Summarized by Pia-Maria Blaas, Manager and Scientific Coordinator (KI)

Animal Workshop Athens June 2013

From the 5th till the 7th of June, the 2nd BTCure workshop on Animal Models took place in Athens, Greece. The second workshop, organized by BTCure partner Fleming with financial support of UCB, could attract nearly 60 participants of highly motivated researchers and experts in this field, including numerous academic partners and EFPIA colleagues from UCB, GSK and Novo Nordisk.

One of the first goals was to pursue the standardization work for the classical RA models, as the CIA, CAIA, PIA and the transgenic TNF model; work which has been initiated during last year`s workshop in Stockholm organized by the Karolinska Institute. KI groups presented first validation results of academic partners, as well as potential reasons for some of the observed variances and open participations. Open discussions were followed by decisions on final validation instructions to further improve the reproducibility across partner laboratories. Exemplary questions that were discussed in more detail:
CIA: recommended genetic background, reagents and providers, amount of tested animals, endpoints, scoring in particular during relapsing phases, collection of feces, etc. **CAIA:** antibody transfer and administration, antibody cocktail providers, and titrating instructions to reach severity, description of genetic backgrounds used **PIA** generally good overlaps in scoring system, use of synthetically derived pristine. **TgTNF:** nice overlap in arthritis evaluation without or upon treatment (TNFi), in vivo read outs, outstanding histopathology. Partner Fleming further presented SOPs for mouse sample handling and processing for -omics data generation. In Sep 2013 during our Annual Meeting in Prague it is further planned to discuss how these procedures could be best aligned to similar human protocols, in order to improve comparability of human and mouse -omics data.
In order to rule out that certain labs cannot follow the outlined SOPs due to different ethical restrictions of local ethical committees (e.g. with regard to

enrichment, endpoint, pain, chronic arthritis, amount of animal, feeding, etc.) a questionnaire to systematically evaluate this question was designed. This anonymous web survey is now open for input and feedback by all internal and external animal researchers.
In response to first results and IMI`s external reviewer feedback, industry interest to engage in on-going validations could be regained, which will be of great support for the project considering EFPIA`s in-house expertise in this area. BI agreed to validate the CAIA and pick up some –omics work, UCB confirmed to contribute with CIA validation, as well as GSK is currently is evaluating internally, if their ethical restriction allow to follow the CIA validating protocol. It was decided that this will be further encouraged and coordinated by BTCure`s EFPIA coordinator, UCB and the respective academic model coordinators.

Another important goal was to present different, new and humanized mouse models that may have certain advantages over the well established and currently internally used classical RA models.
Internal and external researchers were present to introduce their work and first results obtain with numerous alternative models, as the G6PI model, SKG model, KRN model, SCID model, humanized TNF/TNFR transgenic models, TnfΔARE model, NSG and K/BxA^{g7} models, and the ROSA26-iPSC mouse. The talks on humanized models were of particular interest to participants and created very positive reactions. It is planned to endorse different models BTCure internally or to recommend certain models for the certain kind of experiments. Thus, pros & cons of the respective models compared to the classical models and in comparison to each other, could be further highlighted, in particular with regard to the applicability of certain models to investigate specific human disease stages, types, pathways and events, and their feasibility to test certain type of drugs and MoAs.

In addition, the important question of the general usefulness of mice as a model system to study RA, or the general reliability and reproducibility of research results per se, and other ethical questions were thoroughly taken into account. In this context a recent publication questioning the translational value of mouse genomics in comparison to humans suffering from inflammatory disease was discussed. This external publication brought up reasonable arguments. However, preliminary as well first published BTCure results, that were based on optimized tools, and aligned experimental set ups for trans-species comparisons, indicate a reasonable overlap for certain signatures and targets worth further investigating. Future, collaborative BTCure work further identify biomarkers that are relevant in both species and contrast even better which models reflect certain human disease stages and types.

In the coming weeks and before our Annual Meeting, the WP1 expert group will further decide on open question as: -) Which two partner sites will finalize the second round of validations according to the detailed instructions and until when? -) Who will be responsible for histological procedures and documentation? -) How to clearly outline and what is necessary to outline advantages of certain new models? -) If to and which groups could start / continue with the generation of –omics data from different models and upon different treatments, following SOPs.