

## Nucleotide sequence of the rat ornithine decarboxylase gene

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Submitted July 20, 1988

Accession no. X07944

Ornithine decarboxylase (ODC; EC 4.1.1.17) is the first and rate-limiting enzyme in the pathway of polyamine biosynthesis in eukaryotes. Previously genomic ODC sequences have been reported for yeast (1), trypanosome (2) and mouse (3-5). Here we report the complete nucleotide sequence of a 7776 bp BamHI fragment, carrying the complete rat ODC gene (clone pODC821). Comparison of this genomic DNA with rat ODC cDNA (6), reveals that the gene consists of 12 exons and 11 introns, as was also found for mouse genomic ODC (3,5). As in mouse, 2 introns are found in the 5' untranslated leader sequence, which spans 303/304 nucleotides (7). The first of these also represents the largest of all introns, comprising 1877 bp (nt 1344-3220). The organization of the protein coding part of the ODC gene is strongly conserved between mouse and rat. Intron/exon boundaries are found at identical positions in the coding sequence, giving rise to exons of identical length. Intron lengths, however, vary between rat and mouse. At the 3' end of the gene 2 alternate polyadenylation sites are found (see fig.1 and also ref. 6). Besides the TATA-box several other putative promoter- and enhancer elements are discernable: 9 GC-boxes, 5 upstream of the capsite (nt 1157/1158; ref.7), 1 in exon 1 and 3 in intron 1 (see fig.1 and ref. 8); 2 AP-1 binding sites, 1 upstream of the capsite having a single nt mismatch and one perfect copy in intron 1 (see fig.1 and ref. 9); 1 Ap-2 binding site having 2 mismatches in a conserved 13 nucleotide sequence (see fig. 1 and ref.10); 1 cAMP responsive element with 2 mismatches (see fig.1 and refs.3,11).

