Yale Cancer Center

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AZINE

Innovation
in Cancer Care

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director's letter

Innovation in cancer care is essential to our success. Our ability to respond to the fast paced improvements in technology is directly related to our clinical and translational research achievements. This year, Dr. Patricia LoRusso joined Yale Cancer Center as Associate Director for Innovative Medicine to draw attention to the need to continually adapt and develop our research models to ensure we are moving new treatments to the clinics in the most efficient manner. I am confident that her leadership will continually push us to innovate our models of clinical research and care. You will read about some of her goals in this issue of *Centerpoint*.

Like many of our peer institutions, Smilow Cancer Hospital at Yale-New Haven has turned our attention to the Affordable Care Act (ACA) and its impact on oncology care. Dr. Kerin Adelson, Chief Quality Officer for Smilow, is leading a team to build an innovative oncology care model focused on quality and value-based decisions in response to upcoming changes with the ACA. Each new initiative at Smilow will be carefully reviewed to determine its value-added component for patient care and its priority within Smilow Cancer Hospital and our 10 Cancer Care Centers.

We are also planning for our future at Yale Cancer Center. Over the last several months the Cancer Center has engaged in a full strategic plan process, beginning with a survey of our entire membership and continuing through committee workgroups to form recommendations. Four main initiatives have been established: to prioritize areas for research investment that capitalize on strengths; to position Yale Cancer Center to lead in translational team science; to increase the impact of clinical trials; and to unite around a common vision for Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. I look forward to updating you on our progress and the final plan of action.

The incredible advances coming from Yale Cancer Center labs and Smilow Cancer Hospital clinics continue to inspire all of the work we do each day. It's amazing to acknowledge that we're already celebrating 5 years in Smilow Cancer Hospital, and are looking ahead to what we will accomplish over the next 5 years. Innovation will certainly be a key component in our success when we hit the 10-year anniversary mark in 2020!

Sincerely,

Tom Lynch

Thomas J. Lynch, Jr., MD
Director, Yale Cancer Center
Physician-in-Chief, Smilow Cancer Hospital

The Fight to Save a Mother

Emily Fenton **writer** Peter Baker **photographer**

In the summer of 2014, during her last months of pregnancy, Kaitlin Eppinger began experiencing severe headaches and migraines. Her OBGYN prescribed medication and they gradually went away, but returned after the birth of her daughter. When the headaches persisted, she had blood work done that revealed she had Lyme disease. She received treatment and started to feel better, but was still not 100%. Usually a very active person, she noticed lack of energy along with some new symptoms; body tingling and blurred vision. She thought they might be related to the Lyme disease, but her doctor suggested an MRI to rule out further issues.

Kaitlin had started teaching a new school year in her kindergarten classroom, and was feeling overwhelmed and stressed, when normally a new year brought excitement. The day after the MRI, she received a phone call at school with her results; she was instructed to call her husband to drive her to the Emergency Department immediately, as a mass the size of an orange had been found in her brain.

Doctors explained that the mass was of an irregular shape and size, very large, and located near her frontal lobe. Based on the presentation, they were surprised to see that she was up, walking and talking. She was immediately referred to Dr. Jennifer Moliterno Gunel, a neurosurgeon who specializes in the surgical treatment of brain tumors at Smilow Cancer Hospital.

"Upon meeting Dr. Moliterno I could tell she was a very caring person," said Kaitlin. "I was in shock, so my husband asked most of the questions, but she took the time to listen and make sure we understood everything. We both felt very comfortable with her. She put it simply for us, 'this is something that is not supposed to be there, and we are going to get it out.' From that point on I trusted her completely."

While reviewing Kaitlin's MRI, Dr. Moliterno noticed a very small and subtle finding that had been overlooked at the outside hospital. "I was concerned that there was a large, possibly abnormal blood vessel supplying the deep portion of the tumor," said Dr. Moliterno, "so I ordered a special test called a CT angiogram (CTA) that shoots dye into the blood vessels to be performed before her surgery." The CTA revealed the tumor to not only have a robust blood supply, but an aneurysm of one of the main arteries feeding the tumor. According to Dr. Moliterno, aneurysms of blood vessels supplying tumors are exceptionally uncommon and can be acutely life threatening if not found.

