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Cancer prediction model measures tumor diversity

Scientists led by Kornelia Polyak, MD, PhD, and Franziska Michor, PhD, have developed a mathematical model to predict the behavior of tumors and which treatments are most likely to be effective for a particular patient.

Publishing in the journal *Cell Reports*, the scientists combined several types of data from pre- and post-treatment biopsies of breast tumors to obtain a molecular picture of how chemotherapy influenced the evolution of the cancer.

“Better understanding of tumor evolution is key to improving the design of cancer therapies and for truly individualized cancer treatment,” says Polyak, a breast cancer researcher in the Susan F. Smith Center for Women’s Cancers.

A tumor contains a varied mix of cancer cells, and the mix is constantly changing – a property known as tumor heterogeneity. The cells may have different sets of genes turned on and off,

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Scientists led by Kornelia Polyak, pictured, and Franziska Michor have developed a mathematical model to predict the behavior of tumors.

In good company: Clinical floor specialist role connects volunteers with patients and families

With a combined 32 years of volunteer experience, Ron Paglierani and Harriet Kantrowitz are just two of hundreds of volunteers at Dana-Farber. Both discovered that while volunteering here, they enjoyed connecting with patients and families the most.

So, it was a perfect match for Paglierani and Kantrowitz when a new volunteer position was created that allows them to do just that: keep patients company while they navigate the Institute. Clinical floor specialists are assigned to floors in the Yawkey Center and ensure that patients are checked in, interact with them while they wait for appointments, and provide information about Dana-Farber support services.

With eight clinical floor specialists, and more joining the team this month, patients are able to bond with these familiar faces. “This program exists to reinforce the DFCI value of compassionate care,” says Patricia Stahl, manager of Volunteer Services and Programs. “Whether it’s to provide information or keep someone company, clinical floor specialists play a key role in creating a helpful and supportive environment.”

When Paglierani decided that he wanted to volunteer at DFCI after retirement seven years ago, he became a food

cart volunteer, delivering lunch and snacks to patients. Since then, he has adopted a hybrid role as a volunteer, arriving at 7:30 a.m. to sit with patients in between delivering snacks and lunch, combining his regular responsibilities with those of a clinical floor specialist.

“As a food cart volunteer, I tended to spend a little more time with patients than other volunteers,” he says. “I like to talk a lot and strike up interesting conversations with people. I’m also an incorrigible joke teller, so Pat [Stahl] let me know about this role.”

Kantrowitz, who has been a DFCI volunteer for more than 25 years, says she loves Dana-Farber and believes in the mission of the clinical floor specialist role: to make patients feel comfortable and well-informed.

“I love being here and interacting with people,” Kantrowitz says. “They’re just so amazing – the patients, doctors, nurses, and staff. They’re resilient, inventive, courageous, and fascinating people and they bring all of that with them when they come through the doors each day.”

Clinical floor specialists meet with Stahl once a month to share experiences, learn more about support services, and receive ongoing training. [SS](#)

Study finds genomic jungle in multiple myeloma

From patient to patient, and even within a single patient, multiple myeloma is a portrait in diversity. Scientists have not found a single genetic mutation that is common to all cases of the disease. The myeloma in each patient is a jumble of cell clusters with different sets of mutations. The disease is not consistent over time, either, with new mutations cropping up and new genetic subgroups of cells continuously forming.

Those are among the takeaway lessons of a new study by researchers at Dana-Farber and their colleagues in the United Kingdom and France. The study, one of the largest-scale scoutings of the genomic landscape of myeloma yet undertaken, suggests that different targeted therapies will need to be mixed and matched to the particular set of mutations and other abnormalities in each patient’s tumor.



Nikhil Munshi is senior author of a study that suggests that different targeted therapies will need to be matched to mutations in a tumor.

“The great range of genetic mutations that we discovered across many tumor samples suggests that therapies directed at multiple targets will be required for successfully treating this disease,” says Nikhil C. Munshi, MD, director of basic and correlative sciences at the Jerome Lipper Multiple Myeloma Center at Dana-Farber/Brigham and Women’s Cancer Center and senior author of the study, which appeared in *Nature Communications*. “As we move toward an era of personalized therapy

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Vish Viswanath

Viswanath receives two national honors

Kasisomayajula “Vish” Viswanath, PhD, director of the Health Communications Core at Dana-Farber/Harvard Cancer Center (DF/HCC), professor in the department of medical oncology at Dana-Farber, and professor of health communications at the Harvard School of Public Health, recently received two national honors.

