Helder Constantino
Campaign Manager
Research & Toxicology
hconstantino@hsi.org

HUMANE SOCIETY INTERNATIONAL

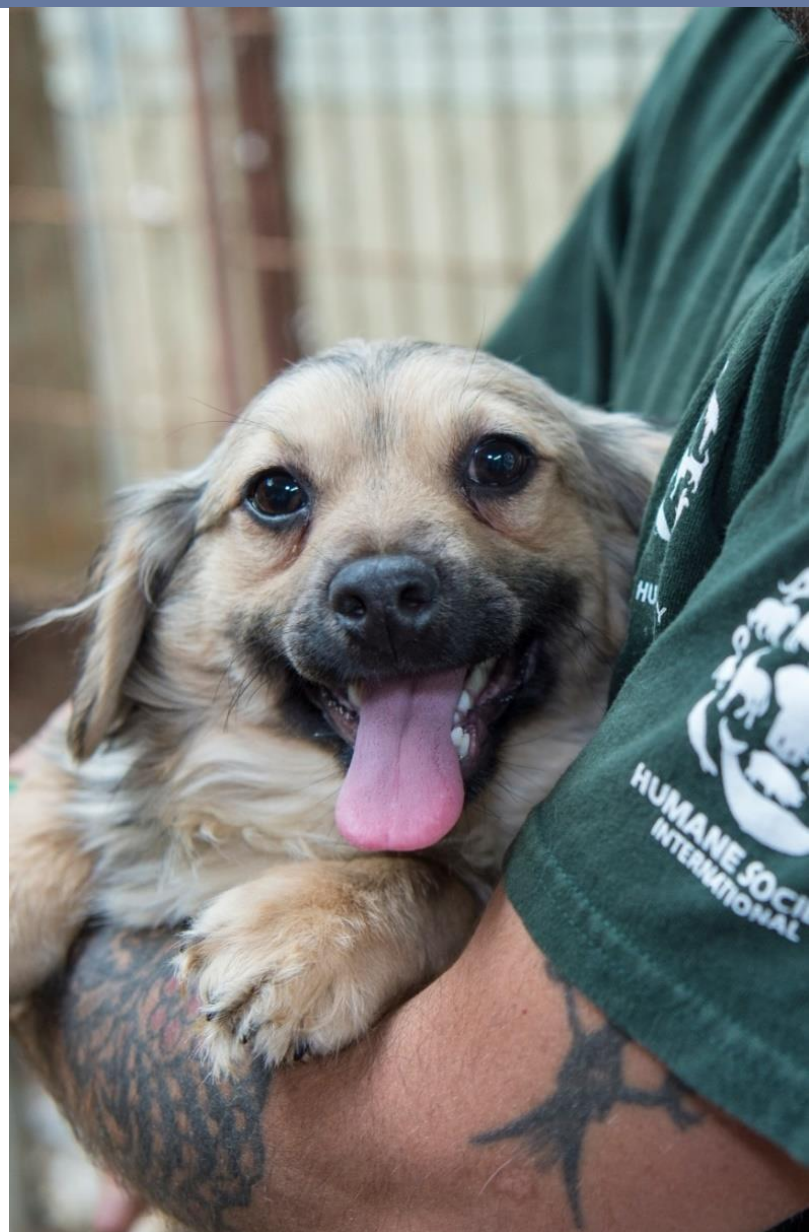
Advancing Science Without Suffering in Brazil

About HUMANE SOCIETY INTERNATIONAL

- **Our mission**
  Humane Society International is a global animal protection organization working to help all animals—including animals in laboratories, animals on farms, companion animals and wildlife.

- **Our approach**
  HSI seeks out innovative and scientifically sound approaches to animal protection and relies on a network of on-staff and external experts to make the case for policy change to improve the lives of animals and people.

- **Our reach**
  HSI's programs are active in more than 50 countries on nearly every continent.