Dr. Moliterno immediately called upon her colleagues, Drs. Murat Gunel and Charles Matouk for their input and expertise. Smilow is the only hospital in Connecticut with an operating room with the capability to perform an intra-operative angiogram right in the operating suite where tumors are commonly removed. Dr. Matouk was able to successfully glue the blood vessel with the aneurysm shut and in the span of minutes, Dr. Moliterno began surgery. Had Kaitlin not been at Smilow and there had been a delay in between the two procedures, the outcome could have been very different.

Heading into surgery, Kaitlin brought with her a book of photos of her daughter. She wanted to be able to see her first thing when she woke up. Kaitlin's surgery, with the treatment of the aneurysm, took over 10 hours. "Dr. Moliterno saw me as a person, not a cancer patient," said Kaitlin. "I knew that she would get me better so that I could continue being a mother to my daughter." Over 98% of the tumor was successfully removed, and Kaitlin received radiation treatments to kill the remaining portion.

Kaitlin still has a long road ahead and will be monitored closely for any signs of a recurrence. Combining surgical expertise with state-of-the-art technology saved her life. She is now hiking, doing Yoga, running, and enjoying all the things she used to. "Sometimes I have to remind myself that I had a brain tumor, and maybe I should slow down," said Kaitlin. "But I don't want to waste any time. The silver lining in all of this is I get to spend time with my daughter. I am taking the time to get healthy and knowing Dr. Moliterno is there for me if I need her is a great comfort."

Kaitlin and Violet Eppinger

innovation IN cancer care

Steve Kemper **writer** Peter Baker **photographer**

Alexandra Minnella, Dr. Patricia LoRusso, Associate Director for Innovative Medicine, and Dr. Joseph McLaughlin

Innovation can be found all over Yale Cancer Center: in research labs, medical clinics, specialty healthcare programs, community care centers, and clinical trials. Those areas of innovation often exist in isolation, however, unaware of each other. Part of Dr. LoRusso's goal at Yale Cancer Center is to link these disparate innovations into bigger and more powerful breakthroughs, and to accelerate the creation of new treatments that benefit patients.

Patricia LoRusso, DO, Associate Director for Innovative Medicine, joined Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven in August 2014. She came to Yale from the Barbara Ann Karmanos Cancer Institute at Wayne State University, where she focused on the development of new drugs for 25 years as director of one of the largest academic Phase I Clinical Trials Programs in the United States. Her hope is to use that immense operational and translational experience to help keep Smilow's leading-edge care constantly sharpened by new advances.

She has spent years thinking about innovation and translational medicine. Innovation has been the key to so many advances in cancer medicine. A driving force that led her to Yale was the capabilities for translational medicine. "Yale has amazing scientists and clinical faculty and an amazing patient population," said Dr. LoRusso. "The opportunities to use my team science and clinical research expertise to enhance the marriage of science and medicine at Yale were the underpinnings that drew me here. Additionally, I felt that my years of experience in operationalizing a clinical trials program could benefit the rapidly growing clinical research portfolio at Yale Cancer Center. There are many components that define a top tier clinical trials program. Yale has all those components. Bringing them together to benefit patients is what I envision as my contribution."

An innovative cancer institute, she added, distinguishes itself by the number of cutting-edge trials it has running, and the number of cutting-edge therapeutics available to patients.

She sees all the raw materials for innovation in place at Yale. "We have phenomenal scientists and clinicians," she said. Her task, she continued, is to integrate them by forming teams to move scientific breakthroughs into clinical trials. That will often translate into more investigator-initiated trials and more peer-review funding, important characteristics of a top tier cancer center. "I think it also brings a different level of excitement to your job, because team science brings the energy of many phenomenal

human beings together for a common goal: improved outcomes for our patients."

She expects some of these collaborations to lead to new innovations that can be tested in early phase clinical trials at Yale. A portfolio of early phase trials tends to build on itself, like compounding interest. Insights and results from such trials, if encouraging, lend themselves to later stage clinical investigation making potentially beneficial therapies available for even greater numbers of patients at Yale and across the world. The more high impact trials that open, said Dr. LoRusso, the more options available for a wider circle of patients, not just at the main hospital in New Haven, but in the Smilow Cancer Hospital Care Centers across the state.

