s8b.m2.p5 Crystallization and structure determination of human low density lipoprotein (LDL) at low resolution, using *ab initio* phases. S. Ritter[1], N.L. Lunina[2], V.Y. Lunin[2], A.G. Urzhumtsev[3], A.D. Podjarny[4], I. Frey[1], K. Diederichs[5]., M.W. Baumstark[1], *[1]University Hospital Freiburg, Germany; [2]IMPB RAS, Pushchino, Russia; [3]University of Nancy, France; [4]UPR de Biologie Structurale, IGBMC, Strasbourg, France; [5]University of Konstanz, Germany.*
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The concentration of small, dense LDL particles in serum is a major determinant for the development of coronary heart disease. LDL particles consist of a single polypeptide chain (apoB) with a molecular weight of 510 kDa, and a lipid core of cholesterol esters and triacylglycerol, surrounded by a monolayer of phospholipids. The total molecular weight of the particles is between 2000 and 3000 kDa. The radially averaged structure of LDL is known from small angle scattering. The determination of the three-dimensional X-ray structure of LDL depends on the availability of suitable crystals of this biomolecular assembly. Presently crystals of human LDL subfractions are reported by two groups. The knowledge of the three-dimensional structure of LDL particles that have atherogenic potential would be an important approach to explain the development of atherosclerosis on a molecular basis.

Human LDL subfraction LDL-2 (d=1.031-1.034 g/ml) was crystallized using polyethylene glycol as a precipitant. Complete native data sets were collected in a resolution range of 130-29Å at cryogenic conditions using synchrotron radiation. Indexing and integration of the datasets was done using XDS (Kabsch W.). The space group is most probably C2 with unit cell dimensions of a = 421Å, b = 183Å, c = 385Å, $\alpha = \gamma = 90°$, $\beta \sim 90°$[1](Ritter et al. 1999). Phases up to a resolution of 30 Å could be assigned by *ab initio* methods[2].

The resulting overall shell structure of the LDL particle is consistent with models obtained by small angle scattering. However, in contrast to the current opinion the electron density does not show a radial symmetric particle but supports a particle with a cylindrical shape. The distribution of electron density levels on the particle surface is asymmetric and regions of highest electron density are interpreted to correlate with the distribution of apoB. Areas of reduced (but still high) electron density on the surface could correspond to the phospholipid monolayer.. Inside the particle core we find layer-like structures of low density corresponding most probably to the acyl chains of layers of cholesterol ester. This model is in agreement with that recently obtained by electron cryo-microscopy[3].

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