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The pentafunctional *FAS1* genes of *Saccharomyces cerevisiae* and *Yarrowia lipolytica* are co-linear and considerably longer than previously estimated

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Summary. The fatty acid synthetase (FAS) gene *FAS1* of the alkane-utilizing yeast *Yarrowia lipolytica* was cloned and sequenced. The gene is represented by an intron-free reading frame of 6228 bp encoding a protein of 2076 amino acids and 229980 Da molecular weight. This protein exhibits a 58% sequence similarity to the corresponding *Saccharomyces cerevisiae* FAS β-subunit. The sequential order of the five *FAS1*-encoded enzyme domains, acetyl transferase, enoyl reductase, dehydratase and malonyl/palmityl-transferase, is co-linear in both organisms. This finding agrees with available evidence that the functional organization of FAS genes is similar in related organisms but differs considerably between unrelated species. In addition, previously reported conflicting data concerning the 3′ end of *S. cerevisiae FAS1* were re-examined by genomic and cDNA sequencing of the relevant portion of the gene. Thereby, the translational stop codon was shown to lie considerably downstream of both published termination sites. The *S. cerevisiae FAS1* gene thus has a corrected length of 6153 bp and encodes a protein of 2051 amino acids and 228667 Da molecular weight.

Key words: Yeast fatty acid synthetases – *Yarrowia lipolytica*/*Saccharomyces cerevisiae FAS1* sequence comparison – *S. cerevisiae FAS1* sequence correction

Fatty acid synthetases exist either as non-aggregated multicomponent enzymes (type II FAS) or as highly integrated multifunctional proteins (type I FAS). Characteristically, type I synthetases are found in the cytoplasm of eucaryotic cells while their occurrence in bacteria is rare (Lynen 1980; Kawaguchi and Okuda 1977). In yeast and other lower fungi, the enzyme is an $\alpha_6\beta_6$ heteromultimeric complex whose subunits are encoded by two multifunctional genes, *FAS1* (subunit β) and *FAS2* (subunit α) (E. Schweizer et al. 1978). The genetic and structural organisation of type I synthetases from other eucaryotic taxa differ from this (Wakil et al. 1983). To date, the multifunctional *FAS* genes of *Saccharomyces cerevisiae* (M. Schweizer et al. 1986; Chirala et al. 1987; E. Schweizer et al. 1987; Mohamed et al. 1988), *Penicillium patulum* (Wiesner et al. 1988), rat (M. Schweizer et al. 1989; Amy et al. 1989) and chicken (Yuan et al. 1988) have been cloned and sequenced. As is evident from these studies the sequences of isofunctional domains in different FAS enzymes are clearly similar, although the extent of sequence conservation is often very low (Beck et al. 1990). On the other hand, the sequential order of catalytic domains along the multifunctional FAS chains is comparable only among related species such as yeast and *Penicillium* (Wiesner et al. 1988) while the animal and fungal *FAS* genes have very different structures (M. Schweizer et al. 1989). The similarity of the *Yarrowia lipolytica* and *S. cerevisiae FAS1* sequences as reported in this study (Figs. 1 and 2) corroborates the above conclusions.

The complete nucleotide sequences of the *S. cerevisiae FAS1* and *FAS2* genes were first reported from our laboratory (M. Schweizer et al. 1986). Subsequent reports from Chirala et al. (1987) and from Mohamed et al. (1988) essentially confirmed our data but came to different conclusions regarding the *FAS1* translational termination site. While the *FAS1* open reading frame was originally proposed to end at position 7002 of the sequence shown in Fig. 1, Chirala et al. (1987) postulated that the stop codon is located at position 7409. Consequently, the corresponding gene products differed by 135 amino acids and 14947 Da molecular weight. This discrepancy prompted us to re-investigate the C-terminal sequence of the *S. cerevisiae FAS1* gene. These studies were complemented by *FAS1* sequence data of another yeast, *Y. lipolytica,* which were obtained in our laboratory at the same time.

Sequencing of the 3′-terminal portion of *S. cerevisiae FAS1* was performed using appropriate genomic and cDNA clones (Fig. 3). The latter allowed us to localize the transcriptional termination/polyadenylation site at

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1    ....................CACCGTGCGCAGTGGAATTGACTATCAGGCCCAAATATTCAATATACGATCGCCATTATAACAACGAAATCGAAACCCT
80   TTTCACCTTCGAAAACTTCGGCGTGAACAGGGGCGATGACCTGGTAAACAATTGTAACGAAGCACTAGCCGTATGCATGGACCTGCACGGTGAGGACGTA
180  CAAGATCAAGACCAGGAACAATACCAAGATCCAAGCATGGCGTTTGAGGGTGCGCAAGATCTCAACGCCACGTATTCTGGGCTTGGAGACACCCTTCACG
280  GGCCGCCCGTGTATCAGAACGACGGGCTGGCAGACGATCTGGATGGCGACCTCGTTATGGACAGCGTGGTCTCTAGGGGTGGTCCAGAAGCAAGTATGTC

1    ...........ctgcagcagaagctaagtttggggaaagcatgggagaaatgttgaatgttgagctagttgggctgtactgggttccgtcactgagccg
380  TATGGAGTTCTACGCAAATCAAAATCTTGCTGGCAGAAAGAACTCCAGAGACAATGAATGAACAACATCTATTATGGGAACATCCCGCTGTACTATGCGG

89   ggctgacatataagaagtctcctgtagtgagatggtttggcaatcgaggcgaaccccattatttgat.ttggtgagttttgctacaggaaacagcgcgg
480  TCTCGTCCTCTACGAATATGGCTATTTGCCTTCGTATATACCTTTCTATACCAAGTAATGAATGTCTTGAGGGCCCGTATGGCCGCGCGAAGGCTTAGTT

188  ccaattgagggcgtgaggcaaccacaacaggagcagggcgatatggagctattgattgtgaacggagaaatacgacactggctgggtggccaccacatt
580  AAGATGTTTCAGCAAACGGCAGCATGTGAAAAAACCCGTAGAAGGTCCGCATCAGCCTTCCATGCCCGTGCACCCACGGCTCCTCGGAGGCCGGGTTATA

288  tgaggggggaaatggaaagagagacgacagattggacttggctgattgggcttgggtgaagatgccgtggaactggaaataccgccattcgacgcctggg
680  GCAGCGTCCGCCGCATCACGATACACGAGGTGCAGGCACGGTTCACTACTCCCCTGGCCTCCAACAAACGACGGCCAAAAACTTCACATGCCGCCCAGCC

