Proc. Natl. Acad. Sci. USA
Vol. 84, pp. 1192–1196, March 1987
Biochemistry

Prokaryotic and eukaryotic RNA polymerases have homologous core subunits

(*Saccharomyces cerevisiae/RPB2*)

DOUG SWEETSER*, MICHAEL NONET*, AND RICHARD A. YOUNG*†

*Whitehead Institute for Biomedical Research, Nine Cambridge Center, Cambridge, MA 02142; and †Department of Biology, Massachusetts Institute of Technology, Cambridge, MA 02139

Communicated by Gerald R. Fink, November 3, 1986 (received for review September 3, 1986)

ABSTRACT **Eukaryotic RNA polymerases are complex aggregates whose component subunits are functionally ill-defined. The gene that encodes the 140,000-dalton subunit of *Saccharomyces cerevisiae* RNA polymerase II was isolated and studied in detail to obtain clues to the protein's function. This gene, *RPB2*, exists in a single copy in the haploid genome. Disruption of the gene is lethal to the yeast cell. *RPB2* encodes a protein of 138,750 daltons, which contains sequences implicated in binding purine nucleotides and zinc ions and exhibits striking sequence homology with the β subunit of *Escherichia coli* RNA polymerase. These observations suggest that the yeast and the *E. coli* subunit have similar roles in RNA synthesis, as the β subunit contains binding sites for nucleotide substrates and a portion of the catalytic site for RNA synthesis. The subunit homologies reported here, and those observed previously with the largest RNA polymerase subunit, indicate that components of the prokaryotic RNA polymerase "core" enzyme have counterparts in eukaryotic RNA polymerases.**

Eukaryotic nuclear RNA polymerases I, II, and III are responsible for the synthesis of large ribosomal RNAs, pre-mRNAs, and small ribosomal and tRNAs, respectively (for reviews, see refs. 1, 2). Similarities in RNA polymerase subunit structure and antigenicity among eukaryotes indicate that these enzymes are highly conserved (for reviews, see refs. 3–5). Each of the three polymerases is composed of 9–14 polypeptides that copurify with transcriptional activity. Some subunits are shared by the three RNA polymerases, whereas the others are unique to each enzyme. How these components contribute to the functions of the three enzymes is not yet established, and additional factors appear to be essential for selective transcription initiation.

The *Escherichia coli* RNA polymerase has been relatively well studied biochemically and genetically (for reviews, see ref. 6 and references therein). The enzyme is composed of four different polypeptides, α (rpoA), β (rpoB), β′ (rpoC), and σ (rpoD), whose molecular masses are 36,511, 150,543, 155,163 and 70,263 daltons, respectively. The core enzyme, whose subunit composition is $\alpha_2\beta\beta'$, can catalyze DNA-dependent RNA chain elongation. Selective initiation requires a holoenzyme containing the core plus a σ subunit, indicating that the σ subunit is essential for proper transcription initiation. Although multiple subunits are involved in most transcriptional activities, the individual subunits can play major roles in these activities. For example, α, β, and β′ all contribute to the fidelity of transcription. However, the β′ subunit appears to be largely responsible for DNA binding, and the β subunit contains binding sites for substrates and products and at least a portion of the catalytic site for RNA synthesis. β and β′ also appear to play a role in promoter recognition because mutations in RpoB and RpoC have been shown to affect selective transcription initiation *in vivo* and *in vitro* (7–9).

The roles that eukaryotic RNA polymerase subunits have in transcription are less clear. The presence of common and unique subunits in the three classes of RNA polymerase suggests one model in which common subunits are responsible for at least some of the functions shared by the RNA polymerases, and the unique subunits perform functions specific to each type of RNA synthesis. Alternatively, the eukaryotic RNA polymerases could contain a core enzyme composed of subunits that are structurally and functionally homologous to their prokaryotic counterpart but that differ sufficiently to be categorized as unique in RNA polymerases I–III. The observation that the largest subunit of yeast RNA polymerases II and III and *Drosophila* RNA polymerase II contain amino acid sequence homology with the large subunit of *E. coli* RNA polymerase (10, 11) is consistent with the latter model. To examine the roles of RNA polymerase II subunits in transcription further, we and our colleagues have begun to isolate and study the *Saccharomyces cerevisiae* genes that encode these proteins (12, 13). Here we report that the 140,000-dalton subunit of yeast RNA polymerase II is homologous to the β subunit of *E. coli* RNA polymerase and propose that the eukaryotic transcription apparatus is composed of a core enzyme that is functionally similar to that of prokaryotes.

