



Lush Prize 2016

Young Researcher Award

Research Paper

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Executive Summary

The Lush Prize¹ is the largest annual global award fund that recognises achievements in the field of animal-free toxicology and development of alternative methods to animal testing. In the four increasingly successful years since its launch, the Prize has awarded a total of £1.2 million in funding, devoted to pioneering scientific research, educational outreach, lobbying on alternative methods and the scientific and ethical imperatives to end, or where necessary, replace the use of animals in chemical safety (toxicity) testing. The prize awards individuals and organisations across six categories: Science, Public Awareness, Lobbying, Training, Young Researchers and finally, the 'Black Box' Prize, where in any one year the total £250,000 may be awarded for a key breakthrough in non-animal toxicity testing. Last year, the Lush Prize team was delighted to award its first Black Box Prize, divided between a number of scientists responsible for groundbreaking research to develop and validate alternative methods which map to three key stages in elucidating the first Adverse Outcome Pathway (AOP) for skin sensitisation². The 2015 Black Box Prize was particularly exciting, as Lush Cosmetics made available a further £200,000, so that all other prize categories could still be awarded.

As in previous years, it is always important to highlight in addition to the winning projects, those which were successfully shortlisted in 2015³. The nominations were, as always of exceptionally high quality and choosing winners remains a challenging task for the judging panel.

The Lush Prize continues its focus on only the final 'R' (replacement) being a genuine alternative to animal testing. No other prize is devoted solely to the '1R' of replacements to toxicity tests using animals.

The purpose of this research paper is to focus on one of the Lush Prize categories in particular- the Young Researcher (YR) Award⁴.

1 <http://www.lushprize.org/>

2 <http://www.lushprize.org/2015-prize/2015-prize-winners/>

3 <http://www.lushprize.org/2015-prize/2015-shortlist/>

4 <http://www.lushprize.org/awards/young-researcher-prize/>

The Young Researcher (YR) Award

The Young Researcher Award is offered to scientific applicants, aged up to 35 years old (inclusive) at the time of nomination and rewards an annual fund of £50,000, usually divided between five winners, for prospective toxicology research projects which do not involve animals. In their nomination for an award, applicants must outline their work and interest in non-animal research to date, as well as future research they intend to carry out and how the prize fund will be used (for example for specific areas of investigation and consumable materials). To date, £210,000 has been awarded to nineteen young researchers from across the world. In 2015, a sixth Young Researcher prize was possible due to a winner from another category accepting an award, but kindly declining the accompanying financial prize. The Young Researcher prize category also received a record twenty nominations in 2015, its highest yet.

The Young Researcher Award remains distinct from the other Lush Prize categories as it is awarded on the basis of *future* work, rather than past successes.

This research paper includes the following:

- A summary of prize winning Young Researcher projects for 2015
- Update on activity of some previous Young Researcher winners
- Young Researcher outreach for 2015-2016 and the 2015 Lush Prize conference
- Exciting new outreach for Young Researcher 2016 - The Lush Prize Young Researcher Award for Asia and America

As each new research paper provides an update on those written in previous years, it is advised that these papers are also reviewed, for a comprehensive picture of the Young Researcher Prize to date. These can be downloaded from the Lush Prize website⁵

5 <http://www.lushprize.org/awards/background-research-papers/>

Lush Prize 2016: Young Researcher (YR) Outreach Project

The objectives of the YR outreach project for the 2016 Lush Prize remain as communicating individually with potential applicants to ensure understanding of the criteria for winning a YR award. It also remains an important objective to highlight effective new communication channels for the Young Researcher Award and in turn, identify potential individual nominees. In the 2015-2016 prize cycle, this has been achieved by making contact via networking and conferences with a number of prospective YR applicants, to notify them of the prize's existence generally and discuss if their work may be considered relevant. Conferences attended during 2015-2016 are discussed in a later section.

