Researchers unlock the potential for exploring kidney regeneration

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It is estimated that up to 10 percent of the U.S. population may have some form of renal disease, with 450,000 patients with end stage renal disease (ESRD) requiring hemodialysis. Researchers at Brigham and Women's Hospital, Massachusetts General Hospital and the University of Pittsburgh have identified a cell in zebrafish that can be transplanted from one fish to another to regenerate nephrons, providing the potential to improve kidney function. These findings are published in the February 3 edition of *Nature*.

Currently, the five-year survival rate for patients on dialysis is 33 percent, worse than the survival rate for many forms of cancer. This epidemic of renal failure is projected to grow as obesity, poor nutrition and lack of exercise increase the incidence of diabetes and hypertension. There is also evidence that intra-uterine growth retardation and low birth weight/prematurity reduce the number of nephrons in each kidney thereby increasing the risk of hypertension and renal failure when these premature infants become adults. The cost of treating end stage renal disease is currently 32 billion dollars annually and is likely to double in the next decade.

One of the reasons renal failure is so common, is that humans are unable to generate any new nephrons, the basic filtration unit of the kidney, after the 36th week of gestation. In contrast, many non-mammalian vertebrates continue to generate nephrons throughout their lives and can generate new nephrons following renal injury. Understanding how non-mammalian vertebrates like zebrafish, carry out this remarkable

regenerative process and why mammals have lost this ability is a fundamental biologic question. We believe that answering this question might provide new ways to repair damaged human kidneys and dramatically extend and improve the lives of hundreds of thousands of patients with chronic renal failure.

In a collaborative effort including two groups that are part of the Harvard Stem Cell Institute, the laboratory of Dr. Alan Davidson, at the Center for Regenerative Medicine at the Massachusetts General Hospital and the laboratory of Dr. Robert Handin, in the Hematology Division in the Department of Medicine at the Brigham and Woman's Hospital, together with Dr. Neil Hukriede's team at the University of Pittsburgh, have identified and characterized, for the first time, a progenitor cell in adult zebrafish kidneys that can be transplanted from one fish to another and generate new nephrons. Now that this cell has been identified it may be possible to better understand how to increase its number and capacity to generate nephrons.

Lead author, Dr. Alan Davidson, said "We hope to eventually be able to cross species barriers and understand why similar cells, present in mouse and human kidneys during embryonic life, disappear around the time of birth". The groups plan to continue studies on zebrafish and apply their data to mouse models and eventually humans.

Provided by Brigham and Women's Hospital