

Making a Difference



In five short weeks, 13-year-old Tess Hackworthy organized a three-mile walk to support her mother, Amie, who was recently diagnosed with breast cancer. Walk for Courage was held on Saturday, May 1 in the village of Maple Bluff with more than 600 participants raising \$50,000 for breast cancer research at the UW Carbone Cancer Center. The entire Hackworthy family is featured in this photo. Major congratulations to Tess and her family on a successful first-year event. Simply amazing!



Steve Ramig, Cancer Center Development Director (left) is pictured with Sue and David Ebert at a recent donor event at the Wisconsin Institutes for Medical Research (WIMR). A lung cancer survivor, Sue is a passionate lung cancer advocate in the La Crosse area. With Sue's leadership along with UW Carbone Cancer Center's Lung Cancer Task Force Co-Chairs Fred Johnson, George and Candy Gialamas and more than 50 lung cancer advocates statewide, the UWCCC is proud to be collaborating with Gundersen Lutheran on a joint endowment that is focused on advancing lung cancer research being conducted at WIMR.

YES! I want to make a difference by giving to the University of Wisconsin Carbone Cancer Center.

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Please call (608) 263-0160 with questions.

Advances

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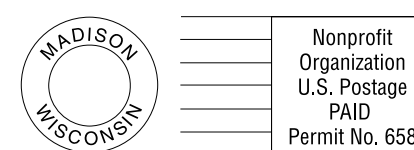
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STAY CONNECTED!

Look inside to learn how to stay connected with the UW Carbone Cancer Center.

On Air Collaborations: Expanding Cancer Center Options

Cancer doctors continually seek optimal treatments for their patients. But staying current about changing technology, new medications and evolving methods of care can be challenging, especially when physicians encounter rare or difficult cancers.

Patients with unusual diagnoses have several options—traveling many miles to a major cancer center, or for many patients in Wisconsin and northern Illinois, staying close to home and receiving care from oncologists affiliated with the UW Carbone Cancer Center.

For nearly a decade, physicians and advanced practice nurses from across the region have been tuning into regularly scheduled video conferences with their colleagues at the UW Carbone Cancer Center in Madison.

Medical and radiation oncologists from Beloit Memorial Hospital; FHN Leonard C. Ferguson Cancer Center at Freeport Memorial Hospital, Freeport, IL; the UW Cancer Center Johnson Creek, Johnson Creek, WI; and from UW Cancer Center at Riverview Hospital, Wisconsin Rapids,

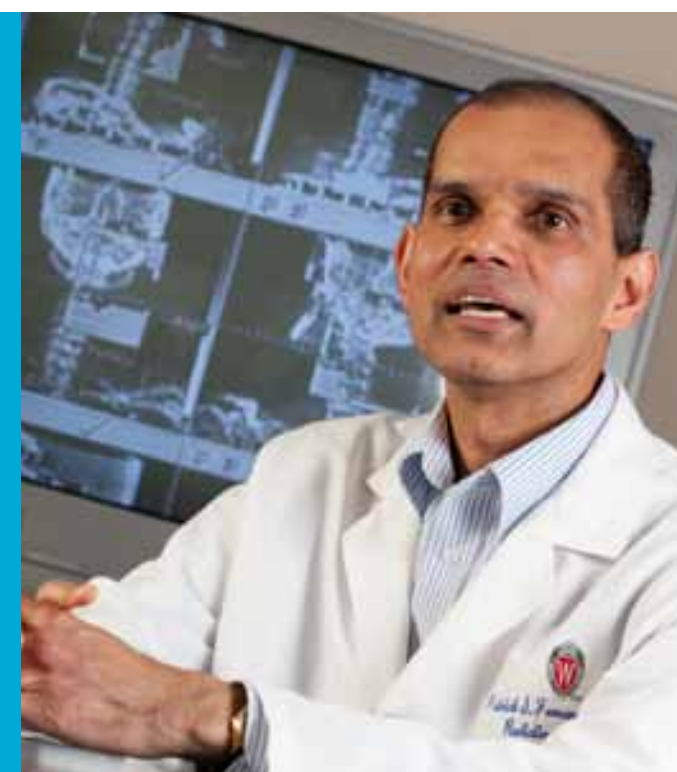
join their counterparts from the UW Carbone Cancer Center to share expertise and consider various options for their patients.

