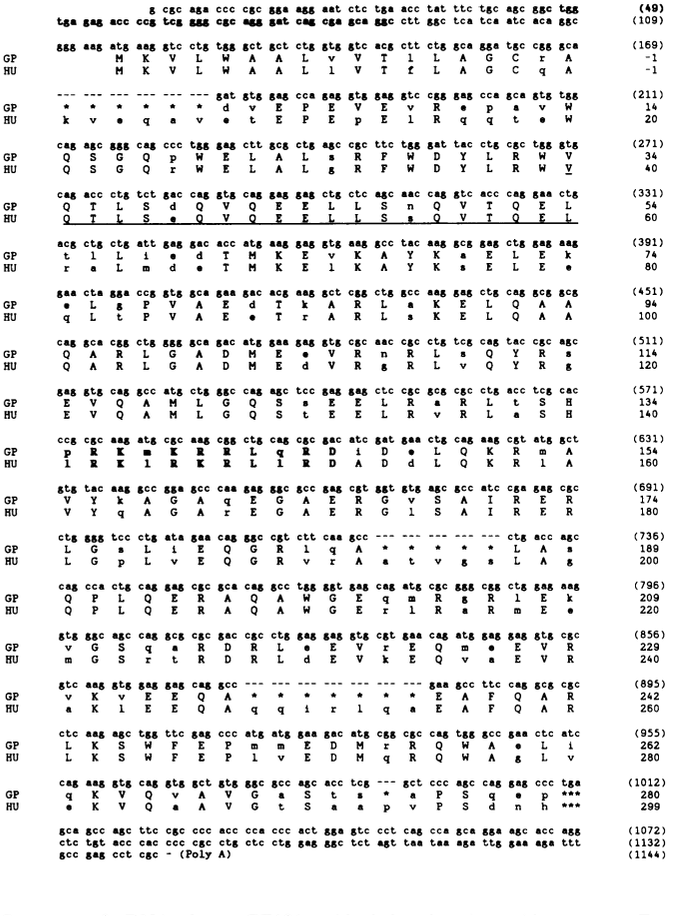
Nucleic Acids Research, Vol. 18, No. 1

Primary structure of guinea pig apolipoprotein E

Teruhiko Matsushima[1*], Godfrey S.Getz[1,2] and Stephen C.Meredith[1]
Departments of [1]Pathology, Biochemistry and [2]Molecular Biology, The University of Chicago, Chicago, IL 60637, USA

Submitted September 25, 1989

Guinea pig apolipoprotein (apo) E has been cloned and sequenced. The calculated M_r is 32,374, about 2000 less than that of human apoE (human apoE), and in agreement with previous results by SDS-PAGE. The 5′ non-coding region is about one and a half times as long as the 115 nucleotide sequence of the rat and human cDNAs, with a unique 44 nucleotide sequence inserted between two conserved regions. The 3′ non-coding region of the cDNA has 132 nucleotides and a poly(A) tail. A polyadenylation signal AATAAA is found 32 nucleotides upstream of the poly(A) tail. Compared to human apoE, guinea pig apoE has four small clusters of deletions: the N-terminal six amino acids of human apoE, and three deletions near the C-terminus, i.e., between residues 186 and 187 (human apoE residues 193−197 missing), between residues 236 and 237 (human apoE residues 248−254 missing), and between residues 274 and 275 (human apoE residue 293 missing). There is high homology between the deduced amino acid sequence of guinea pig apoE and those of 6 other species (human (1, 2), baboon (3), cynomolgus (4), rabbit (5), rat (6), and mouse (7)). The regions deleted from guinea pig apoE are the least conserved among these species. The LDL receptor binding region is among the most highly conserved. The most conserved domain, however, is amino acids 34 through 54 in guinea pig apoE (amino acids 40−60 in human apoE). In humans, baboons, mice, and rats, this domain coterminates with the 3′ end of the third exon (3, 8−10). A synthetic peptide of residues 35−55 guinea pig apoE, was found to be amphiphilic in monolayer studies and helical in circular dichroic spectroscopy (minima at 204 and 217.5 nm). The conservation and strategic location in the genome suggests a hitherto unrecognized importance of this domain of apoE.



Sequence of cDNA clone pGE131, with deduced amino acid sequence. For comparison, the amino acid sequence of human (HU) apoE (1, 2) is aligned with that of the guinea pig (GP). Residues where the human and guinea pig sequences agree are given in upper case letters; other residues in lower case. An asterisk (*) is a deletion of an amino acid; deletions in the cDNA are represented by three dashes (---). Peptide synthesized is underlined; receptor binding region is in boldface. Termination codon is represented by ***. Insert into the 5′ untranslated region of guinea pig cDNA is in boldface.

REFERENCES

1. McLean,J.W., Elshourbagy,N.A., Chang,D.J., Mahley,R.W. and Taylor,J.M. (1984) *J. Biol. Chem.* **259**, 6498−6504.
2. Das,H.K., McPherson,J., Bruns,G.A.P., Karathanasis,S.K. and Breslow,J.L. (1985) *J. Biol. Chem.* **260**, 6240−6247.
3. Hixson,J.H., Cox L.A. and Borenstein,S. (1988) *Genomics* **2**, 315−323.
4. Marotti,K.R., Whitted,B.E., Castle,C.K., Polites,H.G. and Melchior,G.W. (1989) *Nucl. Acids Res.* **17**, 1778.
5. Hao,Q.-l., Yamin,T.-t., Pan,T.-c., Chen,S.-l., Chen,B.-s., Kroon,P.A. and Chao,Y.-S. (1987) *Atherosclerosis* **66**, 125−130.
6. McLean,J.W., Fukazawa,C. and Taylor,J.M. (1983) *J. Biol. Chem.* **258**, 8993−9000.
7. Rajavashisth,T.B., Kaptein,J.S., Reue,K.L. and Lusis,A.J. (1985) *Proc. Natl. Acad. Sci. USA* **82**, 8085−8089.
8. Feng,W.P., Howlett,G.J. and Schreiber,G. (1986) *J. Biol. Chem.* **261**, 13777−13783.
9. Paik,Y.K., Chang,D.J., Reardon,C.A.,Davies,G.E., Mahley,R.W. and Taylor,J.M. (1985) *Proc. Natl. Acad. Sci. USA* **82**, 3445−3449.
10. Horiuchi,K., Tajima,S., Menju,M. and Yamamoto,A. (1989) *J. Biochem.* **106**, 98−103.

*Present address: First Department of Internal Medicine, University of Tokyo Hospital, Tokyo, Japan