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Generating Buzz about Regeneration

University of Dayton, Ohio (url: http://www.udayton.edu/index.php)

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08.20.2009 | Research, Science A University of Dayton biologist has linked natural regeneration in the newt with recent discoveries about stem cells in humans, attracting national attention for his pursuit of the key to one of nature's mysteries: regrowing damaged tissue.

"Regeneration is not one thing. There are lots of different ways animals regenerate," said Panagiotis Tsonis, director of the University of Dayton's Center for Tissue Regeneration and Engineering at Dayton (TREND). "If we can understand how it happens in newts, if we can know the triggers, then the possibility of expanding the process into other animals is there."

Tsonis, who has studied tissue regeneration in the newt for more than 20 years, recently attracted the attention of the National Institutes of Health and national science publications following the release of a study in the June issue of *Developmental Dynamics* in which Tsonis makes a step in bridging the gap between regeneration in newts and regeneration in mammals.

His research followed up on recent studies showing adult cells in humans can be reprogrammed to become induced pluripotent stem cells (iPS), meaning these reverse-engineered cells are able to differentiate into any number of new types of tissue. The reprogramming is induced by expressing – or activating – four factors naturally dormant in cells.

"Lens regeneration in the newt is similar," Tsonis said. "The newt takes a terminally differentiated cell and turns it backward, reverting it to a stem cell-like state."

The big question is whether the reprogramming method in newt regeneration is similar to the newly discovered method of reprogramming adult cells in humans.

Tsonis found that three of the four factors expressed in iPS cells are also expressed in newt lens regeneration.

But while the newt's iris cells are able to differentiate into lens cells, they lack true pluripotency, the ability to become any other type of cell. The absence of the fourth factor expressed in iPS — and another related factor — might hold the key to pluripotency.

"Manipulating these factors in the newt could provide answers of enormous importance in understanding regeneration and how it relates to stem cell research," Tsonis said.

The NIH recently awarded Tsonis a five-year, $1.8 million grant to continue his study of lens regeneration in the newt and its connection to stem cell research in other animals, including humans. The grant, awarded July 31, is the fourth and largest grant Tsonis has received from the NIH, which has funded his research continuously since 1995. In all, he's received nearly $7 million in research funding from the NIH, the Arthritis Foundation and others.

The Scientist also featured Tsonis in its August issue along with several other regeneration researchers — including his wife, Katia Del Rio-Tsonis, who is based at Miami University — in a story called, "The Regeneration Recipe."

The story describes what scientists around the world are learning about different animals with naturally regenerative qualities, such as zebrafish and chicken embryos. Some scientists are collaborating with others in the field of human stem cell research. All of them are focused on understanding how and why some animals and cells naturally regenerate and how they can recreate the phenomenon in animals that lack the ability.

Four years ago, Tsonis and his wife made a breakthrough. They succeeded in causing tissue to regenerate where it never had before. In a newt's eye, the dorsal (upper) iris can regenerate a lens after injury, but the ventral (lower) iris cannot. Both have the same type of cells and both show similar activity after the lens is removed, but the ventral iris naturally stops before it can begin regeneration.

By adding the right mix of certain growth factors – sort of like a recipe – Tsonis was finally able to induce the ventral iris to grow a new lens. *Nature* published the couple's findings in 2005.

The research means that scientists one day may be able to regrow lenses in other animals and eventually humans, which could dramatically reduce the need for cataract procedures, Tsonis said. But he cautions that regeneration of body organs is not around the corner.

"It can take a lifetime to connect research with conclusive evidence to regenerate limbs in humans or prove a cure for cancer," he said. "To me, what matters is good science."

The TREND Center at the University of Dayton includes a research alliance with Wright State University, the Kettering Medical Center Network, Rice University and other universities.

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