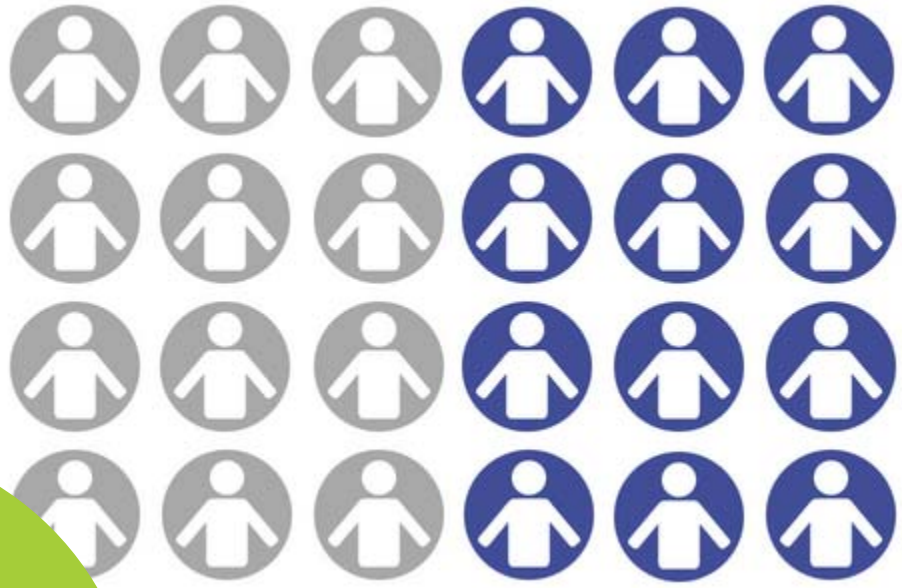
The Canadian Partnership for

Tomorrow Project

Philip Awadalla, PhD
National Scientific Director, CPTP

Ontario Institute for Cancer Research
Canadian Data Integration Centre
University of Toronto

Understanding **disease risk factors** is challenging



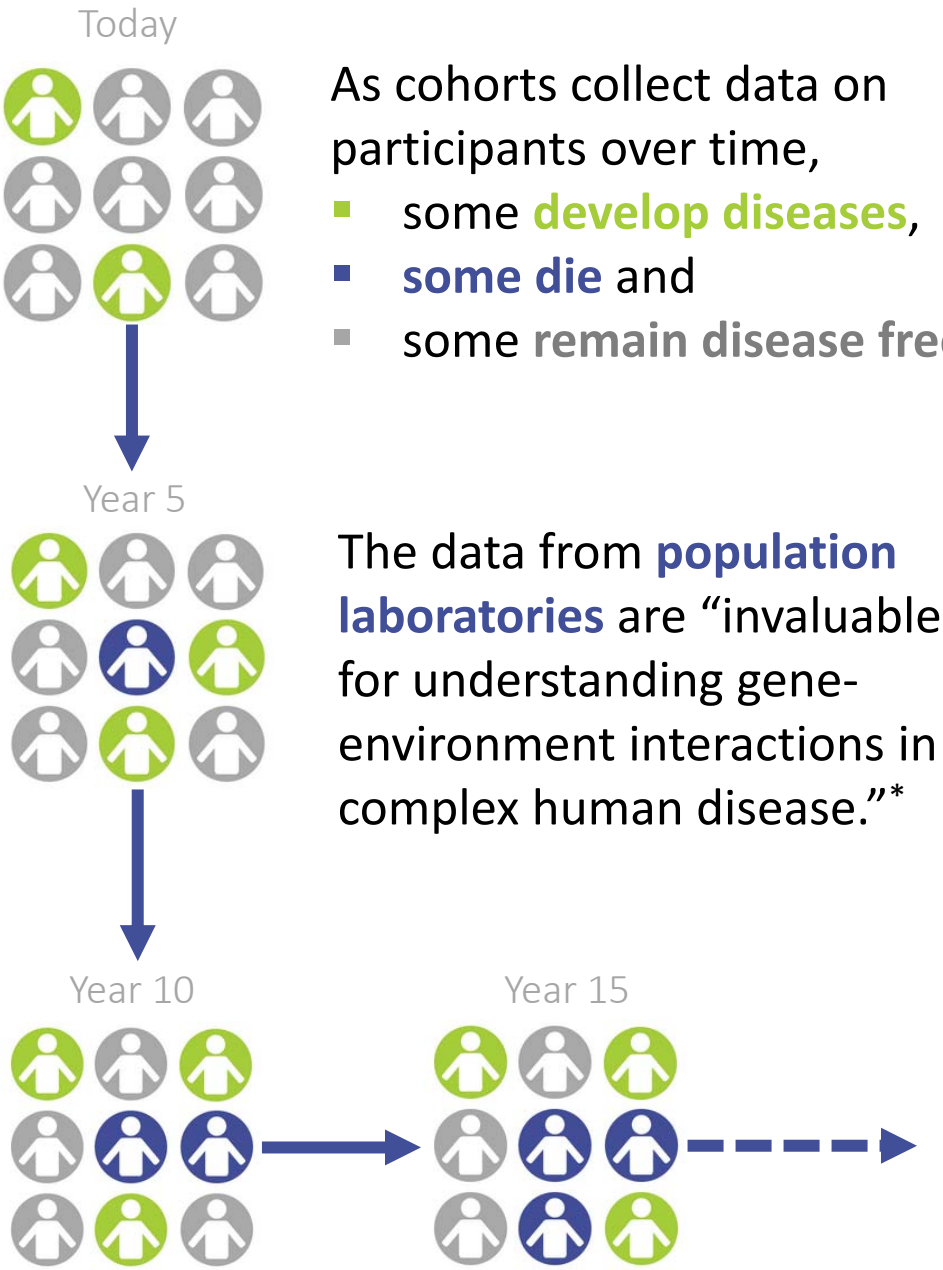
1 in 2

Canadians will die from cancer or a chronic disease*

- 1 in 2 Canadians will be diagnosed with **cancer**
- 1 in 12 Canadians live with diagnosed **heart disease**
- 1 in 10 Canadians live with **asthma or COPD**

*heart disease, respiratory disease or diabetes

Large-scale population health laboratories **help assess disease risks**



As cohorts collect data on participants over time,

- some **develop diseases**,
- **some die** and
- some **remain disease free**.

The data from **population laboratories** are "invaluable for understanding gene-environment interactions in complex human disease."*

**Genes, environment and the value of prospective cohort studies,* Manolio TA, 2006

Large-scale cohort studies drive the discovery of personalized **diagnostics and treatment**

THE GLOBE AND MAIL

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OPINION

As world embraces precision medicine, Canada falls behind

ANDRÉ PICARD ›

PUBLISHED OCTOBER 4, 2016

The United States is going to analyze the genetic information of more than one million Americans. The United Kingdom has a 100,000 Genomes Project and Australia is following suit with its own plan to decode 100,000 genomes.

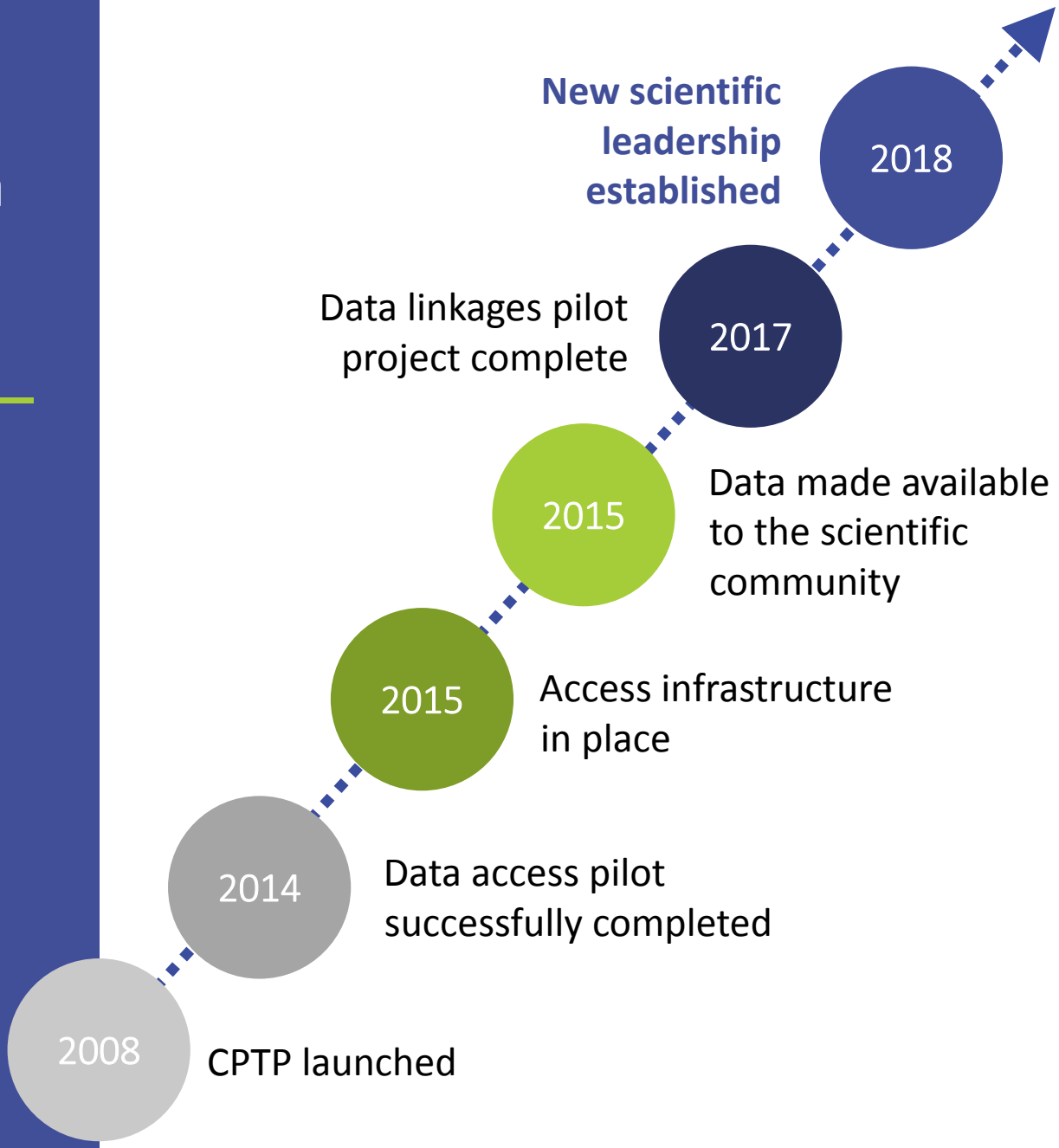
Yet, as the world embraces precision medicine and funds ambitious cohort studies, Canada remains largely on the sidelines. It's a shame.

The Canadian Partnership for Tomorrow Project (CPTP) is a Pan-Canadian platform for research on chronic disease

Canadian Partnership for Tomorrow Project

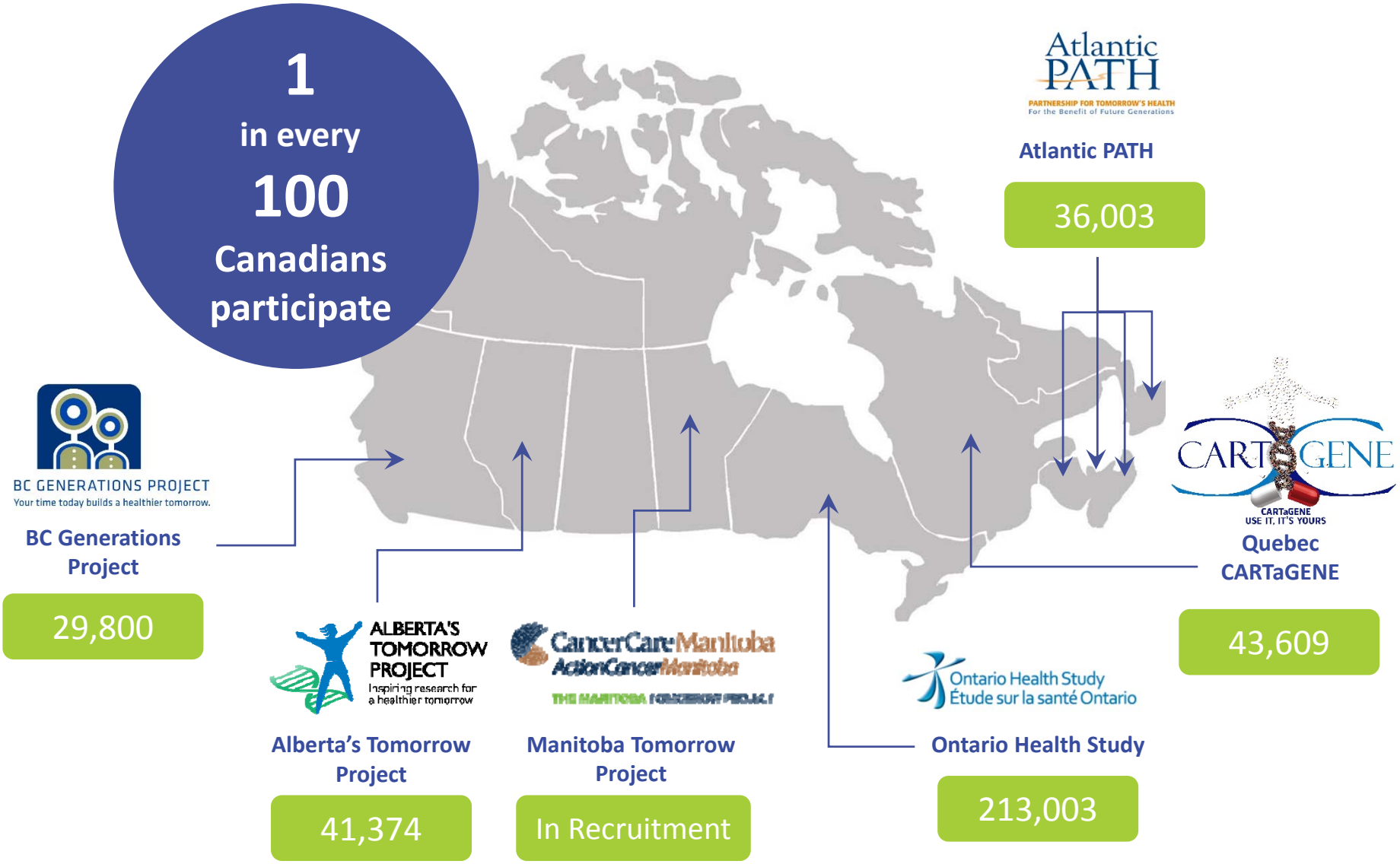
CPTP is a **population-health research platform** for assessing the effect of genetics, behaviour, family health history and environment on chronic diseases.

Entering a new **era** of scientific leadership



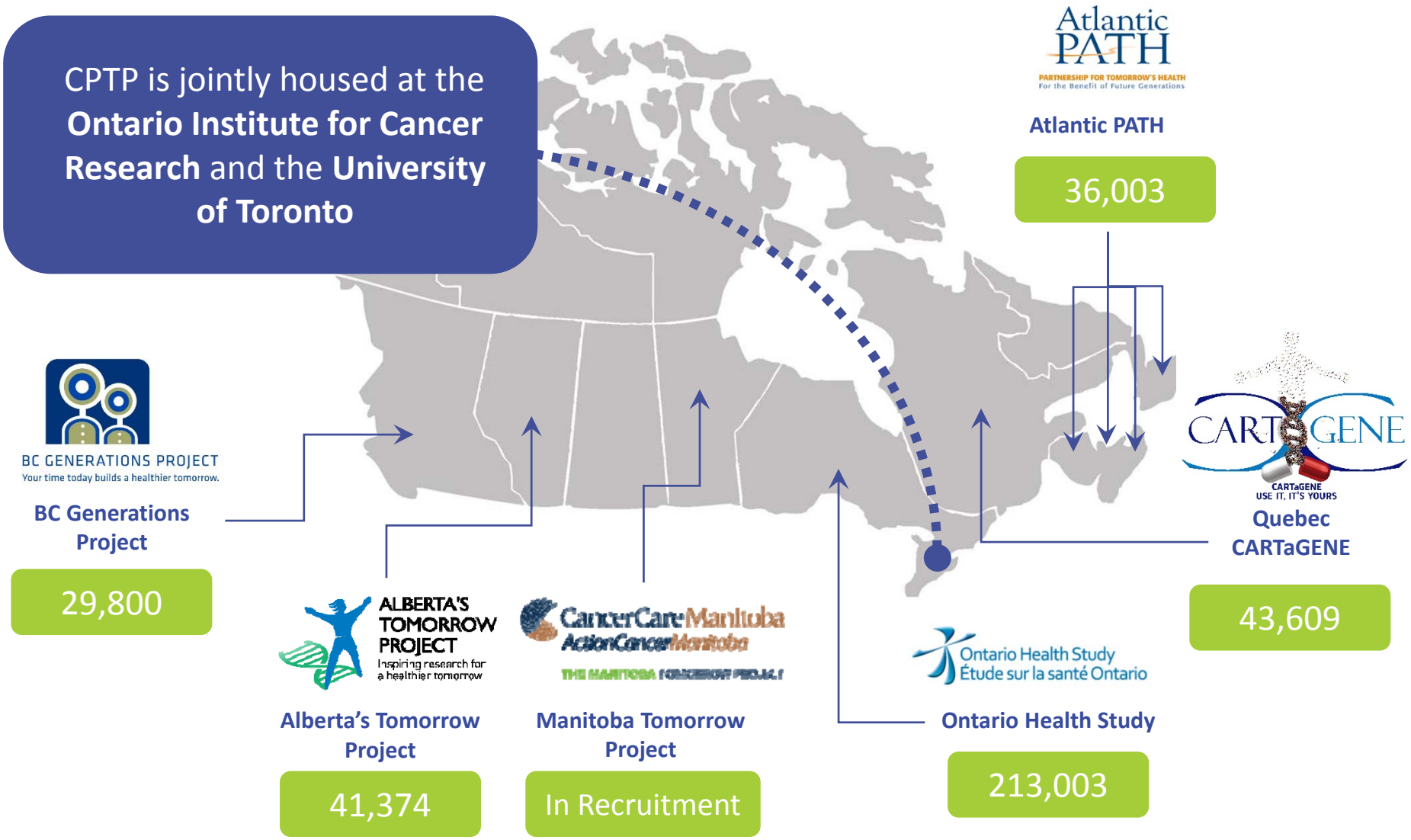
Canada's largest population health research platform

