The MU College of Veterinary Medicine held its 15th annual White Coat Ceremony on Oct. 18, to celebrate the success of Class of 2017 members in completing their first two years of the veterinary curriculum and advancing to their clinical training.

The event marked the midpoint in the students’ professional curriculum. The first two years of preclinical training included courses in anatomy, physiology, cell and molecular biology, pathology, pharmacology, microbiology, virology and toxicology. They also learned fundamentals in clinical disciplines, including anesthesiology, clinical pathology, radiology, public health and medicine and surgery. The students each received a white laboratory coat before starting their next two years working in the Veterinary Health Center in the Small Animal, Food Animal and Equine hospitals, as well as completing preceptorships in private practices or with public agencies.

“Instead of studying late into the night for an equine anatomy test, you may instead be relearning gastrointestinal anatomy as you assist in the surgical resection of 10 feet of small intestine from a horse … at 2 in the morning,” said John Dodam, DVM, MS, PhD, chairman of the Department of Veterinary Medicine and Surgery, as he welcomed the students to the next phase of their education.

Alyssa Thomas gave the response on behalf of her classmates, quoting author A.A. Milne, “You are braver than you believe, stronger than you seem, and smarter than you think.”

“Alyssa Thomas reminded her classmates that they had successfully pushed through mental walls to reach this point in their education. from these past two years, and while life may not be multiple choice, never forget that you do have a phone-a-friend option.”
University of Missouri officials are celebrating the opening of the MU Metagenomics Center, located at Discovery Ridge Research Park. The new center will serve as a comprehensive resource for microbiological research performed at Mizzou, other universities and private entities around the country.

As more and more science is demonstrating the importance of the study of bacteria and other forms of microbiota to cancer research and overall gut health, the need for research on complex communities of bacteria is increasing. Currently, researchers must spend hundreds of dollars and several weeks to characterize the makeups of complex bacterial populations. Now, working with the DNA and informatics core facilities at Mizzou, scientists at the MU Metagenomics Center can perform this study up to 75 percent cheaper as well as faster than previous methods.

“This new metagenomics center will provide a valuable resource for important medical, veterinary and biological research,” said Aaron Ericsson, the director the new center. “Using the methods we have employed..."
WILLIAM GENGLER IS CVM ALUMNUS OF THE YEAR

University of Missouri College of Veterinary Medicine Dean Neil C. Olson announced that William Gengler, DVM ’72, was selected as the 2015 Alumnus of the Year. The announcement came during the CVM’s Alumni Reunion Weekend held Sept. 18-19. A 1966 graduate of the University of Wisconsin-Platteville, Gengler completed a master of science degree in ruminant nutrition at MU and then went on to earn his DVM.

He initially worked in a small animal practice in Newburgh, New York, with a rotating internship at the Animal Medical Center in New York City. He went on to become the co-owner of a small animal and equine practice in Blue Springs, Missouri. In 1978 he founded the Animal Hospital of Verona, which he owned for the next 20 years. After selling the hospital, he stayed on as the chief of staff through 2005.

In 1998 he became a diplomate of the American Veterinary Dental College after completing a specialty board examination in veterinary dentistry and oral surgery. He served as the section head of the Dentistry and Oral Surgery Service at the University of Wisconsin Veterinary Medical Teaching Hospital from 1990 until 2010, and from 2003 until 2010, he also served as the associate dean for Clinical Affairs and as director of the Veterinary Medical Teaching Hospital. He is now an emeritus associate professor in Wisconsin’s School of Veterinary Medicine.

Although he is retired, he continues to work part time at Dallas Veterinary Dentistry and Oral Surgery in Southlake, Texas, and Mission Veterinary Specialists in San Antonio, Texas. He is credited with more than 20 professional publications, and has held numerous leadership positions in veterinary organizations, including as president of the AVDC. He is the recipient of more than a dozen awards, including Veterinarian of the Year by both the Wisconsin Veterinary Medical Association and the Wisconsin Veterinary Technicians Association, the Veterinarian of the Year by the Wisconsin Veterinary Medical Association and the Wisconsin Veterinary Technicians Association, the ...

