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UPMC hospitals named "Blue Distinction Centers for Complex and Rare Cancers"

Hillman Cancer Center is the academic hub of the UPMC Cancer Centers network. The state-of-the-art facility offers cutting-edge cancer care and is also home to the research activities of the University of Pittsburgh Cancer Institute (UPCI). UPMC Cancer Centers and UPCI are the only center in western Pennsylvania with the elite Comprehensive Cancer Center designation from the National Cancer Institute.

## Changing the landscape of oncology



*The New York Times* recently lamented the disparities in cancer care available to patients in a landmark article highlighting the importance of a coordinated care approach to achieving

good outcomes for patients.

At UPMC Cancer Centers and the University of Pittsburgh Cancer Institute, the close collaboration of medical, radiation, and surgical oncologists with referring physicians ensures that patients are being evaluated more quickly and entering treatment sooner — when the cancer is most treatable. Ancillary services, such as behavioral medicine, rehabilitation, social work, palliative care, nutrition, genetic counseling, and patient education, are incorporated into the multi-disciplinary team to ensure that every aspect of a patient's care is addressed. And our physicians work closely with researchers to incorporate the latest therapies into each patient's treatment strategy.

In this issue of *Cancer Insights*, we focus on ways our multidisciplinary model of care is not only enhancing the patient experience, but also advancing the science of cancer prevention,

detection, and treatment. Our Melanoma and Skin Cancer Program is redefining the approach to research of this deadly disease; we are identifying new strategies to improve quality of life for patients undergoing radiation treatment; and our surgeons are employing advanced robotic technology for a less invasive surgical procedure.

UPMC Cancer Centers, one of the nation's top centers for care and research, has been designated a "Blue Distinction Center for Complex and Rare Cancers" by the Blue Cross Blue Shield Association, due in part to the cutting-edge therapies and technologies being developed here in Pittsburgh.

We hope you find this information useful in your day-to-day practice, and welcome the opportunity to discuss our clinical research or patient care opportunities. Please contact us at 412-647-2811 or visit our website at [www.UPMCCancerCenters.com](http://www.UPMCCancerCenters.com).

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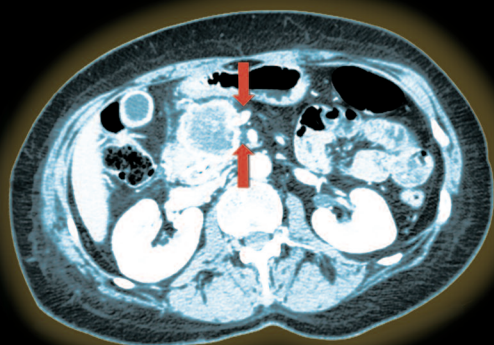
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# medical oncology

## Streamlining the complexities of cancer care

Despite the growing number of advanced cancer therapies, many Americans still are not receiving adequate cancer care. A landmark article in *The New York Times* brought to light this stark reality: A substantial number of patients are getting lost in our complex medical system.

### The multidisciplinary approach



- patient from Texas, age 55, developed liver function abnormalities
- diagnosed with gallstones
- a cancerous mass on the pancreas growing into the portal vein discovered during surgery
- patient comes to Pittsburgh to meet with multidisciplinary team
- treatment plan developed
- patient currently participating in a Phase II clinical trial

**Delivering a coordinated, personalized approach to care is most important during this stressful period for patients.**

This can be especially true for cancer patients. Developing an effective treatment plan for cancer often involves input from a wide variety of specialists. For many patients, the time from diagnosis to the start of treatment can be frustrating and lengthy.

“By the time a patient has seen all the specialists, valuable time may have passed,” says A. James Moser, MD, co-director, Pancreatic Cancer Center of UPMC Cancer Centers. “For certain cancers, the patient may become too frail for treatment that might otherwise have been possible.”

To eliminate the disjointedness that exists for newly diagnosed patients, UPMC Cancer Centers has developed a multidisciplinary model where patients see the entire team of specialists in a concentrated period of time, expediting the development of a treatment plan.

