A Bacterial Compound Linked to Gut Microbiota Diversity and Better Cardiovascular and Metabolic Health

Insulin is produced by the beta cells of the pancreatic islets of Langerhans. Cells which, in type 1 diabetes, are destroyed by the immune system. In this study, the administration of hippurate improved blood glucose control and stimulated insulin secretion in animal models. Credits: Inserm/UMRS975/EndoCells SARL

Good gut microbiota function has an impact on our general physical and psychological health. Understanding how the architecture of the microbiota and the function of the bacteria that inhabit it affect the body has become a key research focus in recent years.

Within this context, researchers from Inserm and Université de Paris, in collaboration with teams from INRAE, Imperial College London and the University of Copenhagen in Denmark, have shown that hippurate, a metabolite derived from gut bacteria, is associated with microbiotal diversity. Hippurate is thought to play an important role in our cardiovascular and metabolic health, particularly by helping to regulate blood sugar. This research has been published in Gut.
For several years, the gut microbiota has been considered to play a key role in our health. Many scientific studies have highlighted the existence of a link between the diversity of the bacterial strains present and certain health parameters, particularly cardiovascular and metabolic.

The team led by Inserm researcher Dominique Gauguier focused on hippurate, a metabolite produced by the gut bacteria and that is found in urine. The scientists combined two methods, DNA sequencing (analysis of the genetic profile) of the gut microbiota bacteria and urinary metabolomic profiling (analysis of small metabolites present in urine) in 271 individuals from a Danish cohort (the MetaHIT study).

From the data obtained, the scientists show that high levels of hippurate in urine are associated with greater gut flora diversity and increased microbiota gene richness, two parameters that protect against cardiometabolic risk (the risk of developing cardiovascular disease and/or diabetes).

The researchers also had information about the participants' dietary habits and body mass index (BMI). They found that in obese individuals with a diet high in saturated fat and a risk of developing cardiovascular and metabolic problems, high levels of hippurate had beneficial effects on weight and metabolic health.

![Figure representing the main study findings.](image)

These findings were supplemented by a validation study in obese mice fed a fatty diet. In these animal models, the administration of hippurate improved blood glucose control and stimulated insulin secretion. "This research confirms the importance in human health of gut flora architecture and function by demonstrating the beneficial role of a metabolite produced by gut bacteria. Something we had already shown with the metabolite cresol," emphasizes Gauguier.

The relevance of these findings is both diagnostic, as hippurate can be considered a biomarker of microbiota diversity, and therapeutic. One could, for example, envisage modifying the microbiota using probiotic systems to produce larger quantities of the gut bacteria that synthesize the precursors of hippurate. This would then increase hippurate levels with their attendant protective effects on cardiometabolic risk.

For the scientists, the next step is to continue their research by studying the cellular mechanisms that explain how hippurate promotes insulin secretion and blood glucose regulation.
Sources

Human and preclinical studies of the host–gut microbiome co-metabolite hippurate as a marker and mediator of metabolic health

François Brial,1 Julien Chilloux,2 Trine Nielsen,3 Sara Vieira-Silva,4 Gwen Falony,4 Petros Andrikopoulos,2,5 Michael Olanipekun,2,5 Lesma Hoyles,6 Fatima Djouadi,7,8 Ana L Neves,2 Andrea Rodriguez-Martinez,2 Ghiwa Ishac Mouawad,1 Nicolas Pons,9 Sofia Forslund,10 Emmanuelle Le-chatelier,9 Aurélie Le Lay,1 Jeremy Nicholson,2 Torben Hansen,3 Tuulia Hyötyläinen,11 Karine Clément,12,13 Matej Oresic,14 Peer Bork,15 Stanislav Dusko Ehrlich,9,16 Jeroen Raes,4,17 Oluf Borbye Pedersen,3 Dominique Gauguelier,1,18 Marc-Emmanuel Dumas2,5,18,19

1 UMRS 1124 INSERM, Université de Paris, Paris, France
2 Section of Biomolecular Medicine, Department of Metabolism, Digestion and Reproduction, Imperial College London, London, UK
3 Novo Nordisk Foundation Centre for Basic Metabolic Research, University of Copenhagen, Kobenhavn, Denmark
4 Laboratory of Molecular Bacteriology, Department of Microbiology and Immunology, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Leuven, Belgium
5 National Heart & Lung Institute, Section of Genomic & Environmental Medicine, Imperial College London, London, UK
6 Department of Biosciences, Nottingham Trent University, Nottingham, UK
7 Centre de Recherche des Cordeliers, Université de Paris, Paris, France
8 Centre de Recherche des Cordeliers, INSERM, Sorbonne Université, Paris, France
9 Metagenopolis, INRAE, Paris, Île-de-France, France
10 Forslund Lab, Max Delbrück Centrum für Molekulare Medizin Experimental and Clinical Research Center, Berlin, Berlin, Germany
11 Department of Chemistry, Örebro University, Örebro, Sweden
12 INSERM, U1166, team 6 Nutriomique, Université Pierre et Marie Curie-Paris 6, Paris, France
13 Institute of Cardiometabolism and Nutrition (ICAN), Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Paris, France
14 School of Medical Sciences, Örebro Universitet, Örebro, Sweden
15 Structural and Computational Biology Unit, European Molecular Biology Laboratory, Heidelberg, Germany
16 Center for Host Microbiome Interactions, King’s College London Dental Institute, London, UK
17 Center for Microbiology, Vlaams Instituut voor Biotechnologie, Leuven, Belgium
18 McGill Genome Centre & Department of Human Genetics, McGill University, Montréal, Québec, Canada
European Genomics Institute for Diabetes, INSERM U1283, CNRS UMR8199, Institut Pasteur de Lille, Lille University Hospital, University of Lille, Lille, France

Researcher contact
Dominique Gauguier
Unit 1124 Environmental Toxicity, Therapeutic Targets, Cellular Signaling and Biomarkers
Email: dominique.gauguier@inserm.fr
Telephone number provided upon request

Press contact
presse@inserm.fr
Access the Inserm press room