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Genetics

Regulation of ribosomal protein synthesis in *Escherichia coli* by selective mRNA inactivation

(gene dosage effect/dominance/λ*spc*2 transducing phages/mRNA turnover)

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ABSTRACT **In an *Escherichia coli* strain lysogenic for λ*spc*2 transducing phage, an extra copy of ribosomal protein (r-protein) genes in the *spc* and α operons are carried on the phage chromosome. Expression of genes in the *spc* operon in this merodiploid strain was compared with that in a control "haploid" strain carrying λ*trkA* phage. It was found that the synthesis rate of *spc* mRNA, relative to other reference mRNA in the merodiploid strain, is about 2-fold higher than that in the control strain; yet, no dosage effect was observed in the synthesis rate of r-proteins in the *spc* or α operon. The *spc* mRNA was found to be more rapidly degraded in the merodiploid strain than in the control strain, and its steady-state amount, relative to reference mRNA, was only slightly higher in the merodiploid strain than in the control strain. Thus, *E. coli* cells have the ability to regulate the rate of r-protein synthesis regardless of the rate of transcription of r-protein genes, presumably by inactivation of the mRNA followed by its degradation. A model is proposed which involves selective inactivation of r-protein mRNA by a feedback mechanism. The model can explain coordinated synthesis of r-proteins and other observations related to selective expression of certain alleles in diploid strains.**

Ribosomes from *Escherichia coli* contain approximately 50 proteins. All of these proteins, with the exception of L7/L12, exist in a single copy per ribosome. In exponentially growing cells, there appears to be neither a significant pool of free ribosomal proteins (r-proteins) nor significant degradation of newly synthesized r-proteins. Therefore, all the r-proteins are apparently synthesized coordinately and stoichiometrically (for a review, see ref. 1). How this remarkable regulation is achieved is not known.

In this paper, we report the results of experiments that show that *E. coli* cells have the ability to regulate the rate of r-protein synthesis regardless of the rate of transcription of r-protein genes. We then describe a new model which involves selective inactivation of r-protein mRNA by a feedback mechanism and discuss various available experimental observations.

EXPERIMENTAL PROCEDURES

Two *E. coli* K-12 strains were used. Both are lysogenic derivatives of strain NO1230 (*trkA*401, *kdpABC*5, *spc*^{r}, *str*^{r}, *fus*^{r}). One (NO1275) carries λ*trkA* transducing phage and λ*cI*857*S*7 helper phage. The other (NO1328) carries λ*spc*2 transducing phage and the same helper phage. These strains and phages have been described (2, 3). All other experimental procedures are described in the figure and table legends.

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RESULTS

We initially asked whether an increase in the number of gene copies leads to an increase in the synthesis rate of corresponding r-proteins or if *E. coli* cells have the ability to regulate the synthesis rate regardless of gene copy numbers. The λ*spc*2 transducing phage carries 14 r-protein genes together with their promoters and 9 additional r-protein genes without their bacterial promoters (3, 4). The former 14 genes are organized into two operons ("*spc* operon" and "α operon"), and the latter 9 genes comprise a distal part of an operon called the "S10 operon" (3, 4) (Fig. 1). We used a λ*spc*2 lysogen (NO1328) as a strain that carries an extra copy of the genes in the *spc* and α operons and a λ*trkA* lysogen (NO1275) as a control strain. λ*trkA* carries a chromosomal segment adjacent to the α operon but does not carry r-protein genes (Fig. 1). Both strains showed identical growth rates as well as ribosome contents under the conditions used in the present experiments (data not shown).

Synthesis rates of individual r-proteins were analyzed by labeling exponentially growing cells with [^{3}H]leucine for 1 min followed by a chase with nonradioactive leucine for 1 or 30 min. Synthesis rates of r-proteins were normalized to the synthesis rate of L1, the gene for which is not carried by λ*spc*2, and these normalized values for the λ*spc*2 lysogen and the control strain were compared (for details, see the legend to Table 1). There was no increase in the synthesis rate of r-proteins coded for by the λ*spc*2 genome relative to r-proteins which are not coded for by this phage (Table 1). We conclude that there are no gene dosage effects on the synthesis rate of r-proteins. Similar experiments were done by Geyl and Böck (8) using a strain carrying the F'141 plasmid, and the same conclusion was drawn.

