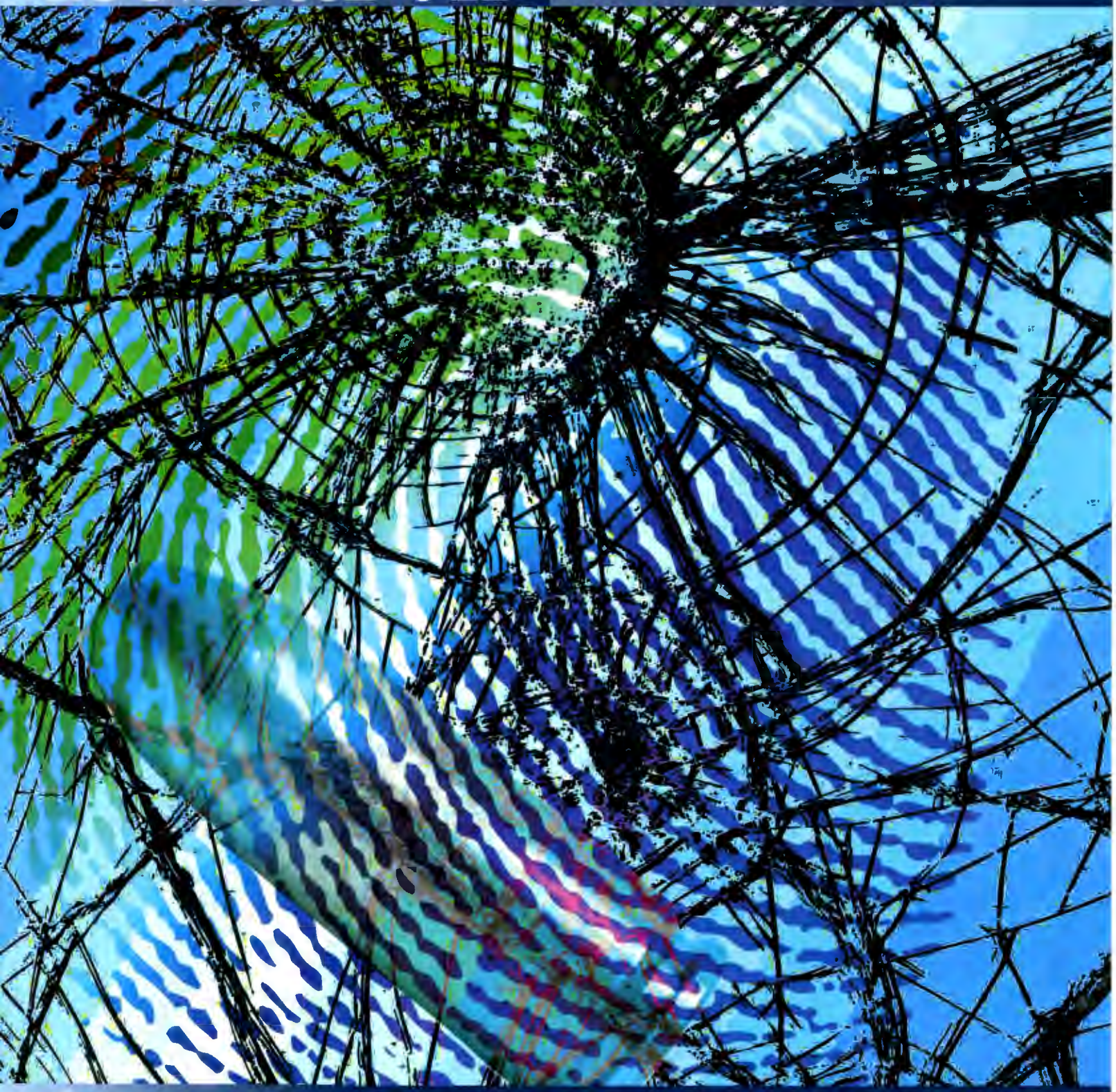
Research

SOUTH DAKOTA STATE UNIVERSITY



South Dakota State University
Fall 2016

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SOUTH DAKOTA STATE UNIVERSITY
SDSU FALL 2016

Cattle primary host for new INFLUENZA VIRUS

Feng Li

Cows get influenza. Six years ago, scientists would have found that assertion laughable, according to virologist Feng Li. "They would have asked us if we were crazy."

Now, researchers in America, Asia and Europe are believers.

"We discovered a new influenza virus and reported cattle as the primary reservoir," said Li, a professor in the biology and microbiology and veterinary and biomedical sciences departments. "This contribution was made in South Dakota, and our theory has been confirmed independently."

Li and immunologist Radhey Kaushik, professor and assistant head of the biology and microbiology department, secured a National Institutes of Health grant for nearly $400,000 to study the biology, genetics and evolution of the new virus. As Li and his collaborators proposed, the International Committee of Taxonomy of Viruses in August approved a new genus Orthomyxovirdae with a single species, influenza D virus, because of its distinctness from other influenza types—A, B and C.

"From a science viewpoint, it's very exciting to work with a brand-new virus," Li said. Ultimately, the goal is to determine whether the virus can cause problems in humans.

In recognition of his research on emerging viruses, Li received the F. O. Butler Award for Research at the 2016 Celebration of Faculty Excellence. Two years ago, he earned the global engagement award for his collaboration with scientists in China and India on avian influenza. During the last six years, Li has received more than $1 million in NIH grants.

Discovering new virus

SDSU alumnus Ben Hause isolated the virus from a diseased pig in 2011 while working at Newport Laboratories, an animal diagnostic lab in Worthington, Minnesota. "It was different from all known influenza viruses," said Hause, who identified and characterized influenza D as part of his doctoral research under Li's tutelage.

His research showed low levels of antibodies in pigs, but high levels of influenza D antibodies in cattle. "A high percentage of cattle with respiratory disease tested positive," he said, pointing out that "it's common for cattle to be infected with this influenza virus."

Li explained, "Out of 100 clinical samples from swine, you will get only one or even no isolations. However, from 100 nasal swabs from diseased cows, you can easily isolate at least 10 to 15 cases." Li and Hause, who is now a research assistant professor at Kansas State University, still collaborate extensively on this virus.

Finding more cases in animals

Their findings have been validated by other research groups. After the SDSU results were published, the University of California-San Francisco identified influenza D as a major player in respiratory disease complex in dairy cattle.

Mississippi State researchers found that 23.6 percent of weaned calves with respiratory disease tested positive for influenza D. The virus has been detected in beef and dairy cattle in seven states, according to a Dec. 2015 article in the journal Virology.

Scientists in France, China, Japan and Mexico have found the virus in cattle, Li reported. However, outside the United States, only scientists from Italy have found influenza D in both cattle and swine. Li suspects "the virus kind of spills over from cattle."

Comparing swine, cattle variants

From a basic science perspective, Li and his team want to figure out what makes the virus replicate so well in cattle. That will then help them unravel how the virus spills over to a new host, crossing the species barrier.

"The two viruses are nearly identical," he said. However, the swine virus has more sugar molecules to coat the virus surface protein that infects the cells. Research assistant professor Dan Wang leads those working on the basic molecular biology of the virus.

Specifically, Li noted, "the swine virus has one additional sugar close to the receptor-binding region. We think the sugar slows down the virus."

Though the virus does not affect poultry, the researchers have identified influenza D antibodies in sheep and goats from the Midwest through blood samples archived at Washington State University. "Small ruminants may get it from the cattle reservoir," he explained. They are also verifying the presence of antibodies in horses.

Gauging human susceptibility

Li's group showed that the virus is spread only through direct contact and proved a guinea pig can be used as an animal model to study the virus. Three doctoral students, two master's students and one undergraduate have worked on the project.

Doctoral student Chithra Sreenivasan is comparing virulence among bovine and swine influenza D strains and human influenza C. Influenza D has about 50 percent similarity to human influenza C.

"Human C affects mostly children," she said, noting that the most common symptom is a runny nose. "It's not a serious disease. We all have some antibodies because we were infected as children."

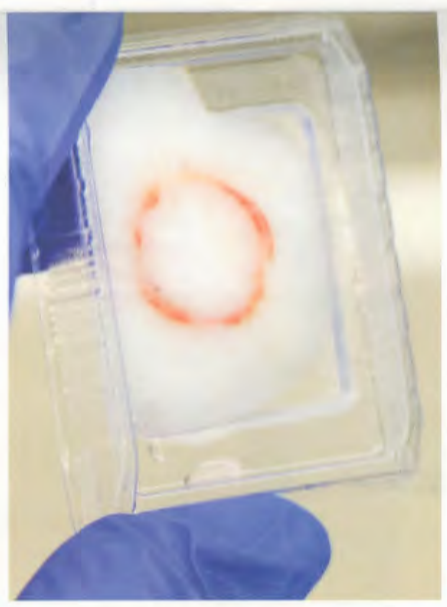
Kaushik, who oversees the development of lung cultures to study the virus, said, "The virus has not been shown to be pathogenic in humans." However, he noted, "if the virus can undergo reassortment in combination with a closely related human influenza virus, it may be able to form a new strain that could pose more of a threat to humans."

