A MONOCLONAL ANTIBODY developed by researchers in the School of Medicine and Biomedical Sciences has been shown to significantly extend the survival of mice with human breast-cancer tumors and to inhibit metastasis to the lungs by more than 50 percent.

The antibody, named JAA-F11, targets a particular disaccharide, an antigen known as TF-Ag, which aids the adhesion and spread of certain cancer cells. In the study—results of which were published in the November 2006 issue of Neoplasia—researchers showed that while the antibody did not kill the cancer cells, it blocked stages of cancer-cell growth that allow the cells to adhere to and organ tissue.

Mice with breast-cancer tumors that received the antibody had a median survival time of 72 days, compared to 57 days for the animals that did not receive JAA-F11, the study found. In addition, exposing cultures of tumor cells to the antibody inhibited cell growth by a statistically significant 16 percent.

“This antibody binds with a carbohydrate on the tumor cell surface that is involved in adhesion of the cell during the metastatic process,” explains Kate Rittenhouse-Olson, PhD, associate professor of clinical and laboratory sciences at UB and senior author on the study. “Not only would drugs attached to the antibody JAA-F11 bind to the tumor cell surface to direct their cytotoxic effect, but the binding of the antibody itself would block the cell from metastasizing.”

The antibody was tested using in vitro models of tumor cell growth, in assays to determine its ability to damage or kill cells (cytotoxicity), in various models of cancer metastasis, and in mice with metastatic breast cancer.

“In addition to providing a survival advantage,” says Rittenhouse-Olson, “JAA-F11 immunotherapy reduced the metastatic tumor burden significantly, reflected by both a dramatic decline in the overall incidence of spontaneous metastasis to the lung—48 percent to 47 percent—and fewer macroscopic metastatic lesions.”

The research group currently is determining if JAA-F11 could increase the effectiveness of existing cancer drugs, she says, as well as studying the possibility of using the antibody as a vehicle for the targeted delivery of drugs to aid cancer diagnosis and therapy.

Jamie Heimbuch and Jun Yan, co-first authors on the paper, were graduate students in Rittenhouse-Olson’s lab at the time of the study.

Also contributing to the research were Susan Morey and Robert Klick, PhD, from the UB Department of Biotechnical and Clinical Laboratory Sciences; Linda Wild, MD ’76, from UB’s Pathology Department; Olga V. Glinsky, MD, Vladislav V. Glinsky, MD, and Virginia H. Huxley, PhD, from the University of Missouri, and René Roux, PhD, from the University of Quebec in Montréal. Glinsky also is affiliated with the Harry S. Truman Memorial Veterans Hospital in Columbia, Missouri.

The research was supported by grants from the National Institutes of Health to Rittenhouse-Olson, Glinsky and Huxley; from the V eterans Affairs Merit Review Program to Glinsky, and from the U.S. Department of Defense to Heimbuch and Rittenhouse-Olson.

A BLOOD COMPONENT called glycated LDL—a form of low-density lipoprotein (the “bad” cholesterol) with a sugar molecule attached—is known to be higher in diabetics than non-diabetics, and extensive research has shown that diabetics are at increased risk of a heart attack.

For the first time, a new study that followed a cohort of elderly people in southern Italy found that glycated LDL levels increase the risk of heart attack in both diabetics and persons without diabetes.

Results of the study, which appeared in the January 2007 issue of Nutrition, Metabolism and Cardiovascular Diseases, show that diabetics with the highest levels of the LDL at the start of the study had nearly three times the risk of developing a heart attack within five years than persons with low levels of the LDL. Even in persons without diabetes, those with high glycated LDL levels had twice the risk of having a heart attack.

“The association of glycated LDL with myocardial infarction could explain why diabetes is a risk factor for MI (heart attack),” says Maurizio Tresivis, MD, dean of the UB School of Public Health and Health Professions and senior author on the study.

