

Disk-like Complex Formation by Apolipoprotein-Lipid Membrane Interaction and Relevance to HDL Formation

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Nascent high-density lipoprotein (HDL) is known to be formed by the interaction of apolipoprotein A-I (apoA-I) with transmembrane ATP-binding cassette transporter A1, but the molecular mechanism by which nascent HDL forms is less well understood. Here, it was studied how reconstituted HDL (rHDL) forms spontaneously on the interaction of apoA-I with model membranes. The formation of rHDL from pure phosphatidylcholine (PC) LUV proceeded very slowly at 37.0°C, but sphingomyelin (SM) -rich PC/SM LUVs, which are in a gel/liquid-disordered (L_d) phase at this temperature, were rapidly microsolvubilized to form rHDL by apoA-I. The addition of cholesterol decreased the rate at which rHDL formed and induced the selective extraction of lipids by apoA-I, which preferably extracted lipids of L_d phase rather than lipids of L_o phase. In addition, apoA-I extracted lipids from the outer and inner leaflets of LUVs simultaneously. These results suggest that heterogeneous interface of the mixed membranes facilitates the insertion of apoA-I and induces L_d phase-selective but leaflet-nonspecific lipid extraction to form rHDL, and are compatible with recent cell works on the apoA-I-dependent HDL generation.