
DISCUSSION

Young Researchers – The Ethical Challenge^a

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Never before has there been a better opportunity for young researchers to focus on replacement alternatives, not only to save animals from unnecessary pain and suffering, but also to pave the way for a career in cutting-edge innovation

Introduction

The Lush Prize awards and encourages individuals or organisations who have contributed to the global initiative to end animal testing, in the fields of science, public awareness, lobbying and training, and also aims to support young researchers who wish to develop a career in animal-free toxicology. The total yearly prize fund is £250,000. The ‘Young Researcher’ category of the Lush Prize welcomes nominations from early-career scientists who are keen to progress in research without animal testing. The award offers four £12,500 bursaries, to reward research and development specifically in methods for the *entire replacement* of animals in toxicity testing.

In this article, Lush Prize refers to testing without the use of animals by using the term ‘non-animal’ methods. They are validated, scientifically robust methods of safety testing in their own right. The use of terms such as ‘alternatives’ or ‘replacement’ methods (while useful for clarity sometimes) may suggest that animal testing is the ‘gold standard’ of safety testing, when much of the scientific industry, along with a wealth of research evidence, confirms that, aside from the suffering involved, animal tests do not reliably predict human responses. In addition, the term ‘alternatives’ is also used to describe the Three Rs methods,¹ previously summarised as follows: *Refinement*: to minimise suffering and distress to animals; *Reduction*: to minimise the number of animals used; and *Replacement*: to avoid the use of living animals.

Whilst reduction or refinement methods are positive steps, they are not achievements according to the ethos of the Lush Prize. We consider only the final ‘R’ (*Replacement*) to be a genuine alternative, as the other two Rs still involve animal use.

A brief review of previous findings

To discuss the relevance of the Young Researcher prize, a number of key animal protection organisations were contacted and interviewed during previous research for the Lush Prize. Some of these contacts are quoted and provide useful updates throughout this article. The key messages are:

- Although the acceptance and recognition of new technologies is growing at an encouraging rate, animal-free toxicology is still the ‘less travelled’ path, and any early-career researcher trying to progress in this area is likely to meet at least some resistance or challenges along the way. That said, the environment for the discussion of alternatives to animal use is expanding, so it is vital to be persistent and remain true to one’s values in pursuing career and networking opportunities.
- A very proactive attitude is needed; ethical scientists must actively seek out their opportunities, but the rewards can be hugely successful.
- Continuing to promote the anti-animal testing message to all relevant individuals in the young/early-career researcher field, as well as communicating this message at an earlier stage of education, is vital.

One of the key positive findings from interviews with previous Young Researcher prize winners is that “*Young scientists don’t always have the prejudices about animal testing being the ‘best’ way of doing things*”.² An unbiased view and fresh perspective on cutting-edge science is essential, combined with raising awareness earlier in the educational system. There is also a strong link between the Young Researcher and Training prizes, as the latter awards are relevant to those involved in the education of a

^aTaken from the 2014 Young Researcher Lush Prize Background Paper.

number of audiences, from children in early-stage schooling, through GCSE/A-level, to the undergraduate and postgraduate levels and beyond.

There is considerable scope for early-career researchers working in a broad range of scientific or technical fields to get involved in non-animal methods. This is coupled with the fact that the *in vitro* toxicity testing market is projected to be worth \$17,227 million by 2018.³ The EU cosmetic testing ban has played a key part in driving this growth.

Mainstream funding and development of Replacement methods

The importance of funding offered by the Lush Prize continues to grow. This is especially relevant to the Young Researcher Prize, as the bursaries awarded will directly fund the development of methods to replace the use of animals in 'frontline' research. As highlighted in previous research conducted for the Lush Prize, lack of finance is a major obstacle to the availability of non-animal methods. The ongoing reliance on animal research means that it continues to receive the vast majority of the available funding. Furthermore, those interested in non-animal research, not only have to maintain the momentum on their specific ideas and methods, but also face a need to continually look for funding or sponsorship, which ultimately impacts on the amount of time they directly spend on their research, as acknowledged by PETA in an interview with Lush Prize in 2012: "...people may have good ideas about non-animal methods, but they're continually going to be seeking support...and funding for those".⁴

