Corners

CAAT feed

Join the Team: Positions Available at CAAT

CAAT is growing its team, and we are looking for professionals at any level of experience in the following areas:
- Communications and Social Media Management
- Event Planning and Logistics
- Metabolomics
- Computational Toxicology

If you, or someone you know, are interested in learning more about these positions, please email Camila Januario at cjanuar1@jhu.edu

Next Generation Humane Science Award

Due by October 24, 2021

The Next Generation Humane Science Award is available annually to young scientists to acknowledge and encourage researchers who focus on replacing the use of animals in experiments. The 2021 award will be a prize of up to $5,000 to recognize the work of one young scientist; this may be shared among two or more young scientists. Please email completed application to caat@jhu.edu

Qualification Criteria

The work must be focused on the replacement of animals used in experimentation. Excellence of research outcome as demonstrated by publications and presentations at scientific meetings. The review committee will also take into account:
- The significance of the potential to replace animal experiments in the future.
- Providing an inspiration to others (fellow students, members of the research group) and outreach to wider audiences.
- The potential for the replacement methodologies to be used in a regulatory context.

2021 Eligibility Criteria

The candidate must be a citizen or permanent resident of the United States working at a US-based institution. The candidate should not have received a PhD or similar degree earlier than 2012. Current and former employees (or their family members) of the Center of Alternatives to Animal Testing at Johns Hopkins University cannot apply.

Article Resulting from CAAT Workshop Published in *Science*

The article "Human microphysiological systems for drug development" by Adrian Roth and MPS-WS Berlin 2019 (Marx, U., Vilén, L., Ewart, L., Griffith, L. G., Hartung, T., Ingber, D. E., Mendrick, D. L., Steger-Hartmann, T. and Tagle, D. A.) has been included in the September 16 issue of *Science*. This perspective article was the direct result of the 2019 workshop "Biology-inspired microphysiological systems to advance medicines for patient benefit and animal welfare." (doi:10.14573/altex.2001241).

CAAT Receives Close to $300,000 for FDA Project on Neurotoxicity

An FDA research project titled "Leveraging human brain organoids for mixture neurotoxicity and the understanding of individual susceptibilities" (PI Thomas Hartung) was awarded to CAAT.

The project is part of the Johns Hopkins Center of Excellence in Regulatory Science and Innovation (CERSI). Thomas Hartung commented "We are thrilled that for the second time we receive one of the rare FDA research grants. It shows the relevance of our work on microphysiological systems for FDA."

CAAT Director Thomas Hartung Honored with EuroTox Merit Award – Honor Recognizes Outstanding Achievement in Toxicology

EUROTOX has recognized Professor Thomas Hartung, MD, PhD, with its 2021 Merit Award. The EUROTOX Merit Award is presented annually at the EUROTOX Congress to a European toxicologist with a long and outstanding career in the discipline.

Dr Hartung is a professor and endowed Doerenkamp-Zbinden chair for evidence-based toxicology in the Department of Environmental Health and Engineering at The Johns Hopkins University. He has joint appointments in Georgetown University and the University of Konstanz in Germany. He directs the Center for Alternatives to Animal Testing (CAAT) in the United States

and Europe and serves as chief editor of Frontiers in Artificial Intelligence. He has authored more than 600 scientific publications. "I was humbled by the fact that this award recognized a European career, even though I've been working almost 13 years now in the United States," Hartung says. "It shows that with the creation of our European joint venture, CAAT-Europe, our work is relevant on the other side of the Atlantic."

EUROTOX is a federation of European toxicologists and societies of toxicology. It has about 6,000 members across Europe and more than 200 members around the world. Merit Award recipients are selected through a member nomination process. "Professor Thomas Hartung's professional career, contributions in the areas of evidence-based toxicology and alternatives methods to animal testing, and extensive list of European and international publications, make him a perfect match for the EUROTOX Merit Award," said Professor Heather Wallace, President of EUROTOX.

WC11 CAAT Presentations

CAAT was well represented at the 11th World Congress on Alternatives and Animal Use held virtually on August 23 to September 2.

Thomas Hartung was co-chair and speaker in the session "Artificial Intelligence for Risk and Safety Assessment" and spoke on "Artificial intelligence and machine learning for chemical risk assessment". He also chaired the session "A Virtual Human Platform for Safety Assessment".

Marcel Leist chaired the session "Challenges of Non-Animal Approaches for Food Safety & Nutrition in the 21st Century: From Inception to Application", and Marcel Leist and Giorgia Pallocca co-chaired the session "A walk through 10 years of CAAT-Europe's highlights", which included Thomas Hartung, Martin Stephens, Costanza Rovida and Francois Busquet as speakers from CAAT and CAAT-Europe.

