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Discovery of gene function may help prevent kidney stones

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The discovery of a gene's function in E. coli and other bacteria might lead to a probiotic to prevent the most common type of kidney stone, according to a Purdue University study.

Human cells can't metabolize oxalate, an acidic chemical found in nearly all plants we eat, so any oxalate we absorb from food must be excreted from the body. Calcium-oxalate urinary stones can form when oxalate reaches a high concentration in the kidneys. About 80 percent of kidney stones are composed of insoluble calcium oxalate.

T. Joseph Kappock, assistant professor of biochemistry, and his research team made the discovery during a study of genes in Acetobacter aceti, a harmless bacterium that is typically used to convert wine to vinegar. Acetobacter aceti, which normally lives on plant tissue, thrives in acidic conditions that easily kill most other bacteria, Kappock said.

The researchers were searching for other acids in addition to acetic acid, the acid present in vinegar, that the bacterium can metabolize.

"We were very excited when we realized E. coli has the same genetic setup as Acetobacter aceti," said Kappock, whose findings were published in the journal *PLOS ONE*.

Kappock and doctoral students Elwood A. Mullins and Kelly L. Sullivan found that Acetobacter aceti and E. coli each contain an enzyme with a previously unknown function, called YfdE in E. coli.

DNA sequencing had identified related genes in each bacterium, but provided little insight about its function.

"When we look at a bacterial genome by DNA sequencing, we can't tell what many of the proteins in the organism do," Kappock said. "I compare it to knowing that a vehicle has an internal combustion engine. You don't know if it's in an Indy car or a diesel truck. DNA sequencing tells us we have an internal combustion engine in this organism, but we don't know what it's for or what it can do."

Many other bacteria have the same genes but don't seem to be capable of using them.

"A few bacteria in the gastrointestinal tract eat oxalate, and we think we know how those work," Kappock said. "But we don't know why so many others are killed by oxalate, even though they have genes that would seem to be able to protect them. Oxalate is a very hard nut to crack. It's a very stable molecule that is difficult to decompose. The enzymes that process it are pretty specialized and don't seem to connect to normal bacterial metabolic pathways in an obvious way."

The researchers determined which chemicals are processed by the YfdE enzyme, following a hunch that it would use oxalate. Their results connected oxalate degradation to the core of bacterial metabolism.

Assigning a function to YfdE may help identify beneficial bacteria that could serve as probiotic agents in the human gastrointestinal tract to reduce the risk of kidney stone formation. Kidney stones, which affect more than 5 percent of the U.S. population, can cause painful blockages of the urinary tract.

"If we understand what bacteria need to degrade oxalate, then we might have a better idea how to identify strains that can do that, and thereby

suppress the uptake of dietary oxalate" he said. "There are probably bacteria out there that have engineered themselves to do this for us."

Genome-sequencing information will increase the speed of the search, Kappock said.

"Because we've figured out what the gene product does, we will be able to find it in any organism and can zero in on those that might be beneficial," he said.

The researchers used X-ray crystallography to pinpoint the most important regions of the YfdE enzyme.

Kappock said the information has other applications, as well. Scientists and engineers who are interested in mapping and reprogramming microbial metabolism now know what one more gene product does.

"Our one piece of the puzzle will help others understand other metabolic networks," he said.

More information: Acetyl-CoA:Oxalate CoA-transferase 1 Function and X-ray Crystal Structure of Escherichia coli YfdE, *PLOS ONE*

Provided by Purdue University