MATERIALS AND METHODS

Yeast and Bacterial Stains. The yeast strain DB1033 (**ura3-52 SUC2*$^+$) is a S288C derivative obtained from D. Botstein (M.I.T.). The *E. coli* strain Y1090 (*lacU169 proA*$^+$ *lon100 araD139 strA supF*[*trpC22*::Tn*10*] (pMC9) is described in ref. 12.

Recombinant DNA Libraries and Clones. The construction of the yeast genomic DNA library in λgt11 has been described (12, 14). The λEMBL3a phage library of yeast genomic DNA was a gift of M. Snyder (Stanford University School of Medicine); it contains 10^5 individual recombinants. Both DNA libraries were constructed with yeast strain S288C DNA. The libraries were screened with radiolabeled DNA probes (15) or with antibodies (16). DNA was manipulated as described (15).

Tetrad Analysis. Genetic manipulation of yeast was performed as described (17).

DNA Sequence Analysis. DNA was subcloned into vector M13mp18 or M13mp19 (New England Biolabs) as suggested by the supplier. Dideoxynucleotide chain-termination reactions and gel electrophoresis of the sequenced products were as described (18). DNA sequences were determined for both strands of DNA. Computer analysis of sequences with UWGCG programs was according to Devereux *et al.* (19).

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

RESULTS

RNA Polymerase Subunit Gene Isolation. DNA clones containing the gene for the 140,000-dalton subunit of *S. cerevisiae* RNA polymerase II (*RPB2*) were isolated. Two DNA clones were previously isolated from a λgt11 library with anti-RNA polymerase II polyclonal antibodies and shown to encode a portion of the second largest RNA polymerase II subunit (12). Clones representing the entire gene were obtained from two different λ phage genomic DNA libraries. Four additional λgt11 clones were isolated by screening with antibodies and a λEMBL3a clone containing a large genomic DNA fragment was isolated using labeled insert DNA from the λgt11 clone Y3015. DNA purified from each of these phages was mapped with restriction endonucleases (Fig. 1). The restriction map determined for the 17-kb genomic DNA insert of the EMBL3a clone Y3053 is identical to that found by Southern analysis in the yeast genome. All of the λgt11 clones contain inserts whose restriction maps overlap with Y3053 DNA, consistent with the observation that *RPB2* DNA sequences occur in single copy in the haploid genome (12).

The *RPB2* Gene Specifies 4- and 4.2-kb mRNAs. The limits of the RNA polymerase subunit gene were determined by S1 nuclease mapping of the 5′ and 3′ termini of RPB2 mRNA (not shown). *RPB2* is transcribed into two poly(A) mRNAs of about equal abundance. These mRNAs are 4 and 4.2 kb, differ in the length of their 3′ untranslated region, and do not appear to be spliced.

***RPB2* Is Essential for Cell Viability.** The single chromosomal *RPB2* gene was disrupted to assess whether the gene is essential for cell viability (20). Diploid cells were transformed with the plasmid Y2059 (Fig. 1), a YIp5 recombinant plasmid (21) containing the 1.4-kb *Hin*dIII–*Bgl* II restriction fragment of *RPB2*, which includes only sequences internal to the protein coding region of the gene. Integration of the recombinant plasmid can occur at loci homologous to either *RPB2* or *URA3* sequences. DNA was prepared from six of the diploid transformants and studied by Southern analysis; four of the transformants had integrations at the *RPB2* locus (Y146–Y149) and the remaining two at the *URA3* locus (Y145, Y150). Disruption of an essential gene should produce a recessive lethal mutation that is detected by standard tetrad analysis. The six independent transformants were sporulated and subjected to tetrad analysis (Table 1). As expected, transformants Y145 and Y150 generally produced four viable spores in which the Ura$^+$ phenotype segregated 2:2. In contrast, transformants Y146–Y149 showed the pattern of viability expected for the segregation of a recessive lethal mutation (2 live:2 dead), and all viable spores had a Ura$^-$ phenotype. We conclude that the *RPB2* gene is essential for yeast cell viability.

