Researchers and physicians collaborate to accelerate advances in cancer care
The partnership between physicians and scientists is the basis for translational medicine. Illustration by Ajay Peckham.
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Chief of the Gastrointestinal Research Program

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Director of Breast Cancer Navigation Program, Margie Petersen Breast Center

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Assistant Professor of Surgery
Acting Director of Margie Petersen Breast Center

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Biostatistics

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Assistant Professor of Immunology

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Director of Complex General Surgical Oncology Fellowship
Director of Donald L. Morton, MD, Melanoma Research Program
Director of Therapeutic Immunology

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Surgical Oncologist

Richard Frierdich, MD
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Assistant Professor of Surgery

Chester F. Griffiths, MD
Professor of Surgery

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Professor and Director of Molecular Oncology
Chief of Scientific Intelligence
Director of Genomics Sequencing

Sharon Huang, PhD
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Director of Brain Tumor Center and Pituitary Disorders Program

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Director of the Dirks/Dougherty Laboratory for Cancer Research

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Diego Marzese, PhD
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Hitoe Torisu-Itakura, MD, PhD
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Professor of Pathology

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Urology

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Medical Oncology

Alistair Cochran, MD
Pathology

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Biostatistics

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Radiation Oncology

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Adjunct Associate Professor of Dermatology

If you have a change of address or would like to be removed from our mailing list, please contact the Public Affairs and Development Office at 310-315-6111.
Our Commitment to Cancer Research—and to You

Cancer is the second-leading cause of death in the country, accounting for almost one in four deaths. This year an estimated 85,720 Americans will be lost to the disease. The devastation caused by cancer is unacceptable.

That’s why my family and I remain steadfast in our fight against the illness. When you support the John Wayne Cancer Institute, you can be assured that our physicians and researchers feel the same way you do about eliminating the pain and suffering linked to cancer.

Cancer research and patient care is not just a career choice, it’s a calling that drives us to do everything we can to unlock the mysteries of cancer and produce better outcomes for patients.

The stories in this issue of Innovations describe the Institute’s commitment to excellence. From the dedication to translational research to the training of our fellows to the creation of the Brain Tumor Center Skull Base and Endoscopic Microdissection Laboratory, the Institute faculty is leading the way toward a brighter future. Your generosity and support make such progress possible. Thank you for joining us as partners in the fight to cure cancer.

Patrick Wayne
Chairman of the Board of Directors

“Cancer research and patient care is not just a career choice, it’s a calling that drives us to do everything we can to unlock the mysteries of cancer and produce better outcomes for patients.”

REMEMBERING THE DUKE

CAST A GIANT SHADOW, 1966

John Wayne joined a star-studded cast that included Kirk Douglas, Frank Sinatra, Yul Brynner and Angie Dickinson in this big-budget film. Cast a Giant Shadow was based on the true experience of Jewish-American military officer Col. David “Mickey” Marcus, played by Douglas, who was asked to help form an Israeli army during the 1948 Arab-Israeli War. Wayne played a senior Pentagon official who overcame initial misgivings to support Marcus’ efforts in the Middle East.

“This dynamite is our artillery, and the night is our armor.”
What It Means to Be on the Leading Edge of Cancer Research

The treatment and prevention of cancer is a fast-moving field. Increasingly, cancer can be cured and lives prolonged with groundbreaking treatments based on personalized medicine and translational research. That is our mission at the John Wayne Cancer Institute.

But what does that mean to you, our friends and supporters? It means we back our words with actions. Every day in our clinical examination rooms, operating suites and laboratories, we are pressing forward with hands-on work that extends lives.

For some institutions, “personalized medicine” is little more than a marketing term. At the John Wayne Cancer Institute, that concept is made real through our state-of-the-art patient care and novel research on immunotherapies, targeted molecular therapies and surgical innovations.

Our commitment to remain a top-flight cancer research organization is verifiable through the scientific papers we regularly publish in peer-reviewed medical journals. It’s apparent through the highly competitive grants we receive from prestigious organizations, including the National Institutes of Health. It’s apparent in the quality of the enthusiastic fellows who seek to study and train at the Institute and who go on to make significant contributions as leaders in the field.

Your investment in the John Wayne Cancer Institute is producing tangible benefits. Thank you for your support and your trust in our dedicated faculty and staff. Together we will continue to lead the way in reducing the global burden of cancer.

Anton J. Bilchik, MD, PhD
Professor of Surgery
Chief of Medicine and
Chief of the Gastrointestinal Research Program

Welcoming Marcel Loh as the New Institute and Health Center Chief Executive

The John Wayne Cancer Institute is pleased to welcome Marcel Loh as the new chief executive for the Institute and Saint John’s Health Center. In Loh, our campus will be guided by a successful health care executive with proven leadership skills. For the past 14 years, Loh has served in various executive roles with the Providence affiliate Swedish Health Services, a five-hospital network in greater Seattle. Loh holds a master’s degree in hospital administration, served as an Army officer in the Medical Service Corps and retired from the Army Reserve as a lieutenant colonel. In addition to being a past chairman of the Washington State Hospital Association, he is a fellow in the American College of Healthcare Executives.
At the Podium

Members of the Institute faculty are invited to speak at many international and national cancer meetings and forums regarding their latest projects and papers. This travel keeps our researchers at the forefront of scientific developments in cancer diagnosis and treatment and communicates the Institute’s work to audiences around the globe.

Seven studies from John Wayne Cancer Institute researchers were presented by invitation in April at the annual meeting of the American Association for Cancer Research in San Diego, the largest and most important annual meeting on cancer research. This impressive body of work encompassed investigations ranging from chemoresistance to biomarker analysis to tumor microenvironment.

An Institute team led by Anton J. Bilchik, MD, PhD, presented data on immunoscopy scoring for prognostic assessment of colon cancer at a plenary session of the Society for Surgery of the Alimentary Tract in Chicago in May. Research has hinted that a patient’s immune system can be an important factor in colon cancer. The research—the first prospective study on the question—demonstrated that even if physicians adhere to surgical and pathological quality standards, the patient’s immune response to a colon cancer can play an important factor in determining whether cancer cells spread. The study, which was recently accepted for publication in the Journal of Gastrointestinal Surgery, also suggests that there are specific targets which may be important in the development of a colon cancer vaccine.

Delphine Lee, MD, PhD, was invited to lecture at the internationally attended American Academy of Dermatology Meeting in Denver in March. Dr. Lee gave two presentations, one on advanced melanoma and the other on tumor immunology. Dr. Lee was invited to speak at the meeting as a recognized expert in research and treatment of advanced melanoma.

Mark B. Faries, MD, presented research findings on adoptive tumor-infiltrating lymphocytes at the Society for Immunotherapy of Cancer meeting in La Jolla in August and at a regional meeting in Portland in October. In addition, an Institute team led by Dr. Faries presented a poster on the use of extensive lymphadenectomy for regional control of stage III cutaneous melanoma at the American Society of Clinical Oncology annual meeting in May in Chicago.

Daniel Kelly, MD, presented a pituitary surgery course at the American Association of Neurological Surgeons in San Francisco in April. Dr. Kelly also gave two talks—on meningiomas and the endoscopic treatment of meningiomas—in April in Milan, Italy, and spoke at the 73rd annual meeting of the Japanese Neurosurgical Society 2014 in Tokyo, Japan, in October.

Dave S.B. Hoon, PhD, presented findings at the American Society of Clinical Oncology annual meeting in Chicago in May on the use of deep sequencing to identify multiple informative genomic mutations associated with cell-free tumor DNA in the plasma of patients with metastatic melanoma. The study was published in Pigment Cell & Melanoma Research.

Dr. Hoon and collaborators published a paper in the Journal of Investigative Dermatology on BRAF mutations that often occur in melanomas. The study demonstrated that EGFR epigenetic activation has important implications in BRAF inhibitor resistance in melanoma.

Dr. Hoon led an institute team publishing findings in the journal Clinical Chemistry on the first detailed single-nucleotide polymorphisms-based (SNPs) genomic confirmation of the close relationship between circulating tumor cells and tumor metastases. The study demonstrates the important role of circulating tumor cells in identification of genomic changes associated with melanoma outcomes.

Publications

Dr. Lee was the lead author of a landmark paper published in May in the journal Frontiers Oncology on data pointing to a new way to predict patients who will respond to the melanoma drug ipilimumab. The data has led to a patent application.

The Journal of Glycobiology published Dr. Lee’s paper on immune response modulation by tumor-secreted glycosphingolipids, a special type of complex lipids (fats) that are present in normal tissues. These fats released by tumors allow them to progress and hide from the immune system. Certain drugs may inhibit production of these glycosphingolipids to block this strategy that helps tumors persist.