This year, Chinese researchers found similarities in the molecular mechanisms that influenza D and human influenza C use to infect cells. They identified a receptor-binding protein called hemagglutinin-esterase-fusion glycoprotein in influenza D that is structurally and functionally similar to its counterpart in influenza C. Furthermore, the Chinese scientists showed that influenza D and C viruses use the same cellular receptor to enter and infect cells.

"These findings suggest that influenza D virus may be a potential threat to human health," Li pointed out. This summer, a University of Florida study demonstrated that 97 percent of people working on Florida dairy or beef farms have antibodies to influenza D. "That provides serological evidence that the virus from cattle can be transmitted to humans especially those within close proximity to cattle," he said.

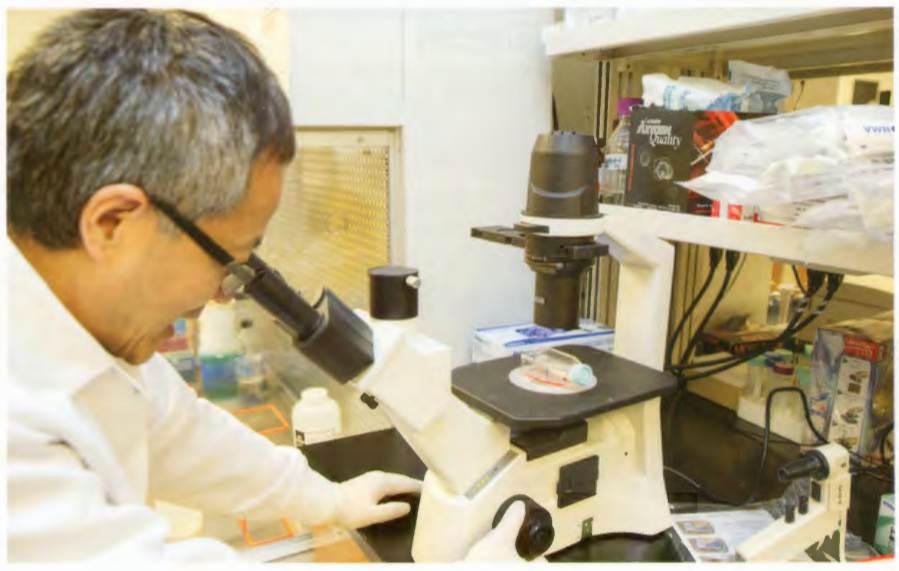
However, Li noted, such a high prevalence seems to be in conflict with a previous investigation showing approximately 1.3 percent of the general human population have antibodies to influenza D.

Those contrasting results show that there is more work to be done. "Environment may be a factor in transmission," Li explained. "We may need to reinitiate a study and focus on people working with cattle."



Above: Replicated virus-derived antigens isolated from tracheal and lung tissues showed that the guinea pig could be used as an animal model to study influenza D.

Below: Professor Feng Li checks the growth of human lung epithelial cells as part of research on influenza D.



Habit of excellence drives researchers

"Excellence is not an act but a habit."

-Artistotle

Making excellence a habit has been at the core of research at South Dakota State for more than 150 years. As our scientists and engineers seek ways to benefit human health, agriculture, industry and the ecosystem as well as enhance sustainability, we see the impact of our university's land-grant mission in action.

This fall, SDSU alumnus Raymond Bushland, an entomologist and U.S. Department of Agriculture research scientist, was recognized posthumously with the Golden Goose award for research that led to the eradication of a parasitic fly that was devastating the cattle industry in the United States. The sterile insect technique that Bushland and his colleague Edward F. Knipling used to defeat this pest may be applied to the Zika virus.

Bushland also received the 1992 World Food prize, an award founded by Norman Borlaug that recognizes research that has improved the quantity, quality or availability of food in the world. As the first South Dakota State graduate to receive these two prestigious awards, Bushland is an example of this university's culture of excellence.

This publication highlights faculty whose work has been recognized at the February 2016 Celebration of Faculty Excellence, including some recent notable firsts:

- For the first time, a group of seven faculty members were named outstanding artists for the College of Arts and Sciences for their work on "An Evening with Harvey Dunn's Feminine Images," part of the Harvey Dunn Collaborative project. The performance, which can be viewed on YouTube, combined original music, dance and poetry to bring to life the joys and sorrows of pioneer women, as depicted in 12 Harvey Dunn paintings.
- The executive committee of the International Committee of Taxonomy of Viruses approved "influenza D" as the name of a new influenza virus that SDSU researchers discovered five years ago. This is the first influenza virus identified in cattle, according to professor Feng Li, who received the F. O. Butler award for his influenza research.
- Two statisticians are applying probability theory to forensic evidence, such as fingerprints, shoeprints and glass fragments. Assistant professor Cedric Neumann, who received the Berg Young Scientist Award, and associate professor Chris Saunders are the first SDSU faculty to receive a grant from the National Institute of Justice to do this type of research.

The scientists, engineers and artists featured in this issue embody the longstanding tradition of excellence that fuels research at South Dakota State.

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Statisticians evaluate probability models for

CRIME SCENE EVIDENCE

Cedric Neumann

Probability versus certainty—that's the dilemma when it comes to connecting a suspect to a crime scene using forensic evidence, such as fingerprints, shoeprints and glass fragments.

Traditionally, examiners have given their conclusions an aura of absolute certainty when reporting evidence in court, thus negating the introduction of less-than certain evidence that may be important to the case, according to an article in Forensic Magazine.

Reaching a conclusion on the link between a piece of evidence, such as a fingerprint recovered from a crime scene, and a particular person in the forensic context involves a great deal of uncertainty, according to assistant professor Cedric Neumann of the Department of Mathematics and Statistics. He was head of the United Kingdom's Forensic Science Service Statistics and Interpretation Research Group for five years. While there, he and a team of scientists developed and tested a statistical model to quantify the probative value of fingerprint evidence.

Handling uncertainty is the purpose of probability theory, Neumann pointed out. He and associate professor Chris Saunders are developing and evaluating statistical models designed to determine probability values for evidence such as glass shards, fingerprints, bullets and handwriting through a three-year $780,300 grant from the National Institute of Justice. They are the first SDSU statisticians to receive such a grant.

For his research, Neumann received the Sherwood and Elizabeth Berg Young Scientist Award at the 2016 Celebration of Faculty Excellence. In addition, the Jerome J. Lohr College of Engineering recognized him with its Young Investigator Award.

Testing statistical models using glass fragments

"There is a strong movement to quantify the probability value of evidence to support the fairness and transparency of the criminal justice system," he said. In 2009, the National Academy of Science cited the need to measure the probability value of evidence using statistical methods.

The first statistical models used in casework dealt with glass evidence, which can be easily described by random variables. "Developing such a model was relatively straightforward," he pointed out, particularly with the computing power available beginning in the 1990s.

As the complexity of the models increased, scientists made assumptions or shortcuts to simplify them, Neumann explained. However, those models can assign radically different probability values to the same piece of evidence.

Doctoral students Danica Ommen and Jonah Amponsah are studying the convergence of these models to the true probability value by applying them to glass fragments for which they have known values from databases collected by FBI scientists. This allows the researchers to define properties and conditions in the statistical models that ensure convergence to the expected values, knowing precisely what those values should be.

"What we have are the refractive index for each fragment as well as the elemental compositions for chemical elements, such as sodium, magnesium, aluminum and silicon," Neumann explained. The statisticians work backward to start from the expected probative value and develop models that converge.

Once the models produce acceptable results for the glass fragments, the researchers can apply those same conditions and properties to other types of evidence, such as handwriting, fingerprint, shoeprint and firearm identification.

Developing other models for fingerprint analysis

Forensic scientists typically have only a partial print from a crime scene with which to identify a suspect using features in the trace evidence. However, Neumann pointed out, "Depending on how you press the finger, this pattern will distort because skin is elastic."

Amponsah is also trying to model how that particular pattern could look under different distortions, he explained. "Given what we know about how the finger of the suspect moves and the resulting deformation, the model can then determine the probability, be it high or low, that a trace pattern originates from the suspect's finger."

This statistical method could also assess the quality of the trace evidence, Neumann noted. Law enforcement agencies often have a backlog of fingerprints to process and this model could give agencies a scientific means of screening evidence to streamline workflow.

"There's no sense treating cases sequentially and being blocked on one case for weeks when there are 10 to 15 cases that could be easily solved and then come back to the hard one," he said.