Summaries of prize winning Young Researcher Projects for 2015

A record six YR prizes were awarded in 2015 to researchers from the USA, Brazil, Italy and Germany. Summaries of their projects are provided below:

Laura Bray, Leibniz Institute of Polymer Research, Germany

Laura's winning proposal used a variety of clinical and in-vitro methods to fulfill three key areas; firstly, a 'toolbox' to study acute myeloid leukemia in vitro; a high throughput screening method to progress potential new drugs to clinical trials faster; and a biopsy testing system to personalise treatment, in order to identify if a patient's cancer has advanced or metastasised.

To do this, Dr Bray proposed to use 3D hydrogel platform cell culture models of breast and prostate cancer which the Leibniz team have already developed, to provide robust microtissue environments which mimic the complex stages of cancer development and metastasis. Work already successfully published by the team has shown exciting promise.

Jeremy Caplin, Hashemi Labs, Iowa State University, USA

Dr. Caplin won a 2015 YR prize for his proposal on ongoing 'placenta on a chip' research, a 3D microfluidic device no greater than 2cm in size which offers highly improved performance in toxicity testing. To overcome well known inaccuracies in the prediction of human responses when using animal based methods, Jeremy's work combines multi organ chip (MOC) methods using combinations of layers of human cells and delivery of media at a constant flow rate into the devices to mimic the human body on a microscale, saving not only animals but expensive *in-vivo* testing costs too, to investigate for example the effects of alcohol (ethanol) transport from mother to foetus.

Elena Kummer, Università degli Studi di Milano, Italy

Elena's 2015 prize winning research proposal is devoted to a better understanding of allergic sensitization in toxicity testing, without animals. To do this, Dr Kummer and the team at Università di Milano are developing a simple test, using human cell lines already available, to assess the potential of chemicals to activate the immune system, by measuring the associated levels of enzymic activation of skin cells resulting in allergic contact dermatitis (ACD). Dr. Kummer's prize winning work was directly relevant to the theme of the 2015 Lush Prize conference on the breakthrough of the skin sensitisation Adverse Outcome Pathway (AOP).

Bianca Marigliani, The Federal University of São Paulo, Brazil

Bianca's award winning project, driven by a long term passion for replacing animals not only in toxicology but scientific research generally, involves the replacement of foetal bovine serum (FBS), widely used as a serum in cell culture and inhumanely obtained from the slaughter of pregnant cows, via cardiac puncture of the foetus. Its use is not only unethical but causes scientific inaccuracies in *in-vitro* research, due to contamination from foreign proteins. Bianca and the team at São Paulo are working to overcome this by making use of the recently approved h-CLAT *in-vitro* skin sensitisation test, which involves a particular type of human leukaemia cell line, THP-1, to investigate if FBS-free adapted THP-1 cells match results to those seen in standard h-CLAT testing. Such research eliminating the use of FBS allows

replacement methods to be truly animal-free and would have global impact in *in-vitro* research.

Ilka Maschmeyer, TissUse, Germany

Ilka and the multi-award winning team at TissUse are developing their 'Human on a Chip' technology by working on systemic connection of different organ chips with microfluidic capillary networks and micro-pumps to ensure steady flow rate of media through the devices, which are capable of maintaining and connecting tissues derived from cell lines, primary cells or biopsies of various human organs like skin, liver, intestine, hair follicle and kidney. This will allow the Multi Organ Chip (MOC) its best performance yet to faithfully replicate the human *in-vivo* system for the testing of drugs, cosmetics and other substances by oral, dermal or intravenous delivery and provide superior results to those obtained from inaccurate animal models.

Dr Lena Smirnova, Center for Alternatives to Animal Testing, USA

Dr Smirnova of CAAT was awarded a 2015 YR prize for her research into human relevant, high-throughput 3D *in-vitro* 'mini-brain' models for chemicals testing, in the much needed area of developmental neurotoxicity (DNT), combined with the use of multi-omics technologies. Lena is using these models to investigate toxicity pathways and molecular mechanisms, with a particular focus on micro RNA (miRNA) which plays a key role in gene expression and development of the nervous system, to investigate response to environmental stress, relevant to conditions such as Parkinson's disease.

