Corners

Alan and Helene Goldberg In Vitro Toxicology Grant Program for 2023-2024

The Center solicits pre-proposals focusing on implementation of the NAS Report: *Toxicity Testing in the 21st Century: A Vision and a Strategy*. For proposals relating to toxicology, the maximum grant amount is $40,000. The objective should be to significantly reduce or replace laboratory animals. Examples of acceptable projects could include: providing mechanistic understanding of *in vitro* responses to toxicants in human cells, development of AOPs, or conducting systematic reviews. Consideration should be given to the translation of this new method to evaluate/predict health outcomes. For proposals relating to refinement, the prize includes $6,000. This award focuses on research projects that help reduce animal use by identifying areas of research and testing where animal models lack reproducibility and translational value or that enhance the housing, handling, and/or experimental procedures for laboratory animals who are still deemed necessary. For those invited to submit, full proposals are due by August 1, 2022.

Article in *Virginia Mercury*

In a recent *Virgina Mercury* newspaper article about Veterans Affairs reducing the use of dogs in laboratory testing, our Director Thomas Hartung said: "Researchers have gotten used to animal experiments being the ultimate proof, but there is a reason 95% of clinical trials in humans fail." He added, "We are not connected perfectly to the biology of animals. This is the reason why there is so much hope for the human relevant organ and chip systems and combined organs."

Hartung & Smirnova Enroll 15,000 in Toxicology Courses

More than 15,000 have enrolled in two Coursera classes taught by Drs Thomas Hartung and Lena Smirnova. The free open-enrollment course titled *Toxicology 21: Scientific Applications* presents the latest developments in toxicology – the shift from animal testing toward human-relevant, high-throughput integrative testing strategies. The novel concepts respond to the breakthrough National Research Council vision. The *Evidence-based Toxicology* class teaches the transparent, objective, and comprehensive use of available evidence in toxicology following the role-model of evidence-based medicine.

Lena Smirnova Selected as Frontiers' Topic Editor

Lena Smirnova has been selected as a Topic Editor for Frontiers' *Emerging Talent in Toxicology: Neurotoxicology*. This series will highlight the work of young talent globally. The collaborative and interactive peer-review process has been designed to make the exercise less daunting for student researchers. There is a commitment to ensuring the success of young scientists in publishing.

Deputy Director Fenna Sillé Awarded JHU Award

Deputy Director Fenna Sillé received as lead-PI a Discovery Award from Johns Hopkins University. The school awards the prize to JHU interdisciplinary teams advancing the field of knowledge and solving complex problems. Sillé's project, *The Next Frontier to Improve Public Health: Exploring the Use of Artificial Intelligence to Assess the Exposome*, was a partnership between the Bloomberg School of Public Health, the Whiting School of Engineering, the School of Medicine and the Berman Institute of Bioethics. Her co-PIs are fellow Public Health colleague Brian Caffo; Engineering collaborators Carsten Prasse and Thomas Pisanic; the School of Medicine's Meredith McCormack; and Joseph Ali of Berman.

CAAT Postdoc Itzy Morales Pantoja Earns Interdisciplinary Fellowship

Dr Itzy Morales Pantoja has been selected as an ASPIRE/IRACDA postdoctoral scholar. Academic Success via Postdoctoral Independence in Research and Education (ASPIRE) is an NIH-sponsored Institutional Research and Academic Career Development Award (IRACDA) postdoctoral fellowship designed to train the future generation of biomedical scientists and engineers, who bridge the disciplines of biology, medicine, and engineering. The program draws on expertise from faculty and mentors from the three partnering institutions: Johns Hopkins University, Morgan State University and Coppin State University.

Video of Alexandra Maertens speaking at SOT Annual Meeting

Green Toxicology Program Director Alexandra Maertens spoke at the Society of Toxicology Annual Meeting in San Diego, California, US, about the need for chemistry students to be taught how to reduce toxicity in chemicals. Her work highlights the need for interdisciplinary study between toxicologists and chemists to decrease toxicity in widely used chemical products. Link: https://youtu.be/a37COXHyTG0

Upcoming Events

Biointerfaces International Conference 2022

Thomas Hartung has been invited to give the keynote address at the Biointerfaces International Conference 2022 from September 13 to 15 in Zurich, Switzerland. This year's program focuses on microphysiological systems, *de novo* tissues, and organoids.

Hartung Debates About AI at SOT

At the SOT Annual Meeting in March, Thomas Hartung debated Craig Rowlands of the Institute for Integrative Toxicology at Michigan State University in a Featured Session. The topic addressed was *Is There a Role for Artificial Intelligence and Machine Learning in Risk Decisions?* The debate will also be included at the XVI International Congress of Toxicology in the Netherlands from September 18 to 22.