388  ccgcctcatccaccaccatcacattggtctgtttcactctattcgaaaaagtgttcggattaattaaggataaacgggatcagcctttttttttcgtgt
780  AAGCATAATTACGCAACAGC.GATCTTTCCGTCGCACAAGTTAAAAGAAATTGTT...GAAAAATACAAATAATCGCGAACAATACGTTGTTGCTATTTA

488  gttcgtgagagaacagacatgtgttgcggagccacaacagagcacgctaccggccgttacactacttgcttgtggcggttacatgagcatcaagccccaa
876  ACGCTTTTGGTCTGACAGTAAGTGTGCCTTTCCCAATCACCGAAAAGTGTTGAACGATTCACTGCGCACAATAATCAGAGATTACAGTCGGCATTTTGGCA

588  ttgtccagaatgagatctatccagtggtggtgcttactggctcccgtttcatgtctcacctgtctgctttgactcgaaatactgcgcagatgctacgcttt
976  TT.TTTGGCATACTTTTTATCGATTGAACCATCTTCTCCAAACACTTTTCCTTTTTCCTTCTATTCTGCAGGACCAACTAAAACTGGGTATATATATCAT

688  caagtatggcactcacagtccctctctaaagtgat....gatacaacgacctcccctgtttttttcttcttcccctcatcaatattcccgcgtctttgct
975  TATCTATATATATAAACGGCTTTCAACAAAGTTATAGGGGAAAACTAAAAATATAAGAAAAAAAAAGGTATTGATTGATAAGGAAAAAGAACCAAGGGAA

784  ctcccccaaagggttataagttaagctatagactctcttgggccaacgctgcactcagccaagcagatcacccctttgcctctccacatgatacatgagt
1175 AAATATAAAAAAGTACATTGGGCCTTTTCATACTTGTTATCACTTACATTACAAAGAAGAACAAACAACTTTTTTAAACGAATTTTCTTTCTTCCTTTTT

884  gatctcgacgaaacacctactaaccacagctc.........tgattccggtttggcgatttcccatttaattactaatctacaaccacacgcaactacaa
1275 CAATTTATTAATTCTTTTTTTTCCATACAATTCAAGGTCAAATATATTCTTATATGCTCTTTGAATATTTCTGAAAAATATATAAAGAAAAGAAACTACAA

975  tggtgagtatcgaccgaagcaggatgatctctacatgagatatgcaacgcgtacgtgattcaattgatcctaacacagtaccctaccacaggtgtcaaca
1375 ....GAACATCATCCGGAAAATCAGATTATAGACTAGGATTCCGCTCTTTTTAGTATATTTATT.........CGCCACACCTAACTGCTCTATTATTCG

1075 ccccccatgagcgccgcctcattaagaccactggtgctatcgcacggccaaactgagcactcgctgctggtgcccacctctctgtacatcaactgcacca
1462 CTCATTATGGACGCTTACTCCACAAGACCATTAACCCTATCTCACGGTTCTTTAGAGCACGTGCTTCTGGTACCAACCGCTTCATTTTTCATTGCTTCGC

1175 cgctccgagaccagttctacgcctctctacctccagccactgaagacaaggccgacgatgatgagccctctctccacagagcttctagctgccttcct
1562 AATTACAAGAACAATTTAATAAAATTTTGCCCGAACCCACTGAAGGGTTTGCTGCAGATGACGAGCCTACCACACCTGCTGAACTAGTGGGGAAATTCCT

1275 gggat...ttactgccaagaccgtcgaggaagagcccggaccatacgacgacgttctctctctcgtgcttaacgagtttgagacccggtacttgcgaggt
1662 TGGCTACGTATCTTCTCTAGTCGAACCTTCCAAGGTCGGTCAATTCGATCAGGTCTTGAACCTTTGCTTAACAGAATTTGAAAACTGTTATTTAGAAGGC

1372 aacgacatccacgctgtggcctcctccttgttacaagacgaggacgtgcctaccaccgttggtaagatcaagagggtgattcgagcctactacgccgcac
1762 AATGACATTCACGCCTTGGCTGCTAAACTATTACAGGAAAACGAC......ACAACTTTAGTGAAGACTAAAGAACTAATTAAAAATTATATTACCGCCA

1472 gaattgcctgcaaccggcccat...caaggcccactcgtcggctctgttccgagccgcatctgaagactcggacaacgtctctctgtacgccatcttcgg
1856 GAATAATGGCTAAGAGACCATTTGACAAAAAATCCAACTCTGCTCTTTTTAGGGCC......GTCGGCGAGGGTAACGCACAATTGGTAGCCATTTTCGG

1569 tggccagggaaacaccgaggactactttgaggaactgcgggagatttacgacatctaccaggggctggtcggcgacttcattcgggaatgtggagcccag
1950 TGGTCAAGGTAACACCGACGACTACTTTGAAGAATTGCGTGATCTATATCAAACTTATCATGTCTTAGTGGGAGATTTAATCAAGTTCTTCGCTGAAACT

1669 cttctggcgctgtctcgagatcacattgctgctgagaaaatttataccaagggctttgatatcgtcaagtggctggaacaccccgagaccatccccgact
2050 TTAAGTGAACTGATTAGAACTACTTTAGATGCTGAAAAAGTCTTTACTCAAGGTTTAAACATATTGGAATGGTTGGAGAACCCTTCAAATACCCCAGACA

1769 ttgagtacctaattctgctcccatctctgtacccatcatcggtgttatccagctggcacactacgctgtcacctgtcgagttttgggtcttaatcctgg
2150 AGGACTATTTACTTTCCATTCCAATTTCATGCCCCTTAATTGGTGTCATTCAATTGGCTCACTACGTAGTTACTGCCAAGCTTTTGGGTTTCACTCCAGG

1869 ccaggtccgagacaacctcaagggtgccactggccattctcagggtctgatcaccgcaattgccatctctgcctccgactcgtgggacgagttctataac
2250 TGAGTTAAGATCTTACTTAAAAGGTGCTACAGGTCACTCTCAAGGTTTGGTTACTGCTGTCGCCATAGCTGAGACGGATTCCTGGGAATCCTTCTTCGTC

1969 tctgcctctcgaattctcaagatcttcttcttcatcggtgtccgtgtccaacaggcttacccctccactttcctgcctccctccactctggaagacagtg
2350 TCCGTAAGAAAAGCAATTACTGTATTATTCTTCATCGGTGTTCGTTGTTACGAAGCATACCCAAACACTTCCCTACCACCATCCATCTTTGGAAGATTCCT

