Alliance for Human Relevant Science

The UK is a world leader in life science research. Yet many breakthroughs are lost in translation from preclinical animal models to humans. There is now a tremendous opportunity to bridge the translational gap with human relevant technologies.

It is time to focus on the human.

Newsletter Spring 2018

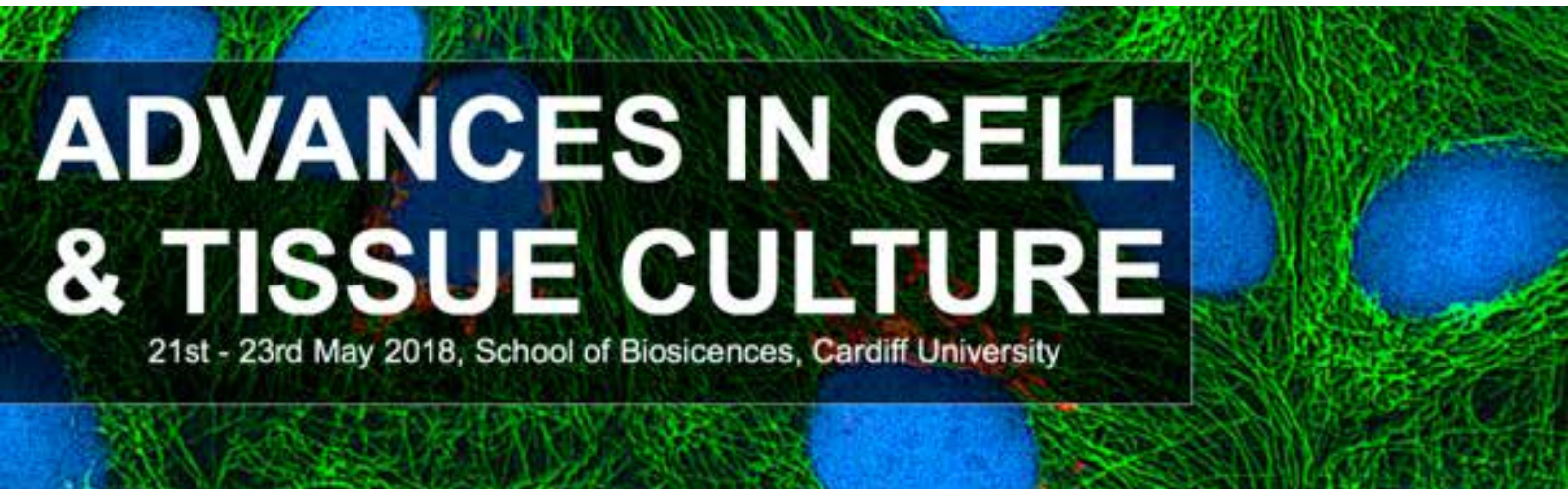
THE ALLIANCE FOR HUMAN RELEVANT SCIENCE WEBSITE HAS BEEN UPDATED

The Alliance website has been updated following the parliamentary launch, meetings and activities during 2017. The site now provides background information on the Alliance and its founder members, as well as new member organisations who have joined to date. Other features include a scientific resources area and updates on forthcoming Alliance events and publications.

New content is still being added and suggestions for content are welcome. For more details in the meantime, visit humanrelevantscience.org

KIRKSTALL ACTC (ADVANCES IN CELL AND TISSUE CULTURE) 2018 CONFERENCE AND ALLIANCE MEETING – 21-23 MAY

This year's Advances in Cell and Tissue Culture (ACTC) conference hosted by Kirkstall will be held at the University of Cardiff's School of Biosciences from 21st-23rd May. The comprehensive scientific programme includes presentations from international keynote speakers on a range of relevant topics, including in vitro models for the study of neurological diseases, creating more realistic gut models, and advanced cell culture (including 3D models, fluid flow and co-culture). The first Alliance for Human Relevant Science meeting of 2018 will also be held at the end of ACTC 2018 on 23rd May. To register for ACTC 2018 and for more details on speakers and exhibitors, visit actc2018.com



WHO WE ARE

The Alliance for Human Relevant Science is an inclusive collaboration of like-minded companies, organisations and individuals. Working together, we will accelerate innovation and create positive change.

Find out more about our founder members:

AIMS OF THE ALLIANCE

- Support better science for better health
- Save lives – human and animal – through improved safety and efficacy testing of medicines and other chemicals
- Save money by promoting more scientifically relevant research

TOX21 WORKING GROUP ON DRUG INDUCED LIVER INJURY COMPLETES FULL TEXT REVIEW OF HUMAN AND ANIMAL DATA

The Evidence Based Toxicology Collaboration (EBTC) Tox21 Working Group has an ongoing study to investigate how the mechanistic data from ToxCast and Tox21 can be used in safety assessment. The group is currently running a pilot study to answer the following question;

'How well do the ToxCast in vitro tests predict the liver outcomes in animals (mice, rats, Beagle dogs and non-human primates) and humans?'

