

# The 3Rs prize 2005-2015

Each year the NC3Rs awards a prize to highlight an outstanding original contribution to scientific or technological advances in the 3Rs, published in the last three years.

Sponsored by GlaxoSmithKline and the NC3Rs, the prize consists of a prize grant of £28k and a £2k personal award\*.

The first award was presented in 2005. There have been 12 winning papers (there were two joint winners in 2015) and 15 highly commended papers recognised by the prize to date.

The winning papers have covered a variety of topics from *in silico* modelling of cardiac electrophysiology, through to complex microphysiological systems and improvements in the welfare of laboratory mice and dogs.

The competition is open to applicants from academia or industry. Since 2012, individuals from establishments outside of the UK have been eligible to apply.

\* the total prize package was increased from £20k to £30k in 2016.



NC  
3R<sup>s</sup>

National Centre  
for the Replacement  
Refinement & Reduction  
of Animals in Research



GlaxoSmithKline

# 2015 joint winner: Dr Madeline Lancaster, MRC Laboratory of Molecular Biology

## Research:

The paper describes the development of the first 3D model of the human embryonic brain using human induced pluripotent stem cells. These cells were able to spontaneously self-organise into a structure that resembles the human brain with discrete, interdependent regions.

Lancaster M *et al.* (2013). Cerebral organoids model human brain development and microcephaly. *Nature* 501 (7497): 373-9.

## 3Rs implications:

The suitability of animal models in studying neural development is limited, as they do not recapitulate the anatomical and functional complexity required to study human brain biology and disease. Developing brain organoids from human tissue is a revolutionary step towards reducing reliance on animals in studying neurological diseases and potentially in the development of new treatments.



# 2015 joint winner: Dr Laura Hall, University of Stirling

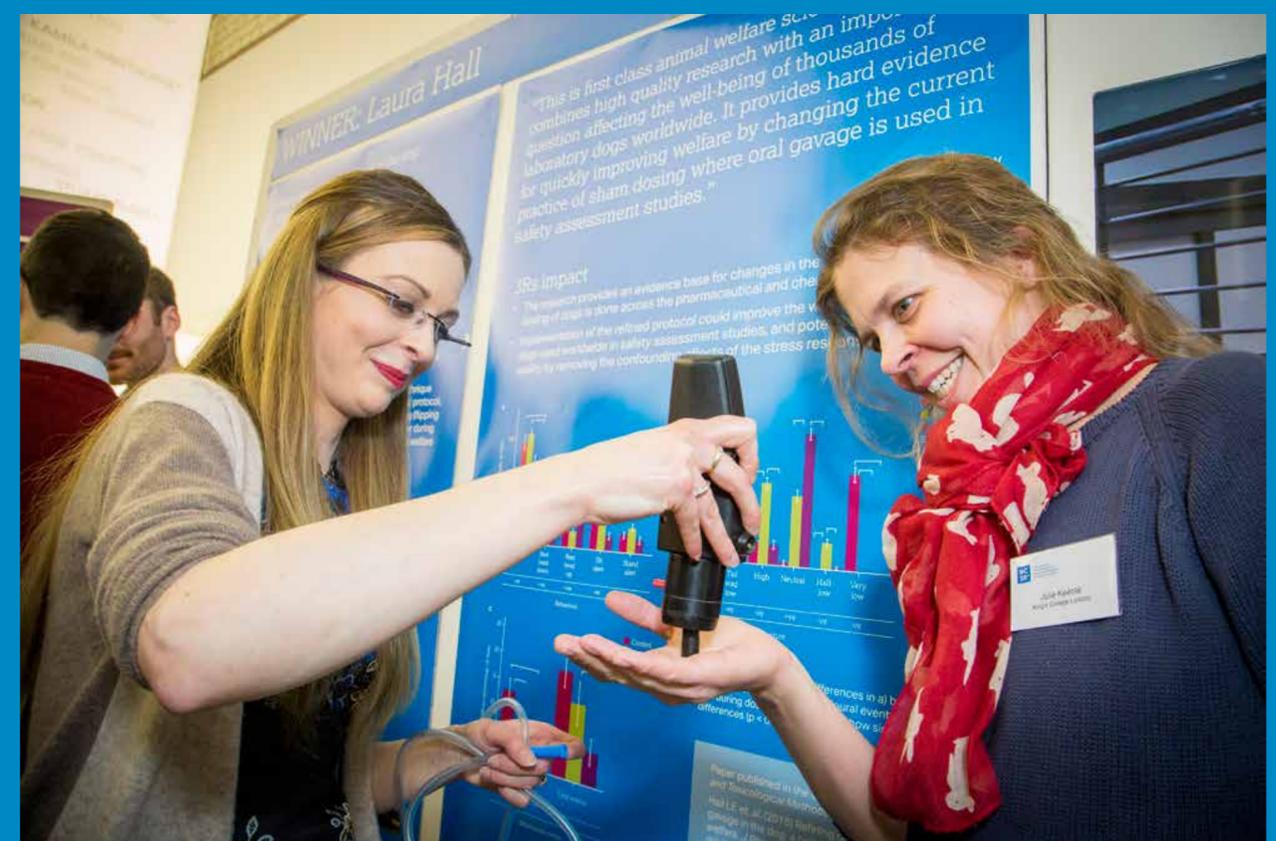
## Research:

