

notes

FALL 2013

Duke Launches Center for Cancer Survivorship

By Angela Spivey



At a breast cancer survivors clinic led by nurse practitioner Kathy Trotter, breast cancer survivors Odessa Thorpe, 73, of Alton, Va., right, and Delray Schulze, 81, of Greenwood, S.C., left, exercise during a group meeting. The DCI is expanding its survivorship care and research through the launch of the Duke Center for Cancer Survivorship.

A cancer diagnosis is life-changing, even if treatment goes well. More than half of patients with cancer report secondary problems such as chronic pain, fatigue, sexual dysfunction, relationship difficulties, fertility issues, fear of recurrence, depression, and financial and job-related concerns.

The DCI has engaged this problem head on with the launch of the Duke Cancer Survivorship Center. “With close to 14 million cancer survivors

nationally and a rapidly growing number of survivors of all types of cancers treated at Duke, we are working to build a single center that can coordinate and augment existing programs to ensure that the individual needs of all patients are recognized and addressed,” says Jeffrey Peppercorn, MD, MPH, the new director of the center. “We will integrate top quality clinical care with research to provide a national model for survivorship care. The new center will provide a centralized infrastructure to

coordinate and expand our research in this area.”

The center will coordinate the care of patients after active treatment is finished and promote research into how to improve quality of life and address the challenges facing cancer survivors.

The center officially launched on September 26, 2013, with a scientific symposium featuring keynote speaker Larry Shulman, MD, Dana Farber Cancer Institute, a national expert in cancer

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Honoring the Memory of O. Michael Colvin, MD

By Angela Spivey

O. Michael Colvin, MD, a former director of the Duke Comprehensive Cancer Center, passed away on March 16, 2013.

Colvin is remembered not only for his leadership of the cancer center but also for his dedicated mentorship and his pioneering research.

One of Colvin’s mentees was Michael Kastan, executive director of the Duke Cancer Institute and William W. Shingleton Professor of Pharmacology and Cancer Biology. “I personally benefitted greatly from his mentorship and his commitment to advancing the careers of both his students and his colleagues,” Kastan says. “His insights into research combined with his calming demeanor and dry sense of humor had a lasting impact on my career and that of many others.”

In 1995, Colvin became the third director of the Duke Comprehensive Cancer Center (now the Duke Cancer Institute), which he led for six and a half years. He had been recruited to Duke after a 34-year career at Johns Hopkins, where he was chief of the internationally recognized Division of

Pharmacology and Experimental Therapeutics.

During his time at Duke, Colvin restructured the administration of the cancer center and appointed senior leaders to oversee major areas such as basic research, clinical research, and cancer prevention, detection, and control. In addition, Colvin was a strong advocate for patient support services, serving on the advisory board of the Duke Cancer Patient Support Program and the board of the Caring House. Colvin retired from Duke as director *emeritus* in 2008.

Colvin was well known for his pioneering research with drugs that damage the genetic material that causes cancer cells to replicate. He was one of the first investigators to use very high dose of cyclophosphamide for the treatment of solid tumors, now a common practice in bone marrow transplantation for breast cancer and other cancers. His work also contributed to the development of current stem cell therapies.


To honor Colvin’s memory, the DCI has established the Michael Colvin Memorial Lecture



O. Michael Colvin, director *emeritus* of the Duke Comprehensive Cancer Center.

in Developmental Therapeutics. The lecture will feature a preeminent researcher in the area of developmental therapeutics annually.

Giving Opportunity

For information about donating to the memorial lecture, please visit dcc.convio.net/colvinlectureseries. 

Cracking the Secrets of a Lethal Pediatric Tumor By Dave Hart

Researchers and clinicians have made dramatic progress in treating pediatric cancer in recent years. Mortality rates have plunged; more than 80 percent of children with cancer now survive for five years or more, and most are cured altogether.

One form of pediatric cancer, though, a type of brain stem tumor called Diffuse Intrinsic Pontine Glioma (DIPG), has stubbornly resisted this encouraging trend. With some 200 to 300 cases in the U.S. annually, DIPGs are the leading cause of death among children with brain tumors.

Despite three decades of clinical trials and therapeutic approaches, no treatment yet developed has managed to significantly slow the inexorable path of this type of tumor, and for parents and children a diagnosis of DIPG is devastating: the majority of young patients die within a year.

"It's difficult to give families that diagnosis," says Oren Becher, MD, of Duke's Division of

Pediatric Hematology/Oncology. "We've had a lot of success in other cancers in children, but with this particular tumor, there has not been any progress. It's completely incurable."

Becher and his team at the Levine Science Research Center are hoping to help change that. By exploring the genetic mutations associated with DIPGs and analyzing the obstacles to effective drug delivery systems, he is working to gain a better understanding of these dreaded tumors in hopes of developing more effective therapies. "Ultimately, the goal is to find a cure for this tumor," says Becher, who came to Duke in 2010 after training at Johns Hopkins and completing two fellowships at Memorial Sloan-Kettering Cancer Center in New York. "That's a long way down the line, but I think we're making some good first steps. Our lab is focusing exclusively on this tumor, and we're attacking it from all angles."

