

**PRISM Project:**  
Precision medicine comes to Neurosymptomatics



February  
**2018**



## this issue:

IMI Mid-term Review Meeting

Multicentre study in mice making progress

Building the molecular landscape of social withdrawal

Save the dates!

[To the website](#)

## Highlights IMI Mid-term Review Meeting

On 22 November, the co-ordination team and work package leaders presented PRISM's progress to the IMI mid-term review panel in Brussels. The three external reviewers commended the progress that has been made. With a few small exceptions, all deliverables and milestones foreseen have been achieved.

All efforts are being made by the consortium to recruit the patient cohort needed to deliver the innovative approach at PRISM's heart, namely, to cluster schizophrenia and Alzheimer's disease patients on the basis of quantitative biological measures, irrespective of their initial diagnosis, and to implement a preclinical platform for the related predictive model systems.



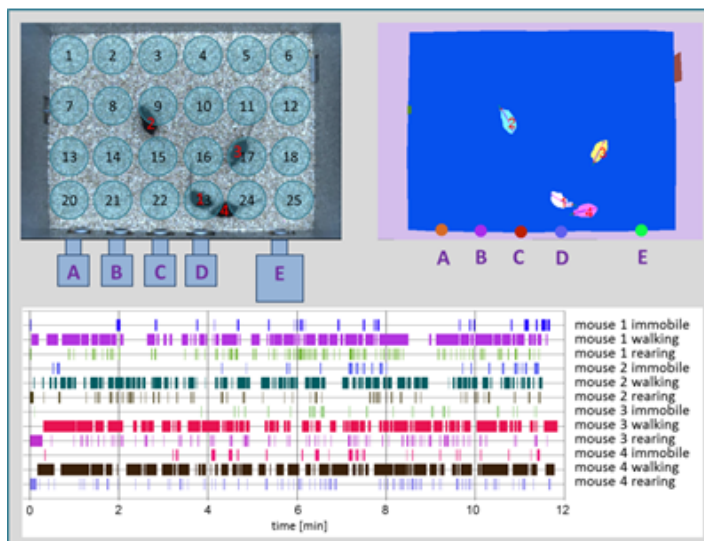
PRISM Steering Committee members at the meeting in Brussels.

## Multicentre study in mice making progress

The setting up of the social arena task is making good progress: the arena boxes including nests of different sizes, food hoppers and bottle holders have been manufactured and distributed to the three participating sites: Boehringer Ingelheim International (BI), the University of Groningen (RUG) and Radboud University Medical Center (RUMC). The RFID sensor boards for tracking individual mice have been optimised and adapted to the second generation arena layout. Nine setups are currently being assembled at the three sites and will be ready for a cross-site validation experiment end of Q1/2018.

In the meantime, the software package for automatically analysing social behaviour has been further improved at BI in collaboration with CleverSys Inc. A pilot experiment with 90 hours of synchronous video and RFID recordings has been performed in Q3/2017. During the analysis of the material, numerous behaviours have been detected, which escaped correct detection by the software or had even led to system crashes. In close collaboration between BI and CleverSys Inc., bug fixes have been generated and numerous software

updates have been released. The resulting product is running stably and various social behaviours are currently being analysed in the pilot study.



[Click here to view the high resolution image](#)

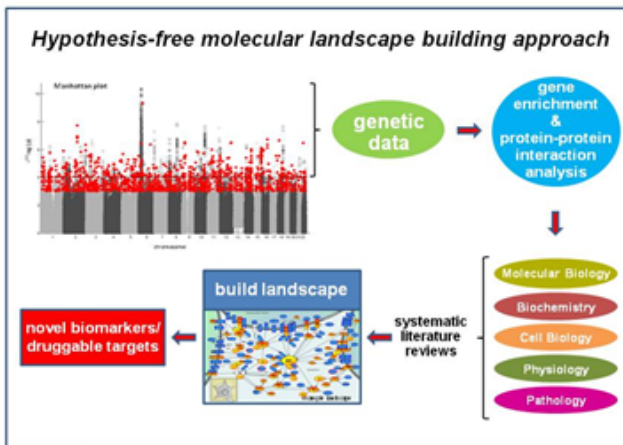
The next milestone for the social arena task will be the cross-site validation study. The general study parameters such as housing conditions or supplier of the animals have been harmonised in face-to-face meetings and in teleconferences. For aligning the exact procedures and discussing final details of the cross-site validation study, a training session with all scientists involved in the social arena task is scheduled for March 2018 at BI.

## Building a molecular landscape of social withdrawal

PRISM project partner Drug Target ID (DTID; <http://www.drugtargetid.com/>) is a SME and has pioneered a highly innovative approach to build so-called 'molecular landscapes' of complex genetic disorders in order to provide insights into the biological processes underlying these disorders and to reveal novel, disorder-specific diagnostic biomarkers and drug targets. This unbiased 'molecular landscape building approach' involves the application of bioinformatics tools as well as extensive literature evaluations to/of the top-ranked genes that have been identified through several types of genetic, epigenetic and expression studies as well as studies on (genetic) animal models and pharmacological studies, and that have been ranked and weighted using statistical approaches.

Recently, papers about molecular landscapes of two neurodegenerative disorders - Parkinson's disease and amyotrophic lateral sclerosis (ALS) - have been published in Nature Partner Journals (NPJ) Parkinson's disease (Klemann et al. ; <https://www.nature.com/articles/s41531-017-0015-3>) and Brain Pathology (Klemann et al. ; doi: 10.1111/bpa.12485). Within the PRISM project, we will apply the molecular landscape building approach to the top-ranked genes from a number of genome-wide association studies (GWASs) of social withdrawal-related traits in general population samples - including a GWAS in the very large sample from the UK BioBank (up to 500.000 people), a study that is currently underway - as well as in case-controls samples for Alzheimer's disease, schizophrenia and major depression.

The figure below provides an overview of the molecular landscape building approach.



[Click here to view the high resolution image](#)

## Save the dates!

The next PRISM General Assembly and Steering Committee meetings are taking place on 8-9 March 2018 at Boehringer Ingelheim International in Mainz, Germany.

This will be the first time that we will have a poster session where selected PRISM early career researchers will present the progress of their work and/or preliminary findings.



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