SAFER MEDICINES
Putting patient safety first

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Newsletter 2018

Driving Progress Forward

Just as a juggernaut takes time to pick up speed, it has taken decades of sustained effort by numerous groups across the world to initiate a transition towards human-focused drug development and testing – but that juggernaut is now unstoppable.

The milestones along the way are too numerous to list here but a pivotal one was the publication in 2007 of the US National Research Council report: "Toxicity Testing in the 21st Century: A Vision and a Strategy". This landmark report provided a blueprint for "a paradigm shift from the use of experimental animals […] toward the use of more efficient in vitro tests and computational techniques."

The report spawned several major ongoing initiatives, including Tox21, of which ToxCast (the use of high-throughput human relevant in vitro assays to predict the safety of thousands of chemicals, including pharmaceuticals) is an important part. The report's authors warned that change would be difficult, and that powerful resistance would need to be overcome. Their words were prophetic: despite so much work and the profusion of impressive new methods now available, major issues continue to delay their implementation.

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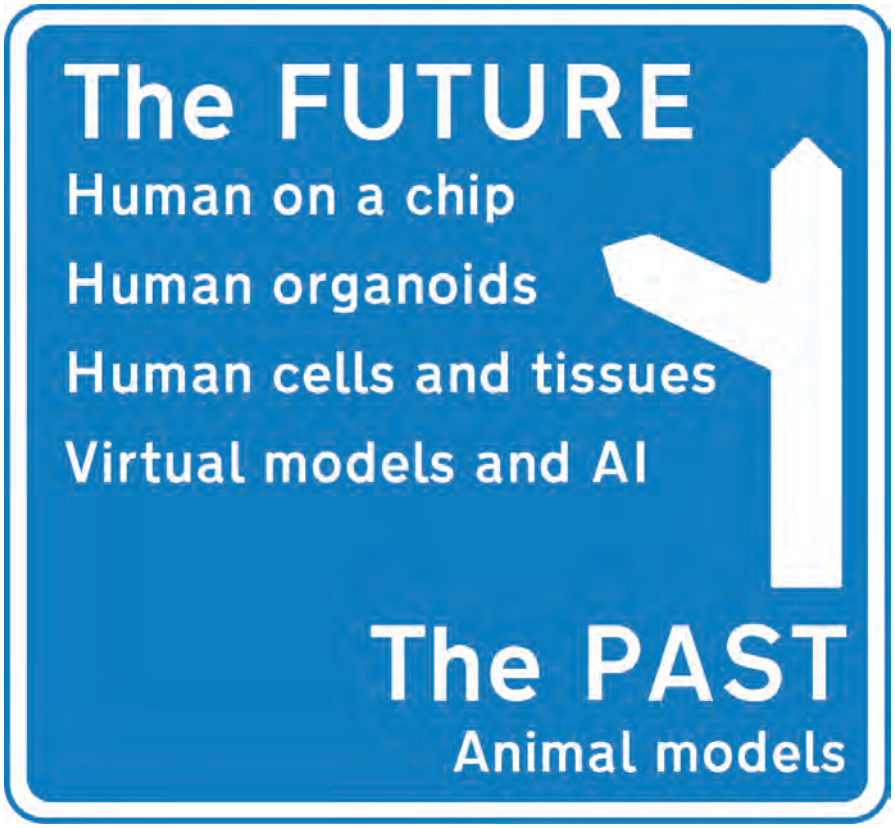


Picture credit: Rich England

Safer Medicines Trust is a patient safety charity whose mission is to change the way medicines are tested, to a system based on *human* biology: the only way to ensure safety for patients.

Safer Medicines Campaign exists to challenge the regulations that still require animal-based safety tests when superior methods exist.

