Received: 16 August 2018 | Revised: 30 October 2018 | Accepted: 6 November 2018

DOI: 10.1002/jgc4.1073

WILEY National Society of Genetic Counselors

SPECIAL ISSUE

Indigenous Peoples and genomics: Starting a conversation

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Abstract

Compared to European ancestral groups, Indigenous Canadians are more likely to have uninterpretable genome-wide sequencing results due to non-representation in reference databases. We began a conversation with Indigenous Canadians to raise awareness and give voice to this issue. We co-created a video explaining genomic non-representation that included diverse Indigenous view-points. We audio-recorded the focus groups including 30 First Nations, Métis, and Inuit individuals living in Greater Vancouver. After watching an introductory video explaining genomic testing, participants discussed issues surrounding collecting Indigenous genomic data, its control, and usage. Transcripts were analyzed, and participants' quotes representing main themes were incorporated into the introductory video. Indigenous participants discussed data interpretation and gave approval for quote usage. The 20 participants who provided feedback concurred with the thematic interpretation: Systemic racism interlaced most conversations, particularly within the theme of trust. Themes of governance emphasized privacy and fear of discrimination. Some participants thought a separate, Indigenous-controlled database was essential; others recognized advantages of international databases. The theme of implementation included creative ideas to collect Indigenous genomes, but prior approval from Indigenous leaders was emphasized. The final video (https://youtu.be/-wivIBDjoi8) was shared with participants to use as they wish to promote awareness and ongoing discussion of genomic diagnostic inequity.

KEYWORDS

First Nations, genetic testing disparities, genomic sequencing, healthcare inequity, Indigenous Peoples, reconciliation, reference databases

1 | INTRODUCTION

1.1 | Background

Genomic sequencing technology is recognized as the best diagnostic test in many situations where a genetic disorder is suspected (Lionel et al., 2018; Tan et al., 2017). When testing leads to a diagnosis, it may enable the family to receive more accurate genetic counseling, lead to a change in management, or, more rarely, point to a treatment (Tarailo-Graovac et al., 2016).

When patients' genomes are sequenced, bioinformaticians and geneticists interpret whether individual differences represent normal variability or pathogenicity. In part, this is done by comparing data to an international database of anonymous sequences (Lek et

al., 2016). The frequency of many genomic variants differs considerably across populations; therefore it is critical to compare each patient's sequence data to a database that includes sequences from people of the same ethnic group. Not doing so may result in misdiagnoses (Manrai et al., 2016). Sequence databases used for this purpose, such as gnomAD (Karczewski & Francioli, 2017), are derived from participants who are predominantly of European, Asian, Latino, and African ancestry (Karczewski & Francioli, 2017; Popejoy & Fullerton, 2016). Canadian First Nations, Métis, and Inuit genomes are virtually or entirely absent from gnomAD despite comprising 5.8% of the Canadian population (Statistics Canada, 2016).

This lack of representation means that analysis of genomic testing from Canadian Indigenous Peoples risks being inherently incomplete. Consequently, Indigenous Canadians do not receive the same quality of genomic healthcare as Canadians of other ancestral backgrounds.

Given an appropriate research study, a group of Indigenous Canadians could volunteer to submit their genomic sequences to an anonymous genomic database, such as gnomAD (Karczewski & Francioli, 2017). But for anyone contemplating donating sequence data, there are many issues to weigh that are based on personal values and beliefs. Exploitive, unethical, and culturally insensitive genetics research in Canada and elsewhere in North America has eroded trust in genetics and genomics for many Indigenous Canadians. This includes use of genomic sequencing for ancestral research without consent, the results of which are viewed as a source of racism and discrimination, as a challenge to culturally held origin stories (Abadie & Heaney, 2015), as potentially being at odds with Indigenous constructs of identity (TallBear, 2013). The lack of reconciling these past abuses of trust has created challenges resulting in reluctance amongst some researchers to include Indigenous participants in studies (McWhirter, Nicol, & Savulescu, 2015), potentially leading to increased healthcare disparities.

Further, the perpetration of colonial research practices, even when well intentioned, continues to marginalize Indigenous groups through Western ethnocentric interpretation of their "needs" whereas Indigenous Peoples have questions and priorities of their own (Smith, 1999). For all these reasons, it is important that a decolonizing lens, supported by Indigenous scholars, be a central framework to begin conversations about the meaning and value of genomic sequence data for medical use, from the perspectives of Indigenous Canadians.

