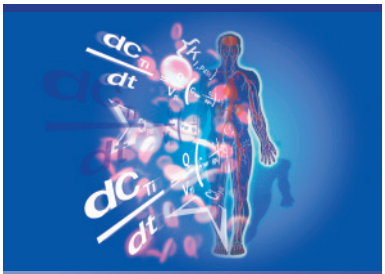
cyprotex AN EVOTEC COMPANY

In Silico Prediction

chemTarget™ - Predicts Biological Target Interaction Directly from Chemical Structure

Background Information



'A virtual screening tool for predicting *in vitro* biological target interaction from chemical structure alone.'

- Predicts binding affinity, inhibition constants or other measures of interaction with biological targets, directly from chemical structure.
- Uses Cyprotex's unique pattern recognition software to build models from existing data sets (provided by the customer or from the literature).
- Analyses approximately 10,000 descriptors using linear, random forest, neural network and nearest neighbour methods.
- Provides clinically relevant binding/inhibition/activation when used in combination with the pharmacokinetic predictor, chemPK™.
- Provides an early-stage filter for directing chemistry and prioritising screening.

chemTarget™ Input Requirements

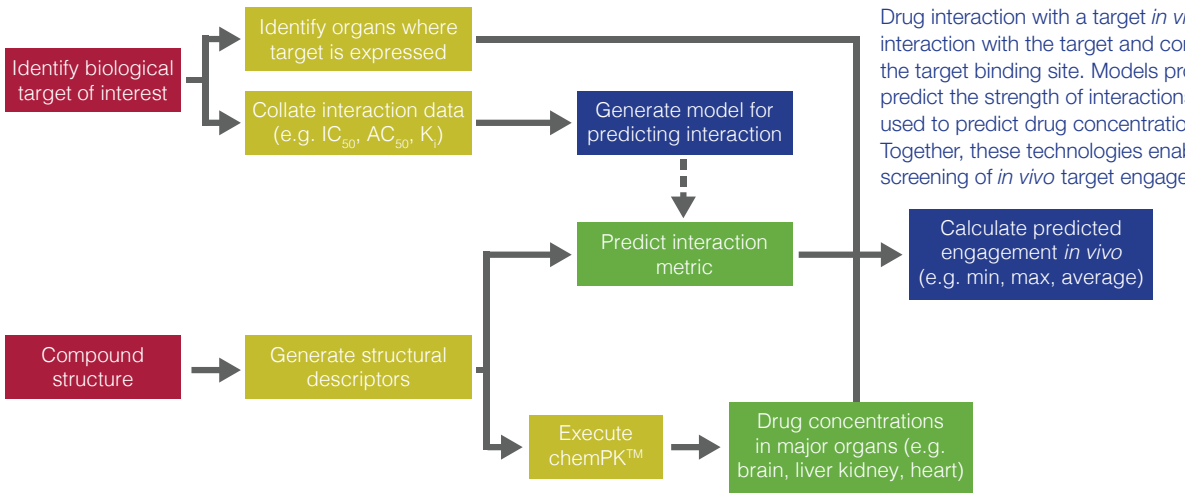
- Chemical structure, e.g., SMILES, mol or sdf.
- Location(s) of *in vivo* target expression.
- Existing target interaction data (e.g. IC_{50}, AC_{50} or K_i).

chemTarget™ Data Delivery

- Predicted target interaction.
- Predicted engagement *in vivo* for specified dose-regimen(s) (minimum, maximum, average) if used in combination with chemPK™.

Figure 1

Schematic illustrating how chemTarget™ can be integrated with chemPK™ to predict clinically relevant biological target interaction.