The study, in collaboration with AstraZeneca, improves the technique of oral dosing in dogs. Following a framework of objective welfare assessments developed by Dr Hall, the authors demonstrate that a modified, refined protocol for gavage can minimise stress in dogs compared to the standard approach.

Hall LE, Robinson S, Buchanan-Smith HM (2015). Refining dosing by oral gavage in the dog: A protocol to harmonise welfare. *Journal of Pharmacological and Toxicological Methods* 72: 35-46.

## 3Rs implications:

Most laboratory dogs in the UK are used for safety testing, and oral dosing is one of the most common procedures used during these tests. This paper shows that using seemingly small refinements (positive reinforcement training with food rewards, a signal for dosing, and covering the dosing tube in palatable paste during training) significantly reduces the negative welfare impact of the oral dosing on the dogs.



# 2014 winner: Mr Oliver Britton, University of Oxford

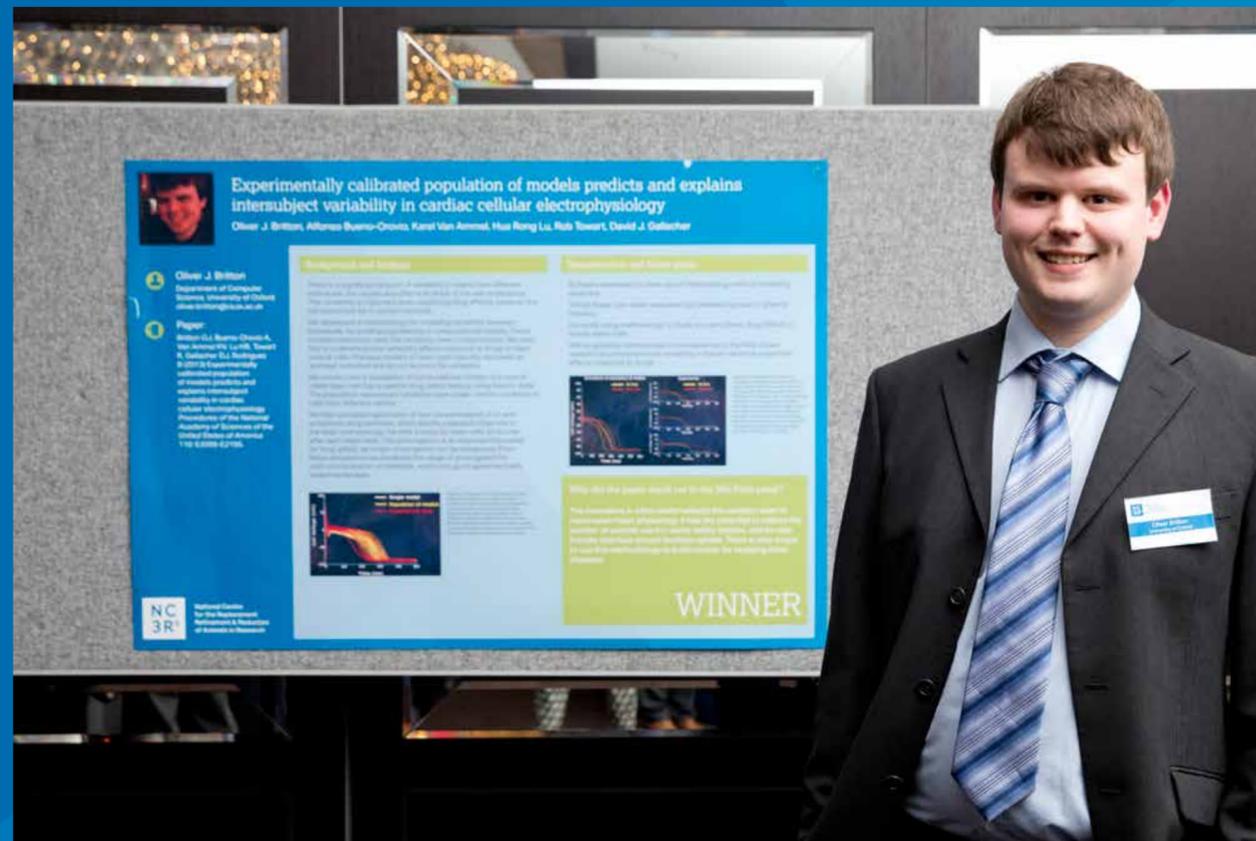
## Research:

