Acknowledgments

Chris Nelson, Bella Coola, BC

Louise Christie, Photographer

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tmccgenetics.org/

Gnomad (Genome Aggregation Database)

Nativereflections.com

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Sources of Info

A Standardized Framework for Representation of Ancestry Data in Genomics Studies, with Application to the NHGRI-EBI GWAS Catalogue *ncbi.nlm/nih.gov/pmc/articles/pmc5815218*

European Bioinformatics Institute *ebi.ac.uk/gwas/docs/*

www.stanfordchildrens.org/en/topic/default?id=studies-for-single-gene-defects-dna-direct-and-indirect-90-P02148

The Broad Institute

V.1, 13 May 2020

Our Indigenous Partners

ASSEMBLY OF FIRST NATIONS

First Nations Health Authority
Health through wellness

Other Research Partners

LifeLabs

Michael Smith Foundation for Health Research

illumina

GenomeCanada

Canada's Michael Smith Genome Sciences Centre

CIHR IRSC
Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

UBC The University of British Columbia

For more information contact:

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ALL MY RELATIONS

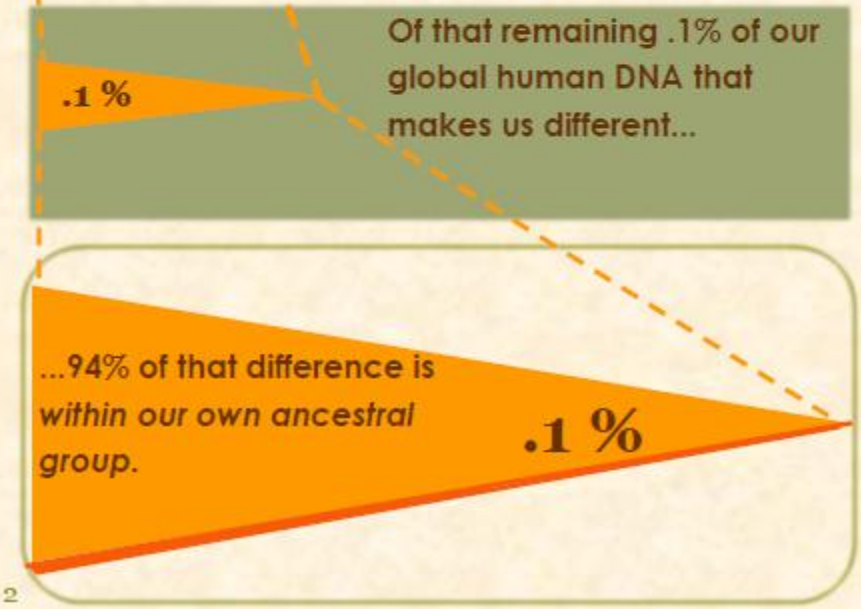
BUILDING A BACKGROUND DNA VARIANT LIBRARY FOR INDIGENOUS PEOPLE

Silent Genomes Research Project

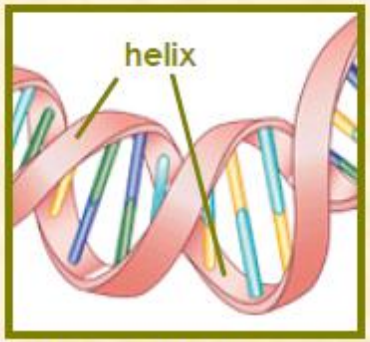
WE ARE RELATED THROUGH DNA

DNA (deoxyribonucleic acid) is the set of instructions that tells our bodies how to work by messages from generation to generation.

As Indigenous peoples, we are even more closely related.

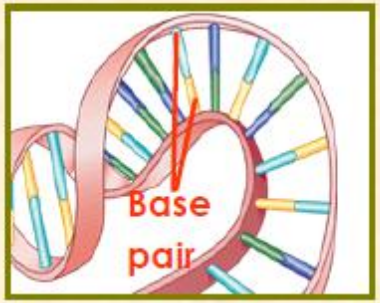


DNA IS INHERITED FROM EACH PARENT



Each rung of the ladder is called a base pair and is represented by the letters C-G and A-T.

Imagine DNA as a long twisted ladder, commonly referred to as a double helix.



We have 3 - 4.5 million different bases between individuals, even those we are related to. This is why no two people are alike, even if we are closely related (except for twins - but that's for another day)!

These differences in DNA bases between individuals are called ***variants***. Although one change in one base can produce dramatic changes, most variants are harmless.

What is a background DNA variant library?

