Summary of Vienna`s 3rd Animal Workshop (May 14-16)

Besides rapping up BTCure`s SOP work, making decisions on their publication and discussing new animal models, that have not yet been presented, the main focus of the 3rd animal workshop was the presentation and discussion of –omics work performed in selected mouse models.
In addition, there has been an own short session on neutrophils and NETs, which are currently actively discussed. Moreover, imaging and in vivo monitoring techniques were presented to follow up on functional impairment over time.

As in previous workshops the mouse as a model in RA was critically reviewed, in particular due to recent, critical publications and views in this regard, which are challenging the mouse as a model system. However, critically voices in this regard only support the goal of BTCure`s animal work which aims to standardize and improve the use of models. Keynote speaker **Cory Brayton (Baltimore)** presented some reasons why mouse data sometimes lack quality and reproducibility, as insufficient documentation and nomenclature, wrong presentation of results and data, as well as the selection of inappropriate models and strains. These examples clearly show a need to improve research performance rather than they challenge the model per se.
Josef Smolen (MUW) outlined the clinical perspective. He explained the current criteria that are used to monitor human disease activity over time as clinical response rates. He also explained the currently used multifactor composite measures that are used to classify and compare patients. Josef Smolen mentioned how difficult it has been in the past to show differences in drug responses of different investigated targets and biologics. He gave some examples for targets that originally showed good results in the CIA model but could not be verified in clinical studies. He outlined the importance to use clinical insights and to more often apply bedside to bench approaches. Josef Smolen also highlighted that there is still a high need for molecular markers to distinguish between responders, to predict a profound response, as well as more markers for the risk of developing RA, and a need for mouse models that reflect RA better than currently most widely used and common models.
Stephan Blüml (MUW) highlighted the academia perspective and the importance of models to understand pathogenic disease, to investigate potential therapeutics and their MoA. *In vitro* cell cultures do not reflect the complexity of organisms, the accessibility and access of drugs to organ. More complex models also play an important role for the visualizations of pathogenic processes. Stephan Blueml explained the need for good models that cover and reflect the adaptive (as CIA and SKG) and innate (CAIA/K/BxN serum transfer, hTNFtg) immune system. He outlined our promising efforts to standardize animal work, and the promising combination of techniques: as conditional KO, imaging tools, -omics technologies.

Adrian Moore (UCB) gave an insight into the industry perspective. Companies have been investing more and more R&D expenditure the last decades. However, while the number of drugs tested increased, the number of drugs approved decreased. Only about 10% of drugs entering clinical trials will make it to approval, with most failing in PhIII. In the future a stronger case will have to be made for species selection. Choosing models based on phenotypes only is of limited value. Moreover, it is becoming more and more obvious to choose the right patient populations and treat the right patients groups for the best effect. Again the need for biomarkers was highlighted. Patient stratification can be complex, thus there is a need of good efficacy biomarkers in humans and mice.
Giulia Superti Furga (CeMM, Vienna) was another keynote speaker and shared his expertise in the area of -omics methods and analysis. He explained pitfalls and highlighted the importance of using more than a single line of analysis since usually one -omics method is not sufficient. If possible results should be aligned with other results, as from transcriptomics, and methylation experiments, etc. We still do not know the MoA of most drugs and we underestimate the complexity of drug targets and the number of genes contributing to one process. He explained the strategy of his group to elucidate and understand the MoA of investigated targets. He recommended using well-characterized single cell systems in addition to more complex systems, as xenograft models.

For a more details on other talks and speakers, please have a look at the workshop program at the end of this report.

For more information on BTCure decisions that have been taken with regard to future SOP and –omics work, please contact Rikard Holmdahl, Günter Steiner, or Adrian Moore.