Help us put patient safety first

> *"We don't have to look for model organisms any more because we are the model organism"*
>
> **Nobel Laureate Sydney Brenner CH FRS**

OUR PATRONS

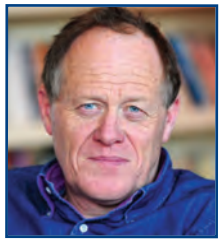

Sir David Amess MP


Caroline Lucas MP


Paul Flynn MP


Mat Fraser


Carol Royle


Dr James Le Fanu

Era of the Roadmap

The report predicted that "toxicity testing will be radically overhauled over the next 10 years" but this has not yet happened, despite great progress in advancing the necessary science and technology. This delay has prompted a plethora of 'roadmaps' spelling out the practical steps required to actually implement change. Useful roadmaps have been issued by important organisations, which include the US Food and Drug Administration, the Interagency Coordinating Committee on the Validation of Alternative Methods (comprising 16 US federal government agencies), the largely European Transatlantic Think Tank for Toxicology and a UK collaboration led by the government's innovation agency, Innovate UK.

Encouragingly, all of the roadmaps point in the same direction. They emphasise the need for a transition to the use of human relevant methods and technologies that can reliably predict the safety and efficacy of pharmaceuticals and chemicals present in cosmetics, foods and agricultural, industrial and household products.

The process of transition has been cautiously underway for some time. Computational models and several human cell- and tissue-based assays are now used routinely in the early stages of assessing the potential for medicines and other chemicals to cause cancer, skin sensitisation or heart rhythm disturbances. But the majority of other possible adverse effects are still assessed primarily through animal tests. Going forward, the strategic focus of the roadmaps should initiate a **wholesale** process of transition to a human-focused approach in the near future. The US initiatives welcome public engagement and are supported by regular public fora and progress reports, which should help to hold them accountable and ensure they deliver on their promises.

In January 2018 the UK BioIndustry Association and the Medicines Discovery Catapult published a very positive and inspiring report (State of the Discovery Nation 2018). They emphasised that "humanising" the process of drug discovery and testing is the most important way to ease the "productivity crisis" in pharmaceutical research and recognised the need for immediate action. The report's authors write: "The priorities seem clear; humanise and validate the many emerging in vitro models and invest in informatics and new methods to query them." We applaud this recommendation, which must be heeded if the UK is to retain its position as a prime location for developing new medicines.

Breaking from the past

Vigilance will always be essential to ensure that new methods are actually used in place of old, inferior methods. Even today, EU legislation mandating the use of available validated non-animal methods is not being enforced, with the result that scientific progress is being delayed by the continued use of unreliable animal tests that have been superseded but not yet replaced.

One way to help consign unreliable models and tests to the past would be to instigate a process of "invalidation". This was first proposed by Professor Michael Balls and Dr Robert Combes in 2005 and reiterated in 2018 (*Alternatives to Laboratory Animals*, Vol. 33, 299-308 and Vol. 46, 103-104). Methods which are demonstrated to be unfit for their stated purpose would be designated as invalid and deleted from the OECD Test Guidelines, to prevent their continued use.

Targets and timelines are essential to drive progress: without them, change can be much delayed or postponed indefinitely. The Netherlands is to be congratulated for its bold initiative to phase out legally prescribed animal-based safety testing by 2025. The Netherlands National Committee for the protection of animals used for scientific purposes (NCad) recommends creating an Innovations Without Laboratory Animals Index in collaboration with other countries, along the lines of the Access to Medicine Index (NCad, Transition to non-animal research, 2016).

The roadmaps and all the related activities provide grounds for great optimism. If they are to be successful, increased collaboration (including internationally) will be essential and substantial reallocation of funding from animal-based to human-focused research must be prioritised. Also, as our ongoing petition to the UK government demands, regulators must clearly require that companies use the best available human relevant methods, to protect the safety of patients and consumers.

"The difficulty lies, not in the new ideas, but in escaping from the old ones..."

