Scientists produce first stem cells from endangered species

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Northern White Rhinoceros. Credit: San Diego Zoo

Starting with normal skin cells, scientists from The Scripps Research Institute have produced the first stem cells from endangered species. Such cells could eventually make it possible to improve reproduction and genetic diversity for some species, possibly saving them from extinction, or to bolster the health of endangered animals in captivity.

A description of the accomplishment appeared in an advance online edition of the journal Nature Methods on September 4, 2011.

Genesis

About five years ago, Oliver Ryder, PhD, the director of genetics at the San Diego Zoo Institute for Conservation Research, contacted Jeanne

Loring, PhD, professor of developmental neurobiology at Scripps Research, to discuss the possibility of collecting stem cells from endangered species. Ryder's team had already established the Frozen Zoo, a bank of skin cells and other materials from more than 800 species and wondered if the thousands of samples they had amassed might be used as starting points.

Just as is hoped with humans, Ryder thought stem cells from endangered species might enable lifesaving medical therapies or offer the potential to preserve or expand genetic diversity by offering new reproduction possibilities.

At the time, although researchers were working with stem cells from embryos, scientists had not yet developed techniques for reliably inducing normal adult cells to become stem cells. But the technology arrived soon after, and scientists now accomplish this feat, called induced pluripotency, by inserting genes in normal cells that spark the transformation.

While Loring's team met with Ryder in early 2008, they realized that these newly emerging techniques might be applied to endangered species. Postdoctoral fellow Inbar Friedrich Ben-Nun, PhD, set out to systematically explore the possibilities.

Ryder suggested two species for initial work. The first was a highly endangered primate called a drill that he chose because of its close genetic connection to humans, and because in captivity the animals often suffer from diabetes, which researchers are working to treat in humans using stem cell-based therapies.

The northern white rhinoceros was the second candidate. Ryder chose this animal because it is genetically far removed from primates, and because it is one of the most endangered species on the planet. There are

only seven animals still in existence, two of which reside at the San Diego Zoo Safari Park.

Initially members of the team thought they would have to isolate and use genes from animals closely related to the endangered species to successfully induce pluripotency. But that line of experimentation didn't work. Instead, to their surprise, after a year of trial and error, the researchers found that the same genes that induce pluripotency in humans also worked for the drill and the rhino. "It has been just amazing," said Ryder of the Scripps Research team's successes.

The process is inefficient, meaning only a few stem cells are produced at a time, but that's enough. "There are only two animals in it," said Ben-Nun, "but we have the start of a new zoo, the stem cell zoo."

Drill primate. Credit: San Diego Zoo

Stem Cells to the Rescue

The scientists view their success as a first step toward greater advancements. Besides the possibility of using stem cells as the basis for diabetes or other treatments, there is great potential for new reproductive technologies as the stem cell research field advances. "The most important thing is to provide these stem cells as a resource for other people taking some of the next steps," said Loring.

One of the greatest concerns with small populations such as the northern white rhinos is that even if they did reproduce, which hasn't happened in many years, their genetic diversity is inevitably and dangerously low, and such inbreeding leads to unhealthy animals.

But researchers are moving toward inducing stem cells to differentiate into sperm or egg cells. With that accomplished, one possibility is that scientists could take skin cells in the Frozen Zoo from long dead animals, induce pluripotency, trigger differentiation into sperm cells, and then combine these with a living animal's eggs through in vitro fertilization. Otherwise-lost genetic diversity would then be reintroduced into the population, making it healthier, larger, and more robust.

Or, both eggs and sperm might be produced from the stem cells, with the resulting embryos implanted in live animals, a process that current research suggests could be much more reliable than existing cloning techniques.

Scientists are already exploring the possibility of producing sperm and eggs from stem cells as a potential solution to human infertility issues. Loring hopes that some of these groups might consider initial technique development using endangered species stem cells. "I think that work would be a lot easier ethically with endangered species than with humans," she said, "so I suspect some people working in this area would

love to have our cells for experiments."

The Real Solution

"The best way to manage extinctions is to preserve species and their habitats," said Ryder, "but that's not working all the time." The rhinos are a perfect example, he said, because there are so few. "Stem cell technology provides some level of hope that they won't have to become extinct even though they've been completely eliminated from their habitats. I think that if humankind wants to save this species, we're going to have to develop new methodologies."

And even when there are reasonable wild populations of a species, they face a range of threats, including loss of habitat and poaching.

Moving forward, Loring said the group is hoping to continue producing stem cells from other species to expand their fledgling stem cell "zoo." For now, they're working to secure funding for what amounts to an unconventional line of research. "It's in between fields," said Loring. "It's not classical conservation and it's not ordinary biological research."

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In addition to Ryder, Loring, and Ben-Nun, authors on the paper, titled, "Generation of induced pluripotent stem cells from highly endangered species," (DOI 10.1038/nmeth.1706) were Susanne Montague, Ha Tran, Ibon Garitaonandia, Trevor Leonardo, Yu-Chieh Wang, Scripps Research, Louise Laurent from Scripps Research and UCSD, and Marlys Houck and Suellen Charter from the San Diego Zoo Institute for Conservation Research.

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