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A Community of Practice that
makes a difference to your work and career!

Predictive Toxicology Workshop

A Hands-On Practical Approach
Oxford, August 2-6, 2010

Interactive pragmatic workshops with leading experts and industry practitioners...

- **Mechanism-guided Strategies**
- **Mining Human Adverse Events**
- **Knowledge-based Modelling**
- **Carcinogenicity Prediction**
- **QSAR Modelling & Validation**
- **Metabolism & Kinetics**
- **Bayesian Nets, Weight of Evidence & Consensus Models**
- **Workflows & Resources**
- **Designing *in vitro* Test Sets**

Use leading-edge methods and software applied to predictive toxicology. Discuss practical examples, case studies and methods.

- Class facilitation and discussions led by Community Manager Dr. Barry Hardy and an international faculty team of predictive toxicology modeling experts and practitioners. Emphasis is placed on collaborative work and learning.
- Use leading modeling software and databases including OpenTox, Leadscope, Lhasa, Ambit, Toxmatch, Titanium, ACToR, SimCyp, SMARTCyp, Meteor, DiscoveryBus.
- Integrating case study approach and group work throughout the week on methods, datasets, challenging problems and discussion of results obtained
- One year's membership of eCheminfo included

The workshops will take place at the Medical Sciences Teaching Center, Oxford University.

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Human Adverse Event Data Mining
Jeffrey Wiseman (Pharmatrope)

- Study Drug-Human Adverse Event Associations in FDA data
- Build models using Titanium™ database of filtered data
- Analyse fragment-based QSAR models for 650 adverse events
- Identify significant adverse event links
- Derive data-driven clustering of event-event relations
- Distinguish adverse events that are linked to off-target activities
- Apply models to the generation of mechanism-based hypotheses

"I learned a lot, made many good contacts and confirmed that I'm on the right way with my projects and goals on safety assessment. We learned about many programs and the differences between them in terms of use, applicability, and endpoints."

You will have ample opportunity to discuss your perspectives and criticisms of the methods studied and you'll take away key nuggets of understanding from these intensive sessions.

Mechanism-Based Models of Chemical Toxicity using ToxCast Data
Richard Judson (EPA, National Center for Computational Toxicology)

- Understand design and results of 600 assays in ToxCast program
- Study chemical activity across pathways & disease-gene collections
- Build signatures of endpoints from ToxCast data
- Model liver toxicity and reproductive fitness
- Judge models for specificity, sensitivity, statistical metrics, and biological merits
- Discuss Prioritization Strategies and Planning
- Select *in vitro* assay data for OpenTox-based model building

NB: This work may not necessarily reflect official EPA policy

Group Work and Discussion on Workshop Case Study Problems

At the beginning of the week Case Study Working Groups will be formed based on individual interests and team diversity. Case studies and associated data will be made available to the groups. The groups will each decide which strategies and problems they will work on as their focus. Throughout the week time will be made available to the groups to work on their case studies using methods and software studied during the workshop.

A fully equipped IT classroom and a variety of software packages will be at your disposal to work through the problems posed by the instructors.

"At the scientific level I obtained an overview of many aspects involved in Toxicity and ADME prediction. I found the topics on predictive model development to assess the toxicity of compounds, the application of knowledge-based reasoning and the consideration of metabolism and reactivity most interesting and useful."

Using Database look-ups, Read Across, and Predictive Models to assess the Toxicity of Compounds, Glenn Myatt (Leadscope)

- Review sources and integration of toxicology data
- Use database look-ups and read across
- Search over toxicity data including US FDA databases
- Discuss issues concerning data mining toxicity
- Finding structural alerts and building categories
- Use partial logistic regression methods to model categorical data
- Use regression to build continuous data models

Integrated QSAR-based Model Building, Applicability Domain Estimation, Validation and Reporting, Nina Jeliazkova (Ideaconsult)

- Apply OpenTox data services to the integration of multiple datasets
- Select and calculate descriptors for model building
- Apply novel algorithms to build classification and regression models
- Evaluate the Applicability Domain of models
- Validate models including the calculation of prediction uncertainty
- Generate reports in QMRF format
- Discuss considerations for QSAR models & REACH regulations

"Excellent workshop. Informative and enjoyable from start to finish. Lots of new ideas and best practices to implement asap. It was a great group with lots of different areas of expertise. Scientists from all over the world meant that discussions were interesting and informative."

Return to your lab with new ideas, best practices & software experiences to maximise productivity in your own predictive toxicology activities.

