Mott Children's Hospital: Fifth in the nation, best in Michigan

An independent national survey has confirmed what thousands of children and parents already know: The University of Michigan's C.S. Mott Children's Hospital is one of the best places in America for kids who need medical care.

Mott placed fifth in *Child* magazine's list of top 10 children's hospitals as published in its February 2003 issue. It was the only children's hospital in Michigan to make the top 10 list. Mott also placed fifth in *Child*'s specialty rankings for cardiology — the highest ranking of any children's hospital in the Midwest.

"We're absolutely thrilled to have this independent recognition of the excellence we strive for every day," says Patricia Warner, the U-M associate hospital director who oversees Mott. "Every member of the Mott team deserves credit for making our hospital the best it can be. Together, our hard work has paid off."

"This ranking is based on solid data that reflect the high quality of care and the broad range of services we provide — making our rank that much more meaningful," says Lazar Greenfield, M.D., the U-M's interim executive vice president for medical affairs.

The rankings were compiled using statistics and information from 178 children's hospitals nationwide. This is the second time the magazine has ranked children's hospitals, but the 2003 rankings were based on a more exhaustive methodology than before. In 2001, Mott ranked ninth overall. This is the first year specialty rankings were included.

Opened in 1969, the 200-bed hospital is named after Flint industrialist and philanthropist Charles Stewart Mott, whose foundation's $6.5 million gift in 1964 helped make construction possible. Today, Mott provides inpatient and outpatient pediatric specialty care in many disciplines. More than 165 physicians from the U-M Medical School faculty see patients at Mott. In fiscal year 2002, U-M received $16 million in research funding from government and private sources to support pediatric research at Mott Children's Hospital.

—KG

Photo: PictureQuest

"Every member of the Mott team deserves credit for making our hospital the best it can be. Together, our hard work has paid off."
—Patricia Warner

Read an expanded version of this story and learn more about C.S. Mott Children's Hospital:
www.med.umich.edu/opm/newspage/2003/childmag.htm

Read the Fall 2001 feature on Mott in Medicine at Michigan:
www.medicineatmichigan.org/magazine/2001/fall/miracles/default.asp

Treating Pancreatic Cancer

RADIATION-CHEMOTHERAPY COMBINATION MAY HOLD A KEY

There is new hope on the horizon for patients with pancreatic cancer. Although it is only the fifth most common cancer (about 29,000 people get the disease each year), pancreas cancer has a disproportionate impact because it is one of the least curable illnesses. A novel treatment regimen being studied at the U-M, however, may provide significant improvement in outcomes for pancreatic cancer patients.

A team led by Cornelius McGinn, M.D., assistant professor of radiation oncology, and Mark Zalupski, M.D., associate professor of internal medicine in Medical Oncology, is testing a pancreatic cancer treatment that combines radiation and gemcitabine, a relatively new chemotherapy agent. Gemcitabine is a compound that resembles cytosine, one of the nucleoside building blocks of DNA. It functions by becoming incorporated into a cancer cell's DNA, inhibiting further synthesis of the DNA and, in turn, hindering division of the cancer cells.

Photo: Martin Vloet

Mark Zalupski and Cornelius McGinn

"We believe, in general, that concurrent radiation and chemotherapy are better than sequential use of the two modalities," says Zalupski. "When chemotherapy is given with radiation therapy, it prevents the cell from repairing the damage caused by the radiation, which cancerous cells can often do, and the cell dies." In this way, the compound functions as what is known as a "radiosensitizer."

Zalupski and McGinn have taken a novel approach to the treatment. Other studies have tested the gemcitabine-radiation treatment using doses of gemcitabine lower than that used for chemotherapy alone, along with a standard, high dose of radiation administered by conventional means to a broad region in the upper abdomen.

"What we did was the flip side," says McGinn. "Not only is gemcitabine a radiosensitizer, it's an effective therapy when used alone. We provide patients a full dose of gemcitabine systemically and combine that with lower doses of radiation targeted more accurately." In an initial phase I study begun in 1997, McGinn and Zalupski used the standard dose of gemcitabine and experimented with different levels of radiation that were all significantly lower than the conventional dose used in other studies. "A lower dose should be adequate to provide local control considering the radiosensitizing properties of the drug that were determined by our laboratory group," McGinn adds.

In addition, the U-M team has incorporated a means of radiation therapy, developed by the Radiation Physics Division, called conformal radiation, which uses three-dimensional treatment planning to allow physicians to better pinpoint a tumor's outer boundary and irradiate cancerous cells while sparing normal tissue. This is one of the factors that enable investigators to safely combine both modalities while providing potentially better treatment than with conventional radiation administration.

Chemotherapy and radiation are typically administered after surgical removal of the tumor. McGinn and Zalupski are also looking into preoperative gemcitabine-radiation therapy, which may make surgery more effective. "If we treat patients first, we might be able to improve the odds of removing the tumor. For some of our patients, even modest shrinkage of the tumor has been enough to allow the surgeon to remove it."