The paper describes a computer model of cardiac electrophysiology, built to incorporate natural variability. The *in silico* model is therefore more representative of the whole population, where natural variations in heart properties occur from person to person.

Britton O, Bueno-Orovio A, Van Ammel K *et al.* (2013) Experimentally calibrated population of models predicts and explains intersubject variability in cardiac cellular electrophysiology. *Proc. Natl. Acad. Sci. USA* 110: E2098–2105.

## 3Rs implications:

This approach has the potential to make computer models that are far more powerful and more predictive of human response, and therefore a more viable alternative to using animals in research. This is the first time that natural variability has successfully been considered in such a model, and the methodology could be applied to other diseases.



# 2013 winner: Dr Meritxell Huch, Gurdon Institute, University of Cambridge

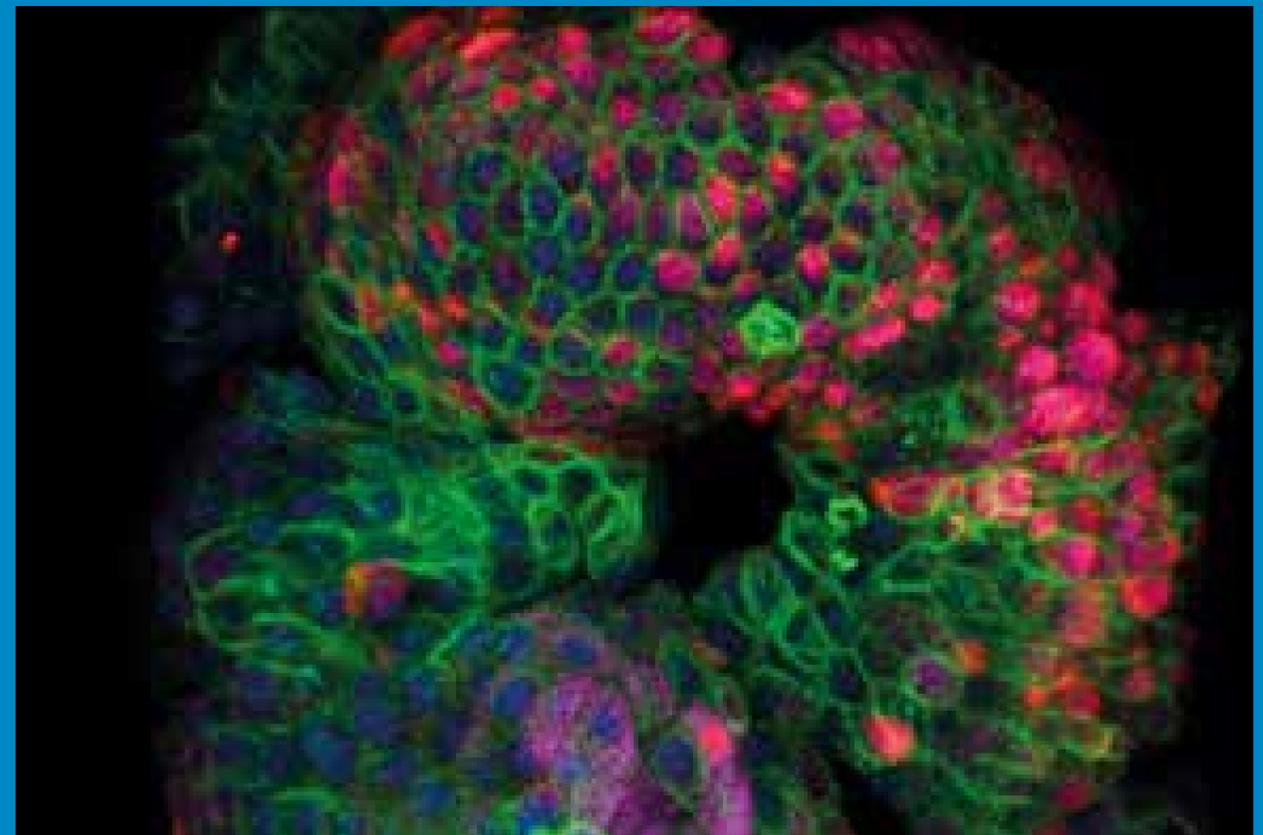
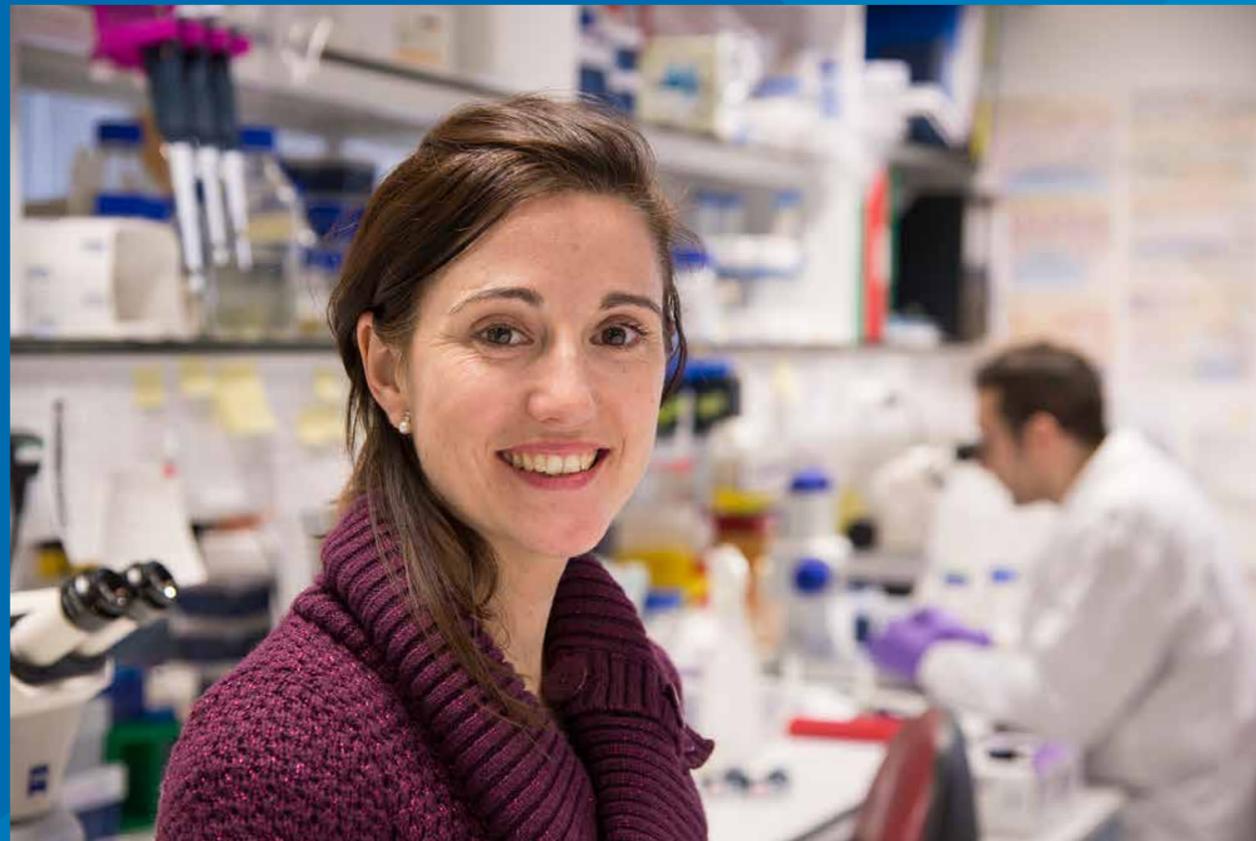
## Research:

The paper describes the development of a culture system that enables adult mouse stem cells to grow and expand into fully functioning 3D liver tissue.

Huch M, Dorrell C, Boj SF, van Es JH *et al.* (2013). *In vitro* expansion of single Lgr5 liver stem cells induced by Wnt-driven regeneration. *Nature* 494: 247252.

