

## Antibiotic effective in breast cancer clinical trial

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Scientists fighting cancer have carried out the first successful trial of the effects of the antibiotic Doxycycline on cancer recurrence in patients after surgery.

Breast <u>cancer patients</u> were given the orally-administered antibiotic for 14 days before surgery and almost all saw a significant drop in cancer <u>stem cells</u>, the aggressive <u>cells</u> that drive tumour recurrence.

Although small – restricted to 15 patients at the University Hospital in Pisa, Italy – the trial is highly significant, giving hope for the efficacy of cheap, over-the-counter drugs being used alongside standard treatments to prevent cancer regrowth. Doxycycline is one of the most commonlyprescribed antibiotics, effective in treating pneumonia, sinusitis, chlamydia, syphilis, cholera and Lyme disease.

The research, reported in the journal *Frontiers in Oncology*, was led by Professors Michael Lisanti and Federica Sotgia at the University of Salford and supported by the Healthy Life Foundation, the Pisa Science Foundation and the Foxpoint Foundation.

Lisanti, chair of translational medicine, said: "We have very few FDAapproved drugs to target and reduce <u>cancer stem cells</u>, so to find that a drug that is effective, readily-available and costs just 10pence per patient per day and is highly significant, particularly as around two-thirds of cancer deaths occur due to recurrence after initial treatment."



The University of Salford specialises in discovering non-toxic remedies and repurposing approved drugs as complementary treatments for cancer.

In the trial, doxycycline was administered to 9 patients whilst a further 6 were observed as 'controls' (no treatment). Immuno-histochemical analysis was performed with known biomarkers of "stemness" (CD44, ALDH1), mitochondrial mass (TOMM20), cell proliferation (Ki67, p27), apoptosis (cleaved caspase-3) and neo-angiogenesis (CD31). For each patient, the analysis was performed both on pre-operative specimens (core-biopsies) and surgical specimens.

Post-doxycycline tumour samples demonstrated a statistically significant decrease in CD44—between 17.65% and 66.67%, in 8 out of 9 patients treated. One patient showed a rise in CD44, by 15%. Overall, this represents a positive response rate of nearly 90%. Similar results were also obtained with ALDH1, another marker of stemness.

"What we infer here is that the stem cells selectively over-express key mitochondrial-related proteins, which means that if we can inhibit mitochondrial function we can disrupt the stem cells," explained Prof Sotgia.

Because mitochondria evolved from bacteria, they explain, many classes of antibiotics including Doxycycline actually target mitochondria and inhibit the reproduction of stem cells. These latest observations, they say, are further evidence that mitochondria are both biomarkers and potential drug targets.

Professor Lisanti added: "Our ability to treat cancer can only be enhanced by utilising drugs that are not only cheap but also widely available. Since Doxycycline first became clinically available in 1967, its anti-cancer activity has been right under our nose, for more than 50



years."

**More information:** Doxycycline, an inhibitor of mitochondrial biogenesis effectively reduces cancer stem cells (CSCs) in early breast cancer patients: A clinical pilot study *Frontiers in Oncology*. DOI: 10.3389/fonc.2018.00452

Provided by University of Salford

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