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The genes for yeast ribosomal proteins S24 and L46 are adjacent and divergently transcribed

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ABSTRACT
        Unlike most yeast ribosomal protein genes studied so far the genes
coding for S24 and L46 are adjacent on the genome. Sequence analysis showed
that the two genes are transcribed divergently, their initiation codons being
630 bp apart. Taking the respective ATG translation start sites as reference
points, the 5'- end of L46 mRNA was mapped at position -26, while the S24 mRNA
showed two major 5'-ends mapping at positions -13 and -16 respectively. Unlike
most other yeast ribosomal protein genes, the gene for S24 does not contain an
intron. Its coding region encompasses 390 nucleotides encoding a protein of
14762 D. The gene for L46 on the other hand is split by an intron of 386
nucleotides starting after its second codon. This gene encodes a small, very
basic protein having a molecular weight of 6334 D. Yeast ribosomal proteins
S24 and L46 show striking homologies with ribosomal proteins from other
organisms. In particular, yeast L46 is clearly the evolutionary counterpart
of rat liver L39. A search of the intergenic region for sequence elements
previously identified as common to most yeast ribosomal protein genes, reveal-
ed the presence of a single conserved box (RPG-box) roughly equidistant from
the transcription initiation sites of both genes. We suggest that this box
acts as a regulatory signal in either orientation and thus influences the
expression of both genes simultaneously.

INTRODUCTION

        With the aim to elucidate the molecular mechanisms underlying the

coordinate regulation of ribosomal protein gene expression in yeast we have

characterized several cloned yeast ribosomal protein genes (1-6). It turned

out that most ribosomal protein genes share some general characteristics:

they are not clustered, occur duplicated on the yeast genome and contain an

intron near their 5'-end. In some cases two different ribosomal protein genes

appear to be physically linked. For instance the split genes encoding S16A and

rp28 are separated by only 600 bp and are transcribed in the same direction

(5). In this paper we describe a second pair of linked yeast ribosomal

protein genes. The split gene coding for L46 and the unsplit gene coding for

S24 were found to be located adjacent to each other in a head-to-head arrange-

ment. The intergenic region consists of about 600 bp and must contain the

signals controlling the expression of both genes.

MATERIALS AND METHODS

DNA preparation and sequence analysis

Plasmid pBMCY135 containing the genes coding for S24 and L46 was purified as described previously (2). Restriction enzyme digestions were performed as recommended by the suppliers (New England Laboratories; Boehringer Mannheim). Appropriate DNA fragments were subcloned in M13 mp8 or mp9, and sequence analysis was carried out according to the dideoxy chain termination method (7).

Primer extended sequence analysis of mRNA

RNA sequencing using reverse transcriptase was performed as described elsewhere (4). The primer for the S24 gene was labelled by repair synthesis of the subcloned BglII-BglII fragment in M13 mp8. Subsequent digestion of the labelled fragment with Sau3A yielded a 162 nucleotides long primer (see Fig. 1). The primer for mapping the 5'-end of the L46-transcript was a 55 nucleotide fragment obtained by digestion with Sau3A plus HinfI of cDNA synthesized using the subcloned HaeIII-HaeIII fragment in M13 mp8 (see Fig. 1) (9).

