Two-time survivor continues to sail through life

By Maxsane Mitchell

2016 has been banner a year for Brenda Cheney. She’s celebrating 20 years as a Hodgkin’s lymphoma survivor and almost one year as a melanoma survivor. When she’s not working at the new job she started this summer, Cheney is busy raising money for research to improve treatment options for other people. She is a Board of Trustees member with the Leukemia & Lymphoma Society-Gulf Coast Chapter (LLS) and occasionally finds herself in the same circles as the oncologist who treated her two decades ago, Fredrick Hagemeister, MD, professor of Lymphoma/Myeloma.

Her lymphoma diagnosis

Cheney was diagnosed with stage II Hodgkin’s when she was 34, about six months after the sudden death of a boyfriend. Devastated, she said she couldn’t eat much or mentally focus. She started losing weight, and experienced drenching night sweats and difficulty breathing. “Then, one morning, I felt like I was about to have a heart attack,” recalled Cheney, who was working in sales for a Houston sports team and immediately contacted the team doctor. He saw her at a Texas Medical Center hospital for an exam and X-rays, which revealed two tumors in her chest—one the size of a grapefruit and the other the size of a golf ball. “One was pushing into my heart and the other one was growing into my lungs,” she said. A biopsy confirmed the diagnosis and what followed was a recommendation for a treatment that was more aggressive than Cheney wanted to undergo without another opinion. So, she came to MD Anderson.

The treatment

“She came in with a treatable disease that we knew at the time was curable, however, we were studying a regimen of less toxic chemotherapy and radiation therapy,” Hagemeister said. Standard therapy back then was ABVD, a regimen of doxorubicin, bleomycin, vinblastine, and dacarbazine, which produced severe nausea, vomiting, and low blood counts. “At the time, it was thought that NOVP would be less toxic, and since we knew from a prior study that NOVP with radiotherapy was an effective regimen, we offered Brenda a place on a randomized study of NOVP versus ABVD followed by radiotherapy. However, she chose therapy with NOVP, which is mitoxantrone, vincristine, vinblastine, and prednisone, followed by radiotherapy to the upper abdomen and chest, instead of going onto the randomized trial, and has done well,” said Hagemeister. Cheney recalled, “As soon I started receiving chemotherapy, I started feeling better and breathing better. The drugs were reducing the two masses in my chest.” She worked during therapy and says she was able to maintain her sales records.

Therapy side effects and improvements

Hagemeister (right) said that in the two decades since Cheney was a lymphoma patient, chemotherapy options and radiotherapy approaches have improved. Instead of radiation to the neck, abdomen, chest, and pelvis, providers now reduce exposure to just the nodes that are involved, which may be in the neck and mediastinum. This has reduced the risk of secondary cancers and heart and lung diseases that can occur 20 to 30 years post-treatment. “Additionally, the amount of chemotherapy is less now, and we’ve been able to introduce non-chemotherapeutic agents into our regimen,” the oncologist said, such as the antibody-drug conjugate brentuximab and, more recently, nivolumab for Hodgkin’s that has relapsed or progressed after autologous stem cell transplantation. Hagemeister added that staging also has improved to reduce the number of bone marrow tissue samples needed.

Catching a 2nd cancer early: Melanoma

Cheney was diagnosed in December 2015 with melanoma, one of the secondary cancers that can occur following treatment. The stage I mole

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The Halo House Foundation was formed in 2009 to help out-of-town leukemia, lymphoma, and myeloma patients with low-cost, temporary housing during cancer treatment. The organization took root after a conversation between Nathan Fowler, MD, professor of Lymphoma/Myeloma, and his mother, Kathleen Fowler, about a patient whose story tugged at his heartstrings. “It involved a young man who traveled to Houston from Florida for treatment for non-Hodgkin’s lymphoma (NHL). He arrived with his wife, leaving two children at home, after failing multiple therapies at home and believing MD Anderson was his only chance of survival,” recalled Mrs. Fowler, executive director and co-founder of Halo House Foundation. “He told Nathan that he wasn’t afraid to die, but that he was afraid to leave his family deep in debt.”

Even with insurance, out-of-pocket expenses for cancer care can be financially burdensome, especially for those who travel outside of their communities to come to Houston. Procedures such as bone marrow or stem cell transplantation can require at least 30 days hospitalization and a commitment from patients to stay close to the hospital for weeks at a time. That takes money, and understanding that is what prompted Mrs. Fowler to postpone her retirement from the apartment management business to help find short-term homes for that NHL patient and others like him. With help from her son’s departmental colleagues, former patients, friends and family of cancer survivors, and Houston-area business leaders, they raised enough money to offer two apartments. Fast-forward six years later and the foundation has 10 furnished apartment units to offer out-of-town patients for $20 per day—quite a bit less than they’d pay per night at a hotel. Patients can be referred to Halo House by doctors in the Texas Medical Center, social workers, the Leukemia & Lymphoma Society of Houston, and other charitable agencies. “As of late July, we have provided over 13,000 days of housing, but the need is still enormous. That’s why we’ve been raising money to build a bigger facility,” said Dr. Fowler. “We have approximately 75% of the capital needed to build it.”

Net proceeds of $250,000 from the foundation’s Nov. 5 gala at the Bayou City Event Center will help fund the completion of the complex, which will include 32 apartment units, a fitness center, a laundry room, a chapel, and a large community room where allied health specialists can give lectures and community groups can host holiday meals and events. The property will also feature a courtyard and outdoor gazebo.

The design was donated by Kirksey Architecture of Houston, with local real estate giants Midway Companies and Morgan Group donating their construction expertise. “The leaders of our partner companies have personal reasons for wanting to help us. They understand how important it is to have a comfortable place to stay during this critical time,” said Mrs. Fowler. “It’s important to have your own space where you can recover, relax, and do normal things like watch television and cook your own meals—instead of having to leave a hotel and go to a restaurant. The apartments also serve as a refuge for caregivers who need a place of peace. What we’re doing is helping entire families.”

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**Expanding the Halo**

**Providing a home away from home for more out-of-town patients**

By Maxsane Mitchell

The Halo House Foundation was formed in 2009 to help out-of-town leukemia, lymphoma, and myeloma patients with low-cost, temporary housing during cancer treatment. The organization took root after a conversation between Nathan Fowler, MD, professor of Lymphoma/Myeloma, and his mother, Kathleen Fowler, about a patient whose story tugged at his heartstrings. “It involved a young man who traveled to Houston from Florida for treatment for non-Hodgkin’s lymphoma (NHL). He arrived with his wife, leaving two children at home, after failing multiple therapies at home and believing MD Anderson was his only chance of survival,” recalled Mrs. Fowler, executive director and co-founder of Halo House Foundation. “He told Nathan that he wasn’t afraid to die, but that he was afraid to leave his family deep in debt.”

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**Survivor continues to sail through life**

was found on one of her legs during a yearly checkup, and was excised at MD Anderson in February 2016. Cheney is unsure that prior radiation triggered the malignancy because of sunburns she experienced as a younger woman. “I’m just grateful the melanoma wasn’t on my face. I can hide the scar on my leg,” she said with a sense of relief. Additionally, Cheney said that one of her three brothers was diagnosed a few years ago with early stage Hodgkin’s. “One of his doctors thinks the Epstein-Barr virus may have contributed. Another doctor thought there might have been something in the Minnesota home where we grew up that exposed us to a disease-causing agent. Who knows?” she questioned.

**Sailing to raise money for lymphoma research**

Now recovered from both cancers, Cheney continues a decade of work she started with the LLS. The first fundraiser she held years ago, “Sip and Sail for a Cure,” is now the organization’s kickoff for the annual Leukemia Cup Regatta. “Over the years I have fine-tuned my campaigning efforts with exciting auctions and an online fundraising page. To date, I’ve raised over $130,000 for blood cancer research,” Cheney said. “As a top fundraiser again this year, I qualify to attend the Leukemia and Lymphoma Society’s Fantasy Sail with Gary Jobson.” He’s the lymphoma survivor, 1977 America’s Cup winner, and sports broadcaster who started the Fantasy Sail as a reward for all volunteers who raise over $12,500 each year. Cheney has qualified for seven Fantasy Sails. This year’s trip will set sail from Newport Beach, CA, in December.

