

Potential drug candidates halt prostate and breast cancer growth

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March 9, 2017 - Scientists on the Florida campus of The Scripps Research Institute (TSRI) have designed two new drug candidates to target prostate and triple negative breast cancers.

The new research, published recently as two separate studies in *ACS Central Science* and the *Journal of the American Chemical Society*, demonstrates that a new class of drugs called small molecule RNA inhibitors can successfully target and kill specific types of [cancer](#).

"This is like designing a scalpel to precisely seek out and destroy a cancer—but with a pill and without surgery," said TSRI Professor Matthew Disney, senior author of both studies.

A Tool to Fight Prostate Cancer

RNAs are molecules that translate our genetic code into proteins. RNA defects can lead to cancers, amyotrophic lateral sclerosis (ALS), myotonic dystrophy and many other diseases.

In their *ACS Central Science* study, Disney and his colleagues used DNA sequencing to evaluate thousands of small molecules as potential drug candidates. The researchers were on the lookout for molecules that could bind precisely with defective RNAs—like keys fitting in the right locks.

This strategy led them to a compound that targets the precursor molecule to an RNA called microRNA-18a. This RNA had caught the attention of scientists who found that mature microRNA-18a inhibits a protein that suppresses cancer. When microRNA-18a is overexpressed, cancers just keep growing.

Disney and his team tested their compound, called Targapremir-18a, and found that it could target microRNA-18a and trigger [prostate cancer](#) cell death.

"Since microRNA-18a is overexpressed in [cancer cells](#) and helps to maintain them as cancerous, application of Targapremir-18a to cancer cells causes them to kill themselves," Disney said.

Disney said the precise binding of Targapremir-18a to microRNA-18a means a cancer drug that follows this strategy would be likely to kill [prostate cancer cells](#) without causing the broader side effects seen with many other cancer therapies.

And there may be even bigger implications. "We could apply the strategy used in this study to quickly identify and design small molecule drugs for other RNA-associated diseases," explained study first author Sai Velagapudi, a research associate in the Disney lab.

Testing the Strategy in Breast Cancer

The same screening strategy led the researchers to a drug candidate to target triple negative breast cancer, as reported in the Journal of the American Chemical Society.

Triple negative breast cancer is especially hard to treat because it lacks the receptors, such as the estrogen receptor, targeted with other cancer drugs. The Disney lab aimed to get around this problem by instead

targeting an RNA called microRNA-210, which is overexpressed in solid breast cancer tumors.

The researchers tested their drug compound, Targapremir-210, in mouse models of triple negative [breast cancer](#). They found that the therapy significantly slowed down tumor growth. In fact, a single dose decreased tumor size by 60 percent over a three-week period. The researchers analyzed these smaller tumors and discovered that they also expressed less microRNA-210 compared with untreated tumors.

Targapremir-210 appears to work by reversing a circuit that tells cells to "survive at all costs" and become cancerous. With microRNA-210 in check, cells regain their normal function and cancer cannot grow.

"We believe Targapremir-210 can provide a potentially more precise, targeted therapy that would not harm healthy cells," said study first author TSRI Graduate Student Matthew G. Costales.

Next, the researchers plan to further develop their molecule-screening strategy into a platform to test molecules against any form of RNA defect-related disease.

Provided by The Scripps Research Institute

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