An innovative cancer institute...distinguishes itself by the number of cutting-edge trials it has running, and the number of cutting-edge therapeutics available to patients.

To increase the number of trials and accelerate them, she added, the process needs to be streamlined. With investigator-initiated concepts, the bottlenecks are often drug availability and funding. "One of the grants that I was fortunate to bring to Yale was the National Cancer Institute Early Therapeutic Clinical Trials Network UM-1 grant. Yale is only one of a few centers in the country to now hold this prestigious grant," she said. The grant enables investigator-initiated clinical trials based on drugs available in the NCI's portfolio of pharmaceutical compounds.

Dr. LoRusso believes that streamlining the clinical trials process will lead to more innovation in drug development. Restructuring is also necessary, she said, because the design of many trials is changing, driven by the genomic revolution. Until recently, a trial typically focused on a single type of cancer. "But now, to be more efficient, early on, pharmaceutical companies want to test drugs on large numbers of patients representing more than one tumor type," said Dr. LoRusso. "To accommodate such demands, we are reassessing and restructuring our clinical trials operations so we can accommodate those kinds of trials more efficiently and offer more new treatments to more patients." Many trials of this sort are already underway—most notably currently, immunotherapy treatments that target several types of cancer. Other types of drug treatments are already beginning to follow this clinical trial paradigm.

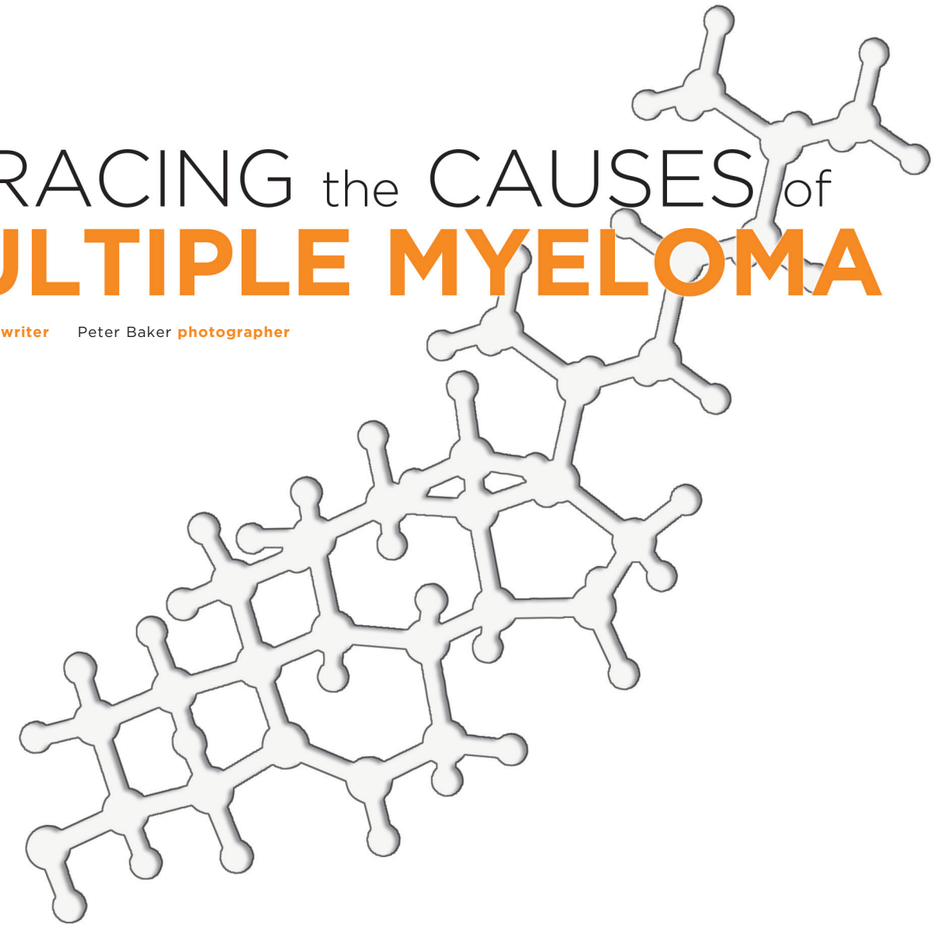
Several new trials using innovative drugs and drug combinations are being conducted at Yale already, focused on a multitude of different tumor types. She commented, "there is phenomenal talent in both the preclinical and clinical landscape at Yale University and Yale Cancer Center. There are phenomenal scientists. The potential to advance patient outcomes with some of the science is enormous. If we can be successful with bringing even just a handful of their discoveries into the clinic, the benefit to patients with a variety of tumors could be enormous." She also expects Yale to attract more trials because of its recent designation by the NCI as one of two national "molecular characterization hubs," which will do molecular profiling for early phase clinical trials.