"This makes a tremendous difference," says Dr. Patrick Fernandes, a radiation oncologist at the Leonard C. Ferguson Cancer Center in Freeport. "It allows me to get opinions from colleagues, doctors who are experts on specific kinds of cancer."

Fernandes meets with fellow radiation oncologists each week for an hour and half. Doctors from each of the facilities present cases to their peers. They assess treatment plans, discuss challenging diagnoses and share years' worth of experience.

"The people who gain the most are the patients; they get university-based care at home. It's like getting a second opinion," Fernandes explains.

Dr. Ron Kirschling at the UW Cancer Center Riverview in Wisconsin Rapids attends similar video conferences with fellow medical oncologists from the UW Carbone Cancer Center and the affiliate cancer centers. Once a month they meet to consult on patient care.



Patrick Fernandes, MD

"We are able to bounce ideas off the physicians in Madison. It is very helpful for physicians with a single practice; it gives us the benefits of a group practice and access to wider resources," says Kirschling, medical director and medical oncologist at UW Cancer Center Riverview.

UW RESEARCHERS:

Stress Causes Poor Mental Health in Parents of Kids with Cancer

Hospital appointments, invasive procedures and the uncertainty of their child's situation produce severe stress in parents of children with cancer. These parents may have worse quality of life than those whose children do not have the disease, but according to a recent study at the UW Carbone Cancer Center, they may not be doomed to poor outcomes.

Whitney P. Witt, PhD, MPH and her research team at the University of Wisconsin School of Medicine and Public Health in Madison studied the role of stress in the relationship between parenting a child with cancer and quality of life.

"Caring for these children can be stressful for families and therefore health professionals may want to consider screening parents for mental and physical health

problems. By reducing the parents' stress, we can improve the health of the entire family," Witt says.

The study included 74 parents of children with cancer or a brain tumor and 129 parents of healthy children. In addition to asking about stress and quality of life, interviewers asked about family characteristics, health behaviors, life events, family functioning and social support.

Parents of children with cancer or a brain tumor were more likely to smoke tobacco, less likely to exercise regularly and had worse sleep quality compared to parents of healthy children.

