Corners

CAAT feed

Textbook by our own Alexandra Maertens

Green Toxicology: Making Chemicals Benign by Design, 1st edition, Alexandra Maertens
Royal Society of Chemistry

Green toxicology is an integral part of green chemistry. One of the key goals of green chemistry is to design less toxic chemicals. Therefore, an understanding of toxicology and hazard assessment is important for any chemist working in green chemistry, but toxicology is rarely part of most chemists' education. Therefore, chemists lack the toxicological lens necessary to view chemicals in order to design safer substitutions. This book seeks to fill that gap and demonstrate how a basic understanding of toxicology, as well as the tools of *in silico* and *in vitro* toxicology, can be an integral part of green chemistry. R&D chemists, product stewards, and toxicologists who work in the field of sustainability can all benefit from integrating green toxicology principles into their work.

Topics include *in silico* tools for hazard assessment, toxicity testing, and lifecycle considerations. This book aims to act as a bridge between green toxicologists and green chemists.

CAAT at SOT 2022

CAAT was well represented at the Society of Toxicology (SOT) Annual Meeting 2022 held in San Diego, CA, USA from March 27-31, 2022. Thomas Hartung debated Craig Rowlands at the "*SOT/EUROTOX Debate: Is There a Role for Artificial Intelligence and Machine Learning in Risk Decisions?*". Each year, the SOT Annual Meeting includes a debate in which leading toxicologists advocate opposing sides of an issue of significant toxicological importance. The debate will take place again with the debaters taking the reverse positions in Maastricht, The Netherlands, during the XVIth International Congress of Toxicology, September 18-22, 2022.

Martin Stephens co-chaired our annual *Society of Toxicology (SOT) Satellite Meeting:* "*21st Century Toxicology: Updates on Relevant Domestic and International Activities*," an event by CAAT and the Animal-Free Safety Assessment (AFSA) Collaboration. This year's session included updates on a spectrum of related projects in the US and abroad, highlighting additional technologies (e.g., microphysiological systems, artificial intelligence, and other new approach methodologies) and additional programs (e.g., EU-ToxRisk). Speakers included Thomas Hartung (Johns Hopkins University), Suzanne Fitzpatrick (US FDA), Catherine Willett (HSI), Ruili Huang (NIH/NCATS), Menghang Xia (NIH/NCATS), Tala Henry (US EPA), Helena Hogberg (NIEHS/NICEATM), Katya Tsaioun (Johns Hopkins University), Seiichi Ishida (Sojo University and NIHS Japan), Allison Harrill (US EPA), Bob van de Water (Universiteit Leiden).

Itzy Morales Pantoja received the Colgate-Palmolive Postdoctoral Fellowship Award in In Vitro Toxicology with her project titled "*In Vitro Microfluidic-3D MEA System to Enable Higher Biocomplexity of Human Brain Organoid Model for the Study of Neurodegeneration*."

Fenna Sillé was chair of "*Current Status and Future Outlook of Developmental Immunotoxicity Testing*" symposium and she presented: "*A Path Forward: Current and Future Perspectives on Alternatives to Developmental Immunotoxicity Testing*." Lena Smirnova presented "*A New Approach Method Using a Brain Organoid-Based Testing Strategy for Neurotoxicity and Research on Countermeasures*." Alex Maertens presented "*Training Toxicologists toward Sustainability: Green Toxicology for a Green New Deal*" and Helena Hogberg (new affiliation NIEHS/NICEATM) was chair of "*Assay Gaps in the Developmental Neurotoxicity (DNT) New Approach Methodologies (NAMs) Battery for Human Health Risk Assessment*" and co-chair of "*Next-Level Neurotoxicology: New Technologies to Advance Visualization of Spatial Molecular Alterations and Behavioral Phenotyping*." Helena also presented "*Microphysiological Systems of the CNS to Bridge between In Vivo and In Vitro*" and "*Ontogeny of Neurotransmitter Function as an Endpoint for Developmental Neurotoxicity Assessment*." Emily Golden co-chaired the session "*Educating 21st Century Toxicologists: Making In Vitro and In Silico approaches Part of the Equation*."

