2nd Predictive Model Systems (PREMOS) activity
The translational value of animal models: Stakeholder meeting

1st of April 2022, Online

The stakeholder meeting was Activity 2 of the PREMOS cluster, conducted as online meeting on April 1st 2022, 9-12 am CEST. Because both projects have similar goals, the attendees were first informed about:

- **Results of previous PREMOS cluster working group meetings**, including the identification of translational gaps in a survey among cluster members and the discussion with clinicians about prerequisites for clinical relevance of model systems
- **Results of the PERMIT (PERsonalised Medicine Trials) project**, in particular their recommendations for robust and reproducible preclinical research in personalized medicine

The main part of the PREMOS stakeholder meeting was the following discussion about the suggestions how to increase the predictive value of model systems for clinical trials resulting from this previous work of PREMOS and PERMIT. The open and critical discussion resulted in the following conclusions:

1. It is important to invite patient organisations into preclinical research discussions, because we need their input to make models relevant, as patients and clinicians do not always concur on what is a priority focus.
2. To achieve this, the language must be more accessible and common to non-experts in the field, and relationships with patient organisations must be nurtured.
3. We need to communicate openly and transparency to normalize the role of animal models in scientific research within the public consciousness.
4. It was consensus among participants that animal studies can test for causality of human clinical findings and that they can expand our knowledge at the mechanistic level.
5. There was agreement that animal models contribute significantly to proving genetic causality in rare neurodevelopmental or neurodegenerative diseases.
6. As the majority of psychiatric disorders are complex, a suggestion also needs to be developed for complex disorders until the PREMOS consensus meeting.
7. Access to existing animal models and their detailed information, including negative results as e.g. available for IMPC models, through national, European and global repositories needs to be reinforced. The extent and regulation of the access, including a grace period for the provider, need to be further debated.
8. To ensure clinical relevance, the biological mechanisms and functions studied in a model must be similar to humans, taking into account species specificity. The use of literature to establish that a model is clinically relevant for the question asked should be reinforced. Symptom, target and drug response similarity are important aspects for clinicians. Preclinical evidence justifying clinical trials should be based on the use of multiple models, not only one, to increase the predictive value of the preclinical evidence for translational success.

9. To enable the provision of clinically relevant model systems, it should be mandatory that human studies provide quantitative and biological data to optimize back-translation of human clinical findings. Closer interactions between preclinical scientists and clinicians need to be fostered on a larger scale to reduce the number of animal studies with irrelevant outcomes.
10. Further discussion is needed on the question if primary endpoints for clinical trials should be based on the indicated quantitative biological and translational parameters used for back translation. Changing of primary endpoints would hamper meta-analyses, and there may be primary endpoints that are relevant for patients but not apt to back-translation.
11. In the position paper resulting from the PREMOS cluster activities, it would be useful to address and respond to the EU goal to eliminate animal research.

The European Brain Research Area project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825348