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New Appointments for Dr. Mark B. Faries

Mark B. Faries, MD, was recently appointed to the melanoma Staging Committee of the American Joint Committee on Cancer. The committee will assess and assign the staging protocols for all melanoma tumor types in its next update. The Staging Committee sets the worldwide standards for assessing prognosis in cancer and helping determine appropriate therapy. Dr. Faries is director of the complex general Surgical Oncology Fellowship Program, director of the Donald L. Morton, MD, Melanoma Research Program, and director of therapeutic immunology at the Institute. Dr. Faries has also joined the editorial board of the *Annals of Surgical Oncology*. This publication is the official journal of the Society of Surgical Oncology and the American Society of Breast Surgeons.

Avon Foundation Funds Breast Cancer Research

Delphine Lee, MD, PhD, director of translational immunology in the Dirks/Dougherty Laboratory for Cancer Research, has received funding from the Avon Foundation for research that will investigate microbial communities in the breast ducts of women. In previous studies—funded in part by the Associates for Breast and Prostate Cancer Studies and the Fashion Footwear Association Charitable Foundation of New York—Dr. Lee’s group found evidence of specific microbes associated with breast cancer. In collaboration with Maggie DiNome, MD, acting director of the Margie Petersen Breast Center, and Susan Love, MD, MBA; Dr. Lee and her team will further investigate microbes in the breast—research that could lead to more accurate ways to determine risk and even new vaccines for breast cancer.

Study Shows the Benefits of Surgery for Cancer in the Liver

For decades, Institute researchers have sought to improve the life expectancy of patients with tumors in the liver. Anton J. Bilchik, MD, PhD, has been at the forefront of using minimally invasive techniques such as radiofrequency ablation and resection. These approaches were evaluated in patients with malignant melanoma that has spread to the liver. In a study published recently in the *Journal of the American College of Surgeons*, Institute researchers demonstrated a survival benefit for removal of cancerous lesions in the liver. Dr. Bilchik was senior author of the paper while Mark B. Faries, MD, was the first author.

Melanoma that spreads to the liver is usually fatal, with most patients surviving only four to six months from the time of diagnosis. The study examined 1,078 patients, the largest single institution experience in the world. After careful evaluation by a multidisciplinary tumor board, only 5.4% of patients were selected for liver surgery; the remainder received only medical therapy, such as chemotherapy and immunotherapy.

The median survival rate was only eight months for the nonsurgical patients compared to 24.8 months for the surgical patients. The study is significant because it’s the largest-ever experience with liver surgery for melanoma, and it will provide guidelines for doctors treating patients with advanced melanoma.

“This is an important study,” Dr. Bilchik says. “Melanoma that spreads can be a very aggressive disease. What this study shows is treatments for melanoma have really evolved over the past few years, and so have surgical techniques. The combination of more effective drugs and more effective surgical techniques is prolonging patients’ lives even after cancer has spread to the liver. Up to 25% of patients may even be cured after such treatment.”

The research points to the need for patients with melanoma to seek care at a specialized medical facility, he adds.

“Everyone with melanoma, even when it’s advanced, should be evaluated by a multidisciplinary tumor board where medical oncologists and surgical oncologists are present, to see if surgery can improve survival in combination with effective medical therapies,” says Dr. Bilchik, the Institute’s chief of medicine, interim chief of science and chief of the gastrointestinal research program.
Expertscape Recognizes Dr. Anton Bilchik as a Top-10 Expert in the World

Expertscape, a Palo Alto, California-based medical search and ranking organization, has named Anton J. Bilchik, MD, PhD, as one of the top 10 experts in colon cancer in the world. Dr. Bilchik is chief of medicine, interim chief of science and chief of the gastrointestinal research program at the Institute. Expertscape uses objective data and algorithms to identify the most knowledgeable and experienced doctors and medical institutions across an estimated 26,000 specific topics, stratified by geography. Expertscape defines an expert as someone who has published peer-reviewed research in the science, therapies and complications for a specific medical topic.

Board of Advocates: Showcasing the John Wayne Cancer Institute and Saint John’s Health Center Talent

The Board of Advocates is a forum for long-standing members of the John Wayne Cancer Institute and Saint John’s Health Center families. Members are kept informed of the latest medical advances and cutting edge technology at the Institute, the Health Center and the Saint John’s Health Center Foundation.

Members of the Board of Advocates serve as ambassadors to the community and encourage the support of various projects and programs deemed to be of highest priority by Institute and Health Center staff. The board, previously known as the Board of Counselors, has been expanded to include representatives of the John Wayne Cancer Institute, the Saint John’s Health Center Foundation, Saint John’s Health Center physicians, nurses, employees, volunteers, and alumni as well as community friends and patrons.

The mission of the board is to support and further excellence in health care and research. The board has approximately 60 members and is co-chaired by Ruth Weil, Robert Amonic, MD, Allan B. Goldman and Sophie Andriaschuk, MD. Ruth Weil is a current member and past president of the John Wayne Cancer Institute Auxiliary board. Dr. Amonic is a plastic surgeon who is a former president of the medical staff and serves as secretary of the Foundation. Goldman has served as chairman of both the board of Saint John’s Health Center and of the Foundation. Dr. Andriaschuk is a retired anesthesiologist and currently serves as program chair of the Physician Alumni Association.

“I’m delighted to help lead this organization,” Weil says. “We are eager to educate the community about the outstanding research and fellowship training underway at the Institute—work that is making a difference around the world.”

“This is a group of people invested with a common interest in the John Wayne Cancer Institute and Saint John’s Health Center,” Dr. Amonic says. “We showcase the outstanding advances made by the medical and research staff, identify potential new trustees and donors, and reach out to encourage others in our community to join us.”

Shop Amazon Smile to Help Fight Cancer

Shopping on Amazon can now benefit the research at John Wayne Cancer Institute. Just log in to your Amazon account at smile.amazon.com and type “John Wayne Cancer Institute” in the search bar. Select the Institute and begin shopping. Amazon will automatically donate 0.5% of your total purchase to the Institute every time you shop. You can share the link with your friends or post it on Facebook. Every little bit helps in the fight against cancer.

GARY VALENTINO, treasurer of the ABCs, passed away on April 21. He will be remembered as a devoted friend and supporter of the organization.
The Institute’s Community Ambassadors

For many years, two groups of enthusiastic supporters have served as ambassadors for our mission, reaching into the community to raise awareness and support for the John Wayne Cancer Institute and promoting its programs. We recognize and thank the members of these two organizations for their dedication to cancer research.

THE JOHN WAYNE CANCER INSTITUTE AUXILIARY

The Auxiliary has raised more than $18 million to fund a wide array of the Institute’s priorities including groundbreaking research, vital new laboratory equipment and the nationally renowned Surgical Oncology Fellowship Program, which trains the next generation of surgical oncologists. The Auxiliary organizes the Odyssey Ball, now in its 30th year. It also holds an annual Membership Luncheon in October and hosts educational evenings highlighting Institute projects with the community.

The Auxiliary is currently led by president Anita Swift, eldest granddaughter of John Wayne, and a dedicated board of 30.

For more information, please visit www.jwci.org or call 310-829-8324.

THE ASSOCIATES FOR BREAST AND PROSTATE CANCER STUDIES (ABCs)

The ABCs was established in 1990 by a group of dedicated philanthropists to devote resources to eradicating breast and prostate cancer—diseases that will be diagnosed in approximately 465,000 people this year. Today the ABCs, led by president Gloria Gebbia, comprises close to 200 members.

The group has raised more than $14 million to support breast and prostate cancer research at the Institute. The ABCs holds two events each year, a Mother’s Day event and the Talk of the Town gala held this year on November 22.

For more information, please visit www.jwci.org or call Grant Associates at 323-904-4400.
Stepping Up to the Plate

The John Wayne Cancer Institute enjoys the support of many community groups. The Premier Girls Fastpitch (PGF) and Surf City Tourneys (SCT) are two sister softball organizations that endorse our mission to eradicate breast cancer. Premier Girls Fastpitch holds a large softball tournament each summer in Orange County that attracts top teams of girls ages 10-18 from around the nation and helps raise funds for the John Wayne Cancer Institute. That tournament and other PGF and SCT events have raised $65,000 in donations for the Institute over the last three years.

The idea for the donations came from Dan Hay, president and chief executive officer of Premier Girls Fastpitch and Surf City Tourneys, who was watching The Western Channel late one night and saw an advertisement about the John Wayne Film Festival. “When I learned of the actor’s advocacy for cancer research, I wanted to support it,” Hay says.

And since the Surf City girls softball tournament is held in October—breast cancer awareness month—Hay took his inspiration one step further. He asked the tournament participants to also support the Institute.

That request fueled additional donations from individual players, parents, coaches, umpires and the tournament announcer. Premier Girls Fastpitch and Surf City Tourneys, based in Huntington Beach, provide a national platform in which fastpitch softball players can demonstrate their skills against the best teams in the nation.

The Institute sponsors a booth at the October tournament to pass out educational materials and answer questions. During a tournament in July, Institute chairman Patrick Wayne and Auxiliary president Anita Swift, John Wayne’s granddaughter, attended the opening ceremonies to thank the teams for their support.

“Coach Hay is not only promoting healthy living, he is demonstrating to these young women the importance of giving back,” says Patrick Wayne. “We’re grateful for his friendship.”

