Acknowledgments

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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/

The Broad Institute

Our Indigenous Partners

ASSEMBLY OF FIRST NATIONS
First Nations Health Authority Health through wellness

Other Research Partners

Building a background DNA Variant Library for Indigenous People

For more information contact:
silentgenomes@uvic.ca
**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.

We share 99.9% of our DNA with the rest of humanity.

Of that remaining .1% of our global human DNA that makes us different...

...94% of that difference is within our own ancestral group.

As Indigenous peoples, we are even more closely related.

Indigenous peoples need better access to health care for Indigenous patients.

Indigenous patients need library for faster and more accurate diagnosis, treatment & disease management.

An Indigenous Background Variant Library needs loans of DNA from Indigenous peoples.

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.
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.

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.
How does this work?

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.

...by a process of elimination.

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!

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).
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.

- **0.03% Native American, Oceanic, Greater Middle Eastern**
- **21.07% European origin**
- **78% The rest of the world**
Why do we need an Indigenous phone book with our own DNA names in it?

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

Some variants are unique to Indigenous peoples in Canada.

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.

2 DNA on Loan by First Nation citizens for the purpose of the research for which consent was obtained.

Vancouver, BC, for analysis & storage of de-identified DNA variant data.
Blood samples collected by Silent Genomes or through other collection method, e.g., community health fair.

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

BACKGROUND VARIANT LIBRARY?

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.

Engagement

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

Thoughts

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
Engagement - a Collaborative Approach

Interest
Introductory presentations upon request

<table>
<thead>
<tr>
<th>Origin</th>
<th># of Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alliance Study-National Aboriginal Working Group biobank</td>
<td>900</td>
</tr>
<tr>
<td>BC participants without severe genetic diseases</td>
<td>200</td>
</tr>
<tr>
<td>Relatives of Activity 2 (diagnosis of children with suspected genetic disease)</td>
<td>400</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1500</td>
</tr>
</tbody>
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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.

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