John Maynard Keynes (1935)

Safer Medicines Trust team expands

We are delighted to announce the appointment of two new team members:

Welcome to our Medical Director

Dr Andrea Wraith

Dr Andrea Wraith BDS, MA, MB BChir, MMedSci has joined us as our new Medical Director. Andrea qualified as a dentist from Kings College London in 1990 and as a doctor from Cambridge in 2002. She has worked as a hospital anaesthetist and in A&E. Her professional life has centred on promoting the provision of safe and effective sedation in medicine and dentistry through both education and regulation. She provides sedation services for dentists in the primary care setting and runs courses teaching the dental team how to manage medical emergencies. From 2016 to 2017, she was President of the Section of Anaesthesia of the Royal Society of Medicine. Dr Wraith has acted as an expert advisor to local health authorities and lectured on sedation related issues to dentists, doctors and nurses both nationally and internationally. Patient safety has always been at her core.

… and to our Research Consultant

Dr Pandora Pound

Dr Pandora Pound BA, MSc, PhD has joined us as our Research Consultant. Pandora has been conducting research since 1990 and has worked within universities and medical schools throughout London and the South West, mainly in the field of public health. She was an early proponent of the need for systematic reviews of animal research and has published widely on the need for an evidence-based approach in this field. Two of her seminal publications, both published in the British Medical Journal, include "Where is the evidence that animal research benefits humans?" and "Is animal research sufficiently evidence based to be a cornerstone of biomedical research?". In 2017 she left academia to focus on this issue. Her research highlights the inconsistencies and limitations of the current approach, while encouraging more human-relevant approaches to the development and testing of medicines.

And a warm welcome to our newest Science Adviser

Dr Azra Raza

Dr Azra Raza MD is Chan Soon-Shiong Professor of Medicine and Director of the Myelodysplastic Syndromes (MDS) Center at Columbia University in New York. During her career, she has established a highly productive translational MDS research programme, which includes a tissue repository containing more than 50,000 samples from MDS patients. She serves on numerous national and international panels as a reviewer, consultant, and advisor, and is well known internationally for several landmark observations related to the biology and treatment of MDS. Some of Dr Raza's awards include The First Lifetime Achievement Award from APPNA, Award in Academic Excellence twice (2007 and 2010) from Dogana, Woman of the Year Award from Safeer e Pakistan, CA, The Hope Award in Cancer Research 2012 and the Distinguished Services in the Field of Research and Clinical Medicine award from Dow Medical College in 2014. Dr Raza was named as one of the 100 Women Who Matter by Newsweek Pakistan in March 2012.

Latest publications in scientific journals

Journal of the Royal Society of Medicine published a Commentary by Kathy Archibald, Katya Tsaioun, Gerry Kenna and Pandora Pound, entitled: "Better science for safer medicines: the human imperative".

Our commentary warns that the UK must not fall behind in the race to 'humanise' drug discovery. We argue that current research models and regulation are blocking the development of human-relevant approaches to drug discovery and perpetuating animal-based approaches. We point out that the UK has world-leading research in this area but that significant investment in non-animal technologies is taking place in the US and Europe. We suggest the UK should seize the initiative to revolutionise medicine through more intelligent, human-relevant research.

Journal of the Royal Society of Medicine, Nov. 2018, DOI: 10.1177/0141076818812783

Journal of Translational Medicine published a Review by Pandora Pound and Merel Ritskes-Hoitinga (Professor of Evidence-Based Laboratory Animal Science at SYRCLE, Radboud University, Netherlands) entitled: "Is it possible to overcome issues of external validity in preclinical animal research? Why most animal models are bound to fail".

The authors make a compelling argument that preclinical animal models can never be fully valid due to the uncertainties introduced by species differences. They suggest that to improve clinical translation and ultimately benefit patients, research should focus instead on human-relevant research methods and technologies.

Journal of Translational Medicine, 7 Nov. 2018, DOI: 10.1186/s12967-018-1678-1

Drug Metabolism and Disposition published a review article by Dr Gerry Kenna and Dr Jack Uetrecht (Professor of Pharmacy and Medicine at the University of Toronto and the Canada Research Chair in Adverse Drug Reactions) entitled: "Do In Vitro Assays Predict Drug Candidate Idiosyncratic Drug-Induced Liver Injury Risk?"

