Metabolic biomarkers for preventive molecular medicine

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One of the big challenges of biomedicine is understanding the origin of illnesses in order to improve early detection and significantly increase recovery rates, as well as being able to do what CNIO researchers call preventive molecular medicine, which consists of identifying those individuals who have a greater molecular risk of suffering certain pathologies in order to prevent them. The ageing of the organism, and therefore of the cells and tissues it is made of, represents the greatest risk factor for the majority of developed-world illnesses, including cancer.

A team of scientists from the Spanish National Cancer Research Centre (CNIO), led by its director, María Blasco, together with Jose M. Mato, the director of the Center for Cooperative Research in Biosciences (CIC bioGUNE), has shown that the metabolic profile of an organism indicates its level of cellular ageing and the general state of health in mice. These results could be of great use for preventive molecular medicine, given that they would indicate the state of health quickly and in a non-invasive manner, and that they would help to prevent illnesses or to diagnose them at the earliest stages.

The metabolism is one of the processes which best defines the general state of organisms. With the aim of studying a possible relationship between the metabolism and ageing, the authors of this study have used a new methodology that, based on liquid chromatography techniques and nuclear magnetic resonance, has made it possible to study up to 1.500 metabolites—intermediate products of the metabolism—in 130 mice using very small samples—just 5-10 µl of blood serum.

"Using this new technique, we have seen that the metabolic profile of mice depends on their age; specifically, we have found 48 metabolites that vary very significantly with age", says CNIO researcher Bruno Bernardes de Jesús, one of the study's authors.

When researchers carried out the same analysis in mice that had increased levels of telomerase —those that age more slowly, according to a study published recently by the Blasco laboratory in the journal EMBO Molecular Medicine—, they observed that the metabolic footprint was very similar to that of the youngest mice. When they studied mice with telomerase deficiencies —those that aged more quickly—, they observed a metabolic profile very similar to that of older animals.

Recent studies in humans indicate a possible relationship between the metabolism and life expectancy. "Our large-scale analysis, that analyses a larger amount of metabolites than has ever been studied before, validates the theory that the metabolome faithfully shows cells' biological clocks", says Mato.

NEW BIOMARKERS TO EVALUATE THE STATE OF HEALTH

Ageing is characterised in large part by metabolic decline that implies

loss of hepatic, renal, coronary or cardiac function, as well as an increased risk of suffering cancer. In fact, some of the 48 metabolites identified in the study have previously been related to illnesses associated with age, such as Alzheimer's or cardiovascular diseases.

The results of this research may be useful for predicting the overall state of health in humans, via the extraction of a small blood sample. They might also be useful for preventing illnesses related to the passage of time, which make up the majority of deadly diseases in developed countries.

From these results, the researchers are also looking into searching for diagnostic biomarkers that are associated to high-impact socioeconomic illnesses such as diabetes, obesity or cardiovascular diseases.

More information: A metabolic signature predicts biological age in mice. Antonia Tomás-Loba, Bruno Bernardes de Jesus, Jose M. Mato, Maria A. Blasco. *Aging Cell* (2012). doi: 10.1111/acel.12025

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