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“Glycated apo B, like glycated hemoglobin (HbA1c), is present also in non-diabetics and its increase could be due to temporary hyperglycemia, caused by a high-glycemic-load meal, by stress and by other factors,” explains Silvano Trevisan, professor of clinical laboratories affiliated with Italy’s National Health Service, not from the general population. “These findings need to be confirmed,” he says, “and if the relationship is confirmed, interventions aimed at lowering the glycation of lipoproteins should be organized to test whether such interventions can lower the risk of coronary heart disease.”

The 20-year follow-up of participants in the study, which began in 1992, should provide more concrete data, he adds.

For the study was Giovanni Misciagna, MD, PhD, a former doctoral student in epidemiology at UB, now at the Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS) in Castellana-Bari, Italy. Additional contributors were Giancarlo Logroscino, from Harvard University’s School of Public Health, and Gianpietro De Michele, Vito Guerra, Annamaria Cisternino and Maria Gabriella Caruso, all from the IRCCS.

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Rewriting Bad Code
Targeting RNA that causes triplet-repeat disorders

A University at Buffalo medicinal chemist has identified compounds to target a ribonucleic acid (RNA) that causes a form of muscular dystrophy called myotonic dystrophy, or DM.

Myotonic dystrophy, a form of muscular dystrophy, belongs to a class of diseases called triplet-repeat disorders in which the genetic code has an abnormal repetition of three letters of DNA.

As with all forms of muscular dystrophy, no treatment currently exists for DM, which is characterized by the inability of muscles to relax at will. Cases of the disease can vary widely in severity based on the severity of the RNA defect and it frequently is diagnosed in the adult years.

According to Matthew Disney, PhD, whose research focuses on developing a chemical code for targeting RNA with small molecules, DM belongs to a class of diseases called triplet-repeat disorders in which the genetic code has an abnormal repetition of three letters of DNA.

“The RNA with the abnormal triplet repeat is made into a defective RNA that forms an unnatural structure that binds to a protein important in muscle function,” explains Disney. Assistant professor in the Department of Chemistry in the UB College of Arts and Sciences. “It is this RNA-protein interaction that causes the disease.”

Disney in 2006 was one of just seven scientists in New York State to be awarded a $200,000 James D. Watson Investigator grant from the New York State Office of Science, Technology and Academic Research. He is using the award for work to target some of these RNA structures with small molecules developed in his lab at UB.

RNA, DNAs chemical cousin, is a template for protein synthesis, which orchestrates protein-building, catalyzes chemical reactions and performs many other essential roles in cells.

Mutations in RNA can alter expression of proteins that can lead to cancer, sickle cell anemia and other diseases, one of which is DM.

Initial research efforts will be focused on validating Disney’s approach for designing compounds to target RNA structures, as well as confirming that the DM RNA target is a viable one for treating this disease.

If the early research is successful, then Disney and his colleagues will tackle the much more challenging issue of developing their compound into a viable pharmaceutical treatment.

In addition to the NYSTAR award and funding from the Camille & Henry Dreyfus Foundation, Disney is supported by, and is a member of, UB’s New York State Center of Excellence in Bioinformatics and Life Sciences.

A UB faculty member since 2005, Disney graduated from the University of Maryland and earned a master’s in chemistry and a doctorate in biophysical chemistry from the University of Rochester.

Depth and Breath
Training breathing muscles improves swimmers’ performances

Swimmers and scuba divers can improve their swimming endurance and breathing capacity through targeted training of the respiratory muscles, researchers at the University at Buffalo have shown.

“Typically, we think it’s the muscles that move the body that are fatigued when we tire;” he notes. “However, the increased work load of the breathing muscles is very important, particularly underwater during prolonged or high-intensity exercise such as swimming.

“As shown by other studies, when breathing muscles become fatigued, the body switches to survival mode and ‘steals’ blood flow and oxygen away from the locomotor muscles and redirects it to the respiratory muscles to enable the diver to continue breathing. Deprived of oxygen and fuel, the locomotor muscles become fatigued.