Many new medicines cause undesired side effects in humans that are not predicted by the largely animal-based safety studies performed currently. This review highlights both the promising progress made in developing human-relevant in vitro methods that can anticipate and reduce the risk of drug-induced liver injury, and the outstanding challenges that remain to be addressed.

Drug Metabolism and Disposition, Vol. 46, Issue 11, 1658-1669, Nov. 2018

C**linical Pharmacology & Therapeutics** published a major review article co-authored by Dr Kenna and an international team of scientists, entitled: "Can BSEP Inhibition Testing In Drug Discovery And Development Reduce Liver Injury Risk? An International Transporter Consortium Perspective."

This group of experts from Safer Medicines Trust, major pharmaceutical companies, universities and biotechnology companies reviews the evidence that inhibition of a liver cell membrane transport protein called the Bile Salt Export Pump (BSEP) can cause drug-induced liver injury, which is poorly predicted by animal tests. They go on to recommend the use of a series of in vitro and in silico methods to evaluate BSEP inhibition during drug development, in order to aid the design and selection of safer medicines.

Clinical Pharmacology & Therapeutics, Vol. 104, Issue 5, 916-932, Nov. 2018

Journal of Animal Ethics commissioned a paper by Kathy Archibald, entitled: "Animal Research Is an Ethical Issue for Humans as Well as for Animals."

Animals are used in biomedical research to study disease, develop new medicines, and test them for safety. This paper argues that a revolution in science and technology has produced a new generation of more relevant and predictive tools, which could be used to create safer medicines more quickly and at less cost: a win-win situation that should be supported by everyone. The obstacle preventing this from happening is governments' continued insistence on animal testing. Yet the evidence is clear that reliance on animals as surrogate humans puts patients at risk, can delay medical progress, and can cause effective treatments to be wrongly discarded. There is a compelling case to be made that animal research is an ethical issue for humans as well as for animals.

Journal of Animal Ethics, Vol. 8, Issue 1, 1-11, Spring 2018

Book chapters

Replacing Animal Tests to Improve Safety for Humans. In this chapter, Kathy Archibald, Robert Coleman and Tamara Drake propose a comparative approach (now being pursued by Dr Katya Tsaioun: see Box on p5) that could accelerate the replacement of most, if not all, regulatory animal tests with superior tests based on human biology. They conclude that there is a clear ethical imperative to replace unreliable animal-based safety tests to protect human safety, and that current regulations are stifling innovation by failing to keep pace with scientific progress. Governments must act to protect the public by updating regulations that now prevent their own aim (patient safety) from being realised.

In: **Animal Experimentation: Working Towards a Paradigm Change.** K Herrmann, K Jayne, (eds). Brill: www.Brill.com. FREE E-Book. Hard copy publication date: April 2019

Safety assessment of pharmaceuticals. Gerry Kenna and Rebecca Ram explain how useful in vitro assays for genotoxicity, skin sensitisation and eye irritancy came to be incorporated into regulatory guidelines. They also describe exciting progress in the development of in vitro human assays for heart and liver toxicity. The challenge now is to ensure that the scientific and regulatory communities accept the value of these assays.

In: **The history of alternative test methods in toxicology.** M Balls, R Combes (eds). 167-174, Academic Press, London, 2018

Interpretation, Integration, and Implementation of In Vitro Assay Data: The Predictive Toxicity Challenge. In this chapter, Dr Kenna and scientists from Pfizer review strategies they used at AstraZeneca and at Pfizer to persuade these pharmaceutical giants to implement novel in vitro test cascades. They offer valuable advice in tackling a challenge greater than the purely scientific one of devising the cascade itself.

In: **Drug-Induced Liver Toxicity.** Chen M, Will Y (eds). Humana Press, New York, 2018

Noninvasive Preclinical and Clinical Imaging of Liver Transporter Function Relevant to Drug-Induced Liver Injury. In this chapter of the same book, Dr Kenna and an international team of scientists review various imaging methods that can be used to investigate cellular processes that can cause liver injury. Medical imaging is one approach that can help to address the translational gap between in vitro toxicity assays and adverse outcomes in patients.