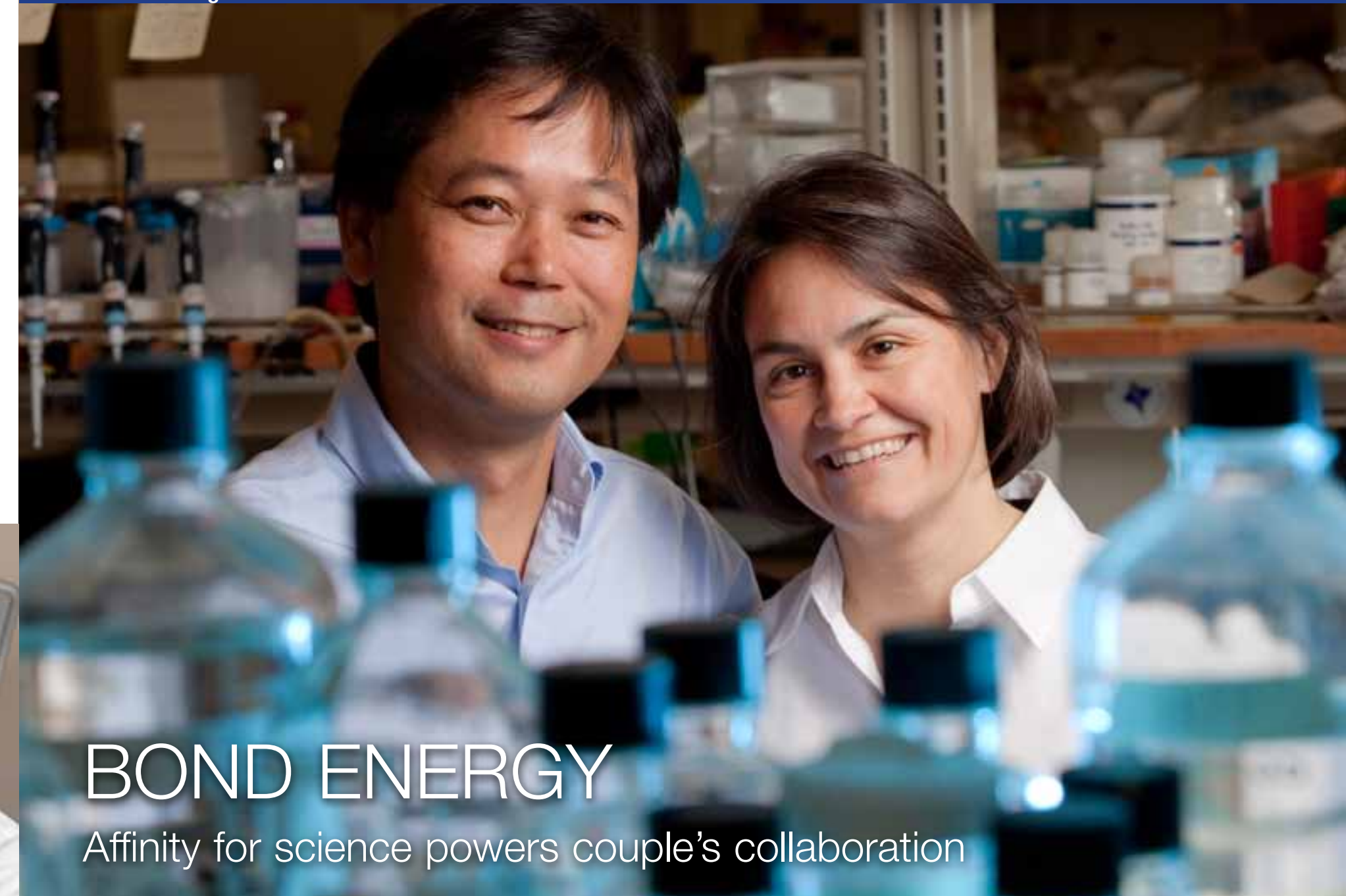
The paper was published in the journal *Quality of Life Research* in May.



Advances

uwhealth.org/cancer

Summer 2010



BOND ENERGY

Affinity for science powers couple's collaboration

Some colleagues were surprised last summer, when cancer researchers Shigeki Miyamoto, PhD, and Elaine Alarid, PhD, willingly moved themselves and their research teams into adjoining laboratories at the Wisconsin Institutes of Medical Research (WIMR).

A few folks simply said what was on their mind: "Are you sure you want to work that close to your spouse?"

They do. "I enjoy spending time with Shigeki," Alarid says. "And we both love to talk science. . . . So why not work together?" (What else would you expect from a couple who met as graduate students when a bomb threat drove their respective laboratory groups into the streets of Berkeley?)

After moving to Madison in 1995, the pair spent 15 years driving to work together then working in separate locations. Miyamoto's initial job at the UW was as assistant professor for the Cancer Center and department of human oncology; Alarid worked as an assistant scientist in the biochemistry department before taking a position in her specialty, physiology.

Their new labs and offices at WIMR provide Miyamoto, now a professor and vice chair of pharmacology at UW School of Medicine and Public Health, and Alarid, now an associate professor of oncology, with many opportunities to collaborate. The seven-story WIMR tower, completed in September 2008, supports translational research by

interdisciplinary teams. The facility's laboratories, offices, meeting spaces and specialized services accommodate 300 cancer researchers. Faculty at WIMR include scientists like Miyamoto and Alarid whose research has clinical implications, doctors who tend to patients and test new therapies, and chemical engineers capable of creating new treatment agents. The fertile mix of people, ideas and resources speeds discoveries that improve treatments and outcomes. "We're learning to think more collaboratively," Miyamoto says.

Since his days as a postdoctoral fellow, Miyamoto's research has centered on the intricate workings of a group of proteins called nuclear factor-kappa-B (or NF-κB) found in most animal cell types. These transcription factor proteins bind to DNA and control activity of several genes, including immune function, growth control and cell death or apoptosis.

