VOLUME #15

NEWSLETTER

cartagene

December 2025

Happy Holidays!

Dear participants,

2025 has been a busy year for CARTaGENE, highlighted by the launch of the cohort's second major health follow-up. This follow-up will significantly expand the data on your health and lifestyle, which are essential for improving our understanding of chronic diseases and supporting population health research in Quebec. Thank you to everyone who has already taken part! If you haven't yet, there's still time to complete your questionnaire.

In this edition of our newsletter, we highlight several advances in genetics made possible by studies using CARTaGENE data. Thanks to your contribution, the platform is now the largest publicly accessible genetic database of the Quebec population. These studies show how important it is to have a resource that truly represents Quebec: it helps researchers interpret genetic data, better understand hereditary diseases, and develop precision health approaches tailored to our population,

In this edition:

especially at a time when Quebec remains underrepresented in major international genetic databases. CARTaGENE's reach goes far beyond genetics. Dozens of projects are exploring public health, chronic diseases, cancer, neuroscience, mental health, the environment, and lifestyle factors. This diversity highlights the wide-ranging impact of research made possible through your participation.

Looking ahead to 2026, we have an exciting year of new initiatives and collaborative projects planned. Thanks to your involvement, we are continuing to develop the platform to better connect genetics, the environment, and living conditions, helping us understand how these factors interact to influence health in Quebec.

As Dr. William Foulkes, a researcher using the platform, says: "*CARTaGENE is an extraordinary resource, and it exists because thousands of people chose to contribute to something larger than themselves*".

Thank you for being part of this collective scientific journey; none of this would be possible without you.

Wishing you happy holidays!

The CARTaGENE team

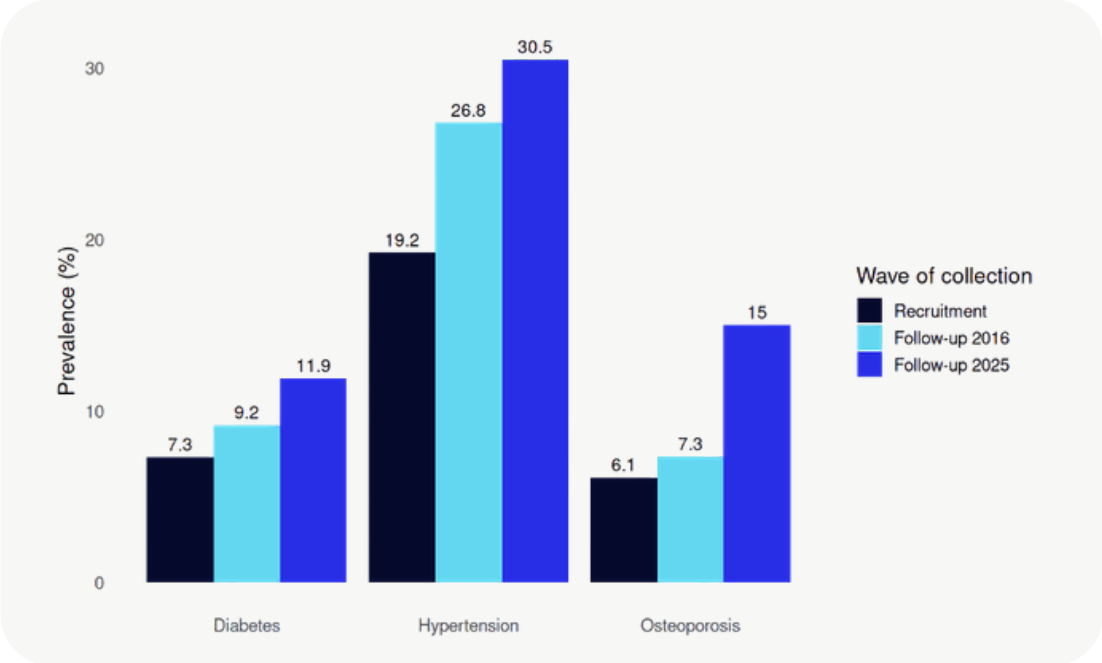
2025 Health Follow-up

In May 2025, we launched the campaign for the second major health follow-up of the cohort. This initiative is designed to gather updated information on your health and lifestyle habits, enriching our databases and supporting research efforts aimed at improving the health of Quebec's population.