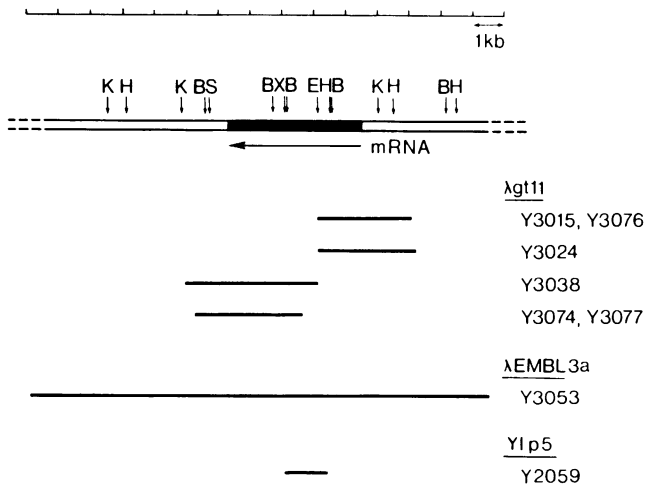

FIG. 1. Organization of *RPB2* DNA. The heavy horizontal line depicts the *RPB2* gene in the yeast genome. The light horizontal lines represent the DNA inserts of the recombinant DNA clones. The DNA clones were mapped with the restriction enzymes *Bgl* II (B), *Eco*RI (E), *Hin*dIII (H), *Kpn* I (K), and *Sal* I (S). The presence of these restriction sites in the yeast genome was confirmed by Southern analysis of S288C DNA. kb, Kilobase.

Table 1. Tetrad analysis of *RPB2* gene disruption

Transformant	Locus of integration	Viable spores/tetrad 4	3	2	1	Ratio of spores URA$^+$:URA$^-$
Y145	*URA3*	14	1	0	0	30:29
Y146	*RPB2*	0	0	7	0	0:14
Y147	*RPB2*	0	0	5	1	0:11
Y148	*RPB2*	0	0	17	2	0:36
Y149	*RPB2*	0	0	6	0	0:12
Y150	*URA3*	10	0	0	0	20:20

To determine whether the *RPB2* is an essential gene, the *RPB2* coding sequence was disrupted in one of the two chromosomes in a diploid cell, and the viability of the meiotic products was ascertained.

RPB2 Protein Is Homologous to *E. coli* RNA Polymerase Subunit β. The amino acid sequence of the RPB2 protein was deduced from DNA sequence analysis of the 6-kb *Kpn* I fragment of Y3053 (Fig. 2). The single large open reading frame predicts a 1224 amino acid polypeptide of 138,750 daltons, smaller than the $NaDodSO_4$/polyacrylamide gel estimate of 150,000 daltons (22).

The amino acid sequence deduced for the RNA polymerase subunit was compared with that of other proteins in the National Biomedical Research Foundation protein sequence database. The *E. coli* RNA polymerase subunit β exhibited a striking degree of sequence homology with the 140,000-dalton subunit (Fig. 3). The nine major segments of homology occur in nearly identical relative positions within the two polypeptides. Within these segments, the amino acid sequences of the proteins align without introducing any spacing (Fig. 4). One-third of the amino acids in the segments are identical, and conservative amino acid replacements account for many of the nonidentical residues. Less significant homology exists between the DNA sequences of the prokaryotic and eukaryotic genes, reflecting different codon usage in the two organisms.

RPB2 protein sequences were analyzed for motifs that are conserved in nucleotide-binding and metal-binding domains of various proteins. The sequence G-X-X-X-X-G-K-(T), where X is any amino acid, is a common motif among purine nucleotide-binding or processing proteins (24). This sequence is found in a conserved region in both yeast and *E. coli* subunits (Fig. 4), although the yeast sequence varies from the consensus by having five rather than four amino acids in the X positions. Nucleic acid binding proteins often contain sites that complex with zinc ions, and a sequence of the form $C\text{-}X_2\text{-}C\text{-}X_{9\text{–}15}\text{-}C\text{-}X_2\text{-}C$ has been implicated in binding metals (25). This sequence motif occurs in the 140,000-dalton yeast subunit (encoded by nucleotides 4295–4363 in Fig. 2), although it is not found in the prokaryotic subunit.

