

Yale Cancer Center

centerpoint

MAGAZINE



**Translational Research:
The Path to the Future**

fall | winter 2012



departments

2 Teaching our Immune System to Fight Cancer, Gives One Couple New Hope

Considering all that they have been through, Joe and Karen DePalma have a surprisingly positive outlook on life. Karen is a 10 year survivor of breast cancer and Joe has been fighting renal cell carcinoma for the last 5 years. Throughout the last 10 years, they have never given up hope, in themselves or each other.

4 The Gilead Project Progress Report

In April 2011 Yale signed an agreement with Gilead Sciences that will bring Yale Cancer Center \$40 million over four years, with an option to extend the collaboration to \$100 million over 10 years. The agreement's purpose is very specific: to encourage Yale scientists to produce breakthroughs with clear potential to make possible new cancer therapies. Nearly a year and a half into the project, both the Cancer Center and Gilead are delighted with the arrangement.



On the Cover

Roy S. Herbst, MD, PhD, Chief of Medical Oncology and Associate Director for Translational Research at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven.

Peter Baker **photographer**

1 Director's Letter

7 Advances

Breakthrough Research from Yale Cancer Center

8 Prevention

Preventing HPV Saves Lives

10 Forefront

Translational Research: The Path to the Future

12 Support

Helping Women Thrive after Cancer

14 Giving

Closer to Free Ride

16 Meet the Physician

Q&A with Dr. Wendell Yarbrough

17 New Faces

Appointments at Yale Cancer Center

yale cancer center

Thomas J. Lynch, Jr., MD
Director

Kevin Vest, MBA, FACHE
Deputy Director, Administration
and Clinical Affairs

Renee Gaudette
Director, Public Affairs and Marketing

art + Production

Greg Stewart
Art Director

contributors

Writers
Emily Fenton
Steve Kemper
Colleen Shaddox

Photographer
Peter Baker
pbakerphoto.com

Design
Ingenuity Design, Norwalk, CT
ingenuitydesign.com

Submit your ideas...

Do you have an idea for a story you'd like to see featured in Centerpoint Magazine?

Submit your ideas to:
renee.gaudette@yale.edu

centerpoint MAGAZINE

Centerpoint Magazine is published two times a year by Yale Cancer Center to inform the public and the Center's friends, volunteers, donors, and staff on current items of interest at Yale Cancer Center.

Yale Cancer Center
333 Cedar Street, PO Box 208028
New Haven, CT 06520-8028
yalecancercenter.org

©Copyright 2012, Yale Cancer Center. All rights reserved. No part of this periodical may be reproduced by any means, prints, electronic, or any other, without prior written permission of the publisher.

Editorial Office
Yale Cancer Center
100 Church Street South, Suite 160
New Haven, CT 06519
renee.gaudette@yale.edu

director's letter



THIS HAS BEEN AN EXTRAORDINARY YEAR at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. In September, we submitted our Cancer Center Support Grant (CCSG) to the National Cancer Institute, which describes the remarkable growth and investment in cancer care and cancer research that has occurred over the past 36 months. The CCSG is the funding and award mechanism that establishes Yale Cancer Center as one of only 41 National Cancer Institute Comprehensive Cancer Centers. I am also pleased to report that our SPORE in Skin Cancer grant was renewed by the NCI for an additional 5 years and we have submitted a second SPORE application for research in lung cancer. Bridging our cancer research successes in our extremely productive laboratories to our clinics at Smilow Cancer Hospital has been one of our main objectives over the last year for the leadership of both the Cancer Center and the Hospital.

Clinical trial management is a priority for all of our physicians and our patients have benefited from their dedication. Over the last twelve months, we have doubled the number of patients who participated in therapeutic clinical trials. I hope to continue this momentum and increase our participation to nearly 1,000 patients in 2013. Importantly we are beginning to do several biomarker driven studies linking Yale science to advances in the personalized care of cancer patients.

2012 has brought major expansion to the cancer enterprise with the addition of 8 Smilow Cancer Hospital Care Centers throughout the state of Connecticut and the integration of 24 medical oncologists who are now full time members of our faculty. We have redesigned cancer care in our state, providing patients easy access to the resources and quality principles standard at Smilow Cancer Hospital at Yale-New Haven within 35 minutes of their home.

I am extremely pleased that our patient satisfaction scores for Smilow Cancer Hospital are strong in both our inpatient and outpatient centers. The inpatient oncology patient satisfaction scores are consistently in the 99th percentile in the nation. In the outpatient setting, we exceed 90th percent for patient satisfaction. Our patients' experience is one of the key areas of focus for the leadership of Smilow Cancer Hospital and we will continue to assess and improve the patient and family experience. We welcome your continued feedback and participation in this process.

I look forward to updating you on our progress in translational research and patient care in the next issue of Centerpoint Magazine early in 2013.

