The cloned double-stranded cDNA isolated from the recombinant pBR322 vector was recloned in the single-stranded DNA bacteriophage M13mp7 in order to develop a specific hybridization probe for mRNA quantitation. The α₁-AGP-specific cDNA probe was used to examine α₁-AGP mRNA levels in total liver RNA during a period of 48 h following the induction of acute inflammation by the administration of turpentine. In normal rat liver, α₁-AGP mRNA comprised about 0.0006% of total cellular mRNA. An increase in the amount of α₁-AGP mRNA was first detected 4 h after the onset of inflammation, and it reached a maximum level of induction at 36 h following the administration of the inflammatory agent. At this point, α₁-AGP mRNA comprised about 0.053% of total cellular RNA, representing a 90-fold increase over its normal level. This induction was associated with a substantial increase in the circulating plasma concentration of α₁-AGP, as measured by quantitative rocket immunoelectrophoresis. These results demonstrate that acute inflammation causes an increased accumulation of a specific mRNA which is responsible for the increased plasma concentration of α₁-AGP.

α₁-Acid glycoprotein is an M₀ = 41,000 plasma protein that is produced by the liver. It consists of a single polypeptide chain and contains five carbohydrate side chains that account for approximately 45% of its mass (1). In normal animals, α₁-AGP has a relatively low plasma concentration. However, in response to various acute inflammatory agents such as turpentine or bacterial endotoxin, the plasma level of α₁-AGP increases rapidly. This response is typical of the class of plasma proteins known as the acute phase reactants (2).

Previous studies suggest that the increased plasma concentrations of the acute phase reactants are due to an increased synthesis of these proteins (3-5). However, little is known about the mechanisms which underly this increased synthesis. In this report we describe a preliminary characterization of the induction of α₁-AGP following the onset of acute inflammation. A cloned cDNA hybridization probe was utilized to demonstrate that the increased plasma concentration of α₁-AGP appears to be the result of a dramatic increase in the level of liver α₁-AGP mRNA.

EXPERIMENTAL PROCEDURES

Animals—Acute inflammation was induced in Sprague-Dawley rats (230-290 g) by a single subcutaneous injection of turpentine (0.5 ml/100 g of body weight) in the dorsal lumbar region. At different times following injection, the rats were anesthetized with ether, plasma was obtained from the inferior vena cava, and the livers were excised and rapidly frozen in liquid nitrogen.

Protein Purification and Antibody Production—α₁-AGP was purified from rat plasma obtained 48 h after turpentine injection by a combination of ammonium sulfate precipitation, DEAE-Sephrose (Pharmacia) and CM-Sepharose (Pharmacia) ion exchange chromatography, affinity chromatography on wheat germ lectin Sepharose (Pharmacia), and preparative polyacrylamide gel electrophoresis. Antibodies to purified α₁-AGP were produced in rabbits with complete Freund's adjuvant (Difco) by the method of Crowle (6). Antibodies to purified α₁-AGP showed a single precipitin line in crossed immunoelectrophoresis (7) with rat plasma.

Preparation of Total RNA—Total RNA was extracted from frozen liver essentially as described by Chirgwin et al. (8). Livers were...
homogenized in 15 volumes of 4 M guanidine thiocyanate, 25 mM sodium citrate at pH 7.0, 0.5% N-laurylsarcosine, 0.1 M 2-mercaptoethanol, and 0.2 M Tris-HCl, pH 8.0 (SIGMA). The homogenate was centrifuged at 6000 rpm in a Sorvall GSA rotor for 15 min at 10 °C. The supernatant fluid was adjusted to pH 5.0 by addition of acetic acid and the RNA was precipitated by 0.75 volume of ethanol at -20 °C for 2 h. RNA was collected by centrifugation and redissolved in 7.5 M guanidine hydrochloride containing 25 mM sodium citrate and 5 mM dithiothreitol. Following two additional precipitations using 0.5 volume of ethanol, the residual guanidine hydrochloride was extracted from the precipitate with absolute ethanol. RNA was dissolved in sterile water, insoluble material was removed by centrifugation, and the pellets were re-extracted with water. The RNA was adjusted to 0.2 M Tris-HCl, pH 8.0 and precipitated by addition of 2.5 volumes of ethanol at -20 °C overnight.

