



With a Special Focus on Research

Exercise as a Prescription to Help Bone Cancer Patients?



Taryne Thomas, PT, DPT, (left) works with 17-year-old Logan on TRX exercises she performed during trial.

Can exercise be the right prescription to improve outcomes for pediatric bone cancer patients? A pilot clinical trial based on the laboratory work of **Keri Schadler**, **PhD**, assistant professor in Pediatrics-Research, and her team, is underway to answer the question for patients with Ewing sarcoma and osteosarcoma, the most common malignant bone tumors diagnosed in children and young adults. Ewing sarcoma is a tumor that grows in the bones or soft tissue around bones, usually the legs, pelvis, ribs, arms or the spine.

Osteosarcoma is usually found in long bones, such as the femur, tibia, and the humerus bone in the upper arm.

Valerae O. Lewis, MD, professor and chair of Orthopaedic Oncology is the principal investigator, and Douglas Harrison, MD, assistant professor in Pediatrics-Patient Care, is a collaborator. The study opened in December 2016 to first determine a safe baseline of supervised exercise. "Conventional therapy for these patients typically yields a 5-year survival rate of 70 percent. One possible reason is inadequate chemotherapy delivery to the tumor largely due to their disorganized, immature and leaky tumor vasculature which prevents the tumor cells from receiving the full dose of the drug therapy," Schadler explained. "Pre-clinical data in mice has shown that exercise can be used as a way to reorganize and improve tumor vasculature, and therefore improve delivery and efficacy of chemotherapy."

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Parents of Former Patient Urge Pediatric Neuro-Oncologists and Researchers to Expand Treatment Options

From our recent Neuroscience Update in Pediatric Neuro-Oncology Conference: James and Debbie Scully standing with Soumen Khatua, MD, section chief of Pediatric Neuro-Oncology and associate professor in Pediatrics-Patient Care (middle). The Scullys lost their 12-year-old son Thomas last year following a battle with anaplastic ependymoma, a form of brain cancer. During certain procedures, doctors and other caregivers often asked Thomas to give them a "thumbs up" if he was doing okay. But Thomas, always positive and hopeful, would give two "thumbs up." Khatua was the neuro-oncologist on his child's multidisciplinary team and the chair of the conference, held April 22, 2017.



Renowned speakers discussed strategies, research and clinical trials including immunotherapeutic approaches to treat pediatric brain tumors. This included infusion of natural killer (NK) cells directly into the brain. Newer surgical approaches that involve delivering drugs directly into the brain, genomic/epigenetic update on pediatric brain tumors, radiation therapy, and novel translational research endeavors were also presented. Additionally, discussion about multiple modality treatment toxicities and short- and long-term survival side effects were discussed.

Research Assistant in Washington, D.C., Learning about the Politics of Healthcare

Jolie Schafer, BS, graduate research assistant in Pediatrics-Research, is now working as a summer fellow at the U.S. Department of Health and Human Services within the Office of the Assistant Secretary for Preparedness and Response (ASPR). She is gaining hands-on experience with legislative processes involving healthcare and interacting with the very leaders who imagine and write policies. This opportunity is part of the Archer Center Graduate Program in Public Policy at The University of Texas System in Washington, D.C., which brings promising graduate students to our nation's capital to interact with recognized leaders of the field.



After completing the fellowship, Schafer will graduate from

The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences (GSBS) with a doctorate of philosophy in immunology. She earned two bachelors' degrees from Houston Baptist University—one in biology and the other in biochemistry molecular biology. What's her motivation? "I have a childhood friend who was very sick growing up with Cystic Fibrosis. He inspired me to go into research to find cures for childhood diseases. I also was very interested in immunology and its use as immunotherapy. When I found Dr. Dean Lee's lab that focused on pediatric cancer and immunotherapy, I knew I had found where I wanted to pursue my PhD," Schafer explained, adding that her passion includes translational studies and clinical trials. "I'm interested in how scientists and the government can work together to improve patient therapy options." In the short term, Schafer plans to enter the clinical trial arena and learn about the trial process. "From there, I would like to serve in a leadership position for a pharmaceutical company or government organization working towards improving clinical treatment options for various diseases," she said.

