A Disruption of the Microbiota Is Linked to the Formation of a Molecule Promoting Type 2 Diabetes

An imbalanced diet has been linked to a disruption of the gut microbiota, which promotes metabolic diseases such as diabetes. Researchers from Inserm, Sorbonne Université, Paris hospitals group AP-HP and the French National Research Institute for Agriculture, Food and Environment (INRAE) in collaboration with a Swedish team have shown, in a large European cohort, that changes in the composition of the gut microbiota lead to increased blood levels of the molecule imidazole propionate. A molecule known to render the body's cells resistant to insulin, thereby increasing the risk of developing type 2 diabetes. Their findings have been published in *Nature Communications*.

Diet plays a major role in the composition of our gut microbiota. From what we consume, the gut bacteria produce organic compounds known as metabolites, which can affect our health. © Adobe Stock
organic compounds known as metabolites, which can affect our health if they are present in too large or too small a quantity in our body.

Previous studies have shown that changes in the makeup of the gut microbiota and the production of certain metabolites can directly influence the development of type 2 diabetes. For example, they have revealed that lower levels of the bacteria that produce butyrate, a fatty acid known to improve insulin sensitivity, are linked to an increased risk of diabetes.

Other recent research suggests that an alteration of the gut microbiota disrupts the metabolism of histidine, an amino acid found in many foods, leading to increased levels of the metabolite imidazole propionate. This molecule blocks the action of insulin, preventing it from lowering blood glucose levels.

The present study published in *Nature Communications* confirms these initial findings in a large European cohort of 1990 participants from France, Germany and Denmark, called METACARDIS. Coordinated by Inserm, the objective of this cohort is to study the impact of changes in the gut microbiota on the onset and progression of cardiometabolic diseases and associated pathologies. "METACARDIS is a unique and valuable database in that it allows us to access very detailed characteristics of each person enrolled in the cohort with large amounts of phenotypic, metabolic, and bacterial genetic data," emphasizes the project’s coordinator, physician Karine Clément, teacher-researcher in nutrition at Sorbonne Université.

She and her colleagues show that in the cohort, subjects with prediabetes\(^1\) or type 2 diabetes do indeed have higher levels of imidazole propionate in their blood. The gut microbiota of these subjects is also characterized by a significant depletion of bacteria.

The researchers suggest that these alterations in the bacterial composition of the microbiota are linked to an imbalanced diet. They cause a disruption in the metabolism of histidine, which in turn leads to an increase in imidazole propionate and problems regulating blood glucose. The risk of developing type 2 diabetes then becomes higher.

"Our study suggests that people with poor diets have increased levels of imidazole propionate and that there is a clear link between the depleted composition of the microbiota, diet and type 2 diabetes. Its aim is to convey a message of prevention, emphasizing that a more varied diet can enrich the microbiota. This study also has therapeutic implications since we could envisage the future development of drugs to modify the synthesis of certain metabolites such as imidazole propionate," explains Clément.

A number of questions continue to be raised and are expected to be elucidated in future research based on METACARDIS. In particular, the researchers want to understand how the elevation of one or more metabolites can predict, in people with diabetes, the risk of developing other complications, such as those affecting the cardiovascular system. They also want to study how increased imidazole propionate levels in people with prediabetes could increase their risk of developing type 2 diabetes earlier on in their clinical course.

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\(^1\) Prediabetes is a blood glucose disorder at a less advanced stage than diabetes itself. It is characterized by fasting blood glucose levels of between 1.10 g/L and 1.25 g/L (normal fasting blood glucose is below 1.10 g/L). The risk of going on to develop type 2 diabetes is increased.
This large-scale research project, based on close collaboration between several European scientific teams, has received support from the European Community (7th Framework Programme FP7-Metacardis), as well as from the Leducq Foundation.

Sources

Imidazole propionate is increased in diabetes and associated with dietary patterns and altered microbial ecology


1 Wallenberg Laboratory, Department of Molecular and Clinical Medicine and Sahlgrenska Center for Cardiovascular and Metabolic Research, University of Gothenburg, 413 45, Gothenburg, Sweden.
2 Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden.
3 INSERM, Nutrition and Obesities; Systemic Approaches (NutriOomics), Sorbonne Université, Paris, France.
4 Assistance Publique Hôpitaux de Paris, Pitie-Salpêtrière Hospital, Nutrition department, CRNH Ile de France, Paris, France.
5 Integromics Unit, Institute of Cardiometabolism and Nutrition, 75013, Paris, France.
6 Medical Department III - Endocrinology, Nephrology, Rheumatology, University of Leipzig Medical Center, Leipzig, Germany.
7 Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Blegdamsvej 3B, 2200, Copenhagen, Denmark.
8 Assistance Publique Hôpitaux de Paris, Clinical Investigation Center Paris East, 75013, Paris, France.
9 Assistance Publique Hôpitaux de Paris, Biochemistry and Hormonology Department, Tenon Hospital, 75020, Paris, France.
10 Experimental and Clinical Research Center, A Cooperation of Charité-Universitätsmedizin and the Max-Delbrück Center, Berlin, Germany.
11 MetaGenoPolis INRAE, Jouy-en-Josas, France.
12 Laboratory of Molecular Bacteriology, Department of Microbiology and Immunology, Rega Institute, KU Leuven, Leuven, Belgium.
13 Center for Microbiology, VIB, Leuven, Belgium.
14 Unité de Modélisation Mathématique et Informatique des Systèmes Complexes, UMMISCO, 93143, Bondy, France.
15 Sorbonne Paris Cité Epidemiology and Statistics Research Centre (CRESS), U1153 Inserm, U1125, Inra, Cnam, University of Paris 13, Nutritional Epidemiology Research Team (EREN), 93017, Bobigny, France.
16 Computational and Systems Medicine, Department of Metabolism, Digestion and Reproduction, Faculty of Medicine, Imperial College London, London, SW7 2AZ, UK.
17 Genomic and Environmental Medicine, National Heart & Lung Institute, Faculty of Medicine, Imperial College London, London, SW3 6KY, UK.
*These authors contributed equally

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**Researcher contact**

Karine Clément

U1269 Nutrition and Obesity: Systemic Approaches (Nutrinomics)

Email:

 karine.clement2@gmail.com
 karine.clement-lausch@sorbonne-universite.fr

Cell phone number on request

**Press contact**

presse@inserm.fr

[Access the Inserm press room](https://www.inserm.fr)