DISTRIBUTION AND FREQUENCY OF THE VARIANT rs10738445 OF BNC2 GENE ASSOCIATED TO IDIOPATHIC SCOLIOSIS IN PUERTO RICO

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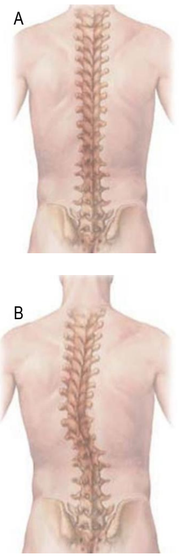
ABSTRACT

Idiopathic Scoliosis is a deformity of the spine, due to the growth of the person, shaped like an “C” or “S”; at a minimum Cobb angle of 10°. Recent studies have found a susceptibility allele (rs10738445) that increases the expression of the BNC2 gene and is expressed as a homozygous for CC. The BNC2 protein is present in the myoblasts and uterus, spinal cord, bone, and cartilage tissue. Thus, suggesting that there is a relationship between the increase in the gene and the etiology of Idiopathic Scoliosis. Other findings suggest a functional role for BNC2 in the development and progression of spinal deformity in patients with Idiopathic Scoliosis. The rs10738445 of the BNC2 gene appeared, in the worldwide genomic study 1000 Genomes Project, in Puerto Rico with a genotypic frequency of 53% for the homozygous CC. Using RT-PCR, 622 samples of the general population of Puerto Rico are going to be genotyped for the SNP rs10738445. In this study, we obtained that the genotype CC of rs10738445 has a population frequency of 5.9% in Puerto Rico, with a higher prevalence in the western area. We are planning to genotype patients diagnosed with Idiopathic Scoliosis and other spinal deformities for this variant in Puerto Rico.

INTRODUCTION

- Idiopathic scoliosis (IE) is a deformity in the spine that is only caused by the growth of the person and not by adjacent conditions.
- It has a curvature shape of “S” or “C”, with a minimum of 10° Cobb angle.



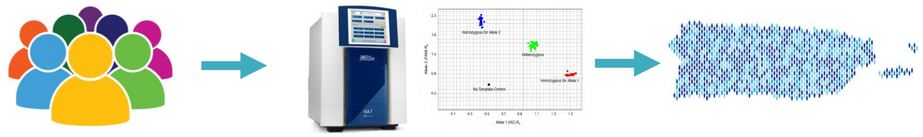
- The protein Basonuclin-2 (BNC2) can be found in myoblasts and uterus, spinal cord, bone, and cartilage tissue.
- Studies has showed an association between a variant of the BNC2 gene (rs10738445) and Idiopathic Scoliosis.
- The variant rs10738445 is an intronic variant, affecting intron 3 of the gene, and is located on chromosome 9 position 22.2.
- The variant rs10738445 will overexpress the protein, thus causing a severe body curvature.
- The ancestral allele of the variant is the allele A, but people who have the CC genotype (which is the mutation caused by the variant), will become a risk factor of developing a severe curvature.

Figure 1. Comparison between a normal spinal column (A) versus a spinal column with Idiopathic Scoliosis (B).

OBJECTIVES

- To confirm the presence of the genetic variant rs10738445 of BNC2 gene in Puerto Rico.
- Determine the distribution and frequencies of the genotypes of the variant rs10738445 of BNC2 gene in Puerto Rico.
- To compare statistical data from this study and the 1000Genome Project.

