Design and Performance of a Xenobiotic Metabolism Database Manager for Building Metabolic Pathway Databases

A. Chapkanov[1], P.Schmieder[3], J. Jones[2], R. Kolanczyk[3], S. Temelkov[1], V. Kamenska[1], M. Velikova[1], S. Stoeva[1], S. Kotov[1], K. Vasilev[1], O. Mekenyan[1]

[1] Laboratory of Mathematical Chemistry, Bourgas, Bulgaria
[2] USEPA/ORD/NERL/ERD – Athens, GA, USA
[3] USEPA/ORD/NHEERL/MED – Duluth, MN, USA

A major challenge for scientists and regulators is accounting for the metabolic activation of chemicals that may lead to increased toxicity. Reliable forecasting of chemical metabolism is a critical factor in estimating a chemical's toxic potential. Research is underway to develop *in silico* approaches to predict chemical metabolism as a component of efforts to screen and categorize chemical risks. The quality of metabolic predictions depends on the amount and quality of data used to train programs to simulate observed metabolic transformations. Two software tools, METAPATH and the DER Composer were developed for rapidly creating and enhancing databases containing various levels of information on metabolism of chemicals. Using the METAPATH platform a database of mammalian liver metabolism of xenobiotics was created. The database contains 566 metabolic pathways (maps) for 441 unique parent chemicals. The metabolites in these maps were observed in various experimental systems (*in vivo* and *in vitro*) primarily for studies using rats. A wide range of additional supporting information was also coded – test species details, experimental conditions, sampling and processing methods, dosing information, etc. An integrated QA system to ensure quality of data coding was included. The METAPATH platform also provides very powerful and flexible data analysis and search capabilities. Search queries can be defined and subsequently combined in complex logical AND, OR, NOT clauses. The search queries can be based on study information, map data, chemical structure or reactions observed within the map. The system also can calculate the similarity between maps and between chemicals. A satellite program called DER Composer has been developed based on Organization for Economic Cooperation and Development (OECD) pesticide metabolism templates as an external stand-alone application allowing coding of information from metabolism studies and saving it in text and XML formats. The XML files can be easily imported into the METAPATH databases. The accumulation of metabolic map information using the DER Composer and METAPATH allows sophisticated metabolism data analysis and will provide high quality data for enhancement of metabolic simulators. *Disclaimer: Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.*

Key words: metabolism, xenobiotics, database, simulator