Population-varied Physiologically-based ADME Simulation for *in vitro-in vivo* Extrapolation and Exposure Estimation, Sebastian Polak & David Turner (Simcyp)

- Analyse *in vitro-in vivo* extrapolation (IVIVE) of experimental data
- Estimate exposure and its physiologically-based variation
- Model metabolism, induction and active transport
- Predict the time-dependent exposure of organs to administered compounds
- Assess inter-individual variability of exposure via *virtual trials*
- Include consideration of Drug-Drug Interactions

"My scientific experience was really good. Our group is starting with using predictive toxicology techniques and for us it was really interesting to learn how to develop and apply the leading methods and software available. My personal experience was incredible as I met open and friendly people. Thank you for two weeks of learning and fun!"

Using Computational Chemistry to Predict Drug Metabolism Mediated by Cytochromes P450, Patrik Rydberg (University of Copenhagen)

- Identify potential metabolites of P450s
- Apply quantum chemical methods to P450 metabolism
- Use fragment matching of pre-computed energies
- Apply statistical methods to relate substrate properties to metabolites
- Design compounds to overcome potential metabolism problems
- Discuss advantages and limitations of different methods
- Combine methods to obtain best possible predictions

Knowledge-based Reasoning for the Prediction of Toxicity and Metabolism, Liz Hardy (Lhasa)

- Use non-statistical approaches for the prediction of toxicity and metabolism
- Obtain toxicity evidence from Derek Knowledge Base
- Apply knowledge-based approach to metabolism prediction
- Examine and discuss predictions and reasoning
- Combine knowledge-based and statistical predictions

Time is set aside throughout the week to work in small groups on case study datasets.

Datamining and Predictive Toxicology Workflows
David Leahy (Discovery Bus)

- Apply workflow approaches to automating QSAR modeling
- Test QSAR modeling methods and parameters without programming
- Learn and use Inkspot Science and Discovery Bus Technologies
- Study QSAR models for more than 10,000 ChEMBL datasets
- Compare modelling method performance
- Discuss model validation and applicability domain

Enjoy the Oxfordshire countryside after an intensive day in the computer lab!

Weight of Evidence approaches: from Consensus Models to Bayesian Integration Methods, Jin Li (Unilever)

- Learn about Weight of Evidence (WoE) approaches
- Weigh qualitative and quantitative evidence
- Apply Bayesian methods to WoE approaches
- Combine prior distribution with data to produce posterior distribution
- Combine evidence from *in silico* and *in vitro* data
- Apply WoE to predicting mutagenicity and skin sensitisation

In vitro Assays that Predict Mechanisms of Human Organ Toxicity, Katya Tsaioun (Apredica)

- De-risking of drug discovery programs
- *in vitro* Toxicity and ADME assays and their validation
- Combining *in vitro* data with *in silico* models and data
- Determining safety windows in the absence of human data
- Assays to analyse Drug-Drug Induced Liver Injury mechanims
- New tissue models and mechanisms

"We applied lots of methods and software for human toxicology including approaches from internet-based communities to hybrids to fully commercial and many different scientific techniques including Bayesian, Graphs, Numeric, and mixed methods"

Design and Planning of Experimental Assays for Testing Predictions

Together the group will discuss the design and planning of *in vitro* assay experiments for the testing of predictive models developed from the workshop case study work, which will then be carried out after the workshop.

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Register now for eCheminfo's Workshop Week on
Predictive Toxicology

5 ways to register...

- ✓ **Online** at
  echem2010-admet.eventsbot.com/
  http://www.echeminfo.com (Ticket Office is only visible after login)
- ✓ **Email** echeminfo at douglasconnect.com
- ✓ **Phone** Nicki Douglas on +41 61 851 04 61
- ✓ **Fax** +44 870 112 38 44 (eFax)
- ✓ **Post** Douglas Connect GmbH, Baermeggenweg 14
  4314 Zeiningen, Switzerland

Payments by bank transfer, cheque or credit card (Amex, MasterCard, Visa)

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Join this international community of leading scientists...

Founded in 2003, eCheminfo is an ongoing Community of Practice (CoP) committed to the core value of outreach with diverse groups in the commercial, government and academic sectors for the sharing of best practices and the development of strategies, resources and methodologies that address specific issues in improved drug discovery and safety.

The network involves a diversity of subject matter expertise comprised of experienced professionals from the life science and pharmaceutical industry, vendors, research institutes, universities and government.

A strong emphasis on science and innovation in addition to networking and personal contacts and discussion is followed at eCheminfo events. Collaborative research projects furthering drug discovery and safety innovation goals are currently being pursued to advance the creation of a community of research approach to challenging problems and issues.

echeminfo.com

Become part of OpenTox

The OpenTox project is developing a predictive toxicology framework that provides a unified access to toxicological data and *in silico* models. We welcome your participation in this Open Source development community! OpenTox is supported by the EC FP7 research program.

www.opentox.org

OpenTox

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