RESULTS AND DISCUSSION

a. Structure of the genes for yeast ribosomal proteins S24 and L46

From a colony bank of HindIII-generated yeast DNA fragments in pBR322 several recombinants containing yeast ribosomal protein genes have been isolated (2). Hybrid-selected in vitro translation followed by two-dimensional gel electrophoresis revealed that recombinant plasmid pBMCY135 carries at least the genes encoding yeast ribosomal proteins S24 and L46 (9). The pertinent physical map is presented in Fig. 1A. Electron microscopic R-loop analysis, successfully used in locating a number of ribosomal protein genes on cloned DNA fragments (9), in this case led to only a rough estimate of the position of the two genes, because of the complexity of the R-loop structures observed (9). However, on the basis of the known N-terminal amino acid sequence of ribosomal protein S24 (which is identical to YS22 – [10]) as well as the preferent codon usage observed within yeast ribosomal protein genes (2), we could predict a BglII site at the very 5'-end of the S24 coding sequence. Starting from these assumptions the sequencing strategy for both ribosomal protein genes as outlined in (the legend to) Fig. 1B was developed. The results of the nucleotide analysis are shown in Fig. 2. The gene coding
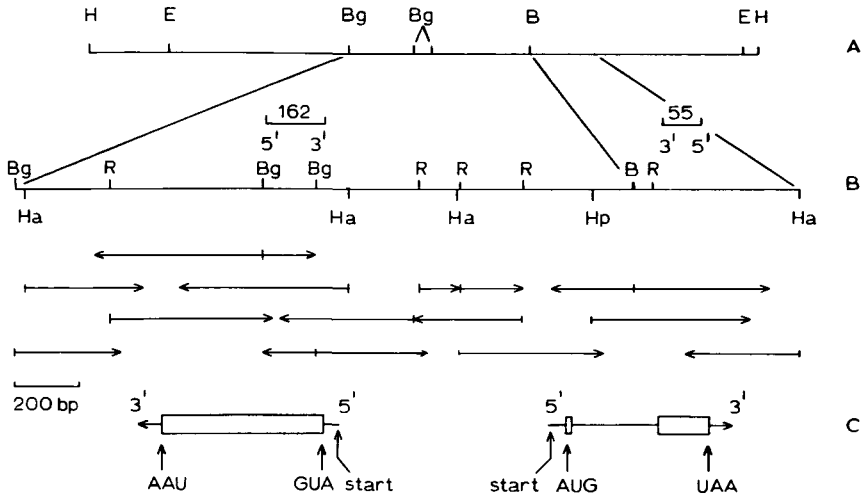
Fig. 1. Map of the insert of pBMCY135 and structural analysis of the genes coding for S24 and L46.
The position of some restriction enzyme sites indicated in A was published previously (9). H = HindIII, E = EcoRI, Bg = BglII, B = BamHI, Hp = HpaI, Ha = HaeIII, R = RsaI.
In B the sequence strategy is shown. The arrows give the extent of nucleotide analysis. The 162 and 55 nucleotides long primers used for the cDNA synthesis are indicated.
In C the structures of the S24 and L46 transcripts are given.

for S24 contains an uninterrupted reading frame of 390 nucleotides, whereas the coding region of the L46 gene comprises 153 nucleotides which is interrupted after the second codon by an intervening sequence of 386 nucleotides. In contrast to the clustered rp28 and S16A genes which are transcribed in the same direction (5), the transcription of the genes for S24 and L46 is divergent. Their translation initiation sites are 630 bp apart. Southern analysis suggested that the L46 gene is unique whereas the S24 gene may be duplicated on the yeast genome (result not shown; [11]).

b. Mapping of the 5'-ends of the mRNAs

The cap sites of both the L46 and S24 gene were determined by primer-extended cDNA synthesis. Using a Sau3A-Sau3A primer fragment for reverse transcription (see Fig. 1) two major 5'-ends of the S24 mRNA were mapped at position -13 and -16. In addition to these major transcription start sites a minor site at -22 was observed (see Fig. 3A). Heterogeneous 5'-ends have also been observed for several other yeast ribosomal protein mRNAs (e.g. Ref. 3). Mapping of the 5'-end of the L46 transcript, by use of a Hinf1-Sau3A primer fragment (Fig. 1), revealed a dominant transcription start site located at