Recruited more than 320,000 participants

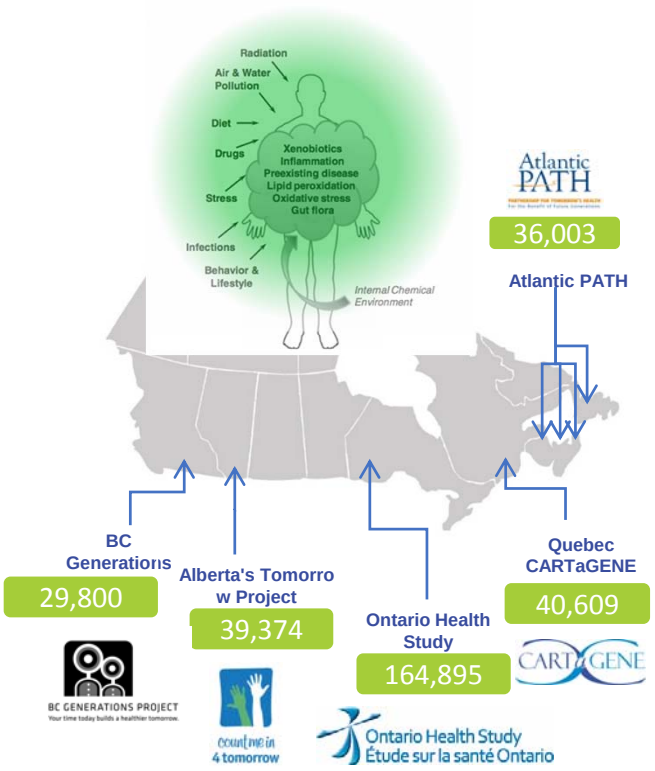


Confederation of 6 regional cohorts

CPTP is jointly housed at the **Ontario Institute for Cancer Research** and the **University of Toronto**



Canadian Partnership for Tomorrow Project (CPTP)



~310,000 participants aged 30-74

No selection criteria
1 in 60 Canadians aged 30–74 have taken part (based on 2016 Census)

Questionnaire data
Lifestyle, health
Physical measures
blood pressure, complete blood count, biochem, MRIs etc.

Biological samples – blood, plasma, serum, DNA, RNA, genotypes, exomes, RNASeq, single-cell, inflammatory markers…

Longitudinal cohort – Canada-wide recontact and linkage to administrative data

Retrospective and Prospective
Data including Drugs and Treatments, Outcomes, Genetic Testing Data etc.

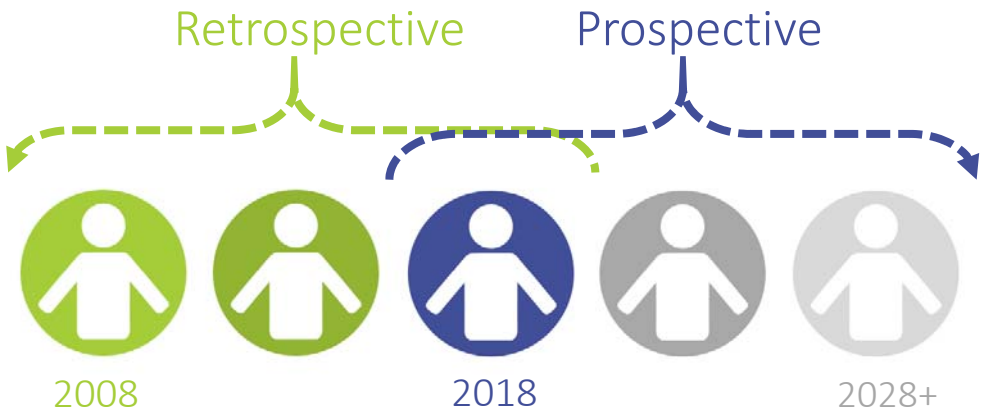
The Canadian Partnership for Tomorrow Project: a pan-Canadian platform for research on chronic disease prevention

Trevor J.B. Dummer PhD, Philip Awadalla PhD, Catherine Boileau PhD, Camille Craig MSc, Isabel Fortier PhD, Vivek Goel MD, Jason M.T. Hicks MSc, Sébastien Jacquemont MD, Bartha Maria Knoppers PhD, Nhu Le PhD, Treena McDonald MSc, John McLaughlin PhD, Anne-Marie Mes-Masson PhD, Anne-Monique Nuyt MD, Lyle J. Palmer PhD, Louise Parker PhD, Mark Purdue PhD, Paula J. Robson PhD, John J. Spinelli PhD, David Thompson MSc, Jennifer Vena PhD, Ma'n Zawati LLM; with the CPTP Regional Cohort Consortium*

Cite as: *CMAJ* 2018 June 11;190:E710-7. doi: 10.1503/cmaj.170292

Enabling health-related research for scientists today and for those in years to come

- Following participants over **25 years**
- Linking 6 cohorts over 9 provinces
- Recruited more than **320,000 actively engaged participants**
- Supported more than **80 projects to date**



Capturing comprehensive health and lifestyle data

Blood

- General hematology
- Basophils
- Eosinophils
- Lymphocytes
- Monocytes
- Neutrophils
- White cells
- Hb
- Hematocrit
- MCHC
- MCV
- Packed cell volume
- Platelets
- Red cells
- RBCDW
- HbA1C

Serum

- Lipid profile
- Cholesterol
- HDL-cholesterol
- Triglycerides
- HDL-ratio
- LDL-cholesterol
- Glycemia
- Glucose
- Hepatic function
- Electrolytes
- Kidney function
- Creatinine
- Nutritional status
- Thyroid function
- Uric acid
- Thyroxine
- TSH

Macro measures

- Arterial stiffness
- Cardiac function
- Blood pressure
- Lung function
- Grip strength
- Weight
- Height
- BMI
- Waist-hip circumference
- Bioimpedance
- Depression
- Anxiety
- Diseases / conditions
- Imaging and MRI data

Environmental measures

- Diet questionnaire
- Smoking status
- Geographical location
- Sun exposure
- Exercise / sedentarity
- Residential history
- Income
- Education level
- Rural / urban
- Siblings
- Medications
- Alcohol consumption
- Sleep

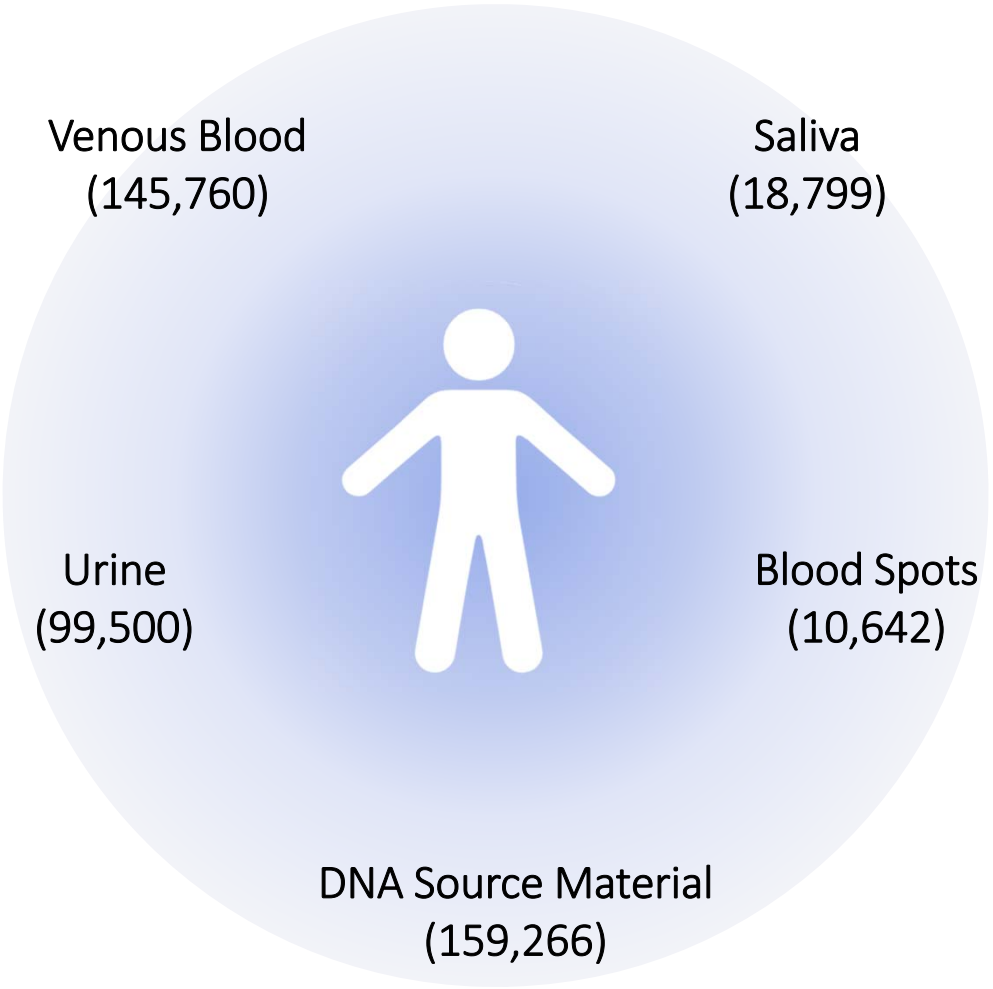
Capturing comprehensive physical measures data

Physical measures

Cognitive test	Reaction time, memory, executive function
Anthropometric measures	Height, sitting height, waist and hip circumference, weight
Bioimpedance	BMI, impedance, % body fat, fat mass, fat free Mass, total body water, basal metabolic rate
Grip strength	Right and/or left hands
Bone density	Heel of non-dominant leg: Stiffness index, % young adult, T score, % age matched, Z-score, BUA and SOS values
Lung function	Timed peak and forced inspiratory and expiratory flow, vital capacity: FVC, FEV1, FEV1/FVC, FEF25, FEF50, FEF75, FEF25-75, FET, FEV3, FEV3/FVC, FEV6, PEF, EVol, FIVC, FIV1, PIF, ELA. MVV.
Blood pressure	Systolic and diastolic blood pressure, heart rate
Arterial stiffness	Heart rate, Aortic Systolic and diastolic pressures, Aortic augmentation, Aortic augmentation index, Ejection duration, and Buckberg ratio
Partial resting electrocardiogram	Leads: I,II, III, aVR, aVL et aVF. Heart rate, PQ Interval, QRS duration, QT, QTC, P-R-T axis, P duration, RR and PP Intervals.
MRI (n=10,000 participants)	Full body, n=10,000 participants, Combination of hospital centres and mobile units.

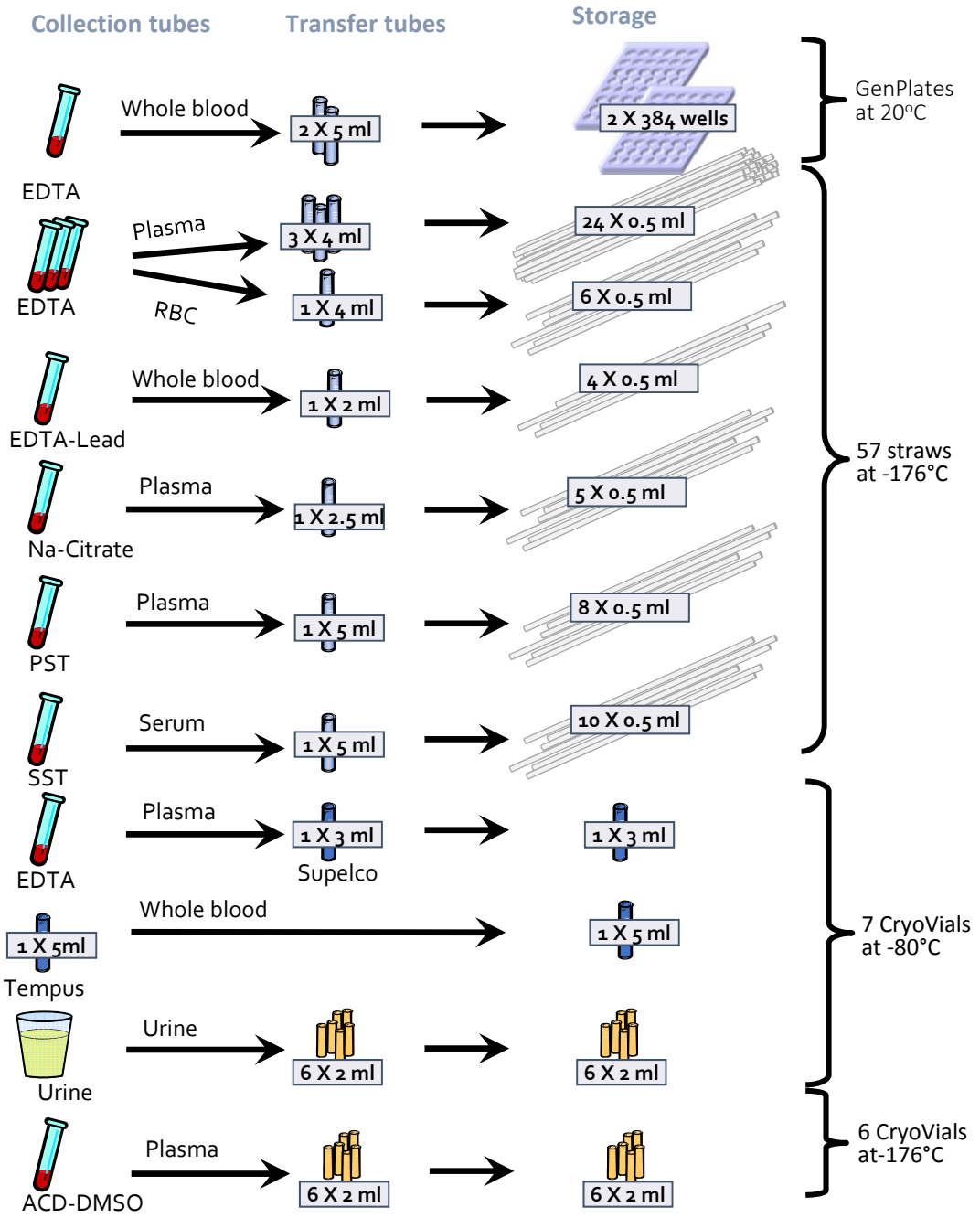
Longitudinal sampling of biological data

