# Integrative Extension of Drug Interaction Ontology (DIO) to Herb-Drug and Food-Drug Interactions

Sumi Yoshikawa, Akihiko Konagaya

Riken Genomic Sciences Center (GSC) sumi@gsc.riken.jp

The safety profile of a drug, including adverse reactions and drug interactions, is not static and varies according to the use patterns of different patients. Drug interaction occurs not only between drugs (i.e. drug-drug interactions) but also between the drug and foods, herbs, supplements and other complementary and alternative medicines (CAMs). Thanks to the ease of Internet shopping, there is an increasing number of patients/consumers who purchase pharmaceuticals or CAMs for self-medication purposes. At the same time, there is increasing concern about safety problems, not only due to the quality of the products but also regarding the availability of appropriate and accurate information on which patients can rely. Even if the documentation is appropriate and of high-quality, most of it is written in natural language and the level of understanding may vary according to the patients' background knowledge including tacit ethnic ones. Moreover, some reports suggest that patients do not tell their physicians about their use of CAMs. This fact also indicates the need for patients to be aware of the potential for drug interactions across non-drug xenobiotics with updated medical information.

I have already reported on Drug Interaction Ontology [1) 2)], which deals with the mechanism of drug interaction events at the pathway level. As it deals with molecule or ingredient level interactions for assertions, it has the potential to cover other xenobiotics including CAMs, with less redundancy compared to ontologies or information models that edealing with every combination of preparation products.

I will demonstrate how to apply ontology using as an example the anticoagulant drug warfarin, which has narrow therapeutic windows and is used for chronic disease (long-term use). The therapeutic effect of warfarin is its inhibitory effect on vitamin K metabolic cycle by inactivating vitamin K epoxy reductase that is essential in the blood coagulation process, thus warfarin negatively influences the process. Pharmaceutical preparations including vitamin K and those that may indirectly increase vitamin K dependent coagulation process are not recommended for concomitant use as they may weaken the above mentioned drug effect. The same thing applies to some foods, herbs and supplements and other CAMs too.

The advantage of employing an ontology is to allow a linkage among different ontology domains: pathway ontology, evidence ontology (literature), preparation formula ontology. I will show how the following knowledge will be addressed: 1) inference of potential drug interaction for a new product (i.e. new drug new supplement products) or ethnic food (e.g. *natto*) by using its ingredients and known metabolites as entities; 2) prediction of the relation between genetic predisposition (e.g. VKORC1) and individual differences in drug response and liability to the effect of drug interaction and, 3) linkage with literature resources.

**Concluding remarks:** There are increasing needs to provide adequate information on adverse reactions and drug interactions in a timely and effective manner. Representation of drug interaction mechanisms (including foods, complementary therapeutics, etc.) by ontology will integrate different domain ontologies, and will contribute to a collaborative effort for health information sharing and promote better understanding of individual differences in drug responses.

1) Yoshikawa S, Satou K, Konagaya K. Drug Interaction Ontology (DIO) for Inferences of Possible Drug-drug Interactions. Medinfo 2004; Proc. of f the 11th World Congress on Medical Informatics. Part1, IOS Press, pp454-458, 2004.
2) Okada M, Sugimoto Y, Yoshikawa S, Konagaya A. Drug Interaction Ontology (DIO) and the Resource-Sensitive Logical Inferences. Lecture Notes in Computer Science Volume 4060, Springer Berlin / Heidelberg. Pp 616-642, 2006.