

## The new definition of plasma remnant lipoproteins

The definition of remnant lipoproteins (RLP) in plasma has been confused for many years because of the variety of methods used to identify RLP. The most common definition of RLP proposed several decades ago has been the intermediate density lipoproteins (IDL) isolated by an ultracentrifugation method as other lipoprotein fractions. The most important RLP characteristic has been recognized as the TG-rich lipoproteins which increase significantly after food intake. However, IDL doesn't increase after food intake, it has become inconspicuous as indicative RLP. There are other methods, such as electrophoresis, NMR and HPLC which are used to identify RLP by charge, particle size and the calculation. However, those methods can't isolate a substantial RLP fraction from plasma.

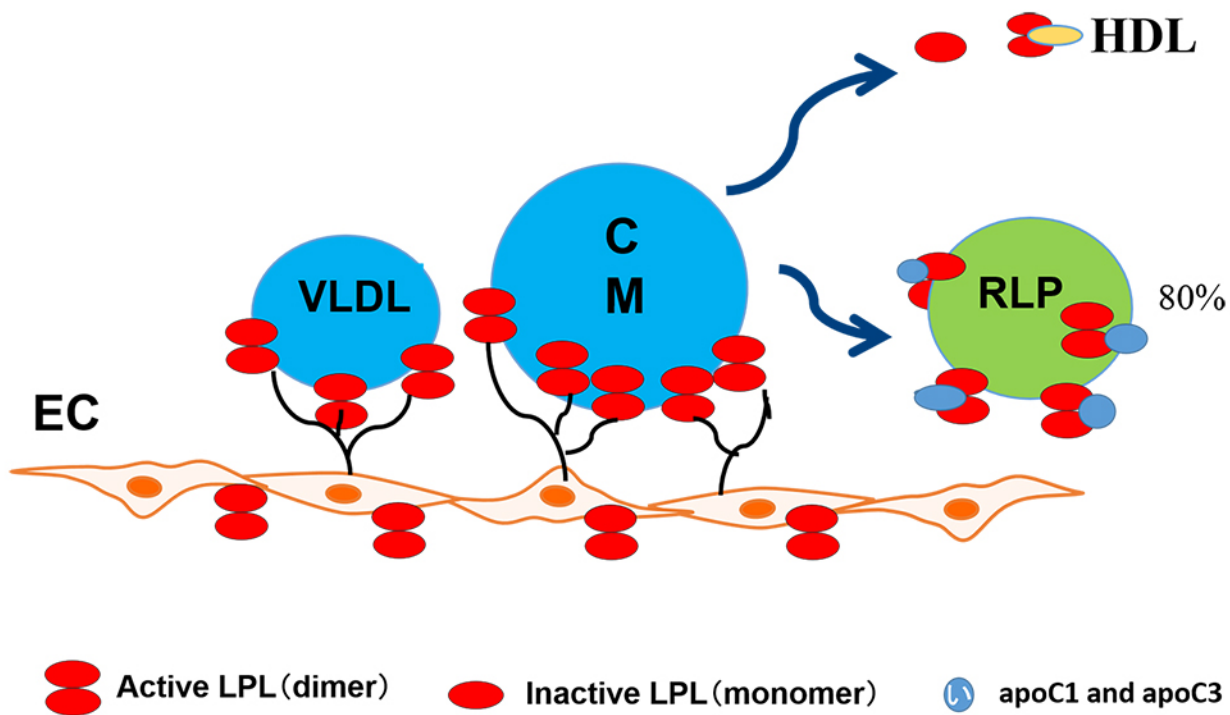


Fig. 1. RLP are formed from chylomicrons (CM) and very low density lipoproteins (VLDL) on the surface of endothelium cells (EC). After hydrolysis of CM and VLDL, most LPL is dissociated from EC as the LPL- RLP complex with dimeric and inactive form.

We have investigated the characteristics and clinical significance of remnant lipoproteins in plasma isolated by an immunoaffinity gel separation method since 1993. Using this method, we found that the majority of LPL in plasma presented in RLP fraction we have isolated as remnant lipoproteins.

The new findings are as follows. 1) More than 80% of circulating LPL in non-heparin plasma was found in RLP as RLP-LPL complex. 2) The circulating LPL found in RLP in the pre- and post-heparin plasma was shown as LPL dimers but in the inactive form with inhibitors such as apoC1 and C3. 3) When lipolytic activity was inhibited by LPL inhibitor (tetrahydrolipstatin; THL) in the post-heparin plasma, most LPL dimers were found in the VLDL elution range, specifically in the RLP.

Those results provided a new insight of LPL and RLP interaction in the circulating plasma and suggested the need of a new definition of plasma remnant lipoproteins. RLP we isolated has been defined as TG-rich lipoproteins with apoE-rich, apoC3-rich and cholesteryl-ester rich VLDL. However, those markers are not specific to remnant lipoproteins. Therefore, LPL could be the only specific marker of remnant lipoproteins which is associated with the formation of RLP at endothelium.

After the reduction in the TG content by LPL, CM and VLDL particles have been generally believed to become smaller remnant particles such as IDL. However, several studies, including our own reported that RLP was predominantly of large VLDL size, which remained without further hydrolysis associated with comparatively low LPL activity and concentration at endothelium. We have shown that LPL does not increase after food intake associated with significant increase of RLP size and resulted less amount of LPL per postprandial RLP.

Chylomicronemia is a typical case which lacks the LPL protein or lipolytic activity. Those cases can't form remnant lipoproteins, therefore, large nascent chylomicrons and VLDL remain in plasma. As those particles don't carry LPL, those lipoproteins can't be defined as remnant lipoproteins. The cases with TG above 800 mg/dL have been controversial, whether atherogenic or non-atherogenic, it can be judged by the concentration of LPL on those TG-rich lipoproteins.

When LPL is detached from the endothelium, LPL is released as the RLP-LPL complex with inactive form into the circulation. The LPL bound to RLP plays a role for the ligand to LRP-1 or VLDL receptor, as Beizegel et al reported that LPL is able to efficiently mediate binding of lipoproteins to the cell surface and to both of the endocytotic receptors.

In conclusion, the present report clarified that the majority of LPL in non-heparin plasma was bound to RLP particles in the dimeric but inactive form.

The presence of LPL on RLP reflect the metabolic condition of remnant proteins. Therefore, we have proposed that the TG-rich lipoproteins bound to LPL dimers is the new definition of remnant lipoproteins.

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## Publication

[The majority of lipoprotein lipase in plasma is bound to remnant lipoproteins: A new definition of remnant lipoproteins.](#)

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