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PRESERVING SPERM THROUGH FREEZING OF SPERMATOGONIAL STEM CELLS

Frozen sperm has long been a mainstay of the cattle and dairy industry. But sperm from many other species do not freeze well because freezing protocols vary from species to species and effective methods have been developed for only a few animals. Now Dr. Ralph Brinster, Richard King Mellon Professor of Reproductive Physiology here at the School, has developed a technique that may eliminate the need to freeze sperm. Dr. Brinster and colleagues developed a method to freeze the cells that give rise to spermatozoa and showed that these cells are productive when thawed. *continued on page 3*

LATE BREAKING NEWS:

The Pennsylvania Legislature has voted to restore the School's funding to 1996 levels and has provided an additional $400,000 to renovate the toxicology laboratory at New Bolton Center, bringing the total to $21,107,000.

Preserving sperm through freezing of spermatogonial stem cells *continued from front cover*

The spermatogonial stem cells can be removed from the testes of prepubertal or adult animals and then frozen and stored. They can later be implanted into the testes of other animals where they will give rise to fully developed spermatozoa.

Dr. Brinster removed spermatogonial stem cells from a strain of transgenic mice that allows sperm cells to be stained blue when incubated in a special material. These cells were frozen for various periods of time, then thawed and implanted into the testes of mice whose own spermatogonial stem cells had been chemically destroyed. Once implanted into the seminiferous tubules, the site in the testis where spermatogenesis takes place, the stem cells established spermatogenesis. In earlier work Dr. Brinster had shown that spermatozoa produced by donor cells were able to fertilize eggs effectively.

Spermatogonial stem cells differ from spermatozoa in that they carry the entire germ line of the male as they are diploid and they divide to replenish the stem cell populations as well as generate sperm. Each stem cell can produce over 4,000 unique spermatozoa. The ability to freeze spermatogonial stem cells has wide implications, not only for agriculture where it could be used to preserve, potentially indefinitely, valuable strains of livestock, but also for the preservation of endangered species. For humans this technique could be utilized for males who have to undergo chemotherapy. The stem cells could be frozen and preserved and then later re-implanted, allowing the male to father children.

In another experiment, Dr. Brinster went a step further. Spermatogonial stem cells from transgenic rats were implanted into the testes of a strain of immunosuppressed mice. The rat stem cells gave rise to viable sperm, establishing that one species can be the host for the sperm development of another even though the length of the period for complete sperm development is different between host and donor. This opens the possibility that immunosuppressed mice could act as *in vivo* hosts for spermatogenesis of other mammalian species.

If scientists can develop a culture medium in which to maintain and grow these spermatogonial stem cells, many other possibilities arise. The stem cells then could be modified to correct a defective gene, eliminating specific genetic diseases forever from that particular male germ line. Modifications could be made in livestock germ cells to produce disease resistant or better producing animals. The technique could also be used to create further transgenic models of human and animal diseases, aiding researchers in their studies of these problems.

The work was published in the June issue of *Nature Medicine* and the May 30th issue of *Nature*. Dr. Brinster's collaborators for the study of *Rat spermatogenesis in mouse testis* were Dr. Shauna D. Maika and Dr. Robert Hammer of the Howard Hughes Medical Institute, Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, Texas, and Dr. David Couthier and Mary R. Avarbock of his laboratory. The collaborators of the study on the *Reconstitution of spermatogenesis from frozen spermatogonial stem* cells were Mary R. Avarbock and Clayton J. Brinster of his laboratory.

The research was supported by funds from the NIH, United States Department of Agriculture, W.M. Keck Foundation, and the Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation.

Dr. Brinster was the co-recipient of the First March of Dimes Prize in Developmental Biology, awarded on April 12, 1996 to him and Dr. Beatrice Mintz of the Institute for Cancer Research, Fox Chase Cancer Center, Philadelphia. The two scientists were honored for their pioneering work in the development of transgenic mice.

"We still don't know enough about the normal processes of biological development and how they sometimes go awry," said Dr. Jennifer L. Howse, president of the March of Dimes. "Basic research is essential to understanding these processes. It is laying the foundation we need to discover the origins of birth defects, and it gives us hope that one day we will be able to prevent many disabling and fatal disorders. We are delighted to recognize Dr. Mintz and Dr. Brinster for their major contributions to basic research."

The March of Dimes Prize will be awarded annually to investigators who have made a seminal discovery in developmental biology, one that has revealed a new principle of relevance to birth defects, and who have not previously received a major prize for their work.

Inaugural Scholarship Recognition Dinner

Dean Alan Kelly and scholarship donors.

Scholarship donors met "their" students at a reception and Scholarship Recognition Dinner on November 8, 1995 in the Marshak Gallery at VHUP. About 80 students and donors got together and spent the evening in lively conversation. The 1996 Scholarship Recognition Dinner will be held on November 13, again at VHUP. If you are a current scholarship recipient or a donor, please mark your calendar.