About the College

Departments

Teaching & Research

Giving to Vet Med

Veterinary Health Center

Veterinary Medical Diagnostic Laboratory (VMDL)

CVM Employment

Zalk Veterinary Medical Library

CVM Course Materials

MyZou

Home

NEWS & EVENTS

Of Mice, Mizzou and the Nobel Laureate

Mutant mice aren't just a plot device for science fiction or apocalyptic disaster tales. The value of genetically engineered mice to scientific research is immeasurable. Since 1901, nearly every Nobel Prize in medicine has been awarded for work that is heavily dependent on data from research animals – most of them mice. According to the Foundation for Biomedical Research, 95 percent of all laboratory animals are mice.

MU's Mutant Mouse Resource and Research Center stores nearly 4,000 strains of genetically modified research mice. Assistant Professor James Amos-Landgraf (left) and Project Manager Joe Waterman helped the MMRRC add a collection of strains developed by Nobel Prize winner Bruce Buetler, MD.

The importance of selectively bred research mice and the dramatic growth of genetically modified mouse strains led the National Institutes of Health (NIH) to establish the Mutant Mouse Resource and Research Center (MMRRC) in 1999 to serve the scientific community. The MMRRC is a consortium of four centers, one of which is located at the University of Missouri.

"Understanding the biology of mutant rodents is really our expertise," says James Amos-Landgraf, PhD, assistant professor of veterinary pathobiology. "With the presences of the MMRRC along with its partner center, the Rat Resource and Research Center (RRRC), we have a very strong rodent biology background. Moreover with the MU Metagenomics Center here as well, we are really at the forefront of understanding the effects of genetics and the microbiota — complex microbial communities that live in and on many parts of the body — on health and disease," Amos-Landgraf stated.

*****

The MMRRC became necessary after developments during the past 20 years allowed researchers to create custom-made mice by making specific, intentional changes to the DNA sequence of a gene in mouse embryonic stem cells in order to research specific conditions. The

Eek, A Genetically Modified Mouse!

Consider the humble mouse. The trigger of many a phobia, mice have startled the daylights out of most of the world's population, damaged uncountable homes, and turned tons of personal possessions into

mouse genome contains more than 23,000 protein-encoding genes, and researchers have produced thousands of genetically modified mice that differ in terms of which gene has been manipulated. Typically, each type has a different gene that has been knocked out, or deactivated.

The Center for the Genetics of Host Defense is a prolific producer of mice with many different mutations and phenotypes. Located at the University of Texas Southwestern Medical Center in Dallas, the center is commonly known as the Beutler lab, after its director Bruce Beutler, MD, a prominent immunologist and geneticist. Beutler shared the 2011 Nobel Prize in Physiology or Medicine for discoveries he made using mutant mice.

shreds. Mice like to party through the wee hours of the morning, squeaking and screaking like tiny gothic hinges, while we grumble and check the alarm clock every 20 minutes.

Particularly discouraging, mice eat 15 to- 20 times a day, yet remain tiny little things.

And, of course, mice can carry more than 100 human pathogens. Mice, it would seem, are naughty by nature.

Still, the mouse is easy to admire. It can jump like Michael Jordan, climb like Tensing Norgay, and swim like Katie Ledecky. And, for more than a century, mice have been helping to save the human race.

[read more]

The staff at the Beutler lab has produced more than 3,550 mutant strains, and counting. The Beutler lab and its collection, however, are not affiliated with the MMRRC.

“We had a few of Beutler’s lines coming in to the MMRRC and we realized that he was doing something much bigger – much bigger than any mouse center had pursued,” Amos-Landgraf said.

“Our director, Craig Franklin, had approached him several years ago about trying to get this entire collection,” Amos-Landgraf said. “We had received a few of his lines, and we have some of the same interests in immunology, understanding cancer, and so forth. At the time, Dr. Beutler was interested in trying to maintain and distribute animals himself. But, he soon realized it was too big of a job to generate animals and do the distribution. That wasn’t the focus of their mission; they just wanted researchers around the world to have access to live animals to study.”

As a cost saving measure, all of the Beutler mice are cryopreserved as sperm samples and brought back to life through artificial reproduction techniques like in vitro fertilization.

