CHU Sainte-Justine
Le centre hospitalier universitaire mère-enfant
Pour l'amour des enfants
Université de Montréal

CARTaGENE

Université de Montréal

Newsletter

Volume 1 - August 2012

Thanks to the much-valued participation of over 20 000 Quebeckers, our first objective has been achieved !

A total of **20 227 people** responded to our health questionnaire and donated blood and urine, allowing us to establish our data and biological samples bank !

The Environment and Nutrition is nearing completion.

We have requested that participants complete two further questionnaires that focus on **environmental exposure and eating habits**.

This additional component enriches our database, which will be available for research into original information with great scientific potential. It will also allow for the investigation of environmental impacts on health.

To this day, we have received **12,556 Environment questionnaires and nearly 7500 Nutrition questionnaires** for this component.

Stay Informed!

Information about the CARTaGENE project is available on our website:
www.cartagene.qc.ca

Contact-us !

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A second wave of recruitment

Starting in October 2012, CARTaGENE is embarking on a new stage of recruitment that will not only provide for the maintenance and expansion of our participant cohort, but will also allow us to access regions of the province not previously integrated into the project (Gatineau, Trois-Rivières).

The questionnaire on health and lifestyle habits used in this new initiative has been improved to delve deeper into the exploration of new areas of health studies such as genetic and infectious diseases.

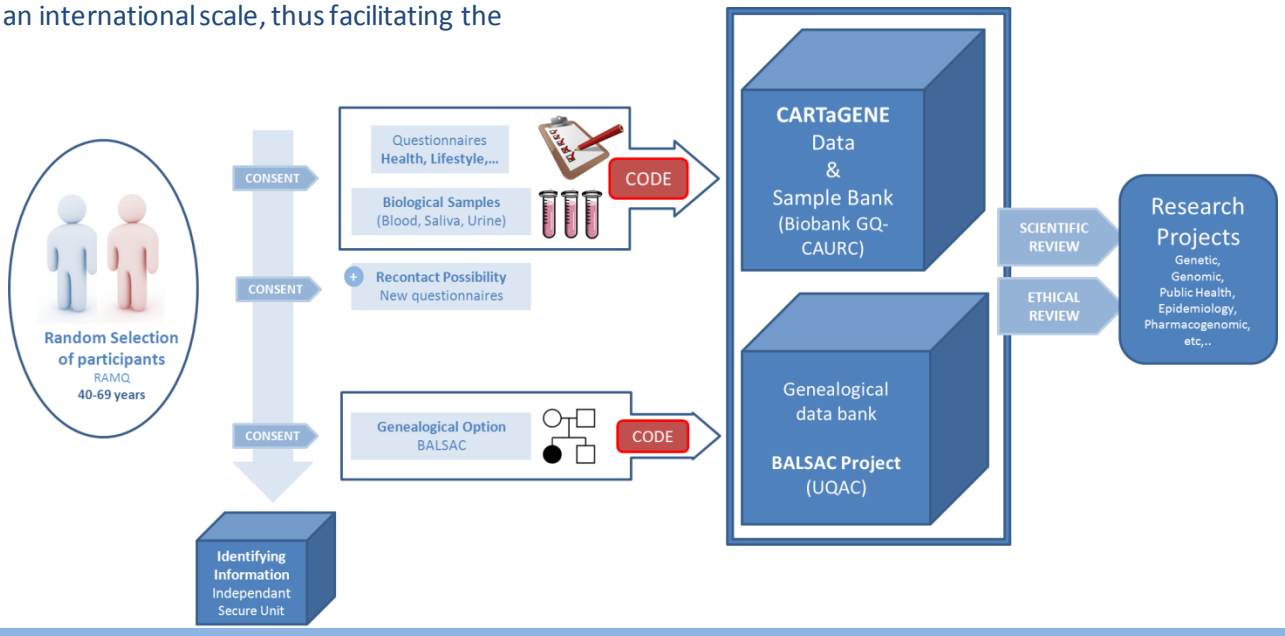
A sample of blood or saliva will be requested as part of this new initiative.

Nos partenaires :

Canadian Partnership for Tomorrow Project
Projet de partenariat canadien Espoir pour demain
GenomeQuébec relier la science à la vie
PARTENARIAT CANADIEN CONTRE LE CANCER
GenomeCanada

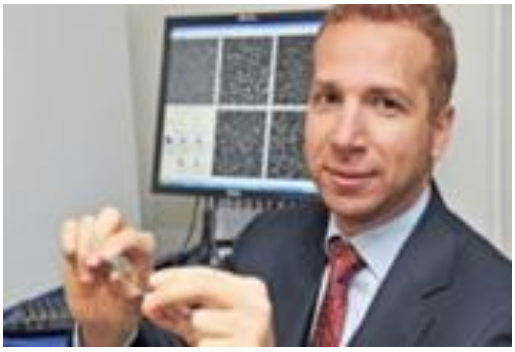
A Brief Summary of the CARTaGENE Project

CARTaGENE's mission is to create and maintain in the long term a bank of data and samples that represent the genomic identity of Quebec and are competitive on an international scale, thus facilitating the emergence of new research projects and knowledge regarding health care for Quebec, Canada, and the international community.