**Not slowing down one bit**

This past July, Cheney started working as a marketing director for a certified public accounting firm, but she still is making time to enjoy a full social life. Some of her down time includes sailing, of course, hitting the road with her dog, hanging out with friends, and participating in other fundraisers that support rodeo outings for special needs children and homeless pets waiting to be adopted. “It’s fun to help other people. I’m doing fine, so I want to enjoy as much life as I can,” Cheney said.
reduce repetitive strain on staff during procedures. Nominators also recognized Cornelison for re-matching physician assistants with faculty to create fair workloads and for teaching clinic administrative employees about the principles of transplantation so they can understand some of the concerns that patients encounter daily. Several patients submitted strong letters of support on her behalf. “There have been many unexpected turns before and after transplantation, some of which we are still dealing with. On top of that, there’s the complication that I live in Maryland with my wife and two kids. You could call us ‘high maintenance,’ but Megan has remained accessible and diligent. The evidence is her quick response to questions about prescriptions, requests for letters to the insurance company to get them to approve treatment, and her concerns about my state of being,” a patient wrote. “We’re figuring out how to make a new life, with a new normal, and Megan’s willingness to care for us as a family has made all the difference.”

Recognizing Epic contributors

Division Head Patrick Hwu, MD, led the way in presenting some special edition awards at the employee recognition program to honor those whose contributions were quite literally deemed as “Epic!” Brenda Brown, RN, MSN, OCN, clinical administrative director for the Ambulatory Treatment Center (ATC), was given the highest honors, Epic Champion. James Yao, MD, chair of Gastrointestinal Medical Oncology and member of the institutional EHR Executive Core Committee, and Martha Salas, MSW, MBA, division administrator, presented the award together. Brown worked for 34 days in a row—including weekends—before she was ordered to take some time off. “Because of Brenda’s leadership and ability to work with multiple groups throughout MD Anderson, the ATC had no patient harm events in the month of go-live,” Salas said. While providers were instructed to reduce patient appointments by 50%, the downstream center saw 256 patients on March 4. The average number of patients on a normal weekday in the ATC is 384. That day, some patients waited as long as six hours prior to start of treatment. Brown worked with Patient Advocacy and Cancer Medicine volunteers to provide
Epic contributors communications assistance, meal tickets, and refreshments, while requesting an emergency Command Center on the main unit where clinical pharmacists, advanced practice providers, and faculty—including department chairs—could work with Epic consultants to check and validate treatment plans to reduce patient wait times. Brown simultaneously worked with Financial Clearance Center supervisors to determine why the new EHR was showing holds or “hard stops” on patient records, which was another major barrier to on-time starts, and she gave daily Top 10 progress/issues reports at the Hickey Auditorium before representatives of the entire institution. “Thank you for this award. There was so much talent and support that showed up at the clinic on March 4 to help us—everyone from Drs. Hwu, Robert Wolff, and Tom Buchholz. Wendy Austin (executive director, Hospital & Clinics) and Martha were there or just a phone call away. I want to thank my patient care nurse managers—Michelle Lawrence and Joy Yates—for taking the position that if I didn’t leave the clinic, they weren’t going to leave the clinic. Special thanks to the entire ATC team,” said Brown. “Everyone worked tirelessly.” Ever the administrator, Brown had a final message. “Sign your orders, sign your consents!”

Dina Patel, RPH, PharmD, manager of clinical pharmacy services, was named Epic Super Star. Patel leads Pharmacy Clinical Programs for DoCM’s Lymphoma/Myeloma and Neuro-Oncology departments, and the Gynecologic Oncology & Reproductive Medicine department in the Division of Surgery. Prior to go-live, she maintained her own clinic practice, participated in departmental projects, mentored employees, and worked on institutional committees to improve medication administration for our patients. But after President Ron DePinho announced that MD Anderson was switching to Epic, Patel began taking an active role to ensure successful transfer of thousands of Clinic Station chemotherapy order sets into Epic’s Beacon treatment plan module. Her schedule changed to spending 40% of her time on Epic, to 80%, and then to 90% in the days leading up to launch. The Epic Stars category recognized pharmacy employees Janna Baganz, MA, Judy Chase, RPH, PharmD, Alison Gulbis, RPH, Laura Michaud, RPH, PharmD, PhD, and Deborah McCue, RPH, PharmD, who also won in the Divisional Support category. “Without their contributions, we couldn’t have done what we did. Without their efforts, I’m not sure it would have been possible to go live on time. Their work made the difference in getting treatment plans converted correctly in the red, green, and blue light processes,” said Yao and Salas.

Several Cancer Medicine employees shared the Epic Star spotlight. Alicia Newton, MHA, MBA, department administrator in Gastrointestinal Medical Oncology, was lauded for introducing the Department Administrator Report (DAR) as a tool to keep the progress of each department organized during the many steps of implementation. Kent Walters, MBA, CMPE, FACHE, department administrator in Stem Cell Transplantation and Cellular Therapy, was honored for keeping things afloat at the ATC Command Center. Cheryl Fullmer, RN, BCN, MBA, clinical administrative director in the Clinical Translational and Research Center, was noticed for participating in a treatment plan conversion workgroup that provided oversight of the Beacon template build, which was largely constructed by non-clinical information systems employees. Salas also thanked divisional employees for administrative help in organizing meetings, disseminating information to clinical staff and faculty regarding Beacon build updates, and participating in teleconferences and institutional town hall meetings.

From left: Yao, Walters, Hwu, Fullmer, Newton, and Salas.
Citations for excellence

**Administration:** Sonya Polk-Davis, RN, BSN, OCN, nurse manager in the Lymphoma/Myeloma Center, was recognized for her willingness to help with patients during crunch situations, for including clinic staff representation during applicant reviews for new positions, for addressing challenges with the APP fast-track clinic, and for serving as an Epic Super User.

**Administrative Support:** Demetria Babineaux, office manager in Thoracic/Head and Neck Medical Oncology, was lauded for superb support of her department's faculty recruitment efforts. This included the time she arranged a second visit for a candidate who wanted to return a week later. In a matter of hours, Babineaux scheduled babysitting and fun activities for the candidate's children, house tours, and appointments for follow-up interviews. Additionally, she's appreciated for taking on facilities asset request processes for South Campus research labs following the departure of a lab manager.

**Advanced Clinical Practice:** Peg Fields, RN, MSN, ACNP, AOCNP, Neuro-Oncology advanced practice registered nurse, was celebrated for having a deep understanding of standard of care and research options that rivals Neuro-Oncology medical trainees. She's appreciated for her ability to teach at all levels, including medical, nursing, and midlevel provider trainees. Patients supported her nomination, including one who came to MD Anderson with stage IV glioblastoma multiforme. He wrote that Fields made him feel as if she were personally invested in his outcome. “She got me through the shock of having cancer and moved to accepting the diagnosis, to helping my doctors develop a strategy, to working on my self-talk so I can forge ahead.”

**Clinical Nursing Practice:** His name is mentioned more than any other employees' names in the Ambulatory Treatment Center, wrote colleagues of Loven Panes, RN, OCN, clinical nurse. He's regarded as an excellent nurse who is relied upon to handle the most difficult patient issues, including tough IV starts. Some patients request him by name and if his schedule is full, nominators say those patients will often change their appointment for a time when Panes can be their nurse. As an Epic Super User, he gave tutorials and created tip sheets to improve functionality. He still takes calls to answer technical issues—even calls to his home as late as 9 p.m.

**Clinical Research:** Nominators say Ly Nguyen, MPH, a clinical studies coordinator in Investigational Cancer Therapeutics, was the top clinical trials enroller in fiscal year 2016. She has a strong rapport with her patients and goes the extra mile for them. This includes the time a refractory patient was about to be removed from a one-year trial even though the medication was working. The pharmaceutical company believed one year was the maximum benefit these patients would achieve. However, Nguyen showed them multiple scans and other results—eventually convincing the pharmaceutical company to allow a compassionate use protocol.

**Communication, Education, and Information Systems:** Sergio Garza, BS, information services supervisor in Genitourinary Medical Oncology, was appreciated for speeding up development of the Prometheus Platform tool that enables users to store all clinical research information in one place. The application has been so successful that other departments, including outside of the DoCM, ask for his help in building their own. In particular, faculty and research employees in the Department of Gynecologic Oncology and Reproductive Medicine have even asked for Garza’s help in identifying a suitable applications expert to build and run a similar system for them.

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Divisional Support: This category recognizes contributions to the division by a non-Cancer Medicine employee. Deborah McCue, RPH, PharmD, clinical pharmacy services manager, was nominated by Leukemia. “Without Debbie, the department would not have had any Beacon treatment plans for hundreds of patients receiving chemotherapy. Because of her, disaster was avoided,” wrote nominators. They said she responded to the conversion crisis by coordinating with her team of clinical pharmacy specialists in Pharmacy Services to review 800 treatment plans line by line to check and revalidate orders. McCue worked an estimated 200 hours on Epic-related issues—much of it beyond her regular 40-hour week. The extra hours spent were uncompensated because she refused to take time off, as her main job—fulfilling orders for blood cancer patients—still had to be done along with sorting through applications to fill two open positions in her group.

