PATHS OF PROGRESS
Research and Care at Dana-Farber Cancer Institute

STOPPING CANCER IN ITS TRACKS
AN UNCONVENTIONAL APPROACH TO DRUG RESISTANCE

PLUS: BRAIN TUMOR INSIGHTS • BILL KAELIN’S RESEARCH • NEW ERA OF SURVIVORSHIP
Dana-Farber Cancer Institute ...

“Dedicated to discovery ... committed to care” is the mission of Dana-Farber Cancer Institute (DFCI), described as one of the world’s premier cancer centers by the National Cancer Institute. Founded in 1947 by Sidney Farber, MD, Dana-Farber is renowned for its unique blend of basic and clinical research and for using its discoveries to improve the treatment of adults and children with cancer and related diseases. It is a founding member of the Dana-Farber/Harvard Cancer Center – one of 41 nationally designated Comprehensive Cancer Centers. A teaching affiliate of Harvard Medical School, Dana-Farber is also one of 21 federal Centers for AIDS Research in the United States, and is consistently ranked one of the top cancer centers in the country by U.S. News & World Report. In addition, it has earned “Magnet” status for excellence in nursing.

Dana-Farber partners with Brigham and Women’s Hospital to deliver care for adults with cancer through Dana-Farber/Brigham and Women’s Cancer Center. It also has a long-standing alliance with Boston Children’s Hospital to care for pediatric cancer patients through Dana-Farber/Children’s Hospital Cancer Center. By bringing together the strengths of three world-class institutions, these partnerships provide an exceptional level of care for cancer patients and their families.

... and the Jimmy Fund

The Jimmy Fund supports the fight against cancer at Dana-Farber, helping to raise both funds and the chances of survival for children and adults around the world. Named to protect the anonymity of one of Dr. Sidney Farber’s young patients, the Jimmy Fund was established in 1948 by the Variety Children’s Charity of New England in conjunction with the Boston Braves baseball team. Later adopted as the official cause of the Boston Red Sox, the Massachusetts Chiefs of Police Association, and the annual Pan-Massachusetts Challenge bike-a-thon, the Jimmy Fund is widely regarded as “New England’s favorite charity.” Individual and corporate gifts, many of them collected through numerous annual Jimmy Fund events, have helped the organization generate hundreds of millions of dollars for cancer research and care at Dana-Farber over the decades.

10% of all designated gifts will support our Faculty Research Fund to advance Dana-Farber’s research mission.
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Dear Readers,

When we discuss the new era of personalized medicine for cancer, we often speak of therapies that are able to hit specific targets – such as mutated genes or abnormal proteins – in tumor cells. While this description is accurate, it can give the impression that cancer is a static, unchanging opponent with a fixed set of molecular targets. In fact, tumors are dynamic, elusive entities, and the genetic programming within their cells is susceptible to new errors. The result is that treatments that stop the advance of the disease sometimes lose their potency over time, allowing tumors to resume their growth and spread.

As scientists and caregivers, we need to be as nimble as the disease we are confronting – to stay several steps ahead of tumors known for their evasive maneuvers. In this issue of *Paths of Progress*, you’ll read how Dana-Farber scientists are using evolutionary principles to devise treatments and dosing schedules that minimize the chance that tumors, once under control, will regrow.

Other articles in this issue illustrate how strategies for fighting cancer are evolving as a result of scientific advances and of our own success in treating the disease. One story describes Dr. Mark Kieran’s victory over medical orthodoxy that held it was unsafe to biopsy tumor tissue from children with a rare form of brain cancer. His work has paved the way for new targeted treatments to be tested in patients – and ultimately, we hope, for better options for these young patients. Another story focuses on a largely unsung group of pioneers – people who have lived for many years after cancer treatment. As survival rates for many cancers increase, the experiences of these long-term survivors serve as a map for the many who will follow.

Edward J. Benz Jr., MD
President, Dana-Farber Cancer Institute
Dana-Farber Unveils Audio Art Tour

Visitors to Dana-Farber’s Yawkey Center can now take in a contemporary art tour on a visit to the center, or virtually, from their computer. The 40-minute audio tour guides visitors through some of the more than 500 works of art from local and internationally renowned artists.

After checking out an easy-to-use handheld device and a map from the Shapiro Center for Patients and Families, individuals can take the self-guided tour to view original artwork and listen to recorded interpretations of the pieces, with an accompanying musical score.

To learn more or take an online version of the tour, visit www.dana-farber.org/audioarttour.

New Targeted Therapy for GIST Patients

Investigators at Dana-Farber led testing for a new molecularly targeted drug, regorafenib, that may help control metastatic disease in patients with gastrointestinal stromal tumors (GISTs) that have developed resistance to Gleevec and Sutent, the only two FDA-approved drugs available.

Dana-Farber’s George Demetri, MD, designed and led an international clinical trial of the treatment. The phase III trial determined that in patients whose tumors were resistant to Gleevec and Sutent, regorafenib prolonged the time in which the disease was under control by more than 70 percent.

“If approved, regorafenib will fulfill an urgent unmet need for patients with GIST who have exhausted all other treatment options,” said Demetri, director of the Center for Sarcoma and Bone Oncology at Dana-Farber/Brigham and Women’s Cancer Center.

It appears to target GIST tumors in a different and possibly more powerful way than the current FDA-approved therapies, making it a potentially significant new option to help patients.”

Regorafenib targets abnormalities in cancer cell signaling pathways driven by an abnormal enzyme called KIT. The drug shuts off the switch that keeps the cancer cells alive and growing, resulting in disease control.

In the News

This year’s annual “Best Hospitals” guide from U.S. News & World Report, published in August, again ranked Dana-Farber/Brigham and Women’s Cancer Center as the top cancer center in New England and fifth overall in the nation.

The magazine also ranked Dana-Farber/Children’s Hospital Cancer Center as the top pediatric cancer hospital in New England, second in the nation, in its 2012-2013 “Best Children’s Hospitals” guide.

The annual “Best Hospitals” guide provides a reference for patients who are reviewing their medical care options. In addition to cancer, the guide ranks medical facilities in 15 other specialties. The overall score a hospital receives is based on professional reputation, mortality rates, patient safety, and a grouping of care-related factors, such as nursing and patient services.
Profile Enrolls More Than 10,000 in First Year

The Profile cancer research project, launched last year by Dana-Farber and Brigham and Women’s Hospital, is helping accelerate the development of personalized treatments for people with cancer. Considered one of the world’s most comprehensive cancer research studies, more than 10,200 adult patients have enrolled in the study since its inception in August 2011.

Patients who agree to participate in Profile have their leftover tumor tissue screened for 471 mutations, in 41 genes, that are known to be linked to cancer. A small number of people who participate in the study will have “actionable” genetic mutations in their cancer. For these patients, a particular drug may be known to be effective for the cancer mutation identified, and this information may be useful for the patient’s care. A second group of patients who participate will have “potentially actionable” genetic mutations – genetic alterations for which new drugs are being tested for safety and efficacy in clinical research trials in which these participants may be eligible to enroll. Still, for most participants, the value of enrolling in the study is in helping future cancer patients in their fight against cancer.