Another element in the recipe for innovation is collaboration with pharmaceutical sponsors, which currently have the most innovative portfolio of novel drugs for clinical research. These companies are looking for new and exciting ways to partner with academic sites, particularly ones like Yale where there is so much expertise in pre-clinical science and cancer medicine. One of Dr. LoRusso's goals in her new position is to increase strategic alliances with several sponsors, with the objective of identifying each party's needs and working with their strengths. "That way we won't have to reinvent the wheel every time we have a new clinical trial from them," she said. "We want to be one of their preferred sites so we can expedite their trials and offer them to patients who could benefit." The result, again, will be more therapies available for more patients.

Innovation in cancer care requires collaborations between various combinations of different parties including scientists, clinicians, the NCI, and pharma. All have their own interests, perspectives, and cultures. However, the common denominator will continue to always be the patient. "The first and main focus," said Dr. LoRusso, "is always what we can do to improve outcomes for patients. Most of us go into oncology because we want to make a difference. It's a war out there, and it's us against cancer. The way to win a war is to bring the troops together with one common goal, and to have them understand who the true enemy is. I've always believed that if we can get everyone working together against our common enemy, we're going to win this battle!"

TRACING the CAUSES of MULTIPLE MYELOMA

Steve Kemper **writer** Peter Baker **photographer**



Science has known for some time that many cancers can be traced to mutated proteins. Now researchers at Yale Cancer Center may have identified a surprising new instigator of multiple myeloma, a bone marrow cancer: lipids. The implications could be profound, both for patients who have this disease and for certain groups known to be at higher risk of developing it, which includes a large number of Americans—the obese.

"Obesity is a national problem that includes about 30 percent of the population," said the leader of the research, Madhav V. Dhodapkar, MBBS, Professor of Medicine and of Immunobiology and Chief of Hematology at Yale Cancer Center and Translational Working Group Leader of the Hematology Program at Smilow Cancer Hospital at Yale-New Haven. "There's an entire field studying the links between lipids, obesity, and cancer, but the insight about how lipids may be directly related to the origins of myeloma is new. It's quite possible that some of the therapies being developed against obesity might

affect the lipid-reactive subset of multiple myeloma."

According to the American Cancer Society, in 2015 about 26,850 new cases of multiple myeloma will be diagnosed in the United States and about 11,240 Americans will die from the disease. The cancer occurs when plasma cells—white blood cells in the bone marrow that normally function as part of the immune system—turn malignant.

Why do cells that should produce antibodies to fight infection become traitors that attack healthy blood cells and promote disease? A partial explanation, in some cases, seems to be genetics. If a parent or sibling has multiple myeloma, the risk for other immediate family members increases by four. African-Americans, for unknown reasons, are more than twice as likely as white Americans to get the disease. For a small group who inherit the disorder called Gaucher disease, the risk is 30 times higher.

But inherited genes don't explain why obese people are diagnosed with multiple myeloma at two or three times the normal rate. Nor can the cause be pinned on outside risk factors, said Dr. Dhodapkar. "For instance, smoking causes lung cancer and UV radiation causes melanoma, but obesity is an acquired disorder." It is characterized partly by the accumulation of excessive lipids. "Basically we have found that the host response to the lipids sets the stage for the mutations leading to multiple myeloma."

Researchers have known for a long time that malignant plasma cells associated with multiple myeloma produce unique antibodies, but the antigen that those antibodies recognize remained a mystery. Identifying it was critical, explained Dr. Dhodapkar, because antibodies are very specific and only recognize one antigen. "We thought for a long time," he said, "that if myeloma is basically a tumor of antibody-making plasma cells, if you could figure out what that antibody recognizes, then you will know how the tumor started."