Our **Research & Toxicology** Department

- **Expert team**
  Toxicology, ecotoxicology, pharmacology, regulatory science, endocrinology, biochemistry, neuroscience, law, etc.
- **Global presence**
  Brazil, United States, Canada, Mexico, Central America, European Union, India, Japan, South Korea, Viet Nam, Australia, Africa and beyond
- **Approach**
  Working with policy makers, regulators, companies, scientists, and other stakeholders to build partnerships for progress

HSI is the leading international NGO working to advance non-animal testing & health research worldwide

HUMANE SOCIETY INTERNATIONAL

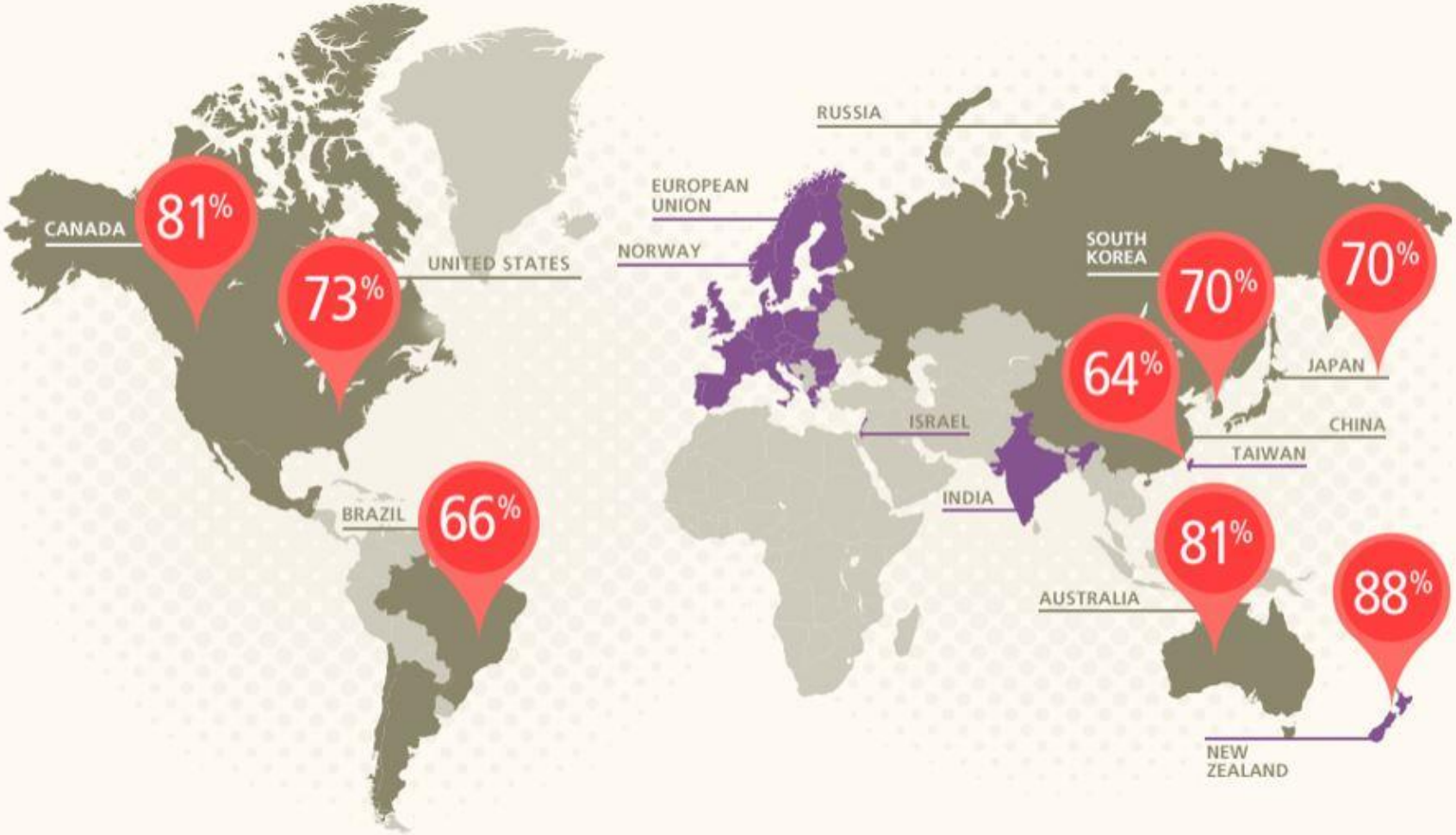
The **#BeCrueltyFree** campaign

Ending Cosmetic Tests on Animals Worldwide

Why we believe the world is ready to end cosmetic tests on animals

- **Public opinion** strongly opposes cosmetic tests on animals.
- **37 countries** have already banned these tests; the EU in India have prohibited the sales of cosmetics tested on animals, creating trade incentives to stop them in other nations.
- **Legislations banning cosmetic tests on animals** have triggered investments in alternative methods, allowing innovation in the cosmetic sector without tests on animals.