> "In my experience, I haven't seen patients do so well for so long."
> *–Mark Zalupski*

McGinn and Zalupski's team are in the process of conducting a phase II trial to further determine the treatment's efficacy. While the phase I study focused on determining a tolerable combination of gemcitabine and radiation, a higher percentage of patients showed measurable tumor response than would have been anticipated by using either gemcitabine or radiation alone, and there was an apparent increase in average survival rate as well. "In my experience," says Zalupski, "I haven't seen patients do so well for so long." ➤

Treating Pancreatic Cancer *(continued)*

Arnold Morawa, former assistant dean of the U-M School of Dentistry, is a personal supporter of the treatment protocol. Four years after surgery followed by the combination therapy, he shows no signs of relapse and continues his prominent Ann Arbor dental practice. "I really believe that this treatment and the way my body responded to it are the reasons I've done so well," says Morawa.

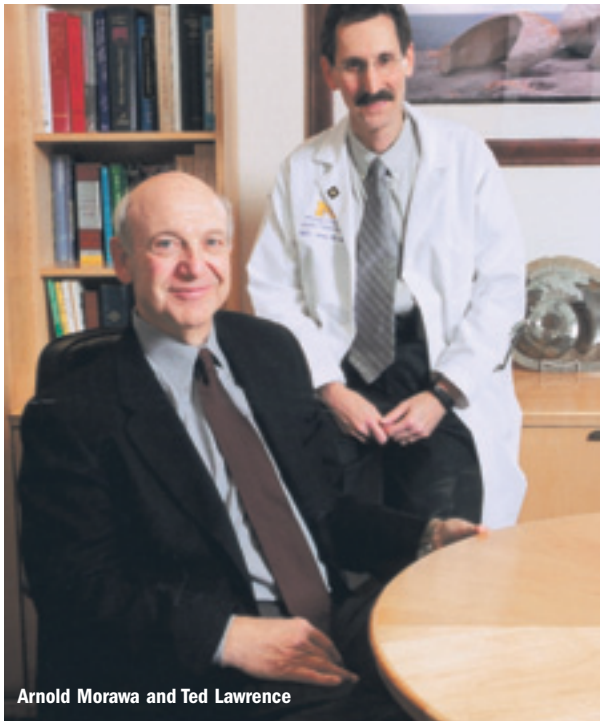
Ted Lawrence, M.D., Ph.D., professor and chair of Radiation Oncology and Morawa's physician, and Donna Schewach, Ph.D., professor of pharmacology, collaborated in laboratory studies to understand the basic mechanism of interaction between radiation and gemcitabine. This information was used by McGinn and Zalupski to design the clinical trials.

–RS

Department of Radiation Oncology:
www.med.umich.edu/radonc

Information on gemcitabine as a pancreatic cancer treatment:
www.nlm.nih.gov/medlineplus/druginfo/uspdi/203038.html

Photo: Martin Vloet

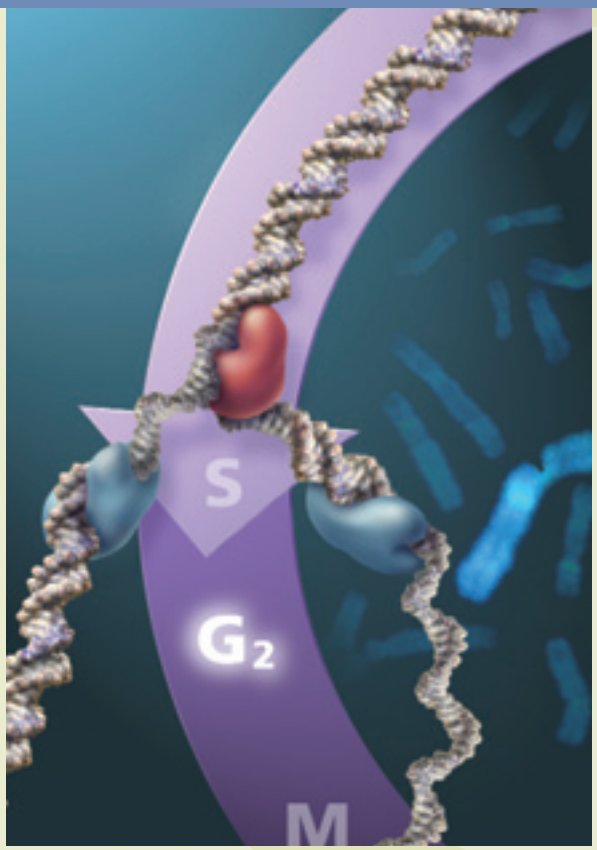


Arnold Morawa and Ted Lawrence

"I really believe that this treatment and the way my body responded to it are the reasons I've done so well."

