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Zebrafish discovery may shed light on human kidney function

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Researchers say the discovery of how sodium ions pass through the gill of a zebrafish may be a clue to understanding a key function in the human kidney. The findings from a collaboration between Mayo Clinic and the Tokyo Institute of Technology appear in the online issue of the *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*.

The researchers discovered a protein responsible for gas exchanges in the fish gill structure. Specifically they studied and characterized the Na+/H+ (sodium/hydrogen) exchanger named NHE3, responsible for controlling sodium and hydrogen ions across the gill. The researchers also directly demonstrated that NHE3 can function as a Na+/NH4+ (sodium/ammonium) exchanger.

"This is significant because the fish tends to mimic the process in humans," says Michael Romero, Ph.D., a Mayo Clinic physiologist who works in nephrology. "This is the true beauty of comparative physiology-– a lot of the organs function by very similar processes, down to ionic transfer."

In this case the protein allows the sodium ions to be absorbed from the forming urine while at the same time discarding waste from normally functioning cells, thus keeping the body in balance and serving as an energy saving system. The researchers say the same NHE3 protein performs a similar function in the intestine, pancreas, liver, lungs and reproductive system.

The gill is used in the fish as a transport system: sodium ions are nutrients and ammonium carries away waste. It's a key process allowing zebrafish to extract sodium ions from fresh water. In humans, NHE3 is involved in the acid-waste control system in the kidney, but there hasn't been a good analysis of that process in humans. Part of this acid-control process in the human kidney is "ammoniagenesis" which requires the initial part of the kidney tubule (proximal tubule) to export ammonia/ammonium. Physiologically, it has been assumed that NHE3 can perform a Na+/NH4+ exchange, but this has never been experimentally demonstrated.

Ammoniagenesis and increased renal sodium bicarbonate absorption are partly under the control of the renin-angiotensin-aldosterone system (RAAS), which means that this work enhances understanding of human hypertension. Researchers say their results in fish can be a clue or starting point for analyzing the process in people. Researchers say they hope to continue their work in other species and ultimately further describe the process in humans.

Provided by Mayo Clinic

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