# ABSTRACT BOOK

## Indigenous Genomics Abstracts

### IG1: Mātauraka, tikaka and Decision Making for Active Protection

Te Aika, B.[1]

[1]Ōtakou Whakaihu Waka

Tikaka Māori (Aotearoas first law) underpin much of te ao Māori (the Māori world), providing direction for virtually all activities in our lives as Māori (and increasingly non-Māori). In recent decades, tikanga informed decision making has become more commonplace in Aotearoa New Zealand, for example, in providing a bases for lawful decision making. In genomics and gene technology spaces, various frameworks have been developed for decision making with consideration of te ao Maori.

Genomic data and algorithmic sovereignty for various applications extends matauraka into the turbulent waters of hard sciences. The role of sciences in colonisation needs to be resolved. This presentation describes characteristics between two worlds and suggests the importance of distinctiveness ahead of points of alignment for the purpose of publication at any cost. Important in this is academic prioritisation of itself and its philosophies against those of matauraka. Decision making within genomic science has recently evolved, culminating in tikaka and mātauranga-informed development of genomic resources: Aotearoa Genomic Data Repository[1] (ADGR) and the Rakeiora[2] projects.

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## IG2: Advancing Māori Leadership, Engagement, and Awareness in Genomics

Nikora, T.[1]

[1]Ira Tātai Whakaeke Charitable Trust Ltd

SING Aotearoa is a transformative initiative fostering Māori leadership, engagement, and awareness in genomic science while centring mātauranga Māori, Te Tiriti o Waitangi, and Indigenous values. The programme provides Māori with a safe, immersive space to explore the technical, ethical, and cultural dimensions of genomics through both scientific and cultural lenses.

The cornerstone of the SING programme is a week-long wānanga, where Māori participants gain hands-on experience in DNA analysis, computational genomics, and ethical decision-making. Designed for all levels of prior knowledge, the wānanga equips attendees with the skills to critically engage with genomics and its implications for Māori.

Since its inception, SING has welcomed over 120 alumni, with two now leading national genomics initiatives, while others pursue advanced research qualifications and careers in the field. SING also convened the 2020 International Indigenous Genomics Conference, amplifying Indigenous voices globally.

This presentation will explore SING Aotearoa's transformative model, which bridges Māori, Indigenous, and Western science. It will highlight the programme's role in empowering Māori to navigate complex issues such as data sovereignty, informed consent, and ethical research practices.

**IG3: [Huti Watson]**

# IG4: 'Whare Atua' - Exploring endemism and ethnomycology in the psychoactive fungal taonga species of Aotearoa

Van Zuylen, E.M.[1,2], Reid, J.[1]

[1]Ngāi Tahu Research Centre, University of Canterbury, Te Whare Wānanga o Waitaha;
[2]Biomolecular Interaction Centre, University of Canterbury, Te Whare Wānanga o Waitaha.

Psilocybin is a naturally occurring prodrug produced by Basidiomycota mushrooms that elicits psychedelic effects when consumed. Psilocybin and other related tryptophan derivatives have garnered interest as potential effective treatments for several mental health disorders including clinical depression, anxiety, PTSD, substance abuse and addiction. While clinical uses of psilocybin and its fungi have only recently been explored, psychoactive mushrooms have long been utilised by Indigenous peoples around the world. Mātauraka Māori tells us our tīpuna utilised numerous native fungi for both kai and rongoā. However, little is known about the presence or use of native psychoactive fungal species in Aotearoa. The Tohunga Suppression Act 1907, which aimed to prohibit traditional Māori healing practices, led to the suppression of Rongoā Māori for over five decades until its repeal under the Māori Welfare Act 1962.

This kaupapa explores the relationships our tīpuna may have had with Indigenous psychoactive fungi, and how this might inform culturally grounded, contemporary approaches to mental health care for whānau. Through the layering of archival ethnographic texts, iwi oral histories with Western scientific methods (genome sequencing, biochemical analyses) we seek to reconstruct our understanding of the whakapapa of endemic *Psilocybe* sp., an area with a history of colonial suppression and limited public understanding. Semi-structured interviews with Rongoā Māori practitioners, and a collaboration with Tū Wairua- the first marae-based clinical trial seeking to provide psilocybin-assisted therapy to whānau Māori suffering from methamphetamine use disorder in Te Tairāwhiti- will also inform this study.

## IG5: Whāia te mātauranga hei oranga mō koutou

Taane, M.[1]

[1]New Zealand Institute for Bioeconomy Science Limited

Growing up in a predominantly pākeha environment, disconnected from my papakāinga, Te ao Māori was not a prominent theme during my early formative years, save for waiata, and a couple of te reo Māori classes at primary school. Travelling internationally, I got a sense of how homogenous the world seemed to be, giving me a new appreciation for how truly important Māori culture was in bringing something unique and different to Aotearoa, distinguishing it from the European countries I had been exploring.

