Research identifies a new drug candidate to starve and suffocate breast cancer cell stem growth

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Michael P. Lisanti. Credit: University of Salford

Scientists have identified a new drug candidate that is able starve and suffocate cancer stem cells, paving the way for new therapies to treat breast cancer patients.

Breast Cancer is one the most common types of cancer in the UK. It is predicted that one in seven women will be affected by the illness in their lifetime.

Research at the University of Salford has uncovered important findings on how to effectively target mitochondria, which normally provide all the necessary energy for driving the proliferation and dissemination of cancer stem cells.

It is well-recognized, by the medical community, that the growth of cancer stem cells (CSC's) is one of the major causes of treatment failure, tumour recurrence and cancer spread, in many different cancer types.

CSC's that are resistant to chemotherapy and radiotherapy, often resulting in tumour recurrence.

In research conducted at the Translational Medicine Laboratory at the University of Salford, a candidate drug was identified, Dodecyl-TPP, that was found to be effective when targeting mitochondria within CSCs. Using this approach when treating cancer patients has the scope to reduce the risk of recurrence and spread of cancer.

Professor Michael P. Lisanti, the chair of translational medicine at the University of Salford, said, "Our pre-clinical research has identified a new drug candidate for targeting mitochondria in CSC. It was found that Dodecyl-TPP treatment can potently starve CSCs to death, this being effective in the nano-molar range, blocking their use of oxygen to generate energy in the form of ATP. The findings make a valid case for future clinal trials in this area."

Scientists at the University of Salford also identified 5 other agents that worked together with Dodecyl-TPP. This includes two FDA-approved drugs (Doxycycline and Niclosamide) and two nutraceuticals (Vitamin C and Berberine).

The research, led by Professors Michael P. Lisanti and Federica Sotgia, was published in the journal *Frontiers in Oncology*, a peer-reviewed research platform that covers cancer research. This metabolic approach using drug combinations, can potentially improve patient survival by preventing tumour recurrence and metastasis, via the high-efficiency targeting of CSCs. Around 90% of all cancer patients die as a result of the cancer spreading and tumour recurrence, this being the basis of the research to identify new mitochondria inhibitors.

About Mitochondria

Mitochondria are the 'powerhouse' of the cell, which

drive the production of cellular energy in the form of NAD and ATP. Research has shown that Dodecyl-TPP acts as a mitochondrial inhibitor, starving the CSCs to death. ATP and NAD are high-energy metabolites required for cell survival and propagation.

About Dodecyl-TPP

Dodecyl-TPP contains a 12-carbon side-chain which is tethered to a TPP (tri-phenyl-phosphonium) moiety. TPP acts as a chemical signal to target the drug to the mitochondria. TPP more efficiently targets mitochondria in cancer stem cells and cancer cells, but is largely excluded from normal cell mitochondria, reducing its potential for toxicity in normal body cells.

More information: Ernestina Marianna De Francesco et al. Dodecyl-TPP Targets Mitochondria and Potently Eradicates Cancer Stem Cells (CSCs): Synergy With FDA-Approved Drugs and Natural Compounds (Vitamin C and Berberine), *Frontiers in Oncology* (2019). DOI: 10.3389/fonc.2019.00615