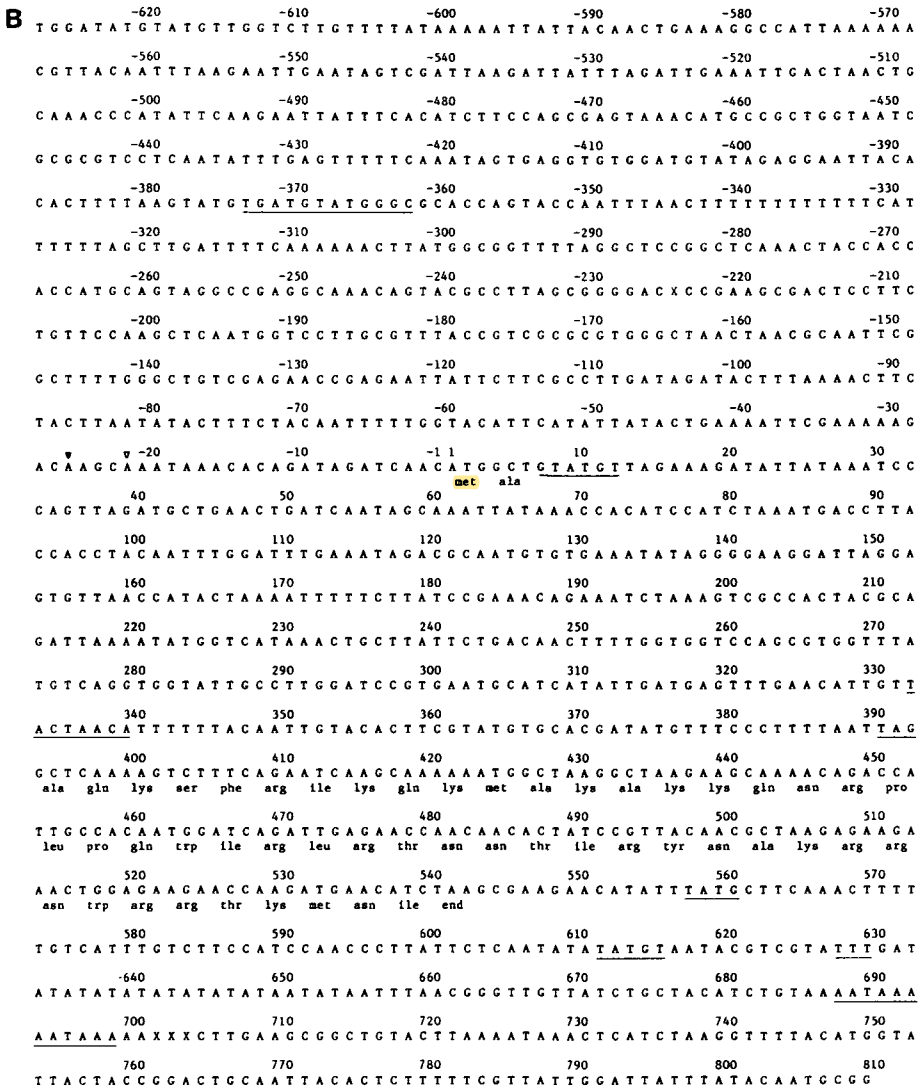26 nucleotides upstream from the translation start codon. A weak primer extended product was found at -22 nucleotides (see Fig. 3B). In this case the mRNA sequence determination also provided definite proof for the presence of an intron within the L46 gene. The nucleotide structure of the transcription initiation regions is in good agreement with the structure of other cap sites previously found for other yeast ribosomal protein genes (3).

A

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       -630          -620          -610          -600          -590          -580
     GTTGATCTATCTGTGTTTATTTGCTTGTCTTTTTCGAATTTTCAGTATAAATATGAATGTA

       -570          -560          -550          -540          -530          -520
     CCAAAAATTGTAGAAAGTATATTAAGTAGAAGTTTTAAAGTATCTATCAAGGCGAAGAAT

       -510          -500          -490          -480          -470          -460
     AATTCTCGGTTCTCGACAGCCCCAAAAGCCGAATTGCGTTAGITAGCCCACGCGCGACGGT

       -450          -440          -430          -420          -410          -400
     AAACGCAAGGACCATTGAGCCTTGGAACAGAAGGAGTCGCTTCGGGGTCCCCGCTAAGGCG

       -390          -380          -370          -360          -350          -340
     TACTGTTTGCCTCGGCCTACTGCATGGTGGTGGTAGTTTGAGCCGGAGCCTAAAACCGCC

       -330          -320          -310          -300          -290          -280
     ATAAGTTTTTTGAAAATCAAGCTAAAAAATGAAAAAAAAAAAAAGTTAAATTGGTACTGGT

       -270          -260          -250          -240          -230          -220
     GCGCCCATACATCACATACTTAAAAGTGTGTAATTCCTCTATACATCCACACCTCACTAT

       -210          -200          -190          -180          -170          -160
     TTGAAAAACTCAAATATTGAGGACGCGCGATTACCAGCGCGCCATGTTTACTCGCTGGAAGA

