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Neurosciences News

A publication for those who support brain, nerve, and muscle disease research, education, and care at the University of Minnesota

One vaccine, multiple cures?

Researchers hope a new vaccine for Epstein-Barr virus could guard against mono, multiple sclerosis, and certain blood cancers

The power of vaccines against deadly diseases cannot be overstated. In fact, "vaccine-preventable diseases" tops the Centers for Disease Control and Prevention's list of the 10 greatest public health achievements of the past decade, which saw the number of diseases successfully targeted with immunizations rise to 17.

Now, a University of Minnesota scientist is determined to see that number rise again as he puts his considerable expertise to work making an Epstein-Barr virus (EBV) vaccine available to the public.

Almost everyone has heard of EBV, but few really understand the havoc it can create inside the body. There's no Epstein-Barr *disease*, after all, so ... what does it mean to contract EBV, and how significant would a vaccine really be?

A good question, says University professor of laboratory medicine and pathology and pediatrics Henry Balfour Jr., M.D., because almost everyone gets infected with EBV at some point in their lives. But while the vast majority of people carry EBV around with little or no ill effect, others suffer acutely from this insidious virus.

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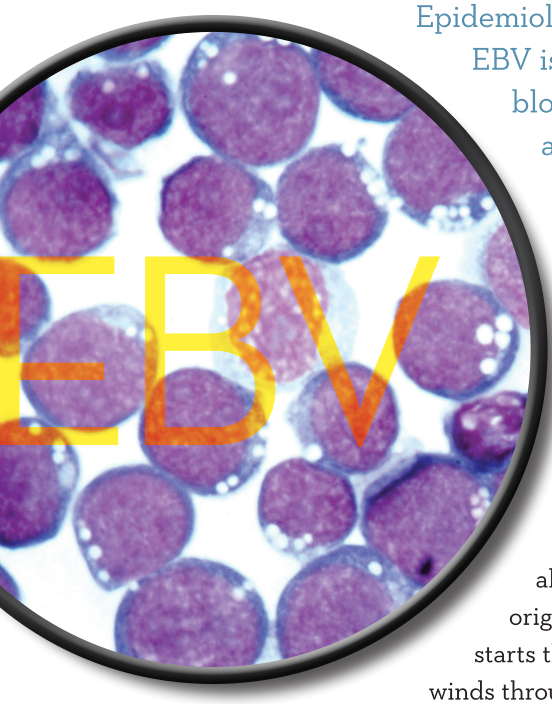
Photo by Scott Streble

Because contracting Epstein-Barr virus is essential to getting multiple sclerosis, vaccinating against the virus could well be vaccinating against multiple sclerosis, says the U's Henry Balfour Jr., M.D.

One vaccine, multiple cures? *(continued from cover)*

"We know that EBV causes infectious mononucleosis [mono] and certain cancers like endemic Burkitt lymphoma and a subset of Hodgkin lymphoma," says Balfour, who founded the U's clinical virology lab and is principal investigator of its International Center for Antiviral Research and Epidemiology. "We also know now that EBV is a major threat to successful blood and marrow transplant, and that it's the most significant environmental risk factor for multiple sclerosis (MS). So a vaccine for EBV could impact millions of people worldwide."



Epstein-Barr virus as seen under a microscope

A tangled tale

An experimental EBV vaccine already exists, and the story of its origins is a tangled tale of stops and starts that crosses two continents and winds through numerous pharmaceutical companies. It's a tale that gives lay people a glimpse into the frustrating world scientists often deal with as they try to move their research ahead.

Back in the 1990s, scientists identified a likely candidate for use in a vaccine—something called glycoprotein 350, or gp350, which can prevent EBV from getting into the cell. The drug company that owned the intellectual property made good progress on the vaccine but was then bought out by another company, which decided to out-license the vaccine to yet another company. That company also then decided not to pursue the research. Happily, its affiliate in Belgium wanted to work on the vaccine, and that's where the story takes a step forward.

In 2007, researchers in Belgium completed and published the results of the first clinical trial, which showed that the vaccine could indeed prevent the development of mono in people who contracted EBV. Finally, it seemed the vaccine was close to reality—but no. After doing more work on the vaccine, the company that owned it was bought out by yet another company, which shelved the project. And there it languished until last year, when the company approached Balfour, offering to give him the rights to further develop the vaccine.

