Newsletter

Issue Num. 6 - March 2013

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Latest Breaking News

eTOX project extension approved

The review of the **eTOX** extension proposal (ENSO) was very positively evaluated by IMI-JU and an extension until 2016 has been approved. The accomplishments of the **eTOX** team were highlighted as commendable and the reviewers also considered it impressive that the **eTOX** consortium has generated such a large number of high quality publications. The extension will build upon early successes by expanding the acquisition of additional toxicology data inputs (species, types of trials, etc) and allowing access to more public databases. For this purpose four new partners will join the consortium, allowing for greater linking between experimental animal and biochemical studies with human outcomes.

PROJECT NEWS

New partners in extension (ENSO):

- Fraunhofer ITEM (FHG-ITEM)
- Erasmus Medical Center (EMC)
- University of Leicester (ULEIC)
- Polytechnical University of Valencia (UPV)

3rd eTOXsys user meeting in Barcelona

The 3rd eTOXsys user meeting took place in Barcelona on the 24th of January. The progress in the development of the integrated prediction system became evident during this meeting when the so-called Virtual Machines (VMs) which encapsulate the system were presented. As a Proof-of-concept of the eTOXsys, the project partners will soon be able to install these VMs behind their firewalls, thus allowing an in-depth evaluation also with confidential structures.

Model Evaluation and Regulatory Acceptance

With the first series of predictive models available in eTOXsys the important step of model evaluation and validation started early this year in work package 7. In order to ascertain a high level of transparency on how a model was constructed, what data was used and what the reliability is, a database containing this information, called eTOXvault, will be implemented in eTOXsys. Each end user will then be able to interpret whether the model is applicable to his/her specific use case question and how reliable the prediction of a certain property will be. This capacity is also a prerequisite to obtain regulatory acceptance of the eTOX predictive system.

KEYNOTE

A global pharma industry perspective on toxicity prediction

Message from ROCHE Global Head Non Clinical Safety & Translational Technologies and Bioinformatics: Thomas Singer, Dr. D.V.M., PhD, DABT

The Pharmaceutical industry faces increasing pressure to improve its productivity. A major challenge is to speed up and improve the discovery and development process to bring better drugs to patients. Nonclinical safety assessments play an important role in supporting not only the early selection of drug candidates but also in prediction and management of safety liabilities in patients.

Avoiding and addressing adverse drug reactions (ADRs) early on has become critical to reduce late stage attrition or market withdrawal due to toxicities. The prediction of drug effects in humans still involves a number of assumptions and extrapolations associated with high uncertainty. However, during discovery and development a massive amount of data is generated across various drugs and projects which improves the basis for prediction of safety. It is necessary to build computational tools which integrate this wealth of information to systematically improve the prediction of *in vivo* toxicity and the extrapolation from animal to man. These predictive tools, built from large datasets, will enable the scientists to design compounds with reduced probability of ADRs. In addition, these tools help to shape the drug discovery/development process by influencing the choice and design of the most informative *in vitro* and *in vivo* experiments. Such strategic use of computational models will certainly help to reduce animal testing as well as to improve efficiency by identifying and dropping early on, candidates that present a high risk of failure.

In this context, *the eTOX project offers the unique opportunity to get access to the wealth of information for safety assessment from both the pharmaceutical industry and the public domain*. Great progress has been made to build a harmonized toxicological database for the development of the required predictive tools that an individual institution would be unable to achieve.

ACHIEVEMENTS

- Apart from legacy reports data sharing, recently, AZ has transferred a set of more than 1000 ABCB11 transporter inhibitors to UNIVIE partner, targeting modeling purposes.

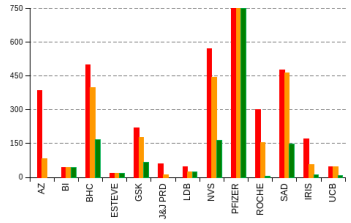
- Early 2013, the **Anatomy pathology** (3075 Preferred Terms, 4400 Synonyms) and **Micro Histopathology** (785 Preferred Terms, 2187 Synonyms) pieces of the common ontology were delivered. Thanks to OntoBrowser use and curation core team input 99.9% of Anatomy related verbatim terms and 63.2% of the Micro related verbatim terms have already been assigned to preferred terms.

- Ending February 2013, Lhasa Limited launched the **fourth release of the Vitic Nexus eTOX database,** with 357 substances (127 confidential) linked to 1392 study design records (166 to confidential structures) collected from Bayer, Boehringer, Esteve, GlaxoSmithKline, Novartis, Pfizer, Sanofi, Servier and UCB legacy reports. In addition, it contains data from the **third release of the ChOX database** (411 toxicology-linked targets; 169,216 distinct compounds and 672,684 activities) and the **Open TG Gates database** (170 substances and 304 records).

- This month, the first Software Evaluation agreements between EFPIA partners (AZ, BHC, GSK and UCB) and Molecular Discovery has been signed for 2 months licenses of Pentacle and MoKa software, to evaluate the Proof of Concept of the **eTOXsys**, which includes 4 models (3 FIMIM and 1 MN) for CACO2 and Phospholipidosis predictions, as virtual machines.

REPORT-O-METER 3589

After more than 1 year, this is the status of legacy reports data processing and sharing from all contributor partners.



Cleared Reports submitted to CROs or in-house facilities for data extraction
Extracted Reports with processing by CROs or in-house facilities completed
Vitic Reports with data available at Vitic Nexus database

PUBLICATIONS

A full list of publications is available on http://www.etoxproject.eu

- GUEST EDITORIAL-(BHC): Advances in Computational Toxicology. Steger-Hartmann T. *Mol Inf* 2013;32(1):9.

- ARTICLE-(FIMIM): The eTOX Library of Public Resources for *in Silico* Toxicity Prediction. Cases M, Pastor M, Sanz F. *Mol Inf* 2013;32(1):24-35.

- ARTICLE-(AZ): Exploiting Pharmacological Similarity to Identify Safety Concerns – Listen to What the Data Tells You. Muthas D, Boyer S. *Mol Inf* 2013;32(1):37-45.

UPCOMING EVENTS

- **04.04.13 |** 1st SCT Workshop on Biological Relevant Molecular Diversity. Paris (France). Info: http://www.SCTworkshopApril2013.org
- **21-24.04.13 |** 7th EFMC Short Course on Medicinal Chemistry: Principles of Molecular Recognition. Oegstgeest (The Netherlands). Info: http://www.ldorganisation.com/produits.php?langue=english&cle_menus=1238915634
- **20-22.06.13 |** 26th IEEE International Symposium on COMPUTER-BASED MEDICAL SYSTEMS. Porto (Portugal). Info: http://staff.icar.cnr.it/cannataro/cbms2013/
- **21-22.05.13 |** Optimizing Pre-Clinical Drug Safety Conference. Boston (USA). Info: http://goo.gl/3BgkS
- **03-05.07.13 |** RICT 2013 - 49th International Conference on Medicinal Chemistry. Drug Discovery and Selection: When Chemical Biology meets Drug Design. Nice (France). Info: http://www.rict2013.org