SILENT GENOMES:
Reducing health care disparities and improving diagnostic success for children with genetic diseases from Indigenous populations.
• Laura Arbour MD - Pediatrician, Medical Geneticist (UBC, UVic, BCCHRI)

• Nadine Caron MD - Sagamok Anishnawbek (Ojibwa) - Surgeon (UBC, UNBC, BCCA, Associate Faculty Johns Hopkins, Co-director of the Centre for Excellence, Indigenous Health UBC)

• Jeff Reading PhD - Mohawk Indigenous Scholar (SFU, Providence Health, FNHA-Chair in Heart Health and Wellness)

• Wyeth Wasserman PhD - Bioinformatics (UBC, Executive Director of the BCCHRI)

• Dean Regier PhD - Economist (UBC, BCCA)
“The genomic health divide must be kept in check and ultimately bridged through equitable economic investment, clinical research, and provision and use of genomic services and technologies globally.”

http://www.who.int/genomics/healthdivide/en/
**THE PROBLEM**

Data from persons who identify as Indigenous are starkly absent from reference databases used for genomic diagnosis.

Therefore access to precision diagnosis is limited - increasing health disparity

**First Nations:** 618 FN communities N = 851,560.  
**The Inuit:** 53 communities N = 59,445.  
**The Metis:** N = 451,795.

• With Indigenous partners (Nationally, regionally and on a community level) we will:
  • build a strong governance model for genomics research;
  • plan together, the necessary steps for development of an Indigenous Background Variant Library (IBVL);
  • offer genomic diagnosis to Indigenous Children across Canada;
  • assess the cost-effectiveness of the system.
The Team

INDIGENOUS HEALTH
Nadine Caron (UBC/UNBC)
Jeff Reading (SFU)
Sonia Isaac Mann (FNHA)
Nanibaa’ Garrison (UW)
Laura Arbour (UBC/UVic)
Sonia Anand (McMaster)

COMMUNITY INFORMED ECONOMICS
Dean Regier (UBC/BCCA)
Michael Burgess (UBC)
Nanibaa’ Garrison
Anne-Marie Laberge (UM)

MOLECULAR GENOMICS
Marco Marra (UBC)
Maja Tarailo-Graovac (UC)
Anna Lehman (UBC)

BIOINFORMATICS
Wyeth Wasserman (UBC)

CLINICAL GENOMICS
Anna Lehman (UBC)
Maja Tarailo-Graovac (UC)
Laura Arbour (UBC/UVic)
Francois Bernier (UC)

National Clinical Network

END USERS / PARTNERS
Assembly of First Nations
Inuit Tapiriit Kanatami (ITK)
Métis National Council (MNC)
First Nations Health Authority (FNHA)
National FN Alliance Working Group
BC Ministry of Health
Nunavut Department of Health
Canadian National Clinical Network (NCN)

POPULATION GENOMICS
Ripan Malhi (UI)
Simon Gravel (McGill)

INTERNATIONAL INDIGENOUS GENOMICS PERSPECTIVES
Nanibaa’ Garrison (USA/Wash)
Kim Tallbear (Canada/AB)
Maui Hudson (New Zealand)
Phil Wilcox (New Zealand)
Ngiare Brown (Australia)
Maile Taualie (USA/Hawaii)
Sharon Edmunds-Potvin (Canada/Nunavut)

COMMUNITY EDUCATION
Sarah McIntosh (UBC)
Anne-Marie Laberge (UM)

CLINICAL GENOMICS
Anna Lehman (UBC)
Maja Tarailo-Graovac (UC)
Laura Arbour (UBC/UVic)
Francois Bernier (UC)

National Clinical Network

MOLECULAR GENOMICS
Marco Marra (UBC)
Maja Tarailo-Graovac (UC)
Anna Lehman (UBC)

BIOINFORMATICS
Wyeth Wasserman (UBC)
The text is organized as follows:

**Activity 1:** First Nations, Inuit, and Métis Engagement, Governance, and Capacity Building

**Activity 2:** Precision Diagnosis of Indigenous Children with Genetic Disorders

**Activity 3:** Build an Indigenous Background Variant Library

**Activity 4:** Economics of Genomic Diagnosis in Indigenous Populations
ACTIVITY 1: First Nations, Inuit And Métis Engagement, Governance, and Capacity Building

ACTIVITY 2: Precision Diagnosis of Indigenous Children with Genetic Disorders

ACTIVITY 3: Build an Indigenous Background Variant Library

ACTIVITY 4: Economics of Genomic Diagnosis in Indigenous Populations
ACTIVITY 1:
First Nations, Inuit And Métis Engagement, Governance, and Capacity Building

ACTIVITY 2:
Precision Diagnosis of Indigenous Children with Genetic Disorders

ACTIVITY 3:
Build an Indigenous Background Variant Library

ACTIVITY 4:
Economics of Genomic Diagnosis in Indigenous Populations
1. Policy Framework: 
   Guidelines
   Best Practices

2. Community educational tools, training and capacity building

3. Indigenous Background Variant Library

4. Precision Diagnosis and Cost effectiveness evaluation
Assembly of First Nations Support

First Canadian **Summer internship for INdigenous Peoples in Genomics (SING Workshop)** enabled by LifeLabs Scholarship program to Silent Genomes
We will take a quantum step forward to address the “genomic divide” through reducing barriers to access in both the diagnosis of genetic diseases and the research that drives it for Indigenous Canadians.