Martin Stephens and Kathrin Herrmann chaired the session "Beyond the 3Rs: Expanding the Use of Human-Relevant Replacement Methods in Biomedical Research", in which Helena Hogberg spoke on "Applications of brain-model technology to study chemical induced neuro(developmental) disorders." Martin Stephens and Kathrin Herrmann also co-chaired the session "Animal Experimentation: Working Towards a Paradigm Change", in which Kathrin Herrmann spoke on "Educating Future Scientists and Raising Public Awareness on Animal-free Experimentation" and Thomas Hartung spoke on "Research and Testing Without Animals: Where Are We Now and Where Are We Heading?". Kathrin Herrman was co-chair and speaker in the session "Barriers of Refinement Use in Practice" and spoke on "Education and training to fully implement refinement methods in practice".

Alex Maertens spoke on "Functionally Enigmatic Genes in Cancer: Are We Still Looking Under the Lamp Post for The Keys?", Lena Smirnova spoke on "From microphysiological to micropathophysiological systems to study neurotoxicity and CNS diseases", and Francois Busquet spoke on "Ways to improve their effectiveness and recognition" and on "Data access and EU institutions" and chaired and spoke at the session "skills4science".

Alan Goldberg Named Ambassador of Compassion for American Visionary Art Museum's Healing & the Art of Compassion (and the lack thereof!) Show

Alan M. Goldberg, PhD, is Founding Director (Emeritus) of the Center for Alternatives to Animal Testing.

From Rebecca Hoffberger, founder of the American Visionary Art Museum: Years ago, I devoted a year to an exhibition entitled, "Home & Beast." As happens with AVAM's magic, the focus on our relationship to animals and how we humans share the one home with all that lives (answer: poorly) coincided with the 25th anniversary of CAAT. Alan Goldberg and I collaborated on a private guided tour, which we led together, and he then held a dinner for the many researchers and physicians who had taken up CAAT's mission as their own.

Alan Goldberg has inspired physicians and researchers from all over the world to find and adopt non-animal testing alternatives. His attendees were powerfully moved by an exhibition so in sync with their ideals. Our national museum and education center, right from its initial twinkle in my eye, always sought to weave together the works and thoughts of creative visionaries throughout all aspects of human endeavor, not limited to simply visionary artists, but rather inclusive of scientists, engineers, philosophers, human rights activists, farmers – all who creatively aim to better lives.

Therefore, I have been privileged to collaborate with truly outstanding human rights activists like Archbishop Desmond Tutu, Julian Bond, Dame Anita Roddick, and Patch Adams MD; inventors and innovators like Martine Rothblatt, Ray Kurzweil, Dean Kamen, Peter Agre MD, and Abel Wolman – my hero for whom I dedicated our exhibition, "Holy H_2O: Fluid Universe,"; and comedians like Matt Groening and Lewis Black, who wield humor to speak truth to power.

In our new year-long focus on the twin forces of healing and compassion, the passion wedded to Alan Goldberg's career is so expressive of intense caring to alleviate animal suffering and at an orchestrated and unprecedented scale. This makes Alan once again an ideal collaborator and worthy show ambassador. Simply put, Alan Goldberg never fails to inspire me with his depth of sincerity and care for ameliorating life. We are so lucky to be working with him yet again.

We are also asking institutions and clergy to adopt, in their own voice, a focus on healing and compassion, to magnify the intention for good of our show. AVAM has never just been about art as object, but rather as mechanism to deepen understanding and inspire better action.

Healing & the Art of Compassion (and the lack thereof!) begins with a private opening on October 8, 2021. The exhibition opens for the public October 9.

CAAT 40th Anniversary Symposium

The celebration of CAAT's 40th birthday on September 21, 2021, featured a program with special guests and friends of CAAT from its 40 year history promoting and shaping the field of alternatives and humane science. Speakers included

Alan Goldberg, Andrew Rowan, Tim Shafer, Danielle Wikoff, Sandra Coecke, Joanne Zurlo, Tony Gaspari, Julia Fentem, Deborah Rudacille, Nick Anastas, Bert van Zupthen, Paul Locke, and Kristie Sullivan.

MPS World Summit 1st Virtual Pre-Event Young Investigator Award Winner

Ilka Maschmeyer, of TissUse GmbH, has been awarded the 2021 MPS World Summit Young Investigator Award for her paper entitled Multi-Organ-Chip Technologies: Towards a Paradigm Shift in Drug Development.

3Rs Webinar Training Series

The 5th webinar in the series was a German talk by Dr Tamara Zietek about organoids and about the NAT database (Non-Animal Technologies, https://nat-database.org), a new database, available in both English and German, that contains information on modern non-animal technologies and methods from various areas of biomedicine and life sciences, based on scientific studies and publications.

The 6th webinar was an English talk by Dr Laure-Alix Clerbaux from the Joint Research Centre (JRC) of the European Commission on the CIAO project, which aims at modelling the COVID-19 pathogenesis via the adverse outcome pathway (AOP) framework.

8th Annual 3Rs Symposium Video Available!

The 8th Annual 3Rs Symposium, jointly organized by the Johns Hopkins University Center for Alternatives to Animal Testing (CAAT), the USDA Animal Welfare Information Center (AWIC), the NIH Office of Laboratory Animal Welfare (OLAW), and the Johns Hopkins Department of Molecular and Comparative Pathobiology, took place via Zoom on June 3 and 4, 2021.

