Altering cancer metabolism helps treatments attack tumors

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Restricting the ability of cancer cells to metabolise sugar could make oncolytic viruses more effective at attacking them, suggests a study published today in the journal *Cancer Research*.

Viruses that are trained to attack cancer cells—known as oncolytic viruses—can kill tumours without affecting healthy cells nearby. They normally work by invading the cells, multiplying and destroying the tumour from inside. They are currently being tested in clinical trials.

In this new study, a team of scientists exposed lung, ovarian and colon cancer cells, and mouse models, to conditions similar to those in the human body, and investigated how manipulating cell metabolism can make cancer more vulnerable to oncolytic viruses.

In the lab, scientists usually keep cells at the perfect temperature and provide them with lots of glucose, as it's easier to grow and store them this way. In this study, the researchers changed the lab conditions to make them reflect what actually happens in the human body, where sugar levels are much lower.

They found that oncolytic viruses worked better when less glucose was available. To investigate whether they could make the virus work even harder, the researchers then used a drug to restrict the cancer cells' ability to metabolise sugar—its energy source—to see if this optimised the virus's cancer killing capability. They found that reducing sugar levels allowed the virus to multiply much faster, making treatment more

effective and destroying cancer quicker.

Arthur Dyer, lead author and Cancer Research UK-funded Ph.D. student from the University of Oxford, said: "Our research in the lab showed that restricting the amount of sugar available to cancer cells makes these cancer-attacking oncolytic viruses work even better. We already know that this virus is effective against cancer—and this sugar-starving technique is a way to make it even better."

This approach may also improve how potential cancer drugs are investigated in the lab.

Arthur Dyer added: "When studying any kind of drug in the lab, we keep the cells in very high sugar conditions—it's a bit like soaking them in Lucozade. But this doesn't reflect the conditions that these cells would be exposed to in the body, which are normally much poorer—in cancer they're even worse because tumours typically have poor circulation. Our approach is more realistic in mimicking the conditions in the human body, which ultimately may help us to better predict how patients will respond to drugs well before any trials are planned."

However, the researchers caution that their early findings should not be misinterpreted by patients who are looking to optimise treatments.

Professor Len Seymour, Cancer Research UK-funded study author from the University of Oxford, explains: "It's important to remember that changing your diet is not enough to starve cancer cells of sugar. A lot of people think that carbohydrates are bad, but that's not the case—we need them, and cutting out sugar won't cure cancer. Because cancer gobbles up glucose so quickly, the cells are very vulnerable to attack from a drug that targets the sugar pathway. The same effect cannot be achieved by eliminating sugar from your diet."

Dr. David Scott, Cancer Research UK's director of discovery research, said: "By making treatments work more effectively, we hope that patients will be able to see positive results faster than before. The next step is to test whether this approach works in clinical trials, and to find out which cancers respond best."

The team are aiming to test their glucose-limiting approach to improving oncolytic virus treatment in clinical trials to assess whether it could be successfully implemented in cancer patients.

More information: Dyer et al. Antagonism of glycolysis and reductive carboxylation of glutamine potentiates activity of oncolytic adenoviruses in cancer, *Cancer Research* (2018). cancerres.aacrjournals.org/con … 008-5472.CAN-18-1326

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