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La Autoantigen Alleviates Translational Repression by the 5′ Leader Sequence of the Human Immunodeficiency Virus Type 1 mRNA

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The *trans*-activation response element (TAR) at the 5′ end of the human immunodeficiency virus type 1 (HIV-1) mRNAs forms a stable hairpin structure which is a target for binding of the virally encoded protein Tat, which activates viral gene expression, as well as several cellular factors. TAR is also inhibitory to translation. One of several host factors that binds to TAR RNA is the La autoantigen, an RNA-binding protein which functions in RNA polymerase III transcription termination and has also been implicated in cap-independent internal translation initiation on poliovirus RNA. Here we show that La autoantigen alleviates translational repression by the HIV-1 leader RNA. In rabbit reticulocyte lysate, La relieves the *cis*-inhibitory effect of the TAR RNA on translation of bacterial chloramphenicol acetyltransferase (CAT) mRNA but not inhibition that is mediated by an artificial secondary structure element. Canonical translation factors exhibited slight (eIF-2 and GEF) or no (eIF-4A, eIF-4B, eIF-4E, eIF-4F, eIF-3, and eEF-1α) stimulatory activity on translation of TAR-containing CAT mRNA. In addition, we show that poliovirus RNA, in spite of being an inefficient template in rabbit reticulocyte lysate, is a strong competitive inhibitor of translation of TAR-containing CAT mRNA but not CAT mRNA. This inhibition can be relieved by La but not by any other translation factor. The results suggest a possible involvement of the La autoantigen in HIV-1 gene expression.

RNA-protein interactions involving the 5′ untranslated region (UTR) of human immunodeficiency virus type 1 (HIV-1) play an important role in regulation of virus gene expression. The best-studied interaction is that of the viral protein Tat with a target *trans*-activation response element (TAR) present at the 5′ end of the HIV-1 transcripts. The TAR sequence forms a stable stem-bulge-loop structure that binds Tat and several cellular factors in vitro (28, 37). The interaction of Tat and TAR leads to a dramatic increase in the abundance of HIV-1 transcripts and accelerates virus production (for a review, see reference 40). Although the detailed mechanism of this *trans* activation has not been established, current data suggest that Tat augments transcription initiation from a processive promoter element (for a review, see reference 8). Interaction with several transcription factors assist Tat in this process (3, 18, 43).

The TAR sequence is present at the 5′ end of all HIV-1 mRNAs. In addition to mediating *trans* activation by Tat, TAR has the potential to regulate the expression of viral genes at the translational level. Indeed, the first 111 nucleotides of HIV-1 mRNA were shown to have a strong inhibitory effect on mRNA translation in vitro as well as in *Xenopus* oocytes (11, 15, 30, 39). Mutations in the sequence of the 5′ UTR that disrupt the secondary structure relieved translational inhibition (30). It was concluded from this and other experiments that the secondary structure in the 5′ UTR of HIV-1 mRNAs and the inaccessibility of the cap structure are responsible for the inhibition of translation (30). It is conceivable that the block to translation of HIV-1 mRNAs by the 5′ UTR must be overcome to allow for efficient synthesis of viral proteins in infected cells. This could be mediated by *trans*-acting factors that interact with the viral 5′ UTR. In addition to Tat, several cellular proteins bind to TAR (13, 14, 23, 35, 41). Recent studies showed that TAR interacts strongly and specifically with La autoantigen (6). La is an RNA-binding protein that elicits an autoimmune response in patients with systemic lupus erythematosus and Sjögren's syndrome (47). La was shown to be an RNA polymerase III transcription termination factor (16, 17, 22). Recently, La was shown to bind to the 5′ UTR of poliovirus, and in vitro translation studies implicated this protein in poliovirus internal translation initiation (24, 26, 46). La does not enhance translation of several other mRNAs such as tobacco mosaic virus or brome mosaic virus RNA (26).

La requirement in translation of HIV-1 mRNAs was tested in a rabbit reticulocyte lysate (RRL). The lysate was programmed with a hybrid RNA consisting of the HIV-1 leader containing the first 111 nucleotides, termed TAR(+111) (30), that was fused to the coding region for bacterial chloramphenicol acetyltransferase (CAT); the resulting construct was called TAR(+111)CAT. We show that La, but no other translation factor, significantly stimulates translation of this mRNA. Moreover, poliovirus RNA exerts a profound competitive inhibitory effect on translation of the TAR(+111)CAT mRNA. The inhibition can be relieved by La but not by any of the canonical translation factors tested.

