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**TITLE:**

**ABSTRACT: (250 words maximum)**

**Background**

Patients with differentiated thyroid cancer (DTC) are managed by total thyroidectomy and radioiodine ablation of the remnant thyroid tissue, requiring L-Thyroxine (LT4) therapy for replacement and thyroid stimulating hormone (TSH) suppression. There is wide variation in L-T4 dose requirement, possibly due to an underlying genetic cause. Therefore, this study aims to identify single nucleotide polymorphisms (SNPs) of 6 genes comprising 3 deiodinases (*DIO1*, *DIO2* and *DIO3*), TSH receptor Beta, PAX8 transcription factor and sodium iodine symporter (*NIS*), involved in thyroid hormone metabolism/action and evaluate their possible association with L-T4 dose requirements and with the risk of developing DTC in Saudi population.

**Methods**

SNPs were identified by sequencing of the genes in 200 individuals using the MegaBACE DNA analysis system, and data analyzed by DNASTAR Lasergene Software. Association studies for 3 *NIS* SNPs (rs4808708, rs4808709 and rs7250346) were accomplished in 409 cases versus 406 controls by rtPCR using Taqman chemistry with the ABI Prism 7900HT Sequence Detection System.

**Results**

Overall, 225 SNPs were captured, comprising 62 novel, 11 nonsynonymous and 9 insertion/deletion polymorphisms. Thus far, association experiments were performed on 3 *NIS* variants showing that the G allele [Odds ratio(95%CI)=1.30(1.05-1.60); p=0.016] and the AG+GG genotypes [1.38(1.05-1.82); p<0.05] of the rs4808708A>G are significantly associated with DTC, independent of age and sex. No association was found for any of these SNPs with L-T4 dose.

**Conclusions**

We identified rs4808708 as a risk variant for DTC. The variability in the L-T4 dose requirement does not appear to be related to *NIS* polymorphisms.