One of those angles involves using genetically modified mice to understand the role a particular genetic mutation plays in the formation of DIPGs. Until recently, Becher said, physicians assumed

structures and, ultimately, to use that knowledge as a basis for developing new therapies.

"The next step will be to look for ways to target these unique genetic alterations," he says. One possibility for doing that may be a drug called Dasatinib, which inhibits one of the altered genes. Dasatinib, an approved treatment for adult leukemia, has been shown to slow DIPG cancer cell growth in vitro, but it has not improved survival times in DIPG mouse models.

Why does the drug inhibit cancer cells in isolation but not in live mice? One possible explanation, Becher says, is that DIPG has a relatively intact blood-brain barrier (BBB), which prevents drugs from crossing from the blood into the tumor in sufficient levels to be effective.

One of the ways the BBB does that, Becher says, is by using tiny pumps within the blood vessels that push drugs back out of the tumor and into the blood stream.

His team also generates DIPGs in mice where these pumps have been genetically deleted. When they compare Dasatinib's effect on DIPG cancer cells in mice without pumps to mice with intact



Pediatric hematologist/oncologist Oren Becher works to develop new therapies for a lethal pediatric brain stem tumor.

"If the data look really promising, we'll try to move forward quickly," Becher says. "We'll see what the next three months show."

DIPGs in children were biologically similar to gliomas in adults, and most therapies were based on therapies developed for those other gliomas.

Those approaches have not worked, and Becher said recent research may indicate why.

"It turns out that there are unique genetic alterations in this tumor that are not found in other gliomas," he says. "So only in the last several years have we begun to analyze this tumor correctly. We finally have the right information about what is driving this tumor, and that gives us a better sense of how to attack it."

Becher was the first researcher to develop a genetic DIPG mouse model in which to study these alterations while he was at Sloan-Kettering. At Duke he is improving those mouse models to better understand the tumors' unique genetic

pumps, the early results are encouraging.

"This work is preliminary, but it suggests that the drug has no efficacy in mice with pumps, but kills tumor cells in mice without pumps," Becher says. "If you quantify the amount of cell death you get with one dose in mice without pumps versus mice with pumps, it's a twenty-fold difference."

That suggests that the pumps may prevent sufficient amounts of the drug from reaching the tumor. The next step is to see if he can produce the same result by inhibiting the pumps pharmacologically rather than genetically.

"If the data look really promising, we'll try to move forward quickly," Becher says. "We'll see what the next three months show." ■

Duke Launches Center for Cancer Survivorship

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survivorship. Also speaking were Peppercorn; Drew Peterson, MD, director of the Urology Survivorship Clinic; and Steve Patierno, PhD, the deputy director of the DCI.

The launch also included the announcement of the Duke Cancer Survivorship Clinic, directed by Denise Spector, PhD. Patients finished with active cancer treatment can be referred to this clinic. "As a nurse practitioner, my role will be to give patients comprehensive assessments of where they are and how we can help them physically, psychosocially, and spiritually," Spector says. "We want survivors living longer and longer, but we also want them living well." Spector aims to offer a multi-disciplinary clinic in which patients would, after the initial

assessment, see all the practitioners they need in one visit, which may include dietitians, physical therapists, and social workers.

The DCI's long-standing Cancer Patient Support Program will continue to operate under the umbrella of the survivorship center and may expand services if needed, says Cheyenne Corbett, PhD, LMFT, director of the program. The program offers services such as individual, couple, and family therapy; support groups; and self-image resources, all free of charge. "Our services are offered throughout the course of the patient experience, to both patients and their loved ones," Corbett says. ■

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A Crucial Juncture in the War on Cancer

When congress declared the “war on cancer” in 1971, scientists did not know the right questions to ask, nor did we have the technologies we needed to answer them.

Over the past 40-plus years, significant advances in the molecular and cellular sciences have revolutionized our understanding of cancer. We are poised to be able to develop new therapies that target the abnormal biology of tumors, making new therapies both more effective at killing cancer cells and also less toxic to normal cells.

Because of these advances, we are at a critical juncture in the war against cancer. To keep our momentum going, we need to continue to make basic discoveries and to translate that knowledge to prevention and treatment of cancer.

The Duke Cancer Institute was created to address those challenges. With a single administrative structure that oversees all cancer-related activities, from basic science research to clinical research to patient care, it is easier than ever for us to take discoveries from the lab to our clinics to patients nationwide.

In these pages we share the latest developments in these efforts, including the launch of the Duke Center for Cancer Survivorship, our progress in developing vaccines to stimulate the immune system against cancer, and exciting new drugs being tested in clinical trials at Duke that target only the specific proteins or genes that are overactive in cancer cells.

