Project title	Inflammation and Arterial Disease		
Key words	inflammation, heart, artery, diet		
Expected duration of the project (years)	5		
Purpose of the project	Basic research	Yes	
	Translational and applied research	Yes	
	Regulatory use and routine production		No
	Protection of the natural environment in the interests of the health or welfare of humans or animals		No
	Preservation of species		No
	Higher education or training		No
	Forensic enquiries		No
	Maintenance of colonies of genetically altered animals	Yes	
Objectives of the project	**<u>Manchester secondary availability</u>** The objective of the project is to understand the biological mechanisms occurring in artery walls that ultimately lead to heart attacks. The focus of these studies will be on molecules that drive inflammatory processes in artery walls. Inflammation is thought to play a key role at all stages of disease but there are no specific treatments available yet that target these in man.		
Potential benefits likely to derive from this project	This research will lead to a greater understanding of the key molecules that control inflammation in diseased artery walls. From this research we will be able to pinpoint the pathways and individual molecules that could be targeted directly or with repurposed or new drugs/treatments as a prelude to first in man studies.		
Species and approximate numbers of animals expected to be used, and anticipated period of time	**<u>Manchester secondary availability</u>** We will use mouse preparations of arteries and expect to use 50-70 mice over the next 2 years.		
Expected adverse effects and the	Arteries (carotid or femoral) will be ligated or be injured with an intraluminal wire and the response to healing in		

likely/expected level of severity. What will happen to the animals at the end.	the artery wall will be followed. Any adverse events relate largely to the surgical procedure e.g. rare stroke due an incomplete circle of Willis or temporary change in gait and are of moderate severity. All the animals are humanely killed at the end of procedures and their arteries are dissected for assessment of the healing pathology.
Application of the 3 Rs	
1. Replacement Why do animals need to be used, and why non-animal alternatives cannot be used.	As well as biological mechanisms responsible for healing, we wish to study the physiological consequences e.g. blood flow using laser Doppler techniques. This is only possible in a whole animal setting.
2. Reduction How the use of minimum numbers of animals will be assured	As much information as possible will be gleaned *in vitro* before proceeding to mouse preparations. We will keep our experimental design and power calculations for group sizes under review to ensure that the minimum number of animals is used. These will be revisited each time a new individual study plan is prepared.
3. Refinement Reasons for the choice of species and why the animal model(s) to be used are the most refined, having regard to the objectives. General measures to be taken to minimise welfare costs (harms) to the animals.	The mouse offers the best benefit/cost ratio for these proposed pre-clinical studies of atherosclerosis and its consequences. We continually refine our models and are fortunate to be able to have the technical expertise to deploy the most appropriate of these to address our objectives. General measures to minimise welfare costs are the use of ventilated caging especially where use of anti-inflammatory treatments is studied, individual study plans and health/welfare recording for each mouse during the more complex procedures.