Project title	**Regulation of pituitary physiology**		
Key words	Pituitary, gene regulation, prolactin		
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	Yes	
Objectives of the project	The pituitary gland produces hormones that control a wide range of body functions. Hormone production is regulated both acutely in response to immediate stimuli such as stress and trauma, and also chronically in response to physiological changes like puberty and pregnancy. It has been found that gene expression in the pituitary is dynamically variable, both in tumour cell lines in vitro, and in normal animal tissue. We are exploring the mechanisms and significance of the dynamic responses of gene transcription in living cells, and how this relates to pituitary growth and development. An important aspect of this work is the ability to study normal pituitary tissue, as opposed to cancer cell lines. In order to achieve this we have created transgenic rats in which marker genes are expressed in the pituitary gland. These marker genes have no detrimental effect on the pituitary gland itself or on the animal's well being, but allow us to study the behaviour of pituitary tissue that has been removed from the animal after death.		
Potential benefits likely to derive from this project	The work will lead to new understanding of the role of tissue structure in coordinating the production of hormones in normal physiology. This in turn will help us understand how tumours arising in the pituitary gland over-produce these hormones, and we hope it will contribute to the development and understanding of new		

	therapies for these tumours in man.
Species and approximate numbers of animals expected to be used, and anticipated period of time	Rats and mice, up to 4,000, over 5 years
Expected adverse effects and the likely/expected level of severity. What will happen to the animals at the end.	Very few if any adverse effects are expected. Most of our studies will be aimed at normal physiology in healthy animals, for example during early development, pregnancy and across the oestrous cycle. In some experiments we will study the effect of oestrogen, using hormone implants similar to those used by women in routine healthcare.
Application of the 3 Rs	
1. Replacement Why do animals need to be used, and why non-animal alternatives cannot be used.	The aim of the work is to study effects of tissue structure on hormone production. Cancer cell lines have been studied until now, and limited work can be performed in this way on individual cells, but for analysis of tissue structure animal work is essential.
2. Reduction How the use of minimum numbers of animals will be assured	We are using microscopic approaches studying the behaviour of individual cells, and this allows us to minimise the numbers of animals to ensure reproducibility of results consistent with achievements of scientific goals.
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 measures to be taken to minimise welfare costs (harms) to the animals.	We are using laboratory rodents as these are amenable to genetic manipulation, and the physiology of the pituitary gland is well understood. Animals are observed at least once a day. No adverse effects are expected from the endocrine manipulations. Analgesics will be administered after surgical procedures to minimise discomfort or pain, and we will seek veterinary advice if we encounter any unexpected occurrences.