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# Targeted cancer therapy kills prostate tumor cells

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A new targeted therapy for prostate cancer halts tumor growth in animals with advanced prostate cancer that is resistant to hormone therapy, a new study finds. The results will be presented Saturday at The Endocrine Society's 93rd Annual Meeting in Boston.

"This targeted therapy may provide a treatment breakthrough that will extend the lives of men with advanced, hormone-refractory prostate cancer," said lead investigator Shuk-mei Ho, PhD, chairwoman of the Department of Environmental Health at the University of Cincinnati.

Men with prostate cancer that has recurred or has spread outside the prostate routinely receive androgen deprivation therapy, which blocks the action of the male hormones. This castration occurs through surgical removal of both testes or more often with medications. Although effective, this hormone-blocking treatment eventually stops working in some patients, Ho said.

"These patients are left with very few treatment options and usually succumb quickly to the disease," she said.

Ho's team previously found they can inhibit the growth of prostate cancer cell lines in culture by targeting and activating a protein called G protein-coupled receptor 30 (GPR30) using the experimental drug G-1, a GPR30 agonist, or stimulator.

In their new study, funded by the Veterans Affairs and the National

Institutes of Health, Ho and her co-workers tested G-1 in an animal model of castration-resistant prostate cancer. They implanted human prostate cancer cells beneath the skin of male mice. The established tumor regressed upon castration and after the cancer relapsed, they injected the mice with a low dose of G-1. They also gave G-1 to noncastrated, or "intact," male mice that had prostate tumors. In these intact mice that still had male hormones, G-1 did not stop growth of the prostate tumors or cause substantial death of tumor cells (necrosis), they found.

"Surprisingly, G-1 was highly effective in halting the growth of the tumors that re-emerged after castration," Ho said.

The castration-resistant tumors showed a 65 percent necrosis. These mice had increased expression of GPR30 after castration, which Ho believes sensitized prostate tumors to the cell growth-inhibiting effects of G-1.

"These results mean G-1 won't work without androgen deprivation therapy," she said.

Therefore, Ho reported, the window of time when this targeted therapy might be effective for treating hormone-resistant prostate cancer is after androgen deprivation therapy. She said she believes G-1 can make androgen blockade more effective. G-1 caused no harm to the prostate or other vital organs in mice, she added.

Although GPR30 may have a role in cell growth in female tissues, Ho said it appears to have the opposite effect in men with hormone-resistant prostate cancer. "The beauty of this GPR30 is that it does not have any estrogen, and so it will not cause any side effects of estrogen," she said.

Provided by The Endocrine Society