Polymorphisms of NAT1 and risk for prostate cancer

The identification of specific polymorphisms at loci 640

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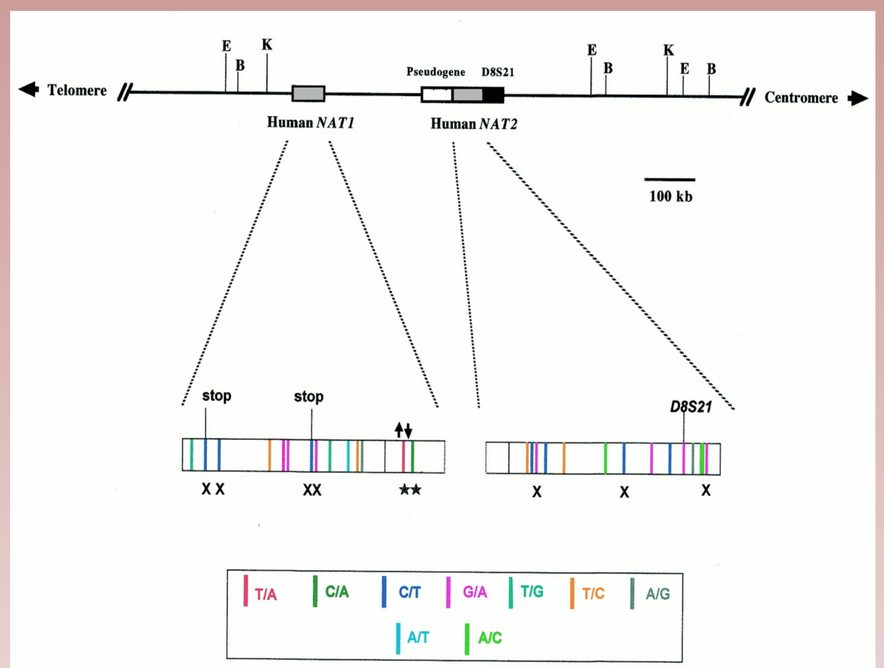
Introduction

Single nucleotide polymorphisms (SNPs) are single nucleotide submissions, insertions, or deletions in the genome, which can produce serious consequences when they occur in specific sequences or genes. Specifically, the N-acetyl transferase (NAT1) gene is polymorphic because of substitutions, which have resulted in the compromise of its function and efficiency as an enzyme.[1,2] The original function of an unaltered NAT1 gene is to encode a specific enzyme that acts as the catalyst in the transfer of an acetyl group from acetyl-CoA to various substrates.[1,2,3] This enzyme is important in the metabolism of drugs and xenobiotics and has implications in chemical carcinogenesis pathways.[1,3] However, the frequency in which SNPs are present in the NAT1 gene at specific loci may correlate with an increased incidence of prostate cancer in males.[1,3]

Hypothesis

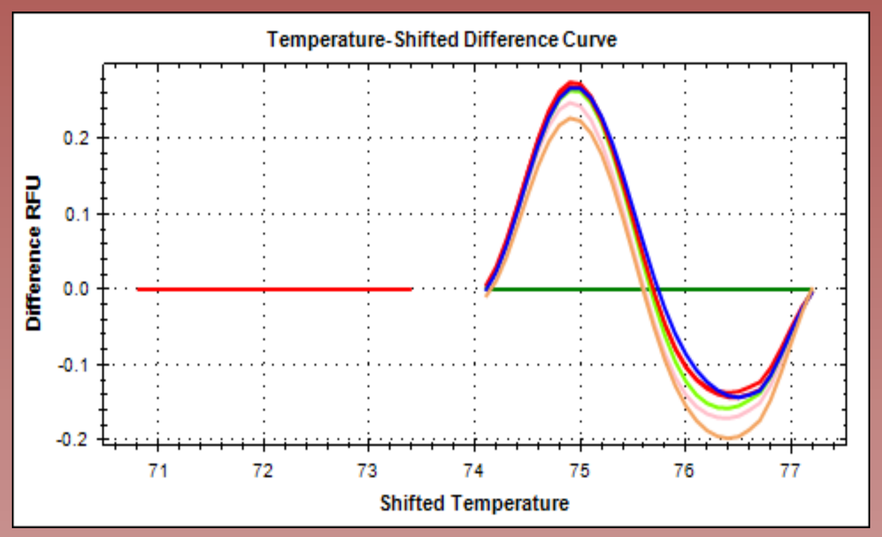
It is postulated that the incidence of benign prostatic hyperplasia (BPH) and prostate cancer may be higher among men with an increased frequency of SNPs within the NAT1 gene.