"Our laboratory studies the regulation of NF-κB as a model system to learn how normal growth control and cell death are regulated, as well as how deregulation of these processes may contribute to the development of cancer," Miyamoto says. Moreover, studies by Miyamoto and others suggest that blocking NF-κB can cause some tumor cells to stop proliferating, to die, or to become more sensitive to anti-tumor agents.

In recent years, working closely with clinicians helped Miyamoto's team

identify new mechanisms and roles of NF-κB in cell samples from patients with lymphoma and myeloma, as well as to identify certain non-cancerous cells that play a critical role in promoting cell survival and drug resistance in some cancer cells.

Alarid has also uncovered novel molecular mechanisms related to a family of proteins that regulate gene transcription. Her work centers on a steroid hormone receptor called estrogen receptor alpha.

"The research in our laboratory focuses on dissecting the molecular mechanisms controlling how cells respond to estrogen, a key driver of tumor cell growth in many cancers affecting women," Alarid says. "Estrogen mediates its actions through its receptor, estrogen receptor (ER), a member of the nuclear receptor family."

Members of this family are key molecular targets in the pharmacological intervention for diseases including breast and prostate cancer, diabetes, cardiovascular disorders, metabolic X syndrome and osteoporosis, among others.

Serving as a reviewer of breast cancer grants for NIH on a panel where most reviewers are physicians has helped Alarid more fully appreciate their clinical perspective. She relishes having physicians as neighbors at WIMR. "Now if I have a question about the clinical implications of an aspect of our work,

I can walk down the hall for an answer, which is so much better than picking up a phone or sending an e-mail."

The diverse, inclusive environment makes WIMR a great place to work. "It's an amazing place," Alarid says. "When you get a good mix of people with a great level of openness, there's a lot of potential. And we certainly have that here."

Things are going well among the dozen students and staff who work in Miyamoto's and Alarid's labs. "We had to make some adjustments early on because our teams have different approaches to our work and different expectations, but now it feels as if we're one large, extended family," she says.

The couple regards many neighbors and academic colleagues as family, too. Miyamoto, who taught sushi-making during grad school, is a popular guest chef at parties. Even so, the pair reserves plenty of time and energy for the two teenage daughters Alarid fondly calls "our biggest collaboration."

Above photo: Shigeki Miyamoto and Elaine Alarid photographed in their adjoining labs at WIMR.

Q. What's new in the management of brain tumors?

A. A primer on brain tumors

Although relatively uncommon, brain tumors have been featured in recent news, and it seems like we all know someone who has a brain tumor. One reason could be that the definition of "brain tumor" includes many different types of both benign and malignant central nervous system tumors. Benign, slow growing tumors such as meningiomas, pituitary tumors and acoustic schwannomas (hearing nerve tumors) are found with modern brain imaging, despite causing little or no symptoms. In contrast, 'brain cancer' describes the various types of aggressive, malignant tumors that arise from seeding from a primary cancer located elsewhere in the body (i.e. cancers of the lung, breast, colon, skin, etc.), and the rare cancers growing directly from brain cells. Since our brain functions to determine who we are and how we interact with others, any extra growths in and around the brain (whether labeled 'benign' or 'malignant') could cause debilitating problems in our daily life in many ways (e.g. headaches; problems with thinking, vision or speech; weakness; coordination issues; seizures, etc.). Therefore, we believe at the UWCCC that the optimal care for the physical, emotional, mental and social needs of people with brain tumors and their families requires a multidisciplinary team of specialist physicians, nurses, therapists and social workers, in addition to the latest technologies.

Modern therapies

Brain tumors and their effects on adjacent normal brain anatomy, wiring and function are now being imaged at high resolution by sophisticated MRI scans, which are used like "GPS maps" during computer-guided microsurgical tumor resections. With special anesthesia monitoring, neurosurgeons can also painlessly detect and avoid the exact locations of critical brain functions (like reading, speech and movement) by having patients awake for part of the surgery, if needed. Sophisticated image-guided delivery of precise radiation therapy is improving tumor control and minimizing risk of damage to normal brain tissue, therefore leading to better quality of life. Recent advances in chemotherapy combined with surgery and

radiation, have significantly improved survival and quality of life even in cases of the incurable primary brain cancer, glioblastoma multiforme (GBM or grade 4 astrocytoma). Avastin, a new drug that helps block cancer blood vessel formation, has just been approved for treating GBM and shows remarkable, albeit only temporary, effects in some patients.

