Gut microbiota regulates antioxidant metabolism

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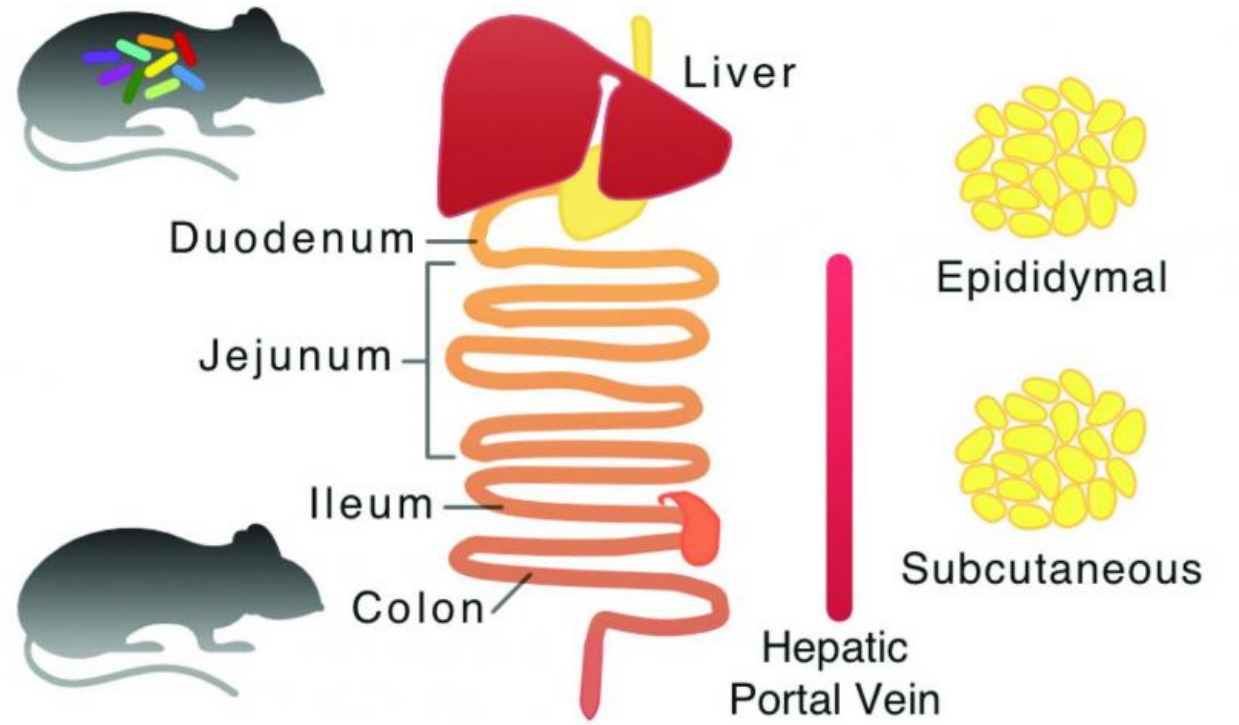

The effect of bacteria has been identified by studying the metabolic differences between the many gut, liver and fat tissues obtained from normal and bacteria-free mice. Credit: Chalmers

A recently published study shows that gut microbiota regulates the glutathione and amino acid metabolism of the host. Glutathione is a key antioxidant, found in every cell in our body. Deficiency of glutathione

contributes to oxidative stress, which plays a major role in several lifestyle diseases.

The functional output and diversity of gut microbiota are important modulators for the development of various human disorders. Obesity, type 2 diabetes, atherosclerosis, non-alcoholic fatty liver disease as well as the opposite end of the spectrum, for example malnutrition, have been associated with imbalance in human gut microbiota. Hence, the interactions between the gut microbiota, host tissues of the gastrointestinal tract and other peripheral tissues as well as diet are known to be highly relevant for the health of the host.

In a recent paper published in *Molecular Systems Biology*, researchers at Chalmers University of Technology, the Royal Institute of Technology and the University of Gothenburg in Sweden revealed that gut microbiota regulates the glutathione and amino acid metabolism of the host. The study, highlighted on the cover of the journal, shows how a novel integrative approach can be used to reveal the metabolic differences between germ-free and conventionally raised mice through a combination of proteomics, transcriptomics and metabolomics data as well as tissue-specific metabolic modeling.

Glutathione is our body's most powerful antioxidant and the main detoxifying agent in the body. It plays a vital role in enabling the immune system, nutrient metabolism and regulation of other important cellular events. Glutathione is a very small protein, produced inside the cells from three amino acids ultimately obtained from our food or supplementation. The deficiency of glutathione contributes to oxidative stress, which plays a major role in the mechanisms of above mentioned complex disorders.

In the study, a generic map of mouse metabolism was created, and tissue-specific computer models for major mouse tissues were generated.

Through integration of high throughput experimental data, the researchers found that the microbiota in the small intestine consumes glycine, which is one of the three amino acids required for the synthesis of the glutathione.

In order to confirm the results of the computer-based simulations, the level of the amino acids in the portal vein of the mice was measured. Moreover, a lower level of glycine was observed in liver and colon tissues, which indicates that the gut microbiota regulates glutathione metabolism, not only in the small intestine but also in the liver and the colon.

"Some bacteria in our gut consume glycine, which is required for the synthesis of the glutathione, and imbalances in the composition of the bacteria may lead to the progression of the chronic diseases", says Chalmers researcher Adil Mardinoglu, first author of the paper.

In previous independent studies, imbalances in the plasma level of glycine as well as other amino acids have been shown to exist in obesity, type 2 diabetes and non-alcoholic fatty liver disease.

"Strikingly, the plasma levels of glycine are decreased in all subjects with the above-mentioned diseases compared to the healthy subjects", says Professor Jens Nielsen at Chalmers. "In this context, it may be of interest to study the microbial amino acids in the human gut in relation to their potential role in the development of such metabolism-related disorders.

"The discovery that the bacteria in our small intestine consume glycine and regulate glutathione metabolism may led to the development of food products that can deliver beneficial bacteria (probiotics) to the gut. The results of the study can help us understand how bacteria play a role in the metabolic processes involved in the development of obesity, type 2

diabetes, non-alcoholic fatty liver disease and malnutrition."

More information: The study "The gut microbiota modulates host amino acid and glutathione metabolism in mice" has been published in the *Molecular Systems Biology* journal: msb.embopress.org/content/11/10/834

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