Hay says he hopes the girls learn not only the value of philanthropy but facts about personal health and cancer prevention. “That’s our responsibility as adults—to help these youngsters.”

Other community groups around the country support the Institute and hold fundraisers each year. We thank the Premier Girls Fastpitch, Surf City Tourneys and the following groups for their continued support:
1. Buehrle Golf Classic is an annual golf tournament held each summer in Missouri to support breast cancer research.
2. Tustin Brewery Charity Golf Tournament is an annual Southern California event that raises funds for melanoma research.
3. Dr. Anton Bilchik and Norma Bilchik with Dennis Fasone at Rod’s Day, an annual event at Mo’s Place in Playa del Rey that raises funds and awareness for gastrointestinal cancer research.
4. Cathy Classic is an annual golf tournament held in Kissimmee, Florida, that funds melanoma research.

For more information on community fundraising, call the Development office at the John Wayne Cancer Institute at 310-315-6111.
October 23
**John Wayne Cancer Institute Auxiliary Membership Luncheon**
*Beverly Wilshire, Beverly Hills, CA*

The highly anticipated annual boutique and luncheon helps support the operations of the John Wayne Cancer Institute Auxiliary, which has successfully raised millions of dollars for the Institute over the past 29 years. Marilou Terpenning, MD, will receive the Auxiliary’s Angel Award and Dan Hay will receive the Public Service Award.

October 23
**Power of Pink 2014: An Acoustic Evening with P!NK and Friends**
*House of Blues, West Hollywood, CA*

Power of Pink is back. This intimate performance, featuring Grammy Award-winner P!NK, will benefit the Cancer Prevention Program at the Margie Petersen Breast Center at Saint John’s Health Center. The event is sponsored by the John Wayne Cancer Foundation/Duke Spirits and Tervis.

October 25
**Caritas Gala**
*Beverly Wilshire, Beverly Hills, CA*

The annual Caritas Gala presented by the Saint John’s Health Center Foundation board of trustees and the Irene Dunne Guild is a black-tie evening of glamour and elegance. Trustee Tonia Hohberg will receive the Spirit of Saint John’s Award. David and Yolanda Foster will be honored with the Caritas Award.

November 22
**ABCs Annual “Talk of the Town” Gala**
*Beverly Hilton Hotel, Beverly Hills, CA*

The Associates for Breast and Prostate Cancer Studies (ABCs) will recognize individuals who have made a difference in the fight against cancer. This glittering, black-tie event attracts more than 800 guests as well as major media attention. Proceeds provide critical funds for the John Wayne Cancer Institute’s innovative breast and prostate cancer research programs.

December 7
**Benefactors Dinner**
*Four Seasons Hotel, Beverly Hills, CA*

Our benefactors are an integral part of the John Wayne Cancer Institute’s continued success and achievements in the fight against cancer. The Institute will honor the generosity of donors who have helped us carry out our mission by supporting innovative cancer research at the highest levels of giving in 2014. Attendees will enjoy an evening with the Wayne family and Institute faculty and fellows and will hear updates and research highlights.

For more information on any of the events, please contact us at development@jwci.org or 310-315-6111.
Welcoming the 2014-2015 Institute Fellows

The oncology fellowship programs at the John Wayne Cancer Institute are among the most comprehensive in the United States. The Surgical Oncology Fellowship Program was the first program on the West Coast accredited for complex surgical oncology by the Accreditation Council for Graduate Medical Education.

These clinical fellowships prepare surgeons to be highly educated, inspired and compassionate future leaders in surgical oncology. The Surgical Oncology Fellowship Program is one of the largest in the country, with more than 150 fellows counting themselves as graduates. More than 75% of the graduates have academic appointments, and 39% are division chiefs, chairs or deans.

This renowned program, and similar programs for laboratory scientists, receive generous support from individuals and foundations. There is no better investment to make a lasting impact in the fight against cancer than by training leaders who will save lives and who will go on to mentor future generations to become leaders in cancer research.

For more information about how you can support the oncology fellowship programs, please contact the Development office at 310-315-6111 or email development@jwci.org.

Dr. Ira Smalberg Joins the Faculty

The Institute is honored to announce the appointment of Ira Smalberg, MD, to the faculty. Dr. Smalberg is a radiologist who specializes in cancer imaging and emergency and trauma radiology. He is an expert in the Response Evaluation Criteria In Solid Tumors (RECIST), clinical trial guidelines that define when tumors in cancer patients improve, stabilize or worsen during treatments. He actively participates in national and international cancer clinical trials as an independent central reviewer to help determine the effectiveness of new cancer drug therapies. Dr. Smalberg has presented scientific exhibits and has spoken at national radiology and industry meetings.

Dr. Smalberg was born in New York City and attended college and medical school at the University of California, Los Angeles. He performed a medicine internship and radiology residency at North Shore University Hospital and a fellowship in abdominal imaging at North Shore University Hospital at New York University Medical Center. He served as medical director of imaging at Saint John’s Health Center from 2008 to 2012. Prior to joining the John Wayne Cancer Institute faculty this year, Dr. Smalberg served as an adjunct faculty member since 2008.

“It’s an extraordinary time for cancer care and research at the Institute and the Health Center,” he says. “And I look forward to greater involvement as part of the team.”
Leaders Made Here
Dr. Travis Kidner credits the Institute for great training—and saving his life.

Travis Kidner, MD, was performing a residency in general surgery at Cedars-Sinai Medical Center in Los Angeles when he heard some of his colleagues talking about the fellowship program at the John Wayne Cancer Institute. What they were saying intrigued him. Cancer therapies were rapidly evolving, and the Institute was at the forefront of research that continued to advance the field. “I had worked with several John Wayne Cancer Institute fellows,” he recalls. “I saw how they treated their patients and the level of expertise they had. I knew that was the place I wanted to be. Donald L. Morton, MD, was there. Who better to learn surgery from than the guy who invented the sentinel node procedure?”

Dr. Kidner applied, was accepted and spent 2010 to 2012 as a surgical oncology fellow. Today he is a surgical oncologist in private practice in Beverly Hills and a medical staff member at Saint John’s Health Center.

Dr. Kidner grew up in Ohio and attended Ohio University and the University of Cincinnati College of Medicine. He became intrigued with medicine early in life. “When I was young, I had a disorder with my bones,” he says. “I saw an orthopedic surgeon quite a lot from the ages 4 to 8. Watching him, seeing his role and how compassionate he was and what he was able to do for me, made an impact.”

His time at the Institute also had an enormous influence on his career, Dr. Kidner explains. During his fellowship, he was mentored by Dr. Morton, the Institute’s co-founder who died earlier this year; Mark B. Faries, MD, professor of surgery and director of the complex general Surgical Oncology Fellowship Program, the Donald L. Morton, MD, Melanoma Research Program and director of therapeutic immunology; and Anton J. Bilchik, MD, professor of surgery, chief of medicine, interim chief of science, and chief of the gastrointestinal research program.

“I was lucky. I wrote nine papers with Dr. Morton and Dr. Faries on melanoma while I was there,” says Dr. Kidner. “I was able to present at several large meetings throughout the country. Before my fellowship, research was never my strong point. But because of the Institute’s vast resources and assistance with technical writing, it was easy to succeed.”

The ability to think critically has served Dr. Kidner well. “In cancer, we have to push forward to advance our knowledge of the disease. The way to do that is with well-supported and focused research,” he explains.

But Dr. Kidner didn’t leave the Institute with only research and technical skills. He became a better physician. “I learned that you really have to care for your patients,” he says. “Patients come from all over the world to the Institute. They are terrified. I watched as Dr. Morton would calm them down, giving them options and spending time with them.”

Dr. Kidner, who is married and has two 3-year-olds, is grateful to the Institute for something else, too. Shortly after his graduation from fellowship training, he found a lesion on his back. He suspected it was melanoma.

“I thought if I had a health problem, where would I go? The John Wayne Cancer Institute of course,” he says.

Dr. Faries operated on him, removing a Stage I melanoma and performing sentinel node biopsy, the technique invented by Dr. Morton that’s used to evaluate the risk of cancer spreading elsewhere in the body. The nodes were negative for cancer, and no further treatment was needed.

Dr. Kidner was cured and is in wonderful health today. A board-certified surgeon, he specializes in melanoma and breast cancer and performs general surgery. He also volunteers his time and energy to educate people on preventing melanoma and on recognizing the warning signs of the disease.

“I was happy and relieved to see Dr. Kidner recover from melanoma,” says Dr. Faries. “He is already helping the public understand the importance of skin cancer prevention. And he’s one of the bright, young physicians who will never stop looking for better treatments for his patients.”
Many people undergoing conventional cancer treatments are interested in complementary health practices. This "Integrative Health" column highlights the research behind various activities and how patients may benefit.

Diet Impacts Cancer, But The Magic May Not Be In Your Favorite Superfood

WRITTEN BY VICTORIA CLAYTON

We’ve all heard the promises: Certain foods or diet strategies are supposed to have the power to prevent cancer. In some cases, ads for special drinks, supplements or potions are targeted to vulnerable cancer patients.