Financial Services: Richarle “Ricci” Ryan, financial analyst in Thoracic/Head and Neck Medical Oncology, was recognized for financial acumen that allows her to manage the accounts of eight physician-scientists. She has oversight of the department’s $40 million research grant portfolio. One of her investigators wrote that prior to Ryan joining the team, his attention to scientific matters was frequently interrupted by issues of how to manage major federal, state, and donor funds. He needed more expertise to help accurately forecast ability to hire postdocs. “With Ricci, I now look forward to our meetings because she provides a clear picture of where we stand,” the researcher stated.

Laboratory Research: Nominators say the talent of Anh Hoang, HT, histology laboratory chief in Genitourinary Medical Oncology, for performing immunohistochemistry procedures can only be compared to that of a musical virtuoso. The work to search for cell or tissue antigens that detect disease biomarkers is tedious, but Anh’s optimization of these staining techniques is second to none. Faculty nominators credit his work as a basis for successful research and manuscripts published in high-impact journals, including Clinical Cancer Research, and they hold him out as a model for safe and efficient lab management.

Patient Services: Carol Williams, CNA, nurse assistant in the Ambulatory Treatment Center, was celebrated for improving safety practices throughout the ATC. One of her suggestions led facilities staff to install sanitizer dispensers for CNAs to use between patients. Previously, the nearest ones were located down a hallway outside of patient treatment rooms. Williams is also appreciated for proactively having equipment repaired or replaced or asking a manager to teach her how to correct a problem in the Tetris scheduling system so she could share the solution with other nursing assistants.

Research Nursing Practice: Colleagues affectionately refer to Vruti Patel, RN, BSN, research nurse in Melanoma Medical Oncology, as the “TIL Queen.” She’s the main contact for patients enrolled in the tumor infiltrating lymphocyte protocols, intense immune system treatments that usually require patients to be hospitalized for 30 days. She knows every detail about the protocols and teaches medical oncologists and other nurses about the intricacies of the trials. She is beloved by patients, including one who wrote a support letter that began with the sentence, “Vruti saved my life.” He detailed his arrival at MD Anderson with what lab tests found to be a low platelet count, which would have prevented him from starting his trial. But Patel suggested to the doctor that they hand-count the platelets, a tedious process that found the patient’s numbers to be in the eligible range. The patient is stable today.
Program Coordinator named September Heart of MD Anderson

By Maxsane Mitchell

“...No way, you’re kidding, right?” This was the first thought in Lurtese Sherrell-Gardner’s mind when told that she would receive the September 2016 Heart of MD Anderson Outstanding Employee Award. However, after the program coordinator in Genomic Medicine accepted it as a real thing, she said she felt very blessed and honored. “It truly melted my heart and I was overwhelmed with joy. It’s a beautiful thing to be appreciated and to know that what you do makes a difference,” she said.

A reception was held in her honor on Sept. 16, at which she received a new employee badge featuring the photo that will be seen around the institution until September 2017, along with a pink marble plaque with her name etched on it, and a cash award of $1,000. In attendance at the jam-packed soiree were some of Sherrell-Gardner’s biggest fans: Cathy Davis, MBA, department administrator, Andy Futreal, PhD, chair ad interim, Jennifer Wargo, MD, professor in Surgical Oncology and Genomic Medicine, and her husband, Tony Gardner.

Sherrell-Gardner was celebrated for having a “can do, upbeat” attitude, and for being a calm current in a sea of deadlines and competing priorities. “We’d be completely lost without her and her organizational skills,” said Futreal. “Lurtese has an amazing capacity to do things in an incredibly professional way, but also with a very warm, caring demeanor.” Someone else in the group noted, “Her positive attitude is contagious, and in the last few years, she has spent countless hours trying to make our new department feel like home.” Nominators also appreciate Sherrell-Gardner for reliably communicating with them about changes that affect their work, helping them overcome administrative and regulatory hurdles, and assisting them in gaining access to professional development organizations.

We have the Best Bosses

Congratulations to Best Bosses Sandi Knight, MSN, CPON, RN, NE, (left) nurse manager in the Genitourinary Cancer Center, and Anna Vardeleon, BSN, MBA, RN, associate director of research planning and development in Melanoma Medical Oncology. Knight and Vardeleon were two of five employees honored at an Oct. 18 ceremony as winners of the 2016 MD Anderson Best Boss Award. Both honorees credited their success to their teams. “This award is really less about me and more about the team of people I’ve been blessed to work alongside and empowering them to become the best version of themselves, and in turn they’ve challenged me to do the same,” Knight said. “I am truly nothing without you. Always remember, you are your own boss. Look beyond yourself as leaders,” Vardeleon said. MD Anderson Human Resources Vice President Shibu Varghese said a total of 348 nominations were received in support of 133 individuals, while Executive Vice President-Administration Dan Fontaine noted that at MD Anderson, “Our most important deliverable is our people.”
Sean Post, PhD, assistant professor of Leukemia, recently received total funding of $1.83 million (including indirect costs)—$366,000 per year for five years—for his new NIH Research Project Grants (R01) entitled “Personalized therapy for AML patients with a newly identified genetic alteration.”

Development of new treatment options for AML patients has stalled in recent decades due in large part to limited understanding of how driver mutations impact pathogenesis and progression of this malignancy. Post and his team are making important strides in the field, having recently identified that deletion of one copy of the gene encoding heterogeneous nuclear ribonucleoprotein K (HNRNPK) leads to downstream ablation of the tumor suppressive p53 and C/EBP pathways and resultant leukemic progression [Cancer Cell 2015:28, 486–499]. While this work linked HNRNPK haploinsufficiency with AML malignancy, the team also found in contrast that HNRNPK amplification and overexpression are common in AML patients, and that this overexpression associates with increased oncogenic c-Myc expression and NPM1 mutation. In the clinic, co-occurrence of HNRNPK overexpression and NPM1 mutation associated with further enhancement of c-Myc expression and dire patient outcomes, a finding of particular importance as patients with NPM1 mutation in the absence of elevated HNRNPK expression typically have favorable prognoses.

Given these preliminary findings, the team developed their R01 proposal around the hypothesis that HNRNPK overexpression cooperates with NPM1 mutation to drive leukemogenesis via activation of c-Myc. Accordingly, their proposal seeks to: 1) globally explore the mechanisms by which HNRNPK enhances AML malignancy, 2) investigate the therapeutic efficacy of several agents in treating disease marked by HNRNPK overexpression, and 3) determine how HNRNPK synergizes with NPM1 mutation to bring about a worse prognosis.

These studies are invaluable for understanding AML disease mechanisms and working toward novel therapeutic options for a malignancy that has seen little forward progress on this front in decades.

Investigations in the first aim will utilize transgenic mice that overexpress HNRNPK in the hematopoietic compartment to molecularly and temporally define how HNRNPK mediates expression of c-Myc and other oncogenic pathways throughout the course of AML disease. Additionally, Post and team will look at global transcriptional and translational changes resulting from HNRNPK overexpression during leukemogenesis to help identify other potential therapeutic targets. Further studies will focus on the self-renewal capacity of hematopoietic cells from these mice and determine the stage at which HNRNPK overexpression blocks myeloid differentiation.

In the second aim, Post will evaluate the therapeutic efficacy of bromodomain inhibitors and BRD-4 specific degraders, which both target c-Myc, in alleviating HNRNPK-dependent malignancy. Studies will be performed with both primary cells from patient samples that overexpress HNRNPK and malignant cells from HNRNPK transgenic mice. Single agents and novel combinations with front-line chemotherapies and bortezomib will be tested, and the most effective options will be recapitulated in vivo in mice. Additionally, the molecular mechanisms governing response to these therapies will be determined through analysis of tissues obtained from mice exposed to the most promising regimens.

The final aim will probe the synergistic relationship between HNRNPK overexpression and NPM1 mutation in influencing leukemogenesis. Genes and pathways altered by the presence of both these genetic events, and specifically exacerbated by NPM1 mutation, will be identified using transgenic mice engineered to both overexpress HNRNPK and carry mutated NPM1. Changes in c-Myc expression and other targets identified in aim 1 will be analyzed over the course of leukemic disease initiation and progression. Additionally, primary patient cells will be used to determine the cooperative impact of these genetic events on therapeutic responses to bromodomain inhibitors, which will be tested for therapeutic efficacy in vivo.

The results of this work will inform clinical trial design to target c-Myc in the context of HNRNPK overexpression, and determine whether HNRNPK expression can be used to risk stratify and choose personalized therapies for AML patients. These studies are invaluable for understanding AML disease mechanisms and working toward novel therapeutic options for a malignancy that has seen little forward progress on this front in decades.
Andreeff: Researching AML in the immunosuppressed microenvironment

Congratulations to Michael Andreeff, MD, PhD, professor of Leukemia, for his recent Multi-Investigator Research Award (MIRA) from the Cancer Prevention & Research Institute of Texas (CPRIT) in the amount of $6 million for research titled “Acute myeloid leukemia in the immunosuppressed microenvironment.” In total for this round of funding, MD Anderson received $17.1 million for research and $2 million for recruitment.

