

A relational framework for microbiome research with Indigenous communities

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Ethical practices in human microbiome research have failed to keep pace with scientific advances in the field. Researchers seeking to ‘preserve’ microbial species associated with Indigenous groups, but absent from industrialized populations, have largely failed to include Indigenous people in knowledge co-production or benefit, perpetuating a legacy of intellectual and material extraction. We propose a framework centred on relationality among Indigenous peoples, researchers and microbes, to guide ethical microbiome research. Our framework centres accountability to flatten historical power imbalances that favour researcher perspectives and interests to provide space for Indigenous worldviews in pursuit of Indigenous research sovereignty. Ethical inclusion of Indigenous communities in microbiome research can provide health benefits for all populations and reinforce mutually beneficial partnerships between researchers and the public.

Recent decades have seen the remarkable growth and consolidation of microbiome science as an established field. The development of next-generation sequencing (NGS) technologies substantially contributed to this rapid expansion, as investigators turned their collective focus to defining community composition through massively parallel microbial profiling and discovery¹. However, the establishment of ethical frameworks for human-associated microbiome studies, in which researchers seek to understand complex relationships between humans and their resident microbiota, has failed to keep pace with the field’s technical development. Communities who have historically been disenfranchised from genomic

and biomedical advances therefore remain at risk of further exploitation.

Scientific research has targeted Indigenous communities around the world through repeated rounds of resource and knowledge extraction, which has resulted in direct harm to people, other organisms and environments. In particular, biomedical experimentation on Indigenous peoples has physically and psychologically harmed individuals, disrupted families and undermined the existence and well-being of communities^{2–6}. These harms continue through the exploitation of other-than-human entities with whom Indigenous people are in relationships.

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We are a group of Indigenous and non-Indigenous researchers who engage with human–microbe interactions and microbial communities from a variety of research perspectives. In this Perspective we voice serious concerns regarding the treatment of Indigenous peoples in human microbiome research, which has been facilitated by historical and ongoing ethical failures in its parental fields of microbiology and genetics. We first document the existing ethical deficiencies in microbiome science and then lay out a framework of relationality and its application to microbiome research in a way that empowers Indigenous communities and advances Indigenous research sovereignty.

Biases in foundational human microbiome research

Human microbiome studies disproportionately include, and advance the health of, majority populations in industrialized nations conducting this research, with implications for how microbiologists understand health and disease across human populations worldwide^{7,8}. Dysbiosis (an imbalanced composition) of the human gut microbiota has been linked to numerous health challenges. However, the demarcation between a microbial community composition associated with disease and interpersonal variation remains unclear, especially across different human populations^{9–11}. Although early studies used large cohorts of individuals to overcome the complications of inter-individual variation, heavy reliance on populations of European descent in microbiome studies^{12,13} mirrored persistent flaws that have plagued genome-wide association studies aimed at identifying causative alleles underlying complex human disease¹⁴. Subsequent work has clarified that microbiome variation can arise through multiple factors, including age^{15,16}, diet and lifestyle^{15,17}, as well as the transition between health and diagnosed disease^{18–21} — all factors that can vary widely across distinct human communities⁸. Nevertheless, microbes linked to diseased states in industrialized populations are now typically distinguished from protective commensal species and instead classified as either ‘pathobionts’ (that is, commensal species with the potential to cause host disease) or pathogens. Microbiome-based treatments, such as the introduction of commensal taxa^{17,22}, antibiotics^{23,24}, changes in diet²⁵, faecal microbiome transplant^{26–28}, phage therapy²⁹ and microbiota-directed foods³⁰, seek to outcompete or eliminate potential ‘pathobionts’ to restore the gut microbiome from perceived dysbiosis, based on understandings of microbial health and disease derived from industrialized populations.

