**MetaCardis project five-year update: Analysis of data from 2000 recruited subjects will yield insights about gut microbiota and cardiometabolic diseases**

*Over five years, physicians and researchers have gathered data on 2000 people's gut microbiomes and their metabolism and cardiovascular health. Here's what they're hoping to find out.*

The world's most ambitious study to date on cardiometabolic diseases and gut microbiota marks its fifth year in 2017, with the upcoming results set to change the way we see a set of complex diseases that create a significant burden for healthcare systems around the globe. The €20 million-Euro MetaCardis (Metagenomics in Cardiometabolic Diseases) project, financed primarily through the European [FP7 initiative](https://ec.europa.eu/research/fp7/index_en.cfm), has completed its data collection phase, and in the final year of the project, physicians and researchers are working to answer clinically-driven questions in order to improve care for individuals at various stages of progression of their metabolic and cardiovascular conditions.

With multiple studies from the past decade showing links between the gut microbiota and cardiometabolic disorders—which include obesity, metabolic syndrome, diabetes, and cardiovascular disease—a group of European investigators initially saw a major opportunity to develop new approaches to treatment and move toward precision medicine for individuals with these conditions. The resulting project was MetaCardis, coordinated by Prof. Karine Clément—physician, full professor in nutrition, and research director of an [INSERM/University Paris 6 group](http://www.obesite-paris.com/ens_site.asp). The study brings together physicians and researchers in fields ranging from obesity, diabetes, and cardiology to microbiology, immunology, molecular biology, physiology, and bioinformatics. Originally slated to last five years (2012 to 2017), the project received a one-year extension to complete enrollment and data analysis.

The combined efforts of investigators from 15 research institutions in six countries have now resulted in the successful recruitment of over 2000 patients from three centres (in France, Denmark, and Germany). The subjects fall into nine clinically defined groups related to cardiovascular and metabolic diseases: (1) Metabolic syndrome, (2a) obesity, (2b) obesity, undergoing bariatric surgery, (3) diabetes, (4) acute coronary artery disease, (5) chronic coronary artery disease without heart failure, (6) chronic coronary artery disease with heart failure, (7) heart failure unrelated to coronary artery disease, and (8) healthy controls.

MetaCardis researchers left no stone unturned when it came to data collection. In total, they examined 1400 patient-related clinical and lifestyle variables, along with stool metagenomics and metabolomics data from serum and urine. So in addition to the standard information about subject age and anthropometric characteristics (waist circumference, BMI, body composition with percentage body fat), the researchers also measured clinical and biological characteristics (cholesterol, blood pressure, fasting blood glucose, inflammatory markers) and lifestyle factors related to medication use and history, physical activity, and dietary/nutrient intake. To complete the picture, researchers also gave each person an oral glucose tolerance test and measured hormonal responses.

This considerable amount of data, which is secured at [ICAN](http://www.ican-institute.org/), was recently copied to a project data hub stored at the [European Molecular Biology Laboratory](https://www.embl.de/) (EMBL) in Heidelberg, Germany. Physicians from [APHP](https://www.aphp.fr/hopitaux) and researchers from [INSERM](http://english.inserm.fr/) detailed the sociodemographic, clinical, and lifestyle variables for the MetaCardis study groups. In 2016, a poster of this data was presented in Magog-Orfod, Canada at a conference hosted by the [Cardiometabolic Health, Diabetes, and Obesity Research Network](http://www.frqs.gouv.qc.ca/en/la-recherche/la-recherche-financee-par-le-frqs/centres-groupes-et-reseaux/groupe/cardiometabolic-health-diabetes-and-obesity-research-network-nkhiaq9g1400704216075) (CMDO).

Previous studies on cardiometabolic diseases have been limited in their ability to combine multiple factors about a patient to carry out an integrated analysis; currently, the MetaCardis researchers are undertaking this formidable task by using sophisticated methods from systems biology—integrating the data and carrying out multi-level analyses. The associations they discover will then be validated in new experimental systems.

Those with cardiometabolic diseases, and the health professionals who care for them, know that new treatment approaches are urgently needed. MetaCardis could lay the groundwork for improving cardiometabolic disease care and progressing toward precision medicine by finding physiological pathways that might lead to new therapies, and by discovering gut microbial metabolites that contribute to the progression of these diseases—but most importantly, the project could help medical researchers learn how to refine the existing diagnostic categories based on new measures (that is, targets or pathways), eventually allowing subsets of patients to be funnelled toward therapies that will work more reliably.

Collaborators are ensuring ethical considerations remain front and centre in MetaCardis through the work of an external ethics expert, Prof. Thierry Magnin, professor of science and ethics and rector of Catholic university in Lyon (France). Prof. Magnin is overseeing communication of the MetaCardis objectives, results, and treatment possibilities to the patient volunteers; he will focus on important ethics-related issues including management and ownership of big data, reliability of statistical results, and development of algorithms for use in personalized medicine.

The sixth and final year of the project may prove to be the most exciting, as researchers work to uncover the answers to these main questions:

* Are factors related to lifestyle/sociodemographic factors, patient physiology, or microbiota associated with different stages of cardiometabolic diseases?
* How do these factors combine to constitute a healthy phenotype?
* Are certain gut microorganisms or metabolites responsible for the onset or progression of cardiometabolic diseases?
* Do certain gut biomarkers flag cardiovascular complications arising from obesity and diabetes?
* Can gut microbiota profile help doctors stratify (sub-categorize) these complex disorders?
* What are the effects and interactions of multiple drugs with lifestyle and the gut microbiome in patient populations?

Project leader Prof. Karine Clément says, “Coordination of MetaCardis has already been a fantastic adventure, involving experienced physicians and researchers from various fields, along with patients and patient associations. We expect a lot of interesting findings from the analytic work—findings that will improve knowledge in cardiometabolic disorders and lead to new ways of improving patients’ health and mitigating risks along the entire spectrum of disease progression.”

The highly-anticipated results will be released late next year, providing the basis for linking the gut microbiota to metabolic and cardiovascular diseases—with potential implications for the quality of life for millions of patients around the globe.

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