"We have a strong team here at the U that sees this vaccine as fulfilling a huge unmet need," Balfour explains. "What people don't always understand is the path in medical research is often as much about money and legalities as it is about science."

The multiple sclerosis impact

Worldwide, more than 2.3 million people have MS, which is an unpredictable disease of the central nervous system that can lead to paralysis, blindness, and even death.

"The role of EBV in MS is very important," Balfour says. "Nearly everyone with MS has been infected with EBV, and the amount of antibodies in their systems is very high, which means the virus is continuously active."

In other words, he says, contracting EBV is essential to getting MS. So, vaccinating against EBV could well be vaccinating against MS.

Cancer complications

Linda Burns, M.D., a professor of medicine in the U's Adult Blood and Marrow Transplant Program, has seen the damage wrought by EBV countless times.

"If a patient who undergoes a transplant has been exposed to EBV," she explains, "it can lead to big problems because the patient's immune system is not functioning properly and may not effectively fight the virus."

One of those complications is an aggressive type of non-Hodgkin lymphoma that can become life-threatening to the transplant patient. EBV also plays a critical role in the development of Hodgkin lymphoma; doctors have known for some time that having had mono increases your chances of developing that blood cancer.

"Reduce the number of people who contract infectious mononucleosis," says Burns, "and we would likely reduce the number of people who get the serious lymphomas associated with EBV."

The staggering cost of success

Once a licensing agreement for the vaccine is in place, which Balfour hopes will happen early next year, his team is ready to begin the preclinical studies necessary to gain U.S. Food and Drug Administration approval for testing in humans. That phase, Balfour says, takes about two years, which will hopefully see the vaccine into the final leg of a decades-long journey. In 2017, Balfour plans to oversee a clinical study of the vaccine to prevent mono involving about 300 U of M student volunteers. He predicts this study will cost at least $5 million.

"Our goal is to see this vaccine get into people to prevent mono and also some very nasty, sometimes deadly, diseases," Balfour says.

