

0477 Mutation Scanning for *MC4R* gene in Saudi Arabia

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Melanocortin-4 Receptor (MC4R) is a seven transmembrane domain G-protein coupled receptor. MC4R is implicated in the central regulation of body weight. *MC4R* mutations constitute the most common monogenic form of human obesity, which appear 5% of severe obesity due to mutation at this locus. The prevalence of overweight and obesity in Saudi was 13.8% and 20.5% respectively. Up to date no obesity genetic study have been taken in Saudi. We have developed a high-throughput system, meltMADGE, which reduces scanning cost to a fraction of PCR cost (1/7) rather than a multiple of it (10-100x). MeltMADGE combines the properties of Microplate Array Diagonally compatible PAGE gels with are configuration of denaturing gradient gel electrophoresis, such that the independent (denaturing) variable is a DNA melting thermal ramp in time instead of a chemical (urea) gradient in space. Two heteroduplexes and two homoduplexes bands should resolve from a heterozygote amplicon. Throughput per worker per day is 40x96 well gels=4,000 amplicons, using two 2l tank staking 10-gels each for 2hr runs. Previously, we have screen *MC4R* gene in UK population and found two 'paucimorphisms' were identified (V103I in 27 subjects and -178A>C in 22 subjects). Anthropometric studies of these variants have the power to detect, for example, BMI effects as little as 0.5 units. Two rare variants were also identified, one previously described (T112M), one unknown (A87D) BMI of 31.5 in the latter might point to mild functional effect.