“Most patients who enroll in Profile are unlikely to benefit directly from the study, but they are helping many others who will be diagnosed with cancer in the future,” says Barrett Rollins, MD, PhD, Dana-Farber’s Chief Scientific Officer. “It’s an effort to build an unprecedented genomic database for studies that seek to improve the effectiveness, safety, and precision of future cancer treatments. Over time, we’re optimistic that this growing body of information will help us discover more about the genetic causes of cancers and increase the development of new, targeted therapies to treat them.”

For more information about Profile, visit www.dana-farber.org/profile.
Voices from Dana-Farber: On Optimism

“Too often we fail to appreciate the amazing progress going on around us. Incredible leaps in cancer biology are allowing us to identify many new cancer subtypes. It’s a golden age.”

Harold Burstein, MD, PhD
a physician in the breast cancer treatment center at Dana-Farber/Brigham and Women’s Cancer Center, on why he’s optimistic about the future of cancer care and treatment.

“We are on the brink of a whole new era in cancer treatment and prevention, but in breast cancer we are building on the research of the last 40 years. We must maintain the momentum, and make breast cancer something women ‘used to have.’”

Judy Garber, MD, MPH
director of Dana-Farber’s Center for Cancer Genetics and Prevention, on why she sees a bright outlook for breast cancer treatment and research.

“We’re getting so much better at tailoring our treatment to the type of breast cancer patients have. The vast majority of patients will survive breast cancer, almost certainly in the short term, and most in the long term.”

Ann Partridge, MD
director of Dana-Farber’s adult survivorship program and oncologist in the breast cancer treatment center at Dana-Farber/Brigham and Women’s Cancer Center

“We’ve made strong advances in treatment, resulting in great outcomes for the majority of childhood cancer patients. For example, the survival rate for the most common pediatric cancer diagnosis is now at more than 90 percent.”

Lisa Diller, MD
chief medical officer and clinical director of Pediatric Oncology at Dana-Farber/Children’s Hospital Cancer Center

Get ‘Paths of Progress’ on the Go

Read about the latest cancer research and treatment on your tablet device, such as an iPad, or on your e-reader, such as a Kindle or Nook.

The interactive edition of Paths of Progress includes all of the content from the print issue, along with special, digital-only enhancements including photo galleries, videos, and more.

Download the Paths of Progress app from the iTunes app store or the Android marketplace (search for “cancer research”). You can also find an e-reader version of the magazine at the Kindle and Nook stores.

Links to the interactive versions, along with a downloadable PDF, are available at www.dana-farber.org/pathsofprogress.
Researchers Activate Cellular ‘Death’ Protein

In a study published in *Nature Chemical Biology*, scientists led by Dana-Farber’s Loren Walensky, MD, PhD, identified a prototype compound that directly activates one of the most powerful cell death proteins, known as BAX, which triggers apoptosis, or self-destruction of unwanted cells. The development could represent a new approach to designing future cancer drugs.

The research exploited the discovery by Walensky’s team of a distinctive groove, or “trigger site,” that activates the BAX protein. When activated, BAX damages the cell’s mitochondria (the cell’s power producers), releasing signals that break the cell apart and digest its pieces. This programmed cell death is part of a natural check-and-balance mechanism to control cellular life and death.

Investigators used computer-based screenings to search for molecular compounds that could jump-start BAX. A small-molecule compound named BAM7 (BAX Activator Molecule 7) was identified, which selectively bound to BAX and activated it.

In search of molecular compounds that could fit snugly into the trigger site and jump-start BAX, the investigators used computer-based screening to sift through 750,000 small molecules from commercially available libraries.

The Walensky group has developed other compounds designed to spur apoptosis of cancer cells, but BAM7 is the first one that avoids combat with cancer cell’s survival proteins and binds directly and selectively to BAX to turn on cell death.

There are concerns that switching on cell-death proteins in a patient would kill normal cells as well as cancer cells, but the researchers say that other compounds now in clinical trials that target the apoptosis pathway haven’t shown such side effects.

Connect with Dana-Farber Online

Whether it’s through Facebook, YouTube, or Twitter, connecting with Dana-Farber online has never been easier. You’ll find our “Insight” blog at www.blog.dana-farber.org/insight, or keep in touch through your favorite social networking sites, such as Google+, Pinterest, or YouTube.

Visit us online at www.dana-farber.org/socialmedia to find links to all of our social media sites, then follow us to keep up with the Institute’s latest news and research, while showing your support for vital research and patient care.

13.7 million Cancer survivors living today in the U.S., according to a report from the American Cancer Society and the National Cancer Institute

18 million Estimated number of cancer survivors living in the U.S. by 2022

10 Years that Dana-Farber’s Mammography Van has been providing breast screenings to women throughout the Boston metropolitan area

31,000 Mammograms performed in Dana-Farber’s Mammography Van since the program’s inception

79 Breast cancer diagnoses confirmed in returning patients on Dana-Farber’s Mammography Van

248 Registered nurses who staff Dana-Farber’s outpatient units

15,000 Average number of people diagnosed each year with myelodysplastic syndrome (MDS), a rare blood and bone marrow disorder. Good Morning America host Robin Roberts this year announced that she has MDS and will undergo a bone marrow transplant to treat the condition.

594 Dana-Farber faculty members who hold one or more advanced degrees (MD, PhD, or both an MD and a PhD)
Bruce Spiegelman, PhD

Dana-Farber’s Bruce Spiegelman, PhD, is a cell biologist at a cancer center. Yet, he’s widely recognized for discoveries relevant to diabetes, obesity, and insulin resistance. Spiegelman explains how research into the fundamental processes of life connects cancer with a variety of other diseases.

Q: What was your original focus as a cancer researcher?

A: I was interested in how cells develop into more differentiated cells with specific roles. Cancer cells have regressed from this differentiated state into a more primitive one. I was using fat cells as a model to investigate how differentiation is regulated – knowledge that could be useful in the treatment of cancer.

Q: How did this lead you to other diseases?

A: Fat cells are important in how the body maintains a balance between food intake, energy storage, and energy expenditure. Imbalances of the system are involved in metabolic problems such as diabetes, insulin resistance, and obesity. So we began to study energy metabolism and discovered some of the molecular switches that control it – and how, for example, they are affected by drugs used to treat diabetes. We’ve also learned what causes some cells to become white, energy-storing fat cells while others develop as brown or beige fat cells that burn energy and may be useful for weight loss.

Q: Are these findings having an impact in treating metabolic diseases?

A: Our findings have helped to explain how certain diabetes drugs work and also how exercise improves the metabolic status of mammals.

Q: So your discoveries are having real-world applications to metabolic diseases, even as you look for solutions to cancer?