Continued on page 4
Alumni, continued

American Veterinary Dental Society Hill’s Research and Education Award, the Seeing Eye Dog Foundation’s Veterinary Award, the University of Wisconsin-Platteville’s Friend of Agriculture Award, and its Outstanding Alumnus Award, and the AVDC Peter Emily Service Award honoring outstanding contributions to the field of veterinary dentistry.

In nominating the honoree, Richard Meadows, DVM, Curators’ Professor at the CVM, said Gengler provided early guidance and support to the Veterinary Dental Educators organization, which teaches dentistry to veterinary students from around the world at no cost. He volunteers during the Student American Veterinary Medical Association annual conference, and at the yearly MU Zoetis Veterinary Dentistry Continuing Education Weekend — all at his own expense.

The announcement of this year’s Alumnus of the Year was made during the reunion banquet Sept. 18 at the Adams Conference Center. Other reunion activities included a brunch with retired faculty prior to the Mizzou Tigers football game, rides with the CVM Mule Team and tours of Clydesdale Hall.

Jewell Taylor, DVM ’61, catches up with classmate James Thorne, who is a professor emeritus at the CVM.

Natural Compound Could Cut Breast Cancer Risk in Some Women

More than 100 women die from breast cancer every day in the United States. The odds increase in postmenopausal women who have taken a combined estrogen and progestin hormone replacement therapy; these women also have an increased risk of developing progestin-accelerated breast tumors. Now, University of Missouri researchers have found that luteolin, a natural compound found in herbs such as thyme and parsley as well as vegetables such as celery and broccoli, could reduce the cancer risk for women who have taken hormone replacement therapy.

“In most circumstances, hormone replacement therapies improve the lives of menopausal women and achieve excellent results,” said Salman Hyder, the Zalk Endowed Professor in Tumor Angiogenesis and professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center. “Nevertheless, research has proven that a higher incidence of breast cancer tumors can occur in women receiving therapies that involve a combination of the natural component estrogen and the synthetic progestin.

“Most older women normally have benign lesions in breast tissue,” Hyder said. “These lesions typically don’t form tumors until they receive the ‘trigger’ — in this case, progestin — that attracts blood vessels to cells es-

Continued on page 5
sentially feeding the lesions causing them to expand.” His newest study shows that when the supplement luteolin is administered to human breast cancer cells in the lab, benefits can be observed including the reduction of those vessels “feeding” the cancer cells causing cancer cell death.

Hyder’s lab has found that as human breast cancer cells develop, they tend to take on stem cell-like properties, which can make them harder to kill. Here, luteolin was used to monitor stem cell-like characteristics of breast cancer cells, and his team saw a vast reduction in this phenomenon, further proving that the natural compound exerts its anti-tumor effects in a variety of ways.

Then, Hyder further tested laboratory mice with breast cancer and found that blood vessel formation and stem cell-like characteristics also were reduced in vivo, or inside the body.

“We feel that luteolin can be effective when injected directly into the bloodstream, so IV supplements may still be a possibility,” Hyder said. “But, until the supplement is tested for safety and commercialized, which we hope will happen after further testing and clinical trials, women should continue consuming a healthy diet with fresh fruits and vegetables.”

The early-stage results of this research are promising. If additional studies are successful within the next few years, MU officials will request authority from the federal government to begin human drug development (this is commonly referred to as the “investigative new drug” status). After this status has been granted, researchers may conduct human clinical trials with the hope of developing new treatments for breast cancer in women who have taken combined estrogen and progestin hormone replacement therapies.

Researchers involved with the study included Matthew T. Cook, a recent doctoral graduate and research scientist at Dalton Cardiovascular Research Center; Cynthia Besch-Williford, associate professor of veterinary pathology; Yayun Liang, a research associate professor of biomedical sciences in the College of Veterinary Medicine at MU; and Sandy Goyette and Benford Mafuvadze, who are graduate students in biomedical sciences.