Dr. Dhodapkar and his colleagues assumed they were looking for a protein. But it turned out that in a third of the cases of multiple myeloma, the antibody wasn't recognizing a protein but a lipid. "So the tumor originated in a lipid-reactive cell," explained Dr. Dhodapkar. This may explain why people with obesity and Gaucher disease show an increased risk for multiple myeloma.

Dr. Dhodapkar discovered a new kind of immune cell—a subset of type II Natural Killer T cells (NKT)—that recognizes lipid antigens. They found that these cells help B cells (another immune cell) to become plasma cells, which in turn make antibodies to help antigens. But accumulation of lipids can drive repetitive activation of these immune cells in the lead-up to multiple myeloma.

"Compared to proteins, lipids have been a relative black box. But now we know that there's a specific immune cell that recognizes them, and these studies provide early insights into precursor states of multiple myeloma—and show that the causes are inside us," said Dr. Dhodapkar.

Understanding the origins of multiple myeloma points the way toward new therapies and drug targets that could prevent or treat the disease.

His lab has done some early studies along these lines and is planning more. He wants to see if full-blown multiple myeloma can be prevented among high-risk populations through newer approaches targeting lipids or the immune system. For the obese, this could include simple lifestyle changes that reduce weight and hence risk. Maybe a medication could lower the level of key lipids, as drugs now do for cholesterol. He also intends to test whether it's possible to use drugs preventatively to activate the immune system against the early tumor cells, and thus stop monoclonal gammopathy of undetermined significance (MGUS) from turning into multiple myeloma.

"Understanding the origins of any cancer," said Dr. Dhodapkar, "sets the stage for new approaches to prevent it."

Compared to proteins, lipids have been a relative black box. But now we know that there's a specific immune cell that recognizes them, and these studies provide early insights into precursor states of multiple myeloma—and show that the causes are inside us.

Madhav V. Dhodapkar, MBBS, Professor of Medicine and of Immunobiology and Chief of Hematology

PETER BAKER

Unleashing the Immune System to Fight Lung Cancer

Scott Gettinger, MD
Associate Professor
of Medicine

Scientists are trained to be skeptical, especially when research results seem too good to be true. Even if the results are confirmed, and confirmed again, scientists often call them preliminary and keep a lid on their enthusiasm.

But cautious dispassion is hard to maintain when it comes to the findings on nivolumab, a new immunotherapy drug against lung cancer that has been in clinical trials for several years at Yale and elsewhere.

"There are two great things about this therapy," said Scott Gettinger, MD, Associate Professor of Medicine (Medical Oncology), and the principal investigator for many clinical trials of nivolumab at Yale/Smilow. "First, unlike with chemotherapy, most patients have little or no side effects."

"Second," he continued, "responses tend to be durable, and unlike chemotherapy, do not appear to be less frequent in patients who have received a number of prior chemotherapies. Truly remarkable are the ongoing responses in some of our chemotherapy refractory patients started four to five years ago, patients who had a prognosis at that time of only a few months." The results of the trials were so impressive that in March nivolumab became the first immunotherapy drug approved by the FDA for lung cancer. (The drug's maker, Bristol-Myers Squibb, markets it under the trade name Opdivo.) At the moment, nivolumab is approved only for patients who have metastatic squamous non-small cell lung cancer that progressed after chemotherapy. That sounds narrow, but according to Dr. Gettinger, much wider applications are sure to follow.

Unlike chemotherapy and other targeted treatments, nivolumab fights cancer by harnessing the body's immune system. Normally, the immune system detects invaders such as viruses or cancer, and attacks them. But lung cancer, like other cancers, has evolved ways to disguise itself and trick the immune system into passivity as cells mutate. Immuno-drugs strip off cancer's disguise, revealing it to the immune system, which then attacks. Moreover, the immune system seems to remember the cancer's disguise and isn't easily fooled if cancerous cells try to slip by it again.

In lung cancer and several others, the disease blocks attack by the immune system with the use of a brake called Programmed Death Ligand 1 (PD-L1), which is generated by the tumor and effectively immobilizes the immune cells that recognize the tumor and are primed to attack. Nivolumab releases this brake, awakening these stunned immune cells that can now do what they are meant to - attack cancer.

