Only 1 percent of human genes lack counterparts in mice, which is what makes the mouse such a great model to study human diseases.

While 99 percent of genes in humans have counterparts in the mouse, 80 percent have identical, one-to-one equivalents.

The similarities are what provide researchers fertile ground in which to create medical breakthroughs. Tens of thousands of human and veterinary medicines in the market today are the results of research using laboratory animals, particularly the mouse.

Since 1 percent of human genes have no mouse counterparts, some human diseases cannot be tested in them, unless the mouse is specially designed to carry human blood and cells.

“Mice are always teaching us,” said Larisa Poluektova, M.D., Ph.D., associate professor of pharmacology and experimental neuroscience, who adapted a specially-designed mouse model for HIV dementia research.

Because mice cannot acquire HIV, UNMC has developed mice with the equivalent of a human immune system that can now “catch” HIV. Such a mouse model enables advanced tests on HIV and its treatment.

“Some things are specifically human and only human. That’s why we were so excited to develop this special mouse,” she said.

She and Santhi Gorantla, Ph.D., assistant professor of pharmacology and experimental neuroscience, and their team were the first to describe the development of changes in the brains of these mice.

Approximately 95 percent of all lab animals are mice and rats. In the past decade, scientists have discovered how to breed mice with genetic alterations that mimic human diseases. This capability has revolutionized medical research and dramatically increased the number of mice used in medical science.

Two types of mice — knockout and transgenic — dominate the research arena. A knockout mouse is genetically engineered to have an inactivated, or “knocked out,” gene that is replaced or disrupted with an artificial piece of DNA. By causing a specific gene to be inactive in the mouse, and observing any differences from normal behavior or physiology, researchers can infer its probable function.

A transgenic mouse contains additional, artificially-introduced genetic material in every
cell and is used to study gene function and regulation because analysis is carried out on the whole organism. Transgenic mice also are used to model human diseases that involve the overexpression or misexpression of a particular protein.

C.B. Gurumurthy, Ph.D., assistant professor of genetics, cell biology and anatomy, directs the UNMC Mouse Genome Engineering Core Facility, funded by the Nebraska Research Initiative and tobacco settlement funds. Since he took this position nearly two years ago, he has become the “mouse guru” to whom researchers turn for advice about mouse models.

“Genes are like stars in the sky — what happens to the rest of the universe when we take out one star?” Dr. Gurumurthy asked.

“That is a question many researchers want to answer. We help researchers create designer mice that could enable them to get to the answer. We take out the star of their interest from the mouse genome universe or insert an artificial star into it.”

Dr. Gurumurthy constantly looks out for newer trends in transgenic technology. One of the biggest drawbacks of the existing transgenic technology is the randomness of gene integration into the genome.

“It is like when you insert a star into the genome universe and it gets lost somewhere,” he said.

But now, a gene can be placed in the mouse genome at a precise location using a novel technique called PITT (Pronuclear Injection-based Targeted Transgenesis). He collaborates with a Japanese group to try this technique at UNMC. The technology could save researchers up to two years and $25,000 in screening each mouse line to determine if it is useful.

He uses a system that cuts in half the time it takes for researchers to change the genetic background of their genetically engineered mouse strain. It normally takes three years of “congenic breeding” to get the desired mouse, but with the “marker assisted speed congenics,” the time is reduced to about a year and a half.

“Just a handful of other labs in the United States, including only one other core lab, offer services using processes similar to ours,” Dr. Gurumurthy said. “The method, not readily available, is up to three times less expensive than a newer method that is used at some core facilities and commercial sources.”

He also has developed a genetically engineered fluorescent mouse model that illuminates individual cells that comprise various organs in the animal body. Called the “rainbow mouse,” Dr. Gurumurthy said it enables researchers to observe cellular interactions and organization during a disease process in real time.

“With this mouse model, researchers could watch how cancer grows and metastasizes to other organs in the body,” he said.

“Researchers could test new medications or use the rainbow mouse for developmental studies. It’s really quite extraordinary.”

Breast cancer researcher Kay-Uwe Wagner, Ph.D., has worked with genetically engineered mice since 1995. Over the past decade, he has developed more than 20 mouse models that are now being used in cancer research around the world. Read more about how he and other UNMC researchers use mice to advance medical research.