Cosmetic tests on animals are rejected by consumers



Changing the rules in Brazil

Bans on testing cosmetics on animals: legislative progress

PODER LEGISLATIVO
ASSEMBLEIA LEGISLATIVA DO ESTADO DO AMAZONAS
LEI PROMULGADA Nº 289 de 03/12/2015

PROÍBE a utilização de animais para desenvolvimento, experimentos e testes de produtos cosméticos, de higiene pessoal, perfumes e seus componentes no Estado do Amazonas, e dá outras providências.

A MESA DIRETORA DA ASSEMBLEIA LEGISLATIVA DO ESTADO DO AMAZONAS, na forma da alínea e, I, do artigo 17, da Resolução Legislativa n. 469, de 19 de março de 2010, Regimento Interno, faz saber a todos que a presente virem que promulga a seguinte

LEI PROMULGADA:

Art. 1.º Fica proibida, no Estado do Amazonas, a utilização de animais p... testes de produtos cosméticos, de higiene pessoal, perfumes e seus ... legislação Municipal, Estadual ou Federal.
Art. 2.º Para os fins dos dispositivos constantes no art... pessoal, perfumes as preparações constituídas por ... partes do corpo humano, pele, sistema ... mucosas da cavidade oral, com o ob... ou alterar odores corporais e ou pr...
Parágrafo único. São exemp...
I - cremes, esmaltes...
II - maquiagem;
III - ba...

2014

- State bans in São Paulo and Mato Grosso do Sul.
- Bill 70/2014 moves to the Federal Senate
- CONCEA Normative Resolution 18 (17 OECD Methods recognized

2015

- State bans in Paraná and Amazonas.

2016

- State ban in Pará.
- CONCEA Normative Resolution 31. (6 OECD methods recognized).

2017

- State ban in Rio de Janeiro
- Senator Randolfe Rodrigues' report is voted by Commission of Science and Technology.

2018

- State ban in Minas Gerais.
- Senator Gleisi Hoffmann's report published. Bill 70/2014 moves to Plenary chamber.

Senator Gleisi Hoffmann's report on Bill 70/2014

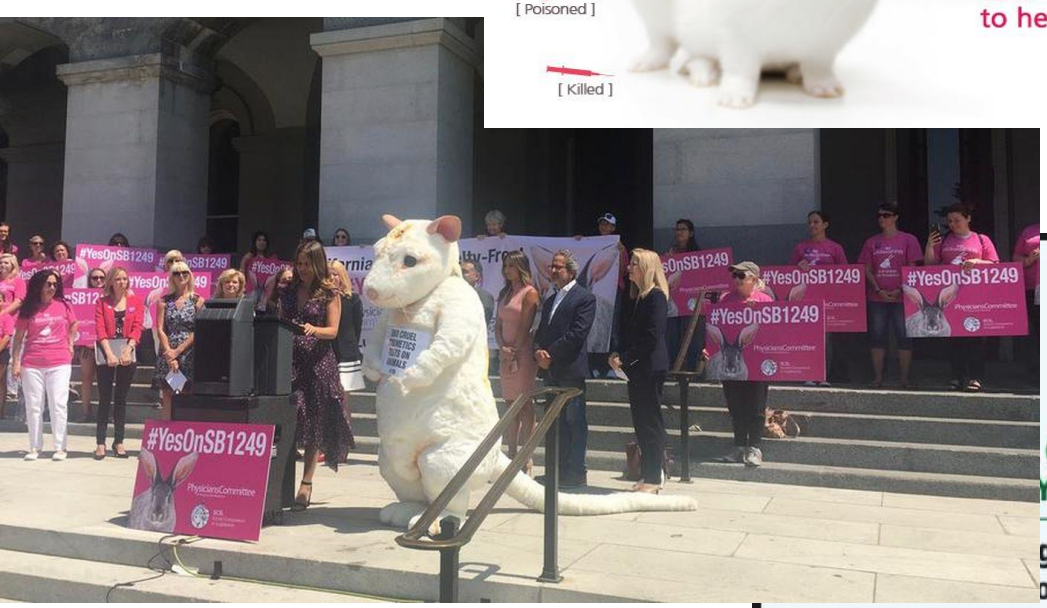
1. Immediate ban on testing cosmetic products on animals.
2. Ban on testing cosmetic ingredients on animals, within three years.
3. Ban on submitting data obtained from tests on animals conducted after the cut-off date, within three years.
4. Derogation for exceptional circumstances.

