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Nonviable Embryonic Stem Cells Used to Create Tissue Transplants in Mice

Two alternative sources of embryonic stem cells have been found to be effective at replacing adult tissue, which can be transplanted without the risk of rejection, according to Penn Vet researchers. The findings of a team headed by Dr. K. John McLaughlin, assistant professor of reproductive physiology at Penn’s Center for Animal Transgenesis and Germ Cell Research, appearing in the February 15, 2007 issue of *Genes & Development*, detail how blood cells in mice are replaced with uniparental embryonic stem cells, generated either solely from unfertilized eggs or sperm from males.

Research has long shown that mammalian embryos inheriting both sets of chromosomes from one parent (uniparental) do not develop. While embryos with two sets of chromosomes from the mother (parthenogenetic) were previously considered a potential source of tissues for the female from which they were derived, this study shows for the first time that parthenogenetic cells can regenerate an organ in an adult mouse. An unexpected bonus was discovering that this could also be done with embryonic stem cells derived from sperm.

“It has been known for over a decade that uniparental cells had some capacity to form tissues in vitro and in vivo, but it was questionable if these embryonic stem cells could generate transplantable material that would proliferate and replace tissues in an adult,” said Dr. McLaughlin.

There are several concerns in using these cells for transplantation as they cause abnormalities during development and are linked to malignant tissue formation. The transplant recipient animals from both egg and sperm derived uniparental cells were, however, healthy over a normal lifespan and with a normal range of blood cell types.

Compared to very low efficiency of deriving embryonic stem cells from clones in mice, the derivation of both androgenetic and parthenogenetic embryonic stem cells is more comparable to normal fertilized embryos. This approach, if translated to humans, could produce patient-derived tissue without the ethical and efficiency issues associated with therapeutic cloning.

Other coauthors of the study from Penn are Dr. Sigrid Eckardt, research associate, and Adrian Leu, research specialist, at the Center for Animal Transgenesis and Germ Cell Research.

“Killer” B Cells Discovered; New Link in the Evolution of Immunity

A unique evolutionary link between the immune systems of fish and mammals in the form of a primitive version of B cells, white blood cells of the immune system, has been discovered by Penn Vet researchers. Their studies link the evolution of the adaptive immune system in mammals, where B cells produce antibodies to fight infection, to the more primitive innate immunity in fish, where they found that B cells take part in phagocytosis (cell eating), the process by which cells of the immune system ingest foreign particles and microbes.

The finding, in the October issue of *Nature Immunology*, represents a sizeable evolutionary step for the mammalian immune system and offers a potential new strategy for developing much-needed fish vaccines.

“When examining fish B cells we see them actively attacking and eating foreign bodies, which is a behavior that, according to the current dogma, just shouldn’t happen in B cells,” said Dr. J. Oriol Sunyer, pathobiology professor. “I believe it is evidence for a very real connection between the most primitive forms of immunological defense, which has survived in fish, and the more advanced, adaptive immune response seen in humans and other mammals.”

Despite the behavioral differences, the fish B cells likely represent a less advanced version of mammalian B cells.

The trout cell in the lower left is in the process of engulfing tiny latex beads (arrow). Dr. J. Oriol Sunyer; image taken with the assistance of R. Meade, Biomedical Imaging Core Laboratory of Penn’s School of Medicine.
Dr. Sunyer found the very cellular structures that medical science has used to define B cells in humans to be present in fish B cells, which is why they are able to label them as B cells in the first place.

Funding for this research was provided by the National Science Foundation and United States Department of Agriculture.

**Friend or Foe? How the Intestine Keeps Us Safe From Microbial Invaders**

How the immune system is switched on and off, or how it detects friend or foe, has baffled scientists for many years. New research from Penn Vet shows tiny intestinal epithelial cells play a central role in both turning on antimicrobial immune responses and turning off harmful responses that can cause chronic inflammation in the intestine. The researchers reported their findings in the February 25, 2007 issue of *Nature*.

“Our findings suggest that manipulating intestinal epithelial cell function could provide a method to improve the efficacy of oral vaccines or help treat inflammatory diseases of the intestine like inflammatory bowel disease or food allergies,” said Dr. David Artis, assistant professor of pathobiology and senior author of the study.

“The body’s intestinal immune system is continually exposed to the food we eat and harmless intestinal bacteria that help us digest that food. It is essential that immune cells do not react to food or harmless bacteria otherwise diseases like inflammatory bowel disease or food allergies can develop,” said Dr. Artis. However, following exposure to dangerous viral, bacterial or parasitic microbes, immune cells must respond and turn on the appropriate immune response to kill the microbe. “Our recent studies identify intestinal epithelial cells as critical cells in making friend-or-foe decisions in the gut,” said Dr. Artis.

Other participants in the study from Penn Vet included Colby Zaph, Amy E. Troy, Betsy C. Taylor, Lisa D. Berman-Booty, Katherine J. Guild, Yurong Du, Evan J. Yost and Michael J. May.

Funding for this research was provided by the National Institutes of Health, the Irvington Institute for Immunological Research, and the Crohn’s and Colitis Foundation of America’s William Shelby Modell Family Foundation Research Award.

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**Deaths**

Marsha Finkelman, biomedical purchasing manager for the Ryan Veterinary Hospital, died November 27, 2006. She started working at Penn Vet in the late 1970s as an anesthesia veterinary technician. Ms. Finkelman was an organizer of the Academy of Veterinary Technician Anesthetists, and in 2003 was president of the Veterinary Technicians and Assistants Association of Pennsylvania. She was among the first to be granted official certification as a veterinary technician specialist in anesthesia.

Dr. David Kritchevsky, emeritus professor of biochemistry at the School of Veterinary Medicine, and one of the first scientists to study the link between cholesterol, cardiovascular risk and cancer, died November 20, 2006. From 1975 to 1991, Dr. Kritchevsky served as associate director of the Wistar Institute. He was president of the American Society for Nutrition in 1979.

Charles E. Wismer, Jr., an overseer of the School of Veterinary Medicine from 1984 to 1988, died September 1, 2006. He also was an agriculture trustee at Pennsylvania State University from 1981 to 1987 and a former member of the Pennsylvania Pesticide Board.