1. Indigenous led Governance will be the model for Canadian Guidelines and International Best Practices
2. Genomic Education Tools for Communities
3. Genomics Capacity Building for Indigenous Students
4. The platform for a sustainable IBVL will be in place with room to grow to provide precision diagnosis for children, their families and communities
In 2015 Canada signed on to the United Nations Declaration of the Rights of Indigenous Peoples confirming Indigenous Canadians:

(Article 24) ‘have the right to access, without any discrimination, to all social and health services’;

(Article 4) ‘have the right to self determination’.

- Indigenous persons deserve to have their genetic disease diagnosed and managed. And they have the right to guide the process.
- Silent Genomes has the potential to lead the world by example in developing Indigenous led policy on Genomic research to be integrated into on-going health care.
- We are uniquely qualified to bridge the ‘Genomic Divide’ for Indigenous Canadians by improving access to genomics diagnosis.
EXTRA SLIDES
Activity 1: Engagement and Capacity Building

Activity 1.1: Gathering Ceremony & Project launch with FN and Inuit Elders and Knowledge Keepers
Dialogue to establish governance and to guide policy development and capacity building

Activity 1.2: Engagement with Alliance communities
Face-to-face meeting to establish process for research and engagement

Activity 1.3: Engagement with non-Alliance communities
Face-to-face meeting to establish process for research and engagement

Activity 1.5.1: Community education
Development of culturally-appropriate and community-specific education aids

Activity 1.5.2: Research, clinical, academic capacity building
SING: Summer internship with Indigenous Peoples in Genomics
IMNPN: Indigenous Mentorship Network of the Pacific Northwest

Deliverable:
Indigenous Focused Community Education Tools and Student Genomics Training
ACTIVITY 1: POLICY

Governance (Oversight) of Silent Genomes project

- Application of FN, Inuit and Métis health research principles
- Privacy (individual/community) consequences of WGS
- Data ownership and stewardship
- Approaches to safe access to IBVL for clinical diagnosis

Survey of funding agencies to establish gaps in processes and policy relevant to Indigenous genomics research

Deliverable – Model Policy

1) Guidelines applicable to Canadian context
2) Best Practices from international indigenous perspective
ACTIVITY 2: DIAGNOSIS

Dr. A Lehman

Dr. M Tarailo-Graovac
ACTIVITY 3: IBVL DEVELOPMENT
Discussion underway with FN arm of Canadian alliance for healthy hearts and minds
ACTIVITY 4: ECONOMIC ASSESSMENT

Figure 4.2 Decision model examining cost-effectiveness of WGS and the IBVL versus standard care

Figure 4.3 Long term decision model examining cost-effectiveness of WGS and the IBVL versus standard care
<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>PLANNED START (dd/mm/yy)</th>
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<th>QUARTER - 3 months Start Date (01/18)</th>
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<td>Activity 1.1 Gathering Ceremony; Project launch</td>
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<td>Activity 1.3 Additional FN and other community Engagement</td>
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<td>Activity 1.4 Model Policy</td>
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<td>Activity 1.5 Capacity building for communities and Indigenous Training Program</td>
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<td>Activity 2.1 Patient Recruitment, Phenotyping, and Biological Sample Collection</td>
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<td>Activity 2.2 WGS for Precise Diagnosis</td>
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<td>Activity 2.3 Validation of the WGS-derived Diagnosis</td>
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<td>Activity 3.1 Database Construction</td>
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<td>Activity 3.2 Sample Processing</td>
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<td>Activity 3.3 Whole Genome Sequencing (WGS)</td>
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<td>Activity 3.4 Data Analysis</td>
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<td><strong>Activity 4: ECONOMICS OF GENOMIC DIAGNOSIS IN INDIGENOUS POPULATIONS</strong></td>
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<td>Activity 4.1 Documenting Community and Individual Acceptibility</td>
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<td>Activity 4.2 Estimating the Cost-effectiveness</td>
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<td><strong>Project Management</strong></td>
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<td>Project Management</td>
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Milestone 1- Act 1.1: Gathering ceremony (Q4)
Milestone 2a- Act 1.4: Governance process in place (Q9)
Milestone 2b Guidelines (Canadian) (Q12)
Milestone 2c Best Practices (International) (Q14)
Milestone 3- Act 3.1: Security system completed for IBVL (Q8)
Milestone 4- Act 3.2: Begin sample transfer of existing samples for IBVL (Q9)
Milestone 5- Act 3.4: Data analysis for IBVL (Q15)

Milestone 6- Act 3.4: Validation of Clinical diagnosis samples with IBVL (Q15)
Milestone 7- Act 1.4: Complete development of process for use of IBVL beyond Silent Genomes (Q16)
Milestone 8- Act 4.1 - Focus groups and qualitative interviews and analyses completed (Q8)
Milestone 9- Act 4.1 - Preference-based analyses completed (Q12)
Milestone 10- Act 4.2 - Chart review and associated analyses completed (Q8)
Milestone 11- Act 4.2 - Decision model 1 completed (Q11)
Milestone 12- Act 4.2 - Decision model 2 completed (Q15)