India-EMBO Lecture Course

Thomas Hartung will speak on the topic *Brain organoids to study neurological diseases* at the India-EMBO Lecture Course in Hyderabad, India. The course, to be held October 31-November 4, 2022, will give an overview of the current research of how human model systems, such as MPS, are being used to understand human disease and development.

Recent Events

MPS World Summit 2022

The inaugural MPS World Summit in New Orleans culminated with the creation of the International MPS Society, the first of its kind in the biotech arena. The conference welcomed 665 in-person and virtual attendees from 26 countries with the largest global contingency arriving from Japan. Attendees heard from the leading medical and engineering researchers about organoids and organ-on-a-chip technologies. The program had 142 speakers; 80 of them were invited and 62 selected from the 318 abstracts submitted. Young investigators submitted 163 abstracts.

Berlin, Germany, will host the MPS World Summit 2023. The next summit will be hosted by CAAT-Europe Co-director Marcel Leist, TissUse CSO Uwe Marx, and EUROoCs Chair Peter Loskill. The second global gathering will be held June 26-30, 2023.

2nd US Summer School on Innovative Approaches in Science

Students and early-career researchers attended the PCRM Summer School on Innovative Approaches in Science to learn about innovative methods to reduce and replace animal tests in toxicology and biomedical science. The program was held in early June at the North Carolina Biotechnology Center. The four-day event aimed to speed up progress in ethical and effective scientific research by supporting a new generation of scientists who utilize and champion nonanimal methods for research and testing. CAAT's scientists Thomas Hartung, Lena Smirnova, and Kathrin Herrmann contributed to the Summer School program by giving presentations, moderating sessions, and mentoring students. For more information, visit www.InnovativeScience2022.org.

The 9th Annual 3Rs Symposium

The 9th Annual 3Rs Symposium on June 22-23, 2022 focused on collaborative efforts to improve animal welfare and rigorous results. It was again a joint program organized by the Johns Hopkins University Center for Alternatives to Animal Testing, the Department of Molecular and Comparative Pathobiology, the USDA Animal Welfare Information Center (AWIC), and the NIH Office of Laboratory Animal Welfare (OLAW). The symposium drew more than 140 participants and 18 speakers attending from North America, South America, Africa, Asia, and Europe, signifying it as the most international 3Rs Symposium in this series to date. Select recordings of the symposium will be published on the website of USDA AWIC in approximately August.

New Publications

Caloni, F., De Angelis, I. and Hartung, T. (2022). Replacement of animal testing by integrated approaches to testing and assessment (IATA): A call for in vivitrosi. *Arch Toxicol 96*, 1935-1950. doi:10.1007/s00204-022-03299-x

Deng, J., Hartung, T., Capobianco, E. et al. (2022). Artificial intelligence for precision medicine. *Front Artif Intell 4*, 834645. doi:10.3389/frai.2021.834645

Lippa, K. A., Aristizabal-Henao, J. J., Beger, R. D. et al. (2022). Reference materials for MS-based untargeted metabolomics and lipidomics: A review by the metabolomics quality assurance and quality control consortium (mQACC). *Metabolomics 18*, 24. doi:10.1007/s11306-021-01848-6

Neuhaus, W., Reininger-Gutmann, B., Rinner, B. et al. (2022). The rise of 3R centres and platforms in Europe. *Altern Lab Anim 50*, 90-120. doi:10.1177/02611929221099165

Pamies, D., Wiersma, D., Katt, M. E. et al. (2022). Human organotypic brain model as a tool to study chemical-induced dopaminergic neuronal toxicity. *Neurobiol Dis 169*, 105719. doi:10.1016/j.nbd.2022.105719

Cruelty Free INTERNATIONAL
Ending animal experiments worldwide

Brussels event raises awareness of European Citizens' Initiative

Cruelty Free Europe, GAIA, Animal Rights Belgium, PETA and MEPs joined forces last month in Brussels to raise awareness and gather vital signatures for a European Citizens' Initiative (ECI) to end animal testing.

Despite huge public support for the bans – 74% of adults in EU member states agree that animal testing for cosmetic products and their ingredients is unacceptable in all circumstances[1] – the European Chemicals Agency (ECHA), supported by the European Commission, continues to demand new tests on animals for chemicals used as cosmetics ingredients under chemicals legislation.

The ECI, launched in collaboration with cruelty free brands including Dove and The Body Shop and over 100 animal protection organizations across Europe, calls for the EU to strengthen and protect the bans on cosmetics testing.

