G. NON TECHNICAL SUMMARY (NTS)

Project title: Targeting the mechanistic drivers of lung tumour progression
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: NO
   (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:
Tumour progression, Therapy, Lung cancer

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):

The overall aim of this project is to characterize the crucial steps that normal cells undergo in order to become malignant tumours. Each of these steps may potentially act as an "Achilles heel" for tumour development and our goal is to determine whether tumours can be prevented or treated using drugs that block those progression steps. Our research is particularly focused on lung cancer, the most lethal malignancy worldwide, and for which little progress has been made over the last decades in terms of survival. Over the last 5 years our lab defined key changes that take place during the progression of lung cancers. Our future research aims to use mouse tumour models to better interrogate how the changes we identified may influence tumour development and therapy. Since mice have a similar physiology to humans and can develop lung tumours comparable to those seen in humans, we hope that our findings can help our understanding of the human disease. Furthermore, while our lab carries out basic research we ensure that our findings are of relevance to the clinic by validating the potential relevance of our data and proposed therapeutic targets on human tumour samples.
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)?
This is a basic research project and as such, our immediate goals are to improve our understanding of lung cancer development and to identify novel strategies to efficiently target tumours in the laboratory using relevant models (including mice). However, our work also has a strong “translational” (from basic science to the clinic) component as we focus only on processes or mutations for which we find relevant evidence of disruption in human cancer samples. The ultimate aim of our work is to contribute to the identification, characterization and pre-clinical validation of novel lung cancer therapeutic targets (e.g. tumour mutations). Once such targets are identified, novel therapies, aimed at killing the cells that carry them, can be proposed for the improved treatment of lung cancer patients. Furthermore, this study may contribute to the identification of biomarkers (molecular signals) of lung cancer that will help us diagnose both early and advanced disease more efficiently.

What types and approximate numbers of animals do you expect to use and over what period of time?
We expect to use 8000 mice over the 5 years of this licence. These will be distributed as follows: Year 1: 1450 Year 2: 1450 Year 3-5: 1700/Year The average of mice/year is similar to our current usage and the values calculated overlap with our current breeding/experimental distribution (60/40%). Of note, our colony is currently being moved to a new facility, so we expect to use slightly lower numbers of experimental mice over the first 2 years, as we focus first on colony re-establishment. As tumour development is a slow process, experimental cohorts will gradually increase over time (we require 6-10 months old mice for most experiments). In the last 3 years of this licence, we expect to be fully functional and the increase shown in number of mice should reflect this.

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?