There have been a number of studies around DNA biobanking involving Indigenous participants. Biobanks differ from reference databases such as gnomAD in that they include specimens that are linked to phenotype or other information, which may or may not be re-identifiable. Several studies have directly addressed models for Indigenous biobanks, including a community-based participatory research design for Pacific Islanders living in Arkansas (McElfish et al., 2017) where participants helped identify the medical concerns to be studied. Abadie and Heaney (2015) performed a small interview-based study of urban-living, off-reserve, mid-western Native Americans about DNA banking. Whereas hopes were expressed about the medical potential for genomics, concerns focused on a range of issues, including privacy, discrimination, and compensation for use, in the context of past exploitation. In this group, genomic participation decisions were seen as individual, not "tribal," but the authors recognized that the role of community in the decision might be different and contentious in other groups of Native Americans. For several of the interviewees, DNA was described as having a personal connection beyond the sample itself, "that's a part of you," and issues of "ownership" included expecting samples to be returned: "It's mine. And I'm just loaning it out." This same concept was described in a Canadian study regarding the relationship between participants and researchers, as "DNA on loan" (Arbour & Cook, 2006). In New Zealand, a Maori culturally informed biobank model has been proposed (Beaton et al., 2017) using Maori-informed practices to guide governance, ownership, ethics, and usage, including oversight by Indigenous guardians. These studies raise some of the issues that we anticipated might be in common with participants' concerns in our study.

To the best of our knowledge, there has been no study of the opinions of Indigenous Canadians regarding their under-representation in clinical sequence reference databases. We therefore aimed to begin a conversation with Indigenous Canadians living in British Columbia, Canada, regarding the consequences (both negative and positive) of their non-representation in genomic databases. We proposed this project as an initial step prior to broader Indigenous-led discussions that might lead to consideration of an Indigenous Peoples' genomic database in Canada.

1.2 | Objectives

Using a collaborative framework, qualitative methods based on community-based participatory research (Arbour & Cook, 2006; Jacobs et al., 2010), and experience-based co-design (Bate & Robert, 2007), our objectives were to:

- hear and record the opinions and values of various people of Indigenous ancestry living in British Columbia, Canada, regarding how they would or would not value the inclusion of non-identifiable sequence data from Indigenous individuals in a public database, and any concerns they may have;
- collaborate with participants to discuss the thematic interpretation of these varied opinions; and
- make a video describing genomic testing, the consequences of non-representation of Indigenous Peoples, an explanation by a genetic counselor of the resultant difficulties in interpretation of genomic test results, and a montage of the opinions about this issue from a diversity of voices of Indigenous participants.

2 | METHODS

2.1 | Research ethics

This study was approved by the University of British Columbia/Children's and Women's Health Centre of British Columbia Research Ethics Board and the Langara Research Ethics Board and received

approval and facilitation from the Langara College Director of Aboriginal Education and Services. Participants were offered a $40 honorarium for the initial 2-hour focus group, and $30 for the follow-up focus group, which was approximately 90 minutes. We used a double consent process. The first consent form was for focus group participation; the second was specifically for quote usage in the final video.

2.2 | Design

The Indigenous (J.M., R.L., R.K., and R.P.) and non-Indigenous (R.R.C., N.M., and P.H.B.) project team members have been guided by the tenet of full participation of Indigenous community participants. This provided a culturally safe approach to inform the project. Project co-leader J.M. is from the Gitxsan First Nation. Co-leader PHB is of British ancestry. Elder R.P. is from the Snuneymuxw and Cowichan First Nations. Focus group scribe and data analyst R.L. is Métis. Focus group scribe and data analyst R.K. is Anishinaabe (Ojibway and Sioux). Focus group facilitator N.M. is of British ancestry. Video creator and data analyst R.R.C. is of Swedish and British ancestry.

We chose a community-based co-design approach, with sharing circle focus groups, in order to develop a respectful and collaborative mechanism for participants to share their range of experiences, thoughts, and concerns (Cochran et al., 2008). Equally important, this approach enabled participants to provide feedback regarding the data analysis and to validate the researchers' thematic analysis and interpretation. Using a participant collaborative data interpretation framework is consistent with the British Columbia First Nation Health Authority's research directive of meaningful collaboration to promote best Indigenous practices (First Nations Health Authority, 2016). Choice of a video as a major outcome was deliberate. The final video belongs to participants and provides an accessible way for them to share it as they wish, thus making it available to a broader group of Indigenous Peoples, as well as to genetic counselors, other healthcare professionals, and institutions. This approach is consistent with a newly developed framework for Indigenous genomic research (Claw et al., 2018).

2.3 | Community participants

We conducted focus groups in Vancouver, Canada between August 2017 and February 2018, enrolling adults who self-identify as Indigenous (First Nations, Métis, or Inuit). Four initial groups were held: The first was in the Indigenous Health offices of British Columbia Women's Hospital, a tertiary care hospital that is the provincial referral centre for high-risk pregnancies. The second group was in Vancouver's Downtown Eastside, an area of Vancouver with a disproportionate number of individuals described as vulnerable due to poverty, homelessness, and a variety of health conditions, and with an over-representation of Indigenous individuals (City of Vancouver, 2013). The third and fourth groups were held at a large urban university and an urban community college, respectively. Recruitment for each focus group was via printed paper flyers posted in the community and word-of-mouth. The flyers had a contact phone number and email address for P.H.B.