Viswanath received the Joseph W. Cullen Award from the American Society of Preventive Oncology (ASPO), which recognizes a researcher for distinguished achievement in national tobacco control efforts through research and advocacy. He will accept the award at the ASPO annual meeting in March in Arlington, Va. Viswanath’s research includes studying the development and execution of strategic communications campaigns to promote tobacco control and understanding how tobacco companies use the media to encourage tobacco use.

He is also the recipient of the inaugural Dale E. Brashers Award from the National Communication Association. Named for the late Dale E. Brashers, who led the department of communications at the University of Illinois, the award recognizes a communications professional who goes above and beyond to mentor students and young professionals.

“It is an incredible feeling to be recognized as a model mentor,” says Viswanath, who mentors students and fellows through the Harvard School of Public Health and his lab at DF/HCC, both informally and through formal advising. “To me, mentoring is a two-way street, and you do it because it is so enriching and you gain a lot from it, just as you hope those you mentor gain a lot.”

Since he joined DF/HCC 10 years ago, Viswanath has studied communication inequalities, such as information access, and how they contribute to cancer-related health disparities. His community-based research in Boston, Lawrence, and Worcester addresses how advances in research can be translated to influence public health practices and policies in the community, and how health information is communicated to the public. [SEW](#)



Catherine J. Wu

Wu receives ‘Quest for Cures’ grant from Leukemia & Lymphoma Society

Catherine J. Wu, MD, physician in the Adult Stem Cell Transplantation Program at Dana-Farber/Brigham and Women’s Cancer Center and Dana-Farber’s Cancer Vaccine Center, and assistant professor at Harvard Medical School, received a \$400,000 “Quest for Cures” grant from the Leukemia & Lymphoma Society. She will use the funding for research into the biology of genetic and epigenetic heterogeneity and its impact on chronic lymphocytic

leukemia (CLL) outcomes. She is one of 14 recipients of the “Quest for Cures” grants, which range from \$200,000 to \$400,000 annually for two years.

“One of the most striking things about CLL is that patients have such varied clinical courses,” says Wu. “Our lab has been very focused on understanding the genetic and epigenetic landscape of CLL to explain why that occurs.”

Wu, who has been with Dana-Farber since 2000, uses next-generation sequencing approaches to better understand why CLL progresses faster in some patients. This grant will help her and her colleagues define the impact of abnormal patterns of DNA methylation, which plays a critical role in whether genes are expressed, on CLL heterogeneity and clonal evolution, and on clinical outcomes. [SEW](#)

Five Dana-Farber researchers selected for ASH Scholar Awards

Five scientists from Dana-Farber/Brigham and Women’s Cancer Center (DF/BWCC) and Dana-Farber/Boston Children’s Cancer and Blood Disorders Center will receive 2014 Scholar Awards from the American Society of Hematology (ASH).

Ranging from \$100,000 to \$150,000, the awards support the research of fellows and junior faculty during the “perilous and uncertain time” of transition from training to becoming independent investigators, said ASH President Janis L. Abkowitz, MD.

The five local recipients are **Suneet Agarwal, MD, PhD**, of Dana-Farber/Boston Children’s; and **Ami Bhatt, MD, PhD**; **Andrew Lane, MD, PhD**; **Sarah Nikiforow, MD, PhD**; and **Baochun Zhang, MD, PhD**, all of DF/BWCC.

The award to Bhatt will support research on the role of the microbiome in the development of pulmonary and gastrointestinal complications related to stem cell transplants, and follows up work on her discovery of *Bradyrhizobium enterica*, a novel bacterium found in the gastrointestinal tracts of patients with cord colitis syndrome.

Agarwal’s funding will support a project to develop models of the human bone

marrow failure syndrome dyskeratosis congenita, both to understand disease mechanisms and to test the therapeutic potential of novel genome engineering tools.

Lane says: “We will use the award to study an aggressive form of leukemia that is almost completely uncharacterized, and for which there are no specific therapies.”