The awards, announced in August with several others, bring CPRIT well over the halfway point for its funding authority. To date, the institute has awarded 1,070 grants totaling more than $1.67 billion to 98 academic institutions, non-profit organizations, and private companies in Texas. The agency was launched in 2009 after Texas voters approved a 2007 bond issue committing $3 billion to the fight to end cancer.

Hong: AACR names new research award for esteemed leader

The American Association for Cancer Research (AACR) has established a new award named in honor of Waun Ki Hong, MD, professor of Thoracic/Head and Neck Medical Oncology and former division head, and AACR Past President (2001–2002). The AACR-Waun Ki Hong Award for Outstanding Achievement in Cancer Research acknowledges Hong’s contributions to cancer research, care, and prevention during his career as a physician scientist. This award will recognize the outstanding research of a young investigator who has conducted highly meritorious laboratory, translational, or clinical cancer research.

The recipient of the inaugural AACR-Waun Ki Hong Award for Outstanding Achievement in Cancer Research will deliver an award lecture at the AACR Annual Meeting April 2017, and will receive an honorarium of $10,000. Hong’s pioneering research resulted in several seminal contributions in cancer medicine. He conceptualized and led the landmark Veterans Administration Cooperative laryngeal preservation trial using induction chemotherapy and radiotherapy, which changed the way the disease is managed and served as a model for organ preservation in many other cancers. Hong also established proof of principle that chemoprevention works in patients with head and neck cancer, thereby helping define a new discipline in cancer prevention. Additionally, he was the main architect and principal investigator for BATTLE (Biomarker-integrated Approaches of Targeted Therapy for Lung Cancer Elimination), the first successful biopsy-driven trial in lung cancer. This formative work opened up a new paradigm of personalized cancer therapy in solid tumors.
The Thoracic/Head and Neck Medical Oncology (THNMO) faculty and staff gathered on Sept. 9 to discuss recent research progress within the department. The departmental retreat was divided into four sessions, each involving talks by researchers about tumor microenvironment, drug resistance, tumor metabolic regulation, and DNA methylation/cell cycle in the context of thoracic/head and neck malignancies.

Lectures in session one provided insights into factors that regulate the tumor microenvironment. Hou-Fu Guo, PhD, postdoctoral fellow in the lab of Jonathan Kurie, MD, professor of THNMO, discussed efforts to assay the activity of lysyl hydroxylase 2 (LH2), an enzyme that adds a hydroxyl group to collagen residues leading to enhanced cell stiffness and heightened invasion and metastasis in lung cancer cells. The group is also working to determine the structure of the LH2 catalytic domain to assist the ultimate design of LH2 inhibitors.

Taghreed Hirz, PhD, postdoctoral fellow in the lab of Ferdinandos Skoulidis, MD, PhD, assistant professor of THNMO, spoke about plans to assess the impact of APOBEC expression on tumor growth kinetics, metastasis, DNA damage, the immune microenvironment, and response to PD1/PDL1 checkpoint blockade in a murine model of non-small cell lung cancer (NSCLC). APOBEC family members contribute to tumor somatic hypermutation by deaminating cytosine to uracil.

Closing the session, Irene Guijarro, PhD, postdoctoral fellow in the lab of John Heymach, MD, PhD, chair of THNMO, discussed recent findings showing that in a murine model of small cell lung cancer (SCLC), the CDK4/6 inhibitor G1T28 not only preserves vulnerable white blood cells, preventing cisplatin-induced cytotoxicity and myelosuppression, it also synergizes with cisplatin chemotherapy to increase tumor volume reduction. Clinical trials testing the combination of G1T28 and chemotherapy in patients with advanced SCLC are currently underway.

Monique Nilsson, PhD, senior research scientist in the Heymach lab, kicked off the second session with preclinical and clinical data demonstrating a role for β2-adrenergic receptor activation and downstream IL-6 upregulation in promoting resistance to tyrosine kinase inhibitors (TKIs) in EGFR mutant NSCLC. This link is thought to occur via modulation of the LKB1/AMPK/mTOR axis. Next, David Peng, graduate research assistant in the lab of Don Gibbons, MD, PhD, associate professor of THNMO, discussed preclinical work revealing a role for the epithelial-to-mesenchymal transition (EMT) in promoting MEK inhibitor resistance in KRAS-mutant lung cancers. MAPK signaling and downstream MEK/ERK activation were decreased in mesenchymal versus epithelial cells, rendering the former cell type resistant to MEK inhibition. These findings are the first to implicate the miR-200/ZEB1 axis, which promotes EMT, in regulating the MAPK signaling cascade. Jacqulyne Robichaux, PhD, postdoctoral fellow in the Heymach lab, presented preclinical and 3D structural modeling data demonstrating that, of seven tested TKIs, poziotinib was the only agent able to potently inhibit the activity of EGFR and HER2 exon 20 insertion mutants in NSCLC cell lines. Structural modeling revealed that both EGFR and HER2 exon 20 mutations led to steric hindrance at the drug binding site.
binding pocket; poziotinib was the only agent that could overcome this obstacle due to its small size and flexible chemical structure. These findings have provided strong rationale for testing poziotinib in the clinical setting for NSCLC patients carrying EGFR and HER2 exon 20 insertions.

Talks in session three focused on tumor metabolic regulation, beginning with findings from Xi Liu, PhD, instructor of THNMO and member of the lab of Ethan Dmitrovsky, MD, professor of THNMO, and provost and executive vice president of MD Anderson. Liu described studies showing that loss of protein USP18, which leads to spontaneous development of leiomyosarcomas in mice, results in repression of thermoregulatory protein UCP-1 and mice that are hypersensitive to cold temperatures. This work illuminated a previously unrecognized link between USP18 and metabolism.

Vaishnavi Sambandam, PhD, postdoctoral fellow in the lab of Faye Johnson, MD, PhD, associate professor of THNMO, performed a drug sensitivity screen for PI3K/mTOR pathway inhibitors in head and neck squamous cell carcinoma (HNSCC) cell lines and oral xenograft mouse models. Results of the screen showed that inactivating NOTCH1 mutation may be a biomarker of response to PI3K/mTOR inhibitors, and that targeted metabolic pathway inhibition could potentially be used to sensitize NOTCH1 wild-type cells to these agents. Kyriante Henry, graduate research assistant in the Johnson lab, wrapped up session three with a related discussion exploring the mechanism of communication between the NOTCH1 and PI3K/mTOR pathways that may underlie sensitivity of NOTCH1 mutants to PI3K/mTOR inhibitors in HNSCC. Ongoing efforts have found that NOTCH1 in HNSCC cell lines appears to regulate expression of multiple HES/HEY protein family members, which connect NOTCH1 and PI3K signaling through PTEN in other cancer types. Future work will refine this putative network of communication in the context of PI3K/mTOR inhibitor sensitivity.

The fourth session centered on DNA methylation and the cell cycle in thoracic/head and neck malignancies. Kelly Quek, PhD, postdoctoral fellow in the lab of Jianjun Zhang, MD, PhD, assistant professor of THNMO, observed significant DNA methylation pattern intratumoral heterogeneity (ITH) within the same tumor and between different patients in lung adenocarcinoma samples. Analyses revealed that larger tumors, advanced age, and patients who had relapsed exhibited higher levels of methylation ITH. Next, Triparna Sen, PhD, postdoctoral fellow in the lab of Lauren Byers, MD, assistant professor of THNMO, presented work demonstrating the potent anti-tumor activity of a CHK1 inhibitor alone and in combination with anti-PDL1 in SCLC cell lines and mouse models. Biomarker analyses to determine expression of immune markers in single agent and combined CHK1/anti-PDL1 treatment are ongoing. The CHK1 inhibitor chosen for these studies, LY2606368 is currently being tested in clinical trials.

The final seminar of the day was provided by keynote speaker Sandra Schmid, PhD, professor and chair of Cellular and Molecular Biology at the UT Southwestern Medical Center. Schmid is a decorated and renowned scientist recognized internationally for her work on clathrin-mediated endocytosis.
Introducing the 2016 incoming class of Hematology/Oncology fellows

By Maxsane Mitchell

Fourteen physicians joined our Hematology/Medical Oncology Fellowship Program in July 2016 to receive the additional training they need to make a long-term impact in cancer care, clinical or translational research, and treatment outcomes metrics. One of the doctors will spend one year with us solely to focus on benign blood diseases.

