eTOX

Newsletter

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PROJECT NEWS

eTOX at EuroQSAR and ISMC

eTOX has had a huge presence at the EuroQSAR (Knowledge Enabled Ligand Design) and ISMC (XXIInd International Symposium on Medicinal Chemistry) conferences held on the 26-30 August and 2-6 September, respectively. With a total of 5 posters presented by several partners and a wide representation of the consortium, these conferences have been a forum for eTOX members.

eTOX presented at FIMEA meeting

eTOX has been presented at the Preclinical Assessors Meeting (FIMEA) held in Helsinki on the 10th of September 2012. The assessors showed great interest in eTOX and an intensified collaboration between eTOX and the regulators is envisaged.

2nd eTOX user meeting

On the 20th of September, the second meeting to advance the integrated data and prediction system of eTOX (eTOXsys) was held in Berlin. With the number of data sets in the eTOX data base constantly growing, the focus of this meeting was on executing complex queries of these data and adequate result presentation. In addition, the experts developed approaches on how the existing prototype will be implemented behind the firewalls of the EFPIA companies to allow for protection of sensitive structural information.

Have a look at the eTOX public resources LIBRARY

As a part of the tasks oriented to extracting information from the public domain, the eTOX has developed a strategy to identify, gather, and store different types of toxicology related information, building a LIBRARY of relevant public resources which have been properly classified and annotated. The content is updated on a monthly basis, and recently has been opened to the general audience.

KEYNOTE

Opportunities to advance predictive toxicology
Message from the Director of EPA's NCCT, member of the eTOX SAB: Robert J. Kavlock

Progress in transforming toxicology from a largely descriptive science to a predictive science continues to accelerate internationally. In the US Environmental Protection Agency (EPAs) ToxCast program (http://www.epa.gov/ncct/toxcast/) is completing Phase 2 of the program that brings the number of chemicals tested in ~600 biological assays to 1060. Included in the chemical library are more than 100 chemicals donated by six pharmaceutical companies (Pfizer, Merck, Sanofi, Roche, Astella and GSK) that failed either in pre-clinical or clinical trials.

This chemical subset will allow ToxCast to probe the ability to detect pathways relevant to adverse effects in humans as it has been doing with rodent bioassays. eTOX members can track progress on this effort by joining EPAs computational toxicology community of practice (http://epa.gov/ncct/communities_of_practice.html). ToxCast is part of Tox21 (http://www.epa.gov.ncct/tox21/), a larger US government effort consisting of the National Toxicology Program from NIEHS, the National Center for Advancing Translational Research at NIH (formerly the National Center for Chemical Genomics) and the Food and Drug Administration. Tox21 is currently testing a library of more than 8000 unique chemicals (including approximately 3000 drugs) in ultra high throughput assays. The initial priority assays include nuclear receptors and stress response pathways. Since the testing began in late 2011, more than a dozen assays have been completed, including ones for estrogen and androgen receptors. The goal of ToxCast and Tox21 is to make all the data publicly available as soon as possible, preferably in conjunction with a journal publication, but no later than a year after data generation.
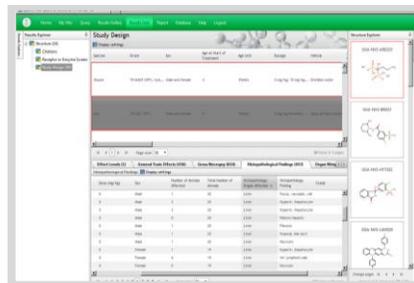
Given the number of drugs in the Tox21 chemical library, there is certainly opportunity for collaboration with the eTOX program.
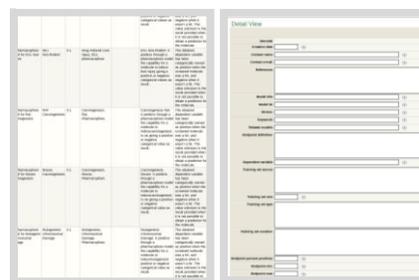
- Ending July 2012, Lhasa Limited launched the **second release of the Vitic Nexus eTOX database**, with 105 structures and 209 study design records collected from Bayer, Boehringer, Esteve, GlaxoSmithKline and Novartis partners.

- Novartis pathologists set up the **beta version of the common ontology** which it is envisaged will facilitate the harmonisation of terms in the Vitic Nexus database using the OntoBrowser, a web application developed to host the different ontologies generated in the framework of the eTOX project and others currently available at the public domain. This tool will map the variety of terms recorded from the legacy reports extraction data process to a preferred terminology thus simplifying the database queries, and will be beneficial for the quality of the models developed.

- A new relational database, named **eTOXvault**, has been created to complete the documentation (following OECD principles) for all the predictive models developed in the project. This database will be linked to the prediction system, the eTOXsys, to allow end users gathering details of the predictive models used, providing highly informative summaries, and a detailed description of how the models were built.

- All model-developing partners have their **first models running in the eTOXsys**, which cover different endpoints prediction based in different methodologies (QSAR, Pharmacophore-based, etc.).
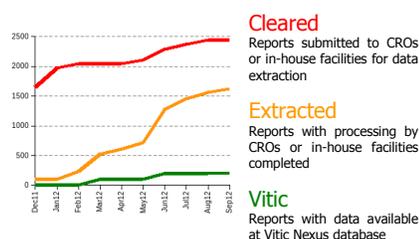
Vitic Nexus database

eTOXvault database

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EFPIA are progressing with the extraction and quality checks. The next Vitic release, planned by mid November 2012, will contain data from over half of the 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

- ARTICLE-(UNIVIE): An *in silico* model for predicting ABCC2 substrates. Pinto M., et al. *Mol Inf*. 2012, 31: 547-553.

- ARTICLE-(UNIVIE): Annotating human P-glycoprotein bioassay data. Zdrazil B, et al. *Mol Inf*. 2012, 31: 599-609.

- PRESENTATION-(FIMIM): Carrió P, Cases M, Schwab C, Sanz F, Pastor M. Development of an integrated *in silico* prediction system of drug toxicity endpoints. International Symposium on Medicinal Chemistry.

UPCOMING EVENTS

- **1-4.10.12 |** Safety Pharmacology Society Annual Meeting and Exhibition - A dynamic forum for best practice sharing between safety pharmacologists, academics and regulators, Phoenix (USA). Information: http://www.safetypharmacology.org/am2012/general.asp

- **16-19.10.12 |** European Society of Toxicology in Vitro 2012 International Conference, ESTIV2012, Lisbon (Portugal) Information: http://www.estiv2012.com/programme.htm

- **23-25.10.12 |** 33rd Annual European Meeting of The Toxicology Forum, Brussels (Belgium) Information: http://goo.gl/vump9

- **11-12.11.12 |** 11th International Semantic Web Conference, Boston (USA) Information: http://www.ontologydynamics.org/od/index.php/evodyn2012/