PRODUCT INFORMATION

ApoE4 (human, recombinant)

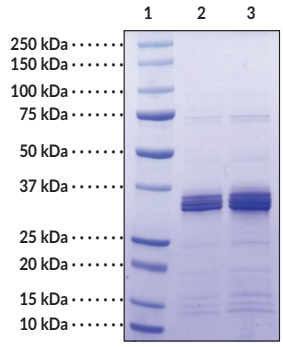
Item No. 37227

Overview and Properties

Synonym:	Apolipoprotein E4
Source:	Active recombinant human C-terminal His-tagged ApoE4 expressed in HEK293 cells
Amino Acids:	19-317
Uniprot No.:	P02649
Molecular Weight:	37.8 kDa
Storage:	-80°C (as supplied)
Stability:	≥6 months
Purity:	≥70% estimated by SDS-PAGE
Supplied in:	50 mM HEPES, pH 7.4, with 150 mM sodium chloride and 10% glycerol
Protein Concentration:	***batch specific*** mg/ml

Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

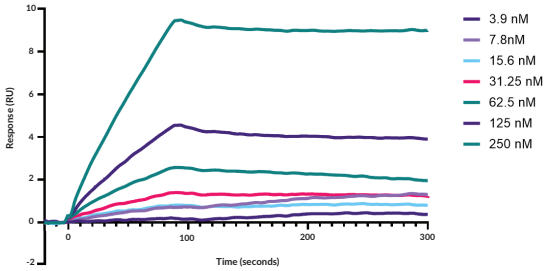
Images



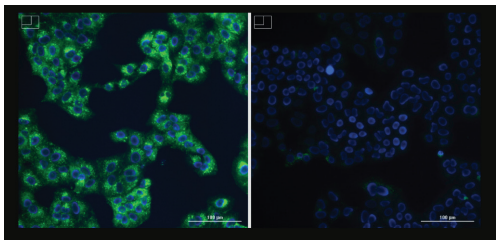
Lane 1: MW Markers
Lane 2: ApoE4 (2 µg)
Lane 3: ApoE4 (4 µg)

SDS-PAGE Analysis of ApoE4.

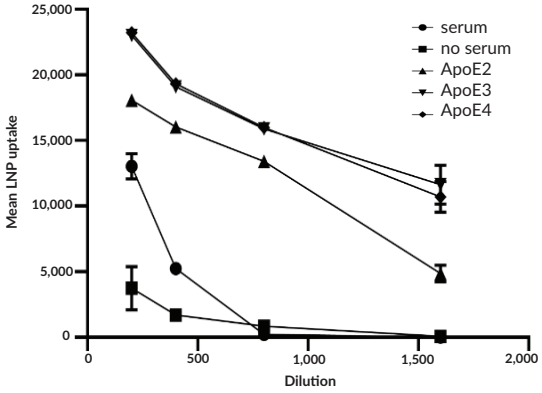
Representative gel image shown; actual purity may vary between each batch.



ApoE4 binds human LDLR with nanomolar affinity. LDLR (FC-tagged) was immobilized on CM5 *via* anti-human IgF FC antibodies. SPR analysis was used to determine APOE4 binding affinity on a Biacore™ 8K, using multi-cycle kinetics with seven concentrations of ApoE4.



ApoE4 activity in cell-based assay. ApoE4 (left) increases the uptake of SM-102 (LNP-102; Item No. 33474) compared with no serum (right).



Fluorescent lipid nanoparticles with SM-102 (LNP-102; Item No. 33474) were diluted in media with 10% serum, no serum, or different ApoE proteins (Item Nos. 37225 | 37226 | 37227) at 1 µg/ml. A549 lung epithelial cells were incubated with diluted SM-102 samples, washed, and stained with Hoechst 33342 dye for nuclei. The cells were imaged on a Cytation V imaging plate reader and analyzed for mean per-cell BODIPY fluorescence, as a measure of LNP uptake.

CAYMAN CHEMICAL
1180 EAST ELLSWORTH RD
ANN ARBOR, MI 48108 · USA
PHONE: [800] 364-9897
[734] 971-3335
FAX: [734] 971-3640
CUSTSERV@CAYMANCHEM.COM
WWW.CAYMANCHEM.COM

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Description

ApoE is a member of the superfamily of amphiphilic exchangeable apolipoproteins and a lipid carrier protein with a major role in lipid homeostasis.[1,2] It is expressed in astrocytes, hepatocytes, monocytes, macrophages, and kidney cells and exists as three major polymorphic alleles, ApoE2, ApoE3, and ApoE4, which occur in the United States population with frequencies of approximately 7, 79, and 14%, respectively. ApoE is composed of an N-terminal domain, which contains sequences for binding to members of the LDL receptor family, and a C-terminal domain, containing the major lipid-binding region, linked by an unstructured hinge region, which facilitates domain mobility essential to protein function.[1] Upon lipid binding, ApoE undergoes a conformational change that orients the α-helices of the C-terminal domain perpendicular to the acyl chains of the bound lipids to stabilize the bound lipids and facilitates recognition and binding to LDL receptors by the N-terminal domain. ApoE isoforms vary at amino acids 130 and 176 (112 and 158, respectively, in the mature protein) with ApoE2 containing cysteine at 130 and 176, ApoE3 containing cysteine at 130 and arginine at 176, and ApoE4 containing arginine at 130 and 176. The lack of cysteine residues in ApoE4 inhibits dimerization and multimerization observed with ApoE3 and ApoE2, respectively. ApoE4 is associated with smaller lipoproteins that promote less cholesterol efflux than ApoE3-containing lipoproteins, and *APOE4*-expressing astrocytes accumulate smaller lipid droplets than those expressing *APOE3*.[3,4] It is associated with increased amyloid-β production and accumulation, as well as impaired episodic memory and global cognition in adults over the age of 60.[2,5] *APOE4* expression is positively correlated with earlier disease onset, faster disease progression, and increased brain atrophy in patients with Alzheimer's disease.[5] Cayman's ApoE4 (human, recombinant) protein can be used for cell-based assays.

References

1. Lanfranco, M.F., Ng, C.A., and Rebeck, G.W. ApoE lipidation as a therapeutic target in Alzheimer's disease. *Int. J. Mol. Sci.* **21(17)**, 6336 (2020).
2. Petros, A.M., Korepanova, A., Jakob, C.G., *et al.* Fragment-based discovery of an apolipoprotein E4 (apoE4) stabilizer. *J. Med. Chem.* **62(8)**, 4120-4130 (2019).
3. Michikawa, M., Fan, Q.W., Isobe, I., *et al.* Apolipoprotein E exhibits isoform-specific promotion of lipid efflux from astrocytes and neurons in culture. *J. Neurochem.* **74(3)**, 1008-1016 (2000).
4. Farmer, B.C., Kluemper, J., and Johnson, L.A. Apolipoprotein E4 alters astrocyte fatty acid metabolism and lipid droplet formation. *Cells* **8(2)**, 182 (2019).
5. Wolfe, C.M., Fitz, N.F., Nam, K.N., *et al.* The role of APOE and TREM2 in Alzheimer's disease-current understanding and perspectives. *Int. J. Mol. Sci.* **20(1)**, 81 (2018).

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