This year's virtual symposium, among other things, focused on current, pandemic-driven developments in refinement, reduction and replacement of animal use in science. Together with international experts and practitioners it aimed to increase awareness of the challenges faced during the pandemic as well as of successes in effectively applying the 3Rs principles to maximize both biomedical discovery and animal welfare.

To watch the authorized presentations: https://www.youtube.com/playlist?list=PL_8uALA03ZsVHZib48Qn31tfrkl7hpqYc

Upcoming events

Challenges and Opportunities for Overcoming Dog Use in Agro-chemical Evaluation and Registration

October 25th, 2021, 9am-1pm EDT, Online

The 90-day dog study is being conducted for agro-chemical authorization when it is not always needed to adequately address hazard identification and human safety and risk. This virtual workshop will host a series of presentations on the role the dog study has played in regulation of agro-chemicals in both the U.S. and Europe during the past 20 years and what approaches may be employed to substantially reduce its use. The public will have the opportunity to submit comments and questions to be discussed during the following invitation-only workshop.

Save the Date! EBTC 10th Anniversary Symposium

November 11, 2021, Online

Please save the date for the Evidence-Based Toxicology Collaboration's 10th anniversary symposium, which will be held online on November 11, 2021.

2-day Early Career Scientists Online Workshop on NAMs in Biomedical Research

November 22-23, 2021, 9am-12pm EST/ 3-6pm CET Online Workshop (via Zoom)

Deadline for applications: 7 November 2021
More information: https://www.berlin.de/lb/tierschutz/alternativen-zu-tierversuchen/artikel.1129019.php

CAAT and the Animal Protection Commissioner of Berlin are inviting early career scientists to a two-day online workshop focusing on animal-free new approach methodologies (NAMs) in biomedical research. The program will include presentations and interactive sessions. Following the call for abstracts, up to ten early-career scientists will be selected to present their own research involving NAMs. The program will also include a session with established scientists from academia, industry, government, and NGOs, who will answer the participants' questions and share advice and guidance on future careers in the field of non-animal methods. In another session, we will discuss topics such as how to tackle the "publish or perish" trap, and where to find funding as well as ongoing training opportunities in NAMs.

The workshop is free of charge. Please use the form on the website to apply and to submit your abstract (if you would like to present your research) via email to Dr Kathrin Herrmann at kherrma1@jhu.edu.

2nd MPS World Summit Virtual Pre-Event:

Systems Engineering of Microphysiological Systems
December 9, 2021, 9am-1pm EST

9:00 am – Welcome, Thomas Hartung, JHU
9:05 am – Keynote Address: Donald Ingber, Wyss Institute, Harvard University
9:35 am – "MPS Hardware and Enabling Technologies" (short talks from submitted abstracts)
10:55 am – Break and poster voting
11:00 am – "Cell Models and Applications for MPS" (short talks from submitted abstracts)
12:20 pm – Panel discussion and Q&A: Adrian Roth, Roche – moderator; Linda Griffith, Massachusetts Institute of Technology; Alysson Moutri, University of California San Diego; Peter Loskill, Tübingen University; Uwe Marx, TissUse; Hiroshi Kimura, Tokai University
12:50 pm – Young Investigator Travel Award announcement and closing remarks

Registration: https://mpsworldsummit.com
Abstracts are invited on the topic of new

developments in MPS: new cellular models (from bio-printing to organoids, etc.) and new approaches in bioengineering of MPS devices. Describe your newest developments: breakthroughs, advantages, challenges, and the field of applications. The top abstracts will be selected for oral presentations in one of two sessions: (1) MPS hardware and enabling technologies; (2) Cell models and applications for MPS.

All accepted abstracts will be invited to submit an electronic poster. There is no submission fee and no conference registration fee.

Abstract submission guidelines:

- Abstracts must be in English.
- All abstracts will be evaluated and selected by the MPS Scientific Advisory Committee (SAC).
- Please limit abstracts to 300 words.
- References must be cited in the text as (First author et al., Year).
- Pictures, figures, attachments are not permitted – text only.
- Please submit abstract as Word document.
- Include no more than five references.
- All accepted abstracts will be published in an abstract/poster book (PDF) and distributed digitally to all registered attendees.

E-mail abstracts to: info@mpsworldsummit.com; Please note "Abstract" in the subject field.

Applicants will be informed of acceptance/non-acceptance by November 25, 2021.

Microphysiological Systems World Summit

May 30 - June 3, 2022: Hybrid Conference,
Hilton New Orleans Riverside,
New Orleans, LA, USA

The MPS World Summit will bring together a global audience – including institutions (government, health foundations, charities), the academic research community (universities, research institutes), environmental and human toxicity researchers, the pharmaceutical and other industries (cosmetics, chemical, and food industries), medical centers and practitioners, patient associations, and policy makers and testing centers – in a series of global conferences to create a roadmap for MPS technologies. NIH NCATS will support the first three Microphysiological Systems World Summits with $450,000. This substantial NIH contribution is still only a fraction of the anticipated costs.