Upon returning, I began my journey through academia and te ao Māori after enrolling at university. From that point on, my science education and reconnection with my whakapapa have been intimately intertwined. Throughout my education and working life, I continue to maintain and grow connections within the Māori science community, the SING program has contributed greatly in this regard, by giving me the opportunity to both meet people, and have productive discussions about mātauranga within the context of science and research.

In this talk I will share with you my story, my roots, my journey, where I am now, and how it all ties into SING and the broader SING community.

## IG6: The Kiwi Whakapapa Project: genomics for kaitiakitanga of North Island Brown Kiwi

Hills, S.F.K.[1], Witehira, R.[2], Hura, A.[1], Undin, M.[3], Lockhart, P.[4], Castro, I.[1]

[1]Zoology and Ecology Group, School of Food Technology and Natural Sciences, Massey University, Palmerston North, NZ, [2]Te Rawhiti 3B2 Ahu Whenua Trust, Bay of Islands, NZ, [3]Department of Natural Sciences, Design and Sustainable Development, Mid Sweden University, Sundsvall, Sweden, [4]School of Agriculture and Environment, Massey University, Palmerston North, NZ.

Active kaitiakitanga of kiwi in Te Taitokerau is needed to arrest decades of population decline and ensure the mauri of surviving populations flourishes in the future. Translocation of birds is currently used to create new kiwi populations or boost others, but translocations are made in the absence of information regarding the health and genetics of the birds. Led by Nga Hapū o te Rawhiti, our research has focused on the ecology and genomics of Northland kiwi to examine the genetic structure and health of key populations. Since 2013 many hapū/iwi have been engaged in the collaboration, allowing blood samples to be collected from kiwi in their rohe for genetic analysis. A Genotyping-by-Sequencing (GBS) approach was taken to generate high-resolution genetic data for approximately 400 individual brown kiwi. The sample set includes birds from 12 populations in the rohe iwi/hapū across Te Taitokerau. Kiwi have also been sampled from Taranaki, the source of some birds historically translocated to Ponui Island and Hauturu-o-Toi (along with birds from Northland). Genetic data from these kiwi has been used to examine the whakapapa of the birds, determine the extent of local adaptation of populations, and to assess the genetic composition of ‘hybrid’ populations. Each of these questions represent key considerations for translocation. The outputs of these analyses will be used by iwi/hapū to help inform decision making for kaitiakitanga. Extending from our investigation of kiwi whakapapa, this project aims to develop the concept of tomo into conservation translocation practices. Tomo is the traditional practice of arranged marriage, often used by Māori to tie bloodlines of different hapū/whanau/iwi closer together for various reasons. Using a tomo based model hapū/iwi would decide the donor and recipient populations for translocations based on the results of genetic investigation, improving the success of kiwi in their rohe.

## IG7: Ruatau: connecting Māori genomic scientists and communities

Alexander, A.[1], Collins, C.[1], Hills, S.[2], Langsbury, Ho.[3], Tamati-Elliffe, P.[3], Cassidy, T.[3], Langsbury, Ha.[3], Keane, A.[4], Flack, B.[4], Russell, K.[4], Vanderburg, P.[5], Walker, M.[4], Rata-Te Raki, J.[4], Davison, E.[5], Kenny, N.[6], Leask, M.[7], Goodwin, D.[8], Charlton, A.[8], Gamlen-Greene, R.[6], Heremia, L.[9], Hema, K.[10], Ehau-Taumaunu, H.[11], Hēnare, K.[12], Rua, H.[13], Taiuru, K.[14], Te Āika, B.[15], Warbrick, L.[13,16], Wilcox, P.[17]

[1]Department of Anatomy, University of Otago, [2]Massey University, Palmerston North, NZ, [3]Te Rūnanga ō Ōtākou, [4]Kāti Huirapa Rūnaka ki Puketeraki, [5]East Otago Taiāpure Committee, [6]Department of Biochemistry, University of Otago, [7]Department of Physiology, University of Otago, [8]DBZ Consultancy Ltd, [9]Department of Microbiology and Immunology, University of Otago, [10]Department of Zoology, University of Otago, [11]Bioprotection Aotearoa and Bioeconomy Science Institute, [12]Faculty of Medical and Health Sciences, University of Auckland, [13]Te Pua Taketake (Indigenous Genomics Institute), [14]Independent STEAM and Property Rights Māori Cultural Adviser, [15]Research and Enterprise, University of Otago, [16]Pou Arataki, Te Pū Oranga Whenua, [17]Department of Mathematics and Statistics, University of Otago

