These are exciting times in the Department of Urology and our Institute for Prostate and Urologic Cancer (IPUC) at the University of Minnesota. Seeds planted in the last decade for research, faculty, clinical care, and collaboration have been flourishing, leading to many new developments we would like to share with you in this issue of Straight Talk.

The Institute continues to grow its robust portfolio of clinical trials and research, including significant ongoing studies for bladder, kidney, and prostate cancers. Physicians, scientists, and other specialists are productively collaborating on a wide variety of projects.

The most exciting new development is the recruitment of Dr. Charles Ryan as the head of Hematology, Oncology and Transplantation. Dr. Ryan is an internationally recognized researcher and clinician who has pioneered the development of abiraterone, a novel hormonal treatment for prostate cancer that is now widely used.

In this newsletter, read about two researchers who are making a difference in genitourinary cancers. Arpit Rao, MD, assistant professor of hematology, oncology, and transplantation, joined the Department of Urology in 2017 from the University of New Mexico Comprehensive Cancer Center. He specializes in developing and providing advanced treatments for cancer patients, especially through first-in-human clinical trials.

Jayanth Panyam, PhD, chair of the Department of Pharmaceutics and an endowed professor of targeted drug delivery, partners with me and other researchers on using nanotechnology to diagnose and treat cancer. He is creating new, effective therapies for patients with breast, bladder, renal, and lung cancers, aiming to improve outcomes for difficult-to-treat tumors.
Other recent highlights include two major studies that were recently published:

- University of Minnesota researchers were involved in a randomized trial evaluating blue light cystoscopy. Compared to white light cystoscopy, this diagnostic identified 20 percent to 40 percent more bladder cancers. The study, “Efficacy and Safety of Blue Light Flexible Cystoscopy with Hexaminolevulinate (HAL) in the Surveillance of Bladder Cancer,” was published in December 2017 in the Journal of Urology.

- IPUC researchers recently completed a study comparing robotic-assisted radical cystectomy to open radical cystectomy for bladder cancer. Awaiting publication, the research shows that patients undergoing the robotic-assisted procedure experienced less blood loss and had reduced stays in the hospital.

Christopher Weight, MD, “Potential Patient Harms from Misinterpretation of Publically Reported Surgical Outcomes” studies the patient misinterpretation of medical care information found through the internet. The information presented in online surgical complication websites is misinterpreted by a considerable proportion of the general population. Failing to appropriately gauge the risk of surgical complications and uncertainty of complication rate estimates from small numbers may have significant financial ramifications to patients, and may disproportionally impact individuals from vulnerable groups such as the elderly, the poor, those with a history of cancer, and those who were unable to properly interpret online healthcare information.

Other exciting developments include work by urologic surgeon Christopher Weight, MD, and urologist J. Kyle Anderson, MD, that pushes the boundaries of robotic surgery. Anderson and Weight belong to a select group of physicians nationwide who use robotic methods for patients with complex kidney cancer, such as tumors growing in major blood vessels.

We have additional research underway that is making great progress, especially in the area of cancer genetics. Our teams are making contributions to the understanding of bladder cancer genomics and precision medicine, as well as advanced prostate cancer. These researchers are investigating the genetics of prostate tumors to better tailor therapy to patients. I also am excited by our outcomes research group. This talented team is doing phenomenal work comparing the effectiveness of different treatments and discovering numerous factors to improve patients’ outcomes.

Thanks to philanthropy, IPUC is able to recognize faculty by supporting their research. Medical oncologist Gautam Jha, MD, this year’s Semmer Scholar, specializes in genitourinary cancers and is currently conducting prostate and bladder cancer research. Post doc Jamie Van Etten, PhD, investigates metastatic prostate cancer, as does Mohammad Saleem Bhat, PhD, whose recruitment was fueled by philanthropy.

On a personal note, I am thrilled about several recent hires that we will announce later in 2018. I also will be assuming a new leadership role as president of the Société Internationale d’Urologie. I hope to bring honor to the University of Minnesota, the Department of Urology, and the Institute for Prostate and Urologic Cancers.