Become a sponsor! Multiple sponsorship levels are available. Information on sponsorship: https://mpsworldsummit.com/s/MPS-One-Sheet-and-Sponsorship-Levels-Flyer.pdf

Please contact Camila Januario (cjanuar1@jhu.edu) if you need more information.

Thank you to our already committed sponsors:
Gold sponsor: Emulate
Silver sponsors: AxoSim, Hesperos, InSphero, Obatala
Bronze sponsor: Nortis
Exhibitors: Aracari, Mimetas, Vitrocel Systems GmbH, TissUse

New Publications

Chesnut, M., Paschoud, H., Repond, C. et al. (2021). Human 3D iPSC-derived brain model to study chemical-induced myelin disruption. *Int J Mol Sci 22*, 9473. doi:10.3390/ijms22179473

Golden, E., Maertens, M., Hartung, T. et al. (2021). Mapping respiratory sensitization: How useful are our current tools? *Chem Res Toxicol 34*, 473-482. doi:10.1021/acs.chemrestox.0c00320

Hartung, T. (2021). Evidence integration in the era of information flooding – The advent of the comprehensive review. *Front Public Health 9*, 763828. doi:10.3389/fpubh.2021.763828

Hoffmann, S., Margliani, B., Akgün-Ölmez, S. G. et al. (2021). A systematic review to compare chemical hazard predictions of the zebrafish embryo test with mammalian prenatal developmental toxicity. *Toxicol Sci 183*, 14-35. doi:10.1093/toxsci/kfab072

Maertens, A., Golden, E. and Hartung, T. (2021). Avoiding regrettable substitutions: Green toxicology for sustainable chemistry. *ACS Sustainable Chemistry and Engineering 9, 23*, 7749-7758.

Modafferi, S., Zhong, X., Kleensang, A. et al. (2021). Gene-environment interactions in developmental neurotoxicity: A case study of synergy between chlorpyrifos and CHD8 knockout in human BrainSpheres. *Environ Health Perspect 129*, 77001. doi:10.1289/EHP8580

Roth, A. and MPS-WS Berlin 2019 [Marx, U., Vilén, L., Ewart, L. et al.] (2021). Human microphysiological systems for drug development. *Science 373*, 1304-1306.

Spoladore, J., Lopes, I. G., Bachinski, R. F. et al. (2021). Standardized pyrogen testing of health products with bacterial endotoxin tests (BET) as a substitute for rabbit pyrogen testing (RPT): A scoping review. *Toxicol In Vitro 74*, 105160. doi:10.1016/j.tiv.2021.105160

Tran, V., Kim, R., Maertens, M. et al. (2021). Similarities and differences in gene expression networks between the breast cancer cell line MCF-7 and invasive human breast cancer tissues. *Front Artif Intell 4*, 674370. doi:10.3389/frai.2021.674370

Vinken, M., Benfenati, E., Busquet, F. et al. (2021). Safer chemicals using less animals: Kick-off of the European ONTOX project. *Toxicology 458*, 152846. doi:10.1016/j.tox.2021.152846

Cruelty Free INTERNATIONAL
Ending animal experiments worldwide

UK publishes 2020 animal testing statistics

According to the latest Home Office annual report, published on 15 July 2021, a total of 2.9 million animal procedures were completed in the UK in 2020. While this represents a reduction of 15% since 2019, the decrease is largely explained by two national lockdowns due to the COVID-19 pandemic.

Approximately 1.44 million procedures (50%) were related to the "creation" and breeding of genetically altered animals, while the remaining 1.44 million (50%) were actual experiments on animals for various purposes including basic and applied research and regulatory testing.

Notably, there was a significant increase in animal procedures conducted to satisfy chemicals legislation (e.g., REACH) – up 64% from 2019 to 59,613 procedures, which includes substantial increases in mouse skin sensitisation tests (up 375% since 2019 to 452 tests), despite the availability of internationally accepted non-animal methods, and animal tests for chemicals designed to be used in household products (up 349% from 2019 to 301 experiments).

EU Commission publishes 2018 animal testing statistics

On 15 July 2021, the European Commission published a new report detailing the number of animal experiments conducted in 2018, including a summary of the number of experiments conducted in each member state.

The 2018 figures show that (excluding Norway – an EEA member included in the reporting for the first time) the total number of uses of animals in experiments was 10.6 million. This represents a decrease of 2% since 2017.

The United Kingdom still features in the reports as it was still in the EU in 2018 and is still the country with the highest number of animal experiments in Europe (2.4 million in 2018), followed by Germany (2.1 million) and France (1.9 million).

Rabbit pyrogen test to be removed from EU Pharmacopeia

At its 170th session in June 2021, the European Pharmacopeia Commission announced its commitment to eliminate the rabbit pyrogen test from the EU Pharmacopeia within the next five years.