Robert Wolff, MD, program director, with the fellowship administrative team, received 448 applications through the Match Program, about a dozen more than the previous year. Fifty-six doctors were invited for interviews. Those selected for the precious few slots are the crème de la crème—they have worked on significant research projects with mentors, served as first authors for papers in high-impact journals, such as Cancer, Clinical Cancer Research, Molecular and Cellular Biochemistry, and presented before leaders of the field at annual meetings of ASCO and ASH.

Aydah Al Awadhi, MBBS

MBBS: United Arab Emirates University Faculty of Medicine & Health Sciences, UAE
Residency: St. Vincent Hospital, Worcester, MA

Driving Al Awadhi’s aspirations to become a master clinician in oncology is her desire to provide the same care and kindness that her grandmother received while being treated for a complex medical issue. Al Awadhi is comfortable interacting with patients during their most challenging health crises, as evidenced by the Ace of Heart Award presented to her during residency for outstanding patient service, and she hopes to return to the UAE to be among a new generation of physicians working to improve the level of specialized cancer care. During her early training, Al Awadhi became particularly interested in breast cancer genetics and survivorship. She has co-authored several research manuscripts, including in a 2013 edition of Molecular and Cellular Biochemistry, examining hereditary hemorrhagic telangiectasia type 2 ALK1 missense mutations.

Kelly Casteel, MD

MD: Case Western Reserve University, Cleveland, OH
Residency: University of Texas Health Science Center, Houston, TX

Casteel trained in a four-year internal medicine/pediatrics residency program and then served as the internal medicine chief resident for one year. She chose to pursue a career in hematology and oncology because of the special doctor-patient relationships she found to be unique to the field. She has participated in poster presentations with supervising faculty and clinical fellows, contributed to book chapters, and participated in a retrospective analysis focusing on outcomes and prognostic markers in an acute leukemia patient cohort. Casteel is looking forward to working with strong clinical mentors in hematology and oncology, and developing her clinical research experience.

Jad Chahoud, MD

MD: Lebanese University Faculty of Medical Sciences, Lebanon
Residency: The University of Texas Health Science Center, Houston, TX

Chahoud aspires to continue developing his career as a clinical investigator. Accomplishments so far include participating in a yearlong joint program of his medical school and the Université of Toulouse in Paris to study the fundamentals of research. As a resident he contributed to two abstracts presented at the 2015 ASCO Annual Meeting and received a Hematology Opportunities for the Next Generation of Research Scientists (HONORS) award from the American Society of Hematology (ASH) in support of a study he worked on with Dr. Elias Jabbour, associate professor of Leukemia. They examined the prognostication value of adjunct cytogenetics in 20q deletion acute myeloid leukemia (AML). Chahoud’s work on cancer-related disparities in the United States was recently published in the Journal of the National Comprehensive Cancer Network (JNCCN) and highlighted in a press release by the National Comprehensive Cancer Network. The Journal of American Medical Association (JAMA) Oncology published his paper on the challenges and future of HPV vaccination. JAMA Dermatology also published his research on the association between HPV and cutaneous squamous cell carcinoma.

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Hematology/Oncology fellows

**Katherine Clifton, MD**
**MD:** Loyola University, New Orleans, LA  
**Residency:** Beth Israel Deaconess Medical Center, Boston, MA  
Clifton joined the fellowship intent on pursuing her interest in breast oncology, genetic screening, and women’s health. During residency, she was especially inspired by women who insisted on living full lives even while in treatment for metastatic disease. Working with a mentor there in the Cancer Genetics and Prevention Program, Clifton gained exposure to the benefit of genetic testing for BRCA 1/2 mutations and how the results assisted women and their specialists in making decisions about prophylactic options. She participated in a study of patient reasoning for having or declining genetic testing and hopes that information will ultimately be used to improve counseling approaches. In proposing the study and getting it approved, Clifton gained valuable knowledge about the institutional review board (IRB) process and hopes to identify a mentor at MD Anderson who can help her develop and execute other clinical research ideas.

**Ryan Huey, MD**
**MD:** University of Oklahoma, Norman, OK  
**Residency:** Duke University Medical Center, Durham, NC  
Huey selected oncology because of the enormous and gratifying responsibilities of not only diagnosing disease and guiding treatment plans, but also of being intellectually prepared to respond to treatment setbacks and providing counsel to patients and their families when curative options are exhausted. In residency, he worked on a project focused on methods to reduce overtesting in internal medicine clinics and performed similar assignments following residency when he spent a year as an inpatient hospitalist on a neuro-oncology ward. Huey is deciding which tumor subspecialty he will pursue, but knows that future goals will include helping to advance personalized and immunotherapy options while improving methods that measure care outcomes and reduce treatment costs. He’s also seeking additional formal training in quality improvement and outcomes research, and looks forward to mentored projects during fellowship that will expand his knowledge base in this area. Huey also wants to be involved in the medical education of upcoming physicians.

**Daniel Johnson, MD**
**MD:** Louisiana State University, Baton Rouge, LA  
**Residency:** Louisiana State University, Baton Rouge, LA  
Johnson’s initial inspiration to become an oncologist is deeply personal. He was impressed by the care and scientific and technological advances that were part of his mother’s treatment for glioblastoma. Once she recurred after frontline therapy, she participated in a Phase I gene therapy trial at MD Anderson that staved off the cancer for five years. Johnson remains appreciative of the doctors’ expertise and human kindness. During medical school, Johnson cofounded the student hematology-oncology interest group. During residency, he was involved with a research committee that worked with AIDS patients diagnosed with cancers. Also a chief resident, Johnson enjoyed training less-experienced residents and medical students, and working to improve their board review program.

**Amy Jones, MD**
**MD:** The University of Texas at Southwestern, Dallas, TX  
**Residency:** Duke University Medical Center, Durham, NC  
Jones became interested in oncology and hematology after losing grandparents to lung cancer and lymphoma. She believes the field offers an opportunity to blend scientific drive, clinical acumen, and empathy. From undergrad through residency, Jones spent many summers abroad doing health education projects in Haiti and Belize, and serving as a public health worker in rural Peru and Guatemala. In college, she was particularly interested in immunology and developed mouse models of susceptibility to *S. aureus*. As a resident, Jones presented a poster at the 2016 ASCO Palliative Care in Oncology Symposium about patient outcomes in metastatic colon cancer and about how symptom burden influences patients’ decisions about future therapy. She contributed to a case study of patients with hemophagocytic lymphohistiocytosis, which she and her research partners hope will uncover clinical patterns that could lead to novel treatment and better outcomes. In this fellowship, she plans to pursue clinical research training to either expand her work in patient outcomes in late-stage disease or capitalize on prior training in immunology.

**Andrew Laccetti, MD, MS**
**MD:** Albany Medical College, Albany, NY  
**MS:** Union College, Schenectady, NY  
**Residency:** University of Texas Southwestern Medical Center  
The former chief resident ultimately aspires to a career that includes leadership opportunities in clinical and health systems research, and work in medical education. In fact, he has already contributed to clinical research and medical education. In residency, Laccetti worked with a mentor using Surveillance, Epidemiology, and End Results (SEER) data to examine the longstanding practice of excluding patients with prior cancers from certain lung cancer trials. The study showed that although up to 18% of lung cancer patients were omitted, their survival rates were as good as patients with no prior cancer. As a result, Laccetti and other researchers suggested that broadening of clinical trial inclusion would not adversely influence trial results. He co-published these findings in the *Journal of the National Cancer Institute*, and presented the work in 2014 to the Eastern Cooperative Oncology Group-American College of Radiology Imaging Network (ECOG-ACRIN) national meeting, which awarded him a Young Investigator Award. In 2015, the ECOG Thoracic Committee dropped its standing practice of automatically excluding patients with prior cancer from its advanced cancer clinical trials.