Sincerely,

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



TEACHING OUR IMMUNE SYSTEM TO
FIGHT CANCER, GIVES ONE COUPLE

new hope

Emily Fenton **writer**

Peter Baker **photographer**

Considering all that they have been through, Joe and Karen DePalma have a surprisingly positive outlook on life. Both school teachers, they married in 1995, saved up money for a house, and four years later, had their first child; they were living the perfect life. Then, in 2002, at the age of 35, Karen found a lump in her breast and was diagnosed with breast cancer. Seven years later, Joe received a diagnosis of renal cell cancer, and his prognosis was not good.

During Karen's treatment with chemotherapy, surgery and subsequent medications, namely tamoxifen to reduce her risk of recurrence, Joe was there to support her by going to appointments and taking over the household duties. They even had a second child during a break from the tamoxifen, something doctors couldn't guarantee would be possible. They thought things were looking up and that cancer would soon be behind them, but on Karen's final check-up after being on tamoxifen for five years, they found that the cancer had returned in her lungs. She went on hormone therapy for 9 months, but when the cancer didn't respond, she went on taxol, a newer drug that is highly effective; she lost her hair for the second time.

"I hated seeing my wife go through this, not knowing what I could do to make it better. I felt helpless, and had no idea what she was truly going through," said Joe. "Then, just as Karen was finishing up her chemotherapy regimen with taxol, I got the news that I had stage IV renal cancer. I had a persistent cough and they did a chest x-ray to see what was going on, my lungs were clear, but they saw a large mass in my kidney."

Karen and Joe were young and healthy, with no real family history of cancer. They couldn't believe that 'lightening had struck their family twice.' Reeling from his diagnosis, Karen took Joe to where she was being treated at the Harold Leever Regional Cancer Center in Waterbury. His case was complicated and they referred him on to Dr. Mario Sznol at Yale, Professor of Medicine in Medical Oncology. At Yale he began a rigorous treatment regimen of Interleukin-2 (IL-2) that was very difficult to tolerate and had no effect on his cancer. Joe developed pain from the cancer that had invaded his left hip, so severe that he required narcotic medications. His hip was treated with radiation and he began taking sunitinib, but after one cycle of this medication the CAT scans again showed that the cancer was progressing. Calcium levels rose in his blood, a sign that the cancer was growing rapidly.

Dr. Sznol then suggested a clinical trial looking at an anti-PD1 drug. Dr. Sznol commented, "Mr. DePalma met the criteria for the trial because his disease had progressed on IL-2 and sunitinib, and other standard therapies were unlikely to be effective. The disease responded very rapidly to anti-PD1, and over time almost all of his disease regressed except the primary tumor in the kidney, which shrank substantially and

has not shown signs of growth. His response to this new agent was quite amazing."

Anti-PD1 is an antibody that works by blocking signals within the cancer which turn off immune cells. Therefore, the immune cells that are already within the tumor attack the tumor cells more effectively. Dr. Sznol commented that anti-PD1 provides meaningful benefit to a subset of patients with metastatic kidney cancer, on the order of 25 to 30%, and some of those patients will have durable remissions of their cancer. "This is the first of several immune therapy drugs that will make a major impact on treatment of cancer and may surpass the effect of other types of treatment including molecular therapies," said Dr. Sznol.

Throughout this process, Karen and Joe have never given up hope, in themselves or each other. They have learned to balance their roles as both caretaker and patient. During a recent MRI, three tumors were found in Karen's brain, and she underwent whole brain radiation, losing her hair for the third time around; she is still receiving chemotherapy. A small tumor was also found in Joe's brain, but he was successfully treated with Gamma Knife surgery and he has had no other signs of recurrence. He was finally able to get the hip replacement he desperately needed to repair the damage that had been done by the cancer. The clinical trial with anti-PD1 gave him his quality of life back. He is now able to get around on his own, and work in his yard again. Most importantly, his children have seen a huge improvement in their dad's condition.

Both Karen and Joe commented that they see themselves as living with cancer, not dying of cancer. "We feel that our children, Josh, 13 and Jessica, 7, have the information that is appropriate, so that they are aware and prepared," said Karen. "Right now we are focused on them and are able to stay involved in school activities, sporting events, etc. Things are improving and we see ourselves as lucky to be here."

Joe and Karen were selected as Teacher of the Year at their schools, Joe for the 2006-2007 school year, and Karen for the 2011-2012, and they continue to teach. For the moment they are focused on enjoying family vacations, the little life moments, and the milestones. The support they receive from family, friends, and their church has been one of the good things to come from their experience; realizing there are so many kind people around them, willing to lend a hand. They recently celebrated Joe's 50th birthday, which he commented was celebrated as normally as possible in an abnormal situation. "We don't want to live to be 99. We just want to live long enough to see our children grow and to know that they are going to be okay," said Joe. "With the new advances that are constantly being made at places like Yale Cancer Center and Smilow Cancer Hospital, we are hopeful that we will get that chance."

In April 2011 Yale signed an agreement with Gilead Sciences that will bring Yale Cancer Center \$40 million over four years, with an option to extend the collaboration to \$100 million over 10 years. The agreement's purpose is very specific: to encourage Yale scientists to produce breakthroughs with clear potential to make possible new cancer therapies. In return, Gilead gets first option to develop any discoveries that emerge from its funding.

