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RESEARCH AS REMEDY

In Nursing and Allied Health, Recent Research Promises Patient Benefits

By Kevin Dunegan
Photography by Aaron Mayes and R. Marsh Starks

During the past decade, UNLV's Schools of Allied Health Sciences and Nursing have expanded their research programs and boosted collaboration among faculty investigators in support of the university's vision of becoming a major research institution.

In Allied Health Sciences, these projects include a range of potentially patient-benefitting areas, among them investigations in health physics and diagnostic sciences, physical therapy, nutrition, and kinesiology. Nursing researchers are also working to improve human health and wellness, most prominently via projects aimed at advancing understanding of issues related to chronic conditions such as diabetes, obesity, and stress. Both schools will benefit from a recent $20 million grant from NIH to support clinical and bench-to-bedside research and to lead a health research group, the Clinical Translational Research Infrastructure Network, or CTR-IN, comprising 13 universities across the Mountain West region.

The following profiles demonstrate the diversity and depth of the two schools' research projects.

Yu Kuang: Dangerous Tumors, Expedited Assessments

YU KUANG, AN ASSISTANT PROFESSOR in the School of Allied Health Sciences, is focused on the early detection of cancer and image-guided cancer treatment. His recent work explores whether testing for genetic markers associated with tumors, coupled with new approaches to quantitative magnetic resource imaging (MRI) analysis, might lead to more effective treatments for sarcomas, malignant tumors that form in bone, cartilage, fat, muscle, or vascular tissue.

Patients diagnosed with sarcoma usually undergo what health care providers call “neoadjuvant” therapy — typically chemotherapy — to shrink their tumors before surgery. Reducing tumor size prior to operating, oncologists have found, not only makes surgery more effective but also enhances patients’ long-term survival rates.

A drawback of this approach is that determining whether neoadjuvant therapy has done its job can only happen via tumor-tissue analysis following surgery. This means that patients don’t learn if they’ve benefitted until after leaving the operating room, an unfortunate reality that ensures some patients will endure the toxic effects of chemotherapy without any therapeutic advantage. For these patients, the harm in superfluous chemo is not just in the unnecessary discomfort it inflicts. Precious time has been wasted — time that could have been spent on potentially life-saving treatment alternatives.

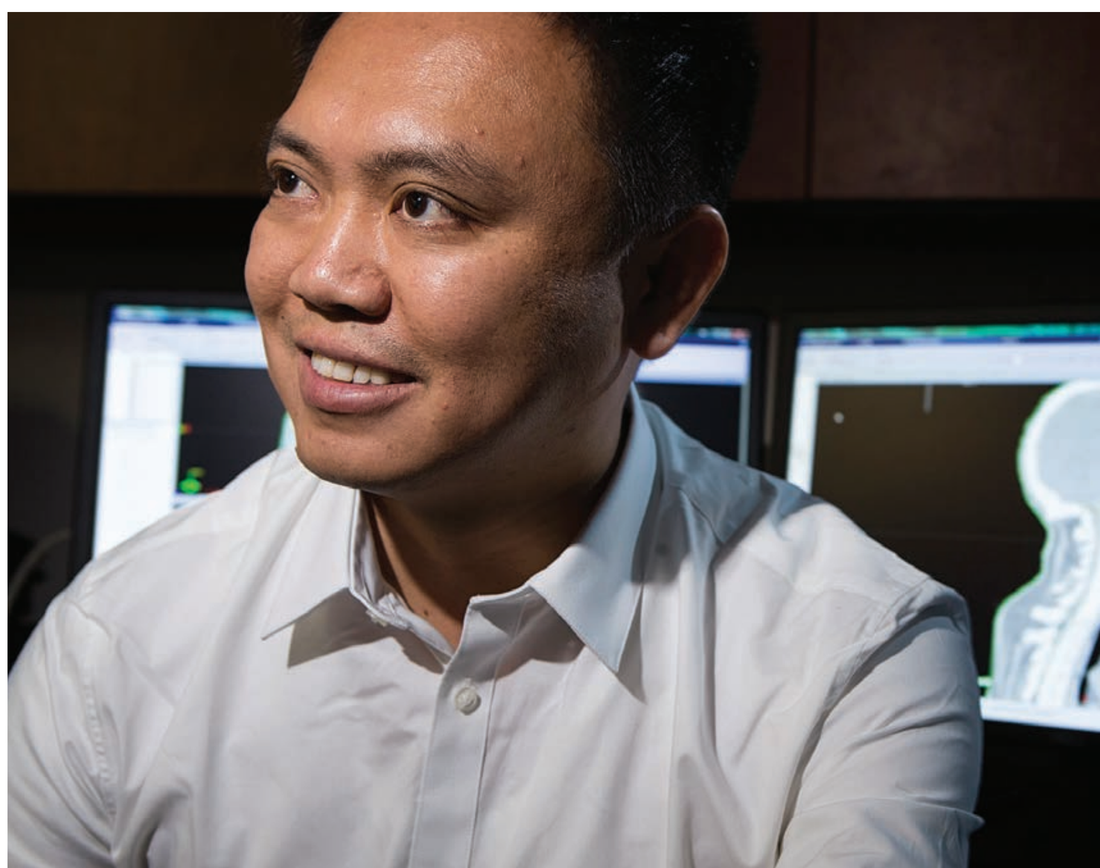
Kuang has teamed up with the Children’s Specialty Center of Nevada and Nevada Imaging Centers to develop an earlier, non-invasive method for predicting success or failure of neoadjuvant chemotherapy. His method involves combining an analysis of tumor markers in mitochondrial DNA from blood draws and diffusion MRI data. The goal, Kuang says, is to identify the early changes of genetic biomarker levels in the blood and the imaging features in the MRI scan that can help clinicians more effectively ascertain how well sarcomas have responded to pre-operative chemotherapy.