3rd BTCure Workshop on Animal Models

May 14-16 2014, Imperial riding school Renaissance Hotel, Vienna, Austria

DAY 1: Wednesday May 14 2014

14:45 Welcome (Günter Steiner, MUV)

Relevance of animal models for Research and Industry		
Chair: Neil Gozzard (UZB), Günter Steiner (MUV)		
15:00 – 16:00	Cory Brayton (Baltimore)	Immunological variation between inbred mouse strains, and sources
16:00 – 16:30	Stefan Blüml (MUV)	The academia perspective
16:30 – 17:00	Adrian Moore (UCB)	The industry perspective
17:00 – 17:30	Josef Smolen (MUV)	The clinician´s perspective
17:30 – 18:00	General Discussion	

19:00 Dinner at Hotel

DAY 2: Thursday May 15 2014

OMICS		
Chair: N.N.		
09:00 – 10:00	Giulio Superti-Furga (CeMM Vienna)	Power and Pitfalls of Proteomics
09:45 – 10:00	Per-Johan Jakobsson (Karolinska)	Proteomics
10:00 – 10:15	Emmanuel Karouzakis (Zürich)	Epigenomics
10:15 – 10:30	Christoforos Nikolaou (Fleming)	Transkriptomics/Epigenomics
10:30 – 10:45	Maria Denis (Biomedcode)	Metabolomics
10:45 – 11:00	Florence Apparailly (Montpellier)	Trans-species miRNomics to unravel molecular control of monocyte subset functions
11:00 – 12:00	General Discussion: What is the goal and expected output of the OMICS within BTCure? Which cells or tissues are investigated across BTCure´s WPs and partners? Who is doing it?	

12:30 Lunch at Hotel

Established and new Animal models of Arthritis		
Chair: Rikard Holmdahl (Karolinska), Adrian Moore (UCB)		
13:30 – 14:15	Johann Bäcklund *et al.*	Short update on SOPs
14:15 – 14:45	Jonatan Tuncel (Karolinska)	What can we learn from PIA?
14:45 – 15:00	Rikard Holmdahl (Karolinska)	SKG and G6PI-induced arthritis
15:00 – 15:15	Marietta Armaka (Fleming)	TNFΔARE
15:15 – 15:30	Karl Skriner (Berlin)	Efficient CAIA in the PWD/Ph inbred strain of the *Mus m. musculus* subspecies
15:30 – 15:45	Marije Koenders (Nijmegen)	Ra synovium SCID model
15:45 – 16:00	Maria Denis (Biomedcode)	Humanized models
16:00 – 16:15	Natacha/Patrice (Paris)	Genetically modified models
16:15 – 16:45	General Discussion: Which models will be investigated/standardized next?	

	Advantages and Limitations of New models? How to publish the finalized SOPs?

16:45 – 17:15 Coffee break

Imaging		
Chair: Silvia Hayer (MUV), N.N.		
17:15 – 17:35	Mette Thorn (Novo Nordisk)	FMT technology in experimental arthritis
17:35 – 17:55	Fons van den Loo (Nijmegen)	Biophotonic imaging of gene expression in experimental arthritis
17:55 – 18:15	Silvia Hayer (MUV)	*In vivo* monitoring of functional impairment and structural damage in Tg197 mice under TNF blockade
18:15 – 18:35	Florence Apparailly (Montpellier)	Monitoring response to treatment in CIA using *in vivo* longitudinal assessment of joint structure and pain

19:30 Conference Dinner at Salmbräu Brewery & Restaurant, Rennweg 8, 1030 Vienna

DAY 3: Friday May 16 2014

Neutrophils		
Chair: Markus Hoffmann (MUV & Erlangen)		
09:30 – 10:20	Mariana Kaplan (NIAMS)	Neutrophil extracellular traps in the pathogenesis of RA and other autoimmune diseases
10:20 – 10:40	Martin Herrmann (Erlangen)	How aggregated neutrophil extracellular traps resolve inflammation
10:40 – 11:00	Litsa Papadaki (Athens)	NETs exacerbate auto-reactive T cell responses in RA

11:00 – 11:30	Ros Walley (UCB)	Use of historic *in vivo* control data to assess assay reproducibility and to reduce the number of control animals

11:30 – 12:00	**Roundup and General Discussion**
Chair: Florence Apparailly (Montpellier), Neil Gozzard (UCB)	
Future directions, Topics for next workshop, open issues	

13:00 Lunch
14:00 End of Workshop