Sincerely,

Badrinath R. Konety, MD
Director of the Institute for Prostate and Urologic Cancers
By: Staff Writer

Like many doctors, Badrinath Konety, MD, and Gautam Jha, MD, receive their fair share of “thank you” messages from appreciative patients. But neither of them have ever received a gift quite like the one they were given on Nov. 15 and 16, when artist and cancer patient Shelley Kerr presented both of them with a pair of custom bronze sculptures she designed.

Shelley, from Colorado, said the gift seemed like a natural decision. “They saved my life,” Shelley said. “The great skill and passion of these two doctors filled me with confidence. I was able to move through this very scary, life-threatening disease with grace. They had my back, allowing me and my husband Dave to make great decisions and participate in my treatments and recovery.”

Immunotherapy helps Shelley

In 2014 Shelley was diagnosed with urothelial carcinoma in her left kidney. Doctors removed that kidney. The cancer was also found in her bladder. In 2015, she started seeing Konety, a M Health urologist, and Jha, a medical oncologist. Under their care, Shelley underwent chemotherapy. Eventually, she had the cancerous bladder removed, and received a “neo-bladder” in its place. Following these treatments there was no residual disease.

Later that year, however, Shelley began experiencing symptoms. After investigating, her care team discovered that the cancer had returned. Running low on options, Jha suggested that Shelley enroll in a clinical trial for immunotherapy, an emerging therapy that uses the body’s own immune system to fight cancer. Three months after starting the new treatment, Shelley was tumor-free. Shelley received a type of treatment called immune checkpoint inhibitors, Jha said.

The body has checks and balances designed to regulate normal immune responses, he explained. For example, checkpoints help govern which cells the body identifies as “self” and which cells it sees as “foreign” so the immune cells don’t attack the wrong things. Unfortunately, cancer cells often exploit the same checkpoints by disguising themselves as normal, thereby avoiding an immune response. Immune checkpoint inhibitors enable our white cells to mount an immune response to these disguised cancer cells.

The treatment is not without its risks, however. The immune system can start to reject and attack other parts of body besides cancer. In Shelley’s case, she developed joint swelling, which made movement painful.

“We had to stop [immunotherapy] and start her on steroids,” Jha said. “They suppress the immune system and reduce side effects, but can extinguish the progress we’ve made.”

Though Shelley’s immunotherapy eliminated the tumors, her cancer is making a slow comeback in her lymph nodes. For now, her cancer care team is safely keeping watch on it.

“I am healthy now, and excited to be back to a life that includes lifting weights, dancing, playing the accordion, and making bronze art,” Shelley said.

The art of a positive attitude

That upbeat attitude has also been an important factor in Shelley’s journey, her doctors said.

“Mentally she’s a tough, resilient lady,” Dr. Konety said. As an example, Konety related a story from Shelley’s treatment. After Shelley’s bladder was removed, Shelley’s sister-in-law wrote a poem describing Shelley’s bladder as a “friend” who left her. “It’s funny and poignant and now we use it in a book as educational material for patients,” Konety said.

“Sure, I shook my fist at the sky,” Shelley said, “And cried myself to sleep. But I did not stay in that place. I’m not a victim of cancer.” She laughed. “I have every right to be mad. I never smoked a cigarette, I don’t have a genetic proclivity. I participate with my success. The doctors did the amazing technical and scientific part and my job is to be third leg on the stool.”

Shelley Kerr (left), presents a handmade bronze sculpture to Urologist Badrinath Konety, MD (right). Konety and Medical Oncologist Gautam Jha, MD, helped treat Kerr for recurrent cancer in her bladder and kidney.
**Driven to excel**

**Arpit Rao, MD**, joined the University of Minnesota Medical School with a bold goal: to transform the genitourinary (GU) oncology specialty into a premier program. His vision includes offering world-renown care in the Twin Cities, fostering a deep bench of clinical trials, and engaging in multidisciplinary care and research that culminates in exceptional treatment for cancer patients.