By determining patients’ response to the treatment early in the course of chemotherapy, Kuang’s team expects this research will ultimately enable oncologists to optimize treatment protocols for individual patients, improving quality of life and enhancing disease-free survival for patients with sarcoma.

If successful, Kuang’s next step will likely involve multi-institutional clinical trials. These will seek to determine how this combined biological- and imaging-biomarker method might be used to guide future chemotherapy treatments.

Kuang is also actively involved in multi-institutional collaborative work related to prostate cancer. Earlier this year, he teamed up with Sandi A. Kwee, a physician and associate professor at the John A. Burns School of Medicine at the University of Hawaii, to develop a positron emission tomography (PET) image guided prostate cancer radiation therapy method. PET scan is an imaging test that helps reveal how patients’ tissues and organs are functioning via a radioactive drug (radiotracer). In this collaboration, the radiotracer Kuang and Kwee are using is a new U.S. Food and Drug Administration-approved investigational drug that could allow for better targeting of radiation treatments used against intermediate- and high-risk prostate cancer.

The collaborative relationship is expected to lead to a multicenter clinical trial initiative between UNLV and University of Hawaii, a trial that could bring this potentially game-changing approach to prostate cancer patients in Southern Nevada.



ACCELERATED ANSWERS A diagnostic tool developed in part by UNLV's Yu Kuang promises to speed physicians' ability to assess the effectiveness of neoadjuvant therapy in sarcoma patients. If successful, the approach could lead to new, more effective ways to combat these potentially deadly malignancies.

SHOCK AND STRESS The human knee takes a continual pounding, a process scientists such as UNLV's Kai-Yu Ho describe as "shock loading." Ho's latest research aims to identify how shock-loading stress on knees may be contributing to arthritis-inducing bone alignment issues.

Kai-Yu Ho: Assessing "Shock-Loading" and Arthritis Risks

OSTEOARTHRITIS OF THE KNEE, AN INcreasingly common health problem among active adults, is a painful condition involving loss of cartilage and deformity of the joint. It is also a major factor in diminished mobility, especially among older people.

Multiple studies have identified stress injuries to the leg bones as a primary contributor to arthritic knee pain and deformity. Little is known, however, about the causes and progression of bone-stress injuries among middle-aged, active adults.

Kai-Yu Ho, an assistant professor in the School of Allied Health Sciences, is directing a study that could remedy this deficiency, while at the same time providing a method for evaluating the probability that osteoarthritis is present. She also hopes to help doctors detect the sort of bone damage that produces osteoarthritis, even before a person experiences pain.

