FRAMING ATHEROSCLEROSIS AS A NANOTOXICOLOGY PROBLEM

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Abstract

With the combination of poor diet, inactivity and aging population in the developed world, cardiovascular disease is the major disease leading to morbidity and mortality. Central to this is atherosclerosis and the role it plays in instigating myocardial infarction and strokes in a high proportion of individuals. Current measures directed at atherosclerosis (and subsequently myocardial infarction and strokes) are either preventative such as controlling blood cholesterol level with drugs such as statins or surgical such as angioplasty to combat stenosis of the arteries and peripheral blood vessels or by-pass surgery. However by taking a different approach to viewing the pathogenesis of atherosclerosis it becomes evident that it is a toxicological problem driven by exposure to a biological, endogenous ‘nanoparticle’. It is well established that Low Density Lipoproteins (LDL) is the crucial driver of atherosclerosis and indeed treatment with statins is aimed at reducing blood concentration levels of LDL. It is also known that LDL is a nanoparticle with a diameter of 20-25nm, placing atherosclerosis into the toxicological paradigm of exposure leading to dose leading to a response. Thus, it becomes clear where the broad targets of therapies lie. Statins and changes in diet seek to control exposure by reducing blood borne LDL levels whilst mitigating endothelium dysfunction (e.g. due to high blood pressure using drugs such as beta blockers) helps reduce the dose of LDL and accumulation of inflammatory cells in the arterial wall which again may help ameliorate a response. However whilst these therapeutic interventions can have a significant improvement in clinical outcome, they are typically long term therapies associated with limiting progressions of the disease yet there remains the need to be able to stabilize and/or regress the disease by targeting the atherosclerotic plaques directly.

In this presentation, the processes leading to Atherosclerosis will be described as a Nanotoxicology problem and the potential development of Nano Delivery Systems (NDS) to target the plaques, for identification and therapy, will be discussed.

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