Early microscopy studies of faecal contents from global Indigenous groups identified many taxa labelled as ‘pathobionts’ in industrialized populations (for example, *Helicobacter* species and intestinal parasites^{31,32}) as common components of the gut microbiota in healthy Indigenous peoples. These early findings motivated scientists in the nascent field of human microbiome research to seek out global Indigenous groups as comparators for emerging definitions of the industrialized human microbiome. Large-scale microbiome profiling reported distinct gut microbial profiles in multiple Indigenous communities engaged in non-industrialized lifestyles^{33–37}. These communities were typically positioned by researchers as maintaining ‘traditional’ or ‘ancestral’ lifeways — a convenient comparison to ‘Western’ or industrialized populations for understanding functional relationships between human-associated microbes and host health^{38,39}. Microbiome research has clearly defined industrialized microbiota as affected by increased antibiotic use, strategies for sanitation, birth intervention and food production efforts, but give no such definitions for ‘traditional’ microbiota, which becomes a proxy for Indigenous or ‘undeveloped’⁴⁰. Similar comparative microbiome studies found an altered community composition between industrialized and Indigenous peoples at other body sites, including the oral cavity⁴¹, the vaginal tract⁴² and the skin³⁴. The outcomes of these comparative surveys highlight inadequacies in the definition of the ‘healthy’ human microbiome, which are oriented predominantly around industrialized populations and predisposed to ascertainment bias.

Human microbiome research in Indigenous communities raises ethical concerns

Global Indigenous peoples and members of minoritized groups have repeatedly been subjected to ethical misconduct from microbiological and genetic studies that lack appropriate consent and community engagement. For example, a recent study of genetic diversity among Indigenous peoples in Peru expanded beyond the initial authorized scope of work to include genetic analysis of neurological and mental disorders and profiling of gut microbiome diversity. Samples for analysis were disseminated to researchers in the United States without formalized oversight or community consent, which was described as ‘a clear example of genetic extractivism’ by Peruvian researchers⁴³. The lack of free and informed consent, as well as harm to those involved in these studies, constitutes ethical malfeasance posing as advancing microbiome science. Extractive practices by researchers from the Human Genome Diversity Project (HGDP) and the Genographic Project, within the closely related field of human genetics, rallied global Indigenous peoples to push back against biomedical researchers obtaining human samples and data without providing benefit to, or seeking consent from, communities^{44–46}. Ongoing programmes to explore genetic diversity in the United States under the auspices of precision medicine initiatives, such as the National Institutes of Health (NIH) *All of Us* project and the *Million Veterans Project*, include Indigenous people either explicitly or implicitly and have faced severe backlash over their lack of consultation and circumvention of Tribal sovereignty^{47,48}.

As interest in human-associated microbes from global Indigenous peoples continues to expand, researchers must engage with the ethics of working in this rapidly advancing field of research. Echoing a pattern in broader human genomic and medical research⁴⁹, the approach of many human microbiome researchers has been to perform science ‘on’ instead of ‘with’ Indigenous communities. Microbiome research in Indigenous communities risks the exploitation of Indigenous peoples and their associated microbes as a resource for the benefit of predominantly non-Indigenous industrialized nations without addressing the health priorities of Indigenous people, otherwise known as ‘extractivism’. Although this term is more commonly used in relation to the commercial exploitation of natural resources and macroscale biodiversity, discussions of monetizing the microbial biodiversity that exists in relation with, and under the care of, global Indigenous peoples indicate that the finite members of Indigenous-associated microbiota are also at risk^{50–54}. This risk is exacerbated when Indigenous communities are not equal partners in the research process, which has been the norm so far for nearly all studies. Indigenous research sovereignty, the right to dictate the direction and terms of research, is required to rebalance this longstanding inequity in microbiome research.

The perception of global Indigenous communities and their associated microbiota by the scientific research community can have a considerable influence on research conduct and interpretation. Framing Indigenous communities as ‘traditional’, meaning that they maintain non-industrial cultural practices such as subsistence gathering^{15,34,36–38,55}, and as ‘ancestral’, implying that the increased diversity of Indigenous peoples’ microbiota represents a temporal and evolutionary baseline for all human microbiomes^{36,38,56}, reinforces harmful hierarchical racial and evolutionary tropes of Indigenous peoples as fundamentally different from and less ‘evolved’ than non-Indigenous counterparts^{57–59}, unless comparing Ancestor and descendant communities directly. Similarly, attempts to link microbiome compositions directly to ethnicity in some studies^{10,41–43} have conflated biological communities of microbes with socially determined race in a way that is overly simplistic and highly problematic⁶⁰. Such current and ongoing studies hypothesize a racial basis for variation in microbiome composition, and downplay the contributions of lifestyle, diet, infrastructural, social and environmental sources towards the increased microbial diversity observed in Indigenous communities when compared to industrialized populations^{36,55}. Furthermore, this research mindset

'others' living populations by representing them as a bank of unique ancestral microbiota and positions Indigenous communities merely as a resource for understanding and improving the health of industrialized populations, increasing the risk of exploitation by researchers without reciprocal benefits.