2069 tcaagcagggtgagggcaagcccactcccatgctgtccatccgagacctgtctctcaaccaggttcaggagttcgtcgatgccaccaacttgcattgcc
2450 TGGAAAACAATGAAGGTGTTCCATCTCCAATGTTGTCCATTTCCAATCTAACTCAAGAACAAGTTCAAGACTATGTAAATAAGACTAACTCTCATTTGCC

2169 cgaagataagcagatcgtcgtgtctctgatcaatggtcctcgaaacgttgtcgttactggccccccccagtctctgtatggtctgtgtcttgtgcttcga
2550 AGCTGGTAAACAAGTTGAAATTTCTCTAGTCAATGGTGCGAAGAATCTAGTCGTATCGGGCCCACCACAATCATTATATGGTTTAAACTTGACTTTAAGA

2269 aaacagaaggccgagaccggtctggaccagagccgagtgccccacagtcagcgaaagctcaaattcacacatcgtttcctgcccatcacctctcctttcc
2650 AAGGCCAAGGCCCCATCTGGACTGGATCAATCAAGAATCCCATTCAGCGAAAGAAAATTGAAGTTCTCCAATAGGTTCTTACCTGTTGCATCACCATTCC

2369 actcgtacctgctggaagaagagcacggatctgatcatcaacgacctggagtcttccggtgtggagtttgtgtcctccgagctcaaggtgcctgtttacga
2750 ATTCCCATCTATTGGTTCCAGCTTCAGATTTGATTAACAAAGACTTAGTCAAAAACAATGTCAGCTTTAACGCTAAAGATATTCAAATCCCCGTTTACGA

2469 cacctttgatggctccgtgctgtctcagctacccaaggggtatcgtcagccgtctggtcaacctcatcactcatctgcccgtcaagtgggagaagccact
2850 CACTTTTGATGGTTCAGATCTAAGAGTCCTTTCAGGTTCCATTTCCGAGAGAATCGTCGACTGCATCATTAGATTACCTGTCAAATGGGAAACTACTACA
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2569 cagtttcaggcctcccacattgtggactttggtcccggtggcgcttctggtcttggtctgttgaccacaaggaacaaggatggaactggagtgcgaacta
2950 CAATTCAAAGCCACCCACATATTAGACTTTGGTCCAGGTGGAGCTTCCGGTTTAGGTGTTTTAACCCATCGTAATAAAGATGGTACTGGTGTTCGTGTTA

2669 ttcttgctggt......gtcattgaccagcccctcgagttcggcttcaagcaggagctgtttgaccgacaggagtcgtccattgtttttgctcaaaactg
3050 TCGTTGCCGGTACTCTCGACATTAACCCAGATGATGATTACGGATTCAAGCAAGAAATCTTTGATGTTACTAGTAATGGTTTGAAGAAAAATCCAAACTG

2763 ggccaaggagttttctcccaagctcgtcaagatctcctccaccaacgaggtctatgtcgacaccaaattctctcgtctgactggccgagcccccatcatg
3150 GTTGGAAGAATACCATCCAAAATTAATTAAGAACAAATCAGGCA...AAATTTTTGTCGAAACAAAATTTTCTAAATTAATCGGTAGACCACCTTTATTG

2863 gtcgctggtatgacccctaccactgtcaaccccaaatttgtggctgccactatgaactccggctaccacatcgagcttggtggtggaggctactttgccc
3247 GTTCCTGGTATGACACCATGTACTGTTTCTCCAGATTTCGTAGCTGCTACCACAAATGCTGGTTATACCATTGAGTTGGCCGGTGGTGGTTACTTTTCCG

2963 ccggtatgatgaccaaggcccttgaacacattgagaagaacactcctcccggatccggtatcaccatcaacctgatctacgtcaaccctcgactgattca
3347 CAGCAGGTATGACCGCCGCTATTGATTCTGTGGTTTCTCAGATAGAAAAGGGTAGTACCTTCGGTATCAACTTGATCTACGTCAATCCATTTATGTTACA

3063 atggggtattcctctgattcaggagcttcgacagaagggtttccccattgaaggtctcaccattggtgccggtgtgccctctctggaggttgctaacgag
3447 ATGGGGTATTCCATTAATCAAGGAACTAAGAAGCAAAGGTTATCCAATTCAATTCTTGACCATTGGTGCTGGTGTCCCATCATTGGAAGTTGCTAGTGAA

3163 tggattcaggatctgggcgtcaagcacatcgccttcaagcctggatccatcgaggccatctcctcggtgattcgaatcgccaaggccaacccagacttcc
3547 TACATAGAGACATTAGGTTTGAAGTACTTGGGTTTGAAACCAGGTTCCATTGATGCTATTTCGCAAGTTATAAACATTGCTAAAGCACATCCAAACTTCC

3363 ctatcatccttcagtggaccggaggtcgaggaggaggacatcattcgtttgaggacttccacgctcccattctgcagatgtactccaagatccgacgatg
3647 CAATAGCTTTACAATGGACCGGTGGTAGAGGTGGTGGTCATCATTCTTTCGAAGATGCCCACACTCCAATGTTACAAATGTACTCCAAGATTAGAAGACA

3363 cagcaacattgtgctgattgccggatctggtttcggtgcttctaccgactcctacccatacctcactggttcatggtcccgagactttgactaccctccc
3747 TCCAAACATTATGTTGATATTCGGTTCTGGTTTCGGTTCTGCTGATGACACTTACCCATACTTAACCGGTGAATGGTCCACAAAATTCGATTATCCACCA

3463 atgccctttgacggtatcctggttggttctcgagtcatggttgccaaggaggctttcacttctctgggagccaagcagctcattgttgactctccgggtg
3847 ATGCCATTCGATGGTTTCCTATTTGGTTCGAGGGTCATGATTGCTAAGGAAGTTAAAACTTCTCCTGATGCTAAGAAGTGTATTGCTGCTTGTACTGGTG

3563 ttgaggattctgagtgggagaaaacctacgacaagcccactggtggcgtcatcaccgttctctccgagatgggtgagcctatccacaagctcgccactcg
3947 TTCCTGATGATAAATGGGAACAAACCTACAAGAAGCCAACTGGTGGTATTGTCACTGTTCGCTCTGAAATGGGTGAACCAATTCACAAAATTGCCACTCG

3663 aggtgtgctcttctggcacgagatggacaagaccgtgttctccctgcccaagaagaagcgtctggaagtgctcaagtccaagcgagcctacatcatcaag
4047 TGGTGTTATGCTATGGAAGGAATTCGACGAAACCATCTTCAACTTACCAAAGAATAAGTTGGTACCAACTTTGGAAGCAAAGAGAGATTACATTATCTCA

3763 cgtctcaacgacgacttccagaagacttggtttgccaagaacgcccagggacaggtgtgtgatctcgaagacctcacctacgcggaggtcatccagcgac
4147 AGATTGAACGCCGATTTCCAAAAACCATGGTTTGC...TACCGTCAACGGTCAAGCCCGTGACCTAGCCACAATGACATACGAAGAAGTTGCAAAGAGAT

3863 ttgttgacctcatgtacgtgaagaaggaaagccgatggatcgatgtcactctccgaaatcttgccggcactttcattcgacgagttgaggagcgattctc
4244 TGGTGGAATTAATGTTCATCAGATCTACCAACTCTTGGTTTGATGTCACATGGAGAACCTTTACTGGTGATTTCCTACGTCGTGTCGAAGAACGTTT...