## 3Rs implications:

The researchers were able to grow small liver organoids, which survive and expand for over a year in a laboratory environment. When implanted back into mice with liver disease they continued to grow, ameliorating the disease and extending the survival of the mice. The *in vitro* liver tissue could be used to study liver diseases, as well as a screen for liver toxicity in pharmaceutical development.



# 2012 winner: Professor Don Ingber, Wyss Institute, Harvard University

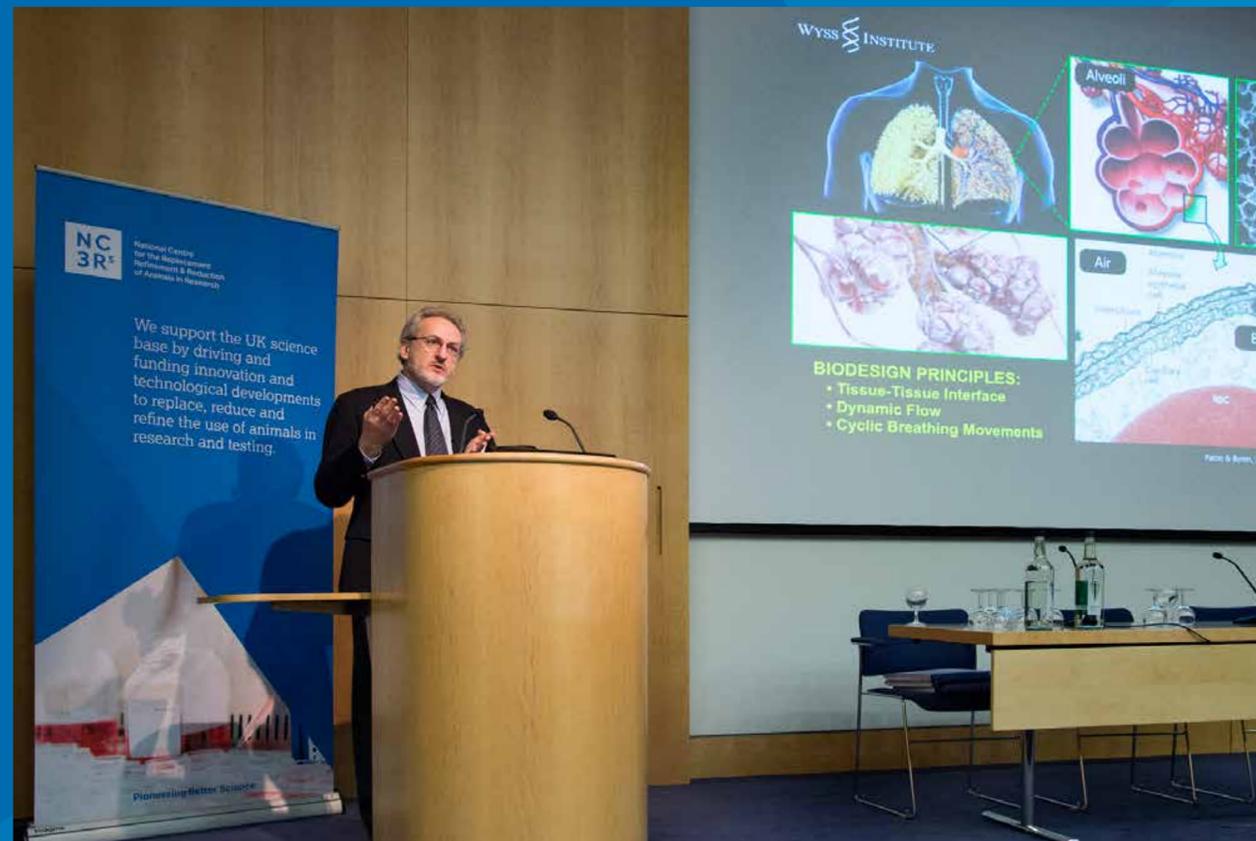
## Research:

The paper describes an innovative 'lung-on-a-chip' microdevice that can accurately replicate conditions in a diseased human lung, including pulmonary oedema.

Huh D, Leslie DC, Matthews BD, Fraser JP, Jurek S, Hamilton GA, Thorneloe KS, McAlexander MA, Ingber DE (2012). A human disease model of drug toxicity-induced pulmonary edema in a lung-on-a-chip microdevice. *Science Translational Medicine* 4 (159): 159ra147.

## 3Rs implications:

Using the microphysiological device it is possible to carry out real-time high resolution imaging on cells, and make accurate measurements of fluid flow and blood clot formation, potentially providing an alternative to traditional animal models.