> **"I think PD-1 axis blockers will become the backbone of systemic therapy for patients with lung cancer and other cancers... This is just the beginning."**

But PD-L1 doesn't seem to be universally present in lung cancer patients, which may partly explain why 75 to 80 percent of the patients in the clinical trials didn't respond. Researchers, including Dr. Gettinger, are working on that. Some patients, he said, don't seem to have immune cells in their tumors, which means that the drug can't activate the immune system there. The solution here might be to help immune cells get to and stay in the tumor, and then add a drug like nivolumab.

Another strategy being tested is to combine immunotherapy with other drugs approved for cancer. For instance, a recent melanoma trial combined nivolumab with another immunotherapy drug approved for melanoma called ipilimumab, which blocks cytotoxic T-lymphocyte antigen 4 (CTLA-4). The results suggest that responses are longer and deeper when the drugs are given in combination rather than alone. Perhaps such combinations could help lung cancer patients who don't respond to nivolumab alone.

Other trials also show great promise. At Yale and elsewhere, nivolumab is being studied as a first-line therapy for lung cancer, meaning for patients who haven't previously had treatment.

"The amazing thing is that some of these patients have had complete responses," said Dr. Gettinger. "That means resolution of every area of cancer on imaging. This is extraordinarily rare in most cancers."

Such results have convinced Dr. Gettinger that immunotherapy drugs will become first-line treatments, used on earlier-stage lung cancers, and also combined with standard chemotherapy and radiation.

"I think PD-1 axis blockers will become the backbone of systemic therapy for patients with lung cancer and other cancers," he said. "Encouraging results of recent trials evaluating nivolumab and other PD-1 axis blockers have provided a glimpse into the potential of one's own immune system to attack and control cancer. This is just the beginning."

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Sun damage as seen with ultraviolet photography.

Sun Damage Occurs Even After Sunset

Skin cancer normally occurs when ultraviolet (UV) radiation from the sun or from tanning beds damages DNA in skin cells, triggering mutations that lead to such cancers as melanoma. The mechanism by which this occurs was understood to take place during exposure to UV light. Researchers at Yale have recently discovered that this damage continues even when we're out of the sun and that melanin, the pigment that gives skin its color, may be both protective and harmful.

Dermatologists have long known that blondes and redheads are more sensitive to sunburn and skin cancer. Melanin helps block UV, so this was thought to be attributable to their light skin. Yet there are light-skinned, dark-haired people in countries near the equator who don't have a high incidence of skin cancer. Furthermore, scientists at Yale and elsewhere found that when skin cells or mice were irradiated with UV, there was more cell death in cells that contained melanin.

When UV light hits the skin, it causes a type of DNA damage known as a cyclobutane pyrimidine dimer (CPD), in which two adjacent bases attach, causing a bend that makes it difficult for the cell to copy its DNA correctly. During UV exposure, many CPDs are instantly created in skin cells, but the DNA is able to repair itself by removing most of the CPDs and replacing them with normal DNA. In a study published in the journal *Science*, Douglas E. Brash, PhD, Clinical Professor of Therapeutic Radiology and Dermatology, and a member of Yale Cancer Center's Radiobiology and Radiotherapy Research Program, and his colleagues found that melanocytes, the cells that form melanin, continued to generate CPDs for several hours after UV exposure ended. Interestingly, cells without melanin generated CPDs only during UV exposure.

"We've been underestimating the amount of UV damage that the sun or sun beds are causing because we measure it immediately after exposure," said Dr. Brash. In fact, over half of a person's DNA damage arises in the car on the way home from the beach. Furthermore, while melanin does act as a shield, it is also associated with skin cell damage.

"We've been underestimating the amount of UV damage that the sun or sun beds are causing because we measure it immediately after exposure. In fact, over half of a person's DNA damage arises in the car on the way home from the beach."

When researchers delved into the details of this process, the results were surprising. Sanjay Premi, PhD, associate research scientist in the Brash laboratory, discovered that UV light activated two enzymes that combined to excite an electron in a fragment of melanin. The energy generated from this process was transferred to DNA in the dark, creating the same DNA damage that occurs in the presence of sunlight. Chemically induced electron excitation – known as chemiexcitation – was previously seen only in plants and lower organisms such as jellyfish and fireflies, where it generates softly glowing light. In humans, however, it is less benign, raising the question of what other diseases might involve similar chemistry.