We then asked whether the absence of gene dosage effects in r-protein synthesis is due to the absence of gene dosage effects on the transcription rate of the genes in question. This was examined by measuring the rate of mRNA synthesis using the same λ*spc*2 lysogen and control strain. Cells were pulse-labeled with [^{3}H]uridine for 0.5–3 min, and the relative amounts of radioactive RNA (called "*spc* mRNA") hybridizing to the 10% *Eco*RI fragment of λ*spc*2 DNA (see Fig. 1) were analyzed as described in the legend to Table 2. Because the efficiency of RNA·DNA hybridization varies depending on the conditions, we used ^{32}P-labeled reference RNAs as internal controls to correct any variations in the efficiency of hybridization. In addition, we also measured, in the same hybridization reaction mixtures, the amount of mRNA corresponding to the *Eco*RI 4.4L fragment of λ*rif*^{d}18 or of mRNA corresponding to the DNA segment carried by hybrid plasmid pNO1003 (cf. Fig. 1). These control mRNAs correspond to r-protein mRNA or r-protein mRNA plus *rpoB* mRNA coming from the *rif* region (88 min) which is far away from the *spc* region (72 min) on the

Abbreviations: r-proteins, ribosomal proteins.

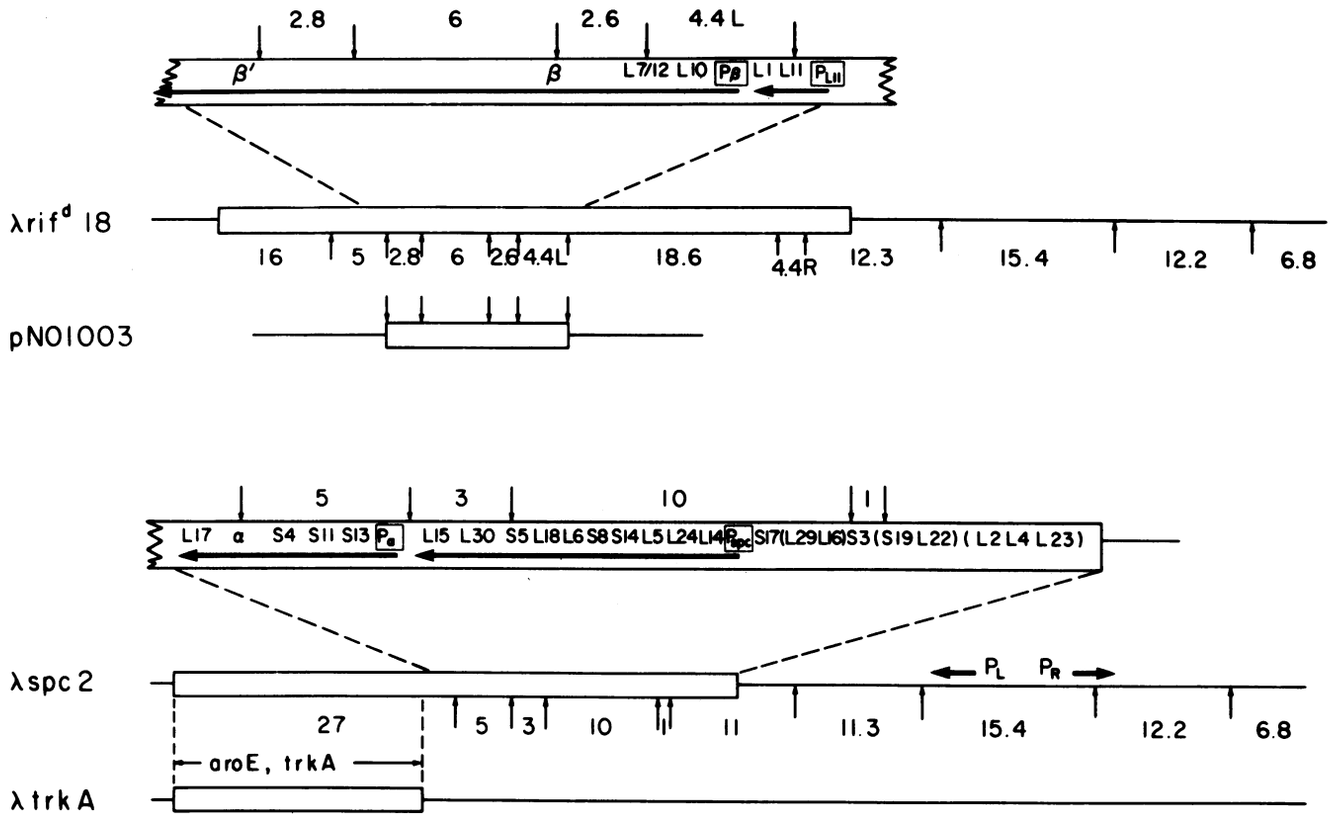

FIG. 1. Genes for r-proteins and RNA polymerase subunits carried by λ*spc*2, λ*rif*^{d}18, and pNO1003. The locations of bacterial genes and their promoters and *Eco*RI cleavage sites are shown (cf. refs. 1, 3, and 4). Approximate sizes of *Eco*RI fragments are indicated in %-λ units (1 %-λ unit is 465 base pairs). Two 4.4% fragments are called 4.4L and 4.4R, as indicated. The thin lines represent λ DNA or plasmid vector DNA; the open area represents the bacterial DNA carried by the phage or the plasmid. The circular pNO1003 plasmid molecule is arbitrarily shown in a linear form. The direction of transcription in pertinent operons is indicated by horizontal arrows.

E. coli chromosome. The genes in the *rif* region are present only in a single copy per chromosome in both the λ*spc*2 lysogen and the control strain. Thus, the ratio of *spc* mRNA to these control mRNAs is a measure of gene dosage effects on the transcription rates in the λ*spc*2 lysogen. This ratio was about 2-fold higher in the λ*spc*2 lysogen (NO1328) than in the control strain (NO1275) (Table 2); that is, a clear gene dosage effect was detected in the rate of transcription of r-protein genes in the *spc* operon.

