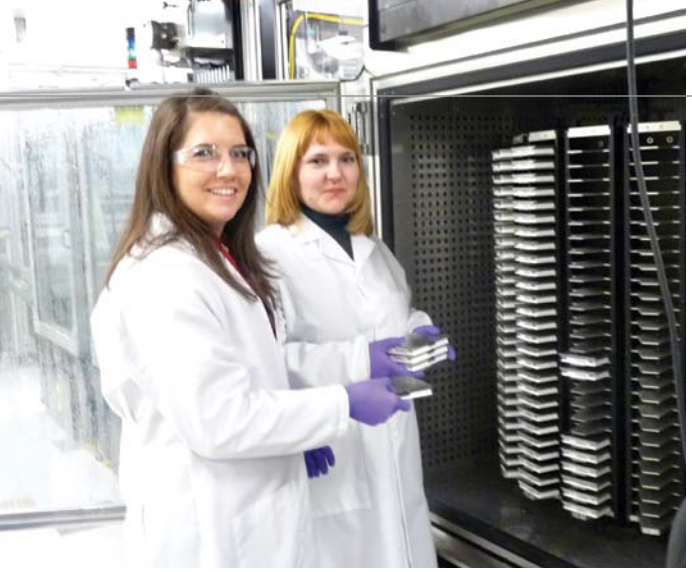

'Team Science' advances technology

Computational toxicology creates new ways to synthesize data

How much exposure to a certain chemical is safe?

What's the right dose of a given drug? So far, agencies charged with answering these questions—the U.S. Environmental Protection Agency and Food and Drug Administration—have not had good ways to account for an immutable fact about human beings—namely, that people are different.

Individual genetic makeup might keep one person from metabolizing a given substance, while another might metabolize so much that it becomes toxic. Ivan Rusyn, MD, PhD, associate professor of environmental sciences and engineering at UNC Gillings School of Global Public Health and director of the Carolina Center for Computational Toxicology (CCCT), leads several projects developing breakthrough methods to consider genetic diversity. Research by Rusyn and colleagues provides substantive data to determine safe levels for pharmaceuticals and environmental chemicals.

"Rapid advances in the technology of genotyping make these types of studies possible," Rusyn explains.

"Five or ten years ago, it was a major undertaking to sequence one individual mouse, yeast or human."

Now, he says, researchers can quickly and inexpensively sequence genetic information. That means genetic data on many individuals can be obtained easily.

It also means dealing with a staggering amount of information.

"For some research, where we screen thousands of compounds on hundreds of people, we have millions of data points," he says.

That's where computational toxicology comes in. The interdisciplinary field merges toxicology, biology and computer science to create new ways to synthesize data and predict chemical hazards.

"Toxicologists need biostatisticians, geneticists and molecular biologists to be part of the team," Rusyn says. "It's team science, and this campus is just great for building these teams."

Fred Wright, PhD, professor of biostatistics, is a key contributor to several research efforts underway at CCCT. "Without his help, we'd be dead in the water," Rusyn says.

The teams don't work on human populations per se, but on collections of human cells from different individuals or on populations of laboratory animals, such as mice.

"We're using cell lines and exposing them to different chemicals," Rusyn says.

"We're looking at whether different cell lines respond differently, and if so, why. Similar experiments can be done in animal models—for example, in mice where we know the genetic makeup of a particular strain. Having in vitro and computational tools allows us to address these risks without doing lengthy and unnecessary animal research."

Dr. Ivan Rusyn

The center's collaborative approach includes partnerships with the EPA and the National Institutes of Health's National Institute of Environmental Health Sciences, National Toxicology Program and National Chemical Genomics Center.

"We work with government stakeholders to engage them in our research and leverage resources and expertise," Rusyn says.

Through this collaboration, he aims to find reliable models to predict how individuals will react to chemicals and drugs. Rusyn hopes that working directly with government agencies also will speed up the flow of information from the laboratory bench to the regulator's desk. ■

–Kathleen Kearns

PHOTOS BY DR. MENGHANG XIA AND SRI SAKAMURU

Collaborative experiments with the National Chemical Genomics Center are vital in generating data for Dr. Ivan Rusyn's research. Master's student Shannon O'Shea (above, left) and research specialist Oksana Kosyk traveled to the center to expose dozens of cell lines to various environmental chemicals, using the center's advanced robotic equipment (right).