Nikiforow’s research will focus on high-throughput sequencing of the T cell receptor to better understand the dynamics of T cells in the rebuilding of a patient’s immune system following stem cell transplant. She says the goal is to develop improved prognostic algorithms and clinical trials for treatment of graft-versus-host disease.

Zhang says he and his colleagues will perform complementary human and mouse studies to understand how B cells infected with Epstein-Barr virus turn into cancers. [RS](#)



Jeannine Sudol

Sudol honored with quarterly DAISY Award

Jeannine Sudol, RN, BSN, of Yawkey 8, was honored with a DAISY Award, a quarterly honor given to an extraordinary member of the nursing department. Sudol, who joined Dana-Farber 26 years ago, received the award from Patricia Reid Ponte, RN, DNSc, senior vice president for Patient Care Services and chief nursing officer, and members of the Nursing Council in a surprise ceremony on her infusion unit Feb. 6.

“Jeannine knows I do not want to spend more time than I have to receiving infusions,” wrote a patient who nominated Sudol. “She is always on top of the medicines and ready to begin when I sit down. I feel very fortunate that Jeannine is part of the staff at Dana-Farber.”

Dana-Farber is one of approximately 1,500 hospitals that participate in the DAISY Award program. The DAISY Foundation (Diseases Attacking the Immune System) established the award in memory of J. Patrick Barnes, whose parents created the foundation in his memory after experiencing firsthand the skills, care, and compassion of nurses. [SEW](#)

United Way of Massachusetts Bay and Merrimack Valley



By the numbers

This year’s United Way campaign is **Feb. 24 – March 7**. Watch your email and the intranet announcements scroller for more information, including a link for donating and information about daily opportunity drawings.

- 20** number of years Dana-Farber has partnered with United Way
- 87** communities across our region that are helped
- 170** partner agencies supported, including the Jimmy Fund
- 63%** children not reading proficiently by third grade in some Massachusetts communities
- \$5** amount per week that provides an entire preschool class with books
- 2-1-1** the national abbreviated dialing code for free access to critical health and human services available in the caller’s community
- 85,000** callers served by Mass 2-1-1 in 2013
- 28,375** youth who received academic support
- 18,300** individuals who avoided homelessness
- \$1 million** amount raised by DFCI employees since 2000
- ONE** number of people it takes to make a difference in our community

Inside the Institute is published by the Dana-Farber Communications Department for staff members and friends of **Dana-Farber Cancer Institute**. The next issue is scheduled for **Tuesday, March 4**.

Story ideas are welcome and may be sent to Naomi Funkhouser at 450 Brookline Ave., OS301, Boston, MA 02215. You may also call 617-632-5560, fax to 617-632-5520, or email Naomi_Funkhouser@dfci.harvard.edu. Visit the Dana-Farber website at www.dana-farber.org or the intranet at www.dfcionline.org.

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Christine Rosati

Operations Manager,
Pediatric Hematopoietic
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Years at DFCI: 3.5

Infantil Teletón de Oncología], a group of physicians and nurses from Mexico who spent time here prior to the opening of their new hospital, The Teletón Children's Hospital of Oncology.

Describe your role here.

I am responsible for the day-to-day operations of the pediatric bone marrow transplant program. These responsibilities include maintaining our FACT accreditation [Foundation for the Accreditation of Cellular Therapy], quality improvement/quality assurance for the program, and collecting and maintaining patient data. I have the opportunity to work with many observers and clinical rotators both locally and internationally. This past summer, I worked with the HITO group [Hospital

What brought you to Dana-Farber?

Good luck. I was hired as a temp almost four years ago. I initially worked with both the Perini Family Survivors' Center and the Bone Marrow Transplant Program. I immediately loved working at DFCI, and I was fortunate to be hired as a permanent employee with the Pediatric Bone Marrow Transplant program.

What is most rewarding about your work here?

Is "everything" an appropriate answer? I love feeling like I make a difference, even in a small way. Every employee of DFCI seems genuinely happy to come to work and willing to go above and beyond to help. The one thing that I find most rewarding is participating in patient satisfaction rounds. I round weekly on the inpatient unit with our medical director, Leslie Lehmann. We check in with all of our patients to see what we can do to make their stay a little bit easier (from a non-medical standpoint). It's a wonderful feeling to be grateful to go to work every day. Not many people can say this.

