

B²¹OMED

EMERGING TECHNOLOGY TOWARD PATHWAY- BASED HUMAN BRAIN RESEARCH

Rio de Janeiro, 29-30 May 2017

WORKSHOP *Flash* REPORT



**HUMANE SOCIETY
INTERNATIONAL**
hsi.org



Latin American scientists and stakeholders call for national strategy and funding boost for human-relevant approaches to health research and safety testing, emphasizing non-animal technology infrastructures such as human stem cells, organoids and organs-on-a-chip.

Leading Brazilian and international health scientists and other stakeholders met in Rio de Janeiro in May 2017 for the workshop *BioMed21: Emerging Technology Toward Pathway-Based Human Brain Research*. The workshop – organized by Humane Society International as part of a global scientific series^{1,2,3,4} and hosted by the D’Or Institute for Research and Education – examined the development and application of various human biology-based tools for modeling brain diseases with the aim of identifying actionable, consensus recommendations to guide future funding and developments in this area.

The workshop was inaugurated with a presentation on the historical path that started in 1906 when the first drops of cell culture were examined under the microscope, through the birth of induced pluripotent stem cell (iPSC) technology in the beginning of the 21st century. Subsequent presentations illustrated how iPSCs are now

being used to study a variety of brain diseases, including microcephaly-causing Zika virus, Dravet disease, autism, neuropsychiatric disorders, Amyotrophic Lateral Sclerosis and Parkinson Disease, and how these modern, human biology-based tools are being used as an alternative to animal models in labs worldwide. Similarly, human ‘mini-brain’ organoids and organs-on-a-chip were presented as promising new tools for pre-clinical research and testing for drug safety and efficacy.

Modern, human-based technologies offer the possibility of using patients’ cells to study diseases, test new drugs and develop tailor-made treatments according to each patient characteristics. Virtually all presentations included work that has been done using patients’ cells. Testing of potential new drugs such as Cannabidiol to treat epilepsy in Dravet Syndrome, Chloroquine to protect from microcephaly-causing Zika virus, or

¹ Langley G, et al. *Environ Health Perspect*. 2015;11:A268-72.

² Langley G, et al. *Drug Discov Today*. 2016;22:327-39.

³ <https://ntp.niehs.nih.gov/go/biomed21>

⁴ <http://www.biomed21.org>

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 strategic science ‘think-tank’**

In view of the complex and often polarized nature of discussions regarding the replacement of animal use in the life sciences, participants recommended that a think-tank inclusive of Brazilian scientific, corporate and civil society stakeholders should be established to help build consensus around challenging topics. Improved stakeholder communication and collaboration through an entity of this nature could contribute for an environment that is more receptive for innovative ideas.

Such a group could also be used to connect research groups across Brazil and South America using non-animal technologies for sharing knowledge and resources. Further, coordinated applications for grants as a group could potentially be facilitated by such a group.

- **The role of scientific journals in driving or impeding a paradigm shift in human health research**

Scientific journal editors and peer reviewers were identified as either a positive force that could contribute to the advancement of human-specific approaches in biomedical research or as a negative force that many times requires that *in vitro* results are also demonstrated *in vivo*. Some participants noted that reliance on non-

animal-based research findings or statements critical of the current paradigm remain a deal-breaker in terms of publication in some peer-reviewed journals due to reviewer conservatism or overt bias. A suggestion was made that an inventory could be created of animal models have not generated useful results as a reference for research funding bodies and institutional ethics committees. A further strategy to reduce the number of animals used in Brazilian health research was suggested by CNPq, which announced its intention to map all animal facilities and register only the few that adhere to national regulations. CNPq also announced the creation of an online platform to provide continuing education to researchers on how to handle animals in the laboratory.

Participants

Dr Patricia Beltrão-Braga, University of São Paulo, Brazil

Dr Gerson Chadi, University of São Paulo, Brazil

Dr Fabio Klamt, Federal University of Rio Grande do Sul, Brazil

Dr Maristela Martins de Camargo, University of São Paulo, Brazil

Dr Joseph R Mazzulli, Northwestern University Feinberg School of Medicine, USA

Dr Carla Molento, Federal University of Paraná, Brazil

Dr Marcelo Morales, National Council for Scientific and Technological Development (CNPq), Brazil

Dr Juliana Minardi Nascimento, University of Campinas, Brazil

Dr Eduardo Pagani, National Biosciences Laboratory (LNBio/CNPEM), Brazil.

Dr David Pamies, Johns Hopkins University, USA

Dr Georgia Quadrato, Harvard Stem Cell Institute, USA

Dr Stevens Rehen, D'Or Institute for Research and Education and Federal University of Rio de Janeiro, Brazil

Troy Seidle, Humane Society International, Canada

Dr Marina Simian, Instituto de Nanosistemas, Universidad Nacional de San Martín, Argentina

Dr Bruno Henrique Silva Araujo Torres, National Biosciences Laboratory (LNBio/CNPEM), Brazil

Dr Marcia Triunfol, Humane Society International, Brazil