2.4 | Introductory video creation and focus group outline

We created a 5-minute introductory video to describe concepts of genomic testing for medical diagnostic reasons and possible effects on genomic testing resulting from the lack of Indigenous representation in existing reference databases (Karczewski & Francioli, 2017; Lek et al., 2016). The video begins with an introduction by a respected Indigenous healthcare leader (J.M.). We then used the example of the diverse traditional blanket designs and fabrics that are seen world-wide as an analogy to describe genomic variability across ancestries. The ancestral representation of gnomAD data is briefly described, leading into an explanation of the difficulties that may occur with variant interpretation in some under-represented ancestral groups. The introductory video then provides a concrete example of the issue: A genetic counselor describes a family whose ancestry, and its lack of representation in reference databases, precluded interpretation of a genomic variant. The video concludes with an invitation to provide thoughts and opinions about the issue of under-representation of Indigenous Peoples in reference databases. This introductory video was shown at the beginning of each focus group and formed the core of the final video, which also incorporated Indigenous voices.

2.5 | Focus group topic guide

We developed a focus group guide via consensus among the authors. The guide was based on themes that arose in a literature review of issues emerging in both Indigenous and non-Indigenous genomic sequencing and biobank research (Abadie & Heaney, 2015; Beaton et al., 2017; Hudson et al., 2016; McElfish et al., 2017). Questions were open-ended, with prompts drafted to promote discussion in the focus groups, although we agreed that the conversation should mainly be driven naturally by participants. The focus groups all began with the facilitator asking participants what they thought about the video. Key topics included whether Indigenous genomes should be contributed to a reference database. When participants raised the issue of a separate Indigenous database, the facilitator probed barriers/facilitators to participation, governance, implementation, and access for such a database.

2.6 | Role of the Elder

Each focus group lasted approximately 2 hours. A First Nations Elder (R.P.) opened the groups with a traditional Indigenous greeting and prayer, introductions of study staff and participants, and the sharing of food. The research team had anticipated that past

TABLE 1 Description of the 30 participants

	Participants (%)
Age	
20s	7 (23%)
30s	3 (10%)
40s	7 (23%)
50s	10 (33%)
60s	1 (3%)
70s or older	2 (7%)
Education	
Elementary school	2 (7%)
High school	9 (30%)
College diploma	10 (33%)
University degree	6 (20%)
Prefer not to say	3 (10%)
Gender[a]	
Female	23 (77%)
Male	7 (23%)
Two-Spirited	1 (3%)
Indigenous identity	
Status First Nations	19 (63%)
Non-Status First Nations	3 (10%)
Métis	5 (17%)
Inuit	1 (3%)
Status First Nations and Métis	1 (3%)
Prefer not to say	1 (3%)
Lives on reserve	
Yes, on reserve	2 (7%)
No	27 (90%)
Prefer not to say	1 (3%)

[a]One person identified as more than one gender.

abuses and colonialization might "trigger" participants when speaking of ancestry. The term "trigger" includes arousal of intense emotions, images, and memories of past abuses, including historical abuses that have occurred to previous generations. We therefore thought that the lack of connection to community and culture that many Indigenous individuals experience might result in triggering if people made a direct connection between genomic testing and ancestry research. As a result of this, the team ensured that the Elder was available during and after the focus groups to debrief with any participant who may have been triggered during these discussions.

2.7 | Data collection

The study process was reiterated, with opportunities for questions. Consent forms were signed, and an optional anonymous demographic information form was completed to enable us to describe participants' Indigenous diversity.

Focus groups were audio recorded and transcribed verbatim. Transcripts were then de-identified, using pseudonyms for participants.

2.8 | Data analysis

A thematic framework approach was used for data analysis (Pope, Ziebland, & Mays, 2000). Transcripts for the first three focus groups were read by authors J.M., P.H.B., R.L., and R.R.C. to generate a list of themes for analysis. We met to discuss and consolidate our themes into eight categories, each with up to seven sub-themes. Each transcript was then coded to the identified themes by at least two authors, one Indigenous and one of European ancestry, using NVivo 11 (QSR, 2016). Representative quotes were selected and organized by two authors (R.C., R.K.), and the team discussed the representative quotes to further refine and reorganize the themes, reducing the data to six main themes. Quotes representative of each theme were then edited into the initial introductory video.

The themes were consistent across focus groups with no new broad themes emerging after the first group; therefore data collection was halted after four focus groups, on the assumption that saturation had likely been achieved. The themes were: Systemic Racism, Trust, Reciprocity, Database Structure, Database Management, and Implementation Practicalities.