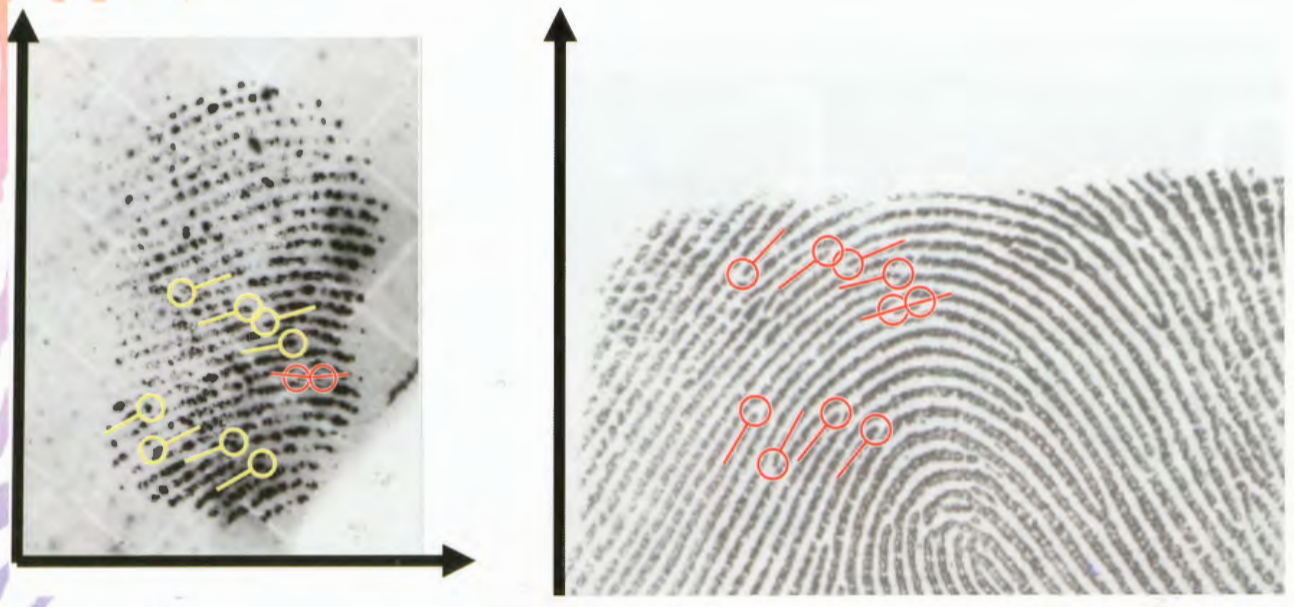
On another front, two other graduate students are trying to leverage current technology to determine the probative value of fingerprint evidence. Commercial fingerprint systems use a score to rank the database prints from the most to least similar to the trace evidence, Neumann explained. "The system we are developing could convert those scores into probabilities."

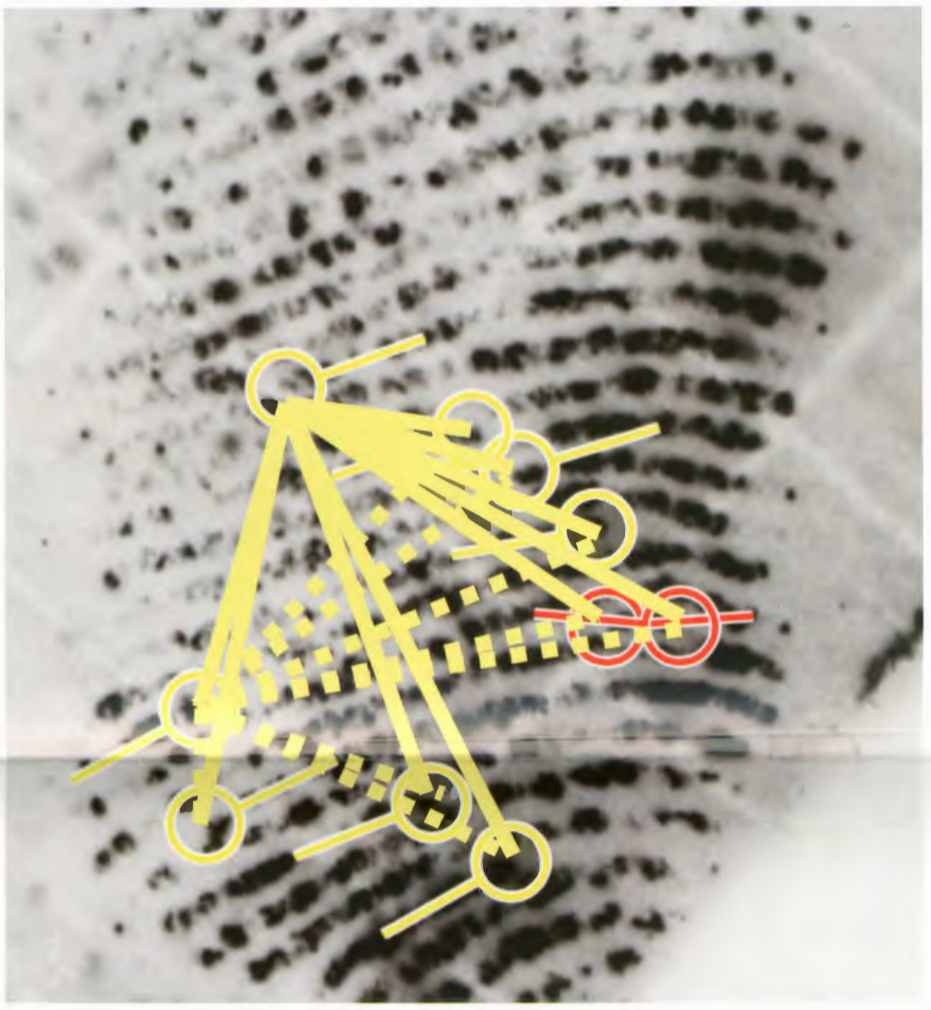
Doctoral student Douglas Armstrong is developing kernel-based methods to quantify the value of forensic evidence through a National Institute of Justice fellowship that provides nearly $35,000 annually for up to 3 years. His approach involves cross-comparisons with all reference material, such as fingerprints or bullets, in a database. He hopes to show that these cross-comparisons can result in a model with a small number of parameters that can be easily deployed in casework.

Master's student Jessie Hendricks is using approximate Bayesian computation to model the spatial relationship among selected features in a partial fingerprint. Her work is supported by a grant from the SDSU Scholarly Excellence Fund.

Ultimately, the researchers could apply these systems directly into the commercial algorithm used to produce the scores. "It would be a win-win for the industry," Neumann said.

All three fingerprint models could also be transferred to footwear evidence, which is underused in the United States, he added.





Examining trace on fibers

Particles of dust attached to fibers may contain clues to help investigators determine the origin of a drug shipment or individual explosive device, Neumann explained. "The fibers themselves can be extremely common, but we're washing those fibers and analyzing the chemical composition of the dust."

Proportions of specific chemicals and even the types of soil and pollen can help locate a suspect, he pointed out. "Cities and even neighborhoods within them have different dust profiles."

Armstrong and master's student Madeline Ausdemore are working on this project, which receives annual funding based on the results through the National Institute of Justice grant.

"When a bomb blows up, some parts are left. If you swab the inside, you can find particles of pollen, for instance, that may give you a target area where the bomb was made," Neumann said.

The intelligence community has attempted to utilize this type of information informally based on experience, he noted. However, use of dust on fibers or on the sole of shoeprint, for instance, for forensic purposes is very new.

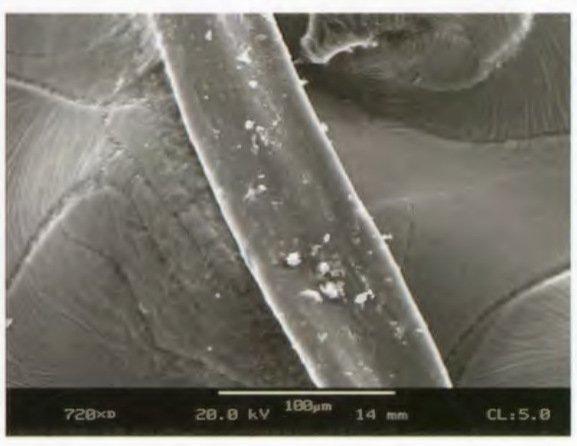
In particular, Ausdemore is focusing on the development of a proper probabilistic inference model and is attempting to separate particles when the dust contains a mixture from multiple locations.

Developing and verifying these statistical models will help build a solid foundation for determining the probability values for forensic evidence and provide an avenue through which law enforcement agencies and courts can systematically weigh that evidence.

Top: Evaluating the relationships among selected features may help determine the probability that the partial print, top left, recovered at a crime scene, could have been made by the suspect's finger, top right.

Right: Assistant professor Cedric Neumann and associate professor Chris Saunders discuss statistical models that will help determine the probability that a piece of evidence can be linked to a particular suspect. Their research is supported by a National Institute of Justice grant.

Bottom row: These transmission electron microscope images show particles of dust attached to fibers recovered from a crime scene that may help investigators determine where a crime occurred.



Beef reproduction research to increase sperm, embryo survival

George Perry.

A pregnant cow is a beautiful sight—to beef producers and to animal science professor George Perry. Normal conception rates among beef cattle run around 60 percent, but Perry's research seeks to increase that number. "We've got a lot of ways to improve that," he said.

To do so, he examines both the female and male sides of the equation.

With 65 percent of his time devoted to research and 35 percent as SDSU Extension beef reproduction management specialist, Perry sees himself as a bridge between basic research and field application. "What we learn on the research side ties to what is practical for the producers to use," he said.