Nearly a year and a half into the project, both the Cancer Center and Gilead are delighted with the arrangement, according to Thomas Lynch, Jr., MD, Director of Yale Cancer Center, Physician-in-Chief of Smilow Cancer Hospital, and the Richard and Jonathan Sackler Professor of Medicine. "We've made terrific progress," said Lynch. "This money has allowed unprecedented resources to be brought to the sequencing effort, and to the cataloguing of tumors. We started with melanoma but have moved into many other types of cancers, at least a dozen specific tumor types, and we have sequenced more than 1,000 exomes."

"We can now sequence all the exomes in genes in the tumor and see what the actual mutations are," Richard Lifton, MD, PhD, Sterling Professor of Genetics and Medicine (Nephrology) explained. "And we can identify which ones are the drivers by finding mutations that either recur in different tumors from different people, or by finding where the same gene is mutated in different tumors much more frequently than would be expected by chance." This revolutionary ability to sequence is helping to propel cancer research; Gilead's support is invaluable to this effort.

The funding has accelerated the research process, said Lynch. "If we identify a unique opportunity, we're able to deliver those funds and make a difference in a matter of weeks, as opposed to applying to the NIH for grant money and waiting eight months to hear back." Because cancer research has become so competitive, Lynch declined to be specific about the project's priorities, but did name lung cancer, breast cancer, and gastrointestinal cancers as areas of current interest.

Earlier this year the project solicited proposals from the Cancer Center's scientists, asking for "transformative ideas" in cancer research. Of the more than 60 proposals submitted, just six were approved for two years of funding by the project's steering committee, which consists of three people from Yale (Thomas Lynch, Joseph Schlessinger, and Richard Lifton) and three from Gilead.

Most of the proposals contained excellent science but were inappropriate for the Gilead Project, said Joseph Schlessinger, PhD, William H. Prusoff Professor and Chair of Pharmacology at Yale School of Medicine, who negotiated the collaboration with Gilead and serves on the steering committee. "The project's goals are very well defined," he said. "To get support from this fund you have to show evidence that your proposal will lead to drug discovery on a reasonable timeline, within a couple of years. Many times when you get a grant, from the NIH for instance, you don't know what your research will lead to. For this, that's not sufficient."

Schlessinger believes that once the Yale research community better understands what Gilead wants, the number and types of funded projects will increase. "I predict that in three or four years we'll be doing a lot of different things as compared to what we're doing now."

Gilead's requirements are stringent partly because it has become so expensive to develop and clinically test new drugs. "As costs go up, picking your targets carefully becomes much more critical," said Lynch. "You need to focus your efforts on the targets most likely to be important to cancer care."

So far the project has concentrated on sequencing different tumors with the goal of identifying new mutations, to give Gilead a focus for new anti-cancer drugs. "If we could find a dozen genetic abnormalities in the coming year we would be

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

THE GILEAD PROJECT PROGRESS REPORT



Richard Lifton, MD, PhD, Thomas Lynch, MD, and Joseph Schlessinger, PhD



very happy,” said Lynch. “That does not mean they would all become targets. Some abnormalities are easier to study than others. We’re looking at tumors where we think there’s an unmet medical need, and also at targets that may be potentially tractable with new drugs.”

In the past year, the project has expanded from its initial emphasis on discoveries made through sequencing. Schlessinger noted that Gilead is also doing early drug discovery work in three areas based on research from other scientific specialties at Yale.

Gilead sought the collaboration with Yale, explained Schlessinger, as a shortcut to establishing itself in anti-cancer drugs. “This is a fantastically clever way for them to get very good cancer research people,” he said. “It’s cheaper for them and it’s also very good for us—it’s like getting 50 NIH grants annually. It’s a win-win situation.”

And not just for Gilead and the Yale researchers who get funding. “It’s a fantastic deal because the project supports many important aspects of research,” said Schlessinger. For instance, though much of the sequencing for Gilead won’t lead to drug development, the data will be invaluable for researchers throughout Yale. Likewise, the cutting-edge equipment and new technologies bought for the project will serve Yale’s entire scientific community. And the people hired to interpret data for Gilead also will assist everyone else at Yale. “It’s a rare opportunity for both sides,” said Schlessinger, “and I expect the project to generate novel cancer drugs in the next five to ten years.”

“It’s a **rare opportunity for both sides**, and I expect the project to generate novel cancer drugs in the next five to ten years.”



Nanoparticles Cut Off ‘Addicted’ Tumors from Source of their Survival
Proc Natl Acad Sci. 2012 Jun 26.

Yale biologists and engineers have designed drug-loaded nanoparticles that target the soft underbelly of many types of cancer — a tiny gene product that tumors depend upon to replicate and survive. The novel therapy successfully stopped lymphoma in mice when injected directly into tumors.

The interdisciplinary collaboration takes advantage of a new concept in cancer research — that tumors become “addicted” to a few genetic abnormalities they need to survive, grow, and spread throughout the body. By studying the microRNA miR-155, the team found that it helps regulate cell survival and is overactive in many forms of cancer. The team discovered that injecting nanoparticles that deliver a compound that specifically targets miR-155 into tumors stopped them from growing in mice.

