Distribution and Allele Frequency of the Gln3060x Variant Present in the ASPM Gene Associated to Microcephaly and Related Disorders in Puerto Rico

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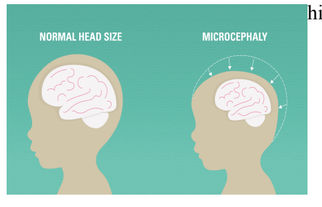
ABSTRACT

Microcephaly is a disorder that affects brain-development and results in infants with smaller heads. The ASPM gene is an important factor in mitotic spindle division during brain development and neurogenesis, meaning that a mutation in this gene could be the cause of neurological disorders of this sort. The Gln3060X variant was used, a missense variant of the ASPM gene previously associated with primary microcephaly. A general population study in Puerto Rican population was done using an array of 625 DNA samples from healthy individuals evenly divided by 30 municipalities around Puerto Rico. The variant was tested using the ViiA 7 Real Time PCR system, using TaqMan and the particular SNP (rs137852994) for the Gln3060X variant. Among these 625 samples, 62 mutated individuals were found; 61 heterocigotes (G/A) and 1 homocigote (A/A). In total, this study found an approximate 5% allelic frequency of the Gln3060X mutation in Puerto Rican population. Therefore, we can confirm the presence and prevalence of this mutation in Puerto Rico, mainly concentrated among North and East regions of the Island. Furthering the project, patients that suffer from Microcephaly and related conditions will be collected to participate in the project to prove allelic frequency in patients that suffer from them, meanwhile associating this variant with the development of Microcephaly and other conditions in Puerto Rico.

INTRODUCTION

Microcephaly is a condition affects brain-development, resulting in neonates with a smaller head-circumference of 3-4 SD below the mean depending on age and gender. The main focus of this research project is the condition **Primary Hereditary Microcephaly (MCPH)**, microcephaly discovered before birth that is commonly caused by genetic factors. Although many genes have been identified as risk factors for MCPH, mutations in the ASPM gene are known to be the biggest risk factor associated with primary microcephaly. The ASPM gene, located on chromosome 1, is known to play a very important role in mitotic division during neurogenesis in a developing brain. Therefore, a mutation in this gene could be the cause of this sort.



The variant studied is Gln3060X, a missense variant of the ASPM gene previously associated with primary microcephaly. This mutation affects the G/A alleles, being G the ancestral allele, while A is our allele of interest or mutated allele.

It can also be noted that in the 1000genome project conducted in 2015, this variant was identified in Puerto Rico with an approximate 1% allelic frequency.

OBJECTIVES

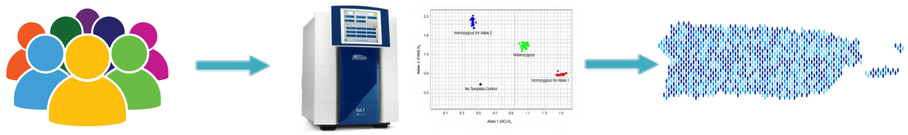
Confirm the existence of the Gln3060X variant in Puerto Rico

Establish allelic frequency of the Gln3060X variant in Puerto Rico.

Determine the difference between allelic frequency established in the 1000genome project and in this one.

Determine the distribution of the Gln3060X mutation in and around Puerto Rican regions.

METHODOLOGY



62X Samples
30 Municipalities
DNA repository
J. C. Martínez-Cruzado Lab

Genotyping by RT-PCR
Allelic Discrimination
TaqMan Assay for SNP rs137852994
Allele Frequencies

Distribution and Frequency in Puerto Rico
Distribution Maps
Map Viewer

RESULTS

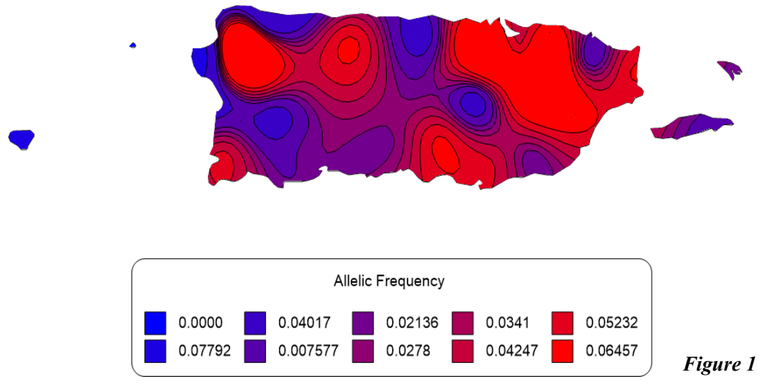


Figure 1

Table 1

Heterocigotes (G/A)	Homocigotes (A/A)	Total Mutated Allele Count
61 individuals	1	63

Table 2

ALLELIC FREQUENCY BY REGION					
North	South	East	West	Center	Total
0.07377	0.02521	0.05944	0.04422	0.0319	0.0504
7.37%	2.5%	5.9%	4.4%	3.2%	5.04%
1000genome project			**0.009615**		**≈1%**

PRELIMINARY CONCLUSIONS

The existence and prevalence of the Gln3060X mutation can be confirmed in Puerto Rican population.

This study shows a significant increment in frequency expected from the 1000genome project.

The variant can be mostly found in the North and East regions of Puerto Rico.

FUTURE PLANS

Repetition of mutated individuals

Adding of 2 West municipalities (San Sebastian/ Lares).

Patient recollection from individuals that suffer from any of the following:

- Microcephaly
- Recurring Convulsions
- Intellectual deficiency
- Autism
- Attention Deficit/Hyperactivity
- Hearing problems.

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Genetic Variants Associated to Risk Factors and Mendelian Conditions in Puerto Rico Research Group