CARTaGENE Team News

The Canadian Society for Clinical Investigation has awarded Dr. Philip Awadalla, Scientific Director and Principal Researcher of the CARTaGENE project, with the 2012 *Joe Doupe Young Investigator* Award. This award recognizes outstanding achievements in the first eight years of an independent researcher's career.



Dr. Philip Awadalla., Ph.D

Transfer to Sainte-Justine

The management of CARTaGENE will soon be transferred to the Sainte-Justine University Health Centre (CHU Sainte-Justine), which will replace the Université de Montréal as the project's host institution. The CHU Sainte-Justine is committed to respecting and implementing CARTaGENE's policies of engagement with its participants, including its consent form. CARTaGENE's operations will undergo no modification as a result of the transfer, which will affect neither staff nor the principal investigators, Dr. Guy Rouleau and Dr. Philip Awadalla.

Dr. Awadalla's Laboratory

The laboratory of Dr. Awadalla specializes in Medical Genomics and Population Genomics at the Université de Montréal, where it investigates how genetics and the environment influence the frequency and severity of diseases impacting human populations, including genetic, infectious, and chronic diseases as well as cancer.

Using state-of-the-art techniques and modern statistical tools, the regions of the genome implied in pathology can be identified and localized, leading to a better comprehension of the mechanism that is causing the mutations.

Dr. Guy Rouleau , M.D., Ph.D, FRCP(c),QC

CARTaGENE's Principal Co-Researcher Team Discovers the Gene Responsible for Essential Tremor

Essential Tremor (ET), the most common motor disorder in the population today, is a neurological disease that can affect the hands, head, vocal cords, or other parts of the body.

The principal characteristic of ET is involuntary tremor that accompanies everyday gestures. Individuals affected by the disorder may find the tremor embarrassing, and it can render ordinary tasks difficult.

The researchers at the Université de Montréal, CHU Sainte-Justine, and the CHUM have identified a gene linked to the onset of the disease. The gene, known as FUS, has previously been associated with the onset of amyotrophic lateral sclerosis (ALS).

Scientists have also found that mutations in the FUS gene can, through different mechanisms, result in cases of ET.

"*This discovery represents the first piece of genetic information that allows for the identification of the pathological mechanism causing ET; this will be beneficial for diagnosis and the development of future medications. The transition toward genetic diagnosis will one day allow for reductions in the misdiagnosis of ET; three-quarters of diagnostic errors occur in 37-50% of ET cases," explains the study's director, Dr. Guy Rouleau, in a communiqué.*

The discovery of this gene is not only able to confirm diagnosis; it can also pave the way for the development of new therapies.
(MaxiSciences, August 3, 2012)

Reference of the scientific article :
«*Exome sequencing identifies FUS mutations as a cause of essential tremor*» - Nancy D. Merner et al. **The American Journal of Human Genetics** (August 2012)

The CARTaGENE Project's Co-Founder is Recognized by the Order of Quebec

On June 7th, 2012, **Bartha Maria Knoppers was honoured with the insignia of an officer of the National Order of Quebec**.

Pr. Bartha Maria Knoppers, LL.D., Ad.E., O.C.

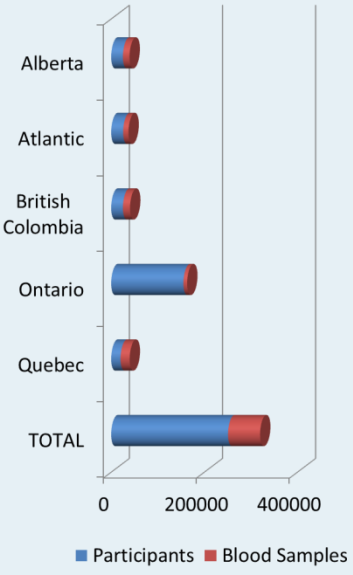
Professor Knoppers is pursuing a successful academic career in the adjoining fields of medical law and biomedical ethics.

For several years, she has focused on highly-debated topics and social issues such as biobanks, population genetics research, pharmacogenomics, and the future of public health.

A world leader in the fight for the "social ownership" of genetics, Prof. Knoppers has played key roles in the foregrounds of Genome Canada, Genome Quebec, and at the heart of the CARTaGENE infrastructure.

(National Order of Quebec)

Quelques chiffres...



250 919 Canadian Participants !