The application of palaeogenomic (ancient DNA) research methods to microbiome science may provide additional insight into the co-evolution of humans and human-associated microbes, but it has its own ethical challenges. Ancient microbial DNA recovered from calcified human dental plaque (calculus)^{61–63} and preserved human faeces (coprolites)^{64,65} allows researchers to assess how physical and social environments shaped human microbiomes in the past, without using living Indigenous communities with 'traditional' lifestyles as evolutionary models. The microbiomes of Ancestors can also be used as a proxy source of genomic data to investigate human population histories⁶⁶, which requires careful collaboration with descendant communities to minimize the risk of harm to Indigenous peoples^{67,68}. However, samples from human Ancestors (that is, calculus and coprolites) used for microbiome analysis are often not considered 'human' tissue⁶⁹, which can allow researchers to circumvent the need for consent and community engagement, despite the risks that the research may bring to a descendant community. Although researchers may view genomic analyses of these biological samples as 'less destructive' to Ancestors' skeletal remains than palaeogenomic analysis of teeth or bones⁷⁰, some Indigenous communities may not agree with this perspective or wish to pursue this type of research. In particular, Indigenous Ancestors held in museum and research collections have been vulnerable to exploitative palaeogenomic research without consent or collaboration with descendant communities^{71–73}.

A lack of ethical approaches to obtaining consent for microbiome research can result in unintentional harm. Many studies of Indigenous microbiomes have failed to meet recommended practices for critical components of the research process, such as obtaining appropriate and truly informed consent^{38,74}. Despite human-associated microbiome samples being collected from an individual host, individual consent alone is generally inadequate when engaging Indigenous communities in microbiome research⁷⁵; instead, larger community consultations about the type of samples and data proposed to be collected, their purpose, and the potential implications of the research results should take place and be followed by community consent. Importantly, data derived from sampling relatively small populations, as is true of many Indigenous communities, can never truly be de-identified⁷⁶. Thus, microbiome or medical data generated from consented individuals in an Indigenous community can provide information about individuals within the same or neighbouring communities who may not have consented to the study. Research findings and their framing in scientific communications can have far-reaching consequences for participants, their communities and broader networks of individuals (that is, through stigmatization of disease or infection⁷⁷).

To minimize the risk of these harms, guidelines for researchers set forth by the World Health Organization (WHO) recommend obtaining consent that extends to the individual, community and larger network of related communities⁷⁸. A multi-tiered approach, requiring consent of the individual, the community and a representative organization for communities, more closely aligns with Indigenous decision-making processes and acknowledges that microbiome research with one individual, group or cohort can substantially impact others. As one example of this three-tiered approach, regional institutional review boards (IRBs) operating under the authority of Indian Health Services in the United States review research involving Tribal entities within similar geographic areas and must approve of biomedical research protocols alongside the tribe and individual participant.

Without carefully restructured informed consent through extensive consultation, microbiome research in Indigenous communities runs the risk of engaging in extractive biocolonialism. The

responsibility lies with microbiome researchers to clearly communicate the research objectives and potential impact, including the global significance of microbiome sciences to human health and the potential commercial value of samples collected to global populations that are unlikely to include the focal Indigenous group, before obtaining consent for the study. Attempts to 'rewild' the microbiome of industrialized populations through the commercialization of Indigenous-associated microbiota, in an effort to cure non-communicable diseases, without directly establishing benefits to Indigenous peoples through equitable profit-sharing models, perpetuates extractivism.

In general, researchers have too rarely demonstrated an interest in pursuing biomedical treatment options for Indigenous peoples who contribute biological materials to advance research. Collectively, these efforts have funnelled benefits from Indigenous people, who are being sought out as a potential source for microbial therapeutics, to non-Indigenous researchers and the industrialized nations from which the studies are conceived. The source of information used to alleviate disease in industrialized people must be acknowledged as having its own history, rights to data governance, and sovereignty⁷⁹.