DISCUSSION

The molecular genetic techniques available in yeast provide a powerful approach to study the functions of the highly conserved eukaryotic RNA polymerases. We have investigated the gene for the second largest RNA polymerase II subunit, *RPB2*. This gene encodes a 138,750-dalton protein and is essential for cell viability. Most important, the RNA polymerase II subunit contains amino acid sequences that have been implicated in binding purine nucleotides and zinc

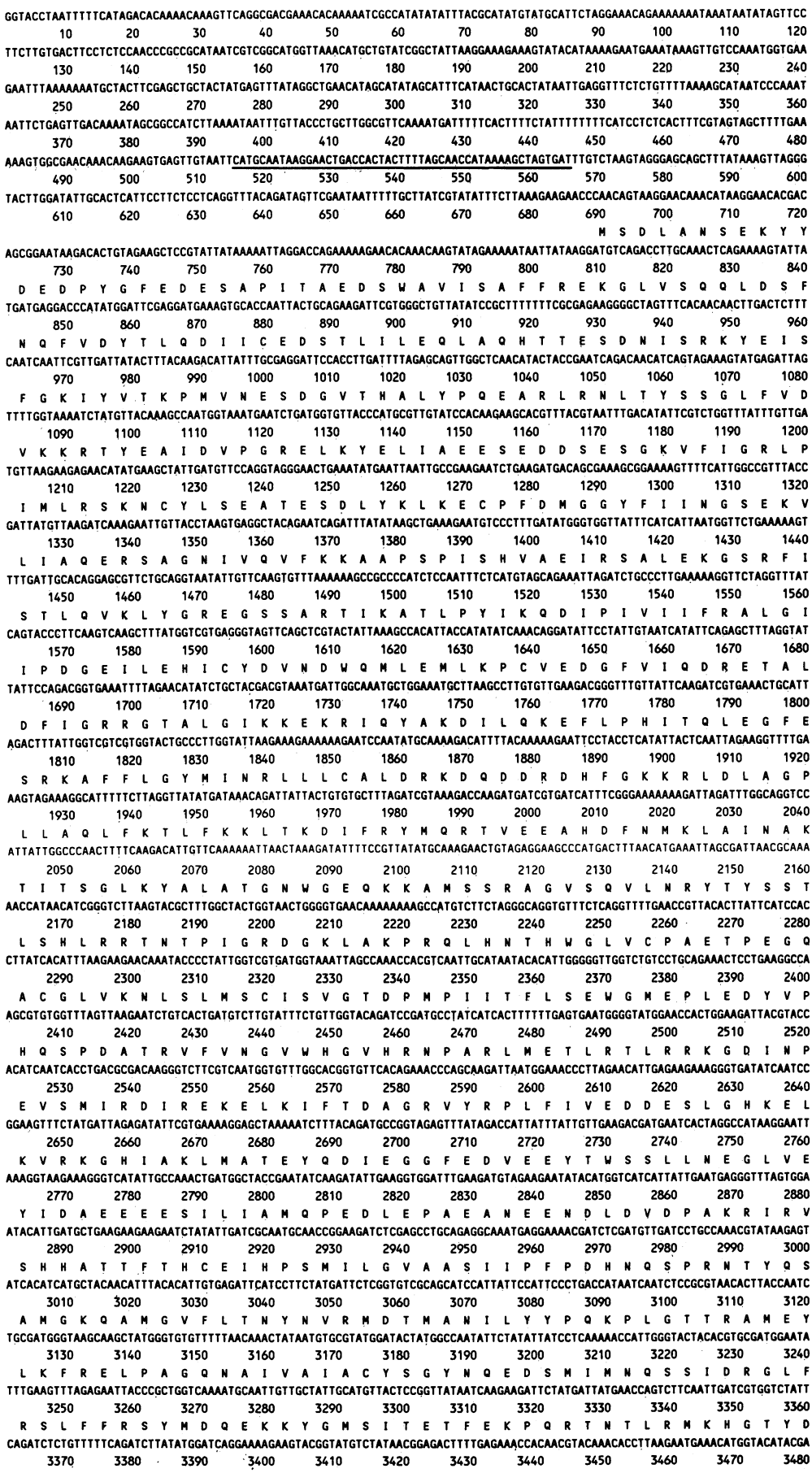

FIG. 2. (*Figure continues on the opposite page.*)

```
K L D D D G L I A P G V R V S G E D V I I G K T T P I S P D E E E L G Q R T A Y
TAAGTTGGACGATGATGGTCTAATTGCGCCTGGTGTTAGAGTTTCAGGAGAAGATGTGATTATCGGTAAAACCACACCAATCTCACCAGATGAAGAGGAACTCGGTCAAAGAACAGCATA
     3490      3500      3510      3520      3530      3540      3550      3560      3570      3580      3590      3600
 H S K R D A S T P L R S T E N G I V D Q V L V T T N Q D G L K F V K V R V R T T
CCATTCCAAACGTGATGCTTCCACACCATTGAGAAGTACTGAAAACGGTATTGTTGATCAAGTTTTAGTCACAACAAACCAAGATGGGTTAAAGTTTGTCAAAGTTCGTGTAAGAACTAC
     3610      3620      3630      3640      3650      3660      3670      3680      3690      3700      3710      3720
 K I P Q I G D K F A S R H G Q K G T I G I T Y R R E D M P F T A E G I V P D L I
AAAGATTCCTCAAATTGGTGACAAATTTGCTTCTCGTCACGGTCAAAAGGGTACTATTGGTATCACATATCGTAGAGAAGATATGCCATTTACCGCAGAAGGTATTGTTCCAGATTTGAT
     3730      3740      3750      3760      3770      3780      3790      3800      3810      3820      3830      3840
 I N P H A I P S R M T V A H L I E C L L S K V A A L S G N E G D A S P F T D I T
TATTAACCCTCATGCTATTCCATCTCGTATGACTGTTGCCCATTTAATTGAATGTTTGTTGAGTAAAGTCGCGGCACTATCTGGTAATGAAGGTGACGCCTCTCCTTTCACGGACATTAC
     3850      3860      3870      3880      3890      3900      3910      3920      3930      3940      3950      3960
 V E G I S K L L R E H G Y Q S R G F E V M Y N G H T G K K L M A Q I F F G P T Y