2.9 | Returning to participants

After drafting the longer video with incorporated quotes, we held two follow-up focus groups with participants to show them the longer video and elicit feedback. We presented the themes and discussed them to ensure that our interpretation of focus group data was consistent with participants' views and that different opinions were well represented in the video. Participants were asked to comment on anything that was missing from the video. Those who were not able to attend the follow-up focus groups in person were invited to provide feedback by email. All participants quoted in the final video signed a second consent form to indicate if and how they would like their quote to be identified in the video. Options were: removing their quote, obscuring their voice, using their name, and/or using their photo. Participants also had the choice of listing their Nation, with their name or a pseudonym. No quotes were used in the final video if we were unable to contact participants for their approval. The video was then finalized based on participants' feedback and consent choices and was distributed to all participants in June 2018.

3 | RESULTS

3.1 | Participants

Forty-one self-identified Indigenous individuals contacted us stating that they would attend one of the initial focus groups. Of those, 30 people attended the groups, with between four and 12 participants in each focus group. Demographics of the participants are described in Table 1. Participants were almost all living in the Vancouver area

but identified with Nations across Canada: There were 12 people from Nations encompassing areas now in the province of British Columbia; six from Alberta and Saskatchewan; two each from Central Canada and the Northwest Territories; one each from Arctic Quebec, Yukon, and the Southern United States; one from multiple ancestral areas; and four not stated.

Twenty of the original 30 individuals participated in the follow-up sessions: 12 participants attended one of the two follow-up groups in person, seven watched the video at home then provided feedback by email (six) or phone (one), and one person watched the video at a community location and provided in-person feedback to P.H.B.

Of 10 individuals who did not attend the follow-up groups, two are known to have moved, leaving no forwarding address, two had no email address and their phones were out-of-service, and one person was unavailable. Messages were left by email and/or phone with the remaining five participants who did not respond to invitations to provide feedback by our deadline, and they have not contacted us since.

Of the 20 individuals who contributed to the follow-up groups, 16 participants were quoted in the final video. None declined to have their quote(s) included in the video.

3.2 | The initial focus groups

The concept of genomic sequencing and the issue of non-representation in reference databases were new to all 30 participants. However, many people had heard of genetic testing and a misunderstanding that emerged in all focus groups was the confusion between genomic sequencing for medical reasons and direct-to-consumer testing for personal interest. Participants also raised personal health experiences in three of four groups and in the same groups the discussion triggered personal or family memories of past abuses including experiences with residential school and the Sixties Scoop. Residential schools were government-funded church-run boarding institutions where Indigenous Canadians were assimilated, their traditions denigrated, and language lost. Physical, emotional, and sexual abuse were commonplace, and thousands of children died due to the poor living conditions. The last residential schools were closed in the 1990s. The Sixties Scoop was the government-sanctioned removal of Indigenous children from their families for adoption or fostering in primarily non-Indigenous homes through to the 1980s (McKenzie, Varcoe, Brown, & Day, 2016). The facilitator took time to allow these discussions while reminding participants not to share confidential health information.

In general, the introductory video was received positively; in particular, people commented favourably on the weaving analogy and the introduction by a respected Indigenous healthcare leader. Most individuals were quite engaged in the topic and in one focus group the conversation increased in intensity when participants expressed different perspectives regarding whether there should be a separate Indigenous Peoples' database or whether it should be integrated to an international database. The facilitator emphasized that different opinions were expected and all views were legitimate. The Elder used a talking stick method (where each participant has the opportunity to share or pass in the circle) to ensure that everyone had a chance to be heard, particularly in the largest focus group.

3.3 | Follow-up focus groups

Discussion in the follow-up focus groups was generally more directed toward the core issue of non-representation and what to do about it. Participants were quite focused on the task at hand of verifying quotes and themes and critiquing the longer video.

Without exception, the draft final video was well-received with general agreement regarding the thematic analysis and quotes. In one follow-up group, three people agreed that there should be a better explanation of current reference databases, specifically describing gnomAD. In response to that, a short section was added to the video to address this identified concern.

3.4 | Focus group thematic analysis

The six themes that emerged from the thematic analyses by the project team were confirmed with participants. These are listed below, followed by the percentage of time coded to each of the themes, averaged over all four groups. Systemic Racism: 14%; Trust: 20%; Reciprocity: 26%; Database Structure: 15%; Database Management: 17%; Implementation Practicalities: 27%.

There was considerable thematic enmeshing, hence some overlapping coding, between many themes, particularly between systemic racism and the theme of trust. All six themes were present in all four groups; however, the percentage of each transcript that was assigned to each theme differed somewhat between groups. Notably, the second group, held in the Vancouver Downtown Eastside, spent proportionally more time discussing systemic racism (23%) and database structure (29%) than the other three groups, whereas the two groups held on university and college campuses, spent more time discussing implementation practicalities (39% and 36%, respectively). The theme of trust was coded approximately equally across all four groups.

Representative quotes for each theme are listed below, along with an attributed pseudonym.

3.4.1 | Systemic racism

Systemic racism included aspects of racial discrimination, past abuses, equity, and human rights. This theme came up repeatedly throughout the groups and was interlaced through many conversations.