       -150          -140          -130          -120          -110          -100
     TGTGAAATAATTCTTGAATATGGGTTTGCAGTTAGTCAATTTCAATCTAAATAATCTTAA

        -90           -80           -70           -60           -50           -40
     TCGACTATTCAATTCTTAAATTGTAACGTTTTTTAATGGCCTTTCAGTTGTAATAATTTT

        -30        ▽ -20       ▼      ▼ -10          -1 1          10           20           30
     TATAAAACAAGACCAACATACATATCCAAGATGACCAGATCTTCCGTTTTAGCTGATGCT
                                          met thr arg ser ser val leu ala asp ala

                     40            50            60            70            80            90
     TTGAATGCCATTAACAACGCTGAAAAGACCGGTAAGCGTCAAGTTTTAATCAGACCATCC
     leu asn ala ile asn asn ala glu lys thr gly lys arg gln val leu ile arg pro ser

                    100           110           120           130           140          150
     TCCAAGGTCATTATCAAGTTTTTTGCAAGTTATGCAAAAGCACGGTTACATTGGTGAATTT
     ser lys val ile ile lys phe leu gln val met gln lys his gly tyr ile gly glu phe

                    160           170           180           190           200          210
     GAATACATCGATGACCACAGATCTGGTAAGATTGTTGTTCAATTGAACGGTAGATTGAAC
     glu tyr ile asp asp his arg ser gly lys ile val val gln leu asn gly arg leu asn

                    220           230           240           250           260          270
     AAGTGTGGTGTTATTTCCCCAAGATTTAACGTTAAGATTGGTGACATTGAAAAATGGACT
     lys cys gly val ile ser pro arg phe asn val lys ile gly asp ile glu lys trp thr

                    280           290           300           310           320          330
     GCCAACTTGTTGCCAGCCAGACAATTCGGTTACGTCATCTTGACCACCTCTGCTGGTATC
     ala asn leu leu pro ala arg gln phe gly tyr val ile leu thr thr ser ala gly ile

                    340           350           360           370           380          390
     ATGGACCATGAAGAAGCCAGA AGAAAGCATGTTTCTGGTAAGA TTTTGGGTTTCGTTTAC
     met asp his glu glu ala arg arg lys his val ser gly lys ile leu gly phe val tyr

                    400           410           420           430           440          450
     TAAGCTATTTTGTTACAACAACCTTTTCGGTAGCTTTATATACTATAAATAAACACACGAT
     end

                    460           470           480           490           500          510
     AGCCTCATAACTTTACTCATTTCTTATTATACATTTTTTTAGTTTTCCTGTTAAATACTA

                    520           530           540           550           560          570
     ATATATTTGTACTTTAAAAACTGTTCAAAAGATTAGACAGAAATGAATTTATCTGCCGCAT

                    580           590           600           610           620          630
     TTCTGCATGCACGAAGTCGAATATGCAAATGTTTATATTGGCTTTATTAATTAAACAAAC

                    640           650           660           670           680          690
     TATATTTATGTGAGAAGGTAAAGCCGTATTTCCATGCGTTAATAGAGTAAAAAAAAGAAA

                    700           710           720           730           740          750
     TCATAATCTTCTACCTCTTCTACCACCCTTCTTTCTGGTGGAGTCTGATGGGACTGGAGT

                    760           770           780
     AACGTCTTCGATACGGCCAATTCTCAAACCAGATC
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B

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        -620          -610          -600          -590          -580          -570
  T G G A T A T G T A T G T T G G T C T T G T T T T A T A A A A A T T A T T A C A A C T G A A A G G C C A T T A A A A A A

        -560          -550          -540          -530          -520          -510
  C G T T A C A A T T T A A G A A T T G A A T A G T C G A T T A A G A T T A T T T A G A T T G A A A T T G A C T A A C T G

        -500          -490          -480          -470          -460          -450
  C A A A C C C A T A T T C A A G A A T T A T T T C A C A T C T T C C A G C G A G T A A A C A T G C C G C T G G T A A T C

        -440          -430          -420          -410          -400          -390
  G C G C G T C C T C A A T A T T T G A G T T T T T C A A A T A G T G A G G T G T G G A T G T A T A G A G G A A T T A C A