Relationality as a framework for human microbiome research

Human microbiome research is still a young discipline, which means that we have an opportunity to establish ethical best practices that can be adopted and implemented broadly. The recommendations we provide build on those developed previously in human microbiome and genomics research^{71,74,80,81}. Specifically, we apply the Indigenous concept of relationality to create a framework to address ethical concerns in research involving Indigenous peoples and their microbes.

Relationality is defined in this Perspective as the interconnected nature of all biological and non-biological entities because of our shared space and interdependent interactions, which requires care and respect for all of these components of the natural world^{82,83}. Relationality is crucial for guiding ethical microbiome research with Indigenous communities because it emphasizes kinship, not only between people, but also between humans and other organisms, as well as their environment. With kinship comes obligation and responsibilities that decentre the self and emphasize consideration of the consequences of our actions for others. Crucially, relationality is contradictory to extractive research practices⁸², which are a central concern regarding microbiome research among Indigenous communities. Relationality is especially well-suited to form the basis of a framework for microbiome research because it links biological, social, land, food and microbial systems. We highlight in this Perspective the importance of relationality in the context of microbiome research by discussing the obligations inherent in establishing and maintaining ethical relations, as researchers, with Indigenous community partners and their associated microbes (Fig. 1). We argue that ethical microbiome research with Indigenous communities must uphold Indigenous research sovereignty, as this is needed to undo the harmful legacy of colonization⁸³.

Writing in an accompanying article, Handsley-Davis et al.⁸⁴ discuss the ethical, legal and social implications (ELSI) of ownership and intellectual property in microbiome research. The authors explore how to protect knowledge, data and the microbes that comprise Indigenous microbiomes using existing global systems of intellectual property rights, while also navigating these systems through a relational lens in which interdependence, stewardship and caretaking relationships between people and microbes are contrasted with Western notions of ownership.

Relationality between Indigenous peoples and microbes

Many Indigenous peoples contextualize their position in the world through reciprocal interactions with the surrounding environment, that is, in a relational context^{82,85}. These world views recognize the

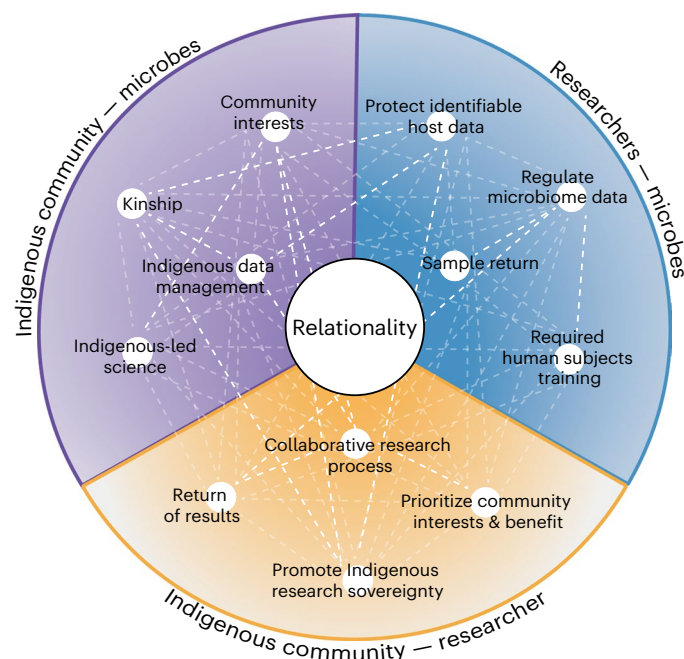


Fig. 1 | Map of relationality concepts in the context of microbiome research with Indigenous peoples. Labels around the exterior of the circle indicate the key relationships between entities embedded in human microbiome research. Within the circle, obligations that guide research ethics are featured for each relational pairing.

influence that humans have on our surrounding environments and acknowledge the power of environmental constituents, including microbes, to dictate relationships between physical and biological entities⁸⁶. It is increasingly acknowledged in the academic canon that microbes play a central role in maintaining balanced relationships among flora, fauna, geological systems, waterways and the air^{87–90}. Although global Indigenous peoples have long recognized the influence of community structure at different ecosystem levels to the health of the whole, these relationships have only recently been codified in non-Indigenous research settings through the ‘One Health’ concept⁹¹.

