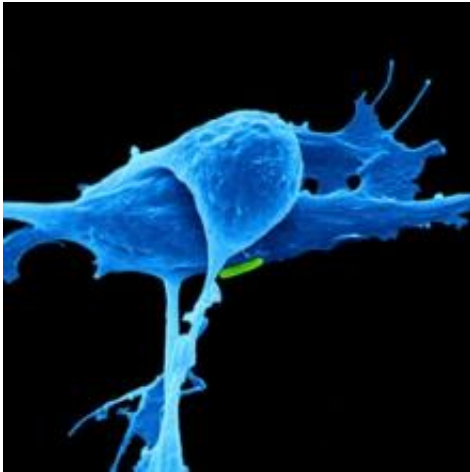


Researchers identify new ways to drain cancer's 'fuel tank'

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Scientists at the University of Manchester have discovered a potential weakness in cancer's ability to return or become resistant to treatment, by targeting the 'fuel' part of stem cells which allows tumours to grow.

Cancer stem cells are particularly difficult to eradicate and are at the heart of why it is so hard to more effectively treat cancer patients, as the post-treatment survival of [cancer stem cells](#) drives tumour recurrence, the systemic spread of cancer and, ultimately, treatment failure.

The researchers, based at the University's Institute of Cancer Sciences and the Cancer Research UK Manchester Institute – both part of the

Manchester Cancer Research Centre - investigated the role of [mitochondria](#) which produce and release energy within cells. In this context, the new Manchester Centre for Cellular Metabolism (MCCM) also played a critical role in these studies.

By observing cancer stem cells in a lab setting, they discovered that mitochondria are especially important for the proliferative expansion and survival of cancer stem cells, also known as 'tumour initiating cells', which would then promote treatment resistance.

The research was carried out in breast cancer stem cells grown in a lab, but the theory was also checked against human [breast cancer cells](#) from patients. In both cases, proteins within the cells were examined. Sixty-two mitochondrial-related proteins showed significantly increased levels. In particular, fuels such as ketone and L-lactate appeared to be critical, and in the past, they have been shown to accelerate the growth of tumours.

Professor Michael P. Lisanti, Director of the Breakthrough Breast Cancer Unit, led the research. He said: "Essentially mitochondria are the "engines" of cancer stem cells and ketone and L-lactate are the high octane fuels, which promote cancer growth.

"This is one of the first times that the actions of mitochondria in cancer stem cells have been fully appreciated and the results suggest new ways in which we can drain the fuel tank – restricting cancer's ability to come back after treatment."

Trials run by Cancer Research UK are currently underway using MCT inhibitors, which also target the mitochondria in cancer cells and the researchers believe that this could, if successful, open up new avenues of treatment.

Dr Federica Sotgia, a Senior Lecturer, who also led the study, said: "Targeting the mitochondria is difficult because of potential side effects, but, if these trials prove successful, then it represents an exciting new way to treat a large number of different cancer types."

Nell Barrie, senior science information manager at Cancer Research UK, said: "Blocking [cancer cells](#)' ability to generate the energy they need to grow and divide is an exciting new avenue for future cancer treatments. This research suggests that MCT inhibitors may be particularly effective against breast cancer 'stem cells' that can resist other treatments, and could prevent the cancer from coming back – but further work is needed to find out if these drugs can help patients. Cancer Research UK is funding trials of these drugs in a range of cancer types."

Dr Matthew Lam, Senior Research Officer at Breakthrough Breast Cancer, said: "Whilst further investigation beyond the lab is needed to test the validity of these findings, this is promising work because in effect the team used one of the unique properties that cancer stem cells have against them.

"Secondary [breast cancer](#) is responsible for all deaths from the disease and we know that cancer stem cells play an important role in its development. If we are going to out-smart cancer once and for all in the future, every step taken towards finding new ways to prevent it from spreading and becoming life-threatening will be an important one."

The work presented in the paper, 'Mitochondria as new therapeutic targets for eradicating [cancer stem cells](#): Quantitative proteomics and functional validation via MCT1/2 inhibition' was funded by Breakthrough Breast Cancer and Cancer Research UK and was published in the journal *Oncotarget*.

More information: "Mitochondria as new therapeutic targets for

eradicating cancer stem cells: Quantitative proteomics and functional validation via MCT1/2 inhibition." [www.impactjournals.com/oncotar ... article&op=view&path%5B%5D=2789&path%5B%5D=5266](http://www.impactjournals.com/oncotar...article&op=view&path%5B%5D=2789&path%5B%5D=5266)

Provided by University of Manchester

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