



Improving the odds

FINDING NEW WAYS TO TREAT MELANOMA

Highly curable when detected early, melanoma has a much bleaker prognosis in its later stages, causing an estimated 7,770 cancer deaths in the United States this year.

At the UW Comprehensive Cancer Center, research in gene therapy and immunotherapy is helping scientists understand how to enlist a patient's immune system to fight melanoma. They are investigating ways to trigger the immune system to recognize and kill tumor cells that can grow and spread through the body.

An increasingly common type of cancer, this year melanoma will be diagnosed in about 60,000 Americans, according to the American Cancer Society. When melanoma is detected in early stages, surgery can cure the vast majority of those patients. But once melanoma metastasizes, the average length of survival is a year.

"Once it has spread, the disease is extremely resistant to various treatments. Study after study has tried to improve upon this, but to date, there really has not been much success," says UWCCC medical oncologist Mark R. Albertini, MD.

Albertini is a member of several UWCCC research teams investigating different types of immunotherapy aimed at improving the prognosis for late-stage melanoma patients. The laboratory research and clinical trials are part of the UWCCC's Immunology and Immunotherapy Program, headed by Paul Sondel, MD, PhD.

"Unfortunately, translating that research into the clinic and finding something that works for patients has been really difficult," says Albertini. "That's really where we're poised right now—between new insights and new discoveries in the lab, and trying to come up with new treatment approaches that, in fact, will work with patients."

To help bring promising therapies to patients, Albertini has received a four-year, \$300,000 award to establish the Gretchen and Andrew Dawes Melanoma Research Fund. These funds will support innovative translational research to specifically improve treatment and diagnostic approaches for melanoma patients.

Immunocytokine treatment

One alternative therapy involves using immunocytokines, which operate on a different principle than conventional chemotherapy, with fewer side effects. Rather than killing dividing cells—both normal and cancerous—immunocytokines recognize specific molecules found on cancer cells, avoiding "collateral damage" to healthy tissues and organs.

In a small fraction of melanoma patients, an immunocytokine called Interleukin-2 (IL-2) has proven to be an adequate treatment by itself. But for the majority of patients for whom IL-2 alone is not sufficient, scientists are trying to find ways to better direct activated immune cells to the tumor site.

"They're potent killers, but they have a hard time localizing to where they need to be to kill the tumor cells," says Albertini.

In a UWCCC study funded by the National Cancer Institute, Albertini and his research team are attempting to use an antibody to bring the IL-2 to tumor sites and then activate so-called "natural killer cells." The theory is, when given in combination as separate molecules, the IL-2 and tumor-reactive monoclonal antibody (mAb) will work together to selectively track and then attack melanoma cells.

In the first phase of the study, Albertini and his team demonstrated a potent immune activation in melanoma patients. In the second phase, the team will try to determine if the therapy will cause tumors to stop growing or shrink in a significant number of patients.

New clinical trial now open

The clinical trial is currently seeking patients with newly metastatic melanoma to distant sites who have not received prior treatment for their metastatic melanoma. Candidates for the study should have good heart and lung function and normal blood tests for liver and kidney function.

"Given the limitations of standard treatment, considering innovative and scientifically-sound experimental studies as first treatment options for patients with metastatic melanoma is, I think,

one important message that is being increasingly appreciated by physicians in this community," Albertini says.

Because melanoma is so difficult to treat in its advanced stages, Albertini says it's important that physicians from several different medical specialties are involved in diagnosis and treatment—from dermatologists and surgeons to medical and radiation oncologists.

Risk factors and warning signs

For patients, being aware of risk factors and the so-called "ABCDs" of melanoma are also critical to detecting the cancer in its early stages. Risk factors include:

- Personal or family history of malignant melanoma
- Light complexion and/or blond or red hair
- Marked freckling of the upper back
- Three or more blistering sunburns before age 20

The first sign of melanoma is often a change in the size, shape, color or feel of an existing mole, but melanomas also may appear as a new mole that can be black, discolored or otherwise abnormal.

The clinical features of early melanoma include:

- **A**symmetry (uneven shape)
- **B**order irregularity (ragged or blurred edges)
- **C**olor variation
- **D**iameter (generally greater than 6 mm).

"In general, I think any pigment or skin spots that are showing change are worth a physician's look," says Albertini. "If caught early, it certainly can be cured in a large fraction of patients. If it gets to be deeply invasive, it's much more difficult to treat."

Patients or referring physicians interested in more information about the study should call Cancer Connect, 800-622-8922.