The follow-up is progressing well. To date, 4,366 participants have completed the questionnaire, and 932 are currently in progress. We sincerely thank you for your continued involvement. Your participation is essential to the success of this study.

As illustrated in the figure below, the **prevalence of several chronic conditions**, including diabetes, hypertension, and osteoporosis, increases with age. For instance, when comparing data from our three major health follow-ups, we observe that the proportion of individuals with hypertension has increased from 19.2% at recruitment to 30.6% based on preliminary data from the 2025 follow-up.

By continuing to share information about your health, you contribute to a deeper understanding of disease risk factors and help advance knowledge that promotes healthy aging.



If you haven't yet contributed to the 2025 Health Follow-up, there's still time! Over the coming months, reminders will be sent to those who have not yet completed their questionnaire. Each email includes a link to the information and consent form. Want to learn more? Watch our webinar to understand the importance of this data collection for chronic disease research and see how easy it is to participate.

NutriQuébec

Our collaboration with NutriQuébec, launched in 2024, continues to collect valuable information on the eating and lifestyle habits of Quebecers. Last year, 2,466 participants contributed by completing at least one food recall. This summer, a second wave of data collection took place, with 1,576 people participating. A third wave is scheduled for June 2026.

Photo source: NutriQuébec

Did you know?

Your nutrition and physical activity data, collected through NutriQuébec, will be combined with data from six other cohorts across Canada. This initiative is part of the Canadian Partnership for Tomorrow's Health (CanPath), where CARTaGENE represents Quebec. Together, we aim to advance nutrition research on a national scale.

The CARTaGENE Platform in 2025

Over the past year, our team has continued working to enhance data quality and strengthen research infrastructures.

We have developed a new portal for researchers, which brings together key information about the cohort, collected data, available biological samples, and the access process. This portal also features an interactive catalog that allows users to explore cohort data in detail.

Additional DNA sequencing data have been generated at the *Centre d'expertise et de services de Génome Québec*. Approximately 1,750 additional genomes will be available for research starting in 2026. To learn more about the value of genetic data, read our Special Feature starting on page 5.

CARTaGENE has also maintained its collaboration with the Maelstrom Research team at the Research Institute of the McGill University Health Centre. This group specializes in data cleaning and harmonization. Through this partnership, we aim to continuously improve datasets, making them more relevant and usable for health research.

Your Genetic Data Supports Research

Thanks to your contribution, CARTaGENE now constitutes the largest publicly available dataset of genotyping and whole genomes from the Quebec population for research purposes. Approximately half of all active scientific projects, or 42 projects, are currently using this data to advance health research in Quebec and elsewhere.

Your genetic information allows scientists to better understand diseases, improve diagnostic tools, and develop more personalized approaches to medicine. Below, we present a few concrete projects that rely on your data, as well as an interview with Dr. William Foulkes, a renowned medical geneticist and long-time user of CARTaGENE.

Sequencing and Genotyping

CARTaGENE has generated two main types of genetic data:

- **Genome sequencing** for about 2,200 participants, which provides the complete DNA code of a person, letter by letter.
- **Genotyping** for about 30,000 participants, which identifies specific variants at selected positions in the DNA.

Sequencing = reading the entire book

Imagine your DNA as a book written with four letters: A, C, G, and T. Sequencing reads every letter, from start to finish.

What is it used for?

- Identifying all variants, including rare ones, that may influence health.
- Studying genetic diversity and evolution.
- Providing a comprehensive reference for research.