        -380          -370          -360          -350          -340          -330
  C A C T T T T A A G T A T G T G A T G T A T G G G C G C A C C A G T A C C A A T T T A A C T T T T T T T T T T T C A T

        -320          -310          -300          -290          -280          -270
  T T T T T A G C T T G A T T T T C A A A A A A C T T A T G G C G G T T T T A G G C T C C G G C T C A A A C T A C C A C C

        -260          -250          -240          -230          -220          -210
  A C C A T G C A G T A G G C C G A G G C A A A C A G T A C G C C T T A G C G G G G A C X C C G A A G C G A C T C C T T C

        -200          -190          -180          -170          -160          -150
  T G T T C C A A G C T C A A T G G T C C T T G C G T T T A C C G T C G C G C G T G G G C T A A C T A A C G C A A T T C G

        -140          -130          -120          -110          -100           -90
  G C T T T T G G G C T G T C G A G A A C C G A G A A T T A T T C T T C G C C T T G A T A G A T A C T T T A A A A C T T C

         -80           -70           -60           -50           -40           -30
  T A C T T A A T A T A C T T T C T A C A A T T T T T G G T A C A T T C A T A T T A T A C T G A A A A T T C G A A A A A G

     ▼       ▽ -20           -10           -1 1          10            20            30
  A C A A G C A A A T A A A C A C A G A T A G A T C A A C A T G G C T G T A T G T T A G A A A G A T A T T A T A A A T C C
                                              met   ala

          40            50            60            70            80            90
  C A G T T A G A T G C T G A A C T G A T C A A T A G C A A A T T A T A A A C C A C A T C C A T C T A A A T G A C C T T A

         100           110           120           130           140           150
  C C A C C T A C A A T T T G G A T T T G A A A T A G A C G C A A T G T G T G A A A T A T A G G G G A A G G A T T A G G A

         160           170           180           190           200           210
  G T G T T A A C C A T A C T A A A A T T T T T C T T A T C C G A A A C A G A A A T C T A A A G T C G C C A C T A C G C A

         220           230           240           250           260           270
  G A T T A A A A T A T G G T C A T A A A C T G C T T A T T C T G A C A A C T T T T G G T G G T C C A G C G T G G T T T A

         280           290           300           310           320           330
  T G T C A G G T G G T A T T G C C T T G G A T C C G T G A A T G C A T C A T A T T G A T G A G T T T G A A C A T T G T T

         340           350           360           370           380           390
  A C T A A C A T T T T T T A C A A T T G T A C A C T T C G T A T G T G C A C G A T A T G T T T C C C T T T T A A T T A G

         400           410           420           430           440           450
  G C T C A A A A G T C T T T C A G A A T C A A G C A A A A A A A T G G C T A A G G C T A A G A A G C A A A A C A G A C C A
   ala   gln   lys   ser   phe   arg   ile   lys   gln   lys   met   ala   lys   ala   lys   lys   gln   asn   arg   pro

         460           470           480           490           500           510
  T T G C C A C A A T G G A T C A G A T T G A G A A C C A A C A A C A C T A T C C G T T A C A A C G C T A A G A G A A G A
   leu   pro   gln   trp   ile   arg   leu   arg   thr   asn   asn   thr   ile   arg   tyr   asn   ala   lys   arg   arg

         520           530           540           550           560           570
  A A C T G G A G A A G A A C C A A G A T G A A C A T C T A A G C G A A G A A C A T A T T T A T G C T T C A A A C T T T T
   asn   trp   arg   arg   thr   lys   met   asn   ile   end

         580           590           600           610           620           630
  T G T C A T T T G T C T T C C A T C C A A C C C T T A T T C T C A A T A T A T A T G T A A T A C G T C G T A T T T G A T

         -640          650           660           670           680           690
  A T A T A T A T A T A T A T A T A A T A T A A T T T A A C G G G T T G T T A T C T G C T A C A T C T G T A A A A T A A A

         700           710           720           730           740           750
  A A T A A A A A X X X C T T G A A G C G G C T G T A C T T A A A A T A A A C T C A T C T A A G G T T T T A C A T G G T A