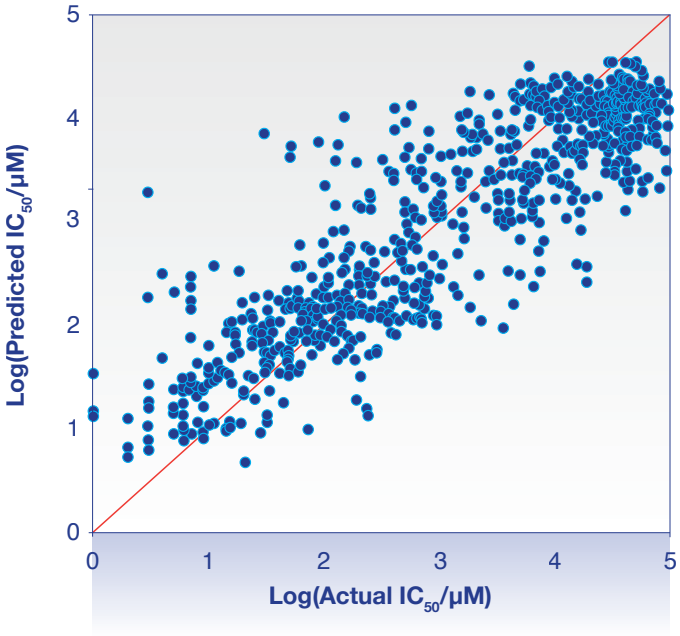
Drug interaction with a target *in vivo* depends on strength of interaction with the target and concentration of the drug at the target binding site. Models produced by chemTarget™ predict the strength of interactions, whilst chemPK™ can be used to predict drug concentrations in organs and tissues. Together, these technologies enable structure-based screening of *in vivo* target engagement.

To find out more contact **enquiries@cyprotex.com**

Performance of chemTarget™ predictions

Figure 2

Prediction of JNK3 binding affinity from chemical structure. Results are from 10 repeats of 10-fold cross-validation for a set of 697 compounds.



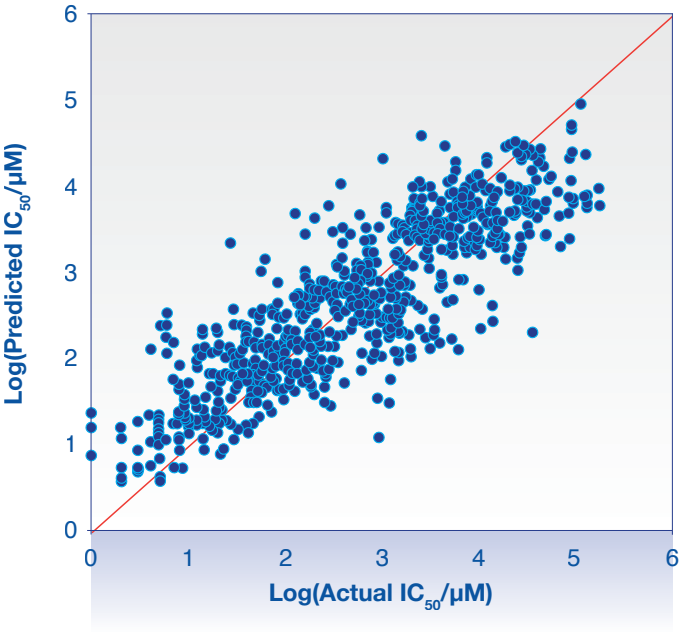
RMSE*	0.68
R^2	0.76
Spearman rank correlation coefficient	0.85

*RMSE = root mean square error

JNK3 is a potential therapeutic target for several neurodegenerative disorders. chemTarget™ predicts JNK3 inhibition directly from structure with a repeated cross-validation R^2 of 0.76 for a set of 697 compounds

Figure 3

Prediction of MK2 binding affinity from chemical structure. Results are from 10 repeats of 10-fold cross-validaton for a set of 670 compounds.



RMSE*	0.64
R^2	0.72
Spearman rank correlation coefficient	0.85

*RMSE = root mean square error

MK2 (mitogen-activated protein kinase (MAPK)-activated protein kinase 2) is a potential therapeutic target in inflammatory disease. chemTarget™ predicts MK2 inhibition directly from structure with a repeated cross-validation R^2 of 0.72 for a set of 670 compounds.

Contact enquiries@cyprotex.com to discuss your project.