

P013 Apolipoprotein-E independent mechanisms in the macrophage uptake of chylomicron remnants-like particles.

M. Napolitano¹, E. Bravo¹, R. Rao², H. Kruth²

¹*Istituto Superiore di Sanità, Rome ITALY;*

²*NHLBI, NIH, Bethesda, USA.*

The main ligand in chylomicron remnants uptake is apolipoprotein E (apoE). Macrophage internalization of chylomicron remnants-like particles (CRLP) containing human apoE induces a several fold increase in triacylglycerol (TG) and about a 30% increase in cholesterol (CH). The lack of apoE on CRLP reduced, respectively, by only about 50% and 10% the induced TG and CH increase, indicating that CRLP uptake is also mediated by apoE receptor-independent mechanisms. To study the latter mechanisms, human monocyte-derived macrophages (HMDM) were incubated with up to 80 µg CH/ml of apoE-free CRLP. Then, macrophage TG and CH content were evaluated by fluorometric assay. First, we investigated whether apoE secreted by macrophages into the medium mediated the apoE-free CRLP uptake. Then, we tested the hypothesis that macropinocytosis, which is responsible for particle uptake in the fluid-phase, functioned in the uptake of apoE-free CRLP. Since the presence of apoE antibodies in the HMDM incubations with apoE-free CRLP and macropinocytosis induction by phorbol esters both did not affect cell TG and CH content, we can conclude that both these mechanisms are not involved in apoE-free CRLP induced macrophage lipid accumulation. On the contrary, an important contribution to the TG accumulation seems to be extracellular lipoprotein lipase hydrolysis of TG, which precedes macrophage uptake of released fatty acids, as suggested by the significant reduction (-34%) of macrophage TG accumulation induced by orlistat.