July Carolina Romero Sandoval presented a poster titled "*Multifluorescent Human Brain Organoid Model for High-Throughput Chemical Toxicity and Drug Efficacy Screening*," Emily Golden, Thomas Hartung, and Alex Maertens had a poster titled "*Impact of Activity Cliffs on In Silico Skin Sensitization Mod-*

el Predictions Using Chemical Similarity Maps and a Human Data Set." Ishita Virmani, Breanne Kincaid, Lena Smirnova, Klara Hilscherova, Thomas Hartung, and Helena Hogberg had a poster titled "*Developmental Neurotoxicity of Brominated and Organophosphorus Flame Retardants Using 3D hiPSC-Derived Brain Spheres*." Katya Tsaioun and Helena Hogberg had a poster titled, "*A Systematic Review of COVID-19 Literature: Neurological Effects and SARS-CoV-2*," and Katya Tsaioun had a poster titled "*Quality of Conduct of Systematic Reviews in Toxicology and Environmental Health: The Current State of the Art*." Sebastian Hoffmann and Katya Tsaioun also presented the poster titled "*Assessment of the Zebrafish Embryotoxicity Test's Capacity to Predict Mammalian Prenatal Developmental Toxicity of Chemicals: A Systematic Review*."

Monthly 3Rs Webinar Training Series

organized by Kathrin Herrmann, Director of CAAT's Beyond Classical Refinement Program:

Since December 2021, Kathrin has hosted five webinars featuring various experts and themes (in chronological order):

- Dr Anne van Veen: The Principles of the 3Rs: Lessons Learned from History
- Julia Menon: Why Preregistration of Animal Studies Benefits Research
- Dr Brianna Gaskill: Experimental Design of Animal Studies
- Dr Joanna Makowska: A Good Life for Laboratory Rodents?
- Debby Weijers, Prof. Sue Gibbs and Dr Evita van de Steeg: Dutch Initiatives to Accelerate the Transition Towards Innovative Animal-Free Science

The webinar recordings can be watched at: https://www.youtube.com/channel/UC7WgnOtO4Ez6HiDRlTLEWZg/videos

Upcoming events

Symposium: "Green Toxicology: Making Hazard and Exposure Part of the Green Chemistry System" at the 26th Annual Green Chemistry & Engineering Conference

June 6-8, 2022 in Reston, Virginia

The symposium will be organized by Alexandra Maertens, Research Associate at CAAT; Thomas Hartung, Doerenkamp-Zbinden Chair for Evidence-Based Toxicology and Director of CAAT; and Emily Golden, Doctoral Student, Johns Hopkins University.

Green Chemistry Principle #4, which states that "*Chemical products should be designed to preserve the efficacy of function while reducing toxicity*," has been described as the least developed principle of green chemistry. While other aspects of green chemistry – such as atom economy – have simple and well-developed metrics, hazard and exposure are more difficult to measure in ways that allow chemists to incorporate them into their design.

Green toxicology is an emerging discipline that seeks to provide a framework for integrating the principles of toxicology into the design of safer chemicals using 21st-century toxicology tools (e.g., including high-dimensional data, computational approaches, and systems-level thinking) to look not just at chemicals in isolation but also at their exposure scenarios, as well as transformation and degradation products.

9th Annual 3Rs Symposium: Collaboration to Improve Animal Welfare and Rigorous Results

June 22 and 23, 2022 and June 24, 2022 – Workshop (extra ticket required)
Baltimore, MD, USA

This symposium will focus on reduction, refinement, and replacement methods to improve laboratory animal welfare while maintaining or improving scientific results. It is jointly organized by the Center for Alternatives to Animal Testing, Johns Hopkins University Bloomberg School of Public Health; the Department of Molecular and Comparative Pathobiology, Johns Hopkins University School of Medicine; the USDA's Animal Welfare Information Center (AWIC) at the National Agricultural Library; and the Office of Laboratory Animal Welfare, National Institutes of Health.

Sessions are designed for investigators, laboratory animal veterinarians, care staff, and IACUC members and staff. Residents, students, and postdocs are also welcome. The sessions on refinements for better science and animal welfare describe cutting-edge advancements in laboratory animal welfare, methods to achieve sound scientific results, and 3Rs success stories. There will also be panel discussions on laboratory animal adoption programs and international perspectives on 3Rs implementation in Asia, Africa, and South America, other TBD presentations, and an optional demonstration of refinement techniques. More information: https://www.eventbrite.com/e/9th-annual-3rs-symposium-tickets-262571677957

Summer School on Innovative Approaches in Science

June 7-10, 2022
North Carolina Biotechnology Center, Research Triangle Park, NC, USA

Applications are still being accepted on a rolling basis for remaining seats on a first-come, first-served basis.