–Arnold Morawa

Illustration: ClearScience

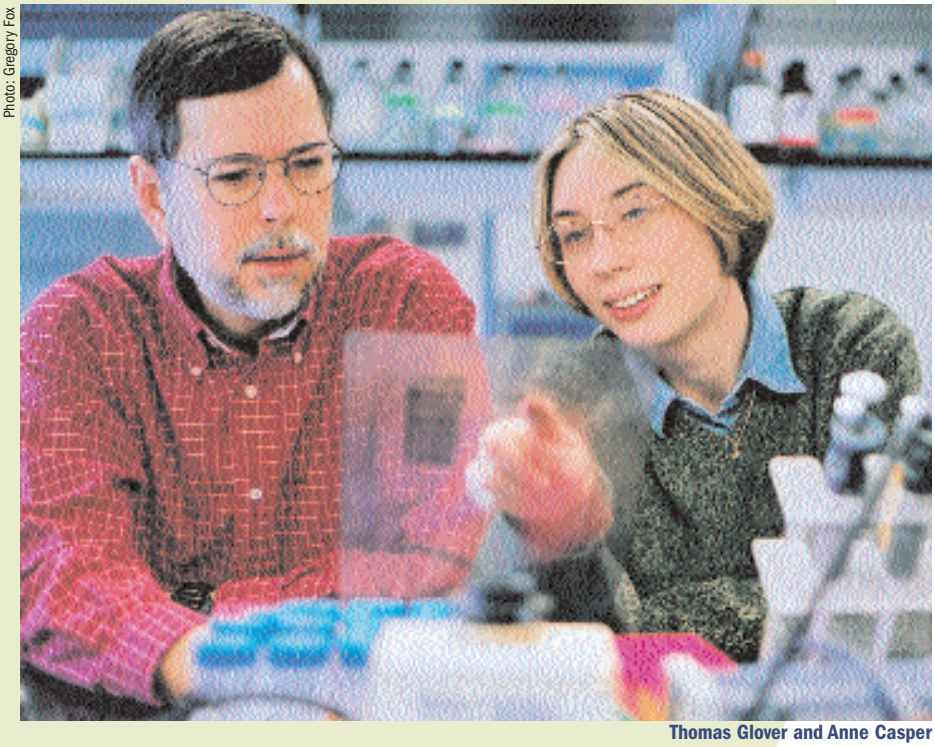


Artist's depiction of a stalled replication fork in DNA.

"When replication starts to stall, ATR sends out a chemical signal telling the cell to shut down replication until it can fix the problem."

–Anne Casper

Photo: Gregory Fox



Thomas Glover and Anne Casper

With 46 chromosomes and six feet of DNA to copy every time most human cells divide, it's not surprising that gaps or breaks sometimes show up in the finished product — especially when the cell is under stress or dividing rapidly, as in cancer.

But what is surprising — according to Thomas Glover, Ph.D., a geneticist at the University of Michigan Medical School — is that these breaks don't always occur at random. Instead, chromosomes break at just a few specific locations during stages in the cell cycle when DNA is being copied, or replicated, and the cell is dividing into two identical daughter cells.

Protein Puts the Brakes on Fragile Site Breaks

Scientists call them fragile sites, but the reasons for their inherent instability have remained a mystery. Now Glover and colleagues at the U-M Medical School and the Howard Hughes Medical Institute have discovered that a protein called ATR in a previously unknown molecular pathway protects fragile sites from breaking during DNA replication. Results of their research were published in the December 13, 2002, issue of *Cell.*

"ATR recognizes areas called stalled replication forks where the DNA-copying process is blocked," says Anne M. Casper, a U-M graduate student in human genetics who is first author of the *Cell* paper. "For reasons we don't understand, fragile sites seem to be difficult to copy. When replication starts to stall, ATR sends out a chemical signal telling the cell to shut down replication until it can fix the problem."

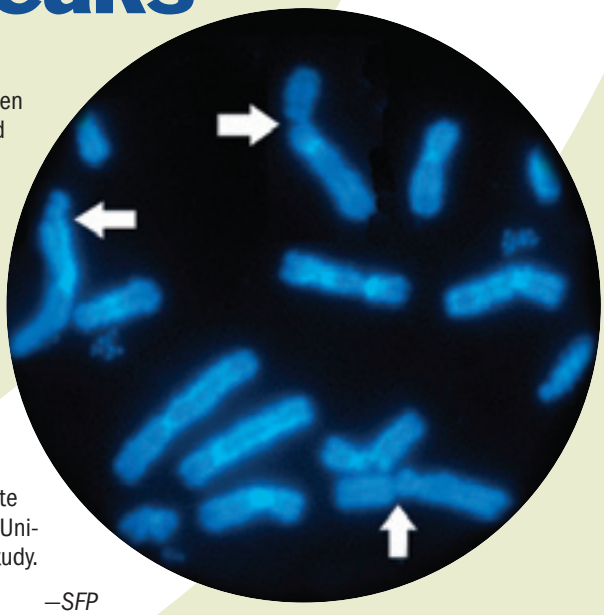
"If you complete the cell cycle without replicating the fragile site and the cell continues into metaphase, our hypothesis is that the cell goes into metaphase with a gap in the chromosome," says Glover. "That can lead to double-strand breaks, chromatid recombination and all sorts of things that aren't supposed to occur." Since fragile site breaks are very common in some tumor cells and often take place near genes associated with tumors, defects in the ATR protein pathway may be involved in the progression of cancer.

The research study was funded by the National Institutes of Health. Casper is supported by a predoctoral fellowship from the National Science Foundation. Martin F. Arlt, Ph.D., a U-M post-doctoral fellow in human genetics, and Paul Nghiem, Ph.D., a Howard Hughes Medical Institute post-doctoral fellow at Harvard University, were collaborators on the study.