The rabbit pyrogen test is one of ten animal experiments on Cruelty Free International's Replace Animal Tests (RAT) list, which highlights tests with internationally accepted non-animal methods.

Despite multiple efforts to encourage developers to use the monocyte activation test (MAT), a cell-based test that was first published in the EU Pharmacopoeia in 2009, the rabbit test continues to be used in the EU. According to the latest statistics, 30,453 rabbit pyrogen tests were conducted in 2018 with 81% taking place in France, Spain and Germany.

To help speed up replacement, the rabbit test will now be deleted and replaced with cell-based methods in 59 texts of the Ph. Eur. covering a range of medical products including vaccines, blood products and antibiotics. It is hoped that this move will ultimately lead to the complete elimination of this controversial test in the EU.

11th World Congress on Alternatives and Animal Use in Life Sciences

The 11th World Congress on Alternatives and Animal Use in the Life Sciences was held virtually from Maastricht, The Netherlands on 23 August - 2 September 2021.

In over 100 symposia, workshops and lectures, over 1,000 scientists shared their expertise and recent work on innovative non-animal methods, good research practice, harmonisation, education, and the transition to animal free research.

Cruelty Free International's Director of Science and Regulatory Affairs, Dr Katy Taylor, and Senior Science Advisor, Dr Emma Grange, both presented at the event. Dr Grange spoke about replacing guinea pig skin sensitisation tests with non-animal methods and about how EU chemicals legislation could be improved to better protect animals while Dr Taylor discussed the key barriers to the implementation of non-animal methods.

Four posters from Cruelty Free International's science team were also presented at the event covering the following topics: endocrine disruptors, estimated global statistics on animal use, prevalence of gavage incidents in regulatory toxicity tests, and barriers to eliminating tests with alternatives, i.e., Cruelty Free International's RAT list.

Opinion poll reveals majority support for deadline to end animal tests in Great Britain

According to a poll carried out by YouGov on behalf of Cruelty Free International in September 2021, 65% of the public in Great Britain want to see a binding plan in place to phase out animal testing. Two-thirds (66%) also agree that a target date should be set for the end of all animal experiments.

A further 80% think it is unacceptable to test on dogs, while 76% think it is unacceptable to carry out tests on monkeys. However, the UK remains one of the top users of dogs and monkeys in Europe.

Despite public opinion being firmly against animal testing, the UK is the big-

gest user of animals in Europe, with Home Office statistics for 2020 revealing that 2.9 million animal experiments took place.

The poll also showed that 85% of the public find it unacceptable to test cosmetic ingredients on animals. However, the UK Government recently stated that it will follow the EU's position and permit the testing of cosmetic ingredients for other purposes such as for chemical safety regulations.

Cruelty Free International together with Animal Free Research UK and OneKind have launched a #TargetZero petition, so far been signed by 78,000 people, calling on the UK Government to set a clear and ambitious plan to phase out animal tests.

European Parliament calls for an EU-wide action plan to phase out animal experiments

On 16 September 2021, cross-party Members of the European Parliament voted overwhelmingly in support of an action plan to accelerate the transition from the use of animals in research and testing to human-relevant science across the EU, stressing the importance of a clear timeline, reduction targets, and milestones to incentivise progress.

The EU Parliament wants officials in the European Commission to set up a high-level working group with member states and other stakeholders to draw up an ambitious plan containing concrete actions that will lead to absolute and sustained reductions in the number of animals used in experiments across Europe.

European Citizens' Initiative to #EndAnimalTesting and #SaveCrueltyFreeCosmetics launched

A European Citizens' Initiative (ECI) – spearheaded by Cruelty Free Europe, PETA, HSI, The Body Shop and Dove – launched in August has already collected over 177,000 signatures. The ECI calls on the European Commission to protect and strengthen the cosmetics animal testing ban, transform EU chemicals regulation, and modernise science in the EU by moving away from cruel and ineffective animal tests and instead embracing animal-free approaches.

If you're an EU national, help us reach the 1,000,000 signatures needed to make this ECI a success by visiting https://eci.ec.europa.eu/019/public/#/screen/home.

Reference

European Parliament resolution of 16 September 2021 on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education. https://www.europarl.europa.eu/doceo/document/TA-9-2021-0387_EN.html

EUSAAT

European Society for Alternatives to Animal Testing

New EUSAAT website to be launched soon

EUSAAT is getting a new, timely website, which will go online soon. After the basic design was voted on together with the EUSAAT members, the work is in full swing. We are very much looking forward to presenting the new website, which will have some new features and will be visually spruced up.