Empowering Māori communities to make informed decisions about important genomics issues such as hauora (health) in humans, or kaitiakitanga (guardianship) of taonga species is critically important. Māori scientists (kaipūtaiao Māori) can help this through understanding community perspectives, priorities, and concerns. However, Māori are under-represented in academia and in genomics research. Furthermore, many Māori genomics researchers grew up Te Ao Pākehā and feel that they lack a sufficiently strong grounding in Te Ao Māori. Developing cultural competency in these Māori genomic scientists in collaboration with Māori communities can increase the understanding of genomics and associated risks and benefits in Māori communities, and enable kaipūtaiao Māori to increase their understanding of mātauranga Māori/tikanga and reconnect with their own whānau/hapū. The Ruatau project has aimed to achieve this by running cultural upskilling wānanga (workshops) for kaipūtaio Māori, and then bringing Māori communities and kaipūtaiao together in wānanga focused on genomics. Ruatau has provided a pathway to extend the knowledge of both groups through a two-way tuakana-teina relationship examining problems and questions about genomics that are relevant to Māori communities. Here, we talk about our journey with Ruatau so far.

A. Alexander – Te Hikutū: Ngāpuhi, Pākehā
C. Collins – Kāi Tahu, Pākehā
S. Hills – Ngati Porou, Pākehā
Ho. Langsbury – Te Rūnanga ō Ōtākou
P. Tamati-Elliffe – Te Rūnanga ō Ōtākou
T. Cassidy – Te Rūnanga ō Ōtākou
Ha. Langsbury – Te Rūnanga ō Ōtākou
A. Keane – Kāti Huirapa Rūnaka ki Puketeraki
B. Flack – Kāti Huirapa Rūnaka ki Puketeraki
K. Russell – Kāti Huirapa Rūnaka ki Puketeraki
P. Vanderburg – Pākehā
M. Walker – Kāti Huirapa Rūnaka ki Puketeraki
J. Rata-Te Raki – Kāti Huirapa Rūnaka ki Puketeraki
E. Davison – Kāti Huirapa Rūnaka ki Puketeraki
N. Kenny – Kāi Tahu, Te Ātiawa
M. Leask – Kāi Tahu

D. Goodwin – Ngāti Tūhoe
A.R. Charlton – Ngāti Tūhoe, Ngati Ruapani
R. Gamlen-Greene – Waikato
L. Heremia – Ngāti Tūhoe
K. Hema – Ngāti Kahungunu ki Wairoa
H. Ehau-Taumaunu – Ngāti Uepōhatu, Ngāti Porou, Te Ātiawa, Te Whānau-ā-Apanui
K. Hēnare – Te Aupōuri, Te Rarawa
H. Rua – Ngāti Tūhoe
K. Taiuru – Ngāi Tahu; Ngāti Rārua; Ngāti Kahungunu; Ngāti Hikairo; Tūwharetoa; Ngāti Hauiti; Ngāti Whitikaupeka
B. Te Āika – Ngāti Mutunga, Te Āti Awa, Kāti Wairaki, Kāti Mamoe, Waitaha
L. Warbrick – Ngati Awa, Ngati Rangitihi, Te Ati Haunui a Pāpārangi
P. Wilcox – Ngāti Rakaipaaka, Rongomaiwahine, Ngāti Kahungunu ki te Wairoa

# IG8: Working With Communities in Aotearoa-New Zealand to Build Climate Resilience in Kaimoana Using Transcriptomics

Gamlen-Greene, R. [1,2], Alexander, A. [1,3], Collins, C. [1,3], Coyle, L.[1,5], Flack, B. [1,4], Gilligan, J. [2], Gnanalingam, G. [1,5], Hepburn, C.D. [1,5], Pritchard, D.W. [1,6], Kenny, N.J. [1,2]

[1]Coastal People Southern Skies Centre of Research Excellence, University of Otago, Dunedin, New Zealand, [2]Department of Biochemistry, University of Otago, Dunedin, New Zealand, [3]Department of Anatomy, University of Otago, Dunedin, New Zealand, [4]East Otago Taiāpure Committee, Dunedin, New Zealand, [5]Department of Marine Science, University of Otago, Dunedin, New Zealand, [6]TMK Research, Dunedin, New Zealand

Climate change threatens marine ecosystems through marine heatwaves and ocean acidification, worsening declines in taonga species. Species used for kaimoana and mahinga kai are of special concern. In Aotearoa-New Zealand, Māori communities and commercial and recreational fishers have observed shifts in kaimoana distribution and health as ocean temperatures rise and marine heatwaves become more frequent and severe.

