New medication treats drug-resistant prostate cancer in the laboratory

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A new drug called pyrvinium pamoate inhibits aggressive forms of prostate cancer that are resistant to standard drugs, according to a study conducted in an animal model. The results will be presented Monday at The Endocrine Society's 95th Annual Meeting in San Francisco.

"Our novel prostate cancer drug works by a unique mechanism of action," said study lead author Jeremy Jones, PhD, assistant professor of molecular pharmacology at City of Hope, Beckman Research Institute, in Duarte, CA. "Thus, it has the potential to treat cancers resistant to currently approved therapies."

Prostate cancer is the second-leading cause of cancer death, after lung cancer, among men in the United States, according to the American Cancer Society. The disease affects about one out of every six men, and more than 29,000 will die of prostate cancer this year alone.

An age-related disease, prostate cancer usually affects men who are 65 or older. In addition to advanced age, genes and certain environmental factors influence the development of prostate cancer, although the exact causes remain unknown.

In a healthy prostate gland, cells express a protein called androgen-receptor, or AR, which is activated by male sex hormones, or androgens, including the primary male hormone testosterone. These same receptors also play a role in promoting the growth of the abnormal cells of prostate cancer.

The drugs that are currently available to treat prostate cancer work by preventing androgen from binding to the AR. Specifically, the drugs block androgen from attaching to a certain part of the AR known as the ligand-binding domain. This domain is the part of the receptor that hormones bind to when they activate the receptor. By blocking all androgen activity, these drugs induce chemical castration.

The problem is that prostate-cancer cells usually become resistant to androgen blockage. After initially responding, these aggressive cancers develop mutations that enable them to spread, or metastasize, without the influence of androgens. For this reason, these aggressive prostate cancers are called castration-resistant.

In contrast, the study drug binds to a different part of the AR that does not require androgen, according to Jones. "Our new lead compound, pyrvinium pamoate, works by a unique mechanism that involves binding to a different site on the AR and inhibiting its activity without preventing androgen binding," he said. "We are hopeful that an optimized derivative of pyrvinium will be able to inhibit all AR activity and inhibit the growth of human prostate cancers that become resistant to other AR-targeted therapies and perhaps result in a curative metastatic prostate cancer therapy."

Investigators conducted this pre-clinical study using prostate-cancer cells in an animal model.

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