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Fighting cancer with food and nutrition

Nutritionists are often asked if a diet, a food or a supplement will help cure cancer or prevent it from recurring. To answer, we need to understand what we know about fighting cancer with food and nutrition.

- The food you eat can increase your body's ability to fight cancer and survive.
- The food you eat can decrease your risk of developing some cancers.
- It makes sense that what you eat to prevent cancer may help in decreasing risk of cancer recurrences.

However, there is no evidence that any special diets or that any single food will cure cancer or prevent it from recurring. In fact, diets that exclude or limit some food groups may be harmful.

Nutrition research on preventing and treating cancer is continually changing as scientists develop studies and report findings. Information on the health benefits or health dangers of a specific food is often interesting and exciting to hear, but is frequently based on preliminary data. To prevent becoming a victim of the "food of the week" syndrome, it is important to wait for collaborating studies and scientific consensus.

Everyday dietary patterns and general eating habits are key in preventing and treating cancer.

- Choose a variety of colorful fruits and vegetables. Although there are many controversies in the area of food and nutrition, there is total agreement that fruits and vegetables are the number one cancer fighters. Choose the most colorful for the highest amounts of cancer fighting phytonutrients, including antioxidants, vitamins and minerals. Among the highest in antioxidant power are:
 - Blueberries, blackberries, strawberries, oranges, cranberries, grapes, cherries, apples and melons;
 - Broccoli, spinach, asparagus, peppers, peas, beets, tomatoes, carrots, squash, pumpkin, sweet potatoes, cabbage, onions and garlic.
- Increase fiber and select whole grains. Hundreds of studies have shown strong associations between high fiber diets and reduced cancer risk. Check the label of food for fiber content. A good goal is 25 – 30 grams of fiber per day. Fruits and vegetables provide some fiber, other high fiber foods include:
 - Breads and cereals made with whole grains, nuts and seeds;
 - Beans and legumes (red, white, black and kidney beans).

- Drink lots of fluids. Any liquid counts as part of your fluid intake—water, juices, tea, even coffee. Studies show that tea has special characteristics that decrease the risks of some cancers and possibly slow some cancer cell growth. Green, white and red teas are best, either caffeinated or decaffeinated.
- Choose good protein foods at every meal. Eat more fish. Poultry, eggs, low fat dairy products, nuts, beans, soybeans and legumes are also good proteins. Limit high fat animal products and other saturated and trans fats. Recent studies found decreased risk of breast cancer and prostate cancer recurrences when a low fat diet was followed.
- Find ways to increase essential omega-3 fats in your diet. These fatty acids are abundant in oily fish, especially salmon. Other choices are olive oil, canola oil, walnuts, flax seed, flax oil and fish oil supplements.
- Multivitamins and mineral supplements with close to 100 percent DV of most nutrients are usually recommended, but large amounts of single vitamins are not. Calcium and Vitamin D supplements are important for those who do not eat dairy products regularly. Check with your physician or nutritionist on any herbal supplements.
- Exercise regularly. Regular exercise decreases cancer risks and may decrease risk of some cancers recurring. Choose an exercise program that works for you. Remember that any exercise is better than no exercise.
- A healthy weight is the goal. Studies show excess weight increases risk of many cancers. The good news is that there is every reason to assume that reaching and maintaining a healthy weight will decrease the risk of cancer.
- And the best news—dark chocolate is a good source of antioxidants. Choose a chocolate treat that does not run around with bad friends (lots of sugar and fat).

Enjoy eating and fight cancer too!



Donna L. Weihofen, RD, MS is a senior nutritionist and lecturer with UW Hospital and Clinics and the UW Comprehensive Cancer Center. Her primary area of expertise is nutritional care of patients with cancer and heart disease. The author of several books, she is a regular guest on WISC-TV 3, in Madison.

MARK YOUR CALENDARS

A Walk With G.R.A.C.E.

August 12-13, 2005
Visit: www.walkwithgrace.com

2nd Annual Brian Howell Lung Cancer Research Golf Outing

August 15, 2005
Contact: Dan Coyne at swimdad5@charter.net

Into the Twilight

September 13, 2005
Awareness and fundraising event for gynecologic cancer. Monona Terrace Community and Convention Center. Call Ann Johnson, (608) 263-1677.

HEADRUSH – A Wisconsin Brain Tumor Event

September 17, 2005
Visit: www.headrushevent.org

Estrogen Open

September 22, 2005
Golf outing for breast and gynecologic cancer research.
Call Ann Johnson, (608) 263-1677.