One of the features will be a section on the *EUSAAT Virtual Seminar Series*. The EUSAAT Virtual Seminar Series ran from April to August 2021 for the 3Rs community and all EUSAAT members as an alternative to the EUSAAT 2021 congress, which had to be postponed so as not to interfere with the World Congress in August 2021. The EUSAAT Virtual Seminar Series provided a platform for both a distinguished researcher and a young scientist every two weeks and thematically addressed each of the 3Rs. We are very pleased that the EUSAAT website will be able to provide almost all lectures in the form of videos or slides for the public. As an appetizer, we provide the program in the following list:

15.4.2021: "Organs-on-Chips/3Rs for Wildlife Animals"

Horst Spielmann "Is it time to request human multi-organ-chip experiments rather than animal experiments?"
Miriam Zemanova "Making room for the 3Rs principles in wildlife research."

29.4.2021: "Toxicology in Chemical Industry"

Barbara Birk "How can alternatives to animal testing bring benefit to chemical industry?"
Andreas Georg Weber "Development of new approach methodologies for the detection of potential thyroid disruptors"

13.5.2021: "*In Vitro* Models – Brain/Neurosystem"

Winfried Neuhaus "The power of *in vitro* models to study the blood-brain barrier in health and disease"
Bettina Seeger "Potency testing of botulinum neurotoxins – Cells can do it better than mice"

27.5.2021:
"Refinement"
Anna Olsson "Big numbers of small animals: Preweaning mortality in laboratory mouse breeding"
Sophie Brajon "Why estimating perinatal mortality of laboratory mice is more challenging than you think"

10.6.2021:
"Bioprinting & ECM"
Anna Sebestyén "3D cell cultures, bioprinted cancer rafts and their potential importance in experimental cancer research"
Johannes Hackethal "Human placenta: medical waste or value for tissue engineering"

24.6.2021:
"Refinement"
Lars Lewejohann "Boredom in laboratory mice – measurements and cures"
Paul Mieske "Mice roaming in a semi-naturalistic environment"
Ute Hobbiesiefken "Preference for different enrichment items from a mouse's point of view"
Katharina Hohlbaum "Lock box – cognitive enrichment for laboratory mice"

8.7.2021:
"Complex 3D Models"
Heike Walles "Divers and complex human skin models and their biomedical application"
Anna Koncz "Application of cardiomyocyte cell lines as models for heart diseases"

22.7.2021:
"*In Silico* & *In Vitro* Models"
Sandra Coecke "A future framework for application of *in vitro* metabolism and QIVIVE models to risk assessment, the validation of advanced non-animal methods (NAM)"
Andrea Volkamer "*In silico* toxicity prediction for risk assessment of small molecules"

5.8.2021:
"QSAR & Dissemination of 3R Information"
Vera Rogiers "Animal-free risk assessment of cosmetic substances in the EU: Today and tomorrow?"
Anne Kienhuis "TPI.tv: A visual platform for animal-free innovations"

19.8.2021:
Topic "Combination of *In Vitro* and *In Silico*"
Manuela Raimondi "Micro-structured tools for cell modeling in the fourth dimension"
Annemarie Lang "Combining *in vitro* and *in silico* modelling to study the pathogenesis of osteoarthritis"

The EUSAAT Virtual Seminar Series organizing committee (Annemarie Lang, Winfried Neuhaus, Györgyi Szabó, Horst Spielmann) would like to thank all speakers for agreeing to EUSAAT disseminating and archiving their excellent contributions to the Seminar Series and to 3Rs research in general.

EUSAAT at WC11

At WC11, EUSAAT sponsored a virtual discussion session entitled "3Rs centers around the world and their role in fostering the implementation of 3Rs in academia", which was well attended.

As reported previously, a substantial number of 3Rs centers have recently been established around the world, all of them covering different aspects of replacement, reduction, and refinement of animal use for scientific and regulatory purposes. The session provided an overview of their diversity and the challenges the various centers are facing in their countries, which particularly depend on their funding status since some are supported by government, others by universities and research institutes, and some have been established by animal welfare activists and NGOs. During the session, the chairs/directors of 3Rs centers discussed synergies and collaborative activities to assist each other in implementing 3Rs at different levels, e.g., research, testing, education, and dissemination.

The session was chaired by *Charu Chandrasekera* (CCAAM) & *Horst Spielmann* (EUSAAT). The following speakers presented overviews on activities of their 3Rs centers:

– *Winfried Neuhaus*, Austrian Institute of Technology GmbH, Austria: "The EUSAAT initiative to establish a European Network of 3Rs Centers"
– *Adrian Smith*, Norecopa, Norway: "Norecopa: A hub of international 3R resources"
– *Monika Schaefer-Korting*, Freie Universität Berlin, Germany: "The Berlin-Brandenburg Research Platform BB3R – Research and Graduate Education since 2014"
– *Charu Chandrasekera*, CCAAM, Canada: "The Canadian Centre for Alternatives to Animal Methods (CCAAM)"
– *Hajime Kojima*, JaCVAM, Japan: "The Japanese Society for Alternatives to Animal Experiments (JSAAE)"
– *Shujun Cheng*, CCARE, Shanghai Jiaotong University, China: "The Consensus Center of Alternatives Research and Evaluation (CCARE)"

The EU-ToxRisk project is finalizing its scientific deliverables. The long-term sustainability activities are now a major focus. The project's regulatory and industry stakeholders' network is being used to promote the implementation of NAM.

