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EDITORIAL

Reverse Translational Pharmacology Research Is Driven by Big Data

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Pharmacology research usually translates *in vitro* pharmacology experiments or animal studies to human proof of principle or phase I clinical studies. This is often referred as the T1 translational research. The clinical pharmacokinetic (PK) or pharmacodynamic (PD) studies usually translate and sometimes even guide the phases II and III clinical studies. This is called T2 translational research. The T3 translational research focuses on the practice, including comparative effectiveness research, postmarketing studies, and clinical outcome research, whereas T4 translational research deals with population level outcome research, monitoring of morbidity, mortality, benefits, and risk, and impacts of policy and change. Usually, T3 and T4 fall into the pharmaco-epidemiology research domain. All T1 to T4 translational researches are very well organized and conducted in most medical centers and pharmaceutical industries.[1]

A new type of translational pharmacology research is now being enabled that was not feasible before because of the emergence of big data, especially the increased accessibility of institutional electronic medical records, the availability of health insurance claims data through health information technology commercially, and many public *in vitro* drug screening data sources. Noticeably, Tatonetti *et al.*[2] tested and validated a large number of drug interactions in two health record databases. Recently, Chiang *et al.*[3] conducted the high-dimensional drug interaction discovery using health record databases and evaluated the pharmacology mechanisms of these drug interactions using pharmacokinetic models. Unlike the conventional T1 to T4 translational research, these translational studies, driven by the big data, reversely connect the pharmaco-epidemiology evidences with *in vitro* pharmacology experiments. In this editorial, we call them "reverse translational pharmacology research."

The early success of this reverse translational pharmacology research is largely due to the fact that biomedical informatics is a powerfully driving force in the current data science era. Biomedical informatics, developed primarily from the data management and analysis needs in the biomedical domains, is fundamentally a translational research field. The innovations of biomedical informatics are motivated from well integrated scientific computing and biomedical research. Here, I would like to point out two challenges that biomedical informatics is facing in the reverse translational pharmacology research. First, the notable early successes of biomedical informatics were directly resulted from our existing computational capability of mining the associations between drugs and adverse drug events (ADEs). In the meantime, a great deal of attention was paid in developing new data mining algorithms that control the confounding variables. However, only limited research has been conducted in selecting proper epidemiology designs using large-scale health record databases. Although there exists extensive literature in pharmaco-epidemiology studies, they were designed for specific drug-ADE hypotheses, not necessarily for data mining. Statistically valid and computational efficient designs are very much needed for the data mining.

Second, PK and PD models are well populated in the preclinical experiments, and phases I–III studies; and they are applied to guide study designs. However, their translational potential is limited by their scalability. For example, if hundreds of drug-ADE signals are tested and validated from the health record data sources, how can we evaluate their PK or PD mechanisms through pharmacometric models? We currently cannot analyze them all at the same time because we do not have all the associated PK and PD models right now. We still do not know what data are available from the literature, what are still missing, and what data are not validated yet. This critical knowledge gap shall be filled with additional informatics and pharmacology research. In this special issue of Reverse Translational Research in *CPT: Pharmacometrics & System Pharmacology*, we further illustrate the challenges and opportunities in various specific pharmacology research areas. Schneider *et al.*[4] discussed the reverse translational research between veterinary and human medicine; system pharmacology studies in pregnant women by Quinney *et al.*[5] and Ke *et al.*[6] reviewed the system pharmacology research in pregnant women; Li *et al.*[7] evaluated physiologically based pharmacokinetic model-based prediction on the food effect on the oral drug absorption; and Zhang *et al.*[8] provided extensive review on the reverse translational research in drug interactions.

Conflict of Interest. The author declared no conflict of interest.

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