In: **Drug-Induced Liver Toxicity.** Chen M, Will Y (eds). Humana Press, New York, 2018

Links to all publications are available on our website

Presentations at scientific conferences

Dr Kenna has presented a number of talks and courses at universities and scientific meetings. His slide presentations can be viewed on our website (see the Resources page).

Evidence, Evidence, Evidence

Evidence for the superiority of human relevant models and approaches continues to accumulate at an ever-increasing rate. We present here a small selection of recent advances.

Study to compare safety prediction of animal versus non-animal tests

Dr Katya Tsaioun, Director of the Evidence-based Toxicology Collaboration (EBTC: ebtox.org) at the Johns Hopkins Bloomberg School of Public Health, USA, is continuing to lead an important study using evidence-based methods to compare drug-induced liver toxicity in humans to preclinical animal data, and to US ToxCast in vitro data.

An EBTC workgroup, including stakeholders from academia, government organisations and industry, are in the final stages of a systematic review of the literature on two marketed drugs for diabetes: Rezulin (troglitazone) and Avandia (rosiglitazone), which caused markedly different adverse reactions in humans. Preliminary results show that in vitro tests reveal a much higher number of positive signals from Rezulin, which reflects its effects on patients. Rezulin was withdrawn in 2,000 after being linked to over 94 cases of acute liver failure and 63 confirmed deaths, although experts estimate the true numbers could be 10 times higher.

Rebecca Ram (from Safer Medicines Trust) and others have screened almost 6,000 papers for the systematic review and are in the process of extracting the relevant data from the selected studies. The next step is to calculate the predictive value of the 'signatures of toxicity' from in vitro tests. We look forward to reporting the outcome in our next newsletter. If you have a biomedical background and would like to help with extracting data from selected studies, please contact us as soon as possible. The study protocol is published at https://goo.gl/v9UcxP

Better prediction of toxicity

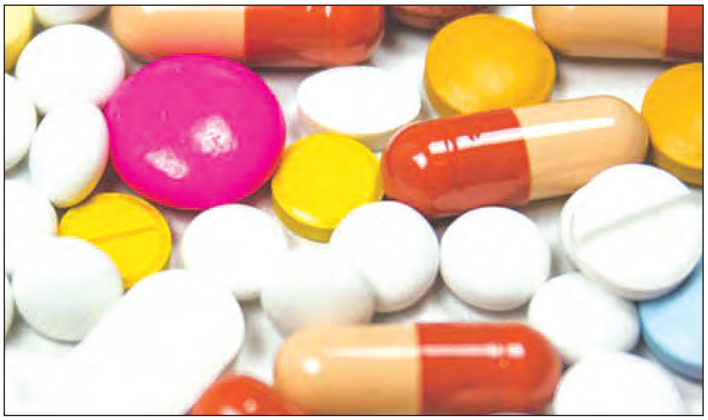
Scientists from the US National Center for Advancing Translational Sciences have conducted the first meta-analysis to compare the performance of animal tests in predicting human adverse outcomes with that of human in vitro assays. Data on 1,511 approved drugs were collected from animal tests, from documented human outcomes and from in vitro assays in the US Tox21 programme. Analysis of the first phase of in vitro assays showed that they predicted human drug toxicities about as well as animal tests do, which is not very well. (This poor performance was probably because the assays in the first phase of the Tox21 programme – selected for their ability to be automated – were only a small subset of the assays required to study all aspects of human biology.) However, combining the in vitro data with information on chemical structures and on pathways that were not covered by the Tox21 assays, produced models that "greatly outperform" the predictive ability of animal toxicity tests. This knowledge will be invaluable for guiding the selection of suites or batteries of in vitro tests for comprehensively predicting toxicity in humans.