New Melanoma Driver Genes Found in Largest DNA Sequencing Study to Date

Nat Genet. 2012 Jul 29.

Yale Cancer Center geneticists, biochemists, and structural biologists have painted the most comprehensive picture yet of the molecular landscape of melanoma, a highly aggressive and often deadly skin cancer.

The Yale study used powerful DNA sequencing technologies to examine 147 melanomas originating from both sun-exposed and sun-shielded sites.

The study revealed an excess of UV-induced mutations in sun-exposed melanomas. Most of these are passenger mutations that do not have a functional role in melanoma.

The analysis identified a frequent “gain-of-function” mutation in the RAC1 gene that has all the hallmarks of UV-damage. The study provided evidence that the mutant protein induces accelerated growth and movements among normal pigment cells, which are melanoma’s cells of origin.

With Drug-Loaded Nanogel, Yale Researchers Attack Cancerous Tumors

Nat Mater. 2012 Jul 15.

Yale University scientists have developed a new mechanism for attacking cancerous tumors that intensifies the body’s immune response while simultaneously weakening the tumor’s ability to resist it.

Tumors — in this case metastatic melanomas, or spreading skin cancers — are adept at overcoming their host’s natural defenses, in part by emitting agents that disrupt production and operation of the immune system.

The Yale team developed a new biodegradable nanoparticle that delivers a combination of two very different therapeutic agents to tumor sites, gradually releasing the agents into the tumor vasculature. One agent, a large soluble protein called a cytokine, stimulates the body’s innate immune response. The other, a small-molecule inhibitor, interferes with the tumor’s ability to suppress the immune response. Other drug combinations are possible.

The War on AIDS: Newly Developed Proteins Inhibit HIV Infection

J Virol. 2012 Jul 18.

Yale Cancer Center scientists have developed a new class of proteins that inhibit HIV infection and may open the way to new strategies for treating and preventing infection by the virus that causes AIDS.

AIDS slowly weakens the immune system and allows life-threatening infections and cancers to thrive. The Yale team isolated six 44- and 45-amino acid proteins that inhibited cell-surface and total expression of an essential HIV receptor and blocked HIV infection in laboratory cell cultures.

The proteins were modeled after a protein from a papillomavirus that causes warts in cows. This bovine papillomavirus is related to the human papillomaviruses that cause cervical cancer and some head and neck cancers.

Yale Team Finds Order Amidst the Chaos within the Human Genome

Nature. 2012 Sep 13.

The massive Encyclopedia of DNA Elements (ENCODE) reveals a human genome vastly more rich and complex than envisioned even a decade ago. In a key supporting paper, Yale University scientists found order amidst the seeming chaos of trillions of potential molecular interactions.

The scientists show it is not just the gene, but the network that makes the human genome dynamic.

Using sophisticated mathematical modeling, the team traced the cascade of a half million molecular interactions triggered by 119 transcription factors — special genes that can simultaneously activate or silence thousands of genes. The model shows that these transcription factors are wired together in a hierarchical fashion, with some factors operating like top-level executives, and some as middle managers or shop foremen. Together they regulate the 20,000 or so genes in the human genome.



1. Come to Yale
2. Get your HPV vaccine
3. Hook-up with Mr./Ms. Right...

Get all your ducks in a row!

Preventing HPV Saves Lives

The most common sexually transmitted infections in the United States are caused by human papillomaviruses (HPV). More than half of all sexually active people will contract HPV sooner or later, often without knowing it, although HPV infection can cause genital warts. HPV encompasses about 150 related viruses, which usually aren't life-threatening. Many infections with high-risk types of HPV disappear without treatment.

But infection with HPV can be serious. They are the second most common cause of cancer in women worldwide, perhaps best known for causing cervical cancer. Yet HPV also accounts for most anal cancers and many penile, vaginal, and head and neck cancers. The incidence of HPV-associated head and neck cancer has increased over the last few decades, probably because of oral sex.

Researchers at Yale Cancer Center are working on several fronts to understand and prevent HPV. Several labs are investigating the virus, said Daniel DiMaio, MD, PhD, the Cancer Center's Scientific Director and the Waldemar Von Zedtwitz

Professor and Vice Chairman of Genetics. One of the Cancer Center's seven research programs, he noted, focuses on molecular virology. "Lots of cancers are caused by mutations, which are hard to find," said DiMaio. "But when a virus causes a cancer, it's pretty discrete, which makes these cancers amenable to prevention and treatment."

DiMaio's own lab is looking into the ways that HPVs get into cells, turn them cancerous, and maintain that cancerous state. "We recently surveyed all 20,000 cellular genes to see which ones are

required for HPV entry into cells," he said. "No one has done this previously. We identified several hundred genes that appear to be important, so we're trying to figure out how they work. The products of these genes might be targets for anti-viral drugs. In addition, our work suggests that we can treat these cancers by turning off the viral oncogenes in cancer cells or inhibiting their activity." Other labs at Yale also are attacking the problem: investigating how HPV suppresses immune responses; trying to develop a therapeutic vaccine to treat cervical cancer; and identifying chemical markers that indicate which infected cells are pre-cancerous.