Scientists Successfully Edit Genes of Dengue Fever Mosquitoes

Mosquitoes are a key contributor to the spread of potentially deadly diseases such as dengue and malaria, as they harbor parasites and viruses that are spread when mosquitoes bite humans and animals. Now, researchers at the University of Missouri have found an effective way to edit the genes of mosquitoes. Shengzhang Dong, post-doctoral fellow in the Department of Veterinary Pathobiology of the MU College of Veterinary Medicine, says this new technique opens the door for future research into genetically modifying mosquitoes so they cannot carry and transmit viruses and parasites that are harmful to humans.

“By successfully editing specific genes in the Aedes aegypti, the mosquito species which transmits the dengue virus, we have established techniques which can be used in future research to target the virus-carrying capabilities of this mosquito,” said Dong, who is the first author of the study.

For their study, Dong and his colleagues used the CRISPR/Cas9 gene editing system, and adapted it for use in mosquitoes to disrupt the blue fluorescent eye color gene in a previously generated genetically-modified mosquito line, which originally expressed both fluorescent blue and red color genes in their eyes. As a consequence, future generations of these mosquitoes no
A
s the dog days of summer come to an end, the University of Missouri welcomes three four-legged members to the campus community. Learn more about these furry new additions and how each through their professional training helps others and enriches Mizzou.

Brass, Explosives Detection K-9

Let’s face it. How we act at work can be quite different from how we act at home. When at work, we are eager to accomplish what we are hired to do, while our time at home is often spent reenergizing and relaxing. Things are no different for a new University of Missouri Police Department officer. His name is Brass. And he’s a K-9.

The 22-month-old German shepherd is friendly and approachable when not working, but as soon as his handler, MUPD Officer Joan Haaf, gives the command, Brass switches into work mode. Brass earned explosives detection dog certification through the North American Police Working Dog Association, and he is the only explosives K-9 in Boone County, according to MUPD Maj. Brian Weimer. He joined the force in mid-August after completing six weeks of training at Shallow Creek Kennels in Sharpsville, Pennsylvania.

Brass will work with Haaf to patrol campus and sporting events, perform building sweeps and respond to bomb threats. The canine is trained to identify the scents of common materials used to make explosives. He performs a sitting action to notify Haaf when the scents are detected.

The dog’s expertise isn’t cheap. His training and upkeep while on the force will cost more than $16,000, Weimer said. But that’s a pittance given the lives that might be saved through the canine’s work.

Rhett, Assistance Canine

During a recent counseling session at the MU Thompson Center for Autism and Neurodevelopmental Disorders in east Columbia, a child with autism was having difficulty reading and had become frustrated. The clinician asked for assistance from a new staff member, Rhett.

Dengue, continued

longer showed the blue color, but still showed the red color expression in their eyes. This new trait was stably inherited over several mosquito generations.

“While, for this study, we simply disrupted a fluorescent marker in the eyes of mosquitoes using CRISPR/Cas9, we were able to prove that this system can be used to perform more impactful gene edits in the future,” Dong said.

Alexander Franz, an assistant professor of veterinary pathobiology at MU and senior author of the study, says future research using this established technique could search for ways to genetically edit mosquitoes so they cannot harbor diseases like dengue.

“Infection of a mosquito with a human pathogen, such as dengue virus, alters the gene expression profile of the mosquito due to innate immune responses produced by the insect,” Franz said. These complex genetic interactions are not well understood. However, being able to knock out an individual mosquito gene that responds to the presence of a virus will allow researchers to understand the gene’s underlying molecular mechanism in order to find ways to genetically block virus infection in the mosquito.”

Franz says in the case of viruses such as dengue, blocking the ability for the virus to reproduce in the mosquito will interrupt the viral disease cycle.

This study was published in *PLOS ONE* and was funded by a National Institutes of Health NIAID grant R01 AI091972.
Service dogs, continued

Rhett works through animal-assisted therapy. With exceptional patience and temperament, the dog radiates unconditional love and a nonjudgmental spirit toward the children.

The 2-year-old Labrador retriever started working at the center in May. As a facility dog, Rhett was trained like a service dog, but instead of working for a single person, he works at a facility to assist many people. Rhett is frequently used to calm children during lab procedures, such as when drawing blood. He can also help relax children performing a frustrating task.

