

# Lombardi Magazine

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Georgetown University

Lombardi Cancer Center  
Research • Education • Treatment

## A Conversation with Lombardi's New Director... Dr. Richard Pestell

On September 3rd, Richard G. Pestell, MB BS, MD, PhD joined Lombardi as the new Cancer Center Director. Dr. Pestell is an internationally renowned expert in oncology and endocrinology who comes to Lombardi from the Albert Einstein Cancer Center of Yeshiva University in New York. Originally from Australia, Dr. Pestell has enjoyed a distinguished career in academic medicine. In this interview, Dr. Pestell tells us about himself and shares his vision for Lombardi.

### **Q. What attracted you to Lombardi? Why do you see Lombardi as a good fit for you personally?**

The quality of Lombardi's clinical care and research is internationally renowned. Kevin Cullen [who served as Lombardi's interim director since October 2000] and Bob Dickson [who led the Department of Oncology as interim chair] provided outstanding leadership during Lombardi's director transition, so I'm taking over a center that is poised to become one of the best cancer centers in the country.

I'm excited by the commitment of Georgetown University and MedStar [a non-profit network of seven hospitals, including Georgetown University Hospital] to Lombardi. Dr. Bill Thomas, who is MedStar's Executive Vice President of Medical Affairs, and the rest of the MedStar leadership are eager to collaborate to improve the quality of cancer care available to the diverse population in the area. As part of this effort, we are working together to make Lombardi's clinical trials and other research studies accessible to all patients in the MedStar network.

Also, Lombardi's physical location makes it ideal for collaboration with the National Institutes of Health and other medical centers and high-tech companies in the area.

### **Q. What are some of your plans for Lombardi?**

I plan to establish an oncology-genetics program to expand our study of the genetic changes involved in cancer, and develop a premier molecular pathology laboratory to identify new markers of cancer risk. I plan to build a program in medicinal



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The Lombardi Cancer Center would like to extend a warm welcome to the research and clinical faculty members who joined us in 2002.

For more information about these doctors, go to <http://lombardi.georgetown.edu/about/physiciansandstaff.htm>

**Asim Amin, MD, PhD**, who completed his hematology/oncology fellowship at Lombardi, returned in April as an assistant professor of medicine (hematology/oncology). Dr. Amin spent the past two years in Pakistan organizing the education and research program of a charity cancer center. Dr. Amin's areas of clinical research include genitourinary malignancies and melanoma.

**Bruce Cheson, MD**, was appointed professor of medicine, head of hematology, and director of hematology research at Lombardi in June. Dr. Cheson's clinical interests focus on the development and evaluation of new therapeutic approaches for hematologic malignancies. Most recently, he was Head of the Medicine Section for the National Cancer Institute's Clinical Investigations Branch within the Cancer Therapy Evaluation Program, and senior staff physician in the NCI's Lymphoma Clinic.

**Corina Gonzalez, MD**, joined Lombardi as assistant professor of pediatrics (pediatric hematology/oncology) in January. She comes to Georgetown from the Pediatric Oncology Branch of the National Cancer Institute. Dr. Gonzalez's research focuses on the development of new therapeutic modalities to treat fungal infections in the immunocompromised host.

**Marja Nevalainen, MD, PhD**, came to Lombardi in March as an assistant professor of oncology and cell biology. Most recently, Dr. Nevalainen was a postdoctoral scientist at the Uniformed Services University of the Health Sciences. At Lombardi, she will investigate hormonal regulation of prostate and breast cancer.



Drs. Gonzalez, Toretzky and Amin



Drs. Nevalainen and Rui

**Hallgeir Rui, MD, PhD**, assistant professor of oncology, came to Lombardi in March after establishing a research program in prostate and breast cancer in the Department of Pathology at the Uniformed Services University. Dr. Rui's research seeks to define the signaling pathways activated by prolactin and related peptide factors that promote breast and prostate cancer cell growth.

**Jeffrey Alan Toretzky, MD**, assistant professor of oncology, came to Lombardi in May from the Departments of Pediatrics and Biochemistry and Molecular Biology at the University of Maryland. Dr. Toretzky is a pediatric oncologist who is dividing his time between Lombardi's pediatric outpatient clinic and the lab. His research interests include pediatric sarcomas, particularly Ewing's sarcoma. ■

Ewing's Sarcoma...

# Unraveling the Mystery

Although he is new to Lombardi, Jeffrey Toretzky, MD, assistant professor of oncology, is already hard at work identifying the key factors responsible for the development and growth of Ewing's sarcoma, a type of bone cancer that most commonly affects adolescents. Toretzky's goal is to learn to manipulate these factors to develop safer, more effective treatments for this disease.

Researchers are not sure what triggers Ewing's sarcoma, or why the cancer typically develops late in childhood. Some of Toretzky's initial lab studies suggest that one cause of Ewing's sarcoma is insulin-like growth factor 1, a hormone whose production is stimulated by growth hormone. His results suggest that IGF-1 not only contributes to the growth and development of Ewing's sarcoma, but also enhances the cancer cells' ability to survive chemotherapy.

These lab findings encouraged Toretzky to study IGF-1 in patients with Ewing's sarcoma. He analyzed blood samples to measure levels of IGF-1 and a protein that binds to it, IGF binding protein-3. His preliminary results indicate that a high ratio of IGF binding protein-3 to IGF-1 in the blood may signify a better prognosis for patients with the cancer.

Toretzky is now engaged in a three-year study to determine if measurement of IGF-1 and IGF binding



Dr. Jeffrey Toretzky

protein-3 can serve as a prognostic tool, and if treatments to manipulate IGF-1 levels can improve survival. The study will enroll about 400 patients.