The relevance of the EU-ToxRisk approach in the strengthening of the communication between research programs and regulatory organizations was a central discussion topic at the virtual event "A new toolbox for citizens' protection: implementing science into EU policy", a joint activity organized by EU-ToxRisk together with the H2020 project PATROLS[1,2]. The objectives of the meeting were to show how the outcomes of two of the most relevant EU toxicological programs support the current European strategies for citizens' health protection. The EU-ToxRisk project built especially on an active and dynamic interaction between academic, industry and regulatory stakeholders. This proved to be key to the successful implementation of NAM for regulatory purposes.

The most relevant proofs of this approach are the EU-ToxRisk case studies, some of which have been submitted to the OECD for review, and the advisory document on NAM-supported read-across. These topics will be presented at the upcoming EU-ToxRisk final symposium, a two-day open event organized by the project and its stakeholders at the Square Brussels Meeting Centre on November 3-4, 2021 in Brussels, Belgium[3]. The meeting will also host the kick-off of the ASPIS project cluster, a direct follow-up activity of the EU-ToxRisk project, which will have the responsibility to implement the learnings from this flagship project to advance towards NGRA.

EU-ToxRisk publications

The EU-ToxRisk Final Symposium will provide a good opportunity to get familiar with the EU-ToxRisk NAM toolbox. A strong component of the toolbox is the omics technology-based methodology: high throughput and high content NAMs. Some examples of these have recently been published.

High-throughput omics techniques have been applied extensively for the *in vitro* investigation of the underlying mechanisms of toxicity of chemicals. For instance, metabolomics has been used to provide a real-time picture of the metabolic effects caused by exposure of cells to xenobiotics. However, it was observed that the metabolomics-based strategy needs improvement concerning reproducibility and robust hazard interpretation. To solve these issues, Moreno-Torres et al. (2021) evaluated the impact of several key experimental and instrumental factors on the outcome of a metabolomic analysis data set. Meta-analysis showed that quality control measures are critical to enable consistent and meaningful estimations of the effects caused by compounds on cells. In Gupta et al. (2021), the use of transcriptomics technology for evaluating putative biomarkers that could help in the early prognosis of hepatocellular carcinoma (HCC), one of the leading causes of cancer death, was proposed. To identify such potential transcript biomarkers, RNA-Seq data for healthy liver and various HCC cell models were subjected to different machine learning algorithms, and various metrics were evaluated. By using RNA-Seq data combined with machine learning approaches, novel transcript biomarkers could be identified.

Bas ter Braak et al. (2021) used a fluorescent protein HepG2 reporter test system in combination with high content imaging to measure induction of the DNA damage response. The reporter lines were cultured as 2D monolayers and as 3D spheroids. This study showed how different culture methods can influence the sensitivity towards diverse genotoxicants and how this provides opportunities for a tiered genotoxicity testing strategy, e.g., in case of metabolically activated toxicity. A similar approach was used in Snijders et al. (2021), where the authors presented a fluorescent human induced pluripotent stem cell (hiPSC) reporter line for a sensitive and reliable biomarker for the oxidative stress response. Fluorescently tagged hiPSC-derived proximal tubule-like, hepatocyte-like, cardiomyocyte-like and neuron-like progenies were exposed to oxidant chemicals. Live-cell confocal imaging and transcriptomics analysis were used as readouts. Point of departure modelling further captured the specific lineage sensitivities towards oxidative stress, indicating how the reporter can become a valuable tool in understanding and quantifying critical target organ cell-specific chemical-induced oxidative stress responses.

Outlook

The upcoming last project months are strongly focused on increasing the confidence and understanding of NAM implementation for risk assessment.

[1] https://eutoday.net/news/environment/2021/implementing-science-into-eu-policy

[2] European Parliament to vote on animal-free research, testing and education – EU Reporter

[3] https://cmt.sym.place/events/event/view/391754/eu-toxrisk-final-open-symposium-2021

The virtual EU-ToxRisk workshop on "Application of a science-driven approach to solve the needs of regulatory and industry communities in the implementation of NAM-supported read-across in regulatory dossiers" is scheduled for October 27-28, 2021 (2-6 PM CEST). The event aims to provide a platform for facilitating the discussion among stakeholders interested in the implementation of NAMs in RAx-based regulatory dossiers. To gain this understanding, regulatory and industry stakeholders will be asked to discuss real examples of successful and failed RAx submissions, focusing on the REACH regulatory framework, where RAx attempts most often fail.

Additionally, a virtual workshop, co-organized by EU-ToxRisk and Cosmetics Europe, will take place on December 3, 2021 (date to be confirmed). The content of the workshop focuses on recently developed and improved NAMs for risk assessment. The event aims to provide a short overview of available NAMs for measuring bioactivity, exposure and hazard, and the associated levels of confidence in the conclusions derived from them to show the advances made. Additionally, the presentations aim to demonstrate the use of NAMs in the risk assessment of cosmetic ingredients and how this approach could be translated into other regulatory frameworks.