Be Cruelty-Free in the Americas

Canada, it's time to **ban** cosmetic testing on animals.

take action to help **www.BeCrueltyFree.ca**

HUMANE SOCIETY INTERNATIONAL · ANIMAL ALLIANCE OF CANADA · LUSH FRESH HANDMADE COSMETICS



Regulatory Toxicology: Reducing animal testing requirements in pesticides regulation

Advances defended throughout the pesticide regulation revision:

- The waving of the one-year dog study;
- The compulsory use of all alternative methods and validated testing strategies already accepted by the OECD;
- The wave of toxicological studies, if this is justified technically.
- Use of the the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Regulatory Toxicology: Introducing strategies to develop alternative methods in Brazilian chemical legislation

as informações e os estudos complementares requeridos será de 120 dias, contados a partir da solicitação do Comitê Técnico, prorrogáveis mediante justificativa técnica do interessado, podendo a avaliação de risco ser concluída somente com base nas informações disponíveis.

Art. 19. A realização de novos estudos com a utilização de animais deve ser o último recurso, depois de esgotadas todas as possibilidades de métodos alternativos.

§ 1º Os métodos alternativos à experimentação com animais a que se refere o caput devem ser reconhecidos cientificamente e apresentarem um grau de confiabilidade considerado adequado para uma tomada de decisão, pelo Comitê Técnico.

§ 2º A autoridade federal responsável pelo setor de meio ambiente, em consulta com instituições afetas, estabelecerá um plano estratégico para promover a utilização de métodos alternativos à experimentação com animais.

Art. 20. O Comitê Técnico poderá constituir grupo consultivo ou convidar especialistas e pesquisadores da academia, indústria e sociedade civil para subsidiar a avaliação de risco das substâncias químicas.

Parágrafo único: O grupo consultivo terá mandato temporário a ser definido pelo Comitê Técnico.

Art. 19. New studies on using animals should be the last resort after all alternative methods have been exhausted.

§ 1 Alternative methods to animal experimentation mentioned in this article must be scientifically recognized and present a suitable degree of reliability in order for the Technical Committee to be able to take a decision.

§ 2 The federal authority responsible for the environment sector, in consultation with impacted institutions, will establish a strategic plan to promote the use of alternative methods to animal experimentation.

Perspectives | Brief Communication

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1510345.

Lessons from Toxicology: Developing a 21st-Century Paradigm for Medical Research

http://dx.doi.org/10.1289/ehp.1510345

SUMMARY: Biomedical developments in the 21st century provide an unprecedented opportunity to gain a dynamic systems-level and human-specific understanding of the causes and pathophysiologies of disease. This understanding is a vital need, in view of continuing failures in health research, drug discovery, and clinical translation. The full potential of advanced approaches may not be achieved within a 20th-century conceptual framework dominated by animal models. Novel technologies are being integrated into environmental health research and are also applicable to disease research, but these advances need a new medical research and drug discovery paradigm to gain maximal benefits. We suggest a new conceptual framework that repurposes the 21st-century transition underway in toxicology. Human disease should be conceived as resulting from integrated extrinsic and intrinsic causes, with research focused on modern human-specific models to understand disease pathways at multiple biological levels that are analogous to adverse outcome pathways in toxicology. Systems biology tools should be used to integrate and interpret data about disease causation and pathophysiology. Such an approach promises progress in overcoming the current roadblocks to understanding human disease and successful drug discovery and translation. A discourse should begin now to identify and consider the many challenges and questions that need to be solved.