Multidisciplinary clinics are set-up by cancer type – including adult neurological, breast, head and neck, lung, leukemia, liver, lymphoma, pancreatic, and thyroid cancers. Newly diagnosed patients work with a coordinator who serves as the point person for the treatment team – reviewing the patient’s history and making appropriate appointments based on the patient’s needs and the team’s recommendations.

“The collaborative framework of the multidisciplinary clinics enables the team to work through the complexities of each individual case to develop the most appropriate treatment plan,” says Frank Lieberman, MD, director of the Adult Neuro-Oncology Program.

Multidisciplinary teams include medical, radiation, and surgical oncologists; disease-specific specialists (such as gastroenterologists, pulmonologists, and neurologists); pathologists and radiologists; as well as ancillary support services including:

- nutrition experts
- behavioral medicine and palliative care
- pain and rehabilitation services
- oncology social workers
- cancer education specialists
- genetic counseling

“Our multidisciplinary approach encompasses a full range of specialized services ranging from risk assessment and early detection to treatment strategies and supportive care,” says Athanassios E. Argiris, MD, co-director, Lung Cancer Center of UPMC Cancer Centers, and associate chief, Multidisciplinary Clinics, Division of Hematology/Oncology. “Delivering a coordinated, personalized approach to each patient and their family is most important during this stressful period.”

Once the patient has been evaluated, the treatment team meets to discuss the case and to coordinate care with referring physicians. Patients leave with a plan of care in place.

“The cornerstone of our approach is the close coordination with the referring physician,” says David L. Bartlett, MD, chief, Division of Surgical Oncology, and director, Multidisciplinary Disease Site Clinical and Research Programs. “Once a treatment plan has been developed, the team provides immediate feedback to the referring physician to ensure a complete continuum of care.”

An important component of the multidisciplinary model is ensuring that a patient’s treatment plan combines innovative and promising clinical trial options with the best standard of care therapies for their specific cancer.

“Integrating research into treatment plans improves care and ultimately improves outcomes,” says Dr. Bartlett.

## Redefining benchmarks leads to better treatments for melanoma

The University of Pittsburgh Cancer Institute Melanoma and Skin Cancer Program is setting the benchmark for the future of melanoma research.

In a multicenter cooperative group overview published recently in the *Journal of Clinical Oncology*, physician-researchers at UPCI evaluated 30 years of Phase II melanoma trials in an effort to determine a better way of gauging clinical trial endpoints to more accurately evaluate the effectiveness of potential treatments.

“Historically, Phase II trials have used tumor response rates as a benchmark to decide whether or not a new therapy is worth pursuing,” explains John M. Kirkwood, MD, leader, Melanoma and Skin Cancer Program, UPCI. “This has not been a reliable indicator for patients with metastatic melanoma because radical differences in response mean nothing in terms of survival. Identifying more reliable endpoints may allow a more effective selection of new therapies to be considered for Phase III trials.”

This analysis underscores the importance of re-evaluating the endpoints of clinical research, and may in fact avoid the use of randomized controls for some studies in the future, to accelerate the pace of melanoma research.

The internationally renowned Melanoma and Skin Cancer Program has employed this forward thinking approach since its inception more than 20 years ago. The multidisciplinary research team comprises 26 experts from the fields of medicine, pathology, dermatology, surgery, and pharmacology.

The program’s major areas of research range from vaccine development and the analysis of novel therapeutic combinations to the search for biomarkers to aid in the development of personalized treatments and improved early detection methods.

Recognizing early detection as one of the best options for combating skin cancer, the program was one of the first centers in the country to use a digital mole mapping system to assess high-risk patients. Specially trained medical photographers use digital cameras and special color-managed lighting to create a mosaic of the patient’s skin. Physicians are able to use the photos obtained at baseline as a reference for

clinical evaluation at each examination and, where indicated, can do side-by-side comparisons of the patient and their digital history.

The Melanoma and Skin Cancer Program is currently focusing on projects addressing key questions pertaining to genes and proteins that govern the development and progression of melanoma and molecules and processes that render melanoma refractory to therapy, with the ultimate goal of developing molecular and immunologic therapies.