Genotyping = reading key words

Instead of reading the whole book, genotyping focuses on specific sections to see which variants are present.

What is it used for?

- Accessing useful genetic information at a lower cost.
- Studying associations between certain variants and diseases or specific traits.
- Examining genetic diversity and population structure.

Tools for estimating disease risk

Part of genetic research involves combining the effects of thousands of small DNA variants to estimate predisposition to certain common diseases with a hereditary component. These estimates are called “polygenic risk scores”. Ultimately, these tools could help doctors better tailor prevention and treatment to each person’s genetic profile, based on the concept of precision health (or personalized medicine). Recently, a team used CARTaGENE data to develop a faster and less expensive algorithm for calculating these scores. This tool is now freely available to the entire scientific community.

Source: Zabad *et al.* 2025 Am J Hum Genet.

Discoveries of regional genetic characteristics

Because CARTaGENE is a representative sample of the Quebec population, it enables researchers to investigate how the province’s settlement history has shaped its genetics landscape. For example, a recent study focused on Beauce, a region whose population descends from a small number of founding families and has remained relatively isolated over generations. This unique history has led to a higher frequency of certain rare genetic variants, some of which are associated with hereditary diseases. By comparing genetic data from Beauce with data from urban areas obtained from CARTaGENE, Simon Girard’s team identified 36 pathogenic variants that are much more common in the region, some of which have never been described before. These discoveries enhance our understanding of rare diseases and help improve their diagnosis. This example also shows that, even though the cohort was recruited in urban areas, the data you provide contribute to a better understanding of genetic diversity across Quebec, including regions outside the recruitment areas.

Source: Gagnon *et al.* 2025 Commun Biol.

A common genetic cause of hereditary cancer in Quebec

In a recent study, William Foulkes, Simon Gravel, and their colleagues identified a genetic variant in the *PMS2* gene associated with Lynch syndrome, a hereditary form of cancer linked to a DNA repair defect. This variant increases the risk of developing colorectal cancer and endometrial cancer.

Initially discovered in 2008 in several members of the same family affected by Lynch syndrome, this variant was subsequently identified in several individuals from families in different regions of Quebec.

By cross-referencing CARTaGENE's genetic data with genealogical information from the BALSAC database, the team was able to trace this variant back to a single ancestor who arrived in Quebec approximately 11 generations ago. This is the most common genetic variant associated with hereditary cancer identified to date in the French-Canadian population.

Source: Chong *et al.* 2025 Clin Genet.

Discovery of a genetic cause for a rare lung disease

Primary ciliary dyskinesia (PCD) is a rare genetic disorder that affects tiny structures called cilia, found in the lungs, nose, and sinuses. People with PCD suffer from chronic coughing, frequent infections, and may develop lung damage.

Adam Shapiro and his team identified five people with PCD caused by changes in the *ODAD4* gene. Among them, three patients from Quebec had the same genetic change, inherited from a common ancestor who lived about 330 years ago.

Data from CARTaGENE was essential to this discovery. The research team identified 59 individuals carrying this genetic variant in the cohort and found that it is more common in two regions: Bas-Saint-Laurent (1 in 111) and Côte-du-Sud (1 in 143).

Source: Bourassa *et al.* 2025 Cells

A resource for hereditary disease screening programs

CARTaGENE data is used to inform public policy development in genetics and to improve hereditary disease screening programs.

A recent study evaluated the screening program for autosomal recessive hereditary diseases for people from Saguenay–Lac-Saint-Jean, Charlevoix, and Haute-Côte-Nord. By examining the frequencies of genetic variants associated with these diseases in other regions of Quebec using CARTaGENE data, the research team led by Luigi Bouchard showed that they are much rarer in the rest of the province, confirming that the risk of being a carrier remains highly regionalized. These results helped document the relevance of the program and support its reassessment.

INESSS relied on CARTaGENE's population genetic data to recommend the addition of two diseases to the program, mucolipidosis type 2 and Zellweger spectrum disorder, bringing the number of diseases covered to six.