TGTAGAAGGTATATCCAAACTACTGCGTGAGCATGGTTATCAATCTCGTGGGTTTGAAGTTATGTATAATGGTCACACAGGTAAAAAACTAATGGCTCAAATTTTCTTTGGTCCTACATA
     3970      3980      3990      4000      4010      4020      4030      4040      4050      4060      4070      4080
 Y Q R L R H M V D D K I H A R A R G P M Q V L T R Q P V E G R S R D G G L R F G
TTATCAACGACTAAGACACATGGTGGATGACAAGATACATGCCAGAGCACGTGGTCCAATGCAAGTATTGACGAGACAGCCTGTAGAGGGTAGATCGAGAGACGGTGGTTTAAGATTCGG
     4090      4100      4110      4120      4130      4140      4150      4160      4170      4180      4190      4200
 E M E R D C M I A H G A A S F L K E R L M E A S D A F R V H I C G I C G L M T V
TGAGATGGAACGTGACTGTATGATTGCTCATGGTGCTGCCTCATTCTTGAAGGAGAGATTAATGGAAGCATCCGATGCCTTTAGAGTCCATATTTGTGGTATTTGCGGGCTGATGACAGT
     4210      4220      4230      4240      4250      4260      4270      4280      4290      4300      4310      4320
 I A K L N H N Q F E C K G C D N K I D I Y Q I H I P Y A A K L L F Q E L M A M N
TATCGCGAAATTAAATCATAACCAATTTGAATGTAAGGGATGTGATAATAAGATTGATATTTACCAAATTCATATTCCATACGCCGCGAAGTTATTATTCCAAGAACTTATGGCTATGAA
     4330      4340      4350      4360      4370      4380      4390      4400      4410      4420      4430      4440
 I T P R L Y T D R S R D F
CATTACACCACGTTTATATACCGATCGTTCGAGAGATTTTTAAGAAATAATGTTGTAACTCTAAGAAAGTAAAATAATAAAAAACATTTCATTTGTGCTGATCTTGCCAAAAAAAGGGTA
     4450      4460      4470      4480      4490      4500      4510      4520      4530      4540      4550      4560
AACAAGTAGGCAATAGTAATAAAATAAGAATGAAGCATTTCTTTTAATAAGCAGAGAGAACTTTCAAGCATTCAAAAAACACAAAAATAATGATGAATAAAATGGGACTCACAGTGTTTA
     4570      4580      4590      4600      4610      4620      4630      4640      4650      4660      4670      4680
TTTATAGTCCTTGTTTCGCATTTTACCAAATTAAAATTTAATTTTATCAAGACATATTAATGAACTTTAGCGGAAAACCTTAAATATCCAAGTCATAAATAATGACTTATGTAAAAAGTT
     4690      4700      4710      4720      4730      4740      4750      4760      4770      4780      4790      4800
```