Two highly effective HPV vaccines have been developed. Both prevent infection with the two most common types of HPV, which cause 70 percent of cervical cancers and some cancers of the anus, vagina, and vulva, and one prevents infection with another two types of HPV that account for most genital warts. These vaccines may also help prevent cancers of the head and neck caused by HPV. Named Gardasil and Cervarix, the vaccines are given in three shots over six months.

In 2007 the vaccine was recommended for all girls in the U.S. aged 11 and 12. Since then about 50 percent of adolescent girls have received at least one shot, but many fewer have received

More than half of all sexually active people will contract HPV sooner or later, often without knowing it.

all three. In 2011, the vaccine was recommended for boys aged 11 and 12, but so far their compliance is much lower, with less than five percent vaccinated.

Since 2008, Linda M. Niccolai, PhD, Director of the HPV-IMPACT Project and Associate Professor of Epidemiology, has been tracking the effects of the vaccine on girls in Connecticut through a partnership with the State Department of Public Health and the CT Emerging Infections Program. "The state has made precancerous cervical lesions a mandatory reportable condition," said Niccolai. "We've been working with all 34 pathology labs in the state to track the incidence of these diseases."

As more girls are vaccinated, Niccolai expected the rate of precancerous cervical lesions to drop. After four years of data collection, she said, there's been a decline in these lesions among women in their early 20s. This could be because they received the vaccine as girls.

Yet large percentages of girls and boys remain unvaccinated. Niccolai is researching the reasons for this and looking for ways to overcome them.

Some parents worry about the vaccination's safety, but approximately 50 million doses have been given nationwide with no serious adverse

effects. Others object that their pre-teen children don't need protection from sexually transmitted disease. "But the point is to give the vaccine before they're sexually active," said Niccolai, "because the vaccine is only effective at preventing infection and not treating them." Even so, she added, the vaccination can be given up to age 26 because it protects against four types of HPV and can prevent future infections.

Pediatricians are accustomed to giving vaccines, noted Niccolai, but sexually transmitted diseases may not be on their radar or they may be reluctant to bring up the topic with parents. OB-GYNs, by contrast, are comfortable talking about STDs. "But by the time they see these young women, many of them will already have an HPV infection."

To surmount these barriers, Niccolai has started collaborating with DiMaio and the Cancer Center to develop programs that reach parents and providers. Within Yale, the Cancer Center is planning to work with student organizations to spread the word during orientation about HPV vaccination, which the university now offers free to all students.

The rationale, said DiMaio, is simple: "Preventing HPV saves lives."



PETER BAKER

Joseph Paul Eder, MD and Roy S. Herbst, MD, PhD

Translational Research: The Path to the Future

One of the keys to the future of Yale Cancer Center is “translational research”—that is, research that moves swiftly from the lab to the clinic so that more cancer patients can benefit more quickly from breakthrough therapies. Roy S. Herbst, MD, PhD, Chief of Medical Oncology and Associate Director for Translational Research has one fundamental goal for the next year: to take at least one anti-cancer substance or compound discovered in Yale’s labs and test it in clinical trials in-house.

One strong contender, said Herbst, is a targeted therapy for lung cancer. “There are 15 of us investigating lung cancer,” he said. “We’re working together phenomenally. I would say in the next two or three years some of these trials will change clinical practice.”

Translational research requires both a steady stream of breakthroughs in the lab and a wide array of clinical trials for testing them. Trials aren’t possible without a

large number of patients, so the Cancer Center has been working to enlarge that pool. “We have achieved a benchmark for the end of the fiscal year,” said Julie L. Boyer, PhD, “which was 450 patients accrued to clinical studies in cancer.” The Center’s new collaborative agreement with Nashville’s Sarah Cannon Research Institute will help as well. “They are experts on running clinical studies and also have access to a huge patient population,” said Boyer. This will

“We want to leverage the scientific expertise of the Yale faculty so that pharmaceutical companies and biotech companies with new drugs will come to us to solve any problems before the drugs get into the clinic.”

Joseph Paul Eder, MD

provide new opportunities to test Yale discoveries on a large scale, as well as opportunities for tissue profiling and DNA sequencing.

To generate more clinical studies and take greater advantage of the expertise at Yale, Herbst and Boyer are encouraging researchers who work on the same cancer to share discoveries and apply jointly for grants. “We have a group of clinical and basic investigators in lung cancer—physicians, scientists, and clinical investigators—who will submit a large grant to the National Cancer Institute this fall,” said Boyer. The breast cancer and melanoma groups will submit similar grants within a year.

Herbst and Boyer also have started a dialogue across departments throughout Yale. Investigators at the Cancer Center now meet monthly with researchers in chemistry, biomedical engineering, and molecular biophysics & biochemistry to hear brief presentations and to talk about how they can work together, including opportunities for joint grant applications. In the past, new compounds and drugs created by Yale chemists and other scientists have typically been handed off to drug

companies for development. Herbst wants to keep those discoveries at home by having the inventors work with Cancer Center researchers, with the goal of moving the discoveries into clinical trials.

