

Primary structure of guinea pig apolipoprotein E

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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.

	<u>g cgc gga ccc cgc gga ags aat ctc tga acc tat ttc tgc agc ggc tgg</u>	(49)
	<u>tga gag acc cag tgc gga cgc ags gat cag cga gca ggc ctt ggc tca tca atc gca ggc</u>	(109)
GP	<u>sss ags atg ags gtc ctg tgg gct gct ctg atg atc acg ctt ctg gca gga tcc cgg sca</u>	(169)
HU	<u>M K V L W A A L V V T f L A G C r A</u>	-1
	--- --- --- --- --- gat atg ags cca gaa atg atg atc cag gca gca gca gca gca	(211)
GP	<u>k v e q a v e t E P E p E l R q q t e W</u>	20
GP	<u>cag agc gga cag ccc tga ggc ctt gca ctg agc ctc ttc tga gat tac ctg ctg tgg atg</u>	(271)
HU	<u>Q S G Q P W E L A L s R F W D Y L R W V</u>	34
	<u>Q S G Q P W E L A L S R F W D Y L R W V</u>	40
GP	<u>cag acc ctg tct gac cag atg cag ags ags ctg ctc agc aac cag gtc acc cag gaa ctg</u>	(331)
HU	<u>Q T L S d Q V Q E E L L S n Q V T Q E L</u>	54
	<u>Q T L S e Q V Q E E L L S s Q V T Q E L</u>	60
GP	<u>agc ctg ctg att gaa gac acc atg ags ags atg agc ctc tac agc gca gca gca gca gca</u>	(391)
HU	<u>t l l l i e d T M K E v K A Y K a E L E k</u>	74
	<u>r a l m d e T M K E l K A Y K s E L E e</u>	80
GP	<u>gaa cta gga ccg atg gca gaa agc agc agc ctc gca gca gca gca gca gca gca gca gca</u>	(451)
HU	<u>q l t P V A E d T r A R L s K E L Q A A</u>	94
	<u>q l t P V A E e T r A R L s K E L Q A A</u>	100
GP	<u>cag gca ctg ctg gaa gca atg gaa ags atg gca gca gca gca gca gca gca gca gca</u>	(511)
HU	<u>Q A R L G A D M E e v R n R L s Q Y R s</u>	114
	<u>Q A R L G A D M E d v R g R L v Q Y R g</u>	120
GP	<u>gag atg cag gcc atg ctg gca cag agc ctc gca gca gca gca gca gca gca gca gca</u>	(571)
HU	<u>E V Q A M L G Q S s E E L R a R L t S H</u>	134
	<u>E V Q A M L G Q S t E E L R v R L a S H</u>	140
GP	<u>ccg cag atg ctg gca gca gca gca gca gca gca gca gca gca gca gca gca gca gca</u>	(631)
HU	<u>p R K m K R R L l R D i D e L Q K R m A</u>	154
	<u>l R K l R K R L l R D i D d L Q K R l A</u>	160
GP	<u>atg tac ags gcc gca gca gca gca gca gca gca gca gca gca gca gca gca gca gca</u>	(691)
HU	<u>V Y k A G A e G A E R G v S A I R E R</u>	174
	<u>V Y k A G A e G A E R G l S A I R E R</u>	180
GP	<u>ctg gaa tcc ctg ata gaa gca gca gca gca gca gca gca gca gca gca gca gca gca</u>	(736)
HU	<u>L G s l i e Q G R l q A * * * * L A s</u>	189
	<u>L G p l v e Q G R v r A a t v s s L A s</u>	200
GP	<u>cag cca ctg cag gaa cgc gca cag gca gca gca gca gca gca gca gca gca gca gca</u>	(796)
HU	<u>Q P L Q E R A Q A W G E q m R s R l E k</u>	209
	<u>Q P L Q E R A Q A W G E r l R s R m E e</u>	220
GP	<u>atg agc agc cag gca gca gca gca gca gca gca gca gca gca gca gca gca gca gca</u>	(856)
HU	<u>v G S q a R D R L e E V r E Q m e E V R</u>	229
	<u>m G S r t R D R L d E V k E Q v a E V R</u>	240
GP	<u>atc ags atg gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa gaa</u>	(895)
HU	<u>v K V E E Q A * * * * * A E A F Q A R</u>	242
	<u>A K l E E Q A q q i r l q a E A F Q A R</u>	260
GP	<u>ctc agc agc tgg ttc gaa ccc atg atg gaa gca atg cag cag cag tgg gca gaa ctc atc</u>	(955)
HU	<u>L K S W F E P m m E D M c R R Q W A e L i</u>	262
	<u>L K S W F E P l v E D M q R R Q W A e L v</u>	280
GP	<u>cag ags atg ctg gca gca gca gca gca gca gca gca gca gca gca gca gca gca gca</u>	(1012)
HU	<u>q K V Q v A V G a S t s * * P S q a p ***</u>	280
	<u>e K V Q a A V G t S a a p v P S d n h ***</u>	299
GP	<u>gca gca agc tbc gca ccc acc cca ccc act gaa gca cct cag cca gca gca agc acc ags</u>	(1072)
HU	<u>ctc tgt acc cag ccc cgc ctg ctg gaa gca cct act gaa gca gca agc acc ags</u>	(1132)
	<u>gca gca cct cgc - (Poly A)</u>	(1144)

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.

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