Toretzky considers it a natural progression to study Ewing's sarcoma in the lab, conduct patient studies, and treat children with the cancer. "It's important for me to have both the clinical and research aspects of my job. When the research can benefit the patients, that's when it gets exciting." ■

## Lombardi's Pediatric Hematology and Oncology Team

Like adults, children suffer from many different types of cancers with unique treatment challenges. And, like adults, children benefit from cancer treatment by physicians with expertise in their particular type of cancer.

"The varied expertise of Lombardi's talented pediatric team allows us to offer specialized care to our patients," said Aziza Shad, MD, Chief, Division of Pediatric Hematology/Oncology, Blood and Marrow Transplantation.

Dr. Shad specializes in leukemia and lymphomas; Dr. Amal Abu-Ghosh in bone marrow transplantation; and Dr. Francisco Bracho in brain tumors and solid tumors. Drs. Corina Gonzalez and Jeffrey Toretzky are the two most recent additions to the Lombardi pediatric team, specializing in hematologic disorders and solid tumors, respectively. ■

To find out more. <http://lombardi.georgetown.edu>

Lombardi CancerLine. (202) 784-4000



# Make a Wish Upon... an Elephant?

Visitors to the Lombardi's Pediatric Clinic, The Children's Cancer Foundation Pediatric Hematology-Oncology Outpatient Clinic, can always expect a surprise. The latest was a four and a half foot long, five foot tall elephant that towered over the children in the waiting room.

The elephant is part of a project organized by the D.C. Commission on the Arts and Humanities to adorn the nation's capital with "party animals." The 100 Democratic donkeys and 100 Republican elephants follow the lead of successful public art displays in other cities, such as the creatively decorated cows in Chicago and fish in Baltimore.

Early this year, Tracy Councill, Senior Art Therapist at Lombardi, read an article about the Party Animals project in the newspaper. Councill called Matt Gerson, a Cancer Research Foundation of America board member and founder of Tracy's Kids – a fund that has supported Lombardi's art therapy program since 1991. Gerson helped Councill apply for the chance to decorate an elephant.

"Our choice to decorate an elephant wasn't political," Councill said, laughing. Rather, during a previous art project, Councill and Lombardi's pediatric patients learned that elephants are considered lucky. "There were two things the kids really wanted to do when decorating the elephant. One was to make wishes, because elephants are lucky. Also, the kids wanted the elephant to relate to their medical experiences, so they chose to have his bones showing, like you are looking at an x-ray."

The children's design was selected from 1,200 international applications.

In March, the "naked" gray elephant arrived at the clinic. Councill and art therapist E.J. Endler

drew on the skeleton; like the rest of the elephant, the bones were then covered with tiles. More than 50 kids and family members worked on the project, creating hand-made tiles, writing wishes, and glazing and attaching the tiles.

"One of the main goals of the art therapy program is to help kids feel like they aren't passive patients things are done to, but active participants in the work of getting well," Councill explained. "Art therapy helps them feel active and engaged and allows them to do something fun, express their goals, and learn what they have in common with other kids with cancer. The wishes especially gave the kids and their family members permission to remember what was really important, what was really in their hearts. It was very meaningful."

Lombardi's pediatric patients are excited to show their work off to others. "It's our hope that the community will find our elephant as rewarding as the kids did," Councill said. The elephant currently is displayed at Market Square, near the Archives Metro and Navy Memorial, where it will remain until late September. Then, Lombardi's elephant will be sold at a public auction.

Councill and the children are hoping that a generous donation will make it possible to bring the elephant back to Lombardi, where it will be put on permanent display. ■



Tracy Councill and pediatric patients create the Lombardi elephant.

To find out more. <http://lombardi.georgetown.edu>

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## Grant Funding...

Selected new grant funding for fiscal year 2002 are highlighted below:

- **Stephen Byers** received \$697,915 from the National Institute of Diabetes and Digestive and Kidney Diseases for "Cross Regulation of Beta-catenin and Retinoid Signaling."
- **Robert Dickson** received \$719,764 from the National Cancer Institute to support the "Training Grant in Tumor Biology."
- **Edward Gelmann** received \$582,416 from the U.S. Army Medical Research and Materiel Command for "Genetic Risk Factor for Prostate Cancer."
- **Robert Glazer** received \$155,200 from the National Cancer Institute for "Structure-Based Discovery of AKT Inhibitors."
- **Radoslav Goldman** received \$351,303 from the U.S. Army Medical Research and Materiel Command for "Mutagen Sensitivity, Apoptosis and Polymorphism in DNA Repair as Measures of Prostate Cancer Risk."
- **J. Milburn "Kim" Jessup** received \$150,000 from NASA for "Use of NASA Bioreactor to Study Cell Cycle Regulation."
- **John Ojeifo** received \$1,367,525 from the National Cancer Institute for "Combined Gene Therapy for Metastatic Breast Cancer."
- **Careen Tang** received a U.S. Army grant of \$349,200 for "A Novel Molecular Targeting of a Tumor-Specific Oncogenic Mutant Receptor in Human Prostate Cancer."
- **Kathryn Taylor** received \$580,713 from the U.S. Army Medical Research and Materiel Command for "Treatment Decision Making Among Early-Stage Prostate Cancer: Evaluation of Computer-Based Patient Education and an Interactive Decision Aid."
- **Todd Waldman** received \$100,000 from the National Cancer Institute for "Genetic Analysis of Beta-Catenin Function in Human Cancer."

