



Contribution ID : 37

Type : not specified

Lipoprotein lipid exchange dynamics with natural membranes probed by time-resolved small-angle neutron scattering (TR-SANS)

In atherosclerosis lipids and fibrous elements accumulate in the blood vessels forming plaques that eventually can lead to myocardial infarction or stroke. HDL and LDL particles have been shown to play a role in the development and the progression of the plaque build-up and are currently used as biological markers in addition to measurements of total lipid and cholesterol. Yet many people still develop the disease even when their blood lipid values fall within the healthy range. The function and the lipid exchange of the HDL and LDL particles seems to be more important than the actual HDL and LDL levels. Understanding the dynamic/structure relationship of different lipoproteins and especially the mode of action with which they release or accept their lipid cargo is therefore a prerequisite for the development of better standards and methods for diagnostics of atherosclerosis to aid in the development of targeted therapies in the fight against CVD. Here, small-angle neutron scattering in combination with selective deuteration was used to follow the molecular lipid exchange between native lipoprotein particles and complex cell-membrane mimics. Focusing on the lipid transport kinetics between both native HDL and LDL and large unilamellar vesicles made of “neutron invisible” natural, monounsaturated, phosphocholine mixtures we show that the lipid exchange is assisted by collision and particle tethering to the membrane. The data also show that the two particles exhibit different kinetic regimes, suggesting that the apolipoprotein plays a key role in enhancing lipid exchange. The method developed here allows for molecular exchange events between complex biological protein-lipid systems to be followed in an elegant, systematic and controlled fashion. For the case of lipoproteins and their function in atherosclerosis, this approach can be used to provide unique information on the role that each lipid species exerts on lipid uptake and exchange, as well as the mode of action of specific apolipoprotein types and subtypes.

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