Mice Become First Animals to Produce Other Species' Sperm

By Stephen Bradt

With pinhead-sized grafts of testicular tissue from newborn mammals, scientists at the School have induced mice to produce fully functional sperm from evolutionarily distant species. The result has important implications for preserving the germ lines of critically endangered species as well as prized livestock.

The study, in which male mice produced functional gametes first from other mice and then from pigs and goats, is reported in the Aug. 15 issue of the journal *Nature*.

"This is the first report of complete spermatogenesis from tissue grafted across species," said **Dr. Ina Dobrinski**, assistant professor of large animal reproduction in the School. "The production of functionally competent sperm from three different mammals indicates that testis tissue grafting may be applicable to a wide variety of species."

The work also yielded the first functional sperm from immature reproductive tissue, meaning sperm could be derived even from individuals that have not reached sexual maturity. Unlike cryonic approaches to preservation, testis tissue grafting offers a potentially inexhaustible supply of male gametes.

Mice with the testis grafts could aid studies of the effects of drugs – including potential male contraceptives – on sperm production. The mice also give scientists a valuable model to better understand testicular function, many aspects of which remain murky.

Dobrinski and colleagues grafted as much as one cubic millimeter of tissue from the testes of newborn mice, goats and pigs onto the backs of mice. As many as eight miniature testes developed, and in vitro fertilization revealed that the sperm produced by those testis grafts were functional.

"At least 60 percent of grafts grew into functional testis tissue under the skin," Dobrinski said, "and those grafts produced as much sperm, gram for gram, as testes in the donor species. Some grafts grew more than 100-fold."

Similar cross-species grafts of testicular tissue have been tried previously, but no sperm cells resulted. Dobrinski speculates that the mice's backs may have provided both an ideal temperature and suitable blood vessels to allow for the growth of functional testes.

"Dr. Dobrinski is one of the few investigators attempting to remove testicular stem cells and transplant them into recipients," said Michael D. Griswold, interim dean of science at Washington State University's School of Molecular Biosciences, who was not involved in the work. "The fact that she can graft portions of testes from other mammalian species into mice and get sperm produced is an important step forward."

Dr. Dobrinski

The work also demonstrates that testosterone and other mammalian hormones can work across species, said David de Kretser, director of the Institute of Reproduction and Development at Monash University in Australia. "These data indicate that the hormones produced by the mouse are adequate to stimulate sperm production in a range of species."

Spermatogenesis is a highly organized process that generates virtually unlimited sperm cells during adulthood. Continuous proliferation and differentiation of germ cells occurs in a delicate balance with various testicular compartments.

"It seems that the testis grafts transferred this entire environment to the recipient mice," Dobrinski said.

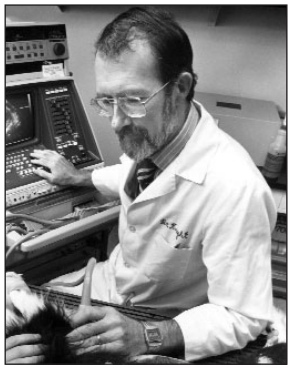
She was joined in the work by Drs. Ali Honaramooz, Amy Snedaker, Michele Boiani and Hans Schöler of Penn's Center for Animal Transgenesis and Germ Cell Research and Dr. Stefan Schlatt of the University Münster in Germany. Schlatt conducted the group's research with mice, Honaramooz and Snedaker conducted the work involving pigs and goats, and Boiani completed the in vitro fertilization.

The work was funded by the National Institutes of Health, the U.S. Department of Agriculture, the Deutsche Forschungsgemeinschaft, the Marion Dilley and David George Jones Funds and the Commonwealth and General Assembly of Pennsylvania.

Dr. David Knight Dies

Dr. David Knight, Emeritus Professor of Cardiology, died on July 15. He suffered a heart attack while bicycling near his home. Dr. Knight had retired on June 30, 2001, after 34 years on the faculty. A 1962 graduate of Cornell University College of Veterinary Medicine, he came to Penn in 1964 to study at the then Division of Graduate Medicine and to join the School's Comparative Vascular Studies Unit, which pioneered the study of veterinary cardiology. Dr. Knight's primary research interests were pulmonary hypertension and heartworm disease. He was a charter member of the American College of Internal Medicine, a member of the American Heart Association and the former president of the American Heartworm Society.

Before taking up bicycling two years ago, Dr. Knight was very involved in water sports. He rowed at Cornell and for Vesper Boat Club and the Bachelors Barge Club in Philadelphia. In 1964, he was an alternate on the U.S. Olympic team. He won the Masters World Championship in 1982 in the Netherlands with former Olympian John B. Kelly, Jr. In 1973 he won a gold medal in a world white water canoeing competition in Switzerland.



Dr. Knight is survived by his wife Krystina, sons Eric and Christopher and his father, Ernest, and a brother.

A memorial service was held on September 26th at Houston Hall.

The David S. Knight Memorial Fund has been established at the School.