Grand Opening of UW Cancer Center Johnson Creek

October 15, 2005
Free and open to the public.
Call Craig Robida, (608) 263-4982.

Breast Cancer: Back to Basics and Beyond

October 20, 2005
Call Ann Johnson, (608) 263-1677.

4th Annual Symposium: Advances in Multidisciplinary Cancer Care

October 21, 2005
Designed for health care professionals, this year's fall cancer conference will focus on screening and prevention.
Call Ann Johnson, (608) 263-1677.

Visit cancer.wisc.edu for more details on all events listed.

State patient protection bill

Will provide continued access to clinical trials

Cancer clinical trials are where the newest cancer drugs are studied, often giving patients the best chance for a response to treatment.

This summer, a bill known as the Cancer Patient Protection Bill will be introduced in the Wisconsin Legislature and is designed to have a significant impact on the number of patients who will be able to participate in cancer clinical trials. As treatment in such trials may be considered "research or investigational," the routine care costs incurred by patients enrolled in these trials are often not covered by insurers. This lack of coverage is a significant barrier to many patients who might otherwise choose to enroll in a trial.

The bill prohibits a health care plan from denying coverage for care costs in a cancer clinical trial if the health plan covers the same costs for standard cancer treatment given outside a trial setting. The bill simply allows for parity of coverage for two types of cancer treatments. The bill does not require coverage for the actual clinical trial costs, just the routine care costs associated with it. To read more, visit www.cancer.wisc.edu.

If you agree that this is worthwhile legislation, please take a moment to contact your state legislators urging their support. To find out who your state legislators are or to leave a message, call the toll-free legislative hotline at 1-800-362-9472. E-mail addresses for legislators can be obtained at the WI State Legislature web page, www.legis.state.wi.us. Just click on "Who are my legislators?" Your contacts can make a difference.

An amazing birth

New cervical cancer surgery preserves woman's fertility

Rockford patient receives treatment and delivers baby

Every time she looks at her son, Zachary, Gina Janovsky is struck by the miracle her family is living.

In 2003, an irregularity in Janovsky's annual Pap test led doctors to discover that she had early-stage cervical cancer, a condition that, as little as five years ago, would have slammed the door on motherhood for the 33-year-old Rockford, IL resident. The standard treatment for early-stage cervical cancer is a radical hysterectomy, a surgical procedure in which doctors remove a woman's cervix and uterus.

"I was more fearful of not being able to have a child than I was about having cancer," Janovsky recalls. "All I could think was, 'This wonderful opportunity is being taken away from me.'"

But Janovsky and her husband Mike didn't realize that less than 150 miles away, David Kushner, MD, an obstetrics and gynecology cancer specialist with the UW Comprehensive Cancer Center (UWCCC), had been traveling internationally to become proficient in trachelectomy, a new procedure that would give the opportunity back to her.

In a trachelectomy, surgeons use laparoscopic techniques to remove only the lymph nodes and the cancerous part of the woman's cervix, preserving her ability to carry a child. A permanent suture called a cerclage is used to hold the remaining part of the cervix in place.

"We put the cerclage in the lower part of the uterus, or the upper cervix if some cervix remains, and we then sew the vagina back to the lower uterus, burying the cerclage," Kushner explains. Women who undergo the procedure must deliver

their babies by Caesarean section; in some cases, women who have undergone trachelectomy have delivered multiple children with no damage to the cerclage.

The modern trachelectomy procedure was pioneered in the mid-1990s by a French surgeon named Dr. Daniel D'Argent. According to Kushner, U.S. surgeons were initially skeptical of D'Argent's work.

"Ultimately, D'Argent has shown that pregnancy and cancer outcomes are excellent in well-chosen patients," Kushner says.

Trachelectomies are routinely performed in Canada and France, although the procedure is quickly gaining acceptance here. Only a handful of other U.S. hospitals offer trachelectomies, and Kushner is the only doctor in this region currently performing them.

Janovsky's case was an instance of almost preternaturally good timing. She was receiving her cancer care from Kushner's UWCCC colleague, Ellen Hartenbach, MD. Hartenbach told Gina and her husband, Mike, about trachelectomy—and that Kushner soon would be traveling to Canada to perform some cases. "These surgeries usually need to be scheduled a certain amount of time after the biopsy—usually a month for any kind of cervical cancer," says Kushner. "It turned out that she could have her surgery right when I was there."