The Canadian Partnership for Tomorrow Project (CPTP) is a prospective cohort study funded by the federal government. Its objective is to recruit 300,000 participants and create a national bank of data and samples on the health of the population, thus facilitating, for the benefit of all Canadians, the acceleration of the fight against cancer and other chronic diseases. To achieve this goal, the project has undertaken to recruit thousands of Canadians between the ages of 35 and 69 years and follow their progress over the course of several decades.

CARTaGENE represents the Quebec cohort of this pan-Canadian project. The four other major cohorts are:

- **Ontario Health Study**
- **Tomorrow Project** *(Alberta)*
- **Atlantic Path**
- **BC Generations Project**

	Alberta	Atlantic	Bristish Colombia	Ontario	Quebec	TOTAL
Participants	25119	25587	25159	155050	20004	**250919**
Samples	14256	11502	15333	8044	19692	**68827**

A Message from Dr. John Potter, *Chair of the Canadian Partnership for Tomorrow Project's International Scientific Advisory Board*

"Each person makes a unique contribution to the project."

Why is this type of study important?

Such a study allows scientists to identify various sets of disease-causing factors by allowing them to observe the evolution of individuals over time and with consideration of the genetic background.

Why include so many participants?

Chronic illnesses are complex, and they generally result from several causes, whether environmental or genetic. To better determine the mechanisms from which such diseases develop, investigators need to look at more than a few rare cases. By having a great number of participants, we are able to more quickly identify risk profiles in the population.

Why participate?

It's a gift to the future. Even if there may be no direct benefit to you as a participant, you will be giving something valuable to the community.

Each individual's participation raises the total number of people in the study and contributes to the diversity of what constitutes a Canadian today.

There are many applications for CARTaGENE's Biobank, particularly in the field of cardiovascular research.

Genome Canada's national competition for funding in the field of personalized medicine and genomics has recently selected four pre-applications for projects, including a CARTaGENE initiative in the cardiovascular field. CARTaGENE is currently the only population-based cohort in Canada considered among the proposals to Genome Canada.

Moreover, the CARTaGENE project, along with all its Canadian partners, will be included in an initiative launched by the Canadian Partnership for Tomorrow Project through two applications focused on cardiovascular traits.

The CARTaGENE's Genomics Project :
Systems Genetics of Cardiometabolic Phenotypes

Spearheaded by Dr. Philip Awadalla and Dr. Youssef Idaghdour (Banting Fellow, Research Associate; CARTaGENE), this genomics program makes use of the wealth of biological samples collected by the CARTaGENE project.

Dr. Youssef Idaghdour, PhD

Dr. Philip Awadalla, PhD

Merging population and quantitative genomics, the project aims to identify markers of disease susceptibility by focusing specifically on the link between the "expression" of genes of the genome set and certain quantitative measures generally associated with cardiometabolic problems such as lipid profile, arterial rigidity, and the body mass index. This approach will allow researchers to determine the relative contributions of certain genes and environmental factors on "cardiometabolic" traits. The team used the genetic material of 1000 individuals at low to high risk for cardiovascular disease garnered by the CARTaGENE cohort. What is more, relevant and detailed genealogical data have been obtained for the participants.

The researchers have thus been able to document a structure in gene expression profiles and transcriptional signatures** correlated with the presence of a lower or higher risk of cardiometabolic disease.

This research project has led to a large number of auxiliary studies with collaborators such as Dr. Mark McCarthy of Wellcome Trust, who studies the side effects and complications that result from diabetes treatments. Similarly, a collaboration examining markers associated with Type 2 diabetes and other factors of comorbidity is underway with Dr. Pavel Hamet of CHUM.

* Denotes a cluster of risk factors for coronary heart disease and the development of metabolic diseases such as Type 2 diabetes.

** Transcription is a biological process of genetic information expression contained in DNA

Diagnostic Aid for Incidences of Zellweger Syndrome in the Quebec Population

Ongoing project led by Dr. Luigi Bouchard (Department of Biochemistry) and Dr. Sébastien Levesque (Department of Pediatry), Université de Sherbrooke

Dr. Luigi Bouchard, Ph.D.,

Zellweger Syndrome is a rare genetic disease that manifests at birth, causes serious neurological problems as well as damage to many organs, and usually results in death during the first year of life. At least four causal genetic anomalies of the condition have been identified in Quebec, with a particularly high incidence in the Saguenay-Lac-St-Jean (SLSJ) region.

Nourrisson atteint du Syndrome de Zellweger

Given the increased frequency of the syndrome in SLSJ and the lethality of the condition, the project aims to determine the prevalence of carriers in the region and elsewhere in Quebec by using participant blood samples available in the CARTaGENE biobank in order to develop an appropriate molecular screening test.