—SFP

Read the complete story:
www.med.umich.edu/opm/newspage/2002/fragilesites.htm

Learn more about research in the Glover lab:
www.med.umich.edu/hg/research/faculty/glover/glover.htm



Arrows point to fragile site gaps or breaks in chromosomes. Photo: Anne Casper

‘You Just Keep Going’

THE UNCOMMON ORDINARY LIFE OF BILL SCELZA

Ask Bill Scelza, M.D. (Residency 2002), to describe himself and he’ll say he’s “just an ordinary person living an everyday life.” The most important thing right now, he’ll tell you, is that he and his wife, Beatriz, are the proud new parents of a baby boy named Dominik William.

Keep him talking and you’ll learn that Scelza is a physician who graduated from Case Western Reserve Medical School in 1998, and then moved to Ann Arbor and the U-M Health System for his residency in physical medicine and rehabilitation. Next fall, after completing a fellowship at the Kessler Institute for Rehabilitation in New Jersey, he’s returning to the U-M to focus on the care of patients with spinal cord injuries. Athletics, especially basketball, have been a major part of his life since high school, and he encourages all his patients to exercise regularly to maintain health and fitness.

Oh, and by the way ... Scelza uses a wheelchair, because a car crash at age 17 left him with a spinal cord injury and no function in his legs. In fact, his injury was the reason he decided to become a doctor. “I wanted to use my personal experience to take care of other people with spinal cord injuries,” he says.

By the time he started medical school in 1994, Scelza had developed self-confidence, a positive attitude and the skills required to negotiate his way through a world that’s not designed for people in wheelchairs. “You have to speak up and advocate for yourself,” he says. “If barriers come up, you have to be flexible, patient and creative on how to get around them. And you just keep going. You don’t let things hold you back. You figure out what needs to be done and then you do it.”

When he started treating patients, Scelza was careful to approach people with spinal cord injuries no differently than patients with other medical conditions. “We deal with patients with serious disabilities after major traumatic life events. Often they are in the early stages of adapting to the changes. It’s a difficult time and there’s a lot of anger. I don’t want to force myself on them, but I want them to see that injuries don’t have to hold you back.”

Scelza was introduced to the intense, competitive world of wheelchair basketball while he was at the Edwin Shaw Hospital for Rehabilitation in Akron, Ohio, recovering from his injuries. “I met some of the guys on the hospital team and they sort of took me under their wing,” he says. Before long, he was playing with the Cleveland Wheelchair Cavs competing all over the country. “There’s a misconception that it’s just people moving around slowly in wheelchairs, but it’s an active and aggressive game,” says Scelza. “We take it very seriously.”

Photo: Gregory Fox

David Gater, Bill Scelza, and Denise Tate

Scelza’s bottom line message is that exercise and physical fitness are important whether you walk or roll through life. “People with spinal cord injuries are just as susceptible to heart disease and diabetes as everyone else,” he says.

People with complete spinal cord injuries like Scelza’s often have little or no leg function, so aerobic workouts can be difficult, because they cannot work the large muscles in their legs. That rules out treadmills and stair-climbing machines, but Scelza says basketball, swimming and upper extremity machines are good alternatives.

U-M's Model Spinal Cord Injury Program:
A COMPREHENSIVE APPROACH TO REHABILITATION

The University of Michigan's Model Spinal Cord Injury Care System is one of only 16 comprehensive programs in the United States funded by the National Institute on Disability and Rehabilitation Research. Directed by Denise Tate, Ph.D., and David Gater, M.D., Ph.D., the program combines advanced clinical care, applied and clinical research, and education of spinal cord injury specialists. Established in 1985, it is the only program of its kind in the Midwest.

The 16 federally-funded spinal cord injury centers in the U.S. aim to improve the quality of life for more than 200,000 Americans living with spinal cord injuries and the 11,000 more who are injured every year.

"Improvements in medical care and rehabilitation are giving spinal cord injury patients a longer life expectancy and better quality of life," says Gater, an associate professor in physical medicine and rehabilitation who has a dual appointment in the VA Ann Arbor Healthcare System. "Now we need to focus on the higher risk of heart disease, diabetes and other disorders that spinal cord injury patients face, because of lifestyle factors and the secondary physical effects of such an injury."

The sudden, dramatic physical changes that come with a spinal cord injury can have psychological effects. "People living with these injuries have a higher incidence of depression and substance abuse than the general population," says Tate, a psychologist working with spinal cord injury inpatients and outpatients at U-M. "Depression can interfere with the drive to exercise or adopt a healthy lifestyle."

—KG

U-M Model Spinal Cord Injury Care System:
www.med.umich.edu/pmr/model_sci/index.htm

Some people with a spinal cord injury can benefit from new technology, which uses electrical stimulation of leg muscles as an exercise aid. When muscles aren't used, they tend to atrophy, but electrical impulses cause the muscle to contract, building bulk and increasing metabolic activity.

"It looks very positive in terms of building aerobic and cardiovascular capacity, because it allows people who have no use of their legs to actually pedal a recumbent bicycle," adds Scelza. "But it's important to work with people who are familiar with this technology and know how to use it safely."