As federal research funding has decreased, we must rely more than ever on industry partnerships and philanthropy to support these and other efforts. Thank you for your support of our efforts at the Duke Cancer Institute. Together, we can ensure success in our quest to understand and defeat cancer. ▀



Michael B. Kastan, MD, PhD
Executive Director, Duke Cancer Institute
William W. Shingleton Professor of
Pharmacology and Cancer Biology



Regional Chemotherapy Targets Melanoma, Sparing the Immune System *By Dave Hart*

Doug Tyler, MD, opens his laptop and scrolls through photograph after photograph of a patient’s leg, which is peppered with dozens of what look like small moles. Each little spot is actually a melanoma tumor, says Tyler, professor of surgery and chief of the Division of Surgical Oncology — “and for every one you can see, there’s one you can’t see.”

Tyler, who directs the Melanoma Program at the Duke Cancer Institute, runs the nation’s largest regional chemotherapy center for the treatment

of skin cancer. He develops novel treatments to battle these stubborn cancers, including innovative approaches that direct drugs to the most seriously affected regions while minimizing the deleterious effects of whole-body chemotherapy. Using catheters, he can channel drugs directly to the stricken limb and then use a carefully applied tourniquet to keep the treatment concentrated for precise periods.

“When you give whole-body chemotherapy, it suppresses immune response,” Tyler says. “By giving chemotherapy regionally, we can give 20

times the normal dose of a therapeutic agent, making it more effective, and the benefit is that we don’t suppress the immune system.”

Tyler is exploring the potential of combining that approach with a systemic therapy that modulates immune response. By applying both a high dose of regional chemotherapy and whole-body antibodies that bolster the immune system, he hopes the treatment will help the patient’s own body fight the cancer. ▀

Golfers Against Cancer Investment Yields Big Returns *By Angela Spivey*

When a patient receives radiation treatment for liver cancer, the liver can move as much as four centimeters, as the patient breathes. “You may think of this as not a big movement, but it has a large impact on the radiation dose,” says

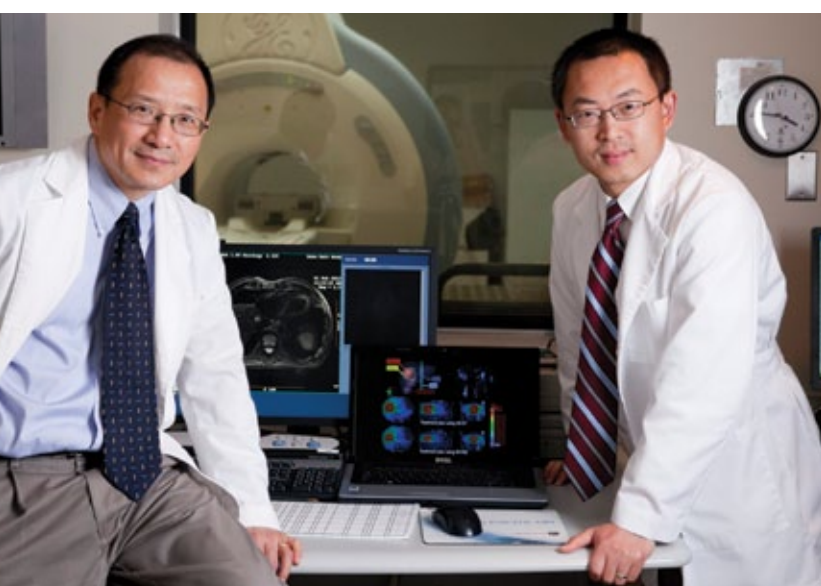
Jing Cai, PhD, assistant professor of radiation oncology. When radiation misses its mark, healthy liver tissue could be damaged, or tumor tissue could be left behind because it didn’t receive the radiation needed to destroy it.

So for tumors in the liver, you can’t see them very well.”

So Cai is developing 4D MRI technology to more precisely target treatment of moving tumors in the liver. The 4D technique includes three dimensions plus time. “It gives you motion in three dimensions,” Cai says. Unlike other MRIs that are used clinically, the 4D MRI is a 3D movie, not a static image or a 2D movie.

In early 2012, Cai received an award of \$70,000 from the Triad chapter of national nonprofit Golfers Against Cancer (GAC). He used the funds to compare his 4D technique to traditional 4D CT imaging in 10 patients.

Cai and his co-principal investigator, Fang-Fang Yin, PhD, professor of radiation oncology, included that data in a grant proposal to the National Institutes of Health. That proposal yielded a \$650,000, two-year grant. “The GAC funding really helped us in getting more preliminary patient data to convince the reviewers that our technique works,” Cai says. ▀



Radiation oncologists plan radiation treatment using CT imaging to map out all the organs and allow for their movement. But Cai wants to do better.

“CT has two problems,” Cai says. “It gives patients an imaging radiation dose. Second, it has insufficient soft tissue contrast.

