Dynacare®

MT-RNR1 m.1555A>G Fact Sheet

What is the RNR1 Gene?

The *RNR1* gene is responsible for regulating insulin and maintaining healthy glucose levels in the human body. The *RNR1* gene is located within the DNA of the mitochondria. Mitochondria are present in every cell of our body and provide the energy needed for our cells to function and communicate with other cells. The mitochondria has its own genetic code (called mitochondrial DNA or mtDNA), separate from the other genes in our cells which are found in the nucleus of the cell (called nuclear genes). Unlike nuclear genes, which are inherited from both parents, mitochondrial genes are inherited only from the mother.

We all have variants/changes in our DNA; most of them do not cause any health-related problems, however, some affect the way our bodies metabolize drugs/supplements, and some are related to the development of certain health conditions. The *MT-RNR1* m.1555A>G variant is passed on from a mother to all of her children (both males and females) and can cause health-related problems. This variant, however, is never passed on from a father to his children.

What does having the *MT-RNR1* m.1555A>G variant mean for me and my family?

Individuals who have the *MT-RNR1* m.1555A>G variant (approx. 2-3% of the population) have adverse reactions to a class of medications called aminoglycosides. Aminoglycosides are a specific type of antibiotic used to treat serious infections caused by aggressive bacteria. Some of the more common names of aminoglycoside medications are gentamycin, tobramycin, amikacin, kanamycin, or streptomycin.[i]

Individuals with the *MT-RNR1* m.1555A>G variant who are treated with aminoglycoside antibiotics will typically experience permanent hearing loss that ranges from severe to profound and affects both ears. This hearing loss is not associated with other physical signs and/or symptoms. The hearing loss experienced by carriers of this variant is typically called "aminoglycoside-induced hearing loss".[ii] As such, individuals who have the *MT-RNR1* m.1555A>G variant should avoid treatment with aminoglycosides.

Individuals with the *MT-RNR1* m.1555A>G variant who are NOT exposed to aminoglycosides may still develop hearing loss, however, the severity and age of onset is variable and is not predictable. Some carriers also experience pigment changes on their skin (light patches) and/or thickening of the skin on the palms or soles of the feet commonly referred to as keratoderma.

Important Facts:

- Individuals with the *MT-RNR1* m.1555A>G variant should not take any form of aminoglycosides and avoid increased noise exposure.
- Patients with hearing loss should be assessed for appropriate rehabilitation including hearing aids, speech therapy, culturally appropriate language training, cochlear implantation, and educational programs for the hearing impaired.
- For individuals with skin involvement, they can consider referral to dermatology to discuss lotions and/or moisturizers for mild keratoderma.
- The *MT-RNR1* m.1555A>G variant is passed on from mother to child. All offspring of females with the *MT-RNR1* m.1555A>G variant are at risk of inheriting the variant. Offspring of males with the *MT-RNR1* m.1555A>G variant are not at risk of inheriting the *MT-RNR1* m.1555A>G variant.
- Prenatal diagnosis options are available to determine the fetal carrier status for the *MT-RNR1* m.1555A>G variant.
- Newborn infants from a female *MT-RNR1* m.1555A>G variant carrier should be flagged to avoid any administration of aminoglycosides to reduce long term hearing loss.[iii]

How Can I Get More Information?

A referral to a genetic counsellor can help clarify individual risks and determine other at-risk family members who could benefit from predictive testing for the 1555A>G *MT-RNR1* variant.

In Canada, genetic counselling is available at provincial genetic clinics by referral. Your healthcare provider can send a referral to Dynacare Genetics Specialty team at 450.901.3076. Our online referral form can be completed here. Alternatively, to locate a genetic clinic near you, visit the Canadian Association of Genetic Counsellors at www.cagc-accg.org.

Genetic Counselling Referral forms:

- Dynacare Pharmacogenomic Genetic Counselling Referral

[i] Usami S, Nishio S. Nonsyndromic Hearing Loss and Deafness, Mitochondrial. 2004 Oct 22 [Updated 2018 Jun 14]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1422.

[ii] Pandya A, Xia XJ, Erdenetungalag R, Amendola M, Landa B, Radnaabazar J, Dangaasuren B, Van Tuyle G, Nance WE. Heterogenous point mutations in the mitochondrial tRNA Ser(UCN) precursor coexisting with the A1555G mutation in deaf students from Mongolia. Am J Hum Genet. 1999;65:1803–6.

[iii] Bardien S, Human H, Harris T, Hefke G, Veikondis R, Schaaf HS, van der Merwe L, Greinwald JH, Fagan J, de Jong G. A rapid method for detection of five known mutations associated with aminoglycoside-induced deafness. BMC Med Genet. 2009 Jan 13;10:2. doi: 10.1186/1471-2350-10-2. PMID: 19144107; PMCID: PMC2630920