A: Yes. We didn’t set out to do that, but we’re very glad to make an impact in biomedicine where we can. And it also works the other way – we now know that diabetes and obesity are major risk factors for cancer; that wasn’t appreciated when I started. By studying fat cells, we’ve learned that they’re not just containers for storing calories. Particularly in obese people, the cells secrete chemical signals that cause inflammation in the body’s tissues in organs, and inflammation is increasingly being implicated in cancer development.

Q: That means people should control their weight and blood sugar in part to reduce cancer risk?

A: It certainly does. And considering the problem of childhood obesity in this country, adopting lifestyle changes to maintain a healthy weight could help lower the risk of cancer over a lifetime.

Q: Should funding for research include basic science, even when it’s not directly aimed at finding, say, a cure for cancer?

A: That’s right. There are a lot of things we don’t know about cancer biology, and it would be a mistake to treat curing cancer like an engineering question with a very specific game plan that has already been worked out. It’s extremely important to recognize that breakthroughs in cancer biology have come from studies in other fields.
Cancer is the cagiest of diseases, notoriously hard to corner. Even when medicine sends a tumor into retreat, the disease often finds a way to return. Science’s response to this phenomenon, known as drug resistance, is personified by researchers like Dana-Farber’s Jean Zhao, PhD, who study the basic workings of cancer to uncover its weaknesses.

For Zhao and her colleagues, drug resistance is less an unalterable fact than a stimulus to new thinking. Much of Zhao’s research focuses on HER2-positive breast cancer, named for a receptor that crowds the surface of the cancer cells. The HER2 molecule stands at the head of a long network of proteins that transmit growth signals within the cell. Although drugs like Herceptin work well against HER2-positive breast cancers, the drugs often lose effectiveness over time, allowing tumors to resume growth.

Zhao and other researchers in the field have found that, in many of these Herceptin-resistant tumors, the culprits are proteins known as PI3 kinases, which take over the growth-signaling duties from the incapacitated HER2 molecule. Biotech and pharmaceutical firms responded by developing drugs that specifically target PI3 kinases.

When Zhao tested PI3 kinase inhibitors in mice, she found that the drugs drove up insulin levels in the blood and harmed bone marrow, potentially dimming their prospects for use in humans. She wondered if drugs that targeted just one version – or “isoform” – of PI3 kinase would have an anti-tumor effect without causing harm to the body.

“When we eliminated the gene for one of these isoforms, known as p110α, in mouse models of HER2-positive breast cancer, tumor formation was blocked,” Zhao relates. “But, surprisingly, when we eliminated the gene for the p110β isoform of PI3 kinase, tumor formation actually increased.”

The results suggest that drugs targeting just p110α may have the best chance of success in patients with Herceptin-resistant breast tumors. But Zhao knows tumors may become resistant to even these agents. She’s currently analyzing such tumors to find misbehaving genes which might make good targets for future therapies.

“Cancer cells are incredibly resourceful,” she says. “It’s a constant challenge to develop therapies that can close off the cells’ escape routes.”

As such therapies are developed, it’s critical that scientists such as Zhao work closely with clinical researchers testing the agents in patients. Zhao and her colleagues established precisely that kind of working relationship with Eric Winer, MD, and other Dana-Farber researchers.

“We love questions from Eric’s team,” she says. “The give-and-take between us makes progress possible.”
Eric Winer, MD, used to tell audiences that getting lab scientists and clinical researchers to collaborate in the area of women’s cancers was like making a vinaigrette: “Our job was to bring them together and shake things up so the boundaries disappeared.”

It’s an analogy that’s no longer valid, he says. Over the past 15 years, Winer and others at the Susan F. Smith Center for Women’s Cancers at Dana-Farber/Brigham and Women’s Cancer Center (DF/BWCC) have created an environment in which collaborations between lab and clinic tend to arise naturally through the everyday interactions of scientists, without the need for outside intervention.

“Scientists and clinicians used to inhabit different worlds,” explains Winer, director of the Breast Oncology Center at DF/BWCC. “Today, researchers are apt to know a bit about the clinical world and clinicians know something of cancer biology. It allows for a degree of give-and-take that results in better research and therapies.”

As a clinical researcher, Winer has found that, as science reveals more about the molecular workings of cancer cells, his own interest in basic cancer biology has increased as well. This is particularly true for research that produced targeted agents that shut down the genetic pathways cancers use to grow and spread.

Currently, Winer is most involved in clinical trials of drugs for two types of breast cancer whose very identities were uncovered through molecular research – HER2-positive cancers and triple-negative cancers. He and his colleagues investigate many new treatments for HER2-positive cancers, including trials that test T-DM1, a tandem therapy of a targeted drug and a powerful chemotherapy agent. For triple-negative cancers, investigators in the program conduct trials of agents known as PARP inhibitors and of the chemotherapy agent cisplatin.

Increasingly, new cancer treatments are built on a finer-grained understanding of the underlying biology of the disease. As a consequence, clinical trials are more complex and valuable, Winer notes. “We try to learn as much as possible from every patient who enrolls on a trial.”

The generosity of a patient’s choice to join a clinical trial to benefit future patients is never lost on Winer. It’s even memorialized in his title. In 2007, when an investigatorship was created to support his research, Winer chose to honor the first patient he enrolled in a trial of the drug Herceptin as a single agent for breast cancer. Within days of the start of treatment, her disease, which had been advancing rapidly, began to regress – a first hint of Herceptin’s effectiveness against her form of cancer.

Today, Winer is the Elizabeth Thompson Senior Investigator in Breast Cancer Research. ■
EVOLUTION

BY ROBERT LEVY
What survival of the fittest teaches us about drug resistance
In the words of Dana-Farber scientist Franziska Michor, PhD, “Why should cancer be the one exception to this rule?”

The notion that tumors are subject to the same evolutionary forces as the necks of giraffes and the wings of hawks has intrigued cancer scientists for nearly a century, but only in recent years, with the introduction of technology for speed-reading the DNA of cells, have researchers been able to capitalize on it. An evolutionary perspective allows scientists to study how tumors change and adapt over time – how they respond to stress and, potentially, how their impetuous behavior can be tamed with therapies.

At Dana-Farber’s Physical Science-Oncology Center (PS-OC), where Michor is principal investigator, researchers use this approach to tackle some key questions about cancer. One project is examining the mechanisms by which gene alterations accumulate in cancer cells, information that can help doctors predict how the disease will progress and which therapies are likely to be most effective against it. Another project aims to identify the cells at the root of human cancers. Researchers are exploring whether cancer originates in stem cells – the living clay from which other cells arise – or in the more “differentiated” cells that comprise the body’s many organs and tissues.

It is in the realm of drug resistance, however, that the PS-OC is set to have its most immediate impact on the treatment of cancer patients. Resistance, the process by which tumors bounce back from drugs that once were detrimental to them, has long been a weak point in cancer therapy, limiting survival rates and often dampening the promise of new treatments. Using evolutionary principles, with a generous assist from applied mathematics, Michor and her colleagues have devised a strategy for slowing or even halting drug resistance in certain patients.

