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ASSOCIATION OF A NOVEL LPL INTRONIC VARIANT G.18704C>A WITH TRIGLYCERIDE LEVELS IDENTIFIED IN KUWAITI ARABS

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Interethnic genetic differences play a role in plasma lipid level variation across populations. Several genes involved in lipid metabolism and transport are candidates for the genetic association with lipid level variation including lipoprotein lipase (*LPL*). This enzyme is important for the hydrolysis of circulating triglycerides into free fatty acids for tissue utilization. It is encoded by a 30 Kb gene, mapped to chromosome 8p22. More than 1000 variants have been identified across the gene including both SNP's and InDel's with variable frequencies across different populations. The objective of the study was first to identify variants across the *LPL* gene among a sample of Kuwaiti's of Arab ethnicity and investigate the genetic association of selected variants with variation in lipid levels among a cohort of 712 apparently healthy Kuwaiti's. The variants were identified by re-sequencing the full gene in 100 sample of Kuwaiti's with document Arab ethnicity. A total of 293 variants were identified and characterized among which were 47 novel variants. The study was the first to report a genetic association of a novel "rare" variant (*LPL*: g.18704C>A) with a significant increase in serum TG (p=0.044) and VLDL (p=0.043) levels. In addition, the variant also showed a significant (p=0.033) association of lower high-density lipoprotein (HDL). The opposing effect of one variant on two lipid levels can be explained by the direct action of *LPL* on TG levels and indirect action on HDL levels (Figure 1). This newly identified variant (g.18704C>A) should be investigated in other populations for its genetic association with serum lipid levels to verify if it is ethnic specific and its role in the gene expression regulation of pathways involved in lipid metabolism and transport. Moreover, the study verified the importance of identifying ethnic specific variants that would explain the interethnic variation in lipid levels.

Biography

Suzanne Al-Bustan has completed her PhD in Human Genetics from the Duncan Guthrie Institute in Medical Genetics at Glasgow University in 1992. She is an Associate Professor of Human and Molecular Genetics in the Department of Biological Sciences and currently the Department Chair of Biological Sciences. She has published numerous papers in reputed journals and has been active in both scientific research and supervision of several graduate students in the areas of human genetics and molecular biology. Her main research interests are in the Genetic Association of Candidate Genes with Complex Traits, specifically Dyslipidemia and Subsequent Disorders. The methods applied include re-sequencing of genes involved in the lipid transport (*APO* gene family) and metabolism (*LPL*) in order to identify variants that may increase the risk to develop dyslipidemia.

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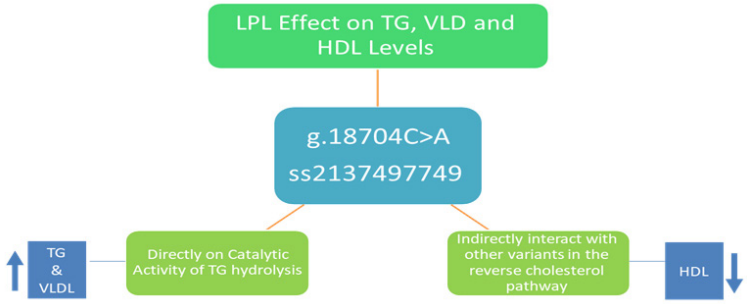

Figure 1: A schematic illustration of effect of the LPL novel variant