New study shows promise for preventing therapy resistance in tumor cells

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A new study led by University of Kentucky researchers suggests that activating the tumor suppressor p53 in normal cells causes them to secrete Par-4, another potent tumor suppressor protein that induces cell death in cancer cells. This finding may help researchers decipher how to inhibit the growth of tumors that have become resistant to other treatments.

Loss of the tumor suppressor p53 often contributes to therapy resistance in tumors. In the study, published in *Cell Reports*, the University of Kentucky's Vivek Rangnekar and his colleagues activated wild type p53 in normal cells to trigger cell death in the p53-deficient cancer cells. Because p53 is intact and functional in normal cells, the researchers harnessed its potential to inhibit the growth of p53-deficient cancer cells.

This paracrine effect was brought about by the tumor suppressor Par-4, which specifically kills cancer cells. Although other tumor suppressors exist, what makes Par-4 so special is that it is not mutated as frequently as other known suppressors, and it's "selective" in its actions in that Par-4 will only kill cancer cells and not normal cells. Importantly, it's secretion from normal cells can be induced by activating p53 so that Par-4 enters circulation, thereby potentially targeting tumor cells at distant sites.

"As normal cells far outnumber the cancer cells in patients, we sought to empower the normal cells to trigger cell death in p53-deficient cancer

cells," said Rangnekar, associate director of transdisciplinary collaborations for the UK Markey Cancer Center. "Our findings have potential for targeting local, as well as metastatic tumors, and future studies will use FDA-approved drugs to induce Par-4 secretion."

Provided by University of Kentucky