MATERIALS AND METHODS

Plasmids. pSP64/CAT and the SP6 constructs containing the HIV-1 5′ long terminal repeat fused to the coding sequence of CAT were essentially as described previously (30). In pSP64/

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TARCAT and pSP64/TAR(+111)CAT, the viral sequences correspond to nucleotides +1 to +80 and +1 to +111 of HIV-1 mRNA, respectively. Plasmids HB0 and HB3, which contains secondary structure contributed by the insertion of three *Bam*HI linkers, 5'-TT(CCGGATCCGG)$_3$AAGCTT-3', in the 5' UTR of the CAT gene, were previously described (19). Plasmids HB3 and HB0 were digested with *Ban*I and *Bgl*I restriction enzymes, and the ~800-bp fragment containing the 5' UTR fused to CAT was blunt ended by Klenow enzyme and ligated into blunt-ended *Hin*dIII and *Bgl*II sites of plasmid pSP64T (20). The correct orientation of the pSP64T plasmid derivatives containing none (A0-CAT) or three (A3-CAT) *Bam*HI linkers in the 5' UTR of the CAT gene was confirmed by sequencing using an SP6 primer. RNAs transcribed from these plasmids were termed A0CAT and A3CAT, respectively.

In vitro transcription. Plasmids were linearized with *Bam*HI, except for plasmid HB3, which was linearized with *Xba*I, and transcribed by SP6 RNA polymerase (Promega) for 2 h at 37°C as described by the manufacturer. m^{7}GpppG was included in the transcription mixtures in 10-fold molar excess relative to GTP to synthesize capped mRNAs (33). Following digestion (10 min, 37°C) with RNase-free DNase I (200 U/ml; Boehringer) RNA was purified by phenol-chloroform extraction and gel filtration through Sephadex G-50 nick translation columns (Pharmacia). RNA was precipitated with 2 volumes of ethanol, washed three times with 70% ethanol, and resuspended in water. The RNA concentration was determined by measuring the optical density at 260 nm. RNA integrity was determined by formaldehyde-agarose gel electrophoresis.

Purification of La, deletion mutant La(1-194), and initiation factors. Recombinant human La protein and deletion mutant La(1-194) were expressed in *Escherichia coli* and purified as previously described (46). Recombinant murine initiation factor eIF-4E was purified to apparent homogeneity by chromatography on an m^{7}G-coupled agarose matrix. Highly purified GEF from rabbit reticulocytes was a kind gift from J. N. Dholakia. Rabbit reticulocyte eIF-2, eIF-4F, and eIF-3 and elongation factor eEF-1α were kindly provided by W. C. Merrick. These and other preparations of translation factors were described previously (46). All factors were at a concentration of 1 mg/ml in buffer A (46). A 0.5 M KCl ribosomal wash fraction from Krebs-2 cells (47) had a protein concentration of 15 mg/ml.

In vitro translation. Micrococcal nuclease-treated RRL was purchased from Promega Corp. In vitro translation of RNA templates was performed under the conditions recommended by the manufacturer. Each reaction mixture (12.5 μl) contained 8.75 μl of the lysate and the following components at the indicated final concentrations: 75 mM potassium acetate, 0.75 mM magnesium acetate, 10 mM creatine phosphate, 50 μg of creatine phosphokinase per ml, 20 mM each unlabeled amino acid minus methionine, 5 mCi of [^{35}S]methionine (1,200 Ci/mmol), 2 mM dithiothreitol, 0.02 mM hemin, and 50 μg of calf liver tRNA per ml. mRNA was added to a final concentration of 48 μg/ml (unless indicated otherwise). Reaction mixtures were supplemented with 1.5 μg of initiation factor preparations and incubated at 30°C for 60 min. Products of in vitro translation were analyzed on sodium dodecyl sulfate–15% polyacrylamide gels, except for Fig. 1, in which translation rates were measured by incorporation of [^{35}S]methionine into trichloroacetic acid-precipitable material. After electrophoresis, gels were processed for fluorography by using En^{3}Hance (Dupont). The intensity of the band corresponding to CAT protein was determined with a BAS-2000 PhosphorImager (Fuji Corp.)