3963 caccgagacaggtgcctcttctgtgttgcagagcttttccgagctggattccgagcccgagaaggttgtcgagcgggtgtttgagctcttccctgcctct
4341 CACTAAAAGTAAGACATTGTCTTTAATCCAATCCTATTCTCTACTAGA...CAAGCCTGATGAAGCTATTGAAAAAGTATTTAATGCTTATCCTGCCGCT

4063 actacccagatcatcaacgctcaagacaaggaccacttcctcatgctgtgtctcaaccccatgcagaagcccgtgcccttcatccctgttctggatgaca
4438 AGGGAACAGTTCTTGAATGCGCAAGATATTGATCACTTTTTGAGCATGTGTCAAAATCCAATGCAAAAACCAGTGCCTTTTGTTCCAGTTTTGGATCGTA

4163 actttgagttcttcttcaagaaggactctctgtggcagtgcgaggacctcgcagctgttgtggacgaagacgttggacgaatctgtattcttcagggtcc
4538 GATTCGAGATTTTTTCAAAAAAGATTCGTTATGGCAATCTGAGCAATTGGAAGCCGTCGTCGACCAAGACGTTCAAAGAACATGTATCCTACATGGACC

4263 cgttgctgtcaagcactccaagattgtcaacgagcccgtcaaggagattctcgactccatgcacgaaggtcacatcaagcagctgcttgaggatggcgag
4638 TGTTGCAGCACAATTCACTAAAGTCATCGATGAACCAATTAAGAGCATTATGGATGGTATTCACGATGGTCACATCAAAAAGTTACT...ACATCAATAT

4363 tacgctggcaacatggccaacatcccccaggtcgaatgctttggtgg...aaagcctgctcagaacttcggtgacgttgctctcgactctgtcatggttc
4735 TACGGTGACGATGAGTCAAAGATTCCAGCAGTTGAGTACTTTGGTGGTGAAAGCCCTGTAGACGTACAAAGTCAAGTTGATTCTTCCTCTGTATCTGAAG

4460 ttgatgacctcaacaagaccgtgttcaagattgagaccggcacctctgctctgccttctgctgcagattggttctctctgctggccggtgacaagaactc
4835 ACTCAGCTGTTTTTAAGGCAACATCCTCTACTGA........................TGAAGAAAGCTGGTTTAAGGCTTTGGCGGGATCCGAAATTAA

4560 ttggcgacaggtcttcctgtccactgacaccattgtgcagaccaccaagatgatctccaaccctctgcatcgacttctggagcccatcgcaggtttgcag
4911 CTGGAGACATGCAAGTTTCTTATGTTCCTTTATCACTCAAGATAAAATGTTTGTTTCTAACCCAATTAGAAAAGTTTTCAAGCCAAGCCAAGGAATGGTT

4660 gttgagattgagcaccctgatgagcccgagaacaccgtcatctctgctttcgagcccatcaacggcaaggtcaccaaggtgctggagctgcgaaagggtg
5011 GTTGAGTTTTCCAACGGCAATACTTCTTCAAAGACTGTTGTCACTCTTTCAGAACCTGTTCAAGGTGAATTGAAACCAACTGTTATTTTGAAGTTGTTGA

4760 ccggagatggcatttcgctgcagctgatcgaagcgcgtggcgttgaccgagtccccgttgctcttcctctggaattcaagtaccagccccagattggcta
5111 AGGAGAACATAATCCAAATGGAAATGATTGAGAACAGAACTATGGATGGTAAGCCCGTCAGCTTGCCATTGTTGTACAACTTCAACCCAGATAATGGTTT

4860 cgctcccattgttgaggttatgaccgacaggaacacccgaatcaaggagttctactggaagctgtggtttggccaggactccaagtttgagattgacacc
5211 TGCTCCAATCTCTGAAGTTATGGAGGACAGAAACCAAAGAATTAAGGAAATGTACTGGAAATTATGGATTGATGAGCCTTTCAATTTGGACTTTGACCC.

4960 gacatcaccgaggaaatcattggcgatgacgttaccatctctggcaaggccattgccgactttgtccacgctgttggcaacaagggcgaggcctttgttg
5310 .....AAGAGATGTCATTAAGGGCAAAGATTTCGAGATCACCGCTAAAGAAGTTTATGACTTTACACACGCTGTTGGAAACAATTGTGAAGACTTCGTT.

5060 gtcgatctacctctgctggtactgtcttcgctcccatggactttgccattgttttgggctggaaggccattatcaaggcaatctttccccgagcaattga
5404 .....TCTAGACCTGATAGAACGATGTTGGCCCCAATGGACTTTGCTATTGTTGTCGGATTGAGAGGCATCATCAAGGCCATTTTCCCTAATACGGTCGA

5160 tgctgacattctgcgtctggtacatctgtccaacggcttcaagatgatgcctggcgccgaccctctgcagatgggtgatgttgtttccgccactgccaag
5499 TGGTGACTTATTGAAGTTGGTTCATTTGTCTAACGGCTACAAGATGATTCCTGGCGCTAAGCCACTGCAAGTTGGTGATGTTGTTTCAACTACTGCTGTT
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Fig. 1 (continuation, see page 312)

Fig. 1. (continued)

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5260 atcgacactgtcaagaactccgctaccggcaagactgttgctgttcgaggtcttctcacccgagacggcaagcctgtcatggaggttgtttccgaattct
5599 ATTGAATCTGTCGTCAACCAACCTACAGGAAAGATTGTCGATGTGGTAGGTACATTATCGAGAAATGGCAAGCCTGTCATGGAAGTCACCTCCTCATTCT

