Introduction

Gout is a severely debilitating inherited disease affecting 10-15% of Māori and Pacific men and 6% of European men. It is caused by too much *urate* in the blood which can form crystals in the joints. This causes an immune reaction leading to inflammation (red, hot joints) and severe pain. Related conditions include type 2 diabetes, obesity, heart and kidney disease.

New Researchers

Dr Cassidy Moeke (Ngāti Porou rāua ko Ngāti Awa) has secured 2 years of funding as a Postdoctoral Fellow in our group under the supervision of Prof. Merriman. Dr Moeke's project is to detect immune material on monosodium urate crystals in people with gout. This will provide new biological information about the immune process of the people who get gout.

Anezka Hoskins (Ngati Porou) is working on the **LIPE** gene which has two roles: it is involved with steroid hormone production; and it can change stored triglycerides to free fatty acids. Anezka will be connecting with the gout community up the Coast over summer.

Local update, new findings

We have identified more gene changes that are specific to Māori and Pacific people. We think the **PRPSAP1** gene results in more urate being produced in the body. A change in another gene, **IL37,** means that IL37 chemical (involved in the immune system) cannot prevent the immune system making gout attacks.

The recent exciting finding is the **CREBRF** gene. A specific change in this gene, found only in people of Māori and Pacific ancestry, causes weight to increase. But it also *protects* from diabetes. This tells us that the causes of obesity and diabetes are different in Māori than overseas populations. We think that increased muscle mass in Māori combined with good fat is behind this apparent contradiction. With the Maurice Wilkins Centre (nationwide but based in Auckland) we are initiating local research to understand this. CREBRF change *may* also control urate levels.

National updates

We know that some **kai** can trigger gout in some people who already have urate crystals. To look at the role of some **foods and drinks** in urate levels we used American data to calculate the role of diet compared to genes.

Genes are overwhelmingly dominant in determining urate levels. Diet has only a very small role. This points to the importance of using allopurinol to lower urate levels to stop gout.

International updates

A United States company (ArdeaBiosciences) has developed a new drug for gout: Lesinurad. It works by increasing the amount of urate excreted in the mimi. This is different to allopurinol which works by slowing the production of urate in the blood. We hope that Lesinurad will be available in New Zealand in the coming years.

We are involved in a very large international study studying the DNA of more than 2.5 million people, and have discovered more than 100 new genes that cause gout. We will be able to test these genes for involvement in gout in Tairawhiti.

Previous findings

ABCG2. We know that the ABCG2 gene plays a strong role in gout by triggering gout attacks. We have also found out that ABCG2 influences how people respond to allopurinol. People with a certain version need more allopurinol to decrease urate levels.

ABCC4. We have also found a version of another gene ('ABCC4') that is involved in making the urate high by getting rid of less uric acid in the mimi. This version is found in Māori and Pacific people, but not in Pākehā. It is part of the explanation as to why urate is naturally higher in Māori and Pacific people.

LRP2. This gene plays a role in gout in Tairawhiti, and in other Māori and Pacific Island people in Aotearoa NZ. What is very interesting about LRP2 is that its genetic function is over-ridden by alcohol drinking. There is one variation of the gene that decreases the chances of gout by about a quarter. This version is present in 1 in 8 of Māori in Tairawhiti. When a person with this version drinks any alcohol their chance of gout is about 4.5 times higher than someone with this version who does not drink. We do not know what LRP2 gene does in the body, but it may be involved in getting rid of urate in the mimi.

What does this mean for improving health care?
How do we improve we prevent and manage both gout and the other related conditions?

We are now considering how whānau and doctors & nurses can use this precise information - about the ways genes work with your kai, and with the drugs used to treat gout (e.g. allopurinol) – to better treat and prevent these conditions.

We look forward to discussing and receiving your feedback on some of these possibilities in community hui and related meetings.

Key Messages

1. Hit the target <0.36 uric acid levels in your blood to avoid a gout attack.

2. Your gout is not 'cured' even if the pain goes away. Take your medication EVERY DAY.

3. Your genes play an important role in gout and related conditions, not just your kai.

Acknowledgements

We recognise the commitment of many people in the successful continuation of this project and take this opportunity to thank the people who have participated, and the technical staff for processing patient samples.

We would also like to thank the funding bodies that recognise gout as an important disease (and related conditions) to be researched and better understood, managed and treated in Tairawhiti.

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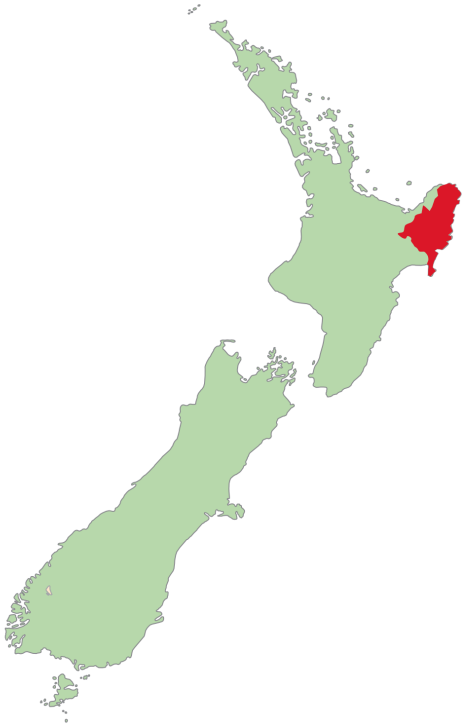
Gout and Related Conditions in Tairawhiti



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