After clearing a few hurdles related to health insurance, Gina, Mike and Kushner traveled to L'Hotel-Dieu de Quebec in Quebec City, where Kushner was part of the surgical team that performed a four-hour trachelectomy on Janovsky. Doctors were able to remove Gina's cancer and give her a clean bill of health. Six months later, she became



Gina Janovsky of Rockford, Illinois smiles as she holds her son, Zachary. A new cervical cancer surgery, trachelectomy, preserved her fertility, allowing her to give birth.

pregnant, and in September of last year, she gave birth to a healthy baby boy.

"I was so thankful, so overjoyed," says Gina. "The doctors were able to treat my cancer and still allow me to become a mom, which was a choice I didn't think I was going to have when I was first diagnosed. Our son is absolutely amazing—Mike and I look at him each day and cry for the joy we feel at having him in our lives."

Cervical cancer affects approximately 12,000 women in the United States each year. A quarter of those women

have early-stage cervical cancer, making them potential candidates for surgical treatment. The best patients for trachelectomy are women under 40, with tumors smaller than 2 centimeters, and who want to maintain fertility.

"Gina's story has been incredible for our whole team," says Kushner. "To be able to get to the next level, to be able to say that we can not only cure people, but also improve their quality of life and give them something they wouldn't have been able to have a few years ago—that's exciting."

Grand opening

UW Cancer Center Johnson Creek



Please mark October 15, 2005 on the calendar for the official grand opening of UW Cancer Center Johnson Creek. A community partnership among Fort HealthCare, Watertown Memorial Hospital and UW Health, UW Cancer Center Johnson Creek will give area patients and families convenient access to cutting edge research and treatment in a nurturing environment.

Cancer care, prevention and education will be provided by medical and radiation oncologists. The center's services will include chemotherapy, radiation therapy and

access to clinical trials. It will also feature support groups, educational programs and complementary medicine designed to encourage patients and families to choose services tailored to their individual needs.

Affiliated with the UWCCC, UW Cancer Center Johnson Creek will be a 14,300 square-foot facility located between Madison and Milwaukee, just south of the Interstate 94 and Highway 26 junction.

To read more about UW Cancer Center Johnson Creek, visit www.uwjohncreek.org.

- **Advances is published semi-annually by the University of Wisconsin Comprehensive Cancer Center (UWCCC), a National Cancer Institute-designated comprehensive cancer center.**
- **For patient services at the UWCCC, please contact Cancer Connect, (800) 622-8922 or (608) 262-5223 or e-mail uwccc@uwccc.wisc.edu.**
- **To learn more about the UWCCC, please visit our website: cancer.wisc.edu**

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You may also contact Craig with a request by telephone at (608) 263-4982 or by e-mail at robida@uwccc.wisc.edu

Patient resources expanded on website

The UW Comprehensive Cancer Center has recently redesigned its website, focusing on more detailed information for cancer patients and their family members. To find out more, visit cancer.wisc.edu and click on the "For Patients" button on the left-hand side of the homepage, or go to uwhealth.org/cancer.

The new patient site offers quicker access to a number of resources:

- Detailed information about specific cancers, including specialized treatments available only at the UWCCC;
- Physician profiles;
- Expanded information on related services, such as the palliative care program, clinical trials and genetic counseling;
- Support groups and classes for cancer patients;
- News and events hosted by the UWCCC;
- Ways to support the UWCCC.

"Patients will have faster access to the cancer resources they are seeking at the University of Wisconsin," said Ruth Bronston, MS, CHES, who was involved in redesigning the patient pages. "Furthermore, our new site offers seamless navigation for all services provided at the UW Comprehensive Cancer Center, as well as the entire University of Wisconsin Hospital and Clinics system."

The new patient pages also offer a direct link to the UWCCC's Regional Cancer Center network, including regional cancer center partners and outreach clinics. The UWCCC has five regional cancer centers in Wisconsin and Illinois, with the sixth one opening in October, 2005—UW Cancer Center Johnson Creek.



Training the next generation

of cancer physician-scientists

Kelly Mackin, 23, from Waupaca, Wisconsin, knows how she is spending her summer vacation. She will be working under the watchful eye of her mentor, Kyle Holen, MD from the UW Comprehensive Cancer Center (UWCCC).

Mackin is one of 50 recipients (16 in cancer) of the 2005 Herman Shapiro Summer Research Award Program for medical students. These awards are made possible by a gift of the Herman and Gwen Shapiro Foundation to support research experiences for medical students. For the last three years, the UWCCC has paid half of the stipend for cancer-related projects carried out in conjunction with UWCCC researchers.