## Selected Publications...

Since January 2002, Lombardi members have authored more than 160 scientific articles, including:

- **Mandelblatt JS, Lawrence WF, Womack AM and colleagues** published, "Benefits and costs of using HPV testing to screen for cervical cancer" in the May 8 *Journal of the American Medical Association*.
- **Kim JS, Krooks H, Dracheva T, and colleagues** published, "Oncogenic  $\beta$ -catenin is required for bone morphogenetic protein 4 expression in human cancer cells" in the May 15 *Cancer Research*.
- **Ellis M, Davis N, Coop, A and colleagues** published, "Development and validation of a method for using breast core needle biopsies for gene expression microarray analyses" in the May issue of *Clinical Cancer Research*.
- **Hughes C, Lerman C, Schwartz M and colleagues** published, "All in the family: evaluation of the process and content of sisters' communication about BRCA1 and BRCA2 genetic test results" in the January 15 *American Journal of Medical Genetics*.
- **Isaacs C, Peshkin BN, Schwartz M and colleagues** published, "Breast and ovarian cancer screening practices in healthy women with a strong family history of breast or ovarian cancer" in the January issue of *Breast Cancer Research and Treatment*.
- **Oberst MD, Johnson MD, Dickson RB and colleagues** published, "Expression of the serine protease matriptase and its inhibitor HAI-1 in epithelial ovarian cancer: correlation with clinical outcome and tumor histopathological parameters" in the April issue of *Clinical Cancer Research*.
- **Boulares AH, Zoltoski AJ, Contreras FJ and colleagues** published, "Regulation of DNAS1L3 Endonuclease Activity by Poly(ADP-ribosylation) during Etoposide-induced Apoptosis" in the January 4 *Journal of Biological Chemistry*.
- **Ackler S, Ahmad S, Tobias C and colleagues** published, "Delayed mammary gland involution in MMTV-AKT1 transgenic mice" in the January 10 *Oncogene*.
- **Feng LX, Chen Y, Dettin L and colleagues** published "Generation and in Vitro Differentiation of a Spermatogonial Cell Line" in the July 19 issue of *Science*.
- **Martin MB, Voeller HJ, Gelmann EP and colleagues** published, "Role of cadmium in the regulation of AR gene expression and activity" in the January *Endocrinology*.

## Grand Rounds...

Lombardi Cancer Center, in conjunction with the Office of Continuing Education, offers an ongoing series of Oncology Grand Rounds. The monthly program features distinguished visiting scientists and focuses on translational research and treatment. Physicians, basic scientists and clinical investigators receive one CME Category 1 credit for each lecture, held on the last Wednesday of the month in the Main Auditorium of the Research Building, at 3970 Reservoir Road, NW, Washington DC, 20057. Refreshments are available at 7:30 a.m. with the hour-long program beginning at 8:00 a.m.

### September 25

#### **Novel Therapeutic Approaches for Malignant Gliomas**

Speaker: Howard A. Fine, MD, Branch Chief, Neuro-Oncology, Division of Clinical Sciences, NCI, NIH.

### October 30

#### **Genes and the Environment in Cancer Etiology**

Speaker: Joseph Fraumeni, MD, Director, Division of Epidemiology and Genetics, NCI, NIH.

### November 13

#### **To be Announced**

Speaker: Carlos Arteaga, MD, Vanderbilt University.

### December 11

#### **p53 Tumor Suppressor Gene: At the Crossroads of Molecular Carcinogenesis and Molecular Epidemiology**

Speaker: Curtis Harris, MD, Chief, Laboratory of Human Carcinogenesis, NCI, NIH.

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chemistry to develop selective, non-toxic drugs that will target specific genetic abnormalities in tumors, and improve the quality of life for patients with cancer. And I'd like to enhance Lombardi's capabilities in biochemistry, biostatistics and bioinformatics. I will continue recruiting outstanding senior faculty to lead our efforts in many of these areas. With these new faculty and the outstanding faculty currently at Georgetown, we can build an extraordinary future at Lombardi.

**Most importantly, we have to stay focused on our true goal: to provide the best care we possibly can to patients with cancer.**

Everything we do here is directly or indirectly aimed at the provision of high quality patient care, especially here in the DC community.

#### **Q. What are your research interests?**

The overall goal of my research is to develop non-toxic therapies to improve the quality of health care for people with cancer. One method that we have been exploring in my lab is using drugs to interfere with the action of a gene called cyclin D1. Researchers in my lab and others have shown that many different cancers – including breast, prostate, head and neck cancers and many lymphomas – require the cyclin D1 gene to grow. When cells are dividing to create these cancers, cyclin D1 is crucial to the division process. Based on this knowledge, we are trying to design drugs that target and interfere with the action of cyclin D1.

We are also studying how to use gene therapy to prevent or treat cancer by turning selected genes on or off. Scientists have developed ways to use gene therapy in cells in the lab, but it is hard to make it work in a living body because it is difficult to get the therapy to the cancerous cells.

My lab is trying to solve this problem by using a plant steroid, which is completely non-toxic to humans, to

turn targeted genes on or off. We developed a gene therapy with a receptor for the plant steroid, so when the steroid is introduced into the body, it acts only on the gene therapy, and only in the cancerous cells. We tested this therapy using a mouse model, and we were able to successfully turn a gene important to breast cancer on or off. We now have developed a number of different gene therapies that can be regulated by these plant steroids.