         760           770           780           790           800           810
  T T A C T A C C G G A C T G C A A T T A C A C T C T T T T T C G T T A T T G G A T T A T T T A T A C A A T G C G G
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Fig. 2. DNA sequence of the genes for yeast ribosomal proteins S24 (A) and L46 (B). The nucleotides are numbered starting from the first nucleotide of the respective initiation codons. The positions of the 5'-ends of the S24 and L46 mRNA are indicated by triangles (▲ major-, △ minor start site).
In addition conserved sequence elements occurring in the non-coding regions are underlined.
For the sake of clarity the intergenic region is shown in both DNA sequences.
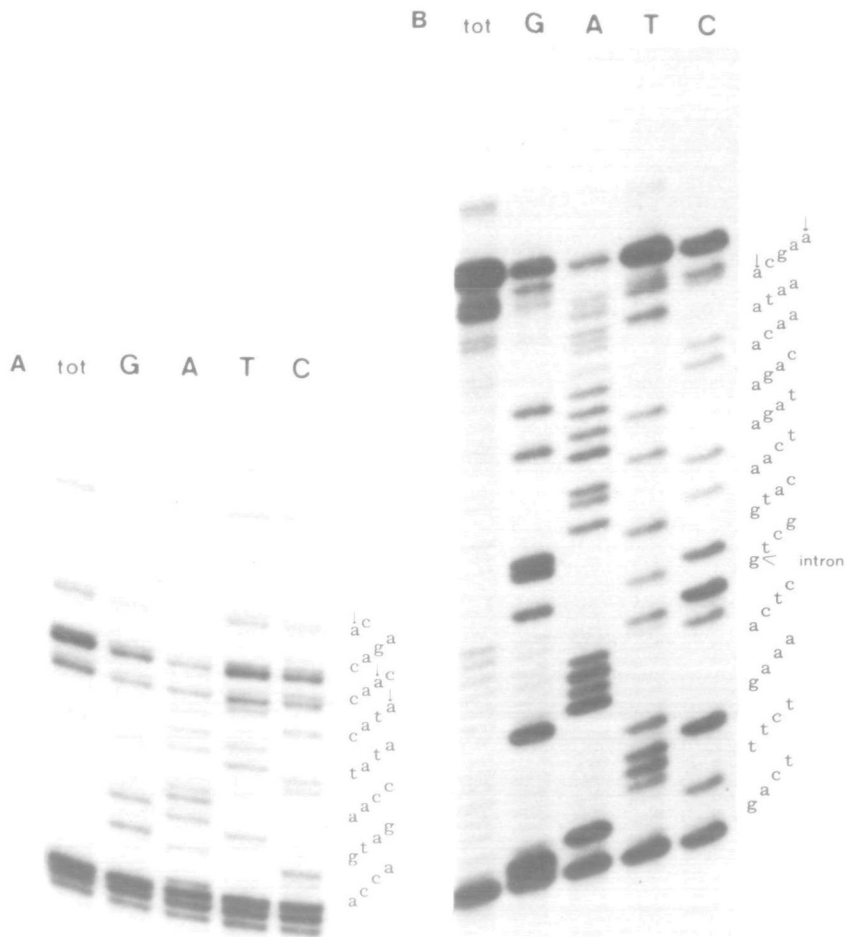
Fig. 3. Sequence analysis of the 5'-ends of the S24 (A) and L46 (B) mRNAs. cDNA synthesis was performed as described in Materials and Methods using the 162 and 55 nucleotides long primers depicted in Fig. 1. The arrows indicate the 5'-termini of the respective mRNAs; 'intron' indicates the splice junction in the L46-gene.

c. The structure of ribosomal proteins S24 and L46

Yeast ribosomal protein S24 as deduced from the nucleotide sequence of its gene is a protein of 14762 D with a net positive charge of +9, while L46 is a very small and extremely basic protein with a molecular weight of 6334 D and a net charge of +17.

