

Scientists discover molecular pathway for organ tissue regeneration and repair

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Scientists have discovered a molecular pathway that works through the immune system to regenerate damaged kidney tissues and may lead to new therapies for repairing injury in a number of organs systems.

The findings, reported in this week's [Proceedings of the National Academy of Sciences](#) (*PNAS*), come from collaborative research led by Cincinnati Children's Hospital Medical Center and the Brigham & Women's Hospital of Harvard Medical School.

The study may have significant medical ramifications as currently there are no effective treatments for acute kidney injury - a growing problem in hospitals and clinics, according to the study's senior co-authors, Richard Lang, Ph.D., a researcher in the divisions of Pediatric Ophthalmology and Developmental Biology at Cincinnati Children's, and Jeremy Duffield, M.D., Ph.D., a researcher at Brigham and Women's Hospital. Acute kidney injury is a significant cause of kidney disease, cardiovascular complications and early death, affecting as many as 16 million children and adults in the United States.

The new molecular repair pathway involves white blood cells called macrophages - part of the [immune system](#) - that respond to tissue injury by producing a protein called Wnt7b. Scientists identified the macrophage-Wnt7b pathway during experiments in mice with induced kidney injury. Wnt7b is already known to be important to the formation of kidney tissues during embryonic organ development. In this study the scientists found the protein helped initiate tissue repair and regeneration

in injured kidneys.

"Our findings suggest that by migrating to the injured kidney and producing Wnt7b, macrophages are re-establishing an early molecular program for organ development that also is beneficial to tissue repair," said Dr. Lang. "This study also indicates the pathway may be important to tissue regeneration and repair in other organs."

Wnt7b is part of the Wnt family of proteins, which are known to help regulate cells as they proliferate, grow and become specific cell types for the body. Wnt proteins have also been linked to the regulation of stem cells in bone marrow and skin, which suggested to researchers of the current study that Wnt might have a role in tissue regeneration.

The researchers conducted a number of experiments of [kidney injury](#) in mice to identify the repair pathway, finding that:

- Silencing macrophage white blood cells through a process called ablation reduced the response level of Wnt proteins to injured kidney cells.
- Deleting the Wnt7b protein from macrophages diminished normal tissue repair functions in injured kidneys.
- Injecting into the injured kidneys a protein called Dkk2, which interacts with and is known to help regulate the Wnt pathway during embryonic development, enhanced the macrophage-Wnt7b repair process. It also restored epithelial surface cells that line internal [kidney](#) surfaces and suggested a therapeutic potential for the pathway.

Drs. Lang and Duffield said the repair pathway may benefit other

injured organs because macrophages act somewhat like a universal emergency responder in the body, rushing to injured tissues wherever damage occurs. Another factor is the central role the Wnt pathway plays in cell regulation and function throughout the body.

Provided by Cincinnati Children's Hospital Medical Center

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