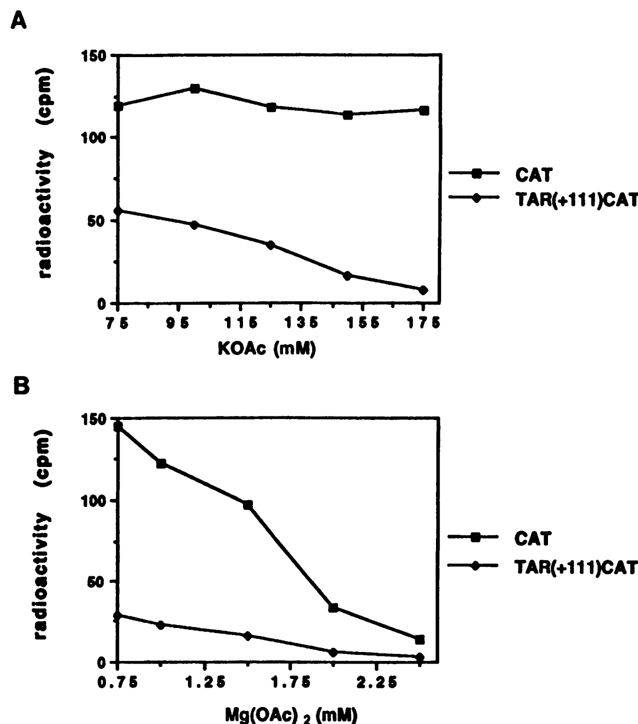

FIG. 1. Comparative effects of salt concentrations on translation of TAR(+111)CAT and CAT mRNAs in RRL. TAR(+111)CAT and CAT mRNAs (0.04 μg) were translated at 30°C at 75 to 175 mM potassium acetate (KOAc) and 1 mM magnesium acetate (A) or at 0.75 to 2.5 mM magnesium acetate and 150 mM potassium acetate (B). After 60 min of incubation, 5-μl aliquots of translation reaction mixtures were assayed by incorporation of radioactivity into trichloroacetic acid-insoluble material as described by the manufacturer (Promega).

RESULTS

Translational *trans* activation of HIV-1 leader RNA by La. Previous results showed that the 5' leader sequence of the HIV-1 mRNA exhibits a strong *cis*-inhibitory effect on translation of downstream cistrons and that the TAR stem-loop structure is responsible for this inhibition. The magnitude of this inhibition was considerably lower in extracts from HeLa cells than in RRL (30). This finding suggests that extracts from HeLa cells possess some factor(s) that could mitigate TAR-mediated inhibition and that this factor(s) is limiting in RRL. A likely candidate for such a factor is La protein, which binds to TAR (6) and is required for efficient translation of poliovirus RNA in RRL (26, 46). To address this possibility, the ability of La to stimulate TAR-mediated translation in RRL was studied.

Hybrid RNAs transcribed from plasmids pSP64/TARCAT and pSP64/TAR(+111)CAT, in which the 5' UTRs correspond to nucleotides +1 to +80 and +1 to +111 of HIV-1 mRNAs, respectively, were used to program translation in a RRL. TAR(+111)CAT mRNA and CAT mRNA displayed similar Mg^{2+} and K^+ concentration dependences for translation, despite their different translation efficiencies (Fig. 1). However, increasing the concentration of K^+ preferentially inhibited translation of TAR(+111)CAT mRNA compared with CAT mRNA. This effect may be a result of stabilization of the RNA secondary structure. Under optimal ionic conditions, TARCAT and TAR(+111)CAT mRNAs translate less effi-