Preparation of Poly(A)-containing RNA—Total RNA was dissolved in 20 ml Hepes buffer at pH 7.2 containing 10 mM EDTA and 1% SDS, heated at 65 °C for 10 min, then quickly cooled to 25 °C. The RNA solution was then diluted with an equal volume of water and adjusted to 300 mM NaCl. Samples containing up to 2400 ng RNA were mixed with 2.5 g of poly(U)-Sepharose (Pharmacia), equilibrated in the above final buffer, and mixed gently at room temperature for 30 min. The affinity matrix was then collected by centrifugation with 70 ml of 0.1 M 2-mercaptoethanol-containing RNA eluted with 70% (v/v) ethanol at -20 °C overnight.

Preparation of Poly(A)-containing RNA recovered from the second poly(U)-Sepharose chromatography step was heated at 65 °C for 10 min, quickly cooled to 25 °C, and sedimented through 5-29.5% isokinetic sucrose gradients (10) containing 1% SDS, 25 mM Hepes (pH 7.4), and 5 mM EDTA in a Beckman SW 41 rotor at 27,000 rpm for 17 h at 20 °C. The gradients were collected in 0.4-ml fractions and the RNA was precipitated twice with ethanol. RNA samples were redissolved in water and used for translation analyses.

Cell-free Translation and Immunoprecipitation—Cell-free translations in the mRNA-dependent protein-synthesizing system derived from rabbit reticulocyte lysates were carried out as described (11). Immunoprecipitation was performed by an initial binding reaction with monospecific antibodies to rat α1-AgP, followed by adsorption to a staphylococcal protein A (IgGisorB, The Enzyme Center Inc., Boston) antibody adsorbent (12). Electrophoresis of translation products and immunoprecipitates was performed on 10% or 10-17.5% gradient polyacrylamide gels containing 0.1% SDS, essentially as described by Laemmli (13). To prepare fluorograms, the gels were impregnated with E. HANCE (New England Nuclear), dried under vacuum, and exposed to Kodak XRP film at -70 °C for several days.

Cloning of pAGP 663 in Bacteriophage M13mp7—Isolated recombinant plasmid DNA (1 µg) was digested with 3 units of Pst I in a final volume of 10 µl. The enzyme was inactivated by heating to 65 °C for 10 min, and the DNA cleavage fragments were diluted to a final concentration of 10 ng/µl. The replicative form of the vector DNA, M13mp7 described by Messing et al. (18), was cleaved with Pst I and used for hybridization with an identical DNA sample (29 ng) from phage DNA (60 ng) in a 10-µl reaction mixture containing 70 mM Tris-HCl (pH 7.5), 7 mM MgCl2, 7 mM dithiothreitol, 0.07 mM ATP, and 0.2 unit of T7 DNA ligase. The reaction mixture was incubated at 15 °C for 2 h and then diluted to 80 µl with 25 mM EDTA.

Competent cells were prepared from E. coli strain JM103 (19) as described by Norgard et al. (20). A portion (2.5 µl) of the ligation mixture was added to 0.3 ml of competent cells, allowed to stand at 0 °C for 40 min, heated at 42 °C for 2 min, and mixed with 3 µl of YT top agar (21) containing 0.2 mg/ml of exponentially growing E. coli strain JM103, 0.33 mM isopropyl-1-thio-D-galactopyranoside (0.033% 5-bromo-4-chloro-3-indolyl-b-D-galactosidase), and 0.2 unit of T7 DNA ligase. The reaction mixture was incubated at 15 °C for 2 h and then diluted to 80 µl with 25 mM EDTA.

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hybridization for 3 h at 47 °C, the filters were washed five times for 15 min each at 47 °C with 1 ml of 75 mM NaCl, 7.5 mM sodium citrate (pH 7.4), and 0.5% SDS. Hybridized RNA was eluted by two successive 10-min incubations at 47 °C in 150 µl of 9% (v/v) formamide, 0.1% SDS, 10 mM Hepes (pH 7.5), 1 mM EDTA, and 33 µg/ml of tRNA. The RNA was precipitated with ethanol and then translated in the reticulocyte lysate protein-synthesizing system.