Introduction

The genomics era opened a door to understanding genetic changes in susceptibility to diseases, such as single nucleotide polymorphisms, gene copy number variations, and gene deletions and insertions (Zerhouni 2014). The subsequent explosion of related "omics" approaches, including transcriptomics, metabolomics, and proteomics, have provided more details of how gene regulation and protein production are implicated in human disease mechanisms.

However, many human illnesses such as cancers, diabetes, immune system and neurodegenerative disorders, and respiratory and cardiovascular diseases are caused by a complicated interplay between multiple genetic and environmental factors (Lango and Weedon 2008). The environmental counterpart to genomics is exposomics, which aims to capture an individual's lifetime exposure to external factors (e.g., infections, environmental chemicals, drugs, radiation) measured via biomarkers in blood, urine, feces, or breath samples. It provides an opportunity to develop an environmental analog of possibility of gaining a dynamic systems-level and human-specific understanding of the causes and pathophysiologies of disease (van de Stolpe and Kauffmann 2015). This understanding is a vital need, in view of current failures (Scannell et al. 2012; Kaitin and DiMasi 2011) in health research, drug discovery, and clinical translation (Collins 2011). But these developments in human-specific models and tools require a new research paradigm to unlock their full potential. We suggest it is time for a novel, overarching paradigm for medical research based on adapting and applying the transitional process underway in toxicology that includes reducing reliance on animal models, and instead emphasizing human biology and approaches based on multiscale pathways.

Discussion

In future health research and drug discovery, diseases can be envisaged as the combined outcome of extrinsic causes that include many types of exposures, not just chemical exposures, and intrinsic genetic and epigenetic changes (e.g., Gohlke et al. 2009) that interact at multiple levels (Figure 1). This combined approach would provide a more coherent "big picture" by linking environmental sciences with medical research.

Some of the thinking required to develop a more comprehensive framework for understanding disease causation has already begun. Toxicologists and environmental health scientists are already devising new models that explore synergies between toxic exposures and infectious pathogens in complex diseases, exemplified by interactions between the hepatitis B virus and aflatoxin in liver cancer (Birnbaum and Jung 2010).

A new medical research paradigm. To maximize the value of advanced models and technologies, we believe that a new paradigm is needed for fundamental research into human diseases and for drug discovery. The focus should move decisively away from preclinical animal studies and overly simplistic cell models toward a systems biology framework to integrate new types of scientific data, such as from omics, novel human-specific *in vitro* models, and clinical studies. Such a framework would help enable a comprehensive and dynamic understanding of disease causation and pathophysiology.