**Melody Becnel Oncale, MD**
**MD:** Tulane University, New Orleans, LA  
**Residency:** Tulane University, New Orleans, LA  
Oncale’s intellectual interest in hematology-oncology began in medical school while caring for a patient with systemic amyloidosis— which can occur with multiple myeloma—but her interest was later solidified on a personal level when a loved one was affected by cancer. This loss allows her to empathize with patients and their families in a way that would not have been possible without this experience. As Tulane is the top referral center in Louisiana for benign blood disorders, Oncale seized opportunities to expand her knowledge and management skills for patients with sickle cell anemia and hemophilia. She gained experience in supportive care and medical education while working as a hospitalist for two years prior to this fellowship. Her work with the underserved population of New Orleans opened her eyes to the issue of health care disparities in cancer medicine. Oncale’s career interests include academic clinical research in malignant hematology, collaborative supportive care medicine, health care disparities, and training future physicians.
Hematology/Oncology fellows

Koji Sasaki, MD

**MD:** Tokyo Medical and Dental University, Tokyo, Japan  
**Residency:** Beth Israel Medical Center, New York, NY

Sasaki joined the program for one year of hematology training after completing two years as a fellow in the Department of Leukemia and one year as a fellow in the Department of Stem Cell Transplantation and Cellular Therapy. He satisfied residency and hematology programs in his home country, as well as a residency program at Beth Israel before first coming to MD Anderson in 2010. During his hematology residency in Japan, Sasaki enjoyed his role as a chief, managing blood cancer patients who received high-dose chemoradiation, and caring for patients who required multiple immunosuppressants after stem cell transplantation. To respond to challenges of relapsed/refractory blood cancers, complications of stem cell transplantation, Sasaki gained experiences with clinical trials targeting oncoproteins, microRNA, mutated DNA sequences, and conducted data-driven research about clinical application of artificial intelligence in patients with CML-CP, which he is scheduled to present as an oral presentation at the American Society of Hematology (ASH) 2016 annual meeting in December. His fellowships at MD Anderson afforded him opportunities to work with Drs. Jorge Cortes, Elias Jabbour, and Muzaffar Qazilbash, and he has published in high-impact journals including *Lancet Haematology.*

Paolo Strati, MD

**MD:** Universita Vita-Salute San Raffaele, Milan, Italy  
**Residency:** Mayo Clinic, Rochester, MN

Strati wants an academic career focused on translational research for chronic lymphocytic leukemia (CLL) and other hematological malignancies. He has fulfilled two residencies in Italy and the United States, a clinical research fellowship in England, and a two-year Department of Leukemia fellowship here at MD Anderson, which afforded him opportunities to work with renowned blood cancer experts, including Dr. Michael Keating, who serves as a co-leader of MD Anderson’s Chronic Lymphocytic Leukemia (CLL) Moon Shot. As recognition of Strati’s achievements at that point, he was appointed to the rank of assistant professor of medicine at the Mayo Clinic. With senior faculty from Mayo and MD Anderson, Strati has co-authored 30 peer-reviewed papers, more than 40 abstracts, and given presentations at annual meetings worldwide, including the American Society of Hematology (ASH) and the American Society of Clinical Oncology (ASCO).

Oluchi Ukaegbu, MD

**MD:** University of Illinois College of Medicine, Peoria, IL  
**Residency:** Vanderbilt University, Nashville, TN

During her undergraduate education, Ukaegbu volunteered at a community health center and saw firsthand how difficult it can be for underserved populations to access quality care. Watching those struggles motivated her to become a doctor and learn a humanistic approach to help those facing healthcare inequities. Prior to medical school, she attended Memorial Sloan-Kettering as a research fellow for three months, where she performed studies on survivorship and quality of life in stem cell transplantation patients. As a resident, she researched organ response related to amyloidosis and effects of JAK inhibitors in patients with myelofibrosis who underwent transplantation. She plans to continue in this subspecialty in an academic setting, and possibly teach hematology courses or direct a fellowship program while finding means to provide healthcare education to community groups.

Jason Willis, MD, PhD

**MD/PhD:** Weill Cornell Medical College, New York, NY  
**Residency:** John Hopkins University, Baltimore, MD

Willis is interested in a physician-scientist career in which he can contribute overall knowledge of how genetics and environmental and social factors play in cancer predisposition, diagnosis, and management. He has been pursuing answers since doctoral studies in which he investigated genetic markers for generating cancer and treatment response outcomes. Among other things, Willis found indications that genetic variants on chromosome 12q21 are associated with worse overall survival from pancreatic cancer. He published first-author findings in *Clinical Cancer Research* and *Frontiers in Genetics.* Additionally, Willis wants to help improve technology that identifies genetic risks as delivery of that information to patients has significant clinical and psychosocial ramifications. On a long-term basis, in research and practice, Willis hopes to explore novel approaches that translate cancer genomic discoveries across environmental and socioeconomic barriers that are faced by underserved communities.

Clinton Yam, MBBS

**MBBS:** National University of Singapore  
**Residency:** University of Pennsylvania, Philadelphia, PA

While in medical school, Yam lost his grandfather to lung cancer. That experience sparked his interest in tumor biology and made him more determined to be an outstanding physician. As a result, Yam worked with mentors to develop a mouse model of liver metastasis in pancreatic cancer. Being a huge fan of quantitative methods, Yam also performed outcomes research in MDS, non-Hodgkin’s lymphoma, and breast cancer where he demonstrated the value of genetic testing for BRCA 1/2 mutations in unaffected individuals. Yam envisions an investigative career in breast medical oncology, focusing on the development of novel therapeutic agents and early phase clinical trials.
Driving targeted therapy in lung cancer
Promising responses when treatments matched to mutation types

By Erica di Pierro

This year, Bruce Johnson, MD, chief clinical research officer at Dana-Farber Cancer Institute and professor of medicine at Harvard Medical School, received the distinction of being named Waun Ki Hong Visiting Professor. This award was developed to honor its namesake physician, one of the most impactful leaders in the history of MD Anderson. Hong has shaped our institution in innumerable ways, especially as a mentor to many faculty members whose careers he has nurtured over the years. In his introduction at Grand Rounds on July 26, John Heymach, MD, PhD, chair of Thoracic/Head and Neck Medical Oncology (THNMO), lauded Johnson’s similar, selfless ability to support faculty through the various stages of their careers and bring together teams of strong-willed independent investigators to move medicine forward. “No one better exemplifies the characteristics that have made Dr. Hong such an important force in oncology as Dr. Bruce Johnson,” Heymach noted. Johnson provided an overview of the genomic characterization of lung cancer, highlighting a number of his team’s contributions.

Following two decades of chemotherapy combinations that yielded no discernible improvements in survival for non-small cell lung cancer (NSCLC) patients, Johnson had a direct hand in driving the targeted therapy revolution for this challenging malignancy. In the early 2000s, Johnson and his team identified several patient-derived NSCLC cell lines that were sensitive to epidermal growth factor receptor (EGFR)-targeting agent gefitinib. Sequencing revealed that these cell lines carried the L858R mutation, now known to be the second most common oncogenic mutation in this receptor. The resultant 2004 collaborative publications reported this mutation as well as G719A, which together cover about 90% of EGFR mutants. A follow-up trial conducted in Japan that randomized patients carrying these mutations to gefitinib or chemotherapy showed a dramatic doubling of progression-free survival (PFS) in the former treatment arm. Longer-term studies in both Japan and at Dana-Farber revealed that 24% and 14% of patients respectively were alive at a five-year follow-up. Taken together, these findings represent a notable leap forward for patients with EGFR-mutant lung cancer, providing targeted therapeutic possibilities for extending survival well beyond what was previously possible with chemotherapy. In addition to EGFR mutation, Johnson also went after the EML4-ALK fusion mutation, which was present in some of the same cell lines harboring mutations in EGFR. Mouse xenograft models generated using these cell lines were treated with a known ALK inhibitor, which brought about significant and dose-dependent tumor regression; Johnson has also observed durable complete responses in EML4-ALK fusion patients treated with ALK inhibitors. The hope is that development of more specific and potent targeted therapies will continue to increase survival times.

While EGFR and ALK mutations are fairly common, together making up about 13–15% of NSCLC cases, there exist numerous mutations which occur in only 1–3% of patients and as a result are much more difficult to study. Johnson spoke about an ongoing Phase II study organized by the Lung Cancer Mutation Consortium (LCMC) combining dabrafenib andtrametinib to treat lung cancer characterized by BRAF mutation, which is found in less than 2% of lung tumors. This therapeutic combination yielded a promising 63% response rate in patients with BRAF V600E mutations including several complete, durable responses. Johnson also briefly mentioned another uncommon mutation occurring in exon 14 of the gene encoding MET, noting that patients carrying this genetic lesion show sensitivity to crizotinib in ongoing clinical trials.

Ultimately, the goal of every clinical trial is to identify treatments that improve patient outcomes. When targeted therapies are involved, the hope is that patients receiving treatment targeting their specific mutation will fare better than those without targetable mutations or without an appropriate drug; this would provide important justification for genotyping patients and selecting therapies based on these results. Johnson discussed LCMC efforts revealing that patients who carried actionable mutations and received treatment specific to these lesions did indeed survive longer than patients without actionable mutations or appropriate therapies. These results are promising for the continued use and refinement of targeted agents.