During his U-M residency, Scelza led a study to identify barriers to physical fitness for patients with spinal cord injuries. The study was part of the Wellness with Spinal Cord Injury Project, a two-year clinical trial started in 2001 by Denise Tate, Ph.D., a professor and director of research in the U-M Medical School's Department of Physical Medicine and Rehabilitation. Funded by the U-M Investment Venture Fund, the project is designed to determine the most effective methods of helping people with spinal cord injuries improve their health with nutrition, exercise and lifestyle changes.

The study surveyed 72 spinal cord injury patients participating in the wellness program in the U-M Health System. "We found that most people want to exercise, but things get in their way. They are afraid of getting hurt or don't know what to do and how to start," says Scelza. "Often, there is a lack of motivation or energy. Lack of accessibility to facilities with proper equipment or knowledgeable people who can help them develop a directed exercise program are additional barriers. And less than half the patients we surveyed said their physician encouraged them to exercise."

Scelza's bottom line message is that exercise and physical fitness are important whether you walk or roll through life. "People with spinal cord injuries are just as susceptible to heart disease and diabetes as everyone else," he says. "Regular exercise improves their overall health and quality of life, and leaves them in better condition to benefit from new treatments for their injury."

—SFP

Photo: Gregory Fox

Leslie Crofford

Read the complete story:
www.med.umich.edu/opm/newspage/2002/pregabalin.htm

General information on fibromyalgia syndrome:
www.med.umich.edu/opm/newspage/2002/pregabalinbackground.htm

U-M fibryomyalgia research:
www.med.umich.edu/intmed/rheumatology/fmweb

U-M-tested Drug Relieves Pain of Fibromyalgia

Pregabalin, a drug developed by Pfizer, Inc., and tested at the University of Michigan, could help reduce the pain associated with fibromyalgia, according to study data presented in October 2002 by U-M researcher Leslie Crofford, M.D., at the annual meeting of the American College of Rheumatology.

"Fibromyalgia syndrome is highly debilitating for patients and difficult to treat," says Crofford, the study's lead investigator and an associate professor of internal medicine-rheumatology in the U-M Medical School. "This study is encouraging, because pregabalin was shown to provide significant relief from the symptoms most troublesome to patients."

Fibromyalgia is a chronic disorder characterized by widespread musculoskeletal pain. It also is frequently associated with fatigue and sleep disturbances. The syndrome is estimated to affect 2 percent of the population, or 5.6 million Americans, and occurs most often in women.

The U-M study included 529 patients diagnosed with fibromyalgia. Patients received either a placebo or pregabalin at doses of 150, 300 or 450 milligrams for eight weeks. Patients kept records of their pain levels in detailed daily diaries.

Pregabalin-treated patients who received 450 mg/day doses showed statistically significant improvements in pain compared to those who received the placebo. Twenty-nine percent of pregabalin-treated patients reported at least a 50 percent reduction in pain, compared with 13 percent of patients who received the placebo. In addition, pregabalin significantly improved sleep quality and lessened fatigue.

—KG

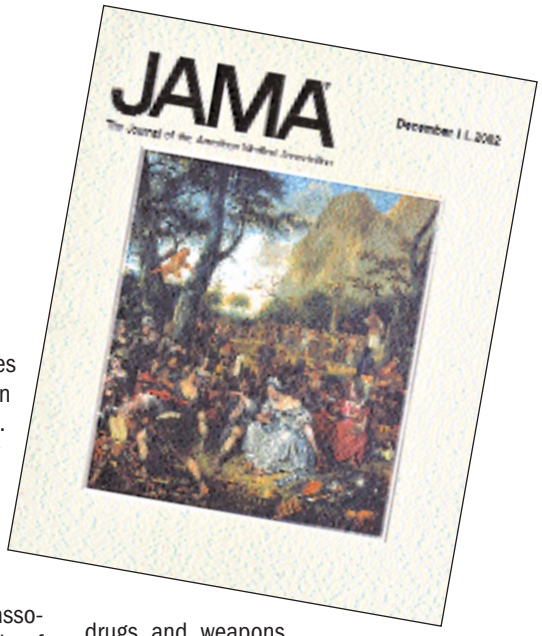
Kimberlydawn Wisdom Is Appointed Michigan's First Surgeon General

Michigan Governor Jennifer Granholm has appointed Kimberlydawn Wisdom (M.D. 1982), assistant professor of medical education in the University of Michigan Medical School, to be the state's first surgeon general. Wisdom, who has been a member of the faculty since 1988, will focus on disease prevention and health risks for the nearly 10 million residents of Michigan.

In addition to her U-M medical degree, Wisdom holds a master's degree from the School of Public Health in clinical research design and statistical analysis. An emergency room physician, she is also an associate research scientist in the Center for Medical Treatment Effectiveness Programs in Diverse Populations at Detroit's Henry Ford Hospital. Wisdom is heavily involved in prevention and minority health care issues, with particular interest in diabetes. She serves on the Centers for Disease Control and Prevention Diabetes Translation Advisory Committee, and is the founder and director of the African-American Initiative for Male Health Improvement, a community-based health-screening program in Detroit.

Blocking Porn — Not Health Information

SETTINGS CAN STRIKE A BALANCE BETWEEN ACCESS AND PROTECTION



A comprehensive U-M study of Internet filtering software finds that libraries, schools and parents can bar access to pornographic Internet sites without blocking access to important health information. Setting Internet filters to their most restrictive level, however, prevents computer users from seeing many health sites — and gives only marginally better protection against pornography than the least restrictive setting.