What is the biggest challenge in your role?

Finding extra hours in the day to be involved in everything you want to do.

How does your role contribute to the mission of Dana-Farber?

By maintaining quality standards and seeking out quality improvement projects that will improve patient care. By demonstrating empathy and compassion to everyone, patients and co-workers alike.

What book are you reading?

I just finished *City of Thieves* [by David Benioff].

If you didn't work in your current role, what job would you most like to do?

Child life specialist or resource specialist.

What do you do for fun in your spare time?

Read, volunteer, spend time with family and friends, and, of course, spend as much time as I can at the beach. [TT]

Why We Work Here

"I have known Dr. Janet Abraham for many years, sometimes it feels like forever. We have cared for many very sick patients together, several at the end of life. Most recently, I was asked to arrange for a home hospice discharge for a 38-year-old man to a rural area in Vermont. Most home hospice discharges are quite complex; however, in this case, the added distance and the agency closing for a holiday made this discharge more complex. Knowing I would be working with Janet made the preparation and planning so smooth. She works on a level that is indescribable. Every single page and phone call was returned in a matter of seconds. She is an amazing professional and even more so as a person. We are so fortunate to have Janet on our staff."

– Carol Ann Bellinghausen, RN, BSN

Multiple myeloma, continued from page 1

for myeloma, we need to understand which genes are most frequently mutated and how they affect the course of the disease and the impact of therapy. This study is a significant step in that direction."

Multiple myeloma is a cancer of the bone marrow in which infection-fighting plasma cells grow out of control. It is diagnosed in more than 22,000 people each year, making it the second most common blood cancer after non-Hodgkin lymphoma. Although scientific advances in the past 15 years have significantly lengthened the lives of myeloma patients, it is still considered incurable in a majority of patients.

In the new study, researchers from Dana-Farber, the Wellcome Trust Sanger Institute in the United Kingdom, and Le Centre Hospitalier Universitaire (CHU) de Toulouse in France analyzed the DNA in

84 myeloma samples, looking for instances of gene mutations, missing genes, and over-copied genes. The research team included Ken Anderson, MD, and Paul Richardson, MD, of Dana-Farber; Peter Campbell, MD, PhD, at the Sanger Institute; and Herve Avet-Loiseau, MD, PhD, and Stephane Minville, PhD, at CHU.

The results showcase how much genetic variation can exist within a single form of cancer. Researchers found that each tumor sample had an average of more than 50 mutations, and no one mutation was present in every sample. The most common mutations – in the genes *KRAS* and *NRAS* and *BRAF* combined – appeared in only 40 percent of the samples. (Investigators also discovered abnormalities in several genes, including *SP140*, *LTB*, and *ROBO1*,

that had never been found in multiple myeloma.)

The researchers further discovered that the cells acquire new mutations in four distinct patterns. In one pattern, for example, the type and number of mutations in the myeloma cells stayed relatively consistent over time. In another pattern, mutations that weren't present at diagnosis became very common later on.

"We found that the pattern by which mutations evolve influences how the disease behaves," Munshi says. "That, in turn, will have an impact on how it is treated.

"We are right at the cusp of the use of targeted therapies for myeloma," he continues. "This study makes it clear that such therapies will work best if they not only block critical mutations, but if they can slow or stop the evolution of new and different mutations in the cells." [R]

Tumor diversity, continued from page 1

or have different numbers of genes and chromosomes.

The study analyzed breast cancer samples from 47 patients who underwent chemotherapy to shrink the tumor so it could more easily be removed by surgery. The biopsy samples, representing the major types of breast cancer, included specimens taken at diagnosis and again after the chemotherapy was completed.

In generating their predictive model, Polyak and Michor, a computational biologist, integrated data on large numbers of individual cells in the tumor samples with maps of the cells' location within the tumors.

"We asked two questions – how heterogeneity influences treatment outcomes and how treatment changes heterogeneity," explains Polyak.

The model revealed that the amount of genetic diversity within tumors didn't change much following treatment with ineffective drugs. But it also showed that certain types of cells – those prone to grow rapidly – were more likely to be eliminated, and that the locations of cell populations changed.