Fang-Fang Yin and Jing Cai are developing a 4D MRI technology to more precisely target treatment of tumors in the liver.

Better, Faster Recovery from Endocrine Surgery

By Dave Hart

Hedwig Bischoff had so many symptoms she couldn't decide which were the worst. The pain or the hot flashes? The racing heartbeat, fluctuating blood pressure, or wild mood swings?

"My husband didn't know who he was living with," says Bischoff, 68, who lives in New Bern, N.C. "He never knew if he was going to wake up to the smiling wife or the other one."

She sought help at Duke University Hospital, where physicians discovered a pheochromocytoma, a neuroendocrine tumor on one of her adrenal glands. On July 8, 2013, Bischoff had surgery by Sanziana Roman, MD, to remove the tumor.

The effects were immediate. Her symptoms vanished. Just as remarkably, she was back on her feet in almost no time, with virtually no postoperative pain or complications.

"I feel fantastic," she says. "It's been less than a month, and I almost can't tell that I just had surgery. People can't believe how quickly I've recuperated."

That rapid rebound is one of the hallmarks of a new minimally invasive approach to adrenal gland surgery adopted at Duke under the new



Hedwig 'Sue' Bischoff with her 1979 Corvette at her home in New Bern, N.C. in August 2013. Bischoff refers to the car as her "toy" and is an active member of the local Twin Rivers Corvette Club. Bischoff had a posterior retroperitoneoscopic adrenalectomy, a new minimally invasive adrenal gland surgery performed at Duke University Hospital and has experienced a quicker-than-normal recuperation.

and potentially injure all the stuff in there, like your spleen, your pancreas, your liver, your bowels. Instead, you access the adrenal glands very quickly, with minimal disruption, minimal chance of injury, and much more rapid recovery."

That swift recovery time is especially important because a number of other cancers—lung, breast, melanoma, and others—frequently metastasize to the adrenal glands.

"Patients who have metastasized lung cancer

increase in incidence worldwide. She also has joined forces with collaborators in pharmacology at Duke to develop additional novel treatments for the disease.

Duke has also begun to routinely test thyroid tumors and nodules for specific molecular markers that can indicate a likely prognosis and help physicians determine the best course of action.

Sosa disputes the common characterization of thyroid cancer as "the good cancer." While 10-year survival rates for the most common type, papillary thyroid cancer, are in excess of 95 percent, she says, survival rates are not the only measure of a disease's disruptive effects. In addition, she points out that another type, anaplastic thyroid cancer, is the most aggressive solid tumor known to science; median survival after diagnosis is about nine weeks.

The bottom line? "There is no good cancer," Sosa says.

If the endocrine surgery section seems to be in a flurry of activity these days, Sosa says, that is due in large part to the strong tradition she inherited from prominent Duke endocrine surgeons such as Samuel Wells, MD, and George Leight, MD.

"There's a huge history here," says Sosa. "And this is a very exciting time. We have three full-time very experienced endocrine surgeons, so we're rapidly becoming one of the largest and busiest endocrine surgery and endocrine neoplasia centers in North America."

The need justifies that activity, she says.

"The incidence of thyroid cancer is skyrocketing," Sosa says. "Adrenal lumps are common. Primary hyperparathyroidism is common. All of a sudden there's a lot going on at Duke, and we've assembled a big multi-disciplinary team. I give the leadership of the Duke Cancer Institute a lot of credit for having the insight to invest in this area." ■

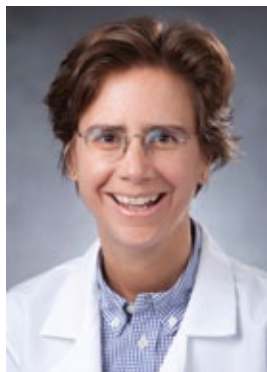
"I feel fantastic," Bischoff says. "It's been less than a month, and I almost can't tell that I just had surgery. People can't believe how quickly I've recuperated."

chief of endocrine surgery, Julie Ann Sosa, MD.

The procedure, known as posterior retroperitoneoscopic adrenalectomy, resembles the standard technique, laparoscopic adrenalectomy, in that each is performed through three or four very small incisions.

The difference is where those incisions are made: while traditional laparoscopic adrenalectomies are done through the abdomen, the new approach reaches the adrenal glands through the back. Duke is one of just a handful of institutions that have begun using the new method.

"The adrenal glands aren't really in your abdomen," says Sosa, who came to Duke in January 2013 and also serves as the leader of the Endocrine Neoplasia Diseases Group at the Duke Cancer Institute and the Duke Clinical Research Institute. "They sit on top of your kidneys. They're much closer to your back than your front, and if you approach them through the back you don't violate the peritoneal cavity



New chief of endocrine surgery, Julie Ann Sosa.

are usually quite debilitated, so going into the operating room to have adrenal surgery is a very big deal," says Sosa. "We have now done adrenalectomies for three lung cancer patients with just a one-night hospitalization. That is absolutely critical, because it allows them to go on to have their definitive therapy for lung cancer much faster. In my opinion, this is revolutionizing the management of adrenal tumors."