FIG. 2. Sequence of *RPB2* DNA and its protein product. The DNA sequence of 4800 base pairs of the 6232-base-pair *Kpn* I DNA fragment (Fig. 1) containing *RPB2* is shown. The sequence is numbered from the *Kpn* I restriction site nearest the beginning of *RPB2* (Fig. 1). The sites of RPB2 mRNA initiation [nucleotide 540 (±25)] and polyadenylylation [nucleotides 4507 and 4787 (±25)] are underlined. The first AUG in the RPB2 mRNA sequence occurs at nucleotide 809, and the protein sequence terminates at a UUA at nucleotide 4481.

ions and is homologous to the *E. coli* RNA polymerase subunit (β) that accommodates a portion of the catalytic site for RNA synthesis.

The homology between the RPB2 protein and the prokaryotic β subunit and the presence of nucleotide-binding sequence motifs in these proteins indicate they share similar functions. The β subunit of *E. coli* RNA polymerase plays several roles in transcription. The binding sites for substrates and products and at least a portion of the catalytic site for RNA synthesis appear to reside on this subunit (7, 26–28). Although the σ subunit is essential for proper transcription initiation, RNA polymerases with mutant β or β' subunits can exhibit altered promoter selection *in vivo* and *in vitro*, and some β subunit mutations can suppress the phenotype of some σ mutants (7–9). The β and σ subunits are probably in close proximity in the initiation complex, as they can be crosslinked to DNA sequences only five nucleotides apart in the *lac* UV5 promoter (29). Several lines of evidence suggest that the yeast 140,000-dalton subunit is responsible for at least some of these roles in eukaryotic mRNA synthesis. The presence of a purine nucleotide-binding motif in the sequence of the 140,000-dalton subunit (Fig. 4) indicates that the yeast subunit is involved in substrate binding. Similarly, a sequence found in zinc-binding domains occurs in the yeast subunit; the Zn ion associated with the β subunit coordinates with ATP and is thought to be involved in RNA catalysis (30). Finally, the ability to affinity label the 140,000-dalton subunit of wheat germ RNA polymerase II with a purine nucleoside analogue (31) indicates that substrate-binding activity is a conserved feature of this subunit in eukaryotes. Whether the 140,000-dalton subunit performs other functions that have been attributed to the prokaryotic subunit is not yet clear. It is tempting to speculate that eukaryotic transcription control factors may interact with the 140,000-dalton subunit, in a manner analogous to that suggested for the prokaryotic β and σ subunits.

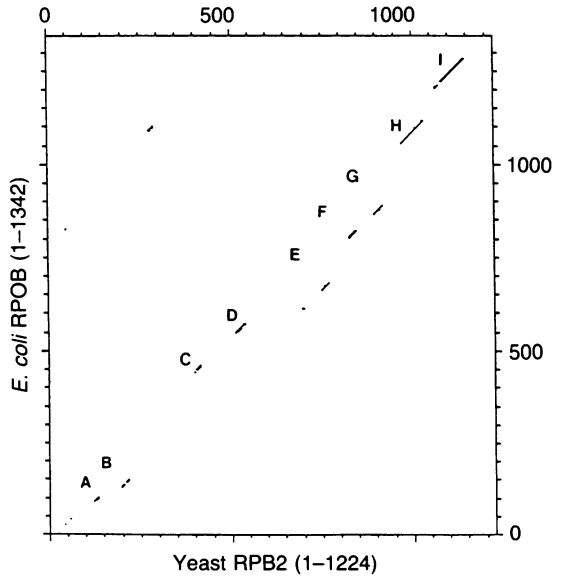

FIG. 3. Yeast RPB2 and *E. coli* RPOB amino acid sequence comparison. RPB2 amino acid sequences are compared with those of the *E. coli* RNA polymerase β subunit using a dot matrix computer program (19), with the window set at 25 and the stringency at 40.