Nature Scientific Reports, Vol. 8, Article number: 3783, 2018

Big data and machine learning

Joint research by UL, a US consumer safety company and scientists from Johns Hopkins University, US has demonstrated that using machine-learning software (artificial intelligence or AI) to analyse mountains of safety data can greatly outperform animal studies in predicting chemical safety. Their new "REACHAcross" method is an automated version of the "read-across" technique, where the toxicity of untested chemicals is inferred by comparison with similar compounds whose effects are known. A database on over 70 million chemicals, containing more than 300,000 biological data points was used to train the algorithms. By analysing billions of chemical combinations, REACHAcross™ software can predict some of the potentially harmful effects of chemicals on health and the environment, including skin sensitisation, acute oral and dermal toxicity, eye and dermal irritation, mutagenicity and acute and chronic aquatic toxicity. These tools have an accuracy of 80–95%, compared with 50–70% for the respective animal tests. Furthermore, they can be performed in a matter of seconds and at a fraction of the cost.

Toxicological Sciences, Vol. 165, Issue 1,198-212, 1 Sept. 2018



Human heart cells predict cardiac safety of medicines

An assay using primary human heart cells to assess the potential of drugs to disrupt heart rhythm or contractility (two serious liabilities responsible for many drug failures) demonstrated excellent prediction (with 96% sensitivity and 100% specificity in the reference drugs tested) of real clinical outcomes. Furthermore, a comparison between human and dog heart cells for two of the test drugs highlighted the inability of studies in dogs (a default model for drug cardiac safety assessment) or dog cells to accurately predict the risk of such effects on the human heart.

Frontiers in Physiology, 19 Dec. 2017
DOI: 10.3389/fphys.2017.01073

Cardiac safety also predicted *in silico*

Human-based computer models offer a fast, cheap and potentially effective alternative to experimental assays, also facilitating translation of in vitro and/or in vivo data to human risk assessment. In an innovative in silico (computational) 'drug trial', 62 reference drugs were tested in more than 1,000 simulations of human cardiac cells. The computer models predicted the risk of human drug-induced heart arrhythmias with 89% accuracy, compared with animal studies that showed up to 75% accuracy.

Frontiers in Physiology, 12 Sept. 2017, DOI: 10.3389/fphys.2017.00668

Computational modelling saves lives

Certara (a member of the Alliance for Human Relevant Science) offers a range of in silico models, which integrate all available evidence to support model-informed drug development. In a letter published in Clinical Pharmacology & Therapeutics, Certara explained how the use of one of their existing models before the clinical trial of BIAL 10-2474 in France in 2016 (in which one volunteer died and five others were hospitalised) could have provided a better prediction of the maximum dose than preclinical animal data and arguably might have prevented the tragic outcome. As mentioned in our 2017 newsletter, human cellular models could also have given a more reliable prediction of the trial's risk.

The Role of Quantitative Systems Pharmacology in the Design of First–in–Human Trials. Piet H. van der Graaf and Neil Benson. *Clinical Pharmacology & Therapeutics,* Vol. 104, Issue 5, 797, 2018

Intestinal organoid transforms treatment for patient with cystic fibrosis

Cell samples were taken from the nose of a patient with cystic fibrosis who was unresponsive to available drugs due to a rare gene mutation. The cells were grown in the lab into mini-organs, or 'organoids', then exposed to different experimental drugs to decide whether any could be of benefit. In this way, doctors were able to select an effective therapy, which was then used successfully to treat the patient. The EU Horizon 2020 programme is funding researchers to create personalised treatments for all cystic fibrosis patients with ultra-rare mutations that preclude their treatment with currently available therapies.