Biological Samples

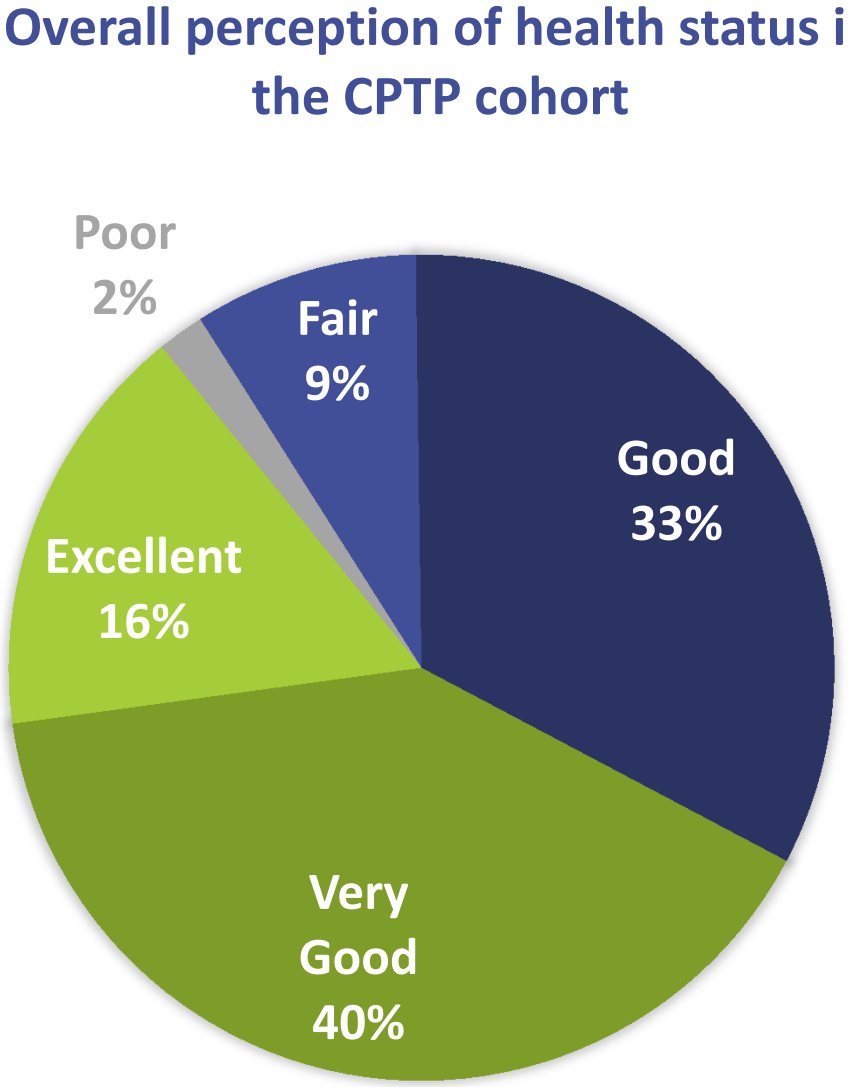


Comprehensive data capture

Total blood volume collected: 160.5 mL

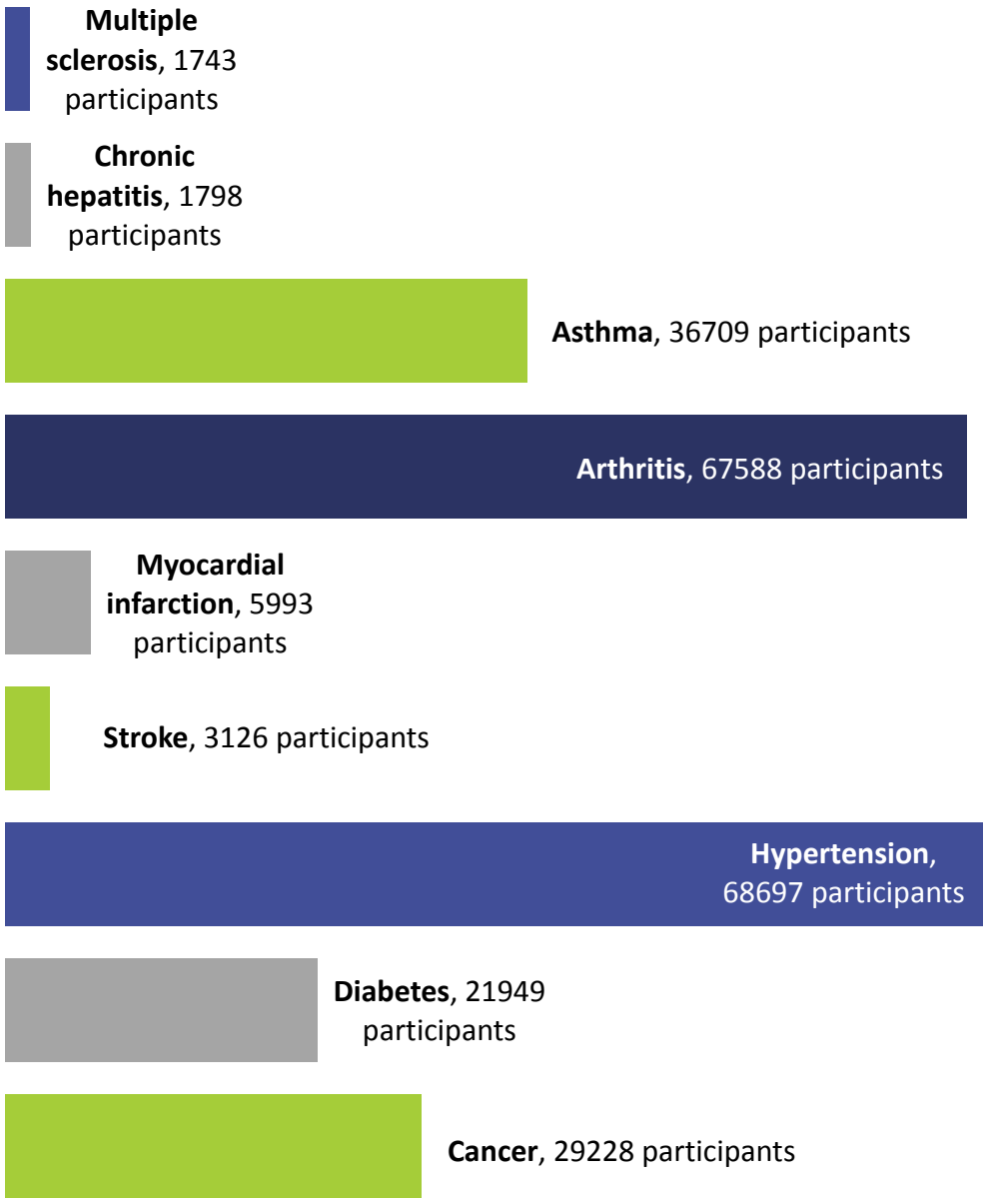


Following both healthy and affected participants over time



Including participants with various chronic diseases and conditions

Diseases and conditions in the CPTP cohort



Working with a network of **internationally recognized** large-scale initiatives

CPTP is Canada's largest population health cohort

1) The International Hundred Thousand Cohort Consortium (IHCC)

2) International Common Disease Alliance

23andMe 

Biobank Japan 

China Kadoorie Biobank 

Canadian Partnership for Tomorrow Project (CPTP) 

EPIC 

Kaiser Permanente Research Program 

LifeGene 

Million Veteran Program 

Million Women Study 

Multiethnic Cohort Study 

MyCode Community Health Initiative 

Nurses' Health Study (NHS/NHSII) 

US Precision Medicine Initiative/ All of Us 

Tohoku Medical Megabank Project 

UKBioBank 

International 100K Cohort Consortium (IHCC)

Linking cohorts, understanding biology, improving health

National Medical Genome Projects and Cohorts

Over 20 million participants will be linked and harmonized through this consoritum

CHPT
CROSS-COHORT HARMONIZATION PROJECT FOR TOMORROW

CANADIAN PARTNERSHIP AGAINST CANCER
PARTENARIAT CANADIEN CONTRE LE CANCER

OBJECTIVE

Leverage the use of existing North American and European cohort studies focused on better understanding of the risk factors that contribute to cancer and other major chronic diseases

CHPT catalogue:
more than 2.5 million participants!!!

Canadian Study of Diet, Lifestyle and Health
epic
EpiHealth
NTNU HUNT Research Centre
LifeGene
Cohort of Swedish Men
LifeLines
CONSTANCES
Nurses' Health Study
csa élcv
Swedish Mammography Cohort
Canadian Partnership for Tomorrow Project
CHPT CROSS-COHORT HARMONIZATION PROJECT FOR TOMORROW
biobank Imaging study

mælstrom

"I am interested in pooling data across cohort studies to explore the effect of physical activity and social participation on quality of life in older adults, adjusting for SES"

Displays only studies collecting all variables of interest for the research project

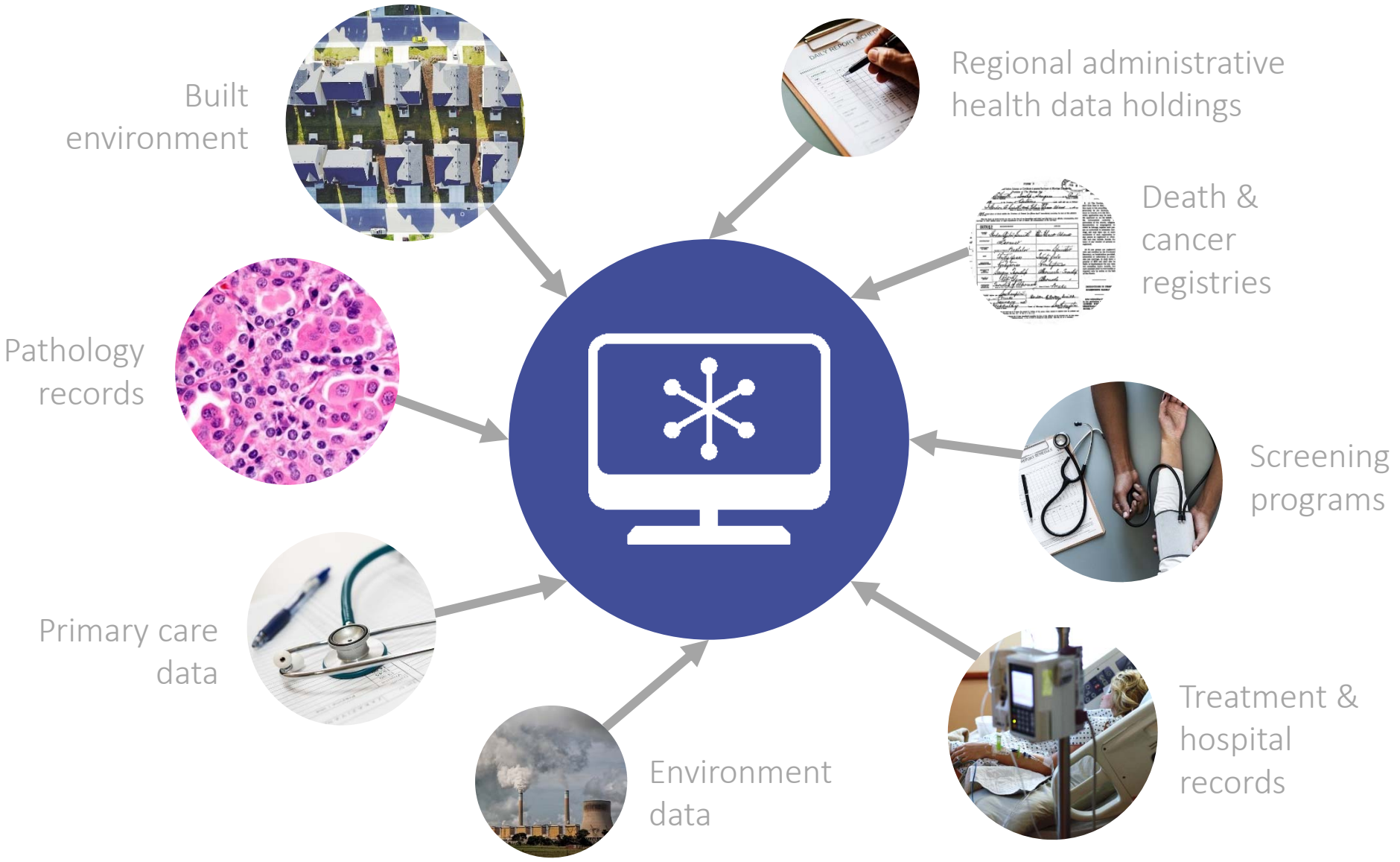
Study | DataSchema

Download

Data Collection Event (DCE)

	Study	Socio-demographic and economic characteristics ×			Lifestyle and health behaviours ×	Health status and functional limitations ×	Social environment ×
		Education ×	Labour force and retirement ×	Income, possessions, and benefits ×	Physical activity	Quality of life	Social participation
☐	ALSA	16	28	198	75	53	177
☐	CaPS	18	37	4	71	2	13
☐	CSHA	24	174	17	48	18	39
☐	ELSA	491	3,325	37,630	295	134	261
☐	FRèLE	12	27	42	120	138	123
☐	NuAge	1	5	14	430	256	93
☐	OATS	34	43	6	121	40	59
☐	PATH	156	228	77	150	261	44
☐	TILDA	16	99	374	21	28	46
☐	VETSA	21	28	9	24	54	1
	All	789	3,994	38,371	1,355	984	856

Linking data to better understand disease risk



Enabling health-related research for **scientists today and for those in years to come**

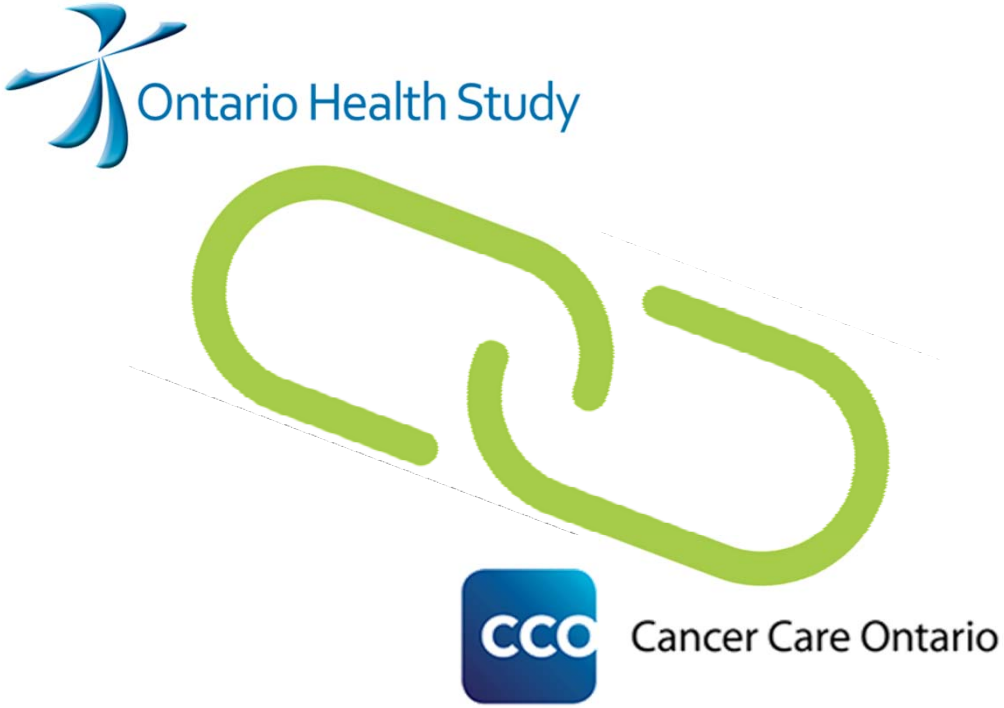
CPTP serves both **retrospective and prospective** research studies.

Case Study

Linking cancer data: a pilot project

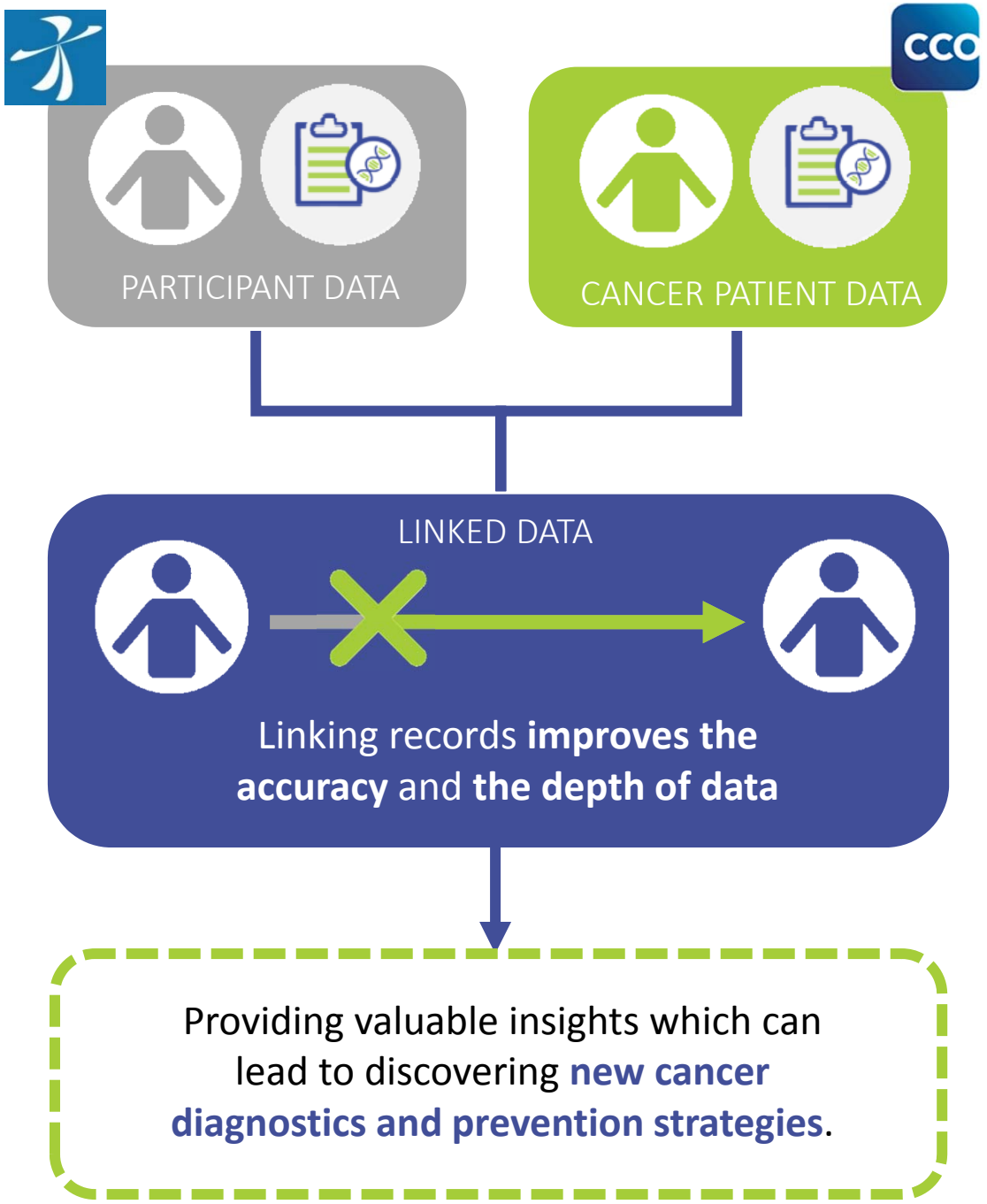
Awadalla Lab Pilot Project, 2018

The Awadalla Lab's pilot project successfully linked Ontario Health Study data with Cancer Care Ontario data, **to analyze the effects of health, environment and lifestyle factors on early cancer development.**