Hope through biology research and clinical trials

The following areas are just a few of the frontiers UW clinicians and scientists are pursuing to develop even better brain tumor therapies for the future. We are studying more sophisticated metabolic and tumor cell-specific imaging to improve the effectiveness and safety of targeting tumors. Lab research is revealing the mechanisms underlying the therapeutic resistance of cancer stem cells—the 'seeds' of tumors. Data is emerging through clinical trials on the possibility of custom-tailored molecular therapies based on an individual patient's tumor biology—thereby maximizing tumor control and minimizing treatment side effects. UWCCC is a leader in the NIH-funded international cooperative clinical trial groups that are working hard to make much hoped for advances in brain tumor therapies in the near future. We owe a debt of gratitude to the many motivated and brave patients and families who participate in brain tumor clinical trials, which are critical for proving whether new treatment strategies improve on the current standard therapies.



Dr. John S. Kuo, a neurosurgeon who specializes in caring for brain tumor patients, is director of the UW Comprehensive Brain Tumor program. He leads brain tumor clinical trials by chairing the UW Carbone Cancer Center CNS Diseases Working Group and supervises the Brain Tumor Research Lab in studies on cancer stem cells. After graduating with MD and PhD degrees from Harvard and MIT, he trained at the University of Southern California and University of Toronto before moving to UW-Madison.



Patti Keely: A Trapeze Artist Mother, Cancer Researcher and Cancer Survivor

It's 5 am in Washington, DC, and I am awake; jittery from lack of enough sleep and compensating with a tall latte. I've been in Washington to attend a scientific meeting of cancer researchers—to hear the latest breakthroughs, to present my own work, to share in an international community of scientists. I am exhausted from the volume of information and the long days. I am exhilarated, as I have had one of those "eureka" moments while talking with a fellow cancer researcher, in which two pieces of the puzzle come together, and a new idea for investigation is launched.

I head a research lab that studies the way that cancer cells spread or metastasize to other parts of the body. This is important to helping fight cancer, as metastasis is the killer. Metastasis can be hard to treat. We are trying to understand how the environment around tumors, an environment made of proteins and connective tissue, contributes to the spread of cancer. In our journey, we have discovered that a particular protein, collagen, becomes rearranged around the edge of tumors. This rearranged collagen provides tracks that allow cancer cells to leave the tumor and spread around the body, providing a sort of highway on which the cells spread.

I am also twice a cancer survivor, having survived Hodgkin's lymphoma 25 years ago, and more recently esophageal carcinoma. In truth, I chose cancer research because, as a budding cell biologist, I found it truly fascinating. But, it is also absolutely important and strikingly relevant, and recently we have found ways to take our basic research closer towards the clinic...to help diagnose and treat this tragically too common disease. As a survivor, this move towards helping patients is very satisfying.

We recently discovered that the changes in collagen arrangement predict which patients are more likely to relapse. Oncologists are always seeking such information, as it is hard to determine who they need to treat aggressively, and who will be fine with more moderate treatment. We are developing ways to use this change in collagen as a predictor of outcome.

But I am not just a cancer researcher and cancer survivor, I am also a mom, and the reason I'm up so early is to catch the earliest flight, as I am trying to get back to Madison in time to see my

son in a school performance. When I arrive, he's happy I'm there, and I'm happy to be there, too, as these moments are the ones that we will both remember years from now. Being a mom is the greatest joy in my life, and it adds a rich texture to all the other parts. Science is one of those professional fields that takes up as much space and time as you allow it; it is quite easy to consume every single bit of your life with scientific endeavors. My son, David, makes sure I don't. I am so thankful for the evenings we spend playing games or reading, for the bike rides and walks we take, for the weekends hanging out, for the camping trips, for the play and the giggles and the hugs.

"How do you balance family and science?" the younger women who are training to be researchers often ask. This is the thing that most scares them, the thing that may keep many women away from ultimately running their own research labs.

