

Forward

Broadening the Conversation About Cancer

FALL/WINTER 2015

CUSTOMIZING CANCER TREATMENT

Through Precision
Medicine, Doctors
Can Identify the
Most Effective
Treatment
for Individual
Patients



ALSO

DAN'S VOICE PROVIDES
SUPPORT TO PATIENTS

VOLUNTEERS PLAY IMPORTANT
ROLE AT THE CENTER

LUNG SCREENING PROGRAM
CONTINUES TO THRIVE

 **FOX CHASE**
CANCER CENTER

TEMPLE HEALTH

LOOKING AHEAD

Discovering new advances that will most effectively treat a patient's cancer requires a sophisticated level of focus. This idea helps form the basis of what we know as precision medicine.

In a broad sense, precision medicine is the understanding that physicians can no longer diagnose and treat patients based on broad definitions of diseases, but instead must examine an individual's unique genetic make-up to offer the most effective treatment.

In this issue's cover story, we discuss the future of cancer care and how precision medicine represents a shift in how we think about treatment. This approach builds on Fox Chase Cancer Center's already rich history of innovative research, which includes discoveries like the Philadelphia Chromosome — the first genetic abnormality linked to cancer, which led to the creation of the drug Gleevec for patients with chronic myeloid leukemia. That same drug is now helping others like Barry Dixon (on page 8) to overcome neuroendocrine cancer.

This year, we established an expert panel of clinicians and scientists — the Precision Medicine Steering Committee — to define and carry out the vision for our efforts in this rapidly evolving field. We have unique technologies, significant grants, and leaders of national clinical trials, as well as key research projects underway to support this pursuit.

Also in 2015, Fox Chase was designated a center of excellence in precision medicine by Caris Life Sciences®, an innovative biotechnology company — paving the way for even more collaborations and discoveries among our faculty and through our relationships with investigators both in industry and academia. The goal is to move the field forward by engaging in these exciting new opportunities.

On page 3, you'll learn how advances in identifying genetic mutations linked to Lynch syndrome — an inherited condition predisposing some to a greater risk of colorectal cancer — may help clinicians determine which patients need more frequent screenings.



Fox Chase researchers are also tracking clues as to why some people respond to certain therapies while others do not — despite being diagnosed with a seemingly incurable cancer. This article on “super responders,” found on page 4, explores the research focused on this remarkable subset of patients.

The exciting impact of precision medicine is already being felt, yet more work remains — work that holds great potential for us all.

Richard I. Fisher, MD
PRESIDENT AND CEO

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FEATURES

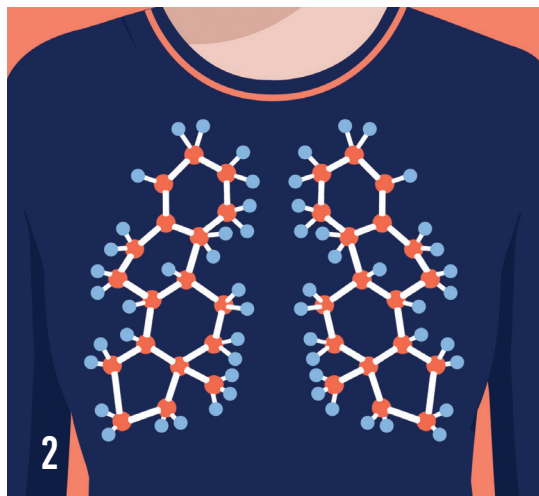
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Precision medicine presents a new way of approaching various diseases, including cancer. Doctors are beginning to treat patients based on individual genetic makeup rather than location of the tumor.
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Brenda Rich wanted to recognize the Fox Chase team who cared for her late husband Dan while he was being treated for throat cancer. As a result, she founded Dan's Voice to raise funds for head and neck cancer treatment.

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Launched in 2011 to help discover lung cancer at an earlier and more treatable stage, the lung screening program continues to expand while servicing the Philadelphia community.



ESTROGEN MAY INCREASE LUNG CANCER RISK IN WOMEN

Recent data pointed to estrogen as a potential culprit behind lung cancer in women, and researchers at Fox Chase Cancer Center are working to find out why that is. Margie Clapper, professor and co-leader of the Cancer Prevention and Control Program, said that her research began when a clinical colleague noted a larger number