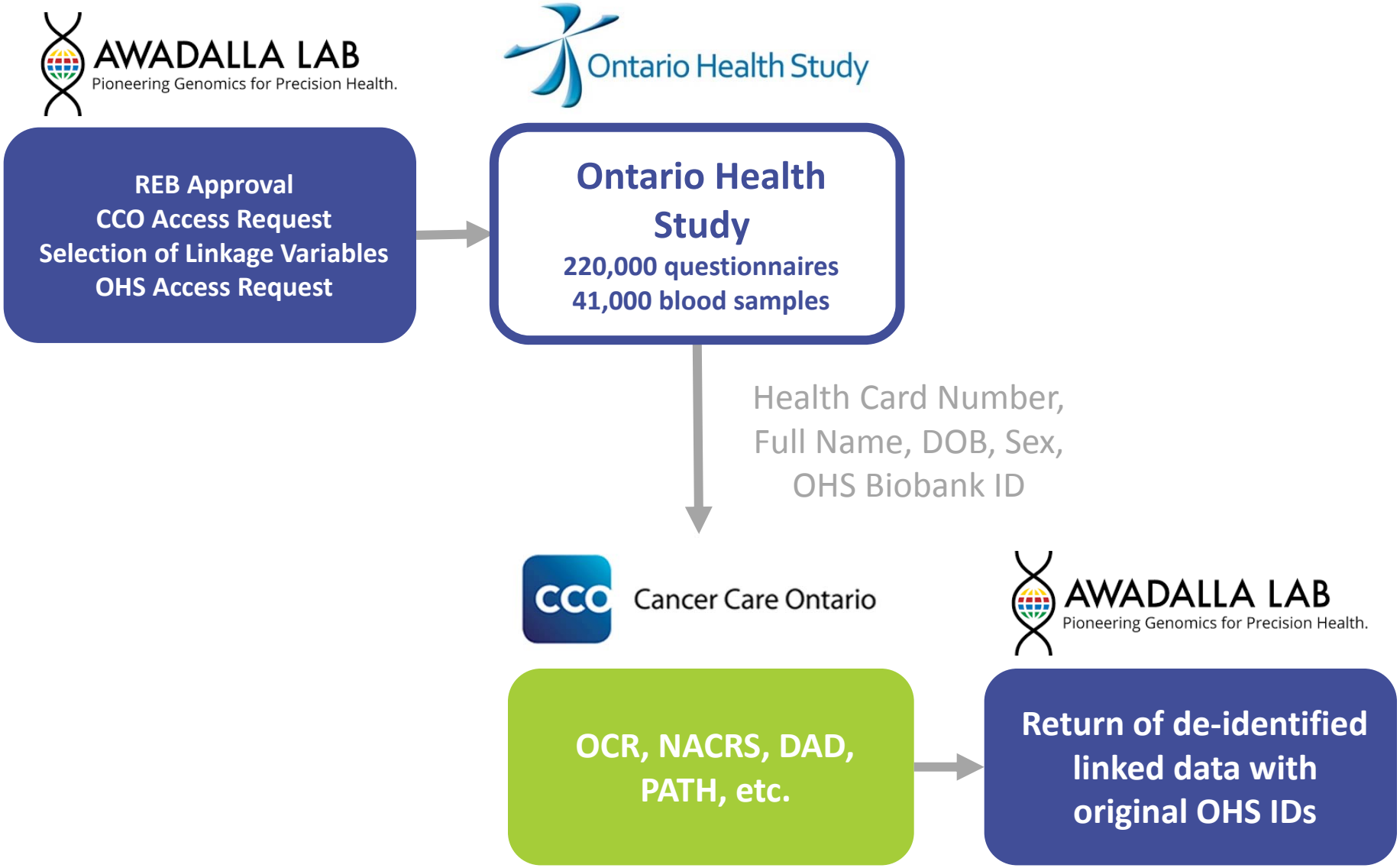
Linking cancer data: the concept

Awadalla Lab Pilot Project, 2018



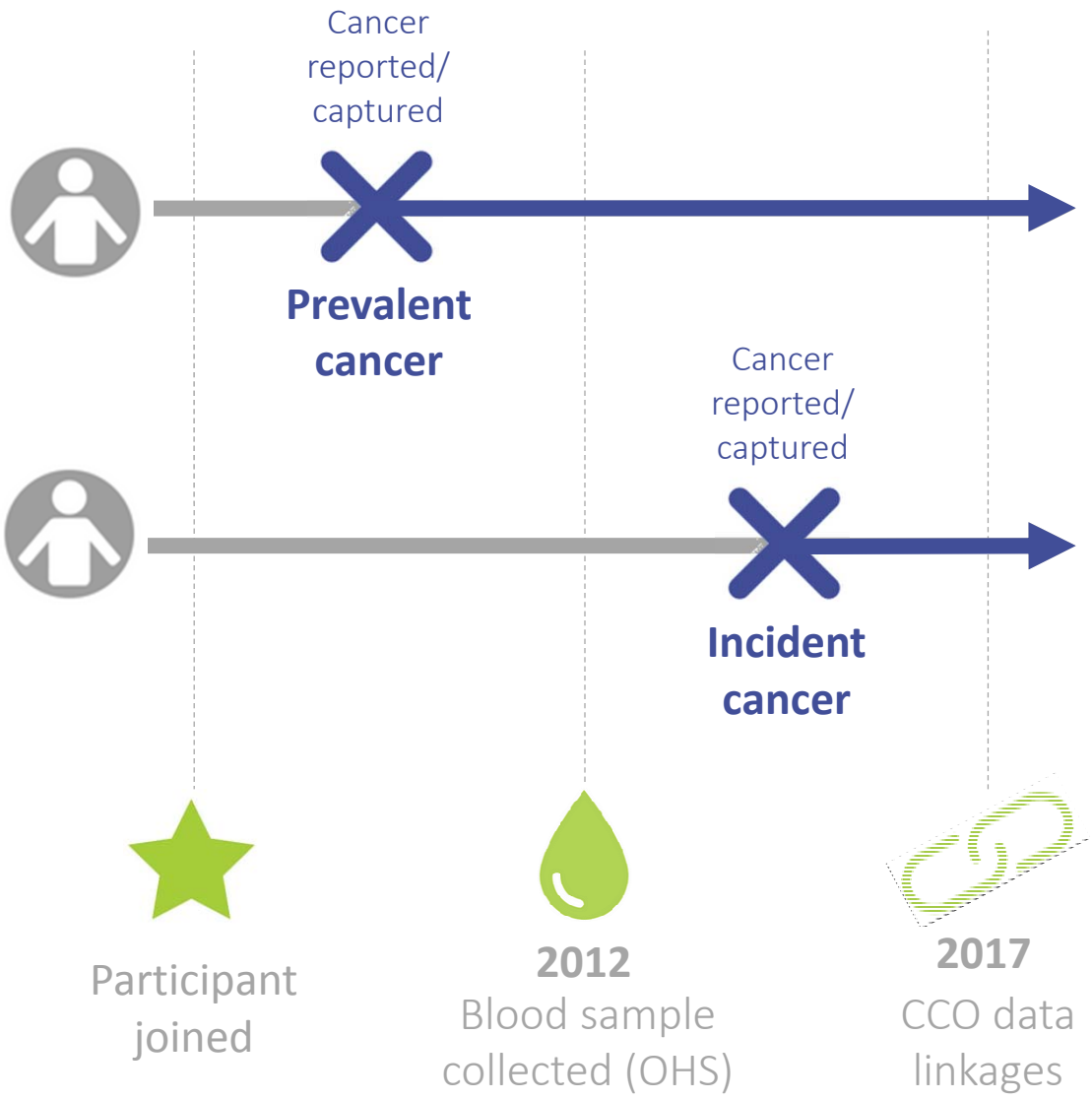
Linking cancer data: the process

Awadalla Lab Pilot Project, 2018



Capturing both incident and prevalent cancers

Awadalla Lab Pilot Project, 2018



Leveraging cohort data to find leukemia years before it surfaces

case study

Acute myeloid leukemia (AML) progresses quickly and **requires treatment soon after diagnosis**. Early indicators of AML were thought to be indistinguishable from healthy aging.

We investigated cohort study data (EPIC and OHS) to find traces of AML in patients samples that were collected before the disease developed

We found traces of the disease up to 10 years before the patients were diagnosed with AML.

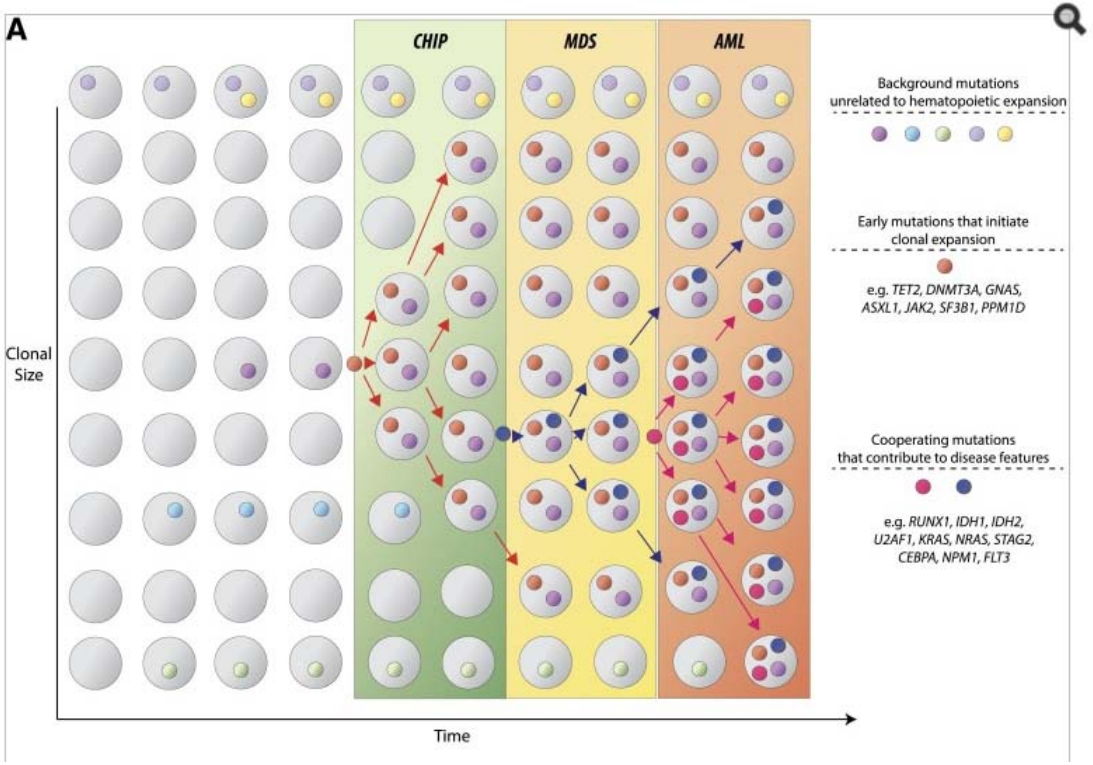
"This could in future enable **earlier detection and monitoring**, and may help to inform intervention."*

**Prediction of acute myeloid leukaemia risk in healthy individuals,* Abelson et al., 2018

Using EPIC and OHS data to evaluate clonal hematopoiesis and AML risk

case study

- Supported by **$10 million from OICR**, Dr. John Dick and collaborators (including Awadalla) are investigating clonal hematopoiesis and acute myeloid leukemia (AML) risk



OICR

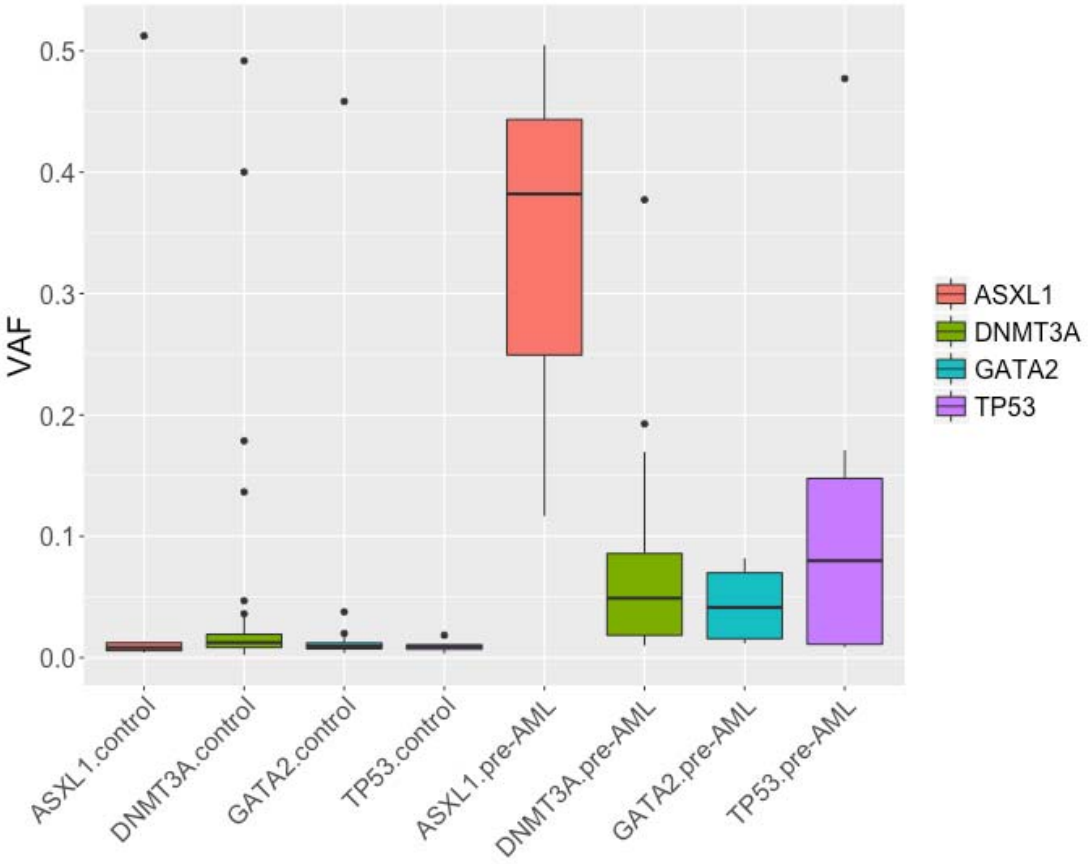
מכון ויצמן למדע
WEIZMANN INSTITUTE OF SCIENCE

UHN Princess Margaret Cancer Centre

Using EPIC and OHS data to evaluate clonal hematopoiesis and AML risk

case study

Pre-AML cases have **higher variant allele frequency** in recurrently mutated AML related genes



(derived from preliminary analysis of EPIC cohort)

Using EPIC and OHS data to evaluate clonal hematopoiesis and AML risk

case study

nature
International journal of science

Letter | Published: 09 July 2018

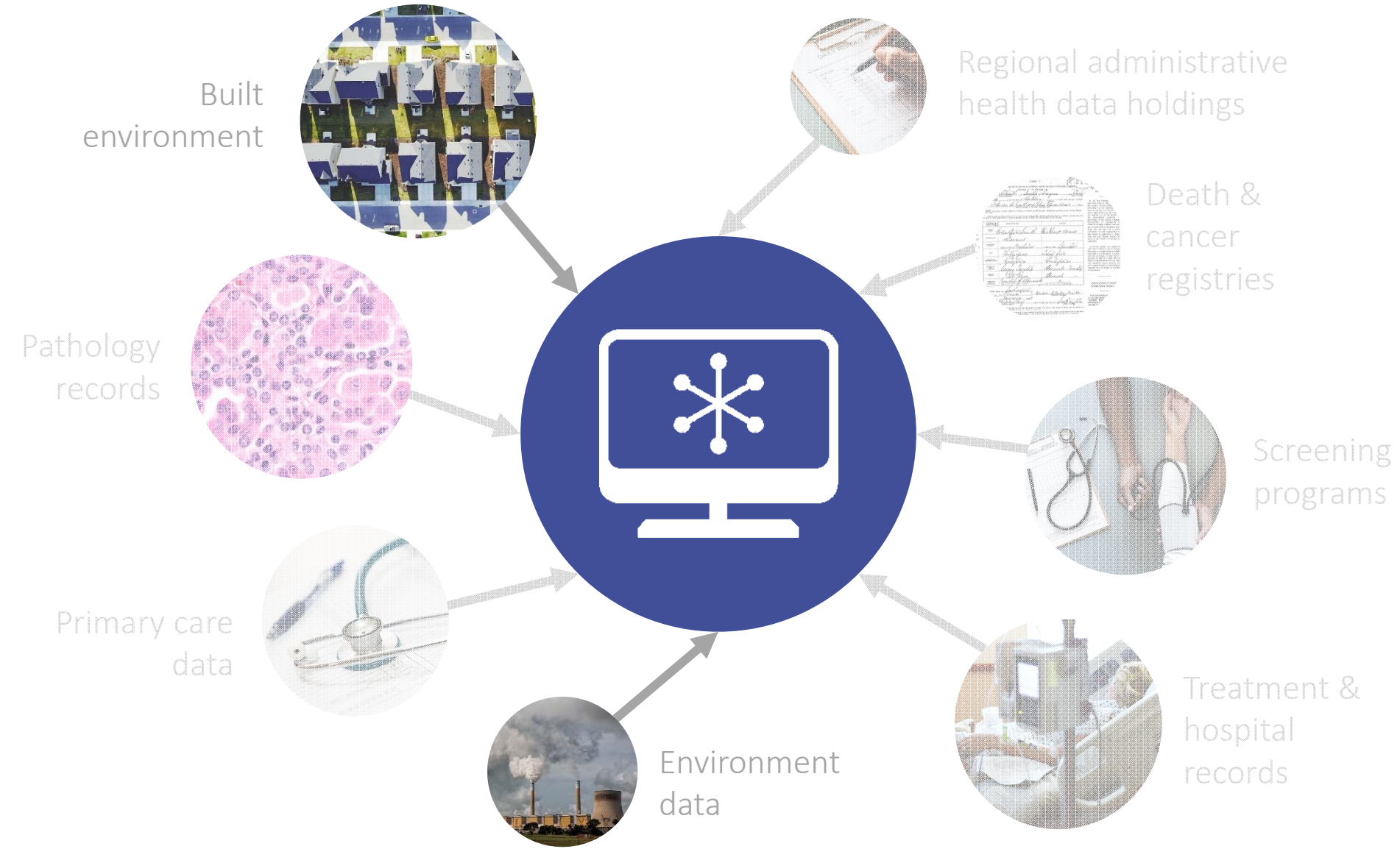
Prediction of acute myeloid leukaemia risk in healthy individuals

Sagi Abelson, Grace Collord, […] Liran I. Shlush

Nature (2018) | Download Citation

- Found how to distinguish between individuals who are at high risk of developing AML and those who are not
- Made possible by long-term health research cohorts
- "This could in future enable **earlier detection and monitoring**, and may help to inform intervention."