**cDNA Synthesis from M13AGP 663m Recombinant DNA**—One microgram of recombinant M13mp7 DNA was mixed with 2 µg of oligo(dT) primer (Collaborative Research) in a buffer containing 125 mM NaCl, 17.5 mM Tris (pH 7.5), 17.5 mM MgCl₂, and 0.1 mM EDTA in a final volume of 11 µl. The DNA was denatured by heating at 100 °C for 3 min, then plunged immediately into an ice water bath for 10 min to allow annealing of the oligo(dT) primer. The reaction mixture was then supplemented to give final concentrations of 30 µM each of unlabeled deoxyribonucleoside triphosphates (dATP, dGTP, dTTP), 5 µM of [α-32P]dTTP (410 Ci/mmole; Amersham), 1 mM dithiothreitol, and 2 units of the Klenow fragment of E. coli DNA polymerase I (New England Nuclear) in a final reaction volume of 25 µl. The reaction mixture was incubated at 25 °C for 1 h, followed by phenol extraction and Sephadex G-100 column chromatography. The DNA was denatured in 0.2 M NaOH by heating at 75 °C for 15 min, then sedimented through 5-27.8% isokinetic sucrose gradients (10% containing 0.1 M NaOH, 0.9 M NaCl, and 1 mM EDTA for 24 h in a Beckman SW 41 rotor at 41,000 rpm at 4 °C. Fractions containing radioactive DNA (∼8×10⁶ cpm µg⁻¹) were pooled and the DNA was collected by ethanol precipitation.

**RESULTS**

**Identification of the mRNA for α₁-AGP**—Total poly(A)-containing RNA isolated from normal and acute phase livers was translated in the mRNA-dependent protein-synthesizing system derived from rabbit reticulocyte lysates. Analysis of the total translation products by gel electrophoresis and fluorography indicated that an abundant Mr = 23,000 peptide had been induced by the action of the inflammatory agent (Fig. 1). Immunoprecipitation of the total translation products with a monospecific antibody to α₁-AGP (Fig. 1) demonstrated a single radioactive band of Mr = 23,000, indicating that this peptide corresponded to the translation product of α₁-AGP mRNA.

An RNA preparation enriched for α₁-AGP mRNA was obtained by sedimenting total poly(A)-containing RNA through isokinetic sucrose gradients. The RNA fractions were translated and analyzed by gel electrophoresis and fluorography. A comparison of normal and acute phase translation products indicated that density gradient fraction 10 (Fig. 2) was substantially enriched for α₁-AGP mRNA. This poly(A)-containing RNA fraction was then used for ds-cDNA synthesis and subsequent cloning in pBR322.

**Construction and Identification of Recombinant Plasmids Containing α₁-AGP cDNA**—A ds-cDNA was synthesized from the gradient fraction enriched for α₁-AGP mRNA and was examined by agarose gel electrophoresis. Most of the radioactive material migrated at a size of 400-800 base pairs (data not shown). The ds-cDNA was digested with S1 nuclease, separated from low molecular weight products by sedimentation through sucrose gradients, and subsequently inserted into the PstI site of the ampicillin resistance gene of the plasmid pBR322 by the oligo(dG)-oligo(dC)-joining technique. The DNA was then transformed E. coli RR1 and approximately 1000 tetracycline-resistant transformants were selected. Transformants were screened as described under "Experimental Procedures," and a recombinant DNA plasmid (pAG 663) containing a 740-base pair insert was tentatively identified as being a candidate for containing α₁-AGP mRNA sequences.

In order to establish the identity of the α₁-AGP candidate plasmid, the ds-cDNA insert was employed to select its corresponding mRNA by hybridization, followed by cell-free translation of the hybrid-selected mRNA and immunoprecipitation of the translation products. Since this procedure requires denatured or single-stranded DNA that is complementary to the mRNA, the ds-cDNA was recloned into the single strand phage vector M13mp7. Single-stranded DNA from one of the cDNA strand clones (M13AGP 663c) was immobilized on nitrocellulose and used to specifically select its corresponding mRNA. Fig. 3 (Lane B) demonstrates that M13AGP 663c specifically hybridizes to an mRNA which then directs the cell-free synthesis of a single peptide with an apparent Mr = 23,000. The translation product is immunoprecipitated with monospecific antibodies to rat α₁-AGP (Fig. 3, Lane C), thus establishing the identity of the recombinant plasmid.