The new approach to adrenal gland surgery is just one of the many initiatives Sosa and her partners, Roman, and Randal Scheri, MD, have launched since Sosa and Roman arrived earlier this year. On the clinical side, they also have implemented a comprehensive minimally invasive surgical procedure to treat a common disease called primary hyperparathyroidism.

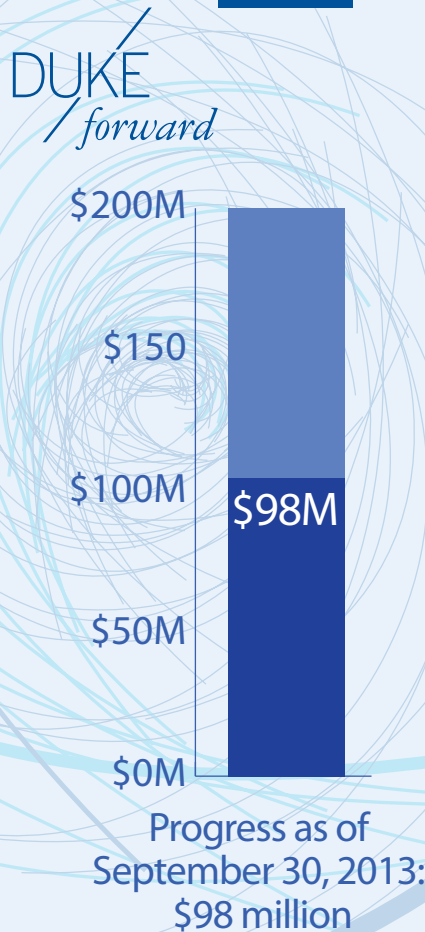
And under Sosa's leadership, Duke is developing its first clinical trials to evaluate what are called "small molecule" drug therapies for thyroid cancer, which has seen an explosive

The Duke Medicine Campaign



Duke Medicine has surpassed the halfway mark in its most comprehensive philanthropic effort to date, a five-year, \$1.2 billion campaign to lead discovery, clinical care, and education. Duke Medicine's campaign, *Medicine that Changes the World*, is part of Duke University's \$3.25 billion campaign, *Duke Forward*, to lead higher education and accelerate advances in science and health care. Both campaigns kicked off in September 2012 and will end June 30, 2017.

As part of the Duke Medicine campaign, the Duke Cancer Institute seeks to raise \$200 million to advance cancer research and care. As of September 30, 2013, the DCI has raised nearly \$98 million. For updates, visit dukeforward.dukemedicine.org/cancer. ▀



TISCH FAMILY CONTINUES THEIR GENEROUS SUPPORT

The DCI campaign recently received a big boost from one of its most generous philanthropic supporters—the family of the late Preston Robert Tisch.

The Tisch family has renewed its support of brain tumor research at the DCI and at the Preston Robert Tisch Brain Tumor Center. In addition, the family has made a matching grant for research that uses a modified poliovirus to defeat one of the most aggressive brain tumors, glioblastoma multiforme. The treatment, developed at the DCI through basic laboratory research, capitalizes on the discovery that cancer cells have an abundance of receptors that work like magnets to attract the poliovirus, which then infects and kills the cells.

In a future issue of DCI Notes, look for a story about the impact of the Tisch family's philanthropy, and for more information about this pioneering research.

Endowment Honors the Career of Jon. P Gockerman, MD

By Angela Spivey

To mark 30 years of contributions to Duke by Jon P. Gockerman, MD, professor *emeritus* of medicine, the DCI established the Jon P. Gockerman Research Endowment Fund on the occasion of his retirement from Duke in March 2013.

The endowment will fund research that will continue the progress made through Gockerman's research on lymphoma, leukemia, and other lymphoproliferative disorders. Gockerman's accomplishments over a 30-year career at Duke include completing a number of new drug discovery studies for lymphoma treatments, including pazopanib, which gained approval for renal cell carcinoma and soft tissue sarcoma from the U.S. Food and Drug Administration.

Gockerman is also known as a great advocate for his patients. "As a physician, Jon impacted the lives of literally hundreds of people. He would go to whatever lengths it took to find the right treatment for a patient," says Gockerman's longtime colleague Joseph Moore, MD, professor of hematology and oncology.



Jon P. Gockerman, professor emeritus of medicine.

In 2012, Gockerman received the Leonard Tow Humanism in Medicine Award, which is presented annually to a faculty member who demonstrates outstanding compassion in the delivery of care, respect for patients, their families, and colleagues, as well as clinical excellence.

"From the very first moment that I had any contact with Jon Gockerman he put my apprehension and fears at rest."

— former patient Gordon Wright.