Ho's study involves an examination of how "locomotion-induced shock loading" — the results of such everyday, bone-jarring movement like walking, running, and stair climbing — affects the physiology of knees. Her work also examines the alignment of bones in legs that have stress injuries, and how injury-related alignment issues might relate to arthritis development.

A normal femur, or upper leg bone, is not perfectly vertical. The bone extends from the hip at a slight angle toward the midline of the body. Normal physical activity can cause micro-damage to the femur and tibia where they meet at the knee. The body repairs the damage by growing new bone, a process called bone remodeling.

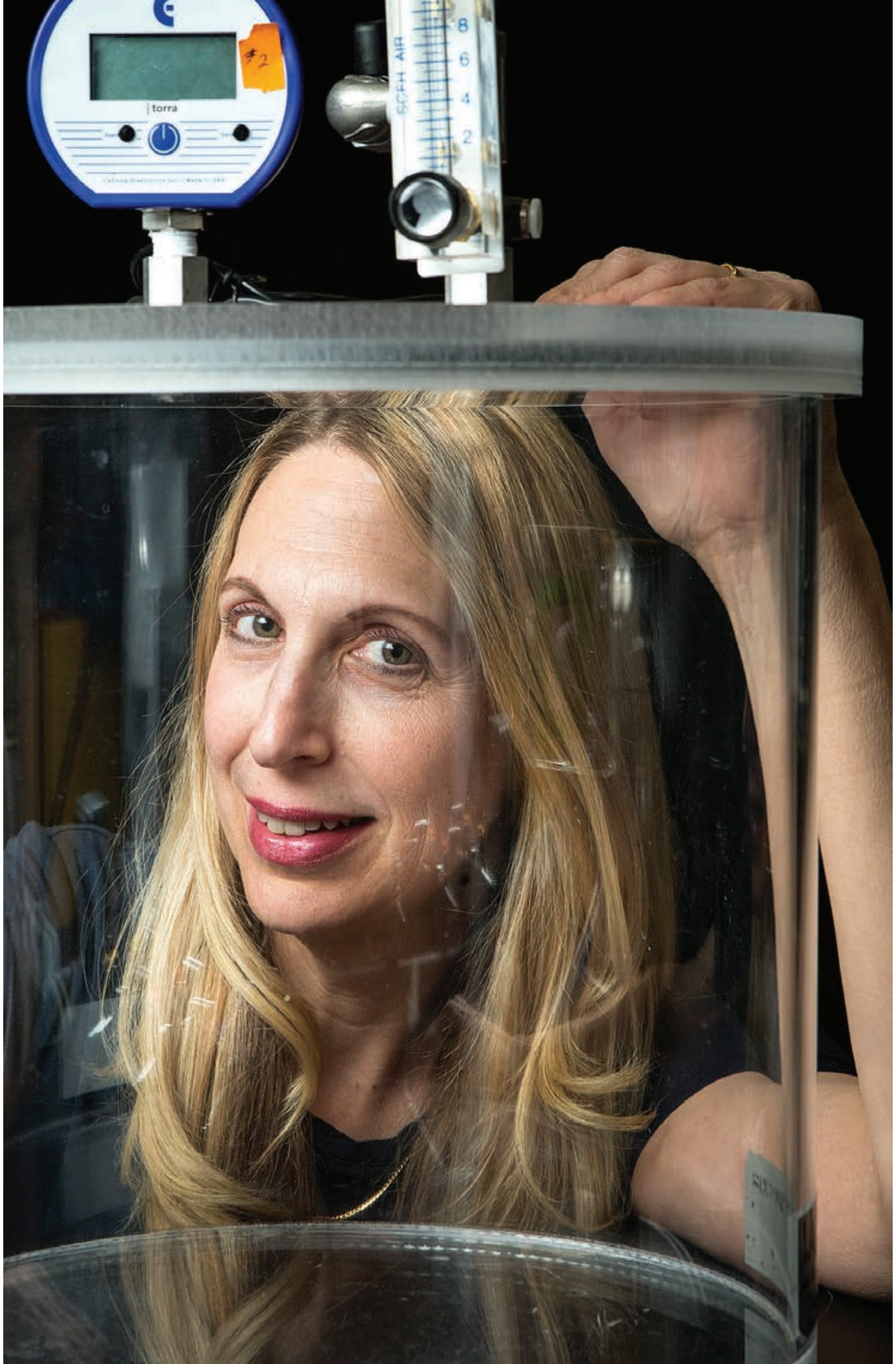
Continual shock-loading damage can cause too much bone remodeling, however, with new bone forcing the femur away from the midline of the body into a "varus angle" (a phrase adapted from the Latin word for "crooked"). When the varus angle is pronounced a person appears bowlegged — the knees do not touch when one stands with his or her feet together.