Linking key environment data to health data



Case Study

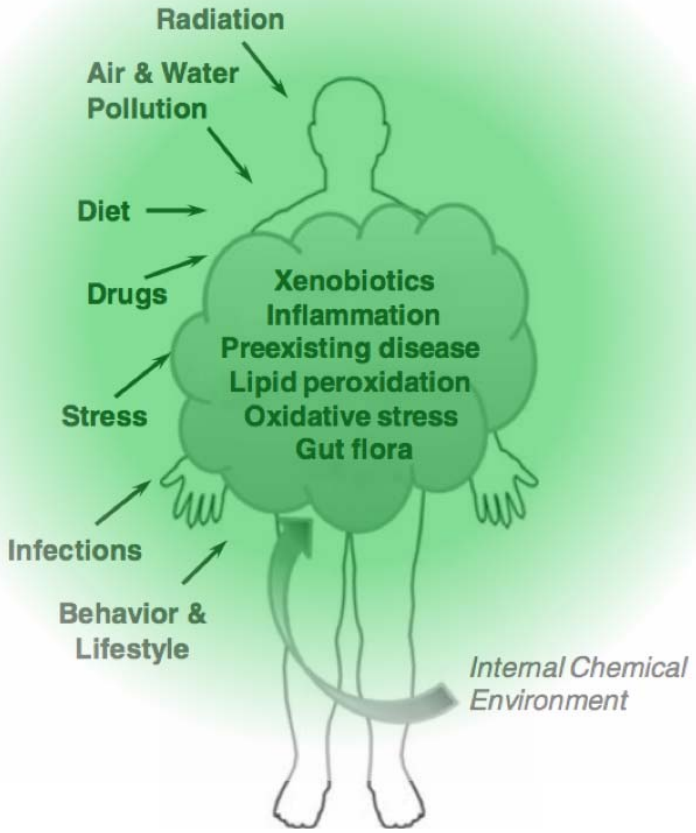
Linking environmental and health research

case study

- CIHR awarded **$4.2 million** to Dr. Jeffrey Brook and Dr. Philip Awadalla to lead CANUE (2016 – 2021), a national platform for big environmental data

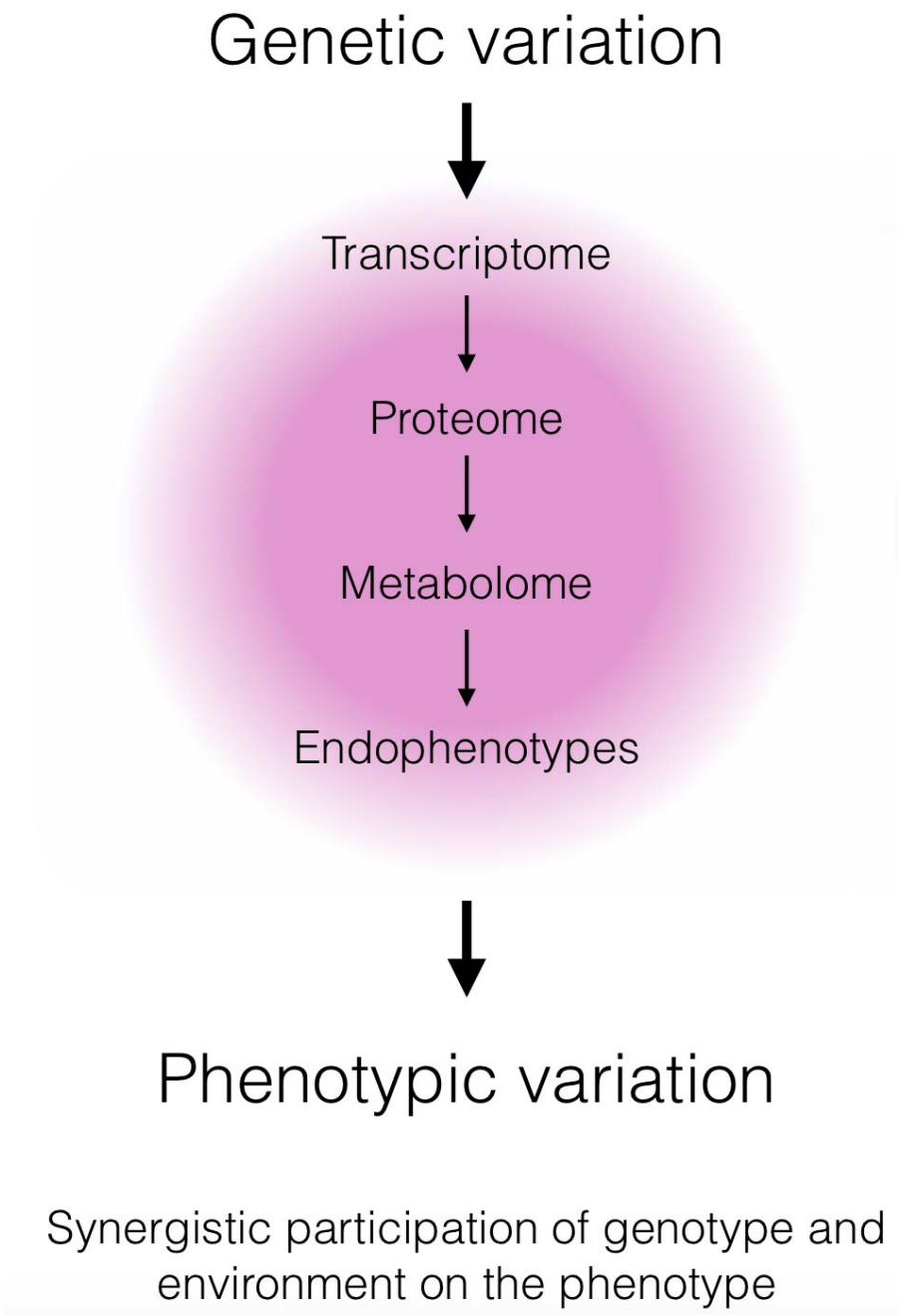
Exploiting the cohort to study gene-by-environment interactions

case study



Exploiting the cohort to study gene-by-environment interactions

case study



Exploiting the cohort to study gene-by-environment interactions

case study

Recombination affects accumulation of damaging and disease-associated mutations in human populations

Julie G Hussin, Alan Hodgkinson, Youssef Idaghd
Jean-Philippe Goulet, Elias Gbeha, Elodie Hip-Ki

Nature Genetics **47**, 400–404 (2015) | Download

nature genetics

High-Resolution Genomic Analysis of Human Mitochondrial RNA Sequence Variation

Alan Hodgkinson,[1]* Youssef Idaghdour,[1,2]*† Elias Gbeha,[1] Jean-Christophe Grenier,[1] Elodie Hip-Ki,[1] Vanessa Bruat,[1] Jean-Philippe Goulet,[2] Thibault de Malliard,[1,2] Philip Awadalla[1,2]‡

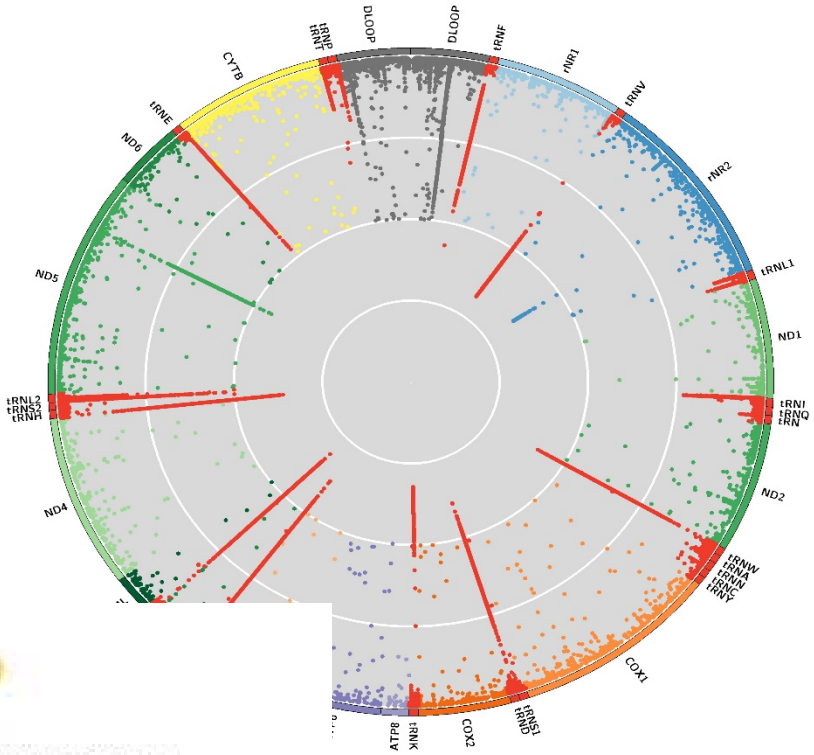
Mutations in the mitochondrial genome are associated w
processes; however, little is known about the extent of s
transcriptome. By ultra-deeply sequencing mitochondrial
blood of ~1000 individuals from the CARTaGENE projec
sequence variation within and across individuals, as well
of posttranscriptional modification. Using a genome-wid
posttranscriptional modification of functionally importan

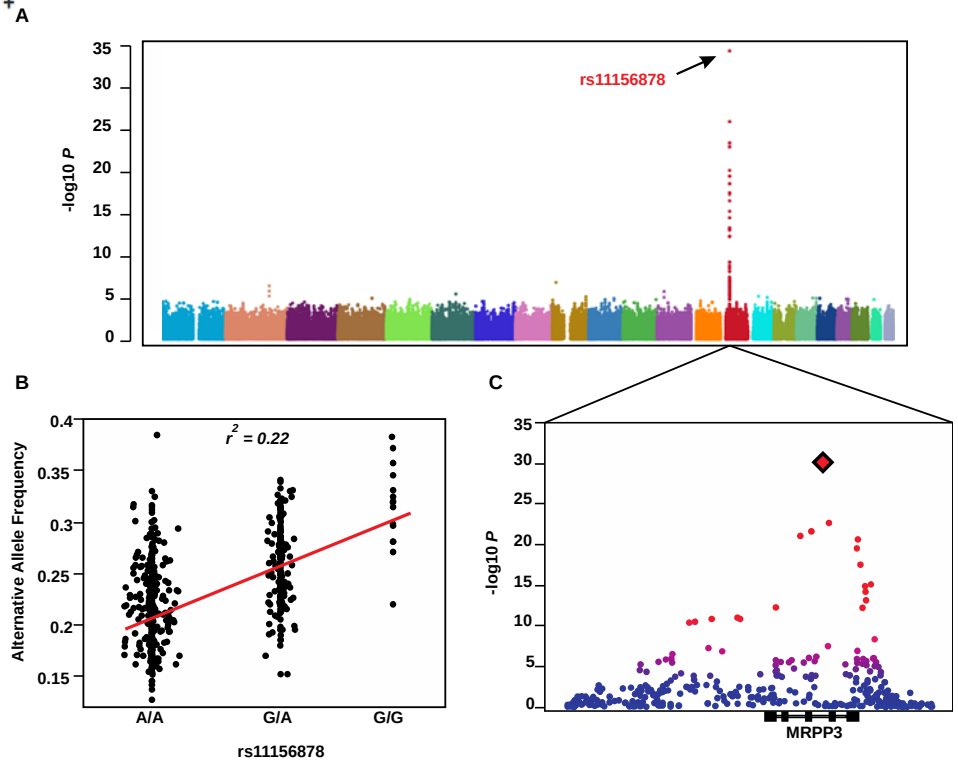
Science
AAAS

High-Resolution Genomic Analysis of Human Mitochondrial RNA Sequence Variation

Alan Hodgkinson,[1]* Youssef Idaghdour,[1,2]*† Elias Gbeha,[1] Jean-Christophe Grenier,[1] Elodie Hip-Ki,[1] Vanessa Bruat,[1] Jean-Philippe Goulet,[2] Thibault de Malliard,[1,2] Philip Awadalla[1,2]‡

Mutations in the mitochondrial genome are associated with multiple diseases and biological processes; however, little is known about the extent of sequence variation in the mitochondrial transcriptome. By ultra-deeply sequencing mitochondrial RNA (>6000×) from the whole blood of ~1000 individuals from the CARTaGENE project, we identified remarkable levels of





Université de Montréal

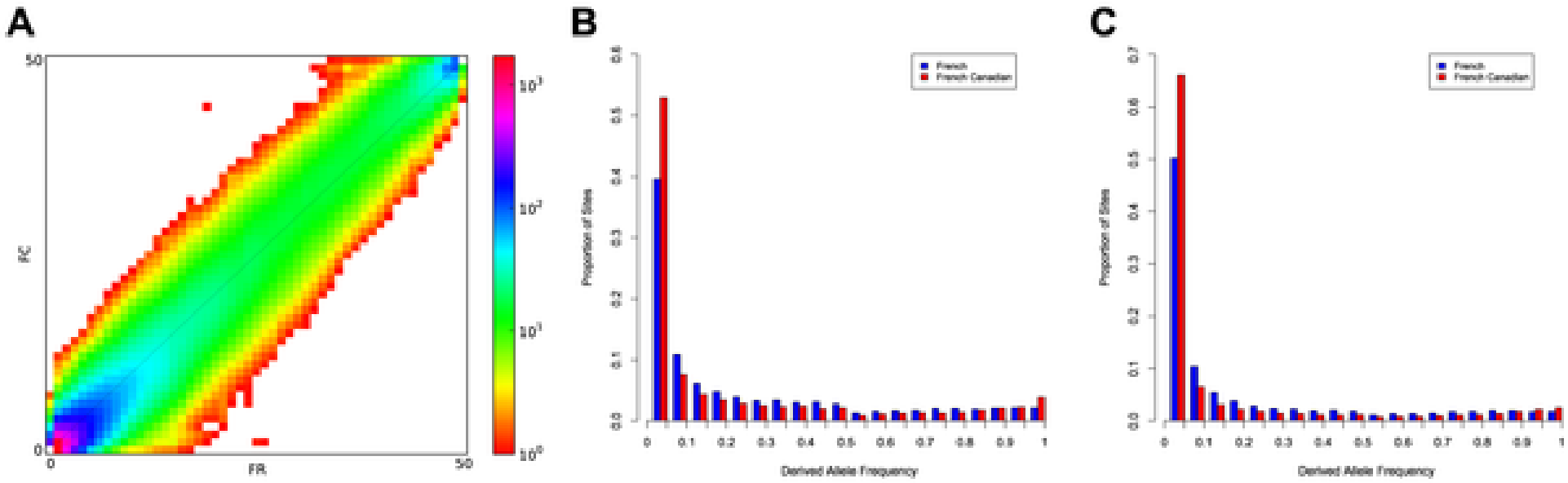
Science AAAS

Sainte-Justine Hospital Foundation

For the love of children

Site frequency spectrum of genetic variation in the French and French-Canadian populations