Your data help support public health decisions, improve the prevention of hereditary diseases, and provide couples with more informed reproductive choices.

Sources:

Fortin *et al.* 2025 Genet Med Open.
INESSS report on Zellweger spectrum disorder (in French).
INESSS report on mucolipidosis type 2 (in French).

Interview with Dr. William Foulkes

Understanding Hereditary Cancer in Québec

Dr. William Foulkes is a clinician and researcher at McGill who has spent his career studying hereditary cancer. We spoke with him about his work, his long-standing use of CARTaGENE, and his team's recent discovery of a founder variant in the *PMS2* gene among French Canadians.

You are both a clinician and a researcher. Could you explain what your work looks like, and how these roles complement each other?

I am both an MD and a PhD, so my work is really divided between caring for patients and doing research. In the hereditary cancer clinic, I see people who developed cancer at a very young age, people who have several relatives affected, and also people who have never had cancer themselves but are worried because someone close to them was recently diagnosed. With our team of genetic counsellors, we try to understand whether an inherited factor might be involved.

A lot of my research actually starts with what happens in the clinic. When we notice something unusual, for example the same rare genetic change appearing in two unrelated families, it naturally raises scientific questions. That is what we then explore through research. Having both roles allows me to link what I see in real families to the genetic discoveries we make, and the research in turn helps us give better answers and better care to the people who come to the clinic.

You have spent many years studying hereditary cancer. What drew you to this field originally, and what questions are you trying to answer today?

My interest in hereditary cancer began when I was a young doctor deciding what direction to take. I was considering oncology, but my wife encouraged me to think about genetics so that I could focus not only on treating people who were already very sick, but also on understanding the causes of disease. That idea appealed to me. I was fascinated by the question of why certain people develop cancer so early or in such unusual ways.

I then completed a PhD in a lab working on ovarian cancer. I had almost no laboratory experience at the time, so I learned everything from the ground up, from collecting samples to running experiments.

That experience, and the early discoveries we made about the genetic basis of cancer, convinced me that inherited factors were a powerful way to understand these diseases.

Today, the same curiosity drives my work. I want to know which inherited changes put people at higher risk and how we can use that knowledge to prevent cancer or detect it sooner. The goal is to translate what we learn in the lab into clearer answers and better options for the families we see in the clinic.

You have been using CARTaGENE for quite a long time. How has the cohort helped your research over the years, and what makes it valuable from your perspective?

We first used CARTaGENE as a source of very reliable control samples. It allowed us to select healthy participants of French Canadian ancestry, with several grandparents from Québec, so we could check whether a genetic variant we found in a cancer patient was actually rare or simply common in the population. Over time, as part of the cohort had their genomes fully sequenced, the value of CARTaGENE grew enormously.

It helped us confirm founder variants, understand how frequent they are, and even map where in Québec they seem to originate. Working with CARTaGENE, and with researchers like Simon Gravel, has opened the door to studies that would have been impossible without such an unbiased and deeply rooted Québec resource.

Your team recently discovered a "founder variant" in the PMS2 gene among French Canadians. Could you explain what a founder variant is, and why this particular discovery is important for families and for cancer prevention in Québec?

A founder variant is a genetic change that begins in a single ancestor and is passed down through many generations. This happens in Québec because of the unique history of the population, where certain lineages expanded rapidly over a few centuries.

The *PMS2* variant we studied raises the risk of colon and endometrial cancer. Many people who have it will never develop cancer, but their risk is clearly higher than average, and there are practical things they can do about it, like regular colonoscopy or even aspirin for prevention. It also helps families understand why cancer may have appeared among their relatives.

In very rare situations, if both parents carry the same variant, a child can develop a serious condition in childhood. Knowing this ahead of time can make a real difference. And from a research perspective, having many people with the exact same variant helps us understand the gene much more clearly.