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1 GGATCCGGC ATCCGGGCTT GAAAGGGGT TTTAGTTGAG AATTAACAAA CCTTAACAG CGTGACATA GTAACAAGTT GGAGTTACTC CTAAGCTTC CCAAATCTGA ATATGTAAGT
121 AACCGAGTC TCCCATTCT TTCTTAAACAG TGTAACTTGC GGATGGGCTTGC TGAGTTGGAG AGGGCTTACAG TAGGAAAGGGC AAGGCCCTGG GTTCGGTCCC CAGCTCCAAA
241 AAAAAGAAAAA AAAAACAAA AAAAACATGTG AACTCTTGGG GATCAAAATT CCTACTGGGAG ACCTCTTTCAC TCTCAAGATG ACTTAGTGTG AGCTTACCTG
361 AAAGATTAA CAGAAATAGG GACAGCTGTG GGCTTGAAAC CCCCTCAACCT CTTCCTCAAA ATCGCAGCTC TGCTTGTAGATA AAAGGCAATTAA TCTTACATGAG CAATCTGGC CTAGAACTCTA
481 GTTGGAGCT ACCAAAGTAA AAGGGAGTGG CTCTCCAGGCT TCCTCTCTCGT AGCTTGTGAG GCTTAAAGGCA AGCACGGGGT TGAGACAGGG CAAATGGCA CAAAGGAGTC
601 TAGTCTACGT CAACTCAAGG CCCATCCTAC GATCTGGCATC CGCCGGTCAAA TAAATACATA CGCGCTGAAAT GCAAAAGCGGA GAAAGAGTTG TGCTAGTCTT
721 CGACGGCAGG GCTCAAGCGT TAGAACGGCCG GGAGAGACT CGTGTATGAG CGCGTGTCAAA GACGGCAGACG CGACGGCTGC TGCGCATGCA CGCGCTGGAT CGCGCTGGT CGCGCTGGATAGGA
841 CCCTGGCGCA AGCTGTGAGT TAGCTGTGTT GGTGTTGGTGC GGCTGGGGCGG GGCTCTGGCGA GGGAGTGTGC GGCAAGGGGC GGGGGGGGGG GCGCTGGGGG ATGGGGGGGGG GGCTGGGGAC
961 GGCGGGGGCC AGCTGTGAGT GACGGCGGGCGG CGGGGGCGCT GGCTGGGGGGAA CGGTGGGGGGC TGCTGGGGGGC CGGGGGGGGGG GAAACGGATCG
1081 GGCTGGGTGTTT GAGCTGGCTG GTCCTCATGA GA CGACGTGTC CGCC TATAAG TAGGGGGGGGGG TGCGGGGGGGC GGGCTTGTGCT AGCTCTCTCA CGGGGGGGGGCCTG CAGCTCAGCA
1201 GCTCGGGCGCC AGCTCTGGTCG GCGGACTGCG CGGGGGCTCGA CGAGGGGGCTG GACGGGGGGGG CGGGGGGGGGT GGGCTCTGGG GTTGAATGGC GGCCTCTICCA TGGGGTCCAGC
1321 CAGGGGGCTG CTGCTGGCTG GAGGTAGGGC GGGGGGGGGG GCGACGGGGGGC GGGGGGGGGG GACAGCTGGC CGGGGGGGGG GACAGCTGGC TGACCTGGC
1441 AGGCCCTGGC CGAAGGGCAAG CAGCTGTGTC TGCCCCCTGG CGTCAAGGGCC CGGAGATGGGG CGCGATGCTG TGACGGGGGG TCAGGGGGCTC ACTTGGGGGGG GGGGGATGG
1561 AGGGCAGGG CAGGGGGAGCC CGGGGGGGTAG CAGC GGGGCGT GCAGTTCTCT GCTTTCTTA GTTTGTCTCA GTGACAGAG CAGAGCTGAT GACTCTGAAGT GGAAAGCTGAT AGACCTAAAT
1681 TAGCTAGGA GTCTCCCTGTA ATGAACTGGT ACCGGCTGTG ACTTGATTG AGAACTGAAC TCTTTGAAATG ACTTGGGGGG TTACGGGGAA CGGGTCTTGG GCTGTCCTGG AGGGCTTGG
1801 CAGAACTCTG AATAACTGGT AGGAGATCTC GTCAAGATG TGCTGGGGAG GAAACATGGG TGAGCTGGCT TTCTTCTTACCT AAACCTAAACCA TGCGGGCAGAA TTTGACTGG
1921 GTTCATTCTT GTTAAATG TGCTGTATCT CATCCAGATT TAATCTCTTG TGCTTAATGTT TAACAGGAT TGAGCTGCTT CCATGCCCCA AGTGTAGGA TTTTTTCTTCT TTTATCTTT
2041 TTTCTTCTT CTTTTTCTT TTGTGTTGAG GCAAAAGATAG GAAAGGGCA AATAATGGTGT ATTAAATAGA AGTITTTCCA GTTAAAGGCC GGAAGGCTGC CTGGAAAATA
2161 CTAAACAGA CCTAAATTA CAAGCTTACT CCTAAAGCTG ATACAGCTG GTTGGCTGGC GCTGGTCTGT AGCTCTACTA TAAGAGAGGT TTATGACGT
2281 AACCGAGGTG ACCAGGCGCA AAAGCTCTT CCTAAAGCTTAA AGTGTGCTTT ATCATGATG GATTTGGGGT TATGACAGG CTCATCCCCGT GGCCTCTCAT AGTGTCTGGT GCTAGAGCAA
2401 ACTGGCTCTT AACCCTGGC CGGGCTGGT GCATGTAGGC TGCTGGACT GAAGTGGGGTC ACACATGGG AAAAGTTT ACCTGGGGAC TTGTGCTGG TGTCCTTGG ATAGACCTCA
2521 GGGAGGGCT TTTTAAAGC GGTTGGTGTG TGCTTATGAA TTGTAGTAAA AAAGTTGGCC AAAAATGTTCT CCATATGGT TATTCATGGT AAGTGGGGAT TAGAGGGCAC TTGGAGACTG