Balance? It's not so much tight-rope walking as swinging from a trapeze.

At any one moment in the day, I am usually either a scientist or a mom, rarely both at once, but often both several times a day. Interspersed moments. My roles flow so seamlessly that I make one phone call to a colleague to discuss how we might better target breast cancer metastasis, and the next to another mom to discuss our volunteer time at the school. In the evening, I might find myself on the phone with a collaborator while chopping onions and making dinner. After dinner is always family time, so is Saturday morning and Sunday afternoon. I volunteer at his school, I chaperone the occasional field trip. And I work from home early in the morning and late in the evening.

I can do this because being a researcher is flexible, and that makes it easier to also be a mom. I can also do this because I have support from my family: my partner, Tom, David's father, Jeff, and my parents all help out in various ways.

In many ways, the skills I've acquired as a mom are useful as a mentor and teacher. Much of the actual research in the lab, the hands on part, is performed by talented graduate students and postdoctoral fellows, who are working with me to learn how to be independent scientists.

Thus, being able to mentor is crucial to advancing our research. Parenting has taught me patience, how to listen and when to give gentle feedback. When to give firm boundaries, how to console bruises, whether they be those obtained as a child on the playground or those obtained as a young scientist at the brutal criticism of a peer reviewer.

The excitement I see in students when they make a discovery is similar to the excitement I see in my child as he grows and explores the world. It is similar to the excitement I feel when another bit of the puzzle falls into place.



And in many ways, the skills I am learning as I mentor students to become cancer researchers are skills that help me as a parent. No one who has mentored simultaneously five independent and very different graduate students has any fear whatsoever of the teenage years. Students finish their thesis and leave, and I expect the sense of loss that accompanies that is preparing me for the day my own son will head off into the world on his own. The continuing relationship I have with some of those who have left assures me that I will always be part of their lives; reminds me I will always be part of my son's life.

Another day. Another 5 am. This time, up early to edit a manuscript while the world lies quiet, before getting my son up, fed and off to school. Then to the lab where I talk with a student about her results, to the school where I sometimes volunteer to help teach science in David's class, back to the lab to peer down a microscope with another student...meetings, papers to read, papers to write, dinner to make, card games to play, books to read out loud, hugs and pajamas.

I am a trapeze artist. I am the luckiest person in the world.

Updates in **Clinical Trials**



Melanoma

A clinical study entitled "A Pilot Trial of Hu14.18-IL2 (EMD 273063) in Subjects with Completely Resectable Recurrent Stage III or Stage IV Melanoma" is open for patient accrual at the UWCCC. This study is for melanoma patients with recurrent regional (Stage III) metastasis or any distant (Stage IV) metastasis who have not received therapy for Stage IV disease and for whom surgical resection would be clinically recommended. To date, no additional medical treatment has been proven to improve survival versus surgery alone for these advanced melanoma patients. The hu14.18-IL2 immunocytokine consists of a humanized anti-GD2 monoclonal antibody linked to interleukin-2 (IL2).

This melanoma study plans to enroll up to a total of 20 patients and will evaluate evidence of anti-tumor activity of hu14.18-IL2 in previously untreated advanced melanoma patients who have achieved a complete response through surgical resection of all known metastatic disease. The use of this combined therapy for patients who have achieved a complete response following surgery is designed to reproduce the "microscopic residual disease" setting where this combination has been most effective in preclinical studies in mice. Since detailed analyses are performed on the removed melanoma tissue, patients need to be enrolled in this study prior to the resection of metastatic disease to be eligible. (CO05601)

Lung Cancer

Lung cancer is the leading cause of cancer death in the United States. Over 60% of new cases are never smokers or former smokers, many of whom quit decades ago. Current standard of care therapy for newly-diagnosed lung cancer involves systemic treatment using chemotherapy drugs that circulate through the body to kill rapidly dividing cells, including cancer cells. Studies are currently being done at the UW Carbone Cancer Center using new therapies that specifically target cancer cells. IMC-3G3 is one of the targeted agents being studied for the treatment of lung cancer.