“Studies of tumor and mole biopsy tissues of melanoma patients show the effects of new treatments that will accelerate the pace of our progress,” says Dr. Kirkwood.

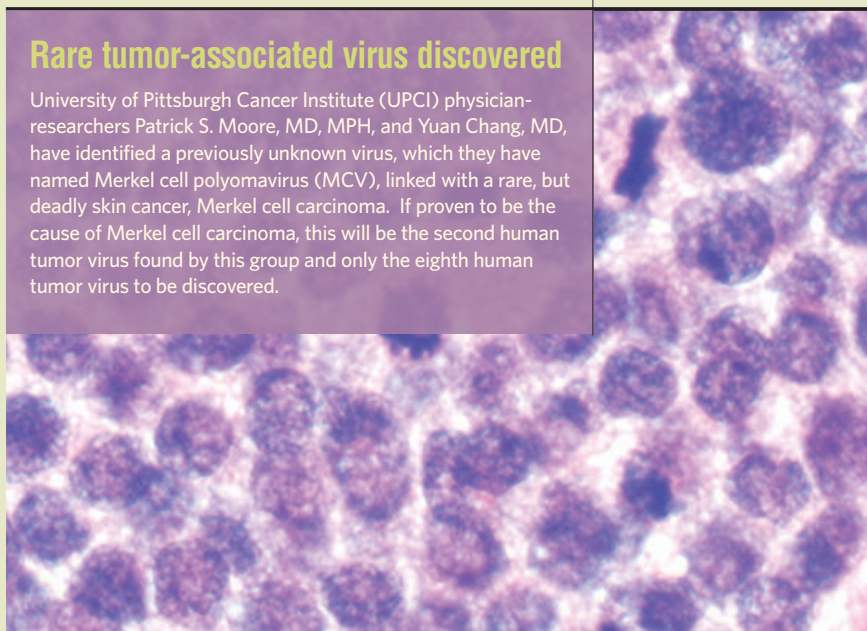
To learn more about the program’s clinical research or patient care opportunities, contact Dr. Kirkwood, at [kirkwoodjm@upmc.edu](mailto:kirkwoodjm@upmc.edu).

**“This has not been a reliable indicator for patients with metastatic melanoma because radical differences in response mean nothing in terms of survival. Identifying more reliable endpoints may allow a more effective selection of new therapies to be considered for Phase III trials.”**

— John Kirkwood, MD

### Rare tumor-associated virus discovered

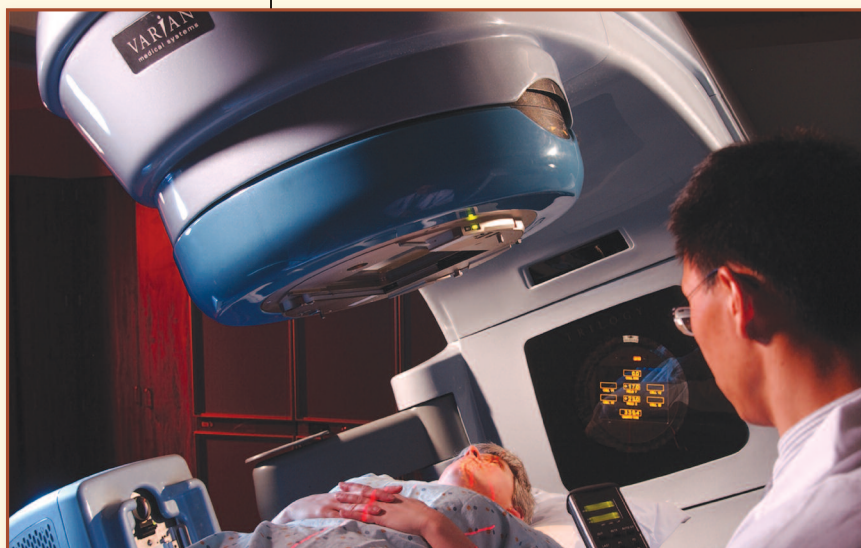
University of Pittsburgh Cancer Institute (UPCI) physician-researchers Patrick S. Moore, MD, MPH, and Yuan Chang, MD, have identified a previously unknown virus, which they have named Merkel cell polyomavirus (MCV), linked with a rare, but deadly skin cancer, Merkel cell carcinoma. If proven to be the cause of Merkel cell carcinoma, this will be the second human tumor virus found by this group and only the eighth human tumor virus to be discovered.