Discrimination was explicitly stated by some participants:

> I always feel that there's a step missing because … First Nations people don't have access to health, not the way the general population has. Mainly due to still discrimination against them. (Samantha)

There was also some sense of incredulity expressed, with undertones of systemic racism:

> But I guess I find it so shocking that there isn't a single First Nations DNA sequence in the system. Like I find that so crazy. (Abigail)

Current and past inequity was mentioned directly or inferred:

> I'm wondering if this will help get faster diagnosis and, you know, get our people treated the same as the general population. (Samantha)

> Because they're not in the database, they're losing out on all this western medicine. (Maria)

3.4.2 | Trust

The theme of trust fell naturally into discussions of lack of trust and what can be done to help build trust in the future. Although we considered *Trust* as one theme, we have separated the theme into the two aspects for ease of presenting results.

Lack of trust

Participants talked about the mistrust that many Indigenous Peoples may feel when considering contributing to a potential database. They listed residential schools, the Sixties Scoop, and abuses within healthcare as sources of erosion of trust.

> One roadblock I see is that there is a general mistrust of any physicians or doctors or institutions. (Irene)

> I can see how people wouldn't trust it too. Like is this ever going to be used against us? Do you know what I mean? Turn from genomics to genocide? (Isaac)

The concept of "being researched to death" (Cochran et al., 2008) was also alluded to under the umbrella of lack of trust:

> I guess my concern would be that it would be just another research project…. (Raven)

> That it's just another experiment. (Emily)

Building trust

Most agreed that a database that included Indigenous genomes would be beneficial, and offered suggestions for building trust:

> Express your knowledge of their fears. Acknowledge the past…. (Raven)

> Emphasize it's not government related. (Yousef)

> I think it has to be a safe environment. (Madeline)

Many participants mentioned the importance of involving community leaders and elders in discussions of possible Indigenous contributions to a genomic database:

> I would want to see other Aboriginal people at those higher levels … directly involved. (Sarah)

> Go to the elders. [Yeah.] Go to the community. Go to like Indigenous communities. Reserves. Have a talking circle like this, and having the elders there…. (Gracie)

> Making it personal and acknowledging where Indigenous people are coming from will create that trust that you need. (Yousef)

However there was some recognition that this approach might not always result in support for Indigenous contributions toward a database:

> There's certain little bands … that would not want anything part of this. (Isaac)

3.4.3 | Reciprocity

This theme includes perceived benefits for donors, family, community, and others. Many mentioned concrete benefits for themselves or their extended families:

> Maybe you want to find out your health problems faster or determine if you're healthier. (Lenore)

> I'm looking at the long term … at my grandchildren. (Gracie)

Others discussed specific benefits that might emerge, such as treatment:

> We could find the links to these genes to certain diseases and that we can make better treatment plans for individuals because some … respond better to this treatment from this ethnic background. (Avril)

> It's not just for Indigenous Peoples. Everybody benefits. Everybody, not just Indigenous Peoples. (Roxanne)

> I would do it for the greater good. (Meredith)

> I'm seeing that, you know, this is an opportunity to participate in something larger than myself. (Sarah)

3.4.4 | Database structure

This theme included differing opinions regarding whether there should be a separate Indigenous database. Some participants felt very strongly that the database should be separate:

> I think it should be separate. (Gracie)

> We need to have more control. (Madeline)

Other participants felt that a separate database may have downsides, especially for those who do not know or wish to disclose their ancestry:

> What if you didn't want to … fill out the ancestry part? (Maria)

Several felt that a combined database would be optimal, stating the possible future need for analysis from people of mixed ancestry:

> So, what if a person is biracial? Or has more than one ethnicity? (Raven)

> Each of our family situations is different and my children are not full Indigenous.... I would want [my genomic sequence] to be in the … big general database because of heritage from [both] sides of the family. (Roberta)

> There might be somebody who needs that information that lives in Romania? (Kaylee)

Finally, participants remarked on the artificial nature of political borders, inferring that the Canadian-US border is inappropriate to consider in such a database:

> Before colonization happened, we travelled. There were very few boundaries. (Sarah)

> There's Coast-Salish in the States, and there's Coast-Salish here. (Isaac)

3.4.5 | Database management

Database management included issues of sample ownership, control of use, and access, as well as concerns about privacy and security.