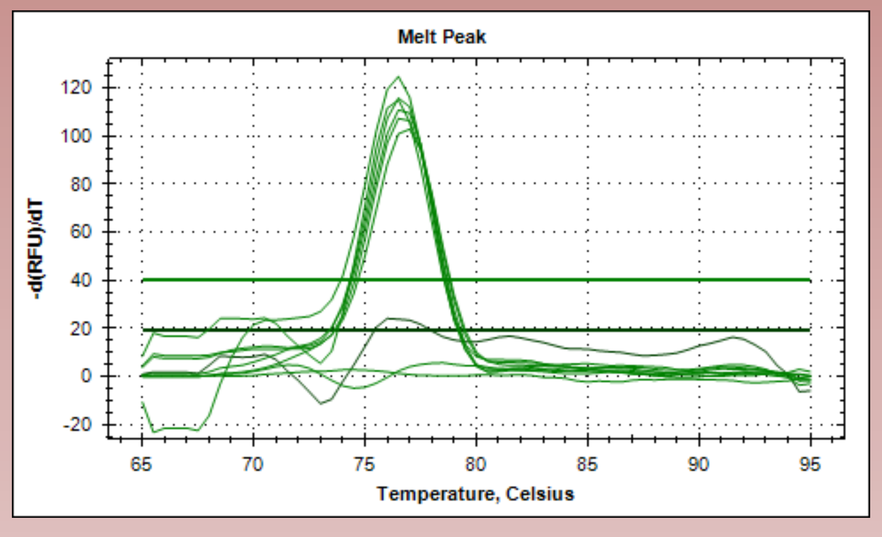


Source: Edith Sim et al. Hum. Mol. Genet. 2000;9:2435-2441

Results

The literature supports a potential involvement of NAT1 polymorphisms in prostate carcinogenesis.[5,7] It was concluded that polymorphisms in carcinogen-metabolizing enzymes increases the risk or prostate cancer development.[6] NAT1 gene polymorphisms therefore have tremendous potential as biomarkers for the risk of developing prostate cancer in males.[7]





Suggestions/Future Directions

The next step could be to identify which polymorphisms exist in cases or control samples. Ultimately, these findings may establish protocol that can be utilized for the future development of pre-screening techniques for males at a higher risk of developing prostate cancer.

Methodology

Literature Review (PubMed) – efficacy and function of NAT1 in the presence and absence of polymorphisms.

DNA samples from case and control groups were analyzed to determine the presence or absence of the mutation at loci 640.

Polymerase Chain Reaction (PCR) was used to amplify the sample DNA sequences with the suspected 640 mutation.

These samples were observed using a High Resolution Melt (HRM) technique to determine what the mutations looked like in graphical form.

Conclusion

Polymorphisms were selected as determinants of prostate cancer because many studies suggested a link between polymorphisms of metabolic enzymes and tumour susceptibility.[4] These polymorphisms have a causal relationship with cancer by rendering protective enzymes ineffective.[4]

The goal of this research was to develop a protocol permitting proper PCR-based identification and screening techniques to efficiently mark deviations within the NAT1 gene at loci 640. Based on the results, the HRM curves indicate conclusively the presence or absence of polymorphisms at the NAT1 640 loci. The presence of mutations increases the risk of prostate cancer development. It is possible to determine the presence and absence of mutations using the designed PCR protocol with the correct primers and probes.

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