

Study shows why prostate cancer cells develop resistance to treatment

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A new study at the University of York has shown that a standard hormone supplement, used to boost energy levels in prostate cancer patients following radiotherapy, could potentially increase the chances of the cancer returning.

Previous studies led by Professor Norman Maitland at the University's Department of Biology, have shown that stem cells inside the cancer are resistant to radiotherapy treatment. This means that the bulk of the cancer dies following treatment, but the 'core' does not, increasing the risk of the cancer returning.

Until now, however, it was not clear why stem cells - which are present in all cells of the body - should survive when the rest of the cell is killed off by radiotherapy. Using [cancerous cells](#) from patients diagnosed with prostate cancer, researchers showed that proteins called SMARCs, inside the stem cells, help to keep the 'core' of the cancer alive.

The research team, including York scientists Dr Jayne Rane and Dr Holger Erb, were surprised to find, however, that [cancer cells](#) that had been treated in the laboratory with a glucocorticoid hormone, which is normally administered to patients in tablet form to boost [energy levels](#) following radiotherapy, became more resistant to cancer treatment.

Professor Maitland said: "This was a really unexpected result of our investigation, so we took a slightly different direction in order to find out why these stem cells would become more resistant to [cancer treatment](#)."

Tiny molecules that respond to changes in the body are present in all 'normal' cells and can be regulated by hormones. These are kept at very low levels in [cancer stem cells](#). The researchers found, however, that any increase in these molecules, called MicroRNAs, impacts on the levels of SMARCs in the stem cells.

Professor Maitland continued: "When more glucocorticoid hormones are ingested, the levels of MicroRNAs decrease even further, resulting in an increase in SMARCs. These SMARC proteins wind up chromosomes inside the cancer cells to make them resistant to treatment.

"Hormone injections to counter the energy-sapping effects of radiotherapy and chemotherapy have been a standard part of after-care for 15 years or more, so we were surprised to find that the treatment was actually to the detriment of radiotherapy."

When the researchers looked at what would happen if the natural levels of glucocorticoids were blocked, they saw an increase in the number of MicroRNAs and the expected decrease in the levels of SMARCs. It is now possible that the same radiotherapy dose could kill more cancer stem cells - the root of cancer recurrence after treatment.

Professor Maitland added: "We now need to move into clinical trials to see whether blocking, rather than boosting, the glucocorticoid in patients could bolster the success rate of [radiotherapy](#). It would ultimately mean that the patient is more tired after treatment, but there are other non-hormone treatments that could be used to improve energy levels that would not interfere with how we now believe [stem cells](#) to behave in cancer."

More information: Jayant K. Rane et al. Inhibition of the glucocorticoid receptor results in an enhanced miR-99a/100-mediated radiation response in stem-like cells from human prostate cancers,

Oncotarget (2014). [DOI: 10.18632/oncotarget.10207](https://doi.org/10.18632/oncotarget.10207)

Provided by University of York

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