IMC-3G3 is a monoclonal antibody that targets the PDGFRa receptor which is present on lung cancer cells. PDGFRa plays a role in cell growth. It is hypothesized that when given with standard chemotherapy IMC-3G3 can potentially slow the spread of lung cancer. This study will enroll newly diagnosed lung cancer patients with advanced or metastatic disease. Half of the participants will receive IMC-3G3 in addition to the standard chemotherapy treatment. Blood draws will be done throughout the treatment to further explore IMC-3G3 activity. Archived tumor tissue will also be collected to evaluate PDGFRa receptors present. (CO09503)

Neuroendocrine Tumors

Providing clinical trials for rare cancers is a specialty of the UWCCC Gastrointestinal Oncology Clinical Research Program. A Phase II Trial of Panobinostat in Patients with Neuroendocrine Tumors, is now open at UWCCC. Neuroendocrine tumors are a range of rare and diverse tumors arising from the neuroendocrine system. Gastroenteropancreatic neuroendocrine tumors include pancreatic islet cell tumors and carcinoid tumors and are the most common of the neuroendocrine tumors. Despite being the most common neuroendocrine tumors, gastroenteropancreatic neuroendocrine tumors represent only 2% of all gastrointestinal malignant neoplasms.

Approximately 33 patients will be enrolled in this study to receive panobinostat. The study will take approximately 24 months to complete. (CO08209)

For more information about these and other clinical trials at the UW Carbone Cancer Center, contact Cancer Connect, (800) 622-8922 or (608) 262-5223 in the Madison area.

A complete listing of clinical trials at the UWCCC is also available on our website, uwhealth.org/cancertrials

MARK YOUR CALENDARS

Tomorrow's Hope Walk Fest
Benefit for UW Carbone Cancer Center
July 23, 2010
www.tomorrowshope.org

Drive for Hope Golf Outing – Beaver Dam
Benefit for lung cancer program
July 26, 2010
Contact: Mary Stoltz, (608) 575-5429 or marystoltz@gmail.com

Heads Up! Golf Outing
Benefit for head and neck cancer program
July 26, 2010
(608) 263-0160

Drive for Hope Golf Outing – Madison
Benefit for lung cancer program
August 9, 2010
www.drivetorhopemadison.com

Walk with GRACE
Benefit for UW Carbone Cancer Center
August 13, 2010
www.walkwithgrace.com

Rudy's Road Trip
Benefit for UW Carbone Cancer Center
August 21, 2010
www.rudysroadtrip.com

Pardeeville Car Show
Benefit for UW Carbone Cancer Center
September 4, 2010
www.pardeevillecarshow.com

Please visit uwhealth.org/cancer for more details on all events listed.

Jewel of an Evening
A gathering to honor & remember those affected by gynecologic cancers
September 10, 2010
(608) 263-0160

Mississippi Ridge Walk for Life
Benefit for UW Carbone Cancer Center
September 11, 2010
Contact: Michelle, (608) 778-9821

Gynecologic Cancer Retreat
September 13, 2010
Contact: Libby Caes, ecaes@uwhealth.org

Ovarian Cancer Survivors Course
September 25, 2010
wcn.org/courses

Scramble for a Cure Golf Outing
Benefit for breast cancer program
September 29, 2010
(262) 723-5722

Sparkle of Hope
Benefit for UWCCC gynecologic oncology program
October 11, 2010
(608) 263-0160

4th Annual Toast to a Cure
October 15, 2010
Benefit for UWCCC melanoma program
Presented by Ann's Hope Foundation
www.annshope.org

Funk Out Cancer
November 20, 2010
Presented by Widen Enterprises
www.funkoutcancer.com

9TH ANNUAL SYMPOSIUM
ADVANCES IN MULTIDISCIPLINARY
CANCER CARE

Do You Hear What I Hear?

CONFIRMED KEYNOTE SPEAKERS:
Matthew Kreuter, PhD, MPH ■ Washington University in St. Louis
Paul Smith, MD ■ UW Department of Family Medicine
Teresa Gilewski, MD ■ Memorial Sloan-Kettering Cancer Center
Ellen Foley ■ Former Editor of Wisconsin State Journal

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SAVE THE DATE
FRIDAY, OCTOBER 22, 2010
MONONA TERRACE, MADISON, WI