More information about the upcoming events can be obtained by following the project on social media or subscribing to the project distribution list.

References

Moreno-Torres, M., García-Llorens, G., Moro, E. et al. (2021). Factors that influence the quality of metabolomics data in in vitro cell toxicity studies: A systematic survey. *Sci Rep*, preprint. doi:10.21203/rs.3.rs-724307/v1

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Gupta, R., Kleinjans, J. and Caiment, F. (2021). Identifying novel transcript biomarkers for hepatocellular carcinoma (HCC) using RNA-Seq datasets and machine learning. *BMC Cancer 21*, 962. doi:10.1186/s12885-021-08704-9

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Giorgia Pallocca and Marcel Leist

LUSH PRIZE

SUPPORTING ANIMAL-FREE TESTING

Lush Prize 2021 Virtual Conference "The role of public awareness in replacing animals in safety testing" 24-25 November 2021

The Lush Prize is pleased to host its 2021 virtual conference on 24 and 25 November, 1pm-4pm UK time. The theme of this year's event is "*The role of public awareness in the replacement of animals in safety testing*" with live presentations, panel discussions, and interactive content over a two-day programme.

The Lush Prize hosts a conference in each prize year alongside an awards ceremony. The events provide an opportunity for scientists, policymakers and animal protection campaigners to meet and exchange ideas about progress towards a human-relevant safety testing paradigm without animals.

The Lush Prize is now a biennial event, with the next awards cycle commencing in Spring 2022, so to allow some discussion and exchange of ideas before then, we are holding a conference in November. Sessions will include presentations from regulators, legislators, campaigners and scientists to discuss the importance of public awareness in the campaign to achieve a 21st century, "fit for purpose", human-relevant safety (toxicity) testing paradigm.

Day 1 will discuss the themes of "Public Awareness Through Campaigns and Investigations" and "The Role of Regulators and Legislators in Creating Awareness of Animal Research and Replacements".

Day 2 will switch focus to "Creating Awareness of Animal Research and Replacements Amongst Scientists and Young

Researchers" and a special final session on "REACH, Cosmetics, Current Changes and Their Implications". These sessions have been created with the aim of stimulating discussion on themes we know are of great interest to Lush Prize audiences.

All speaker sessions will include an international panel of experts, and there will be live audience Q&A.

Following success and positive feedback from our 2020 event, throughout the programme there will once again be "fireside chat" interviews with award winning experts in the field.

Lush Prize continues to increase its engagement via virtual platforms for exchange of ideas and discussion. The conference is free to attend and open to anyone around the world. We welcome all interested attendees to register at: https://www.eventbrite.co.uk/e/lush-prize-conference-2021-tickets-185998094307?aff=ebdssbeac

Rebecca Ram,
Scientific Consultant, Lush Prize

RISK-HUNT3R is the newest European project to develop a new modular framework for animal-free next-generation risk assessment (NGRA).

In the first months, the consortium has built its visual identity and its platforms to communicate effectively. The project website has been tailored to display scientific outcomes like publications, newsletters, and news and press releases[1]. Additionally, the project website includes an interactive presentation of RISK-HUNT3R's impact areas: health, economy, regulatory processes, environment. As a consortium, RISK-HUNT3R aims to unite academic researchers, regulators, and safety scientists from industry to foster regulatory acceptance and direct practical application of NGRA in line with the European Commission's Green Deal. This activity will be strongly pursued within the ASPIS cluster.

The research cluster ASPIS (Animal-free safety assessment of chemicals: Project cluster for implementation of novel strategies) comprises the three projects, RISK-HUNT3R, ONTOX, and PrecisionTOX. The cluster gathers 70 research organizations and will receive €60 million over the next 5 years to develop animal-free solutions for the advancement of regulatory testing.

The coordinators of the projects, Prof. John Colbourne, Prof. Mathieu Vinken, and Prof. Bob van de Water, have recently produced a joint letter to support the EP initiative on "facilitating the transition to innovation without the use of animals in research, regulatory testing and education"[2]. The letter supported its adoption and eventual translation into the EU legislative framework[3]. The resolution "on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education" was adopted by the EP on September 6 with 667 votes to 4.

Events & News

The first opportunity to meet the RISK-HUNT3R experts will be at the kick-off meeting of the ASPIS cluster on November 4, 2021, in Brussels, Belgium (Square Brussels Meeting Centre). Please register via the event website[4].

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Giorgia Pallocca and Marcel Leist

1 https://www.risk-hunt3r.eu
2 https://blogs.mediapart.fr/jeanne-laperrouze/blog/070921/eu-action-plan-accelerate-transition-towards-non-animal-testing-0
3 https://www.risk-hunt3r.eu/wp-content/uploads/courrier-cluster-sept2021-_-ENG.pdf
4 https://cmt.sym.place/events/event/view/391754/eu-toxrisk-final-open-symposium-2021