The Summer School on Innovative Approaches in Science aims 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. To address the diverse needs of students and early-career researchers, the Summer School will offer two tracks – toxicology and biomedical science, featuring specific applications of current innovative non-animal methods. The program consists of scientific talks, career development workshops, poster presentations, laboratory tours and demonstrations, networking opportunities, and more.

A portion of the Summer School may be available online for those who are not able to attend in person. No conference fee will be charged. However, participants

will need to cover the costs of their travel and accommodation. A limited number of travel awards is available.

The Summer School on Innovative Approaches in Science is geared towards undergraduate and graduate students, postdoctoral and other trainees, as well as early-career professionals, typically within five years of completing their studies/training. More info: https://www.ascctox.org/innovativescience2022

Microphysiological Systems World Summit

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

The Center for Alternatives to Animal Testing together with more than 50 other organizations is organizing the Microphysiological Systems World Summit, which 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.

Late-breaking submission of posters is still open and multiple sponsorship levels are available.

More information is available at: https://mpsworldsummit.com/ or contact Camila Januario (cjanuar1@jhu.edu).

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Bronze: ALTEX, The Humane Society, Nortis, Pfizer, Syngenta, SynVivo, Tessara, TissUse, Unilever
Exhibitors: Aveolix, Ananda, Aracari, LellLink, Mimetas, React4Life, Vitrocel Systems GmbH, Yokogawa

New publications

Barreras, P., Pamies, D., Monaco, M. C. et al. (2022). A human-derived 3D brain organoid model to study JC virus infection. *J Neurovirol*, online ahead of print. doi:10.1007/s13365-022-01062-7

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

Cruelty Free INTERNATIONAL
Ending animal experiments worldwide

Vigil held in Brussels to save Europe's ban on animal testing for cosmetics

To mark the 9th anniversary of the European Union's cosmetics animal testing bans, Cruelty Free Europe, together with Eurogroup for Animals and GAIA, held a vigil for the bans in front of the headquarters of the European Commission and Council of Ministers in Brussels. The groups were joined by French street artist Ckeja, who painted live throughout the vigil to create a striking visual representation of the threat to the bans.

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.

Cruelty Free Europe and others last year launched a European Citizens' Initiative to save cruelty free cosmetics (www.savecrueltyfree.eu).

More animals saved as a result of last year's Board of Appeal decision

Last year, Cruelty Free Europe successfully intervened in an ECHA Board of Appeal case, in which the Board overturned ECHA's decision demanding a test using hundreds of fish and clarified that ECHA must take changes in the production volume of a chemical into consideration during its decision-making process.

As a result of that win, ECHA has since withdrawn two further decisions concerning other substances that required new animal tests to be performed despite reduced

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

production volumes. We estimate that withdrawing these two decisions alone saved 1,385 rats and 580 rabbits.

Underwhelming European Commission response to Parliament's animal test phase-out resolution

Six months after the historic resolution of the European Parliament asking for an action plan to phase out the use of animals in science, the European Commission released a disappointing response signaling its intention to largely ignore the wishes of the Parliament and stick with the *status quo*.

The Commission's response listed various initiatives in place that aim to reduce the use of animals but failed to address the need for a coordinated, EU-wide action plan for the active phase-out of the use of animals in experiments. An action plan, complete with targets and timelines, would speed up a phase-out of animal experiments.

Cruelty Free Europe has proposed ten actions that EU decision-makers could take immediately to significantly reduce the number of animals suffering in laboratories in Europe (https://bit.ly/3LHquBs).

Hungarian group receives second Geoffrey Deckers Award

On the day of Geoffrey's birthday, January 13, Cruelty Free Europe presented the second Geoffrey Deckers Award to Hungarian animal protection group Ébredő Bolygó Alapítvány (EBA).

The €6,000 award – made annually to groups showing commitment to ending animal tests – honors Geoffrey Deckers, the much respected and loved former Chair of the European Coalition to End Animal Experiments and Cruelty Free Europe, who passed away in 2020.