# radiation oncology

## Breast cancer patients get extra boost

A European study published last year in the *Journal of Clinical Oncology* confirmed what many radiation oncologists have hypothesized for many years — an extra boost dose of radiation after breast conserving surgery reduces the risk of local recurrence for women with early-stage breast cancer.



**When given the extra boost, the risk of relapse was lowered significantly.**

The European Organisation for Research and Treatment of Cancer (EORTC)-sponsored Boost-No Boost trial found that the relapse rate after 10 years in women who received an additional 16-Gy boost dose of radiation to the tumor bed, following a lumpectomy and standard 50-Gy whole breast radiation, was nearly cut in half when compared to participants who did not receive the boost.

Heather Jones, MD, who recently joined UPMC Cancer Centers, worked on the study while completing a fellowship at the Netherlands Cancer Institute in Amsterdam.

According to Dr. Jones, using a boost dose of radiation for breast cancer patients is not new.

“Radiation oncologists have been employing boosts for a while now,” says Dr. Jones. “This study further validates this practice.”

As part of a sub-study analysis, Dr. Jones and colleagues evaluated central pathology results from the original study to identify which patients benefited the most from the boost. The greatest absolute risk reduction was found in women ages 40 or younger. Women in this subset who received the boost had a 13.5 percent risk of relapse at 10 years versus 23.5 percent in patients who did not receive the boost.

The study also revealed that the grade of tumor was a significant prognostic factor.

“Women diagnosed with a high-grade invasive tumor or high-grade ductal carcinoma *in situ* (DCIS) have a high risk of relapse,” explained Dr. Jones. “When given the extra boost, the risk of relapse was lowered significantly.”

Dr. Jones presented the group’s 10 year update on the EORTC trial, with emphasis on the subset analysis, at the annual meeting of the American Society for Therapeutic Radiation and Oncology (ASTRO).

UPMC Cancer Centers, which has been employing a 16-Gy boost for the past five years, is investigating how to make this labor-intensive regimen more patient friendly.

“With new, advanced equipment, it is now possible to use a simultaneous integrated boost technique,” says Dr. Jones. “With this technique, the boost dose is integrated into the standard dose fractions, thus reducing the number of times a patient has to be irradiated.”

To implement this technique networkwide, UPMC Cancer Centers is planning a clinical investigation on higher boost doses and more conformal treatment techniques.

“The integrated boost treatment is labor intensive and requires profound knowledge of the radiotherapy treatment planning system and treatment unit,” said Dwight E. Heron, MD, director, Radiation Oncology Services, UPMC Cancer Centers. “Our existing telemedicine capabilities will allow us to standardize the treatment throughout the network more quickly.”

## Educating the “plain” community

Clusters of Amish throughout western Pennsylvania are gaining access to valuable cancer education and screenings thanks in part to a grant funded by the National Cancer Institute.

The Amish education program was developed as part of the Radiation Oncology Community Outreach Grant (ROCOG) project, which promotes the use of nontraditional outreach to make state-of-the-art cancer care available to disadvantaged communities.

Dwight E. Heron, MD, principal investigator of the grant and director, Radiation Oncology Services, UPMC Cancer Centers, underscores the importance of building trusted relationships and making cancer education understandable and relevant to people in communities like the Amish.

“Trust was an essential component,” explains Dr. Heron. “By understanding their needs and respecting their values, we have been able to make great strides in bringing cancer education to the Amish communities throughout western Pennsylvania.”