We then measured the *amounts* of *spc* mRNA in the λ*spc*2 lysogen relative to the control strain. Cells were grown in the presence of an excess of [^{3}H]uracil for several generations, and relative amounts of ^{3}H-labeled *spc* mRNA in the λ*spc*2 lysogen and the control strain were compared. The values were only slightly (about 20%) higher in the λ*spc*2 lysogen than in the control strain (Table 3).

Because measurements of both the *rates* and the *amounts* of *spc* mRNA were done under similar conditions, the above results indicate that the presence of extra gene copies increases the synthesis rate of mRNA but that the decay rate is also increased in the λ*spc*2 lysogen. To confirm this, [^{3}H]uridine pulse-labeling experiments were repeated, samples were taken at various times after the [^{3}H]uridine addition, and the relative amounts of ^{3}H-labeled *spc* mRNA were analyzed in the same way as described above. As noted in the legend to Fig. 2, most of [^{3}H]uridine was incorporated into RNA within a few minutes under the experimental conditions used, and, therefore, unstable RNA was soon replaced by nonradioactive RNA synthesized from endogenous precursor substrates. Results of four experiments are shown in Fig. 2. Nearly 2-fold overproduction of radioactive *spc* mRNA in the λ*spc*2 lysogen, relative to the control strain, was seen only shortly after the [^{3}H]uridine addition. The degree of relative overproduction decreased with time, reaching in 10 min values which were only slightly higher than unity.

DISCUSSION

We have demonstrated that the synthesis of r-proteins (at least 14 r-proteins in the *spc* and α operons) is regulated such that a 2-fold increase in the gene copy numbers (see note in the legend to Table 2) does not affect the synthesis rate. However, contrary to previous speculations (8, 10), this regulation does not appear to take place at the level of transcription but appears to involve selective inactivation of mRNA, presumably by nucleolytic cleavages followed by rapid degradation. In merodiploid strains (a λ*spc*2 lysogen in this study), the synthesis rate of mRNA appears to be gene-dosage dependent, and yet, the *amount* of functional r-protein mRNAs is independent of the gene dosage. Apparently, *E. coli* cells have the ability to detect the presence of an excess amount of mRNA and then inactivate the excess mRNA, leaving only a "correct" amount of functional mRNA for each r-protein and thereby ensuring a balanced synthesis rate of individual r-proteins.