Thus, Indigenous peoples may have already considered how microbiome research in their community not only produces benefit to humans or other species of interest, but also affects the microbes and the rest of the interconnected landscape as relational partners. Dr Nicole Redvers, Deninu K’ue First Nation member and Indigenous community and health researcher, writes “Microbiome science underscores the importance of accumulated experiences within the total lived environment linking biological, psychological, and social equations critical to personal, public, and planetary scales”⁸³. Little difference is seen in obligations to components of the ‘unseen world’ (for example, environmental and host-associated microbiota) versus land, fauna, flora and other people in the community because of these relational understandings of place and people. As researchers, we must consider how we responsibly and respectfully join this network of relationships as we seek to understand the biological relationships between microbes and their human hosts.

Relationality between researchers and microbes

Researchers working with ancient and/or contemporary human-associated microbial samples and DNA sequences must recognize the interconnectedness of microbes with their human host and broader environment. One clear example of microbes’ interdependent ecological relationships is demonstrated by the failed attempts to remove microbes from their host context and culture them in isolation^{92,93}.

Adopting a relational framework requires researchers to consider the microbiota in relation to their human hosts and to extend the same ethical obligations owed in human research to research centred on microbiota. Indigenous scholars from multiple Tribal Nations highlight the importance of a “more-than-human network of relations” that includes ecosystems, other organisms and humans⁹⁴. Similarly, the importance of host-associated microbiota in host health and homeostasis is clearly signified by the popular description of the microbiome as an ‘organ’⁹⁵. This phrasing situates microbial communities as integral to the identity and function of the host and blurs the distinction between microbial communities and host cells. Microbial populations associated with the host can consequently inform the physiology of the host itself. In human systems, distinct microbiome profiles can point to key features of the host (for example, diet, environmental exposures, health status and age) that may more readily enable the de-identification of populations or individuals in cohorts^{15,96–98}. In Indigenous communities with distinctive microbiome profiles^{36,37} or where relatively small cohorts include Indigenous individuals⁹⁹, the potential for de-identification is high. Additionally, the tight physical association between host and microbe causes DNA extraction and shotgun metagenomic sequencing of the microbiome to inadvertently produce large caches of host genome information^{100,101}. This information, while not the focal point of the study, raises ethical concerns in studies that include either living Indigenous peoples or Indigenous Ancestors^{67,71}. Researchers have spent decades attempting to access American Indian and Alaska Native genetic material for inclusion in population studies, leading to legal action in cases of misconduct and more general ‘cease and desist’ letters from the National Congress of American Indians^{47,77}. It is crucial to remember that the by-product of microbiome research with Indigenous people can reveal more than associative features of the host — it can reveal the host genome itself.

Current standards of training and established guidelines do not adequately prepare microbiome researchers for the potential implications of inadvertent human DNA recovery and de-identification. In the United States, for example, trainees working in microbiome science with discarded clinical samples and ancient DNA research are often exempted from human subjects research (HSR) training because of the perceived disconnect between human subjects and the host-associated microbiome. They may receive only brief ethics-based training from the federally mandated Responsible Conduct of Research (RCR) certification. All those with the potential to engage human DNA or human-informative microbiome data in their research — whether ancient or contemporary and host-associated or environmental — should be required to complete HSR training offered through the Collaborative Institutional Training Initiative (CITI) Program or similarly endorsed resources.

Approval of microbiome research by an IRB (or similar ethical review board) should also be implemented much more comprehensively than is currently done. We propose that ethical oversight should be required for all microbiome research that is human-associated (that is, involving microbial samples sourced from human hosts) and/or Indigenous centred. ‘Indigenous-centred’ microbial samples may not be directly sourced from human bodies but are culturally linked to Indigenous communities, such as microbes found in Indigenous traditional foods or Tribally protected locations. This requirement should apply regardless of the project’s direct engagement with analysis of human materials or perceived clinical relevance. In the case of research that seeks to understand human health conditions as a result of microbial interactions, emphasizing the intertwined relationship between microbes and their human hosts will not eliminate the potential for harm to come to participating individuals or communities, but can remind researchers of their obligations to protect participants in study design and execution.