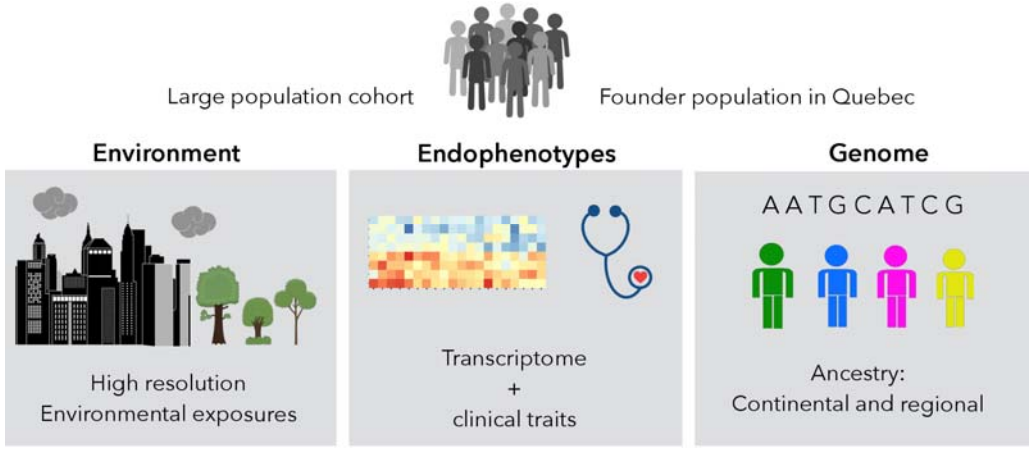
Unique demographic history : original bottleneck less than 20 generations ago followed by a demographic explosion and genetic isolation



nature genetics

PLOS | GENETICS

Canadian Partnership for Tomorrow Project



Gene-by-environment interactions in urban populations modulate risk phenotypes

Marie-Julie Favé, Fabien C. Lamaze, David Soave, Alan Hodgkinson, Héloïse Gauvin, Vanessa Bruat, Jean-Christophe Grenier, Elias Gbeha, Kimberly Skead, Audrey Smargiassi, Markey Johnson, Youssef Idaghdour & Philip Awadalla

Nature Communications **9**, Article number: 827 (2018) | Download Citation

Allele-specific expression reveals interactions between genetic variation and environment

David A Knowles, Joe R Davis, Hilary Edgington, Anil Raj, Marie-Julie Favé, Xiaowei Zhu, James B Potash, Myrna M Weissman, Jianxin Shi, Douglas F Levinson, Philip Awadalla, Sara Mostafavi, Stephen B Montgomery & Alexis Battle

Nature Methods **14**, 699–702 (2017) | Download Citation

bioRχiv

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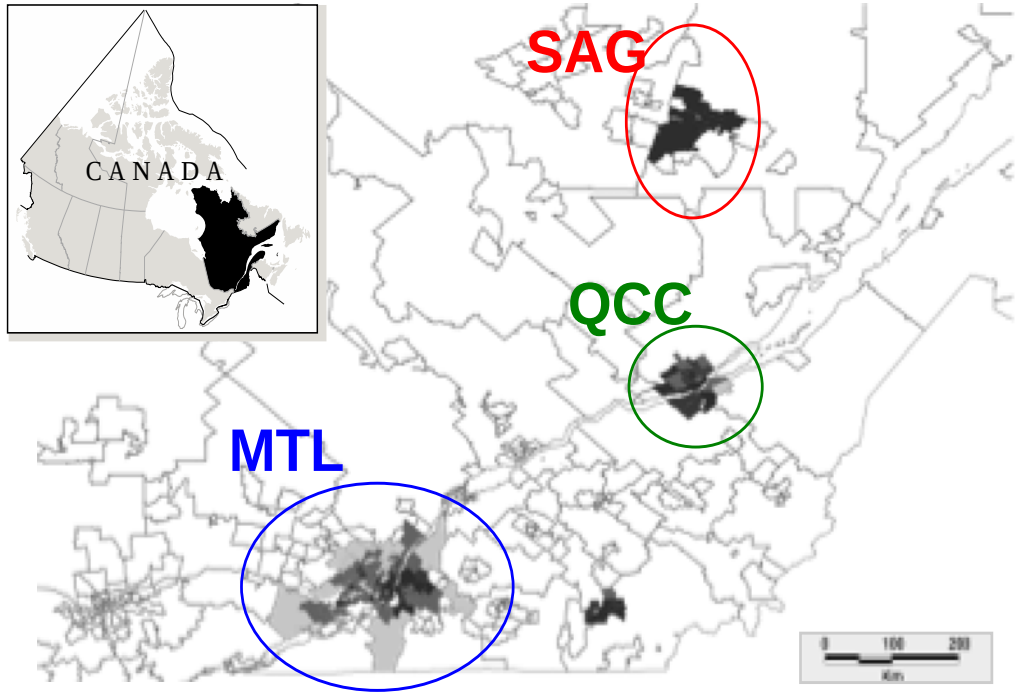
New Results

Comment on this paper

Unraveling the polygenic architecture of complex traits using blood eQTL meta-analysis

French Canadian Genetics

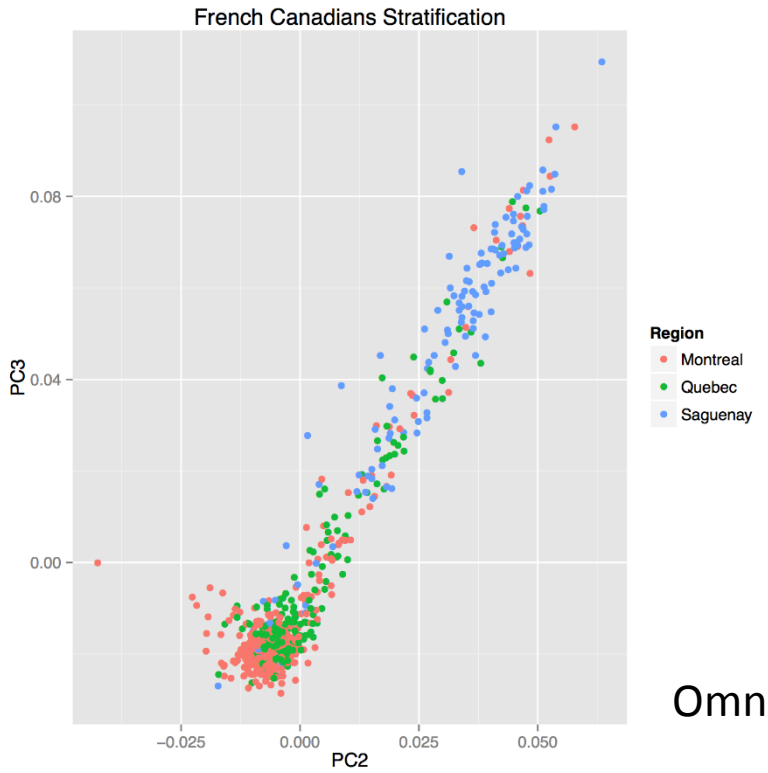
case study



- The French Canadian (FC) gene pool is spatially structured with genetic diversity following a West-East gradient of similarity
- Regional founder effect in the Saguenay region

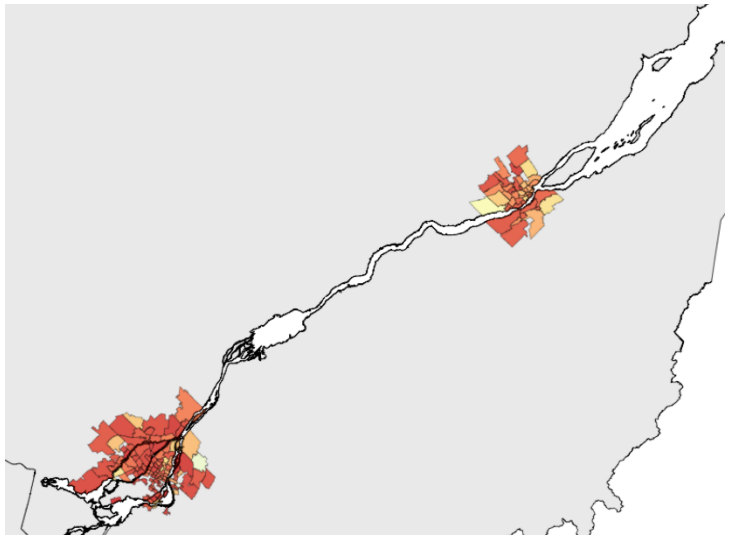
Genotype structure follows a geographic cline

