Activity 3: Indigenous Background Variant Library (IBVL)

Background

A Background Variant Library (BVL) is a list or collection of DNA variants in a group of people without severe genetic conditions, which helps to determine if variants are common or rare within the population (group). There are BVLs for many populations in the world, such as the gnomAD database, but none serving the needs of Indigenous peoples. The proposed Indigenous Background Variant Library (IBVL) will be a database to show the frequency of each DNA variant found within a population of Indigenous people of Canada who have not been diagnosed with a severe genetic condition. To date, no IBVL exists, and Indigenous peoples of Canada are not well represented in the BVLs that are currently available. As seen in activity 2, many children cannot obtain a confirmed diagnosis because it cannot be determined if the variant is common or rare within the Indigenous population without the IBVL. With the generation of the IBVL, we hope to help families get quicker results, thus lessening the stress they may face due to unanswered questions about their child's diagnosis.

Where are we in our efforts to build consensus for Governance of the IBVL?

Silent Genomes Indigenous Rare Disease Diagnosis Steering Committee (S-GIRDD SC)

The mission of the Committee is to provide 'cultural oversight & strategic advice in support of the collaborative creation, implementation, and utilization of the IBVL including respectful, culturally safe policies regarding access to data for clinical diagnoses [and related research]'. The SC is comprised of Indigenous community members, patients and parents of children with rare disease, representatives from Indigenous organizations (MNC, FNHA) and from the First Nations arm of the Canadian Alliance for Healthy Hearts and Minds. The SC has had thirteen meetings to date where participants developed the above mission statement, contributed to the terms of reference, discussed the process for variant release, and are in the midst of ongoing discussion to define acceptable clinical research as it pertains to the IBVL.

Where are we in our efforts to build an IBVL?

Agreements

Currently, agreements are being finalized to initiate DNA sample transfer for communities that want to move forward with the project, these agreements include Material and data Transfer Agreements (MTA) between the Alliance biobank who will provide the samples and BC Children's Hospital Research Institute (BCCHR) who will process the data, Research Ethics Board (REB) approval, etc.

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Security Audit

In order to have a secure informatic system to process the data to generate the IBVL, an independent audit of the informatics system (Information and Security Assessment) was performed. The results of the audit showed that our system is overall well protected. Still, we have implemented yearly training and expanded our existing effort on documenting procedures to ensure that we are constantly keeping our system safe and secure.

IBVL Generation

To prepare for the generation of the IBVL, a start-to-finish analysis is being tested to ensure that we will be ready for the processing of Indigenous data. The dry run analysis is being conducted using fastq data files. Fastq data files are text files that contain sequence data. The fastq data files we are using for the dry run are publicly available, non-Indigenous genomes.

IBVL Access Model and Interface

The IBVL variant frequencies will be accessed in a controlled manner through the web. The construction of the interface has been progressing throughout the year. We asked the Silent Genomes Indigenous Rare Disease Diagnosis Steering committee (S-GIRDD) their thoughts on three different access models for the IBVL. After much consideration and thought, the Silent Genomes team decided to implement a restricted access model, for which the user will need to login to access the variants frequencies. We then started building the IBVL interface using Oracle APEX, which provides high data security and allows detailed tracking and auditing of user actions. We are currently releasing a test version (with no Indigenous data) with features such as a registration page, sign-up page, and variant query page. With more input from our partners, we will then be able to further improve the interface.