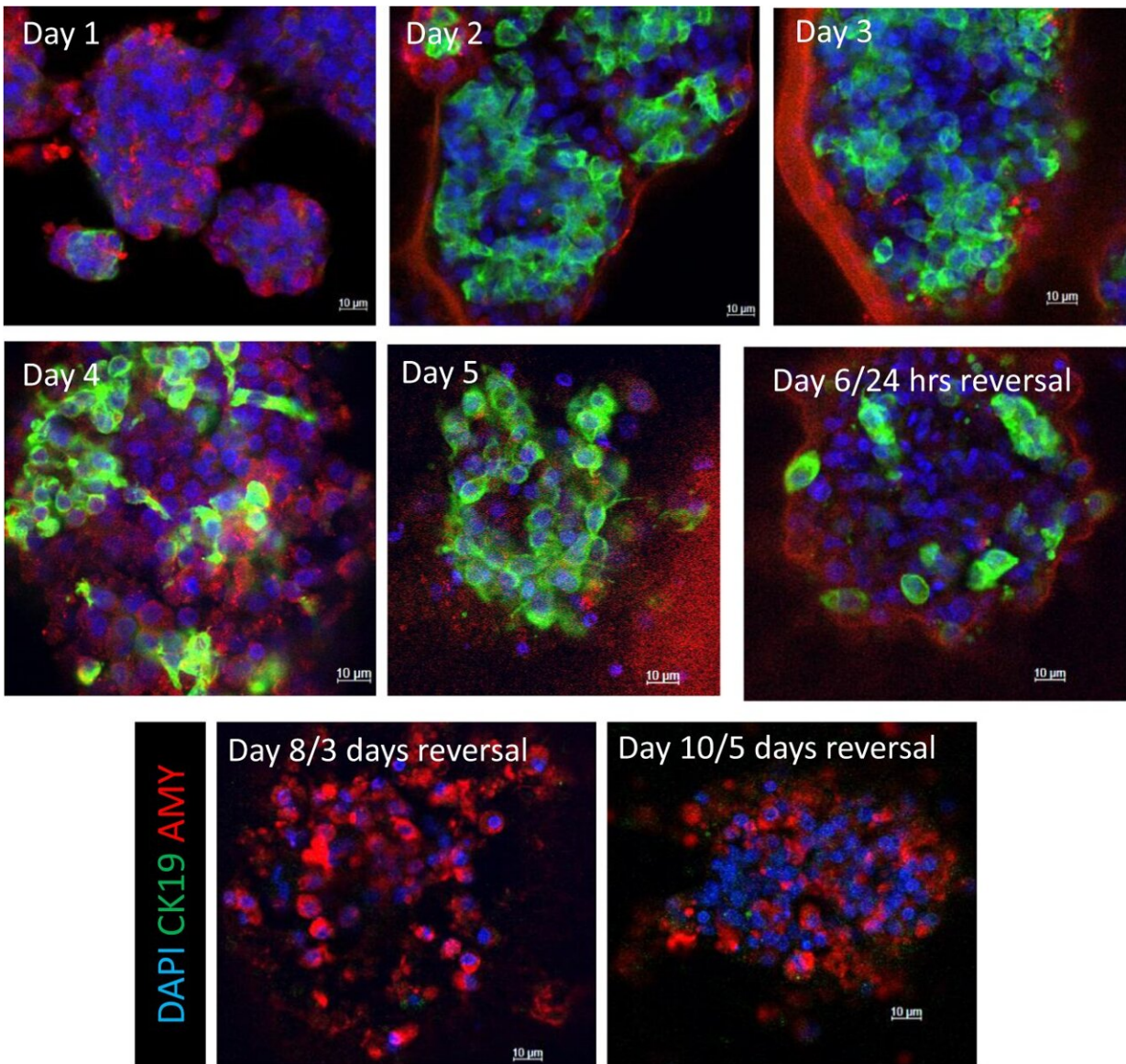


Two drugs reverse a key pancreatic cancer step in the lab

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Reversal of ADM by TSA in primary human acinar cultures. Primary, human

acini were cultured in Matrigel on glass chamber slides for 5 days. On day 5 of culture, 500 nM of TSA was added and the cells were cultured for 5 additional days. The cells were processed for immunohistochemistry and imaged for amylase (red) and KRT19 (green) using confocal microscopy. Credit: *Cell Death Discovery* (2022). DOI: 10.1038/s41420-022-01165-4

Pancreatic cancer often lurks as a silent disease. With no known symptoms, it can progress undetected and spread to other organs.

According to the National Cancer Institute, more than 60,000 Americans will be diagnosed with [pancreatic cancer](#) this year, and only about 1 in 10 of those diagnosed will survive the next five years. The disease ranks as the third leading cause of [cancer](#) deaths in the U.S. because it is rarely detected in the early stages when treatment options are most effective.

Pancreatic cancer's stealth-like nature has the attention of University of Florida scientists, who have discovered a way to reverse a key cellular process involved in its progression. Their study, "Pharmacological Inhibition and Reversal of Pancreatic Acinar Ductal Metaplasia," was published in the journal *Cell Death Discovery*.

The UF researchers identified two [small molecules](#) that inhibit precancerous cell progression. The molecules also reversed a process known as acinar ductal metaplasia, or ADM, which precedes pancreatic cancer.

"To our knowledge, this is the first time researchers have been able to pharmacologically reverse ADM," said Tom Schmittgen, Ph.D., the study's senior author and chair of the department of pharmaceuticals in the UF College of Pharmacy, part of UF Health, the university's academic health center. "With these compounds, we could potentially treat a

pancreatic cancer patient at an earlier stage of the disease and hopefully improve the treatment options available."

ADM often occurs when [inflammation](#) is present. It is a defense mechanism to avoid having the pancreas make too many digestive enzymes and destroy itself. During ADM, stable, enzyme-making [acinar cells](#) turn into protective ductal [cells](#) that line the pancreatic duct. If certain genes mutate during the transition, then the cells can become precancerous and eventually develop into cancer.

To study ADM, UF scientists built a laboratory model using [animal cells](#) with pancreatic cancer and tissue from a healthy human. They introduced the cells to two compounds—one of which was developed by Chenglong Li, Ph.D., the Nicholas Bodor Professor in Drug Discovery in the UF College of Pharmacy. The ductal cells responded by changing back to acinar cells. Pancreatic cancer can be prevented when acinar cells are maintained in their natural state.

"The findings are significant because we have now demonstrated that ADM can be reversed using drugs," said Schmittgen, who also serves as the V. Ravi Chandran Professor of Pharmaceutical Sciences in the UF College of Pharmacy. "This research may lead to developing treatments for patients who are at a high risk for pancreatic cancer development."

Schmittgen hopes this discovery will encourage scientists to think about new ways to treat pancreatic cancer by manipulating ADM. Future research will involve testing other compounds in collaboration with Hendrik Luesch, Ph.D., a co-author of the study and a professor and chair of medicinal chemistry and the Debbie and Sylvia DeSantis Chair in Natural Products Drug Discovery and Development in the UF College of Pharmacy. These compounds may prove to be more effective, as scientists seek new treatments for a disease with very few treatment options.

More information: Lais da Silva et al, Pharmacological inhibition and reversal of pancreatic acinar ductal metaplasia, *Cell Death Discovery* (2022). [DOI: 10.1038/s41420-022-01165-4](https://doi.org/10.1038/s41420-022-01165-4)

Provided by University of Florida

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