John G. Moes, owner/manager of Moes Feedlot near Florence, agrees. He has seen increased and earlier pregnancy rates as well as better longevity of pregnant cows, thanks to collaborating with Perry. "He has been able to establish his results in a true working environment," said Moes. Animals in his herd have been part of Perry's research trials since 2006.

Robert Cushman, research physiologist at the U.S. Department of Agriculture Meat Animal Research Center in Nebraska, wrote, "George brings a unique blend of an understanding of basic science and an ability to translate that to field applications that allow him to educate cow-calf producers about cutting-edge biotechnologies while keeping the subject matter relevant to industry needs."

For his work, Perry received the F. O. Butler Award for Excellence in Research at the university's Celebration of Faculty Excellence this February. In the last six years, he has secured more than $1 million in external funding. Nine graduate students have completed their degrees under his tutelage.

Increasing sperm viability

"Artificial insemination is the greatest biotechnology a producer can use," Perry said. While one bull can breed 30 to 50 cows in a year, a single ejaculate can breed 300 to 400 cows. "If you have a sire with great genetics, artificial insemination is the way to get it out."

When semen is collected, it must be kept frozen using liquid nitrogen and then thawed, shortly before being used for breeding. In developing countries, that's simply not feasible, Perry pointed out.

Sperm from the testes can live in the bull's epididymis, where they mature and are stored, for two weeks, but once ejaculated and put into a female, they last only 24 hours, he explained. Researchers in other countries have been able to extend the viable lifespan of semen to three to four days post-collection.

Through a National Science Foundation Basic Research to Enable Agricultural Development grant, he is investigating how to get sperm to live longer outside the bull's body.

Perry, graduate student Emmalee Northrop and technician Stephanie Perkins have collected and cultured ejaculated and epididymal sperm from nine bulls. Though this type of research is in its early stages, the researchers found that even when cultured in the same media, epididymal sperm remain motile longer than ejaculated sperm.

"In every way, epididymal sperm have a longer life span and more activity than ejaculated sperm," Perry said. The next step will be to analyze the proteins that are bound to the sperm surfaces, which they suspect play a key role in longevity.

Improving embryo survival

For cows that are inseminated when they show what is called standing estrus, meaning they stand to be mounted, fertilization occurs 90 percent of the time. However, 27 days later, the earliest time at which a pregnancy can be detected, the conception rate hovers around 70 percent, according to a 2013 SDSU study.

Finding out how herd management practices affect embryo survival is another focus of Perry's research. After the animal is bred, maternal recognition of the pregnancy does not occur for 15 to 17 days, he explained. "All the dramatic changes—fertilization, hatching, elongation—happen without the cow even knowing she's pregnant." Essentially, Perry pointed out, "The embryo lives totally off the secretions within the uterus." Attachment begins at Day 19 and the placenta is in place by Day 25; however, definitive attachment of the embryo to the uterus does not take place until Day 42.

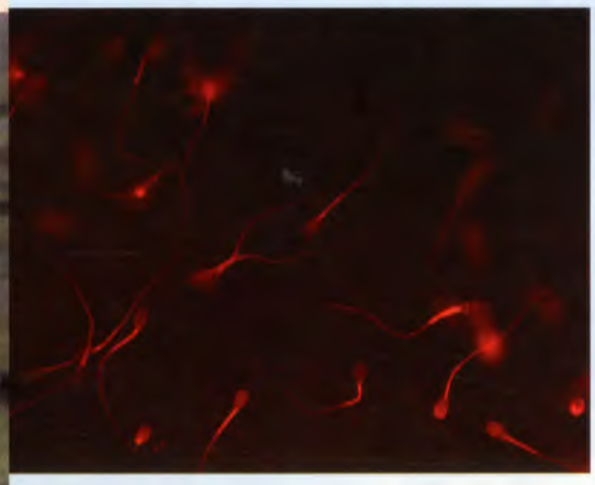
Consequently, he noted, changes in nutrition after insemination can affect embryo survival rates. One study compared pregnancy rates of 207 heifers that had been on pasture since weaning and 214 that had been in the feedlot.

All were artificially inseminated and then turned out on pasture. Those heifers who were accustomed to grazing had a 10.3 percent higher pregnancy rate when tested at 42 days post-insemination than those who grew up in a feedlot.

Assessing activity level, nutritional needs

In another study, Perry traced the activity levels of 69 heifers using pedometers. Half were kept in a 200-by 200-foot feedlot, while the rest were in a 30-acre pasture.

Professor George Perry and graduate students Jerica Rich and Emmalee Northrop use ultrasound to pregnancy check cows and determine the age of the fetus.



"In every way, epididymal sperm have a longer life span and more activity than ejaculated sperm."

—George Perry
animal science professor

"The ones in the feedlot were walking 2,000 to 3,000 steps a day, while those in the pasture logged more than 6,000 steps a day," he explained. However, when the heifers from the feedlot were moved to pasture, they walked over 16,000 steps their first day and over 10,000 per day for the next four days.

The university pasture is small in comparison to those producers use, Perry pointed out. "On a quarter section, they are liable to walk even more."

Those increased activity levels make a difference when it comes to nutrition. "We've seen animals lose 3 pounds a day for the first week when turned out on grass."

"That's a big negative energy change," he said, with embryo losses typically in the 8 to 10 percent range. "That's 8 to 10 calves per 100 cows."

Another research project showed that when the diets of feedlot heifers were supplemented with dried distillers grain at a rate of 5 pounds per head per day when let out on pasture, they gained weight and had a 76 percent pregnancy rate at 42 days post-insemination. Those that did not receive the supplement lost weight and had only a 61 percent pregnancy success rate.

"Diet plays a role in embryo survival," Perry said. Managing the herd to assure that the animals, particularly those raised in feedlots, can maintain their body weight during this crucial period is essential.

Through Perry's research, beef producers can make management decisions that will help increase the number of calves their herds produce.

Top: Detecting when cows initiate estrus and are ready for artificial insemination is difficult, particularly when they are on pasture, as with this herd at the Antelope Research Station.

Right: The brighter the red in this microscope image, the higher the activity level in this ejaculated bull semen specimen.

State veterinarian Russ Daly and professor George Perry prepare to collect ejaculated sperm as part of research to extend the viable life of semen.

A cow showing estrus stands to be mounted by another animal as a sign that she is ready to be bred.

Using pedometers allows the researchers to determine the activity levels of heifers let out to pasture after artificial insemination. Increased activity levels can cause heifers to lose weight and result in embryo losses in the 8 to 10 percent range.

Chemicals in ice core reveal climate-changing events


1

1 Former postdoctoral researcher David Ferris, professor Jihong Col-Dai and doctoral student Kari Peterson work on the West Antarctica Ice Sheet Divide Ice Core project during the 2012 Christmas break. Ferris, now at Dartmouth College, is part of the drilling crew.


2

2 Kari Peterson, who completed her doctoral degree this year, gathers specimens from a snow pit more than 8 feet deep to look for signs of volcanic eruptions in Indonesia and Africa.


3

3 A drilling crew member removes the outer casing of the drilling cylinder.

4 The barrel is then pulled up to a level position.


4

5 A plunger is then used to push the ice core out of the core barrel.

6 Once the ice core has been removed, Ferris and fellow drilling crew member Mike Jared reassemble the unit.

7 Using a special band saw, Cole-Dai slices a piece of ice core from Western Antarctica. The specimens are stored at -4 degrees Fahrenheit in the SDSU Ice Core and Environmental Chemistry Lab freezer.


5

8 The piece of West Antarctica ice core is positioned on a device that captures only the inner section as it melts and then sends the meltwater directly to the analysis machines in the adjoining lab. The device was developed by the SDSU ice core team


6

"We determined the age of each ice layer over thousands of years. We made it possible to look back 70,000 years without leaving a gap."

—Jihong Cole-Dai
chemistry and biochemistry professor

Jihong Cole-Dai

7

Analyzing the kinds and quantities of chemicals trapped in accumulating polar snow can help scientists identify events that have led to global climate change—that's what chemistry and biochemistry professor Jihong Cole-Dai has been doing for more than 20 years. Knowing what's happened in the past through ice cores can increase our understanding about how human activities can influence climate in the future, he explained.

Cole-Dai got into ice core research by chance. When he finished his doctorate in chemistry at the University of Maryland in 1987, the Byrd Polar Research Center at Ohio State University needed a chemist. "I had to learn everything about this type of research from scratch," he said, adding, "It kind of grew on me."

In 2000, Cole-Dai came to SDSU, having already secured a National Science Foundation grant to begin building a lab focused on ice core chemistry. During the last 15 years, he has received nearly $3.5 million in NSF funding and made four trips to Antarctica and one to the Arctic.

The SDSU Ice Core and Environmental Chemistry Lab, led by Cole-Dai, specializes in measuring trace chemicals in polar ice cores. Through NSF funding, the lab has worked on multiple ice core projects in Greenland and Antarctica. Most recently, the researchers were part of the 2006-2013 West Antarctica Ice Sheet Divide Ice Core project, which involved more than 20 universities and national laboratories.

"Research on ice cores is essentially global," Cole-Dai said. He has collaborated in scientific publications with scientists from France, the United Kingdom, China, Japan and Australia. In addition, he has hosted visiting scientists and graduate students from other countries.