There was general agreement in all groups that there should be Indigenous involvement in whatever structure was decided upon. This was stated most strongly by a participant who advocated for a separate Indigenous database:

> Us collecting the information. Us maintaining the information. (Madeline)

Indigenous governance was specifically mentioned and supported by many in several groups:

> …a governing board. Made up of [Indigenous leaders]. (Kaylee)

There was some discussion whether genomic data should be anonymous or whether there should be optional linkage to the sequence donor. Some felt that anonymity was essential for confidentiality:

> So if you apply for a job and somehow they get that information and you're predisposed to mental health issues or whatever, then they don't want to hire you. (Maria)

One person was concerned about anonymity:

> The fact that it's anonymous might scare some people. (Roxanne)

However, in another group, there was general agreement that anonymity should be a personal choice:

> Well you know I think that'd be up to the individual [Yeah.] whether you want to be anonymous or put your name. [sounds of general agreement] (Patrick)

When probed about usage of the database, there were strong feelings that medical use was appropriate but commercial use was not. Regarding access by the pharmaceutical industry:

> Hands down no. The pharmaceutical industry is in direct conflict with Aboriginal traditional healing values. (Madeline)

Other privacy concerns related to insurance:

> …guaranteeing that the data's not going to be used, to be sold to insurance companies to exclude you from getting benefits. (Yousef)

There were also statements that were related to sample ownership and respect for the sample:

> If you were to really be spiritual and an Aboriginal person, you're technically giving a piece of your ancestors away. Because our ancestors live within us. (Madeline)

The concept of respect for usage of the sample was raised by several others:

> I would have to know that my blood and my DNA is going to be used in a good way. (Emily)

And the concept of receiving the sample back was also raised:

> I know there's a lot of Nations that don't want their blood taken away. If it is, they want it returned. (Samantha)

3.4.6 | Implementation practicalities

This broad theme included ideas on how to motivate people to donate to a genomic database and had many practical suggestions including piggybacking genomic donations to blood donor or stem cell donor clinics or other community events:

> The Red Cross comes around on wheels in a great big van. (Kelly)

> When you go [for] a flu shot, say, … we're also going to take a swab. (Matthew)

> Pay them! (Robert)

> I just recently became a blood donor…. They also offered me registration to become a stem cell donor … because again, the Indigenous population is very small; they have only 1% of Indigenous stem cell donors…. So could [DNA collection] possibly be piggybacked off of something like that? (Jennifer)

Several people suggested that potential donors need to be able to understand the situations of families that have been helped by genomic medicine.

> I think it's connecting to them that way, and storytelling is huge. If you can tell a story, and they can connect to that story, they can feel that story. (Yousef)

Several individuals acknowledged both the necessity and the potential challenges of negotiating with individual communities:

> We speak a lot about community engagement, and when you want to go and plan for a community, you should go in and learn from the community. (Anne)

> Starting in an urban setting would be way easier … off reserve; on reserve you have to respect self-government. You have to get consent to do it. Each one is going to be different. (Matthew)

There was some agreement that recruiting younger people, including using social media, would be easiest:

> Getting the young generation. I think they're more open to the opportunity. (Avril)

Various participants stated the need for broader, pan-Canadian consultation, including with Indigenous leadership, prior to any consideration of collecting Indigenous genomic sequences:

> All of our Nations across Canada need to have … discussion…. Because we all don't think the same. (Roberta)

> It would have to be Aboriginal people who [are] higher up in the senate and the government. (Owen)

3.4.7 | Other minor themes

Several other conversations did not emerge often enough to become a major theme. Two individuals questioned the relevance of genomic testing when so many First Nations communities have more basic problems to address, such as poor living conditions. Although these quotes overlap with the theme of systemic racism, they also relate to perception of Indigenous communities' priorities.

> Going and doing something like this is probably not on our radar, considering that we are facing really poor conditions in communities. (Matthew)

> I don't see the point to it…. This isn't really what people think about. They're thinking about, you know, just being healthy and trying…. (Roxanne)

Importantly, the need for more information was mentioned by people in several of the focus groups:

> I'm not really sure, I'm not 100% sure…. I don't really know a whole lot about this stuff…. (Bradley)

4 | DISCUSSION

This project represents an initial exploration of the opinions and values held by a group of 30 predominantly urban Indigenous individuals of diverse self-identity, living in British Columbia. The resulting video (https://youtu.be/-wivIBDjoi8) incorporates an explanation of genomic testing, the genomic testing interpretation difficulties that may result from non-representation in reference databases, and participants' thematically organized opinions.

The issue of Indigenous non-representation in genomic databases was new to all participants and was perceived as important information by almost all participants. Many participants thanked the research team for informing them of the issue, and for the mechanism chosen for the discussion, namely facilitated focus groups, which included a respected Indigenous Elder. Several expressed

surprise that the research team considered the completed video to be equal property of the study participants and investigators.

There was widespread agreement across groups about the existence of past and present systemic racism and resulting mistrust, particularly of institutions, and that this would need to be overcome by anyone developing an Indigenous genomic database. This is consistent with findings of other studies relating to healthcare research, specifically to biobanks (Abadie & Heaney, 2015). Suggestions were made that to build trust, one would have to understand and recognize past wrongs and involve Indigenous leaders in healthcare, government, and at the band level in any discussions or plans to develop an Indigenous genomic database. We observed that participants appeared to feel safe and comfortable sharing past experiences with the healthcare system, both positive and negative, where they felt this would contribute to the conversation. This connection then led to other themes that emerged around the importance of trust.