Ho hypothesizes that increased shock loading among middle-aged persons will lead to greater bone stress, which can increase the onset of osteoarthritis in the joint. She put her hypothesis to the test in a study involving 20 adults ranging in age from 50 to 65. None of her subjects had been diagnosed with arthritis in the knee.

Participants were asked to complete a locomotion-induced, shock-loading activity. When finished, they receive a magnetic resonance imaging (MRI) scan to verify bone stress injuries. Participants next allowed the researchers to measure the angle between the long axis of their femurs and tibias.

Ho says she and her team are now analyzing the data they've collected to determine whether there is an association between lower extremity alignment and MRI-detected bone stress injury. If there is, she says, the finding could provide health-care providers with an early detection method of bone abnormalities. This, in turn, will enable them to recommend physical therapy intervention to ward off future bone-stress injuries to patients' knees.

Research related to this study has been published in the *European Journal of Sports Science* and *Magnetic Resonance Imaging*.



INJURY AND OXYGEN When soldiers and others experience "crush injuries," their treatment often includes evacuation by air. UNLV's Barbara St. Pierre Schneider is exploring why the cabin pressure during such flights may be harmful and what to do about it.

Barbara St. Pierre Schneider: Enhanced Care After Extreme Compressions

EARTHQUAKES, EXPLOSIONS, INDUSTRIAL accidents, car crashes — each are forms of mayhem that leave crushing trauma in their wake. Barbara St. Pierre Schneider, an associate professor in the School of Nursing, is working to better understand the biological processes characterizing such "skeletal and muscle-crush injuries," and how they might best be treated. She is especially concerned with U.S. service personnel who have been injured on the battlefield.

Whether these injuries occur in military combat, during a terrorist attack, or in a natural disaster, crush-related injuries involve significant compression, a traumatic event that interrupts blood flow and damages the cell membrane of muscle fibers. Although the injury itself may not be immediately life threatening, damaged muscle can increase the risk for death down the road: In many cases ruptured muscles spill cellular contents, such as the muscle protein myoglobin, into the bloodstream. Myoglobin, for example, can cause kidney damage and failure.

Soldiers who experience skeletal muscle-crush injuries during combat face additional challenges. Often, the wounded must endure long flights to treatment centers. While unavoidable, these evacuations by air expose the wounded to hypobaria, a situation in which tissues may be deprived of sufficient oxygen, which can become a factor when the air pressure is equivalent to an altitude of 8,000 feet, or that of a typical plane's cabin pressure.

St. Pierre Schneider and her team are studying how hypobaric hypoxia affects the healing of injuries and are searching for potential treatments that counteract its effects. A previous St. Pierre Schneider study, for example, simulated the effects of air transport and examined the effect of hypobaric hypoxia on genes within skeletal muscle. One major finding was that the simulated flights affected the genes affiliated with skin integrity, but had no apparent effect on inflammatory genes in skeletal muscle.

To further her hyperbaric hypoxia crush-muscle research, St. Pierre Schneider is expanding the capabilities of her lab. She recently received grant funding to purchase a combined cell sorter/flow cytometer, an instrument that allows scientists to measure and analyze the inner workings of cells. Having the instrument, says St. Pierre Schneider, will enhance UNLV's research capacity and the university's science, technology, engineering, and mathematics (STEM) program.

St. Pierre Schneider's studies in muscle injury recovery are guiding techniques in aeromedical evacuation, and her work has been featured in multiple publications, including *Aviation, Space and Environmental Medicine* and *Innate Immunity*.

A PLAN FOR PAIN UNLV's Jennifer Kawi is helping both back-pain sufferers and their doctors embrace new ways of thinking about managing the condition. It's an approach that promises to boost patient outcomes while reducing healthcare costs.