5360 tctaccgaggcgaattctccgacttccagaacactttttgagcgacgagaggaggtacccatgcaactgaccctcaaggacgccaaggccgtggccattct
5699 TCTACAGAGGCAACTATACTGACTTTGAAAACACTTTCCAAAAGACTGTTGAACCTGTTTATCAAATGCACATCAAAACTTCTAAAGATATAGCTGTCTT

5460 ctgctccaaggagtggtttgagtacaatggcgacgataccaaggacctcgagggcaagaccattgtgttccgaaactcgtcattcatcaagtacaagaat
5799 GCGCTCTAAGGAGTGGTTCCAAT...TGGACGATGAAGACTTCGATCTGTTAAACAAAACTTTGACTTTCGAAACTGAAACTGAAGTTACTTTCAAGAAT

5560 gagaccgtcttctcttctgtgcacaccaccggtaaggtattgatggagctgccctccaaggaggtcattgagattgccactgttaactaccaggctggcg
5896 GCTAACATCTTCTCTTCAGTGAAATGTTTTGGCCCAATTAAAGTTGAATTGCCAACCAAAGAAACCGTGGAGATCGGTATTGTCGATTACGAAGCCGGTG

5660 agtctcatggcaatcccgtcattgattacctggagcgaaatggaaccaccattgagcagcctgttgagtttgagaagcccatccctctgtccaaggcaga
5996 CCTCTCACGGTAACCCTGTTGTTGATTTCTTGAAGAGAAACGGTTCCACATTGGAACAAAAGGTCAATCTAGAAAATCCTATTC...........CAAT

5760 tgatcttctctccttcaaggctccttcttccaacgagccctacgctggtgtgtccggtgactacaatcccatccacgtgtctcgagcctttgcttcctat
6084 TGCAGTACTTGATTCGTACACTCCAAGTACCAACGAACCATACGCTAGAGTTTCTGGTCATTTGAATCCAATTCACGTTTCACGTCATTTTGCCTCTTAC

5860 gcatcccttcctggaaccatcacccagggtatgtactcttctgctgctgttcgatctctgattgaggtctgggctgccgagaacaatgtgtctcgagttc
6184 GCAAACTTGCCAGGTACTATCACGCACGGTATGTTTTCTTCTGCTTCCGTCCGTGCTTTGATTGAAAACTGGGCTGCTGACAGTGTTTCATCCAGGGTAC

5960 gagccttctcctgtcagttccagggcatggttttgcccaacgacgagattgtgactcgactggagcacgttggcatgatcaacggtcgaaagatcatcaa
6284 GTGGCTACACTTGTCAATTTGTTGACATGGTTTTGCCTAACACTGCTTTGAAAACATCGATTCAACATGTTGGTATGATCAATGGTAGAAAATTGATAAA

6060 ggttacctccaccaaccgggagaccgaggctgttgttctgtctggcgaggctgaggtcgagcagcccatctccacctttgtctttactggccagggctct
6384 GTTTGAAACTAGAAA...TGAAGATGACGTTGTAGTTTTGACTGGTGAAGCCGAAATTGAACAACCTGGTACTACCTTCGTTTTCACTGGTCAAGGTTCA

6160 caggagcagggcatgggtatggacctgtacgcctcttccgaggtggccaagaaggtctgggacaaggctgacgagcacttcttgcagaactacggtttct
6481 CAAGAACAAGGTATGGGTATGGACTTATACAAAACTTCTAAAGCTGCTCAAGATGTTTGGAATAGAGCTGACAACCATTTCAAGGACACTTATGGTTTCT

6260 ccatcatcaagatcgttgtggagaaccccaaggagctggatattcatttggaggccccaagggtaagaagatccgagacaactatatctctatgatgtt
6581 CTATCTTAGACATTGTCATTAACAACCCAGTTAACTTAACAATTCACTTCGGTGGTGAAAAGGGTAAGAGGATCAGAGAAAACTATTCTGCTATGATCTT

6360 cgagaccattgatga.........gaagaccggcaacctcatttccgagaagatcttcaaggagattgacgagacaaccgactctttcaccttcaagtcc
6681 TGAGACTATCGTGGATGGAAAATTGAAGACTGAAAAAATTTTCAAGGAAATTAATGAGCACAGTACTTCTTACACATTTAGATCTGAAAAAGGTTTATTG

6451 cccaccggtctgctttctgctacccagttcactcagcccgctctgaccctcatggagaaggcgtcctttgaggacatgaaggctaagggtcttgtccccg
6781 TCTGCTACTCAATTTACACAACCAGCTTTAACTTTGATGGAAAAAGCTGCTTTCGAAGACTTGAAATCTAAAGGTTTGATCCCAGCCGATGCTACTTTTG

6551 tggatgcaacctttgctggtcactcccttggtgagtactccgctcttgct.tctcttggtgatgtcatgcccatcgagtctcttgttgatgtcgtcttct
6881 CTGGTCACTCTTTAGGTGAGTATGCTGCTTTGGCCTCTTTGGCTGATGTTATGTCTATCGAATCTTTAGTTGAAGTTGTGTTCTACAGAGGTATGACTAT

6651 ac.....cgaggtatgactatgcaggttgctgttccccgagatgcccagggtcggtccaattacggtatgtgcgctg..tcaacccctctcgaatctcta
6981 GCAAGTTGCTGTTCCAAGAGATGAGTTGGGCAGATCCAACTATGGTATGATTGCCATTAACCCAGGTAGAGTCGCTGCATCATTCTCTCAAGAAGCTTTG

6744 ccacct.................tcaacgacgctgctcttcggtttgtcgttgaccatatctccgagcagaccaagtggctgcttgagattgtcaactac
7081 CAATATGTTGTTGAGAGAGTTGGTAAGAGAACCGGCTGGTTGGTTGAAATCGTCAACTACAACGTTGAAAACCAACAATATGTTGCAGCTGGTGATCTAA

6827 aacgttgagaactctcagtacgtgactgccggtgacctgcgagctctcgacaccctcaccaatgtgctcaacgtgctcaaactcgagaagatcaacattg
7181 GAGCTTTAGACACCGTTACCAATGTTCTAAACTTCATCAAATTACAAAAAATTGATATTATTGAACTACAAAAGTCCTTATCTTTGGAAGAAGTTGAAGG

6927 acaagctgctcgagtctctgcctctggagaaggtcaaggagcacctttctgagatcgtcaccgaggtggccaagaagtccgttgctaagcctcagcccat
7281 TCATTTGTTTGAGATCATTGACGAAGCTTCCAAGAAATCTGCTGTCAAGCCTCGCCCACTTAAATTGGAGAGAGGTTTTGCTTGTATCCCATTAGTTGGT

