Cancer: Tumors absorb sugar for mobility

29 July 2014

Cancer cells are gluttons. We have long known that they monopolize large amounts of sugar. More recently, it became clear that some tumor cells are also characterized by a series of features such as mobility or unlikeliness to join in an ordered set. Researchers are calling this behavior "mesenchymal," and they suspect it promotes metastasis.

At EPFL, Etienne Meylan's research team was able to demonstrate that the two observations – appetite for sugar and mesenchymal behavior – result from the same mechanism, at least in "non-small cell lung cancer." They also showed that the intensity of the phenomenon significantly influenced the chances of patient survival. Published in *Cancer & Metabolism*, this discovery opens up new potential targets for future therapies.

A useful mechanism, but put to work by cancer

Mesenchymal behavior is not in itself an anomaly. During embryonic development, some cells acquire these characteristics. In adults, a few cells retain this disposition.

"Mesenchymal behavior is a quite useful feature, but is abnormally reactivated in non-small cell lung cancer, which we studied," says Etienne Meylan.

The mesenchymal cancer cells studied by the researchers produce a protein called GLUT3. The latter serves the function of capturing glucose to activate various growth processes. This is the protein responsible for meeting the cell's need for sugar.

By artificially inducing mesenchymal behavior in cancer cells, the researchers found that the cells spontaneously produced GLUT3. This observation clearly shows that the same mechanism is at work. "This shift from one behavior to another, called epithelial-mesenchymal transition, is a highly debated issue. We have clearly established a cause and effect relationship between this transition and the glucose consumption of cancer cells," explains Mark Masin, lead author and PhD student at EPFL.

A case study confirms the results

Lung tumor cells produce widely varying amounts of GLUT3. This is because the gene is itself regulated by an element called ZEB1, and the amount of the latter is a function of many causes.

These variations in the amounts of GLUT3 seem to be a strong indicator of the aggressiveness of the tumor. By analyzing data from 450 patients with metastatic non-small cell lung cancer, researchers were able to show that the larger the quantity of GLUT3, the lower the chances of survival.

Patients were diagnosed relatively early and were followed for several years. Depending on whether they produced high or low amounts of GLUT3, their survival rates over seven years spanned almost 20%. "Our data don't permit us to conclude that the mechanism promotes metastasis, but it reinforces the assumption," says Mark Masin.

The discovery identifies a potential target for future medications. Etienne Meylan imagines, for example, a toxic molecule that could be specifically incorporated by GLUT3 to destroy the cell from within. "Protected by the blood-brain barrier, neurons that also produce GLUT3 would not be affected," says the researcher.

Provided by Ecole Polytechnique Federale de Lausanne