Joseph Paul Eder, MD, the Center’s new Director of Developmental & Experimental Therapeutics, believes that once Yale becomes known for developing its own discoveries, the promising compounds will flow into Yale rather than out of it. “We want to leverage the scientific expertise of the Yale faculty so that pharmaceutical companies and biotech companies with new drugs will come to us to solve any problems before the drugs get into the clinic,” he said. “And then those companies are also more likely to do their phase I trials here. Anybody who’s developing a drug will get not only greater scientific expertise at Yale but also the best possible clinical care.”

An important aspect of translational medicine is that it is not only research that moves from the research bench to the clinic but also the information and data that moves from clinical trials back to the bench. This enables researchers to learn what worked and what did not.

“It’s like a chess match with a grandmaster where we need to anticipate two or three steps beyond. Analyzing the actual experience in the clinic enables us to use additional therapies in combination or to make entirely new agents to address the mechanisms cancer uses to avoid being stopped by our therapies,” Eder explained.

Eder was recruited for his hybrid experience: 20 years of phase I clinical trials at Harvard’s Dana-Farber Cancer Institute and five years in the pharmaceutical industry. “He knows about early drug development and how to take drugs from the lab to clinic,” said Herbst. In short, Eder has ideal preparation for boosting translational research.

So,” said Herbst, summing up, “we’re not just increasing clinical trial accrual numbers, but at the same time building strong disease-specific translational working groups, and identifying new ways to work with other Yale collaborators to get Yale discoveries into the clinic. That’s the logic we’re using to build a strong translational program at Yale. To advance cancer care based on scientific discoveries made at Yale or elsewhere.”



PETER BAKER

Elena Ratner, MD, Director of the SIMS Clinic

Helping Women Thrive after Cancer

Noa Benjamini's natural optimism didn't flag when she was diagnosed with uterine cancer. "I knew it was treatable," she recalled. She was home recovering from surgery when she got her first hot flash. "That's when I cried," she said. Nobody had warned her that she would experience hot flashes after her ovaries were removed. She suddenly saw herself on a fast track to old age. "I thought I'd shrivel up," she explained.

Three years later, Noa, 48, describes herself as "in a good place," as a combination of herbs, prescriptions, and diet and exercise have tamed her menopausal symptoms. She attributes that turnaround to The Sexuality, Intimacy, Menopause, and Survivorship (SIMS) Clinic at Smilow Cancer Hospital at Yale-New Haven, one of a few programs of its kind in the country. The clinic is the brainchild of gynecologists Dr. Mary Jane Minkin, who specializes in menopause, and Dr. Elena Ratner, who specializes in oncology. They partner with psychologist Dr. Dwain Fehon to provide interdisciplinary care to cancer survivors. After a thorough evaluation, they offer women a variety of services, including medical and herbal remedies, Reiki, acupuncture, and

individual or couples counseling.

More than 6 million American women are cancer survivors. The treatments that saved many of them can cause life-altering symptoms that go untreated for various reasons. The problems can be embarrassing for women to discuss with their doctors, or they can be dwarfed by concerns about the cancer.

Dr. Minkin is not a big fan of stigma, particularly when it keeps women from having frank discussions with their doctors. "I say the word vagina out in public all the time," she declared with a broad smile. "That's what I do. I'm a

vagina doctor." Nor does she think that aftereffects ranging from body image problems to vaginal dryness should be dismissed as unimportant in the face of cancer. "I think many cancer specialists are of the belief that the patients sort of adopt: You're a survivor; you should be happy," said Dr. Minkin, who is also not a big fan of settling. "This is what you're surviving for, to have quality of life."

Dr. Ratner got the idea for the clinic

Dr. Ratner also connected the woman to a therapist to address the horrible fear of recurrence that hung over her relationships. Often the physical solution is far more straightforward than the psychological issues around intimacy. "These women have been through so much," Dr. Ratner said.

The medical and psychological health providers work as a team through the SIMS Clinic to create a suggested


course of treatment. Women may see a psychologist for a brief course of cognitive behavioral therapy or couples counseling. The cancer experience can also bring up past traumas that need to be addressed through longer-term treatment, explained Dr. Fehon. In those cases, patients can be connected to community providers.

thirties to prevent cancer. Counseling these women ahead of their treatment about the menopausal symptoms they will experience is critical. Many can be helped by estrogen, a remedy that is often underused because of misconceptions about its use. "There are definitely women who shouldn't be taking it, but there are women who can take it with very good effect," Dr. Minkin explained.

"We're making sexuality and intimacy OK for providers to talk about. We're making it OK for women to talk about."

Elena Ratner, MD

and speak about their work in hopes that more doctors will develop a comfort level with these issues and that more cancer centers will offer this kind of care to survivors. "We're making sexuality and intimacy OK for providers to talk about," said Dr. Ratner. "We're making it OK for women to talk about."