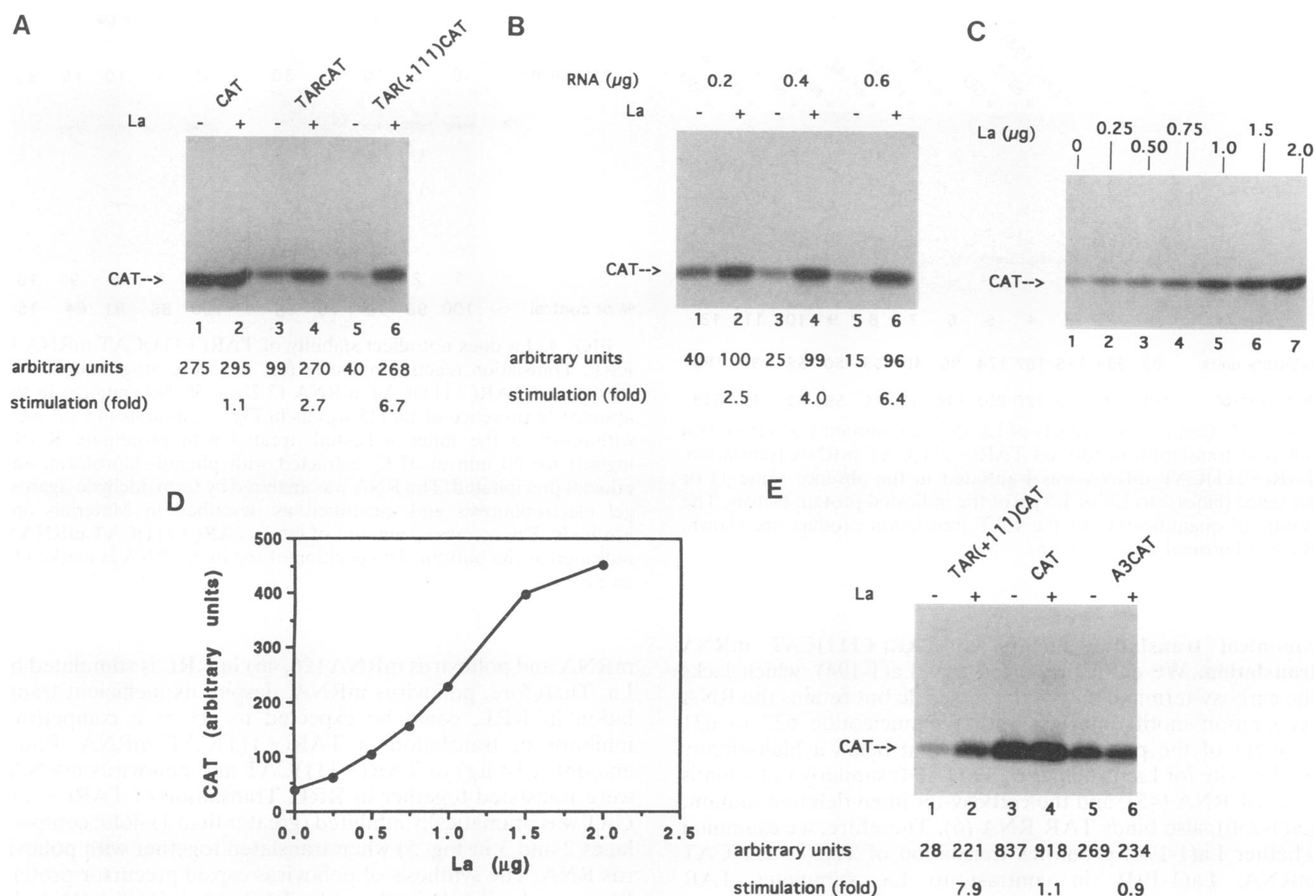

FIG. 2. Effects of La on translation of mRNAs containing the HIV-1 leader sequence. (A) CAT, TARCAT, and TAR(+111)CAT mRNAs were translated in RRL at a concentration of 0.6 µg for 60 min in the absence or presence of 1.5 µg of La protein under conditions specified in Materials and Methods. (B) Titration of mRNA concentration. Translation was carried out at the indicated concentrations of TAR(+111)CAT under the conditions described for panel A. (C) La dose response of translation. TAR(+111)CAT mRNA was translated at a concentration of 0.6 µg in the absence (lane 1) or presence (lanes 2 to 7) of the indicated amounts of La protein. (D) Quantitative representation of the data shown in panel C. (E) Comparative effects of La on translation of TAR(+111)CAT, A0CAT (CAT), and A3CAT mRNAs. The results of quantification of the CAT translation product are given at the bottom of panels A, B, and E.

ciently (about three- and sevenfold, respectively) than CAT mRNA (Fig. 2A). La significantly stimulated translation of TAR(+111)CAT mRNA (6.7-fold) and to a lesser extent the translation of TARCAT mRNA (2.7-fold). No stimulation was seen with CAT mRNA. This result was also reproduced when smaller amounts of CAT mRNA were tested (data not shown), therefore excluding the possibility that another factor was limiting for CAT translation. Thus, La clearly relieves the translational inhibition mediated by TAR and TAR(+111) RNAs in RRL.