European Respiratory Journal, 2018
DOI: 10.1183/13993003.02457-2017

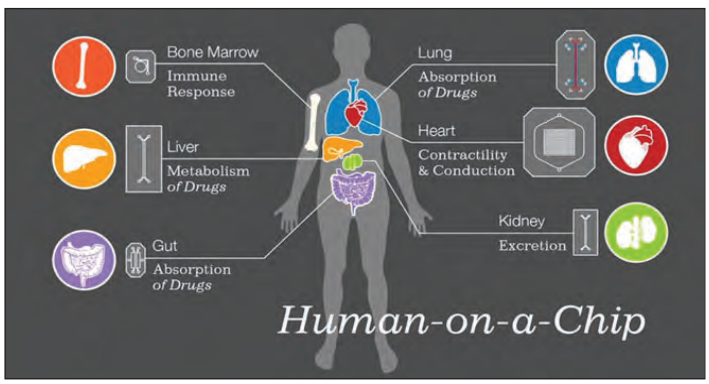
Mini-organs for many diseases

Scientists have created mini-hearts, mini-brains, mini-lungs and many other organoids, which can be used (among other things) to screen drugs in a way that is not possible in humans or animals. Such models can be derived from human induced pluripotent stem cells (hiPSCs) from skin, for example, and are radically more reflective of human organs for preclinical experimentation than any previously available models.

They can be personalised by using cells from individual patients, as in the cystic fibrosis example above. Such 'avatars' are also being used for cancer patients, to select the best treatment combinations. Genetically modified mouse avatars have been used for some time in the hope that they would help guide treatment decisions for cancer patients. However, they often have proved disappointing, not least because they are too slow to produce results and are extremely expensive. Conversely, pancreatic organoids have recently been created from patients' cells for high-throughput drug screening to target pancreatic cancer. The technology is now ready to be used to screen large chemical libraries in the hunt for drugs for patients with this most difficult to treat and deadly cancer.

SLAS DISCOVERY: Advancing Life Sciences R&D, 23(6), 574–584, 2018
DOI: 10.1177/2F2472555218766842

The EU Horizon 2020 programme is funding projects including "Organoid", "Toxanoid" and "in3", which aim to demonstrate that hiPSC-derived tissue technology can outperform current in vitro systems and replace a significant portion of animal-based toxicology studies.



Picture credit: Wyss Institute

Multi-organoid platforms are the logical progression of organoid and organ-on-a-chip technologies and will allow for the realisation of truly predictive in vitro modelling of human physiology. Several teams have integrated multiple different organ types into interconnected micro-physiological systems (organs-on-chips), which then recapitulate in vivo biological processes, such as metabolism of test drugs by liver tissue. The drugs then affect the other connected tissues, e.g. heart or lung just as they would in the human body. An international team, including CN Bio Innovations (a member of the Alliance for Human Relevant Science) successfully integrated 10 different organ types on one platform and kept them fully functioning and continuously interacting for 4 weeks. The technical challenges were huge but this provides an important proof of principle that it is already possible to create a physiome-on-a-chip that can predict human responses before trials in real humans. Of course, even with 10 organs represented, the platform falls short of replicating an entire human, hence the term physiome-on-a-chip – but many groups are working towards the ultimate human-on-a-chip. Nevertheless, the value these systems already offer, not just to drug discovery and development but also to disease modelling and wider biological research is incalculable.

Nature Scientific Reports, Vol. 8, Article number: 4530, 2018

New insights not previously possible

Organ-on-chip systems are yielding invaluable insights into the human body and disease processes that would be impossible to achieve in any other way. For example, scientists from Imperial and King's Colleges, London, used a model liver-chip developed by CN Bio Innovations to study hepatitis B infection. Every step of the virus's life cycle was recapitulated in the model, which even mimicked the immune response seen in infected patients. Remarkably, the model revealed how the virus evades the body's immune response, contributing to a better understanding of the disease, which should enable the development of new treatments.

Nature Communications, Vol. 9, Article number: 682, 2018

In another example, a blood vessel chip was able to accurately model and predict thrombosis induced by monoclonal antibody drugs that caused thrombosis in clinical trials. This life-threatening adverse reaction was not predicted by preclinical toxicity tests in animals. The human vessel-chip is a promising new model for assessing thrombosis risk during drug screening, for evaluating anti–coagulant or antiplatelet agents and for providing insight into the mechanism of clot formation.