The Amish, who are known for their plain lifestyle, typically shun the outside world and modern conveniences. Through an existing relationship with professionals from the Pennsylvania Department of Health, nurse educators from the project were introduced to Amish communities in western Pennsylvania. The nurses held discussion groups with Amish women from two different sects to assess the communities’ needs and to identify ways to provide cancer education.

The idea to print articles in a local newspaper that had a section dedicated to the Amish came from the discussion groups. The articles are written by the cancer education staff and edited by an Amish volunteer to accommodate language barriers. The articles are printed every few months and cover a variety of topics, ranging from basic information about specific cancer types to dealing with death.

In October 2007, ROCOG coordinators brought the first breast and cervical cancer screenings to an Amish community in Somerset, Pa., located southeast of Pittsburgh. Seventeen women came to the screening, with three of the women showing abnormal test results. These three women, who were not insured, were then assimilated into the Healthy Woman Project, a state program dedicated to helping economically disadvantaged women gain better access to care.

“Community outreach and patient navigation go hand-in-hand,” says Karen Schwaderer, RN, BSN, OCN, director, Patient Navigation and Clinical Services. “You can’t go into an underserved, uninsured community like the Amish and not help them gain access to treatment.”

To date, more than 125 Amish have been helped directly through screenings and education provided by the program.

## Gene therapy may improve quality of life for lung cancer patients

A Phase I/II trial at the University of Pittsburgh Cancer Institute (UPCI) is using gene therapy to improve the quality of life for patients with non-small cell lung cancer who develop esophagitis while receiving radiation therapy.

Radiation-induced esophagitis, a painful and often severe complication, affects 30 to 50 percent of lung cancer patients. Local anesthetic syrup is frequently prescribed to control the pain, but is not always effective and does not prevent tissue damage.

“Damage to normal tissue during radiation therapy is a major limitation to the effective treatment of lung cancer,” says Joel Greenberger, MD, professor and chairman, Radiation Oncology. “Many patients have had to temporarily stop or forego treatment, because of complications caused by esophagitis.”

Previous studies have shown manganese superoxide dismutase plasmid liposome (MnSOD-PL) can be used to successfully protect healthy tissue from the effects of radiation. The main goal of this Phase I/II trial is to evaluate the safety and toxicity of administering liquid (MnSOD-PL) to patients undergoing radiation therapy.

“Current treatments only mask the pain caused by the esophagitis,” explains Dr. Greenberger. “MnSOD-PL will prevent the tissue damage from occurring, allowing the patient to complete radiation therapy.”

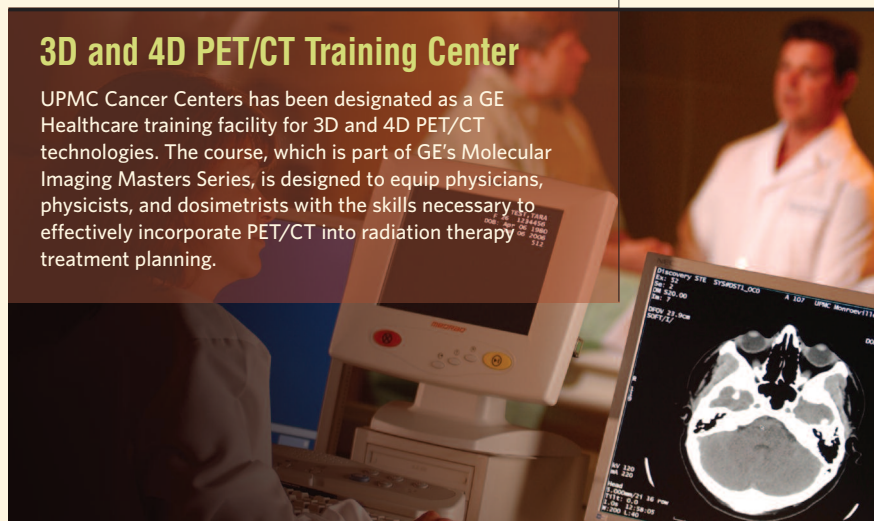
This trial, which is available throughout the UPMC Cancer Centers network, is currently accruing patients. Patients with a previous cancer diagnosis are ineligible.