# 2011 winner: Dr Ludovic Vallier, University of Cambridge

## Research:

The paper looks at the use of 'artificial' liver cells to model inherited metabolic disorders of the liver. The new method shows it is possible to take skin cells, reprogramme them back into stem cells, and then use them to generate liver cells which are able to mimic a broad range of liver diseases.

Vallier L *et al.* (2010). Modelling inherited metabolic disorders of the liver using human induced pluripotent stem cells. *The Journal of Clinical Investigation* 120(9): 3127–3136.

## 3Rs implications:

The innovative study describes the development and validation of a method to produce cells similar to those found in a human liver without the use of animals. These cells could replace animals for some types of early drug testing and could also help to predict adverse clinical reactions.



# 2010 winner: Professor Jane Hurst, University of Liverpool

## Research:

This research has shown that a new way of handling laboratory mice can improve their welfare and the quality of the science they are used for.

J Hurst, R West (2010). Taming anxiety in laboratory mice. *Nature Methods* 7(10): 825–842

## 3Rs implications:

By simply catching the mice using a plastic tunnel or cupped hands anxiety can be greatly reduced. This small change can be easily applied and has the potential to make a big difference to the welfare of every mouse used for research.



# 2009 winner: Dr Jenny Nichols, University of Cambridge

## Research:

The paper describes the development of an optimised culture medium for growing mouse embryonic stem (ES) cells. The study showed that it was possible to derive ES cells from non-obese diabetic (NOD) mice.

Nichols J, Jones K, Phillips J, Newland S, Roode M, Mansifield W, Smith A, Cooke A (2009). Validated germline competent embryonic stem cell lines from non-obese diabetic mice. *Nature Medicine* 15(7), 814–818.

## 3Rs implications:

The ability to derive ES cells from NOD mice could dramatically reduce the number of animals used to study type 1 diabetes. The direct manipulation of the NOD mice genes avoids lengthy rounds of breeding to produce mice with the required genetic background.



2008 winners:

Dr Keith Martin and Mr Thomas Johnson, University of Cambridge

Research:

The paper investigates the potential of stem cells to protect vulnerable nerve cells in the injured retina and could have implications for the development of treatments for glaucoma, the leading cause of irreversible blindness worldwide, and other eye diseases.

Johnson TV, Martin KR (2008). Development and characterization of an adult retinal explant organotypic tissue culture system as an *in vitro* intraocular stem cell transplantation model. *Invest Ophthalmol Vis Sci* 49(8): 3503–3512.

3Rs implications:

The new method for retinal tissue culture could replace the need for some live animal studies of retinal injury.



# 2007 winner: Dr Charlotte Gower, Imperial College London

## Research:

The paper described a new use of DNA fingerprinting, applied to the collection of parasite DNA samples directly from people infected with schistosomes, the worm-like parasites that cause bilharzia.

Gower C *et al.* (2007). Development and application of an ethically and epidemiologically advantageous assay for the multi-locus microsatellite analysis of *Schistosoma mansoni*. *Parasitology* 134: 523–536.

## 3Rs implications:

This method avoids the use of rodents to grow parasites in the laboratory from human faeces in order to produce sufficient material for analysis, by enabling the study of smaller DNA samples taken directly from human subjects.



# 2006 winners: Professor Alan Fairlamb and Dr Susan Wyllie, University of Dundee

## Research:

The paper compared two different methods of infection (intracardial versus intraperitoneal) when infecting hamsters with the parasite *Leishmania donovani*.

Wyllie S, Fairlamb AH (2006). Refinement of techniques for the propagation of *Leishmania donovani* in hamsters. *Acta Tropica* 97(3): 364–369.

## 3Rs implications:

The research found that the intraperitoneal route of infection is a simpler, safer and more effective method of inoculating the hamsters, showing a significant refinement in terms of animal welfare.



# 2005 winner: Dr Siouxsie Wiles, Imperial College London

## Research:

Traditionally mice are individually infected with *E.coli* through a gavage. This paper showed that it is possible to achieve higher infection rates by infecting just one mouse, before placing them in a cage with uninfected mice and allowing the infection to spread naturally.

Wiles S, Dougan G, Frankel G (2005). Emergence of a 'hyperinfectious' bacterial state after passage of *Citrobacter rodentium* through the host gastrointestinal tract. *Cellular Microbiology* 7(8): 1163–1172.

## 3Rs implications:

The new approach refines the procedure, as only one mouse is subject to the gavage procedure, and the total number of animals used is reduced due to the improved reliability of infection.

