Experimental report

15/02/2021

Proposal: 8-03-979 **Council:** 4/2019

Title: Real time studies of the formationof ApoE-based reconstituted High Density Lipoprotein-mimics

Research area: Biology

This proposal is a resubmission of 8-02-845

Main proposer: Sarah WALDIE

Experimental team: Yubexi CORREA
Sarah WALDIE
Trevor FORSYTH

Local contacts: Sylvain PREVOST

Samples: ApoE3 POPC + cholesterol discs
ApoE4 POPC + cholesterol discs
DMPC/POPC +/- cholesterol vesicles
ApoE3/ApoE4 proteins
ApoE3 DMPC + cholesterol discs
ApoE4 DMPC + cholesterol discs

Instrument	Requested days	Allocated days	From	To
D11	2	2	08/09/2020	10/09/2020

Abstract:

In westernised societies, atherosclerosis constitutes the leading cause of death. The development of this disease is directly related to the concentration of high and low-density lipoproteins (HDL and LDL, respectively) in the blood. These particles remove and deposit lipids from and into the artery walls leading to plaques of fat building up and the progression to cardiovascular diseases such as heart attacks and strokes. Essential information regarding the kinetics of lipid exchange and the role played by the apolipoprotein isoform present in the particles is missing – the understanding of which could play a huge role in developing treatment for this disease. The aim of this study is to better understand the formation of the reconstituted HDL particles and the roles the apolipoproteins isoform play in relation to the lipid phase it is interacting with.

Experimental Report for experiment: **8-03-979**

Real time studies of the formation of ApoE-based reconstituted High Density Lipoprotein-mimics

The aim of the experiment was to follow the formation of the reconstituted HDL particles focussing on the protein variant and protein-lipid ratio. Two protein variants were measured, ApoE3 and ApoE4, and 4 protein-lipid ratios were investigated also: 1-25, 1-50, 1-100 and 1-200.

During our beam time we successfully measured the formation of ApoE3- and ApoE4-rHDL at various time points across the two days of beamtime. We started with 1-100 and 1-50 ratios and followed their kinetics during the first hours every 10 minutes at one specific q-range. Periodically the full q-range of interest was measured to obtain an overall view of the sample. We cycled through these samples to obtain measurements at various time points (see figure 1). We later started the 1-200 and 1-25 ratios, however as little change had been seen in the initial hourly kinetics with the previous samples only periodical measurements were taken (every hour for example) to obtain well-spaced out data sets (see figure 2).

After initial preliminary analysis it was seen that ApoE4 took up the lipid vesicles at a higher rate than ApoE3 and that the 1-100 ratio was the most suitable for forming discs at the most efficient rate.

Further analysis is required for these data sets which will be carried out in the coming months, in hopes to publish later this year.

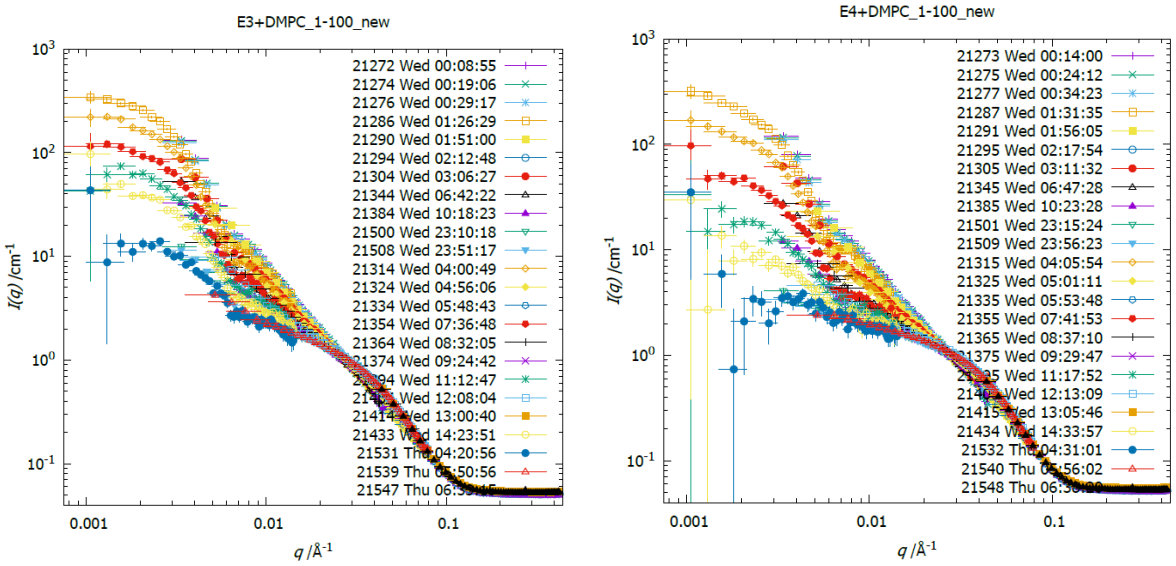

Figure 1. SANS data of ApoE3 (left) and ApoE4 (right) incubating with lipid vesicles at a 1-100 ratio and forming nanodisc-like reconstituted HDL particles.

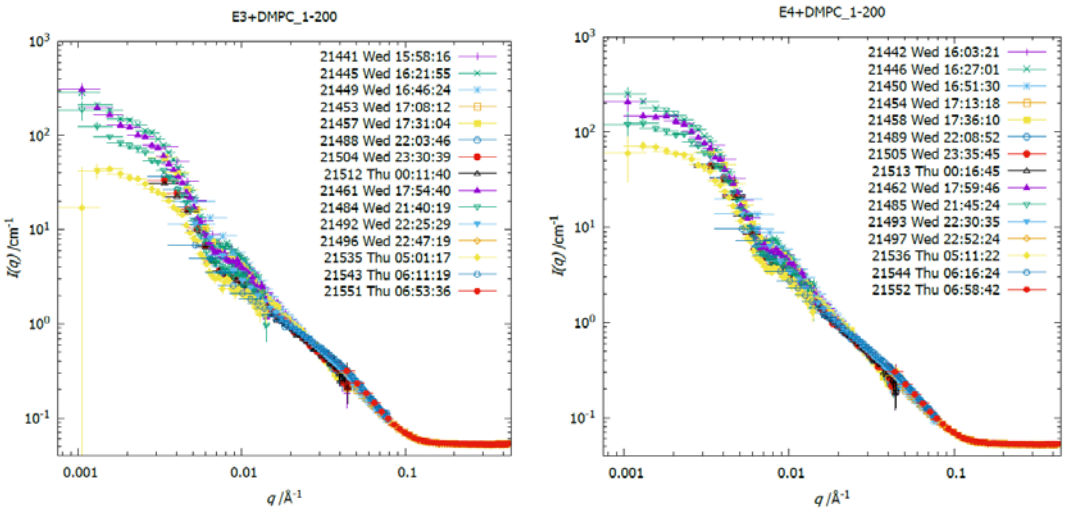

Figure 2. SANS data of ApoE3 (left) and ApoE4 (right) incubating with lipid vesicles at a 1-50 ratio and forming nanodisc-like reconstituted HDL particles.