

## Study of correlation between the NAT2 phenotype and genotype status among Greenlandic Inuit

N-acetyltransferase 2 (NAT2) is the main enzyme metabolizing isoniazid and genotype-based treatment has been studied for years without becoming common practice. To investigate whether genotype-based isoniazid treatment is feasible in Greenland, we sequenced the coding sequence of NAT2 and determined the NAT2 enzyme-activity by caffeine test.

No additional genetic variants were identified in the coding sequence of NAT2, so that genotype status in 260 study participants could be assessed by a well-established 7-SNP panel. Studying the enzyme activity by the ratio of the two caffeine metabolites AFMU and 1X in 260 participants showed a high rate of slow phenotypes with intermediate or rapid genotype. These misclassifications were mainly observed in urine samples with pH3, we observed a moderate level of discrepancies (19 of the 116 individuals with intermediate or rapid genotype status having a slow phenotype). Further investigation showed that drinking coffee and not tea or cola was the most important factor for high levels of both metabolites.

The concordance between phenotype and genotype status with regard to slow metabolism supported the recommendation of lower isoniazid doses in individuals with slow genotype status in order to avoid liver injury, a frequent side effect. The phenotypical variation observed for individuals with intermediate or rapid genotype status warrants further research before increased dosing of isoniazid can be recommended.

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