Eukaryotic polymerases I–III are each composed of 2 large and 5–10 distinctly smaller subunits. The prokaryotic core RNA polymerase is composed of 2 large and 2 smaller but identical subunits. This conservation of overall structure, the sequence homologies between the 2 large subunits of eukaryotic and prokaryotic RNA polymerases, and the similarities in DNA and substrate-binding properties of the subunits all indicate that eukaryotic RNA polymerases have structural and functional homologues of prokaryotic RNA polymerase core subunits. We propose that eukaryotic RNA polymerases contain subunits homologous to all 3 core subunits of the *E. coli* enzyme. The yeast RNA polymerase II 45,000-dalton subunit is a candidate for such a homologue; subunits of similar size occur in all eukaryotic RNA polymerase II enzymes investigated thus far.

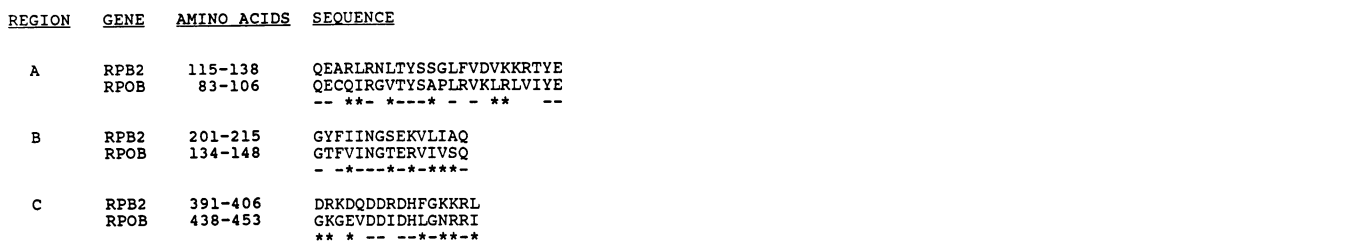

FIG. 4. Subunit amino acid sequence homologies. The nine segments of amino acid sequence homology in Fig. 3 are shown in detail. Identical sequences are underlined. Conservative amino acid replacements, those with a value of at least +1 (23), are starred. The purine nucleotide-binding motif (24) is overlined.

If eukaryotic RNA polymerases contain a core enzyme whose components are homologous to those found in *E. coli*, then what are the functions of the additional subunits found associated with the three eukaryotic RNA polymerases? Some of these polypeptides are unique to one class of RNA polymerase and others are shared by two or all three of the enzymes. It seems likely that some of these additional subunits fine tune the specificity and efficiency of the transcription reaction and others are involved in regulation of the relative levels of active RNA polymerases I–III. Detailed genetic and biochemical analysis of these components should reveal their contribution to the transcription apparatus and may enhance our understanding of the molecular mechanisms involved in the regulation of gene expression.

We are grateful to Gerry Fink and Robert Roeder for discussion and comments on the manuscript and thank J. Sexton for technical assistance and C. Carpenter for preparing the manuscript. This work was supported by a grant from the National Institutes of Health (GM34365).

