



## Gout and Related Conditions in Tairāwhiti

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### *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. As urate builds up in the blood it forms crystals in the joints, which cause an immune reaction leading to inflammation (red, hot joints) and severe pain.

Related conditions include type 2 diabetes, obesity, heart and kidney disease.

### *International updates*

We are involved in a very large international study that has studied the DNA of more than 2.5 million people and discovered more than 100 new genes that cause gout. We are going to test these genes for being involved in gout in Māori.

With coronavirus we are doing a study with UK and US hospital data to see if having gout changes peoples' chances of having a worse outcome if they develop COVID-19.

**IL37.** We have finished a study with researchers from Nijmegen in The Netherlands. We found a version of a gene called 'IL37' that is only in Māori and Pacific people. The version stops IL37 from preventing gout. We think that this version previously allowed people to be resistant to infectious diseases. The folks in Nijmegen are developing a drug for people with this version.

### *National updates*

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

Genes are overwhelmingly dominant in determining urate levels. With diet having such a small role this points to the importance of using allopurinol to lower urate levels to get rid of the gout.

### *Local update, new work on genetic risk score*

MSc student Anezka Hoskin (Ngāti Porou) has studied all the genes at once and is producing a 'genetic risk score' that may be able to help predict in advance people who are at risk of getting gout. This work is being extended this year by Ngāti Porou student Ben Rangihuna. Moving forward we would like to work with Ngāti Porou Hauora to see if this test might work in routine health care.

### *Local updates, previous findings*

**ABCG2.** The biggest previous highlight was that the ABCG2 gene plays a strong role in gout by triggering the gout attack. It is also able to increase the amount of urate in the blood, meaning that this gene gives a 'double whammy' for gout. ABCG2 is also interesting because its function is changed by a chemical called curcumin that is found in the spice turmeric. We are now working with University of Auckland scientists to test if an existing drug can work on ABCG2 to stop gout. We are also planning a clinical trial in Samoa to test if curcumin works to lower urate levels and reduce gout attacks.

We have also found out that ABCG2 influences how people respond to allopurinol. People with a certain version need more allopurinol to get the urate levels down.

**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 Tairāwhiti, and in other Māori and Pacific Island people in Aotearoa NZ. What is very interesting 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 Tairāwhiti. 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 the gene does in the body, but it may be involved in getting rid of urate in the mimi.

**Tomatoes.** We found that tomatoes play a role in triggering gout in some people. This confirms what people with gout have been telling us. How tomatoes do this is not known, but probably triggers gout when urate is already high and the crystals are there. There is no need to avoid tomatoes if they don't cause your gout. The best way to stop gout is getting the urate low with the drug allopurinol.

A recent exciting finding is the **CALCRL** gene. A specific change in this gene, found only in people of Māori and Pacific ancestry, causes kidney disease but only when people have diabetes. We think that the variant blocks release of insulin from the pancreas. We are working with a researcher from Auckland (Prof Alan Davidson) to understand more about how the gene works in

the body. (We studied this gene because we knew it was involved in the kidneys, and we know that how the kidneys work and their ability to get rid of urate in the mimi is very important in gout.)

Another recent finding we have relates to the energy powerhouses in your body, the **mitochondria**. There are dozens of these in your body and they convert the energy from your food (e.g. glucose and fats) to the energy that your body actually uses ('ATP'). We have found that part of the cause of gout may be when the mitochondria get stressed – this helps trigger off the gout attack. We do not yet know exactly how the mitochondria get stressed. Interestingly this seems to be specific to Māori and Pacific people, we don't see it happening in Pākehā.

***What does this mean for improving health care?***  
What does this mean for improving how we prevent and manage both the gout, and the other related conditions?

We are now considering how whānau and doctors & nurses can use the precise information - about the ways genes work to increase the chance of getting gout, how the 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 the research and receiving your feedback on some of the new research we are thinking about in community hui and related meetings.

### ***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 Tairāwhiti.

### *Key messages:*

- 1. Hit the target <0.36 urate 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.**