In other studies (6), we have examined the effects of larger gene dosages on the synthesis of r-proteins and r-protein mRNAs by using a strain carrying a hybrid plasmid containing a cloned *Eco*RI 10% fragment from the *spc* region. Although a definite overproduction of two promoter-proximal proteins was observed, only a weak or insignificant increase was observed in the synthesis of the remaining promoter-distal proteins, even though the genes for these proteins existed in about 15 copies per haploid chromosome. Again, the rate of synthesis

Table 1. Relative synthesis rates of r-proteins in λ*spc*2 lysogenic cells

Class	Protein	Relative synthesis rate 1-min chase	Relative synthesis rate 30-min chase
A	L1	1.00	1.00
	L3	0.93	1.10
	L10	0.96	1.00
	L13	0.96	1.01
	L25	0.90	1.02
	S7	0.91	1.07
B	L2	0.88	1.06
	L4	0.96	1.07
	L23	0.86	0.96
	S19	1.01	1.10
	L22	0.94	0.99
	S3	0.86	0.97
	L29	0.90	1.01
	L16	0.82	1.07
C	L14	0.88	1.10
	L24	0.93	1.11
	L5	0.97	1.15
	S14	0.90	1.17
	S8	1.00	0.91
	L18	0.97	1.18
	L30	1.04	1.11
	L15	1.03	1.15
D	S13	1.08	0.94
	S4	0.92	1.10
	L17	0.98	1.11

Cells were grown at 30°C in AB medium (5) supplemented with thiamine (1 μg/ml) and glucose (0.4%). Both the experimental strain (NO1328) and the control strain (NO1275) had a doubling time of 85 min under these conditions. At a cell density of 50 Klett units, [^{3}H]-leucine (540 pmol/ml; 55 Ci/mmol; 1 Ci = 3.7×10^{10} becquerels) was added. After 1 min of labeling, the [^{3}H]leucine was chased with an excess of nonradioactive leucine (0.5 mg/ml). At 1 and 30 min after the chase, 10-ml samples were rapidly chilled on ice and centrifuged. [^{3}H]Leucine-labeled cells were then mixed with an appropriate amount of [^{14}C]leucine-labeled carrier cells (NO1275). The cells were pelleted and disrupted as described (6). Unlabeled 70S ribosomes (100 A_{260} units) were added, and r-proteins were extracted and separated by two-dimensional gel electrophoresis (7). After the gels were stained, relevant protein spots were cut out, dried, and oxidized in a Packard sample oxidizer. The amounts of ^{3}H and ^{14}C were determined separately. The relative synthesis rate of each r-protein was calculated by the formula: (^{3}H/^{14}C in protein *i* in experimental cells) ÷ (^{3}H/^{14}C in protein *i* in control cells). The ratio obtained for each protein was normalized to the ratio obtained for protein L1. In the table, the proteins are divided into four classes. Genes for class A proteins are not carried by λ*spc*2; genes for class B proteins are carried by λ*spc*2 but do not have their bacterial promoter (P_{S10}); genes for class C proteins are carried by λ*spc*2 and are transcribed in the order listed from the *spc* promoter; and genes for class D proteins are carried by λ*spc*2 and are transcribed from the α promoter (see refs. 1, 3, and 4).

of mRNA for these distal proteins was 10- to 20-fold higher than that of the control strain, and the overproduced mRNA appeared to be rapidly inactivated, presumably by nucleolytic cleavages followed by degradation. These results in general are consistent with the conclusion obtained in the present study—that is, r-protein synthesis can be regulated by selective inactivation of mRNA.

How can cells detect overproduction of certain r-protein mRNAs and inactivate (and degrade) these "excess" mRNAs, leaving a correct amount of the mRNA intact? How can cells increase the decay rate of only one kind of r-protein mRNA (the one being overproduced) without increasing the decay rate of