Nevertheless, Yale is currently the only center offering this kind of comprehensive, interdisciplinary care in the region. That is why Noa, who now lives in Massachusetts, makes regular trips back to New Haven. The clinic has helped her address a number of menopausal symptoms, often through lifestyle changes. "They helped me stay young," she said. "They helped me not to feel defeated." 

Dr. Ratner helped her find solutions to the physical pain intercourse brought on as a result of the surgery. Increasingly, the clinic serves women who have a genetic predisposition for breast and ovarian cancer and are choosing to have mastectomies and oophorectomies in their twenties or



The 2012 Closer to Free Ride

Closer to Free Ride

The spirit of the riders and volunteers at the Closer to Free Ride on Saturday, September 8th showed with a sea of smiling faces at the starting line as the sun came up over the Yale Bowl. Over 500 riders raised money and rode 25, 65, or 100 miles in honor or memory of cancer survivors and to support cancer research and care at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. Forty-six of the riders were cancer survivors and 41 of the 350 volunteers were! Their courage and strength was a symbol throughout the day as riders pushed through the hills of the Connecticut shoreline.

“The enthusiasm and dedication of the riders, many of whom were patients, staff members, and physicians, is inspirational. Their support will help to fund new initiatives in cancer therapy at Yale, and will ultimately benefit our patients with new treatment options for their disease,” said Dr. Thomas J. Lynch, Jr., MD, Director

of Yale Cancer Center and Physician-in-Chief of Smilow Cancer Hospital at Yale-New Haven. Dr. Lynch rode 65 miles with his son Donovan; his wife Laura Pappano rode 100 miles.

“This event is filled with hope, support, and encouragement for all those who have been afflicted or affected by this dreaded disease. Many of the volunteers and supporters that line the bike route and fill the Yale Bowl are many of the same individuals who cared

for us when we were undergoing our cancer treatments. Their dedication and enthusiasm empowers many “Closer to Free” bike riders way beyond their physical capabilities. This event makes everyone who participates, whether you’re cheering, riding, or volunteering, feel like we are all on the same team,” explained rider Tom Capobianco of Team Capobianco.

rideclostotofree.org





Q+A

meet the physician

Wendell Yarbrough, MD

Section Chief, Otolaryngology
Co-Director, Molecular Virology Research Program

How have the surgical options for patients with head and neck cancers improved over the last decade?

Major advances have been in less invasive approaches (including laser, endoscopic, and robotic) for resection of cancers. These approaches allow for faster healing and better cosmetic appearance. In addition, reconstructive options have advanced so that post-operative function and patient appearance are improved.

How does multidisciplinary care help our patients?

Multidisciplinary coordination is critical for the care of patients with head and neck cancer because these cancers typically are treated with multiple modalities (surgery, chemotherapy, and radiation), and both the cancer and its treatment can affect swallowing, communication, and appearance. A multidisciplinary team effort improves delivery of care to maximize cure rates and quality of life. Pathologists, radiation oncologists, medical oncologists, and head and neck surgeons are all involved in recommending the most appropriate care; the team also includes many medical, dental, and ancillary specialties such as speech therapists, care coordinators, dentists, and physical therapists.

What plans are in place to continue to strengthen the care for our patients treated by the Head and Neck Cancer Program in Smilow Cancer Hospital?

We have a weekly multidisciplinary tumor conference where representatives of all disciplines meet and discuss care of patients. The head and neck team also includes translational researchers who are pushing to individualize or personalize care based on each tumor's molecular defects. Our ultimate goal is to improve outcomes and decrease morbidity of patients with head and neck cancer.

What should our research priorities in head and neck cancer be?

We are testing head and neck cancers to determine molecular defects of individual tumors so that we can individualize therapy based on molecular characteristics or weaknesses of the tumor. Ultimately the goal is to improve survival and decrease morbidity by personalizing cancer treatment based on each patient's tumor.

What are the risk factors for cancers of the head and neck?

Tobacco use (smoking, dipping snuff, chewing tobacco) and alcohol have been known risk factors for many years. More recently, the human papillomavirus (HPV) has been shown to cause an increasing number of diagnoses of head and neck squamous cell carcinoma.

Are there early warning signs that people should recognize?

A lump in the neck, sore in the mouth or throat, hoarse voice, coughing or spitting up blood, and swallowing difficulty.

NEW faces

Emily Christison-Lagay, MD

Dr. Emily Christison-Lagay recently joined the department of surgery at Yale School of Medicine. She is a pediatric surgeon specializing in patients with cancer and has a special interest in neuroblastoma and childhood sarcomas. She will serve as the pediatric surgical representative for the Pediatric Thyroid Center at Yale, working with both benign and malignant diseases of the thyroid and parathyroid.