To provide some figures to illustrate the above points, in the UK in 2012-2013, over £300 million of public funding was spent on projects which "include an element of animal use".⁵ In contrast, a sum of just under £9 million was awarded to Three R projects broadly termed as 'alternatives', with the NC3Rs awarding £7 million of this total.⁵ The NC3Rs state that, of the funding they provide, "around 55 per cent of research awards are directed primarily at replacement, 25 per cent for reduction and 20 per cent for refinement".⁶ Therefore, within this £9 million, a much lower sum was awarded to genuine non-animal (*Replacement*) methods, as a significant amount of 'alternatives' funding is donated to the other two Rs, which still involve animal use. For example, previous NC3Rs funding includes projects which develop scales for recognising facial expressions of pain in monkeys⁷ or facial grimace scales in rabbits.⁸ To add further perspective, since it was established in 2004, the NC3Rs has awarded just over £37 million in project funding. Based on the above figures, this equates to 12% of just one year's Government funding of projects which include animal research.

Research carried out by the BUAV in 2013 revealed the stark lack of funding devoted to alternatives to

animal testing across the EU Member States. Just €18.7 million were devoted to methods relating to the Three Rs in 2013, by only seven countries, with most Member States failing to assign any funding at all, and half of them not responding to the survey. Given that the available figures for 2011 show the total combined annual science R&D (research and development) budget for the EU to be almost €257 billion, the amount spent on alternatives is wholly inadequate, equating to just 0.007% of the total expenditure.⁹

These disappointing figures demonstrate the importance of independent funding for non-animal research, such as that which the Lush Prize offers. At its launch in 2012, the £50,000 total prize money for the Young Researcher Prize was allocated to five potential winners. This has now changed to award four prizes of £12,500, in order to increase the funding awarded to each individual, whilst still recognising the work of several researchers. Feedback from previous prize winners has indicated that these bursaries provide a meaningful amount, so the slight increase in funding across four awards will be of even more benefit, to go toward both research expenses and the cost of consumables.

Current and ongoing opportunities for keen young researchers

Banning animal testing will stifle innovation?

The claim that a ban on animal testing would stifle innovation was regularly made by industry as the 2013 EU cosmetics testing ban came into effect.¹⁰ Far from impeding research, the ban (both the 2009 and 2013 phases) had the opposite effect, and was the direct driver for the launch of new research into non-animal methods through large-scale, multinational projects (e.g. ReProTect¹¹) as these two critical deadlines approached. R&D on new methods is innovation in itself, and it provides the perfect opportunity for those who genuinely want to be involved in cutting-edge, next-generation science, without causing animal suffering. The EU has led the way in progress on the development of alternative methods of testing to animals, and is considered 'a leader in innovation', something which should be reflected in the opportunities it offers young researchers and emerging graduate scientists.

Toxicity testing is toxicity testing, regardless of purpose

The validated and accepted non-animal (replacement) toxicity testing methods that are now available have

been developed largely due to the phased EU ban on the animal testing and marketing of cosmetic ingredients and finished products. As a result, discussions on the replacement of animals in toxicity testing are far more common and perhaps are considered more acceptable in the cosmetics field. However, young researchers working or studying in other areas of toxicity may feel less able to speak out about their research interests, especially if they involve replacement/non-animal methods, as these are seen as more controversial than ‘two Rs’ (*reduction or refinement*) approaches. It is therefore important to recognise that these methods are now of essential use in other chemical testing sectors, such as the food or pharmaceutical industries. This demonstrates that when a non-animal method is developed and accepted, it can potentially be applied to the testing of any substance, for any purpose. This may encourage young researchers to voice their interests in the development and use of non-animal methods.

