Advanced glycation end-products uptake by macrophage

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Advanced glycation end-products (AGEs), which comprise non-enzymatically glycosylated proteins, play an important role in several diseases and aging processes including angiopathy, renal failure, diabetic complications, and neurodegenerative diseases. Among AGE-associated phenotypes, toxic AGEs, glyceraldehyde-derived AGE-2, and glycolaldehyde-derived AGE-3 are involved in the pathogenesis of diabetic complications. In addition, macrophages are reported to remove extracellular AGEs from tissues via scavenger receptors, leading to the progression of atherosclerosis. In the present study, we found that AGE-2 and AGE-3 enhanced their own endocytic uptake by RAW264.7 mouse macrophage-like cells in a concentration-dependent manner. Furthermore, we demonstrated the morphology of phagocytic macrophages and the endocytosis of AGE particles. The toxic AGEs induced the expression of a scavenger receptor, CD204/scavenger receptors-1 class A (SR-A). Notably, an antibody against CD204 significantly prevented toxic AGE uptake. Moreover, an SR-A antagonistic ligand, fucoidan, also attenuated the AGE-2- and AGE-3-evoked uptake in a concentration-dependent manner. These results indicated that SR-A stimulation, at least in part, plays a role in AGE uptake.