Students Awarded Postdoctoral Credentials

Three students working in our Research department received their doctoral degrees this past spring from the MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, all mentored by **Eugenie Kleinerman, MD**, professor in Pediatrics-Research. They are:

- Pooja Dhupkar, PhD, Experimental Therapeutics
- Simin Kiany, PhD, Immunology
- Rocio Rivera-Valentin, PhD, Cancer Biology

Espejo Earns CPRIT-Funded Fellowship in Prevention

Alexsandra Espejo, PhD, postdoctoral fellow in Pediatrics-Research, was awarded a CPRIT-funded postdoctoral fellowship in cancer prevention. The program supports her research for two years, allows her to receive mentoring and career coaching, and helps to develop her scientific communication skills. This additional training is designed to provide a foundation to help recipients become independent investigators who can grow into leaders of the field in cancer prevention

science. Espejo, who earned her doctorate in epigenetics and molecular carcinogenesis at MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences, is investigating the impact of obesity among pediatric cancer survivors as it increases their risk of second malignancies. To learn more about CPRIT, click http://www.cprit.state.tx.us/

Exercise as a Prescription, cont.

Both faculty members are excited about the study's potential. "Deconditioning in these patients is significant during their cancer course, and this program has the potential to prevent it by aiding in better functional outcome and improved recovery," said Lewis.

The study is open to patients who are five to 31 years of age receiving standard Children's Oncology Group (COG) regimens. Investigators want to enroll a total of 30 participants, half of whom will be asked to complete three 45-minute sessions with a physical therapist doing specific things: aerobic exercise on a bike or arm ergometer, strengthening and stretching exercises, and engaging in age-appropriate fun activities, such as throwing a basketball. The sessions last for 10 weeks during the long phase of treatment when patients are receiving chemotherapy alone or combinations of chemotherapy and radiation before surgery. "Participants will undergo MRIs to allow us to see the tumor at various time points during the exercise program. This will help us determine if we are increasing blood flow and improving chemotherapy delivery," said Schadler. She explained that when a healthy person goes on a brisk walk, his blood vessels dilate and then contract when he stops walking. "But in a person's malignant bone tumor, the blood vessels are not mature enough to dilate as they are, so instead, the cells have to change their structure and go from rapidly growing to slowing their growth to become mature vessels, which we'll be able to see in 'really cool imaging,' for up to three days after each session." Additionally, investigators will receive tumor samples from surgeries to see under a microscope if the tissue behaved as expected, and they'll get blood samples from surgery to look for biomarkers that indicate whether the level of exercise caused the changes they want to see.

Pedal Power: Hitting the Streets on Bikes to Raise Money for Cancer Research

The University of Texas students travelling 4,000 miles on bicycles from Austin to Alaska in 70 days made a stop at our campus on June 7. The riders are members of the Texas 4000, an organization dedicated to cultivating student leaders and raising money for cancer research. During their visit, they met some of our patients, hosted a tie-dying activity for them, toured the Children's Cancer Hospital, and presented a \$65,000 check to support cancer research, bringing the group's total donation over the years to \$1.52 million.



Their annual charity ride is believed to be the longest in the world, with teams named Sierra, Rockies, and the group that visited us, Ozarks. The route will take them through New Orleans, Memphis, St. Louis, Chicago, Milwaukee, Minneapolis, the Canadian cities of Winnipeg, Manitoba; Edmonton, Alberta; and Whitehorse, Yukon Territory. The final stop is scheduled for Aug. 11 in Anchorage, AK. Why are they doing this? Most said they have a personal connection to cancer, such as having a childhood friend who battled the disease. "In the seventh grade, a friend was diagnosed. She was in treatment for three years and had to stop coming to school with us and start taking classes online.

We never talked about 'if' she'd pull through, but 'when.' But she didn't. She passed away in 2009. As I'm riding to Alaska, I'll carry her with me in my thoughts," explained Al.

Gopalakrishnan Graduates Faculty Leadership Academy



Vidya Gopalakrishnan, PhD, professor in Pediatrics-Research, successfully completed the Faculty Leadership Academy in May. The program was established in 2002 to enrich the management training of competent leaders within MD Anderson. The academy offered each cohort approximately 60 hours of curriculum over a seven-month period focusing on selfawareness, emotional intelligence, communication skills including conflict resolution, mentoring and coaching, and building and managing productive teams. "We were not assigned specific projects, but institutional leaders offered their insights into skillsets they felt were needed to succeed as a leader based on their own personal experiences. Simulations of situations were created in which your ability to problem solve was tested, either individually or in a group setting,' said Gopalakrishnan. After the curriculum, she believes she can better

'diagnose team dynamics' and develop strategies for maintaining team alignment. "Also important is celebrating small victories while striving for bigger ones, setting clear goals and expectations, and establishing boundaries and holding others accountable for their commitments and actions," said Gopalakrishnan.