To be considered by the European Commission, the ECI – available at www.savecrueltyfree.eu – must attract at least one million signatures by the end of August.

EU project aiming to revolutionize chemicals risk assessment launches

May saw the launch of the European Partnership for the Assessment of Risks from Chemicals (PARC) project – an EU-wide program, coordinated by the French regulatory authority ANSES, which aims to revolutionize the way that risks posed by chemicals are discovered and understood.

The project, which involves 200 partners encompassing authorities from across the European Union as well as research organizations, looks to support the EU Chemicals Strategy for Sustainability's ambition of a "toxic-free" environment by developing better approaches for assessing the effects of chemicals on humans and the environment.

We estimate that to date over 2.6 million animals have been used in tests under the EU's existing chemicals regulatory framework, and proposed changes under the Chemicals Strategy for Sustainability could see millions more animals used in new tests. We are hopeful that PARC will deliver new, animal-free approaches to protecting humans and the environment from the toxic effects of chemicals and urge decision-makers to make full use of the project's outputs.

New US bill presents cosmetics threats and opportunities

A new bill introduced in the US, the Food and Drug Administration (FDA) Safety and Landmark Advancements Act, would give the FDA greater oversight of cosmetics, but it lacks any mention of prohibiting animal testing for cosmetics and – worse still – contains a clause that could threaten the state-level bans in effect.

Hawaii, Maryland and Virginia enacted cruelty free cosmetics laws earlier this year, joining five other states to end the sale of newly animal tested cosmetics. New York is close behind, with its Cruelty Free Cosmetics Act passing floor votes in the Assembly and Senate and currently under final consideration by Governor Hochul.

The FDA Safety and Landmark Advancements Act, as it stands, could nullify these state laws without replacing them with similar animal testing restrictions, but there's still time for language based on state legislation and the federal Humane Cosmetics Act to be incorporated into the bill and finally achieve what we and many others have been working towards for many years – a national restriction on animal testing for cosmetics.

Cruelty Free International is encouraging US citizens to contact their Senators about this issue.

World Federation for Animals publishes global strategy

The World Federation for Animals has published a new strategy to make a global impact in animal welfare by 2030.

The strategy calls on the United Nations to recognize the importance of animal protection in international policies and integrate animal protection into existing and future work on sustainable development, and demands the inclusion of animal welfare in laws and policies on biodiversity, climate change, pollution, intergovernmental trade, aid, subsidy and investment.

Cruelty Free International is a founding member of the World Federation for Animals and our CEO, Michelle Thew, is a board member.

European Chemicals Agency could do more for animal-free science

The European Chemicals Agency (ECHA) recently published its 2021 annual report and, while we welcome the steps it is taking to reduce reliance on an-

[1] Poll conducted by Savanta ComRes on behalf of Cruelty Free Europe; https://comresglobal.com/polls/cruelty-free-europe-animal-testing-in-the-eu/

imal tests, it could do more to accept animal-free methods and approaches.

The report details ECHA's efforts to minimize animal testing by assessing substances in groups, developing tools to improve data sharing, and working with agencies in the US and Canada to explore how to increase the application and acceptance of non-animal methods.

Despite these positive steps, ECHA continues to insist on animal testing for chemicals that are used exclusively as ingredients in cosmetics, and its acceptance of animal-free methods and approaches proposed by companies remains low. We urge ECHA to look to its sister agencies the European Medicines Agency and European Food Safety Authority, which are both taking concrete steps to accelerate the transition away from animal testing.

EUSAAT

European Society for Alternatives to Animal Testing

A new EUSAAT BOARD is elected

This spring, a new EUSAAT Board was elected. It is composed of an excellent mix of young and established personalities in the 3Rs field:

Winfried Neuhaus (President)
Annemarie Lang (Vice President)
Mario Rothbauer (Vice President)
Horst Spielmann (Secretary General)
Kristina Wagner (Board member)
Györgyi Szabó (Board member)
Marketa Dvorakova (Board member)
Arti Ahluwalia (Board member)

They start their challenges for the next four years with full vigor. More information and pictures can be found under the following link: https://eusaat.eu/about-us/board-members/

We would like to thank the former EUSAAT Board members for their extraordinary commitment and efforts for EUSAAT:

- Former Vice President *Dagmar Jirova*, M.D., PhD. The National Institute of Public Health Centre of Toxicology and Health Science, CZ-Prague
- Former Vice President FH-Prof. Mag. Dr *Dominik Rünzler*. University of Applied Sciences Technikum Wien, Department of Biochemical Engineering, AT-Vienna
- Former Board member Dr *Candida Nastrucci*. The AlternativesEU, IT-Rome

Update on the EUSAAT Congress 2022 in Linz/Austria on 26-28 September

The EUSAAT Congress 2022 will be held on 26-28 September in Linz/Austria. The planning is already well advanced. A large number of high-quality abstracts on a wide range of topics have been submitted, which means that we can expect an exciting congress.