Feedback and update on activities of current and previous Young Researcher prize winners

One of the 2015 YR winners, Dr. Bianca Marigliani, along with 2014 YR winner Dr. Rober Bachinski and Lush Prize judge Professor Thales Trez are three of the founder members of the 1R Institute of Promotion and Research for the Replacement of Animal Experimentation in Brazil.⁶ Based in Sao Paulo, the institute, like the Lush Prize, dedicates itself to the promotion of the '1R' of *replacement*, rather than reduction or refinement, as the only true alternative to animal testing. The team have worked very hard since the institute's launch a decade ago, to raise awareness on the ethical and scientific problems of using animals in research and to promote their replacement via presentations, political activities, workshops and conferences as well as projects and initiatives on humane education, without the use of animals to collaborate with schools, universities and industry.

There is an ongoing need for the YR Prize and outreach to new early career researchers, as reflected in feedback provided by some of last year's winners, who described how winning a YR award has opened new communication channels, to liaise with other scientists working in similar fields.

Further feedback included a continued need to communicate to universities, both to encourage individuals to nominate and to circulate and raise awareness of the Prize within their institutions, as well as showcasing the prizes at relevant events and conferences. Lush Prize is active in this area and sends regular mailouts to new academic contacts on an ongoing basis, as well as attending and providing sponsorship to annual congresses and events on alternatives to animal testing, to present information on the YR and other prize categories.

6 www.Instituto1R.org

Young Researcher Project- Outreach for 2015- 2016

The Lush Prize team has attended several conferences during 2015 and 2016 so far, including in September 2015, the 51st Congress of the European Societies of Toxicology (EUROTOX) held in Porto. The theme of this year's conference was 'Bridging Sciences for Safety'. EUROTOX is very much a mainstream toxicology conference which maintains largescale focus on animal use, so Lush Prize attended to raise awareness and present a poster entitled 'Rewarding innovative animal-free science around the world', giving an overview of the prize categories available. Of particular relevance to the Lush Prize and YR outreach project were EUROTOX's 'Continuing Education Courses' (CEC) which are described as well attended by young scientists and offering 'cutting edge' information on various themes including use of the 3RS in toxicity testing. The 2015 programme included a number of relevant topics such as non-animal methods in toxicokinetics and progress in replacing repeat dose toxicity testing with new technologies.

Following EUROTOX, Lush Prize also attended the 16th Congress hosted by the European Society for Alternatives to Animal Testing (EUSAAT) in Linz⁷, again submitting a poster presentation to allow visitors and potential prize applicants to find out more.

On 10th December, Lush Prize was very pleased to sponsor and attend the annual Animal Replacement Science⁸ conference, hosted by the Dr. Hadwen Trust (DHT) at Charles Darwin House in London. The theme of this year's conference, the second hosted by the DHT was '*Fundamental biology in the 21st century: Innovative solutions and accelerating change*'. The morning session included a very successful scientific discussion on current animal use in cancer research, as well as relevant non-animal methods. The afternoon session was open to further attendees and Lush Prize was pleased to sponsor the event again this year, which included presentations from FRAME (Fund for Replacement of Animals in Medical Research), the Blizzard Institute and organisations pioneering organ on a chip technologies.

7 <http://www.eusaat.org/>

8 <http://www.animalreplacementscience.com/>

Also in December 2015, an article by Lush Prize and published in ATLA (Alternatives to Laboratory Animals) was entitled ' Young Researchers - the ethical challenge' ⁹. Extracted from the 2014 YR background paper, it outlines the opportunities for early career scientists to pursue a professional path in non-animal technologies, not only saving animals but gaining expertise in cutting edge methods to end or replace the use of animals. Such methods, far from stifling scientific research (as is still rather disingenuously claimed by many invested in *in-vivo* animal -based methods) are themselves a driver for innovation in research and development (R&D).