“Increasing the strength and endurance of the respiratory muscles prevents their fatigue during sustained exercise, enabling divers and swimmers to work load of the breathing muscles is very important, particularly underwater during prolonged or high-intensity exercise such as swimming.

The type of training, adds Lundgren, also may be useful for patients who suffer from respiratory stress.

Julia A. Wysocki, PhD, UB clinical assistant professor of rehabilitation sciences, is first author of the paper. Pendergast, Luc E. Gosselin, PhD, associate professor of exercise and nutrition sciences, and Dan E. Warkander, PhD, research assistant professor of physiology and biophysics, are additional authors.

The research was supported by a grant from the Naval Sea Coastal Systems (Naval Experimental Diving Unit).
Imagine having a decayed tooth repaired, painlessly, without drilling or shots of anesthesia to numb the area.

Researchers study no-drilling, no-shots dentistry

The second study, set to begin this spring, will test the use of ozone to kill bacteria in a decayed tooth and its potential to eliminate the need for the dreaded drill, at least to repair simple cavities.

At least 85 patients should be completed by the end of January; it then will be followed by a second study in March. Once the results, researchers study no-drilling, no-shots dentistry

Health Fair for All

Medical students reach out to underserved communities

"I think it's critical for students who are developing professionally as doctors or dentists or nurses to understand the importance of serving the community in which they live."—Tamara Thomas, Class of 2009

UB medical students hosted a health fair for the general public on March 18 in an effort to foster contact with local residents, as well as to increase awareness about a wide range of health issues of concern to the Buffalo community.

The health fair was sponsored by the UB chapter of the Student National Medical Association (SNMA), and was held in the Buffalo Museum of Science.

The fair is an annual tradition of the SNMA at UB—"the local chapter of the nation’s oldest and largest independent, student-run organization focused on medical students in under-represented minorities," organizers point out that this was the first year the fair also was designated as the regional health fair for SNMA Region IX, which includes chapters at medical schools throughout New York State and New Jersey.

"Every year every region has a health fair," says Tamara Thomas, copresident of the SNMA chapter at UB. "This year, UB was honored to be the place where the regional health fair was held."

"I think it’s critical for students who are developing professionally as doctors or dentists or nurses to understand the importance of serving the community in which they live," adds Thomas. "This is a perfect opportunity for them to be involved and really give back to the community." Surbhi Bansal, a second-year student in charge of organizing this year’s event, says regional sponsorship helps the health fair achieve its mission because additional assistance means a larger event can be held than in previous years.

"Our goal," she says, "is to let the students be more out there in the community, get to know the community, and also let the community know about the involvement of students."

Students staffed information booths on a wide range of topics, including those that dominate the health-care landscape in Buffalo, such as cardiovascular disease, diabetes, hypertension, weight control and obesity. Free blood pressure screenings were available and attendees had an opportunity to meet representatives from Buffalo Free Clinic Services and local medical insurance companies.

Regular contributors to this, as well as past SNMA-sponsored health fairs, include the School of Dental Medicine, the Department of Exercise and Nutrition Sciences in the School of Public Health and Health Professions, Kaleida Health and the Lighthouse Free Medical Clinic, a program run by UB medical students in one of the poorest neighborhoods in Buffalo.

Lynn Ven, a second-year medical student who performed blood pressure screenings and operated a booth at the 2006 health fair, says the event provides a casual environment in which people feel comfortable enough to open up and ask questions about their personal health situations.

"It is a good setting to talk about all sorts of things," she says. "It’s a little bit of a friendlier environment—not an office where I’m wearing a white coat. I’m just another person. They can ask me questions that they might not want to ask their doctor, for various reasons."

She points out that last year’s health fair was held at a neighborhood church on the East Side of Buffalo in an effort to target populations that had limited access to health-care information.

This year’s location at a prominent site, Bansal notes, Bansal, aimed to attract greater numbers of people from throughout the entire Buffalo community.

“We wanted to make it accessible to the general public,” she says. “The first thing that came to mind was the Buffalo Museum of Science.”

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