“We’re interested in determining which genetic alterations cause cancer, which increase cancer cells’ ability to reproduce and spread, and how we can use that knowledge to improve treatment,” says Michor, who helped establish the PS-OC at Dana-Farber in 2009. “By applying evolutionary theory to the study of cancer cells, we want to identify the mutations that are driving the disease – and make the best targets for new therapies – and those that are simply ‘passengers.’”

Michor’s unconventional approach to biological science reflects her unique background. The daughter of a mathematician father and a nurse mother, she earned a PhD from Harvard at age 22. She “wanted to combine the area of expertise of my father with the humanitarian mission of my mother, to help come up with a quantitative approach to cancer.”

**Group Dynamics**

To understand how evolution can shed light on drug resistance, it’s useful to view cancer from a different vantage point than the customary focus on individual cells. It requires a closer look at group behavior – at how populations of cells are shaped by their environment – and a reckoning with forces that extend far beyond the life of a single cell.

In one sense, cancer represents
Mathematics provides a language for Franziska Michor, PhD, to understand genetic change in cancer cells.
a turning back of the clock about 3.8 billion years, to a time when life is thought to have first appeared on earth. The original life forms were single-celled creatures whose sole concern was their own survival and reproduction. Footloose and unencumbered, they had no need to coordinate their activities with any other cell. That changed with the rise of multicellular life in the Precambrian period about a billion years ago, when cells had to form “pacts” to cooperate with one another for the good of the entire organism.

“Cancer represents, in essence, the breakdown of this pact,” Michor remarks. “With cancer, we have cells that behave as if they’re not part of a multicellular organism anymore. They’re selfish: they ignore all the commands that are meant to keep the agreement intact.”

Tumors result from mutations in genes that are the guardians of this pact. When enough mutations have occurred in genes that restrain a cell’s growth or prevent it from invading neighboring tissue, the cell becomes an outlaw, a renegade cancer cell.

If evolution once led cells to organize into multicellular creatures, it also, by a perverse logic, underlies the development of cancer cells, which can sometimes be hardier and scrappier, better equipped for survival than normal cells are.

**Subtle Differences**

When thinking about how evolution operates on cancer – and how it can be turned to therapeutic advantage – it helps to recognize that tumors are not collections of identical cancer cells, but aggregations of different kinds of cancer cells, some differing only very slightly from the others. “Cells within a tumor are always evolving, always acquiring new mutations,” Michor explains carefully. “Some have Mutation A, some may have Mutation B – there can be an enormous variety. Each population of cells responds to drug agents differently.”

In classic evolutionary fashion, the cells not killed by a particular drug gradually come to dominate a tumor as their more-susceptible cousins die. These resilient cells pass their survival skills on to their offspring. Over time, a drug that originally decimated cancer cells becomes powerless against a more transformed tumor.

“Evolutionary pressures drive these tumors to be more and more aggressive and invasive,” Michor says. “The thrust of these pressures is toward the benefit of the tumor but the detriment of the patient.”

The good news is that unlike earlier generations of cancer scientists, today’s researchers have developed...
The results: the one-a-day schedule was not the best of all the alternatives for delaying the emergence of resistance. The optimal schedule, which pushed resistance back the furthest, is now being put to the test in a clinical trial. Patients will take the drug according to either the standard or the new, optimized schedule, and researchers will track which group develops resistance first.

“Mathematical modeling of this type won’t replace clinical research or animal studies of cancer,” Michor observes. “But it provides a tool for speeding up the process of determining which treatment method may be most effective.”

If that tool proves to be a hybrid approach as distinctive as Michor’s own background and ambition, few will be surprised.


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Dana-Farber scientist Kornelia Polyak, MD, PhD, remembers reading *The Beak of the Finch*, a book about two researchers who observed evolution unfold among certain songbirds on the Galapagos Islands, and thinking, “This could be applied to tumors.”

A self-described “fan of evolution,” Polyak has made several trips to the Galapagos, a group of islands off the coast of Ecuador famous as the inspiration for Charles Darwin’s theory of evolution by natural selection. The visits have not only fed her fascination with the diversity of life but also stimulated her interest in the behavior of cancer cells.

In the mid-2000s, Polyak met a similarly evolution-minded scientist, Franziska Michor, then a graduate student in Harvard’s Evolutionary Biology Department, now the principal investigator at the Physical Science-Oncology Center at Dana-Farber. Their conversations “evolved” into a full-fledged partnership that has resulted in several research projects in recent years.

In one study, they explored the order in which genetic alterations occur in certain types of breast cancer, information that may improve doctors’ ability to detect the disease in early stages, gauge a patient’s degree of risk, and even prevent the disease. In another study, they found that cells within a single breast tumor are far from identical in terms of the genetic mutations they carry, suggesting that such tumors may best be treated with several mutation-targeting drugs.

“The idea that evolution plays a role in the growth and development of tumors is not new, but our ability to study it at a molecular level is,” Polyak says. “The better we understand heterogeneity – the genetic and non-genetic diversity of cells within a tumor – the smarter we can be about selecting the best treatment.” –RL

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**An ‘Evolving’ Partnership Yields Success**

models that describe in a very precise way how this evolutionary process unfolds. The core of these models, the language in which they are written and the physical laws they express, is a set of mathematical formulas.

In retrospect, Michor relates, it’s bewildering that math has come so late to the study of the basic biology of cancer. After all, “Math permeates everything; it’s the foundation of physics, we use it to map the movement of the stars,” she comments. “It gives us a set of rules for describing physical forces and making predictions. Why hasn’t it been used more widely in medicine?”

In devising equations to study drug resistance in cancer, Michor and her colleagues accounted for several factors: the rates at which mutations arise in populations of cancer cells, and the growth and death rates of cells exposed to different doses of a drug. The formulas – all algebraic symbols and Greek letters, like something scrawled on the blackboard of a physics lab – allow researchers to calculate the chance that drug resistance will occur, and how quickly.

In a recent study, Michor’s team used their mathematical modeling strategy to predict how frequently a drug targeting a common form of lung cancer should be taken to slow or even prevent the emergence of resistance. “What if, instead of one pill a day, every day – the dosing schedule approved by the Food and Drug Administration for this agent – patients would be better off taking two pills every second day, or three every third day, or some other combination?” Michor asks. The model allowed researchers to test millions of different possibilities simply by running the variables through a computer.

The results: the one-a-day schedule was not the best of all the alternatives for delaying the emergence of resistance. The optimal schedule, which pushed resistance back the furthest, is now being put to the test in a clinical trial. Patients will take the drug according to either the standard or the new, optimized schedule, and researchers will track which group develops resistance first.

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TURNING CANCER ON ITS HEAD

How neurosurgical and molecular biology advances – and one doctor’s dogged pursuit – have changed the way we think about brain stem tumors.