The effects of marine heatwaves on kaimoana remain poorly understood. Identifying whether some populations are more resilient than others is important for management. We focus on two taonga: pāua (*Haliotis iris*) and kōura (*Jasus edwardsii*). We'll present preliminary data from an experiment and the 2025 marine heatwave in Aotearoa.

This project is co-designed with Māori and other local community members to establish a baseline for the resilience and vulnerability of taonga species to marine heatwaves. Communities include Kāti Huirapa ki Puketeraki and the East Otago Taiāpure (Otago), Ōnuku Rūnanga and the Akaroa Taiāpure (Canterbury), and Te Rūnanga o Makaawhio and the Makaawhio Mātaitai (Westland). Using transcriptomic analysis to measure heat stress responses, we aim to understand species responses and identify genetic mechanisms supporting resilience, informing future management strategies.

## IG9: From Service to Science: A Research Journey from Hospitality and Tourism to Aotearoa's Virosphere

Lia Heremia[1]

[1] Department of Microbiology and Immunology, University of Otago, Dunedin, New Zealand

People often assume scientific careers are linear, however, some researchers arrive via unconventional routes. My research journey began with tertiary study at a Polytechnic before transitioning into the hospitality and tourism industries, later enrolling at university to undertake research spanning microbiology, chemistry, and forensic analytical science. Each stage developed complementary technical skills and perspectives that now inform my doctoral research in viral ecology.

My initial training included investigating whether bacterial load influences complete tail regeneration in *Xenopus laevis* tadpoles (Microbiology), developing phantom tissues for spectroscopic probe testing (Chemistry), and exploring hydrogel-based diagnostic methods for breast cancer detection. Forensic analytical science work examined mercury levels in 19th century Central Otago gold miners via hair analysis. These diverse projects have provided experience in molecular biology, spectroscopy, bioinformatics, and environmental sampling.

My postgraduate research examined viral diversity in urban waterfowl across Aotearoa using metatranscriptomic sequencing of faecal samples collected from sites on both the North and South Islands. This work detected both novel and previously described viruses, including members of Orthomyxoviridae, Coronaviridae, and Astroviridae analysing their potential for cross-species transmission. Minimal differentiation between North and South Island samples highlights a global connectedness in viral transmission, with links extending to distant locations such as Brazil.

This interdisciplinary journey shows how diverse experiences, both within and beyond science, build the skills and perspectives needed to address complex questions across a range of scientific disciplines. It highlights that impactful research is not limited to those who follow a traditional academic path, but that determination, curiosity, and a willingness to embrace new challenges are equally valuable. By combining technical expertise from multiple disciplines with a commitment to community engagement and Indigenous genomics outreach, this work contributes to improved biosecurity preparedness and fosters a more inclusive, collaborative scientific community in Aotearoa.

## IG10: Embedding Principles of Partnership and Data Sovereignty in Genomic Research

Kenny, NJ[1]; Stephens, J[2]; Gamlen-Greene, R[1]; Bailie, M[1]; Eason, C[3,4]; Mead, A[5]; Stephens, M[2]; Foster, M[2,6]

[1]Department of Biochemistry Te Tari Matū Koiora, University of Otago, Dunedin, Aotearoa New Zealand, AuOra Ltd, Wakatū Incorporation, Nelson, Aotearoa New Zealand, [3]Wakatū Incorporation, Nelson, Aotearoa New Zealand, [4]Faculty of Agricultural and Life Sciences, Lincoln University, Lincoln, Aotearoa-NZ, [5]Independent Research Principal, Wellington, Aotearoa New Zealand, [6]Edible Research Ltd, Ohoka, Aotearoa New Zealand

Genomic sequencing is increasingly being used in fields of importance to indigenous populations, such as healthcare and agriculture. It provides data that can be used for processes such as selective breeding, screening for disease, and for identifying and generating novel products. This information has not always been generated in an equitable or culturally appropriate fashion, and benefits have not always been returned to source communities.

In several novel projects, we have adopted a tikanga-informed approach to sample acquisition, processing, and data sovereignty, combined with cutting-edge genomic sequencing. This methodology is being used to establish an Aotearoa-centred framework for molecular biology and genomics, cognisant of the need for partnership in this field. This has been aided by advancements in Nanopore sequencing, allowing us to assemble world-class resources locally and at reasonable cost.

As part of this work, we are sequencing the genome of Kopakopa (the ribbed mussel *Aulacomya atra maoriana*), a species of cultural and commercial interest to Wakatū and the Iwi of Te Tauihu (the top of the South Island). We will use this resource to underpin commercial aspirations for this species as an aquacultural product, while supporting kaitiakitanga.