Gordon to Continue Work on Faculty Senate



Nancy Gordon, MD, assistant professor in Pediatrics-Research, will begin her second, three-year term on the Faculty Senate starting Sept. 1. "I am certainly very excited to serve for three more years and represent our Pedi Faculty, and I look forward to three years of prosperity at our institution," she said. The panel meets regularly on the third Tuesday of each month in the Hickey Auditorium, and gathers as necessary for other business. The primary role of the Faculty Senate is to work collegially in the best interest of our institution while promoting a climate of freedom of expression and opinions—even in disagreement—and to fairly represent all faculty institutional governance. Three other Pediatrics faculty members serve on the senate, with their terms ending on Aug. 31, 2019. They are:

- Cesar Nunez, MD
- Shehla Razvi, MD
- Pete Stavinoha, PhD

Kleinerman Elected as a Fellow of the American Association for the Advancement of Science



Eugenie Kleinerman, MD, professor in Pediatrics, has joined the ranks of an elite membership of MD Anderson faculty by becoming an elected fellow of the American Association for the Advancement of Science (AAAS) in the fall of 2016. The designation extols her distinguished efforts to advance science through innovation, education, and leadership. "I am extremely honored to be one of the newly elected fellows to the AAAS, and to be the first faculty from the Division of Pediatrics to be recognized by this prestigious organization for my accomplishments in clinical and laboratory research in osteosarcoma and Ewing's sarcoma," said Kleinerman. "I am very grateful to Drs. Elizabeth Travis, Ray DuBoise, and R. Sanford Williams, president of the Gladstone Institutes in San Francisco, and a professor in medicine at the University of California San Francisco, for supporting my nomination." She is among 40 members at

MD Anderson to be recognized by the "world's largest general scientific society," which was founded in 1874. Additionally, Kleinerman, who served as division head for Pediatrics from 2001 to February 2015, has the distinction of being the only woman of the seven most recently elected fellows from MD Anderson.

Investigating Use of Circulating Tumor Cells and Technology to Predict Treatment Response

Though the work of **Shulin Li, PhD**, professor in Pediatrics-Research, and his team specializes in immune therapy development across different types of tumors, the group has discovered a universal circulating tumor cell (CTC) detection marker/tool for detecting tumor cells from blood samples.

Through partnerships with clinical researchers, such as **Drs. Najat Daw** and **Jessica Foglesong**, this tool has been used in the detection of CTCs in sarcoma, neuroblastoma, Wilm's tumor, acute myelogenous leukemia (AML) and T- cell acute lymphoblastic leukemia (T-ALL) blood samples. Longitudinal analysis of CTCs from neuroblastoma

patients in remission found that the absence of CTCs may serve as a valuable predictor of no relapse and that the presence of CTCs can indicate a high risk of relapse. The kinetic change of CTCs can be found during treatment, which may be used for developing novel maintenance therapy. This technology was licensed to Abnova, Inc. to explore the full clinical utility in both pediatric and adult patients.

Li's team is investigating additional means of financial support to explore this tool further and to explore new circulating markers for predicting chemotherapy and immune therapy response since current federal funding does not cover these liquid biomarker discoveries.

Research laboratory leaders have published manuscripts in high-caliber journals in the past quarter. They are:

Joya Chandra, PhD

 Raber M, Crawford K, Chandra J. Healthy cooking classes at a children's cancer hospital and patient/survivor summer camps: initial reactions and feasibility. Public Health Nutr:1-7. e-Pub 5/2017. PMID: 28463101.