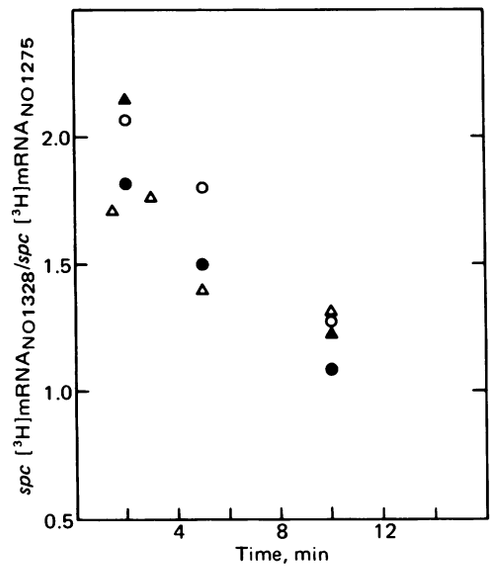

FIG. 2. Relative overproduction of *spc* mRNA in λ*spc*2 lysogenic cells. Experiments were performed as described in the legend to Table 2, except that samples for [^{3}H]RNA analysis were taken at various times after [^{3}H]uridine addition as indicated. Calculations were made as described in Table 2, and the values corresponding to those in the last column of Table 2 are shown to indicate relative amounts of ^{3}H-labeled *spc* mRNA. Results of four different experiments are shown, each represented by different symbols. In one experiment (△), the amounts of *spc* mRNA were first normalized to the amounts of mRNA corresponding to bacterial DNA carried by pNO1003; in other experiments, normalization was to the amount of mRNA corresponding to 4.4L *Eco*RI DNA. It should be noted that about 50% of added [^{3}H]uridine was incorporated into RNA in 2–3 min and the incorporation was practically complete in 6–8 min under the conditions used.

other r-protein mRNAs? One model to explain our observations is a feedback mechanism for this inactivation (and degradation). The model assumes that r-proteins synthesized can recognize their own mRNA and cause inactivation of their own mRNA. As long as the assembly of ribosomes removes r-proteins, the corresponding mRNA escapes from the inactivation and continues to direct synthesis of r-protein.

The proposed model explains the observed balanced r-protein synthesis in merodiploid cells and may also be used to explain the coordinated r-protein synthesis in normal (haploid) cells. However, the model is not concerned with questions such as what determines the normal decay rate of r-protein mRNA or whether there are additional degradation mechanisms for the "normal" mRNA decay. In addition, the model certainly does not exclude the presence of transcriptional regulation in response to other kinds of signals. We also note that there are reports of the presence of gene dosage effects in the synthesis of S20, S21, and L21 which map outside the *str-spc* region (8, 11). The significance of these observations is not clear.

The proposed model could be used to explain several observations concerning dominance and recessiveness in gene expression. It is known that the *str*^{s} allele is dominant over the *str*^{r} allele in merodiploid cells. Flaks and his coworkers (12) have reported that, in such diploid cells, regardless of the location of *str*^{s} allele, more than 90% of the ribosomes contained the *str*^{s} gene product S12. Combined with the conclusions obtained in the present study, we conclude that in these merodiploid cells the synthesis of S12 takes place almost exclusively from mRNA transcribed from the *str*^{s} gene. Flaks and his coworkers showed that wild-type S12 is preferentially used in *in vitro* reconsti-

Table 2. Synthesis rate of *spc* mRNA in λ*spc*2 lysogen (NO1328) relative to λ*trkA* lysogen (NO1275)

Exp.	Strains, (total input RNA, cpm)	DNA for hybridization	[^{3}H]RNA hybridized: Obs. cpm	Obs. − control	Corrected cpm (% input)	*spc* mRNA normalized	Relative *spc* mRNA synthesis rate*
1	NO1275	Calf thymus	187				
	(2.10×10^6)	4.4L *Eco*RI	2,385	2,198	1,725 (0.082)	(1.0)	
		10% *Eco*RI	4,836	4,649	4,246 (0.22)	2.46	(1.0)
	NO1328	Calf thymus	141				
	(1.55×10^6)	4.4L *Eco*RI	1,186	1,045	1,083 (0.070)	(1.0)	
		10% *Eco*RI	5,462	5,321	4,933 (0.32)	4.56	1.85
2	NO1275	Calf thymus	375				
	(4.06×10^6)	pNO1003	13,345	12,979	12,877 (0.32)	(1.0)	
		10% *Eco*RI	7,633	7,293	7,312 (0.18)	0.57	(1.0)
	NO1328	Calf thymus	498				
	(3.37×10^6)	pNO1003	14,286	13,808	12,609 (0.37)	(1.0)	
		10% *Eco*RI	12,339	11,861	12,426 (0.37)	0.99	1.74