Since TAR(+111)CAT mRNA responded to La better than TARCAT mRNA, all subsequent experiments were performed with the former template. Figure 2B demonstrates the effect of La on translation at different mRNA concentrations. The stimulatory effect of La is more pronounced at high (0.6 µg, 6.4-fold) than at low (0.2 µg, 2.5-fold) or intermediate (0.4 µg, 4-fold) RNA concentrations. A similar effect of RNA concentration on the La response was also described for poliovirus RNA translation (46). This observation suggests that La becomes limiting for translation at high mRNA concentrations. La stimulates the translation of TAR(+111)CAT mRNA in a dose-responsive manner (Fig. 2C and D). An amount of La of 1.5 µg, which is subsaturating, was used throughout the rest of this work.

Since an extensive secondary structure is characteristic of both HIV-1 and poliovirus 5′ UTRs (1, 25, 28), it was important to determine if any secondary structure element capable of inhibiting translation will confer La responsiveness to the 5′ UTR. To address this possibility, three *Bam*HI linkers that are predicted to generate in the mRNA a secondary structure comparable in stability to TAR(+111) ($\Delta G = -57.7$ and -53 kcal [1 kcal = 4.184 kJ]/mol, respectively) were introduced in the 5′ UTR of CAT mRNA. This mRNA (termed A3CAT) was assayed for La translational response. The stable hairpin structure element decreased (about threefold) the efficiency of CAT mRNA translation (Fig. 2E; compare lanes 3 and 5). However, translation of this mRNA, in contrast to TAR(+111)CAT mRNA, was not stimulated by La. La also failed to stimulate the translation of A5CAT mRNA (19), harboring five *Bam*HI linkers ($\Delta G = -81.7$ kcal/mol) (data not shown). Thus, La is likely to require specific structural elements in the 5′ UTR of mRNA for its binding and activity.

Comparative effect of La, deletion mutant La(1-194), and

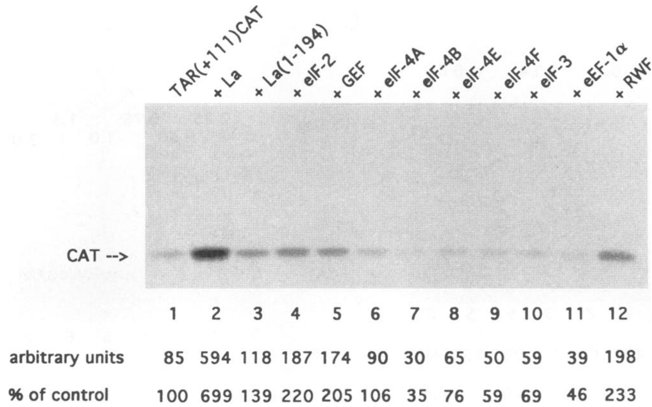

FIG. 3. Comparative effects of La, deletion mutant La(1-194), and different translation factors on TAR(+111)CAT mRNA translation. TAR(+111)CAT mRNA was translated in the absence (lane 1) or presence (lanes 2 to 12) of 1.5 μg of the indicated protein factors. The results of quantification of the CAT translation product are shown. RWF, ribosomal wash fraction.

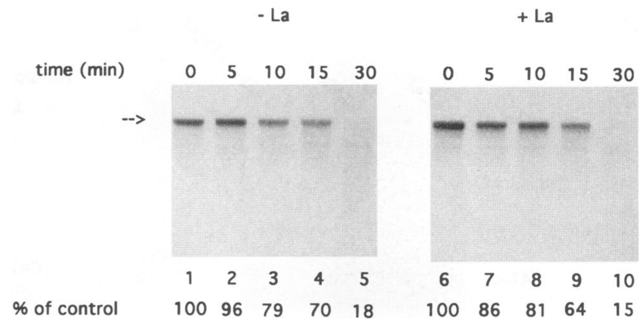

FIG. 4. La does not affect stability of TAR(+111)CAT mRNA in RRL. Translation reaction mixtures (0.1 ml) were programmed with ^{32}P-labeled TAR(+111)CAT mRNA (3.2 μg, 30,000 cpm/μg) in the absence or presence of La (15 μg) as in Fig. 2. Aliquots (15 μl) were withdrawn at the times indicated, treated with proteinase K (0.4 mg/ml) for 30 min at 37°C, extracted with phenol-chloroform, and ethanol precipitated. The RNA was analyzed by formaldehyde-agarose gel electrophoresis and quantified as described in Materials and Methods. The recovered amount of intact TAR(+111)CAT mRNA is indicated at the bottom. The position of the intact RNA is marked by an arrow.

