

Why combination drug treatment ineffective in cancer clinical trials

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Medical researchers at the University of Alberta have discovered that combination drug therapy didn't work well in clinical trials for cancer patients because one drug was making the other drug ineffective.

Faculty of Medicine & Dentistry researcher Michael Sawyer and his colleagues, including first author Vijaya Damaraju, recently published their findings in the peer-reviewed journal, *Clinical Cancer Research*.

In the '80s and '90s, cancer research focused on finding out which proteins "drove" cancers. New drugs targeting these proteins worked well by themselves, and some in the field believed combining the new drugs with the older chemotherapy drugs would work better than either drug by itself.

"So the pharmaceutical industry developed a combination of drugs in which we thought we were giving two drugs at once, but in actual fact the one drug we were giving was completely blocking the actions of the other drug," said Sawyer, who works in the Faculty's Department of Oncology.

"The old chemotherapy drugs required special proteins to get inside of cells to work. What our team discovered is that the new chemotherapy drugs prevented these proteins from carrying the old [chemotherapy drugs](#) into the cell. No one was able to figure out why this combination of drugs didn't work, but now we have discovered what went wrong." Sawyer says the findings will guide oncologists about how [cancer](#) drugs should be combined, or whether certain drugs should be combined at all.

"This will save us from doing millions of dollars in [clinical trials](#) that have no chance of working out. These findings show oncologists we have to be careful about which drugs should be combined. You have to think about how they actually work,

especially in ways which no one understood before.

"Our research was actually like peeling an onion. Once we figured out the answer to one question, then other things the drugs did make more sense. Ultimately, the findings mean we'll be able to design better combination drug therapies. We'll know which drugs to combine, and when and how drugs can be combined. This will require more precise scheduling and dosing than what we've done to date."

He stressed the only patients impacted were those in clinical trials – the [combination drug](#) therapy had not yet become common clinical practice because it wasn't working the way oncologists had hoped. And for those patients who took part in the clinical trials, the one chemotherapy [drug](#) was still very effective – so those patients still received excellent care and drugs that properly targeted their cancers.

Sawyer and his team are continuing their research in this area. Their research was funded by the former Alberta Cancer Board, the Alberta Cancer Foundation and Alberta Innovates – Health Solutions.

Provided by University of Alberta Faculty of Medicine & Dentistry

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