But as we all recognize, cancer is a pretty formidable opponent. Can what we ingest really have an impact on it?

Absolutely, says surgical oncologist Anton J. Bilchik, MD, PhD. Dr. Bilchik is the chief of medicine, interim chief of science and chief of the gastrointestinal research program at the John Wayne Cancer Institute.

“Emerging science, particularly over the last 10 to 20 years, points to an undeniable link between diet and cancer,” says Dr. Bilchik.

Diet is the cause of some 20% of all cancers, including endometrial, gallbladder, esophageal, renal, leukemia, thyroid, breast, pancreas, multiple myeloma, colon, non-Hodgkin lymphoma, liver and lung, according to a 2008 study in the journal *Pharmaceutical Research*. For cancers such as endometrial and colon, the link is thought to be even stronger.

Now prepare to be a little, well, underwhelmed. Fighting cancer isn’t about ingesting exotic—and expensive—nutrients or even eating organic magic foods celebrated for their cancer-preventing properties. It’s not about hard-to-follow diets that entirely eliminate, for example, carbohydrates or sugar. It’s not about shakes, teas or enemas. Studies such as the ones published in the journal *The Oncologist* in 2010 and the 2008 *Pharmaceutical Research* paper conclude that being obese or overweight is the most convincing connection between diet and cancer.

“Weight is a very serious issue. It’s just behind cigarette smoking in terms of increasing our risk of so many cancers,” says Dr. Bilchik. “This doesn’t mean that average-weight people don’t get cancer, but it does mean that there is something we can do to decrease our risk.”

A recent study in the journal *The Lancet* demonstrates that obesity increases the risk of 22 different cancers, he says. It also suggests that different mechanisms are associated with different cancer sites.

Researchers believe that being overweight alters insulin, various other hormones, and the body’s inflammatory responses—all mechanisms that play a role in particular cancers. Furthermore, research suggests that cancer patients who are overweight tend to have worse outcomes than patients who are average weight.

Dr. Bilchik says, though, that he very often hears from patients who are convinced that certain
INTEGRATIVE HEALTH

THE ROLE OF DIET IN CANCER

This chart shows the percentage of cancer-related deaths thought to have roots in various factors:

- **Tobacco**: 25–30%
- **Diet**: 30–35%
- **Genetics**: 5–10%
- **Other**: 10–15%
- **Obesity**: 10–20%
- **Infections**: 15–20%
- **Alcohol**: 4–6%

* Radiation, stress, inadequate physical activity, environmental pollutants

Source: Pharmaceutical Research, Vol. 25, No. 9, September 2008

nutritional strategies will help them. “If someone feels better—whether that’s physically or even psychologically—eating a certain way or taking a supplement in moderation, I don’t have a problem with that,” he says. “But I always warn against drastic measures, spending too much money or taking high doses of anything.”

He notes that many supplements or specialized diets haven’t been rigorously studied. He worries that some could even cause the exact opposite effect of what any patient wants.

“People make all kinds of claims. They’ll say that a certain diet works because it starves the cancer cells. But if you’re starving your cancer cells, you’re also starving the healthy cells that contribute to your body’s immune system to help fight the cancer. If you consider some of these claims carefully, they just don’t make much sense,” he says.

Furthermore, he warns that because a product is labeled “natural” or is widely available over the counter or online doesn’t mean it’s safe—particularly at high levels.

“We know that too much of certain supplements, for example, can damage the liver or kidneys. Other supplements can interfere with a patient’s medication,” he says. “So if you’re going to take something, it’s a good idea to clear it with your doctor first.”

There is data that points to the benefit of reducing red meat, fatty foods and alcohol, as well as eating plenty of fruits and vegetables, but Dr. Bilchik says the absolute best advice is even less complicated than focusing on particular foods.

“I recommend exercising and just eating a very balanced diet, including all the food groups, in moderation,” he explains. “That’s it. For right now, that’s what the scientific research concludes is effective because that’s what we know helps control body weight in a healthy way.”

† Dr. Bilchik’s research receives generous support from the John Wayne Cancer Institute Auxiliary, the Doornink Family Foundation, Marguerite Perkins Mautner and the Sequoia Foundation.
CLOSE COLLABORATORS

In translational medicine, scientists and physicians work together to speed the pace of discovery.

WRITTEN BY SHARI ROAN
Imagine a footbridge over Santa Monica Boulevard linking Saint John’s Health Center with the John Wayne Cancer Institute. All day, Institute researchers would cross the bridge to confer with physicians at the hospital. And the physicians would use the bridge to bring their questions and experiences treating their patients to the Institute laboratories.

In fact, this is what goes on every day—minus the bridge. This dynamic, interactive communications loop between scientists and physicians is referred to as “translational medicine.”

“Everyone who is here, whether it’s a clinician or a laboratory researcher, always has in mind what’s happening on the other side of the street,” says Mark B. Faries, MD, professor of surgery and director of the complex general Surgical Oncology Fellowship Program, the Donald L. Morton, MD, Melanoma Research Program, and the director of therapeutic immunology. “The lab scientists here are always thinking about the clinical implications of their research, and our clinicians are always looking for research tools to investigate the mechanisms of disease.”

Translational medicine is a relatively new term that began to surface about 15 years ago, although a few pioneering physicians, such as the late Institute co-founder Donald L. Morton, MD, embraced the concept throughout their careers. Traditionally, medical scientists (such as people with PhDs) and physicians (MDs) didn’t interact all that much or really understand each other’s worlds, notes Delphine Lee, MD, PhD, professor of immunology and director of translational immunology in the Dirks/Dougherty Laboratory for Cancer Research.

Laboratory scientists typically perform “basic science” experiments on cells to understand fundamental questions about biology. For example: What is the chemical environment that causes cells to grow or divide abnormally and become cancerous? While that’s an important question, it may not really help a physician who is wondering why two patients with the exact same type of cancer and exact same chemotherapy have different outcomes, with one dying from the disease and the other recovering. This disparity shows why discoveries made in the lab must be tested in real patients. Translational medicine reflects research in a more realistic setting.

“People trained in medicine have a cultural and linguistic background,” Dr. Lee explains. “They have a certain vocabulary and mindset and approach to problems. The scientist has been trained to think about one variable at a time, to ask specific questions to understand how things work. These questions, while very important, may not address the immediate questions that trouble patients and physicians. Translational scientists use their skills to ask sophisticated scientific questions that will be more applicable to human health.”
Translational medicine aligns laboratory research with clinical trials—experiments performed on patients to test new medications or therapies to see if they’re more effective than the current therapies,” says Anton J. Bilchik, MD, PhD, professor of surgery, chief of medicine, interim chief of science and chief of the gastrointestinal research program. At the Institute, translational medicine is augmented by the fact that many of the physicians are also researchers with PhDs.

“One of the problems we have in cancer research is that what you discover in the test tube or in a cell does not necessarily translate to an effective treatment for the patient,” he explains. “If we discover a new gene in a mouse and discover a way of blocking that gene in the mouse, that does not mean the same benefit will necessarily occur in a human being. We have to be able to link the two.” (Institute scientists do not perform research on laboratory animals.)

For example, says Dr. Lee, a basic scientist might study what makes plants green. But a translational scientist will study what is in green vegetables that helps prevent cancer.

“Translational research is rigorous research that’s going to have a clinical impact,” she says. “It may still take time to do the research, but the practical implication is never very far away from one’s mind. The end goal is to have a clinical impact on patients.”

The concept of translational medicine has always been practiced at the John Wayne Cancer Institute, says Dr. Bilchik.

“A phrase used a lot by Dr. Morton was ‘bench-to-bedside research’—seeing the patient in the clinic; identifying a problem or cancer; removing the cancer in the operating room; taking a piece of tumor from the patient and growing the cells in culture so the particular cells in that patient can be studied; learning about those cancer cells from the molecular and immunological standpoint; and then potentially using that knowledge to help the patient,” he says.

The Institute’s founders were not content to just treat their patients with the best-available therapies, says Dr. Faries. They wanted to understand the biology involved: Why did patients have the experience they had? Who had a recurrence of cancer? They would look at the blood and data that came from those patients and would study it,” he notes.

The Institute’s tumor and tissue repository contains samples donated by patients and supports much of the translational research performed at the Institute.

Dave S.B. Hoon, PhD, professor and director of molecular oncology, chief of scientific intelligence and director of the gene sequencing center at the Institute, is studying the molecular and genetic aspects of solid tumors to identify the cancer better and develop diagnostic tissue biomarkers and therapeutic targets. The program has multiple, worldwide collaborations in translational research.

Biomarkers can help determine which cancers will metastasize and which ones will respond better to specific treatments. Dr. Hoon’s team has discovered a receptor on the cell surface—a variant of the CD44 receptor—which increases the probability that...
melanoma will spread to the brain. Brain metastasis melanoma cells spread more aggressively when inflammation occurs in the tumor microenvironment. These translational studies were carried out in collaboration with the Institute, combining innovative minimally invasive brain tumor surgery with the expertise of molecular genetics.