EBA will use the funds to start projects securing an end to animal experiments at university level, starting with negotiating with the Veterinary University of Budapest. Also, a campaign will be planned to raise awareness for the animals in laboratories in Hungary.

UK parliamentarians call for transition to animal-free science

In March, the UK All Party Parliamentary Group (APPG) for Human Relevant Science – for which Cruelty Free International forms part of the secretariat – published its report, "Bringing back the human: transitioning from animal research to human relevant science in the UK".

The report is the result of a year-long inquiry led by cross-party Members of Parliament and Peers who heard evidence from expert scientists and regulators highlighting the need for a central role for human-relevant science in the UK.

Cruelty Free International plans to use the report in its work with decision-makers to secure a UK animal testing phase-out strategy – something that over 100,000 Brits showed their support for by signing the #TargetZero petition calling for a plan to phase out animal testing in the UK. The petition – jointly organized by Cruelty Free International, Animal Free Research UK, and OneKind – was delivered to the Prime Minister in January.

Big wins for cruelty free cosmetics in the US

Recent months have seen fantastic progress for cruelty free cosmetics in the US. Cruelty free cosmetics laws came into effect in Hawaii, Maryland, and Virginia in January, ending the sale of newly animal tested cosmetics in those states. Eight US states now have cruelty free cosmetics legislation in place.

New York is close behind, with its Cruelty Free Cosmetics Act passing committee hearings in both chambers of the state legislature and due to go to a floor vote in the Assembly and Senate. Passing the legislation in New York, widely regarded as a global fashion and beauty capital, could be the tipping point that leads to the passage of a federal Humane Cosmetics Act that would harmonize cruelty free rules across the US – something that Cruelty Free International is working hard to secure.

EUSAAT

European Society for Alternatives to Animal Testing

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

The EUSAAT Congress 2022 will be held on September 26-28 in Linz, Austria. We are convinced we can meet again in an "in-person" conference this year.

We are very proud and happy that many 3Rs experts and biomedical professionals have agreed to join our scientific committee. The number is growing day by day and can be viewed on the EUSAAT Congress website. The registration platform is online, and the first proposals for sessions have been discussed. If you want to propose additional topics or sessions, now is a good time to join the planning.

In 2022, topics will cover all of the 3Rs – refine, reduce, replace – ranging from new technologies for risk assessment and basic science (keywords: disease models, microphysiological systems, organs-on-chip, *in silico* methods, AOPs, NAMs, QIVIVE, experimental design, good cell culture practice) to ethics, animal welfare, guidelines, 3Rs policy, 3Rs in education, etc. 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.

Highlights

Again, we are announcing the "*Young Scientist Travel Awards*" (YSTA), supported by the SET Foundation. We will be able to award about 15-20 young scientists with an YSTA to cover their costs for actively participating in the congress. We are also happy to announce that the journal *ATLA* will give out awards for the three best lectures in the YSTA sessions. EUSAAT particularly wants to encourage young scientists to participate in the EUSAAT 2022 Congress with our moderate registration fees and these awards.

In addition, the European Partnership for Alternative Approaches to Animal Testing (EPAA) is sponsoring 3Rs student grants for the EUSAAT Congress 2022 and has provided a lump sum of €1500. Two levels of grants are offered by the EPAA partners: 1 half grant and 1 full grant. The deadline for applications is July 11, 2022. More information on eligibility criteria, application, and the selection processes can be found via following the link: https://ec.europa.eu/growth/calls-expression-interest/3rs-student-grants-2022-call-submissions_en.

To demonstrate that the EUSAAT society supports scientists in the Ukraine who are affected by the war, EUSAAT is sponsoring the participation of three scientists from the Ukraine in the EUSAAT 2022 Congress in September. EUSAAT is also encouraging scientific institutions in Europe to hire scientists from the Ukraine with high priority.

Detailed information on the highlights of the EUSAAT Congress 2022 can be found at: https://eusaat.eu/eusaat-congress/23rd-edition/highlights-2022/

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

Happy Birthday Prof. Dr Horst Spielmann!