However, simply reclassifying all microbiome research wholesale as ‘human subject research’ would not adequately address all risks

unique to Indigenous communities, given their lack of representation among global and national research administration and investigators. Therefore, the development of standardized ethical training that extends beyond HSR for those engaging with Indigenous communities and other historically marginalized groups is sorely needed so that a common groundwork for scientific engagement can be laid and supplemented with more discipline-specific guidelines to meet the relational obligations researchers have to respect and protect microbiome samples, data and Indigenous community partners.

Relationality between researchers and Indigenous community partners

One motivation of human microbiome researchers is the prospect of improving quality of life. To accomplish this goal, researchers must ensure that the benefits of these scientific advancements are shared with the communities whose contributions make them possible. Microbiome research oriented around relationality includes the communities' research priorities and perspectives on 'benefits' throughout the research process, from inception to completion, thereby avoiding extractive practices. Indigenous concepts of 'relational accountability'⁹⁴ and 'ethical relationality'¹⁰² explicitly require researcher accountability to all community collaborators – human and non-human. Examples of collaboration between microbiome researchers and Indigenous communities clearly demonstrate that innovative work with benefit to the participant community is feasible (Box 1). Heavy emphasis must be placed on conversations with Indigenous communities to identify projects of mutual interest before proposal development and work begins, prioritizing Indigenous data sovereignty at the onset of any study. Too often, microbiome scientists formulate a question of interest a priori and seek out Indigenous communities who can supply the answer, most often with little to no benefit for the participating community. Indiscriminately soliciting Indigenous communities for letters of support or seeking affirmation following completion of a study fails to genuinely include their interests and circumvents their sovereignty. Indeed, these practices are exploitative, as they prevent community members from including their own research questions and having a voice in the study narrative, reducing the likelihood of any meaningful outcomes for the community.

The inclusion of community members in the design of research projects will facilitate the introduction of Indigenous research sovereignty. Inclusion of the community will assist in the interpretation of trends found in data analysis and build a foundation of trust that can continue beyond the initial study, potentially into subsequent projects that could receive even more widespread community support¹⁰³. As data analysis begins, scheduling discussions to establish expectations with the partner community on the boundaries of anticipated research and information dissemination will define areas that can be explored for mutual gains and beneficial outcomes and those that are outside the scope or potentially harmful to the partner community. During the course of the study, these boundaries may shift based on findings or community perspectives, and scheduled discussions will increase the likelihood of adjusting the study early on. Community members must also be involved in preparing results for publication, which will expand mutual understanding of the project's results and importance by facilitating the two-way exchange of expertise between researchers and community partners. Collaborative communication and dissemination of research results can also safeguard against stigmatizing language when communicating the project to the broader public and scientific community. Researchers should also develop an agreement with the community regarding acceptable use and long-term deposition of all project data (see 'Relational obligations to uphold Indigenous microbiome research sovereignty'). To facilitate respectful engagement and collaboration with Indigenous communities, microbiome researchers should seek out training in cultural competency and use this training to be responsive to unique community histories, concerns and cultural

BOX 1

Examples of collaborative microbiome research frameworks engaging Indigenous peoples

Yanomami gut microbiome research in the Amazon rainforest.

Researchers seeking to establish long-term relationships with the Yanomami took time to identify what community members hoped to gain from the interaction and to establish mechanisms for providing these deliverables, which included providing requested healthcare and medicines during subsequent visits. Studies unveiled diversity in the Yanomami's associated microbes that exceeded that found in industrial populations³⁴. The inclusion of a Yanomami descendant in the research team helped reaffirm the researcher's obligations of communication and healthcare in the relationship¹¹¹.

Analysis of microbiome composition in members of the Cheyenne and Arapaho Tribes in Oklahoma, United States.

The project started with conversations between researchers and tribal members to discuss fundamental microbiological principles, how the study would be performed, and why it could provide insight into higher levels of autoimmune disorders experienced in Native American populations. The results showed that Cheyenne and Arapaho participants harboured unique microbial signatures in the gut and oral cavity, indicating potential points of intervention in community health^{41,112}.