Pictured left: Digitally enhanced scans of a female brain, using magnetic resonance imaging.
Hamstrung. That is how Mark Kieran, MD, PhD, felt when treating children diagnosed with diffuse intrinsic pontine glioma (DIPG), a rare and deadly form of childhood brain cancer.

Little is known about DIPG tumors because, for a long time, no one was able to look inside them. The tumors grow aggressively in the pons, a nub in the brain stem at the base of the head, making biopsies particularly risky. “The brain stem is the nervous system’s central relay station,” says Liliana Goumnerova, MD, director of Neurosurgical Oncology at Dana-Farber/Children’s Hospital Cancer Center (DF/CHCC). “It is so condensed that, if you injure even a small area, it can cause devastating effects.”

Attempts to biopsy these tumors stopped in the 1980s because, far too often, the surgery resulted in paralysis and death. When it came to pontine gliomas, the dogma among neurosurgeons was clear: Do not touch them.

When biopsies stopped, so did progress in treating DIPG. About 200 children in the United States, typically between ages 4 and 10, are diagnosed with DIPG each year. For the last three decades, no treatment has increased survival times for those young patients. Without biopsies, researchers can only examine tumors after the fact, at which point the tumor has been changed by radiation and chemotherapy, leaving doctors with little but guesswork and frustration.

Shifting the Tides

In 2003, Kieran, director of Medical Neuro-oncology at DF/CHCC, started lobbying to reintroduce DIPG biopsies to learn more about the disease and guide therapy. By then, surgical advances had made brain stem biopsies, which surgeons perform for other types of cancer and other conditions such as infection or multiple sclerosis, less risky.

While serious complications are still possible, modern techniques significantly lower risks by increasing precision and accuracy. Surgeons create a 3-D map of the tumor using magnetic resonance imaging (MRI). Computers then generate a point of entry at the skull base and map a safe needle trajectory to the tumor. Surgeons use laser sights and computer guidance to track the needle throughout the 2- to 3-hour procedure.

Despite the advances, no one wanted to consider DIPG biopsies. Year after year, Kieran stood up at conferences in front of fellow oncologists and neurosurgeons and presented his idea. And year after year, his colleagues were unmoved. “We thought that after 30 years of abject failure, people would be desperate to consider something new,” says Kieran. “I guess they call it dogma for a reason. It is not easy to change.”

The frustration grew, but Kieran did not stop trying. Then, in 2007, French surgeons broke ranks. They biopsied 24 children with DIPG with no mortality and only two complications. Soon after, Kieran convinced neurosurgeon Nalin Gupta, MD, PhD, from the University of California at San Francisco, to join him in advocating for change. For the first time, people were receptive. “Asking a surgeon to propose a surgical procedure was a fundamental twist,” says Kieran.

Meanwhile, tumor tissue was becoming diagnostically valuable. Researchers started analyzing tumor tissue to identify oncogenes, genetic drivers of cancer that can be targeted by drugs. Today’s technology allows decoding of a tumor’s entire genome using just a tiny sample of tissue. “The surgeons made it so getting the sample wasn’t as risky and the molecular biologists made it so we can actually learn something,” says Kieran. “The two together made it possible to move forward.”

Finally, in December 2011, Kieran and his colleagues received approval to start a phase 2 clinical trial to biopsy tumors of children with DIPG, test them for two molecular markers, and assign the children to one of four treatment strategies based on the results. The trial is now open at DF/CHCC. Nineteen other centers...
out what’s going on and we’re going to help other kids.”

Hailey’s biopsy, performed by Goumnerova in mid-December, went smoothly. As with all participants in the trial, Hailey will receive radiation therapy for 6 weeks and a drug called Avastin, which restricts the growth of blood vessels in and around the tumor, for one year. The doctors will use the biopsy to test for the presence of two proteins that indicate whether either or both of two additional drugs might be beneficial.

The immediate aim of the trial is to determine if any of the treatment strategies improve survival. “We used to treat everyone the same,” says Goumnerova, who helped design the surgical protocols for the trial. “It is very exciting to be able to test for genetic abnormalities and assign each patient personalized therapy.”

The trial will also scan the tumor tissue in an effort to find new molecular targets and, potentially, new drugs to treat the disease. For the families supporting this trial – all $2.5 million in funding came from family foundations – this effort brings hope that future families who face a DIPG diagnosis will have better treatment options.

So far, Hailey is doing well and has even shown some improvement with radiation. Her family is hopeful, but realistic. “There was never a question about the trial,” says Jeannie. “What if somebody had done this 10 years ago and it saved Hailey?”

**The Road Ahead**

While only a handful of children have signed on to Kieran’s trial, he has already – with the help of the pioneering French surgeons – begun to use tumor samples to better understand pontine gliomas. In 2011, Kieran convinced the French surgeons to share 20 of their samples with him. Molecular analysis of those samples revealed that about 20 percent expressed a mutation in the PI3K pathway, a cellular signaling pathway that controls cell death. That same mutation has been seen in other forms of cancer.

Kieran is now working with the pharmaceutical firm Novartis, which has developed an experimental drug that targets that pathway, to design a phase 1 clinical trial to test the safety of this drug in children confirmed – based on their biopsies – to have the PI3K mutation. “It’s a proof of principle that this whole strategy could work,” says Kieran.

It also stands as proof of the power of persistence, and how Kieran’s relentless pursuit may soon begin to offer promise to a group of patients who once had none.

Watch Mark Kieran, MD, PhD, Discuss Advances in Pediatric Brain Cancers: Visit www.bit.ly/TrNzJY.
Cancer is caused by mutations—changes in the DNA—allowing cells to grow uncontrollably. Somatic or spontaneous mutations occur randomly in body cells during life and aren’t inherited. Germline mutations are present in every cell of a person at birth, and account for cancers that “run in families.”

It typically takes mutations in both copies of a cancer-causing gene to trigger a tumor. Germline mutations affecting one such copy in every cell creates a high risk that a second, somatic mutation will occur randomly early in life to cause cancer.

Individuals lacking germline mutations have a lower risk, but may still develop cancer from two somatic mutations occurring at different times.
Later on, a somatic mutation occurs on the other chromosome.

Later in Life

Somatic (Spontaneous) Mutation

Sometime after birth, a somatic mutation hits one chromosome.

Later on, a second somatic mutation occurs.

Cancer

Somatic (Spontaneous) Mutation

Cancer
The Vision of Bill Kaelin

BY RICHARD SALTUS

Initially, Dana-Farber’s William G. Kaelin Jr., MD, thought he would be a full-time doctor. He loved the puzzle-solving challenges associated with clinical medicine and the gratification of treating patients. He was intrigued with cancer biology from an early age and had also contemplated a laboratory-based career. But some discouraging experiences in the lab – one lab closed down four months after he moved in – led Kaelin to decide he was better suited to taking care of patients.

“I was getting sign after sign that laboratory research was not for me,” he says.

However, a sobering year on the front lines of cancer care proved a powerful eye-opener – and a reminder of what drew him to research in the first place.