Vidya Gopalakrishnan, PhD

 Dobson THW, Hatcher RJ, Swaminathan Jr, Das CM, Shaik S, Tao RH, Milite C, Castellano S, Taylor PH, Sbardella G, Gopalakrishnan V. Regulation of USP37 Expression by REST-Associated G9a-Dependent Histone Methylation. Mol Cancer Res. 2017 May 8. doi: 10.1158/1541-7786.MCR-16-0424. PMID: 28483947

Eugenie Kleinerman, MD

Lindsey BA, Markel JE, Kleinerman ES. Osteosarcoma Overview. 2017 Jun;
 4(1):25-43. Doi: 10.1007/s40744-016-0050-2.
 EPUB 2016 Dec 8. Rheumatol Ther. PMID:27933467 PMCID: OMC5443719

Shulin Li, PhD

- Mitra A, Yan J, Xia X, Zhou S, Chen J, Mishra L, Li S. IL6 mediated inflammatory loop reprograms normal to EMT(+) metastatic CSCs in pre-neoplastic liver of TGFβ deficient β2SP(+/-) mice. Hepatology. 2017 Apr;65(4):1222-1236. doi: 10.1002/hep.28951. Epub 2017 Jan 2. NIHMSID: NIHM830906.
- Batth IS, Mitra A, Manier S, Ghobrial IM, Menter D, Kopetz S, Li S. Circulating Tumor Markers: Harmonizing the yin and yang of CTCs and ctDNA for precision medicine. Ann Oncol. 2017 Mar 1;28(3):468-477. doi: 10.1093/annonc/mdw619. PMID: 27998963.
- Hu J, Bernatchez C, Zhang L, Xia X, Kleinerman ES, Hung MC, Hwu P, Li S. Induction of NKG2D Ligands on Solid Tumors Requires Tumor-Specific CD8(+) T Cells and Histone Acetyltransferases. Cancer Immunol Res. 2017 Apr;5(4):300-311. doi: 10.1158/2326-6066.CIR-16-0234. Epub 2017 Feb 21. PMID: 28223282.

Duo Wins Grant Supporting Development of T Cell Immune Therapy for Fungal Infections

Pappanaicken Kumar, PhD, instructor in Pediatrics-Research and Dimitrios Kontoyiannis, MD, professor in Infectious Diseases were recently awarded as co-principal investigators an R21/33 grant from the National Institute of Allergy and Infection Diseases (NIAID) to support their research on bioengineered T cells as therapy for drug resistant invasive fungal infections, such as those caused by Aspergillus, Candida, or mucor. Leukemic and hematopoietic stem cell transplant patients are highly susceptible to invasive Aspergillus infection and the estimated survival rate is only 15-40 percent. Drug resistant strains are on the rise, and therefore it is very important to find new approaches to fight this lethal infection.

"Chimeric antigen receptor (CAR) T cell therapy gives new hope to patient suffering from these infection," wrote Kumar in their grant application. "This is the first time that a pattern-recognition receptor (Dectin-1) from innate immune system has been adapted to redirect T cell specificity to control fungal infection." The normal T-cells do not attack fungal germlings or hyphae but secrete cytokines (cell stimulants) to boost the innate immune system to fight against fungal infection. On the other hand, Dectin-1 CAR Tcells directly recognize the sugar moiety present in the fungal cell wall and secrete cell wall degrading enzymes and give protection from fungal infection. Serious fungal infections cause approximately 1.5 million death every year worldwide. Besides cancer patients, fungal infections are a major threat to immunocompromised patients such as AIDS patients and solid organ transplant patients. Kontoyiannis and Kumar believe that patients suffering from primary immunodeficiencies, such as HIV infection, cancer, or transplantation, are highly likely to benefit from this immune adjuvant therapy. Special by Pappanaicken Kumar, PhD.

Mahadeo Joins to Lead Pediatric Stem Cell Transplantation and Cellular Therapy

We are pleased to announce that **Kris Mahadeo**, **MD**, has joined MD Anderson Children's Cancer Hospital as an associate professor, section chief and medical director of Pediatric Stem Cell Transplantation and Cellular Therapy. Prior to this role, he was an assistant professor in pediatrics at Albert Einstein Cancer Center and director of Marrow and Blood Cell Transplantation, where he specialized in providing care for children with malignant diseases as well as inherited genetic diseases. Mahadeo will continue this work with us. His research is focused on novel applications of allogeneic stem cell transplantation and immunotherapy for solid tumors and genetic diseases, and improving critical care outcomes for all children undergoing SCT. Mahadeo plans to work closely with inter-disciplinary team members to expand pediatric cell therapy access to include immune effector cell and gene therapies.