“We are a boutique sequencing center capable of deep sequencing analysis in specific types of tumors and blood,” Dr. Hoon explains. The aim is to identify some genomic property to understand what is unique about a tumor and how to control it.

“Previously, physicians were providing treatments for brain tumors and didn’t have accurate tests to know whether they would work,” he adds. “It was a pretty inefficient approach, and it prevented people from getting their tumors profiled and assessed. But now it’s much more focused. We can profile the tumors and see which drugs they’re more likely to respond to.”

Making those specific connections between a patient and a therapy is the essence of translational medicine.

In Dr. Lee’s lab, researchers are seeking to improve breast cancer treatment by exploring the role of bacteria in the breast. Dr. Lee has found bacteria capable of consuming estrogen that could perhaps be used to lower the estrogen levels of patients with estrogen-fueled breast cancer.

Dr. Lee and Dr. Faries are also studying why some cancer patients who receive immune-system therapies respond well to the treatment while other patients don’t. “If we can figure out what is wrong with the immune systems of
people who received an immune stimulation and didn’t do well, perhaps we can find the pathway that’s missing,” Dr. Lee explains.

While basic scientific research helps explain the importance of the immune system in fighting cancer, translational medicine takes the research full circle. By seeking answers to why the immune-system therapies don’t work in everyone, the research moves from bedside back to bench—and eventually back to bedside to benefit the patient.

“Among patients receiving immunotherapy injections, we also biopsy the tumors and take blood samples,” Dr. Faries explains. “Dr. Lee is looking at the immune cells and samples and reactions to correlate that information with the destruction of cancer. If she’s able to determine the mechanisms, we may be able to harness that and modify the treatment or combine it with other immune treatments to make it better.”

Likewise, Dr. Bilchik is collaborating with Hitoe Torisu-Itakura, MD, PhD, assistant professor of immunology, to better understand which patients with colon cancer require chemotherapy after surgery. By looking at the characteristics of immune cells of the tumor, the Institute researchers are hoping to identify which patients are at low risk for cancer recurrence and thus don’t require chemotherapy.

The Institute’s culture and size allow for this kind of productive translational research, Dr. Bilchik notes. The Institute’s many supporters can be assured that their contributions go to projects that aim to directly impact cancer care.

“Most institutions have clinicians in one department and scientists in another department, not necessarily on the same floor or in the same building,” he says. “The Institute has all the clinicians and scientists in the same building with neighboring offices. So we have the ability to meet and talk with the scientists to develop research projects, to determine ways of answering questions that involve the patient in the clinic.”

—Dr. Anton Bilchik

The enormous success of the specimen repository has triggered a pressing need for additional space and equipment, including larger freezers specifically designed to store valuable biological materials. We welcome additional private support to help us maintain and augment this unique and extraordinary resource.

For more information or to find out how you can help, please contact the Development office at 310-315-6111 or email development@jwci.org.
Cryoablation to trigger immune system stimulation

Cryoablation uses freezing temperatures to destroy tissue with high accuracy while protecting surrounding healthy tissue. The treatment may be a viable option for removal of small breast cancers.

Cryoablation was the focus of a pilot study at the John Wayne Cancer Institute which has led to the Institute’s participation in a multi-center trial on using cryoablation as an alternative to surgery for control of localized breast cancer.

Maggie DiNome, MD, acting director of the Margie and Robert E. Petersen Breast Cancer Research Program, and Delphine Lee, MD, PhD, director of translational immunology in the Dirks/Dougherty Laboratory for Cancer Research, are further investigating the idea that, in addition to destroying cancer cells, cryoablation may stimulate an immune response that fights tumor cells. Cryoablation research at the Institute receives generous support from the Fashion Footwear Charitable Foundation of New York.

Institute Houses a Broad Array of Promising Breast Cancer Research

Our breast cancer research encompasses a wide range of projects that focus on some of the most novel thinking in the field, including work in molecular medicine, minimally invasive surgeries, immunology and genetics. Here is a brief look at this exciting collection of scientific work in progress at the Institute and the Margie Petersen Breast Center at Saint John's Health Center.
Improving the measurement of immune response during treatment

Pioneering work is in progress to expand strategies for harnessing a woman’s own immune system to fight those cancer cells not destroyed by conventional treatments such as surgery, radiation and chemotherapy. In earlier-stage, high-risk breast cancer, treatment with chemotherapy prior to surgery (neoadjuvant chemotherapy) stimulates the immune system to react against cancer cells. The hope of this “self-vaccination” through stimulation of the immune system has Institute scientists keenly interested in expanding the use of neoadjuvant chemotherapy to better treat earlier-stage breast cancer.

Similarly in metastatic cancer, successful treatment will include managing the immunologic response to treatment and monitoring a woman’s immune status. To lay the ground-work for an expanded focus on immunology, scientists must first define metrics for strong immune function and the effects of chemotherapy on immune function. This project is led by Marilou Terpenning, MD.

Breast microbes to help fight cancer

Researchers led by Dr. Lee are looking at microbial communities in breast cancer tissue, comparing healthy tissue and cancer tissue. Investigators can identify the minute quantities of bacteria present in the breast to address whether certain microbes contribute to breast cancer. Several projects are underway at the Institute including an examination of breast duct microbial communities and a study to determine if bacteria in the breast promote an immune environment that protects against cancer.

Isolating T cells to stop cancer

The spread of a primary breast cancer to the lymph nodes predicts a poor diagnosis. Identifying factors that contribute to lymph node metastasis is therefore critical for the development of new diagnostic tools and therapies.

The immune system plays a key role in whether cancer spreads, and immunotherapies show enormous promise in treating even metastatic cancer. Work led by Peter A. Sieling, PhD, assistant director of translational immunology in the Dirks/Dougherty Laboratory for Cancer Research, will isolate immune cells found in breast cancer tissue and identify the dysfunction of the immune cells associated with cancer that spreads to the lymph nodes.

Acupuncture may reduce pain

For postmenopausal patients with breast cancers that are hormone-sensitive, blocking the body’s production of estrogen by taking an aromatase inhibitor has been shown to be an effective treatment strategy. Unfortunately, because this therapy can also cause significant joint pain, almost 20% of breast cancer patients discontinue the treatment.

Institute scientists believe the estrogen


depression induced by treatment may trigger an inflammatory response that causes the joint pain. Acupuncture has been used for centuries to successfully treat inflammatory conditions.

Dr. DiNome will examine whether acupuncture can successfully reduce treatment-related joint pain. Cathryn Hu, PhD, will participate as the acupuncturist.

Mindful movement to improve quality of life

Rebecca Crane-Okada, PhD, RN, director of breast cancer navigation at the Margie Petersen Breast Center, will investigate the psychological and physical effects of “mindful movement” after breast cancer. Dr. Crane-Okada seeks to build on earlier research which found that a combination of mindfulness and dance/movement therapy reduced worry and improved wellbeing in older breast cancer survivors. In this study, the research team will also examine the effects of “mindful movement” on immune function, sleep and fatigue.

Improved therapies for basal-like breast cancer

Basal-like breast cancers, a subtype of aggressive breast cancers having a specific pattern of gene expression similar to normal breast basal cells, make up 15% of all breast cancers. Basal-like breast cancers are the most aggressive and difficult to treat, especially when the cancer spreads to other organs.

It’s unclear why basal-like breast cancer is so aggressive and resistant to chemotherapy. Understanding the mechanisms driving this aggressive type of cancer will provide new therapeutic opportunities for advanced, metastatic breast cancer.

Jinhua Wang, PhD, assistant professor of molecular oncology, is leading a team of researchers who are studying the molecular mechanisms involved in development of basal-like breast cancer. Previous studies (Cancer Research, 2010; Oncogene, 2012) demonstrated that a gene known as FOXC1 plays an important role in the progression of basal-like breast cancer. An improved knowledge of this gene and the mechanisms involved could lead to therapies against aggressive basal-like breast cancer by targeting FOXC1.

Dr. Hoon’s group has been working with the Genome Institute Singapore for the last several years and found important epigenetic regulators of basal-like breast cancer. This study was recently reported in Proceedings of the National Academy of Sciences.

Next-generation sequencing for monitoring and detecting cancer recurrence

Doctors need better ways to determine which patients with early-stage breast cancers are at risk for recurrence of the disease. However, there are few blood tests to monitor for recurrence. A study underway by Institute scientists, led by Dr. Hoon, is looking at circulating free DNA (cfDNA) released into the blood from tumor cells.

The Institute’s molecular oncology department has pioneered research on cfDNA since 1997 and is now studying a cfDNA test on patients with early or later stages of breast cancer who are at high risk of recurrence or progressive disease. The department has an ongoing, joint program with Guardant Health in developing the clinical utility of cfDNA detection using highly-sensitive, digital, next-generation ultrasequencing of both blood and archival tumor tissues. A successful blood test was approved by the Clinical Laboratory Improvement Act/College of American Pathologists to permit better monitoring of treatment and earlier detection of cancer recurrence.