In Rhett’s presence, the child having trouble reading relaxed, picked up a book and started reading to the animal.

Rhett can also demonstrate tasks to children. For children with special needs who are starting school, for example, Rhett teaches them classroom etiquette, such as pushing in their chair, which Rhett accomplishes with his nose. Rhett makes learning more fun.

The black Lab was brought to Mizzou through a collaboration between the Thompson Center and the MU Research Center for Human-Animal Interaction (ReCHAI), which works to educate and conduct programs and research about the benefits of human-animal interaction. Gretchen Carlisle, a ReCHAI postdoctoral fellow, led the effort to bring Rhett to MU. The MU Student Occupational Therapy Association donated $600 to purchase initial supplies.

Due to the high volume of patients at the Thompson Center, Rhett has more than one handler so that he can serve both medical and therapy services.

Rhett lives with his primary handler, Anna Hogg, a Thompson Center behavior analyst. The two other handlers are Krista Hughes, a registered nurse and the clinical services manager, and Tammy Hickman, a licensed practical nurse. Support Dogs Inc., an assistance dog organization in St. Louis, trained the handlers and Rhett. Identical dog commands are used by the handlers.

Support Dogs Inc. will provide ongoing training support for the handlers. “The use of a facility dog for children with autism requires specials skills, so his integration into the Thompson Center will remain gradual,” Carlisle said.

Emma, Docent Dog

For children taking the Docent Dog Tour at MU’s Museum of Art and Archaeology at Mizzou North, the day is brightened by the smile of Emma, the official canine tour guide and ambassador for the museum. Emma shows her Mizzou pride through her black poodle fur and shiny gold bandana.

Docents at the art and archaeology museum are trained volunteers who share knowledge about the art collections and exhibitions with museum visitors. Emma’s owner and handler, Kathryn Lucas, has been a museum docent for five years. Emma received certification through the American Kennel Club Canine Good Citizen award, which assures proper obedience and temperament. Emma has also earned certifications through Therapy Dogs International, MU’s Pet Assisted Love and Support for Seniors program, and the College of Veterinary Medicine’s Pet Assisted Love and Support program.

Lucas uses Emma to model calming energy to the children. Before each tour, she introduces Emma to the children and teaches them how to approach the dog, encouraging them to move slowly and speak softly. Children are free to gently stroke Emma’s fur as they sit circled on the gallery floor discussing their favorite art pieces. The children are asked to demonstrate the same calm energy during the tour.
Resveratrol, a compound found commonly in grape skins and red wine, has been shown to have several potentially beneficial effects on health, including cardiovascular health, stroke prevention and cancer treatments. However, scientists do not yet fully understand how the chemical works and whether it can be used for treatment of diseases in humans and animals.

Now, researchers at the University of Missouri have found that resveratrol does affect the immune systems of dogs in different ways when introduced to dogs’ blood. Sandra Axiak-Bechtel, an assistant professor in oncology at the MU College of Veterinary Medicine, said this is a first step in determining how the chemical causes immune systems to react.

“This study makes it clear that resveratrol does cause the immune systems of dogs to change, but the changes it causes have created more questions,” Axiak-Bechtel said. “We found that resveratrol simultaneously causes dogs’ immune systems to increase and decrease in different ways. If we can better understand why resveratrol makes these changes and learn to control them, the chemical may have valuable uses in treatments of cancer and other diseases in dogs and humans.”

For their study, Axiak-Bechtel; Rowena Woode, a veterinary medical student at MU; and Amy DeClue, an associate professor in the MU College of Veterinary Medicine; added resveratrol to canine blood and measured innate immune system function. They found that resveratrol caused the stimulated white blood cells to release more pro-inflammatory and fewer anti-inflammatory cytokines, which are signals cells use to communicate with each other during infection and inflammation. These cytokines point to a stimulated immune system.

However, the researchers also observed a decrease in the ability of neutrophils, which are immune cells that help fight diseases, to kill bacteria. Axiak-Bechtel says this points to decreased immune system strength.

