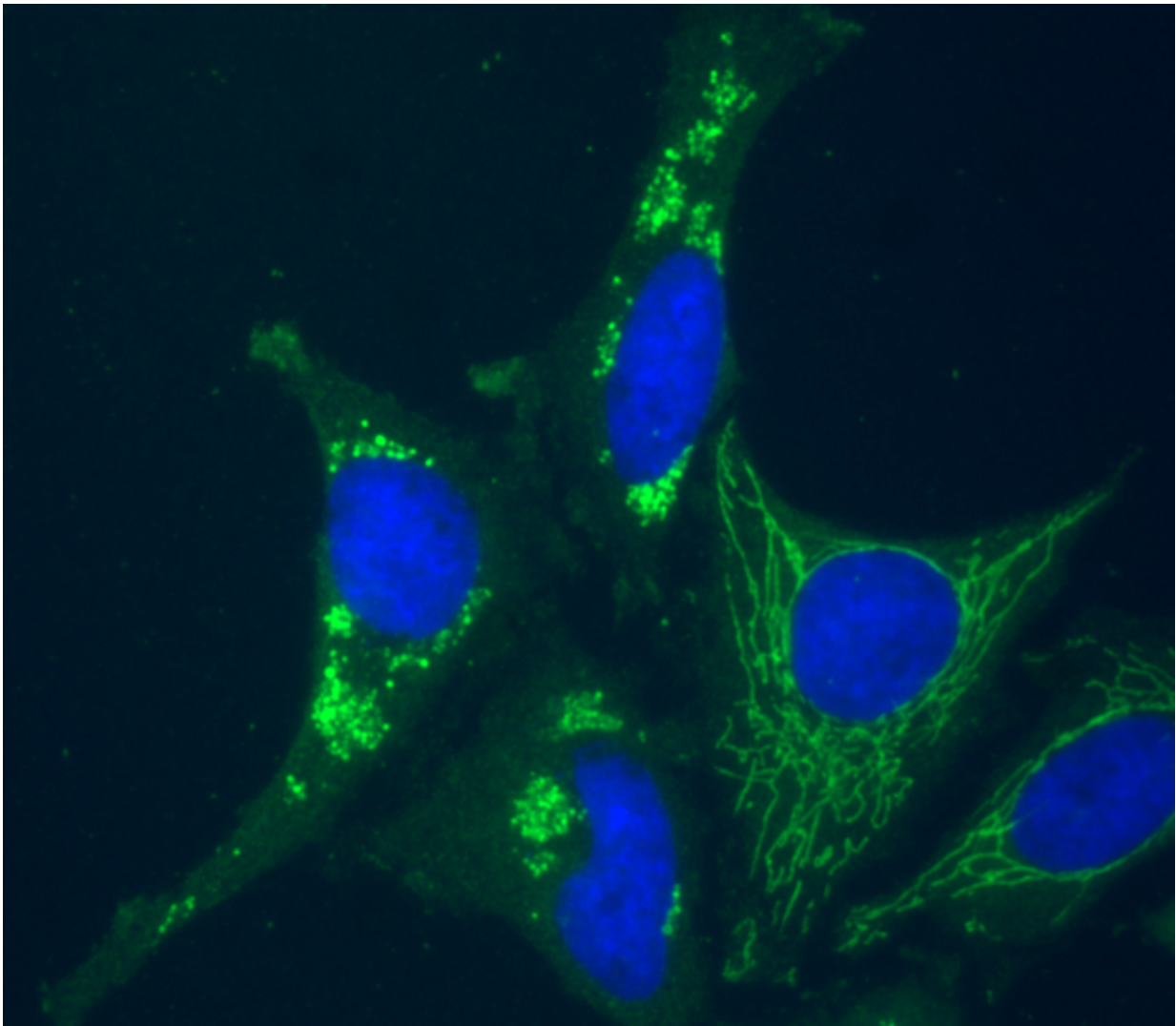


# Observing live energy production by malignant cells

August 6 2015

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Cells whose fluorescent labeling reveals dot shaped or filamentous mitochondria (green), nuclei (blue) or the cytoplasm (greenish-black). Credit: Jean-Claude Martinou

To be able to function, cell mitochondria import "fuel" using a carrier, the Mitochondrial Pyruvate Carrier (MPC). In order to determine whether the MPC is still functional in malignant cells, the team of Professor Jean-Claude Martinou, at the University of Geneva (UNIGE), Switzerland, has just developed a biosensor to measure its live activity. The biologists observed that the MPC displays a very low activity in tumor cell lines, with respect to healthy cells. They then treated the cancer cells with a new kind of antitumoral product, which restored a normal activity of the MPC. These results are published in the journal *Molecular Cell*.

Tumor cells consume an abnormally high quantity of glucose to ensure their rapid growth. To convert this nutrient into energy, and in contrast to healthy cells, they have little use for their mitochondria, these cytoplasmic organelles whose essential role is to produce and stock energy thanks to the cellular respiration. They proceed as such in spite of the optimal energetic yield they could thus obtain. However, they compensate this shortfall by overexploiting other metabolic pathways.

One of the current therapeutic approaches aims at forcing cancer cells to use their mitochondria. "To be able to work, these organelles import a "fuel" named pyruvate by means of a carrier that we discovered in 2012 and baptized Mitochondrial Pyruvate Carrier (MPC)", says Jean-Claude Martinou, Professor at the Department of Cell Biology of the Faculty of Science of UNIGE, Switzerland.

## **A lifeless carrier in malignant cells**

The researchers scrutinized the activity of the MPC in cancer cells. To this end, they transformed the MPC into a sophisticated biosensor, capable of indicating its own live activity: "we genetically modified the

MPC so that it emits fluorescent signals of different intensities according to its level of activity", explains Vincent Compan, first author of the article.

In collaboration with the Swiss Federal Institute of Technology in Zurich (ETHZ), Switzerland, and the University Nice Sophia Antipolis (UNICE), France, the researchers then generated various human cell lines expressing the biosensor. "We measured a very low MPC activity in all the tumor lines, in contrast to that observed in [healthy cells](#). The access of the pyruvate fuel to mitochondria is thus already inhibited at the level of the carrier", notes Jean-Claude Martinou.

## **A reversible effect, however**

In order to force [cancer cells](#) to use their mitochondria, it was necessary to assess whether the MPC was still functional in these cells. The researchers thus subjected the cells to a treatment which induces an increase of pyruvate in the cytoplasm. "This restored a normal MPC activity in the [malignant cells](#), indicating that it is the lack of fuel, rather than a dysfunction of the carrier, that affects the process", details Vincent Compan.

The treatment chosen by the scientists belongs to a group of small chemicals that target another carrier within the cell membrane, the lactate carrier. One of these drugs is in fact currently tested in a clinical trial, as a therapy-candidate. "The biosensor we developed also serves as a tool to identify compounds capable of modulating MPC activity and, thus, new potential treatments", concludes Jean-Claude Martinou.

Provided by University of Geneva

Citation: Observing live energy production by malignant cells (2015, August 6) retrieved 27 April 2024 from <https://phys.org/news/2015-08-energy-production-malignant-cells.html>

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