A collection of variants from people unaffected by **rare genetic diseases**. Some variants may be more common within a population but rare outside of it (or vice versa).

Using the symbols above for variants, if a patient has a + variant, is it in the library? Pssst...no!

How does this work?

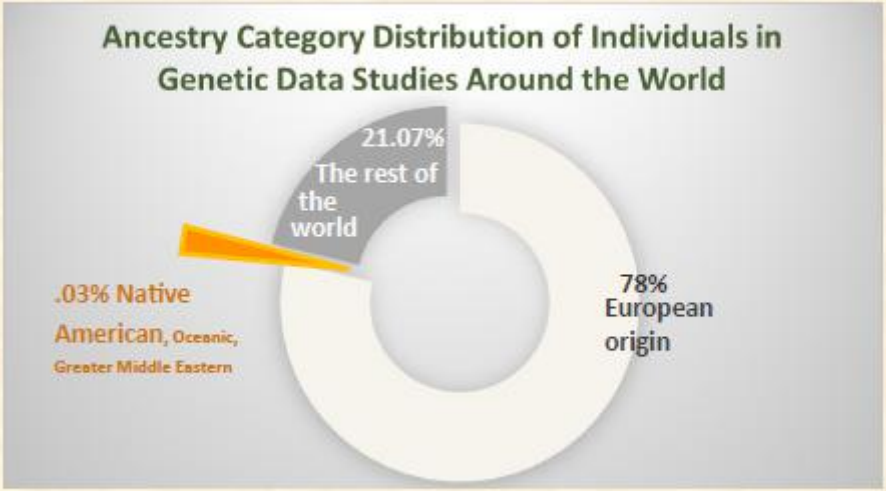
...by a process of elimination.

Rare genetic diseases are difficult to diagnose. A patient's genetic tests are to try to find the cause of their disease amongst millions of their own variants. The library allows doctors to quickly eliminate all of the variants common to the general population and the patient — variants are unlikely to be disease-causing. This step narrows the suspects for diagnosis.

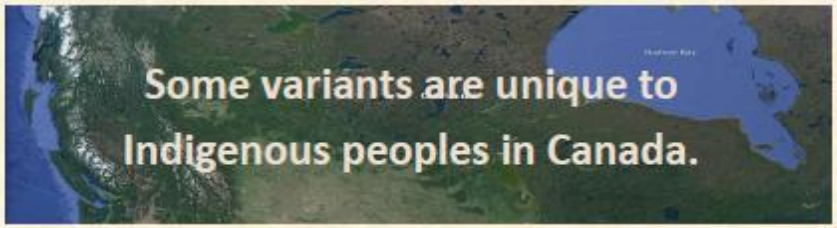
A patient's variant can also be compared to rare disease libraries around the world to see if there is a match.

DID YOU KNOW? **Not all variants are inherited. They can also spontaneously occur within an individual's cells.**

There is a problem: very little is known about Indigenous DNA variation—what is common & rare

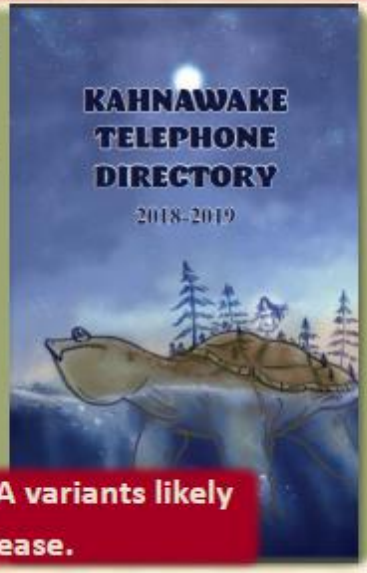


WHY DO WE NEED AN INDIGENOUS BACKGROUND VARIANT LIBRARY?



Imagine looking for the name of a relative in a pile of phone books. What are common and rare last names in your community?

If we have our own phone book with our own DNA names in it, it would be easier to focus on and eliminate healthy variants.



Matching DNA variants likely means no disease.

If we don't find what we are looking for, the search continues for a possible disease-causing DNA variant.

The more contributions of potential relatives' healthy variants, the greater the potential to eliminate those safe DNA variants & focus on what might be causing disease.

This is why a Background Variant Library is an effective tool that can increase the odds of an accurate diagnosis for a suspected genetic disorder. It is the first step towards proper management of a complex health condition.

The goal is 1500 DNA samples from Indigenous peoples across Canada by 2022 ...for starters

Eventually, these first donations will become the foundation for an **Indigenous-controlled** Background Variant Library for Indigenous peoples in Canada.