“It became painfully clear that the treatments we had were inadequate,” says Kaelin of that period, more than 20 years ago. “But at the same time there was an explosion in cancer biology, with the potential to have a deeper molecular understanding of cancer, and to translate that knowledge into more-effective therapies.”

He returned to the lab with a renewed sense of purpose, committed to using genetic tools to go after major cancers that had resisted most therapies and remained poorly understood.

It was the beginning of Kaelin’s prominent career as a cancer biologist and as an adviser on cancer research, not just among his colleagues and collaborators at Dana-Farber, but also in government science circles (such as the National Cancer Institute), high-level scientific meetings, and the boardrooms of drug companies that are trying to figure out what the next generation of cancer drug targets should look like.

What makes Kaelin particularly effective, colleagues say, is an unusual gift for seeing the essence of the problem and crystallizing a discussion with a penetrating comment or question.

“He sees things more clearly than other people,” says Barrett Rollins, MD, PhD, Dana-Farber’s chief scientific officer. “You’re in a seminar and Bill will raise his hand and ask a question and you think, why didn’t I see that or ask that?”
Molecular discoveries led by William Kaelin, MD, have won major awards in areas beyond cancer.

Kaelin serves on the Institute’s Executive Committee for Research, where, Rollins says, “He brings to the table a rational view of what we should be doing with our resources at Dana-Farber – and he does the same thing for the cancer research community at large.”

Kaelin’s accomplishments and promise have been recognized across the scientific community. The Howard Hughes Medical Institute, a major non-government supporter of cutting-edge biomedical research, named him an Investigator in 1998 and funds a portion of his laboratory. He is also a member of the National Academy of Sciences and the Institute of Medicine. Recently, Kaelin received two prestigious awards for a landmark discovery about how cells sense oxygen, and how that mechanism is hijacked in kidney cancer.

A Breakthrough Discovery

Kaelin, who joined Dana-Farber faculty in 1991, projects intensity. Tall and rangy, with slightly graying hair and a youthful face, his eyes convey clarity and focus. His manner and speech are precise and terse, yet tinged with a dry sense of humor. He can seem intimidating, quick to home in on flaws when his postdoctoral fellows and students present research updates.

“It’s something you get used to,” sighed one postdoc after running a gauntlet of sharp questions from his mentor.

Kaelin’s precision has been honed by nearly 25 years of focused cancer research. He came to Dana-Farber for an oncology fellowship in 1987, when he saw patients in the clinic and was drawn back to laboratory research. Not only had he realized that patients above all needed new treatments based on biological research findings, but he had the “sheer luck,” he says, of joining the lab of David Livingston, MD. “He was the ideal mentor and it was the ideal environment to work on important and interesting problems,” Kaelin says.

Livingston, who now heads the Executive Committee for Research, is known for research on tumor suppressor genes, including the RB gene which, when mutated, causes retinoblastoma, a childhood eye cancer. Tumor suppressor genes produce proteins that halt the growth of damaged cells before they can form tumors. In cancer, mutations in these genes are often responsible for out-of-control cell growth.

In Livingston’s lab, Kaelin isolated a protein called E2F, which promotes cell proliferation. E2F is normally kept in check by the RB tumor suppressor protein, but cells harboring a mutant RB divide uncontrollably, leading to retinoblastoma tumors.

In 1992, Kaelin, now in his own laboratory, read about the isolation of VHL, a tumor suppressor gene which is mutated in a cancer syndrome called von Hippel Lindau disease. Kaelin knew about the syndrome from his clinical training. Patients with von Hippel Lindau typically develop kidney and other cancers that, curiously, involve an overproduction of red blood cells and new blood vessels. To Kaelin, it looked like the cancers were acting as if they were low in oxygen – although they were not.

Studying VHL led Kaelin to his most acclaimed discovery – identifying the molecular explanation to a long-standing biological puzzle: How
does the body sense and adapt to changes in oxygen – for example, when people adjust to thinner air at high altitudes?

Pursuing this question, he discovered that the VHL protein normally helps regulate the levels of an oxygen-sensitive protein called HIF, which can trigger or suppress the production of red blood cells and the formation of new blood vessels, and discovered the molecular switch that renders HIF oxygen-sensitive. Cancer cells with mutated VHL genes commandeers this system to surround themselves with new blood vessels – a process called angiogenesis – to feed their growth.

Kaelin’s insights in the mid-1990s, along with findings by two other scientists, earned the trio the 2012 Canada Gairdner International Award and the Grand Prix of the Fondation Lefoulon-Delalande from the Institute of France in June 2012, for contributions to the field of cardiovascular research.

“Discovering the molecular basis of oxygen sensing by cells has turned a whole field’s head around,” comments Livingston. It has already led to experimental therapies being tested for treating cardiovascular diseases like heart attack and stroke, and potentially anemia as well.

Moreover, Kaelin’s linking of VHL to the overproduction of blood vessels led him to propose treating kidney cancer with drugs that block angiogenesis. They are now approved for kidney cancer.

The oxygen-sensing mechanism “turned out to be simpler than many anticipated; there were a number of competing theoretical models, and they were much more complicated,” Kaelin said. The mechanism, in fact, involved a type of chemical modification that had never before been observed in a cell.

The Kaelin lab continues to study tumor-suppressors as a window into the biology and behavior of cancer and a strategy for next-generation therapies. For example, it might be possible to develop drugs that mimic the behavior of a tumor-suppressor protein. It might also be possible to design methods of killing only cells in which a particular tumor suppressor protein has been inactivated (thus sparing normal cells).

Kaelin remains optimistic that cancer research is moving in the right direction, and though progress has been incremental, brighter days lie ahead.

“We’re at a critical point with targeted therapies – exactly where we were with TB and AIDS, when we could only treat those diseases with single agents,” he observes. “I’m stunned when people are surprised that success with new single targeted drugs is so short-lived. Anyone would have predicted that.

“There’s no question that we’re on the right track with targeted therapy,” he adds. “But we have to combine those therapies and use them earlier.”

Given the high esteem in which Kaelin’s ideas are held, his optimism should be reassuring.

Watch Dr. Kaelin explain how cells sense changes in oxygen availability: Visit www.bit.ly/NVwZNf.

Illustration: How cells adapt to oxygen levels. The VHL protein (shown in red) regulates the HIF protein, which can increase red blood cell production and raise oxygen levels. In normal conditions (left), an oxygen-hydrogen molecule (black ball) modifies HIF so that VHL can mark it for destruction. In low oxygen (right), VHL does not mark HIF, so it goes to the nucleus to raise oxygen levels. Mutations in the VHL protein can cause von Hippel Lindau disease and kidney cancers.
Going the Distance

A New Era of Survivorship
The estimated 13.7 million cancer survivors today will grow to nearly 18 million in the next 10 years, according to a report by the American Cancer Society and the National Cancer Institute. Aided by genetic breakthroughs and clinical trials, decades of focus primarily on cures are helping more people live longer.