In each group, a consistent theme emerged that participants felt they could not speak for all Indigenous individuals, and they provided suggestions of ways to engage with Indigenous communities to gather collective opinions and perspectives. There was broad agreement that such a database would be beneficial to Indigenous Peoples and majority agreement that people would participate by donating sequence data if it would improve the health of community members, although the definition of "community" varied somewhat. The desire to help community is not unexpected and has been reported in other studies including one of Pacific Islanders living in the United States, a community also affected by historical abuse (McElfish et al., 2017).

There was, however, disagreement regarding whether sequence data should be integrated into existing international databases, such as gnomAD, or should be a free-standing Indigenous database. Regardless of the model, there was general agreement that some form of Indigenous governance and control would be essential. There was recognition that broader Canada-wide consultation is needed prior to any possible implementation. Issues of privacy and potential discrimination, including worries about health insurance, were raised, as are common in discussions of genetic databases world-wide (Amendola et al., 2018). However, in these focus groups there were also concerns regarding potential use of data for purposes resulting in racial discrimination. It was also raised that some Indigenous communities may hold spiritual beliefs about the ownership of sample tissues and their connection to ancestors that may prevent them from donating, though most participants did not see this as a barrier to their own potential participation.

Several people from each focus group observed that more information and more time were needed to fully comprehend and contemplate these topics. The fact that this was a new topic for people and that the information is complex is supported by the observation that people changed their mind or perspectives on several occasions during the focus groups. For example, in one group, opinions appeared to change over the course of the conversation from initial preference for a separate Indigenous database to favouring combining Indigenous genomic data with an international database.

Also possibly reflecting the magnitude and newness of this topic, we noted that specific consideration of a framework for consent was not discussed. Although respect for individual samples and appropriate database usage were raised, a mechanism to enable individuals to determine the ultimate fate of samples, as summarized by Bardill and Garrison (2015), was missing from the conversation. It is important to note that this concept, and that of "DNA on loan" (Arbour & Cook, 2006) was not raised by the facilitator.

There were many creative and novel ideas for collection of samples for genomic sequences. Various participants stated that consultation with community leaders and elders is important but acknowledged that it would likely be easier to recruit younger, urban individuals than those living on reserve.

As expected, in each focus group, one or more participants spoke of ancestry testing, and the facilitator had to explain that genomic testing for medical reasons was distinct from ancestry research. People discussed the positive and negative aspects of direct-to-consumer testing to find out their personal ancestry and non-medical attributes. Despite these conversations about ancestry, participants did not discuss the possibility of ancestral research being used in the negative way that has been reported in other studies such as the Human Genome Diversity Project (HGDP) (Dodson & Williamson, 1999), which used genomics for human migration and evolution research (Li et al., 2007). It is possible that this might have emerged if the facilitator had asked directly about negative consequences of ancestral genomic research for groups of Indigenous Peoples.

However, eligibility questions prior to study participation from people of partial Indigenous ancestry may have reflected participants' concerns as raised by TallBear (2013): They feared they might not be considered by researchers or other participants to be legitimate members of the group and/or their genomes may be too admixed to be of value as an Indigenous genome. This may reflect perceived harms that have resulted from a number of genetic and genomic projects (Pullman & Arbour, 2009), including HGDP. Despite considerable scientific success (Li et al., 2008), HGDP has been criticised for its lack of Indigenous consultation and its potential for scientific racism (Alper & Beckwith, 1999), which could lead to definitions of race that are based solely on genetics, rather than Indigenous self-identification.

HGDP is one of many examples of research that is based on concepts identified as important by non-Indigenous people who then proceed with research without reconciling past abuses of trust and without ensuring Indigenous perspectives are considered. We recognize the importance of Indigenous-focused research emerging from Indigenous communities, and although this project is a partnership between Indigenous and non-Indigenous researchers, it does not meet that standard and was criticized for this reason. The concept behind our research resulted directly from several clinical genetic encounters, and therefore initial identification of "the problem" was by medical genetic professionals in our hospital, who are non-Indigenous. "The problem" could be reframed as an issue within the healthcare system that results in inequitable genomic testing for Indigenous Peoples

rather than being perceived as an example of Indigenous Peoples having a "problem" that requires assistance from external experts to "solve" (Cochran et al., 2008). In keeping with Smith's writings (1999), "Nothing about us without us," this project was an equal partnership between leaders of the hospital's Indigenous Health Program (J.M., R.L., R.K., R.P.) and academic medical genetics healthcare professionals (P.H.B., R.R.C., N.M.).

