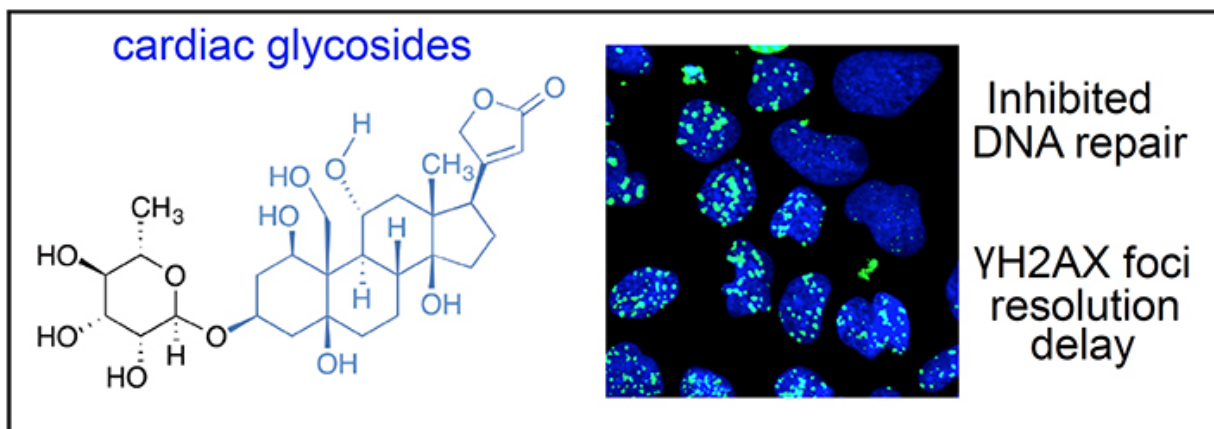


Team screens cardiac drugs that also attack cancer

March 14 2016, by Jim Shelton



Several drugs now being used to treat heart failure and atrial arrhythmia also show promise as DNA disruptors in cancer cells and could be readily repurposed as anticancer agents, according to a new study by Yale researchers.

Cardiac glycosides, which are bioactive natural products found in certain plants and insects, aid in cardiac treatment because they cause the heart to contract and increase [cardiac output](#). They are used in prescription medications such as Digoxin and Strophanthin.

Now researchers at Yale have also discovered that cardiac glycosides block the [repair](#) of DNA in tumor [cells](#). Because [tumor cells](#) are rapidly dividing, their DNA is more susceptible to damage, and inhibition of DNA repair is a promising strategy to selectively kill these cells. Several other researchers have noted that cardiac glycosides possess anticancer properties, but the basis for these effects was not well known. The Yale scientists showed that cardiac glycosides inhibit two key pathways that are involved in the repair of DNA.

"We performed a high-content drug screen with the Yale Center for Molecular Discovery, which identified some interesting cardiac drugs that affect DNA repair," said Ranjit Bindra, assistant professor of therapeutic radiology and of pathology at the Yale School of Medicine. "This has many therapeutic implications for new cancer drugs."

Bindra and Yale professor of chemistry Seth Herzon are the principal investigators of the study, which appears in the *Journal of the American Chemical Society*. Herzon and Bindra also are members of the Yale Cancer Center.

"Our approach focused on damaging the [cancer cells'](#) DNA using radiation, and then measuring the rate of repair in the presence of different compounds. All in all, we evaluated 2,400 compounds," Herzon said. "Surprisingly, we think that the cardiac glycosides inhibit the retention of a key DNA repair protein known as 53BP1 at the site of DNA double-strand breaks. This is a very interesting activity that was unexpected."

Herzon and Bindra said the same approach can be applied to screen hundreds of thousands of compounds. "We are partnering with industry to gain access to their large compound collections. Not only will this help us find new [anticancer agents](#), it can help us elucidate more of the fundamental biology underlying DNA repair," Herzon said. The next

step in their research will be to improve the cancer-fighting properties of cardiac glycosides, while modulating their other biological effects.

Provided by Yale University

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