Toxic treatment

Getting to the heart of the problem

By Marcia Locke

Cancer treatment saves lives, but it can also be hard on the body. Some treatments damage the heart and vascular system. Kansas State University integrative physiologists are doing laboratory and clinical research to get to the heart of the problem.

According to Carl Ade, associate professor of kinesiology, 14 million U.S. cancer survivors experience cardiotoxicity, or damage to the heart and vascular system, after cancer treatment. Their hearts and vessels become weaker, stiffer and less efficient at pumping blood, which can lead to disease and premature death.

Moreover, to avoid that risk, patients may be given reduced doses of chemotherapy or radiation, resulting in less destruction of cancer cells. This raises their chances for cancer recurrence and decreased overall survival.

"There are chemotherapies that are really effective at targeting cancer cells, but some patients, who are maybe older or have underlying risk factors, can't be given the optimal dose because of the potential adverse side effects," Ade said.

Ade and his team study how chemotherapy, immunotherapy, hormone deprivation and radiation change cardiovascular function. Their big-picture approach involves basic research with cell cultures, pre-clinical research in animals and clinical research in humans actively receiving treatment.

In the laboratory, the researchers examine heart muscle and vascular cells and the changes they undergo when exposed to a chemotherapy drug. For their clinical research, they observe heart size, blood flow and small blood vessel function using imaging technology like echocardiography and vascular sonography.

"So, we have this nice translation from very basic science to clinical practice," Ade said. "We're in the lab observing the effects of a drug at the cellular level and then in the clinic taking measurements in patients before and after they get the same chemotherapy."

The team aims to identify and characterize patients at risk of developing cardiotoxicity. If they can predict cardiovascular dysfunction, they can take early steps to mitigate it while also fighting the cancer.

A couple of Ade's studies look at the effects of two specific drugs.

Fluorouracil is effective against colorectal cancers but can cause cardiovascular problems. The researchers apply a small amount of the drug to the skin, where it won't compromise the whole treatment, and see how the small blood vessels react. This less invasive method can inform them about what may happen in the larger cardiovascular system.

The breast cancer drug, Doxorubicin, alters heart function and stiffens the aorta and other vessels around the heart. The researchers are investigating whether the changes occur in the vessels before they do in the heart. If so, they could gather data and set criteria for predicting heart problems by simply observing vessels.

The ultimate goal is to develop screening, diagnostic and management strategies — whether lifestyle or pharmacological — to integrate with cancer treatments and alleviate or reverse cardiotoxicity.

A partnership with Stormont Vail Health's Cotton O'Neil Cancer Center and Heart Vascular Clinic, in Topeka, Kansas, has made it possible to work directly with cancer patients, many of whom are eager to support research.

"We've had an outstanding collaboration with Stormont Vail," Ade said. "We have our own dedicated space there, so patients can go to their oncology and heart appointments and also visit us fairly seamlessly."

Ade is doing some other cancer research as well. For the Cancer Research Collaboration of Excellence in Tumor Microenvironment Studies, an initiative supported by the Johnson Cancer Research Center, he studies vitamin D's effect on ovarian tumors.

This work could not be done without the students, Ade said.

"I have outstanding graduate students who interact professionally with patients, do rigorous data collection and are first authors on almost every paper," he said.

He applauds the Johnson Cancer Research Center for offering students funding that makes their contributions possible. And he recognizes that, in turn, he can have a bigger impact.

"After they help do our work and get trained to do research, they go on to be scientists themselves, so our impact as professors grows as the students go out and make a difference in their fields."

Our faculty averages 25 publications of research findings per year.