Novel therapeutic strategies for triple-negative breast cancer

Hormone receptor negative and Her2 negative (triple negative) breast cancer is an aggressive cancer that’s challenging to treat. Patients affected by triple-negative breast cancer do not benefit from endocrine or immune therapy.

Institute researchers are testing a combination of low doses of multiple epigenetic drugs aimed at improving survival and decreasing the high toxicity experienced using single epigenetic drugs. Dr. DiNome and Dave S.B. Hoon, PhD, chief of scientific intelligence and director of molecular oncology and genomic sequencing, are investigating epigenetic-modifying drugs and their effects on estrogen receptor expression upregulation in triple-negative breast cancer cells.

In addition, Diego Marzese, PhD, assistant professor of molecular oncology, is working to identify enzymes that regulate epigenetic alterations in tumor cells that could be potential targets for the treatment of aggressive breast cancer. Recent grant funding will help generate genome-wide maps of active genomic elements contributing to the disease.
Marc Ezralow is a man of many interests. As president of The Ezralow Company, he directs the family-held company’s real estate portfolio. In the entertainment field, he produced 15 feature films, starting his own production company called Revolution Films.

Interest in technology led him to launch an internet company called Revolution Multi-Media, which has since been acquired by a public company. He is a member of the World Presidents’ Organization and was featured in the Los Angeles Business Journal as one of the Top 20 “Angel” Investors in Los Angeles.

But an interest nearer to his heart is that of cancer research. Ezralow’s mother, Renette, survived 12 years with Stage IV ovarian cancer before passing away in 2002 at age 60. So it was only natural that Ezralow took a specific interest in the John Wayne Cancer Institute when he joined the Saint John’s Health Center Foundation board of trustees two years ago and became a member of the Health Center’s board of directors last year.

“My mother inspired me at a young age with the idea that it’s important to give back,” Ezralow says. Renette Ezralow founded and chaired the Women’s Cancer Research Fund, which raised more than $15 million for cancer research. In 2005, Ezralow’s father funded the Renette and Marshall Ezralow Family Chair at USC/Norris Comprehensive Cancer Center and Hospital, which Marc and his brother, Bryan, oversee.

“I am looking forward to getting more involved with the John Wayne Cancer Institute and more specifically involved with cancer research,” Ezralow says. “I am really a big believer in giving back to your own community. National
(philanthropy) is great, but local is amazing. The Westside is my community, and I choose to be involved with the John Wayne Cancer Institute and Saint John’s."

His presence has already been felt at the Institute, says Anton J. Bilchik, MD, PhD, professor of surgery, chief of medicine and chief of the gastrointestinal research program at the John Wayne Cancer Institute. "Marc is very passionate about giving. He’s passionate about cancer research and saving people’s lives. He is very committed to making a difference in the community. He takes immense pride in helping scientists find a new drug or a new test that may prolong and improve quality of life. He gets involved, follows through and makes a difference."

When not involved in work and fundraising efforts, Ezralow, 50, a Pepperdine graduate, and his wife, Gayle, are busy with their three children, Bryce, Riley and Caden, ages 7 to 16, who attend school in West LA. The family enjoys skiing, golf and school-related activities.

Among Ezralow’s goals for his involvement with the Institute is to get the West LA community more tuned in to the Institute and the work it does. He has high praise for Providence Health & Services, the health care system that assumed sponsorship of Saint John’s earlier this year.

“I am really a big believer in giving back to your own community. National (philanthropy) is great, but local is amazing. The Westside is my community, and I choose to be involved with the John Wayne Cancer Institute and Saint John’s.”

“The John Wayne Cancer Institute is a renowned research institution," Ezralow says. “We are so fortunate to have this wonderful resource. I hope to serve as a link to encourage budding philanthropists in West LA to support this community treasure."

Ezralow and his wife did just that as honorary dinner committee co-chairs of the Institute Auxiliary’s 29th annual Odyssey Ball in April. Among the honorees was Dr. Bilchik, who received “The Duke” Special Service Award. Also honored was the family of Nelson Mandela, which received the “True Grit” Humanitarian Award.

“I was very happy to be involved in honoring Dr. Bilchik and to draw in some new supporters who hadn’t yet donated to the Institute,” Ezralow says. ■
In November 2011, Justine Cogan was given what should have been a death sentence. Doctors found that the severe abdominal pains she had been stricken with were caused by two large cancerous tumors in her intestines.

“I thought I had food poisoning,” recalls the 41-year-old Silver Lake resident. “I was very healthy. I worked out and had never been sick before. Cancer was the furthest thing from my mind. I was totally blindsided.”

Subsequent tests revealed even worse news: The bouts of blurry vision and persistent cough Cogan had been experiencing were the result of metastatic melanoma, an aggressive cancer. The disease had spread to her lungs, intestines and brain before it was detected.

In fact, an MRI showed a large brain tumor near the back of her head in the left occipital lobe, the area responsible for processing visual information. There was also bleeding and swelling around the tumor, typical of melanoma, making it far too large to be treated with radiation.

“The thought of someone operating on your brain is terrifying,” says Cogan, who was on an operating table less than a week later, where surgeons at Saint John’s Health Center fought to save her life.

That was the start of Cogan’s scary, yet ultimately astonishing, battle with one of the most aggressive types of cancer. By the time her treatment concluded, she had been treated or received consultations with several of the top physicians and researchers on the John Wayne Cancer Institute faculty who worked together on her case. The collaborative arrangement was a key to her survival, says Daniel Kelly, MD, director of the Brain Tumor Center & Pituitary Disorders Program at Saint John’s Health Center.

Dr. Kelly’s team performed surgery to remove the tumor. But instead of tunneling through brain tissue at the top of the skull to remove the mass—which often causes collateral damage to the visual pathways—they performed an endoscopic tumor removal...
by entering the skull above the cerebellum to reach the occipital lobe melanoma with minimal manipulation of normal brain tissue.

“If we had gone the conventional microscopic route from above, working through the brain to reach her tumor, as opposed to this endoscopic keyhole approach, reaching the tumor from below, she would likely have lost much of her vision,” says Dr. Kelly, one of the few neurosurgeons in the country who perform this minimally invasive technique.

Afterwards Cogan underwent targeted radiotherapy to ensure that any microscopic cancerous cells remaining in her brain were eradicated. She also endured more surgeries, in which half of her left lung, her adrenal gland and a tumor in her leg were removed. Cogan was then given four infusions of ipilimumab (Yervoy), an immune system booster that helps the body attack melanoma cells more effectively and thwarts production of a protein that cripples the action of T cells, the immune system’s foot soldiers.

Three years later, Cogan is not only still here but living life to the fullest. She works full time, got married in April 2013 and earlier this year went on a delayed honeymoon to Scotland.

She’s beaten incredible odds. Melanoma is the deadliest form of skin cancer, and more than 76,000 Americans will be diagnosed with the disease in 2014, according to the American Cancer Society. About 9,700 people are expected to die from the disease this year.

If the cancer is detected early, melanoma has an excellent cure rate. But if left untreated, these aggressive malignancies spread swiftly throughout the body. Moreover, melanoma has the highest propensity to metastasize to the brain of all common cancers, including lung, breast, renal or colorectal cancer.

Up to 50% of patients with advanced melanoma suffer from brain metastases, and once this fast-growing cancer takes up residence in the brain, it is almost always fatal, Dr. Kelly explains. In fact, historically, few patients with melanoma brain metastases survive long-term after the lesions are detected, and only a small minority survive more than a year.

“It’s much more dangerous because the brain is so critical and this type of cancer is so fast-growing,” says David S.B. Hoon, PhD, chief of scientific intelligence at the Institute. “If the cancer attacks other organs, you can still survive. But once it gets into the brain, that’s nearly always the end of that patient’s life.”

Because melanoma doesn’t respond well to chemotherapy, and chemotherapy often does not reach the brain, therapeutic options for melanoma brain mets—shorthand for the malignant lesions that metastasize—were limited to surgery, radiotherapy or whole brain radiation to destroy tumors. But each approach has limitations.

Radiosurgery can target smaller tumors, and generally is reserved for patients with no more than four lesions—though more recent studies show patients with 10 or more lesions can be well treated with radiosurgery. Whole brain radiation is used when metastases are more widespread and can augment surgery, but this technique can cause severe side effects.

“Radiosurgery can only target lesions that are about two inches or smaller,” says Robert Wollman, MD, medical director of radiation oncology at Saint John’s Health Center. Dr. Wollman also consulted on Cogan’s case. “If a patient has more than 10 tumors, we usually need to radiate the whole brain—but that raises risks of radiation necrosis, where some of the brain cells die near where you’re giving the radiation and can cause
cognitive and motor deficits.”

But Justine Cogan’s seemingly miraculous recovery exemplifies what can now be accomplished using a treatment approach that combines the latest treatment advances: minimally invasive neurosurgery, more precisely targeted radiotherapy that doesn’t cause collateral damage, and immune-boosters like ipilimumab, which is one of a new class of promising therapeutics.