“Seeing a decrease in neutrophil function typically means an immune system is losing the ability to kill invaders like bacteria,” Axiak-Bechtel said. “Combining this loss of bacteria-fighting ability with an increase in inflammatory cytokines creates a very interesting mixed message in terms of what resveratrol is doing to the immune system. It is clear that resveratrol is having a distinct effect on how the immune system reacts, but we still don’t fully understand how this reaction can be best used to fight disease. Once we have a better understanding of this process, resveratrol could be a valuable supplementary treatment in fighting diseases like cancer.”
Previous studies have shown that diabetes adversely affects breathing and respiratory function. However, in the past, researchers have not differentiated diaphragm muscle cells and the muscle cells of limb skeletal muscle in their studies. Now, researchers from the University of Missouri have found that diaphragm muscle cells and other skeletal muscle cells behave differently — a finding that could influence future research on respiratory ailments associated with diabetes.

“One of the crucial problems facing individuals with Type 2 diabetes is that small blood vessels essentially disappear making it harder for muscle cells, even those cells that make up the diaphragm, to respond to insulin,” said M. Harold Laughlin, Curators Professor and recently retired chair of the Department of Biomedical Sciences in the College of Veterinary Medicine and an investigator at the Dalton Cardiovascular Research Center at MU. “Previous research on respiratory distress has focused on the similarities in limb skeletal muscle cells and diaphragm cells. What we found essentially contradicts previous findings and could guide future research in respiratory distress in diabetics.”

Diabetes has been proven to trigger breathing difficulties and even respiratory failure in patients who have the disease and fail to maintain healthy weights. Medical treatment and care guidelines for those with diabetes often call for a combination of aerobic and endurance training to maintain healthy weights and good respiratory function. Because diaphragm muscle cells are similarly arranged as other skeletal muscle cells, the two have often been studied together.

Using rats predisposed to obesity and insulin resistance, Laughlin and his team exposed the rats to two types of exercise programs over a period of several weeks. One was an endurance exercise training program in which rats performed on a treadmill for longer periods of time. The second program exposed the rats to an interval training program during which rats ran on the treadmill for shorter bursts. Then, the team evaluated which genes were turned on or off in diaphragm arteries in the diabetic rats during exercise training.

“We found that smooth muscle cells in the arteries of the diaphragm do undergo adaptive changes in response to exercise training,” Laughlin said. “However, common knowledge among researchers is that limb skeletal muscle and diaphragm muscle behave in the same manner and can thus be studied jointly. Our results indicate just the opposite — in obese patients suffering from diabetes skeletal muscle arteries and diaphragm arteries adapt to exercise in different ways. Therefore, future research studies should disassociate the two. In the future, scientists who study respiratory distress in insulin-dependent patients should seek out causes in the diaphragm independent of other skeletal muscles.”

The study, “Exercise training causes differential changes in gene expression in diaphragm arteries and 2A arterioles of obese rats,” recently was published in the Journal of Applied Physiology with funding from the National Institutes of Health (RO1HL036088).
Insects Can Spread EIA from Asymptomatic Horses

By Philip Johnson, BVSc, MS, MRCVS

A number of horses in the United States have recently tested positive for the virus that causes equine infectious anemia. Equine infectious anemia (EIA) is an infectious disease of horses, mules, donkeys and zebras caused by the equine infectious anemia virus (EIAV).

Also known as “Swamp Fever,” EIA was one of the first diseases to be recognized as caused by a virus in 1904. The EIAV is endemic throughout the Americas, parts of Europe, the Middle East, Far East, South Africa and Russia. This equine-specific virus is closely related to the HIV-1 virus that causes AIDS in people; both viruses are classified as retroviruses. However, unlike HIV-1 in people, the EIAV does not cause immunodeficiency in infected horses. The disease is transmitted to horses by biting insects that transfer the virus from infected horses to non-infected horses. Biting insects that are important for EIA transmission include horseflies, deerflies and stable flies. This virus can also be transmitted when hypodermic needles are used between different horses or when blood products that were produced in infected horses are administered to equine patients. It should be noted that most modern commercial plasma producers will use donor horses that have been rigorously tested and shown to be negative for EIA.

