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EDITORIAL

Database: A New Article Type in *CPT: Pharmacometrics & Systems Pharmacology*

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The immediate impact of big data to systems pharmacology research is highly significant and growing stronger. Current successful big data-driven pharmacology research comes from two major sources: population-based health record databases and molecular databases. The other driving force of big data research is the bioinformatics approach. Remarkably different from traditional hypothesis-driven research, bioinformatics resides in its natural power to inspire discovery. For example, using cutting-edge data mining methods and chemo-informatics data, Tatonetti *et al*. conducted association analysis between drugs, or drug interactions, and adverse events (ADEs) to assess all the US Food and Drug Administration's (FDA)-approved drugs and ADEs.[1] Their much-expanded pharmacovigilance research was based on the FDA's Adverse Event Reporting System (FAERS) and their local electronic medical record database (EMR). Another example is Duke *et al*.'s drug interaction data mining research using the EMR database.[2] Their work further integrated a large-scale cytochrome P450 enzyme pathway-based pharmacokinetics interaction evidence to support epidemiological drug interaction signals identified from the EMR database. The eMERGE (Electronic Medical Records and Genomics) network is another salient example (http://www.genome.gov/27540473). It integrates both population data and genomics data with Biobank samples. Denny *et al*.[3] extended a Biobank-based genome-wide association study (GWAS) to 86 reported disease phenotypes in the National Human Genome Research Institute GWAS Catalog using eMERGE. They successfully replicated a majority of prior GWAS associations. A comprehensive description of the impact of big data and bioinformatics in pharmacological research is documented in a recent review article.[4]

Bioinformatics and big data have increasingly become a core component of publications in *CPT:Pharmacometrics & Systems Pharmacology* (*PSP*). Examples are recent articles on a new drug combinatory effect prediction based on gene expression data by Goswami *et al*.[5]; and the medication-wide adverse event association analysis using medical record databases by Vilar *et al*.[6]

However, there is a major barrier in delivering reproducible and transparent scientific findings if databases are not being made available. At the same time, scientists who pull together databases are not always recognized for their effort and contribution. It is obvious that the very first data collection and processing step is absolutely critical before pharmacometrics or system pharmacology models can be developed. The data can be collected from pharmacology experiments in raw or processed format, in which the valuable information includes experimental designs and conditions. Biological and pharmacokinetics ontologies have been developed to achieve this goal.[7,8] Databases can also be derived from population-based health records, in which the valuable information include data standardization and annotations, e.g., adverse event dictionaries such as MedDRA, drug dictionary RxNORM and ATC codes, lab test dictionary LONIC, etc. The other data type includes curated data and databases from the published literature. The important elements include a data curating protocol, annotation scheme, and quality controls. For example, the pharmacogenomics data curated in the PharmGKB database was well documented in a recent publication.[9] All these significant database development efforts possess a tremendous value to the follow-up model development and warrant its independent recognition in publication.

The Editorial team of PSP has therefore decided to add "Database" to its article types. The scope of the Database article includes a significant effort of data collection from either pharmacology experiments, population databases, and/or is curated from the published literature or various public databases. In our PSP journal, we welcome all databases that attempt to address quantitative pharmacology-related research questions, especially relating to pharmacometrics and system pharmacology. The Introduction of the article should stress the background and significance of the data. The database devel-

Table 1 Database article guide to authors

Scope	This article type describes a database that can be utilized by others for further pharmacometric or systems pharmacology analysis and model development. The database should be freely and readily accessible.
Word limit	4,000 words excluding abstract, references, tables, and figures.
Abstract	150 words maximum.
Reference	50 maximum.
Figures/tables	7 maximum.
Database paper structure	The article paper shall have an Abstract, Introduction, Construction and Content, Utility, Discussion, Summary, and Study Highlights.

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opment will be illustrated in the Construction and Content section, in which the data collection and quality control processes should be thoroughly documented. The scientific applications of the data shall be exemplified by case studies in the Utility section. Finally, the potential usage of the database and its pros and cons shall be discussed in the Discussion section. More detailed Database paper guidance is illustrated in **Table 1**. An example is the recently published Database paper by Yeung and FDA coworkers, "Organ Impairment—Drug–Drug Interaction Database: A Tool for Evaluating the Impact of Renal or Hepatic Impairment and Pharmacologic Inhibition on the System Exposure of Drugs."[10] This is the first rigorously assembled database of pharmacokinetic drug exposure from publically available renal and hepatic impairment studies.[11] In the article, the data curation and validation among different curators was documented, analyzed, and presented as the quality control processes. The utility of this database is demonstrated in two examples: the AUC change comparison between hepatic impairment studies and the pharmacologic inhibition of CYP3A4, and the AUC change comparison between renal impairment and pharmacologic inhibition studies. Using this database, the article concluded that the accurate estimation that the contribution of renal clearance from mass-balance studies may still be the most reliable indicator of the effect of changes in the AUC with renal impairment, while the current pharmacologic studies with available transporter inhibitors do not reflect the worst-case scenario.

Database articles will be reviewed and assessed based on several criteria. Obviously, the article needs to demonstrate innovation in the field of pharmacometrics and systems pharmacology. For example, what is the difference between the new database and the existing ones and what are the advantages of the new database? The article needs to show substantial effort and contribution in the data generation, collection, and the construction of the database. This can be evaluated by the amount of time, or the number of investigators, that was used to generate the data; and sometimes the cost of the data generation. The reproducibility of the database construction is very important. The article needs to provide enough documentation of a database construction process, such that the readers can regenerate the data accordingly. In addition, quality control analysis shall be provided to assess the data collection process. Also, the utility of the database shall be exemplified by a few examples. Finally, the article needs to show where and how the database can be accessed.

We expect this Database article type in PSP will provide much-needed resources to the pharmacometrics and systems pharmacology research community, and increase the impact.

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