7027 tgagctggaacgaggctttgc.....cgtgatccctctcaagggcatctctgtgcctttccactcttcgtacctgcgaaatggtgtcaagcccttccaaa
7381 ATTTCTGTTCCTTTCCATTCCACCTACTTGATGAATGGTGTTAAACCATTCAAGAGTTTCTTGAAGAAGAATATCATAAAAGAAAATGTGAAGGTTGCTA

7122 acttcctggtgaagaaggtgcccaagaacgctgtcaaacctgccaacctcattggcaagtacatccccaacctcactgccaagcc...ctttgagatcac
7481 GATTGGCCGGAAAGTACATTCCAAACTTGACTGCAAAACCATTCCAGGTTACTAAGGAATATTTCCAGGACGTTTATGATTTGACTGGCTCCGAACCTAT

7218 caaggagtactttgaagaggtttacaagctcaccggttccgagaaggtcaagagcatcatcgacaactgggagtcttatgagtccaagcagtaagttgct
7581 CAAGGAAATCATCGACAACTGGGAAAAGTATGAACAATCCTAATTTCTTAAGTGATTATATAACCGTAAGAAATATT........TAACTTTGAAACTCC

7318 ggatctctcgtggaggatttagaaggaatattagaggagattaaaggaggattttgtttatatatgtttaatggattattgttattgaccctcattgt
7673 TGTATACTAATGTTTAATATAGCTGGCTTATGATTTAGTTCTCTTCTCCTATTATAAATAGATACATTGATTAGGTATTTTTATAATATACTTGGGATT

7418 atttactgcactatgtatttacgagtacaatggttgctacagtacatactgtaca.atggtctatggcagcttgatgctgtggttgttttacaacttcgc
7773 AAGAGATGCTATATGAATTTTTTTTCCGCCGCAAGCCCTCGCTAGGGCGGGGCAGATGCTGAAGAAAAAATTTCTGTTCCATTGGGTTATGTTTAAAA

7517 tttaaccgtcttcttcaat..cgcatagtcttcttcagcagcgtcttgtgtcgac.............................................
7873 ATCAACGATATTCGAACATAATCGATGACCTTGATGATTAGCGAAGTTCTGCTCTAAAGAAATTAGCTTTAAAAACAGCTCCATTATTAGTGTAAACTGC