Vision Mātauranga policy framework, Aotearoa, New Zealand.

At a national scale, approaches to engage Indigenous peoples in research have been codified as part of the Vision Mātauranga initiative¹¹³. Researchers requesting New Zealand governmental funding are required to provide details on what consultation with Māori, the Indigenous peoples of Aotearoa, has occurred, how discussion will continue throughout the proposal, and the relevance and/or significant research outcomes for Māori peoples. This policy provides an Indigenous-centred research framework for scientists working in Aotearoa, including those investigating human-associated microbiota.

sensitivities. Prior work calling for Indigenous research and data sovereignty in biomedical sciences serves as a strong starting point for those still learning to engage these concepts^{71,79}. Ultimately, researchers must be willing to establish accountability to the community throughout a project's lifetime, as accountability is key to building and maintaining operable relationships.

Relational obligations to uphold Indigenous microbiome research sovereignty

Indigenous research and data sovereignty is a centerpiece of researchers' relational obligations to their Indigenous community partners when engaging in microbiome science. Efforts by the scientific community to increase the accessibility of large datasets can be problematic for Indigenous communities wrestling with knowledge extraction and unconsented sampling, compounding potential research harms and continuing legacies of extractivism¹⁰⁴. Microbiome researchers should

position themselves as stewards, not owners, of samples and data for the Indigenous communities with whom they work. This position obliges researchers to return unused samples and data to Indigenous communities following completion of a study, so that those communities can dictate the terms of dissemination with other researchers based on their own sovereignty and governance structures. Initiation of new data availability standards by the NIH in the United States should not supersede data sovereignty of Indigenous entities. Researchers should avoid pressure to deposit data from Indigenous communities into publicly available repositories, where researchers may access open-source data from Indigenous peoples without engaging communities for consent for future research. Instead, allowances should exist for Tribal Nations and communities to negotiate data management agreements with the NIH and other federal entities on their own. Conversations about shared intellectual property agreements⁸⁴ must begin early on, be clear in scope and detail to the partner community, and be free of all language that tilts ownership towards the non-tribal entity, which is common in federal, private and academic agreements. The First Nations Information Governance Centre Principles of OCAP (ownership, control, access and possession) provide training aligned with these principles of Indigenous research sovereignty (<https://fnigc.ca/ocap-training/>). This does not exclude interested researchers from engaging tribes in conversation about subsequent projects but shifts the power to Indigenous communities to determine what studies are pursued with their samples. The inclusion of biocultural labels and traditional knowledge metadata tags for samples and data encodes Indigenous provenance information and cultural responsibility, and will more clearly indicate to researchers the cultural significance of microbiome research to Indigenous peoples¹⁰⁵.

Indigenous-led research organizations could serve as key arbiters in the management of data and samples. Genomics Aotearoa (<https://www.genomics-aotearoa.org.nz/>) is an alliance of ten academic and research institutes in Aotearoa that works to centre genetics research as by, for and with Māori, using Māori methods of data management. Partnerships across Aotearoa enable research under Te Ao Māori (Māori world view) principles that respect both people and Taonga (treasured/endemic) species, which can include studies of the microbiome. Biobanks with Indigenous governance structures have expanded to the United States, Canada and Australia, and could operate as intermediaries if insufficient infrastructure exists in the partner community. Affiliated biobanks can then function as a regulatory distribution checkpoint for partner communities to authorize the release of samples or data, including prior microbiome data deposits in publicly accessible repositories. This model supports the retention of samples and data ownership and management by the community, while researchers hold access to the material through documented temporary or 'on loan' agreements¹⁰⁶. Release of materials and data for secondary use from the biobank should follow the CARE Principles (collective benefit, authority to control, responsibility and ethics) recently laid out by Indigenous researchers that enhance the FAIR principles of data management and stewardship (findable, accessible, interoperable and reusable)¹⁰⁷. Implementation of dynamic consent models for data stored in these repositories could further increase the ease of regulation by empowering individuals and communities to quickly and easily vet applications for microbiome data use in the future¹⁰⁸.