In April, the EUSAAT Board would like to celebrate its secretary general, Prof. Dr Horst Spielmann, who has been and still is the heart and soul of EUSAAT. He is turning 80, and while this anniversary in itself is enough reason to celebrate, Horst Spielmann's scientific achievements and encouragement of the 3Rs cannot be praised enough.

Some might say turning 80 would be the time to rest and enjoy retirement. But that is not true for Horst Spielmann. Not only is he still Honorary Professor for Regulatory Toxicology at the Free University of Berlin, Germany. He is also still very much involved in EUSAAT and the planning of the upcoming EUSAAT Congress 2022. We appreciate his immense knowledge, energy and enthusiasm, and his contribution to EUSAAT every day. He has been active in MEGAT and EUSAAT, filling several different Board positions, for decades, and it is due to his dedication that the EUSAAT Congresses were and are so successful and are the major European 3Rs scientific event to bring together scientists, representatives from industry, regulatory authorities, political institutions, and NGOs. With his constant efforts for alternative methods and the 3Rs, he has changed minds, laws, and science. Spielmann was trained as a medical doctor, pharmacologist and toxicologist and received his degree from the Free University of Berlin, Germany. His impressive career spans over 50 years. Before he started to act as an advocate for replacing animal use in research and testing and paving the way for innovative and humane new testing and research methods, he focused his research on embryonic pharmacology and the early stages of pregnancy. It is also thanks to his efforts that *in vitro* fertilization became possible. Thus, he is also deemed the "father" of the first test-tube baby born from *in vitro* fertilization at the gynecological hospital in Berlin in 1984. He has (co-) authored almost 400 scientific publications, most of them dealing with ways

to replace animal tests. In every position he held, he used his influence to make a difference. First and foremost, in his function as the head of ZEBET (National Centre of the Documentation and Evaluation of Alternatives to Testing in Animals) at the BfR (Federal Institute for Risk Assessment) in Berlin, Germany from 1989-2007. Since 1989, he also was a chairperson and member of management teams of national and international validation studies that were funded by the German Ministry for Education and Research (BMBF), by the European Commission (DG Environment), by ECVAM (European Centre for the Validation of Alternative Methods at the JRC in Ispra, Italy), and by COLIPA (the European Cosmetic, Toiletry and Perfumery Association). Several of these successful validation studies resulted in the acceptance of the first *in vitro* toxicity tests for regulatory purposes at the international level (EU, OECD, Japan, and USA), e.g., *in vitro* alternatives to the Draize eye test, *in vitro* phototoxicity tests, *in vitro* corrosivity tests, an *in vitro* embryotoxicity test using a mouse embryonic stem cell line, and the ECVAM skin irritation validation study using human skin models. His work has been awarded with various accolades, amongst others the Lush Prize's Andrew Tyler Award for outstanding contributions to ending animal testing in 2018 and the Björn Ekwall Memorial Award in 2012. But his engagement is not limited to lab animals – this clearly showed when he was serving as Berlin's animal welfare officer from 2012 to 2017, where amongst other things he campaigned for the introduction of a license of competence for dog owners, worked to introduce education in animal welfare to schools and nursery schools, and closely cooperated with the local animal welfare societies.

One can only admire such extraordinary engagement and marvel at what one person can achieve in a lifetime. Even though there is still a long way to go in the 3Rs field, we would never have achieved the goals we already have without a true pioneer for alternative methods – Horst Spielmann.

Dear Horst, we wish you many happy returns and hope to have you with us on the EUSAAT Board for a long time to come to keep working side by side and create the change that we want to see! Thank you for inspiring us. It is an honor to be able to share your wisdom and passion for the 3Rs.

LUSH PRIZE

SUPPORTING ANIMAL-FREE TESTING

Lush Prize 2022

The biennial Lush Prize, the global prize fund to support initiatives to end or replace animal testing, opens for nominations on Monday, April 18.

The £250,000 prize fund is divided into five main categories:

– *Science:* For individuals, research teams or institutions for work most likely to lead to practical non-animal tests which could be accepted by regulators.
– *Training:* For individuals, teams or organizations establishing training programs in using non-animal methods.
– *Young Researcher:* For young scientists (up to 35 years of age) focused on an animal-test free future.
– *Lobbying:* For exceptional individuals, groups or organizations pushing for change.
– *Public Awareness:* For individuals, teams or institutions raising awareness of animal testing.

