Medical Xpress

Researchers map the effects of dietary nutrients on disease

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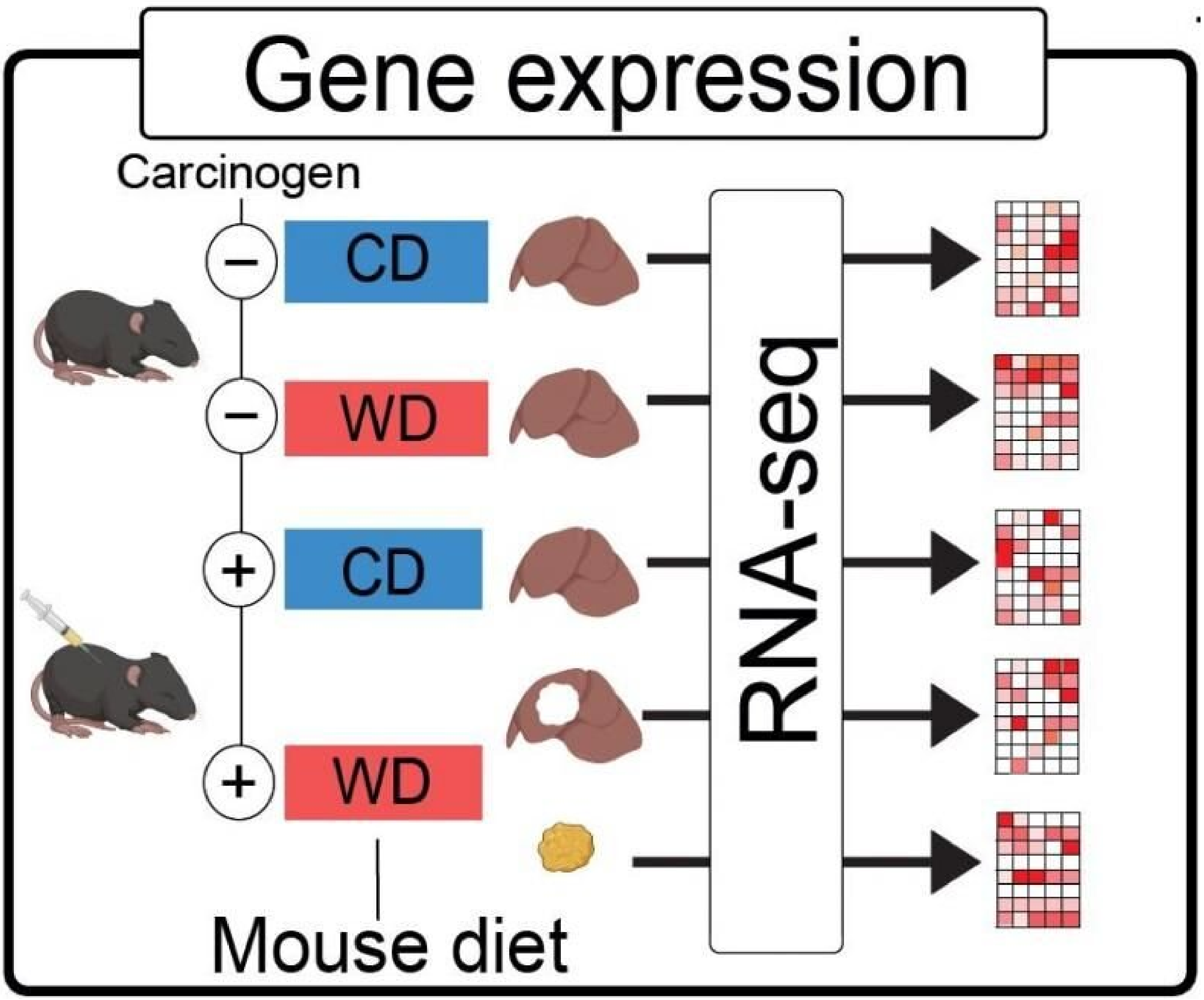

Researchers gathered experimental data to put into the model by measuring the levels of gene expression in liver and liver tumours from mice that had been fed either 'healthy' diets or 'unhealthy' diets, rich in fats and sugars. Credit: The Francis Crick Institute

Researchers at the Francis Crick Institute and King's College London have created a tool to predict the effects of different diets on both cancerous cells and healthy cells.

Their work could help disentangle the subtle metabolic changes associated with different types of nutrients, and improve our understanding of the link between diet and disease.

Metabolism refers to the set of processes that allow an organism to use nutrients from its environment in order to function. Relative amounts of sugars, fats and protein in the diet determine what "fuel" is available for the cells, and also how those cells process the nutrients. Cancer cells, like other diseased cells, change their metabolism to support survival and growth.

As part of the study, published in *iScience*, the research team at the Center for Host-Microbiome Interactions at King's College London first created a comprehensive map of all metabolic pathways in the mouse. The Crick team then gathered experimental data to put into the model by measuring the levels of gene expression in liver and liver tumors from mice that had been fed either "healthy" diets or "unhealthy" diets, rich in fats and sugars.

They found specific changes in metabolism associated with unhealthy diets, which were seen to promote the production of glycerol and succinate in both cancerous and healthy tissues. They also observed that the differences in metabolism between healthy and cancerous cells were highest in the context of an unhealthy diet, suggesting that tumors are able to better exploit unhealthy diets to promote survival and growth.

Patricia Nunes, Senior Laboratory Research Scientist at the Crick, said, "By using experimental data from the lab, the model allows us to start understanding the complex metabolic changes that happen in tissues due to specific nutrients in the diet."

Dimitrios Anastasiou, head of the Crick's Cancer Metabolism Laboratory, said, "We know that poor diet wreaks havoc in our body's metabolism. It can cause obesity and promote liver disease, which, in turn, can progress to liver cancer. We want to understand which nutrients in our diets, and in what combinations, drive these detrimental outcomes."

The team then modeled the effects of a change in dietary components—from healthy to unhealthy, and unhealthy to healthy—in various combinations. They observed that, although some cancer-specific metabolic functions persisted on healthy diets, they could also reverse many of them, but only when both fats and carbohydrates were limited.

Frederick Clasen, first author and Ph.D. student jointly at the Crick and King's College London, said, "The potential applications of this work are far reaching. We can now see which changes in diet actually impact cell metabolism, and which have very little effect because the cells are already programmed to draw missing nutrients from their surroundings."

Saeed Shoaie, head of the Translational Systems Biology group from the Faculty of Dentistry, Oral & Craniofacial Sciences at King's College London, said, "To further increase the accuracy of our model's predictions, we are now generating more sophisticated models of metabolism, that take into account how different organs exchange metabolites, and how bacteria in the gut influence what nutrients are available to tissues."

Anastasiou concludes, "Our approach can be used to help guide dietary changes that complement treatments for different diseases. But the most effective use of this understanding will be in preventing more disease by helping us select the foods we eat."

More information: Frederick Clasen et al, Systematic diet composition swap in a mouse genome-scale metabolic model reveals determinants of obesogenic diet metabolism in liver cancer, *iScience* (2023). DOI: 10.1016/j.isci.2023.106040.
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