case study



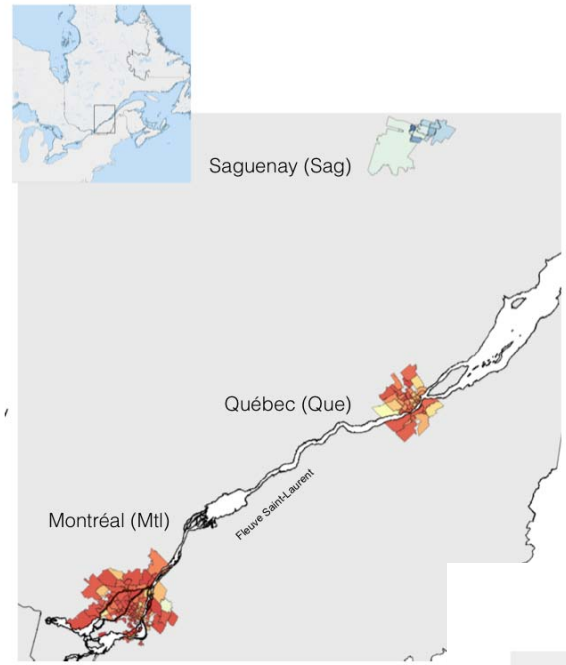
Omni2.5

PC2 + PC3

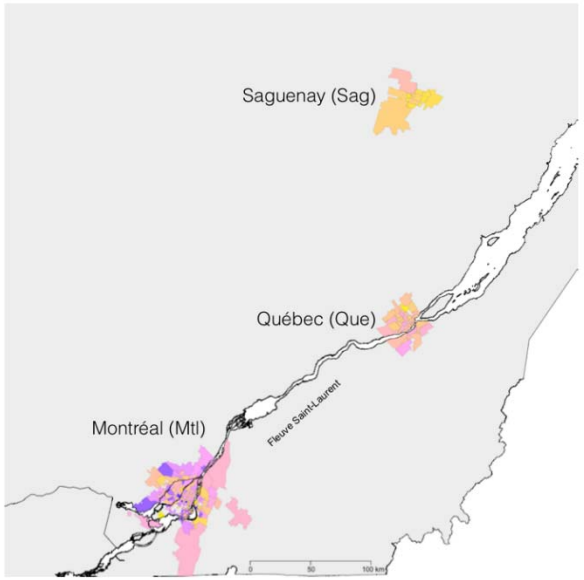


Transcriptomic variation

case study



Genotypic cline



Transcriptomic cline

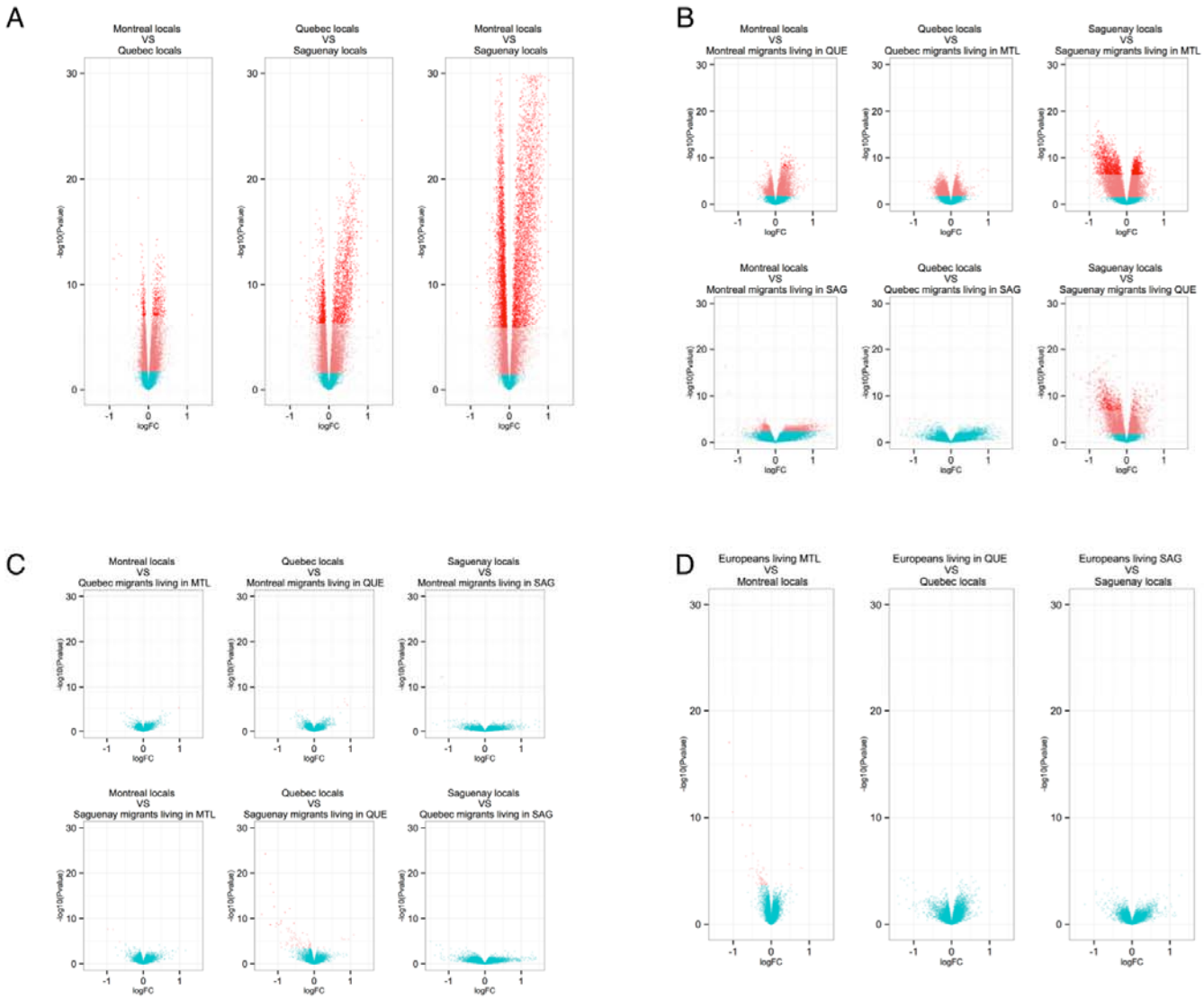
DGE after SVA removals of SVs

Different environments / diff origins

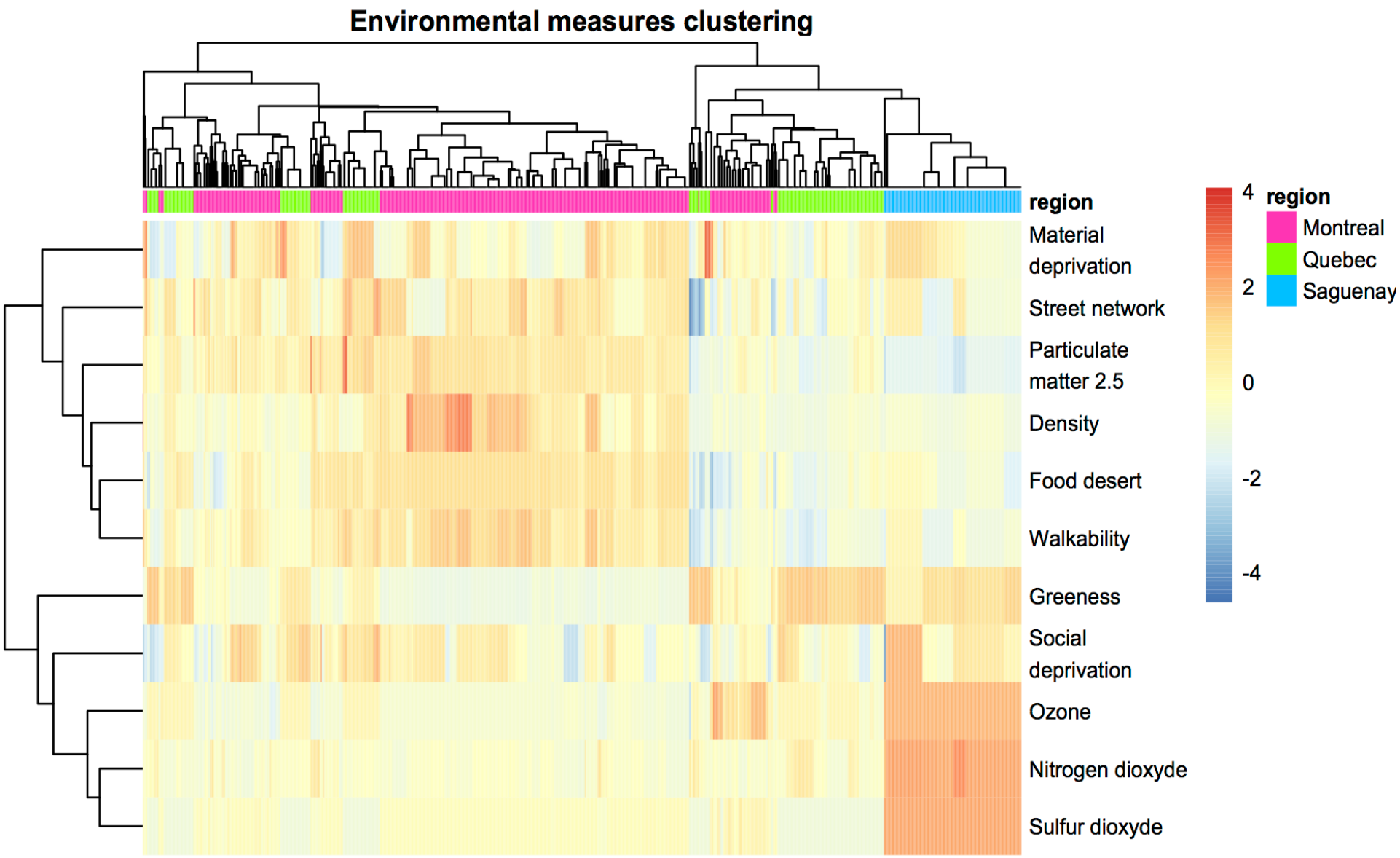
Different environments / same origin

Same environments / different origins

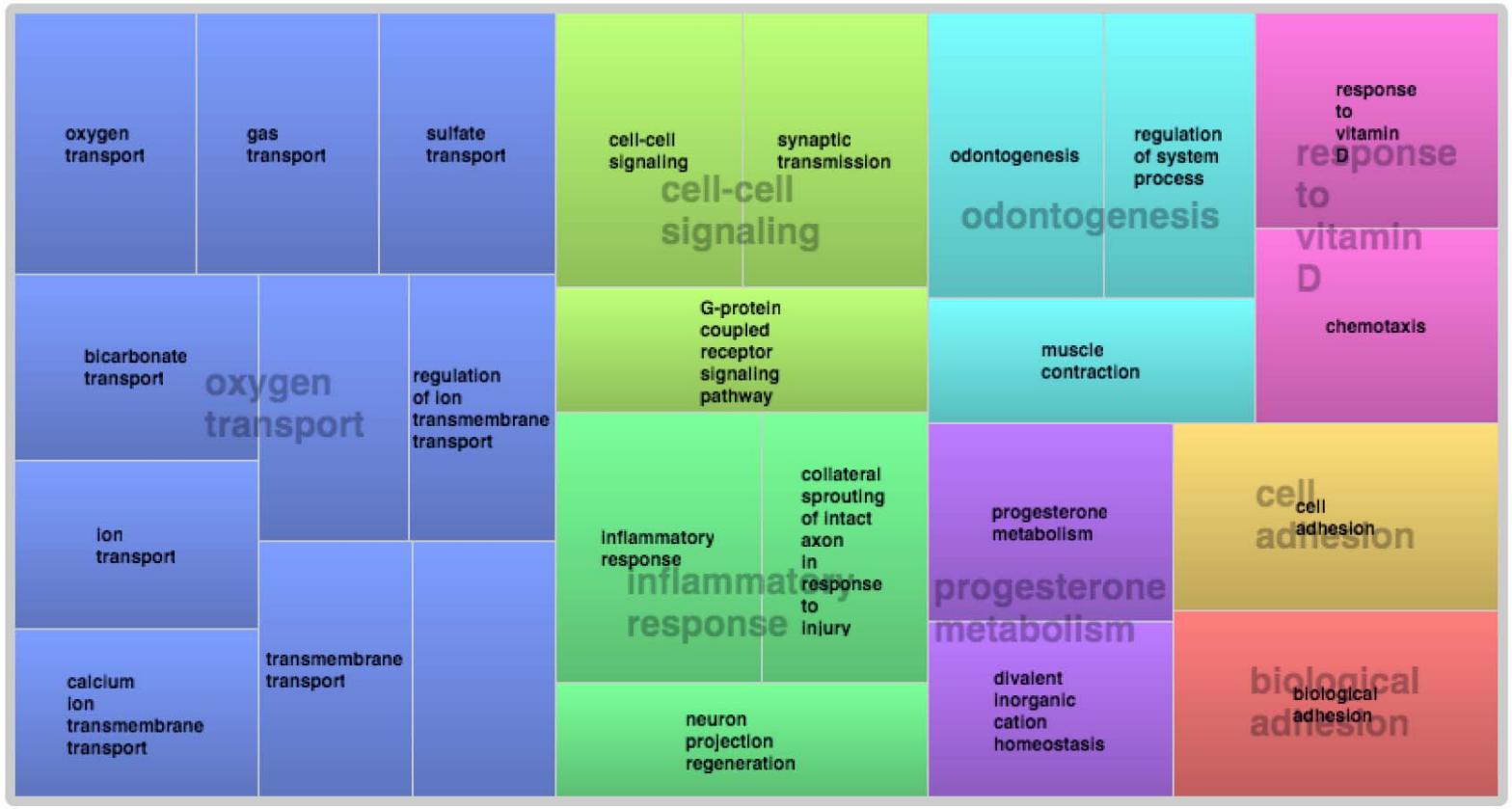
Same environments / different origins



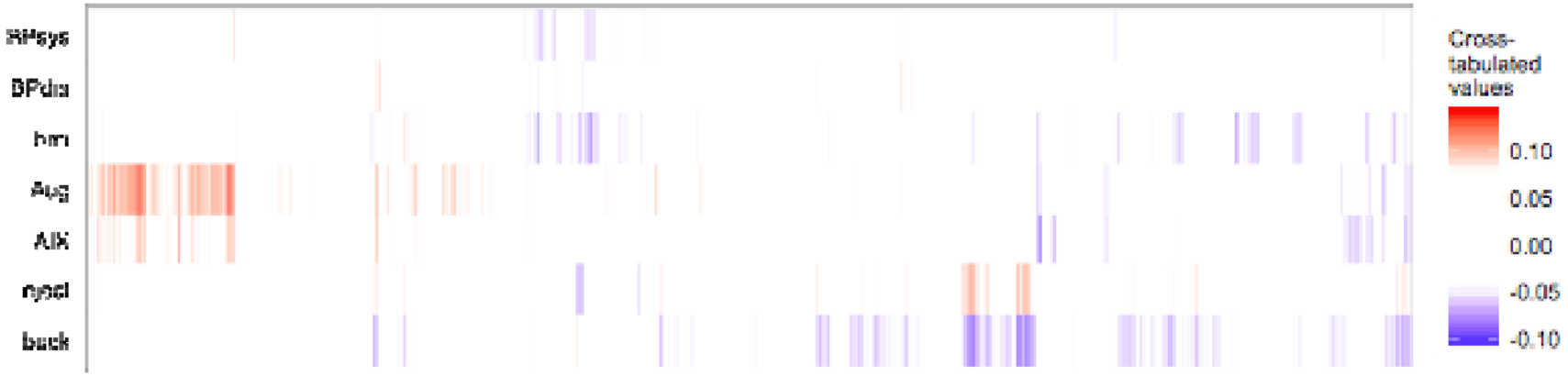
Marie-Julie Fave


Environmental measures clustering
region
Material deprivation
Street network
Particulate matter 2.5
Density
Food desert
Walkability
Greeness
Social deprivation
Ozone
Nitrogen dioxyde
Sulfur dioxyde
4
2
0
-2
-4
region
Montreal
Quebec
Saguenay

Gene enrichment - top 500 DE genes



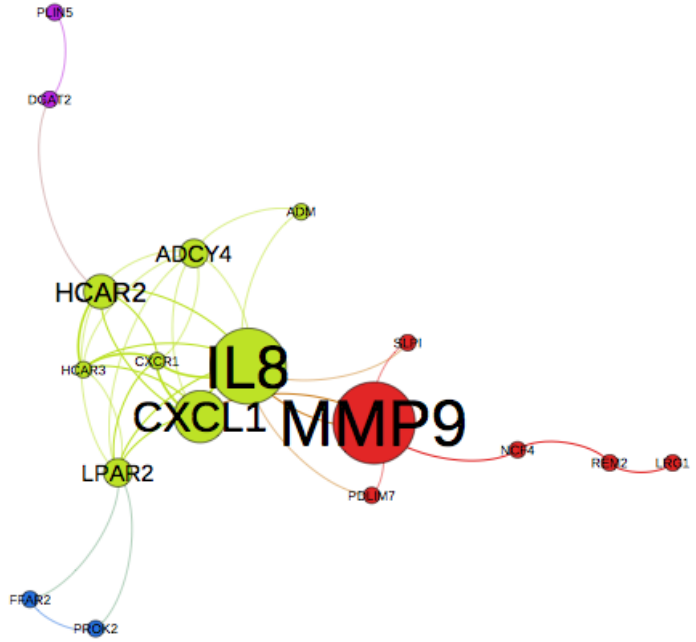
Rare variant eQTLs interact with environment and are associated with arterial stiffness



Matrix 1: DEG between Mtl and Sag

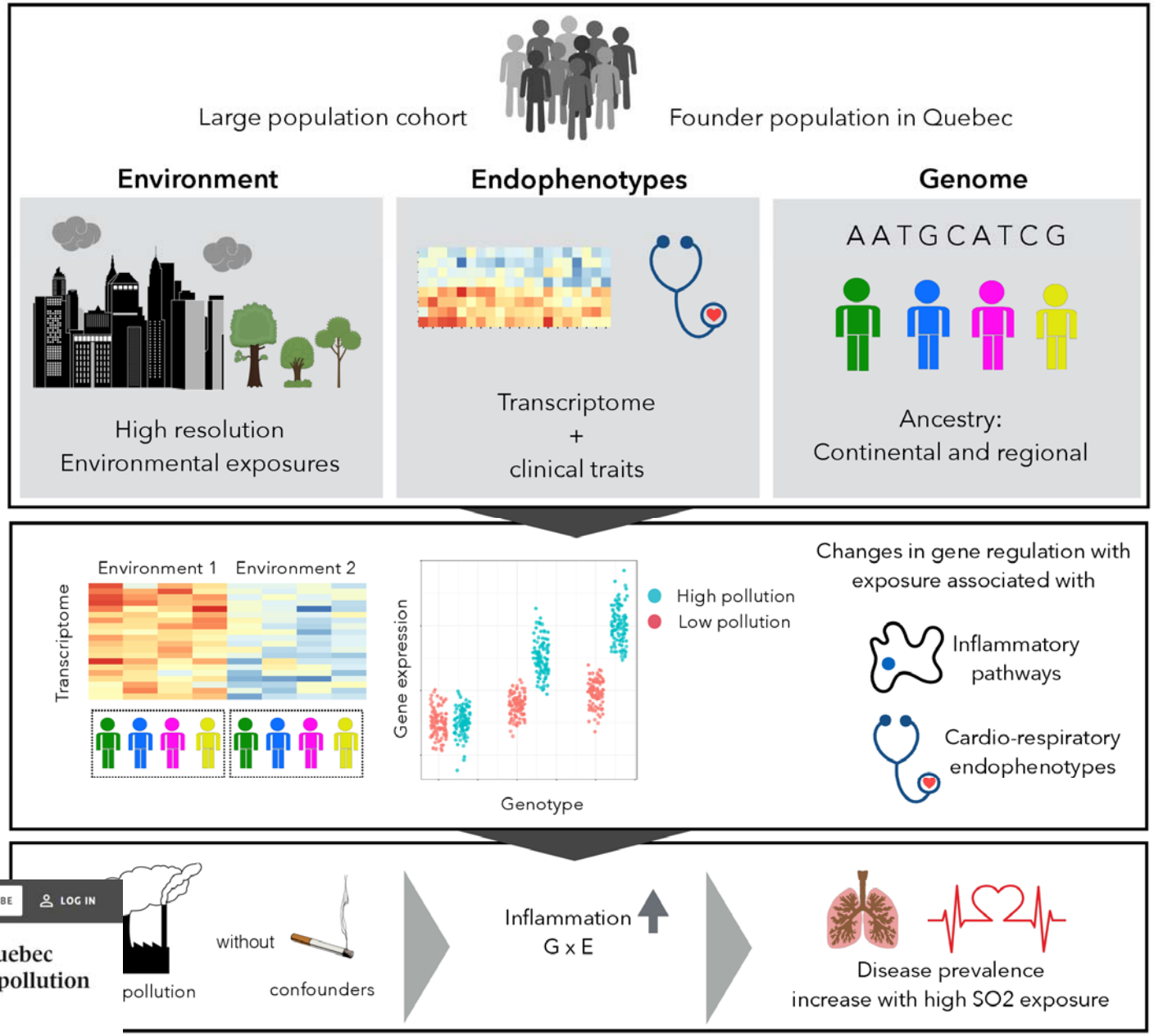
Matrix 2: Phenotypes

Association with AIX: among the genes that show the strongest association, we find 12 out of 18 genes from our MMP9 network (which was identified as associated with the pollution gradient).



Marie-Julie Fave, Nature communications

Summary


Large population cohort
Founder population in Quebec
Environment
Endophenotypes
Genome
AATGCATCG
High resolution
Environmental exposures
Transcriptome
+
clinical traits
Ancestry:
Continental and regional
Environment 1
Environment 2
Transcriptome
Gene expression
Genotype
High pollution
Low pollution
Changes in gene regulation with exposure associated with
Inflammatory pathways
Cardio-respiratory endophenotypes
pollution
without
confounders
Inflammation
G x E
Disease prevalence
increase with high SO2 exposure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Genetic study of Quebec residents finds air pollution trumps ancestry

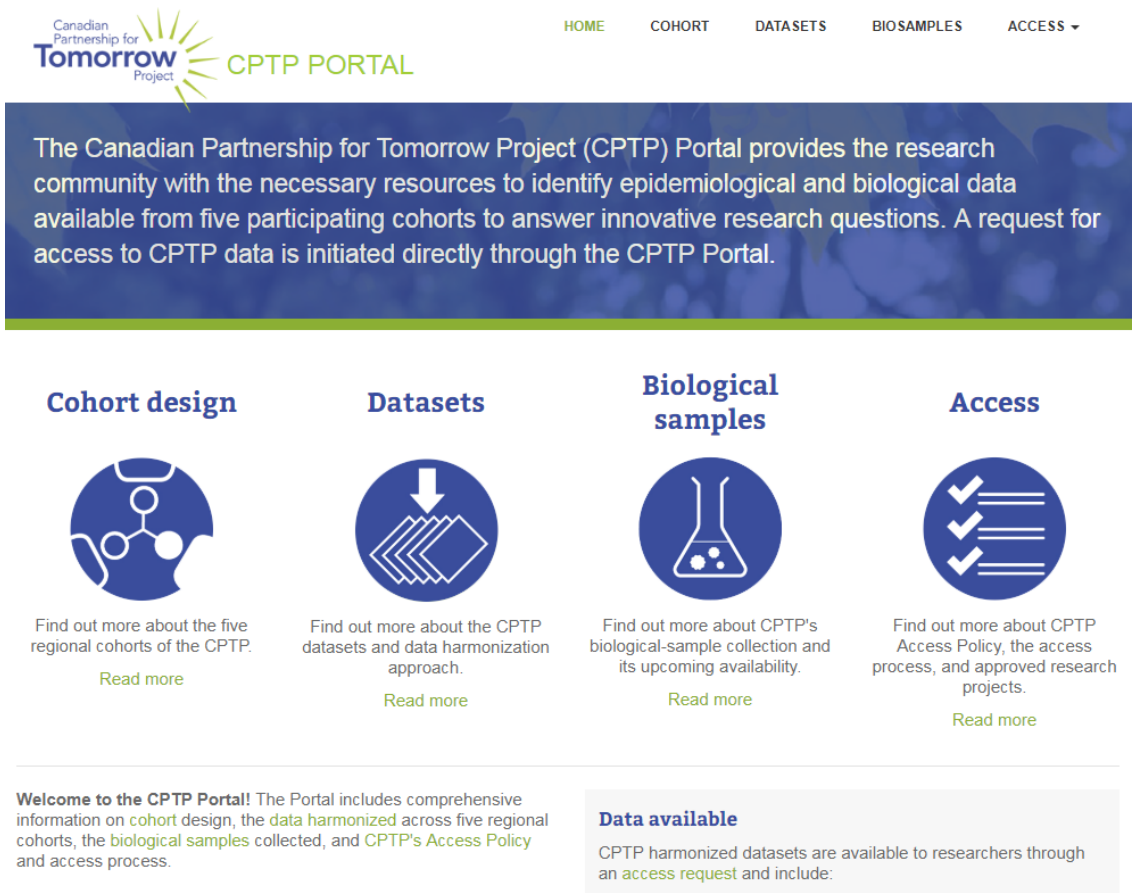
Ongoing and future **enrichment**

Strategic Priorities (2017-2021)

1. Enrichment of the cohort with **biomarkers**
2. Linkages to **environmental data**
3. Collection of **residential and occupational histories**
4. **Regular follow-up** questionnaires
5. **Linkage of participants** to their health-related records
6. Continued development of **key strategic partnerships**

Accessing the CPTP Data

portal.partnershipfortomorrow.ca



Canadian Partnership for Tomorrow Project CPTP PORTAL

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Variables

- Areas of Information
- Source & target
- Properties

List Coverage

Variables 1,581

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20 « ‹ 1 2 3 ... › » 1 - 20 of 1581

Name	Label	Data	Dataset
ALE06_02	Intersection density in 2006	CANUE	CPTP_BL_ALE
ALE06_03	Dwelling density in 2006	CANUE	CPTP_BL_ALE
ALE06_04	Z-score of the intersection density measure in 2006	CANUE	CPTP_BL_ALE

