# Experimental Report



**Proposal:** **8-04-745** **Council:** 10/2014

**Title:** Dynamics of lipoprotein particles under high pressure

**This proposal is continuation of: 8-04-694**

**Researh Area:** Biology

**Main proposer:** **PETERS Judith**

**Experimental Team:** PETERS Judith
MARTINEZ Nicolas

**Local Contact:** PETERS Judith

**Samples:** Lipid-enriched LDL
Minimally oxidized LDL
native Low Density Lipoprotein

| Instrument | Req. Days | All. Days | From | To |
|---|---|---|---|---|
| IN13 | 11 | 9 | 04/05/2015 | 13/05/2015 |

**Abstract:**

We propose to investigate molecular dynamics of native and biochemically modified low density lipoprotein (LDL) nanoparticles,
which are macromolecular assemblies of phospholipids, cholesterol and fat stabilized by a protein moiety, under high hydrostatic
pressure. The conception of a dynamic landscape similar to natural membranes seems to be reasonable for lipoprotein species,
which we assume to be highly sensitive to pressure. Thus this project aims to study the impact of specific modifications of LDL on the
dynamics, organization and interplay of lipids and protein under high pressure conditions. By combining all data we expect to obtain a
more comprehensive picture of the structure and dynamics of LDL to be discussed in relation to its biological role.

Report 8-04-745 and CRG 2230 – IN13

**Dynamics of lipoprotein particles under high pressure**

R. Prassl, B. Lehofer, J. Peters, N. Martinez

Low density lipoproteins (LDL) are naturally occurring macromolecular assemblies of lipids, fat and a single protein component, termed apolipoprotein B100 (apo-B100). Apo-B100 stabilizes the structure of the lipid nano-assembly and triggers the function of LDL in human circulation. The major role of LDL in humans is the transport of cholesterol and fat to tissues and cells. Apart from its vital role in physiology, LDL is intimately involved in the progression of cardiovascular diseases, in particular atherosclerosis. Chemical modifications of LDL e.g. by lipid oxidation cause an accumulation and retention of oxidized LDL in the subendothelial space for ingestion by macrophages to be transformed into foam cells. In combination with inflammatory reactions LDL retention in the arterial wall constitutes the first stage of atherosclerosis. Atherosclerosis dramatically increases the risk for myocardial infarction and stroke, which are amongst the major causes of morbidity and mortality in Western civilization resulting in substantial economic burden imposed on health care systems (1).

To date specific information on molecular motions, intrinsic flexibility or conformational stability is missing, especially with respect to the structural integrity of modified LDL. Ultimately, it is primarily the combination of above mentioned physicochemical parameters that determine the physiological function of LDL in humans. Lipoproteins, which are macromolecular assemblies of lipids and proteins, have shown a distinct dynamical behavior as function of temperature (2), which is very similar to membranes, and we assume lipoproteins to be highly sensitive to pressure as well. Thus, the conception of a dynamic landscape for lipoprotein species similar to natural membranes seems to be reasonable; however, this has never been shown experimentally before.

First we studied structural changes up to 3 kbar and a temperature range between 280 and 310 K at a SANS instrument of the PSI. It is a matter of fact that the core-lipids of LDL undergo a liquid crystalline phase transition at temperatures close to physiological (3), what makes this temperature range particularly interesting. We investigated 3 types of samples: native LDL (nLDL), lipid-enriched LDL (triglyceride (TG) rich LDL) and minimally oxidized LDL (oLDL). One representative example is shown in Figure 1. This experiment made clear that with respect to pressure the main structural changes occurred between 2 and 3 kbar.

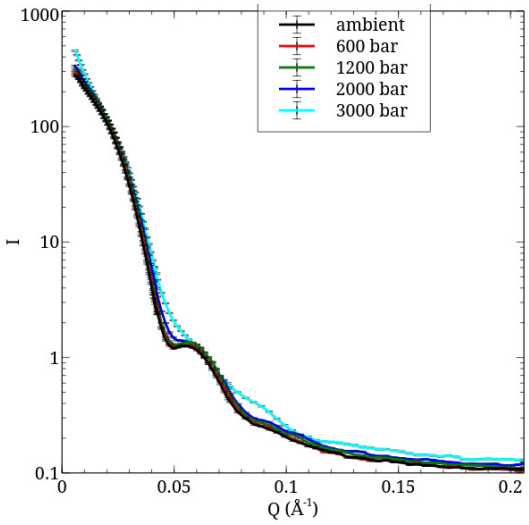


**Figure 1:** SANS spectra at different pressures and 10 °C for the lipid - enriched LDL sample taken on the SANS-II instrument of the PSI.

Therefore, we investigated the molecular dynamics of the same three samples on IN13 at 20 and 3000 bar and at the three temperature values of 280, around 295 (varying slightly depending on the sample) and 310 K, corresponding to the states below, on and above the phase transition, respectively (see Figure 2).

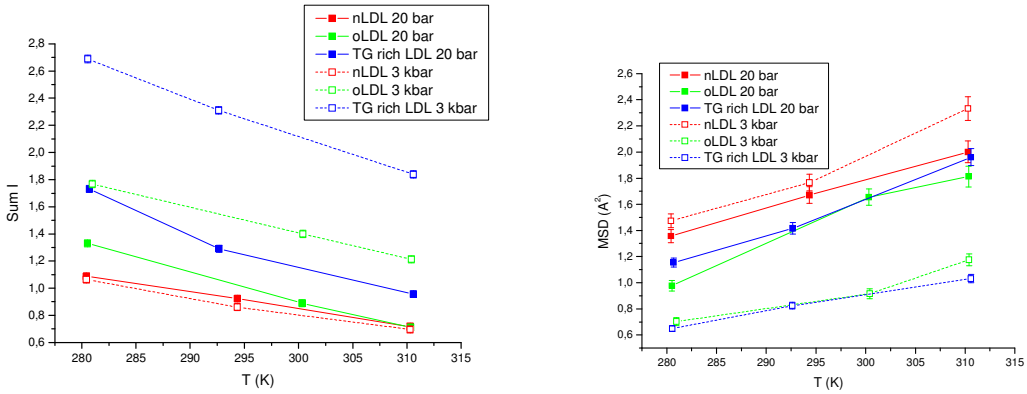


**Figure 2:** Summed intensities and mean square displacements of all three samples as function of pressure and temperature.

Our results showed that oLDL and TG rich LDL became much more rigid at higher pressure (as expected), but surprisingly almost no effect was visible within error bars for nLDL. It could be an indication that the native LDL is able of coping with pressure better than the modified LDL particles, because it is optimized in a way that high pressure does not have so much influence on the dynamics as for the two other particles. Further analyses are under progress to investigate this question.

## References

1. V. L. Roger et al., Circulation (2011) **123,** e18-e209.
2. Mikl, C., Peters, J., Trapp, M., Kornmüller, K., Schneider, W. and Prassl, R., Journal of the American Chemical Society 133 (2011), 13213 - 13215.
3. Prassl R, Pregetter M, Amenitsch H, Kriechbaum M, Schwarzenbacher R, Chapman JM, Laggner P. PLoS ONE 2008;3:e4079