

Common heartburn medications may help fight cancer and other immune disorders in dogs, researchers find

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Dr. Emily Gould, Dr. Abby Ostronic and Dr. Keerthi Bandaru are part of a team at Texas A&M University's School of Veterinary Medicine and Biomedical Sciences studying potential benefits of proton pump inhibitors — medications commonly used to treat heartburn and acid reflux — as a cancer treatment. Credit: Alyssa Moore/Texas A&M University School of Veterinary Medicine and Biomedical Sciences

Researchers at the Texas A&M School of Veterinary Medicine and Biomedical Sciences (VMBS) have discovered that proton pump inhibitors (PPIs)—medications commonly used to treat heartburn and acid reflux in people and animals—may be effective at fighting cancer and other immune disorders in dogs, building on similar ongoing research in human medicine.

Proton pumps are "channels" that regulate how different molecules are distributed throughout bodily systems. While PPIs are designed to inhibit the proton pumps that govern stomach acid production, new research suggests they also may affect other types of pumps, including those in cancer and [immune cells](#).

"While we can't use PPIs alone to treat cancer, we're hopeful that we may be able to improve the effectiveness of chemotherapies by combining them with PPIs sometime in veterinary medicine in the future," said Dr. Emily Gould, a VMBS assistant professor in the Department of Small Animal Clinical Sciences (VSCS). "Using them at certain stages of cancer treatment may improve treatment success."

As [published](#) in the journal *Veterinary Immunology and Immunopathology*, the researchers hope to uncover exactly which cellular systems are affected by PPIs to grant experts in both human and animal medicine a more holistic understanding of their effects.

An acidic connection

Acid isn't important only to the stomach; [cancer cells](#) also prefer an acidic environment.

"Cancer cells have their own microenvironment; acidic conditions help

drive inflammation and metastasis—the growth of additional cancer tumors," Gould explained. "They have their own proton pumps called vacuolar ATPases, or V-ATPases, that, among a lot of other factors, help create those [acidic conditions](#). Our research suggests that PPIs might inhibit these pumps in addition to the ones in gastrointestinal cells."

In addition to creating a pro-tumor microenvironment, V-ATPases are one mechanism some tumors use to assist cancer cells in resisting chemotherapies.

"If we can turn off or stop the ability of cancer cells to resist chemotherapy, we could potentially make those kinds of cancer treatments much more successful," Gould said. "That's where it might be helpful to combine PPIs with chemotherapy."

Immunity toolboxes

One challenge of using PPIs to treat cancer is that they also appear to inhibit proton pumps inside immune cells, including [mast cells](#), a type of white blood cell.

"Mast cells, and other innate immune cells, also have V-ATPase pumps, and they play a role in regulating when the white blood cells release critical molecules that help fight off disease and inflammation," Gould said.

"They keep many of these molecules in what are called granules—they're basically little toolboxes inside the white blood cells. We think that PPIs can inhibit some white blood cells from using their toolboxes effectively.

"Other types of [white blood cells](#) don't have those toolboxes, but that doesn't mean PPIs aren't affecting them, likely via several different

mechanisms," she said. "That's something we want to examine in future studies."

Because PPIs may keep both cancer cells and immune cells from functioning properly, timing will likely be a key element to using PPIs in cancer treatment.

"It all depends on what the immune system is doing," Gould said. "If you have a really bad infection, we wouldn't want you dampening your immune cells with any medication that inhibits them, but in a cancer or immune-mediated disease setting, it could be that these drugs are actually helping the chemotherapy or immunosuppressives be more effective."

Filling in knowledge gaps

PPIs have a long track record of helping patients—both animal and human—manage gastrointestinal problems like [acid reflux](#). However, there is still a lot that scientists don't know about this family of drugs. Trainees such as Drs. Keerthi Bandaru, a doctoral student in the Texas A&M Gastrointestinal Lab, and Abby Ostronic, a VSCS internal medicine resident, are part of the team investigating more about PPIs.

"PPIs can do more than just manage pH levels in the stomach," Gould said. "For example, they also have anti-inflammatory and antioxidant properties.

"This project really began because we wanted to better understand these drugs that we prescribe very commonly in veterinary medicine," she explained. "Then we read about the studies being done in human medicine with PPIs and cancer and decided we need to see how they might translate to helping dogs."

Gould is currently running a clinical trial for dogs with mast cell tumors on their skin to see whether PPIs have a positive effect on reducing side effects of the cancer.

More information: Emily N. Gould et al, Esomeprazole induces structural changes and apoptosis and alters function of in vitro canine neoplastic mast cells, *Veterinary Immunology and Immunopathology* (2022). [DOI: 10.1016/j.vetimm.2022.110539](https://doi.org/10.1016/j.vetimm.2022.110539)

VSCS [Study Pages site](#)

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