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Background

Obesity arises from a complex interaction between genetic variance, environment, and lifestyle changes, and has become a major public health problem as a result of its increasing prevalence in most developed countries. Several genes have been implicated in obesity, namely ADRB1, ADRB2, ADRB3, BDNF, FTO; IGF2, IGF2R, LEP, LEPR, LRP2, MC1R; MC2R; MC3R; MC4R; NEGR1, NPY, NPY2R; NPY1R; NTRK2, PCSK1, POMC; SH2B1; SIM1; SLC6A14 SORCS1; UCP1; UCP2; UCP3. All these genes have mutations associated with monogenic obesity.

Aim

We aimed to investigate the presence of mutations in the mentioned genes in a Portuguese population with obesity using an enrichment method and all exome sequencing.

Methods

Thirty obese individual were included in the study. Inclusion criteria for obese subjects were body mass index >30 kg/m².

Genotyping of the 28 genes was conducted on buccal swab samples following DNA extraction with Qiagen DNA extraction kit.



The exome sequencing experiment was performed by the TruSight One[®] Sequencing Panel, with the NextSeq550, from Illumina.

Results

A total of 185 variable sites were detected, one deletion and 2 insertions, 142 as heterozygous. Two missense variants were detected for the first time, and both probably damaging according to polyphen prevision SORCS1 2491A>C, Thr831Pro, and LRP2 12385A>G Asn4129Asp. One substitution in 3rd nucleotide of exon 1 ADRB3 (1205+3A>G) was also detected for the first time, that can affect splicing. Two individuals were heterozygote for the MC4R V103I obesity risk allele, and two others to the POMC, 706C>G Arg236Gly susceptibility allele to obesity early-onset. Moreover a splice donor variation in intron 6-7 of UCP3 gene with unknown function was observed (824+1G>A).

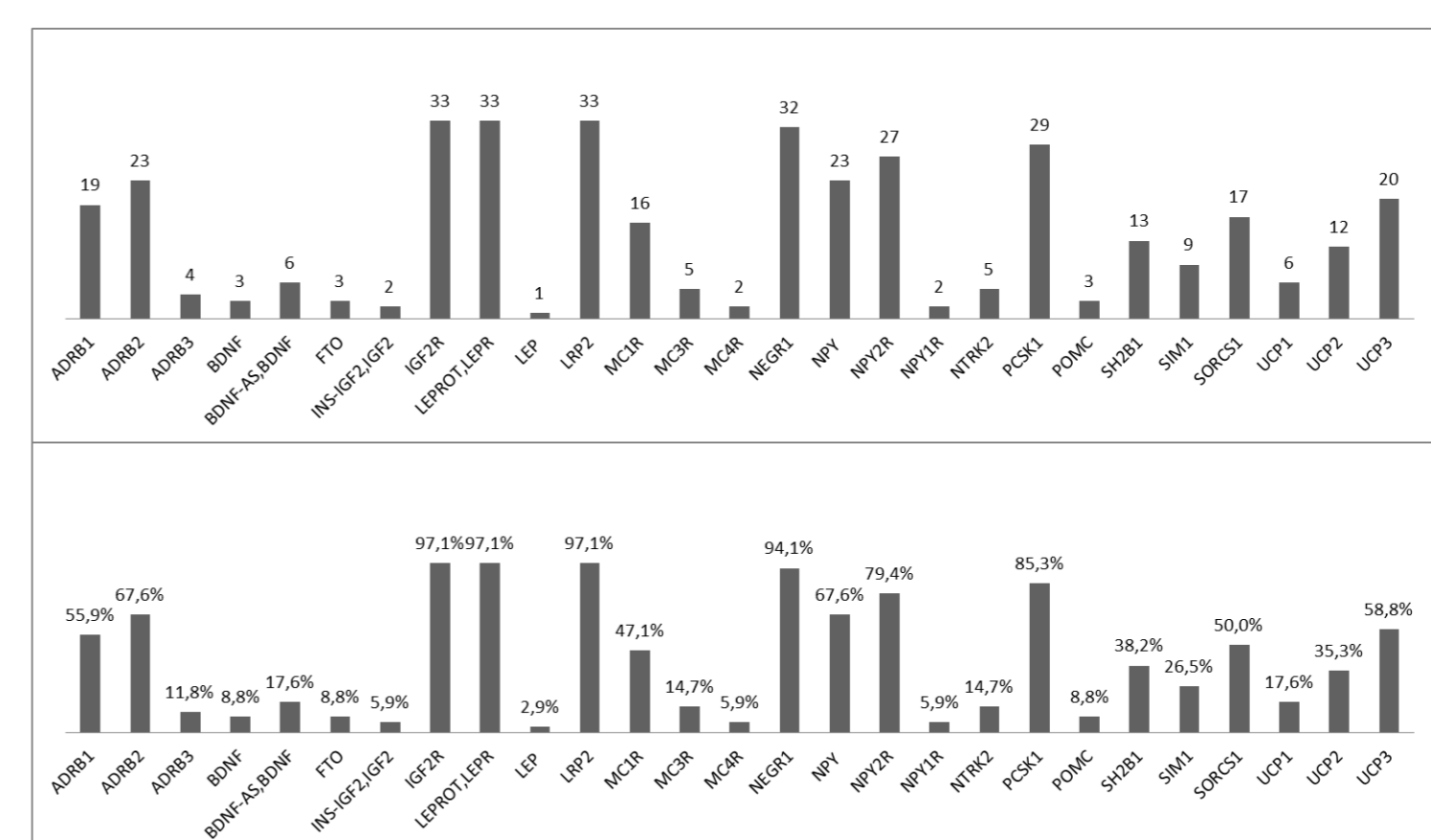


Figure - Number/Percent of samples with variants in each gene

Discussion

Presented data is useful for the clinical management of obesity. Molecular diagnosis of monogenic obesity is of supreme importance for both the patient and the society, as it can result in personalized medicine associated with a better life and it eventually saves health care spending. NGS methodologies are the most adapted methodologies that can give those results with fast and affordable costs.

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