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THE USE OF NEXT-GENERATION SEQUENCING IN THE STUDY OF MONOGENIC OBESITY

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Introduction:

Technological innovation opens the possibility for scientific discovery, especially in biology and medicine, which allows the development of different perspectives that can bring a new understanding regarding different pathologies. Technologies such as the Next-Generation Sequencing (NGS) allow us not only to decode the human genome but also to describe and identify gene polymorphisms that lead to the development of diseases, as it happens with monogenic obesity.

Objectives:

Identify new mutations associated with monogenic obesity

- DNA samples taken from 36 obese patients from Portugal
- Use NGS technology for DNA sequencing

Methodology:

From 36 obese individuals (BMI > 30 kg/m2) from Portugal, all patients from Curry Cabral Hospital, DNA was extracted from mouth epithelial cells (ExtractMe®, from BLIRT SA®) and then analysed in NGS equipment (Illumina NexTSeq550 with the kit TruSight One® from Illumina, Inc.) using a 24 gene panel associated with monogenic obesity:

Gene Panel:

ADRB1	ADRB2	ADRB3	BDNF	FTO
IGF2R	LEP	LEPR	LRP2	MC3R
MC4R	NEGR1	NPY	NPY1R	NPY2R
NTRK2	PCSK1	POMC	SH2B1	SIM1
SORCS1	UCP1	UCP2	UCP3	

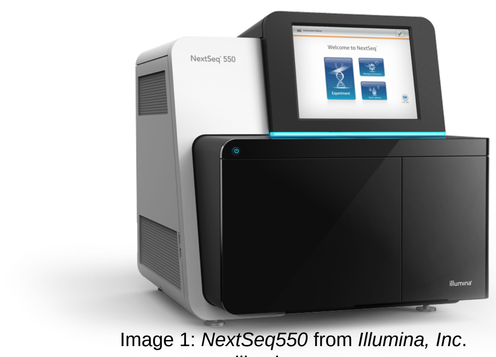

Image 1: *NextSeq550* from *Illumina, Inc*. source: www.illumina.com

Image 2: *kit TruSight One® Illumina, Inc*. Source: www.illumina.com

Results:

A total of 183 snv variants and 3 indels were identified, where 141 were heterozygous:

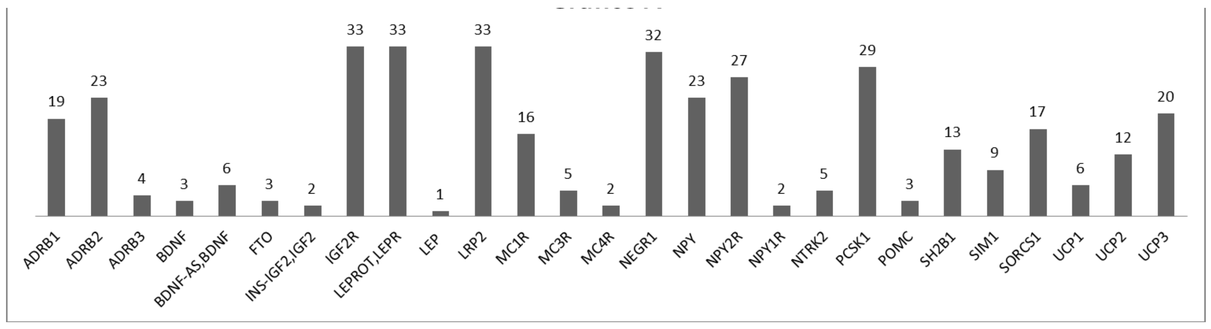

Figure 1 - Number of samples with variants in each gene.

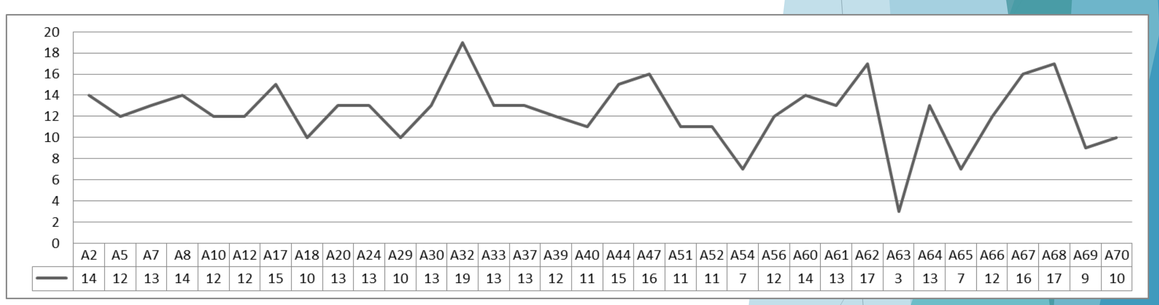

Figure 2 – Number of variants in each sample.

2 samples showed possibly damaging mutations, according to polyphen classification, for the POMC gene.

AND

2 nondescribed missense mutations were identified

- LRP2 12385A>G gene
- SORCS1 2491A>C gene

Conclusion:

NGS shows potential not only as a diagnostic tool in pathologies such as obesity, but also as a research tool by identifying undescribed and unclassified gene mutations. These methodologies can open new possibilities for the medical field not only in diagnosis but also in preventive medicine and new approaches in personalized treatments.