Even though we now know that melanin has a dark side, it is nonetheless evolution's best solution to absorbing harmful UV radiation. "The imperfect melanin strategy does serve to spread CPDs out over time, which may be better than occurring all at once during sun exposure and possibly overwhelming the DNA repair system," said Dr. Brash. It also creates an opportunity. The delayed pathway should be interceptable at several points, creating an opening for an "evening-after" sunscreen that might prevent the enzyme activation or divert the energy from the excited electron into heat before it can damage DNA.

"This finding doesn't really change the habits of UV exposure," said Dr. Brash. "I tell people to enjoy the sun but don't lie on the beach between 10 and 2, and wear a hat." Sunscreens are useful, as long as they block both UVB and UVA, the two types of harmful radiation in sunlight. But once a new generation of sunscreens is developed, a new habit would need to be added: Putting on a different sunscreen when you go inside.

New Program Aims to Bring Prevention to the Forefront

Erin Hofstatter, MD
Xavier Llor, MD, PhD

Streamlining is key when it comes to the Smilow Cancer Genetics and Prevention Program and their mission to be at the forefront of patient care at Smilow Cancer Hospital. With plans to move into a new suite on the Saint Raphael's campus this summer, the Program will now have exam rooms where patients can meet with physicians and counselors together and focus on preventative measures based on an individual's family history and genetics. Under the leadership of Erin Hofstatter, MD and Xavier Llor, MD, PhD, Co-Directors of the Program, all services related to high-risk families will be incorporated into one comprehensive program, including not only genetic counseling and testing, but also an integration of all aspects of care.

The Cancer Genetics and Prevention Program consists of geneticists, genetic counselors, physicians, and nurses working together with the goal of providing cancer risk assessment and taking steps to prevent the development of cancer. Patients are referred either through self-referral, or more commonly, by a physician that has identified them as possibly high-risk based on certain criteria.

Although programs like the one at Smilow are not standard of care yet, they hope to be an example for other centers by demonstrating the effect that prevention plans can have on outcomes. "There is a lack of awareness by some providers and families are falling through the cracks," said Dr. Llor. "We are committed to educating families and their providers to identify who may benefit from a cancer genetics evaluation. Once they are on the radar, our team can follow-up with them as needed."

Dr. Hofstatter commented that when a patient comes to her with a diagnosis of breast cancer and a mutation is found, it feels like a missed opportunity for prevention. Even if a woman is found not to have a mutation but is still considered high-risk, there are preventative steps that can be taken. Dr. Hofstatter explained that a new term, 'previvor,' is being used more often to describe individuals who are living with a predisposition to cancer but who haven't yet had the disease. This group includes people who carry a hereditary mutation, a family history of cancer, or some other predisposing factor.

"More attention needs to be paid to these 'previvors' and their families. We are making huge strides in the treatment of cancer, but there are still toxicities, and no matter what, a cancer diagnosis affects people and their quality of life. In order to put a dent in cancer incidence, prevention needs to be a part of the conversation, not an afterthought once a diagnosis has been made," said Dr. Hofstatter.

> **"We are making huge strides in the treatment of cancer... Prevention needs to be part of the conversation, not an afterthought once a diagnosis has been made.**

Karina Brierley, MS, is Chief Genetic Counselor for the Cancer Genetics and Prevention Program and meets with patients that are considered high-risk based on personal and family history. She explained that each cancer program within Smilow will have a Program Leader assigned to identifying patients that might be high-risk. For example, Dr. Llor will work within the Gastrointestinal Cancers Program and patients with colon cancer, and Dr. Hofstatter as part of the Breast Program for breast and ovarian cancers.

Ms. Brierley commented, "Genetic testing is getting more complicated as more genes and mutations are discovered. Hereditary colon cancer is now the second biggest mutation we test for, but breast and ovarian are still the largest population of patients. Our physicians see patients with an array of diseases and therefore, our testing becomes more diverse as well. It is not uncommon for us to see rare hereditary cancers either."

The World Health Organization (WHO) reports that one-third of all cancer cases are preventable. "People with a strong family history, or that have tested positive for a mutation, don't want to wait around thinking there is nothing they can do, they want a plan," said Dr. Hofstatter. Whether it is following a patient with screening, referring them to the Smoking Cessation Program, or a nutritionist to talk about diet and exercise, the goal ultimately is to provide the resources and options needed so that cancer never becomes an issue.

