Identification, characterisation and functional assessment of microRNA regulation of foam cell macrophage formation during atherosclerosis progression

Collectively, cardiovascular pathologies including atherosclerosis, aneurysms and heart failure, account for more deaths world-wide than other diseases. Accordingly, a better understanding of the cellular and molecular mechanisms underlying these pathologies is paramount for the identification and development of both biomarkers and treatments of these diseases. The past decade has highlighted the prominent role of monocyte/macrophages in the development and progression of cardiovascular diseases, however more current research has demonstrated that it is the transformation of macrophages into lipid-laden foam-cell macrophages that drive the progression of atherosclerotic plaques and contribute to aneurysm formation in man. We have recently identified that foam-cell macrophages can co-exist as varying phenotypes which display an array of differing properties. Moreover our latest findings have suggested that foam-cell macrophage subsets divergently harbour the ability to utilise microRNA to alter their proteolytic potential and consequently atherosclerotic plaque and aneurysm progression. Furthermore, our data imply that microRNA are regulated during the transformation of specific macrophage subsets into foam-cell macrophages. The aim of this current studentship is to identify novel microRNA that are regulated during foam-cell macrophage formation in numerous macrophage subsets, and robustly assess the potential of selected microRNA to regulate foam-cell macrophage formation. Such an approach should result in the identification of specific novel microRNA which can serve as new therapeutic targets and biomarkers for such debilitating cardiovascular diseases as atherosclerosis and aortic aneurysms. The techniques to be used are all routine in our group and include flow cytometry, tissue culture, molecular biology, microscopy and imaging, in vitro and in vivo cell behavioural assays, as well as numerous in vivo models of cardiovascular disease.

This project would suit a student with an interest in the understanding of human disease and inflammation. It offers the opportunity to study in an excellent research environment, in a research institute with world class facilities and resources, devoted to understanding the cellular and molecular mechanisms of cardiovascular disease, and driving new translational therapies and identification of biomarkers for patients susceptible to cardiovascular diseases. We have an opportunity available for exceptional candidates with an interest in the areas of human biology, immunology, cell culture, in vitro and in vivo disease modelling, and of course the cardiovascular system and its diseases.

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