

Treating aggressive breast cancer with an anti-diabetic drug

April 22 2021

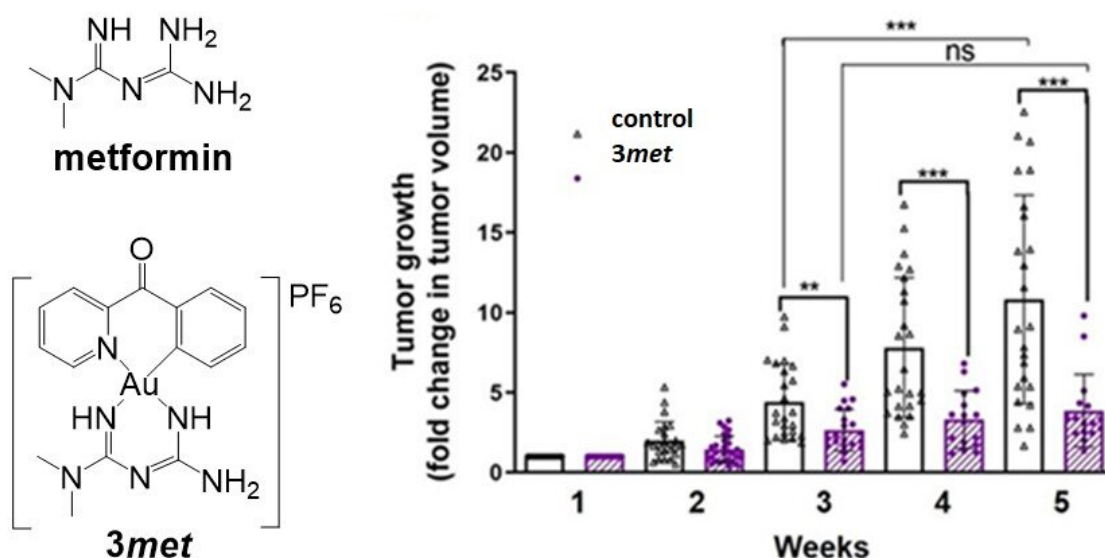


Figure shows the effects of gold-metformin drug candidate *3met* on aggressive breast tumour growth in vivo. Growth of breast tumours in murine models from week 1 (before treatment) presented as a fold change in tumour volume. Starting from week 2, the tumours became palpable and their volume was measured using calipers on a weekly basis. No significant tumour growth was observed after week 3 in a drug-treated group (purple colour). Chemical structures of metformin and *3met* are given on the left. Credit: *Angewandte Chemie International Edition*

National University of Singapore researchers developed an approach to

target highly resistant triple-negative breast cancers (TNBCs) by interfering with their energy production using cytotoxic gold-metformin prodrugs.

Metformin is a widely prescribed "over-the-counter" medication for Type 2 diabetes. There is some evidence that patients taking metformin for a long time have significantly reduced risk of developing [cancer](#). However, despite well-characterized [anticancer effects](#) and the low cost of metformin, its use as an anticancer agent has serious drawbacks. Metformin is poorly taken up by cells. In order to achieve therapeutic concentrations, it has to be taken repeatedly in high doses, which may cause serious side effects in cancer patients.

A team of researchers led by Prof Ang Wee Han from the Department of Chemistry, National University of Singapore and Prof Maria Babak from City University of Hong Kong devised an approach to chemically conjugate metformin, as well as its analog phenformin. This is achieved by using a gold-based active molecular fragment to improve bioavailability and to achieve synergistic action of the two key components (metformin and gold molecules). By taking advantage of the electrochemical activity of the gold-based molecule, the team successfully delivered metformin into cancer cells with high selectivity. The anticancer activity of the lead drug candidate developed by the team named *3met*, was found to be more than 6,000 times higher when compared to [metformin](#).

Prof Ang said, "TNBCs represent an especially dangerous subset of breast cancers with the poorest prognosis and limited treatment options. However, this particular aggressiveness of TNBC cells is related to their increased dependence on glucose and lipids, which provide additional energy to sustain rapid cancer growth. Since our drug candidates interfered with [energy production](#) in the cancer cells, we hypothesized that TNBCs might be particularly responsive to such treatment."

The research team injected the drug candidate into murine models having breast tumors at their nipple region and monitored the growth of the tumors (see Figure). They found that the growth of tumors in a drug-treated group completely stopped after three weeks, indicating the unique anticancer potential of the [drug](#) candidate. A patent application has been filed on this discovery. The research team is actively working on the development of other efficient drugs for the treatment of chemo-resistant cancers.

More information: Maria V. Babak et al. Interfering with Metabolic Profile of Triple-Negative Breast Cancer using Rationally-Designed Metformin Prodrugs, *Angewandte Chemie International Edition* (2021). DOI: [10.1002/anie.202102266](https://doi.org/10.1002/anie.202102266)

Provided by National University of Singapore

Citation: Treating aggressive breast cancer with an anti-diabetic drug (2021, April 22) retrieved 27 April 2024 from <https://medicalxpress.com/news/2021-04-aggressive-breast-cancer-anti-diabetic-drug.html>

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