Because of the vast amount of information, we present the most relevant links here:

- General link to the congress: https://eusaat.eu/eusaat-congress/23rd-edition/congress-2022/
- Highlights and news from the congress, where you can also find news about various Young Scientist Travel Awards or other activities such as YOU: https://eusaat.eu/eusaat-congress/23rd-edition/highlights-2022/
- If you would like to see some pictures of the congress venue: https://eusaat.eu/news/eusaat-congress/the-congress-venue/
- We are very proud of our Scientific Committee and grateful for their excellent work, for example in reviewing abstracts: https://eusaat.eu/eusaat-congress/23rd-edition/scientific-committee-2022/
- We are very grateful for the great number and quality of our co-organizers, and we would also like to thank our sponsors and supporters: https://eusaat.eu/eusaat-congress/23rd-edition/organizers-2022/
- Here you can find the preliminary program: https://eusaat.eu/eusaat-congress-2022/highlights/announcements/tentative-program-2022/
- And here you can find the tentative topics: https://eusaat.eu/eusaat-congress-2022/highlights/announcements/eusaat-congress-2022-practical-info-tentative-topics/
- Sponsors and exhibitors can find initial information here: https://eusaat.eu/eusaat-congress/23rd-edition/practical-information-2022/for-exhibitors-sponsors/
  or write directly to: congress@eusaat.eu
- If you wish to register, you can find the relevant information, including on hotels, here: https://www.touristik.at/en/eusaat-kongress.html

Keynote speakers at the EUSAAT 2022 Congress

We are overjoyed to announce that *Susanna Louhimies* from the European Commission has agreed to give a keynote lecture on the development of the 3Rs field in Europe at the EUSAAT 2022 Congress on Monday, September 26.

We are just as happy that Prof. *Merel Ritskes-Hoitinga*, recently appointed Professor for Evidence-Based Transition to Animal-free Innovations at the University Utrecht, will give her keynote lecture "Evidence-based transition to animal-free innovations: Let's make it happen!" on Tuesday, September 27.

On September 28, *Sasha Mendjan* will talk about "Cardioids unravel human heart development and defects" in the third keynote lecture of the EUSAAT 2022 congress.

We are delighted to have these outstanding keynote speakers covering highly topical areas of the 3Rs field from policy, academia and basic science. See also: https://www.uu.nl/en/news/merel-ritskes-hoitinga-new-professor-of-evidence-based-transition-to-animal-free-innovations; https://www.oeaw.ac.at/imba/research/sasha-mendjan

As in the past, the EUSAAT 2022 Congress will serve as a meeting place for all 3Rs stakeholders to exchange ideas with colleagues, whom you haven't met for several years. Special attention will again be given to the 3Rs centers.

We are very much looking forward to welcoming the international 3Rs community to the EUSAAT 2022 Congress in Linz, and we appreciate any suggestions for additional sessions and topics to the program. The organizers will circulate updates and news via newsletters, LinkedIn and the website www.eusaat.eu.

Publication "The Rise of Three Rs Centres and Platforms in Europe" is online

A major effort by over 60 co-authors from 3Rs centers, platforms and institutes resulted in an overview of the development of 3Rs centers and platforms, with a focus on the respective stories in each country, now published in the 50th edition of the journal *Alternatives to Laboratory Animals: ATLA* (doi:10.1177/026119292210 99165).

This paper is intended to be the first of three, highlighting the development and role of 3Rs institutions and presenting the diversity of roles and activities of individual 3Rs centers and platforms. The idea development and data collection for this series of articles was conducted during the 3Rs center meetings of the last few years and can thus be counted as another output of EU3Rnet.

EU-COST Action "3Rs concepts to improve the quality of biomedical science (IMPROVE)" approved

We are very happy to announce that a COST Action focusing on the 3Rs and 3R-relevant concepts will be funded. The main components and contents of this COST Action were worked out during several meetings of the 3Rs Centers and EU3Rnet. 40 stakeholders from 21 countries contributed to the submission.

The COST Action with the number CA21139 will start on 21.10.2022 with a kick-off meeting in Brussels.

