G: NON-TECHNICAL SUMMARY (NTS)

NOTE: The Secretary of State considers the provision of a non-technical summary (NTS) is an essential step towards greater openness and requires one to be provided as part of the licence application in every case. You should explain your proposed project clearly using non-technical terms which will be understandable to a lay reader. You should avoid confidential material or anything that would identify you, or others, or your place of work. Failure to address all aspects of the non-technical summary may render your application incomplete and lead to it being returned.

This summary will be published (examples of other summaries can be viewed on the Home Office website at http://scienceandresearch.homeoffice.gov.uk/animal-research/).

(WORD LIMIT: 1000 WORDS)

Please complete the following:

<table>
<thead>
<tr>
<th>Project Title (max. 50 characters)</th>
<th>FAP+ STROMAL CELL RESPONSE TO BIOLOGICAL STRESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Key Words (max. 5 words)</td>
<td>Cancer, lymphocytes, cachexia, metabolism, development</td>
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<tr>
<td>Expected duration of the project (yrs)</td>
<td>Five</td>
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<td>Purpose of the project (as in Article 5)¹</td>
<td>Basic research Yes</td>
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<td>Translational and applied research Yes</td>
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<td></td>
<td>Regulatory use and routine production No</td>
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<td></td>
<td>Protection of the natural environment in the interests of the health or welfare of humans or animals No</td>
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<td></td>
<td>Preservation of species No</td>
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<td></td>
<td>Higher education or training No</td>
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<tr>
<td></td>
<td>Forensic enquiries No</td>
</tr>
<tr>
<td></td>
<td>Maintenance of colonies of genetically altered animals² No</td>
</tr>
</tbody>
</table>

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

1. To understand the interaction of cancers with the immune system, and to discover new methods of cancer immunotherapy.

2. To understand the role of stromal cells in the development and maintenance of organs and tissues.

3. To understand the metabolic and immunological responses to diseases, such as cancer, that may manifest as cachexia and immunological dysfunction.

What are the potential benefits

1. Improved cancer immunotherapy.

¹ Delete Yes or No as appropriate.
² At least one additional purpose must be selected with this option.

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**Version Date** 21/1/14

### Likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?

- New insights into tissue regeneration.
- Therapies for cancer-associated cachexia.

### What species and approximate numbers of animals do you expect to use over what period of time?

**Mouse**: 30,000 over 5 year period.

### In the context of what you propose to do to the animals, what are the expected adverse effects and the likely expected level of severity? What will happen to the animals at the end?

The expected level of severity of the overall application would be moderate. In all cases maximum effort will be undertaken to ensure that this level will be adhered to. With regards to individual expected adverse effects of specific protocols, study of cancer cachexia may result in significant weight loss, the pancreatic murine model of cancer (KPC) has well described adverse phenotypic characteristics that will be closely monitored. In all cases of tumour study, anaemia, weight loss, ascites; pronounced lethargy and decreased interaction may be observed and will be addressed immediately as they occur to minimise any and all suffering in the mice. At the end of planned procedures, mice will be humanely killed by competent and trained persons working under the project license.

### Application of the 3Rs

1. **Replacement**
   
   State why you need to use animals and why you cannot use non-animal alternatives
   
   The biological and health-related questions of cancer immunotherapy and the maintenance of tissues and organs cannot be addressed by in vitro methodology. In addition, the capacity to genetically modify mice has enabled the development of models that allow discrete and informative experiments to be performed.

2. **Reduction**
   
   Explain how you will assure the use of minimum numbers of animals
   
   Every opportunity will be taken to decrease the number of animals used for each experiment whilst still maintaining the statistical relevance of the subsequent data. To maximise information, multiple body sites will be examined from each animal and multiple analysis types will be conducted on each sample, where possible. Breeding of animals will be carefully monitored to ensure no excess breeding occurs.

3. **Refinement**
   
   Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.
   
   We will use unique, genetically modified mouse strains that refine our capacity to design and conduct precise experiments that focus on the genes and cells that are most important and relevant to human biology and diseases.

### For Office Use Only

- **Will the project be subject to Retrospective Assessment?**  
  - Yes
  - No
  - Date due: 12 September 2018

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3 The retrospective assessment should be completed, agreed with the establishment AWERB, and submitted to the Home Office within 3 months of this date (or when the project terminates if earlier).

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