

**JOHN COPLAND:** Hi I'm Dr. John Copland. Everyone calls me Al. I'm a cancer biology researcher and faculty member at Mayo Clinic in Jacksonville, Florida.

We've just made some recent discoveries that will be published soon related to thyroid cancer, and it's actually the most deadly thyroid cancer, called anaplastic thyroid carcinoma. It's rare, thank goodness. But if you're diagnosed with this cancer, it's almost like a death sentence within months.

And we currently have a phase-two clinical trial ongoing in this rare cancer. Dr. Bob Smallridge, who I collaborate with, is the national principal investigator of this trial, testing two drugs in combination, efatutazone and paclitaxel, which we most often refer to as Taxol. And in the laboratory, we've been trying to improve to see if we can improve upon this combination therapy with paclitaxel and had come across these inhibitors called HDAC inhibitors.

HDACs are proteins that bind to DNA and suppress gene transcription and enhance tumor growth. So there are now inhibitors that are FDA approved for cancer therapy. And we had found that these HDAC inhibitors can synergize with paclitaxel in inhibiting tumor growth in these anaplastic thyroid cancers.

Interestingly, though, we had tested a number of HDAC inhibitors, and some worked and some didn't. And this is the basis of our publication, where we've identified the mechanism by which they work. And so HDAC inhibitors that up regulate this gene called BIM will synergize with paclitaxel and enhance its ability to kill tumor cells and have what we call anti-tumor synergy and have a greater effect when these two agents are combined. And so it's important to know which HDAC inhibitors you're going to test. And so this is another therapeutic direction that we're going in currently to see if we can enhance our ability to increase survival of patients diagnosed with this deadly cancer.

The significance of this is our ability to better design trials with more effective HDAC inhibitors in combination with paclitaxel. And, also, knowing the molecular mechanisms of this signaling pathways, we can now predict whether an HDAC inhibitor will synergize with paclitaxel. And this also has benefits in other cancers that are responsive to HDAC inhibitors and can clearly benefit other cancers as well. The HDAC inhibitors are now being tested clinically in solid cancers and clearly will need to be used in combination with other therapies. And so these findings will clearly help guide clinicians in selection of HDAC inhibitors in combination with other drugs that may benefit patient survival.