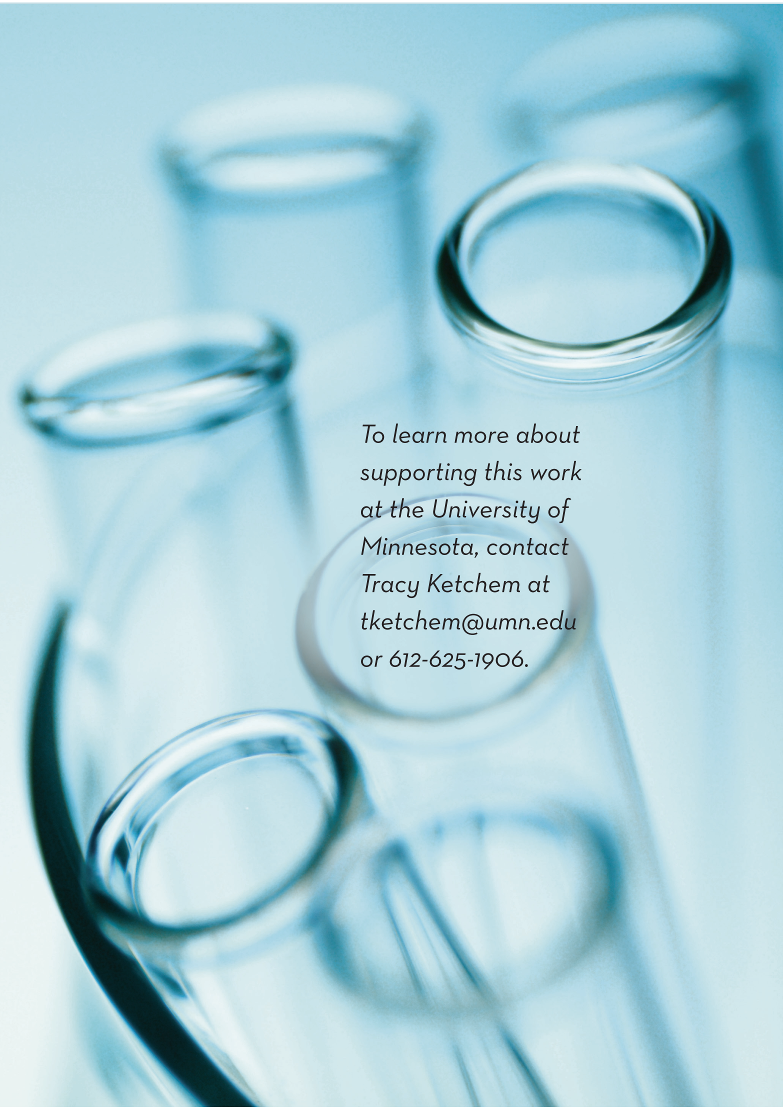
Eager for the next step

Photo by Patrick O'Leary

Among those eagerly awaiting movement on the next big step in this Epstein-Barr virus (EBV) vaccine research is former University of Minnesota first lady Susan Hagstrum, Ph.D. Her mother, Shirley Hagstrum, was diagnosed with progressive multiple sclerosis (MS) when she was 40 years old but had symptoms of the disease for many years before that.

"I am very excited about the prevention possibilities of this vaccine," says Hagstrum, who, with her husband, former University President Robert Bruininks, Ph.D., is already a major donor to the U's ongoing fight against MS; the two established the Susan and Shirley Hagstrum Multiple Sclerosis Research Fellowship in honor of Susan's mother, who died of MS in 1999 at age 76. "It makes me feel so good that the University has researchers like Dr. Balfour, and others, who can produce products like this that will change lives—even save lives—for millions of people around the world."

In the meantime, scientists and those affected by diseases that follow in the wake of EBV watch, wait, and raise dollars to keep the vaccine research on track—once and for all.



To learn more about supporting this work at the University of Minnesota, contact Tracy Ketchem at tketchem@umn.edu or 612-625-1906.

Neuroscientist takes the path less charted

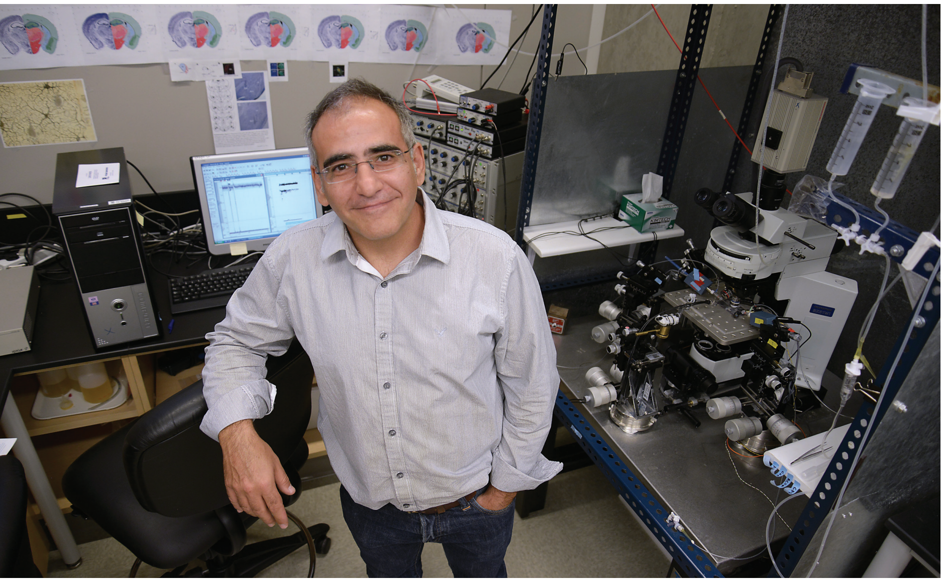


Photo by Jim Bovin

Alfonso Araque, Ph.D., shipped this elaborate equipment, being used here to measure the electrical activity of a neuron, to the U from his lab in Spain.

In the world of brain research, it's been all about neurons—those electrically excitable cells that process information—for the past 100 years. But a few lone wolves are more intrigued by the brain's "glial cells," so named for the 19th century belief that these non-neuron brain cells were simply the "glue" that held everything else together.

Alfonso Araque, Ph.D., professor in the Department of Neuroscience and holder of the Robert and Elaine Larson Neuroscience Research Chair, is one of those investigators taking the path less charted, one who believes that solutions for brain diseases could lie in the shadowy world of the glia.

"We do know now that glial cells are more important than once thought," says Araque, who came to the University last fall from Madrid's prestigious Cajal Institute. He has already shown that astrocytes, a type of glial cell, regulate how neurons communicate with one another. Now he's working on defining the properties of that communication.

"When something goes wrong, is it because the glial cells are not functioning properly? Once we fully understand the role of those cells, it may bring us new understanding of how brain diseases develop," he says, "and how to treat them."