For his work, Cole-Dai received the award for faculty engagement in global research at the university's Celebration of Faculty Excellence. During the last 15 years, two postdoctoral scientists, seven doctoral students and two master's students have worked on ice core research.

8

Uncovering climate-changing events

The main goal of the WAIS Divide project, Cole-Dai explained, "was to get an ice core more than 2 miles deep to give us nearly 70,000 years of history of the Earth's climate." Because the accumulating snow carries chemicals from the atmosphere, the ice contains a history of the changing atmospheric environment and dynamic climate.

For instance, collaborating with scientists from France and the University of California-San Diego, Cole-Dai and his team found evidence of a large volcanic eruption in 1809 that contributed to global cooling. From 1810 to 1819, temperatures worldwide were nearly 1 degree Fahrenheit cooler than normal.

Cole-Dai and his team analyzed the trace chemicals while the California scientists measured the isotopes of the elements in the chemicals. "We found large amounts of volcanic sulfuric acid in snow layers between 1809 and 1810 in both Antarctica and Greenland," Cole-Dai said.

With large eruptions, the plume reaches the stratosphere where the wind patterns carry the volcanic material across the globe, including both poles, he explained. The isotopic composition can determine if the chemicals spend time in the stratosphere. These bits of sulfuric acid scatter and reflect sunlight, which then reduces the amount of energy that reaches the Earth.

Analyzing brittle ice

Figuring out the age of ice layers is a critical part of any ice core research. By measuring trace chemicals, the researchers generate a dataset that essentially reveals the years in the core, he explained. "We created a map like a tree stump where you can see the rings and figure out how old the tree is at any stage of growth."

To analyze the chemical content of the ice, the researchers cut the core into samples the size of ice cubes, Cole-Dai explained. "That translates to thousands and thousands of samples."

For the West Antarctica project, the SDSU team analyzed more than one-half mile of ice core, including a segment of what is known as the brittle ice zone. "It's brittle to the touch and has more fractures," Cole-Dai explained. Tiny air bubbles remain in the snow, which is then compressed underground to form ice. This then makes that section of the ice extremely brittle. "It was the most challenging part in terms of analysis."

Their work on the fragile section was critical to accurately dating the entire ice core. "We determined the age of each ice layer over thousands of years," he noted. "We made it possible to look back 70,000 years without leaving a gap."

To do this, the team developed a specialized instrument that allowed them to analyze their section of ice in less than three years. If done manually, the work would take 10 years or more. "That's a big improvement," Cole-Dai said. "Our lab is the first one in the world to do chemical analysis through the brittle part of the ice core."

Detecting direction of climate change

The precise age of ice layers helped scientists in the WAIC project determine that climate change begins in the Artic and moves southward. A comparison of the Western Antarctica ice core results to those from an ice core from Greenland in the Arctic showed that when the Earth's climate was oscillating between warm and cold in the last ice age, warming began in the North Atlantic and spread southward over the next 200 years.

The SDSU team's expertise with brittle ice led to another collaborative project that began last year. "We're getting a 1500-meter section of ice core from the South Pole," he explained.

That will give Cole-Dai and his team more opportunities to uncover clues about climate change. "By studying these things in the past in a very detailed, systemic way, we can do a better job of forecasting the future," he concluded.

New pediatric drug delivery method uses corn, milk proteins

Developing medications for children can be challenging. "They are growing and their taste preferences are changing," said pharmaceutical sciences professor and department head Om Perumal, who is also co-founder and chief scientific officer of Tranzderm Solutions.

Safety is a major concern, he noted, but when it comes children taking their medicine, taste and texture are important. Perumal has adapted the corn protein-based drug delivery method he developed to oral pediatric formulations.

"Our core technology is the same, but we've refined it and are finding new ways to utilize it," Perumal said. His patented drug delivery system uses zein, a protein found in dried distillers grain, a co-product of ethanol production, to encapsulate the medication. The nanoparticles are approximately 500 times smaller than the diameter of a human hair.

For oral pediatric formulations, Perumal explained, "We've modified the nanoparticles by coating them with milk proteins. Our idea is to use products kids like.

Doctoral student MD Saiful Islam and professor Om Perumal use a spray dyer to encapsulate zein nanoparticles with milk powder as part of research to develop oral pediatric formulations.

For his success at commercializing SDSU technologies, Perumal received the Pat and Jo Cannon Intellectual Property Commercialization Award at the 2016 Celebration of Faculty Excellence. In 2014, Tranzderm received the TechConnect National Innovation Award, which recognizes the top 20 percent of technologies that can have a positive impact on a specific industry sector.

Perumal's research has resulted in four issued patents and six technology development license agreements as well as two new patent applications. "Dr. Perumal has led the College of Pharmacy and Allied Health Professions in invention disclosures, and his work with Tranzderm continues to open new avenues to commercialization, not only for his research but also the work of colleagues in other departments and colleges," said Will Aylor, assistant vice president of the Office of Technology Transfer and Commercialization.

Providing federal incentive

Before 1998, about 70 percent of the drugs used for children had not undergone clinical testing for the newborn to 17-year-old population, according to the National Institutes of Health Medline Plus.

"Drugs behave differently in children than adults," Perumal explained. However, the pharmaceutical industry did not have much incentive to do the testing because the pediatric medications make up only 10 percent of the pharmaceutical market.

To encourage the development of drugs customized for children, the federal government in 2002 passed the Best Pharmaceutical for Children's Act. It grants incentives to drug companies conducting Food and Drug Administration-requested pediatric studies.

Adapting to pediatric market

"We are developing formulas customized for children that are safe and can be flexible based on the age of the patient," Perumal explained. Their initial work targets infants and toddlers, who need either an oral suspension or a chewable form.

"Dissolving a drug that is not water soluble can result in a thick, uninviting suspension," he explained. However, diluting it with water can lead to errors in dosage.

In addition, using an excipient, such as high amounts of alcohol, to dissolve the drug is out of the question for young children.

The zein nanoparticles, which are not water soluble, protect the drug and the milk protein coating makes them more water soluble. "We have the best of both worlds," Perumal noted. In addition, the milk powder masks the drug's taste.

"We can put the nanoparticles into a liquid, a chewable tablet or a capsule," he said. "We could even use them as food sprinkles."

Identifying potential medications

The patent-pending drug delivery method can be optimized based on the matrix using different milk proteins, such as casein, lactoferrin and lactoglobulin. To mimic how the delivery system works, Perumal is testing the formulations using simulated gastric and intestinal fluid.

"We don't want it to release in the stomach," he explained. The medication should be absorbed, typically within 24 hours, in the intestinal tract. Milk has thus far worked best, but experiments are underway to test the formulation in yogurt and other food matrices.

His first target medications are antiretrovirals, which HIV-positive children must take for a lifetime. Using a rat model, Perumal and his team found that his formulation has two to four times higher absorption than what's currently on the market.

Another target medication is a drug under investigation to treat neuroblastoma, a cancer that affects infants and children up to 10 years old. Though neuroblastoma accounts for 6 percent of cancer in children, Perumal said no pediatric drug formulation is available for the investigational compound.

In addition, what works for children will be useful for patients who have swallowing difficulties, such as the elderly. However, Perumal cautioned, the delivery platform is in the early stages of development. Pharmaceuticals can take anywhere from 15 to 20 years to reach the market.

Strategic application key to biochar application

A carbon-rich substance called biochar, which is produced from agricultural waste, has been used for years to enrich soils for small producers in developing countries. However, the same biochar properties that help trap soil nutrients and water can negatively impact production when it comes to herbicide application.

"We must use biochar in a deliberate, well-planned manner," explained professor Sharon Clay of the Department of Agronomy, Horticulture and Plant Science. In a recent study, graduate student Kaitlynn Krack and others on Clay's research team documented a decrease in herbicide efficacy when biochar was added to the soil.

Clay began doing research on soil-herbicide interactions as a postdoctoral researcher nearly 30 years ago and has been involved in multiple U.S. Department of Agriculture research projects on the use of biochar as a soil amendment.

Clay calls herself "a Jill-of-all-trades," as she does research in precision agriculture, remote sensing, biological weed control, pesticides in the environment, pesticide residue studies on minor crops, and weed physiology and biology.

For her accomplishments, Clay was named distinguished professor, the highest level of scholarly distinction granted to a faculty member, at the university's 2016 Celebration of Faculty Excellence.

Examining biochar in two soil types

Biochar can be made from corn stalks and leaves, forestry byproducts or even manure. The thermochemical process, known as pyrolysis, involves burning the feedstock in a structure that limits the amount of oxygen, according to the International Biochar Initiative website.

In addition, pyrolysis is typically optimized at high temperatures, above 752 degrees Fahrenheit, and high pressures to convert plant materials into bio-oil or biogas. The remaining carbon-rich materials, known as biochars, are byproducts of this process.

In the USDA Agricultural and Food Research Initiative-funded project, Clay examined how the use of biochar made from corn, switchgrass and Ponderosa pine affected the soil retention and efficacy of two herbicides—atrazine and 2, 4-D. She collaborated with colleagues Thomas Schumacher, now professor emeritus, and Sharon Papiernik of the USDA Agricultural Research Service in Brookings.