“MU ended up nurturing a relationship with the Beutler lab and was assigned most of these strains,” said Franklin, DVM, PhD, DACLAM, professor of veterinary pathobiology. “Subsequently, Joe Waterman, our project manager, and Jim Amos-Landgraf, one of our co-investigators, worked tirelessly to find a way to obtain the whole collection and get it here in good order.”

“I had met up with Bruce at a mouse meeting and had said that we were really interested in trying to get this all together and keep it as one collection, so the resource wasn’t lost,” Amos-Landgraf said. “That’s where Joe came in and facilitated all of that.”

*****

MMRRC & RRRC Project Manager Joe Waterman served as MU’s boots on the ground for the operation.

“Once we got the go-ahead to bring the collection here, I worked with Dr. Beutler’s group to put together a list of strains,” Waterman recalled. “And then, we started working with our informatics group to transfer all the data; we’re talking about genetic data for more than 3,000 lines.”

Compatibility issues were almost immediate and impossible to ignore.

“We had to find a way to get the data from their system into our system,” Waterman said. “That took a while, even with IT guys from both groups working on it. There were even some communications trending toward our need to manually enter all the information. That would have been problematic. Finally, the IT guys figured out a way to make it work.”

“After we got all the data figured out, it just became a matter of getting them transported,” according to Waterman. “We’re talking approximately 3,000 strains, and each strain has a half-dozen or so straws of sperm, so we were dealing with nearly 20 thousand straws.”

“Getting them here was a challenge,” Amos-Landgraf interjected. “All of the strains are stored in

liquid nitrogen, so it wasn't a simple task."

Liquid nitrogen temperatures range from minus 346 to minus 321 degrees Fahrenheit; its boiling temperature is minus 320 degrees. The substance presents a freezing hazard to humans. The material can also act as an asphyxiant. Small amounts of liquid can evaporate into very large volumes of gas, which can simply displace the oxygen in air to levels below that required to support life. Heat leak, and the resulting vaporization, is always present.

And Waterman was heading to hot, sunny Texas the week before the Fourth of July.

"I went down to Dallas to help get the materials organized and to arrange all of these samples," Waterman said. "I spent a week in Texas working on this. It was a lot of work because we had so many samples to organize. Their cryopreservation structure — or, freezer organization — is different than ours. We had to adapt ours to theirs. We were very meticulous in getting it all organized.

"Then, we had to get those lines up here," Waterman continued. "That was kind of a big deal. We hired a transportation company to send a truck capable of transporting up to 20,000 sperm straws in liquid nitrogen for us, and we shipped 2,931 strain samples from Dallas to our lab."

*****

A comprehensive collection of the Beutler lines now resides inside MU's Discovery Ridge facility. The MMRRC considers the lines to be one of its major collections.

Beutler still resides in Dallas, continuing his research in immunology and genetics in his lab at the University of Texas Southwestern Medical Center.

"He is a really nice guy; very easy going." Waterman said. "I met with him about some of the nuts-and-bolts of the move, and he was very accommodating."

"He's a true visionary," Amos-Landgraf observed. "I think it required a lot of bold foresight and enterprise to make the big investment he made. The Beutler lines are unique: 3,000 lines, they all carry multiple mutations, and they've all been sequenced to identify the mutations in the genome."

"The reason why that's really so important, or why that's fundamentally different than all other mouse collections, is that when you think about humans, we all have lots of different variants in our genomes — that's why we're all different. No two people, except for twins, are genetically identical.

"So, the genetics and the genetic variation between people are really important to understand," Amos-Landgraf said. "Understanding how variants — not necessarily mutations, just variations of a certain gene — can influence whether or not you get a disease. They may influence the disease process only very slightly, or only under certain conditions, but that can make all the difference. These lines are on the forefront of the effort to understand precision medicine. In other words, how multiple mutations interact or how very subtle variations in a gene can affect the phenotype of disease. That's one way we are trying to understand personalized medicine. Here at Mizzou we can look at these mice to gain a better understanding of why certain people get diseases like cancer. This makes Mizzou truly a unique research institution."

Return to News and Events home

College of Veterinary Medicine
W-203 Veterinary Medicine Building
Columbia, MO 65211
Phone: (573) 882-3554
E-mail: cvmwebmaster@missouri.edu