Many former patients of Gockerman's have supported the endowment, including J. Gordon Wright, DDS, PA, of Lexington, N.C.

Gockerman diagnosed Wright with stage 4 lymphoma but assured him that he expected to cure him. "From the very first moment that I had any contact with Jon Gockerman he put my apprehension and fears at rest," Wright says. Wright was in Duke hospital for two different stays that totaled six weeks. "Jon

Gockerman was attentive to my every need and answered my every question literally on a daily basis. After my initial consultation, he gave me his home phone number and told me if I had any

questions to call him at home. That is not a trait that is universally seen in health care anymore," says Wright, who is now cancer free.

Gockerman is also known as a hard-working clinician and teacher who expected hard work from others. "He would ask very penetrating questions of students, residents, and house officers, and he would expect deep thought and hard work in return," Moore says. In 2008, Gockerman won the Master Clinician/Teacher Award from Duke University Medical Center.

Gockerman continues to contribute to developing new therapies to fight cancer, working part time as senior medical director for oncology at Novella Clinical, a clinical research organization in Morrisville, N.C. ▀



Nadine Barrett, founding director of the DCI's Office of Health Equity and Disparities, talks with Latino faith leaders from the Durham community as part of their tour of the Duke Cancer Center building. The faith leaders also participated in community focus groups.

Community Voices on Cancer *By Angela Spivey*

Ernesto Lember is a pastor with Kings Park International Church/Celebración Cristiana in Durham, N.C. When people in his congregation get sick, they look to him mostly for prayers, but Lember and more often, his wife, Martha, do get asked to accompany church members on doctor's visits, as both a comforting presence and as advisors.

In the Latino community, faith is a very important part of daily life. And immigrants who are in the U.S. solely to work may have no family here, so the pastor becomes an even more important source of support.

But at doctor's appointments, especially when the topic is about something serious, such as cancer, there comes a point when Lember feels at a loss. He wants more education about cancer screening and treatments. "We would like a small crash course on the Duke Cancer Institute—how to point people in the right direction," Lember says.

That's one suggestion that Lember and other Latino pastors gave during a series of 10 focus groups, called "Community Voices on Cancer," held by the DCI's Office of Health Equity and Disparities. The DCI heard from more than 100 participants from the Latino, African-American, Asian, and other underserved communities. In addition to clergy members, participants included cancer survivors and their caregivers, social agency representatives, community leaders, and other community members.

"We wanted to find out from the community members themselves, what are their perceptions around cancer, cancer care, and research; what are the challenges their community is facing in accessing care; and how can we work together to address some of those challenges," says Nadine Barrett, PhD, founding director of the

Office of Health Equity and Disparities. The OHED conducted the focus groups with help from Rebecca Reyes, coordinator for Latino health services at Duke University Health System.

Now the OHED is implementing some of the suggestions, which included the need for increased education about cancer risks and symptoms and the reasons why clinical trials are conducted, the need for workshops for caregivers and cancer survivors, and access to services such as counseling, childcare options, transportation, as

well as information about insurance resources. In response, the OHED has begun participating in several community health fairs in Durham by sending DCI patient navigators—people who can provide assistance for anyone needing access to cancer resources and screening services. In addition, the OHED has launched several new programs, including the Health Ambassadors Program, in which Duke employees and community volunteers are trained to raise awareness in their communities about cancer, as well as monthly educational

A WINNING TEAM

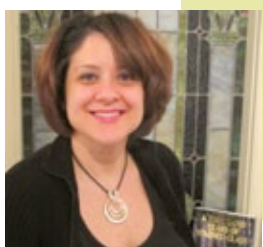
In 2010, Ana Quintana was living in Puerto Rico when she was diagnosed with locally advanced breast cancer. Her pathologist, a friend of hers, encouraged her to seek treatment at Duke. Her doctor, Kimberly Blackwell, MD, treated her with radiation then with a combination of therapies, including Tykerb® (lapatinib).

Blackwell advised Quintana to return to Puerto Rico to be with her children while she took her chemotherapy. Then she came back to Duke for surgery. But her pre-surgery mammography showed no trace of a tumor. The surgeon removed her lymph nodes as a precaution. "The pathology report came back that I was already cancer free," Quintana says. "God and Duke together are a winning team."

One day in the clinic, Blackwell introduced Quintana to Neil Spector, MD, co-director of the Experimental Therapeutics Program at the Duke

Cancer Institute, who played a large role in developing Tykerb when he was a researcher at GlaxoSmithKline. "I just went and hugged the guy," Quintana says.

Cancer has changed Quintana's life. After her diagnosis and recovery, she didn't want to go back to her career running a family business. She and her husband decided to move to North Carolina. "There is just something about this place," Quintana says. "The people have been amazingly supportive." Quintana had always been a part-time minister. Now she works full time as associate minister at Unity Church in Raleigh, NC. In addition, she has worked with the DCI's patient navigator program, and she participated in the community focus groups held by the Office of Health Equity and Disparities. "I want to give back; I will do anything to help," she says.