“It’s a very exciting time in the world of metastatic melanoma because these immune-stimulating drugs and other targeted therapies are having a big impact on survival,” says Dr. Kelly. “Previously, the average survival of people with brain metastases was eight or possibly 10 months, but Justine is now almost three years out and remains disease-free.”

Physician scientists at John Wayne Cancer Institute, both in the clinic and in the lab, are looking at new treatment paradigms that could translate into longer survival rates and better quality of life for patients with melanoma brain metastases. These approaches include deciphering the genetics of the cancer, which may lead to better treatments, devising tests that can spot which tumors are likely to spread so they can be stopped before they infiltrate the brain, and testing experimental drugs in the development pipeline that may be better, more potent and safer.

In Dr. Hoon’s lab, researchers are searching for biomarkers that can predict which primary tumors have a probability of spreading to the brain. They’ve already identified key genes that contribute strongly to the development of brain metastases.

“We’ve compared these tumors to other metastases in organs such as the liver and lung and to other primary tumors to see why they behave differently and why they travel to the brain rather than other organs,” says Dr. Hoon. In the near term, this information will help oncologists identify and monitor patients who may be at higher risk of cerebral metastases. Eventually, understanding these pathways could identify new targets for treatments and accelerate drug discovery.

On other fronts, Delphine Lee, MD, PhD, director of translational immunology, is studying how immunotherapies can be used to fight melanoma. Targeted therapies also hold great promise. Omid Hamid, MD, chief of translational research and immunotherapy and director of melanoma therapeutics at The Angeles Clinic and Research Institute, was an investigator in the early clinical tests of two drugs that have proven significant survival benefits: the immune-boosting ipilimumab and vemurafenib, which blocks the action of a rogue, cancer-causing gene called BRAF. BRAF is a culprit behind the unchecked growth of metastatic melanoma. His research team is now looking at a class
of drugs called PD-1 inhibitors which unleash an immune response against cancer by blocking the immune suppression that some tumors can create in the body.

The early results led to the approval in September, by the Food and Drug Administration, of the first PD-1 inhibitor, called pembrolizumab (Keytruda) for the treatment of patients with advanced or inoperable melanoma. Pembrolizumab is the sixth new melanoma treatment approved since 2011.

“Early evidence indicates that the PD-1 inhibitors can control the disease and shrink tumors in the body and even in the brain,” says Dr. Hamid, who is hopeful about the future. “With these new drugs—through clinical trials, using them individually or in combination—we’re making significant inroads, leading to better quality of life and extended survival for our patients. These breakthroughs may have begun in melanoma but are benefiting patients with other tumors also.”

Cogan was also treated by Dr. Hamid and by Leland J. Foshag, MD, a surgical oncologist at the Institute and expert in advanced melanoma. Patients benefit greatly from seeking care at a center of excellence, adds Mark B. Faries, MD, professor of surgery and director of the Donald L. Morton, MD, Melanoma Research Program and of therapeutic immunology. At the Institute, multidisciplinary teams of physicians and researchers work collaboratively to explore the most advanced options.

“Cancer is not treated in silos the way it used to be,” Dr. Faries explains. “The way cancer treatment has advanced in recent years requires constant collaboration. A surgeon may see that it’s better to have medical treatment before surgery, for example. For more and more cancers, the standard of care is to get input from the surgeon, from the radiation oncologists and from the medical oncologists. In fact, one of the most interesting current questions in oncology is in which order the treatments should be given.”

That all-hands-on-deck approach is making a distinct difference in cases of melanoma metastasis to the brain. There have been so many advances in treatments in the past decade that seemingly miracle cures like Justine Cogan’s case will become more commonplace.

“Many things have come together—better surgical and radiosurgery techniques, a deeper understanding of the genetics of tumors and immune-based therapies, and stronger collaboration among colleagues—that have helped tremendously,” says Dr. Kelly. “We’re definitely going to see more and more outcomes like hers.”

To learn more about supporting innovative metastatic melanoma research, please call the John Wayne Cancer Institute Development office at 310-315-6111.
For almost 150 years, physicians and surgeons have relied on the book *Gray’s Anatomy of the Human Body* and its hundreds of vibrant, detailed sketches to guide them in the treatment of medical conditions. But for today’s leading neurosurgeons and their students, the beloved *Gray’s Anatomy* is not enough.

That’s why the administration of Saint John’s Health Center and the John Wayne Cancer Institute—supported by a prestigious group of donors—created the world-class Brain Tumor Center Skull Base and Endoscopic Microdissection Laboratory. Opened in 2012, the lab is a testament to the Institute’s desire to continue to push the boundaries of knowledge in one of the final frontiers of modern medicine: the brain.

“The microdissection anatomy lab is really key for a high-level training program,” says Garni Barkhoudarian, MD, a neurosurgeon and director of the Skull Base and Endoscopic Microdissection Laboratory. “Keyhole and endoscopic skull base neurosurgery requires a detailed understanding of very complex bone, cranial nerve and brain anatomy to help ensure an optimal outcome for our patients.

“Neuroanatomy is not something you learn and then you’re done,” Dr. Barkhoudarian explains. “Our understanding of the brain, blood vessels, cranial nerves and the surrounding skull has advanced dramatically over the last two decades, in large part helped by advances in endoscopy (surgical telescope) and navigational techniques. Using such high-definition visualization and better instrumentation—such as high-speed drills—we are learning more and more about the intricacies of how these different structures fit together and how to safely navigate through them to remove brain tumors. This brain and bony anatomy is so complicated, so amazing and so beautiful, it intrigues me. We’re still learning, and that’s why having this lab is so important.”

—Dr. Garni Barkhoudarian

Minimally invasive neurosurgery has many advantages, including reducing the risk of collateral damage to the brain and its supporting structures. Patients often experience a speedier recovery compared to the traditional larger-scalp incisions and bony openings and may benefit from improved cosmetic results. However, a relative minority of neurosurgeons are skilled in these techniques.

The lab is utilized by the veteran surgeons and the fellows who come to the Institute to train, including many international neurosurgeons who would not otherwise have access to a state-of-the-art surgical training theater. The lab is set up like an actual operating room with surgical instruments, high-speed drills, high-powered microscopes, endoscopes (the tool that is inserted through small openings in the skull to see inside the brain), a neuronavigational system to produce detailed images of the brain, and cadaver heads that meet specific medical and anatomical criteria and that are obtained from a national vendor.

“There are many cadaver labs around the world, but there are relatively few like ours with this type of cutting-edge technology at our fingertips,” says Dr. Barkhoudarian, who helps train the Brain Tumor Center’s clinical and international fellows. “We train ourselves, our current fellows and the international fellows who come here from all over the world to learn these techniques and practice on these specimens. Physicians hone their skills and take those skills back home to improve the care of patients in their countries.”

This type of continual training is necessary because the brain and skull base anatomy can vary among individuals, he explains. “Most people think that anatomy is something you learn and it’s done. But there is always more to learn. There are variations that people have in their anatomy, and there are also changes that occur as a result of tumor growth. We need to understand these anatomical variations so we can safely and effectively perform surgery. Every time I’m in the lab, I learn something new.”
Doing What Comes Naturally

Since childhood, giving has been a way of life for Maria Lim McClay.

WRITTEN BY SANDI DRAPER

Giving comes naturally to Maria Lim McClay. You might say it’s in her genes. “My great aunt was a Buddhist nun. My grandmother and mother were caregivers in their villages. When I was a little girl, I would give away my things to people who needed them,” McClay says. “Then one day my mother said, ‘You are a good girl to give away your things, but you better not give away your bicycle.’ It was during the war, and a bicycle would have been impossible to replace.”

With that kind of generosity in her nature, it was no surprise she found kindred spirits in the people and the passion of the John Wayne Cancer Institute at Saint John’s Health Center.

“I fell in love with Saint John’s and the Institute long ago,” McClay says. “They don’t treat you like a number; they treat you like a person. Everyone is kind and warm—not once or twice, but always.”

Her many friends at the John Wayne Cancer Institute know McClay to be just as kind—and intelligent, generous and loyal.

McClay was born in the Philippines and relocated to China, where she was raised. During the Communist Revolution, her family was stripped of its wealth and fled to the United States. As a young woman, she came to New York City and worked her way through college as a hatcheck girl in a Chinese restaurant. She joined Danny Kaye’s television variety show, which launched her career in both television and movies. She then became a model and worked steadily in New York City, Los Angeles, London, Paris and throughout Asia for Jacque Griffe and other famous designers.

She left modeling and acting behind when she met and married her late husband of 51 years, Booker, a film publicist for major studios in Los Angeles. She and Booker became supporters of the Institute and Health Center in 2002.

Their support includes donations for the Saint John’s Capital Campaign, the Child and Family Development Center and the creation of the Maria and Booker McClay...
GUARDIANS OF THE FUTURE at THE JOHN WAYNE CANCER INSTITUTE

What Will Your Legacy Be?
When you designate a planned gift to the John Wayne Cancer Center Institute, you not only become a member of the Guardians of the Future, you empower our physicians and scientists to advance the frontiers of scientific knowledge and cancer care for future generations.

