Mathematical models target disease with drugs chosen by your DNA

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Medicines that are personally tailored to your DNA are becoming a reality, thanks to the work of U.S. and Chinese scientists who developed statistical models to predict which drug is best for a specific individual with a specific disease.

"Traditional medicine doesn't consider mechanistic drug response," said Rongling Wu, director of the Center for Statistical Genetics and professor of public health sciences within the division of biostatistics and bioinformatics at the Penn State College of Medicine. "We want to look at how an individual person responds to an individual drug by deriving and using sophisticated mathematical models, such as differential equations."

The current method of prescribing medication now sometimes includes a pharmacogenomic approach, but researchers recognize the limitation of this approach in predicting a response to a particular drug and dosage combination.

Pharmacogenomics uses a person's genes to explain the difference between how one person responds to a drug compared to another. The team's equations take this field one step further by also including information about how the body processes a drug and how the drug acts in the body.

Wu focused on the big picture by studying drug response and drug reaction. In particular, the team looked at pharmacokinetics, which

influences the concentration of a drug reaching its target, and pharmacodynamics, which determines the drug response. Metabolic, environmental and developmental factors also play a role in medication response.

The researchers created a statistical analysis framework of differential equations that they expect will help doctors and pharmacists, by simulating such variables as protein-protein and protein-DNA interactions a drug has in a patient. The framework characterizes a drug's absorption, distribution and elimination properties, yielding information on pharmacological targets, physiological pathways and, ultimately, disease systems in patients, resulting in predictions of treatment effectiveness.

"The results from this framework will facilitate the quantitative prediction of the responses of individual subjects as well as the design of optimal drug treatments," the researchers noted in a recent special issue of *Advanced Drug Discovery Reviews*.

This framework will expand to shed light on the variability of drug response based on information the medical community continues to gather about how an individual responds to a particular drug and dose combination. The information collected is then combined with information about the patient's genes, proteins and metabolism to help determine what drug and dose might be best for that person.

"If we know how genes control drug response, we can create a statistical model that shows us what will happen before using the drug," said Wu, who is also a member of Penn State's Huck Institutes of the Life Sciences. This means a future with more effective medications, faster healing and fewer side effects. "That is our final goal," Wu said.

Working with Wu were Yaqun Wang and Ningtao Wang, both graduate

students in the Center for Statistical Genetics at Penn State; and Jianxin Wang, professor, information science, and Zhong Wang, computer scientist, both at the Center for Computational Biology at Beijing Forestry University.