2641 TTGGATTCTT CGAGAGGGCC AGAGTGGTAGA CAATCCAGGC TCTAGAATAG TGATGTTCA TAACAGTAC ATATACTGT GAATTGAATT TTTTTTAAATG CTAGTACTGC ATAAAGGTA
2761 GGGAGGTGTT GTGCGATTCG ACACATACAT TGAGTGGCTC GGATACCCGA TAATCTGTG TCAACTAAGT ATTCAGCATA ACTCTGCAAG TGGGGAGAAA AGACCTTGGT AGGACTCTAT
2881 GTTACTGTGAT GCGCAATTAAA GTTGTGAG AGCTGGAGT GCTCAAGTA AGCAGATGG ACACATGTG ATAGCGAGTA AGTACGCTGTT TACTCCGTT CGGTTTGGG GAGGGGGCAAG
3001 GATGGAGATG TTCTATGTGT ATAGACCTGTG CGCATTAGT GTGGAATCTA TTGTGAGTATT GGAGATATT GGGGGGGGGG TCTTCAAGGTG GTTCTGACCT CACAGTGT
3121 CTTCCTGTAC TGTGACTCT GTGGTATACT GTGCGATGT GTAACTCTTA ATGGTAAAGT TTCAAGGGAG ATAGCAACAT GTTGTGTTTC TACTCACTAG ACTCCAGGAG
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3241 ACAGCATTCA GAGTTGACCT TGTGAGAGCT GCCCATAATT TAATTCATC TCTAGGTTT CTGTGAAGT ATCGTTGAAT TTGTYGTGAA GCAGTGTCAA GACTTTGAGT  
 3361 GCATTCACTT ATTATCTGCT TATTGTCAGC TATTTGTTTC AGAGGGCACAT CGAGAAACCAA CCTTGGCAG CTTCATAGAG GAAGAGTTG ACTGCCATAT CCTCGATGA GTTTTCAGC  
 3481 CTAAGGACAT TCTGGACCAAA AAAATCAATG AAGTTCTTC CTCCTGTAAGT ACGGGAAAGC CACAGCCACA ACTCTAAAAGT TCCATAAAAAG AGCATGCCCT GCGAGAGAT CTAGAATTG  
 3601 ACTGACTGG CTCTTAGTGT AGTGTGTCATG TCAGTACTGC TAACGGAGT AGGGTTTGT TAGGGAAGG GAAAAAGAT CTTCAGTGTG GCAGGAGTC AGACTGTATA TGAGGTCCT  
 3721 GAACCCACTC ACTCTCATTC CAGGATGATA AGGATGCTT CTATGTTGG GACCTCGGAG ACCTCTAAA GAAGCATGAT CGGTGCGTA AAAGCTCTCC CCGGTGTACT CCCCTCTATG  
 3841 CTGCAAGTG TAATGCAAGCAG AGGACAGCATG TTGACGACCTT GGGACAGGAT TTGATTTGTC ACAGCAAGTA AGACTGTATA TCTCACCCA AAAGGGTAT CAGTGTATG  
 3961 GCTTGTGTT GTCAACTCT GCTATATATC ATCTGATCTC TCTTCAGAC TGAATAACAG TTGGTGCAGA GCGCTGGGGT GCGTCAGAG AGAGATTATC ATGCAAATTC TGTGAAAGCA  
 4081 GIGTCTCAGA TCAAGTATG TGCCAGTAAI GGAGGCCAGA TGATGACTT TGAGCAGTAA ATGGAGTGA TGAAGAGTGC CAGAGCACAT CCAAAGGCCAA AGTANGTCTT CTGATGAGC  
 4201 ACAAAGGG TGGGCTTGT AGCCGACATA TAATCTTGTG TCCCTATTGCT TATACATAGT AAAGAACAGG CTAAACCCCTT GGTTAGAATC AGACCCACAA CGACTGATGC CTAGACAGC  
 4321 TGATTTGATG ACAGTGTACA GAGTGTGATG CACTTGTTC TGTCACCTA GTTGTGTTG GCGGATGTCG ACTGTGATGTT CCAAAGCAGT TTGTCGGCCTC AGCTGTAAAGT  
 4441 TTGGTCAAGC ACTGAAACAC AGGAGCCTTC TCTTGTGAACT GCGAACAGAG CTAAATATTG ATGTCATGG TGTCAGTGA GTGTCAGTGA ATAGTTACAG ACTGACATC TAAATTTAA  
 4561 GCCCCCTTTT TCTCTGAGA ACTAGTCAA GAACGACATC TTGTTTTAT TTCAGCTTC ATGTTGGCAG TGTTGCTACT GACCCCTGAGA CCTTGTGCA GGCACTGTCA GATGCGCGCT  
 4681 GTGCTTGA CATGGGATG AGTACATGAC TTGCTGAGA GGGCTGTTG TATTGAAATAA ACCAACCAA TQAATCTGA ATTGGCTCTT TGAGAAGGT GTCTGACATC CAGATTTAA  
 4801 AACCATCTG CTCTGGCAT TAAACTCTG ATACTACAA TTGTTACTTC ATTCATGCTT GTCAGTACG AGAAAGTGTG TTCAAGCATG ATCTGCTGGA CATTGGTGGT CTTCTCTG  
 4921 GCTGTGAAAGA CAGCAAGCTT AAATTGAGG AGGTAAATTAC TACAACATTA ACCTACAGAC GGTTGAGATAT GTTACCTACCA TTGTTGTTGTT TTACTGATT AAAGGAGCCA ACATGCCCTGG  
 5041 TGTTTGTTC TCACTACTG TTATGTTGCA CTGAGCCCA GGGTCTGCAAA GAACTCTCTG TTCTCTGG TGTTTGTGTT ATTTAATGTT TTAGCTTACT GCTTCTACT ATTTGACTAT  
