CSL112, A NOVEL FORMULATION OF HUMAN APOA-I, ROBUSTLY ENHANCES THE ABILITY OF SERUM TO EFFLUX CHOLESTEROL

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The greatest risk for recurrent cardiovascular events lies in the first several weeks following ACS, and current therapies (e.g. statins) do not target cholesterol efflux from plaque in this time frame. ApoA-I is able to rapidly remove cholesterol from plaque, and cholesterol efflux from macrophages is a functional serum marker that has an even stronger inverse association with coronary heart disease than HDL cholesterol (Khera et al. 2011, NEJM 364;2;127). Statins have minimal effects on apoA-I and no measurable effect on cholesterol efflux. We recently described CSL112, a novel formulation of full length human apoA-I and phospholipids designed to resemble nascent HDL and to maximize efflux from macrophages. Infusion of CSL112 in rabbits has been shown to cause an immediate elevation in cholesterol efflux capacity. Here we studied the effects of adding CSL112 ex vivo to human serum on cholesterol efflux capacity. Samples were obtained from five subjects with a range of lipid phenotypes including normolipidemic subjects and subjects with low HDL and high triglycerides. Serum samples were spiked with a range of concentrations of CSL112 (low, medium, high; corresponding to clinical concentrations) and cholesterol efflux was assessed as previously described (Khera et al.). Cholesterol efflux at baseline was ~30% lower in the two subjects with low HDL compared to subjects with normal HDL. When spiked into human serum, CSL112 robustly increased cholesterol efflux capacity in a concentration dependent manner. At the medium concentration tested, efflux increased by a mean 291% ± 65%. All subjects showed a similar rise in efflux, regardless of initial lipid profile. We conclude that CSL112 robustly and rapidly enhances the capacity of human serum to promote cholesterol efflux to levels substantially higher than those seen in prior studies of normal individuals. CSL112 may thus provide a novel option for rapid reduction of systemic atherosclerotic burden and the potential of cardiovascular event reduction in ACS.