Department of Neuroscience Chair Timothy Ebner, M.D., Ph.D., for one, couldn't be happier that Araque is moving this line of research forward at the University of Minnesota. "I cannot stress enough that Dr. Araque is the world leader in this groundbreaking area of neuron-glia interactions," says Ebner, who recruited Araque with the help of University philanthropists.

Araque and his family are thrilled to be in Minnesota—he calls Minneapolis the "hidden gem of the United States"—and he's grateful for the support he's received in his quest to explore new frontiers in brain science.

"I'm very optimistic about the future," he says. "I believe we've opened a door that will lead us to new understanding of how the brain functions and, ultimately, to treat or even cure serious brain diseases."

Beyond the ice bucket: the U of M ALS Clinic

You've seen the ALS Ice Bucket Challenge, but did you know that the University of Minnesota ALS (Amyotrophic Lateral Sclerosis) Center is an ALS Association Certified Center of Excellence? That's the highest designation the ALS Association gives to recognize and support clinics it considers the best in the field.

The University of Minnesota ALS Center is actively engaged in major national research consortia and is participating in several research studies, including studies involving state-of-the-art imaging and a patient-centered clinical research initiative linking nine ALS centers in the Midwest. And to accelerate local efforts to find better treatments, the University and Hennepin County Medical Center have partnered to create a unified Twin Cities ALS research consortium.

To learn more, contact Tracy Ketchem at 612-625-1906 or tketchem@umn.edu.

A boost for the next generation of neurologists

Sometimes a good story keeps getting better.

Four years ago, University of Minnesota neurology professor emeritus Arthur Klassen, M.D., donated $50,000 to start the Neurology Resident Educational Travel Scholarship, which was designed to help cash-strapped young residents attend important national conferences. A former Department of Neurology chair, Klassen had spent 37 years training neurologists at the U and understood just how essential it was to give them the learning and networking opportunities these conferences provided.

Klassen found a willing partner in fellow professor and another former neurology chair David Anderson, M.D., also a fund contributor, who is quick to direct the spotlight back to Klassen. "Art Klassen is really the hero here for so generously starting this important fund, and I was happy to pitch in when he asked for help," Anderson says.

Because residents are now required to attend at least one conference per year, Klassen and Anderson targeted $300,000 for the fund, which they felt would create a solid endowment to provide ongoing travel support to six residents per year. Then the two got busy spreading the word about the fund.

And they've done well in that mission. So far, the fund has received support from 77 donors who have made 91 gifts totaling more than $131,000.

"We are a continuum of doctors who have come from a very special place, the University of Minnesota," says Anderson, "and we owe it to each other to do whatever it takes to ensure that the younger generation becomes the best doctors they can be, for our patients and for all of neurology."

With advocates like Klassen and Anderson, it's not hard to see that continuum of outstanding neurologists stretching well into the future.

Make a gift to the Neurology Resident Educational Travel Scholarship at **give.umn.edu/giveto/klassen** *or by contacting Tracy Ketchem at 612-625-1906 or tketchem@umn.edu.*

U receives two NIH grants originating from President Obama's BRAIN Initiative

The University of Minnesota's Center for Magnetic Resonance Research (CMRR) is among the first to be awarded a federal grant resulting from President Obama's BRAIN Initiative, an effort to develop next-generation brain imaging technology.

The CMRR, an international pioneer in the imaging field, will receive two grants.

The first is to develop a smaller, portable magnetic resonance imaging (MRI) device that will allow research on human behavior and brain disorders to expand around the world. Today MRIs are only available to an estimated 5 percent of the world's population, primarily in large, developed cities and countries. In contrast to laboratory-bound MRI machines that weigh several tons and occupy large areas in hospitals, a new head-only magnet would allow for imaging of people who have biomedical implants or other metal objects embedded in or attached to their bodies and will weigh roughly 1,000 pounds.

A second award is focused on providing an efficient, cost-effective engineering solution to lead to next-generation MRI technologies and instruments. The goals are to transform the understanding of human brain function and dysfunction and enable noninvasive and reliable assessment of the brain at the cellular level.

Addiction and the factors that fuel it

Photo by Jim Bovin

Sheila Specker, M.D., studies the complex interplay of factors that keeps some people in the grips of alcohol or drug dependence.

Addiction doesn't happen in a vacuum.

