Scientists identify mammal model of bladder regeneration

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While it is well known that starfish, zebrafish and salamanders can re-grow damaged limbs, scientists understand very little about the regenerative capabilities of mammals. Now, researchers at Wake Forest Baptist Medical Center's Institute for Regenerative Medicine report on the regenerative process that enables rats to re-grow their bladders within eight weeks.

In PLOS ONE, a peer-reviewed, online publication, the scientists characterize this unique model of bladder regeneration with the goal of applying what they learn to human patients.

"A better understanding of the regenerative process at the molecular and cellular level is a key to more rapid progress in applying regenerative medicine to help patients," said George Christ, Ph.D., senior researcher and professor of regenerative medicine at Wake Forest Baptist.

In a previous study by Christ's team, research in rats showed that when about 75 percent of the animals' bladders were removed, they were able to regenerate a complete functional bladder within eight weeks. The current study focused on how the regeneration occurs.

"There is very little data on the mechanisms involved in organ regeneration in mammals," said Christ. "To our knowledge, bladder regeneration holds a unique position – there is no other mammalian organ capable of this type of regeneration."

The ability of the liver to grow in size when lobes are removed is sometimes referred to as regeneration, but this is a misnomer, said co-author Bryon Petersen, Ph.D., who was a professor of regenerative medicine at Wake Forest Baptist during the period the research occurred. Instead, through a proliferation of cells, the remaining tissue grows to compensate for the lost size. In contrast, the hallmark of true regeneration is following nature's "pattern" to exactly duplicate size, form and function, Petersen said.

"If we can understand the bladder's regenerative process, the hope is that we can prompt the regeneration of other organs and tissues where structure is important – from the intestine and spinal cord to the heart," said Petersen.

The current study showed that the animals' bodies responded to the bladder removal by increasing the rate at which certain cells divided and grew. The most notable proliferative response occurred initially in the urothelium, the layer of tissue that lines the bladder.

As the proliferative activity in the bladder lining waned, it continued elsewhere: in the fibrous band (lamina propria) that separates the bladder lining from the bladder muscles and in the bladder muscle itself.

The researchers have several theories about how the process works, said Christ. One possibility is that cells in the bladder lining transition and become a type of stem cell that can proliferate throughout the bladder. Other theories are that cells in the bladder lining signal other cells to replicate and that injury prompts stem cells to arrive through the blood stream to repair the bladder damage.

In future studies, the scientists will work to identify the exact regenerative process and will expand the work into mice. The ability to breed mice that lack specific genes will enable the team to explore how

genes and proteins may affect the regenerative process and possibly help identify therapies to prompt regeneration.

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