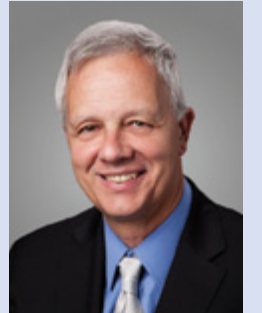
Dr. Christison-Lagay is a graduate of the University of Virginia and received her medical degree from Harvard Medical School. She completed her general surgical residency at Massachusetts General Hospital. She did a pediatric surgical fellowship at the Hospital for Sick Children (SickKids) in Toronto, followed by a "super"-fellowship in Pediatric Surgical Oncology at Memorial Sloan-Kettering Cancer Center.



Joseph Paul Eder, MD

Joseph Paul Eder, MD, a leader in drug development and clinical research, was recently appointed as Director of Experimental Therapeutics and of the Phase I Research Group. Dr. Eder joined Yale Cancer Center and Smilow Cancer Hospital from AstraZeneca, LP and the Dana-Farber Cancer Institute. His unique combination of academic medicine and pharmaceutical experience, and proven leadership in early clinical trial development, will continue to expand the options for translational research at Yale.

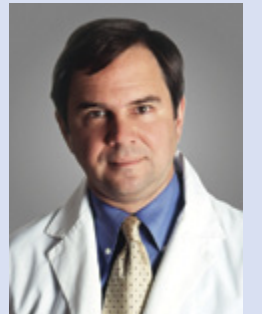
Dr. Eder received his medical degree from Georgetown University School of Medicine, where he also completed his internship and residency. He completed a clinical fellowship in hematology and oncology at Beth Israel Hospital and the Dana-Farber Cancer Institute, both in Boston, MA.



Daniel Petrylak, MD

Daniel P. Petrylak, MD has joined Yale Cancer Center and Smilow Cancer Hospital as leader of the genitourinary cancers medical oncology team and as director of the prostate cancer research group and co-director of the Signal Transduction Research Program. Dr. Petrylak is a national leader for clinical trials for men with prostate and bladder cancer and continually searches for innovative therapies for his patients.

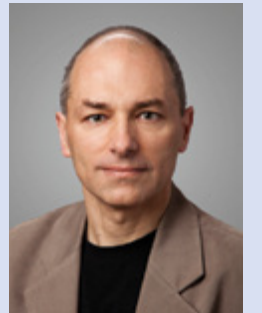
Prior to joining Yale, Dr. Petrylak was a Professor of Medicine at NewYork-Presbyterian/Columbia Medical Center in New York. He received his undergraduate degree from Columbia College and his medical degree from Reserve Case Western Reserve University School of Medicine. He completed his internship and residency at Albert Einstein College of Medicine and his fellowship in medical oncology at Memorial Sloan-Kettering Cancer Center.



Lajos Pusztai, MD

Lajos Pusztai, MD, DPhil, was recently appointed director of the breast cancer research group and co-director of the Cancer Genetics Research Program at Yale Cancer Center and Smilow Cancer Hospital. Dr. Pusztai's research focuses on developing pharmacogenomic markers of response to breast cancer therapy and identifying methods to select the optimal treatment for each patient. He is the principal investigator of several clinical trials investigating new drugs and molecular predictors of disease outcome.

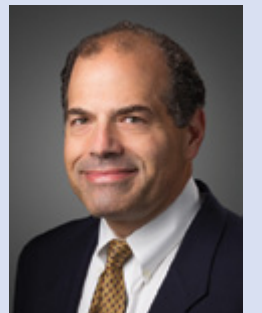
Dr. Pusztai joins Yale from The University of Texas MD Anderson Cancer Center. He received his medical degree from Semmelweis University of Medicine in Budapest, Hungary and his doctorate degree from the University of Oxford. He completed his internship at the University of Rochester and his medical oncology fellowship at The University of Texas MD Anderson Cancer Center.



Theodore Tsangaris, MD

Dr. Theodore Tsangaris has been appointed the Medical Director of Breast Services for the Smilow Cancer Hospital Network. Through this position, he will oversee the collaborations with other Smilow network sites and focus on maintaining quality breast cancer care standards throughout the network.

Dr. Tsangaris' research interests include breast cancer prevention, identification of tumor markers, and sentinel lymph node dissection, as well as other surgical procedures in the treatment of breast cancer. Prior to joining Yale, he was the Chief of Breast Surgery and Director of the Johns Hopkins Avon Foundation Breast Center at the Sidney Kimmel Comprehensive Cancer Center. He is also a Commander in the United States Navy Reserve.



Yale CANCER
CENTER
A Comprehensive Cancer Center Designated
by the National Cancer Institute

 **SMILOW CANCER HOSPITAL
AT YALE-NEW HAVEN**

NON-PROFIT ORG.
U.S. POSTAGE
PAID
NEW HAVEN, CT
PERMIT #526

333 Cedar Street, P.O. Box 208028
New Haven, CT 06520-8028



Be part of our mission to bring the world **Closer to Free.**

The **Closer to Free Fund** provides essential financial support for breakthrough cancer research and compassionate patient care by combining the gifts of many donors. Your contribution is critical to ensure that new research can be pursued without delay, promising treatments are aggressively developed, and patient care is continuously enhanced.

closer to free

The fund to advance cancer research and enhance patient care

givecloserstofree.org