We are also using a transcriptomic approach to understand Kawakawa diversity. Using samples sourced from Te Tauihu takiwā and beyond, we are gaining an understanding of the population structure and genetic diversity of this taonga. A robust framework for relationships between Kawakawa from different areas will inform decisions around eco-sourcing to protect biodiversity in revitalisation or horticulture initiatives.

This data will add to our scientific understanding of the biological landscapes of Aotearoa, and align with research investigating chemical composition and bioactivity. Our approach will allow for the benefits of this sequencing to be returned to hapori Māori, while also providing data of broad interest to science and of utility to conservation.

# IG11: Development of Education Resources and Initiatives to Enhance Māori Participation in Modern Genetics and Genomics

Wilcox, P.L.[1,2,3]

[1]Department of Mathematics and Statistics, University of Otago, NZ, [2]Maurice Wilkins Centre, NZ, [3]Ira Tātai Whakaeke Charitable Trust, NZ

Over the last decade various education-based initiatives have been started that seek to enhance Māori participation in genetics and genomics research. From a base of virtually nothing and with limited funding, these initiatives have targeted multiple demographics ranging from pre-NCEA level 1 taurira Māori, to university undergraduate and graduate students, to 'flax roots' pākeke living and working in Māori communities. In parallel, Māori-specific content has been introduced to genetics (and other) courses at both undergraduate and graduate level at the University of Otago. Beginning in 2016 with the Summer Internship of iNdigenous peoples in Genomics Aotearoa (SING-A, www.singaoearoa.nz ), subsequent initiatives included the University of Otago's genetics module in its 2018 Science Wananga series that targets young high school-level tauira Māori. More recently, Te Roopu Kōkiri (TRK) has been established, which is a collective of Māori biomedical researchers across the Maurice Wilkins Centre partner organisations, including Māori health organisations. There is also the Ira Hāpai collective – of SING-A alumni and faculty, consisting of over 100 tāngata Māori. In addition, the Ruatau project specifically targets genomics researchers who are Māori by descent but raised in te ao pakeha. At the more senior pakeke/kaumātua-level, a Māori-specific charitable trust, Ira Tātai Whakaeke, has been established which involves multiple senior health and genomics researchers, most of whom have represented their hapori in other matters, and two of whom were recently acknowledged among the 100 Māori leaders (https://100maorileaders.com/leaders/irene-kereama-royal and https://100maorileaders.com/leaders/dr-kimiora-henare ). However, despite the formation of these initiatives there are still many challenges. These include a lack of committed long-term financial resourcing for these efforts despite demonstration of considerable benefits arising from them for non-Māori researchers. Other challenges stem from ongoing structural bias, systemic racism, and false allyship. In my introduction to this panel session, I will set the scene by providing an overview of both the aforementioned education initiatives as well as the ongoing challenges, along with examples.

## IG12: Epigenetic Origins of Diabetes Disparities Among Native Hawaiians and Pacific Islanders

Maunakea, A.K.[1]

[1]Epigenomics Research Program, Department of Anatomy, Biochemistry, and Physiology, John A. Burns School of Medicine, University of Hawai'i, Mānoa

Indigenous peoples, including Native Hawaiians and Pacific Islanders (NHPIs), experience a disproportionately higher prevalence and earlier onset of Type-2 diabetes mellitus (DM) than other racial/ethnic groups. This health disparity may result from the social environment shaping an individual's health behaviors (*e.g.* nutrition, physical activity, and education) and innate, interindividual variability in physiological responses that may mediate gene-environment interactions. The detrimental effects of social environments may include an increase in systemic inflammation, a hallmark of DM where monocytes of the immune system play a major role. Epigenetic mechanisms, including DNA methylation, regulate transcription of pro-inflammatory genes in monocytes. Taken together, we posit that DM disparities may in part result from social environment-induced changes to the epigenomic landscape in monocytes underlying their inflammatory states, which is also shaped by the gut microbiome. Herein, we address whether the social environment impacts epigenomic variability in monocytes across different ethnic populations in Hawaiʻi and account for DM disparities among NHPIs by integrating clinical/immunologic and monocyte-specific epigenomic data with social environment data from our Multiethnic Cohort Study (MEC) over a 20-year followup. This study provides the basis for continued efforts linking social-environmental impacts on diseases of health disparities through epigenomic-microbiome interactions with implications for disease prevention in the Native Hawaiian and Pacific Islander population.

## IG13: Te Ira Tātai Whakaheke: A National Centre of Indigenous & Māori Genomics

Henare, K.; Kereama-Royal, I.R.; Rolleston, A.; Sporle, A.; Wihongi, H.; Wilcox, P.