Another theme of my research is developing treatments specific to an individual's cancer. By looking at a "genetic fingerprint" of a person's cancer, you can identify the genetic events that occurred in the transformation from healthy cells to cancer. Those events are the key to killing that particular patient's cancer. So the idea is to fingerprint the cancer, find the genetic abnormalities that led to the cancer, and tailor-make the therapy for the patient.



Dr. Pestell and sons Alex and Tim.

This method also will be useful in preventing cancer. For instance, recent research is helping us predict which women with benign breast disease will go on to develop breast cancer. We hope to soon be able to determine, based on the genetic fingerprint of a woman's benign breast tissue changes, if she is likely to develop cancer, and prescribe drugs specific to

her to prevent her breast cancer from even starting. And this method can be extended to many other types of cancer.

I'm excited about the progress we are making in my lab, and I'm eager to collaborate with the researchers at Lombardi. In the end, my main goal is for research to improve the quality of care we provide to patients at Lombardi.

#### **Q. What is your background?**

I received my MD and PhD degrees from the University of Melbourne in Australia. After my residencies in oncology, radiation oncology and hematology, and a fellowship in endocrinology, I treated cancer for about 10 years. Then I went back for a PhD in molecular biology, focusing specifically on cancer-causing genes. After I completed my PhD, I received an award, called the Winthrop Award, from the Royal Australian College of Physicians. This award allowed me to travel to the Harvard Medical School and Massachusetts General Hospital in Boston, where I stayed for two years. Then I continued my clinical work and research at Northwestern University Medical School in Chicago. I joined the faculty of the Albert Einstein College of Medicine in 1996, and two years ago I became chair of the Division of Endocrine-Dependent Tumor Biology at Albert Einstein Cancer Center. And late this summer I began the exciting transition to Lombardi.

#### **Q. What do you do when you're not directing a comprehensive cancer center?**

My wife, Nicky, and I have two sons, Tim and Alex, aged 14 and 12. They are the joys of my life. Although I've been a competitive track and field athlete, I now run mainly to enjoy nature and exercise with the boys. They love camping and enjoyed white water rafting this summer – it reminded us all how important it is to work together! ■

October is Breast Cancer Awareness Month, and a good opportunity to address the controversy surrounding hormone replacement therapy and breast cancer risk.



Clinical Commentary...

## HRT and Breast Cancer Risk

Until recently, research studies have provided conflicting evidence about the connection between HRT and breast cancer. Then, in July, a large clinical trial of more than 16,000 healthy menopausal women found that those taking combined estrogen and progestin (the combination usually given as hormone replacement therapy) for about five years had a 26% increased risk for invasive breast cancer as compared to those taking placebo pills.

This risk was so much higher among HRT users that the studies' sponsor, the National Heart, Lung and Blood Institute, stopped the study several years early. There were benefits to HRT use, such as fewer cases of colon cancer and hip fractures, but the overall harm, including increases in heart disease, stroke and blood clots, outweighed the benefits.

What does this mean if you are one of the approximately 6 million US women taking combined estrogen and progestin therapy? First, it's important to know that the study population's risk for developing breast cancer and an individual's risk are much different. For each woman in the study, the increased risk of invasive breast cancer due to HRT use was only about 8 cases per 10,000 women per year. Still, the risks associated with long-term use of HRT are serious enough to warrant prompt discussion with your doctor to re-evaluate your goals and treatment options.

Regardless of past HRT use, it is crucial that women remain vigilant about regular breast cancer screening. Studies have shown that physical exams and mammography help detect breast cancer and save lives. In fact, recent data from a study in Sweden showed a 50% reduction in breast cancer mortality for screened women, while there was no change in mortality among unscreened women. In the US, statistics showing a decline in breast cancer death correspond directly to increased use of screening mammograms. It is recommended that women aged 40 and over get regular screening mammograms.

New technologies for breast cancer screening are in development, ensuring that women will have access to more sensitive and reliable techniques in the years to come. Just as important, researchers are improving upon prevention strategies and treatment for breast cancer at every stage. Here at Lombardi, numerous breast cancer studies are underway, a few of which are highlighted in this Breast Cancer Special Section: digital mammography has improved upon mammography technology; Dr. Isaacs is using new methods to identify early cellular changes likely to progress to cancer; Dr. Furth is developing techniques to treat early cellular changes and prevent the onset of cancer; and Dr. Hilakivi-Clarke is identifying risk factors for breast cancer to aid in prevention. ■

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*Clinical Commentary is a regular feature from Lombardi's Director of Clinical Affairs, Robert Warren, MD.*

Digital Mammography...

# Latest Advance in Breast Cancer Screening

Using a lower dose of radiation than a traditional mammogram, the new system produces images of the breast on a computer rather than on X-ray film. Women no longer have to wait while the films are developed, and the radiologist can adjust the contrast and size of the image on the computer screen.

Lombardi's Betty Lou Ourisman Breast Health Center is the first public facility in the Washington region to offer digital mammography, the "wave of the future in breast cancer screening," according to Gale Sisney, MD, director of breast imaging.

"Digital mammography is a meaningful advance in the way we perform and read mammograms," said Sisney. Using a lower dose of radiation than a traditional mammogram, the new system produces images of the breast on a computer rather than on X-ray film. Women no longer have to wait while the films are developed, and the radiologist can adjust the contrast and size of the image on the computer screen.

Computer-assisted diagnosis also helps in the identification of calcifications that cannot be seen with the naked eye. The ability to adjust the contrast of the image sometimes allows the digital mammogram to be more accurate in patients with dense breasts or implants, explained Sisney.