Understanding how the highly reactive biochar affects the herbicide's ability to control weeds is crucial, particularly since the carbon material remains in the soil long-term, she explained. The biochar effects were examined on two types of soil—sandy loam and clay loam.

Experiments were conducted in the lab and greenhouse using air- and water-cooled biochar applied at a rate of 1 percent, which is often recommended, and a high rate of 10 percent.

Interaction with herbicide

Adding biochar increased the amount of herbicide adsorbed in both soil types, Clay reported. Essentially, biochar traps the herbicide, thus decreasing its weed-fighting ability. The biochar itself could soak up 100 times or more of either herbicide compared with the amount held by either type of soil. When biochar was added to soil, the herbicide retention was less than biochar alone but still much greater than the amount retained by either soil.

"Even 1 percent made a difference—that effect increased dramatically at 10 percent," she said. Biochar increased atrazine adsorption rates anywhere from 7 to 90 times when compared to soil alone.

"The adsorption was huge," Clay said, even at the lower biochar rate. This was true of 2, 4-D as well.

On the plus side, the researchers found that the addition of biochar counteracted the negative impact of herbicides on seed germination for Daikon radishes and winter wheat, even increasing germination speed. However, the presence of biochar decreased the herbicide's ability to kill broadleaf or grass weeds.

"Though the biochars had slightly different baseline properties, basically they all worked about the same in our experiments," Clay said. Based on these findings, producers must consider the consequences and use biochar strategically. She emphasized that site-specific application of biochar has the potential to help reduce herbicide and probably nutrient runoff into waterways.

"The application of biochar in grass filter strips may reduce mobile chemicals in the pass-through water," noted Clay. "This would be a win-win scenario for all."

Professor Sharon Clay adds Ponderosa pine biochar to soil. This type of biochar had the greatest variation in terms of processing method, with the air-cooled powder form adsorbing less atrazine than the water-cooled.

After adding herbicide-laced water to the biochar-amended soil, Clay shakes the tube to form a slurry.

Outstanding Scholars

Collaborative project brings pioneer women to life

The struggles and the strength of the pioneer women depicted in 12 Harvey Dunn paintings came to life on the stage and on public television, thanks to the creativity of seven artists from the College of Arts and Sciences.

"An Evening with Harvey Dunn's Feminine Images" combined music, dance, poetry and visual imagery to give audiences what assistant journalism and mass communication professor Rocky Dailey described as "an immersive experience."

Lynn Verschoor, director of the South Dakota Art Museum, said, "This event helped expand the meaning and impact of Dunn's work by providing numerous access points and fresh interpretations in multiple forms of expression." Verschoor was the performance coordinator and State University Theatre produced the show as part of its fall 2015 season.

For this production, Dailey; English lecturer Darla Biel; associate music professor Aaron Ragsdale; associate professor Cable Hardin of the School of Design; and professor Corey Shelsta, associate professor Billy Wilburn and assistant professor Melissa Hauschild-Mork of communication studies and theatre were named outstanding artists for the College of Arts and Sciences. This is the first time the honor has been given to a group of faculty members.

The South Dakota Humanities Council and SDSU Women and Giving provided financial support for the performances. This was the second production for the Harvey Dunn Collaboration Project. The video aired on South Dakota Public Television in January and can be viewed on YouTube.

Combining poetry, dance

For each painting, Biel wrote poetry describing the imagery and emotions that Dunn captures as the women perform tasks such as mending fences, herding cattle and caring for their children.

Biel tapped into the unrelenting toil, calling it "the hard day of working with no end in sight." She drove home the loneliness and isolation with "sing yourself to sleep in something between a lullaby and a sob."

In another segment, she celebrated the courage with which these women faced the challenges saying, "you are your own anchor."

"The thematic context of the feminine images in the paintings, the words of Darla Biel's poetry and the landscape of Aaron Ragsdale's musical compositions inspired the dance and movement," explained Hauschild-Mork, who choreographed and danced in the production. "Bringing the painting to life through movement offered another layer from which audiences could view Dunn's work."

Shelsta and Wilburn designed the costumes, while Hardin did the graphic art. Shelsta also did the theatrical lighting for the performance.

"Many voices come together to celebrate the work of Dunn," said Verschoor, referring to the more than 150 student dancers and musicians involved in the production. In addition, one number featured the 100-member SDSU Women's Choir.

Filming segments on prairie

"The hope is that we are creating a new appreciation for Dunn's art among those who are familiar with it, while also sparking an interest in those who may think art is not accessible to them," said Dailey. He worked on the images and animation projected during the performance and did a stand-alone video for Dunn's "After School" painting that was paired with Biel's poem "Fearlessness."

Multimedia associate Bruce Anderson and Lowell Haag of the Yeager Media Center shot video of the performers dancing on the prairie at EcoSun Prairie Farms and scenes in Flandreau for the stand-alone video.

"It was amazing to see how people from different departments came together, met for an hour or two a month and then walked away and knew what to do," Anderson said. "We all had confidence in each other and knew we were going to make everything happen."

Nurses to learn substance abuse intervention technique

Using a nationally recognized curriculum known as Screening, Brief Intervention and Referral to Treatment will help South Dakota health-care professionals identify patients who are at risk for substance abuse, according to assistant nursing professor Heidi Mennenga. The screening tool asks questions about drug and alcohol use and gauges the client's willingness to change those behaviors.

This year, undergraduate and advanced practice registered nursing students at all four SDSU College of Nursing locations—Brookings, Aberdeen, Sioux Falls and Rapid City—will learn the SBIRT technique through a three-year, nearly $550,000 grant from the U.S. Department of Health and Human Services. The grant is part of an effort by the Substance Abuse and Mental Health Services Administration to increase SBIRT usage.

As grant project manager, Mennenga will work with other nursing faculty to integrate the unit into the undergraduate nursing curriculum. Clinical assistant professor Robin Arends is responsible for incorporating SBIRT into the graduate nursing program.

In addition, the SBIRT research team will offer training sessions for practicing health-care professionals, according to Mennenga. Plans are underway for one session at an East River location and another West River, possibly next spring.

For her leadership in this and other research projects, Mennenga was named outstanding scholar for the College of Nursing at the 2016 Celebration of Faculty Excellence. This year, she became the first SDSU faculty member to participate in the National Rural Health Association's Rural Health Fellows Program.

Identifying at-risk individuals

"The curriculum has proven so helpful in decreasing substance abuse that insurance companies are willing to reimburse health-care professionals for providing this intervention," explained SBIRT project director Marylou Mylant, a nursing professor at the West River campus in Rapid City. "It's the first step to addressing substance abuse and connecting it to one's health before addiction develops."

Using the tool, health-care professionals ask patients about their use of illegal drugs, prescription drugs for nonmedical reasons, tobacco and alcohol, according to Mennenga. For instance, a video illustrating the SBIRT technique shows a nurse in an emergency room interviewing a patient with a head wound regarding how alcohol use may have contributed to the accident.

A University of Pittsburgh study showed that 5 percent of the population are what Mennenga called "true alcoholics," while 40 percent don't drink at all.

"The ultimate goal is to use this screening technique to evaluate the remaining 55 percent who consume alcohol in varying amounts," she noted. "We want to identify those people who are very high functioning but are partaking, for instance, of alcohol in too high amounts." That figure is more than four alcoholic drinks a day for a man or three for a woman.

As part of the training process, nursing students will perform SBIRT prescreens on a patient in lab simulations and may also have a chance to do so during clinicals, Mennenga explained.

Gauging motivation, making referral

Students will practice motivational interviewing to encourage high-risk patients to consider cutting back or quitting, according to Mennenga. They will ask questions such as "Have you ever been drinking and done something you've regretted?" to get those individuals to realize the impact that substance abuse is having on their lives.

For those patients who are ready to change, the undergraduate students will learn how to collaborate with health-care providers—nurse practitioners, physician assistants or doctors—to determine the appropriate referral path.

"This grant is very timely," said Mennenga, pointing to increasing concerns over opioid useage, which is part of the drug prescreen. During the second year, the SBIRT training will expand to graduate counseling students and, in the final year, to pharmacy students.

Heidi Mennenga

Using the Screening, Brief Intervention and Referral to Treatment curriculum, a nurse asks her patient about use of illegal drugs, prescription drugs for nonmedical reasons, tobacco and alcohol.

Outstanding Scholars

Dietitian targets weight management, goal-setting to improve health

Improving the health of South Dakotans—that's what assistant professor Lacey McCormack of the Department of Health and Nutritional Sciences hopes to accomplish through her research. Two unique projects focus on improving a weight management program and teaching young Native American mothers goal-setting skills that may lead to better health for themselves and their families.

In 2015, the South Dakota Academy of Nutrition and Dietetics recognized McCormack as the state's Young Dietitian of the Year. She is also a licensed nutritionist and certified exercise physiologist.

For her work, McCormack was named the outstanding researcher for the College of Education and Human Sciences at the 2016 Celebration of Faculty Excellence.

