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Change of temperature causes whole body reprogramming

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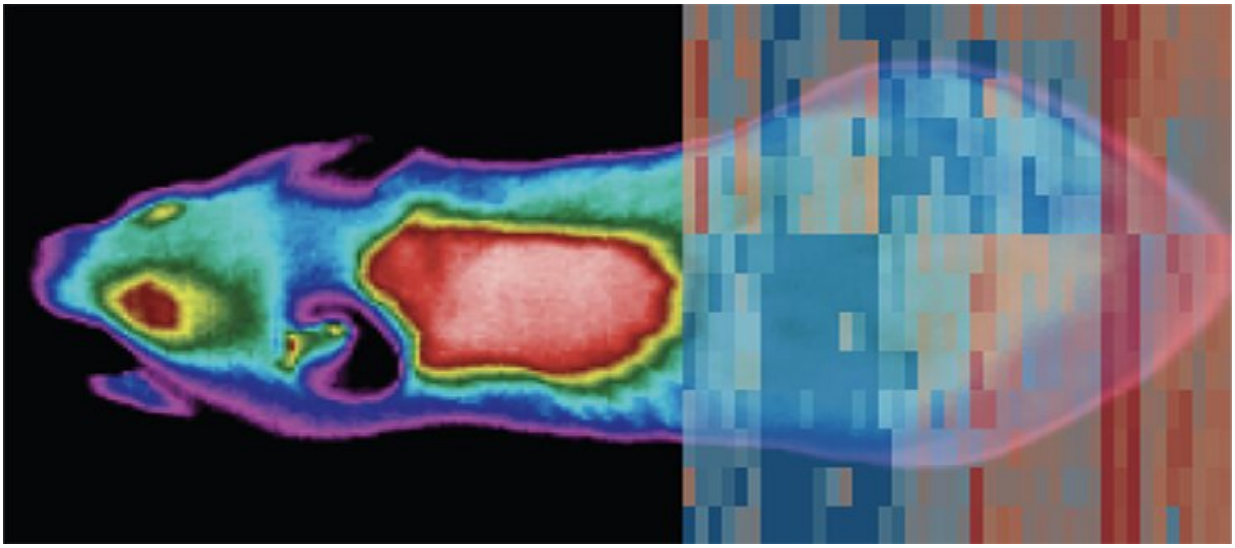

Exposure to cold or warmth causes strong changes in gene expression in various organs of a mouse. Credit: © UNIGE, Laboratory of Prof. Mirko Trajkovski

Human beings, like most organisms, are constantly exposed to alternating colder or warmer temperatures. These environmental variations cause striking metabolic effects and require constant adaptations. While some of these adaptations confer certain beneficial effects on health, the impact of cold and warmth on the various organs in a whole-body context was not known. To understand the overall biological mechanism at stake, a team from the University of Geneva (UNIGE) analyzed changes in gene expression simultaneously in various

organs in mice. They discovered that all organs strongly react to temperature changes, each showing its own specific modulation. To stimulate research and potential therapeutic applications, the scientists created a web-based application where thousands of gene expression profiles are freely accessible. These results can be read in the journal *eLife*.

Temperature is one of the main environmental factors to which living beings are subjected. Exposure to cold or warmth has striking effects on metabolism and health, and the implication of temperature on the human health is also evident by the geographic distribution of the incidence of certain diseases. But beyond the physiological response of some tissues, to which extend living in a colder or warmer environment does contribute to whole-body biological changes?

"In our previous studies, we had already observed that temperature had major effects on the functioning of certain organs," explains Mirko Trajkovski, Professor in the Department of Cell Physiology and Metabolism and in the Diabetes Centre in the UNIGE Faculty of Medicine, who directed this research.

"We now know that exposure to cold promotes weight loss due to the increased thermogenesis, and alleviates the symptoms of multiple sclerosis, while exposure to warmth has protective effects on certain age-related diseases, such as osteoporosis. But what happens on the scale of the whole organism? Indeed, our previous results point to context-dependent effects of temperature alterations on various organs and diseases, but the overall adaptation of the organism needs to be addressed in an integrative way."

All organs react differently

To address this aim, the scientists analyzed the expression of genes in

eleven organs (all adipose (fat) tissues, muscle, liver, brain, hypothalamus, ileum, spinal cord, spleen and bone marrow) of three groups of mice exposed to a temperature of 10°C, 22°C, or 34°C. "The data show that the whole body profoundly reacts to temperature changes," says Mirko Trajkovski. "However, there is no uniformed response: each organ changes its gene expression in its own way, somewhat differently from the rest of the tissues."

To better understand whether this phenomenon was due to the unique expression of genes specific to each organ, the research team performed additional analyses, focusing on genes that are expressed in all organs. And even when considering only this restricted set of genes, the differences in activation were still striking.

Toward therapeutic recommendations?

"Knowing that exposure to alternating temperatures causes major effects on metabolic diseases such as obesity and osteoporosis, or even on auto-immune diseases, indicates use of temperature shifts as potential therapeutic lifestyle intervention. However, we first need to decipher the temperature-induced effects in an integrative manner throughout the body, and not only at a single organ level. Our work allows precisely that—investigating and understanding the mechanisms at work in various organs simultaneously," says Mirko Trajkovski.

To accelerate research in this emerging field, the Geneva team created a free-to-use and easily accessible web-based application that allows users, both scientists as well as the general public, to search for the expression of thousands of genes in response to exposure to cold or warmth in various organs. "These results will be most useful if they are shared and exploited by a large number of people," concludes Mirko Trajkovski.

More information: Noushin Hadadi et al, Comparative multi-tissue

profiling reveals extensive tissue-specificity in transcriptome reprogramming during thermal adaptation, *eLife* (2022). DOI: 10.7554/eLife.78556

Application and the database: metlabomics.unige.ch/Search

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