OBESITY-ACCELERATED ARTERIAL AGING: INTERPLAY BETWEEN FREE FATTY ACIDS AND LIPOCALIN-2

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Obesity is a major culprit for the high prevalence of cardiovascular disease, the leading cause of death in elderly patients. Obesity accelerates ageing-associated arterial dysfunction by causing metabolic disturbances, such as insulin resistance, hypertension and increased plasma lipid levels. Elevated plasma free fatty acids (FFA) are found in both obese and aged human subjects and contribute to the impairment of endothelium-dependent vasodilatations. Lipocalin-2 is a pro-inflammatory adipokine upregulated in obese and ageing subjects. Circulating lipocalin-2 is positively correlated with increased plasma insulin, glucose and lipid levels, as well as arterial blood pressure. In humans, genetic variantions in the gene encoding lipocalin-2 favor the development of hypertension. Mice without lipocalin-2 are protected against endothelial dysfunction induced by both dietary obesity and aging. By contrast, administration of lipocalin-2 induces endothelial dysfunction in ageing and obese animals. Lipocalin-2 possesses specific lipid-binding activity and has been proposed to act as lipid chaperones to enhance lipotoxicity. The presence of FFA serves as a trigger for lipocalin-2 to elicit detrimental effects on endothelial function. Thus, the interplay between FFA and lipocalin-2 not only addresses the close relationship between lipotoxicity and inflammation, but also represents important common mechanisms underlying ageing- and obesity-associated vascular abnormalities.