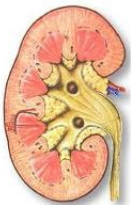
This project is funded by the GO Foundation

Dr. François Madore, M.D., M. Sc

Determining the Prevalence of Chronic Renal Disease in the CARTaGENE Cohort

Ongoing project led by François Madore (Université de Montréal Hôpital du Sacré-Coeur de Montréal Research Centre.)

Chronic renal failure is an alteration in the filtration function of the kidneys. In its early stages, the condition displays few or no symptoms, but by the time symptoms appear, kidney damage may already be advanced.



Thanks to health data and blood and urine samples collected by the CARTaGENE project, an estimate of the renal function of nearly 20,000 individuals has been arrived at. The prevalence of chronic renal failure in the CARTaGENE cohort is approximately 7%.

Nearly 90% of individuals suffering from mild to moderate renal disease have claimed to suffer from no kidney problems. If we relate these figures to the population of the whole of Quebec, we can estimate that 550,000 Quebeckers suffer from chronic renal disease, and more than 470,000 are unaware of their condition. The CARTaGENE project's data has thus demonstrated the prevalence of renal disease in the Quebec population as well as an alarming rate of ignorance of the issue.

Evaluating Mercury Exposure in the Native Population of Northern Quebec

Completed project led by Pierre Ayotte (Université Laval CHUQ Research Centre, Human Toxicology Administration INSPQ)

Dr. Pierre Ayotte., Ph.D

Researchers at the Public Health Research Unit of the CHUQ, in collaboration with the Cree Board of Health and Social Services, have launched a study to examine the relationship between exposure to environmental contaminants such as mercury and certain effects on health in the Cree communities of Northern Quebec.

This study aims to compare the metabolic profiles of urine samples obtained from Cree individuals to those of individuals from Southern Quebec with little history of mercury exposure and recruited in the context of the CARTaGENE project's optimization phrase in order to identify a metabolic urinary profile representing the signature of chronic mercury exposure, which is prevalent in Native populations due to fish consumption.

This project has allowed us to validate the applicability of a method of analysis that can be used in future research projects in the context of a prospective population-based study such as CARTaGENE.

A New Cause of Blindness in Children

Falk MJ. Et all, *Nature Genetics* (July 2012) Leber Congenital Amaurosis (ACL) is a devastating form of hereditary blindness affecting newborns. A new gene recognized as essential to supporting life has been linked to this condition; it has never before been associated with any disease impacting humans.

A Mutation of the Cystic Fibrosis Gene CFTR has been Associated with a Severe Phenotype and High Prevalence in the French-Canadian Population

De Bie I. et al, *Genetics in Medicine* (May 2012)
A rare mutation has with an allelic frequency of 0.7% has been found in a cohort of French-Canadian patients afflicted by cystic fibrosis. The mutation has been associated with a severe expression of the disease and intestinal manifestations from childhood. This mutation can thus be included in the DNA-based screening panel of mutations for the French-Canadian population.

A New Genetic Cause Explains a Significant Proportion of Joubert Syndrome Cases in the French-Canadian Population

Srour M. et al, *The American Journal of Human Genetics* (April 2012)
Joubert Syndrome is a recessive autosomal disorder characterized by a specific cerebral malformation, developmental delay, difficulties with hand-eye coordination, and respiratory anomalies. Though the syndrome was first described over 40 years ago, its cause in many French-Canadian families remains unknown. Out of 16 patients participating in this study, 9 have exhibited a rare mutation; this suggests that the mutation could explain a large proportion of cases of Joubert Syndrome in the French-Canadian population.

A Modification in the Expression of Ovarian Cell Genes of French-Canadian Women with Breast and Ovarian Cancer Susceptibility Syndrome

Diala Abd-Rabbo D. et al, *Cancer Prevention Research* (February 2012)
The objective of this study is to identify early warning signs representing strategic preventative targets for the aggressive tumor that is ovarian cancer. This research shows the first molecular signature associated with French-Canadian mutations in the genes BRCA1/2 ("BReast CAncer"). A single mutation in one of these genes would be sufficient to alter the expression of the normal ovarian epithelial cells gene set, thus modifying the invasiveness of the mutation and the aggressiveness of the associated tumor.

A Mutation Explains a Proportion of French-Canadian Cases of Hereditary Spastic Paraplegia

Noreau A. et al, *Canadian Journal of Neurologic Science* (January 2012)
Hereditary Spastic Paraplegia corresponds to a progressive motor neurodegenerative disorder characterized by uncontrollable contractions and weakness in the lower limb. To this day, 20 genes linked to the cause of the disease have been identified. One of these corresponds to a recessive autosomal form of the condition and codes for an enzyme expressed primarily in cerebral tissue. The study shows that mutations in the gene can explain the onset of the disease in certain patients. In the near future, research into this mutation in patients could take place, and a diagnostic tool could thus be developed, providing for the targeted treatment of patients with the gene.