Looking ahead, how do you see CARTaGENE helping future discoveries in hereditary cancer? What types of

data, tools, or improvements would be most useful for researchers like you?

Sequencing the entire cohort's genomes would be incredibly valuable. Even though some information can be imputed, many geneticists feel strongly that nothing replaces having the actual genome sequence. It would allow us to study the frequency of important variants across the whole population rather than in a limited subset.

Another improvement would be long term follow up. The original questionnaire was completed when participants enrolled, but to advance hereditary cancer research we need to know what happened afterward. Linking to cancer diagnoses and, when possible, collecting tumor samples would transform the resource. Having both the genetic data and the tumor material would create something truly unique and very attractive for future research.

Finally, is there a message you would like to share with CARTaGENE participants who volunteer their data and samples to support research?

I would like to thank every participant. None of this work would be possible without people who take the time to give samples and answer questions simply because they want to help. This kind of contribution cannot be replaced by money. It is a gift to society.

Your participation allows discoveries to be made and helps improve prevention and care for future generations. CARTaGENE is an extraordinary resource, and it exists because thousands of people chose to contribute to something larger than themselves.

The content of this interview has been revised for improved readability.

A Hidden Cardiovascular Risk Factor Revealed Thanks to Your Data

Study shows that invisible hormonal imbalances double the risk of cardiovascular disease.

A recent study using CARTaGENE has shed light on a hormonal issue that is often overlooked: subclinical primary hyperaldosteronism. This condition involves the excessive production of aldosterone, an important hormone that regulates salt and blood pressure, even when blood pressure appears normal or only slightly elevated.

Why does this matter? Because this imbalance, long considered harmless, doubles the risk of serious cardiovascular events such as heart attack, stroke, heart failure, or death from heart-related causes. It is also much more common than previously thought: nearly one in five participants in the study exhibited this hormonal profile.

Rémi Goupil and his team analyzed data from 2,017 individuals recruited into CARTaGENE in 2009–2010. Using blood samples provided, they measured two key hormones: aldosterone and renin. They then followed these individuals for more than ten years using administrative health data from RAMQ, which identifies hospitalizations and cardiovascular-related diagnoses.

The result: Two simple markers can identify people at risk:

- very low renin (≤ 4 ng/L)
- high aldosterone-to-renin ratio (≥ 70 pmol/L/ng/L)

These thresholds are much lower than those currently used to screen for primary hyperaldosteronism, meaning many cases may go undetected. Importantly, the risk exists even in people without hypertension, challenging the current practice of screening only those with severe hypertension.

These findings pave the way for a new preventive approach: detecting these hormonal imbalances earlier and taking action before complications develop. Effective treatments already exist, including medications that block aldosterone's action, and new therapeutic strategies are in development.

Thanks to your contribution, we now know that a simple hormone test could help prevent serious cardiovascular events in people who appear healthy.

Source: Goupil *et al.* 2025 Circulation.

Polluted Air, Troubled Memory? New Study Offers Insights

A research team led by Stéphane Buteau at the School of Public Health, Université de Montréal, analyzed the links between air quality and cognitive health in more than 7,000 CARTaGENE participants.

Why this research matters

Air pollution is well known for its effects on the heart and lungs, but its impact on the brain is less understood, especially in regions with relatively low pollution, like Quebec.

How the Study Was Conducted

The team estimated exposure to two common pollutants based on data provided by the Canadian Urban Environmental Health Research Consortium (CANUE):

- $PM_{2.5}$: fine particles suspended in the air
- NO_2: a gas mainly produced by traffic

These exposures were calculated over the 11 years preceding cognitive tests, which measured reaction time, visual memory, and reasoning skills.

Key Findings

- $PM_{2.5}$: linked to slightly slower reaction times
- NO_2: associated with slightly lower visual memory performance

Surprisingly, both pollutants were also linked to better reasoning scores, a finding that requires further investigation. Factors such as sex, education level, and smoking appear to modify these effects.

