

Cloning of two distinct copies of human phosphoribosylpyrophosphate synthetase cDNA

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Phosphoribosylpyrophosphate synthetase (PRS) catalyzes the phosphoribosylation of ribose 5-phosphate to 5-phosphoribosyl-1-pyrophosphate (PRPP), which is necessary for the *de novo* and salvage pathways of purine, pyrimidine and pyridine biosynthesis (1). In the rat, two nearly identical cDNA transcripts (PRS I and PRS II) have been cloned (2). Additionally, a human cDNA homologous to the rat PRS II cDNA has been cloned (3). We report the isolation of a human PRS cDNA homologous to rat PRS I and confirm the nucleotide sequence of an independently isolated human PRS II cDNA. Published rat cDNA sequences were used to design flanking oligonucleotide primers, and a partial length human PRS cDNA probe was generated from human lymphoblast mRNA by the polymerase chain reaction (4). Human PRS I was isolated from lymphoblast cDNA libraries cloned into lambda gt10. Human PRS II was isolated from human kidney cell cDNA libraries cloned into lambda gt10. Both human PRS I and PRS II cDNA were sequenced by the Sanger method (5).

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REFERENCES

1. Palella, T.D. and Fox, I.H. (1989) In Scriver, C.S., *et al.* (eds.), *The Metabolic Basis of Inherited Diseases*. McGraw Hill Book Co., New York, 6th edition, pp. 965-1006.
2. Taira, M., Ishijima, S., Kita, K., Yamada, K., Iizasa, T. and Tatibana, M. (1987) *J. Biol. Chem.* **262**, 14867-14872.
3. Iizasa, T., Taira, M., Shimada, H., Ishijima, S. and Tatibana, M. (1989) *FEBS Lett.*, **244**, 47-50.
4. Lee, C.C., Wu, X., Gibbs, R.A., Cook, R.G., Muzny, D.M. and Caskey, C.T. (1988) *Science* **239**, 1288-1291.
5. Sanger, F., Nicklen, S. and Coulson, A.R. (1977) *Proc. Natl. Acad. Sci. USA* **74**, 5463-5467.

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I      GACTTCGGTTCGGTCTCTGCAGCAGCCGTGATCGCTTACTGGAGTGCTTAG
II     CGCGTCGCTGCTGCTGTTGGCTCCGGCCACTCTCCGCCGCCGGCCGCCCTCGGAG
      M P M I K I F S C S S H Q D
GGTAGTGGCCAGGATGCCAATAATCAAAATCTTCAGCGGCAAGTCCACCAGGACT 43
      T T C C G C C C C C C A C T G C C C A A C A T C G T G T T T C A G C G C A G T C G C A T C A G A C C
      M P M I V L F S C S S H Q D
L S O K I A D R L G L E L E L G K V V T K
TATCTCAGAAAATTCCTGACCCCTGGGCCGGAGCTAGGCAAGGTGGTGAATAA 100
      T A T C C A G C C G T G C C A C C C C T G G C C T G G A G C T G G C A A G G T G G T T A C A A G A
L S O K I A D R L G L E L E L G K V V T K
K F S N O E T C V E I G E S V R G E D
AGTTCAGCAACCAGGAGACCTGTGTGGAAATCGGTGAAAGTGTACGTGAGAGGATG 157
      A G T T C A G C A A C C A G G A C C A G C T G G A G A T T G C T G A A A G C T G A G A G G G G A G A T G
      K F S N O E T C V E I G E S V R G E D
V Y I V O S G C G E I N D H L M E L L
TCTCATTTTCAGAGTGGTTGTGGCGAAATCAATGACAATTTAATGGAGCTTTGA 214
      T C T A C A T C A T C C A G A C C G C T G C G G G A A A T A A C G A C A A C C T G A T G G A A C T C T C A
      V Y I I O S G C G E I N D H L M E L L
I H I N A C K I A S A S R V T A V I P
TCATGATTAATGCCTGCAACATTCCTTCAGCCAGCCGGGTTACTGCACTATCCCAT 271
      T C A T G A T T A A T G C C T G C A A C A T T C C T T C A G C C A G C C G G G T T A C T G C A C T A T C C C A T
      I H I N A C K I A S A S R V T A V I P
C F P Y A R O D K E D K S R A P I S A
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      G T T C C C A T A C G C C C A C A G A T A A A A G A C A A G A G T C T G C C C C A A T T T C T G C A A
      C F P Y A R O D K E D K S R A P I S A
K L V A N H L S V A G A D H I I T M D
AGCTTGTGCAAAATATGCTATCTGTAGCAGGTGCAGATCATATATACCACTGGACC 385
      A G C T T G T G C A A A A T A T G C T A T C T G T A G C A G G T G C A G A T C A T A T A T A C C A C T G G A C C
      A A C T T G T G C C A A T A T G C T G C G T G C T G G C G A T C A C A T C A T C A C C A T G G A C C
      K L V A N H L S V A G A D H I I T M D
L N A S Q I O G F F D I P V D N L Y A
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      T G C A T G C T C T C A G A T A C A G G A T T C T T G A T A T T C T G T G G A T A A T T G T A T G C G G
      L N A S Q I O G F F D I P V D N L Y A
E P A V L E W I R E N I S E W R H C T
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      A G C C C G C T C T C T A A A G T G G A T A A G G G A G A A A T A T C T G A G T G G A G C A C T G C A C A T A
      A G C C C G C A C T C T G C A G T G A T T C G G G A A A C A T T C C G A G T G G A A G A A C T G A T C A
      E P A V L Q W I R E N I S E W R H C I