For more information on eligibility criteria or for patient referrals, contact Joel Greenberger, MD, at [greenbergerjs@upmc.edu](mailto:greenbergerjs@upmc.edu).

MnSOD-PL therapies have shown not only to be effective in preventing esophagitis, but also may have wide reaching potential to protect the population against terrorism. In 2005, the National Institute of Allergy and Infectious Diseases (NIAID) awarded the University of Pittsburgh School of Medicine a \$10 million grant to create a Center for Medical Countermeasures Against Radiation. Through this grant, the team has investigated the use of MnSOD-PL therapies to protect vital organs and tissues against the effects of ionizing radiation in the event of large scale exposure from a radiological or nuclear bomb.

## 3D and 4D PET/CT Training Center

UPMC Cancer Centers has been designated as a GE Healthcare training facility for 3D and 4D PET/CT technologies. The course, which is part of GE’s Molecular Imaging Masters Series, is designed to equip physicians, physicists, and dosimetrists with the skills necessary to effectively incorporate PET/CT into radiation therapy treatment planning.



# surgical oncology

## Robotic surgery reducing patient recovery time

UPMC Cancer Centers is changing the landscape of surgical oncology — incorporating minimally invasive surgical (MIS) technology into every aspect of surgical cancer care.



**The enhanced visualization and dexterity the robot provides allows the surgeon to perform many complex procedures.**

Very few centers worldwide offer the range of MIS available at UPMC Cancer Centers. The comprehensive program includes the recent expansion of the Surgical Robotics Program, where experts in the field are utilizing a surgical robot to expand the number of abdominal procedures that can be performed with a minimally invasive technique.

To date, the division has performed a wide variety of cases – ranging from liver and pancreatic resections to colon, rectal, adrenal, spleen, and many non-oncologic abdominal procedures with great success.

“We are excited about the technology and have used the robot to enhance many of our clinical applications,” says Sricharan Chalikonda, MD, director, Surgical Oncology Robotics Program at UPMC. “The enhanced

visualization and dexterity that the robot provides allows us to perform many complex procedures that would otherwise have to be performed with conventional open incisions.”

Robotic surgery outcomes are consistent with standard MIS. With recovery times reduced, patients with malignant cancer can start follow-up chemotherapy or radiation therapy almost immediately, giving the drugs a chance to work before the tumor potentially returns.

Data shows that treatment plans that combine surgery with chemotherapy, radiation therapy, and clinical trials when appropriate result in optimal patient benefits.

“Very few places offer convenient access to novel therapeutics or the extent of MIS and robotic surgical options available at UPMC Cancer Centers,” says David L. Bartlett, MD, chief, Division of Surgical Oncology.

## MRI enhances screening for breast cancer in high risk patients

A multi-institutional study conducted by the American College of Radiology Imaging Network, and reported in the *New England Journal of Medicine* demonstrated that magnetic resonance imaging (MRI) detected contralateral breast cancers missed by mammography and clinical examination in three percent of women with biopsy-confirmed unilateral breast cancer.

“The role of MRI in the diagnostic evaluation of patients with breast cancer is evolving,” says Gretchen M. Ahrendt, MD, director, Breast Surgical Services at Magee-Womens Hospital of UPMC, part of the Magee-Womens Breast Cancer Program of UPMC Cancer Centers. “With the development of dedicated breast magnets, improved surface coils for whole body magnets, and enhanced software for scanning and image interpretations, breast MRI has proven to be a highly sensitive and useful screening method for detecting occult cancers.”

Although annual mammography remains the gold standard in breast-cancer screening for women at average risk, some women can benefit by the addition of annual breast MRI. Based on current concepts of lifetime risk for breast cancer, the American Cancer Society (ACS) has issued new guidelines for the use of MRI in breast-cancer screening.

For asymptomatic women at average risk (lifetime risk less than 15 percent), the ACS recommends against breast MRI as a routine screening method. Women in this category should receive annual mammography and clinical breast examination beginning at age 40.