In recognition of his impact on the field of oncology, Johnson was recently elected president of the American Society of Clinical Oncology (ASCO) and will start his term next year. He has contributed invaluable to our understanding of the genetic alterations that drive lung malignancies and best practices for implementing targeted therapeutic agents in the clinic.
This year, the ninth annual John Mendelsohn Visiting Professorship was awarded to Steven Rosenberg, MD, PhD, chief of the Surgery Branch at the National Cancer Institute and a central figure in the area of adoptive cell therapy. Patrick Hwu, MD, head of the Division of Cancer Medicine, introduced Rosenberg as an immunotherapy pioneer who “kept [the field] alive during what we call the dark ages when no one thought that it actually worked.” Rosenberg expressed his deep honor to deliver his address in the name of Dr. Mendelsohn, noting their close, long-term personal and professional relationship and his sincere admiration for Mendelsohn as a scientist, clinician, and “just a wonderful human being.”

Rosenberg’s Oct. 11 seminar focused on his work over the past several decades in the field of T cell adoptive immunotherapy using tumor infiltrating lymphocytes (TILs). This form of immunotherapy involves the administration of large numbers of a patient’s own ex vivo generated tumor-reactive T cells that are reinfused into the body ready to mount a response against the tumor. Rosenberg explained the initial application of this technique in metastatic melanoma patients; about one-quarter of patients treated attained rapid, long-term, and potentially curative responses after only a single infusion. The next step was to understand which exact antigens the TILs were reacting against to bring about such effective responses, and to expand the technique into other cancer types including solid epithelial cancers.

Rosenberg and his team explored the ability of specific cancer mutations to elicit these potent anti-tumor TIL responses, and developed an assay to identify such mutations in individual patients. The process involves determining all mutations in a patient’s tumor through whole exome sequencing and then generating a series of tandem mini-genes containing each mutated amino acid flanked by its 12 neighboring amino acids. These mini-genes are then injected into a culture of the patient’s antigen presenting cells (APCs), which process and present only those peptides that meet the requirements for that patient’s specific major histocompatibility complex (MHC) molecules. Cultured APCs are then exposed to a patient’s TILs to provide an opportunity for the T cells to recognize and react to presented tumor antigens. To determine which specific mutations elicit TIL responses, each mutation is systematically reverted back to wild type and then loss of TIL reactivity is assayed. Once identified, pure populations of specific tumor-reactive T cells can be infused into the patient in an effort to bring about immune-targeted regression of the cancer. Rosenberg’s team has used this technique to identify patient-specific tumor antigens in melanoma, lung, cervix, bladder, esophagus, and breast cancers. In almost every case, the mutations were unique to each patient and often had no known relationship to oncogenesis. This emphasizes that many types of cancer encode random somatic mutations that T cells recognize and react against to bring about disease regression—a critical advance for epithelial cancers with limited treatment options.

In identifying which specific T cells react against a patient’s cancer, Rosenberg also discussed evidence defining PD1, a cell determinant most commonly associated with checkpoint blockade, as a decisive marker of TIL anti-tumor activity. In fact, isolation of PD1-positive cells from the peripheral blood leads to 97% purification of anti-tumor cells. These cells can then be tested for reactivity to tandem mini-genes as described above; this technique is particularly useful for identifying additional antigens in solid cancers with few mutations. Rosenberg also mentioned the use of CAR T cells directed against B cell-determinant CD19 for treatment of follicular non-Hodgkin’s lymphoma, lymphocytic leukemias, and most recently diffuse large B cell lymphoma. Many of these patients attain objective responses, some complete and durable.

The collective impact of Rosenberg’s work in the field of adoptive immunotherapy has allowed us to understand that T cells can seemingly attack any tumor cell type, provided the appropriate antigen is present. Therefore, if a patient has T cells that can mount a response against a tumor-specific antigen, regression of these tumor cells is theoretically attainable. Efforts in the Rosenberg lab are now focusing on improving mutation detection and T cell purification strategies.
Team to tackle HPV-related malignancies along cancer continuum

By Erica di Pierro

Representatives from the Human Papillomavirus (HPV) Moon Shot shared recent progress within the three flagship projects at Grand Rounds on July 12. In a brief introduction, Erich Sturgis, MD, MPH, professor of Head and Neck Surgery and co-leader of the moon shot, emphasized the growing global health burden of HPV-related cancers. In the developing world, HPV-associated cervical cancers are among the leading causes of cancer deaths in women. In the United States, oropharyngeal cancer incidence rates are on the rise particularly among men while anal cancer incidence is consistently increasing particularly among women. The collective Moon Shot Program organizes itself into three flagships (prevention/screening, discovery, and immunotherapy/novel trials) in order to tackle the four key priority areas determined through a collaborative retreat in 2014: prevention through vaccination, screening for earlier diagnosis, improving the efficacy of available treatments, and addressing survivorship by decreasing treatment toxicity.

Lois Ramondetta, MD, professor of Gynecologic Oncology and Reproductive Medicine discussed efforts in Flagship 1 (prevention/screening) to increase HPV vaccination rates through policy change and education. She emphasized that the overwhelming majority of new cancers at HPV-related sites including cervical, oropharyngeal, anal, and penile cancers can indeed be attributed to infection with the virus. The most straightforward way to bring down these numbers, Ramondetta said, is to improve preventive vaccination rates in girls and boys. Increasing vaccination rates will depend on improving provider education in medical schools and clinics across the state, continuing to influence policy change to make a statewide plan for vaccination, and survivor mobilization to bring a real face to the impact of these malignancies.

Curtis Pickering, PhD, assistant professor of Head and Neck Surgery reported from Flagship 2 (discovery), which centers on discovery of novel therapeutic targets and genomic characterization of HPV-associated cancers. He spoke about a project utilizing shRNA libraries to find such targets and pathways involved in HPV-related malignancy. In these experiments, short hairpin RNA (shRNA) pools are introduced into HPV-positive and -negative cell lines to silence expression of a large selection of genes, such that one cell takes in only one shRNA knock-down construct. These cells are then injected into mice to allow for in vivo tumor development, and candidate targets are identified by sequencing cells from the resultant tumor to determine shRNA frequencies. Reduced frequency of a given shRNA in the tumor cell population indicates that knock-down of its target gene leads to poor growth of affected cells, which suggests that gene could be a promising therapeutic candidate. This approach can also shed light on which genes contribute to therapy response. So far, this screening technique has been used to identify focal adhesion kinase (FAK) as both a candidate target for HPV-associated tumor formation and a sensitizer to radiotherapy. Additionally, Pickering discussed a large-scale drug screening pipeline led by Faye Johnson, MD, PhD, associate professor of Thoracic/Head and Neck Medical Oncology. A total of 22 HPV-positive and -negative cell lines are being run through 900 unique compounds to find agents with therapeutic activity. So far, the screen has turned up a number of agents that demonstrate activity across both types of cell lines, and continues to search for drugs with specific activity in HPV-positive cells.

Flagship 3 focuses on developing novel trials, particularly those employing immunotherapies, to test promising agents in the clinic. Michael Frumovitz, MD, MPH, professor of Gynecologic Oncology and Reproductive Medicine introduced a number of ongoing and upcoming trials that the HPV Moon Shot is involved with. These include a soon-to-open Phase I study investigating dual mTOR and aurora kinase inhibition in all HPV-associated malignancies, an ongoing Phase II trial combining nivolumab and HPV-16 E6/E7 vaccination in HPV-16 positive solid tumors, and an upcoming Phase II study combining novel HPV-16/18 E6/E7 vaccine MEDI0457 with durvalumab (anti-PD1) in patients with HPV-16 or -18 positive tumors, among others. The team is also actively exploring tumor infiltrating lymphocyte (TIL) therapy for HPV-associated tumors following reports of unprecedented durable and complete responses in recurrent cervical cancer patients after receiving TIL.

This institution-wide group is working hard along the disease continuum of HPV-related malignancies to develop novel, effective treatments for patients. Importantly, they are also pushing to spread the knowledge that the vast majority of these cancers can be prevented and lives can be saved in the future through vaccination.

The most straightforward way to bring down these numbers, Ramondetta said, is to improve preventive vaccination rates in girls and boys.
**Events**

**GRAND ROUNDS**

**Advanced Scholars present new regimens, pathways**

*By Erica di Pierro*

Jennifer Goldstein, MD, is well-tolerated and promotes efficient hematopoietic recovery.

Fludarabine, as well as safety of post-transplant long-term maintenance and busulfan, the trial aimed to determine a safe dose of pre-effect when romidepsin was combined with fludarabine, clofarabine, and busulfan, the trial aimed to determine a safe dose of pre-allograft conditioning romidepsin therapy combined with busulfan and fludarabine, as well as safety of post-transplant long-term maintenance romidepsin treatment. Preliminary results suggest this regimen is well-tolerated and promotes efficient hematopoietic recovery.