Managing weight

McCormack and associate professor Jessica Meendering are identifying factors that help and hinder clients enrolled in the Profile by Sanford weight management program. The two-year, nearly $83,000 research project is funded jointly through Sanford Health, South Dakota State University and the South Dakota Board of Regents.

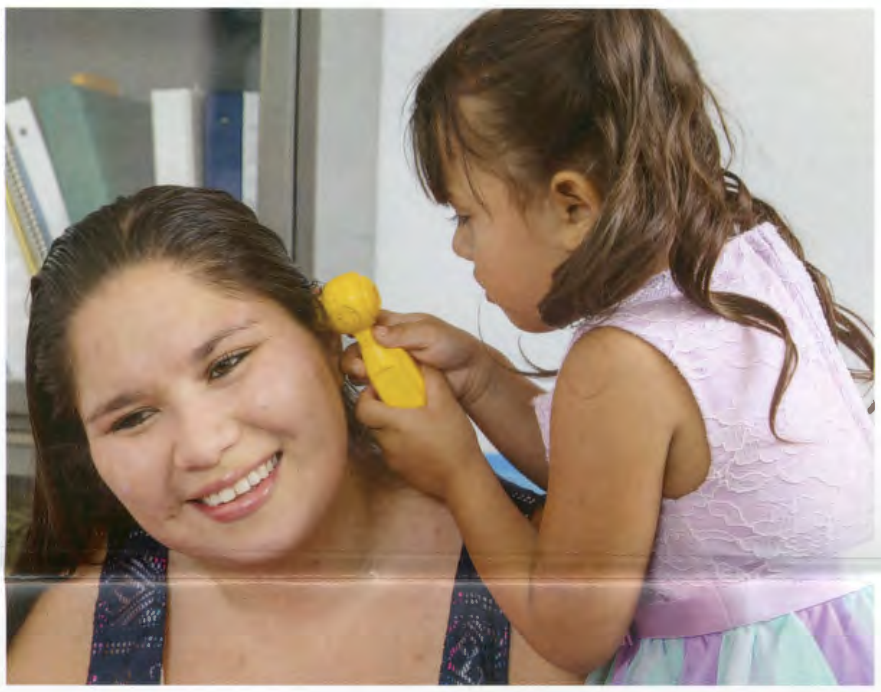
Preliminary results indicate that adapting a weight management program to the client's personality may help health coaches improve success rates. Further work should also be done to guide clients transitioning from the structured Profile meal plan to grocery store foods, according to McCormack. Results from the larger survey of 1,200 Profile clients are under analysis.

McCormack also collaborates with Meendering as part of a research team training graduate students from multiple disciplines through the transdisciplinary obesity prevention program. The graduate certification program emphasizes experiential learning to develop strategies to combat obesity in children and adolescents.

In addition, McCormack works with SDSU Extension Food and Families program director Suzanne Stluka on a Centers for Disease Control and Prevention project targeting obesity and two U.S. Department of Agriculture projects—Better Choices, Better Health program and Voices for Food.

Empowering Native American mothers

This summer, McCormack received funding for We RISE—raising income, supporting education—a project to help young Native American mothers on the Cheyenne River Indian Reservation set and achieve goals related to income, education or career. The one-year pilot project is supported by a $96,000 grant from the Collaborative Research Center for American Indian Health through the National Institute of Minority Health and Health Disparities of the National Institutes of Health.



Helping young Native American mothers, such as Christen Turning Heart, set and achieve goals related to education and income, may help improve the overall health of their families. That's what the We RISE—raising income, supporting education—project seeks to accomplish.

Lacey McCormack

McCormack and her co-investigator, Rae O'Leary, a nurse and public health advocate at Missouri Breaks Research Industries in Eagle Butte, will use a six-month intervention that focuses on defining and then working toward a goal and accessing at least one community resource.

"The idea came about because health disparities research typically controls for socioeconomic status in analyses," McCormack explained. "We decided to try to change those socioeconomic variables." The Missouri Breaks staff will help participants select a goal and identify a support person, someone they see regularly to encourage them as they work toward their goal.

Once the women have achieved one goal, O'Leary explained, "the hope is that they gain the skills and confidence to ask themselves, 'What other potential do I have that I have not yet uncovered?'"

If this model proves useful, it could be integrated into an existing tribal program or school curriculum. "It's a long journey from goal-setting to changes in health outcomes, but we're hoping this will have a ripple effect," McCormack said.

Photovoltaic group helps Pakistani scientists harness sun's energy

Experts from the Center for Advanced Photovoltaics are helping researchers in northwestern Pakistan gain the expertise needed to exploit their nation's solar energy-generating potential.

Associate electrical engineering professor Qiquan Qiao is collaborating with professor Muhammad Hassan Sayyad of Ghulam Ishaq Khan Institute (GIKI) of Engineering Sciences and Technology on fundamental techniques used to develop dye-sensitized solar cells. The joint project, which began in 2013, is made possible through a grant from the National Academy of Sciences.

"This is a good way to expand our research through collaboration on a global scale," said Qiao, who is coordinator of the electrical engineering graduate program. When he came to SDSU in 2007, Qiao established a lab devoted to studying organic electronic materials and devices. This year, he secured more than $1 million in federal research funding.

For his leadership in photovoltaic research, Qiao was honored as the outstanding researcher for the Jerome J. Lohr College of Engineering at the 2016 Celebration of Faculty Excellence.

This fall, Qiao became the second Harold C. Hohbach Endowed Professor in Electrical Engineering. Professor Emeritus David Galipeau was the first recipient of the five-year position, which was created in 2011.

Tapping into huge potential

Pakistan, which is located near the equator, could generate more than 90 percent of its electricity using solar power, according to estimates from research groups at Massachusetts Institute of Technology, Stanford University and the University of California.

The purpose of the project is to help Pakistan build solar energy infrastructure, Qiao explained. Before the project began, GIKI had just begun building its facilities and expertise in solar cells.

In 2013, Qiao went to Pakistan to participate in the first GIKI-SDSU International Symposium on the Design of Dye-Sensitized Solar Cells for Cost Effective Solar Energy Harvesting, which GIKI hosted. The following summer Sayyed trained at SDSU, learning how to fabricate, test and optimize dye-sensitized solar cells.

Two more conferences, one in 2015 on alternative energy solutions for Pakistan and the other this year on next-generation energy technologies, have further developed the collaborative effort.

"This collaborative project is an integral part of helping us acquire the equipment and the skills needed to do cutting-edge solar cell research and to move our nation forward in developing renewable energy technologies," Sayyad said.

Making solar cells

In May, GIKI doctoral student Nazia Nasr came to SDSU for six months through the collaborative research program. For her master's degree in nanotechnology, she worked on the synthesis of nanoparticles and wants to learn about devices related to energy.

"There are more facilities and knowledge here because the United States is a developed country," explained Nasr. During her residency, she learned to fabricate dye-sensitized solar cells. To do this, she worked with the solar cell simulator, impedance spectroscopy and pulsed laser and ultraviolet-visible absorption spectrometry.

"This collaboration will also help our program grow," Qiao said, pointing to the opportunity to bring graduate students from Pakistan along with research funding to SDSU. Two more graduate students will participate in the exchange program within the next year.

Nasr added, "I came here to gain knowledge and go back to my country and transfer that knowledge."

Nazia Nasr, a doctoral student at Ghulam Ishaq Khan Institute of Engineering Sciences and Technology, injects electrolyte into a dye-sensitized solar cell under the tutelage of associate professor Qiquan Qiao.

New capabilities will advance soybean nodule research

Associate professor Sen Subramanian is on a mission—to increase the nitrogen-fixing power of soybeans and thereby reduce the need for chemical fertilizer.

And now, he's got some new tools to do it, thanks to the Biosystems Networks and Translational Research, South Dakota's newest collaborative research center, and a five-year, nearly $660,000 National Science Foundation Faculty Early Career Development award he received in 2014.

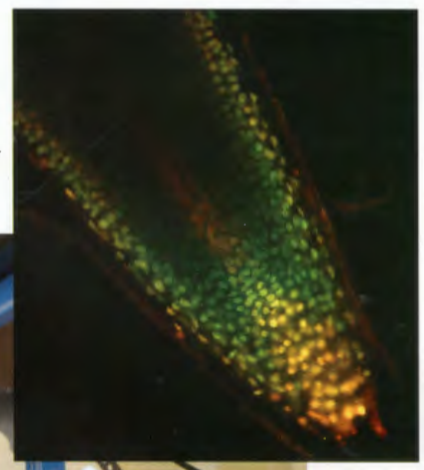
"Both are meant to be capacity-building," said Subramanian, who is the first SDSU plant scientist to receive the prestigious NSF career award. He is also part of a statewide team of researchers collaborating on BioSNTR, which seeks to build infrastructure and encourage collaboration among South Dakota scientists, biochemists and biomedical engineers to improve human health and agriculture.

Adapting microscope to soybeans

A multiphoton microscope, purchased through BioSNTR, will allow Subramanian and his team to do deep imaging of live tissues. "It can image depths up to 200 microns—a five to six times increase for us," he explained. This instrument utilizes four different color channels to examine what's happening within the cells of plant, animal and human tissues.