"Based on this knowledge," says Polyak, "we could predict which tumor cells will likely be eliminated or slowed down by treatment, and how this may change the tumor overall." She adds that this information might help design further treatment strategies for patients who didn't respond well to the initial therapy.

Another finding was that tumors with less genetic diversity shrank more in response to chemotherapy than did tumors with more genetic complexity.

"In general, high genetic diversity is not a good thing," comments Polyak. "The results show that higher diversity is making you less likely to respond to treatment."

The researchers suggest that in the future, cancer doctors may use models of this type to analyze a patient's tumor at the time it's diagnosed; the results could help tailor specific drugs and plan treatment strategies matched to the tumor's predicted behavior.

First author of the report is Vanessa Almendro, PhD, of Dana-Farber/Brigham and Women's Cancer Center. [R]

Brain cancer **SPORE** takes targeted approach to glioma

The era of precision medicine – of drugs matched to the rogue genes within tumor cells – is within sight for patients with glioma, the most common form of brain cancer. Hastening its arrival are the Dana-Farber scientists involved in the Dana-Farber/Harvard Cancer Center (DF/HCC) Specialized Program of Research Excellence (SPORE) in brain cancer.

Unlike many other forms of cancer, where treatment is often targeted to the key genetic abnormalities within tumor cells, the treatment of glioma currently is based on the tumor's size and location, the patient's age, and the degree to which the mass reduces the ability to perform ordinary tasks. Precision medicine for gliomas is near due to the recent discovery of molecular "biomarkers" – genetic mutations that underwrite the tumor's growth – and the development of drugs for blocking those abnormal genes.

The brain cancer SPORE – one of several SPOREs within DF/HCC, each focused on a different type of cancer –

brings together scientists from various disciplines, with a goal of bridging the traditional dividing lines between laboratory and clinic. Funded by the National Cancer Institute (NCI), SPOREs have become a prime engine for translating basic science breakthroughs into better treatments for patients.

"Primary cancers of the brain present a challenge to biomedical researchers," says Charles Stiles, PhD, co-chair of the Department of Cancer Biology at Dana-Farber and co-principal investigator of the DF/HCC brain cancer SPORE. "On one hand, the most aggressive forms of brain cancer – anaplastic astrocytomas or malignant gliomas – are to all intents and purposes incurable. On the other hand, these tumors are far less frequent than cancers of the breast, colon, lung, or prostate. The ability of two large research-oriented hospitals to combine their case loads, tissue banks, and other resources on these cancers was a major strength of the program in the eyes of the NCI advisory panel that reviewed our SPORE application."

The brain cancer SPORE includes four projects, all involving targeted therapies for glioma.

- One project is exploring improved techniques for choking off the blood supply to gliomas. While current "anti-angiogenic" drugs are capable of accomplishing this, they tend to lose effectiveness over time. The DF/HCC team plans to test a drug that blocks a blood vessel-promoting molecule.
- A second group led by Dana-Farber's Patrick Wen, MD, Thomas Roberts, PhD, Jean Zhao, PhD, and Keith Ligon, MD, PhD, will conduct preclinical studies and a clinical trial of an agent called BKM 120, which targets a key cell-growth pathway abnormally activated in gliomas. The pathway, which involves the protein PI3K, may represent a vulnerability for a targeted agent to exploit.
- A third group, co-led by Dana-Farber's William Kaelin, MD, will examine whether attacking another abnormal signaling pathway in glioma cells can impede their growth. In this pathway, a mutation in the gene *IDH* results in increased levels of a chemical called 2-HG. Researchers will study a technique for determining whether glioma cells are overproducing 2-HG. They also will test the effectiveness of drugs that block the production of this chemical.
- The fourth project, led by Stiles, focuses on what's known as the *p53* paradox. The *p53* gene is the most frequently mutated gene in cancer, yet, strangely, it is mutated in only about 25-35 percent of gliomas. One explanation is that while *p53* itself may be intact, its activity is hindered in glioblastoma cells by a protein known as OLIG2. This suggests that drug agents that target OLIG2 could indirectly affect *p53*, and potentially cause glioma cells to become vulnerable to radiation and chemotherapy. The research group will test this hypothesis in the lab. ^{RL}

BROADWAY ON BINNEY... VIVA LAS VEGAS!

