Abstract

Introduction: Cardiovascular disease is the number one killer of Australians. The major cardiovascular disease is atherosclerosis. Atherosclerosis is characterised by the build up of lipid-filled plaques in arteries that eventually rupture causing death through myocardial infarction or stroke. High density lipoproteins (HDLs), the good cholesterol, can reverse advanced atherosclerosis, slow down progression of the disease as well as retard the initial steps in early plaque formation. HDLs exert their protective effects through a number of different mechanisms but notably, HDLs are potently anti-inflammatory. HDLs decrease cytokine-induced inflammatory responses in endothelial cells, the cell type that line artery walls and represent the first line of defence against atherosclerotic plaque formation. The anti-inflammatory effects of HDLs persist in endothelial cells even after the HDLs are removed. It was therefore hypothesised that HDL induces the expression of a protein in endothelial cells that protects the cells against a subsequent inflammatory insult.

Methods and Results: Microarray analysis revealed that HDL increased the gene expression of 24-dehydrocholesterol reductase (DHCR24 or seladin-1) by ~8-fold. Knockdown of DHCR24 expression abrogated the anti-inflammatory effects of HDL.

Conclusion: Anti-inflammatory effects of HDL are mediated, at least in part, by DHCR24. DHCR24 has a potent cellular protective role in endothelial cells. These findings may now provide a potential new therapeutic target for the treatment of atherosclerosis.

Dr Alison Heather’s Other Selected Publications