This is especially relevant as, despite the development of alternatives for use in areas such as cosmetics, toxicity testing in animals continues in many other industries. For example, in the UK in 2013, over 375,000 toxicity tests (from a total 4.12 million procedures) were performed on animals (mice, rats, rabbits, guinea-pigs, dogs, cats, monkeys, birds and fish).¹² Another important point with regard to the Young Researcher Lush Prize, is that almost half of all animal experiments in the UK are carried out at universities. One of the most concerning findings is that the increase in the use of genetically-modified animals (mainly mice) and the increasing use of zebrafish are, in some contexts, being considered as ‘alternatives’. This was highlighted by FRAME in a report on the Home Office annual statistics on animal use in Great Britain in 2012.¹³

The 2011 EU figures¹⁴ showed that over 1 million animals (1,004,873, from a total of just under 11.5 million animals) were used in toxicity testing across the EU states in that particular year. Of these, 111,166 animals were used in tests that were not even required by law (categorised as ‘no regulatory requirements’). The archaic and much criticised LD50/LC50 (lethal dose or lethal concentration test, which tests the amount of substance required to kill 50% of the animals tested) accounts for the majority of the animals used each year, along with other lethal tests (34%). The other main use is simply categorised as ‘other’ toxicology tests (22%), followed by chronic/sub-chronic toxicity and reproductive toxicity. There is no official figure for the number of toxicity tests still conducted on animals worldwide (from the estimated yearly total of 115 million animals¹⁵ used in all experiments), as many countries omit this information or do not even count the numbers of animals used. However, a revised estimate by Lush Prize researchers puts the number of toxicity tests carried out on animals worldwide at almost 9.5 million (from a total 118 million animal experiments).¹⁶

After the 2013 marketing ban, much work is still to be done

Although the EU cosmetics legislation has been the major driver of the development of non-animal toxicity testing methods in recent years, there is still much more to be done. This is illustrated very clearly, given that “*Over 80% of the world allows animals to be used in cruel and unnecessary cosmetics tests and these animal tested cosmetics can be purchased in every country across the globe.*”¹⁷

The proposed 2013 EU marketing ban on animal-tested cosmetics did finally go ahead, though the European Commission had previously considered the possibility of delaying the deadline on the basis of recommendations that necessary but still ‘missing’ alternative methods would take much longer to be developed. For example, estimates of another 5-9 years were proposed for methods for skin sensitisation and toxicokinetics to be developed, and possibly even longer for full replacement in these areas. No estimates were provided at all for when repeat-dose toxicity, reproductive toxicity or carcinogenicity tests on animals might be developed. These timelines were estimated in a report published by the Commission in 2011.¹⁸ In the three years since that time, aside from the introduction of the 2013 ban itself (which went ahead *regardless* of the lack of alternatives available, which was great news), further work had been ongoing in the areas of toxicity testing which still need development. For example, in 2013, the Joint Research Centre (JRC) published its *EURL-ECVAM Strategy to Avoid and Reduce Animal Use in Genotoxicity Testing*.¹⁹ Similarly, the five-year long NOTOX project,²⁰ launched in 2011 and involving a network of scientific expertise from several countries, works “*towards the replacement of current repeated dose systemic toxicity testing in human safety assessment*”. NOTOX is part of a wider project, funded under the EU Seventh Framework Programme (FP7), known as SEURAT (Safety Evaluation Ultimately Replacing Animal Testing). This project combines the research efforts of over 70 European universities, public research institutes and companies, and regularly posts open vacancies and research opportunities.²¹ Of particular relevance is that SEURAT hosted a *Young Scientists Summer School* to discuss replacement of repeat-dose toxicity testing in animals.²²

Focusing on key areas

As highlighted by EURL-ECVAM,²³ a key factor in the development of non-animal methods is the integration of a number of alternative test methods into a ‘battery’ that successfully addresses a number of endpoints, especially those which are considered more complex or need to be considered in-depth. For example, several alternatives available for skin testing, examine how a substance may react in

various stages of topical application, absorption, irritation or corrosion, and provide very targeted and quantitative results, especially when compared to a crude skin test in rabbits or guinea-pigs. Therefore, non-animal methods which are still under development or undergoing validation, or ‘gaps’ in the development of methods where the greatest use of animals still occurs, such as reproductive or chronic toxicity, could be helped by awarding the Lush Prize to young researchers to allow them to potentially channel their ideas or research themes for specific replacement projects and encourage them to specialise in key areas.