Background: Awareness of the existence of a reproducibility and predictability crisis in biomedical science has increased in recent years. The reproducibility crisis refers to the problem that researchers struggle to replicate or reproduce scientific studies. There have been many publications reviewing why preclinical research is irreproducible and lacks predictability, pointing to deficiencies in reporting and statistical practices. Confounding factors, which are part of the laboratory environment and influence both the dependent and independent variables, continue to be identified, suggesting that our knowledge of their existence is far from complete. Better statistical methodology will play a central role in improving the reproducibility of science to produce robust and reproducible research. Another area of improvement is the development of novel methods to better define and assess replication success and improve predictability. Under this light, the development and introduction of new, powerful concepts for biomedical research is essential to reduce the production of non-reproducible and non-predictive data. This has immense scientific, economic and social significance. In this context, we propose that the findings and concepts from the 3Rs field can greatly help to improve biomedical research on several levels.

Therefore, the main aim of the COST Action is to establish a network that will work to refine, harmonize, and promote 3Rs concepts, data, and documents in order to improve the quality of biomedical science.

COST Actions support the creation of networks and networking activities. These networks are generally open for everyone. There are several ways to contribute, e.g., by participating in the Management Committee, in individual working groups, or in specific activities of the Action. Up to two persons, who are nominated by the COST National Coordinators (CNC), can represent their country in the Management Committee. To apply to join the Management Committee, it is best to contact your CNC, which can be found at the following website: https://www.cost.eu/about/who-is-who/#tabs+Name:National%20Coordinators

Everyone can apply to participate in the individual *working groups*, which are Quality and Translatability of Science, Implementation, Dissemination, and Education. For this, first establish an e-COST profile and then apply using https://e-services.cost.eu/user/login.

Please find more details on https://www.cost.eu/actions/CA21139/, where you can also read the Memorandum of Understanding (MoU), which is basically the description of the content of the COST Action.

Everyone who would like to join is very welcome!

You can also directly contact the main proposer, Winfried Neuhaus, via: winfried.neuhaus@ait.ac.at

During the first week of July, the RISK-HUNT*3R* consortium convened at the North Sea for its third annual project retreat. Overall, eighty participants from the 37 project partners met in Egmond aan Zee (The Netherlands) to closely interact and discuss the progress of the project and future plans. Following tradition, the advisory board members kicked off the plenary session. They outlined obstacles and opportunities of applying novel approach methodologies (NAM) for next-generation risk assessment (NGRA) from an industry and regulatory perspective. The different teams then met in breakout groups; they dived into detailed discussions of four main challenges concerning (i) the use of omics-derived data, (ii) the integration of toxicokinetic information derived from PBPK tools, and the implementation of (iii) advanced models and (iv) computational tools for hazard identification and quantification. Many early stage researchers (ESR) participated for the first time in the annual meeting. They presented their work to the consortium during the poster session and in a speed presentation competition. The general assembly also hosted several hands-on training sessions focused on risk assessment, uncertainty analysis, and *in silico* models for toxicokinetics assessment. The ASPIS cluster, the collaborative framework uniting RISK-HUNT*3R* with the projects ONTOX and PrecisionTox, was also a relevant point on the meeting agenda. The responsible working group coordinators presented progress and common goals of the cluster toward animal-free chemical risk assessment.

RISK-HUNT*3R* press review

In this issue of ALTEX, readers can find the first RISK-HUNT*3R* strategy publication (Pallocca et al., 2022). In this article, the authors have introduced the NAM-based chemical risk assessment strategy suggested by the consortium. The project addresses the implementation of a comprehensive NAM toolbox into different regulatory frameworks for chemicals, pesticides, food additives, and drugs. This framework was also presented at the ONE conference, organized in Brussels on June 21-24, 2022 by EFSA and its sister agencies – the European Centre for Disease Prevention and Control (ECDC), the European Chemicals Agency (ECHA), the European Environment Agency (EEA), the European Medicines Agency (EMA) – and the European Commission's Joint Research Centre (JRC).

Engagement with the regulatory stakeholders is critical for promoting a broad implementation of NAM in risk assessment. The project's research on NAM provides a dynamic platform allowing scientists and regulators to work together on case studies. These will inform on NAMs' practical applicability and help design strategies for moving forward toward NGRA.

News and events

The 2nd ASPIS cluster symposium will take place on November 24-25 in Sitges (Spain) 2022, hosted by the ESTIV annual conference. The open meeting will host several exciting talks from the partners of the three consortia. Free registration is possible via the ESTIV conference website.

References

Pallocca, G., Moné, M. J., Kamp, H. et al. (2022). Next-generation risk assessment of chemicals – Rolling out a human-centric testing strategy to drive 3R implementation: The RISK-HUNT*3R* project perspective. *ALTEX 39*, 419-426. doi:10.14573/altex.2204051

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Giorgia Pallocca and Marcel Leist