MedicalXpress

Acidic blood not cause of rare disease pRTA, new study reveals

May 1 2019, by Ellen Goldbaum

A University at Buffalo researcher studying a very rare disease characterized by acidic blood has found that most of the symptoms of the condition are caused by something other than low blood pH.

The paper was published in the *Journal of the American Society of Nephrology* on April 30. The research was conducted by a team led by Mark D. Parker, Ph.D., assistant professor in the Department of Physiology and Biophysics in the Jacobs School of Medicine and Biomedical Sciences.

First author on the paper is Emily Salerno, a graduating senior at the University of Notre Dame, who spent a summer working in Parker's lab.

"To be first author as an undergraduate on a publication in a prestigious journal, such as this one, is a noteworthy and unusual achievement," said Parker.

In addition to having a prestigious publication on her resume, Salerno learned firsthand the value of doing research.

"I think it's important for every undergraduate to gain some sort of research experience within the topic they're studying," she said.

"Not only does it connect you with more senior members of the field but you're able to see a whole new side of academia," she said. "You're right on the front lines, helping discover information that no one had before.

Research is the very foundation of everything in science. Medicine would become stagnant without it.

"I liked that even studying just one kind of protein could have a significant impact on disease," she added.

The disease, called proximal renal tubular acidosis (pRTA) is associated with loss of a sodium bicarbonate transporter (NBCe1) and is extremely rare, with only about 15 known cases worldwide. In addition to low blood pH, the disease causes developmental impairments and may lead to tooth loss and vision loss.

"The only treatment is alkali therapy, which literally involves ingesting baking soda tablets to normalize the pH of the blood," said Parker. He noted that the treatment can be very effective in conditions where the only symptom is low blood pH.

"However, the alkali therapy has never been applied to pRTA patients at an early enough age to determine whether it could prevent the developmental impairments. Our research suggests that these symptoms persist even when blood pH is normalized from birth," he said.

To conduct the experiments, the UB researchers developed an animal model analogous to a patient who has been treated with alkali therapy in utero and beyond. The mice have the sodium bicarbonate cotransporter NBCe1 in their kidneys, which is missing from patients with pRTA, so their blood pH is normal, but both in patients and the mice it's missing from all other cells in the body. That means they cannot take bicarbonate up into their cells.

"This mimics the situation where the blood pH has been cured of its defects, but the patient still lacks NBCe1," said Parker.

"In short, we found in these mice nearly every single sign that individuals with this disease have, except the low blood pH. The mice have corneal edema, weak enamel, are short, are underweight and have increased mortality," Parker explained. "So it turns out that few of the signs of this disease are due to acidic blood. Thus, alkali therapy is not a panacea for this disease."

Parker continued that potential therapies that might address symptoms would need to involve replacing the pathway that would allow sodium bicarbonate to get into cells, possibly involving gene therapy.

The research also provides some insights into the genetic mutation that causes the condition. Parker said that some of the scientific literature suggests that this gene, SLC4A4, may also be involved in cystic fibrosis and other more common diseases. For that reason, these results may become relevant to conditions such as kidney failure and osteoporosis that may present with similar symptoms.

The animal model was generated by the Gene Targeting and Transgenic Shared Resource at the Roswell Park Comprehensive Cancer Center.

More information: Emily E. Salerno et al. Extrarenal Signs of Proximal Renal Tubular Acidosis Persist in Nonacidemic Nbce1b/c-Null Mice, *Journal of the American Society of Nephrology* (2019). DOI: 10.1681/ASN.2018050545

Provided by University at Buffalo