G. NON TECHNICAL SUMMARY (NTS)

Project title: Gene Function in Tumorigenesis
Duration of project - years: 5
Duration of project - months: 0

Purpose of the project (as in ASPA Section 5C(3)):
(a) basic research: **YES**
(b) translational or applied research with one of the following aims:
(i) avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality, or their effects, in man, animals or plants: **YES**
(ii) assessment, detection, regulation or modification of physiological conditions in man, animals or plants: **NO**
(iii) improvement of the welfare of animals or of the production conditions for animals reared for agricultural purposes: **NO**

(c) development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feedstuffs or any other substances or products, with one of the aims mentioned in paragraph (b): **NO**
(d) protection of the natural environment in the interests of the health or welfare of man or animals: **NO**
(e) research aimed at preserving the species of animal subjected to regulated procedures as part of the programme of work: **NO**
(f) higher education or training for the acquisition, maintenance or improvement of vocational skills: **NO**
(g) forensic inquiries: **NO**

Keywords:
Cancer, drug targets, non-invasive imaging

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):
Cancer is responsible for more than one in four deaths in the UK and four cancers, lung, bowel, breast and prostate, account for almost half of all cancer deaths in the UK. Colorectal cancer is the second commonest cause of cancer related death in the UK with over 16 000 deaths annually. Cancer incidence is also increasing and highlights the need for improvements in cancer prevention strategies, diagnosis and more effective treatments, particularly in the context of an ageing population.

To achieve the required improvements in cancer diagnosis and treatment, a more detailed understanding of the molecular mechanisms that promote cancer formation, its growth and spread. are required. This will lead to the identification of novel biomarkers for diagnosis and diagnostic imaging as well as new drug and treatment strategies.

What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?:
Pre-clinical investigation and translation using animal models of human cancers will, in time, facilitate a more personalized approach to cancer treatment where the right treatment is given to the right patient at the right time. This will lead to an improvement in outcomes and quality-of-life for cancer patients.

What types and approximate numbers of animals do you expect to use and over what period of time?:
Mice will be used in this project up to 2250 over 5 years

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected levels of severity? What will happen to the animals at the end?:
The animals used in this project may be genetically engineered to develop spontaneous tumours or be experimental tumour models which use implanted human cancer cells or tissues . The development of tumours in these animals is likely to cause some adverse effects of a moderate severity. Tumour growth and development will be closely monitored to ensure that adverse effects are minimised and humane endpoints are observed, as well as the moderate severity limit. All animals will be humanely killed at the end of the study.

Application of the 3Rs

Replacement:
Cancer is a very complex disease involving all spects of human physiology, including different cell and organ systems along with the cardiovasular system, nervous system and immune responses. In order to fully understand the molecular mechanisms that drive this complex disease, it is essential at some point to study gene function and tumorigenesis in the context of the whole living organism. This is equally true for the development of novel therapeutics and treatment approaches.

Reduction:
We strive to use the minimum number of animals possible in a number of ways. Firstly, extensive in vitro analysis is performed prior to animal experiments to ensure that appropriate studies are undertaken and the likelihood of success optimised. All new studies use pilot study groups to ascertain any given effects and also to provide data for statistical analysis to determine sample sizes in further studies. Non-invasive imaging will be used wherever possible to reduce the numbers of animals used by enabling longitudinal studies to be performed and therefore reducing the need for large cohort studies.

Refinement:
The range of mouse models available for cancer research and the ethical framework in place makes the mouse one of the most important models for cancer related research. The availability of genetically altered animals means that models have been created and are available where tumours arise spobtaneously in specific organs and therefore closely resemble the human disease. We select the most appropriate cancer models available to achieve our specific objectives.

Non-invasive imaging will be used where possible to accurately detect and measure tumour growth. This will facilitate use of more humane endpoints as sensitive detection and measuring of tumour size/growth will inform decision making.