A planned gift may be made via a will or living trust, charitable gift annuity, IRA, life insurance policy or other gift vehicle. By planning ahead, our Guardians can create income for their families, avoid capital gains taxes and save significant amounts on income and estate/gift taxes.

If you would like additional information on becoming a member of Guardians of the Future, sample bequest language or gift illustrations for you and your financial advisor, please call Tanya Lopez at 310-582-7095 or email Tanya.Lopez@stjohns.org.

To ensure proper fulfillment of your bequest, the correct legal description of the Institute is:
John Wayne Cancer Institute
2200 Santa Monica Boulevard,
Santa Monica, CA 90404
Federal ID # 95-4291515
The faculty, staff and supporters of the John Wayne Cancer Institute have enjoyed numerous gatherings in recent months aimed at sharing Institute news, cancer education and fundraising. Here's a look at some recent events. For information on how to get involved with future special events, please contact us at 310-315-6111.

Fellowship Graduation

The John Wayne Cancer Institute hosted its annual Surgical Oncology Fellowship graduation on June 21 at the home of Institute benefactor Ruth Weil. The commencement ceremony featured guest speaker and former John Wayne Cancer Institute fellow Tracy Cordray, MD, with faculty remarks from Anton J. Bilchik, MD, PhD; Mark B. Faries, MD; and Daniel Kelly, MD. The ceremony was followed by a garden reception with live music.

The 2014 graduates are:

Joslyn M. Albright, MD
Co-chief administrative fellow, Tarble Foundation fellow
Elizabeth A. Arena, MD
Nefertiti A. Brown, MD
JWCI Auxiliary breast fellow
Manabu Fujita, MD, PhD
Co-chief administrative fellow, William Randolph Hearst Foundations fellow
Robert G. Louis, MD
Neurosurgery fellow
Victoria O'Connor, MD
The Harold McAlister Charitable Foundation fellow
MEMORABLE EVENTS

FFANY Shoes on Sale

Representatives of the John Wayne Cancer Institute were on hand October 8 in New York City to celebrate the 21st annual QVC Presents “FFANY Shoes on Sale” event. The Fashion Footwear Association Charitable Foundation of New York raises funds in support of breast cancer research.

PHOTOS
Mike George, president and CEO, QVC, Inc.; Dr. Delphine Lee; Ronald A. Fromm, president and CEO, Fashion Footwear Association of New York, Inc.; Dr. Maggie DiNome; and Patrick Wayne

ABCs Mother’s Day Luncheon

The Associates for Breast and Prostate Cancer Studies (ABCs) hosted its annual Mother’s Day celebration with a luncheon and check presentation on May 7 at the Four Seasons Hotel in Beverly Hills. Special guests included Carlton Gebbia and Brandi Glanville of The Real Housewives of Beverly Hills, and actress Nicky Whelan. The luncheon featured an informal fashion show by Los Angeles designer Mark Zunino, as well as a luxury boutique of select vendors who donated a portion of proceeds from their sales to the ABCs. The event benefits breast and prostate cancer research at John Wayne Cancer Institute at Saint John’s Health Center.

The luncheon honored actor Morris Chestnut and presented Paul Dreher, assistant director of catering at the Beverly Hilton hotel, with “A True Gentle-Man of The Year Award” for his longtime support of the organization. Beverly Cohen served as the luncheon chair, and Sheri Rosenblum served as the boutique chair. The event was hosted by actress, comedienne and radio personality Lisa Ann Walter.

PHOTOS
1. Sheri Rosenblum, Patrick Wayne, Beverly Cohen and Gloria Gebbia
2. Paul Dreher and Lisa Ann Walter
Avon Walk for Breast Cancer

The John Wayne Cancer Institute at Saint John’s Health Center was once again a proud partner of the Avon Walk for Breast Cancer on September 6–7 in Santa Barbara. The Institute served as the medical sponsor for the two-day, 39-mile walk, led by Maggie DiNome, MD, acting director of the Margie Petersen Breast Center, medical director of the Cancer Prevention Clinic and chief of general surgery at Saint John’s Health Center.

Several surgical oncology fellows and Health Center nurses provided support in the medical tent, while Institute staff hosted a cheer booth along the route to offer encouragement to the walkers. Cheer booth volunteers distributed ice-cold, pink John Wayne Cancer Institute bandanas and offered walkers a chance to be photographed with “the Duke.”

Proceeds from previous Avon Walks have helped support innovative breast cancer research led by Delphine Lee, MD, PhD, director of translational immunology in the Dirks/Dougherty Laboratory for Cancer Research. This year the Avon Foundation presented Dr. Lee with her second grant of $300,000 to continue her breast cancer research.

PHOTOS

1. Walkers visiting the Institute cheer booth to receive ice cold bandanas
2. Kevin Honeycutt, Dr. Delphine Lee and Cheryl Heinonen
3. Dr. Maggie DiNome
4. Dana McCormick, Teddi Gilderman and Cynde Wilen
5. Fans take a moment to be photographed with “The Duke.”
Planned Giving Luncheon

The John Wayne Cancer Institute was pleased to honor our planned giving donors, Guardians of the Future, on September 10 at the Riviera Country Club. Guardians of the Future is a distinctive group of individuals who have thoughtfully provided for the Institute through their estate and/or charitable plans. Luncheon attendees enjoyed an informative presentation from Delphine Lee, MD, PhD, titled Emerging Ideas in Cancer, which described the most recent theories, trends and advances in cancer treatment. The group also received updates from Institute and Foundation leadership on all of the great things happening at the Institute and Saint John’s. Saint John’s Health Center Foundation’s Friends for the Future were also in attendance.

PHOTOS
1. Dr. Delphine Lee addresses the group.
2. Dr. Sophie Andriaschuk, Arthur Akouris, Elaine Akouris and Ruth Weil
3. Andrew Trilling, Janice Burrill and Robert Klein
4. Dr. Delphine Lee and Steaven Jones, Jr.
The Joy of Giving Back

Attorney Paul R. Kanin guides others on charitable giving.

Paul R. Kanin became acquainted with the wonders of modern medicine at a young age. At age 8 he fell through a plate-glass window and suffered deep cuts on both hands. After a brief stop at one Los Angeles area hospital, he was transferred to Saint John’s Health Center where he was nursed back to health and regained full use of his hands—against considerable odds.

Kanin was also born at Saint John’s and has been a patient, friend and supporter of both the John Wayne Cancer Institute and Health Center for many years. With a successful Beverly Hills-based law practice in estate planning and trust administration, Kanin spends his days helping clients think about the eventual distribution of their wealth.

Kanin is a supporter of the Institute and takes pride in the Surgical Oncology Fellowship Program, which trains surgeons to specialize in the most challenging cancer surgeries. The program is supported with philanthropic gifts.

“I tear up when I go to the fellowship graduations,” Kanin says. “I think about what these doctors are doing and what they’re teaching others, who will then teach others.”

Kanin also is a board member of the Harold McAlister Charitable Foundation, which is operated by the McAlister family, long-time supporters of the John Wayne Cancer Institute and the Health Center.

“We are most grateful for Paul’s friendship and his support of our most important programs,” says Michael Wayne, an Institute board member and grandson of John Wayne. “We’re honored that Paul recognizes the significance of the Surgical Oncology Fellowship Program and that we’ve earned his confidence and trust.”

When the Institute and Health Center come up in conversations as targets for charitable giving, Kanin has no trouble endorsing his clients’ choice.

It’s important for families to discuss their estate plans, seek counsel and make wise decisions. To do so often brings his clients great joy, Kanin says. Estate planning results in tax advantages and helps people realize that they can impact society in a truly meaningful fashion, perhaps more than they thought possible, by leaving a legacy.

“If you can benefit someone, why wouldn’t you?” he asks. “There is such satisfaction in that. It gives people peace of mind that they know where their estate is going. By not doing estate planning, you’re saying, ‘Let everyone else decide how to spend my money.’”

Kanin helps his clients carefully consider how their charitable dollars will be used. For example, does a charity have high administration costs (meaning that fewer dollars will be distributed to the actual cause)? He reviews dozens of proposals for charitable giving and must often make hard choices about which organizations are deserving of support.

“There is huge competition for charitable dollars,” he notes. “There are a lot of good causes out there. The key thing we’re looking for is efficacy. And what better way to be effective than by training oncology surgeons who will go on to train others?”
Your life is filled with generosity – toward family, friends and your community. Remembering the John Wayne Cancer Institute at Saint John’s Health Center in your estate plans ensures that the legacy you have created is never lost. By including the Institute in your Will or Trust, you make it possible for us to continue as a leader in cancer research resulting in significant breakthroughs. All of this can be done without impacting resources during your lifetime. You will create a lasting legacy of giving and make a significant difference for generations to come.

If you would like additional information or sample bequest language, please call Tanya Lopez at 310.582.7095 or email at Tanya.Lopez@StJohns.org or visit www.jwcigiving.org
Scientific advancements and collaboration between physicians are translating to significant success in treating melanoma that has spread to the brain.