A new methodology quickly reveals metabolic fluxes in cells

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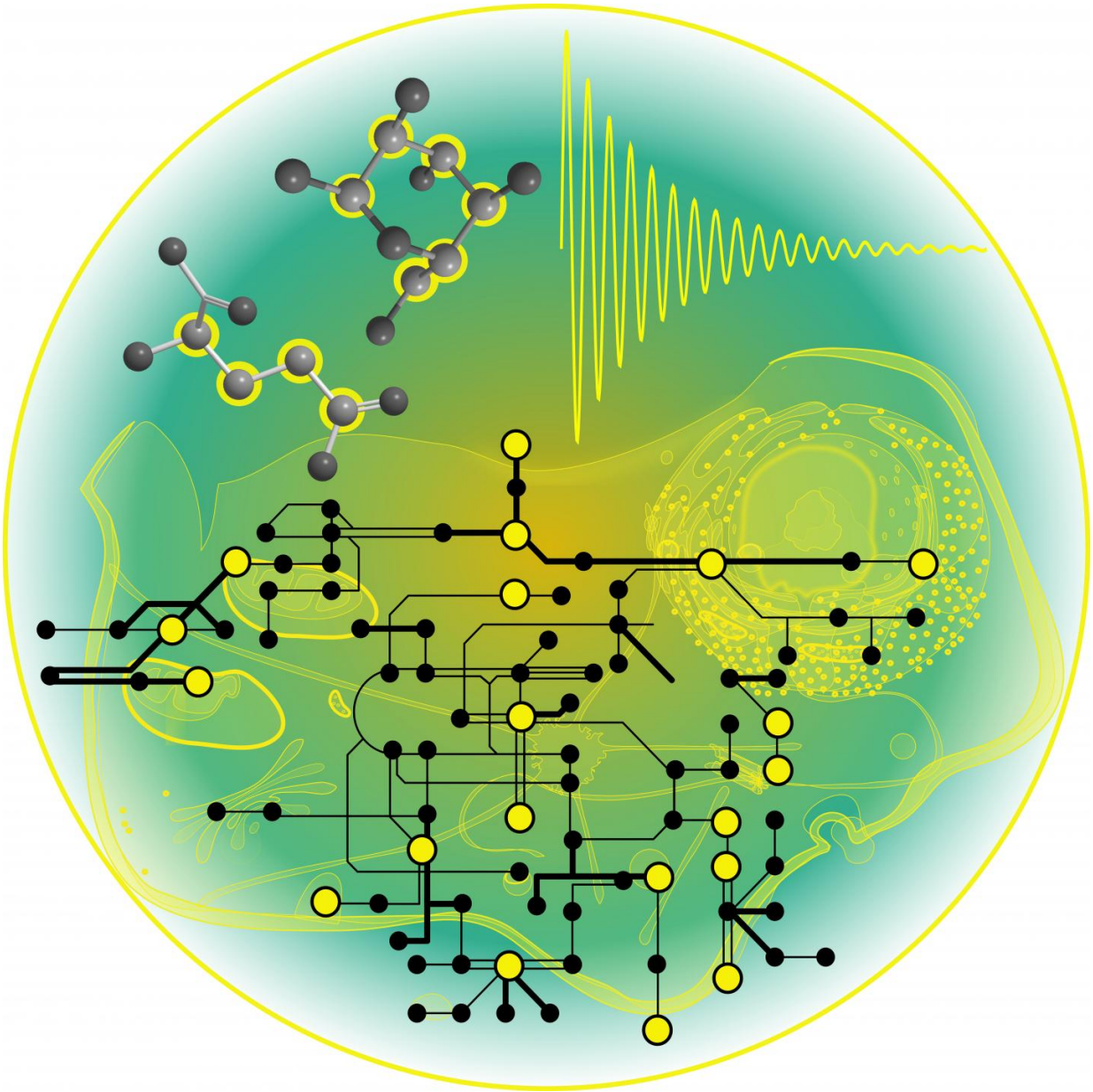

This graphic image simulates the metabolic fluxes in cells, with the nutrients marked with a stable isotope that allow to study the fluxes and the transformation dynamics of these nutrients. Credit: ©URV

Although photographs of the underground stations in Barcelona would reveal the number of people waiting, when rush hour takes place, and offer clues about why some stations are busier than others, they can't reveal whether something has happened between two stations that has caused disruptions. Biologists studying cells confront a similar problem.

The metabolism of a cell is like an underground network in which the chemical structures of the metabolites go from one station to another by means of biochemical transformations. Up until now, it has been possible to determine the number of metabolites in a cell, tissue or organism, but studying their fluxes is technically much more complex and time consuming. Now, however, a group of researchers from the URV, CIBERDEM and IRB Barcelona have developed a new tool that makes this possible.

Via nuclear magnetic resonance (NMR) techniques, it can take researchers hours to measure every sample, and the data are difficult to interpret. The new approach takes only 10 minutes per sample and obtains many more metabolites. Additionally, the results are much easier to interpret, as, metabolic traffic can be determined much more easily and effectively.

It is a methodology based on NMR that measures hydrogen atoms (protons) in order to indirectly determine the number of carbon atoms that are marked in the chemical structures of the metabolites. The experiment is as follows: A nutrient that cells consume is marked with a stable isotope. Stable isotopes such as carbon 13 are not radioactive and

do not represent any danger to organisms or the people who handle the samples. The proton is measured by NMR much more quickly and sensitively than the carbon, making it is possible to study the fluxes and the transformation dynamics of these nutrients inside the cell. So far, the efficacy of this new technique has been validated using human cancer cells, but it is directly applicable to any biological model.

Understanding the reasons for some illnesses

Diabetes, for example, is a metabolic syndrome in which the process begins long before the levels of glucose in the blood increase, because the body uses a variety of mechanisms to ensure that the concentration of this nutrient remains stable. And high levels of glucose are only seen in the blood when the disease is at an advanced stage. The new study describes a technique of studying the mechanisms that cause some tissues in the organism (for example, liver or pancreatic cells) to be unable to regulate levels of glucose or to become insensitive to it. The study of metabolic fluxes helps researchers to understand the reasons why the disease develops and the mechanism by which it does so. Therefore, it also helps in the process of diagnosis. In short, the new methodology offers great potential for practising physicians and molecular biologists to acquire greater understanding of certain diseases. The new technique, unlike more traditional techniques, does not use radioactivity to study the metabolism.

The article, which has been published in the scientific journal *Angewandte Chemie*, shows the results of this work on cancer cells, but the researchers are sure that glucose, amino acids and fats marked with stable isotopes can be studied in other cells and even animals. The fact that they are not radioactive makes them much easier to work with because there is no need for special laboratory conditions.

More information: Maria Vinaixa et al, Positional Enrichment by

Proton Analysis (PEPA): A One-DimensionalH-NMR Approach forC Stable Isotope Tracer Studies in Metabolomics, *Angewandte Chemie International Edition* (2017). DOI: 10.1002/anie.201611347