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Changing Lives Through Research



Dr. Shruti Lal, PhD is conducting groundbreaking research on how the HuR protein regulates cell growth in pancreatic cancer cells.

Plant Biologist Shruti Lal, PhD, Identifies New Molecule That Could Prove Key in Treating Pancreatic Cancer

When Shruti Lal, PhD, joined the Division of Surgical Research as a post-doctoral researcher, she brought an intriguing blend of experience to the lab.

A veritable Renaissance woman, Dr. Lal has earned Master's degrees in both Botany and Computational Biosciences. She holds a two-year diploma in e-commerce and web design, and has more than six years of professional experience in software development, teaching and research. She also studied Molecular Biology techniques at the U.S. Department of Energy's Joint Genome Institute and explored microarray printing, scanning and hybridization at the University of California, San Francisco.

As a doctoral student at the University of California, Riverside, Dr. Lal studied the molecular mechanism that controls floral specification in the model plant *Arabidopsis thaliana*. Her goal was to establish the gene regulatory networks (GRNs) that promote flowering and floral specification in *Arabidopsis*. She applied a variety of approaches – including molecular, genomic and bioinformatics – to understand these networks.

As Dr. Lal explains, plants and animals have a fundamental difference. While human children are essentially

miniature versions of human adults, a young plant is not simply a mini-model of an adult plant: “The plant at juvenile stage has leaves and stems, but upon transition to adult stage it initiates new organs such as flowers,” Dr. Lal says. “My doctoral research was focused on understanding what changes occur that drive plants to start producing flowers.”

Despite opportunities to work in the field of plant research, Dr. Lal was eager to apply her skills to studying human disease. That desire led her to Jonathan Brody, PhD, Director of the Division of Surgical Research, who offered Dr. Lal a position focusing on cancer research. While it might not seem like the most logical career move, Dr. Brody explains, “Dr. Lal brings an intense dedication and fresh perspective to my research team that is invaluable.” From the outset, he posed two challenging questions to her: How do pancreatic cancer cells live with genetic mutations, and how do they become resistant to chemotherapies?

Identifying a novel HuR-regulated molecule

Jefferson scientists previously identified the RNA binding protein HuR (**H**uman **a**ntigen **R**) as a key molecule in pancreatic cancer cells. More than half of patients with pancreatic cancer express high cytoplasmic levels of HuR

Randi Altmark, RN, BSN, CNOR

Through the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP®), the Department of Surgery continually searches for ways to further improve the quality of surgical care delivered to our patients. As our NSQIP Surgical Clinical Nurse Reviewer, Randi Altmark plays a pivotal role in collecting and maintaining the data necessary to identify and act on opportunities for improvement.

When she returned to Jefferson to assume this role in 2006, Altmark brought more than 20 years of experience in nursing – including seven years as a Jefferson OR nurse and experience as an OR manager and business manager for surgical services as well as labor and delivery.

Altmark maintains Jefferson's ACS NSQIP database by abstracting relevant clinical data from patient charts. With data points spanning pre-op, intra-op and post-op variables, the database enables Jefferson to generate risk-adjusted reports and trend the quality of surgical care. As a participant in this program, Jefferson can benchmark itself against other hospitals in order to evaluate its own performance and cultivate best practices. In addition to maintaining the database, Altmark works closely with Surgeon Champions Herbert E. Cohn, MD, Scott Cowan, MD, and Stacey Milan, MD and other health care providers to develop and execute process improvements.

and those patients are more likely to respond well to the drug gemcitabine than those with relatively low levels of HuR. While this knowledge is important, understanding exactly *how* HuR functions in pancreatic cancer cells is critical. This has been the focus of Dr. Lal's research since joining the Jefferson team in November 2011.

“...if a chemotherapy drug can be designed to inhibit the interaction between HuR and WEE1, pancreatic cancer cells will be much more likely to die.”

In that time, Dr. Lal has identified the mechanism by which HuR regulates the WEE1 molecule (a gate keeper of cell growth) when cancer cells are exposed to certain chemotherapeutic drugs. “When chemotherapy is used, pancreatic cancer cells with the HuR protein incur some damage but protect themselves by putting themselves on ‘hold,’ and thereby prevent cell death,” Dr. Lal explains.

On the Job



The NSQIP program enables surgeons, anesthesiologists, nurses and other clinicians to view summaries of patient outcomes based on objective clinical data. Working with others, they can modify their practice to provide improved care to surgical patients. For example, NSQIP data has been used to help drive improvements in rates of surgical site infections.

“It's rewarding to know that my relatively small but vital contribution can greatly benefit patients receiving surgical care,” Altmark says. “And, I enjoy collaborating with surgeons and clinicians, who all contribute their expertise and unify around a common goal of providing the best-quality care possible for Jefferson patients.”

“Above all, I'm very grateful to work in a collaborative environment with people who recognize that while we're doing a great job, we can always do better,” she concludes.

Through the research, Dr. Lal has found that removing the HuR protein impairs WEE1 function and promotes cell death. Thus, Dr. Lal explains, if a chemotherapy drug can be designed to inhibit the interaction between HuR and WEE1, pancreatic cancer cells will be much more likely to die.

With her groundbreaking manuscript currently in review, Dr. Lal's long-term goal remains clear: “We want to quickly get this information from the bench to the bedside,” she says, noting that pancreatic cancer deaths are rising at an alarming rate, while other types of cancer deaths are steadily declining. “Our objective is to reverse that trend.”

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