Ana Quintana



workshops on cancer and clinical trials held in partnership with the Durham Public Library. As for Lembert, he has become chair of the Latino Interfaith Leadership Advisory Council, an organization the DCI set up to work with the faith leaders to respond to community recommendations.

Some of the clergy said that they wanted to learn strategies for talking to their congregations about how God can work to heal them through medicine, rather than in opposition to medicine. “Faith can help people get through some of their most difficult times, without a

doubt, but faith can also become a barrier,” Barrett says. “Someone can go to the point of saying, ‘I’m not going to go to the doctor, or I’m not going to get screened, or I’m not going to get treatment for cancer. I have faith that God will take care of me.’”

Xiomara Boyce, a patient navigator with the OHED, agrees. “A lot of the clergy feel that by reaching out to them, Duke is helping them to be better faith leaders,” she says. ■

Celebracion Cristiana pastors Martha and Ernesto Lembert at Kings Park International Church in Durham, N.C. Ernesto Lembert is chair of the Latino Interfaith Leadership Advisory Council, an organization the DCI set up to work with the leaders to respond to community recommendations.

Making Progress with Cancer Vaccines

By Dave Hart

The principle behind employing therapeutic vaccines as a means to fight cancer is beguiling: use the vaccines to teach the body’s own immune system to recognize and destroy cancer cells. If that could effectively be done, more patients could forgo more difficult treatments and their deleterious side effects.

Far easier said than done, of course. But progress is being made. Among the researchers making it is oncologist Michael Morse, MD, who is working on several fronts to develop and improve cancer vaccine therapies. “One advantage of vaccine therapy is that you don’t have to keep giving it,” he says. “With most drugs, you have to keep taking them, every day or every week. With a vaccine, once it is given three or four times initially, it may only need to be given occasionally in the future as booster. The immune system has ‘memory’ so it can keep working against a cancer by itself, once stimulated.”

One avenue of investigation Morse and colleagues H. Kim Lyerly, MD, Amy Hobeika, PhD, Takuya Osada, MD, PhD, and Kim Blackwell, MD, are pursuing explores the prospect of combining vaccine therapy with standard breast cancer therapy in the hopes of boosting the effectiveness of both to battle a particularly aggressive form of breast cancer that over-expresses a gene known as HER2 (Human Epidermal Growth Factor Receptor 2).

“Unlike some targets for cancer vaccines, HER2 isn’t just present as a marker; it also has functions within the cancer cells,” Morse says. “It actually drives them to be more aggressive. It signals cells to divide and invade and spread more rapidly. So what we’re looking for with the vaccine is not just activation of immune cells that can attack the cancer, but also stimulation of antibodies that can bind to and inhibit the function of HER2.”

Morse is in the midst of a Phase 1 clinical trial that involves giving 12 subjects with HER2-positive breast cancer a vaccine based on an alphavirus particle, into which the gene for HER2 has been cloned.

“The alphavirus particle, although it cannot replicate in humans so it can’t cause an infection, is able to get into immune cells called dendritic cells and directs them to activate T cells and antibodies against the tumor cells which have HER2 present. What we hope to see is T cells attacking the cancers but also antibodies inhibiting the function of the HER2,” Morse says. Following the initial group of participants, another group will receive the vaccine plus the drug therapy Herceptin, and, after that, a third round that would add another drug, lapatinib.

Earlier research Morse conducted in mice indicated improved efficacy against HER2 by combining vaccines and standard anti-cancer therapies.

“We’re pretty excited about the possibilities of combining immunotherapy with Herceptin to double-team HER2,” Morse says.

Another avenue Morse is pursuing involves colorectal cancer and is geared toward solving a common problem in cancer immunotherapy.

“For vaccines using very immunogenic viruses such as adenovirus, it is hard to vaccinate someone multiple times because the immune system attacks the virus so fast that it obliterates



Oncologist Michael Morse works to develop and improve vaccines to treat cancer.

it before it has a chance to do anything,” he says. “We tested an adenovirus that has been modified to activate the immune system against its payload even if the immune system can attack it.”

In a Phase 1 clinical trial involving patients with advanced colorectal cancer, Morse found that a genetically modified adenovirus encoded with a tumor marker called CEA avoided the neutralizing antibodies and induced a significant immune system response. In the study, which has been accepted by

Cancer Immunology and Immunotherapy, the 25 patients experienced a 12-month survival probability of 48 percent, which Morse said was very encouraging in a group for whom all prior therapies had failed. A much larger Phase 2 study is needed to better evaluate those results.

A great deal of work remains to be done, Morse said, but bit by bit he and other researchers are advancing the potential clinical use of therapeutic cancer vaccines not only to treat patients with cancer but to help protect those who don’t yet have it.