Jennifer Kawi: Self-Service for Back Pain

WHEN IT COMES TO PAINFUL CONDITIONS affecting the mobility of millions of Americans, bum knees take a back seat to bad backs. Chronic low-back pain is the most common health complaint in the United States, afflicting nearly 30 percent of people older than 18. In addition to the physical discomfort it causes, chronic low-back pain sufferers also incur high health care costs.

In recent years, more physicians and specialists have recommended self-management strategies to help reduce pain, improve quality of life, and lower associated treatment costs. Jennifer Kawi, a chronic pain specialist and assistant professor in the School of Nursing, is among those who have noted its effectiveness, and she is currently working to identify those chronic low-back pain sufferers who might benefit.

In general, self-management strategies not only encourage patients to actively direct and improve their health, but they also inspire and reinforce patient confidence. Such positive feelings, Kawi says, help patients set realistic goals and action plans, and make lifestyle changes that often include increased exercise and activity levels, better eating habits, and greater use of non-pharmacological pain remedies such as heating wraps and relaxation techniques.

While self-management has improved outcomes and lowered health care costs for a host of conditions, its effectiveness with chronic low-back pain sufferers has not been fully explored. Kawi's project aimed to remedy this using a two-pronged approach.

She first sought to identify variables, such as perceived support from health care providers, pain intensity, and functional ability, that might predict which low-back pain sufferers would respond best to self-management strategies. Her second goal involved evaluating differences in those variables among patients seeking help in specialty pain centers and primary care clinics. Understanding these variables, she reasoned, could help maximize self-management effectiveness in clinical settings, while enabling health care providers to tailor self-management strategies to fit the needs of individual patients.

Kawi and her team analyzed data from 230 people with chronic low-back pain — 110 from specialty pain centers and 120 from primary care clinics. Her research revealed five variables to be predictors of self-management for patients in both settings: age, self-management support, education levels, overall health, and the helpfulness of pain management.

She also discovered differences among key variables in patients who sought care from a specialty pain center versus those who sought care in a primary care clinic. For example, participants in specialty pain centers were more apt to self-manage if they were active in their religious or spiritual beliefs or if they received support from their significant others. On the other hand, low-back pain patients in primary care clinics who had higher incomes tended to self-manage more than those with lower incomes. These important preliminary findings have been tabbed for future research.

Kawi's research has already provided essential intervention data that health care providers can use to bolster the odds that chronic low-back pain patients will be able to successfully self-manage their conditions. The results also identified a need to formulate additional strategies for patients who may not be the best candidates for self-management programs.

The study, which was funded by an external grant from the Nurse Practitioner Healthcare Foundation, appeared in the journal *Applied Nursing Research*.

Susan VanBeuge: For Ailing Seniors, Coordinated Solutions

PEOPLE OFTEN FACE MULTIPLE CHRONIC ailments during their senior years, clusters of conditions that demand a collaborative approach to treatment. But today there are few, if any, training opportunities aimed at preparing the next generation of practitioners and specialists for the challenges of providing the collaborative, interprofessional elder care that is so desperately needed.

Susan VanBeuge is changing that.

VanBeuge is an assistant professor in the School of Nursing who is co-principal investigator with Georgia Dounis, an associate professor of clinical sciences in UNLV's School of Dental Medicine, and Sue Schuerman, an assistant professor in the School of Allied Health Sciences. The UNLV team is a sub-awardee of the Nevada Geriatric Education Consortium, a state-wide initiative aimed at improving the health care delivered to older adults.

The UNLV objectives include developing a Type 2 diabetes management training program for interprofessional faculty with emphasis on communication, prevention of co-morbidities, and cultural sensitivity.

At its core, VanBeuge's program aims to develop a series of provider training for senior health issues to include Type 2 diabetes and Alzheimer's disease. The UNLV team, for example, has developed a one-day training program focused on Type 2 diabetes and offered it statewide to health care providers and faculty who work with professional students. The program includes video-recorded encounters with "standardized" patients — individuals trained to simulate the needs of real patients — and hands-on training with high-fidelity manikins.