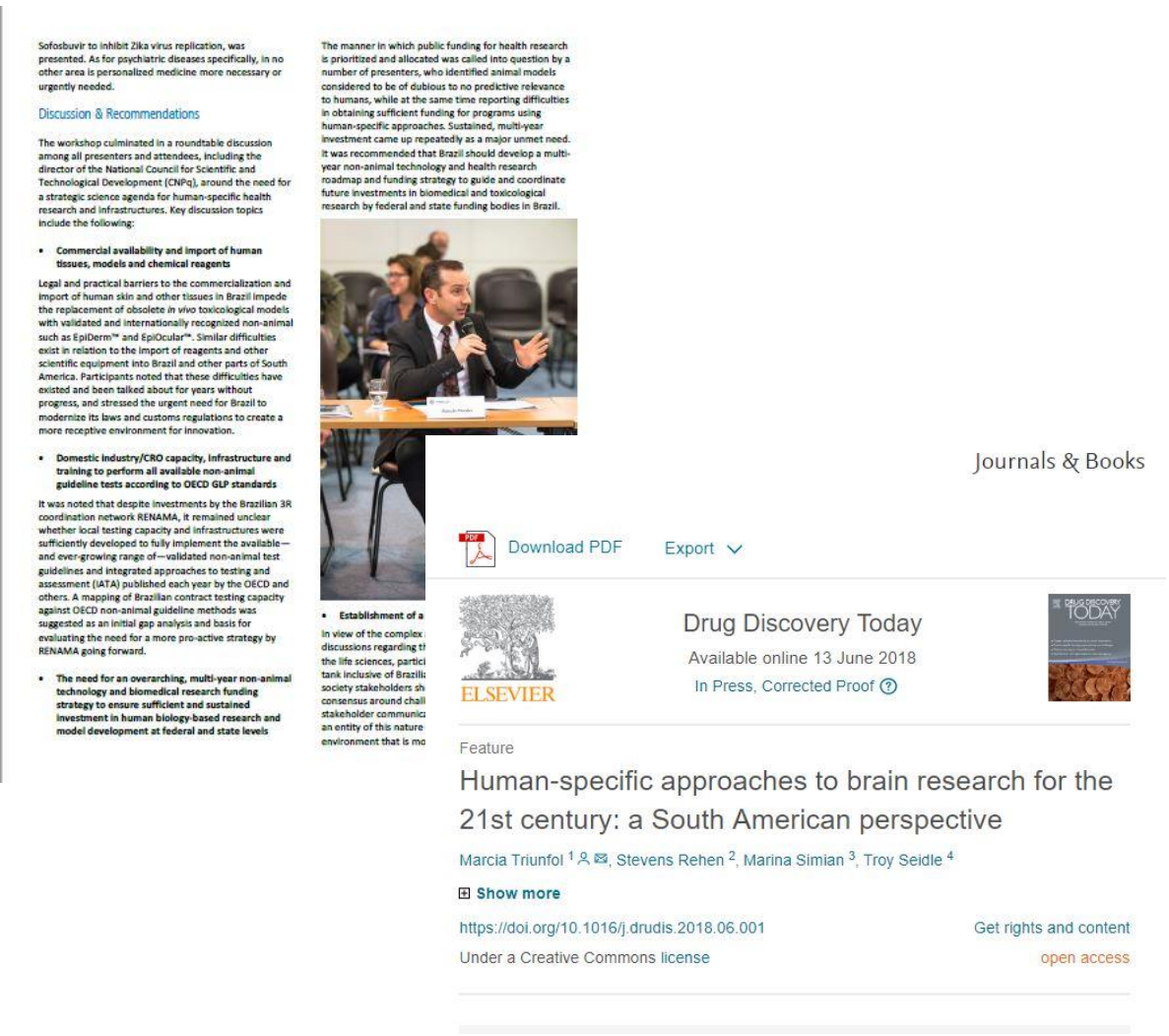
A concept that systematically describes links between causes of disease and outcomes could be repurposed from 21st-century toxi-

Peer review studies supported by Biomed21

Alzheimer's disease: "Many novel compounds for AD have entered clinical trials, but so far none has successfully completed a Phase III trial."
Amyotrophic lateral sclerosis: "Over the past decade, investigational new drug applications based on data collected using animal models of ALS have resulted in 11 human clinical trials, all of which failed to demonstrate efficacy."
Asthma: "In addition to the documented immunological differences between mice and humans …one must question whether continued reliance on the animal model is simply a case of remodelling an inadequate model."
Autism spectrum disorder (ASD): "The lack of pharmacologic treatments for the core symptoms of ASD may be a consequence of the lack of a human model."
Autoimmune disease: "Even mice with a "humanized" immune system lack the complex human genetics underlying autoimmune disease, while organ/tissue antigens remain non-human, interfering with recapturing human immune response and tolerance mechanisms."
Non-alcoholic steatohepatitis (liver disease): "Animal models, mostly based on specific diets and genetic modifications, are often employed in anti-NASH drug development. However, due to interspecies differences and artificial pathogenic conditions, they do not represent the human situation accurately and are inadequate for testing the efficacy and safety of potential new drugs."
Tuberculosis: "To further reflect the complex environment and structure of the human lung, a growing body of studies are resorting to the use of new technologies in the tissue-engineering field to advance human-based TB research models into the 3D era."

The BIOMED21 Workshops

Rio de Janeiro 2017 Workshop: Summary of Key Conclusions



Sofosbuvir to inhibit Zika virus replication, was presented. As for psychiatric diseases specifically, in no other area is personalized medicine more necessary or urgently needed.