“Way down the line, you might start to look at it as a preventative,” he says. “You might treat people who don’t have active cancer but have a high risk of recurrence, or a high risk of developing cancer in the first place. That’s a long-term strategy.” ■

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ask the expert

New Treatments for Chronic Lymphocytic Leukemia

Mark Lanasa, MD, PhD, is assistant professor of medicine at Duke University School of Medicine and the Duke Cancer Institute. He leads efforts at Duke to test several new treatments for chronic lymphocytic leukemia (CLL), a cancer that affects white blood cells called b-lymphocytes. CLL is the most common form of leukemia in the United States.

When is CLL treated? Can treatment cure it?

CLL is incurable but also very treatable. Some people have CLL for years and don't ever need treatment. About one-third of patients will have progressive disease in which symptoms quickly develop. Those people will need treatment in the first few years after diagnosis. Most patients have slowly progressive disease. Overall, about 70 percent of patients will need treatment at some point.

Effects of CLL that may signal the need for treatment include worsening anemia, low platelet counts, or growing lymph nodes. A patient who is anemic will typically feel weak, have low energy levels, and can be short of breath with exertion or have chest discomfort. A patient with a low platelet count will tend to feel fine but will be at risk for complications such as easy bruising or bleeding. Enlarged lymph nodes can be uncomfortable, can compress adjacent organs, or cause cosmetic concerns.

What is the current standard treatment for CLL? Why are new treatments needed?

Most current treatments involve cytotoxic chemotherapies that kill cancer cells but that will also potentially harm normal cells. The response rate to these treatments among CLL patients who have not had prior treatment is as high as 95 percent. But we need new treatments for two reasons. First, chemotherapies cause side effects such as suppression of the immune system and have additional risks such as infections, nausea, and general fatigue. Second, patients develop resistance to cytotoxic therapies. This happens because an initial chemotherapy treatment will kill, for instance, 99 out of 100 CLL cells. That one cell that remains gives rise to all of the new CLL cells when the disease recurs. So the recurrent CLL won't respond nearly as well to the chemotherapy used previously. Chemotherapy works less well the second time around, and

even less well on the third treatment. Eventually chemotherapy stops working completely for these patients.

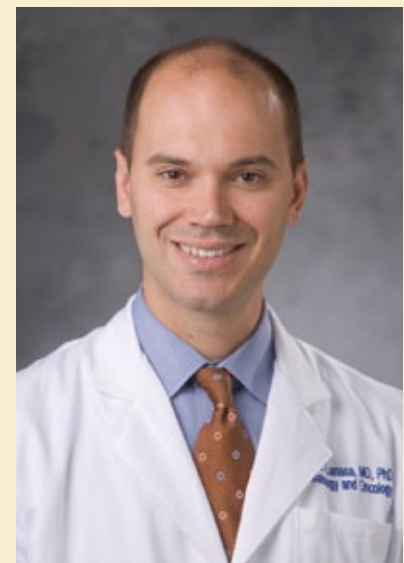
What new CLL treatments are in the pipeline?

There are several very exciting drugs in development for CLL that target only the specific proteins or genes that are overactive in cancer cells of all types. Most of these new treatments are also more convenient for patients because they can be administered orally, rather than through an intravenous infusion. Many of these treatments are being offered to patients at Duke through clinical trials.

To help solve the resistance problem, we have developed a trial available here at Duke that combines two treatments—lenalidomide (Revlimid) and plerixafor (Mozobil). We anticipate that plerixafor will make CLL cells more vulnerable by forcing them out of the lymph nodes and bone marrow, where they receive signals from other cells that make them resistant to treatment. By forcing the cancer cells out into the bloodstream, we hope to increase the chances that lenalidomide will kill them. That trial is in the Phase 1 stage (safety and efficacy testing) and is enrolling patients now. (Sponsors: Celgene and Genzyme.)

Another trial we are offering tests a treatment produced by Amgen, AMG-319, which inhibits a particular enzyme named PI3K that is highly expressed by CLL cells but not to a large degree in other cells. Duke is a participating site of a multi-center trial of this drug that has shown encouraging responses in other CLL patients so far.

Other trials at Duke are in development, including a nation-wide Phase III trial of a drug that looks very promising for previously untreated patients (ibrutinib), and another trial of a drug for patients with relapsed CLL (ABT-199).



What do these trials mean for patients?

With all these new treatments that work in different ways, we have good clinical trial options for almost all patients with CLL. Earlier data show that if CLL patients ever need treatment, they are at risk to ultimately die from a CLL-related cause. The majority of those patients die from infections, such as pneumonia or the flu; CLL weakens the immune system, and the chemotherapy weakens it even further. I genuinely believe that by more efficiently killing cancer cells while producing fewer side effects, these new drugs will significantly prolong survival for people with CLL. ♥

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For information about enrolling in these or other CLL trials at Duke, contact Lanasa's clinical office at **919-684-8964**, or visit centerforcll.duhs.duke.edu.