The program focused on Type 2 diabetes because of its multiple symptoms, prevalence among older adults, and the need for multiple health care professionals to involve themselves in treatment and management of the condition.

During the training, each participant received a chart detailing a standardized patient's medical and social history, physical attributes, clinical findings, and chief complaint. Teams had 15 minutes to complete the examination. During the encounter, each group assessed their patient's physical status, formulated treatment goals and intervention options, noted potential outcomes, and identified opportunities for coordination of care. They also developed a plan for how responsibility for that care would transpire.

The teams next participated in a debriefing session with the project's instructors (who were observing the interactions in real time on video monitors). Finally, instructors led a group discussion and encouraged self-assessments from participants.

Thus far, the five-year grant, now in its fourth year, has seen close to 100 participants complete the course. Early findings were published after the study's second year. Participants at that time told the researchers that they had gained a better understanding of inter-professional team building, a stronger ability to communicate effectively with team members, and greater confidence in recognizing that meeting the needs of geriatric patients often requires an interprofessional response.

The project has been featured in the *Journal of Interdisciplinary Healthcare* and has been presented during multiple national clinical conferences. The team recently received additional funding to include Alzheimer's disease and dementia to the course training for the coming year.

COLLABORATIVE CARE Managing Type 2 diabetes and Alzheimer's disease is one of senior care's greatest challenges. UNLV's Susan VanBeuge leads a team that is teaching a more coordinated approach.

Steen Madsen: A Nano-Sized Weapon Against Glioblastoma

MASTERING MACROPHAGES A new, nano-particle–based drug delivery system being developed by UNLV's Steen Madsen offers hope against primary brain tumors.

SCHOOL OF ALLIED HEALTH SCIENCES' Steen Madsen is exploring new treatment methods for primary brain tumors — tumors that originate in the brain — using nanoparticles and lasers.

Madsen, professor and chair for the department of health physics and diagnostic sciences, is collaborating with Henry Hirschberg, a researcher at the University of California-Irvine's Beckman Laser Institute and Medical Clinic, on a particularly promising approach. It involves using a type of white blood cell that ingests foreign material as a therapeutic-drug delivery vehicle.

There are approximately 34,000 new cases of primary brain tumors diagnosed each year in the U.S. and Europe. Close to 40 percent of these tumors are of the most aggressively malignant variety, glioblastoma multiforme (GBM). Less than 5 percent of patients diagnosed with GBM will live more than five years.

Glioblastoma tumors are notoriously aggressive and difficult to treat. When removed during surgery, they almost always reappear. Madsen, Hirschberg, and their research team are exploring a small solution to this big problem: employing macrophages, the aforementioned, material-ingesting white blood cells, to transport nano-sized particles of therapeutic gold to surgical resection sites. If successful, it's a system that could greatly enhance the effectiveness of photothermal therapy, a process that destroys tumor cells using laser light.

Why gold? The precious metal offers two particular advantages. First, it has already been used safely in humans for a variety of medical applications. Second, and more to the point, gold has the ability to convert infrared laser energy to thermal energy. When exposed to photothermal therapy, gold nanoparticles act as heat generators and burn the tumor cells.

In preliminary studies, Madsen and Hirschberg demonstrated the feasibility of using macrophages as delivery vehicles for gold-based nanoparticles. This was a particularly welcome finding given that, being part of the body's natural defenses, macrophages can be easily extracted from a patient, loaded with the desired therapeutic agents and re-injected into the body.

During the study's next phase, Madsen and Hirschberg's team showed that using gold-loaded macrophages in concert with photothermal therapy was effective in treating tumor cells in the brains of laboratory animals. Animals that received the macrophages and photothermal therapy, in fact, showed zero tumor cells when the treatments concluded. These findings and others have been published in the *Annals of Biomedical Engineering* and *Lasers in Surgery and Medicine*.

Hurdles remain, however. Part of Madsen and Hirschberg's current research involves searching for a means to allow nanoparticle-loaded macrophages to pass through the body's "blood-brain barrier," the biological mechanism preventing most external cells and other matter from passing through to the brain. Thus far, the answer has eluded them.

Madsen and Hirschberg say they are confident that this obstacle, too, can be overcome, and that, once bypassed, they will be that much closer to improving the dismal five-year survival rate of GBM patients.