To further confirm the identity of the recombinant plasmid, a partial nucleotide sequence of the ds-cDNA insert was determined. The restriction endonuclease cleavage map used in the nucleotide sequence determination is shown in Fig. 4. The 271-base pair AvaII fragment was labeled at the 3' end, then subjected to DNA sequence analysis by the method of Maxam and Gilbert (Fig. 5A). Fig. A shows the sequence of 78 nucleotides of this fragment and the amino acid sequence predicted from one of the six possible reading frames. Multiple termination codons were observed in each of the five other reading frames. Fig. 5B shows the alignment of the inferred amino acid sequence with the known protein sequence (1) of human α₁-AGP. Of the 26 amino acid residues shown in the rat sequence, 19 are identical with the corresponding residues in the human protein, providing further support for the identity of the recombinant plasmid.

**Size Estimation of α₁-AGP mRNA**—Total poly(A)-containing RNA samples from normal and acute phase livers were denatured by reaction with glyoxal followed by electrophoresis...
in agarose gels (27). Following electrophoresis the RNA was transferred to diazotized paper (28) and hybridized to a $^{32}$P-labeled cloned DNA probe. As shown in Fig. 6, the cloned cDNA probe hybridized to an RNA species of about 850 nucleotides in length. Furthermore, the relative amount of $\alpha_1$-AGP mRNA in the acute phase liver is increased greatly compared to normal liver. The broad width of the mRNA gradient fraction from which the RNA was collected. $N$ indicates RNA obtained from normal liver, and $A$ indicates RNA obtained from acute phase liver. The molecular weight markers as indicated are $\alpha_2$-macroglobulin (180,000), phosphorylase $b$ (92,500), bovine serum albumin (68,000), ovalbumin (45,000), carbonic anhydrase (30,000), and cytochrome $c$ (12,300).

**FIG. 2. In vitro translation and gel electrophoresis of size-fractionated poly(A)-containing RNA.** Poly(A)-containing RNA samples from normal or 36-h acute phase livers were subjected to sucrose density gradient centrifugation, in vitro translation, SDS-polyacrylamide gel electrophoresis, and fluorography as described under "Experimental Procedures." The numbers refer to the density gradient fraction from which the RNA was collected. $N$ indicates RNA obtained from normal liver, and $A$ indicates RNA obtained from acute phase liver.

**FIG. 3. Positive hybrid selection and in vitro translation.** The details of the experiment are described under "Experimental Procedures" and in Fig. 1. Lane A, total translation products from 36-h acute phase liver; Lane B, total translation products of hybrid-selected mRNA using the M13 cDNA strand clone. The lower band in this lane represents the translation product of residual reticulocyte globin mRNA; Lane C, immunoprecipitation of the translation products of hybrid-selected mRNA (Lane B) with antibodies to purified rat $\alpha_1$-ACP.

**FIG. 4. Restriction endonuclease map of the $\alpha_1$-AGP ds-cDNA insert.** The shaded area represents the inserted sequence in the plasmid pAGP 663 with the indicated restriction endonuclease sites. The numbers indicate the length of these fragments in base pairs. The upper horizontal line indicates the length of $\alpha_1$-AGP mRNA correlated with the relative position of these restriction endonuclease sites in $\alpha_1$-AGP ds-cDNA.

**FIG. 5. Nucleotide sequence of a portion of the coding strand of the $\alpha_1$-AGP ds-cDNA insert.** A, DNA from plasmid pAGP 663 was cleaved with restriction endonuclease Ava II and labeled at the 3' ends with $E. coli$ DNA polymerase I (Klenow fragment) and [$\alpha$-$^{32}$P]dCTP (25). The 5'-terminal Ava II fragment was isolated by polyacrylamide gel electrophoresis and its sequence was determined as described by Maxam and Gilbert (25). The amino acid sequence predicted from the only open reading frame is shown. The numbers above the line indicate the corresponding position in human $\alpha_1$-AGP as described by Schmid (1). B, the boxes enclose amino acid residues that are identical in both rat and human $\alpha_1$-AGP. The one-letter notation for amino acids is according to the recommended convention of Dayhoff (26). The double letter code for three of the amino acid positions represents normal variation in the human protein as described by Schmid (1).
### Measurement of α1-AGP mRNA Levels—The M13-derived α1-AGP DNA was employed in RNA-driven hybridization reactions to determine the relative concentrations of α1-AGP mRNA in total cellular RNA extracted from rat liver before, and at various times after the animals received a single subcutaneous injection of turpentine. Representative hybridization curves are shown in Fig. 8 and the $R_{0.1/2}$ values for all time points are indicated in Fig. 8. The hybridization reaction went to greater than 90% completion with pseudo first order kinetics, occurring over a log $R_{0.1/2}$ range of approximately 2. The S1 nuclease-resistant background of the cDNA in the absence of RNA was about 4% of the input probe.