For many cancers where survivorship was once measured in months, people are now living far longer after treatment. The reasons vary: advances in surgical techniques; better and more targeted chemotherapy and radiation; improved follow-up care; more advanced screening procedures; and a better understanding of the role diet and exercise play in survivorship.

And while this success offers proof that research and enhanced treatment are making a major impact, it also hints at a growing challenge. There is a mounting need to address the myriad physical, emotional, and psychosocial challenges that can arise in the years after initial therapy. These effects usually vary depending on a patient’s age and the treatment received. For example, a baby or toddler who receives radiation for a solid tumor might not grow normally in the area of radiation. And people treated for a variety of cancers as children can have fertility problems 10 or 20 years later.

As survivors progress through middle age and beyond, challenges that affect all individuals during these periods can be especially problematic. Survivors are also at a 14 percent higher risk of developing a new (or secondary) cancer later in life.

As oncologists continue to learn more about how to predict and handle these “late effects,” they say a greater emphasis needs to be put on getting survivors the specialized care they need.
When patients enter survivorship, they are often seeing doctors and other health care providers who are not experts in their particular cancer,” says Ann Partridge, MD, MPH, director of the Adult Survivorship Program at Dana-Farber/Brigham and Women’s Cancer Center (DF/BWCC). “These providers may not be aware of all the potential risks of the therapy, problems that may arise in the future, as well as the likelihood that somebody might hear from that cancer again with a late recurrence.”

By studying patients with very complex after effects from their treatment, Dana-Farber clinicians have been able to help these individuals, emotionally, physically, and vocationally. By understanding more about the risks associated with treatment, they can also make recommendations about specific screening tests (such as breast cancer screenings for childhood cancer survivors). And, by taking what they have learned and bringing it to the next generation of patients, they are able to alter treatments – so that long-term effects are lessened.

**Bridging the Gap**

Led by Partridge and Lisa Diller, MD, chief medical officer of Dana-Farber/Children’s Hospital Cancer Center (DF/CHCC) and director of Dana-Farber’s Perini Family Survivors’ Center, clinicians are developing embedded survivorship clinics within each of Dana-Farber’s 14 treatment centers. The goal is to ensure that all patients seen at DF/CHCC and DF/BWCC get the most focused, comprehensive care possible not only to treat their cancer, but also to manage the aftermath of the disease.

“In this model, patients get the important survivorship attention they need, but they get it from a health care professional who has experience in caring for patients with the disease that they’ve had,” says Partridge. “Ultimately, we want to disseminate this approach all around the world, so that more...
patients can benefit from the availability of embedded experts and high-level, across-the-board care.”

Diller, who also leads efforts to provide survivorship care for patients treated for childhood cancer, says the Dana-Farber survivorship community sees part of its mission as providing primary care physicians (PCPs) with the necessary tools to take on cancer patients requiring routine follow-up care.

“There are services in the community where the care of the patient is best integrated by a PCP,” Diller says. “As a long-term goal, we want every patient who completes primary therapy in our cancer program to have a plan going forward that includes the right cancer follow-up and integration with primary care.”

The work being done for pediatric cancer survivors through Dana-Farber’s David B. Perini, Jr. Quality of Life Clinic serves as a successful model. All pediatric patients completing therapy at DF/CHCC have a “transition visit,” in which they receive a treatment summary detailing all their stages of care and the risks of after effects, as well as a notebook with more detailed information about their specific cancer. The summaries are passed on to the patients’ PCPs, with another copy placed in the child’s DF/CHCC medical record, so that doctors here can best communicate with outside providers. The goal is to make the records entirely electronic and extend them to adult survivors.

“Survivorship programs at a cancer center can provide important services for survivors, especially consultations and care for cancer-related health problems,” explains Diller. “Most survivors will do well with a model of PCPs partnering with treatment center-based survivorship experts at Dana-Farber.”

In addition, Partridge will be advancing the development of a group of treatment center-based nurse practitioners and other caregivers focused on survivorship.

Thinking in a New Way

For this model to work, of course, there need to be strong lines of communication between oncology providers – including those focused on survivorship – and PCPs, along with better ways for PCPs to access knowledge about what cancer survivors need.

“When I see patients in my survivorship clinic and I send notes back to the PCP, there have been several occasions when I’ve gotten calls along the lines of, ‘Thank you – I had no idea that certain kinds of chemotherapy can put people at risk for heart problems later on,’” says Saul Weingart, MD, PhD, vice president for Quality Improvement and Patient Safety at Dana-Farber. “There is a knowledge deficit out there in the primary care world, and we need to do something about it.”

Some outside physicians are already doing their part. For example, Larissa Nekhlyudov, MD, MPH, an internist at Harvard Vanguard Medical Associates in Boston and associate professor in Population Medicine at Harvard Medical School, recently wrote an editorial in the *Journal of Clinical Oncology* on the opportunities and challenges PCPs face when providing comprehensive care for cancer survivors. She says that a growing percentage of her current general medical practice are cancer survivors referred from Weingart, Diller, Partridge, and other Dana-Farber oncologists; she agrees with Weingart that the key is more education – as early as possible.

“When I went through my medical training in the 1990s, oncologists didn’t think about cancer survivorship; the goal then was getting people treated and into remission,” Nekhlyudov explains. “We really need to change our approach in medical education and training and get it into the minds of young medical students and residents, so they really think about survivorship in a different way – or think about it, period.”

Jarrod Marto, PhD, works in a crowded laboratory. Equipment occupies virtually every inch of free space on bench tops and much of the floor. Loops of plastic and silica tubing feed liquid biological samples from large pumps to detection instruments encased in housings the size of a small freezer. Mass spectrometers measure minute amounts of proteins in the fluid stream, their abundance displayed as sharp peaks on a continuous graph on computer monitors.

These are the components of what Marto calls a “comprehensive protein sequencing platform.” At its core, it’s an automated liquid chromatography-mass spectrometry system.

This technology is at the heart of the Dana-Farber Blais Proteomics Center, which studies how proteins function in both normal and cancer cells. Genomics is the study of all the genes in a cell; proteomics is the study of all of the cell’s proteins.

“The majority of drugs target proteins, so if you want to know how the body’s cells and tissues respond to drugs, you want to be able to characterize as many of the proteins as you can,” explains Marto, director of the center.

Researchers here also hunt for early detection biomarkers – proteins produced by cancer cells, and not normal cells, that betray the presence of otherwise undetectable cancer. Marto and his colleagues extract and purify proteins from samples of normal and cancerous tissues, which may contain tens of thousands of proteins. “You can reach into a sample and pull out a certain type of protein – like protein kinases, which are often bad actors in cancer,” he says.

Often, proteins of interest are present in such scarce quantities, Marto says, that detecting them is comparable to “counting ants on the ground, from the top of Mount Everest.”