In April 2016, Lush Prize attended the first Pan American Conference on Alternative Methods, hosted by The Centre for Alternatives to Animal Testing (CAAT) based at The Bloomberg School of Public Health at Johns Hopkins University in Baltimore¹⁰.

The conference, held over three days allowed attendees to hear a number of presentations which aimed to address a new concept of 'The 6Rs'- in addition to the well-known criteria of 'Reduction', 'Refinement' and 'Replacement' of animal experiments, further interesting areas of 'Roadmaps'; 'Relevance' and 'Read-Across' were covered. This was the first conference of its kind hosted by CAAT as part of its 35 year anniversary and the centennial of the Bloomberg School of Public Health.

A key message of the conference was that innovative alternative methods will protect people as well as animals, in chemicals safety testing. Former Lush Prize winner CAAT works with all major industry stakeholders to develop non-animal methods. CAAT aims for its first Pan-American event to provide a good starting point to team up with other countries (e.g. Canada) to develop further initiatives. Also of particular positive note was the attendance of researchers from Cuba for the first time. As part of its exciting international outreach strategy for 2016, Lush Prize networked with a number of contacts to raise awareness of the award categories and engage with potential nominees.

Maintaining existing, as well as making new contacts at toxicology and pharmacology institutions, faculties and scientific departments of universities and in

9 Ram, R. (2015) Young Researchers - the Ethical Challenge. ATLA 43; 72-77
[<http://www.ncbi.nlm.nih.gov/pubmed/26753946>]

10 <http://caat.jhsph.edu/programs/workshops/PanAmerican/reg.html>

industry continues via email, subscription to regular mailings and social media outlets , as outlined in previous Young Researcher background papers.

The 2016 Young Researcher Awards - Asia and the Americas

This year in addition, there are exciting overseas developments with the official launch of Young Researcher Prizes in both the Asia and America regions. Individual prize funds of £50,000 have been allocated to each of these areas, thereby seeing this year's YR awards offer up to £150,000 in prize money for new research. In its international outreach, so far the Lush Prize has engaged with teams in the USA, Japan, Korea and the Middle East to provide initial discussions, support and guidance in launching Young Researcher Award communications locally.

The 2015 Lush Prize conference

The third Lush Prize conference was held in November 2015 with the theme of 'Adverse Outcome Pathways - what, how and where next?'¹¹ The conference was an opportunity to showcase all prizewinners and their work (including the winning YR projects described above). Some presentations, as in previous years were enjoyed during individual breakout sessions and, in 2015, the additional success of the Black Box Prize winners was a central focus of the conference and awards, for their pioneering research on the skin sensitisation AOP to replace animal testing.

As in previous years and now becoming a popular format, the audience was invited to put questions to our expert panel. Interviews were also held with all young researchers and other prizewinners during the conference and subsequent awards gala in the evening, all of which can be seen on the Lush Prize website.

Conclusion

¹¹ <http://www.lushprize.org/2015-prize/2015-conference/>

The Lush Prize Young Researcher project is ongoing in 2016 and outreach continues with academic institutions, toxicology departments and research teams to raise awareness of the YR Awards and other Lush Prize categories.

Preparations are now underway for the 2016 Lush Prize conference and awards and, at the time of writing this paper, nominations are open to welcome applications for Young Researchers and other award categories for this year. Further international activity for USA and Asia outreach provides exciting opportunities to raise awareness of the Young Researcher awards and the concept of early career pathways in non-animal toxicology, well into the 2016-2017 prize cycle and beyond.

New references for 2016

In addition to the updated references below, it is recommended to review comprehensive reference sections provided in previous Lush Prize YR papers.

EUSAAT 2016 Young Scientists Travel Awards

<http://eusaat-congress.eu/index.php/congress/2016/young-scientist-travel-award>

International Foundation for Ethical Research (IFER): Graduate Fellowships for Alternatives to the use of animals in science-2016

www.ifer.org/fellowships.php