

18 July 2014

<b>Project title</b>	<b>Microenvironment signalling in cancer</b>		
Key words	Cancer, microenvironment, therapy		
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		No
Objectives of the project	In the UK, cancer kills over 400 people per day (this means over 730,000 people over a period of 5 years). Modern cancer therapies very efficiently target the cancer cells within a tumour, but there are other non-cancer cells in the so called 'tumour microenvironment', which can help the cancer cells to resist the therapy. We want to understand how the complex 'tumour microenvironment' can communicate with the cancer cells.		
Potential benefits likely to derive from this project	Understanding how the 'tumour microenvironment' communicates with cancer cells will allow the identification of drugs that can suppress the help that the 'tumour microenvironment' offers the cancer cells, and ultimately can improve the overall survival of patients receiving cancer therapies.		
Species and approximate numbers of animals expected to be used, and anticipated period of time	We are planning to use approximately 700 mice over a period of 5 years.		
Expected adverse effects and the	The expected level of severity is moderate. Animals (including immunocompromised animals) will undergo		

<p>likely/expected level of severity. What will happen to the animals at the end.</p>	<p>surgery or receive injections, and appropriate anaesthetic drugs and drugs for pain relief will be given to the animals. Discomfort can occur from the growth of a tumour, including swelling of tissue covering the tumour, skin ulceration and weight loss. Laboured breathing may suggest the existence of tumour cell spread in the lungs. If any of those signs are observed, the mouse will immediately be sacrificed following a protocol for humane killing.</p> <p>At the end of each experiment all animals will be humanely sacrificed, so that we can perform all relevant analyses.</p>
<p><b>Application of the 3 Rs</b></p>	
<p>1. Replacement Why do animals need to be used, and why non-animal alternatives cannot be used.</p>	<p>The 'tumour microenvironment' is extremely complex; it consists of other non-cancerous cell types, a connective tissue, a lymphatic system and blood supply. Although many researchers, including our group are currently developing more sophisticated cell culture systems that resemble certain components of these complex conditions, we are far from being able to reconstitute the full 'tumour' situation; which means that it is currently impossible to adequately study the 'tumour microenvironment' outside the body.</p> <p>If appropriate alternative non-animal models become available that allow replacing the use of animals, these will immediately be adopted. Before the start and throughout the project we will make sure that our research does not unnecessarily duplicate experiments.</p>
<p>2. Reduction How the use of minimum numbers of animals will be assured</p>	<p>The number of animals to be used will be calculated with the advice from designated statisticians. The experiments are designed in a manner that will allow using one animal for a whole series of cell culture experiments in the lab. Furthermore, by combining the animal experiments with our cell culture experiments will allow using the minimum number of animals to achieve our objectives.</p>
<p>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</p>	<p>The mouse is the lowest vertebrate that offers a 'living body' situation relevant to human cancer and that can be manipulated in a manner that will allow producing meaningful data relevant for the treatment of human cancer. Due to the nature of cancer, unfortunately we cannot use an invertebrate, and even the use of other vertebrates such as zebrafish larvae is limited due to the lack of the formation of blood-borne secondary cancers (metastasis). As such, the mouse is the only available</p>

measures to be taken to minimise welfare costs (harms) to the animals.

animal model to achieve the stated objectives.

All chosen regulated procedures will be performed by highly trained staff, which ensures brevity of the procedure and the lowest level of discomfort. By responsibly considering the adverse effects associated with what will be done to the animals, mechanisms are in place to minimise these.