The demands of cancer science are such that Marto and his team are always working to improve the system, to be able to identify even finer amounts of protein in samples. “Our goal,” he says, “is to do the equivalent of seeing an ant on the earth’s surface, while standing on the moon.”
Building on an Important Victory
A legacy of support for pediatric palliative care

BY ERIC SCHULLER

In 2006, Massachusetts legislators voted to create the Pediatric Palliative Care Network, an innovative, state-funded program that ensures children age 18 and younger can have palliative care at home, while still receiving standard therapies in the hospital, such as radiation or blood transfusions. The effort marked an early victory for Dana-Farber, which for more than five years helped bring together patients, families, and staff members to lobby for the legislation.

Dana-Farber’s efforts to support palliative care for young patients didn’t end in 2006. Every budget year, funding for the Pediatric Palliative Care Network must be re-approved by Massachusetts legislators. And every year, the Institute and its Legislative Action Network join with partners like the Hospice and Palliative Care Federation of Massachusetts to make sure that legislators recognize the importance of the network.

“Palliative care programs are growing throughout the country, not because more children are dying, but because they are living longer with serious illnesses,” says Anne Levine, vice president of External Affairs at Dana-Farber. “It’s a testament to just how important these programs are, and it’s why we’re at the state house every year to make sure our voice is heard.”

Before the Massachusetts palliative care legislation was signed into law, families who wanted to qualify for hospice-care coverage faced an “all or nothing” choice. Most health insurance plans would not cover palliative care for children unless treatment ended completely. And for a child to be eligible for such care, a physician needed to certify that the patient’s life expectancy was six months or less.

“In the past, parents were placed in an untenable situation, facing the artificial choice between disease-directed therapy or supportive care, and this legislation ensures that no one in Massachusetts ever needs to face that choice,” says Joanne Wolfe, MD, MPH, chief of pediatric palliative care at Dana-Farber/Children’s Hospital Cancer Center (DF/CHCC). “Today, families can qualify for palliative care without ending treatment or having a physician declare a life expectancy. It gives young patients access to a blend of services and treatment aimed at quality of life.”

The legislation was the result of several years of lobbying from Dana-Farber and parents like Christine Reilly, whose 5-year-old son, Mikey, was a DF/CHCC patient who died of cancer in March 1999. Testifying before a joint committee, Reilly told legislators that parents should not be forced to choose between treatment for their child’s disease or palliative care. They should be allowed to concentrate on only one thing: quality time with their child.

The Massachusetts legislation appears to be achieving its intended goals. A study published last year in the Journal of Palliative Medicine showed that less than 5 percent of children enrolled in the Pediatric Palliative Care Network in 2010 died. The same study reported that a majority of parents participating in the program felt their child received excellent care.

To learn more about Dana-Farber’s legislative work and key advocacy issues, visit the Legislative Action Network online at www.dana-farber.org/legislative-action-network.
Barbara Fine, RN, BSN, sits on the edge of her chair, ready to spring into action. During her short interview for *Paths of Progress*, Fine’s mobile phone rings often. A patient arrives without an appointment ... can he be seen? The chemotherapy infusion unit on another floor is more crowded than the one on Fine’s floor ... can some patients come up? Each time, Fine solves the problem gently and calmly.

As a clinical nurse coordinator on the 10th floor of Dana-Farber’s Yawkey Center for Cancer Care, Fine is responsible for the safe and orderly flow of patients through the clinical exam and infusion areas. Here, patients receive care for gynecologic, head and neck, or thoracic cancer. The floor also includes a desensitization unit for patients who have become allergic to their chemotherapy. “If I do my job well, the nurses and clinic assistants do theirs well, and the patients have a better experience,” says Fine.

She’s done her job so well, in fact, that she earned the title Employee of the Year in 2011 for touching the lives of hundreds of patients, family members, and employees.

“Barb epitomizes excellence in nursing practice,” says Anne Gross, PhD, RN, vice president for adult ambulatory services. “She is a critical thinker, collaborator, mentor, advocate, innovator, and educator.”

Fine, who has worked at Dana-Farber for 20 years, began her career in a pediatric bone marrow transplant unit at the National Cancer Institute, and values Dana-Farber’s research mission. Many patients on her floor receive experimental therapies through clinical trials, so there are always opportunities for learning about new treatments and approaches.

As a self-described “air traffic controller” for the 10th floor, Fine looks to make the flow of patient care smoother and safer. For example, she co-leads Team Training, an effort to decrease the risk of medical error and improve communication among clinicians in exam and infusion areas, especially at critical transition points for patients.

Fine also values the Institute’s real-time locating system, a pilot program in which staff and patients wear badges that can be detected by sensors around the unit. “We always know where people are,” she says.

Perhaps most important, Fine points out, is the joy of working with people committed to Dana-Farber’s mission. “As a specialty institution, we attract a certain kind of person. We all support the goal of providing the best possible care for patients and taking part in discovery and research. Every person’s job counts.”

“We all support the goal of providing the best possible care for patients and taking part in discovery and research.”

BARBARA FINE, RN, BSN
Joe Andruzzi knows something about heroes. He has three brothers who were on duty as New York City firefighters on 9/11. His dad was a New York City cop and Army reservist who held three jobs, and his mother kept the house in order while working part-time.

Andruzzi has emerged as a hero in his own right. He played right guard on three Super Bowl championship teams with the New England Patriots. After being diagnosed in 2007 with Burkitt’s lymphoma – a rare, aggressive form of non-Hodgkin lymphoma – he retired from football and started the Joe Andruzzi Foundation, which provides financial assistance to families facing cancer and supports pediatric brain tumor research. Here, he shares some thoughts on what it takes to be a survivor.

Do your best with what you have. In college, I majored in special education, and I still love being involved with the Special Olympics. Seeing how these kids and adults go all-out with whatever abilities they have is simply amazing. They don’t get down on themselves; they strive for what they can get.

Be ready. My second year with the Patriots, in 2001, we lost our quarterback – Drew Bledsoe – to injury. Tom Brady had worked hard for months as a back-up, and when his opportunity came, he ran with it, leading us to three Super Bowl titles. It’s the same with everything in life, including cancer: You need to be ready for what gets thrown at you and push yourself to get through it.

Laughter can be the best medicine. The nurses at Dana-Farber/Brigham and Women’s Cancer Center are some of the greatest people I’ve ever been around. They were always trying to get me to smile or laugh, and it got me through a lot of ups and downs.

Lean on others. A lot of people may not want to reach out to others when they are sick. They don’t want to take what folks are offering, but they should. Your family and friends are the ones who are going to help you move forward. Keep them close.

Cancer is tougher than blocking a 330-pound defensive tackle. Nothing is more of a battle than fighting cancer. It can affect anybody, and it takes a team of family, friends, and caregivers to beat it.

Joe Andruzzi
Carlos Rodriguez-Galindo, MD (left), director of the Solid Tumor Program at Dana-Farber/Children’s Hospital Cancer Center, examines patient Tiffany Tran in Dana-Farber’s Jimmy Fund Clinic.