Clinical Pharmacology & Therapeutics, 2018, DOI: 10.1002/cpt.1054

Too many examples to mention

The pace of advances in the many fields of human relevant science is now so fast that it is virtually impossible to keep up to date. Space precludes any further examples here but if you would like to see more, the twitter feed on our website (SaferMedicines.org) gives links to many exciting news stories as they are published. Also, the Lush Prize website at LushPrize.org has 1-minute videos of all the winning technologies. These are well worth viewing, particularly the 2018 Science Prize clip, with its blinking eye on a chip, smoking lung on a chip, infected astronaut's lung on a chip, placenta on a chip and cancer immunotherapy on a chip.

US company Emulate (a spin-out company from the Wyss Institute for Biologically Inspired Engineering at Harvard University), is developing a variety of individualised "patient-on-a-chip" models, which enable studies of complex human biology that are not possible with other techniques. Watch their 2-minute video at https://emulatebio.com/insight/patient-on-a-chip

All of these examples, and many more, clearly show that powerful human relevant technologies are now available, which have many advantages over the use of non-human surrogates. Where comparisons with animal models have been made, the human-based models compare very favourably. In many cases, direct comparisons are not possible because the new models offer capabilities that were simply not available before. The opportunities before us now are so exciting – they are limited only by our imagination and, of course, funding. What is needed now is a **full-scale** effort to optimise and implement these impressive new tools, to create unprecedented medical advances and a genuinely effective system for chemical risk assessment: something that we have never had before. This requires – and deserves – massive reallocation of resources, coupled with clear regulatory language to encourage and incentivise companies to use methods that they can demonstrate are truly fit for purpose.

We are extremely grateful to all of our supporters for helping to spread the word and for your generous donations: we couldn't do what we do without you!

We are also deeply grateful for and humbled by the generous legacies bequeathed to us by Ann Lander and Kathy Manovitch.

How to help

If you would like to fundraise for us in any way, we would be extremely grateful, and more than happy to provide collecting tins and literature for the event.

One of the best ways to reach people with our message is through our leaflet. If you can help by distributing leaflets to friends and family, at a stall or event, or via a friendly shop or cafe, we would be delighted. Just let us know how much literature you would like (please see back page) – thank you!

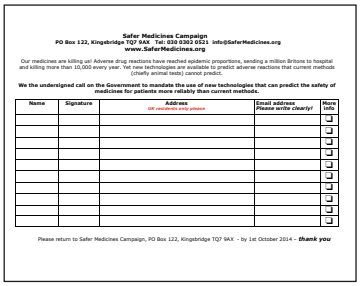
ACTION

Leaflets

If you can help by distributing our leaflets we will be delighted. Donations to help with postage and printing costs will be greatly appreciated.

Petition

Sign our petition calling for the use of more reliable safety tests. You can sign on our website or on paper: download a form from our website or order by email, phone or post.



Newsletters

Please order further copies of this newsletter to distribute if you can.

DVDs

Watch ***Safer Medicines*** on our website or order a copy: **free** but please send stamps or a donation. If you know any secondary school teachers or lecturers, please encourage them to ask us for a free copy.

Donate

Please help us to modernise and humanise the safety testing of medicines, and to distribute our resources to teachers, students and MPs.

You can donate on our website or by post – please see below.

Regular gifts by standing order help us to plan ahead with confidence – if you would like to help us in this way, we will be delighted to send you a standing order form: please contact us or download one from our website.

We rely completely on your generosity. We receive no corporate or government funding and have no expensive overheads: all of our office space is donated without charge.

If you want to see real progress towards a future where medical research is based on studying humans rather than animals, please give generously today.

Booklets

A Critical Look at Animal Experimentation:
Free booklet examining the impact of animal research on medical progress and outlining more valid human-focused methods of research.

Please copy this section or cut it off and return to us – thank you

Please send _____Leaflets _____Newsletters_____DVDs

_____Booklets_____Petition Sheets

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Thank you for your invaluable support – we simply can't do this without you.

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