Newsletter Issue #3
December 2018
Translational quantitative systems toxicology to improve the understanding of the safety of medicines

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We are pleased to present the **TransQST-Newsletter** Issue 3

Key Note

2018 has been a busy and productive year for the TransQST consortium. We have convened for two General Assembly meetings, in Helsinki in April (hosted by Orion Pharma) and in Paris in October (hosted by Sanofi). In addition, our progress was evaluated by an external expert panel who were impressed by our achievements and the team ethic that we have nurtured.

I have been particularly pleased by the fact that we have already been able to deliver outputs that are being used by our industry partners. These include the TransQST data management platform and a new R Shiny tool to visualise and explore WGCNA modelling outputs.

Our unique combination of data scientists, modellers and experimentalists have made this a reality, and I am confident that there is a lot more to come as we enter the third year of our joint endeavour.

I hope you find this newsletter both interesting and informative.

Prof. Kevin Park (co-ordinator)

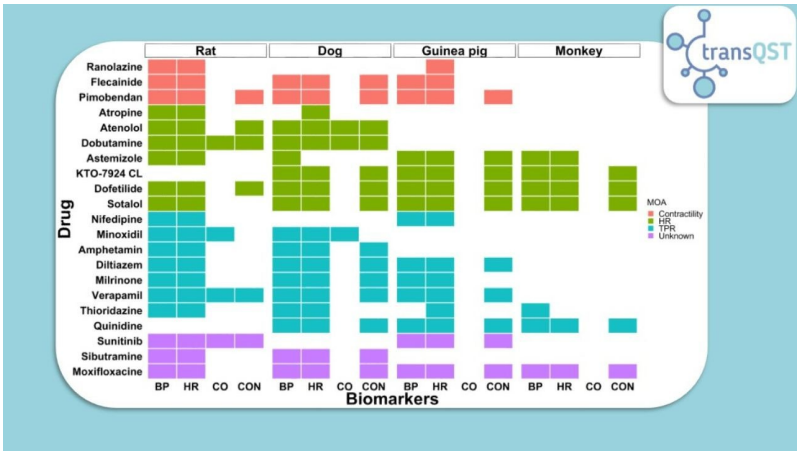
Project News Visit our website News section

TransQST WP7 achievements

Cardiovascular hemodynamic modeling framework

The Leiden University group for been working in the last period to obtain in-depth insight into available data across species to support the cardiovascular hemodynamic modeling framework in order to identify gaps that WP7 aims to fill (see figure).

Furthermore, the group is currently running identifiability analyses to fully characterize the possible mode of actions of drugs and the systems model, and is working to establish a user-friendly web-application to make the modeling framework available to non-expert users.



TransQST GAM2

The second TransQST General Assembly meeting held in Sanofi premises in Chilly Mazarin (Paris, France) on the 17th and 18th of October 2018

The consortium members had the opportunity to meet for the first time after the early review that took place in June 2018 and discuss the so-far progress.

The TransQST project is gathering together existing data and will generate new data under the project goals to support the development of tools that should make it easier to assess the safety profile of drug candidates before undergoing clinical testing phase.

During the first day, parallel sessions of Organ WPs with representatives from WP3 (data) and WP4 (modelling) were organised. On the second day, the consortium met at the plenary session for the WP updates round and discussion on project next steps. The experimental studies already started, and the first data have been shown.

The TransQST Scientific Advisory member Dr. Adriano M. Henney (Avicenna Alliance for Predictive Medicine) attended the meeting on both days. He was able to learn about TransQST progress by attending the sessions and discussing with the key drivers of the project. His recommendations were highly appreciated and will be valuable for the project progress and dissemination of TransQST approaches and achievements.

TransQST posters at the IMI 10th anniversary scientific symposium

TransQST young researchers presented two posters at the IMI 10th anniversary scientific symposium in October 2018

The Innovative Medicines Initiative celebrated its 10th anniversary in 2018, and several activities took place to mark the occasion, certainly the most prominent one was the Scientific Symposium held on 22nd– 23rd of October in Brussels. During the two full days, young scientists were in the spotlight, showcasing the IMI projects stellar science and great scientific output that the IMI projects delivered in the last ten years. The event featured 72 posters and 28 oral presentations, clustered around four topics.

Rowena Sison-Young (ULIV): presented ‘Integration of models of drug-induced liver injury for risk assessment’ poster. The poster focussed on translatability of acetaminophen (APAP) response across species as well as in vitro versus in vivo, ensuring that these were reflected in the computational models being developed. Rowena showed in vitro and in vivo APAP work on human, mouse and rat, and how it is being used for parameterising the APAP PBPK model that is currently being built within TransQST.

Emre Guney (IMIM) presented a poster entitled "Network-based modelling of APAP-induced hepatotoxicity using interactomics and transcriptomics data", showing the characterisation of the biological pathways activated in human liver in response to APAP (paracetamol) treatment. iPath was presented, a systems biology approach in which tissue-specific interactomics data and drug-induced transcriptomics changes are combined to identify pathways involved in APAP-induced hepatotoxicity.

Both Rowena Sison-Young and Emre Guney agree that the event was a great opportunity to learn about wide breadth of research areas of exciting IMI projects, but also to meet new scientists and points of contacts for scientific exchange.

TransQST @

SPS conference in Washington (US)

A poster of the TransQST work contributed by the University of Oxford partner to the project was presented at the **Safety Pharmacology Society annual meeting**, 30th September – 3rd October in Washington, DC.

EUROTOX in Brussels (Belgium)

A poster of the TransQST work contributed by the University of Maastricht partner to the project was presented at the **EUROTOX**, 2-5th September in Brussels.

UM colleagues were also invited to present this poster in the AstraZeneca Educational Event, organized in the framework of the conference on the 3rd of September.

Publications **Visit our website Publications section**

Characterisation of the NRF2 transcriptional network and its response to chemical insult in primary human hepatocytes: implications for prediction of drug-induced liver injury. Copple IM, den Hollander W, Callegaro G, et al. *Arch Toxicol.* 2018. 1–15

Network, Transcriptomic and Genomic Features Differentiate Genes Relevant for Drug Response Piñero J, Gonzalez-Perez A, Guney E, Aguirre-Plans J, Sanz F, Oliva B, Furlong LI. *Front. Genet.* 2018 9:412.

PROJECT INFORMATION **Visit our website**

Next issue in June 2019

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