Triglyceride-Rich Lipoproteins From Normotriglyceridemic Subjects and Hyperlipidemic Patients Differently Affect Endothelial Cell Activation and Gene Expression Patterns

To the Editor:

We read with interest the article by Ting et al showing that post-prandial triglyceride-rich lipoproteins (PP-TGRL) from healthy human volunteers (NTG) fail to promote endothelial inflammation but increase the tumor necrosis factor-α response of endothelial cells. We would like to add further information on this topic recently obtained in our laboratory that may contribute to the understanding of the role of TG-rich lipoproteins in modulating endothelial function(s).

Ting et al showed that PP-TGRL are unable to elicit pro-inflammatory responses and this finding is based on the lack of effect of PP-TGRL on ICAM-1, VCAM-1 and E-selectin mRNA expression. An observation confirmed by the lack of monocyte recruitment by endothelial cells exposed to PP-TGRL. However, and consistent with our findings, postprandial TGRL per se activated p38MAPK a key pathway of intracellular signaling in inflammation.

In addition we showed that postprandial TGRL from type IV hyperlipidemic patients induce to a larger extent, compared with fasting TGRL, phosphorylation of p38 MAPK, CREB and IκB-α in human endothelial cells and increase the DNA binding activity of CREB, NFAT and NF-κB. These results prompted us to investigate the differences between PP-TGRL from NTG subjects and HTG patients on endothelial cell gene expression. We observed the induction by PP-TGRL from HTG patients but not by NTG subjects of a large set of proinflammatory genes including VCAM-1, PECAM-1, ELAM-1, ICAM-1, P-selectin, MCP-1, IL-6, TLR-4, CD40, ADAMTS1 and PAI-1. Furthermore, in vivo, the endothelium-dependent flow mediated dilatation (FMD) decreased in both NTG and HTG subjects after 4 hours from the intake of an oral fat load and returned to basal levels in NTG subjects while remained impaired in HTG subject up to 8 hours. Therefore only PP-TGRL from HTG patients modulated a proinflammatory gene set in endothelial cells.

Thus our data suggest that in hypertriglyceridemic patients TGRL in the fasting state and more so in the post prandial phase may increase the endothelial dysfunction by inducing a proinflammatory activation of the endothelium. In normotriglyceridemic subjects accordingly to Ting et al the postprandial response only prime the endothelium toward a high sensitivity to a pro-inflammatory environment.

In conclusion we believe that the composition of TGRL that profoundly differs in hypertriglyceridemic patients versus normotriglyceridemic subjects is crucial and needs to be taken in account when discussing the effect of TG-rich lipoproteins on endothelial function.

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5. Raw data on cDNA microarray experiments are available at the following address http://www.sisalombardia.it/dati/dati.htm.
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