The amino acid sequences of S24 and L46 as deduced from the nucleotide

sequence are in perfect agreement with the N-terminal amino acid sequences determined by Otaka et al. (12,13) for the proteins YS22 and YL40, which are identical to S24 and L46 respectively (10,14). The amino acid sequence of yeast S24 is partially homologous to that of HS20 from Halobacterium cutirubrum (12), while yeast L46 shows a strong similarity to L36 from Schizosaccharomyces pombe (13). Even more striking is the extended sequence homology of yeast L46 and rat liver L39 (|15|; see Fig. 5). This finding indicates the existence of evolutionary constraints on the structure of at least some ribosomal proteins which suggests a fundamental role of these proteins in the structure and function of the ribosome.

d. Conserved sequences in the non-coding regions

The intergenic DNA region of 588 nucleotides between the transcription initiation sites of the divergently transcribed L46 and S24 genes is expected to contain the signals controlling the expression of both ribosomal protein genes. Previous computer analysis has revealed several conserved boxes upstream of most yeast ribosomal protein genes that might act as regulatory signals (16). The most striking of these boxes is a 12-nucleotide long element (HOMOL 1) having the consensus sequence $AACATC^{TG}_{CA}T^G_ACA$. Neither strand of the intergenic region, however, contains this sequence element. On the other hand, another, recently detected, conserved sequence element (17), is present in the intergenic region. This element, the RPG-box, having the consensus sequence ACCCATACATTT, occurs once on the non-coding strand of the S24 gene at position -268 relative to the translation start site, which corresponds to position -363 relative to the translation start of the L46 gene (Fig. 2A,B).

In the latter case the RPG-box of course is located on the coding strand and its orientation relative to the gene is reversed. Since the RPG-box is found at about the same relative position upstream of most other yeast ribosomal protein genes (17) sometimes in one and sometimes in the other orientation, we suggest that the single box present in the intergenic region

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S24     ATAATCTTAATCGA-CTATTCAATTCTTAAATTGTAACGTTT
        ... . .... ..    ..... ... .  ... .......
L16-1   ATACTGTTAAGAGAGGCATTCATTTCGTGTATTATAACGTTT


S24     -12 n-TCAGTT-16 n-AACA-ACCAACATACATATCCAAG ATG
               ...... .. ..        . ....
L16-1   - 4 n-TCAGTT-14 n-AACATACAAAAATACGCGTTCAAG ATG
```

Fig. 4. Sequence homology in the upstream regions of the genes for S24 and L16-1 (16). The positions of identical bases are indicated by a dot.

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L46      (Met) Ala Ala Gln|Lys Ser Phe Arg Ile Lys|Gln Lys Met|Ala Lys|Ala Lys
RL-L39         Ser Ser His|Lys Thr Phe Arg Ile Lys|Arg Phe Leu|Ala Lys|Lys Gln
               1                                    10

               |Lys Gln Asn Arg Pro Leu Pro Gln Trp Ile Arg|Leu|Arg Thr|Asn|Asn|
               |Lys Gln Asn Arg Pro Ile Pro Gln Trp Ile Arg|Met|Lys Thr|Gly|Asn|
                            20                                        30

               Thr|Ile Arg Tyr Asn|Ala|Lys Arg Arg|Asn|Trp Arg Arg Thr Lys|Met
               Lys|Ile Arg Tyr Asn|Ser|Lys Arg Arg|His|Trp Arg Arg Thr Lys|Leu
                                           40

               Asn|Ile|
               Gly|Leu|
                   50
```

Fig. 5. Comparison of the primary structure of yeast ribosomal L46 with
ribosomal protein L39 from rat liver (15). Identical amino acids are boxed,
functional identical ones are indicated by dotted lines.

of the L46 and S24 genes is involved in controlling the expression of both

genes.

The upstream sequence of the S24 gene shows a remarkable homology with

the 5'-flanking region of a gene encoding yeast ribosomal protein L16 (see

Fig. 4). Similar homologies have been found for other pairs of different

yeast ribosomal protein genes (17). It is therefore tempting to speculate that

these regions are involved in the coordinate transcription of the respective

genes. No sequence conservation could be detected comparing the upstream

sequence of the L46-gene with any other of the known yeast ribosomal protein

gene sequences.

The sequences 3' to the coding regions contain the conserved boxes

implied in termination and/or polyadenylation (Fig. 2A,B; Ref. 18,19).