canonical translation factors on TAR(+111)CAT mRNA translation. We earlier reported that La(1-194), which lacks the carboxy-terminal half of the molecule but retains the RNA recognition motif, interacts with the nucleotide 522 to 631 segment of the poliovirus 5′ UTR that bears a high-affinity binding site for La protein (46). La(1-194) similarly to La binds to TAR RNA (45), and the carboxy-terminal deletion mutant, La(1-250), also binds TAR RNA (6). Therefore, we examined whether La(1-194) promotes translation of TAR(+111)CAT mRNA. La(1-194), in contrast to La, stimulates TAR (+111)CAT mRNA translation only marginally (Fig. 3; compare lanes 1 and 3). Thus, the La carboxy-terminal portion is important for La activity. It is likely, although not proven yet, that the interaction of the La RNA recognition motif with TAR RNA is necessary for La activity, but it is clear that it is not sufficient for translational activity.

Next, we tested several translation factors (eIF-2, GEF, eIF-4A, eIF-4B, eIF-4E, eIF-4F, eIF-3, and eEF-1α) for their effects on translation of TAR(+111)CAT mRNA in RRL. None of these factors stimulated the translation to the extent displayed by La (Fig. 3). eIF-2, GEF, and a crude initiation factor preparation (ribosomal wash fraction) from Krebs-2 cells showed some stimulation (~2.0-fold).

TAR(+111)CAT mRNA stability in RRL is not affected by La. TAR(+111)CAT mRNA relatively unstable (half-life, ~20 min) in RRL (30), and La could potentially stimulate translation by protecting the mRNA against nuclease degradation. To examine this possibility, ^{32}P-labeled TAR(+111)CAT was incubated in RRL in the presence or absence of La under the translation conditions. The RNA was extracted from translation mixtures at different time points and fractionated by electrophoresis in formaldehyde-agarose gels (Fig. 4). As judged by the fraction of intact RNA remaining, the half-life of TAR(+111)CAT mRNA in RRL is approximately 20 min, and La has no appreciable effect on the mRNA stability. Thus, the primary effect of La on translation of TAR(+111)CAT mRNA is likely to be at the level of translation initiation. This view was further supported by our finding that La stimulated initiation complex formation of TAR(+111)CAT mRNA (data not shown).

Competitive inhibition of TAR(+111)CAT mRNA translation by poliovirus RNA. Translation of TAR(+111)CAT mRNA and poliovirus mRNA (26, 46) in RRL is stimulated by La. Therefore, poliovirus mRNA, despite its inefficient translation in RRL, could be expected to act as a competitive inhibitor of translation of TAR(+111)CAT mRNA. Equal amounts (0.4 μg) of TAR(+111)CAT and poliovirus mRNAs were translated together in RRL. Translation of TAR(+111) CAT was dramatically inhibited (greater than 11-fold; compare lanes 2 and 3 in Fig. 5) when translated together with poliovirus RNA. The synthesis of poliovirus capsid precursor protein P1 was only slightly inhibited by TAR(+111)CAT mRNA. In

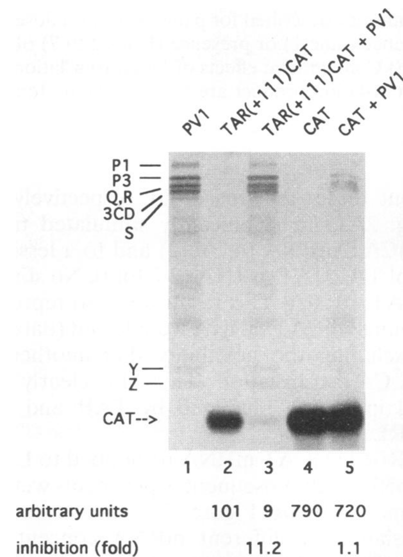

FIG. 5. Poliovirus RNA efficiently competes with TAR(+111)CAT but not CAT mRNA in RRL. Poliovirus type 1 Mahoney (PV1), TAR(+111)CAT, and CAT mRNAs were translated at a concentration of 0.4 μg either separately or together. Following translation, samples were processed, and the CAT product was quantified as described in Materials and Methods. The positions of CAT, poliovirus capsid precursor polypeptide P1, and the aberrant translation products, named as specified by Dorner et al. (10), are indicated on the left.