It is predicted that this will narrow the health care gap by improving diagnostic success for Indigenous peoples with rare genetic diseases.

1 Consultation at each step of the way to acquire free, prior & informed consent.

I'm in. I agree to loan my DNA to the Indigenous Background Variant Library. What is in place to protect my DNA and privacy?

2 From blood sample to non-traceable computerized data, measures are in place to protect your identity. Biological material is stored only for the length of time to build library.

TELL ME MORE ...

3 Controlled, safe access to computerized data by doctors helping First Nation patients.

Interest

Introductory presentations upon request

Engagement

What would a governance framework look like? We present options for discussion.

Thoughts

1 Engagement - a Collaborative Approach

Decision-making Time

Discuss whether we want or need an Indigenous Background Variant Library. If we don't, we stop. If support present, we move forward.

Thoughts

Origin	# of Participants
Alliance Study-National Aboriginal Working Group biobank	900
BC participants without severe genetic diseases	200
Relatives of Activity 2 (diagnosis of children with suspected genetic disease)	400
TOTAL	1500

Blood samples collected by Silent Genomes or through other collection method, e.g., community health fair

2 DNA on Loan

by First Nation citizens for the purpose of the research for which consent was obtained

Vancouver, BC, chosen for sequencing (reading) your DNA from blood

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atggctat
taccgata
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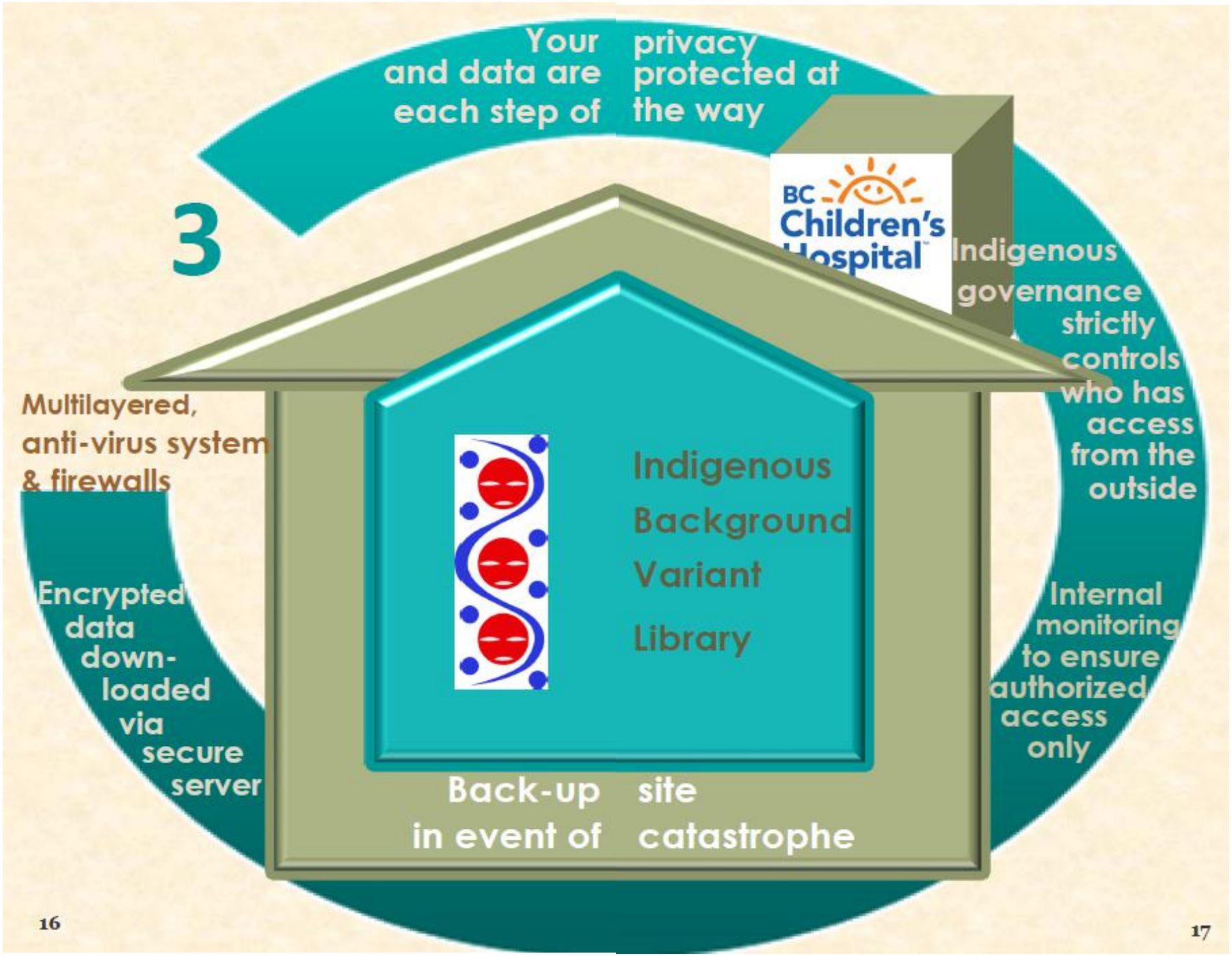
Vancouver, BC, for analysis & storage of de-identified DNA variant data