Cells were grown at 30°C in AB medium supplemented with thiamine (1 μg/ml), glucose (0.4%), and Casamino acids (0.2%). At 40 Klett units, cells were labeled with [^{3}H]uridine (41 mCi/μmol; 50 μCi/ml) for 2 min (Exp. 1) or 3 min (Exp. 2). Samples (3 ml) were removed, mixed with the lysis solution containing sodium dodecyl sulfate, heated, and treated with phenol as described (6). RNA was recovered by alcohol precipitation and dissolved in 1 ml of 0.3 M NaCl/0.03 M sodium citrate, pH 7.0 (6). [^{3}H]RNA samples were mixed with reference [^{32}P]RNAs (one made *in vitro* with 10% *Eco*RI DNA as template and the other made with 4.4L *Eco*RI DNA as template) and then hybridized to various DNAs (6, 9). For each [^{3}H]RNA sample, two different amounts were used. The values of [^{3}H]RNA hybridized to 10% *Eco*RI DNA (or reference DNAs) after correction for differences in hybridization efficiency (see below) were proportional to the amounts of samples used. The values obtained with 0.2-ml samples are given. Corrections for small differences in hybridization efficiency among different reaction mixtures were made by comparing the amount of [^{32}P]RNA hybridized to a specific DNA filter with the average of all the corresponding ^{32}P values (6). No corrections were made for absolute efficiencies of hybridization (which was estimated to be about 10–20% and varied depending on kinds of DNA fixed to filters). The *spc* mRNA is defined as the mRNA hybridized to the 10% *Eco*RI DNA fragment (see Fig. 1). The amounts of the *spc* mRNA were normalized by dividing the observed values by the amounts of [^{3}H]RNA hybridized to purified 4.4L DNA in Exp. 1. In Exp. 2, pNO1003 DNA was used instead of 4.4L DNA. These normalized values were then used to calculate the relative *spc* mRNA synthesis rate. It should be noted that only about 70% of the 10% *Eco*RI DNA segment corresponds to the functioning (*spc* operon) genes, and, therefore, if the λ*spc*2 genome is present in one copy per haploid chromosome, the theoretical maximal value for the gene dosage effect, measured in the way described above, would be about 1.7. Furthermore, the *spc* operon on the chromosome is closer to the origin of replication than the *att*λ site, where λ*spc*2 is probably located. Therefore, the expected gene dosage effect in the lysogen may be even less than 1.7. We have not studied the reason why the observed values are higher than 1.7. It is possible, for example, that the λ*spc*2 genome is present in multiple copies per haploid chromosome.

* (*spc* mRNA normalized in NO1328)/(*spc* mRNA normalized in NO1275).

tution with a mixture of proteins containing both the wild type and the mutant (*str*^{r}) S12. According to our model, inactivation of *str*^{r} mRNA would take place, because its translational product fails to compete in the assembly reaction. Thus, the postulated inactivation of mRNA by r-proteins will take place only (or mainly) in *cis* and not in *trans*.

What are the biochemical mechanisms involved in the postulated mRNA inactivation? Our speculation is that some specific nuclease(s) is involved that uses r-protein–mRNA complexes, but not free mRNA, as substrates. There is a precedent for such a hypothetical nuclease. It is known that colicin E3 cleaves various bacterial 16S rRNAs present in 70S ribosomes but fails to cleave these 16S rRNAs in a free state (13–15). Regarding the *cis*-acting mRNA inactivation discussed above, we imagine that newly synthesized r-proteins stay with their mRNA for most of the time before their incorporation into ribosomes, and that it is these r-protein–mRNA complexes (or r-protein–mRNA–ribosome complexes) that are the substrate of the nuclease. Because most of the r-proteins are basic proteins, formation of such complexes at the site of r-protein syn-

Table 3. Relative amounts of *spc* mRNA in λ*spc*2 lysogenic cells during steady-state growth

Strains (total input RNA, cpm)	DNA for hybridization	[^{3}H]RNA hybridized: Obs. cpm	Obs. − control	Corrected cpm	*spc* mRNA normalized	Relative amounts of *spc* mRNA*
NO1275	Calf thymus	417				
(1.64×10^7)	4.4L *Eco*RI	1118	701	730	(1.0)	
	10% *Eco*RI	3946	3529	3369	4.62	(1.0)
NO1328	Calf thymus	428				
(1.86×10^7)	4.4L *Eco*RI	1329	901	889	(1.0)	
	10% *Eco*RI	4785	4357	4575	5.15	1.11

Cells were grown at 30°C in the same medium as used for pulse experiments (see Table 2) except that [^{3}H]uracil (10 μg/ml; 100 μCi/ml) was present for at least three generations before samples (10 ml) were taken at 40 Klett units. The amounts of ^{3}H-labeled *spc* mRNA were analyzed as described in the legend to Table 2. Similar experiments were done six more times. The following values were observed as relative amounts of *spc* mRNA: 1.00, 1.23, 1.20, 1.36, 1.24, and 1.34. Thus, the mean of seven measurements is 1.21.

