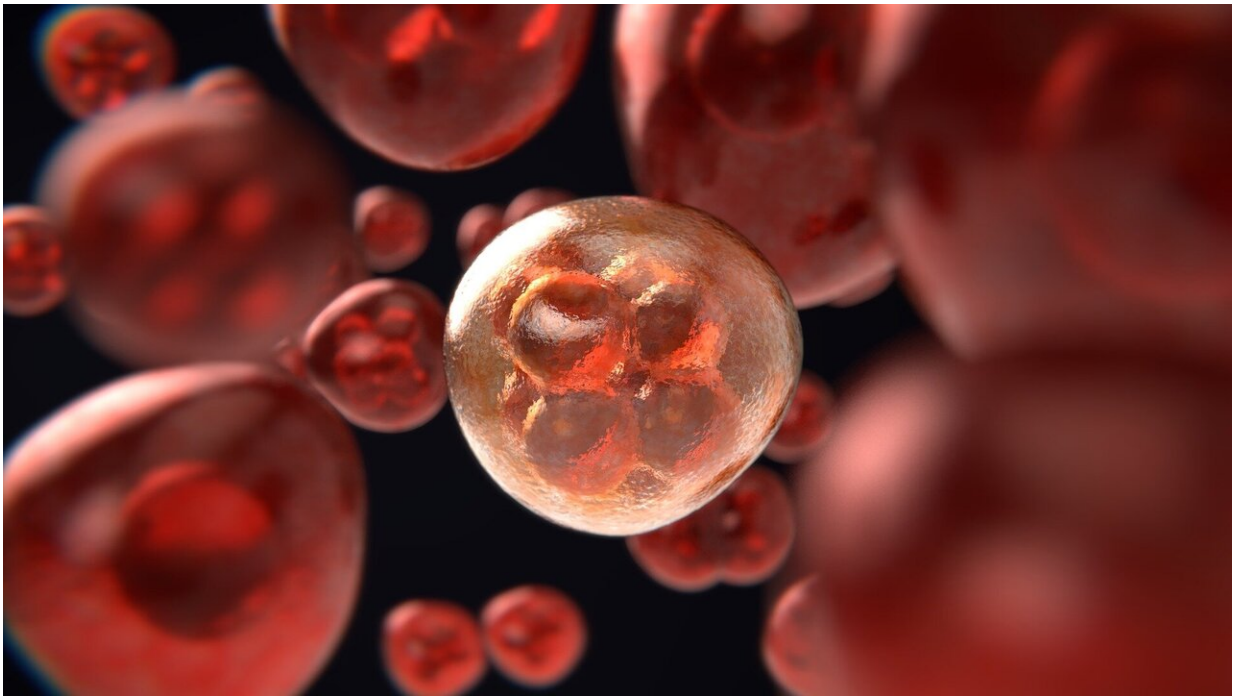
Anti-androgen therapy can fuel spread of bone tumours in advanced prostate cancer

July 7 2021



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Anti-androgen therapy is commonly used to treat patients with advanced prostate cancer at stages where the disease has spread to the bones.

However, new research reveals that anti-androgen treatment can actually facilitate prostate cancer cells to adapt and grow in the bone tumor microenvironment model, which has been developed by QUT

biomedical scientists led by Dr Nathalie Bock.

Dr. Bock, under the mentorship of Distinguished Professor Dietmar Hutmacher, from QUT Centre for Biomedical Technologies, has focused her research on bone metastases from breast and prostate cancers.

She developed 3-D miniature bone-like tissue models in which 3-D printed biomimetic scaffolds are seeded with patient-derived bone cells and tumor cells to be used as clinical and preclinical drug testing tools.

The research team investigated their hypothesis that traditional anti-androgen therapy had limited effect in the microenvironment of prostate cancer bone tumors. The team's findings are published in *Science Advances*.

"We wanted to see if the therapy could be a contributor of cancer cells' adaptive responses that fuelled bone metastasis," Professor Hutmacher said.

"We developed an all-human, microtissue-engineered model of metastatic tissue using human bone-forming cells, prostate cancer cells and 3-D printing."

Cancer biologist Distinguished Professor Judith Clements said the team bioengineered the microenvironment of a bone tumor to assess the effects of two clinically routinely used anti-androgen therapies—enzalutamide and bicalutamide—on the tumor cells.

"We found that the interactions between the cancer cells, the bone and the anti-androgens significantly impacted the progress of cancer in the mineralised microenvironment of bone tumors," Professor Clements said.

"This means that the efficacy of these therapies is compromised in the presence of the bone microenvironment."

Professor Hutmacher said an important outcome of the study was the need to upscale the bone tumor microenvironment model platform and make it available to other research groups.

"This would enable the prostate cancer research community to develop therapies for a more effective treatment of advanced prostate cancer."

In future, Dr. Bock will use her model with patient-derived cells from patients undergoing prostatectomy, so that it could be used as a personalized preclinical diagnostic and drug testing tool.

"By screening existing and novel drugs using the bone tumor model in the laboratory, doctors will be able to treat individual patients with an anti-cancer therapy that can best suit their clinical need," Dr. Bock said.

"This has the potential to considerably improve the quality of life of patients, because patients will not have to trial a succession of drugs, each of which carry the potential of severe side-effects, and which may not work for them."

This research was supported by the National Health & Medical Research Council of Australia, Australian Research Council and the Prostate Cancer Foundation of Australia.

Prostate Cancer Foundation of Australia CEO Professor Jeff Dunn AO said the findings were significant.

"This is an important discovery that will help us to better target treatments for men with different types of prostate cancer," he said.

"The findings also demonstrate the importance of ongoing research to improve our understanding of how different treatments impact disease progression and spread.

"Notably, Australia has one of the highest incidence rates of prostate cancer internationally, with 1 in every 6 Australian men likely to be diagnosed during their lifetime and around 17,000 men diagnosed each year.

"While survival rates for prostate cancer are high, with over 95% of men likely to survive at least five years, we must keep up the pace of work to find curative treatments, especially for advanced disease in the bone.

"There can be no doubt that this research will build on previous discoveries to help us save lives by stopping cancer from spreading and claiming the lives of more than 3,000 men a year, as is currently the case.

"We commend the research team and congratulate PCFA grant recipient Dr. Nathalie Bock for her research achievements.

"This is Australian research excellence at its finest," he said.

More information: Nathalie Bock et al, In vitro engineering of a bone metastases model allows for study of the effects of antiandrogen therapies in advanced prostate cancer, *Science Advances* (2021). DOI: 10.1126/sciadv.abg2564

Provided by Queensland University of Technology