Through BioSNTR, the SDSU plant scientists worked with nanoscience experts from the South Dakota School of Mines and Technology to develop techniques to scan soybean roots and nodules to track activities of key biomolecules. Protocols for microscopy were developed using Arbidopsis, a small flowering plant, as the baseline, Subramanian explained. "It's easy to grow on a plate in clean conditions. We grow soybeans in soil so we have to modify a lot of the methods."

With the new instrument, Subramanian said, "we can image roots and nodules of a live soybean plant, for instance, every six hours as it grows and see what is happening within the cells."



Targeting genes, hormones

Soybean plants form mutually beneficial relationships with rhizobia bacteria in the soil to fix nitrogen. The plant provides the bacteria with carbohydrates and gets nitrogen in return. The bacteria enter the root cells of young plants and trigger the formation of nodules to house the bacteria.

Within the nodules, two distinct zones—one that fixes the nitrogen and another that transports it to the plant—are formed from the pre-existing root cells. The expression of specific genes in a particular root cell determine its function, Subramanian explained. Consequently, he is identifying which microRNAs direct gene expression to achieve this differentiation.

"We need to know what signal makes a cell contribute to one zone or another," he explained. During the last five years, Subramanian and his team of three postdoctoral associates, three doctoral students and two master's students have identified nearly 150 microRNAs that may potentially affect nodule development but are focusing primarily on microRNA 160.

Through a new three-year, $441,000 U.S. Department of Agriculture grant, Subramanian and his team will evaluate how auxin response factor 10, a protein regulated by microRNA160, determines the balance between two key hormones, auxin and cytokinin. This balance is crucial for determining nodule cell function and growth.

Tagging 3-D image, isolating cell types

Using output from the new instrument, the researchers can reconstruct a 3-D image in which cells with auxin activity are tagged in green and cytokinin in red. Cells containing both hormones appear yellow.

Through BioSNTR, Subramanian's team worked with professor Steve J. Smith, director of the SDSMT nanoscience and nanoengineering program. Smith and nanoscience graduate student Jon Fisher developed and applied image analysis techniques to identify each cell's position and nucleus and to determine the auxin-cytokinin outputs within each cell.

At the same time, a method to isolate individual cell types from plant tissue was developed through collaborations with Emory University assistant professor Roger Deal, University of California-Davis associate professor Siobhan Brady and UC-Riverside professor Julia Bailey-Serres.

Armed with these new tools, Subramanian and his team hope to gain the knowledge to produce the optimal soybean nodule growth and reduce reliance on expensive nitrogen fertilizers.

Using multiphoton microscopy, associate professor Sen Subramanian will examine the molecular-signaling networks that control soybean root growth. The instruments allows the researchers to obtain 3-D images of living plant and animal tissues. In the image of a soybean root tip, shown inset, plant cells with activities of two major plant growth hormones, auxin and cytokinin, are tagged in green and red, respectively. Cells containing both hormones appear yellow.

Understanding L1 elements in mouse model can impact human health

A team of graduate and undergraduate researchers led by associate pharmaceutical sciences professor Wenfeng An has successfully cloned more than 30 long interspersed elements type 1 from a mouse model. These L1 elements are DNA segments that can copy and paste themselves to a new position on the same or another chromosome.

"When these L1 elements land inside a gene, they may inadvertently shut down its normal function," explained An, who has been working on L1 elements for 13 years. Using the mouse model, An and his research team are investigating how L1 elements can cause mutations within human body and reproductive cells that may lead to diseases, such as birth defects and cancer.

Although about half of human DNA is made up of a variety of repeated segments, L1 elements constitute the largest portion—17 percent of the human genome. The long-term goal is to moderate the adverse effects created by abnormal L1 activities.

Since he moved his lab to SDSU in late 2014, he has secured nearly $800,000 in National Institutes of Health funding to study L1 elements in a transgenic mouse model. His lab is also part of the Center for Systems Biology of Retrotransposition funded by the National Institute of General Medical Sciences.

One postdoctoral researcher, four doctoral students, one research assistant and three undergraduate researchers work at the lab. By 2018, total federal funding is expected to reach approximately $1.4 million. Cloning mouse L1 elements is one facet of the overall research effort.

For his accomplishments, An was named outstanding researcher for the College of Pharmacy and Allied Health Professions at the university's Celebration of Faculty Excellence. He is the college's first endowed scholar, a cancer research position created through a trust established by SDSU alumni Barry and Sharon Markl.

Working with undergraduates to clone L1s

"Though human and mouse L1s are similar, the mouse genome has potentially more active L1 elements than the human genome," An explained, "There also appear to be more active families or subfamilies in mouse L1 elements."

Previous studies aimed at categorizing the activities of mouse L1 elements were done in what An called "the pregenomic era," working with an incomplete genome. As a result, he noted, "Our understanding of L1s in this important animal model is limited. Our goal is to take a more systematic and comprehensive approach to survey the activity of mouse L1 elements."

The task of cloning full-length mouse L1 elements began as an undergraduate independent studies project last fall. "We started with a list of the active or potentially active L1 elements in the mouse genome," explained An, who refers to the group as "L1 Hunters." Thus far, six undergraduates and one doctoral student have been involved in the project.

Undergraduate biology major Mason Jones explained that the group first

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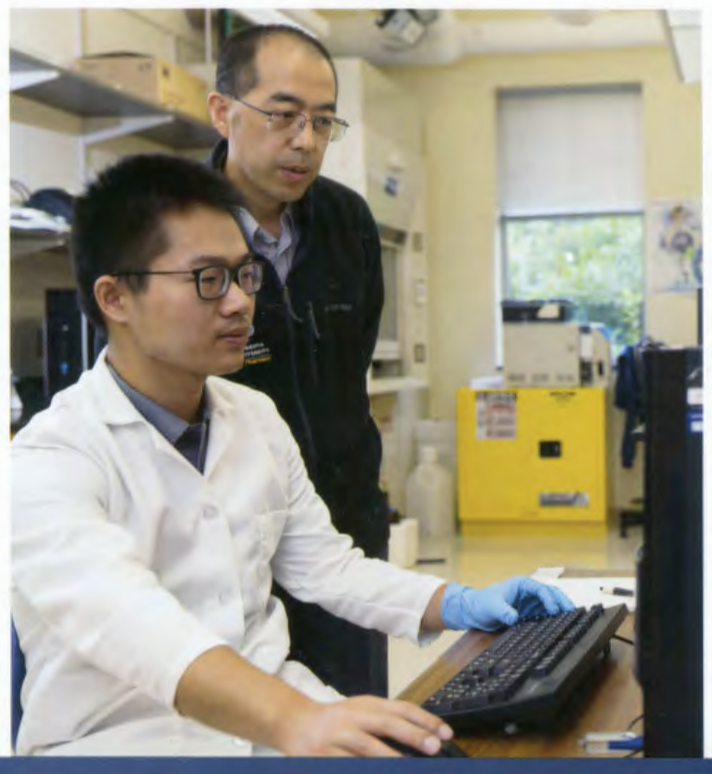

Associate professor Wenfeng An and doctoral student Lingqi "Birch" Kong analyze patterns of DNA fragments from L1 clones.

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Understanding L1 elements in mouse model can impact human health

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experimented with a procedure to amplify full-length L1 elements using polymerase chain reaction, or PCR, en route to establishing a robust protocol for cloning 7,000 base pair DNA sequences. Jones presented his work at the spring Undergraduate Research, Scholarship and Creativity Day and won first place in the health category. This summer, his research was supported by a Joseph F. Nelson Mentorship Scholarship.

The group uses a plug-and-play modular strategy, partially based on An's published work, to clone full-length L1s into an assay vector, An explained. "It took a fair amount of trial and error for the team to map out the entire protocol."

Jones explained: "We used TA cloning for the first six L1s—and then the approach stopped working. It was a frustrating time, but a good learning experience."

The group eventually switched to a more efficient restriction ligation-based approach, An explained. In addition, they developed a written, standard protocol.

Research assistant Nicole Vanden Berg, who spearheaded that effort, said, "We were able to incorporate new things we hadn't tried that changed the protocol and made it easier for individual lab members to follow." The December 2015 SDSU animal science graduate, who began working in the lab her senior year, also maintains the lab's mouse colonies.

Doctoral student Lingqi Kong, who began work in January 2016, developed the base assay vector into which the individual L1 loci were placed.

"Now we have a library of L1 vectors to work with," An explained. The next step will be using reporter assays the lab has developed to test the activity of the L1s in cell cultures using human cell lines.

Research assistant Nicole Vanden Berg and undergraduate biology major Mason Jones transfer bacterial culture from test tubes to microcentrifuge tubes. They will place it into the centrifuge and then collect the bacterial cells. They are cloning the L1 sequence from mouse genome.

Victoria Bishop selects a colony and drops it into the tube that Chase Habben holds. The colony will be grown overnight and screened for the presence of mouse L1 sequence. Both undergraduate researchers are biology majors.

Read more about the L1 research at:
http://www.sdstate.edu/pharmacy-and-allied-health-professions/laboratory-wenfeng

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