Researchers say chemo drug may prevent heart failure

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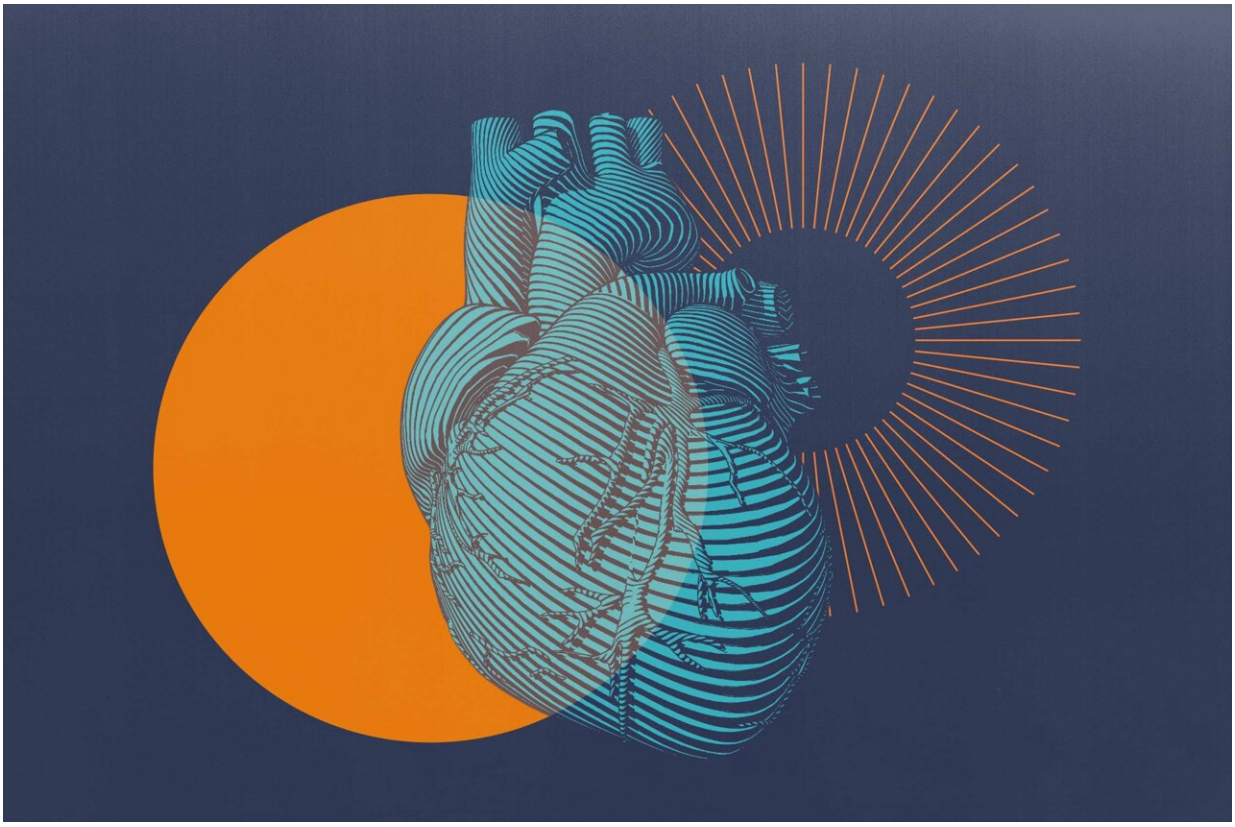

A sophisticated computer model created by UVA Health researchers led to the discovery of how a cancer drug could also be used to fight heart failure. Credit: Emily Faith Morgan, University Communications

A chemotherapy drug used to fight bone-marrow cancer has the potential to treat and prevent potentially deadly heart failure, a powerful

new drug-screening tool developed at UVA Health suggests.

The tool was created by University of Virginia researchers Jeffrey J. Saucerman and graduate student Taylor G. Eggertsen. The sophisticated computer model suggested the drug midostaurin could help prevent the enlargement of heart muscle cells that often precedes heart failure. Subsequent lab results bore that out.

While additional human testing is needed, Saucerman says the new computer model has demonstrated great potential for identifying already available drugs that can be repurposed to battle heart failure, a condition affecting millions of Americans.

"This new computer tool helps us find new uses for old drugs, and it also explains how they may work in the heart," Saucerman said. "New drugs take decades to develop. We hope this tool will help us find drugs for heart failure that are already known to be safe and effective for other diseases."

The researchers have published their findings in the *British Journal of Pharmacology*.

Heart failure is a progressive condition that grows worse with time. The heart loses the ability to pump blood, which can lead to fatigue, wheezing, weakness, swollen legs and feet and, ultimately, death.

While there are drugs used to treat heart failure, more than half of people with the condition die within five years of diagnosis. That speaks to how urgently new and better treatments are needed.

With that in mind, Saucerman and Eggertsen created a complex computer model of the harmful growth of heart muscle cells prior to heart failure. This model allowed them to run sophisticated simulations

demonstrating how existing drugs would affect the process known as cardiac hypertrophy.

"This approach has identified a number of drugs that show initial promise for heart disease that we would not have suspected," Eggertsen said.

The researchers screened more than 250 candidate drugs and found 38 that slowed the harmful heart changes. In addition, the model let the scientists understand how the drugs were having this effect, helping the researchers narrow their options. They then tested the most promising drugs in heart muscle cells. They ultimately found that midostaurin, a chemotherapy drug used to treat acute myeloid leukemia, a cancer of the blood and bone marrow, had the potential to slow the damaging changes to the heart.

"Now that we have found interesting drugs in computer simulations and heart muscle cells, we plan to test these drugs in experimental models that are more similar to humans," said Saucerman, who is part of UVA's Department of Biomedical Engineering, a joint program of the School of Medicine and School of Engineering.

"This computational treasure hunt for drugs may eventually lead to more options for treating heart failure patients," he said.

More information: Taylor G. Eggertsen et al, Virtual drug screen reveals context-dependent inhibition of cardiomyocyte hypertrophy, *British Journal of Pharmacology* (2023). DOI: 10.1111/bph.16163

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