The Betty Lou Ourisman Breast Health Center provides all breast health services in one facility. In

addition to screening and diagnostic services, the center also offers breast-health education, prevention information and a resource center for patients and families. If cancer is diagnosed, women have seamless access to the physicians at Lombardi. A nurse case manager coordinates a woman's diagnostic and treatment experience, scheduling all the

necessary testing and physician appointments and serving as a liaison to other services such as social work, pastoral care, support groups and community resources. Most important, Ourisman Center clinicians are dedicated solely to

breast health. "This is what truly sets us apart," explained Sisney. "Our staff offers a level of quality and knowledge that ensures patients the best possible care."

The Betty Lou Ourisman Breast Health Center was made possible by the generosity of the Ourisman family. Betty Lou Ourisman, who died of breast cancer in 1992, was the wife of Mandell J. Ourisman, who attended Georgetown University and is owner of Ourisman Automotive Enterprises. ■

— D. Arbogast

**"Digital mammography is a meaningful advance in the way we perform and read mammograms."**

To find out more. <http://lombardi.georgetown.edu>

Lombardi CancerLine. (202) 784-4000

# New hope for breast cancer

Researchers at Lombardi are helping us find and treat the earliest precancerous cellular changes to prevent the onset of breast cancer. Here, we examine the research of two Lombardi investigators: Dr. Claudine Isaacs, who is studying methods to identify these early precancerous changes, and Dr. Priscilla Furth, who is developing methods to treat the precancerous changes themselves.

## Early Detection Among High-Risk Women...



Dr. Claudine Isaacs

Breast cancer detection is rapidly evolving. Instead of screening for a mass in the breast, which is the goal of mammography and physical exams, new early detection techniques hold the promise of identifying precancerous changes in breast cells themselves.

At the forefront of this research is Claudine Isaacs, MD, clinical co-director of Lombardi's Breast Cancer Program. Isaacs is collaborating with several researchers at Lombardi to study new methods to detect the earliest changes in the cells that line the milk ducts in the breast, called mammary epithelial cells. Studies have shown that changes in mammary epithelial cells – where the majority of breast cancers originate – are associated with an increased risk of breast cancer.

The development of early detection techniques is especially important for women who have mutations in the genes BRCA1 or BRCA2, inherited from one of their parents. Women with mutations to these genes have a markedly higher risk of developing breast cancer than women without the mutations. Isaacs is focusing on women with mutations in BRCA1.

Specifically, Isaacs and her colleagues are evaluating the efficacy of a new technique known as ductal lavage in identifying premalignant changes in the breasts of these high-risk women.

Ductal lavage is a minimally invasive technique that involves the insertion of a tiny catheter into the milk ducts of a woman's breast. The ducts are flushed with saline to collect a cell sample, which is then analyzed to search for cellular or genetic changes that signal an increased risk of breast cancer.

Isaacs also is collaborating with radiologists at Lombardi and the Washington Hospital Center to study the use of positron emission tomography scans to detect premalignant breast cell changes. Already, the PET scan is an important imaging technique for women with breast cancer; by detecting the increased glucose use of breast cancer tumors, PET scans can help stage the cancer, evaluate a woman's likely response to therapy, and rule out recurrent disease. Recently, Isaacs and her colleagues began testing the idea that premalignant cellular changes also are characterized by increased glucose use. She is now scanning women with BRCA1 mutations to see if PET scans are able to detect premalignant changes.

Isaacs and her colleagues hope that these screening techniques will prove effective and one day offer women an easy way to identify the early warning signs of breast cancer – before the cancer has a chance to grow. “Now that we are able to identify BRCA1 mutation carriers, we need to develop good methods to detect premalignant changes as early as possible,” Dr. Isaacs said. “This would empower high-risk women by allowing them to take steps that prevent their cancer from developing.” ■

# prevention...



Dr. Priscilla Furth

## Stopping Breast Cancer Before It Starts...

Priscilla Furth, MD, professor of oncology, is conducting research at Lombardi to develop treatments for the early cellular changes that can lead to cancer, or preneoplasia. “Identifying preneoplastic changes and treating the cells at this early stage may enable us to prevent some cancers from developing altogether,” Furth said.

Not all preneoplastic changes in cells lead to cancer, Furth explained; some revert to a normal state. She is looking for the molecular factors that dictate when preneoplasia is reversible and when it is not. To identify these factors, Furth has developed a new mouse model that replicates the cellular changes that lead to cancer in the human body. The model is unique because the researchers are able to “turn off” the cancer progression at different points and see if the cells regress to normal, or continue to become cancerous. “If we can understand the difference between the preneoplastic cells that return to normal and those that become cancerous, we may be able to interfere with the process that causes the progression to cancer,” Furth said.

Based on current scientific knowledge, Furth expected to find changes to the genes of the cells that became cancerous. Instead, she found minimal gene changes, but significant structural changes to proteins associated with the cells. Her research clearly indicates that the altered proteins are the factors that prevent the preneoplastic cells from returning to normal. She is now working to identify exactly how the proteins are modified and if this modification can be prevented, halting the progression of the preneoplastic cells toward cancer.

In related research, Furth is investigating methods to replicate key steps in a natural process called mammary gland involution. Mammary gland involution occurs in lactating women after they stop breastfeeding, and involves the death of unneeded cells and restructuring of breast tissue, returning it to

## Are You at High Risk for Breast Cancer?

The Cancer Assessment and Risk Evaluation (CARE) Program is a free genetic counseling and testing program offered by the Lombardi Cancer Center. If you answer YES to any of the questions below, you or your relative may be eligible to participate in the CARE program.

