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Crystal Structure of Human Apolipoprotein A-I: Insights into its Protective Effect Against Cardiovascular Diseases. A. Abdul Ajees^{*}, G.M. Anantharamaiah[†], Vinod K. Mishra[†], M. Mahmood Hussain[§] & H.M. Krishna Murthy^{*}, ^{*}Center for Biophysical Sciences and Engineering, [†]The Atherosclerosis Research Unit, Depts. of Medicine, Biochemistry and Molecular Genetics, Univ. of Alabama @ Birmingham, 1530 3rd Ave. S., Birmingham, AL. [§]Depts. of Anatomy, Cell Biology and Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY.

Despite three decades of extensive studies on human apolipoprotein A-I (apoA-I), the major protein component in high density lipoproteins, the molecular basis for its antiatherogenic function is elusive, in part due to lack of a structure of the full-length protein. We describe here the crystal structure of lipid-free apoA-I at 2.4 Å. The structure shows that apoA-I is comprised of an amino-terminal four-helix bundle and two carboxy-terminal helices. The N-terminal domain plays a prominent role in maintaining its lipid-free conformation, indicating that mutants with truncations in this region form inadequate models for explaining functional properties of apoA-I. This structure provides for the first time a much-needed structural template for exploration of molecular mechanisms by which human apoA-I ameliorates atherosclerosis and inflammatory diseases.