Database tracks toxic side effects of pharmaceuticals

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Sometimes the cure can be worse than the disease. Pharmaceutical drugs are known for their potential side effects, and an important aspect of personalized medicine is to tailor therapies to individuals to reduce the chances of adverse events. Now researchers from North Carolina State University have updated an extensive toxicology database so that it can be used to track information about therapeutic drugs and their unintentional toxic effects.

"Environmental science actually shares a common goal with drug makers: to improve the prediction of chemical toxicity," says Dr. Allan Peter Davis, lead author of a paper on the work and the biocuration project manager of the Comparative Toxicogenomics Database (CTD) in NC State's Department of Biological Sciences.

The scientific literature contains vast information about the adverse effects of therapeutic drugs. But collecting, organizing and making sense of that published information is a daunting task. NC State's CTD team, which historically focused on environmental chemicals, read and coded more than 88,000 scientific papers for this effort.

It took the CTD team one year to efficiently extract information from those 88,000 papers about therapeutic drugs and their involvement in toxic endpoints, such as hypertension, seizures, kidney failure and liver disease. "The project quickly added lots of new data that complements environmental toxicity," says Davis.

The results include more than 250,000 statements collected from seven decades' worth of scientific articles. Putting the data into the CTD framework helps investigators develop and test hypotheses about how drugs might cause adverse events.

"Coding the information in a structured format was key," insists Davis. "This allowed it to be combined with other data to make novel predictions." For example, the drug bortezomib is used to treat certain types of cancer, but it also causes unintended nerve damage in some patients. By linking the data, CTD was able to connect the dots and find genes that that may be key to connecting the drug and the possibility of nerve damage.

"Investigators can now test and validate which genes might be critical to the drug-induced event," explains Davis. "This could be useful in gene-testing patients to tailor the correct medicine or it could help design future therapeutics by alerting safety researchers to avoid those pathways and potential toxic outcomes."

The CTD group also designed a new phenotype module. In this context, phenotypes are events that happen in a cell or system before the toxicity or full-blown disease is recognized at the clinical level. Drugs can affect phenotypes as well as diseases. Independently coding drug-disease and drug-phenotype interactions from the literature and then storing them in the same database allows the system to connect certain phenotypes to diseases, based upon their shared drugs. These connections may allow scientists to resolve, and ultimately prevent, how chemicals – from the environment or from the medicine cabinet – cause toxicity.

More information: The paper, "A CTD-Pfizer collaboration: manual curation of 88,000 scientific articles text mined for drug-disease and drug-phenotype interactions," is published online in the journal *Database*.

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