 5161 GAAGTACACA GGGGTGAAGG AGTTATATCT TTGTCGATG TATTGAGAT TGCACTTTC GCGCCCTCTG TAATTCATTG TTGCTGATT TATTAAATAT TATATAATACT TATTCTATAA  
 5281 TTGTTAGAAA GAGATGGTCC TGAGGGAGT GGGAAAGTGTG TGATGACAG ACTAGTTTC AGAGAGTTT GTGCTCTG TTGCTGTAG ACAGACCTGC TATGCTAGT CATGCTCTG  
 5401 TCTTACACAC AGGAGCTGA TCTTCTCTC CAACATACAA ATATGCTGC TCCCCTCTC CACTAGATC AGGACTGAA TCAACCCAGC TCTGACAAAG TACTCTCTC CGGACTCTGG  
 5521 AGTGTGAGC ATAGCTGAGC CAGGGAGGATC CTACGTCGA TCACTTCA CACTTCAGT GAATATCATT GCGAAAAAAA CCTGCTGAA GGAGCAGACG GGCTCGGGAGC GTATGTTGG  
 5641 CGAGGATGAG TGAATGATGTT GGTTGATGCT TTGTTTCTA TAGGGTGTAC TGTTTCTA GATGAGATG AGTCAACAGA GCAACATTTG ATGTTATTAGC TGAATGATGG  
 5761 AGTGTATGG CTATTTAACT GCATCTTCA TGACCATGCA TCACTGTCGAC CCTCTGTCGA GAAAGGTGAGT TCTGACGCCA TGAGTGTAGT CATAGGACATC AGAGAACATT  
 5881 GGGGCAGAG TCTCTGAGC AGTAAAGAGC ACTGACTGCT CTCAGAGGCC CTGAGTCTAA TCCCAAGAAC AACATGGTG CTCAACCAAGA TCTGATGATA ATGATGCCCT TTGTTGTTG  
 6001 TCTGAAAGA TAGTCTACAGT JTATTTAAA TTCTTAAA AAAAACAAA AACATGGTAA ACTGAGGATG TTGCTCTTAA TGAGCAGAC CAAAGCAGAT GAGAAGTATT ACTCTACAGC CACTCTGGGA  
 6121 CACCAATGTTG ATGGCCCTGA CGGGCCGCTGA GCTCTGCCGA ATATGCTGTC GGTTGATGTTG TGCTGCTTC TGATGCTCTT TTGGCTGTC AGTGTAAATGT TTGCGCAGA  
 6241 AATGGTTCTC AGGGCCCAA CATCTACTAC GGTCAATGTC GTGATGTTGGG CTGTCCTGC TCATGCTCTT TTGGCTGTC AGTGTAAATGT TTGCGCAGA  
 6361 GCTCTGGTGA TGCCCTGATG ACACACAC ACTATCTG GGGGAAAGC AGATGCTGCT GAGGGGAGG ATCTCCGTC TGCTCTCAA GGAGCTGAAT TTGTCCTTCTT TTCTTGTG  
 6481 TGTAATGTT TTCTTCTTAC TTGAGCTAA TAGACAAAGT GAGTTTTTC AAGTAATTAC TGCTCATCTT CAGATGTTTACT CTAGTAGAG AGGCTTACAA AGTAACCCAT TGAATCTTCTT  
 6601 TGCAACTAAA ATATTCAGT TGCATGATG TGCCTGTTG TGCTCTTAAAT ATGTAAGT ACATGGTAT GTTCTCTGGT ATAGTGACAG GTGGAGGGTG CAGGAGGCTT CTTCGGGG  
 6721 TGCCCTTGGTGA TTGGGTTGATTA TATGGCTCATAT TTCTCTGGCA ACTCATGAG CAAATTCAGGA CCTCTGGCTT CCCCCCAGAA GTGGAGGGAGC AGGAATGTTG  
 6841 CACTCTGGCC ATGCTCTGIG CCCAGGAGAG CGGGATGGAC CGTCACCTTC CAGGGCTTGC TTCTGCTAGT ATCAATGTA AGATGGCCATT CTTGTAGCTC TTACCTGCAA GTTACCTG  
 6961 AGTTAACCGC ATTTGGGGG ACCATTAAAC TTAAATCTG TGAGTTGTTG AGAGTAGGGG TTGGCACCAGA TGCAGATGTT AGAAGCTAGG AGATGGGGGT CACACTTAC  
 7081 GIGTTCCTAT GGAAACATTG ATATTTATG ATGCAATTG ATTCACCTT CAGACAGCT ACTAATGAGT GCTCTCTGGC TGCTGACAA GCAATTGAG TCTGTCATAC GCGAGATGG  
 7201 GTCTAAAGGAT TATGTTGTA CCACTTCTGA AATAAAATAA TCTTGAATG ATTTGGACATT GGAGGAATG TGAGCAATGCT CCTTACAGAA GCGACAAACT TCTGACAGG CTTGTTGITA  
 7321 CAGGAGTGA TCTAGCCCCAG CAGAGATGTC GATGACATAA AGCTGTGCC CCTCTGATACA GCATGAACTG GCTTGTGAA TCTCAAGTGT TCTGTTGCCC AAAGCTCTT  
 7441 AAAGGTGCA TCTAGCTCTG GGGCTCTGA CTGAGGGACT AGGGCTCTG ACCTCTGCTT ACCTCTGCTT GCAGAAACCC TGACTGTCTC CTGACCCCTT GGGCTCAGC  
 7561 GCATCACCCAC CTAGTAAACG TGAAGGACTA TGCGACATCA CCTCTGAA TAAATCAAC AACAGCAACT ATCTGTTGT AAATTCTAC CTGACCTT CATATTTATG  
 7681 TCTCTGCTCA TTTATACAC TATGTCATCC CAAAGAAAGT GCCTAGCTT TAACCTAGT AGTATTGAGG ACCTGTAGG CAGGAGGAAGG GGTATC