Compassionate Use Protocol Employed to Prevent Recurrence in Osteosarcoma Patients

Two osteosarcoma patients are receiving care under a Compassionate Use Investigational New Drug (CIND) protocol using the immunotherapy drug Liposomal Muramyl Tripeptide Phosphatidylethanolamine, known simply as MTP. The goal is to prevent recurrence or metastasis to the lung—the most common site for the disease to spread. The agent, developed in the laboratory of Eugenie Kleinerman, MD, professor of Pediatrics-Research and Cancer Biology, activates macrophages—a part of the immune system—to find and destroy microscopic osteosarcoma cells in the lung which were not killed by chemotherapy or excised in surgery. MTP was shown to be effective in prolonging both the disease-free and overall survival for relapsed osteosarcoma patients in a Phase II trial at MD Anderson and later in newly diagnosed patients in a Phase III trial sponsored by the Children's Oncology Group (COG). Combining MTP with chemotherapy resulted in a 30% reduction in mortality rate compared to patients who received chemotherapy alone. MTP was approved by the European Medicine Agency (EMA) and the National Institute for Clinical Excellence in the United Kingdom (UK) and is part of the standard of care in the UK, Spain, Portugal, Italy, and used in other European countries. MTP has also received approval in Israel, South America, Mexico, Taiwan, and Thailand, but has not yet been approved by the Food and Drug Administration (FDA) in the United States. Because the FDA has not approved MTP as a standard drug for osteosarcoma, it can only be obtained under a "compassionate use protocol" and insurance does not support the cost, so patient families pay out of pocket. This mechanism has been used by oncologists at several institutions around the country including Memorial Sloan-Kettering, the Lucile Packard Children's Hospital at Stanford and the Children's Hospital of LA. "Under the compassionate use protocol for our patients MTP is administered on an outpatient basis, twice a week for 12 weeks and then once weekly for 24 weeks. The nine-month treatment takes about one hour to administer each time," said Douglas Harrison, MD, assistant professor in Pediatrics-Patient Care. He is managing the care of one of the two CIND patients. "My patient is a 20-year-old man who lives and works in Houston and is hoping to return to college in the fall. We'll follow him with chest CTs every three months. This patient currently does not have active disease. He's been treated and we're now trying prevent recurrence." The other patient is a 10-year-old boy.

US News & World Report Ranks Children's Cancer Hospital Among Top 50 in the Nation

US News & World Report's "America's Best Children's Hospitals" survey has ranked MD Anderson Children's Cancer Hospital among the Top 50 hospitals in the country for pediatric cancer care. Richard Gorlick, MD, says the US News ranking is an important source of information regarding pediatric hospitals. "We are pleased to again participate in the rankings," said Gorlick. "With our strong team in place, a growing list of outstanding new recruits and our world-class care and research, our focus is on serving our patients and continually improving our outcomes."

Mote a Finalist for Research Nurse of the Year

Estella Mote, RN, BSN, research nurse in Pediatrics-Patient Care, was a finalist for the 2017 Clinical Research Nurse Committee's (CRNC) Research Nurse of the Year Award. She was nominated by colleagues within the division. "I'm grateful for the nomination and feel thankful for the confidence placed in our research nursing team's ability to carry out MD Anderson's vision. It's an exciting time to be a research nurse," said Mote.

Nurses Appreciation Week Observed in May

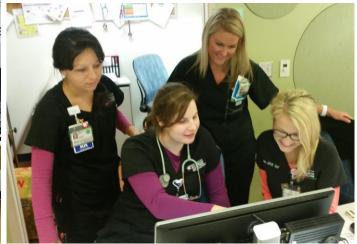
We observed Nurses Week at MD Anderson Children's Cancer Hospital by publicly thanking outstanding clinical care team members for their dedication to our patients. Several were featured on our <u>Facebook</u> and <u>Twitter</u> pages.











Employee Appreciation Week

The division had a few get-togethers In May to thank employees, doctors, and researchers who work hard for our patients. Treats included a roving candy bar that was driven by several Pediatrics managers, a day for ice cream sundaes and games, and a day in which everyone was treated to lunch—and some people even served up "interesting" Karaoke performances. Take a look!



San Diego Zoo Kids Channel Introduced in a Big Way



A great time was had by all on the May 24th launch of our <u>San Diego Zoo</u> Kids channel. It's now part of our inpatient room television lineup as Channel 44. Families sitting in our waiting areas can also ask staff to tune into the channel—45.1. On launch day, our young patients got up close and personal with a North American porcupine, a Madagascar tenrec hedgehog, and an eastern screech owl. A team from the <u>Houston Zoo</u> presented the animals in partnership with the <u>San Diego Zoo</u>. On this channel, our patients will learn about the care and conservation of zoo animals worldwide—including in Houston. The beautiful stories will educate, entertain, and be a source of calm and comfort for our patients.