METHODOLOGY



622 Samples
30 Municipalities

DNA repository
J. C. Martínez-Cruzado Lab

Genotyping by RT-PCR
Allelic Discrimination

TaqMan Assay for SNP rs10738445
Allele Frequencies

Distribution and Frequency in Puerto Rico

Distribution Maps
Map Viewer

RESULTS

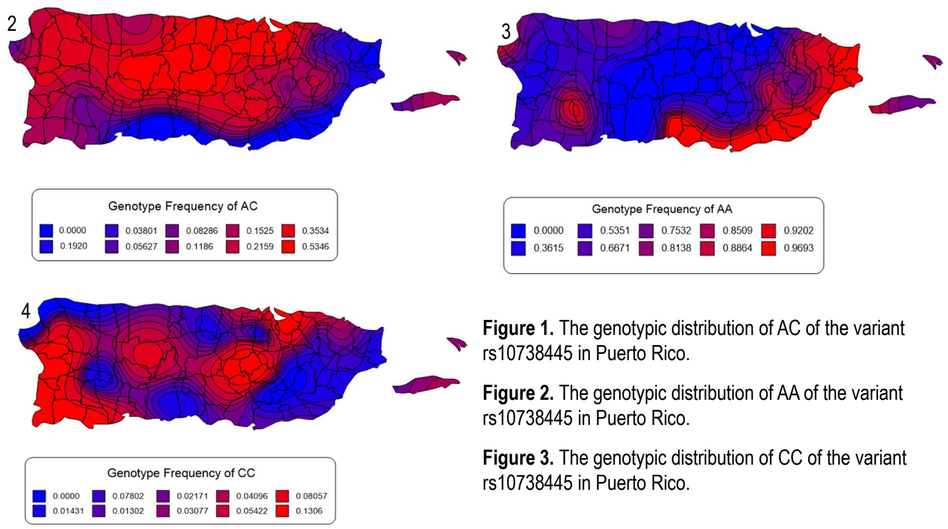


Figure 1. The genotypic distribution of AC of the variant rs10738445 in Puerto Rico.

Figure 2. The genotypic distribution of AA of the variant rs10738445 in Puerto Rico.

Figure 3. The genotypic distribution of CC of the variant rs10738445 in Puerto Rico.

Table 1. The genotypes frequencies of the variant rs10738445 in Puerto Rico.

	AA Frequency	AC Frequency	CC Frequency
West	0.638	0.268	**0.094**
North	0.500	0.451	0.049
Center	0.280	**0.634**	0.086
East	**0.885**	0.101	0.014
South	0.710	0.230	0.060
Puerto Rico	**0.627**	**0.314**	**0.059**
1000 Genome	**0.058**	**0.404**	**0.538**

PRELIMINARY CONCLUSIONS

- The genotype frequencies of the susceptibility allele rs10738445 of the BNC2 gene were successfully determined.
- We obtained that for the genotype CC of rs10738445 has a population frequency of 5.9% in Puerto Rico, with a higher prevalence in the western region.
- In contrast with the 1000 Genome Project, our study showed a lower genotypic frequency for the genotype CC in Puerto Rico. This difference could be explained by the sampling bias in the 1000 Genome Project (Figure 5).

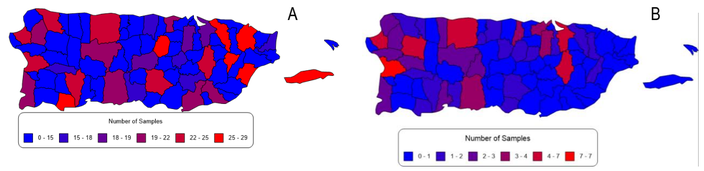


Figure 5. Municipalities sample distribution for our study and Puerto Rican in the 1000 Genomes Project. Our study sample distribution by municipality is shown in A (n= 622) and in B municipality distribution of Puerto Rican volunteers for the 1000 Genome Project until October 10, 2009 (n=77).

FUTURE PLANS

- Genotype patients diagnosed with Idiopathic Scoliosis in Puerto Rico in order to:
  - Determine the genotypes frequencies of the variant rs10734585
  - Determine a relationship between variant rs10738445 and Cobb angle
- Also, patients with other spinal deformities will be genotype, in order to confirm that the variant is exclusive to Idiopathic Scoliosis. This will include the following conditions:
  - Kyphosis
  - Lordosis
  - Spina Bifida
  - Others

ACKNOWLEDGEMENTS

Edwin G Ramírez Aponte

Dr. Juan Martínez Cruzado

Group of students that work on the *Study of Genetic Variants of Risk Factors and Mendelians Conditions in Puerto Rico*