The team leaders felt that the project aims were consistent with the Truth and Reconciliation Commission of Canada's (2015) call to action to identify inequity in healthcare and to close the gaps. In order to do so, we chose to engage Indigenous individuals in the project using a participatory research model and by attempting to be responsive to the research participants. However, lack of engagement in project design by Indigenous leaders external to the team meant that we were not able to capture their view-points.

4.1 | Study limitations

We were constrained by circumstances that limited which research participants we could approach and how we could approach them. Our funding was for 1 year and despite completing our research ethics review prior to the start of funding, we had insufficient time in this project to obtain permission and collaboration from leaders in specific Indigenous communities. We had hoped to engage participants living both on and off reserve, in urban and rural communities, but challenges contacting the appropriate community leaders and travelling during winter weather proved too limiting in the time available.

This meant that our participants are predominantly urban-living, with only two of 30 participants living on reserve. Greater variety in community structure and customs would likely provide more varied participant opinions. Other biases include the excess of female participants and the under-representation of individuals over the age of 60. These, and other factors that we may be unaware of, limit the generalizability of our findings and speak to the need for a broader, pan-Canadian study, including a greater diversity of individuals and proportional representation of Métis and Inuit, as well as consultation with Indigenous leaders, as pointed out by study participants.

4.2 | Practice implications and research recommendations

Genomic sequencing technologies have been developed by research on individuals of predominantly European ancestries; therefore, benefits based on testing or treatment will disproportionately help people of those ancestral groups. The result of this will be a widening genomic medicine divide between people of European ancestry and Indigenous Peoples (and other unrepresented populations). Reducing this disparity requires an understanding of the underlying reasons that contribute to under-representation of Indigenous groups in genomic research, which is the primary source of sequence data for reference databases. These reasons include historical abuses, residual systemic racism, and in particular, multiple examples of deception in genetic research (Cochran et al., 2008). Cultural competency in genetic counseling practice (Warren & Wilson, 2013) requires that genetic counselors understand the necessity for meaningful Indigenous community engagement (Mathew et al., 2017) and involvement of Indigenous leadership as central to raising awareness of (Cornel & Bonham, 2017) and resolving Indigenous genomic healthcare inequities. Genetic counseling research relating to these inequities is necessary but should be led or co-led by Indigenous individuals. The community-based participatory research design used in this study proved to be a good framework for this purpose and is congruent with counselors' collaborative practice.

5 | CONCLUSIONS

This is the first study that we are aware of to discuss the non-representation of Canadian Indigenous Peoples in international medical genomics reference databases. The study was positively received by participants, who engaged in a community-based participatory research model. They provided their views regarding many issues that need to be addressed prior to collecting genomic sequences from Indigenous Peoples, regardless of whether such sequences are stored in a major international reference database or in a separate Canadian Indigenous genomic resource. The video that resulted from this study (https://youtu.be/-wivIBDjoi8) may form the basis for a broader, Indigenous-led conversation.

6 | COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest

Authors Jenny Morgan, Rachel R. Coe, Rochelle Lesueur, Ruth Kenny, Roberta Price, Nancy Makela, and Patricia H. Birch declare that they have no conflict of interest.

Human Studies and informed consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all participants included in the study.

ACKNOWLEDGEMENTS

This project was conducted on the unceded traditional and ancestral lands of the Coast Salish Peoples. We would like to thank the participants for sharing their opinions with us and the time and thought they put into this project. Dr. Rick Ouellet, Director of Aboriginal Education and Services, and Mr. Jimmy Aitken, Indigenous Student Engagement Officer, both of Langara College,

and the staff of the UBC Xwi7xwa Library and UBC Learning Exchange all provided invaluable assistance and allowed us to use their facilities for the focus groups. We appreciate the advice and support of Dr. J.M. Friedman and Dr. Anna Lehman, both of the Department of Medical Genetics, and Dr. William McKellin, Department of Anthropology, University of British Columbia. Ms. Cheryl Davies, Chief Operating Officer, BC Women's Hospital and Health Centre provided Agency partnership for this project. Dr. Susan Law, Trillium Health Partners, Mississauga, and the IHPME, University of Toronto, provided the initial idea for the video to P.H.B. This project was funded by a Societal Issues Grant from Genome British Columbia to P.H.B. and J.M. The authors confirm that this work was not completed as part of a degree requirement and is not eligible for the student paper award.

AUTHOR CONTRIBUTIONS

P.H.B. and R.R.C. conceptualized the study; P.H.B., R.R.C., J.M., and R.L. designed the study; R.R.C. created the video. J.M., R.R.C., R.L., R.K., R.P., N.M., and P.H.B. were involved in acquisition, analysis, or interpretation of data for the study, drafting or critical revision of the article for important intellectual content, agreement to be accountable for all aspects of the article in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved, and final approval of the paper.

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How to cite this article: Morgan J, Coe RR, Lesueur R, et al. Indigenous Peoples and genomics: Starting a conversation. *J Genet Couns*. 2019;28:407–418. https://doi.org/10.1002/jgc4.1073