Accessing the CPTP Data

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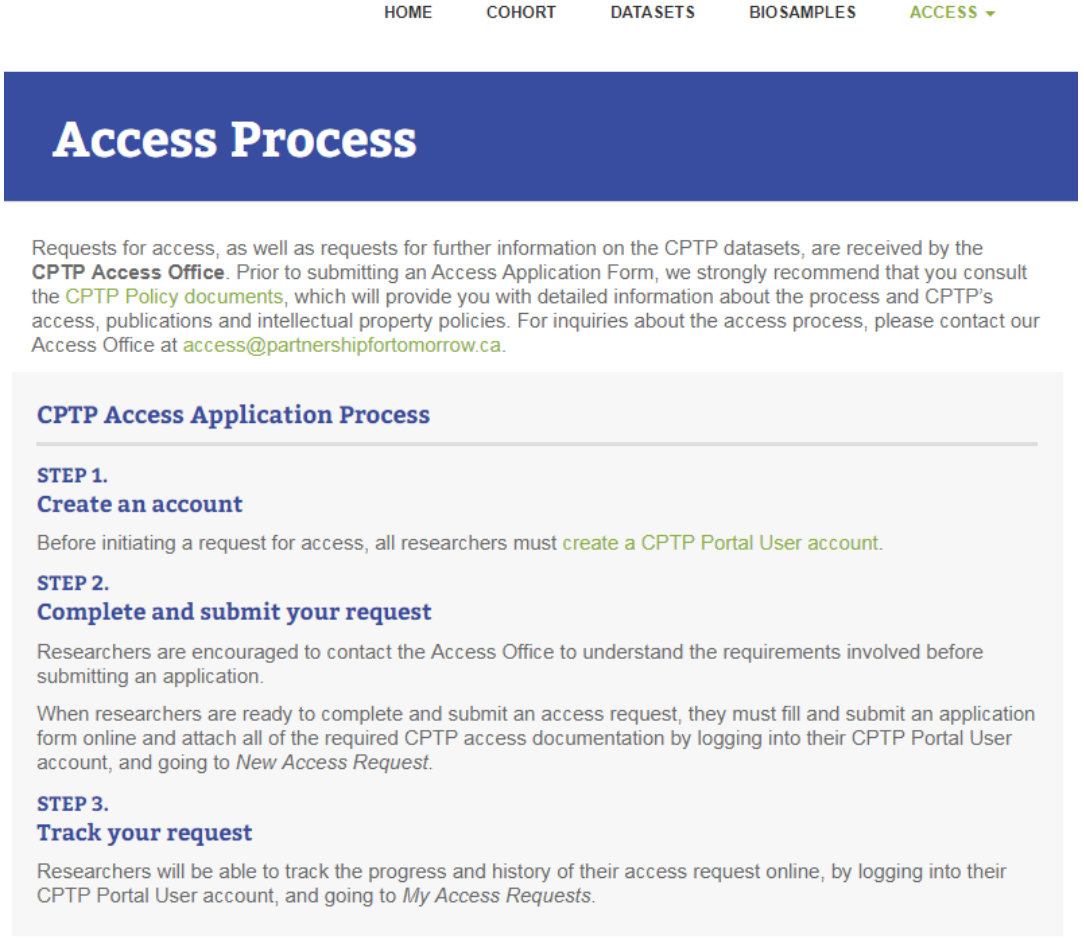
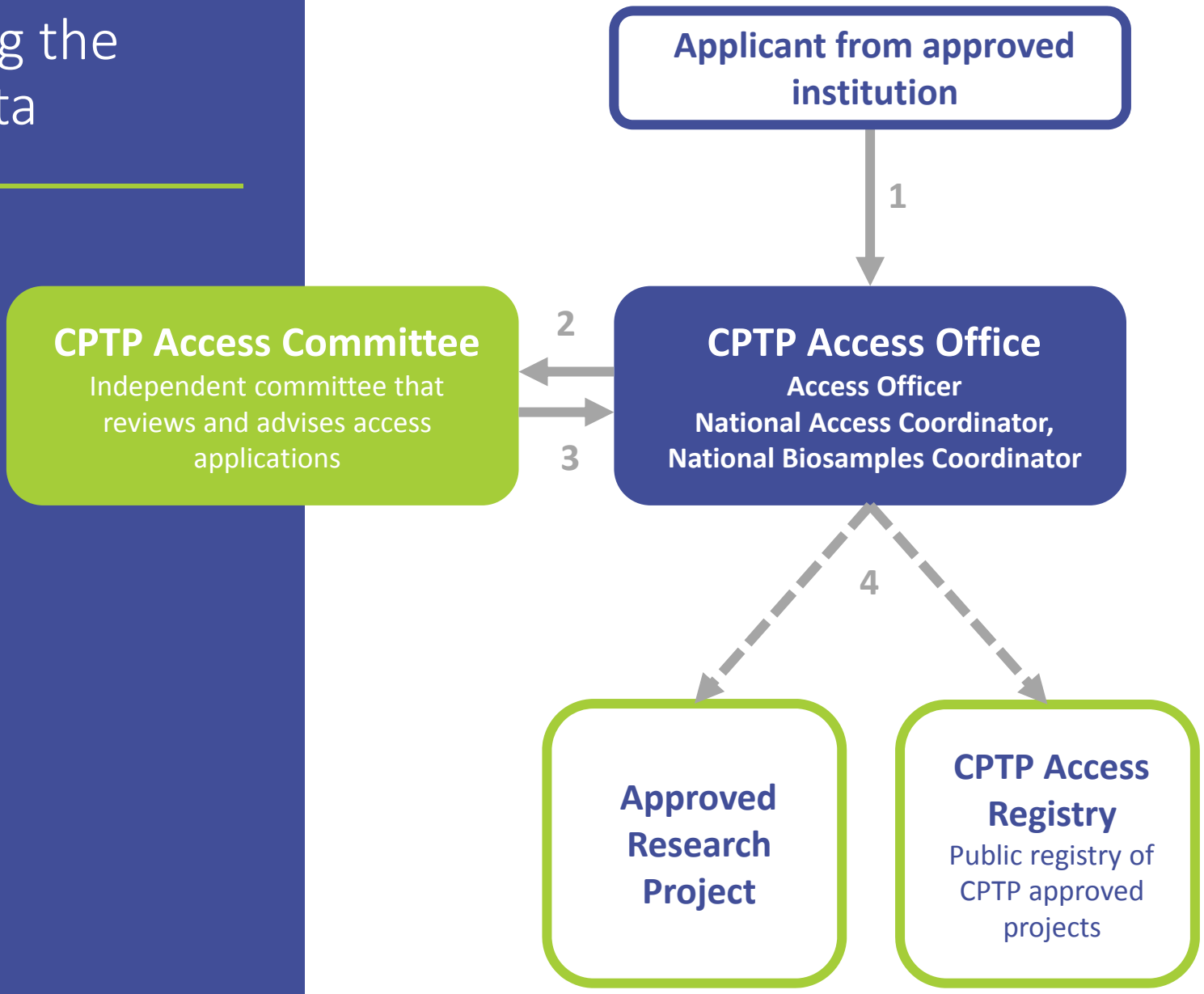
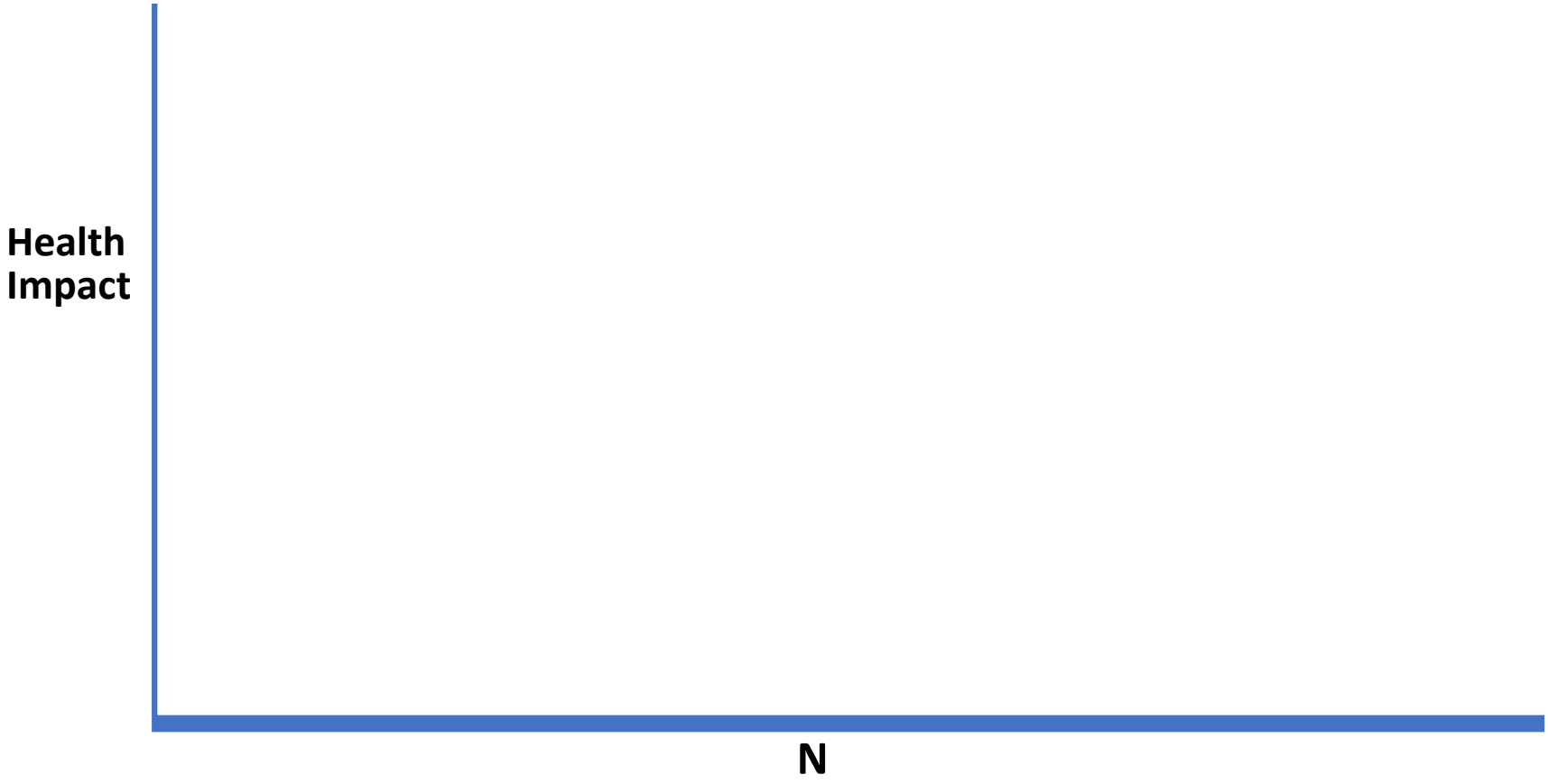


Accessing the CPTP Data



National cohorts to individual cells…
Precision Medicine to Population Health



National cohorts to individual cells…
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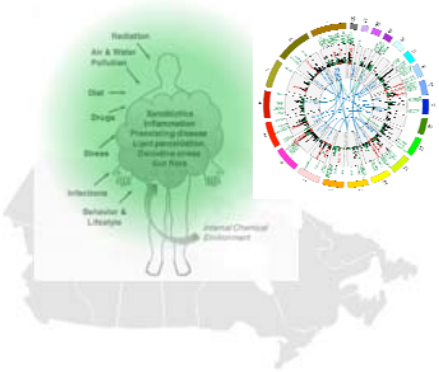

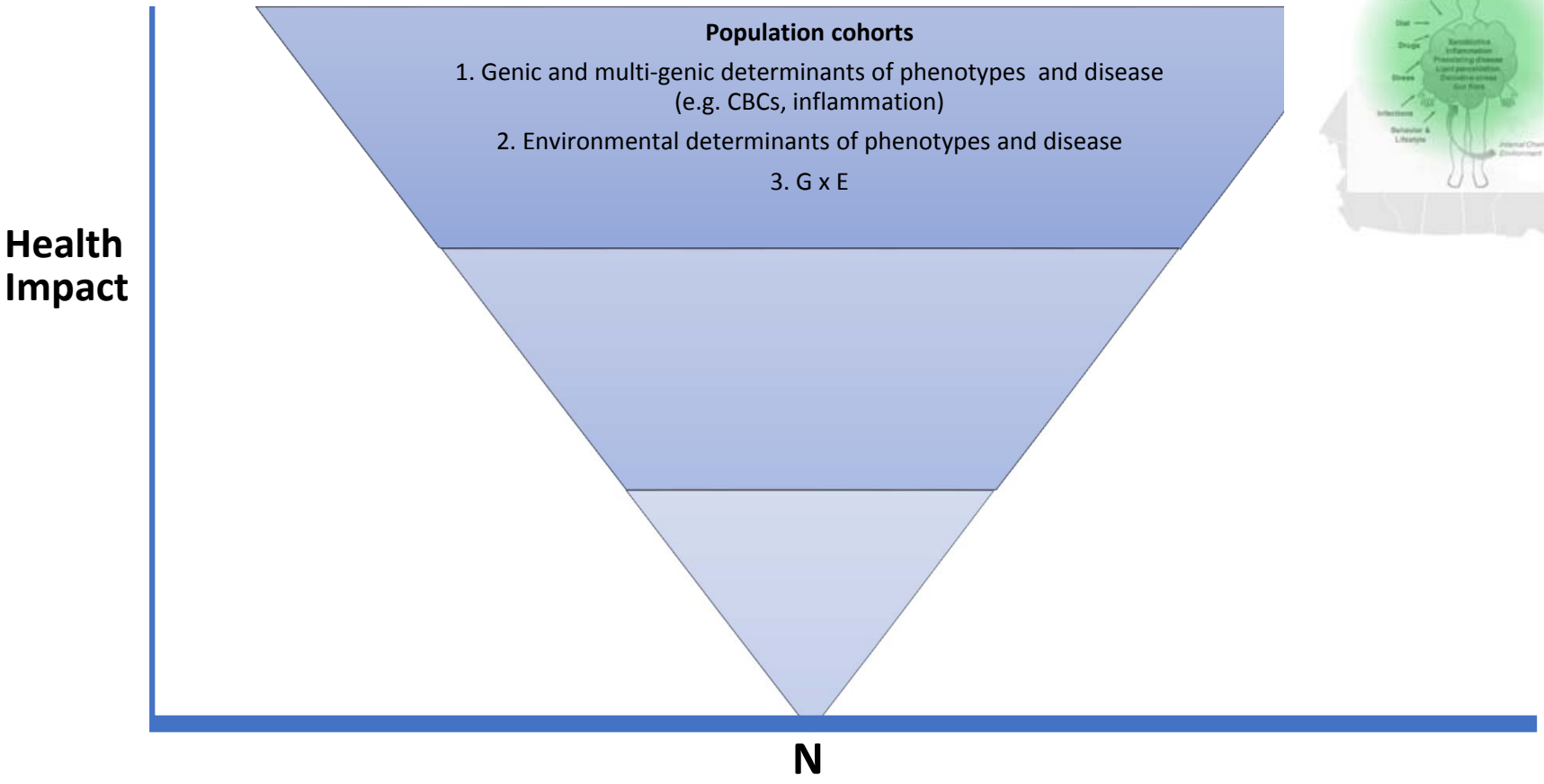

National cohorts to individual cells…
Precision Medicine to Population Health

Health Impact

Population cohorts

1. Genic and multi-genic determinants of phenotypes and disease (e.g. CBCs, inflammation)
2. Environmental determinants of phenotypes and disease
3. G x E

Disease Cohorts

1. Genomic determinants (mutational and epigenomic)
2. Evolutionary dynamics of blood aging and malignancies.

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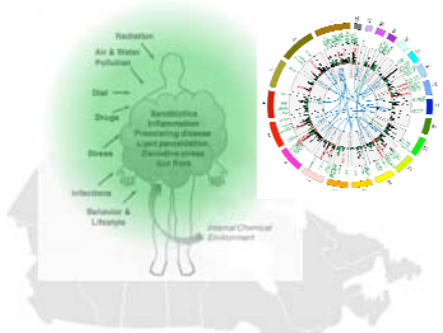

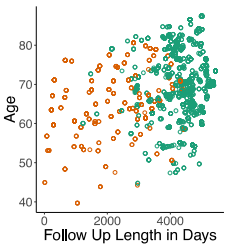

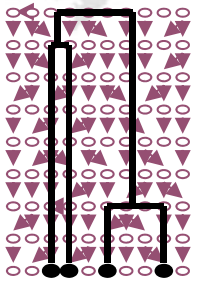

National cohorts to individual cells…
Precision Medicine to Population Health

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Disease Cohorts

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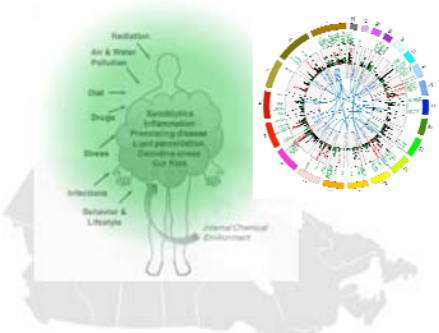
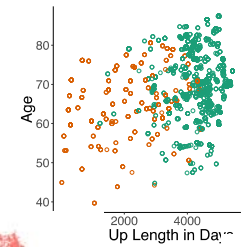
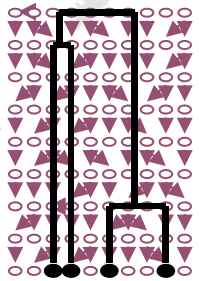
2. Evolutionary dynamics of blood aging and malignancies.

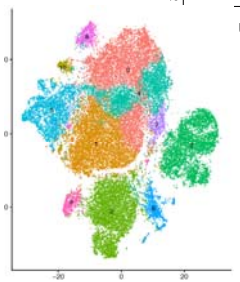
Individual Cellular populations

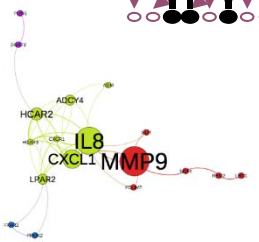
1. Functional impact of aging on hematologic cellular populations
2. Gene expression and phenotype or disease











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Canadian Partnership for Tomorrow Project

Thank you to the Tomorrow Project participants across the 6 regional cohorts who generously donate their time, information and biological samples. **The CPTP is a success because of the participants' ongoing commitment.**

Canadian Partnership for Tomorrow Project

Thank you to our sponsors and partners

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