Te Ira Tātai Whakaheke ("the Centre") is a Māori-led initiative in medical genomics built to ensure research is inclusive of and informed by tīkanga Māori, te reo Māori, and mātauranga Māori, is ethically rigorous, and responsive to Māori communities and whānau needs. The Centre provides a culturally resonant and safe space for Iwi, hapū, and Māori communities to engage with genomic research that reflects an enduring responsibility for the care and protection of their tāonga. It embeds Māori authority and protection through Iwi and hapū representation in governance, through Māori expert boards and decision-making systems that affirm genomic data and samples as tāonga tuku iho - protected as whakapapa and preserved for future generations.

The Centre responds directly to Aotearoa's history of extractive research and institutional racism that excluded Māori communities and withheld benefits and the means of authority over their mātauranga, tīkanga and kaitiakitanga. By embedding Māori authority and Te Tiriti-based partnership in governance, the Centre can ensure genomic resources are stewarded by their rightful kaitiaki. This shifts Māori from subjects to leaders in genomic innovation, restoring trust and enabling benefits to flow back to Iwi, hapū, and whānau. The Centre thus forms an intergenerational foundation, ensuring future generations inherit genomic systems upheld by both scientific excellence and cultural integrity (Hudson et al., 2016; Carroll et al., 2020).

The interdisciplinary expertise within Te Ira Tātai Whakaheke - as Māori health leaders, Treaty lawyers, and data scientists, genomic clinical, research and academic specialists - drives scientific excellence while advancing Māori governance and researcher development. For example, the Rakeiora Pathways program has demonstrated how co-designed genomic research delivers tangible benefits to Māori through precision health frameworks centred on whānau wellbeing and health equity, and also mentoring and training emerging Māori scientists (Rye, Wilcox, Wihongi, Print, Sporle, & Jefferies, 2025). By institutionalising tikanga-based governance and Iwi-led authority over genomic resources, the Centre addresses inequities, builds enduring Māori research capacity, and contributes to global Indigenous data sovereignty (Kukutai & Taylor, 2016). Te Ira Tātai Whakaheke thus marks a vital step for Māori health equity in Aotearoa and exemplifies Indigenous-led genomic governance with international relevance (Carroll et al., 2020).

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## IG14: Role of a *CALCRL* gene variant in blood pressure regulation and kidney disease

Hao-Han George Chang[1] , Ruoxi Li[1] , Megan Leask[2,3,5], Prasanna Kallingappa[1] , Tony Merriman[3] , Huti Watson[4] , Rinki Murphy[1] , Peter Shepherd[1] , Christopher Walker[1] , Debbie Hay[2] , Alan J. Davidson[1,5]

[1] The University of Auckland, Aotearoa/New Zealand, [2] The University of Otago, Aotearoa/New Zealand, [3] The University of Alabama at Birmingham, USA, [4] Ngāti Porou Oranga, Aotearoa/New Zealand, [5] Kai Tahu

Precision medicine tailors medical treatment to individuals, particularly using genetic information, in order to improve health outcomes. However, global strategies largely exclude Māori and Pacific genomes, potentially exacerbating health inequities. We are addressing this gap by focusing on a missense *CALCRL* gene variant (Ile446Thr) that is highly enriched in people with Māori and Pacific ancestry. This variant in a hormone receptor gene implicated in blood pressure regulation, correlates with reduced kidney function, altered blood pressure and increases the risk of kidney failure in carriers with type 2 diabetes. Knock-in rats with the orthologous gene variant show increased weight gain, decreased systolic blood pressure and increased nitric oxide signalling (NO; a potent vasodilator) but high levels of Angiotensin II (a vasoconstrictor). As NO antagonises the effects of Angiotensin II on vascular tone, we hypothesise that the *CALCRL* variant perturbs the homeostatic balance of these vasoactive agents and this may play a role in driving the severity of kidney injury in diabetes. This work paves the way to developing precision medicine strategies for Māori and Pacific people, with significant potential for health benefits.

## IG15: *E koekoe te tūī, e ketekete te kākā, e kūkū te kererū* - A Molecular Tumour Board in Aotearoa

Henare, K.[1]
[1]Waipapa Taumata Rau

## IG16: Mapping the Māori Genome - learnings, risks and utilising technology to support whānau hauora management

Dunn, K.M.

