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Apolipoprotein E (apoE), a two domain protein, plays a key role in cholesterol metabolism through interaction with the low density lipoprotein receptor (LDLR). Previous studies have demonstrated that, to be biologically active in terms of high affinity LDL-receptor binding, apoE must be associated with lipids. To gain insight into the structural properties of apoE associated with lipids, apoE complexed with dipalmitoylphosphatidylcholine (DPPC) was crystallized. Each apoE•DPPC particle contains two biologically active apoE molecules and 92 DPPC molecules. Because the crystals contain 50% DPPC by weight, extensive experimentation was required to optimize cryoconditions to achieve a maximal diffraction of 8Å. The apoE molecular envelope was determined to 10Å by molecular replacement from a theoretical model. Binding to DPPC causes the NH₂-terminal domain to refold from a biologically inactive four-helix bundle into one arm of a helical hairpin structure with the COOH-terminal domain forming the other arm. The internal symmetry of the molecular envelope indicates that the residues implicated in LDLR binding (residues 135-150 and Arg-172) are located in close proximity near the apex of the hairpin which suggests that the complete LDLR binding site is contained within the apex of the hairpin.