Experimental report

15/02/2021

Proposal: 8-02-859 **Council:** 10/2018

Title: Lipid exchange dynamics between native lipoprotein particles and human cell mimics

Research area: Chemistry

This proposal is a new proposal

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Samples: lipoproteins (lipids+apolipoproteins)
D2O invisible PC
D2O invisible cholesterol

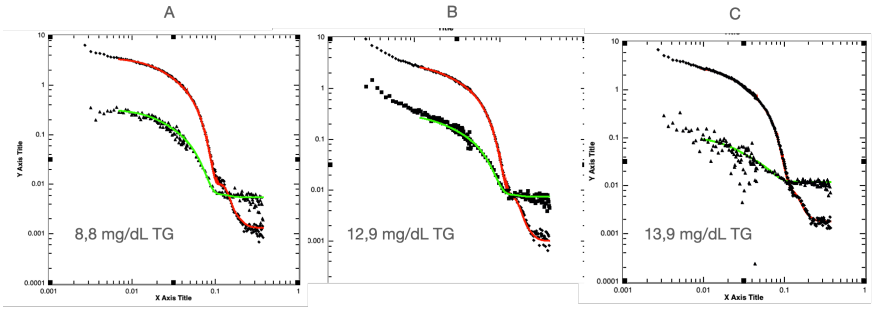
Instrument	Requested days	Allocated days	From	To
D22	3	2	19/09/2019	21/09/2019

Abstract:

In atherosclerosis lipids and fibrous elements accumulate in the blood vessels forming plaques that eventually can lead to myocardial infarction or stroke. High and low density particles, HDL and LDL respectively, 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. 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 and aid in the development of targeted therapies in the fight against cardiovascular disease. Here, SANS in combination with selective deuteration was used to follow the molecular lipid exchange between native lipoprotein particles and cell-membrane mimics.

In this proposal, we looked at Lipid exchange dynamics between native lipoprotein particles and human cell mimics. We focused on the total HDL fractions, and 3 main subfractions, of healthy (individual A) and hypertriglyceridemic individuals (Individuals B and C).

First static data was collected for the different HDL fractions and subfractions. We observe a clear trend as described below:



	A HDL T	B HDL T	C HDL T
Rcore	23,5	18,1	16,7
t tail	13,9	12,1	14,6
T shell	8,0	8,3	8,5
fraction water	0,025	0,083	0,10
number lipid P	**178**	**97**	**117**
Nprot	3,0	2,2	2,2
Nclu	5,7	7,5	5,0
D	94,7	82,9	93,8
f_clu	0,19	0,12	0,30
Sigma_Gauss_SD	0,28	0,348	0,45
ApoA1 mg/mL	0,320	0,500	0,310
PL x Nprot	**81,2**	**47,2**	**51,8**
TG x Nprot	5,4	10,1	9,3
FC x Nprot	22,6	6,8	7,3
CE x Nprot	94,5	39,7	53,5
PL + FC	103,8	54,0	59,1
Volume/ Å3 HDL Bio	154223	90453	99532
VOlume/ Å3 HDL SANS	394574	239954	263522

The higher the TG levels, the smaller the particles (driven by the core)
The outer shell and tail shell remain constant
Total size decreses with TG levels
The estimated number of lipids per particle is larger for the model than as calculated from biochemistry data, typically by a factor of 2

Similar trends are observed for the subfractions.

We then measured the lipid exchange for total HDL fractions and liposomes at different ratios. This data is currently under analysis. Our plan is to prepare this data for publication soon.