Discussion & Recommendations

The workshop culminated in a roundtable discussion among all presenters and attendees, including the director of the National Council for Scientific and Technological Development (CNPq), around the need for a strategic science agenda for human-specific health research and infrastructures. Key discussion topics include the following:

- **Commercial availability and import of human tissues, models and chemical reagents**

Legal and practical barriers to the commercialization and import of human skin and other tissues in Brazil impede the replacement of obsolete *in vivo* toxicological models with validated and internationally recognized non-animal such as EpiDerm™ and EpiOcular™. Similar difficulties exist in relation to the import of reagents and other scientific equipment into Brazil and other parts of South America. Participants noted that these difficulties have existed and been talked about for years without progress, and stressed the urgent need for Brazil to modernize its laws and customs regulations to create a more receptive environment for innovation.

- **Domestic industry/CRO capacity, infrastructure and training to perform all available non-animal guideline tests according to OECD GLP standards**

It was noted that despite investments by the Brazilian 3R coordination network RENAMA, it remained unclear whether local testing capacity and infrastructures were sufficiently developed to fully implement the available—and ever-growing range of—validated non-animal test guidelines and integrated approaches to testing and assessment (IATA) published each year by the OECD and others. A mapping of Brazilian contract testing capacity against OECD non-animal guideline methods was suggested as an initial gap analysis and basis for evaluating the need for a more pro-active strategy by RENAMA going forward.

- **The need for an overarching, multi-year non-animal technology and biomedical research funding strategy to ensure sufficient and sustained investment in human biology-based research and model development at federal and state levels**

The manner in which public funding for health research is prioritized and allocated was called into question by a number of presenters, who identified animal models considered to be of dubious to no predictive relevance to humans, while at the same time reporting difficulties in obtaining sufficient funding for programs using human-specific approaches. Sustained, multi-year investment came up repeatedly as a major unmet need. It was recommended that Brazil should develop a multi-year non-animal technology and health research roadmap and funding strategy to guide and coordinate future investments in biomedical and toxicological research by federal and state funding bodies in Brazil.

- **Establishment of a**

In view of the complex
discussions regarding t
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Drug Discovery Today

Available online 13 June 2018

In Press, Corrected Proof

Feature

Human-specific approaches to brain research for the 21st century: a South American perspective

Marcia Triunfol [1], Stevens Rehen [2], Marina Simian [3], Troy Seidle [4]

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https://doi.org/10.1016/j.drudis.2018.06.001

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- A 21st century roadmap for biomedical research is needed.
- To advance 21st century human-specific scientific progress, funding should be focused on acquiring critical human information.
- International and interagency collaboration is critical: formal collaboration between major organizational and funding bodies should be established.

BIOMED 21
COLLABORATION
Toward a human-focused paradigm in health research

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BioMed21 Workshop Series

Chris Austin, director of NCATS, explains »

ICCVAM Strategic Roadmap now available in five languages

Earlier this year, the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) published its new Strategic Roadmap for Establishing New Approaches to Evaluate the Safety of Chemicals and Medical Products. This seminal document offers a consensus perspective, incorporating the views of 16 federal regulatory and research agencies, several interagency workgroups and public opinion. [Read more...]

2018 Lush Prize Nominations Open

Are you working on an initiative that seeks to replace animal use in toxicology or research? Then you may be eligible for a Lush Prize in one of five categories: Lobbying; Public Awareness, Science; Training and Young Researcher. [Read more...]

UK Report Advocates "Humanizing" Drug Development

A new joint report by the BioIndustry Association and Medicines Discovery Catapult advocates humanizing drug development to reduce drug attrition rates, improve research productivity, and generate better drug candidates for clinical trials. The report recognizes the low predictive power of existing preclinical models and states the need for improvements in humanizing drug discovery—focusing on patient biomarkers, better use of emerging toxicology tools and models, more data sharing (beyond just clinical trial data), and the validation and dissemination of novel, complex in vitro models beyond their current, siloed academic applications. [Read more...]