### If you or your family member have had breast cancer:

- Were you or your relative diagnosed before age 50, and are you of Jewish descent?
- Were you or your relative diagnosed before age 50 and do you also have a first-degree relative (mother, sister, daughter) who had breast cancer before age 40, or ovarian cancer at any age?
- Were you or your relative diagnosed before age 50, and do you also have 2 other relatives on the same side of the family with breast and/or ovarian cancer?

### If you or your family member have had ovarian cancer:

- Were you or your relative diagnosed with ovarian cancer before age 60, and are you of Jewish descent?
- Do you or your relative also have a first-degree relative who had breast cancer before age 50 or ovarian cancer at any age?

### If you have a family history of breast and/or ovarian cancer and are of Jewish descent:

- Do you have three relatives on the same side of the family who were diagnosed with breast and ovarian cancer (not necessarily in the same individual)?

Please call the CARE referral line at (202) 687-1750 for more information.

# Breast Cancer Risk and Pregnancy Weight Gain

Research at Lombardi has shown that women who gain more than 38 pounds during pregnancy may increase their risk of postmenopausal breast cancer by as much as 40%. These findings were reported by Leena Hilakivi-Clarke, PhD and colleagues at the American Association for Cancer Research Annual Meeting in April.

“Our results also indicate that women who retain the additional weight after pregnancy are at the highest risk for breast cancer,” said Hilakivi-Clarke, professor of oncology. “The extra weight may cause changes in the breast tissue that increase susceptibility to cancer later in life.”

Working with colleagues in Finland, Hilakivi-Clarke analyzed data from more than 27,000 Finnish women. Information about breast cancer diagnosis and pregnancy weight gain were obtained from a national cancer registry, maternity center registries and from a questionnaire completed by the study participants. The researchers found that weight gain during pregnancy did not affect premenopausal breast cancer risk, but each kilogram (2.2 lb) increase in pregnancy weight raised the risk of postmenopausal breast cancer by 3.9%, when adjusted for body mass index before pregnancy.

The exact reason for this increased risk is not clear, but other studies suggest that increased weight gain during pregnancy results in higher estrogen levels.

“Women with the highest estrogen levels during pregnancy are more likely to develop breast cancer,” according to Hilakivi-Clarke.

Currently, Hilakivi-Clarke is involved in several studies to identify dietary influences on breast cancer, including the possible effects of fish oil, soy and whole grains. She is interested especially in the timing of these exposures in life (before birth, during childhood, or during pregnancy).

“We still have a lot to learn about the causes of breast cancer,” Hilakivi-Clarke said. “It is clear that there are some risk factors women are not able to change, like genetic predisposition to breast cancer, and some they are able to change, like diet and weight gain. As research continues to identify risk factors, women have more opportunities to change specific behaviors to decrease the likelihood of getting breast cancer.”

“The results of this study provide another reason for pregnant women to stay within the recommended 25 to 35 pounds weight gain,” Hilakivi-Clarke

noted. “We’ve seen that women who gain too little weight during pregnancy put their babies at risk for low birth weight, and now it seems that women who gain too much weight put themselves at risk for breast cancer after menopause.” She recommends that pregnant women and their health care providers discuss diet and exercise that will have benefits for both Mom and baby. ■



Dr. Leena Hilakivi-Clarke

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the normal, pre-lactation state. According to Furth, the same steps could be applied to the reversal of preneoplasia and the restructuring of preneoplastic tissue into normal tissue.

Furth is focusing on a protein called Stat5, which is important to both breast cancer growth and mammary gland involution. Furth has shown that Stat5 must be inactivated for the death of unnecessary cells during mammary gland involution, and that it promotes survival of breast cancer cells. She and her research team

believe that deactivating Stat5 may help to inhibit cancer growth, reduce the ability of cancer cells to survive, and increase the effectiveness of chemotherapy.

Furth’s research is bringing us closer to the day when the earliest cellular changes can be treated, before cancer can develop. “Breast cancer is extremely complex, but we are learning more and more about the pathways that lead to its development. My goal is to identify preneoplastic changes and, ultimately, develop well-tolerated drugs that prevent the onset of cancer.” ■



16th Annual Lombardi Gala. Left to right: John Jaffe, recipient of Lombardi Symbol of Caring; John Safer, sculptor and donor, Lombardi Symbols of Caring and Courage; Jill Kirkpatrick, recipient of Margaret L. Hodges Leadership Award; and Vincent T. Lombardi, II.



16th Annual Lombardi Gala. Left to right: The Honorable Carol Crawford, Gala chair; Lance Armstrong, four-time Tour de France champion and recipient of Lombardi Symbol of Courage Award; and Margaret Hodges, Gala founder.



16th Annual Lombardi Gala. Left to right: Lance Armstrong; Mrs. Gamble; and Jaye Gamble, regional vice president, Comcast Cable, and Gala underwriter.

## Mark Your Calendars for the Seventeenth Annual Lombardi Gala...

Saturday, November 2 • Hilton Washington Hotel

For the seventeenth year, the **Lombardi Gala** will raise crucial funds for the Lombardi Cancer Center while offering attendees an enchanting night exploring the “Treasures of the Sea.” The black-tie dinner dance will feature a silent auction with over 300 items and a select live auction including a 2003 Jaguar, courtesy of Manhattan Jaguar and Rosenthal Jaguar. The silent auction and cocktail reception begin at 6 p.m., followed by dinner, the live auction, awards and dancing at 8 p.m. For the second year, Comcast Cable Communications, Inc. will underwrite the event. The 2002 Gala leadership includes: the Hon. Carol T. Crawford; Mrs. Margaret Hodges; H.E. the Ambassador of Australia and Mrs. Thawley; the Hon. and Mrs. John Breaux; the Hon. and Mrs. Pat Roberts; Mr. Paul S. Schweitzer; Mr. Stephen G. Yeonas, Jr.; Ms. Nancy Chistolini; and Ms. Linda O. Haan.