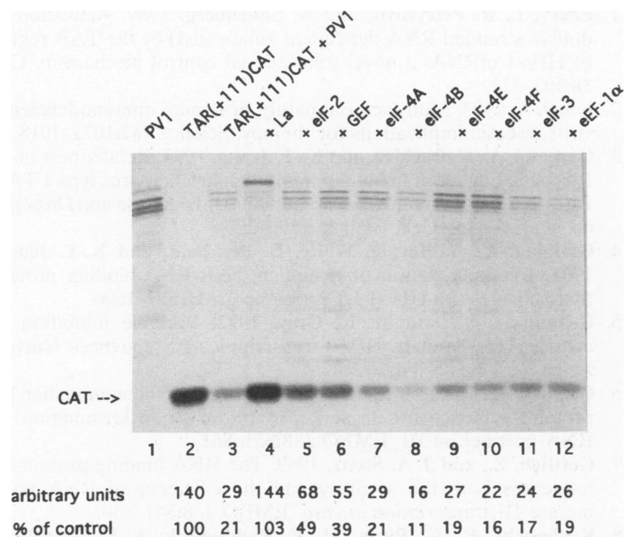

FIG. 6. Ability of different translation factors to relieve translation competition between TAR(+111)CAT and poliovirus mRNAs. Poliovirus type 1 (PV1) and TAR(+111)CAT) mRNAs were translated at concentrations of 0.2 and 0.4 μg, respectively, either separately (lanes 1 and 2) or together (lanes 3 to 13) in the absence (lane 3) or presence (lanes 4 to 13) of 1.5 μg of the translation factors indicated. Translation samples were processed, and the amount of CAT product was quantified as described in Materials and Methods.

contrast to this dramatic inhibition of translation of TAR(+111)CAT mRNA, no inhibition of translation of CAT mRNA by poliovirus RNA was observed. On the contrary, CAT mRNA markedly inhibited (about fivefold) the accumulation of correct and aberrant products of poliovirus. Also, poliovirus RNA failed to inhibit translation of poly(A)$^+$ RNA from mouse liver (data not shown).

To determine whether TAR(+111)CAT and poliovirus mRNAs compete for La binding in RRL, we assayed La as well as other factors for the ability to relieve the translation inhibition. Figure 6 shows that La, but no other factors, completely restored translation of TAR(+111)CAT RNA in the RRL. eIF-2 and GEF restored the translation to a much lesser degree.

DISCUSSION

The 5′ leader of HIV-1 mRNA is a potent down-regulator of translation (11, 15, 30, 39). In this report, we examined whether La autoantigen affects the translational repressor activity of the 5′ leader. The grounds for this work were provided by the findings that (i) La is a TAR RNA-binding protein (6) and (ii) the *cis*-inhibitory effect of the HIV-1 leader RNA is more pronounced in RRL than in HeLa cell extracts, in which La protein is abundant (30). Our results show that TAR(+111)CAT mRNA is a weak template in RRL and that translation is enhanced by La. The inhibitory effect and La response of TAR RNA were less prominent than those of TAR(+111) RNA, implying that both of the two stem-loop structures at the 5′ end of HIV-1 mRNA are required for maximal *cis* inhibition and La *trans* activation of translation. However, not every stem-loop structure that is capable of inhibiting translation when introduced in the 5′ UTRs (33, 34) confers La responsiveness to the mRNA. This is clearly demonstrated by the inability of La to stimulate the translation of the A3CAT mRNA, which possesses a stable hairpin upstream of the initiator AUG. This finding suggests that La recognizes some but not all double-stranded RNAs. This implication is consistent with the results of Chang et al. (6), who showed by direct binding that only specific secondary structures are recognized by La. The mechanism of stimulation of TAR(+111)CAT mRNA translation by La is not known but may involve melting of secondary structure at the 5′ end of the mRNA. La could perform such unwinding in cooperation with established helicases, such as eIF-4A, eIF-4B, and eIF-4F (27, 31, 32, 38). The ability to *trans* activate translation that is mediated by the HIV-1 leader RNA was also described for the viral Tat protein (39). However, we could not show any enhancement of TAR(+111)CAT mRNA translation by recombinant Tat protein in RRL, nor did Tat appear to synergize with La in stimulation of translation (45). The reasons for these discrepancies are not known. It is, however, possible that different preparations of RRL can respond differently to the addition of Tat. For example, it was demonstrated that different preparations of RRL vary considerably in the magnitude of the translational inhibition by the HIV-1 leader (15).

