WP1 standardization workshop – Summary for external communication

On Mar 26, 2012 the first standardization workshop for animal models in Experimental Arthritis took place. The workshop was organized by the Karolinska Institutet (KI) and involved BTCure partners from academia and industry from all over Europe. Additionally, external speakers from the US, China and Germany were invited to consider a broad input and seek international recognition beyond the BTCure network and consortium. For the first time, key opinion leaders in the field of Rheumatoid Arthritis (RA) were meeting to build a critical mass of experts to discuss the standardization of rodent RA models and related work, the advantages and disadvantages of various models, as well as the correlation of different models with actual human disease subtypes.

Background

Prior to this meeting - during BTCure's first Steering Board Meeting in Prague in autumn 2011 - BTCure partners decided on the most interesting and most commonly used, "classic" RA animal models that are currently employed for Experimental Arthritis by BTCure partners:

1) CIA – collagen induced arthritis mouse model

2) CAIA – collagen antibody induced arthritis mouse model

3) PIA – pristane induced arthritis rat model and

4) TNFtg mouse model, i.e. a humanized transgenic model, which is genetically engineered to produce Tumour Necrosis Factor, a common pro-inflammatory mediator of autoimmune disease.

These models were chosen for the first of the annually planned animal workshops, which will also consider other models in future workshops.

Main aim and expected outcomes of standardization

The main aims of this workshop were:

-) to suggest best practice protocols not only allowing inter-lab comparison of research results within BTCure but also internationally in the future, thereby allowing better comparisons between results form different laboratories and improving scientific quality and the drug development processes

-) to improve the description of disease pathogenesis by characterizing and describing each RA animal model in more detail, to be able to compare with the human situation by elucidating which model correlates best with which disease pathway /or disease stage and, thereby, patient subgroup.

Validated protocols and model descriptions will improve the predictability of preclinical models for clinical studies and will lead to a more targeted testing of drugs and, in the following, to a more targeted and improved treatment of patients, which is in the sense of ethical animal research, industrial interests and patient benefit.

The near term aim of this workshop is to commonly decide on these best practice protocols, validate them with the help of industrial partners and to publish validated protocols in high impact journals to reach international recognition.

The workshop at a glance – summary and outcome

The workshop including all preparations was organized highly professionally under the lead of Rikard Holmdal of the KI. Four coordinators familiar with the respective model were assigned to organize and lead the according sessions and working groups (CIA-Johan Bäcklund; CAIA- Kutty Selva Nandakumar; PIA- Jonatan Tuncel and TgTNF -Maria Denis). The coordinators prepared initial general descriptions for each of the models and distributed questionnaires in advance to the workshop to request detailed feedback of partners on important areas with need for standardization, as e.g.

-) used mouse/rat strains and genetic background, -) details to injected materials and adjuvants as well as their mode of administration, -) general and experimental study planning, -) tested treatments and used positive controls, -) disease evaluation, -) presentation and calculation of data, -) animal housing and environment, and -) ethical considerations.

During the workshop, each model was introduced with a session, in which external and internal, internationally recognized speakers and the respective coordinator presented previous experiences with each model. Moreover, the first feedback of the questionnaire was analysed briefly and all participants had the chance to comment and raise open questions.

It became clear early in discussion that more commonly used models, such as the CIA model, show higher diversity in experimental set ups and need immediate attention, while other models used by defined groups correlated better with each other.

Important general areas of improvement could be outlined already during the model sessions, such as disease definition in animal models and correlation with the human situation (definition of acute/early stages of RA vs. relapsing and chronic/established stages), comparison with human syndromes and differences in arthritic disease scoring scales (visual and histopathological), type of disease induction, dosing and mode of administration, general reproducibility of models, onset of disease and time window for research and drug testing.

In the following, working groups with expertise for each model were formed and these groups were meeting during two days to agree on the standardization and the best practice protocols / recommended use.

EFPIA industry partners were further meeting to decide on how these protocols could be validated internally and to decide on responsibilities and prioritization.

Main outcome and decisions: Although the formulation of the new standard protocols were successful and determined in a very positive and collaborative way, there are still adjustments needed to be done both in each model but also to compare the SOPs for the different models. Therefore the meeting agreed on:

1) That the coordinators decide on the final SOP for the 4 different models, based on additional advice taking in from WP1 leaders and others
2) All models described by final SOPs should be validated within BTCure and also outside by interested labs
3) The CAIA, TNF and PIA models are ready to go by also adding in additional characterisation such as various “omic” protocols during the first validation. The coordinators and the providers of the validations will detail this with advice from the WP1 leaders.

Aim of follow up meeting in 2013

Some new interesting humanized RA models were also briefly presented and new inventive models can be further suggested until the next Steering Board Meeting of BTCure, where the WP1 team will decide which models will be further elucidated under 2013.

The emphasis of next year`s workshop will therefore be the presentation and discussion of new RA models.

However the team will also meet to further define the alignment of new as well as old animal models with human disease subtypes and stages, since to improve the predictability for the human situation is one of the long-term goals of this BTCure project.

It was suggested to have alternate workshop organizers and hosts for this annual workshops and that industry could take over the lead for next year. The WP 1 team will decide on the actual host and organizer for next year`s workshops in one of the next internal WP 1 meetings to come.

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