1. Chambon, P. (1975) *Annu. Rev. Biochem.* **44,** 613–638.
2. Roeder, R. G. (1976) in *RNA Polymerase*, eds. Losick, R. & Chamberlin, M. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY), pp. 285–329.
3. Paule, M. R. (1981) *Trends Biochem. Sci.* **6,** 128–131.
4. Lewis, M. K. & Burgess, R. R. (1982) in *The Enzymes* (Academic, New York), Vol. 15, pp. 109–153.
5. Sentenac, A. (1985) in *CRC Crit. Rev. Biochem.* **18,** 31–91.
6. Chamberlin, M. J. (1982) in *The Enzymes* (Academic, New York), Vol. 15, pp. 61–86.
7. Yura, T. & Ishihama, A. (1979) *Annu. Rev. Genet.* **13,** 59–97.
8. Nomura, T., Ishihama, A., Kajitani, M., Takahashi, T., Nakada, N. & Yoshinaga, K. (1984) *Mol. Gen. Genet.* **193,** 8–16.
9. Glass, R. E., Jones, S. T., Nene, V., Nomura, T., Fujita, N. & Ishihama, A. (1986) *Mol. Gen. Genet.* **203,** 487–491.
10. Allison, L. A., Moyle, M., Shales, M. & Ingles, C. J. (1985) *Cell* **42,** 599–610.
11. Biggs, J., Searles, L. L. & Greenleaf, A. L. (1985) *Cell* **42,** 611–621.
12. Young, R. A. & Davis, R. W. (1983) *Science* **222,** 778–782.
13. Riva, M., Memet, S., Micouin, J., Huet, J., Treich, I., Dassa, J., Young, R., Buhler, J., Sentenac, A. & Fromageot, P. (1986) *Proc. Natl. Acad. Sci. USA* **83,** 1554–1558.
14. Snyder, M. & Davis, R. W. (1985) in *Hybridoma Technology in the Biosciences and Medicine*, ed. Springer, T. (Plenum, New York), p. 397–406.
15. Davis, R. W., Botstein, D. & Roth, J. R. (1980) *Advanced Bacterial Genetics: A Manual for Genetic Engineering* (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY).
16. Young, R. A., Bloom, B. R., Grosskinsky, C. M., Ivanyi, J., Thomas, D. & Davis, R. W. (1985) *Proc. Natl. Acad. Sci. USA* **82,** 2583–2587.
17. Mortimer, R. K. & Hawthorne, D. C. (1969) in *The Yeast*, eds. Rose, A. H. & Harrison, J. S. (Academic, New York), Vol. 1, pp. 385–460.
18. Sanger, F., Nicklen, S. & Coulson, A. R. (1977) *Proc. Natl. Acad. Sci. USA* **74,** 5463–5467.
19. Devereux, J., Haeberli, P. & Smithies, O. (1984) *Nucleic Acids Res.* **12,** 387–395.
20. Shortle, D., Haber, J. E. & Botstein, D. (1982) *Science* **217,** 371–373.
21. Botstein, D. & Davis, R. W. (1982) in *The Molecular Biology of the Yeast Saccharomyces: Metabolism and Gene Expression*, eds. Strathern, J., Jones, E. & Broach, J. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY), pp. 607–636.
22. Sentenac, A. & Hall, B. (1982) in *The Molecular Biology of the Yeast Saccharomyces: Metabolism and Gene Expression*, eds. Strathern, J., Jones, E. & Broach, J. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY), pp. 561–606.
23. Dayhoff, M. O., Schwartz, R. M. & Orcutt, B. C. (1979) in *Atlas of Protein Sequence and Structure*, ed. Dayhoff, M. O. (Natl. Biomed. Res. Found., Washington, DC), Vol. 5, Suppl. 3, pp. 345–362.
24. la Cour, T. F. M., Nyborg, J., Thirup, S. & Clark, B. F. C. (1985) *EMBO J.* **4,** 2385–2388.
25. Berg, J. M. (1986) *Science* **232,** 485–487.
26. Zillig, W., Palm, P. & Heil, A. (1976) in *RNA Polymerase*, eds. Losick, R. & Chamberlin, M. (Cold Spring Harbor Laboratory, Cold Spring Harbor, NY), pp. 101–125.
27. Panka, D. & Dennis, D. (1985) *J. Biol. Chem.* **260,** 1427–1431.
28. Hanna, M. M. & Meares, C. F. (1983) *Proc. Natl. Acad. Sci. USA* **80,** 4238–4242.
29. Simpson, R. B. (1979) *Cell* **18,** 277–285.
30. Chatterji, D., Wu, C.-W. & Wu, F. Y.-H. (1984) *J. Biol. Chem.* **259,** 284–289.
31. Cho, J. M. & Kimball, A. P. (1982) *Biochem. Pharmacol.* **31,** 2575–2581.