A genitourinary oncologist and assistant professor of hematology, oncology, and transplantation, Rao came to the University in 2017 from the University of New Mexico Comprehensive Cancer Center, where he completed a fellowship in hematology/oncology.

“People shouldn’t have to travel somewhere else to get the latest medical care. What keeps me motivated is the desire to make our GU oncology program truly one of the best in the country,” Rao says. “We want to have at least one clinical trial option available for patients for all GU diseases and all of the stages. Then we can sit them down and say, ‘Here is an option to participate in this trial.’”

At the University, Rao works closely with urologists, radiation oncologists, other caregivers, and researchers on providing and developing advanced care for patients with prostate, testicular, bladder, kidney, adrenal, and rare genitourinary cancers. He also serves as co-chair of the University of Minnesota Health oncology quality and patient safety committee. Rao oversees all quality improvement and patient safety efforts at the University and Fairview Health Services facilities, including nearly 20 hospitals and clinics.

Rao graduated from the premier medical school in India, All-India Institute of Medical Sciences. His education included rotations at UCLA and Memorial Sloan Kettering Cancer Center, which piqued Rao’s interest in oncology.

He decided to focus on genitourinary cancers after becoming attracted to its diverse spectrum of diseases and patients. A GU oncologist’s caseload includes treating and often curing young men with testicular cancer, providing immunotherapy treatments to people with kidney cancer, and helping grandfathers with prostate cancer control their condition.

“It’s a fascinating spectrum in terms of patients’ ages and the biology of the diseases,” Rao says. “Plus, prostate cancer is the most common cancer in men, and kidney cancer and bladder cancer are in the top 10. These cancers kill hundreds of thousands of people each year, and we definitely need someone with a razor-sharp focus on these malignancies working as part of a multidisciplinary team.”

One way Rao seeks to attack these cancers is through cutting-edge research. He brings rich experience in clinical trials from his time in New Mexico, including six first-in-human clinical trials. “That was one of the most gratifying experiences of my life. These patients had no hope and no options; they were told it was the end of the road,” Rao says. “To help some of them was a great success.”

He aims to be involved in clinical and translational research at the University of Minnesota, such as novel treatment strategies that stop the cell cycle in prostate cancer. Rao is particularly excited to partner on new therapies with basic scientists at the U— who have a national reputation for excellence, backed by significant funding from the NIH—and build bridges between them and other clinical research.

“I want to encourage our investigators to get their own trials up and running,” Rao adds. “That’s one of the ways the University truly gets on the map.”
Cancer warrior
Jayanth Panyam always believed in the power of cutting-edge drug delivery systems to fight foes like cardiovascular disease and cancer. He earned a doctorate in pharmaceutical sciences and focused on targeted drug delivery to engage in research and therapy development that extends or saves people’s lives.

Chair of the Department of Pharmaceutics and an endowed professor of targeted drug delivery, Panyam concentrates on finding new methods to battle difficult-to-treat cancers. He joined the University of Minnesota in 2007 with experience in breast cancer therapies, later extending that knowledge to treatments for bladder, lung, and renal cancers.

“The hope is that you can make a positive impact on how patients are treated,” Panyam says. “We all know that cancer is a hard disease to treat or cure because cancer cells evolve and mutate after new therapies. If you can increase the number of years or months or days of a patient’s life, that’s a great success.”

Panyam, who earned his Ph.D. from University of Nebraska and first worked at Wayne State University in Detroit, came to Minnesota to collaborate with other researchers and take advantage of the University’s rich resources. He has made progress with developing therapies for triple negative breast cancer—a more aggressive and harder-to-treat form of the disease.

First Panyam developed a nanomolecular antibody that binds to a protein on the surface of metastatic breast cancer cells. Now he is working on deploying that antibody for diagnostic purposes. This involves determining whether the antibody detects tumor cells that are circulating in patients’ blood—thought to be the generators of metastases.

“The idea is that you take the blood out for a liquid biopsy instead of surgery to cut out a solid tumor. That’s more difficult than sampling the blood,” he says. “Then you use the antibody and other biophysical methods to isolate or study the circulating tumor cells.”