Advice to Graduating Fellows:

"The Day after You Accomplish Something Big, Start Working on What's Next"

Congratulations to a trio of outstanding physicians who completed a three-year Pediatrics Hematology/Oncology Fellowship! Their accomplishments were recognized in a ceremony on June 8. Winston Huh, MD, associate professor in Pediatrics—Patient Care and program director (wearing lab coat) stands with Drs. Ryuma Tanaka (I-r), Angela Shaw, and Pamela Camacho. Huh presented them with gifts and gave a personal recollection of each. He described Camacho as the calm one of the group, Shaw as the one who passionately stands up for a principle, and former chief fellow Tanaka as a leader in the making who has a great laugh.



"After many years of education and training, this graduation program is the beginning of the next phase in your careers. It's a great time in medicine to be where you are, but I have to warn you that there will be some disappointments along the way, such as not getting grants approved on first submission or receiving rejection letters for papers or other efforts that will be important to you. But this is the process," said **Richard Gorlick, MD**, division head for Pediatrics and the Children's Cancer Hospital. "You'll learn from those times and improve and start getting those approvals. But keep those rejection letters and look back on them because they'll keep you going and not allow you to become complacent." He also urged the departing fellows to accept future accolades with humbleness because the lauded successes not only recognize their abilities, but that of all the people who support them. "Also important to remember is that on the day after you accomplish something big, start working on what's next. Just keep looking forward." Most immediately, Camacho is considering multiple offers; Shaw will remain at MD Anderson for a fourth year to complete a master's degree in clinical research; and Tanaka will take on a fourth year of neuro-oncology training at another institution.

Prom Party Palooza

Our teen pediatric cancer patients danced the night away at Prom Party Palooza, held Saturday, April 29.



This special event -- which included a red carpet entrance, makeovers, music, photography and great food -- was made possible through the generous support of many Houston restaurants and businesses. There were separate parties for parents and younger MD Anderson Children's Cancer Hospital patients which featured lots of fun, too. To learn more about the bash and the vendors who made it possible, log on http://bit.ly/2pxU9UQ.

Camp Star Trails

Our patients and their siblings had a blast at Camp Star Trails, held in Burton in June. A whopping 170 kids attended the event that included arts and craft, horseback riding, handling a variety of animals, cooking and baking, archery, photography, water sports, relay races, and nights by the campfire.



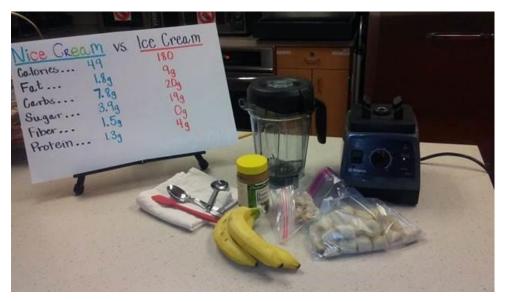
Seven *Division of Pediatrics* faculty were recipients of a 2017 President's Recognition for Faculty Excellence Award in April. The awards honor contributions in several areas.

- Joya Chandra, PhD, for Excellence in Education and Mentorship
- Douglas Harrison, MD, for Excellence in Prevention Outreach
- Cindy Herzog, MD, for Excellence in Network Development
- Winston Huh, MD, for Excellence in OneConnect Leadership
- Shulin Li, PhD, for Excellence in Research
- Demetrios Petropoulos, MD, for Excellence in Clinical Quality Improvement
- **Cindy Schwartz, MD**, for Excellence in Financial Stewardship

Ever hear of "Nice Cream?"

The cool treat was prepared as a lower-calorie version of ice cream at a cooking class held in June. Our families enjoyed it, said **Karla Crawford**, **MPH**, **RD**, **LD**, research dietitian in Pediatrics-Research. "The bananas were precut and frozen, so the patients were able to add all the ingredients with verbal instructions. At first, some were skeptical, but everyone ended up raving about how delicious it was," she reported. The basic recipe also included peanut butter and ice. The group also talked about the nutritional content and how the recipe could be altered to make different flavors. For more delicious, healthy food options, patients can log onto http://www.mdanderson.org/recipe.





Editorial Team

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