Answering the Question:'Which Drug Therapy Is Right for Me?'

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Graduate assistant Alicia Bolt demonstrates the preparation of microarrays measuring human genome expression to pharmacogenomics students.

(PhysOrg.com) -- UA pharmacy researchers aim to unravel a mystery: why do genetically similar people react differently to the same drug.

In the world of pharmaceutical science, the question of why two very similar individuals can react differently to a drug is the subject of intense interest.

At The University of Arizona College of Pharmacy, researchers are striving to find answers to seemingly simple questions asked by patients, such as, "Why did I have to try three different high blood pressure medications before my doctor found one that worked for me?" and

"Why did my cancer stay in remission with drug treatment, but my friend who had the same treatment was not so fortunate?"

At the basis of the answers to these questions is a field of study called pharmacogenomics, the analysis of how the expression of the human genome, the DNA code that instructs the making of the machinery of a cell, is key to the body's response to drugs.

"Importantly," said Walt Klimecki, assistant professor at UA College of Pharmacy, "pharmacogenomics helps us understand why two apparently similar individuals could have very different responses to the same drug. It holds the promise that drugs might one day be tailor-made for individuals and adapted to each person's own particular makeup."

In his lab at the UA's BIO5 Institute, Klimecki and Alicia Bolt, a graduate student in pharmacology and toxicology, are conducting pharmacogenomic research on a collection of white blood cells taken from about 200 healthy individuals from diverse global populations in the United States, China and Africa. The cells have been manipulated experimentally so that they can easily be grown in a plastic flask with growth media. Klimecki stores stocks of these individuals' cells in a lab freezer at the BIO5 Institute – a "town in a tube," he said.

This system allows Klimecki and Bolt to explore the diversity of individual variation in drug response in a much more controlled way than could be possible with the short-lived samples taken directly from human study participants.

In the lab, Klimecki and Bolt expose the white blood cells to arsenic trioxide, a relatively recent addition to the cancer-treatment arsenal in the United States, to measure how different expression patterns of the genome can predict response to this anti-cancer drug.

To measure differences in drug response, they use a technology called microarrays, a highly miniaturized analysis technology that allows scientists to measure the levels of each and every product contained in the master recipe book that is the human genome. For example, on one typical microscope slide, 44,000 such products can be measured four separate times.

Bolt reported he results of the research this month at the Mountain West Society of Toxicology meeting. In her abstract, Bolt states that a frequent observation in humans is the scenario of a relatively uniform toxicant exposure that is associated with a variable response. "The results are exciting," said Bolt. "Our observations suggest that this cell line model reproduces the inter-individual variation seen in arsenic-induced cell-killing observed in humans."

"Our research to date is encouraging," Klimecki said, "but these are complicated problems to solve. We need to study the effects of both genetics and the environment. The long-term solutions to these complex problems are going to involve multidisciplinary teams that include pharmacist-scientists, pharmacologists, toxicologists, chemists and computational/statistical scientists. But the results will be worth the work. These approaches and tools are an important part of the movement away from ‘trial-and-error' drug selection to the more individually targeted drug choices that are on the horizon."

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