The project brings together multiple evidence streams to compare the observed Adverse Event profiles in experimental animals and patients, to be compared with the pathway signatures based on ToxCast and Tox21 data. In March, the group completed a full text review resulting in 333 papers (of 615 reviewed) being selected for the next stage of data extraction, following inclusion from a first stage analysis of almost 6,000 abstracts.

THE LORD DOWDING FUND JOINS THE ANIMAL RESEARCH NEXUS

The Lord Dowding Fund for Humane Research has recently become a member of the Programme Advisory Committee for AnNex: Animal Research Nexus. AnNex is a five-year collaborative programme bringing together academics, who study the practice of animal research without using animals such as through the history and culture of animal experiments, and stakeholders across the animal research community (industry, medicine, 3Rs, patient protection and animal protection). The LDF will be advising on matters of animal replacement in relation to the advantages of more relevant human based research methods.

LORD DOWDING FUND
FOR HUMANE RESEARCH

SIMCYP (CERTARA) PROVIDES TRAINING IN HIGH QUALITY IN VITRO AND IN SILICO PBPK MODELS

Systems toxicology approaches are integral to elucidating mechanisms of toxicity and for implementation of new assessment methods (NAMs). Alliance member organisation Simcyp (a Certara company) has partnered with the Altertox Academy (formerly the CAAT academy) to provide training to *in vitro* experimentalists on modelling nephrotoxicity using mechanistic models within a physiologically based pharmacokinetic/toxicokinetic (PBPK/TK) framework. Further training on the prediction of drug-drug interactions (DDIs) using PBPK/TK models will occur as part of a workshop scheduled for October 2018. Simcyp scientists will also contribute to a short course at the 22nd North American ISSX meeting on *in silico* modelling of *in vitro* metabolism, transport and toxicity data. Through contributing to these educational activities Simcyp seeks to promote the wider application of PBPK/TK modelling approaches, better dialogue between experimentalists and modellers, and ultimately the robust application of high quality modelling that can inform regulatory decision making.

HEPATITIS B RESEARCH USING CN BIO ORGAN-ON-CHIPS PUBLISHED IN NATURE COMMUNICATIONS

A Nature Communications publication in February reported that scientists at Imperial College London have demonstrated how pathogens interact with human organs, using Liver-on-a-Chip technology originally developed by Alliance member CN Bio Innovations. The Imperial team found that the device could be infected with hepatitis B virus at physiological levels and had similar biological responses to the virus as a real human liver, including immune cell activation and other markers of infection. Furthermore, the technology demonstrated specifically how Hep B evades the body's immune response - a finding which could be exploited for future drug development. The researchers hope the technique will provide a better understanding of the resulting disease and improve the development of new treatments. Following this, in March CN Bio published details of its joint work with the Massachusetts Institute of Technology (MIT) on the microfluidic platform PhysioMimix for vastly improving the human relevance of predictions in drug evaluation. PhysioMimix works by connecting engineered tissues from up to 10 organs, accurately replicating human organ interactions for weeks at a time and allowing them to measure the effects of drugs on different parts of the body with a 'plug and play' type system. Publication of the success in **Nature Scientific Reports** showcases the final milestone of the program to bring ten organs together on a chip. CN Bio was a co-recipient with MIT of a US$26M federal contract. At the end of 2017, CN Bio announced their research collaboration with AstraZeneca, following receipt of a £670K award from Innovate UK. CN Bio is also hosting an Organ on a Chip workshop in May (see Events below). More details on www.cn-bio.com

SAFER MEDICINES TRUST WELCOMES DR. ANDREA WRAITH AND DR. PANDORA POUND

Safer Medicines Trust welcomes Dr. Andrea Wraith and Dr. Pandora Pound to its team of research consultants.

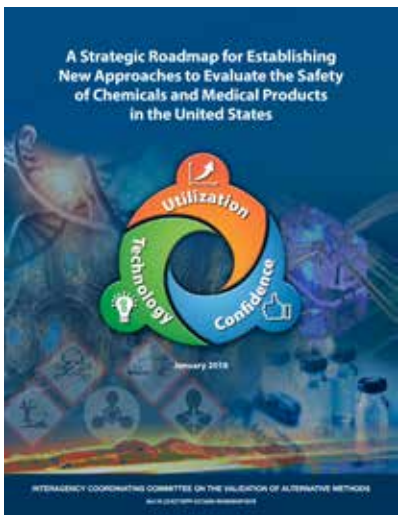
Andrea Wraith qualified as a dentist from King's College London in 1990 and as a doctor from Cambridge in 2002. She has worked as a hospital anaesthetist and in A&E. Her professional life has centred on promoting the provision of safe and effective sedation in medicine and dentistry through both education 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 and 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.

Pandora Pound 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. In 2017 she left academia to focus on this issue and to work towards more human-relevant approaches to the development and testing of medicines.

OTHER NEWS

ICCVAM PUBLISHES STRATEGIC ROADMAP FOR ESTABLISHING NEW ALTERNATIVE METHODS

In January 2018, the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) published its 'Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products in the United States'. Its main goals are to improve human relevance in the safety testing of chemicals and replace the use of animals. Activities are already underway in addressing key endpoints including acute systemic toxicity, eye irritation, skin irritation and skin sensitisation. Each area is set out clearly under four main goals which are i) definition of testing needs; ii) identification of available alternative tests and computer models; iii) developing IATA* and defined approaches and iv) addressing regulatory and other challenges.

