Report on HuSCID Mice and Applications event at ACTREC

Webinar on "Humanized Mice and Applications in Healthcare Research" was conducted at ACTREC on 19th August, 2021. Event was inaugurated by Dr Sudeep Gupta, Director, ACTREC at 5.30pm. His talk was followed by speech by Dr Prasanna Venkatraman, Event Chairperson and Deputy Director, CRI-ACTREC. This event was conducted in memory of late Dr Shyam Somasundaram, CRI-ACTREC alumni and alumni of The Wistar Institute, Philadelphia, USA. Dr Shyam had published landmark paper in the field of Melanoma Therapeutics research using Humanized Mice model just a month prior to his journey to heavenly abode. Dr Robin Mukhopadhyaya, an ex- senior scientist at CRI-ACTREC and a close friend of Dr Shyam, spoke about his association and strong bonding they shared on personal as well as professional front.

We had 627 registered participants for this webinar. Event was streamed live on You Tube channel (https://bit.ly/2WgZIeX). Total of 790 views were reported on 24th August on You Tube video of the event proceedings.

First talk of event by Dr Jyoti Kode on "Humanized Mice: ACTREC Experience" covered basics of mice in cancer research, history and development and how to choose mice models based on requirements. Later she discussed her work on humanized mice using NOD-SCID mice and enriched CD34+ cells from mobilized peripheral blood of stem cell transplant donors. Her work demonstrated using this model how ex-vivo expansion of CD34+ hematopoietic cells can be expanded using chemokine cocktail while retaining its stemness and homing capacity. This was followed by talk by Dr Loui Madakamutil. He covered the use of humanized mice in drug discovery and development. This talk primarily covered the humanized immune system (HIS) models used during drug development in immune oncology and autoimmune diseases. Specifically, case studies in the use of humanized mice in CAR-T cell discovery and development were highlighted. Later on, case studies for the use of humanized mice in anti-TNF therapies for Rheumatoid arthritis was used as example to show the value of humanized TNFa transgenic mice for development of Remicade, Humira, Enbrel and other drugs. Loui also showed example for the use of human HLA-DR transgenic mice for the development of antigen specific tolerance inducing modalities. Finally, the use of humanized mice in the study of cytokine release syndrome (cytokine storm) was discussed. Dr. Eric Ramirez-Salazar paid tribute to Dr. Shyam at the onset of his talk and shared his memories of association with Dr. Shyam while he joined his lab recently. Dr. Eric later talked about data on a recently published paper where they created humanized mice model which reconstitutes all significant components of human immune cells. This model helps understand the role of immune cells in the tumor microenvironment. In a first approach, this model has been used to understand the drug resistance of melanoma patients to immune checkpoint blockers. Dr Balaji Ramchandran spoke on utility of humanized mice models in immuno-oncology studies. Humanized mice models are more sophisticated and robust platform for screening IO check point inhibitors (eg. anti-PD1, anti-PD-L1, anti-CTLA4 etc.). He presented a case study on effect of immune check point inhibitors (as standalone and in combination) in huNOG:EXL mice bearing subcutaneous PC-3 (Prostate) tumor and second case study on selective recruitment of a subset of T cells by a bispecific antibody in acute myeloid leukemia (AML) animal model.

Panel discussion was moderated by Dr Narendra Chirmule and participants were Dr Loui Madakamutil, Dr Eric Ramirez-Salazar, Dr Balaji Ramachandran, Dr Purvi Thakkar and Dr Jyoti

Kode. In the short discussion, the panel listed some of the questions that the field of HuSCID mice for the use in Immuno Oncology.

1. How can we stop using fetal tissue for generating HuSCID mice? (e.g., with iPSC)
2. How can variability in generating HuSCID mice be studied, and reduced?
3. How can these mice be used for understanding safety and efficacy studies in breast cancer, and other solid tumor t
4. How can we study non-immune cells, other clinical indications (e.g. autoimmunity etc.).
5. How do we design these HuSCID mice studies that can inform human responses faithfully?
6. How can we develop and qualify predictive biomarkers using HuSCID mice?
7. What is the value of this model to regulatory requirements?

Rapid Final Comments

Requirements	Measurements	Challenges
CD34	T cell function	Cost
IL3	Tumor efficacy	Time
IL7	Roles of other cells	Autoimmunity (e.g., Lupus)
Beyond T cells	Non-immune cells	Autology models
Hematogical Differentiation	Multiplex imaging	Larger therapuetic windown
Housing needs	Macrophges	Laboratory requirements
Special requirement	NK cells	Animal requirements
Training animal handling	Tumor response	Biomaterials
Understading of biology	Innate	3D printing technology
Colllaboration	Microbiome	Define regulatory

Event supporters included BD India Pvt. Ltd., BioTechne Brands and Ateos Foundation of Science, Education & Research.

Dr Nirmal Kumar, Mr Naythan Dcunha, Ms Priyanka Patole, Ms Pallavi Ellango, Ms Arti Patil and IT team Mr Rohit and Rajesh helped enthusiastically in financial, administrative matters and conducting event smoothly.

Meeting ended with Vote of thanks delivered by Dr Ojaswini Upasani, Event Coordinator at 8.15pm.