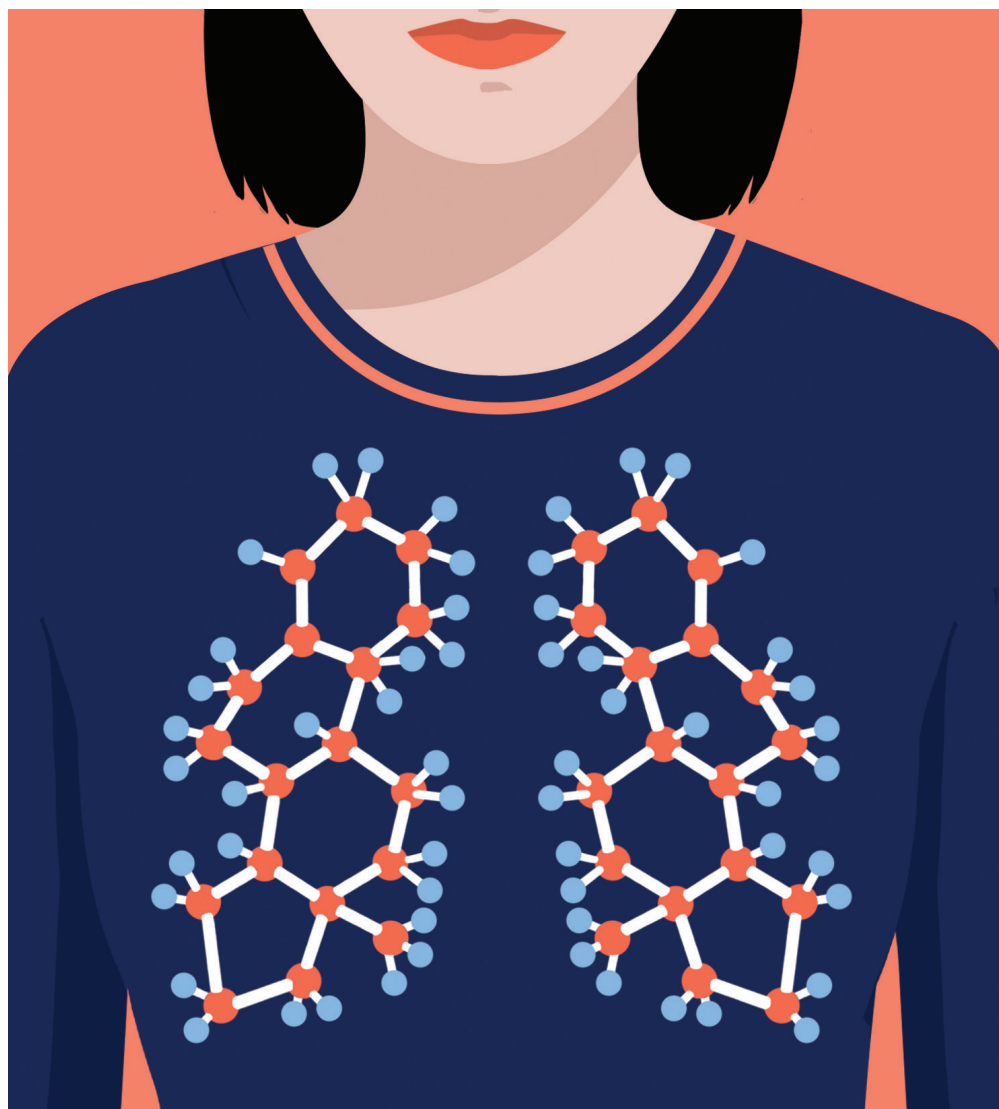
of women required surgery for the disease.

“We wanted to figure out why women seemed to be more susceptible,” says Clapper. “Aside from smoke exposure, there were also many non-smoking women who were affected, and no one understood why.”

Clapper and her team demonstrated that the human lung can

“We wanted to figure out why women seemed to be more susceptible [to lung cancer].”

— MARGIE CLAPPER,
CO-LEADER, CANCER
PREVENTION AND CONTROL
PROGRAM



metabolize estrogen, a female hormone produced naturally by the body, and convert it into a cancer-causing substance. They also found that the levels of “bad” estrogen were higher in women than in men, and its production was accelerated by tobacco smoke.

In collaboration with Grace Ma, director of the Center for Asian Health at Temple University, Clapper also found that Chinese women produced twice the amount of “bad” estrogen as Caucasian women of the same age. “Based on the elevated risk for lung cancer among Asian women, it is critical to determine the role of this estrogen product in lung cancer susceptibility,” explains Clapper.

The goal is to identify women at highest risk for lung cancer because of their capacity to metabolize estrogen and to further explore what other substances in the environment can enhance estrogen metabolism and potentially increase a woman’s risk for lung cancer.

DOES FAMILY HISTORY LEAVE YOU AT A GREATER RISK FOR COLORECTAL CANCER?

Lynch syndrome is one of the most common forms of inherited predisposition for cancer, particularly colorectal. It is caused by mutations in one of several genes that help cells copy DNA correctly. Roland Dunbrack, professor and director of the Molecular Modeling Facility at Fox Chase Cancer Center, and his team strive to make mutations that are linked to Lynch syndrome more easily identifiable. As a result, patients will know if they are at a greater risk for developing colorectal cancer.

“[Researchers] can make more accurate predictions and hopefully inform clinicians on their patients’ level of risk.”