Photo: Gregory Fox

Caroline Richardson

Researchers in the U-M Medical School and School of Information used 24 health search terms and six pornographic terms to compare the Internet search performance of pornography-blocking software filters. Results of the study were published in the December 11, 2002, issue of the *Journal of the American Medical Association.*

"We found that filters, when set at the least restrictive setting, were remarkably good at distinguishing between health information and pornography. At highly restrictive settings, however, almost a quarter of health sites were blocked with little improvement in porn blocking," says Caroline R. Richardson, M.D., a lecturer in family medicine and a research scientist at the Veterans Administration Health Services Research and Development Service in Ann Arbor.

Working with Paul J. Resnick, Ph.D., an associate professor in the U-M School of Information, and colleagues from the U-M Health Media Research Laboratory and the Kaiser Family Foundation, Richardson conducted the study with an eye toward teens who often turn to the Internet for health and sexuality information on issues such as pregnancy, sexually transmitted diseases and birth control.

The research team used six search engines popular with teens — Yahoo!, Google, America Online (AOL), Microsoft Network (MSN), Ask Jeeves and Alta Vista. They tested six commercial software packages, all widely used by schools and libraries. More than 3,000 health and 500 pornography sites were ultimately tested against the filters.

> "We found that filters, when set at the least restrictive setting, were remarkably good at distinguishing between health information and pornography."
>
> *–Caroline Richardson*

At the least restrictive setting, designed to filter out only pornographic pages, the filter software blocked an average of 1.4 percent of health information sites and about 87 percent of porn sites. At moderate settings, designed to filter pornography and a few other categories such as nudity and information on drugs and weapons, the filters blocked an average of 5 percent of health sites and 90 percent of porn sites. But at the most restrictive settings, which barred a broad range of categories, the blocking of health sites reached an average of 24 percent, while pornography blocking increased only to 91 percent.

The study was funded by the Kaiser Family Foundation. In addition to Richardson and Resnick, the study's co-authors include senior author and Kaiser Family Foundation Vice President Vicki Rideout; Holly Derry, U-M Health Media Research Laboratory; and Derek Hansen, Ph.D., a graduate student in the School of Information.

—KG

Read the complete story:
www.med.umich.edu/opm/newspage/2002/filter.htm

An executive summary of the study and complete results are available on the Kaiser Family Foundation's Web site:
www.kff.org/content/2002/20021210a

New U-M Program Preserves Dreams of Parenting for Cancer Treatment Patients

If you have just been diagnosed with cancer, having a baby may be the last thing on your mind. But cancer is not the death sentence it used to be. Powerful new anti-cancer drugs, chemotherapy and radiation treatments are saving more lives every day.

Unfortunately, the same cancer treatments which save lives can also cause infertility and destroy dreams of becoming a parent forever. So cancer patients must consider this very personal decision carefully, before beginning therapy. Too often, in the shock and worry that follow a diagnosis of cancer – especially in a child or adolescent – the issue of infertility is overlooked or avoided, says Gary D. Smith, Ph.D., a U-M associate professor of obstetrics/gynecology who directs the new U-M Fertility Counseling and Gamete Cryopreservation Program.

"With increasing success in curing cancers, issues pertaining to quality of life after cancer treatment become more relevant," Smith says. "For many people, becoming a parent is one of the most important things in life."

Supported by the U-M Comprehensive Cancer Center, the U-M Department of Obstetrics and Gynecology and the U-M Assisted Reproductive Technologies Laboratory, the program was developed to provide accurate information and help U-M patients and their families handle the complex legal, technical and personal issues involved in fertility preservation and cancer.

> "With increasing success in curing cancers, issues pertaining to quality of life after cancer treatment become more relevant."
>
> —*Gary Smith*

Because cryopreservation technologies used to freeze eggs and ovarian tissue are still experimental, the U-M program currently accepts only semen and sperm-producing cells found in testicular tissue.

"It all comes down to the size of the cell and what you expect it to do following thaw," Smith explains. "Sperm are easy to preserve, because they are small and their primary function is to contribute genetic material. Eggs are large with multiple components and complex functions. When eggs are frozen, ice crystals form inside causing intracellular damage which compromises the egg's viability and/or ability to support the many tasks required for normal embryo development."

Photo: Martin Vloet

Gary D. Smith

Marcia Leonard, R.N., is the nurse-practitioner who counsels men and boys referred to the Gamete Cryopreservation Program by U-M physicians. "People don't understand how complicated it is," says Leonard. "They just want to know if they will be infertile after treatment, but in most cases the data are too incomplete to predict an individual outcome. The incidence of sterility varies widely depending on the location of the cancer, the patient's age, the fertility level before cancer, and the type, amount and intensity of treatment." One of the most difficult and sensitive parts of her job is counseling teenage boys who must deal with issues involving sexuality and reproduction before they have the emotional maturity to handle them.