For “high-risk” patients — such as those with a known BRCA gene mutation, or a high likelihood of carrying such a mutation — the ACS recommends annual breast MRI in addition to annual mammography. This high-risk category includes:

- patients with known BRCA mutation
- untested, first-degree relatives of a known BRCA carrier
- patients with a lifetime risk of 20 to 25 percent or greater, as defined by BRCAPRO (a computer model used by genetic counselors for determining genetic risk)
- patients with a history of having received chest irradiation — as for Hodgkin’s disease, acne, thymoma — between the ages of 10 and 30 years
- patients with Li-Fraumeni syndrome and their first-degree relatives
- patients with Cowden or Bannayan-Riley-Ruvalcaba syndromes, and their first-degree relatives

Others for whom MRI may be an appropriate adjunct to screening mammography include those whose family history strongly are suggestive of a genetic mutation, as determined by a genetics counselor. Characteristics known to be associated with an increased likelihood of genetic mutation include:

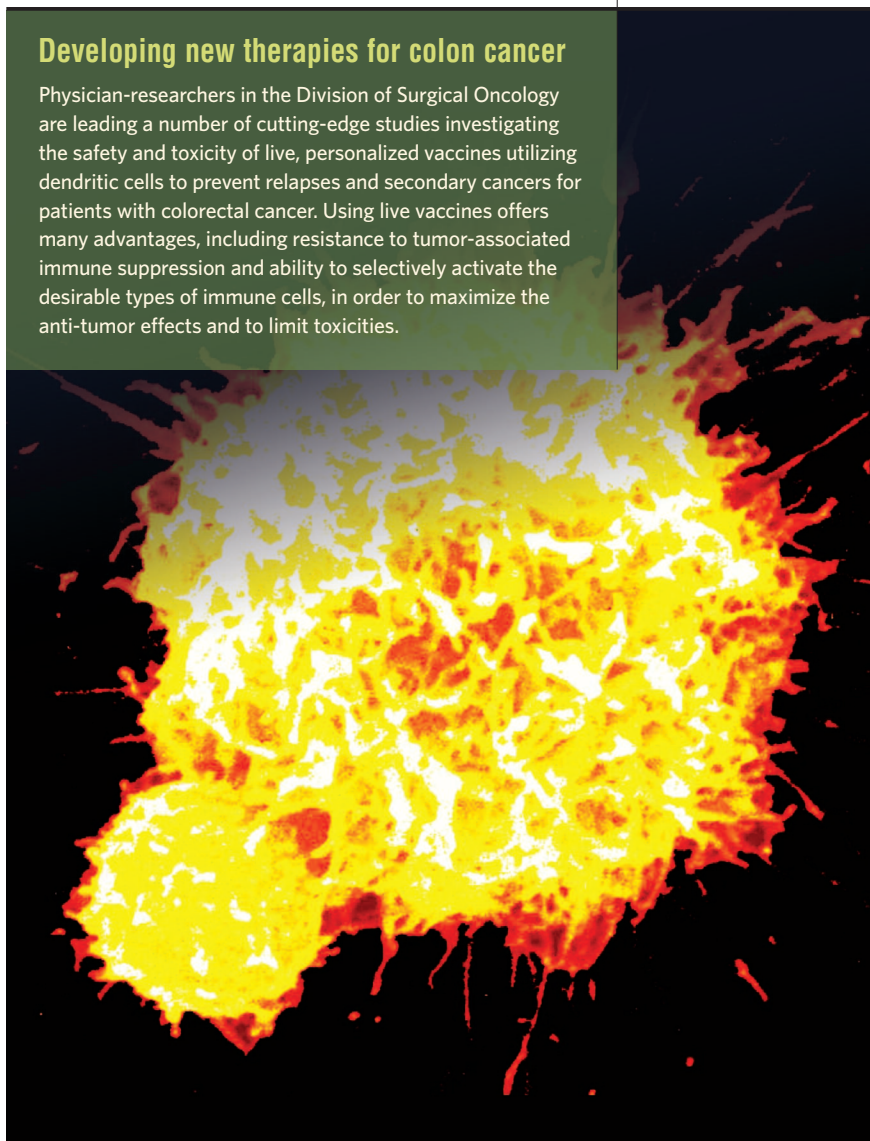
- **A personal history of:**
  - early-onset breast cancer (diagnosed prior to age 50)
  - bilateral breast cancer
  - both breast and ovarian cancer
- **A family history that includes:**
  - multiple cases of early-onset breast cancer (diagnosed prior to age 50)
  - diagnosis of breast cancer in one or more male family members
  - Ashkenazi Jewish background and a family history of breast and ovarian cancer