The relative increase in the concentration of α1-AGP mRNA sequences following the induction of acute inflammation was measured by comparing the $R_{0.1/2}$ values of the hybridization reactions; 2 h after the onset of inflammation no change could be detected in the mRNA levels for α1-AGP (Figs. 8 and 9). At 4 h after injection there was a 3.4-fold increase in these levels, followed by a progressive increase which reached a maximum level 36 h after injection (Fig. 9), at which point the level was 90-fold higher than that of the normal liver. This induction was then followed by a decline which could be detected by 48 h after the onset of inflammation.

α1-AGP mRNA levels were correlated with the plasma levels of its corresponding protein. Rocket immunoelectrophoresis (35) of rat plasma samples indicated that the α1-AGP concentration in the plasma of untreated rats was 0.064 mg/ml. Fig. 9 shows that an increase in the plasma level of α1-AGP was first detected between 4 and 6 h after the onset of inflammation. This induction was followed by a progressive increase to a concentration of 2.5 mg/ml, a value that is in excellent agreement with the serum concentration of 2.7 mg/ml previously reported by Nagashima et al. (36), under conditions of inflammation identical with those in this report. However, we observe 2.7-fold lower levels of α1-AGP in normal plasma than that which was reported by Nagashima et al. These results suggest that basal levels of plasma α1-AGP may

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3 G. A. Ricca, J. M. Taylor, and J. E. Kalinyak, manuscript in preparation.
**α1-Acid Glycoprotein mRNA**

**FIG. 7. Protocol for the synthesis of M13-derived α1-AGP cDNA hybridization probe.** The upper horizontal line represents the replicative form of the M13mp7 vector DNA containing the α1-AGP insert. The positions of restriction endonuclease sites within this DNA, and the sequence information given, are taken from the descriptive literature supplied by Bethesda Research Laboratories, compiled by Joachim Messing, Department of Biochemistry, University of Minnesota, St. Paul, MN. The lower horizontal line represents the position of these restriction sites in the viral (+) strand of the recombinant mRNA strand clone (M13AGP 663m) showing the poly(A) segment at the 3′ end of the insert. The evidence supporting the hairpin structure shown in the lower part of this figure is described elsewhere. For diagrammatic purposes the M13 DNA is shown in a linear form, although the genome is a single strand covalently closed circular molecule.

**FIG. 8. Quantitation of α1-AGP mRNA sequences in rat liver during acute inflammation.** Total liver RNA samples isolated from rats at various times following turpentine injection were hybridized in excess to 32P-labeled α1-AGP cDNA derived from M13AGP 663m. Hybridizations were performed as described, where hybrids were measured by assaying the completed reactions for S1 nuclease (Miles)-resistant radioactive material. The $R_{0.5}$ values for the hybridization reactions were obtained by using a computer program to analyze the data to solve the equation $C / C_0 = 1 - \exp(-ln 2) (R_d / R_{d/2})$, where $C_0$ is the initial amount of single-stranded cDNA, and $C$ represents the amount of cDNA in hybrid at time $t$. RNA for each time point was prepared from pooled livers of 4 adult rats. Representative hybridization curves are shown. Total RNA from normal liver (O) and liver obtained 2 h (O), 4 h (□), 10 h (△), and 36 h (■) after a single subcutaneous injection of turpentine was hybridized to 30 pg of α1-AGP cDNA. The $R_{d/2}$ values (in moles−s−liter−1) for these data and for additional hybridization data not shown were: 3.16, 12 h; 1.19, 18 h; 1.05, 24 h; 0.75, 36 h; and 1.54, 48 h. The fraction of α1-AGP mRNA present in total RNA can be calculated as follows: $R_{d/2}$ of pure α1-AGP mRNA = $R_{d/2}$ of pure rat albumin mRNA (complexity of α1-AGP mRNA)/(complexity of albumin mRNA). The complexity of pure albumin mRNA in 2265 nucleotides (34) and the complexity of α1-AGP mRNA is 850 nucleotides. Under identical conditions purified albumin mRNA hybridizes to albumin cDNA with a $R_{d/2}$ of 0.001. The value of $R_{d/2}$ for hybridization of purified α1-AGP mRNA to α1-AGP cDNA would be 0.0004. Comparison of this value to the $R_{d/2}$ value obtained upon hybridization of α1-AGP cDNA to total RNA from normal rats (66.9) indicates that α1-AGP mRNA comprises approximately 0.0006% of total normal liver RNA.