7973 TACTTCAACTCTTTACTCGAAAAGTTGAAACAAGTGTCTATTCCGCACATCTCTGCAATAACCGAACCTTCACGATTTAGCTACAATCCCACATCTGCAG
8073 ATTCTACCGTTTAATAGTCTTAATTTGAAGAGAAATAAAAATGCGTAAGTGTAAAATTTTTGTTGGTAACTCTCACCCAGAGTTGGGTAATATGGTTTGC
8173 CAAAGATTAGGTATCGAACCAGCTCCATGTACATTAAAAAAATTTGCAAATGGTGAAACGTCAGTTCAAATCGGTGTATCTGTTCGTGACGAAGATGTGT
8273 ATGTCATTCAATCTGGTTCTCCATCCATAAATGATGACATTATGGAACTGTTGATTTTAGTTTCTGCCTGTAGGGGCGGATCTGCTAGGAAAATTACAGC
8373 AGTCATTCCTCAATTTCCTTACTCTAAACAATGTAAAATGAAGAGACACAGAGGCGCTATTACTGCAAGGATGTTGCCAATCTGTTGGTCATGGCTGGC
8473 GCTGATCATGTTGTGTCTATGGACCTTCATGCTTCTCAAATGCAGGGGTTTTTCACCAACCAGTCGATAACCTATACGGGGGCC
```

Fig. 2

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   1 MSAASLRPLVLSHGQTEHSLLVPTSLYINCTTLRDQFYASLPPATEDKADDDEPSSSTELLAAFLGFTAKTVE.EEPGPYDDVLSLVLNEFETRYLRGND
   1 MDAYSTRPLTLSHGSLEHVLLVPTASFFIASQLQEQFNKILPEPTEGFAADDEPTTPAELVGKFLGYVSSLVEPSKVGQFDQVLNLCLTEFENCYLEGND

 100 IHAVASSLLQDEDVPTTVGKIKRVIRAYYAARIACNRPIKAHS.SALFRAASEDSDNVSLYAIFGGQGNTEDYFEELREIYDIYQGLVGDFIRECGAQLL
 101 IHALAAKLLQEND..TTLVKTKELIKNYITARIMAKRPFDKKSNSALFRAVGE..GNAQLVAIFGGQGNTDDYFEELRDLYQTYHVLVGDLIKFFAETLS

 199 ALSRDHIAAEKIYTKGFDIVKWLEHPETIPDFEYLISAPISVPIIGVIQLAHYAVTCRVLGLNPGQVRDNLKGATGHSQGLITAIAISASDSWDEFYNSA
 197 ELIRTTLDAEKVFTQGLNILEWLENPSNTPDKDYLLSIPISCPLIGVIQLAHYVVTAKLLGFTPGELRSYLKGATGHSQGLVTAVAIAETDSWESFFVSV

 299 SRILKIFFFIGVRVQQAYPSTFLPPSTLEDSVKQGEGKPTPMLSIRDLSLNQVQEFVDATNLHLPEDKQIVVSLINGPRNVVVTGPPQSLYGLCLVLRKQ
 297 RKAITVLFFIGVRCYEAYPNTSLPPSILEDSLENNEGVPSPMLSISNLTQEQVQDYVNKTNSHLPAGKQVEISLVNGAKNLVVSGPPQSLYGLNLTLRKA

 399 KAETGLDQSRVPHSQRKLKFTHRFLPITSPFHSYLLEKSTDLIINDLESSGVEFVSSELKVPVYDTFDGSVLSQLPKGIVSRLVNLITHLPVKWEKATQF
 397 KAPSGLDQSRIPFSERKLKFSNRFLPVASPFHSHLLVPASDLINKDLVKNNVSFNAKDIQIPVYDTFDGSDLRVLSGSISERIVDCIIRLPVKWETTTQF

 499 QASHIVDFGPGGASGLGLLTTRNKDGTGVRTILAGVID..QPLEFGFKQELFDRQESSIVFAQNWAKEFSPKLVKISSTNEVYVDTKFSRLTGRAPIMVA
 497 KATHILDFGPGGASGLGVLTHRNKDGTGVRVIVAGTLDINPDDDYGFKQEIFDVTSNGLKKNPNWLEEYHPKLIKNKSGK.IFVETKFSKLIGRPPLLVP

 597 GMTPTTVNPKFVAATMNSGYHIELGGGGYFAPGMMTKALEHIEKNTPPGSGITINLIYVNPRLIQWGIPLIQELRQKGFPIEGLTIGAGVPSLEVANEWI
 596 GMTPCTVSPDFVAATTNAGYTIELAGGGYFSAAGMTAAIDSVVSQIEKGSTFGINLIYVNPFMLQWGIPLIKELRSKGYPIQFLTIGAGVPSLEVASEYI

 697 QDLGVKHIAFKPGSIEAISSVIRIAKANPDFPIILQWTGGRGGGHHSFEDFHAPILQMYSKIRRCSNIVLIAGSGFGASTDSYPYLTGSWSRDFDYPPMP
 696 ETLGLKYLGLKPGSIDAISQVINIAKAHPNFPIALQWTGGRGGGHHSFEDAHTPMLQMYSKIRRHPNIMLIFGSGFGSADDTYPYLTGEWSTKFDYPPMP

 797 FDGILVGSRVMVAKEAFTSLGAKQLIVDSPGVEDSEWEKTYDKPTGGVITVLSEMGEPIHKLATRGVLFWHEMDKTVFSLPKKKRLEVLKSKRAYIIKRL
 796 FDGFLFGSRVMIAKEVKTSPDAKKCIAACTGVPDDKWEQTYKKPTGGIVTVRSEMGEPIHKIATRGVMLWKEFDETIFNLPKNKLVPTLEAKRDYIISRL

 897 NDDFQKTWFAKNAQGVCDLEDLTYAEVIQRLVDLMYVKKESRWIDVTLRNLAGTFIRRVEERFSTETGASSVLQSFSELDSEPEKVVERVFELFPASTT
 896 NADFQKPWFA.TVNGQARDLATMTYEEVAKRLVELMFIRSTNSWFDVTWRTFTGDFLRRVEERF.TKSKTLSLIQSYSLLD.KPDEAIEKVFNAYPAARE

 997 QIINAQDKDHFLMLCLNPMQKPVPFIPVLDDNFEFFFKKDSLWQCEDLAAVVDEDVGRICILQGPVAVKHSKIVNEPVKEILDSMHEGHIKQLLEDGEYA
 993 QFLNAQDIDHFLSMCQNPMQKPVPFVPVLDRRFEIFFKKDSLWQSEQLEAVVDQDVQRTCILHGPVAAQFTKVIDEPIKSIMDGIHDGHIKKLLHQ.YYG

1097 GNMANIPQVECFGGKPAQNFGDVALDSVMVLDDLNKTVFKIETGTSALPSAADWFSLLAGDKNSWRQVFLSTDTIVQTTKMISNPLHRLLEPIAGLQVEI
1092 DDESKIPAVEYFGGESPVD.VQSQVDSSSVSED..SAVFKATSST....DEESWFKALAGSEINWRHASFLCSFITQDKMFVSNPIRKVFKPSQGMVVEF

1197 EHPDEPENTVISAFEPINGKVTKVLELRKGAGDGISLQLIEARGVDRVPVALPLEFKYQPQIGYAPIVEVMTDRNTRIKEFYWKLWFGQDSKFEIDTDIT
1185 SNGNTSSKTVVTLSEPVQGELKPTVILKLLKENIIQMEMIENRTMDGKPVSLPLLYNFNPDNGFAPISEVMEDRNQRIKEMYWKLWI..DEPFNLDFDPR

1297 EEIIGDDVTISGKAIADFVHAVGNKGEAFVGRSTSAGTVFAPMDFAIVLGWKAIIKAIFPRAIDADILRLVHLSNGFKMMPGADPLQMGDVVSATAKIDT
1283 DVIKGKDFEITAKEVYDFTHAVGNNCEDEVSRPDR..TMLAPMDFAIVVGLRGIIKAIFPNTVDGDLLKLVHLSNGYKMIPGAKPLQVGDVVSTTAVIES

1397 VKNSATGKTVAVRGLLTRDGKPVMEVVSEFFYRGEFSDFQNTFERREEVPMQLTLKDAKAVAILCSKEWFEYNGDDTKDLEGKTIVFRNSSFIKYKNETV
1381 VVNQPTGKIVDVVGTLSRNGKPVMEVTSSFFYRGNYTDFENTFQKTVEPVYQMHIKTSKDIAVLRSKEWFQLDDEDF.DLLNKTLTFETETEVTFKNANI

1497 FSSVHTTGKVLMELPSKEVIEIATVNYQAGESHGNPVIDYLERNGTTIEQPVEFEKPIPLSKADDLLSFKAPSSNEPYAGVSGDYNPIHVSRAFASYASL
1480 FSSVKCFGPIKVELPTKETVEIGIVDYEAGASHGNPVVDFLKRNGSTLEQKVNLENPIPIAVLDSY....TPSTNEPYARVSGHLNPIHVSRHFASYANL

1597 PGTITQGMYSSAAVRSLIEVWAAENNVSRVRAFSCQFQGMVLPNDEIVTRLEHVGMINGRKIIKVTSTNRETEAVVLSGEAEVEQPISTFVFTGQGSQEQ
1576 PGTITHGMFSSASVRALIENWAADSVSSRVRGYTCQFVDMVLPNTALKTSIQHVGMINGRKLIKFETRN.EDDVVVLTGEAEIEQPVTTFVFTGQGSQEQ

1697 GMGMDLYASSEVAKKVWDKADEHFLQNYGFSIIKIVVENPKELDIHFGGPKGKKIRDNYISMMFETIDEKTGNLISEKIFKEIDETTDSFTFKSPTGLLS
1675 GMGMDLYKTSKAAQDVWNRADNHFKDTYGFSILDIVINNPVNLTIHFGGEKGKRIRENYSAMIFETIVD..GKLKTEKIFKEINEHSTSYTFRSEKGLLS