Awards will be presented to remarkable individuals for their fight against cancer. The “Lombardi Symbol of Courage” will be awarded to **Patti (P.J.) Cooksey**, jockey at Churchill Downs. The “Lombardi Symbol of Caring” will be awarded to **Don Shula**, former head coach of the Miami Dolphins and founder of the Don Shula Foundation, which is dedicated to breast cancer research. The “Margaret L. Hodges Leadership Award” will be presented to **Nancy Chistolini**, senior vice president of Fashion & Public Relations at Hecht’s.

Tickets begin at \$350 each; sponsorships begin at \$5,000. For information call (202) 687-2604 or go to <http://lombardi.georgetown.edu> and click on Events & Activities. ■

## American Cancer Society Supports Young Lombardi Investigators

For the third year, the **American Cancer Society** has awarded Lombardi an institutional grant to provide research funding for three junior faculty members and one medical student or health sciences graduate student at Georgetown University Medical Center. The funding is used as seed money for cancer-related research.

Congratulations to the 2002 award recipients: Ann O’Malley, MD; Anna Cabanes, PhD; Sheau-Ling Lee, PhD; and Anoushka Alfonso, medical student.

2001 award recipients presented their research

findings during a special minisymposium on September 6. Presentations included: Elena Silva Casey, PhD, “Identification of Regulatory Factors Required for Control of Sox3, a Transcription Factor Expressed in Proliferating Neural Precursor Cells”; Beth Peshkin, MS, “Tamoxifen as Chemoprevention in Breast Cancer Patients with BRCA1 Mutations: A Survey of Physician Attitudes and Predictors of Recommendations”; and York Tomita, PhD, “Structure Determination of Bcl-XL Inhibitor Complex for a Novel Anticancer Drug Development.” ■

# Community Events...

Guests at the **Polo Shopping Event** on March 21 were treated to champagne and hors d'oeuvres while viewing the Ralph Lauren Spring Collection at the Georgetown Park store. Ten percent of all purchases that day benefited the breast cancer research program at Lombardi. The event was facilitated by Polo Ralph Lauren and Jill Kirkpatrick, Lombardi volunteer and winner of the Margaret L. Hodges Leadership Award presented at last year's Lombardi Gala. ■

The 2002 **Thomas R. Schafer Memorial Lecture**, entitled "From Bench to Bed: The Use of Translational Research to Help Patients with Pancreatic Cancer," was presented on May 29 by Dr. J. Milburn Jessup, MD, professor of oncology at Lombardi. The Thomas R. Schafer Memorial Fund was established to sponsor an annual lectureship to share the latest innovations in pancreatic and gastrointestinal cancer therapy at Lombardi. ■



Dr. J. Milburn Jessup



Team Georgetown, 2002 Race for the Cure

"Team Georgetown," comprised of over 150 members of the Georgetown University community, participated in the June 1 **National Race for the Cure**, the world's largest 5K run/walk and 1-mile fun walk. The event, a program of the Susan G. Komen Breast Cancer Foundation, raises millions of dollars each year to benefit breast cancer research, education, screening and treatment programs, including those at Lombardi. For more information about the National Race for the Cure, visit [www.nationalracefortheure.org](http://www.nationalracefortheure.org). ■

The Washington, DC third annual **Men's Event for Prostate Cancer**, benefiting the Lombardi Cancer Center, was hosted on June 17 by the Washington Palm Restaurant, in cooperation with the National Cancer Prevention Fund.

Washington event co-chairs were Clifford J. Alexander, Kirkpatrick & Lockhart, LLP; Tommy Jacomo, Washington Palm; Kevin Cullen, MD, Lombardi Cancer Center; and Thomas A. Keating, Thomas Keating Investigations. The Grand Door Prize was a trip to Jamaica courtesy of Air Jamaica and The Ritz-Carlton Rose Hall. Four people bid \$10,000 each to have their caricature on the wall of the Palm. A trip to the upcoming PGA Tour Championship, courtesy of American Airlines, with entry tickets from Paul Schweitzer of Julien J. Studley, Inc., brought in \$6,500. For information on the 2003 event, contact Bonnie Roberts at [robertsb@georgetown.edu](mailto:robertsb@georgetown.edu). Tickets begin at \$500 each. ■



Third Annual Men's Event: Clifford Alexander, Kirkpatrick & Lockhart; J. Richard Gaintner, MD, Interim EVP Health Sciences, Georgetown University Medical Center; Don Bowman, Associate Vice President, Medical Center Development; John Lynch, MD, Professor of Urology; Tom Keating, Thomas Keating Investigations.

Founded and chaired by Bob Schmidt in memory of Vince Lombardi, the **Lombardi Tournament of Champions** has raised crucial funds for the Lombardi Cancer Center for almost a quarter of a century. The 24th Tournament of Champions was held on June 24. For information on the Annual Tournament of Champions, please call (703) 827-5480. ■

# Upcoming Events...

## September 23

The **Richard J. Fox Memorial Golf Tournament** will be held on **September 23** at the Tournament Players Club at Avenel. The Fox Tournament provides funding for patient support and education activities and the annual prostate cancer-screening program organized by the Lombardi Cancer Center. For more information, call **(202) 333-7626**. ■

## September 27

The second annual **Par for the Cause**, a golf tournament benefit established in memory of Jeanette S. Moore, will provide funds for the advancement of sarcoma research at Lombardi. In 2001, the inaugural Par for the Cause raised over \$12,000. The Moore family looks forward to another successful event on **September 27**. For more information about Par for the Cause, visit [www.lmsfund.org](http://www.lmsfund.org). ■



The Moore family presents a check to Dr. Kevin Cullen, Lombardi Interim Director, following the 2001 Par for the Cause.