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: V S P D A G C A R R V T S I A D R L
TTGCTGCACCTGATGCTGGTGAGCTAAGAGAGCTACCTCCATTCGCAGACAGCCGTA 556
      T T G T T C A C T G A C C A G G G G G A G C C A A A A G G C T T A C A T C A A T T C G A C A C A G G T T G A
      I V S P D A G C A R R V T S I A D R L
M V D F A L I H K E R R K A N E V D R
ATGTGGATTTGCTTGAATCACAAGAACGGAAGAAGGCCAATGAAGTGGACCCGA 613
      A T G T G G A A T T T G C T T G A T C C A A A G A G A G A A A G G C A A T G A A G T G G A C C G G A
      M V E F A L I H K E R R K A N E V D R
M V L V G D V K D R V A I L V D D M A
TGGTCTGTGGGAGATGGAAGATCGGGTGGCCATCCTGTGGATGACATGGCTG 670
      T G G T C T G T G G G C A C G T G A A G G A C C G T G G C C A T C C T G T G G A T G A C A T G G C T G
      M V L V G D V K D R V A I L V D D M A
D T C G T I C H A A D R L L S A G A T
ACACTTGTGGCACAATCTGCCATGCAAGCTGACAACCTCTCTCAGTGGCCACCA 727
      A C A C T T G T G G C A C A A T C T G C C A T G C T G C G G A A A G C T G T G C A G T G G A G C C A C C A
      D T C G T I C H A A D R L L S A G A T
R V Y A I L T H G I F S G P A I S R I
GAGTTATGCCATCTGACTATGGAATCTCTCCGGCTCCTGATTTCTCGCACTCA 784
      G A G T T A T G C C A T C C T T A C C A T G G G A T C T C T G G A C C A G C A T T T C C A G A A T A A
      R V Y A I L T H G I F S G P A I S R I
H N A C F E A V V V T N T I P O E D K
ACAAGCATGCTTGGAGCAGTAGTACCAATACCATACTCAGGAGGACAGA 841
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M R H C S K I Q V I D I S H I L A E A
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I R R T H N G E S V S Y L F S H V P L
TCAGGAACTCACAAATGGAGAACCGTTTCTACCTATTCAGGCATGCTCCCTTA 955
      T C C A A G G A C A C A C A A T G G G A A T C C G T G C T A C C T G T C A G C A T G T C C C C T A I
      I R R T H N G E S V S Y L F S H V P L
AATAGATTAAGGTATTGATGACAAATCAGCAGAAGACCAGCCGCTGCTCAGTGTAG 1012
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      C T T T C A C A T C C C A C A T G A G A T T A G A G T T A T C G A A C T G G G A A A G A C G G A T T
      T T C T G G A T T T T A G C T G A G T A T C A C A A T G A T A G G T T A A T C A C T G G C A A A A G C A
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      C T G T
      C T T T C A G T T T G G A A

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