* (*spc* mRNA normalized in NO1328)/(*spc* mRNA normalized in NO1275).

thesis would be easy to imagine. Thus, the *cis*-acting mRNA inactivation could be explained.

In the above discussion, we have assumed that the unit of r-protein mRNA inactivation is an individual cistron, rather than a polycistronic mRNA corresponding to an operon. In some cases, it might be a group of cistrons, and a complex of some or all of the translational products from these cistrons could act as a feedback regulator. In preliminary experiments (unpublished), we have found that a lysogen carrying a hybrid λ phage with a cloned *Eco*RI 10% fragment from the *spc* operon synthesizes proteins (from L14 to L18 in Fig. 1) coded for by the diploid segment of the *spc* operon and those (L30 and L15) coded for by the haploid segment in approximately equal molar ratios as in nonlysogens. In addition, when the hybrid phage carried the wild-type L24 allele (*rplX*$^+$) and the chromosome carried a mutant-type L24 allele (*rplX*165; cf. ref. 6), the wild-type L24 was preferentially synthesized. This implies that the mutant L24 gene on the chromosome is rarely or only weakly used to make the protein, whereas the distal chromosomal genes (for L30 and L15) are fully active in making the proteins, even though all of these genes belong to the same operon. Such experimental results are difficult to reconcile with regulatory mechanisms based solely on regulation at the level of transcription, while they can be easily explained by the model proposed here. In addition, these results support the assumption made in the model that the unit of inactivation of mRNA is an individual cistron, or a group of cistrons, and not polycistronic mRNA corresponding to an entire operon. In this connection, it should be noted that our previous experiments have shown cotranscription of many r-protein genes (and other related genes) and defined various operons (refs. 1, 3, and 4; cf. Fig. 1). However, these genetic experiments do not necessarily imply the presence of one polycistronic mRNA coming from one transcription unit.

Genes for r-proteins are organized into several operons (as many as 10 or more; see refs. 1 and 16 for reviews). DNA sequences for promoters for some of these operons have been determined (17, 18), but no obvious common structure has been discovered that could be used to explain coordinated regulation. According to the present model, strict coordination of transcription of these operons is not needed to achieve the coordinated synthesis of r-proteins. In addition, the model can explain, in principle, regulation of the synthesis rate of proteins present in multiple copies in the ribosomes (or in any other supramolecular structures; see below) in accordance with the copy numbers needed for the assembly. For example, protein L7/L12 is present in four copies per ribosome (19, 20). It is known (21, 22) that the gene for L7/L12 is in the same operon as the gene for L10 which is present in a single copy per ribosome and that the synthesis rates of L10 and L7/L12 also appear to be 1:4 in molar ratio (cf. ref. 23). The present model can explain the stoichiometric relationship in the synthesis rates and thus provides an alternative to the hypothesis of different efficiencies of translational initiation of these two genes.

Regulation of protein synthesis by selective mRNA inactivation might also be used in other systems, especially in the synthesis of proteins that are components of multisubunit enzymes or supramolecular structures. For example, apparent autogenous regulation of RNA polymerase β and β′ subunit synthesis (for a review, see ref. 24) could be explained by a mechanism similar to the one discussed above. In fact, some of the published results are difficult to explain in terms of transcriptional regulation. The data published by Glass (25) (see also ref. 26) indicate that in a diploid strain carrying the wild-type *rpoB* gene on a F′ plasmid and a suppressed amber mutant allele (*rpoB*12) on the chromosome the synthesis of β is mainly from the operon carried by the F′ plasmid, even though the synthesis of β from the chromosomal operon takes place at the normal rate in the absence of F′ plasmid. Because the promoters for both of the *rpoB* genes in the diploid are presumably identical, preferential expression of one allele over the other must involve a posttranscriptional mechanism similar to that discussed above. Such possibilities have not been considered previously.

In conclusion, we have demonstrated the presence of a posttranscriptional regulation in the coordinated synthesis of r-proteins. Various experimental results, including the present ones, can be explained by the model which involves selective mRNA inactivation by a feedback mechanism. Further experiments will be able to test the generality as well as the validity of this proposed model.

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