As Department of Psychiatry associate professor Sheila Specker, M.D., has seen time and again, it's often accompanied by depression, bipolar disorder, an eating disorder, or another mental health problem. Sometimes it's one thread in a tangle of issues; often it's tough to tease out which problem came first.

Two decades ago, when Specker was running an outpatient treatment program she'd developed for women battling addiction and eating disorders, she learned that in many cases, depression had often preceded both.

"And we were surprised at the high rates of sexual and physical abuse" in patients' histories, Specker says. "We were also surprised at the high rates of suicide attempts, and of compulsive behaviors like shoplifting—and just the severity of other mental health problems."

Those patterns informed the big-picture approach she would take—and continues to take—in her work. Aiming to improve both the prevention and treatment of addiction, Specker studies the complex interplay of different factors that keep some people in the grips of alcohol or drug dependence.

Currently, she's a lead investigator in a five-year study through the University's Center for Women's Health and the National Institute of Drug Addiction examining differences between men and women in impulsivity and addiction.

She's also partnered with the Hazelden Foundation to explore the role of impulsivity in young adults addicted to cocaine and other stimulants. "We used brain imaging to look at connections in the brain in those who relapsed versus those who didn't. It does appear there's a difference," Specker says.

Specker spends about a third of her time in the clinic, often treating health professionals with addiction. And recovery rates are markedly higher among health care providers, she says. "There's a lot at stake: reputation, livelihood. They tend to have more of a support system. They tend to have better access to effective treatment options. Especially for physicians, the resources available are better."

As a consultant to Tapestry, a women's residential treatment program in St. Paul, Specker continually sees how unemployment, homelessness, and "psychosocial instability" undermine patients' efforts to break free.

Across all demographics, a few things have become clear to Specker over time. "The genes are most critical," she says, when it comes to addiction—and, therefore, so is the role of early counseling for youth who have it in their family history.

Perhaps most important, "People who have ongoing support from others in recovery, and those who do ongoing treatment activities, do better."

Ataxia research pioneer named to Institute of Medicine

A career of discovery and research progress has earned the University of Minnesota's Harry Orr, Ph.D., a spot in the prestigious Institute of Medicine (IOM).

Orr, a professor in the Medical School's Department of Laboratory Medicine and Pathology and director of the Institute for Translational Neuroscience at the U, is among 70 new members and 10 foreign associates elected to the IOM in 2014. This is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

The Line Up

News from the Bob Allison Ataxia Research Center

A milestone year

What a difference 25 years can make.

It was during an old-timers game at the Metrodome that Minnesota Twins great Bob Allison first noticed problems with his coordination. Later, family and friends noticed a stagger in his walk, and his speech was often slurred. Eventually, Allison learned that he had a progressive form of ataxia known as Olivo-Ponto cerebellar atrophy.

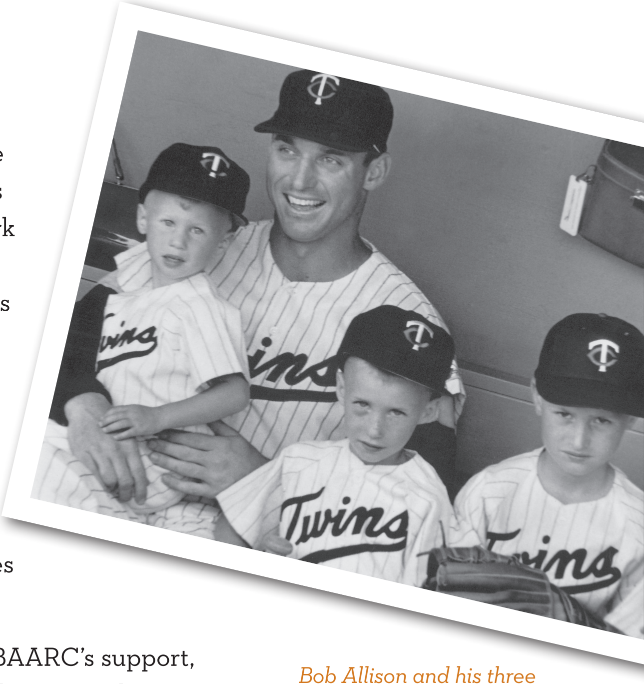
He and his family soon found out what that meant, and it was devastating: it meant trouble coordinating the basic muscle movements required to walk, talk, hold objects, and swallow.