It turns out that this same protein is expressed in many forms of the disease, including bladder and ovarian cancers. That led Panyam to partner with Badrinath Konety, MD, chair of the Department of Urology, on applying his breast cancer findings to bladder cancer. Their recent work involves testing whether the antibody can be used to target bladder cancer cells with cytotoxic anticancer drugs. They aim to reduce side effects associated with bladder cancer therapies and more effectively treat the cancer, Panyam says. “Once a patient has advanced disease, it becomes very hard to treat,” he adds. “We are hoping that because this antibody seems to identify metastatic cells, conjugating the drug to the antibody would be a way to target metastatic disease.”

A prolific researcher, Panyam has several other initiatives going, including a study with Thomas Griffith, Ph.D., an associate professor in the Department of Urology, and David Ferguson, Ph.D., a professor of medicinal chemistry. They are developing immune therapies for renal and kidney cancers. Panyam’s role includes turning a new compound that triggers an immune response into nanoparticles, which are more effective than traditional drug platforms.

It all gets back to Panyam’s mission to make a difference for people facing a life-changing diagnosis of cancer. He is driven to turn his research into more effective therapies for people with cancer, making their treatments easier, better, and more life-sustaining. “If we can do that,” he says, “I think we’ve all done our jobs.”
FACULTY PROFILE: PAARI MURUGAN, MD

Paari Murugan, MD

Cutting edge research
The urological pathology service under the leadership of Dr. Paari Murugan is involved in numerous research projects focusing on prostate, bladder and kidney cancer. Dr. Murugan has studied an innovative model for prostate biopsy processing using a proprietary biomimetic matrix (BxChip) and demonstrated that it reduces cost, test time and improves accuracy of prostate cancer diagnosis. He is in the process of studying the biomarker profile of some of the major genes involved in frequently altered pathways in bladder cancer. The knowledge of these will aid in obtaining prognostic information, chemotherapy response prediction and may provide data for potential targeted therapy. Dr. Murugan is collaborating with other researchers on several ongoing cutting edge projects including 3D printed prostate models for preoperative planning and rehearsal, genomics of low grade prostate cancer in African American men, cell cycle proliferation in non-muscle invasive bladder cancer, efficacy of MRI guided prostate biopsies, molecular signature of metastatic prostate cancer, molecular profile of DNA damaging agents in kidney cancer, chemical markers of cooked meat carcinogens in prostate tissue, AR gene rearrangements and therapeutic targeting of AR variant prostate cancer, efficacy of nivolumab based chemotherapy in bladder cancer and expression of CD133 in neuroendocrine carcinoma of prostate. He has recently authored a section on squamous carcinoma of bladder for the upcoming edition of the International Consultation of Urological Diseases. Dr. Murugan also participates in bladder and prostate cancer patient support groups, offering them a unique opportunity to understand the role and intricacies of pathology diagnosis in formulating treatment plans.

DR. CHARLES RYAN TO LEAD MEDICAL SCHOOL’S HEMATOLOGY, ONCOLOGY AND TRANSPLANTATION DIVISION

Published by: Maddie Eaton, Marketing Specialist

The University of Minnesota Medical School is proud to announce Dr. Charles J. Ryan, MD, as the new Director of the Hematology, Oncology and Transplantation Division in the Department of Medicine. He will also serve as Associate Director for Clinical Research in the Masonic Cancer Center and will hold the B.J. Kennedy Chair in Clinical Medical Oncology.

Most recently, Dr. Ryan was a Professor of Clinical Medicine and Urology at the University of California, San Francisco, a Thomas Perkins Distinguished Professor in Cancer Research, and the Associate Director for Clinical Science at the Helen Diller Family Comprehensive Cancer Center.