1797 ATQFTQPALTLMEKASFEDMKAKGLVPVDATFAGHSLGEYSALASLGDVMPIESLVDVVFYRGMTMQVAVPRDAQGRSNYGMCAVNPSRISTTFNDAALR
1773 ATQFTQPALTLMEKAAFEDLKSKGLIPADATFAGHSLGEYAALASLADVMSIESLVEVVFYRGMTMQVAVPRDELGRSNYGMIAINPGRVAASFSQEALQ

1897 FVVDHISEQTKWLLEIVNYNVENSQYVTAGDLRALDTLTNVLNVLKLEKINIDKLLESLPLEKVKEHLSEIVTEVAKKSVAKPQPIELERGFAVIPLKGI
1873 YVVERVGKRTGWLVEIVNYNVENQQYVAAGDLRALDTVTNVLNFIKLQKIDIIELQKSLSLEEVEGHLFEIIDEASKKSAVKPRPLKLERGFACIPLVGI

1997 SVPFHSSYLRNGVKPFONFLVKKVPKNAVKPANLIGKYIPNLTAKPFEITKEYFEEVYKLTGSEKVKSIIDNWESYESKQ*
1973 SVPFHSTYLMNGVKPFKSFLKKNIIKENVKVARLAGKYIPNLTAKPFQVTKEYFQDVYDLTGSEPIKEIIDNWEKYEQS*
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Fig. 1. Sequence comparison of the *Saccharomyces cerevisiae* (*upper case*) and *Yarrowia lipolytica* (*lower case*) *FAS1* genes. Translational start and termination sites as well as the cDNA polyadenylation site are marked by *arrows*. Presumptive transcriptional initiation and termination signals are *underlined*

Fig. 2. Comparison of the *Saccharomyces cerevisiae* (*lower line*) and *Yarrowia lipolytica* (*upper line*) FAS subunit β protein sequences

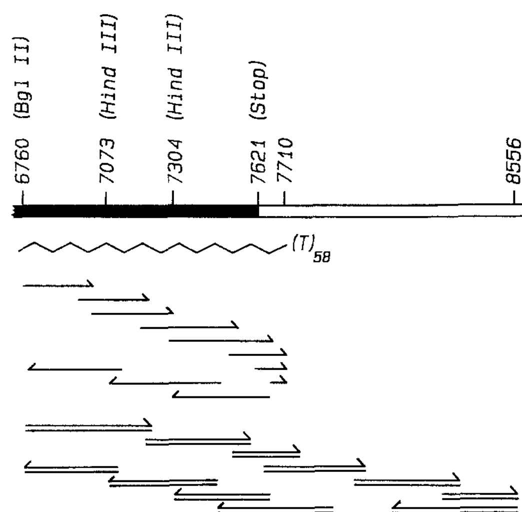

Fig. 3. Sequencing strategy of the *Saccharomyces cerevisiae FAS1* genomic (*upper bar*) and cDNA (*wavy line*) 3′ termini. *Arrows* indicate sequenced portions of the genomic (*double lines*) and cDNA (*single lines*) subclones

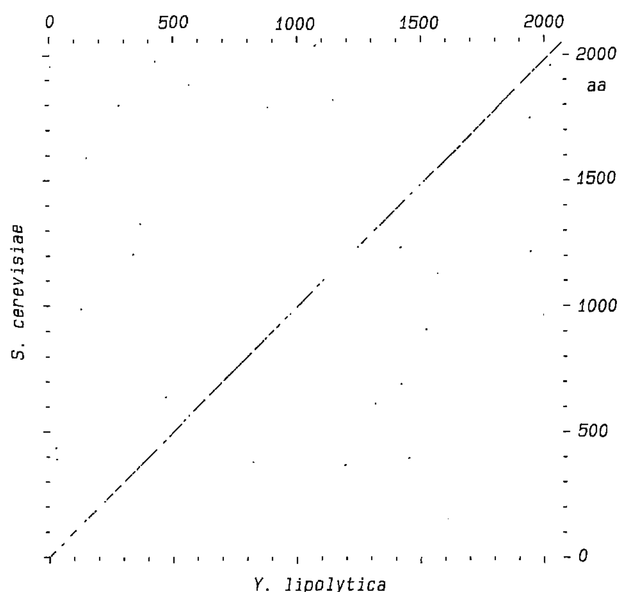

Fig. 4. Matrix comparison of the *Saccharomyces cerevisiae* and *Yarrowia lipolytica* FAS subunit β amino acid sequences. The Compare/Dotplot programs of the UWGCG software package version 6.1 were used with a window of 10 and a stringency of 5

position 7710 of the *S. cerevisiae FAS1* sequence shown in Fig. 1. The re-examined 3′-terminal sequence comprised a total of 1780 bp. Within this region, 48 individual positions were found to conflict with either one or other of the two previously published sequences. Three of these differences involve our own original data (M. Schweizer et al. 1986) while the rest referred to the sequence of Chirala et al. (1987). Most significantly, the translational stop codon is now unequivocally located at position 7621 of the *S. cerevisiae FAS1* DNA sequence (Fig. 1). This location therefore differs from both end-points previously published (positions 7002 and 7409, respectively). The correct size of the *S. cerevisiae* FAS subunit β is thus 228667 Da, corresponding to a protein of 2051 amino acids. A very similar size (2076 amino acids, 229980 Da) is derived for the *Y. lipolytica* FAS subunit β from the corresponding *FAS1* sequence data shown in Fig. 1. The pentafunctional subunit β of yeast FAS is thus distinctly larger than the trifunctional subunit α (E. Schweizer et al. 1987). By Western blot analyses using specific antibodies against the individual FAS subunits of both yeasts this conclusion was confirmed for the *Y. lipolytica* enzyme but not for *S. cerevisiae* FAS (R. Grünbein, unpublished). The same irregular mobility of subunit β is observed upon heterologous expression of *FAS1* in *Escherichia coli* cells (D. Stratmann, unpublished). It therefore appears to be an inherent characteristic of this protein rather than a consequence of post-translational degradation events.

Comparison of the *S. cerevisiae* and *Y. lipolytica FAS1* sequences reveals that both genes are co-linear in both their nucleotide and component enzyme sequences (Fig. 1 and 2). The average sequence similarities are 54% at the DNA and 58% at the protein level. This high degree of sequence conservation varies somewhat along the gene but is not restricted to distinct catalytic domains (Fig. 4). The *Y. lipolytica FAS1* sequence was determined by sequencing both strands over the entire length. The gene is considered to be intron free since it lacks the yeast specific TACTAAC box (Langford et al. 1984) and is functionally expressed in *S. cerevisiae* (R. Grünbein and W. Harrer, unpublished). Both *FAS1* genes are flanked, at comparable distances, by canonical transcriptional start and termination signals (Fig. 1). Recently, a similar colinearity was also observed for the *FAS2* genes of *S. cerevisiae* and *P. patulum* (Wiesner et al. 1988). The high degree of sequence conservation among fungal *FAS* genes appears to be correlated with the known overall structural similarity of their gene products.

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