WELCOME TO Fabulous LAS VEGAS BOSTON

PROUDLY PRESENTED BY
DANA-FARBER CANCER INSTITUTE LGBT & Friends ERG

Performers, volunteers sought for Broadway on Binney staff talent show

Before Sarah Winawer-Wetzel ever saw Dana-Farber's "Broadway on Binney" staff talent show, the popular annual event had already made an impression.

"Broadway on Binney is one of the things that attracted me to Dana-Farber when I was applying here," says Winawer-Wetzel, manager of Clinical Planning and Network Operations. "I was hoping to land at a place that understands that even though we all have a lot of work to do, sometimes it's important to stop and have some fun together."

As soon as she joined DFCI in April 2012, Winawer-Wetzel contacted DFCI's Lesbian, Gay, Bisexual, and Transgender (LGBT) and Friends employee resource group, which hosts the talent show, and got involved. Now, she's communications director for the show, which will take place March 20 from 4-6 p.m. in the Jimmy Fund Auditorium. This year's theme is "Viva Las Vegas!" – but you don't need a Vegas-like act to participate.

"We're looking for anybody who wants to be involved," says Michael Jendrysik of Finance, who is artistic director for the show. "If you don't want to perform, there are lots of other ways to help."

Jendrysik, Winawer-Wetzel, and technical director Rob Mersereau of Quality and Patient Safety all agree that the show brings together Dana-Farber's diverse staff. Performers feel the same way.

"It's great to step away from the lab or desk and share a part of yourself that most people don't get to see," says Elise Krob of the Adult Survivorship Program, who last year sang "Who Will Love Me As I Am?" from "Side Show." "It was really cool to see a pediatrician play the piano and a locksmith bust out some dance moves."

Robson Goulart of Learning, Development, and Inclusion has sung, danced, and played the guitar at the last four shows, and says Broadway on Binney is part of what makes Dana-Farber "an inclusive, caring, and unique place for employees and patients and their family members."

"It's a wonderful collaboration of many departments across the Institute: Conference Services, Food Services, Facilities, and Communications," adds Mersereau. "They've all played a huge part, and the sense of community that builds is inspiring." ^{SW}

Want to join the fun? Attend an open call for performers on Friday, Feb. 21, from 3-7 p.m. in the Jimmy Fund Auditorium. Sign up online at <http://bit.ly/broadway2014>. To learn more about other ways to help, contact Michael Jendrysik at michaele_jendrysik@dfci.harvard.edu.

Rwandan cancer center is off to a successful start



Lawrence Shulman (third from left) and others tour the Rwanda cancer center.

The first comprehensive cancer center in rural Rwanda, established in July 2012, is busy treating patients, and serves as an inspiring model for battling cancer in resource-limited countries.

"The cancer center is operating at a very high level," both in treating patients and in training physicians, nurses, and other caregivers, says Lawrence Shulman, MD, Dana-Farber's senior vice president for medical affairs and director of DFCI's Center for Global Cancer Medicine.

Dana-Farber/Brigham and Women's Cancer Center (DF/BWCC), together with Boston Children's Hospital and Massachusetts General Hospital, is collaborating with Boston-based Partners in Health (PIH) and the Rwandan government to support the Butaro Cancer Center of Excellence. Shulman serves as senior oncology advisor for PIH.

The center opened in Butaro Hospital, which is operated by PIH and was built in 2011 in northern Rwanda, near the country's border with Uganda. With expertise provided by DF/BWCC physicians, nurses, and medical students, as well as through weekly phone consultations and email guidance, the center has brought team-based management of all cancer types to an area that previously had no oncologists at all.

In its first year, the oncology program enrolled 1,107 patients ranging from newborns to age 92, with a variety of solid tumors and blood cancers, according to a report presented by Shulman and his Rwandan colleagues at the African Oncology Research and Training in Cancer Conference in Durban, South Africa. The most common type of cancer in adults was breast, followed by other solid tumors and cervical. In children, Wilms tumor and acute lymphoblastic leukemia were the most common.

The Butaro center offers pathology-based diagnosis, chemotherapy, surgery, referral for radiotherapy, and long-term follow-up. An outpatient infusion facility to supplement the inpatient beds is scheduled to open this year. ^{RS}