## October 14

The fifth annual **Swing Fore the Cure** golf tournament will be held **October 14** at the Westfields Golf Club in Centreville, Virginia. The second annual Shuck & Putt, hosted by McCormick & Schmick's restaurant in Reston, will kick off the event on the evening of October 13, featuring live and silent auctions, games and contests, and food and drink. Swing Fore the Cure has raised more than \$325,000 for breast cancer charities, primarily the Nina Hyde Center for Breast Cancer Research at Lombardi. For more information, call **(202) 687-7269**. ■



Swing Fore the Cure committee members present a check to Dr. Kevin Cullen, Lombardi Interim Director. Left to right: Len Kurtzmann, Nancy Andrews, Skip Tendall, Walter Andrews, Kevin Cullen, Kevin McNerney, Val Bundren, Sarah Wells, Dave Seager, Ann McNerney, Tim Healy.

## October 27

On **October 27**, **Team Lombardi** will join 16,000 runners for the 27th Marine Corps Marathon. In 2001, the inaugural Team Lombardi, including 100 participants and 2,000 donors, participated in the marathon and raised \$250,000 to support Lombardi's vital programs and services. Call **(202) 687-7269** or email [teamlombardi@georgetown.edu](mailto:teamlombardi@georgetown.edu) for more information or to sign up! ■



2001 Team Lombardi



## Making a Difference at Lombardi

Each year, hundreds of individuals, foundations and corporations make gifts to support the Lombardi Cancer Center. Words cannot express the deep appreciation we feel for their overwhelming generosity and their strong belief in our mission. Philanthropic support of Lombardi's friends will continue to be vital to our success. Without their help, our clinicians, scientists, educators and staff would not be able to maintain the level of excellent care that contributes to Lombardi's standing as a world-class leader in cancer care.

If you are interested in making a gift to Lombardi, please use the enclosed envelope and gift form, or give online at <https://lombardi.georgetown.edu/contribute>. Should you have questions about charitable gifts, memorial donations, or special giving opportunities, please contact our Development Office at **(202) 687-8246**.

For more information about Lombardi community events, visit the Lombardi web site at <http://lombardi.georgetown.edu>, and click on Events & Activities. ■

To find out more. <http://lombardi.georgetown.edu>

Lombardi CancerLine. **(202) 784-4000**

Patients should call the facilitator before their first visit to a support group. Groups are free and open to the public; free parking is available. Contact the facilitator listed below for the group location, or go to <http://lombardi.georgetown.edu/events/upcoming.htm>.

### Head and Neck Cancer Support Group

- Third Monday of each month, 12:15-1:45 p.m.
- Contact: Joanne Assarsson, LICSW, (202) 784-3755

### Look Good... Feel Better

- An education program to address appearance-related side effects of cancer treatment.
- Second Monday of each month, 9:30-11:30 a.m.
- Contact: Joanne Assarsson, LICSW, (202) 784-3755

### Lung Cancer Support Group

- First Wednesday of each month, 11:30 a.m.-1:00 p.m.
- Contact: Mary Kardauskas, LICSW, (202) 784-1684

### Us-Too Prostate Cancer Support Group

- A meeting of discussion and sharing. Wives and significant others welcome.
- Second Tuesday of every month, 7:00-9:00 p.m.
- Contact: Sharon Saquella, RN, (202) 687-4613

### Young Women with Breast Cancer Support Group

- For women under the age of 40.
  - First Wednesday of each month, 6:00-7:30 p.m.
  - Contact: Anne O'Connor, RN, OCN, (202) 687-2318
- Registration required.

The Lombardi Cancer Center, part of Georgetown University Medical Center and Hospital, is a full-service cancer center that includes a strong core of basic science and clinical research, a program of high-priority clinical trials, and a commitment to community service and outreach activities related to cancer prevention and control. Lombardi is one of only 40 National Cancer Institute-designated comprehensive cancer centers in the nation, and the only one in the Washington DC area.

*Lombardi Magazine* is produced four

times a year for patients and their families, community members, and friends of the Lombardi Cancer Center. For information about cancer, please call Lombardi CancerLine, (202) 784-4000. For correspondence about the magazine, please email [lcceditor@georgetown.edu](mailto:lcceditor@georgetown.edu) or write to: Editor, *Lombardi Magazine*, The Research Building, Suite E501, Box 571468, 3970 Reservoir Rd, NW, Washington, DC 20057-1468.

To view the *Lombardi Magazine* online, or learn more about the Lombardi Cancer Center, visit <http://lombardi.georgetown.edu>.

#### LOMBARDI CANCER CENTER

Richard Pestell, MB BS, MD, PhD  
Director

#### GEORGETOWN UNIVERSITY MEDICAL CENTER

J. Richard Gaintner, MD  
Interim Executive Vice President  
for Health Sciences

#### GEORGETOWN UNIVERSITY HOSPITAL

M. Joy Drass, MD  
President



A Comprehensive Cancer Center  
Designated by the  
National Cancer Institute

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MedStar Health

To find out more. <http://lombardi.georgetown.edu>

Lombardi CancerLine. (202) 784-4000

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