He is internationally recognized for his research on prostate cancer. His studies have unraveled the roles of androgens and the androgen receptor in castration-resistant prostate cancer. Dr. Ryan received his BA from Marquette University, and his MD from the University of Wisconsin. He completed an internal medicine residency at the University of Wisconsin and medical oncology fellowship at Memorial Sloan-Kettering Cancer Center. Dr. Ryan joins the University of Minnesota Medical School in April 2018.

Charles Ryan, MD
CURRENT CLINICAL TRIALS

**Randomized Controlled Trial Comparing Relapse Rates between Standard Symptomatic Urinary Stone Removal and Standard Removal with Additional Ureterorenoscopic Clearing of Non-Symptomatic Stones in the Kidneys**

Michael Borofsky, MD

Investigation of Non-Invasive Hydration Monitoring with Smart Water Bottle to Increase Fluid Intake in Patients with Nephrolithiasis and Low Urine Volume

Michael Borofsky, MD

**Non-Muscle Invasive Bladder Cancer**

A Phase II Clinical Trial to Study the Efficacy and Safety of Pembrolizumab (MK-3475) in Subjects with High Risk Non-muscle Invasive Bladder Cancer (NMIBC) Unresponsive to Bacillus Calmette-Guerin (BCG) Therapy

Badrinath Konety, MD

**Maintenance Setting**

A Phase 3, Multicenter, Multinational, Randomized, Open-Label, Parallel-Arm Study Of Avelumab® (MSB0010718C) Plus Best Supportive Care Versus Best Supportive Care Alone As A Maintenance Treatment in Patients with Locally Advanced Or Metastatic Urothelial Cancer Whose Disease Did Not Progress After Completion Of First-Line Platinum-Containing Chemotherapy

Gupta, Shilpa

**Testicular Cancer Investigator Initiated Study**

Phase II Study of Brentuximab Vedotin and Bevacizumab in Men with Refractory CD-30 Positive Germ Cell Tumors

Gupta, Shilpa

**Prostate Cancer**

A Phase 1/2, Open-Label, Dose-Escalation/ Dose-Expansion, Safety and Tolerability Study of INC057643 in Subjects with Advanced Malignancies

Gupta, Shilpa

A phase 1b dose-escalation and dose-expansion study of enfortumab vedotin (ASG-22CE) in combination with immune checkpoint inhibitor (CPI) therapy for treatment of patients with locally advanced or metastatic urothelial cancer Gupta, Shilpa

**Kidney Cancer**

A Phase II Study of TAK-228 in patients with previously treated metastatic renal cell carcinoma

Gupta, Shilpa

Phase Ib/II Trial of Interleukin-2 and PD-1 Checkpoint Inhibitor, Nivolumab In Metastatic Clear Cell Renal Cell Cancer

Gupta, Shilpa

**Chemical markers of heterocyclic aromatic amines for human biomonitoring**

Principal Investigator: Robert Turesky, PhD; Co-Investigator: Christopher Weight, MD

**Non-Muscle Invasive Bladder Cancer**

A Phase III Clinical Trial to Study the Efficacy and Safety of Pembrolizumab (MK-3475) in Subjects with High Risk Non-muscle Invasive Bladder Cancer (NMIBC) Unresponsive to Bacillus Calmette-Guerin (BCG) Therapy

Konyet, Badrinath, R

A Randomized, Double-Blinded, Phase II Study of Maintenance Pembrolizumab versus Placebo after First-line Chemotherapy in Patients with Metastatic Urothelial Cancer

Gupta, Shilpa

**Neoadjuvant Setting Investigator Initiated Study**

Phase II Trial of Neoadjuvant Nivolumab with Cisplatin and Gemcitabine in Muscle-Invasive Bladder Cancer (MIBC) Patients undergoing Radical Cystectomy

Gupta, Shilpa

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Gupta, Shilpa

**Adjuvant Bladder Cancer**

A Phase III, Open-Label, Multicenter, Randomized Study Of Atezolizumab (anti-PD-L1 antibody) Versus Observation As Adjuvant Therapy In Patients With High-Risk Muscle-Invasive Urotheial Carcinoma After Surgical Resection

Konyet, Badrinath, R

**Metastatic Setting**

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