Finally the intron of the L46-gene contains all conserved sequence

elements found in the other split yeast nuclear (ribosomal) protein genes

(16,17,20,21,22), viz. GTATGT at 5'-splice site, TAG at the 3'-end and

TACTAACA which in the L46 intron is located 61 nucleotides from the 3'-splice

junction. The latter sequence element has recently been suggested to represent

the target-site for generating a lariat-like structure intermediate in the

splicing of pre-mRNAs in yeast (J. Abelson cited in 23;24).

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REFERENCES

1. Leer,R.J., Van Raamsdonk-Duin,M.M.C., Molenaar,C.M.T., Cohen,L.H., Mager,W.H. and Planta,R.J. (1982) Nucl. Acids Res. 10, 5869-5878.
2. Leer,R.J., Van Raamsdonk-Duin,M.M.C., Schoppink,P.J., Cornelissen,M.T.E., Cohen,L.H., Mager,W.H. and Planta,R.J. (1983) Nucl. Acids Res. 11, 7759-7768.
3. Leer,R.J., Van Raamsdonk-Duin,M.M.C., Hagendoorn,M.J.M., Mager,W.H. and Planta,R.J. (1984) Nucl. Acids Res. 12, 6685-6700.
4. Leer,R.J., Van Raamsdonk-Duin,M.M.C., Mager,W.H. and Planta,R.J. (1984) FEBS Lett. 175, 371-376.
5. Molenaar,C.M.T., Woudt,L.P., Jansen,A.E.M., Mager,W.H., Planta,R.J., Donovan,D. and Pearson,N.J. (1984) Nucl. Acids Res. 12, 7345-7358.
6. Schaap,P.J., Molenaar,C.M.T., Mager,W.H. and Planta,R.J. (1984) Curr. Genet., in press.
7. Sanger,F., Coulson,A.R., Barrell,B.G., Smith,A.J.H. and Roe,B.A. (1980) J. Mol. Biol. 143, 161-178.
8. Bollen,G.H.P.M., Cohen,L.H., Mager,W.H., Klaassen,A.W. and Planta,R.J. (1981) Gene 14, 279-287.
9. Bollen,G.H.P.M., Molenaar,C.M.T., Cohen,L.H., Van Raamsdonk-Duin,M.M.C., Mager,W.H. and Planta,R.J. (1982) Gene 18, 29-37.
10. Bollen,G.H.P.M., Mager,W.H. and Planta,R.J. (1981) Mol. Biol. Rep. 8, 37-44.
11. Molenaar,C.M.T. (1984) Ph.D. Thesis, Free University, Amsterdam.
12. Otaka,E., Higo,K. and Osawa,S. (1982) Biochemistry 21, 4545-4550.
13. Otaka,E., Higo,K. and Itoh,T. (1983) Mol. Gen. Genet. 191, 519-524.
14. Michel,S., Traut,R. and Lee,J. (1983) Mol. Gen. Genet. 191, 251-256.
15. Lin,A., McNall,J. and Wool,I.R. (1984) J. Biol. Chem. 259, 487-490.
16. Teem,J.L., Abovich,N., Käufer,N.F., Schwindinger,W.F., Warner,J.R., Levy,A., Woolford,J., Leer,R.J., Van Raamsdonk-Duin,M.M.C., Mager,W.H., Planta,R.J., Schultz,L., Friesen,J.D. and Rosbash,M. (1984) Nucl. Acids Res., in press.
17. Leer,R.J., Van Raamsdonk-Duin,M.M.C., Mager,W.H. and Planta,R.J. (1985) submitted.
18. Fitzgerald,M. and Schenk,T. (1981) Cell 24, 251-260.
19. Zaret,K.S. and Sherman,F. (1982) Cell 28, 563-573.
20. Miller,A.M. (1984) The EMBO J. 3, 1061-1065.
21. Langford,C.J. and Gallwitz,D. (1983) Cell 33, 519-527.
22. Langford,C.J., Klinz,F.J., Donath,C. and Gallwitz,D. (1984) Cell 36, 645-653.
23. Ruskin,B., Krainer,A.R., Maniatis,T. and Green,M.R. (1984) Cell 38, 317-331.
24. Padgett,R.A., Konarska,M.M., Grabowski,P.J., Hardy,S.F. and Sharp,P.A. (1984) Science 225, 898-903.