In 1990, Allison helped found the Bob Allison Ataxia Research Center (BAARC) at the University of Minnesota, which even then was known as the best place to find leading-edge ataxia treatment and research. Allison's efforts were joined by his wife, Betty; sons, Mark, Kirk, and Kyle; and former teammates Jim Kaat and Frank Quilici.

Although Allison died of complications of ataxia in 1995 at age 60, his legacy lives on through BAARC's work. And as the organization rounds out its 25th year, board chair Mark Allison says there's plenty to be proud of. BAARC has raised nearly $7.5 million. It has granted more than $2.3 million to 27 U of M researchers, who in turn have attracted an astounding $29.6 million from the National Institutes of Health.

Today, largely because of BAARC's support, a renowned ataxia research team at the U is making big strides toward a gene therapy that could become the first ever ataxia treatment.

"There are a lot of good things happening," says Mark Allison, who is stepping down as BAARC board chair after more than two decades in the position. "We're hoping to have the big celebration someday when we cure this disease. That's the next step."



Bob Allison and his three sons in the Minnesota Twins dugout

Don't miss the chance to celebrate baseball and philanthropy at Target Field. Proceeds from this 10th annual event support the University's innovative research and patient care in ALS, ataxia, multiple sclerosis, muscular dystrophy, and Parkinson's disease.

Get your tickets at **minnesotadiamondawards.org.**

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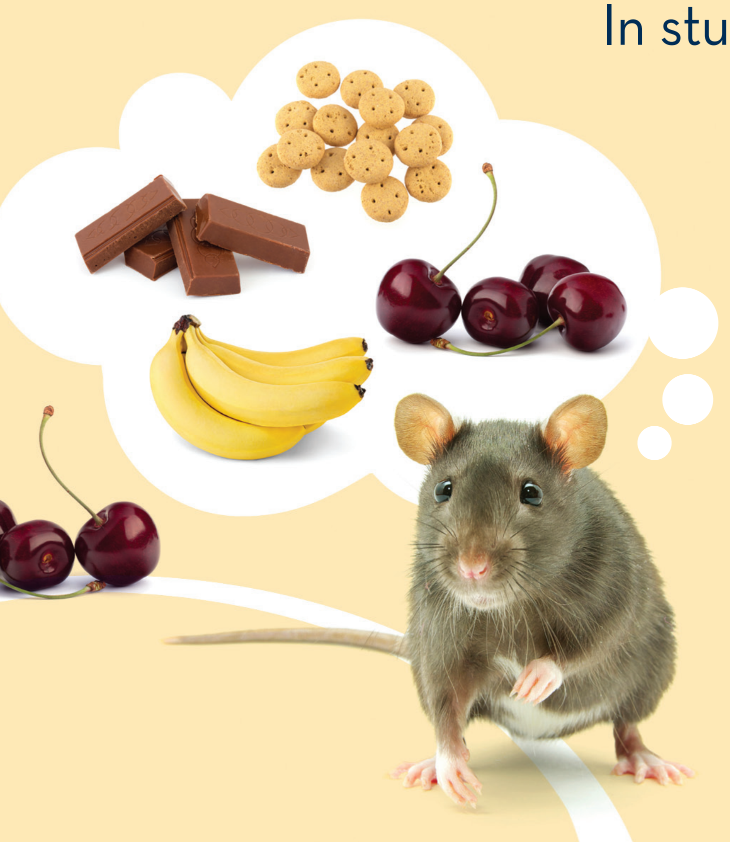
In studies, rats show evidence of regret



When graduate student Adam Steiner walked in and announced, “My rats are expressing regret,” Department of Neuroscience Professor A. David Redish, Ph.D., could hardly believe it.

Redish uses rats to probe fundamental mechanisms of decision-making and sees no reason other animals’ brains shouldn’t resemble humans’. But the idea of regret in rats still came as a surprise, and it required solid evidence—which he and Steiner have now supplied.

In June the researchers reported in the journal *Nature Neuroscience* that rats can recognize when they’ve made a bad choice and change their behavior in response. That, says Redish, is the essence of regret. And it means rats may act as stand-ins for humans as researchers probe how the brain makes decisions.

“When we understand how rats make decisions, it tells us something about how humans do it,” says Redish. “The more we understand about how decision-making processes work, the more we can understand about how they go wrong and how to fix them.”

Learn more about the experiment at ***z.umn.edu/ratregret.***

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