In addition to counseling, one of the most important areas of the new program is its emphasis on research. Smith and other scientists affiliated with the program are currently working to evaluate new technologies that could improve a woman's chances of preserving eggs or ovarian tissue that would be viable years later when they are thawed. A "flash-freeze" technique called vitrification, which eliminates ice crystal formation, shows a great deal of promise, according to Smith.

Photo: Gregory Fox

Marcia Leonard

"Some laboratories will freeze eggs now on the assumption they will figure out how to maintain viability later," Smith says. "But there's a fine line between reality and hype. We hope to be able to offer the service to women soon, with a realistic expectation of success."

—*SFP*

Information on the program:
www.cancer.med.umich.edu/clinic/fertilityclinic.htm

"We understand from PET scans which parts of the brain are most damaged in different disorders and how these changes relate to patients' symptoms." *–Norm Foster*

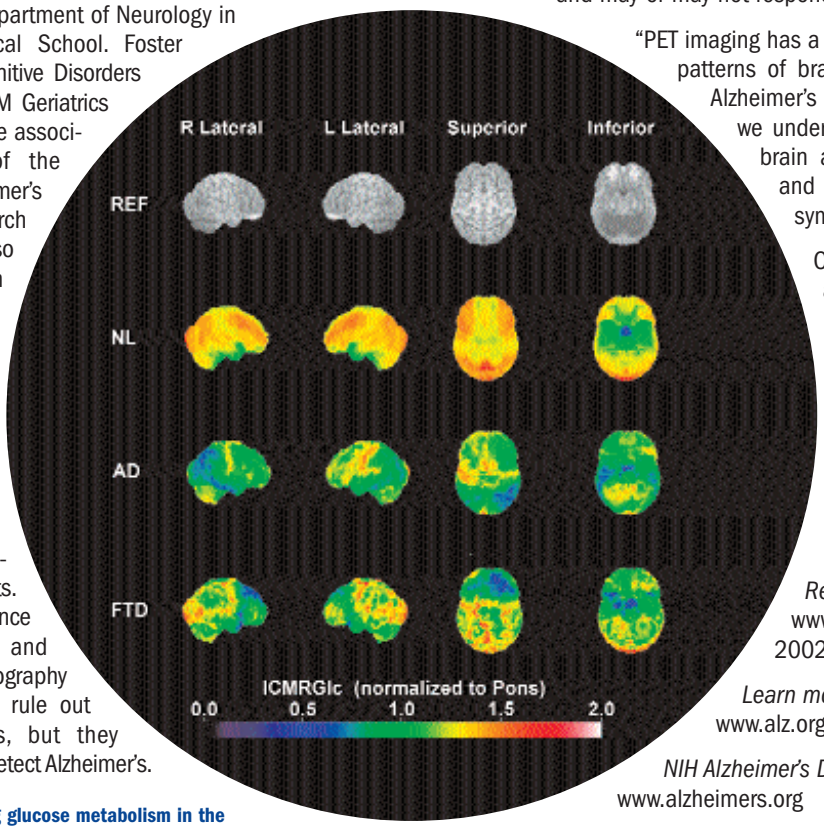
Scanning for Alzheimer's Disease

Alzheimer's is a disease that takes a terrible toll on the memories and lives of millions of adults and their families each year. Unfortunately, there is no definitive test for Alzheimer's disease, and other disorders can mimic its symptoms. New drugs and therapies can slow the spiral of memory loss and behavior changes in Alzheimer's patients, but they work best if the disease is diagnosed and treated early.

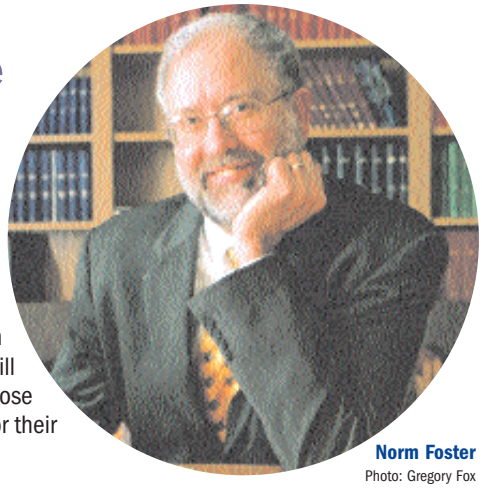
U-M neurologists, working with researchers at three other universities, are evaluating positron emission tomography, or PET scanning, as a diagnostic aid in Alzheimer's disease. Norman Foster, M.D., who leads the research team, says initial results from the study show PET scanning can help physicians differentiate Alzheimer's disease from other neurodegenerative disorders.

PET scans show activity in different parts of the brain and how each part is reacting to disease. Brain activity — or the lack of it — is what matters in Alzheimer's disease, says Foster, a professor in the Department of Neurology in the U-M Medical School. Foster directs the Cognitive Disorders Clinic in the U-M Geriatrics Center and is the associate director of the Michigan Alzheimer's Disease Research Center. He is also a senior research scientist at the U-M Institute of Gerontology.

Researchers have tried other medical imaging techniques to detect the disease, with disappointing results. Magnetic resonance imaging (MRI) and computed tomography (CT) scans can rule out other disorders, but they can't positively detect Alzheimer's.