Prevention and genetics are becoming a vital part of patient care at Smilow. The hope is to include new research and develop clinical trials for families that are found to carry a mutation, and those with a strong family history as well. "Using this method," said Dr. Llor, "we hope to eradicate the predisposing factors that cause cancer to grow, thereby stopping cancer in its tracks. There is a lot of potential here and we plan to hit the ground running."

Mr. and Mrs. Stephen Neuwirth with
Dr. and Mrs. Roy Herbst

Dr. Thomas Lynch, Stephen Neuwirth,
and Dr. Patricia LoRusso

Neuwirth Gift will Advance Translational Research

Thanks to a transformational gift from Stephen and Nataly Neuwirth, the Beatrice Kleinberg Neuwirth Fund for Pancreatic and Lung Cancer Research will support several aspects of translational research at Yale Cancer Center. A partner at the New York law firm Quinn Emanuel, Stephen Neuwirth has made a career in antitrust litigation since graduating from Yale College in 1984 and Yale Law School in 1987. But cancer has taken a toll on his family: His mother – for whom the new research fund is named – died of pancreatic cancer and his sister-in-law was successfully treated at Smilow Cancer Hospital just a few years ago.

Led by Mr. Neuwirth's undergrad college roommate at Yale, Roy S. Herbst, MD, PhD, Associate Director for Translational Research and Chief of Medical Oncology, the research efforts supported by the Neuwirth Fund will identify drugs that bind and inhibit Ras, a commonly mutated gene in cancer. Tumors that are Ras mutated rarely respond to chemotherapy, making them an important target for next generation targeted therapies.

"Ras is an elusive target," Dr. Herbst said. "So far, no one has made major inroads with this group of mutations – it's one that needs a totally out of the box approach. Steve and Nataly's gift makes this possible."

PETER BAKER

Q+A

meet the physician

Jeremy Kortmansky, MD

Medical Director, Smilow Cancer Hospital Care Center – North Haven

Your office integrated into the Smilow family just over three years ago. What has been the biggest change for your daily practice?
Our daily routine is quite similar since joining Smilow. The Care Center physicians remain hands-on in the care of our patients: we see our own patients in the hospital, have office hours daily, and return our own calls. We have largely maintained the same administrative staff, PCAs, and nursing staff as before, and we work well together. Since joining Smilow, we have also added important services like on-site nutrition counseling, social work, and clinical research. The hardest change has been adjusting to the mandates of the electronic medical record. But I suspect this is not unique to Yale. Also, I drink more coffee.

Have your professional goals changed over the last 3 years?
My primary focus remains providing state-of-the-art care in a compassionate manner. However, melding the convenience and service of a community office with the resources of a major comprehensive cancer center is no easy task. In my role as Medical Director, I work closely with the Smilow administration to realize this vision. In doing so, I have rekindled my interests in clinical operations, research, and teaching. I am very excited about the future.

Making clinical trials available to patients in community offices is a priority for Yale. Are your patients benefitting?
I am very proud of our efforts to build a clinical research program in the community. The importance of clinical trials to find better treatments cannot be overstated. In the past, patients balked at the opportunity to participate because of the inconveniences of traveling into New Haven or other major cities. While we don't always know whether an investigational therapy will become the next true advance, patients still benefit from participating in clinical trials. This includes early access to promising treatments that may not otherwise be available and multiple levels of oversight of their treatment. It is a privilege to work with the clinical and research staff at Yale that make this level of care possible.

How are you able to focus your expertise on GI cancers in a community office setting?
I have had an interest in GI cancers since I arrived to this community 10 years ago. I have established important relationships with primary care providers, gastroenterologists, and surgeons within the community, and I am grateful for the trust they have in me to care for their patients. To maintain my level of expertise, I have aligned with the Gastrointestinal Cancers Program at Smilow and participate regularly in the tumor board and the research program meetings. Nonetheless, practicing in the community requires a broad competence in treating several types of malignancies. The scope of my practice includes patients with breast cancer, lung cancer, lymphoma, and many other malignancies.

Yale CANCER CENTER
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