There is also a non-financial *Political Achievement Award* for elected political officials at any level and in any country in recognition of work to create lasting legal change for animals and science.

Nominations for all prize categories are open for two months and close on Friday, June 17.

Further information on each category can be found on the Lush Prize website http://lushprize.org, and nominations can be submitted via the website from 18 April.

2022 marks the tenth anniversary of Lush Prize. We have so far awarded £2.44 million to 120 projects in 28 countries.

The Lush Prize Conference and Awards Ceremony in November will again be virtual events this year.

One of the RISK-HUNT*3R* project's missions is close interaction with regulatory bodies to translate results, methods, and solutions into safety assessment practice. This approach includes a substantial and early involvement of critical end-users, including regulators and industry, to jointly build next-generation risk assessment (NGRA) strategies that are fit for purpose and meet regulatory needs.

To reach its objectives, the RISK-HUNT*3R* consortium has organized a series of workshops to define urgent regulatory needs and identify the role and possibility of new approach methodologies (NAMs) to address them.

More than 70 international experts attended the first virtual workshop, "Current and future regulatory needs for chemical risk assessment," which took place on January 31. The main objective was to identify particularities and differences among regulatory frameworks' needs. Another issue that was addressed was the confidence in NAM implementation in different fields. During the event, the participants actively engaged in breakout group discussions.

Due to the broad interest in the first event, the consortium organized a follow-up virtual mini-symposium. The event took place on March 14 and aimed to inform a general audience about the workshop's preliminary outcome. It also collected feedback from a wider group of interested stakeholders. Around 175 participants attended the online symposium "Orienteering for regulatory needs," where they could actively participate via virtual polls and Q&A sessions. This format allowed the project to collect very comprehensive and valuable input.

Together with more experts from the ASPIS cluster and the workshops' participants, the RISK-HUNT*3R* team will further consolidate the regulatory needs in a public report.

RISK-HUNT*3R* press review

RISK-HUNT*3R* experts, including members of its advisory board cooperated on a publication with the ECETOC Transformational Programme team (Ball et al., 2022). This paper describes a stepwise implementation framework for NAMs in chemical risk assessment. The authors address the unbalanced situation between continuously increasing technological progress of *in silico* and *in vitro* methods and limited implementation of these technologies into the existing regulatory systems. The authors stress that it is time to capitalize on the long-term investments in NAMs. They propose that implementing a tiered approach, as described in the publication, would be an effective way to generate the necessary information and assess safety with minimal use of animals.

An example of highly advanced technologies for hazard identification has been shown by van der Stel et al. (2022). In this work, the authors used high-content imaging and high-throughput transcriptomics tools to address mitochondrial perturbation as a critical event in chemical-induced organ toxicities. The approach successfully explored quantitative, time- and concentration-resolved cellular responses to mitochondrial perturbation. It also identified and validated genes associated with adaptation to exposure to active inhibitors of the electron transport chain.

Tricot et al. (2022) reviewed current liver cell differentiation protocols and *in vitro* iPSC-based liver models that could be used for disease modeling and drug discovery. They also addressed issues related to using *in vitro* liver models to assess efficiency in drug discovery pipelines and to identify potential drugs and their toxicity profiles.

News and events

The first issue of the official RISK-HUNT*3R* newsletter has been recently made available. The newsletter offers a glimpse into the project via interviews, graphics, and press reviews. The newsletter can be downloaded from the RISK-HUNT*3R* webpage (https://www.risk-hunt3r.eu).

References

Ball, N., Bars, R., Botham, P. A. et al. (2022). A framework for chemical safety assessment incorporating new approach methodologies within REACH. *Arch Toxicol 96*, 743-766. doi:10.1007/s00204-021-03215-9

Tricot, T., Verfaillie, C. M. and Kumar, M. (2022). Current status and challenges of human induced pluripotent stem cell-derived liver models in drug discovery. *Cells 11*, 442. doi:10.3390/cells11030442

van der Stel, W., Yang, H., Vrijenhoek, N. G. et al. (2022). Mapping the cellular response to electron transport chain inhibitors reveals selective signaling networks triggered by mitochondrial perturbation. *Arch Toxicol 96*, 259-285. doi:10.1007/s00204-021-03160-7

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement n° 964537.

Giorgia Pallocca and Marcel Leist