The clinical outcome of EIAV infection can be quite variable between different horses depending on the general susceptibility of the patient to infectious disease, the number of viruses that were introduced into the patient’s blood, and the pathogenicity (virulence) of the viral strain involved. In general, the clinical pattern of an EIAV infection has been categorized into three distinct stages. First, there is a transient acute phase immediately following infection during which there is fever, lethargy and lack of appetite for a few days.

The acute phase is followed by a chronic phase that lasts approximately 12 months during which the patient suffers from recurrent and intermittent bouts of malaise, fever, anemia, soft tissue swellings (edema), loss of condition, jaundice, reduced neurological functions and cachexia (wasting). Some horses die during the chronic phase. If the patient survives the chronic phase, it may seem to recover and return to a normal healthy-appearing state. This third recovery phase is known as the inapparent carrier stage during which the patient does not exhibit any clinical symptoms — this final stage may persist for the life of the horse.

As with many infectious diseases, some patients follow a clinical course that does not fall into these three stages of classification and may have constant fever with unprovoked bleeding problems and die. Other horses develop signs of organ disease as a result of EIA, including problems with the lungs, liver, spleen, kidneys and even the spinal cord.

Many infected horses do not exhibit any clinical signs of infection, therefore the true extent of this infectious disease is often underestimated. The diagnosis of EIA is based on the demonstration of circulating antibodies against the virus in the patient’s blood. There are two blood tests for this purpose, and the best known of these is the Coggins test. Following infection by the EIAV, it might take 45 to 60 days for the patient to develop antibodies, so veterinarians may perform more than one test when concerned with diagnosis of EIA. Unfortunately, there does not presently exist a curative treatment or an effective vaccine.

In North America, horses are routinely tested for EIA, and positive horses are subjected to either euthanasia or lifelong segregation. A majority of horses that test positive for EIA are not exhibiting any signs of disease. These asymptomatic horses still represent a source of the virus and risk of infection to other horses. Both the horse industry and the veterinary profession agree that the risk from asymptomatic carriers of EIA is sufficiently severe to warrant their segregation or euthanasia to protect healthy horses.
Past research has shown that the pleasure and reward centers of the brain are activated similarly by dangerous drugs as well as by exercise, which is why therapies that include lots of exercise have been developed for drug addicts. Now, researchers at the University of Missouri have found that activating these pleasure and reward receptors in the brain could provide the “reward” of dangerous drugs without having to consume those drugs.

For the study, a team of scientists led by Frank Booth, a professor at the MU College of Veterinary Medicine, selectively bred rats that exhibited traits of either extreme activity or extreme laziness. The researchers then gave chemicals to the rats to either activate or shut off their mu-opioid receptors, which are the genes in the brains of rats and humans that release dopamine, a pleasure-inducing chemical.

Greg Ruegsegger, a doctoral student in the MU College of Veterinary Medicine and lead author of the study, says that when the receptors of the extremely energetic rats were activated, those rats were much less inclined to exercise.

“These highly active rats would run on their wheels constantly,” Ruegsegger said. “However, when we chemically activated their mu-opioid receptors, those rats drastically reduced their amounts of activity. Since exercise and addiction to substances follow this same chemical process in the brain, it stands to reason that activating these receptors in people with dangerous addictions could provide the same rewards they are craving without the use of dangerous drugs or alcohol.”

When MU researchers studied the brains of the rats, they found 400 percent more of the reward receptors in the extremely active rats than the extremely lazy rats. They believe this indicates that the extremely active rats were active to receive “rewards” from their mu-opioid receptors, which may explain why they voluntarily run such extreme amounts.

The researchers also used chemicals to shut off the mu-opioid receptors in the active rats, but found that it similarly reduced activity in the rats, though not as drastically as turning on those receptors in the active rats. Researchers found that activating and shutting off the receptors in the lazy rats seemed to have no significant effect on those rats’ overall activity levels.

This study was published in the journal *Neuropharmacology.*