

**P009** Oxidation inhibits the uptake of chylomicron remnants by macrophages

**Fatos Bejta, Peter Gough\*, Keith Suckling\* and Kathleen Botham**

*The Royal Veterinary College, London, UK. \*GlaxoSmithKline, Stevenage, UK*

There is considerable evidence indicating that chylomicron remnants (CMRs) are atherogenic. Having established that CMRs are taken up by macrophages and cause extensive lipid accumulation, and that antioxidants increase their uptake, our objective was to investigate the uptake of CMRs in different oxidative states by macrophages. The role of the LDL receptor (LDLr), LDLr-related protein, scavenger receptors and phagocytosis was tested using chylomicron remnant-like particles (CRLPs) and THP-1 macrophages. The CRLP oxidative state was varied by exposure to  $\text{CuSO}_4$  (oxCRLPs), or by the addition of probucol (pCRLPs). OxCRLPs were taken up by macrophages at a significantly slower rate than CRLPs, while pCRLPs were taken up significantly faster. Uptake of all 3 types of particles was inhibited to a similar extent by lactoferrin (an LRP ligand) (-80-90%) and by excess LDL (-30-40%). In the presence of both inhibitors, however, the differences in the rates of uptake were abolished. Modest inhibition of uptake of CRLPs, oxCRLPs and pCRLPs was also observed with blockers of CD36 (anti-CD36) (-40%) and phagocytosis (cytochalasin D) (-35-40%). These results indicate that CRLPs are taken up by THP-1 macrophages mainly via the LRP with some contribution from the LDLr, CD36 and phagocytosis, and suggest that the lower rate of uptake of oxidised particles is due to differential interaction with apolipoprotein E-dependent receptors.