

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 programme of work clearly using non-technical terms which can be understood by 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 will 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 www.gov.uk/research-and-testing-using-animals).

Word limit; 1000 words

Project Title	Brainstem and spinal cord circuits
Key Words	neurogenesis, neuronal networks
Expected duration of the project	5 year(s) 0 months

Purpose of the project (as in ASPA section 5C(3))

Purpose	
Yes	(a) basic research;
	(b) translational or applied research with one of the following aims:
No	(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.

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

To understand how the central nervous system controls homeostatic functions such as blood pressure.

To understand how neural stem cells in the adult spinal cord can be harnessed and controlled for therapeutic repair.

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)?

Manipulating the central nervous control of the autonomic nervous system is currently under investigation for several different therapies e.g. vagal nerve stimulation to treat heart failure. This work will investigate the circuitry and mechanisms underlying such approaches and may inform future trials. Even in the adult the spinal cord continues to make new cells from the division of stem cells. Manipulating the production and/or fate of these cells holds promise for future therapies. For example, in the spinal cord, conditions such as spinal cord injury, motor neurone diseases and multiple sclerosis may benefit from increasing cell production and promoting specific fates. On the other hand, these stem cells may also contribute to some CNS tumours and so in this case it could be beneficial to slow cell proliferation or promote fate to a non-dividing cell type. However, the mechanisms controlling stem cell division are poorly understood and it is vitally important to understand how their behaviour is regulated.

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

We expect to use 2550 rats and 8750 mice.

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 majority of the procedures will be carried out under non-recovery anaesthesia where the animal is killed by anaesthesia prior to organ removal. In some cases experiments will require recovery from anaesthesia following surgical procedures. Adverse effects are not anticipated and post-operative analgesia will be applied to limit suffering. At the end of experiments animals will be terminated for tissue collection.

Application of the 3Rs

Replacement

State why you need to use animals and why you cannot use non-protected animal alternatives

Replacement

The work will study how the CNS controls the autonomic nervous system and how spinal cord stem cells can be manipulated for therapeutic benefit. These will involve mammals which have similar circuits and cell types to humans which will help us translate our research to human benefit. Non-protected animal alternatives do not have such cellular organisation.

Reduction

Explain how you will ensure the use of minimum numbers of animals

Reduction

The number of animals used will be minimised in several ways. Tissue from the same animal will be used for different objectives where possible. This reduces the total number of animals that would otherwise be required if a single animal was used for each project. We have also developed a method of storing tissue long term for future use which also reduces animal use as well as an organ culture for slices of nervous system that allows several tests to be conducted on tissue from one animal. In addition, each experiment is designed to maximise the amount of information gleaned since they often combine different approaches to verify this information.

Refinement

Explain the choice of animals 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.

Refinement

Rats and mice will be used since they contain cell types and assemblies of cells that are similar to those known in humans. Transgenic animals will be used when they make identifying specific cell types possible with fluorescent markers, helping to minimise numbers used.

Suffering of animals will be minimised as the majority of the procedures performed will have a minor severity where the animal is killed by anaesthesia prior to organ removal. In some cases experiments will require recovery from anaesthesia following surgical procedures. Post-operative analgesia will be applied in these cases to limit suffering of the animals.