Indigenous peoples have been systematically excluded from microbiome science. Addressing structural barriers, more inclusive training and increasing access to microbiome technologies would create opportunities for Indigenous scientists to engage in microbiome research and improve the quality and ethics of the field¹⁰⁹. Support of Indigenous trainees builds the next generation of Indigenous scientists, who bring often unique world views compared to their peers, which will shape the research questions and understanding of the research results. Within academic, private and federal laboratories,

Indigenous trainees can acquire the experimental and computational skill sets required for microbiome research. Integrated Indigenous and industrial scientific perspectives and practices allow these trainees to do better science for their home communities and other groups historically excluded from scientific benefit, and broadly drive innovation in microbiome science. The Indigidata workshop (indigidata.nativebio.org) and the Monitoring Environmental Microbes (MEM) workshop (<https://faculty.fortlewis.edu/jslee/MEM/>) have brought together Indigenous trainees, Indigenous instructors and participating Tribal community members to integrate cultural perspectives into environmental microbiome research. Programmes that integrate participants' identities into the curriculum promote trainee retention in science and enable individuals to envision themselves in research contexts in the future. Importantly though, investigators and research programmes should not seek out Indigenous trainees as a means to gain inroads into Indigenous communities or for the extraction of other knowledge systems.

Although efforts by academic and federal institutions or researchers to train Indigenous scientists and ethically engage Indigenous populations in microbiome research will reduce harm, they fail to empower Indigenous people directly. Access to kit-based methods for DNA extraction, paired with decreasing costs of large-scale sequencing, have made microbiome research accessible to non-academic research groups¹¹⁰. We argue that being good relatives, practising ethical relationality in the context of microbiome research, entails facilitating Indigenous groups to independently pursue microbiome studies so that they are no longer dependent on external entities. Providing education in microbiological and bioinformatic principles, equipment, training in specialized techniques, data analysis tools and computing resources to Indigenous communities seeking to explore microbial systems will enable new and more powerful research directions. Even smaller infrastructure projects, such as server banks for data storage, dramatically improve community access to microbiome research, while larger-scale infrastructure such as high-performance computing clusters and satellite systems for data transfer may be feasible in the future. Investment in capacity-building projects increases the ability of Indigenous communities to establish independent research programmes and supports long-term data sovereignty. The Native BioData Consortium (NBDC; <https://nativebio.org/>) serves as a landmark example of building Indigenous research capacity. Seated on the Cheyenne River reservation in the United States, NBDC is the only Indigenous-owned and -operated biobank and data repository in the Western Hemisphere. Through material investment and training provided by multiple biotech companies and academic partners, researchers at the NBDC are now carrying out microbiome experiments to explore how land management practices by Tribal members influence soil microbiomes and lead to the production of altered flora on the prairie. An understanding of the prairie microbiome and how grazing by cattle and/or buffalo changes the soil composition will help maintain this ecosystem and serve as an economic resource for the tribe.

Outlook

As microbiome science continues to grow and innovate, researchers must develop field-specific ethical standards to guide best research practices, particularly when research involves Indigenous communities. We propose that the concept of relationality operates as a guide to developing and implementing more ethical microbiome research with Indigenous peoples, with the ultimate goal of advancing Indigenous research sovereignty.

Individual researchers, research groups and the broader microbiome research community all have a role in setting the standards of accepted research practices by adopting these principles for ethical microbiome research with Indigenous peoples. There are also opportunities for funding agencies, and the broader research support infrastructure, to accelerate the adoption of higher ethical standards

by requiring proposals that include human-associated microbes from Indigenous peoples to provide resources that can be used to support community members' direct involvement in every stage of the research process or establish formalized community oversight, as occurs in Aotearoa. Funding for researchers and Indigenous communities to establish relationships in the research design phase, before proposals are written, would greatly encourage more community-collaborative research practices. Continued funding could then be contingent on community approval of the research plan and the research team. Each of these mechanisms would enable Indigenous communities' direct involvement in human microbiome research, not as subjects but as partners, and in so doing would help to avoid extractivism and thereby provide benefit to all global peoples.

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M.Z.A. is a board member of the Native BioData Consortium. The other authors declare no competing interests.

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