— ROLAND DUNBRACK,
DIRECTOR OF MOLECULAR
MODELING FACILITY

“The challenge is that there are mutations in these genes that are completely benign: they do not affect the function of the genes,” says Dunbrack. “People who are diagnosed with colorectal cancer in their thirties, forties, or fifties are typically evaluated for Lynch syndrome mutations. However, when we sequence the person’s DNA and see a mutation, we don’t immediately know whether this mutation is linked to Lynch syndrome.”



Dunbrack and his team are developing a program to predict Lynch syndrome genes from a large set of mutations found only in the Lynch-associated genes. When new mutations are found in patients, the program compares the properties of the mutation with those in the training data set and makes a prediction on whether the new mutation is harmful or benign.

Their predictor focuses on how mutations affect the structure and function of proteins within the Lynch genes and how the proteins interact with each other as they perform DNA repair. “With these data, we can make more accurate predictions and hopefully inform clinicians on their patients’ level of risk,” Dunbrack says.

CANCER “SUPER RESPONDERS” THRIVE FAR BEYOND EXPECTATIONS

A group of “miracle” cancer patients, known as “super responders,” may hold valuable clues as to why some patients respond exceptionally well to treatment while others do not.

According to Marijo Bilusic, a Fox Chase Cancer Center medical oncologist, a super responder is a patient with incurable disease

were treated at Fox Chase in the hope of identifying genes that may have played a role in their extremely positive responses. “We want to learn about biomarkers that can predict why some patients respond to therapy better than their peers, even when it’s the same cancer under the microscope,” says Bilusic.

Bilusic and colleagues identified

37 patients from Fox Chase for their study, and at the time of publication, the patients’ tissue samples were undergoing genomic analysis. “If you ask any oncologist, there are patients they remember immediately because of their exceptional response,” says Bilusic. “These are patients who were told they have one year to live, and they live several years. There have been

“I continue my normal activities and still work. ... I’m in pretty good health and have been all along.”

— BERNARD CAMINS,
CANCER SUPER RESPONDER

who has a complete response or remission for more than one year after treatment, or someone who has stable disease — no tumor growth — for at least three years. This unique group may also help clinicians and researchers revolutionize the treatment of patients across all cancer types.

Last year, the National Cancer Institute (NCI) launched a study to analyze tissue samples from super responders to find possible molecular reasons for the exceptional response. Now, Bilusic’s team will be launching their own study at Fox Chase — one of 45 NCI-designated Comprehensive Cancer Centers in the country. The researchers are evaluating a group of super responders who



Bernard Camins

COLIN LENTON

“Why did I respond so well? Maybe because I had excellent care and maybe because of divine intervention.”

— MARCELLE SHAPIRO,
CANCER SUPER RESPONDER

some people who live 20 to 30 years with metastatic disease, which is really extraordinary.”

One of Bilusic’s notable super responders is Bernard Camins. In 2009, Camins developed bladder cancer but was successfully treated with robotic surgery. However, in 2013, he developed a 2-centimeter mass on his right scrotal skin, which was confirmed to be metastatic bladder cancer. It spread quickly through his scrotal and groin skin. “Skin metastases from urologic cancers are very uncommon and usually associated with widespread metastatic disease and a poor prognosis,” Bilusic explains.

After one cycle of chemotherapy, the treatment was discontinued due to adverse side effects. Camins then started chemotherapy again. After four cycles, he completed treatment in September 2013 and has been in remission since. “I continue my normal activities and still work,” he says. “I have a computed tomography (CT) scan and see Dr. Bilusic every four months, but I’m in pretty good health and have been all along.”

Sometimes super responders inform future research and trials based upon their responses to treatment. Another super responder is Marcelle Shapiro. In 2010, she was diagnosed with acute myelogenous leukemia (AML). It was

secondary AML resulting from previous treatment with adriamycin, a chemotherapy drug used to treat breast cancer. After six weeks of intense chemotherapy for the AML while in a medically induced coma, Shapiro was in remission. Her family, including her husband and two daughters, were amazed by her recovery. However, that was not the end. “The chances of me maintaining a long-term remission were limited because of my exposure to adriamycin,” says Shapiro, an interventional radiologist.

Patricia Kropf, assistant director of the Fox Chase Cancer Center—Temple University Hospital Bone Marrow Transplant Program, says that Shapiro had an aggressive leukemia that typically has a fairly low chance for a cure. Shapiro received

an intense regimen of induction chemotherapy, consolidation therapy, and a stem cell transplant.

“Response to chemotherapy and transplant ranges across a spectrum,” says Kropf. “Not only has Marcelle been cured of her leukemia, but she tolerated the transplant very well, without significant complications.” She was told she had a 50/50 chance of long-term survival. In 2015, she marked five years being cancer free. Her follow-up includes bloodwork every three months and an annual bone marrow biopsy.

“Why did I respond so well? Maybe because I had excellent care and maybe because of divine intervention,” Shapiro says. “I live moment to moment. I don’t ask questions for which I have no answers.”



Marcelle Shapiro