Why It Matters

Even at low levels, air pollution may subtly affect cognition. These findings underscore the need for continued research to better understand these effects and safeguard cognitive health.

Source: Fliaguine *et al.* 2025 SSRN.

CARTaGENE in numbers

130 projects, 81 still ongoing

273 independent researchers with data access

16 years of progress in research

82 theses and dissertations

194 peer-reviewed **scientific articles**

Replay Available!

Webinar on CARTaGENE's 2025 Health Follow-Up

Town Hall for CanPath Participants
Webinar organized by CanPath.

La génétique des Québécois jouerait un rôle dans l'apparition de maladies cardiaques, published in La Presse, March 10, 2025

Une mutation génétique fréquente en région reliée à un seul ancêtre?, published in Le Soleil, August 14, 2025

Variation génétique propice au cancer colorectal, Ici Première. C'est encore mieux l'après-midi

Effet fondateur et syndrome de Lynch Le Saguenay-Lac-Saint-Jean est moins consanguin que l'on peut le penser! 95.7 - KYK

CARTaGENE in 2026

In this section, we offer a preview of what's coming up for CARTaGENE in the year ahead. Get ready!

New data collection phase for the CAHHM study

Between 2015 and 2017, some individuals took part in the first phase of a partnership between CARTaGENE and the Canadian Alliance for Healthy Hearts and Minds (CAHHM) study, which investigates heart and brain health among Canadians.

The CAHHM study aims to better understand how the environment, lifestyle, and access to care influence heart and brain health. It focuses on memory, blood circulation, fat distribution, and the development of chronic diseases in adults in Canada.

Starting in 2026, a new phase of data collection will begin. Some participants from the initial phase will be invited to take part again, and detailed information will be sent to them by email.

Towards More Participatory Research with the CEPPP

The CARTaGENE team greatly valued its collaboration with the Center of Excellence on Partnership with Patients and the Public (CEPPP) during the CARTaGENE Symposium in October 2024.

To strengthen transparency and collaboration, CARTaGENE is launching a project to involve cohort participants directly in its decision-making processes, in partnership with the CEPPP. This initiative will help define practices for managing the return of research results and support key steps such as the implementation of data-collection campaigns.

Together, we aim to move CARTaGENE toward a more participatory and inclusive model.

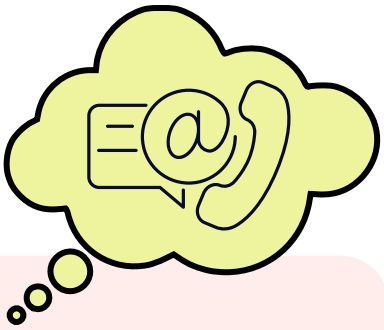
WHAT WE HAVE IMPLEMENTED THANKS TO YOUR FEEDBACK:

Creation of a Participant Committee
We're partnering with the CEPPP to create a committee made up of CARTaGENE participants.

A more comprehensive health follow-up
Our questionnaire now includes additional questions on mental health to better reflect what matters to you.

Exploring the return of individual results
We are working to define the best way to share certain study results with you.

More webinars for you
We plan to offer more accessible science webinars to showcase the research made possible by CARTaGENE.



Have you relocated, retired, updated your email address, or changed your phone number?

Please assist us in maintaining the accuracy of your information.

Please take a moment to provide us with your updated contact information. Even if you relocate outside of Quebec or Canada, you can continue to be a participant!

Maintaining communication with you is crucial for the success of this project!

Get in touch with us!

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1 (877) 263-2360

For additional details:
https://www.cartagene.qc.ca/

Our collaborators

CHU Sainte-Justine – Le centre hospitalier universitaire mère-enfant – Université de Montréal

CanPath – Canadian Partnership for Tomorrow's Health – Partenariat canadien pour la santé de demain

Économie Innovation et Énergie Québec

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