Jennifer Goldstein, MD, detailed her work exploring the role of BRCA pathway mutations in resistance to PARP inhibitors in pancreatic cancer cells. Goldstein determined BRCA-ness within numerous PDAC cell lines and demonstrated that known BRCA-mutant cell lines show increased sensitivity to the PARP inhibitor BMN673. She plans to repeat treatment with BMN673 at increasing concentrations to create resistant cell lines, identify mutations that confer this resistance, and then devise synthetic lethal therapy combinations that can overcome therapy resistance in these cell lines. Jin Im, MD, PhD, explained her work on invariant natural killer (iNK) T cells, exploring their role as immune regulators in the stem cell transplantation setting. She has determined that iNK T cells expressing T regulatory markers CD25 and FoxP3 are enriched in cord blood compared with adult stem cell donor transplants, and that this cell subset undergoes activation and clonal expansion. Additionally, Im presented a method for ex vivo expansion of iNK T cells that preserves both their immunosuppressive and anti-tumor effector functions, allowing for simultaneous prevention of graft-versus-host disease and promotion of graft-versus-tumor effect. She aims to develop iNK T cell-based therapy for clinical application.

**Hematology/Oncology fellows practice for ASCO**

*By Erica di Pierro*

On May 31, four Division of Cancer Medicine Hematology/Medical Oncology fellows were provided the opportunity to share their findings that were later presented at June’s annual meeting of the American Society of Clinical Oncology (ASCO) with the Grand Rounds audience. Second-year fellow Kenneth Kehl, MD, (pictured) spoke about his analysis of the medical provider network landscape under the Affordable Care Act’s (ACA) federal exchange. He found that most networks under the exchange contain American College of Surgeons Commission on Cancer-accredited hospitals, but less than half contain NCI-designated centers. Further, Kehl observed significant geographic variation with regard to access to NCI centers. In all, he found that while in-network access to accredited cancer hospitals is common within exchange plans, more must be done to optimize access to specialized care centers and clinical trials. Vivek Subbiah, MD, assistant professor of Investigational Cancer Therapeutics, presented on behalf of second-year fellow, Tina Cascone, MD, PhD. Cascone’s work includes preclinical and clinical findings that revealed the ability of combined RET inhibitor vandetanib and mTOR inhibitor everolimus to overcome resistance to single-agent vandetanib in non-small cell lung cancer with RET fusion. This therapy regimen showed activity both systemically and in the central nervous system. Matthew Reilley, MD, analyzed the constitution of the immune microenvironment in primary and liver-metastasized colorectal cancer specimens. He found that primary samples with higher mutational burden due to mismatch repair defects had significantly elevated PDL1 expression, supporting the use of PD1/PDL1 blockade in such cancers. Additionally, Reilley identified OX40 and ICOS as potential targets for primary specimens with low mutational burden. He also found increased presence of macrophages in liver metastectomy samples versus primary samples, indicating a unique immune suppressive environment. Shiraj Sen, MD, PhD, evaluated mutations co-occurring with BRAF-V600 in non-melanoma cancers and their impact on progression-free and overall survival. He found that patients with added mTOR pathway mutations suffered significant declines in both of these clinical measures relative to two other subsets of co-occurring mutations. Sen also analyzed results from a combined BRAF/mTOR inhibitor (vemurafenib/everolimus) Phase I trial to reveal that this combination brings about tumor shrinkage in patients with BRAF-mutated advanced cancers, even those that have been heavily pre-treated, and is safe and well-tolerated.
Retondo returns to Cancer Medicine to oversee ICT

Yagut Retondo, MHA, returned to the Division of Cancer Medicine as department administrator in the Department of Investigational Cancer Therapeutics on Sept. 1. “I am excited at the opportunity to serve as the next administrative lead for the department,” she said. “My goal is to build on the existing infrastructure and expertise to further enhance our internal operations and collaborations with industry partners.”

During the past three years, Department Chair Funda Meric-Bernstam, MD, has shepherded the department to become one of the largest Phase I programs in the world through relationships with pharmaceutical companies and academic collaborators. Retondo has been at MD Anderson for eight years. Since 2013, she was the administrator of the Department of Health Services Research, a new department that she launched in the Division of Cancer Prevention and Population Sciences. In this role, she established the administrative and financial structure of the department, created policies and procedures, supported the chair in recruiting faculty, and hired and trained all support staff.

Retondo originally came to MD Anderson as an administrative intern in the Leukemia Department upon completing her Master’s in Healthcare Administration at Texas Woman’s University in 2008. She took on the role of Administrative Manager in Leukemia the following year, where she was the primary business officer for Leukemia’s Clinical Research Services program, developing budget proposals for over 100 new research protocols and amendments to existing projects, and managing a $5 million budget and 20 employees. In 2011, Retondo was promoted to Program Manager. She directed all administrative and operational activities of Leukemia’s Clinical Research Services program including strategic planning, laboratory operations, data and financial management, and personnel management. In addition, she managed collaboration with research investigators and industry sponsors and monitors, reviewed new research proposals for feasibility and ensured contractual obligations, and managed the program’s $7 million budget. Before MD Anderson, Retondo held administrative and project management positions in the oil industry in Houston as well as in Azerbaijan. She earned her bachelor’s degree in Education at the Institute of Foreign Languages in Baku, Azerbaijan, and served as a translator when she was first out of school.

Corbett hits the ground running in Lymphoma/Myeloma

Kimberly Corbett, MBA, new department administrator for Lymphoma/Myeloma, has a significant “list of things to do” for the first year in the division. She joined Cancer Medicine on Aug. 1 from The University of Texas Medical Branch (UTMB) in Galveston, after serving for three years as assistant administrator for basic science in the School of Medicine and as the strategic planning analyst in the Institutional Office of Strategic Management. Other academic experience includes administrative leadership roles at Rice University, where she oversaw graduate and undergraduate academic programs, and at Texas A&M University, where she performed audits, responded to public information requests, and contributed to research initiatives from multiple departments within her college.

Corbett took the reins from Randy Vidrine, MS, who served as ad interim for nine months while managing two departments of his own—Melanoma Medical Oncology and Sarcoma Medical Oncology. In the next year, Corbett will be working on several operational goals. These include increasing patient activity, enhancing Press Ganey patient satisfaction scores, and expanding strategic alliances with industry partners such as Kite Pharma, which is receiving a lot of attention now for developing CAR-T drugs for B cell blood cancers, and Celgene Biopharmaceutical Company, which is a giant in the manufacture of therapies for various cancers and inflammatory disorders. Additionally, Corbett will be working with Penny Philips, RN, MSN, on measures to achieve top-quartile performance in clinical effectiveness and safety.

Corbett earned a Bachelor of Business Administration degree from the University of Houston-Clear Lake and a Master of Business Administration degree from Texas A&M University-Commerce. Additional professional development includes Quality Texas Examiners Training (Malcolm Baldrige National Quality Framework) and membership in the Texas Quality Board of Examiners, the Society for College and University Planning (SCUP), and the National Council of University Research Administrators (NCURA).
R11 redevelopment project earns excellence prize

Remodeling of CCTT, BMA, Supportive Care Center took two years to complete

Experts who know what a well-put-together building looks like have given the R11 Redevelopment Project the gold stamp of approval. In fiscal year 2016, three Division of Cancer Medicine clinics were relocated from Rose 10 to a larger space on Rose 11. Vaughn Construction of Houston renovated the Clinical Center for Targeted Therapy, Bone Marrow Aspiration Clinic, and the Supportive Care Center, and then submitted their project for consideration in the Houston division of the Associated General Contractors of America’s prestigious APEX awards. That annual event bestows upon its winners gold, silver, and bronze level recognition to laud excellence among commercial building general contractors, subcontractors, suppliers, manufacturers, and service firms. The R11 Redevelopment Project, which took about two years to complete, earned gold in the Best Small Healthcare Project category. The area previously housed the president’s office and faculty dining hall.

Pound for Pound

Experimental Therapeutics leads division donations to Houston Food Bank

The Division of Cancer Medicine (DoCM) turned in 15,999.45 pounds of food for the Houston Food Bank this past July. The institution, which commits yearly to this effort in the summer because the food bank experiences a shortage of donations at this time, collected a grand total of 133,030 pounds of bottled water, rice, pasta, beans, canned goods, and other non-perishable supplies to support area families.

The HR Rewards and Retention office reports the Department of Experimental Therapeutics was the top collector in the DoCM, turning in 3,925.5 pounds. Trailing the south campus team very closely was the Department of Leukemia, with 3,474.25 pounds. Rounding out the top three biggest contributors in Cancer Medicine was the combined effort of the Clinical Translational and Research Center (CTRC) and its laboratory partner for 2,217 pounds. Thanks to all employees and faculty who participated in the campaign to help our neighbors.

Leukemia employees had to make a lot of room to pack and store boxes of food and supplies for the institution’s food drive.