3
Your privacy and data are protected at each step of the way
BC Children's Hospital
Indigenous governance strictly controls who has access from the outside
Multilayered, anti-virus system & firewalls
Indigenous Background Variant Library
Encrypted data down-loaded via secure server
Internal monitoring to ensure authorized access only
Back-up site in event of catastrophe

An Indigenous Background Variant Library is expected to improve the current situation

WE DID THIS BEFORE:

Assembly of First Nations Resolution #9-2012

Support for Further Work, Education, & Awareness of Canadian Blood Services One Match Stem Cell & Marrow Network in Partnership with Aboriginal Nurses Association of Canada

Of roughly 7,000 known rare diseases, about 80% of them are genetic

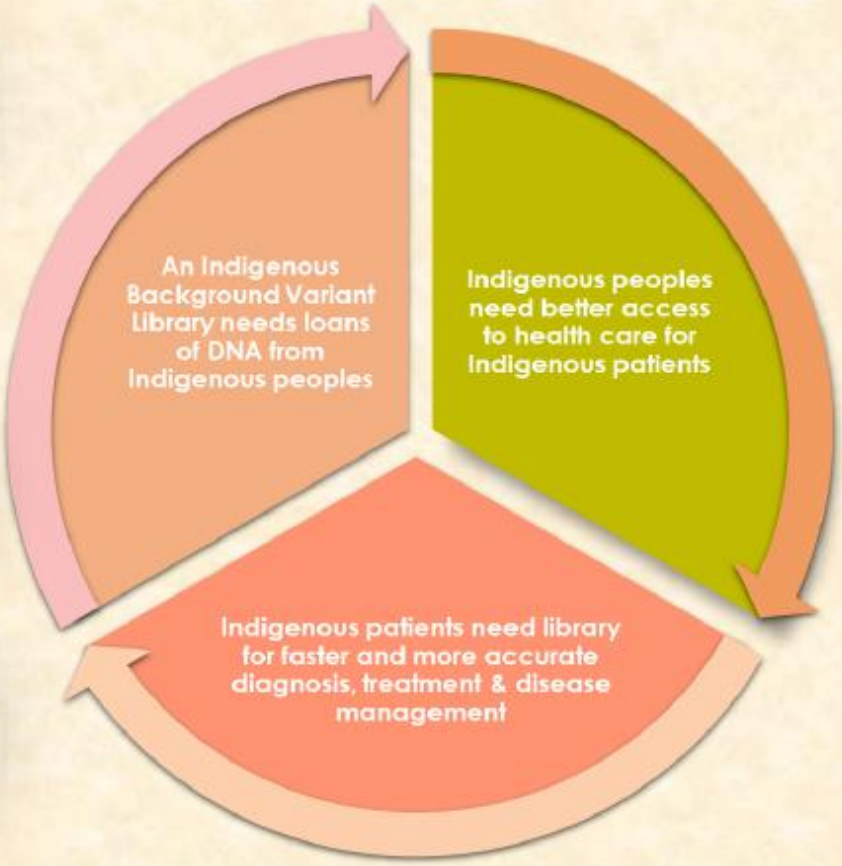
MORE THAN 50% OF RARE DISEASES START IN CHILDHOOD

The length of time from symptom onset to an accurate diagnosis is around 4.8 years for a rare disease.

PATIENTS SEE AN AVERAGE OF 7.3 PHYSICIANS BEFORE A DIAGNOSIS IS MADE

There is no 100% guarantee of finding the gene variant suspected of causing the health condition, especially at start-up.

For a broad collection of disorders, kids are diagnosed 30-40% of the time through DNA libraries. The rate increases each year.



WE PERSONALLY MAY NOT BENEFIT FROM OUR DNA ON LOAN TO THE SILENT GENOMES RESEARCH PROJECT.

However, by moving forward on an Indigenous Background Variant Library, we are helping all our relations, even those we do not yet know — and those unborn.