



The impressive pancreatic cancer research team at Jefferson, led by Jonathan Brody, PhD, and surgeon Jordan Winter, MD, FACS, recently received a \$100,000 donor-funded grant for two promising studies.

Innovative Projects Explore Metabolism, Chemotherapy Resistance in Pancreatic Cancer Cells

A generous contribution via the Gail V. Coleman-Kenneth M. Bruntel Charitable Grant Fund (see “Those Who Give” on p. 4) has enabled Jordan M. Winter, MD, FACS, Associate Professor of Surgery, and his team to initiate two innovative studies in pancreatic cancer. Here, Dr. Winter provides an overview of the purpose – and potential impact – of each project.

Studying Cancer Cell Metabolism

As Dr. Winter explains, metabolism is a fundamental biologic process for the viability of any cell – including cancer cells. “If you can find a way to impair that biology, you have an opportunity to treat cancer by killing those cells,” he says.

The challenge: Metabolism in cancer cells isn’t the same as in healthy cells. In pancreatic cancer cells, a protein called HuR appears to be an important regulator of metabolism – pancreatic cancer’s “secret weapon” in withstanding austere conditions.

“Even with very low levels of oxygen and other nutrients, such as glucose and glutamine, pancreatic cancer cells not only survive but thrive,” Dr. Winter says. Prior work by Dr. Winter and Director of the Division of Surgical Research, Jonathan R. Brody, PhD, has focused on the role of HuR as a pro-survival protein. In other words, remove HuR and pancreatic cancer cells die.

Thanks to the Coleman-Bruntel contribution, Dr. Winter and his laboratory team will be conducting a

sophisticated metabolic experiment to better understand the “how” and “why” of HuR. They will do so by mapping the flow of carbon through metabolic pathways in cells with and without HuR.

“Along with genetics and immunology, cancer cell metabolism is one of the hottest fields in cancer biology,” Dr. Winter notes. “This experiment is the first time anyone has examined how HuR affects metabolic pathways. It’s also the deepest exploration into how RNA biology plays a role in cancer cell metabolism.”

“Analysis of the pre-treatment and post-progression biopsies will provide us with clues as to how the cancer evolves to gain resistance to the chemotherapy.”

Understanding Chemotherapy Resistance

The Coleman-Bruntel gift has also enabled Dr. Winter and his team to take on a second, more translational study – in other words, work that will be more directly applicable in patient care. This one aims to enhance understanding of the mechanisms of chemotherapy resistance in pancreatic cancer.

“We’re studying patients with advanced pancreatic cancer who receive the most common treatment for stage 4 cancer, which is FOLFIRINOX and GEM/ABRAX,” explains Dr. Winter.

Jamie Jay Rothstein, RN, CCRC

As Clinical Research Nurse and the Project Manager for the Department of Surgery, Jamie Jay Rothstein builds systems for implementing and managing all aspects of the Department’s clinical trials – from protocol development to fiscal management. She also guides the Department’s research coordinators, interacting with them regularly for ongoing education and training.

Before joining Jefferson in July 2013, Rothstein created, developed and managed a research department of 10 physicians. Through strategic planning, analysis, business plan development, quality and performance improvement, the department grew to a staff of several coordinators. She says that while she enjoyed the position, she jumped at the chance to move from pharmaceutical to academic research.

“I love having the opportunity to work with the physicians and research coordinators at Jefferson,” she says. “Their passion for research – and compassion for patients – is unparalleled.”

Rothstein has been a nurse since 1991, when she was the first Graduate Nurse hired into the Cardiac Intensive Care Unit at the Children’s Hospital of Philadelphia. By 1995, she was serving as Primary Nurse and Clinical Research Nurse Coordinator at CHOP.

Over the past two decades, she has worked in a variety of clinical nursing fields and

“About half of these patients have some benefit, with the tumor remaining stable or shrinking. Eventually, though, the biology of every tumor adjusts to develop resistance.”

The team wants to understand how the tumor adapts at the genetic level.

For five to 10 patients, the team will first take a blood sample to obtain germline DNA to sequence (a laboratory process used to find mutations that may cause disease). Any mutations inherited from the germ cells (egg cell and sperm cell) of the patient’s parents will be found in this germline sequence. This will give the researchers a baseline for comparison.

Second, the team will take a tumor biopsy prior to starting chemotherapy. They will grow the cell line in the lab,



clinical research positions, including serving as a nurse educator for the OR in the Same Day Surgery Unit at several hospitals and surgical centers. In addition to being a Certified Clinical Research Coordinator, she holds certifications in Good Clinical Practice from the National Institutes of Health and is a member of SOCRA (Society of Clinical Research Associates) and ACRP (Association of Clinical Research Professionals).

Rothstein lauds the quality of research underway at Jefferson: “We’re doing innovative and groundbreaking work, such as studies of immunotherapy for specific kinds of cancer and growth of cell lines. The physicians are committed to the studies’ success.”

She lives with her husband in Cherry Hill, NJ, and enjoys being a mother to two daughters—and three Newfoundland dogs.

extract DNA and sequence the genome of the cancer before treatment. Finally, they will take a second biopsy during treatment once the tumor stops responding to chemotherapy and begins progressing. In other words, they will re-sample the tumor only after the biology of the cancer has changed – likely as a function of new mutations.

“Analysis of the pre-treatment and post-progression biopsies will provide us with clues as to how the cancer evolves to gain resistance to the chemotherapy,” Dr. Winter explains. “A better understanding of which genes or pathways change may help in better targeting those pathways and, ultimately, in improving chemotherapy.”

Dr. Winter is quick to note that this is the first pilot of its kind and was made possible solely through the Coleman-Bruntel gift. It’s already serving as a springboard for further funding – and will likely be the first in a series of studies into chemotherapy resistance.