“Women who meet any of these criteria should meet with a genetics counselor for a detailed assessment of breast-cancer risk,” says Jules H. Sumkin, DO, chief of radiology at Magee-Womens Hospital of UPMC.

The final ACS classification includes women with a history of atypical cytology on breast biopsy, but with no known genetic mutation. ACS guidelines currently make no recommendation either for or against breast MRI screening in women with atypia or lobular carcinoma *in situ* (LCIS) on biopsy. Neither of these pathologic results is a cancer or a known precursor of cancer. However, because atypia and LCIS can indicate increased risk of invasive breast cancer, women with these abnormal biopsy results should be assessed for chemoprevention.

### Developing new therapies for colon cancer

Physician-researchers in the Division of Surgical Oncology are leading a number of cutting-edge studies investigating the safety and toxicity of live, personalized vaccines utilizing dendritic cells to prevent relapses and secondary cancers for patients with colorectal cancer. Using live vaccines offers many advantages, including resistance to tumor-associated immune suppression and ability to selectively activate the desirable types of immune cells, in order to maximize the anti-tumor effects and to limit toxicities.



## news briefs

### UPMC Cancer Centers

UPMC Cancer Centers and  
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UPMC Cancer Centers has consistently received national recognition from *U.S. News & World Report* magazine as one of America's top centers for cancer care and research. For more information about UPMC Cancer Centers' clinical services, or University of Pittsburgh Cancer Institute research, call 1-800-533-UPMC (8762) or visit [www.UPMCCancerCenters.com](http://www.UPMCCancerCenters.com).

#### UPMC hospitals named "Blue Distinction Centers for Complex and Rare Cancers"

UPMC Presbyterian Shadyside, with a campus in the Shadyside section of Pittsburgh, and UPMC Passavant, located north of the city, have been designated "Blue Distinction Centers for Complex and Rare Cancers" by the Blue Cross Blue Shield Association.

This designation signifies that these centers have met or exceeded standards set forth by the Blue Cross Blue Shield Association developed in collaboration with leading clinicians and medical societies across the United States. These standards highlight the critical importance of comprehensive, multidisciplinary treatment planning; depth of expertise across cancer disciplines; ongoing quality management and improvement programs for cancer care; ongoing commitment to using clinical data registries, and providing access to appropriate clinical research for complex and rare cancers; and a proven, sufficient volume of experience in treating rare and complex cancers.

Ronald B. Herberman, MD, director, UPMC Cancer Centers and University of Pittsburgh Cancer Institute, says, "This distinction recognizes our strong commitment to superior and expert cancer care for every patient."

Complex and rare cancers compose 15 percent of new cancer cases in the United States each year, making it difficult for patients to identify facilities with oncologists and surgical teams experienced in treating these malignancies. The types of cancers designated by Blue Cross Blue Shield as complex and rare include: acute leukemia (inpatient/nonsurgical), bladder cancer, bone cancer, brain cancer (primary), esophageal cancer, gastric cancer, head and neck cancers, liver cancer, ocular melanoma, pancreatic cancer, rectal cancer, soft tissue sarcomas, and thyroid cancer (medullary or anaplastic).

#### Save the date

The 50th Annual American Society for Therapeutic Radiation and Oncology (ASTRO) meeting will take place Sept. 21 to 25, 2008 in Boston. Visit UPMC Cancer Centers at booth 1045 in the ASTRO Exhibit Hall.