An array of cellular proteins bind to TAR RNA. These include p68 (23), TRP-1 (41), and TRP-185 (49), which bind to the loop of TAR RNA; TRP-2 (41), which binds to the bulge of TAR; and PKR (36), SBP (35), and TRBP (13, 14), which bind to double-stranded stem portions of TAR RNA. The interplay between the different TAR RNA-binding proteins and their function in HIV-1 replication is ill defined. One possibility is that La cooperates with some of these factors in activation of HIV-1 translation. In particular, the carboxy-terminal portion of La may be involved in protein-protein interactions relevant to *trans* activation, in view of the finding that the deletion of this part of the molecule renders La inactive in stimulation of TAR(+111)CAT mRNA translation (Fig. 3) without affecting its binding to TAR RNA (45). The significance of the carboxy-terminal half of La for its function in poliovirus translation has also been documented (46). On the other hand, some of the proteins can potentially compete with La for the binding with TAR RNA and interfere with La function in translation. For example, mutually exclusive binding of proteins to TAR RNA was described for TRP-1 and TRP-2 proteins (41).

The finding that La interacts with TAR RNA also in vivo (6) strongly supports the hypothesis of physiological significance of this protein in regulation of HIV-1 translation. La is predominantly a nuclear protein. However, in poliovirus-infected cells, La relocates from the nucleus to the cytoplasm in the course of infection (26). Similar findings were also reported for herpes simplex virus type 1 (2). How poliovirus infection affects the transport of La is not known. A similar mechanism might operate in HIV-1-infected cells. However, in the latter case, it is also possible that La binds to the TAR sequence of HIV-1 transcripts and is transported to the cytoplasm as a ribonucleoprotein. In this regard, it is intriguing that in *Xenopus* oocytes, translation of TAR-CAT requires a nuclear-specific activation (5). It should be of interest to determine if La is involved in this phenomenon.

The finding that certain viruses (HIV-1 and poliovirus) exploit a noncanonical initiation factor for their translation might provide new approaches for antiviral therapeutic intervention. Recent results show that a small yeast RNA with an extensive secondary structure is able to block poliovirus replication apparently by binding and sequestering La (7, 9). Similar mechanisms might operate in CEM SS cells overexpressing TAR-containing sequences (TAR decoys). Overexpression of TAR RNA renders cells resistant to HIV-1 replication (44). Our results (Fig. 5) show that poliovirus RNA competes more efficiently than

TAR(+111)CAT mRNA for a limiting factor in RRL, even when present at a five-times-lower molar concentration. The limiting factor in this translation was identified as La protein (Fig. 6). These results are compatible with the view that the poliovirus 5′ UTR has a higher affinity for La than TAR RNA. Gel shift and UV cross-linking experiments show that the RNA 522-631 fragment of poliovirus has an ~6-fold higher affinity for La than TAR RNA (45). It is not clear whether the conditions of translation which provide the competitive advantage to poliovirus over HIV-1 in RRL are met in intact cells, specifically in brain and lymphoid cells, which are the sites of replication of both HIV-1 and poliovirus (4, 12, 21, 42, 48). If this appears to be the case, then one could speculate that a mild poliovirus infection (such as that established after vaccination with attenuated poliovirus) will interfere with production and accumulation of HIV-1 in the brain and in lymphoid tissues of HIV-1-infected individuals.

Recently, La became implicated in several processes in the cell in addition to RNA polymerase III transcription termination. These include translation (references 26 and 46 and this report) and possibly splicing (29). An intriguing hypothesis is that La, which is considered a promiscuous RNA-binding protein, recognizes many different RNAs to serve as an RNA chaperone by facilitating the folding of higher-order structures that are optimal for activity (25). This activity could be analogous to the action of protein or DNA chaperones (28a). This activity would facilitate diverse processes involving RNA metabolism in the cell.

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