

Cancer cell line developed that is resistant to new cancer therapy

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Cancer cell line developed that is resistant to new cancer therapy. Credit: Medical College of Georgia

A cancer cell line that is resistant to one of the newest classes of cancer treatments has been developed by researchers who already are using it to determine what else to give patients when this happens.

“The ultimate goal is to be able to understand how cancer cells develop resistance and to have forward-thinking strategies about how to combat that resistance,” says Dr. Warren Fiskus, postdoctoral fellow in the laboratory of Dr. Kapil Bhalla, director of the Medical College of Georgia Cancer Center.

Resistant cells emerged by treating human leukemic cells with regular, increasing doses of histone deacetylase, or HDAC, inhibitors, similar to what patients would receive. “At each dose level, there were some cells that did die,” says Dr. Fiskus. “Ultimately, we isolated a population of cells that were resistant to very high concentrations of these agents and other agents in the same class.”

Dr. Fiskus is presenting the findings Dec. 11 during the American Society of Hematology’s 49th Annual Meeting and Exposition in Atlanta.

They found the HDAC inhibitor-resistant cell line resistant to many therapies, including more standard treatment such as chemotherapy, but highly sensitive to heat shock protein 90, or hsp90, inhibitors, another emerging cancer treatment.

“As part of their resistance mechanisms, they acquired greater sensitivity to hsp90 inhibitors,” says Dr. Bhalla, Cecil F. Whitaker Jr., M.D./Georgia Research Alliance Eminent Scholar in Cancer. “This creates a potential combination that can be tested in mouse models and ultimately clinical trials.”

HDAC and hsp90 inhibitors are both being studied in combination with other cancer therapies but not each other. However the MCG researchers, who already have published work indicating a synergistic effect, were not surprised by what they found.

“Resistance to HDAC inhibitors is going to emerge, so you need a cellular model to understand mechanisms of resistance and an in vivo model, a mouse model typically, to test new combinations you design based on studies in culture,” says Dr. Bhalla.

The researchers have put the cell line into a mouse model and other scientists already are asking for the resistant cell line, he says.

“This particular cell line can be used to really look at newer agents and new combinations in vitro and in vivo and see if they are safe and effective together,” Dr. Fiskus says.

Heat shock proteins are protein caretakers, activating genes that ultimately make proteins, move them around cells and fold them into shape for proper function. Misfolded proteins can cause cancer.

MCG is participating in an early-phase clinical trial of the oral HDAC inhibitor, LBH589, developed by Novartis Corp. Studies also are underway for some innovative uses of hsp90 inhibitors, including Dr. John Catravas’ studies of its potential as an anti-angiogenesis agent and Dr. Abdullah Kutlar’s studies to see if it can reduce morbidity and related lung problems in sickle cell disease by suppressing inflammation.

Source: Medical College of Georgia

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