# IG17: Omics and molecular pipelines for precision medicine for and by Māori

Megan Leask[1], Hannah Darroch[1], Ben Rangihuna[1], Calvin Young[1], Oluwatobi Eboda[1], Christian Mosimann[2], Robert Lalonde[2], Caleb Calhoun[1], Emily Morice[1], Elizabeth Ledgerwood[1], Alan Davidson[3], Nicola Dalbeth[3], Rinki Murphy[3], Tristan Pascart[4], Janak de Zoysa[3], Lisa Stamp[4], Julia Horsfield[1], Philip Wilcox[1], Tony Merriman[5]

[1]University of Otago, Dunedin, NZ,[2]University of Colorado, Aurora, Colorado, USA, [3]University of Auckland, Auckland, New Zealand, [4]University of Otago, Christchurch, New Zealand, [5]University of Alabama at Birmingham, Birmingham, Alabama, USA

Background: Precision medicine that uses genetic signatures of cardiometabolic disease is poised to revolutionise healthcare. However, the genetic studies driving these advances lack Māori and Pacific data, threatening to exacerbate the health inequities these populations already face.

Methods: We have identified genetic signals that are enriched in Māori and Pacific populations and influence metabolic traits (gout and type-2-diabetes) and in some cases can link to metabolites (metQTL) and gene expression (eQTL). We are establishing methods for functional analyses of individual variants. To assay the functional effect of these non-coding variants we have pioneered an alternative approach to the usual cell-based assays by testing enhancer activity *in vivo* using zebrafish. This allows us to test the function and tissue-specificity of DNA variants in regulatory/enhancer elements in the full complement of cell types that exist *in vivo*.

Results: Our showcase T2D-associated variant near *JAZF1* drives gene expression with tissue specificity in the brain and the kidney. Using CRISPR/Cas9 for *JAZF1* in zebrafish and iPSC we have begun to unravel the role that *JAZF1* plays in these tissues that leads to metabolic dysfunction. We can also apply the same bioinformatic and molecular pipelines to various other non-coding variants that we have recently begun to identify in our analyses of a Polynesian gout GWAS while training the next generation of Māori researchers!

## IG18: SING: Growing Kaupapa Māori Biomedical Researchers

Lima, J.S.[1]

[1]Te Tari Matū Koiora, Ōtākou Whakaihu Waka, Ōtepoti, Aotearoa.

The Summer Internship for INdigenous peoples in Genomics (SING) programme brings together leaders in tikanga, genomics, data protection, and more to empower Indigenous scientists to use our unique cultural lenses to drive science research innovation. In 2020, I attended my first SING workshop where I was introduced to a cohort of scientists from around the globe with shared experiences of creating space for their Indigenous identities in sciences.

This opportunity ignited my passion for conducting biomedical research with a tikanga Māori strategy and focus, which I was able to further develop in subsequent years through the SING programme. A whole village was required to support me through my postgraduate studies where I was subsequently able to produce a doctoral thesis with mixed methodologies, informed and co-designed by iwi, and written for and with my local communities.

In this presentation, I will discuss some of the mixed methodologies employed in my thesis, the approaches to co-designing a doctoral project with communities, and pay homage to the leaders in Indigenous sciences that helped to build my understanding of kaupapa Māori biomedical research.

# IG19: Ngā Tapuwae o te Kairangahau – The Role of the Researcher

Kerekere, T. [1]

[1]Department of Pathology and Biomedical Science, University of Otago, Christchurch, NZ,

He mokopuna tēnei nō Te Tairāwhiti. I currently live in Gisborne, where I'm carrying out my PhD research involving working with whānau from Te Tairāwhiti with cardiovascular inherited disease who have had a negative result returned for standard gene panel testing, to then carry out whole genome sequencing to try and identify the disease-causing variant/s.

I was drawn to this project because there was a shift in the research priorities of Ngāti Porou Oranga toward metabolic health including cardiovascular disease. Three years earlier I worked for Ngāti Porou Oranga as a research assistant. During this time, I realised that as researchers we are tools in our respective community's toolkit to utilise, when needed, to reach their health aspirations. As researchers, we can trust that each community knows themselves best and knows what their research priorities are, to reach their health aspirations and maximise positive health outcomes.

While I was at Ngāti Porou Oranga, precision medicine research was a priority. Accordingly, I did my Honours project the following year, looking at genetic diversity in the pharmacogene *CYP2C19* in a cohort of Māori sourced from Ngāti Porou Oranga. Following this, there had been a shift in research aspirations focusing on metabolic health including cardiovascular disease. In response, I shifted my research towards cardiovascular disease.

Although my current research is not co-designed or community-led, having been designed before I joined the project, I continue to take steps toward becoming a responsive researcher who is guided by community. As researchers, we should ask ourselves, who are doing our research for? Why am we here? For me, it is to serve my people. In the future, I will be a tool for my Tairāwhiti community's toolkit.