**Figure 1.** Rat ornithine decarboxylase genomic sequence: exons are underlined. Translation initiation - (ATG, nt 3423) and termination site (TAG, nt 6920) are indicated by closed circles. Conserved sequences are depicted by boxes: TATA-box (nt 1125); 9 GC-boxes (nt 922, 935, 943, 971, 1044, 1255, 1446, 1549 and 1594); c-AMP responsive element (nt 1108); 2 AP-1 binding sites (nt 856 and 1680); AP-2 binding site (nt 822); 2 polyadenylation signals (nt 7232 and 7619).

#### Acknowledgement

We are indebted to H.M. Hodemaekers for her skillful technical assistance. We thank Deborah Dil for typing and preparing the layout of the manuscript.

#### REFERENCES

1. Fonzi, W.A. & Sypherd, P.S., J. Biol. Chem. (1987) 262, 10127.
2. Phillips et al., J. Biol. Chem. (1987) 262, 8721.
3. Coffino, P. & Lichuan Chen, E. Nucl. Acids Res. (1988) 16, 2731.
4. Brabant et al., Proc. Natl. Acad. Sci. USA (1988) 85, 2200.
5. Katz, A. & Kahana, C., J. Biol. Chem. (1988) 263, 7604.
6. Van Kranen et al., Gene (1987) 60, 145.
7. Van Steeg et al., manuscript in preparation.
8. Dynan, W.S. & Tjian, R. Nature (London) (1985) 316, 774.
9. Chiu et al., Nature (London) (1987) 329, 648.
10. Imagawa et al., Cell (1987) 51, 251.
11. Montminy et al., Proc. Natl. Acad. Sci. USA (1986) 83, 6682.