Never before has there been a better opportunity for young researchers to focus on replacement alternatives, not only to save animals from unnecessary pain and suffering, but also to pave the way for a career in cutting-edge innovation. As highlighted by the New England Anti-Vivisection Society (NEAVS) in a previous interview with Lush Prize, linking an early-career scientist’s research to increased income and sponsorship is key:

*“I think the solution for graduate students who want to do more progressive in vitro research is to find the granting agencies that will help bring money in [to an institution]. ...The key to changing institutions is bringing in grant dollars. When someone who wants to develop in vitro alternatives can show that they can bring in million-dollar grants, then institutions are going to have to accept it. They’re not going to turn money away, even if they want to try to suppress a certain ideology”.*²⁴

What this means, in effect, is that, if a researcher has ideas, but can also say “if you fund me, I propose to cut your costs, save you time, increase income and improve your business”, whilst this might be viewed as a challenge, their proposals are much more likely to be considered.

Challenges for ethical early-career scientists

As previously highlighted, there remain ongoing prejudices toward switching from animal to non-animal research. Resistance to change, combined with ‘comfort’ in repeating accepted, conventional methods, allows the animal research industry to maintain the *status quo*, despite ever-increasing recognition that animal testing is a flawed, over-rated and outdated system. It must also be noted that the industry has, for decades, consisted of a network, not only of researchers, but also breeders, suppliers and transporters of animals across the world, who rely on animal testing to continue.

There are other factors to consider – for example, some scientists (especially senior-level researchers) have based their entire careers on the use of animals,

and are unable or unwilling to consider anything else; they may view switching to non-animal research as the daunting and unattractive option of ‘starting again’. This may also apply to earlier career individuals, who have followed the mainstream route into animal-based toxicology to progress their careers to date, for example, since leaving university. This is echoed by several previous prizewinners, who felt that the undergraduate level of their education was the most challenging arena in trying to avoid the use of animals. Nevertheless, one positive finding from interviews with previous Young Researcher Prize winners is that “*Young scientists don’t always have the prejudices about animal testing being the ‘best’ way of doing things*”.²

Finally, to provide some useful insight into the types of scholarships available to young researchers, Appendix 1 gives a summary of 15 PhD studentships recently funded by the UK NC3Rs. A full list is shown to illustrate the types of research being undertaken – however, it must be noted that the studentships cover the broader remit of the Three Rs, rather than the ‘*replacement only*’ criterion that the Young Researcher Prize demands.

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Appendix 1: A summary of 15 PhD studentships recently funded by the UK NC3Rs	
Location	Description
University of Aberdeen/Marine Science Scotland	Development of a method for non-lethal sampling from individual fish to investigate host responses to ectoparasites.
University of Birmingham/University of Oxford	Creating an <i>in vitro</i> model of pathogenic ossification to explore methods for dispersion.
University of Edinburgh	Motor neuron regeneration in larval zebrafish.
The Babraham Institute, University of Cambridge	Towards engineering a multi-cell lineage multi-organism intestine.
University of East Anglia/University of Liverpool	Development of a non-mammalian, pre-clinical screening tool (FETOX) for predictive analysis of drug safety.
University of Glasgow/University of Edinburgh	An <i>in vitro</i> model to investigate the role of oestrogen and oestrogen metabolism in pulmonary vascular disease.
University of Hertfordshire/GlaxoSmithKline	DM-MAP: Drug and Metabolite Microsampling Analytical Platform for preclinical medicines development.
University of Leeds	Development of an <i>in vitro</i> system to determine the causes of aberrant, leukaemogenic V(D)J recombinant reactions.
University of Liverpool	Developing molecular therapies for glaucoma using an <i>ex vivo</i> human organ culture system.
University of Oxford	Development of a patient-derived cellular model of circadian disruption in bipolar disorder.
Royal Holloway, University of London/University College London	Find the target of valproic acid; pioneering the use of a non-animal model for basic biomedical (epilepsy) research.
Royal Veterinary College	Replacing rodent models for investigating the influence of the microbiome upon innate immune responses and resistance to pathogens.
University of Southampton	Exploitation of an <i>ex vivo</i> disease model to characterise early events in retinal degeneration.
University of Strathclyde	Developing microfluidic systems for high-throughput studies of functional neuronal networks.
University of Sussex	Development of a refined model of neuropathic pain: A model without frank nerve injury.