Living with females extends the reproductive life of the male mouse

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Living with a female mouse can extend the reproductive life of a male mouse by as much as 20 percent, according to a study conducted by Ralph Brinster and a team of other researchers at the University of Pennsylvania School of Veterinary Medicine. The study was reported online today in the journal *Biology of Reproduction*.

The researchers hypothesize that the females' effect on the environment of the spermatogonial stem cells likely occurs through the male's endocrine and nervous systems, but other systems are likely involved. The change amounts to a reduction of fertility six months earlier in "lonely" mice as opposed to those who have female companionship.

The results have significant implications for the maintenance of male fertility in wildlife, livestock and even human populations.

Brinster and his team housed male mice with and without female companions for 16-32 months. Each male was placed with two novel females at two-month intervals to test its ability to impregnate the females. The results indicated that males housed with females did not show a drop in fertility until 32 months of age, a six-month increase in fertility over males housed alone.

The study also indicated, however, that once male fertility began to decrease, the rate of decrease was the same for both those that lived with females and those that did not. The decline in fertility appeared to be due in part to defects in the sperm-production process.

"It appears that housing females with a male mouse delays the decline of reproductive processes at the cellular level by somehow affecting the cells surrounding the stem cells that produce spermatozoa in the testes," said Brinster, professor of physiology at Penn Vet. "Whether this female influence occurs in other species is not known."

While it is commonly known that reproductive aging of males includes decreased fertility, the factors that delay aging are largely unknown. Histological analysis indicated that abnormal spermatogenesis occurred sooner in isolated males, suggesting that defects in spermatogenesis may play a role in the greater decrease in fertility in isolated males.

"If it turns out that this reproductive effect is mimicked in other species, for example, livestock animals that affect food production, then a 20 percent increase in male fertility could mean an extension of the male reproductive life span of years," Brinster said. "This finding may also have relevance for the protection of some large endangered species."

This research continues 10 years of study on the relationship between the stem cell environment, called the "niche" and spermatogonial stem cells, or SSCs. Brinster's team first discovered that the niche in the testis of the newborn male mouse supports the stem cell and its differentiation to produce complete spermatogenesis better than the niche in the mature adult male testis. In subsequent studies, Brinster determined that when the SSCs of young males were transferred into new young testes every three months, the SSCs survived for more than three years, a greater than 50 percent increase in life of the stem cell. Therefore, in old males it was the SSC niche in the testis that was failing long before the SSC, which was relatively long-lived.

The female is just one of many environmental cues that may influence the niche and cells, and thereby fertility, of the male. Whether this female influence occurs in other species is not known, but it is known

that the female profoundly modifies a variety of responses in males in many areas of male physiology and psychology.

The study was performed by Brinster of the Department of Animal Biology in the School of Veterinary Medicine at Penn, as well as Jonathan A. Schmidt and Jon M. Oatley, now of the Department of Dairy and Animal Science at Pennsylvania State University. The research was supported by the National Institutes of Health and the Robert J. Kleberg Jr. and Helen C. Kleberg Foundation.

Brinster, the Richard King Mellon Professor of Reproductive Physiology at Penn, has been a leader in the biology of germ cells, such as egg or sperm, whose genes are passed along to offspring. Early in his career, he established techniques to grow and manipulate eggs and later used these methods to generate genetic changes in mice and other animals. More recently, Brinster has created a technique of altering genes in spermatagonial stem cells, the cells that produce sperm.

Source: University of Pennsylvania