A second-year UW Medical School student, Mackin is splitting her time between the lab and clinical work this summer. In the lab, she is helping to elucidate the mechanism of action for a novel compound, ZM336372. This drug has been shown to reduce the growth of tumors *in vitro* and is currently being tested

for possible clinical development. Mackin is also gaining clinical experience, shadowing Holen in his role as a gastrointestinal oncologist and clinical researcher.

"The purpose of the program is to fund student participation in a full-time summer research project for eight to 12 weeks under the mentorship of a faculty member," according to George Wilding, MD, director of the UWCCC. "Projects are in all areas of basic science, clinical, translational, health services, global and public health research."

The program is designed to provide students with an appreciation for the nature of scientific research and to develop skills in data collection, analysis and presentation of results to the medical community.

Typically, these summer research projects are at a more advanced level than those undertaken by medical students in their undergraduate years. Proposed projects have a central hypothesis or research goal,



with experiments designed to test the hypothesis by collecting quantifiable data. Students play an active role in conducting experiments or gathering and analyzing the data.

Updates in

Clinical Trials

Clinical trials are UWCCC's key to progress in the battle against cancer



New and improved listing of all clinical trials

The UWCCC has recently upgraded the system which highlights nearly 200 clinical trials available for cancer patients. The new system makes it easier to find clinical trials for patients' specific situations. Patients and family members can search by type of cancer, drug names, keywords, age appropriateness and type of clinical trial.

The clinical trials search tool will find treatment clinical trials, as well as cancer prevention and cancer control trials. Cancer Treatment clinical trials test innovative treatments such as a new cancer drug, new approaches to surgery or radiation therapy, or new combinations of treatments. Cancer Prevention clinical trials test whether taking certain medicines, vitamins, minerals, or food supplements may lower the risk of a certain type of cancer. Cancer Control clinical trials test whether certain drugs reduce side effects from chemotherapy and other primary treatments.

To use this new system, visit cancer.wisc.edu and click on "clinical trials" and then "UWCCC Clinical Trials Listing."

Melanoma

The incidence of melanoma continues to rise throughout the world at an alarming rate. In the year 2005, it is estimated that approximately 60,000 Americans will be diagnosed with melanoma and almost 7,700 Americans will die because of melanoma. With early detection, melanoma can often be successfully treated. However, no current therapy has been found to prolong survival for the vast majority of patients with advanced melanoma. Patients diagnosed with metastatic melanoma have an average survival of less than one year.

A study has recently opened at the UW to determine if immunological treatment with an experimental agent, hu14.18-IL2, can help people with advanced melanoma. Hu14.18-IL2 contains an antibody that binds to melanoma cells and is fused to interleukin-2, a molecule that may activate the immune system to kill tumor cells. Thirty people will be treated in this investigator initiated, National Cancer Institute-sponsored, phase II clinical trial. Research subjects will be admitted to the General Clinical Research Center of UW Hospital and Clinics for treatment and will receive a maximum of four cycles of therapy.

Lymphoma

A study evaluating a new combination of chemotherapy plus an antibody is currently open for patients with Mantle cell lymphoma. It will evaluate the combination therapy's overall effectiveness, tolerability and side effects. Eligible patients must not have received any prior chemotherapy, immunotherapy or radiotherapy for their lymphoma except for one cycle of CHOP or CHOP-like chemotherapy.

Physical exams and safety assessments will be conducted throughout the study. Patients will receive the combination therapy every 21 days (one cycle) for a maximum of six cycles. Patients may have the option to continue maintenance treatment with antibody therapy alone.

For more information about these and other clinical trials at the UW Comprehensive 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, cancer.wisc.edu

Making a Difference



On May 7 & 8, 2005 more than 250 participants braved the cool spring weather for Tour De Dells, a unique fundraiser held in Wisconsin Dells. The event included a 32-mile bike road race, a 10-mile mountain bike race and a USCF-certified criterium race. Cyclists could participate in any of the three races, and had an opportunity to test their endurance by performing in all three to compete for the Triple Threat Award. A portion of the proceeds from the event benefited cancer research at the UWCCC. To find out more information about the Tour De Dells event go to www.tourdedells.com.



Participants from The Wabeno Spring Dual Sport Rally are shown presenting a \$7,000 check for breast and colon cancer research at the UW Comprehensive Cancer Center. The two-day event held in the Nicolet National Forest had more than 100 participants riding more than 110 miles each day.

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

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