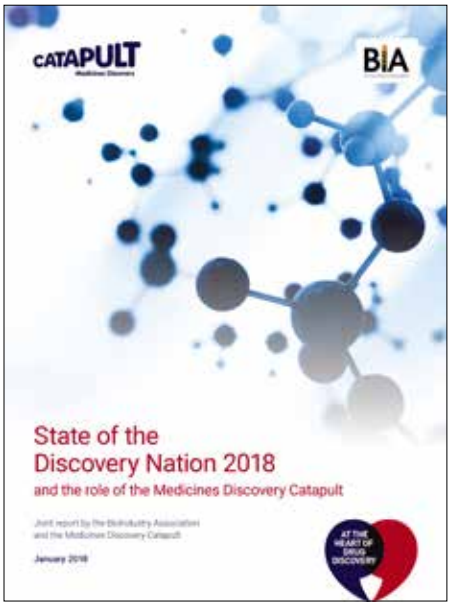


ICCVAM includes a number of government agency members and the roadmap will incorporate key project timelines to update the stakeholder community on how progress is being made.

* IATA = Integrated Approaches to Testing and Assessment

REPORT PUBLISHED BY UK BIOINDUSTRY AND MEDICINES DISCOVERY CATAPULT CALLS FOR HUMAN RELEVANT DRUG DISCOVERY

The UK BioIndustry Association and the Medicines Discovery Catapult have published a report which fully recognises the need for immediate action and emphasises that "humanising" the process of drug discovery and testing is the most important way to ease the "productivity crisis" in pharmaceutical research. The report, State of the Discovery Nation 2018 and the role of the Medicines Discovery Catapult, based on surveys and in-depth interviews with more than 100 senior executives of drug discovery companies, identifies many emerging technologies that can humanise research, which will make the early stages of research more predictive of how a drug will work in real life. The result will be better drug candidates entering human trials, benefitting trial participants and the pharmaceutical industry, through lower attrition and improved productivity.



The Medicines Discovery Catapult's mission is to help UK biotech SMEs transform as necessary to reverse the productivity paradox, and to maintain the UK's heritage position as one of the world's best places for developing new targeted, high value medicines. They say: "The priorities seem clear; humanise and validate the many emerging in vitro models and invest in informatics and new methods to query them." Some of the most important needs include:

Retooling the R&D model with human relevant preclinical models

Joint efforts, such as public-private partnerships to validate the humanised in vitro models developed in academia

Catalysing "disease syndicates" to bring together patients, industry and other stakeholders to conduct high-impact research

Making collaborative R&D the norm, not the exception

Reusing and mining the wealth of information, through appropriate data sharing – especially negative results from failed preclinical experiments

Improving access to patient samples and data

Performing Phase I trials in appropriate patients rather than healthy volunteers would give early evidence of potential efficacy.

NC3RS PRIZE AWARDED FOR IN SILICO PREDICTION OF CARDIAC SAFETY

In March, the 2017 NC3Rs prize was awarded to researchers from Oxford University and Janssen Pharmaceuticals, for their success in developing an *in silico* model which predicts cardiac safety better than animal studies. Their research describes how 62 drugs and reference compounds were tested in more than a thousand simulations of human cardiac cells. The in silico method predicted the risk of drug-induced heart arrhythmias in humans with 89% accuracy, compared to only 75% for data obtained from previously conducted animal studies.

NC 3Rs
National Centre for the Replacement Refinement & Reduction of Animals in Research

US ENVIRONMENTAL PROTECTION AGENCY RELEASES DRAFT STRATEGY TO REDUCE ANIMAL USE FOR TSCA (TOXICOLOGICAL SUBSTANCES CONTROL ACT) TESTING

In March, the U.S. EPA released its draft strategy for public consultation on reducing the use of animals in chemical testing. The draft was open for public consultation until April 26, with a subsequent strategic plan to be developed by late June. The Frank R. Lautenberg Chemical Safety for the 21st Century Act, which amended the Toxic Substances Control Act (TSCA), mandated development of the strategy. The announcement of the draft strategy release is available at https://www.epa.gov/newsreleases/epa-meets-another-tsca-milestone-releases-draft-strategy-reduce-animal-testing

EVENTS

21-23 May
Kirkstall ACTC 2018 - limited places now available

22 May
CN Bio Organ on a Chip Workshop

10-13 June 8th
Alternatives Conference hosted by CCARE (Chinese Centre for Alternatives Research and Evaluation, Shanghai

23-24 August
2nd Pan-American Conference for Alternative Methods, Rio de Janeiro, Brazil

2-5 September
EUROTOX 2018, Brussels – this year's theme is 'Toxicology Out of the Box'

23-26 September
EUSAAT 2018, Linz, Austria

15-18 October
ESTIV 2018 (20th International Congress on In Vitro Toxicology), Berlin

2020
11th World Congress - Maastricht. Register for updates at the WC11 website