Advanced Maturation of NIH-Funded Human iPSC Cardiac Model

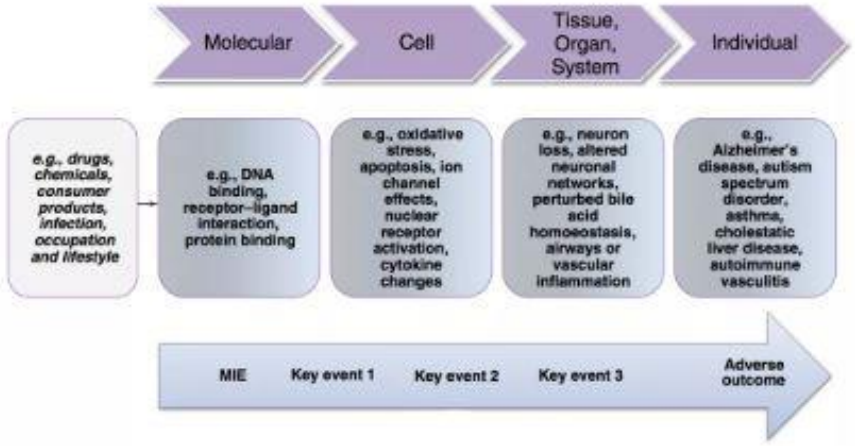
Excerpted from the National Institutes of Health:

"Researchers are now able to use induced pluripotent stem cells (iPSC) to form a model of human adult-like cardiac muscle by introducing electric and mechanical stimulation at an early stage. Since this muscle is similar to the adult heart, it could serve as a better model for testing the effects of drugs and toxic substances than current tissue-engineered heart models. The study, performed by scientists at Columbia University, New York City, and funded by the National Institutes of Health, was published today in Nature."

Our Collaboration brings together scientists and institutions from across Europe, Asia and the Americas who share a vision of a new, human-focused paradigm in health research. This unique mix of health research stakeholders provides both a broad, global outlook as well as deep ties at regional and national levels. We welcome new collaboration opportunities with like-minded organizations and individuals.

What would a new approach look like?

A cornerstone of a new approach is an organizing framework linking molecular initiating events in disease pathways and networks with adverse outcomes, akin to the "adverse outcome pathway" (AOP) approach under development in toxicology. Such a framework could provide a more predictive and effective rubric for understanding disease pathophysiology across levels of biological organization, and for targeting and evaluating new interventions using the growing toolbox of modern, human-specific approaches such as 3D tissue models, microfluidic organs-on-a-chip, computational systems biology modelling, and others.



Regional contacts

North America
Catherine Willett, PhD
HSI/HSUS Senior Director for Science & Regulatory Affairs
Research Gate
LinkedIn

Europe
Lindsay Marshall, PhD
HSI/HSUS Science Communications Officer
Research Gate
Linkedin

Latin America
Marcia Triunfol, PhD
HSI Science Advisor, Latin America
Linkedin

Asia
Brinda Poojary, PhD
HSI Science Advisor, India
Research Gate

Call for Proposals: Latin America

Roadmaps to Human Biology-Based Disease Research

To support strategic scientific dialogue around the concept of extending the vision of "21st century toxicology" to the wider biosciences, Humane Society International is offering grants of $5,000 (USD) to support the development and open-access publication of in-depth, independent review articles in discrete areas of human disease/biomedicine by health scientists with relevant expertise.

Each review should:

- Examine the state of the science in a specific area of human biomedicine, including current understanding of the underlying pathophysiological pathways and networks;
- Critically evaluate the human relevance, translational success and limitations of conventional research models;
- Offer concrete recommendations/roadmap for optimizing the funding and use of advanced, human-specific tools and approaches (pathway paradigm as an organizing framework, primary human cells/tissues, iPSC, organoids, bioengineering, computational systems biology modeling, etc.) in the disease area under discussion; and
- Be accepted for publication in a high-visibility, peer-reviewed journal.

A scientific workshop will be convened in 2019 to explore the findings and recommendations of funded review articles. Lead authors will be invited to attend and present their work, and contribute to a subsequent workshop report. Travel, accommodations and meals will be arranged.

Key Dates | Who can apply | How to apply | Funding conditions | Related documents


25 Years of
Celebrating Animals
HUMANE SOCIETY
INTERNATIONAL
Thank you!