The translation assay was utilized to monitor the partial purification of the mRNA and to confirm the identity of recombinant bacterial plasmids containing ds-cDNA sequences specific for α1-AGP. Recloning the ds-cDNA insert differs substantially, depending on a variety of hormonal and environmental factors.

**DISCUSSION**

By employing a monospecific antibody to rat plasma α1-AGP, we have identified a peptide with a $M_r = 23,000$ as being the primary translation product of rat α1-AGP mRNA. This size is similar to the molecular weight of the peptide portion of human α1-AGP determined from the amino acid sequence by Schmid (1). When the same antibody is employed to immunoprecipitate a [3H]leucine-labeled rat liver perfusate, a protein with an apparent $M_r = 44,000$ is observed, in agreement with a previous report (36) on the molecular weight of rat α1-AGP.

The translation assay was utilized to monitor the partial purification of the mRNA and to confirm the identity of recombinant bacterial plasmids containing ds-cDNA sequences specific for α1-AGP. Recloning the ds-cDNA insert

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*W. S. L. Liao, unpublished results.

*Unpublished result.*
into the single-stranded bacteriophage M13mp7 was found to be particularly advantageous with regard to identifying recombinant clones by hybridization selection of mRNA and subsequent transcription. Since the M13 bacteriophage DNA is obtained in a single strand form, potential problems associated with renaturation of the DNA during binding to the nitrocellulose are completely avoided. We have found that hybridization selection of mRNA using M13 recombinant DNA is far more reproducible than the same procedure with denatured double-stranded DNA inserted derived from bacterial plasmids such as pBR322. The usefulness of recoding a CDNA sequence into a single-stranded form is underscored when one considers the ease of obtaining a hybridization probe from this vector, using the method described in this report.

Our results demonstrate directly that administration of an inflammatory agent can result in a dramatic accumulation of the mRNA coding for an individual component of the seromucoid fraction (2) of plasma, \( \alpha_1 \)-acid glycoprotein. It is noteworthy that no change in mRNA levels occurs within 2 h after the onset of inflammation, but a significant increase has occurred by 4 h. This lag time may be required for the host response to inflammation through the production of various leukocyte factors or other intermediate humoral factors that may stimulate the liver to increase the production of the acute phase proteins (2). Our observations are in agreement with the results of Neuhaus et al. (4), who found that the increased synthesis of the seromucoid fraction, following inflammation, could be blocked by the administration of actinomycin D not later than 4 h after injury.

The 90-fold increase in the relative amount of \( \alpha_1 \)-AGP mRNA at 36 h after the onset of inflammation results in this mRNA species becoming a major component of the liver mRNA. Assuming a sequence complexity of 850 nucleotides for \( \alpha_1 \)-AGP mRNA, it can be calculated (see Fig. 8) that this mRNA is induced to become about 2.7% of the total liver mRNA at the height of the acute phase response. In this regard, albumin mRNA levels show a transient 5-fold decrease, to about 2.2% of total liver mRNA during the acute inflammatory reaction. Thus, \( \alpha_1 \)-AGP mRNA may be induced to become a major liver mRNA species during the maximum response of the liver to acute inflammatory agents. The mechanism responsible for this apparent induction of \( \alpha_1 \)-AGP mRNA is currently under investigation.

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