PET scans showing glucose metabolism in the brain. The color scale at the bottom indicates how glucose metabolism is measured in the scans. The first row (REF) shows the brain as it is oriented in the PET scans below. The second row (NL) shows a "normal" elderly subject, the third row (AD) a patient with Alzheimer's disease, and the fourth row (FTD) a patient with frontotemporal dementia. Courtesy of Norm Foster



Norm Foster
Photo: Gregory Fox

Based on the U-M study and other evidence, Foster feels that early diagnostic testing with PET could become common practice within a few years, and will help physicians choose the best treatment for their patients.

"In some cases, memory loss isn't the first symptom," says Foster. "It could be behavioral or language changes, or difficulty with everyday activities. All symptoms can be caused by different conditions requiring different kinds of treatments and may or may not respond to the same medications.

"PET imaging has a great advantage because it shows specific patterns of brain activity, which differ in normal aging, Alzheimer's disease and other kinds of dementia. And we understand from PET scans which parts of the brain are most damaged in different disorders and how these changes relate to patients' symptoms."

Other universities participating in the study are the University of California-Davis, the University of Pennsylvania and the University of Washington. Funding was provided by the National Alzheimer's Coordinating Center, part of the National Institute on Aging.

—KG

Read the complete story:
www.med.umich.edu/opm/newspage/2002/alzpet.htm

Learn more about Alzheimer's disease:
www.alz.org

NIH Alzheimer's Disease Referral and Education Center:
www.alzheimers.org

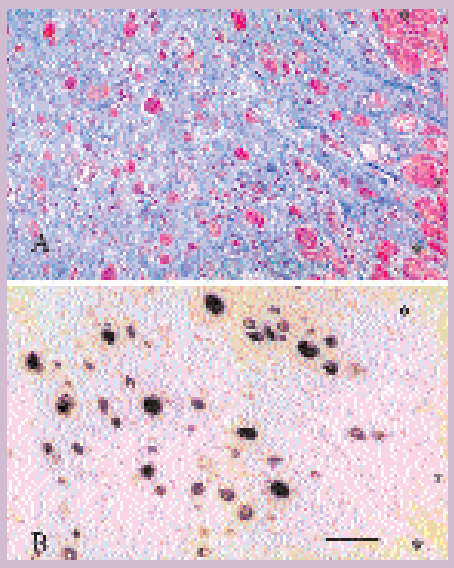
Cell Transplants Could Help Damaged Hearts Heal Themselves

Muscle cells, transplanted from elsewhere in the body, could one day be used to help heal a patient's damaged heart, according to new research led by Francis Pagani, M.D., Ph.D., an associate professor of surgery in the U-M Medical School and director of the Heart Transplant Program.

Photo: Gregory Fox

Frank Pagani

Photo: Arizona Heart Institute



These images show that transplanted cells multiplied and began to form muscle fibers in the damaged hearts of patients in the study.

In addition to the encouraging finding that the injected cells "grafted" into their new environment, the results showed that the patient's heart did not reject the transplanted cells.

In the phase I study, several U-M cardiac patients who were waiting for heart transplants had cells from the quadriceps muscle in their thighs injected into their hearts. After the transplant, their old, damaged hearts were examined for signs of new cell growth. Scientists found that the injected cells not only survived in their new environment, they also began forming muscle fibers. Researchers noticed an increase in the formation of small blood vessels near the injection site. None of the patients developed immune reactions to the transplants. Results were announced at the American Heart Association meeting in November 2002.

The multi-part study, sponsored by Diacrin, Inc., of Charlestown, Massachusetts, involved patients at several medical institutions. U-M Health System patients received injections of skeletal muscle cells during implantation of a heart-assist device called an LVAD, which boosts the failing heart's pumping power and helps patients survive until a new heart is available for transplant. Satellite muscle cells, which occur naturally in skeletal muscle and help repair damage, were injected into the wall of the heart's pumping chamber during the LVAD procedure.

After the heart transplant, the old heart was removed and sent to Diacrin for testing. "We found direct evidence of skeletal muscle cell survival and differentiation into mature muscle fibers, measured using antibodies that specifically target skeletal muscle cells," says Pagani, who directs the Heart Transplant Program in the U-M Cardiovascular Center. "Because cardiac muscle and skeletal muscle are two distinct types of tissue, the antibody test shows conclusively that the transplanted cells survived."

In addition to the encouraging finding that the injected cells "grafted" into their new environment, the results showed that the patients' hearts did not reject the transplanted cells. No evidence of an immune reaction was found in either grafted or non-grafted areas.

"Because the skeletal muscle cells are from the patient's body, we don't expect the kind of immune reaction and rejection we often see in transplants of whole hearts from donors," says Pagani. Pagani stressed that these early results, while encouraging, are merely the first steps in evaluating the potential of using muscle cell transplants to heal damaged hearts.

In addition to Pagani, the research team included Keith Aaronson, M.D., U-M assistant professor of internal medicine and medical director of the U-M Heart Transplant Program, research coordinator Sue Wright, R.N., and several collaborators from Massachusetts General Hospital. Physicians and patients from the Arizona Heart Institute and Temple University were also involved in the study.

—KG

Read the complete story:
www.med.umich.edu/opm/newspage/2002/musclecell.htm

U-M Cardiovascular Center:
www.med.umich.edu/cvc