The Monogenic Forms of Obesity in Saudi Families

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Abstract:

Background: Obesity is a complex biological and hereditary disorder. Most of the monogenic changes that causing obesity discovered in samples of interrelated families and peoples, and other different races. In this present study we have tried to identify missing heritability in obesity by looking at extreme phenotypes that are likely to be enriched with rare variants. This will be improving the power of their discovery by identifying the loci that may reveal more rare variants. We employed the strategy of using "extreme" sub-groups of obese patients to identify known and novel loci for obesity in the population of Saudi Arabia.

Aims of study: To explore the genetics contribution in the progression of obesity in Saudi Arabia. Also, we determine monogenic mutations responsible for obesity among Saudi adults have BMI ≥ 30 kg/m² and children have BMI respectively above the 90th and 97th percentiles in consanguineous families.

Method: In this study we analyzed the samples from 8 Saudi families, each family has 9 individuals that are between healthy and obese individuals. We used Whole Exome Sequencing (WES) to screen for known monogenic and possibly novel obesity genes in multiplex Saudi consanguineous families. Deep statistical analysis was carried out by using manual filtration of variant VCF files and artificial intelligence software called Diploid (Moon). Candidate genes from our analysis were then validated using Sanger Sequencing.

Results: For the manual filtration analysis to 14 candidate genes, we do PCR for 7 genes results were negative, and there is a report for variants and got a list of genes becoming out from Diploid (Moon) artificial software for diagnosis of rare variants. The result indicates that list of rare genes and classification were associated with the phenotypic. The list of the rare genes, variants and candidate obesity genes is totally 35 genes for all families and 40 variants. The candidate genes are 19 genes had 28 variants. Overall, results show the positive between a novel and previously described mutations.

Conclusion: Our study confirmed that homozygous and heterozygous mutations is occur in candidate obesity genes of these families. The affected individuals have shown extreme obesity phenotype. Also, this study confirms that obesity is a polygenic disease that has strong interaction with environment.

Keywords: Consanguineous families, Syndromic of Obesity, Monogenic, Rare disease, Obesity, Bioinformatics, Artificial intelligence, Novel, Heterozygosity, Homozygosity.