## IG20: Characterising the CYP2D6*71 Allele in Aotearoa: Pharmacogenomic Insights for Māori and Pacific Peoples

Holloway B[1], Miller A, Magon N, Kettle T, Faatoese A, Lacey C, Merriman T[2], Kennedy M[1], Leask MP[3]

[1]Department of Pathology and Biomedical Science, University of Otago, Christchurch, NZ, [2]University of Alabama at Birmingham, Birmingham, Alabama, USA, [3]University of Otago, Dunedin

Background: CYP2D6 is a key enzyme involved in the metabolism of a wide range of medications, including some opioids, antidepressants, cardiac drugs and cancer medications. The enzyme is encoded by the highly polymorphic CYP2D6 gene, with genetic variation represented as star alleles. These variants are associated with distinct metabolic phenotypes: Ultra Metaboliser (UM), Normal Metaboliser (NM), Intermediate Metaboliser (IM), and Poor Metaboliser (PM). The frequency of CYP2D6 variants differs between populations, including those in Aotearoa New Zealand and the Pacific Islands. Previous studies have shown that the *71 missense allele is highly enriched in Māori and Pacific Peoples but not observed in European populations. It is important to understand whether this variant has an impact on CYP2D6 enzyme function, and therefore whether it should be included in pharmacogenetic tests offered in Aotearoa New Zealand and elsewhere.

Methods: We examined low pass genome sequencing data from a large cohort of people with Māori and Pacific ancestry, to identify participants who were heterozygous or homozygous for the CYP2D6*71 allele. We identified 708 heterozygotes and 74 homozygotes. 708 of the *71 heterozygous alleles were in trans to a non-functional allele, and these plus the *71 homozygotes, provided a cohort in which the activity of *71 could be accurately measured. To analyse activity, we applied a mass spectrophotometric assay for a potato toxin called solanidine and its metabolites, which was recently shown to be an effective in vivo biomarker for CYP2D6 function.

Results and discussion: Preliminary mass spectrometry analysis of these samples strongly suggests that the *71 allele has low activity. These data extend initial findings in samples from the Pasifika Heart Study and CHALICE cohorts (unpublished data) and provide strong evidence that the CYP2D6*71 allele should be included in pharmacogenetic testing panels. Ongoing work will focus on solanidine metabolism profiling via mass spectrometry and CYP2D6 analysis using nanopore sequencing in all future samples.

# P71: Identifying epigenetic changes underpinning drug resistance in lung cancer

Farry, S.[1], Davis, W.J.H.[1,2], Drummond, C.J.[1,2], Reid, G. [1,2], Kumar, R.[3], Rodger, E.[1], Chatterjee, A.[1]

[1] Department of Pathology, University of Otago, Dunedin School of Medicine, NZ

[2] Maurice Wilkins Centre

[3] Department of Medicine, University of Otago, Dunedin School of Medicine, Dunedin, NZ

Lung cancer is a leading cause of cancer-related mortality in Aotearoa New Zealand. Molecularly targeted therapies as a treatment for this disease offer greater specificity and efficacy in comparison to chemotherapy. Despite the significant initial benefit, patients often relapse due to the development of drug resistance. The pathways behind the onset of this resistance remain poorly understood, justifying the exploration of epigenetic changes as a mechanism for cancer cells to adapt to therapies. Our research investigates the role of epigenetic reprogramming in resistance to targeted therapies using a multi-omic approach.

We analysed DNA methylation and gene expression patterns in three lung cancer cell lines, each with a unique mutation commonly found in lung cancer patients (EGFR, KRAS, ALK). Cells were treated with their respective targeted therapies, where remaining cells post-treatment were collected over 3, 7 and 19 days to track epigenetic changes associated with the development of resistance. We identified a total of 4436 differentially methylated regions (DMRs) across all timepoints and cell lines ($FDR<0.05$, methylation difference $\geq 0.2$) where the associated genes of 368 DMRs were differentially expressed ($FDR<0.05$, $Log2Foldchange > 2$). Temporal expression patterns appeared to be largely stochastic, whereas methylation changes were predominantly established early and sustained over the treatment timeline. These patterns highlight methylation changes as potential predictive markers of drug response.

We are expanding this study to include analysis of cell-free DNA (cfDNA) from blood samples of lung cancer patients receiving targeted therapy, including a cohort of patients from Aotearoa New Zealand. Many patients, including Māori, often face systemic barriers to tissue biopsy, but blood-based epigenetic markers offer a more accessible and equitable diagnostic tool. Building on our analyses in lung cancer cell lines, we aim to define an epigenetic signature of drug resistance that will inform the development of minimally invasive markers to support precision medicine approaches and help improve outcomes for patients with lung cancer.