Investigational agent shows promise in reducing spread of prostate cancer

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A drug developed to treat Ewing's Sarcoma, a rare childhood cancer, may also help prevent human prostate cancer from spreading, as seen in new lab studies say researchers at Georgetown Lombardi Comprehensive Cancer Center, a part of Georgetown University Medical Center (GUMC).

Published online April 29 in PLoS ONE, the researchers report that if the agent continues to work well in further laboratory and preclinical studies, it may be the first prostate cancer drug specifically designed to stop cancer spread, or metastasis.

"This agent does not kill prostate cancer cells, but limits their ability to spread, which could be hugely beneficial in patients," says the study's lead investigator, Aykut Üren, M.D., an associate professor at Georgetown Lombardi. "This study is an early proof of principle that such an approach might be feasible in the clinic, but we have a lot of work to refine and test the drug."

The agent, YK-4 279, was designed in the GUMC Drug Discovery Program, directed by Milton Brown, M.D., Ph.D., a co-author on the paper. YK-4 279 is also being investigated for the treatment of Ewing's sarcoma and is expected to move quickly into a clinical study. Üren participated in the development of YK-4 279, an effort that was led by Georgetown Lombardi researcher Jeffrey Toretsky, M.D., also a co-author of this study.

Recent research has shown that 40 to 70 percent of prostate cancer cells express novel proteins when normal genes such as ETV1 and ERG break off from a chromosome and fuse in to a new location. These new genes produce proteins that push prostate cancer cells to become more aggressive and spread.

Noting that Ewing's sarcoma is produced by a similar fusion gene, the researchers decided to see if their drug would work in prostate cancer cells.

They applied the agent to prostate cancer cells with chromosomal translocations that expressed either an ERG protein or an ETV1 protein and found that the YK-4 279 did inhibit functions of these proteins, which reduced their motility and invasiveness. Tests in cancer cells that did not have either translocation show the agent had no effect.

The researchers also found that although the male hormone androgen turns on genes involved in progression of prostate cancer, including these fusions genes, the presence or absence of androgen is not necessary for this agent to work.

"That means, if successful, YK-4 279 could work in androgen sensitive prostate cancer cells or in cancer that has become resistant to androgen treatment," Üren says.

He says the agent will likely need to be reformulated for prostate cancer use since the fusion gene that causes the Ewing's sarcoma is similar but not identical to ones in prostate cancer.

Provided by Georgetown University Medical Center