Humanized models to study immunity and to accelerate the development of new solutions for human health

Les Pensières Fondation Mérieux Conference Center Veyrier-du-Lac - France

26-28 April 2017

Steering Committee:

- Jacques Banchereau
- Nicolas Burdin
- James Di Santo
- Markus Manz
- Jacques Louis
- Valentina Picot



Background

Translational research has emerged as one of the main pillars of the development of new vaccines or drugs over the past decade. It is indeed an absolute requirement for the pharmaceutical industries to better de-risk their candidates between preclinical proof of concept (PoC) in conventional animal models and the uncertain outcome of an efficacy study that usually takes place several years to a decade after, implying several hundreds of millions of dollars invested with a probability of success very often poorly controlled. A large number of parameters differ in the course of an immune response between laboratory animal models and human beings. Some of them are intrinsic to the host such as genetic polymorphism, metabolisms, physiology and specificities of the immune system (innate immune receptor distributions, differences in cell subset phenotype and functions, some variations in lymphatic or organic immune macro- and micro-architectures ...). Others are environmental such as susceptibility or resistance to infections, co evolution of the host with the pathogen, impact of stress stimuli, role of the flora or of concomitant infections and immune history.

The development of new models to refine candidate selections has been the focus of many efforts to credentialize the preclinical PoC established in classical in vivo models such as laboratory mouse strains and non-human primates. This includes the use of simple to very sophisticated in vitro models based on human cells to test the potency of the compounds in vitro (from PBMCs in a well, to 3D cell cultures and organs on a chip). The latters, limited by their inherent in vitro attributes, have been nicely complemented by the development of animal models which have been humanized in order to better mimic the human responses so as to hopefully better predict outcomes in the targeted populations. Efforts towards the successful engraftment of human genes or gene loci first, of human hematolymphoid cells thereafter and finally of other human tissue cell types, started in the early 1990's. Since then, the discovery and introduction of multiple targeted mutations into the host have continuously improved the quality and duration of such genetic, cellular and tissue engraftments.

The symposiums will be dedicated to the review of the most recent advancement in the development of such chimeric animal models and the impacts of the improvements of their humanization on the translation of new drug, mabs or vaccine candidates as well on the discovery of mode of actions, the identification of correlates of protection and of relevant biomarkers to human diseases, in the fields of oncology, autoimmunity, inflammatory and infectious diseases.

Scientific programme

Wednesday	26th	April 2017

17:30 - 18:30	Registration	
18:30 - 19:00	Welcome address	Fondation Mérieux Nicolas Burdin
19h00	Welcome dinner	

Thursday 27th April 2017

Session 1

New development for the construction of humanized mice			
Chair: Jim Di Santo			
8:30 - 8:50	Generation of improved humanized mouse models for human infectious diseases	Lenny Shultz	
8:50 - 9:10	Discussion		
9:10 - 9:30	Humanized mice to study human hematopoietic stem cells differentiation	Claudia Waskow	
9:30 - 9:50	Discussion		
9:50 - 10:10	Next generation humanized mouse models for normal and malignant hematopoiesis	Alexandre Theocharides	
10:10 - 10:30	Discussion		
10:30 - 11:00	Coffee break		
11:00 - 11:40	Key-note address: Genetic engineering of human hematopoiesis and its preclinical modeling in hematochimeric mice	Luigi Naldini	
11:40 - 11:55	Discussion		

Session 2

Humanized mouse models for the study of the physiopathology of infectious diseases

Chair: Nicolas Burdin & Jacques Louis

11:55 - 12:15	In vivo platforms for analysis of HIV persistence and eradication	Victor Garcia
12:15 - 12:35	Discussion	
12:35 - 14:00	Lunch	

Scientific programme

14:00 - 14:20	Humanized mice to study the role of lymphocyte trafficking in HIV dissemination	Maud Deruaz
14:20 - 14:40	Discussion	
14:40 - 15:00	Modeling human liver development, chronic hepatitis virus infection, immunopathogenesis and therapy in mice	Lishan Su
15:00 - 15:20	Discussion	
15:20 - 15:50	Coffee break	
15:50 - 16:10	Animal models of human oncogenic gamma- herpesvirus infection	Christian Mûnz
16:10 - 16:30	Discussion	
16:30 - 16:50	Humanized mouse models of Filovirus infection and disease	Joseph Prescott
16:50 - 17:10	Discussion	
17:10 - 17:30	Application of humanized mice models in exploring novel therapy strategies against human diseases	Jian Zheng
17:30 - 17:50	Discussion	
19:00	Dinner	

Friday 28th April 2017

Session 3a)

Humanized mouse models for the study of cancers development and therapy (personalized medicine).

Tumors of the hemopoietic origin.

Chair: Alexandre Theocharides

8:30 - 8:50	The use of the AML xenograft model to translate leukemia stem cell biology to the clinic	Jean Wang
8:50 - 9:10	Discussion	
9:10 - 9:30	Humanized models to study myeloid malignancies	Dominique Bonnet
9:30 - 9:50	Discussion	
9:50 - 10:10	A leukemia xenograft model that is representative of de novo drug resistant and very high risk ALL in NOD/SCID/gamma null mice	Jean-Pierre Bourquin
10:10 - 10:20	Discussion	
10:20 - 10:45	Coffee Break	

Scientific programme

Session 3b)

Humanized mouse models for the study of cancers development and therapy (personalized medicine).

Solid Tumors

Chair: Nicolas Burdin

10:45 - 11:05	Evaluation of cancer immunity in cancer mouse models	Jacques Banchereau
11:05 - 11:25	Discussion	

Session 4

Humanized mice models for the study of the human immune-induced diseases in humans

Chair: Jacques Banchereau		
11:25 - 11:45	A humanized mouse model to study atopic dermatitis	Jim Di Santo
11:45 - 12:05	Discussion	
12:15 - 14:00	Lunch	
14:00 - 14:20	A humanized mouse model to study insulinspecific tolerance and islet autoimmunity	Carolin Daniel
14:20 - 14:40	Discussion	
14:40 - 15:00	Concluding remarks and general discussion	Members of the Steering Committee

