

Identification of New Genetic Variants Associated With Coronary Artery Disease in African Americans

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Background and Hypothesis

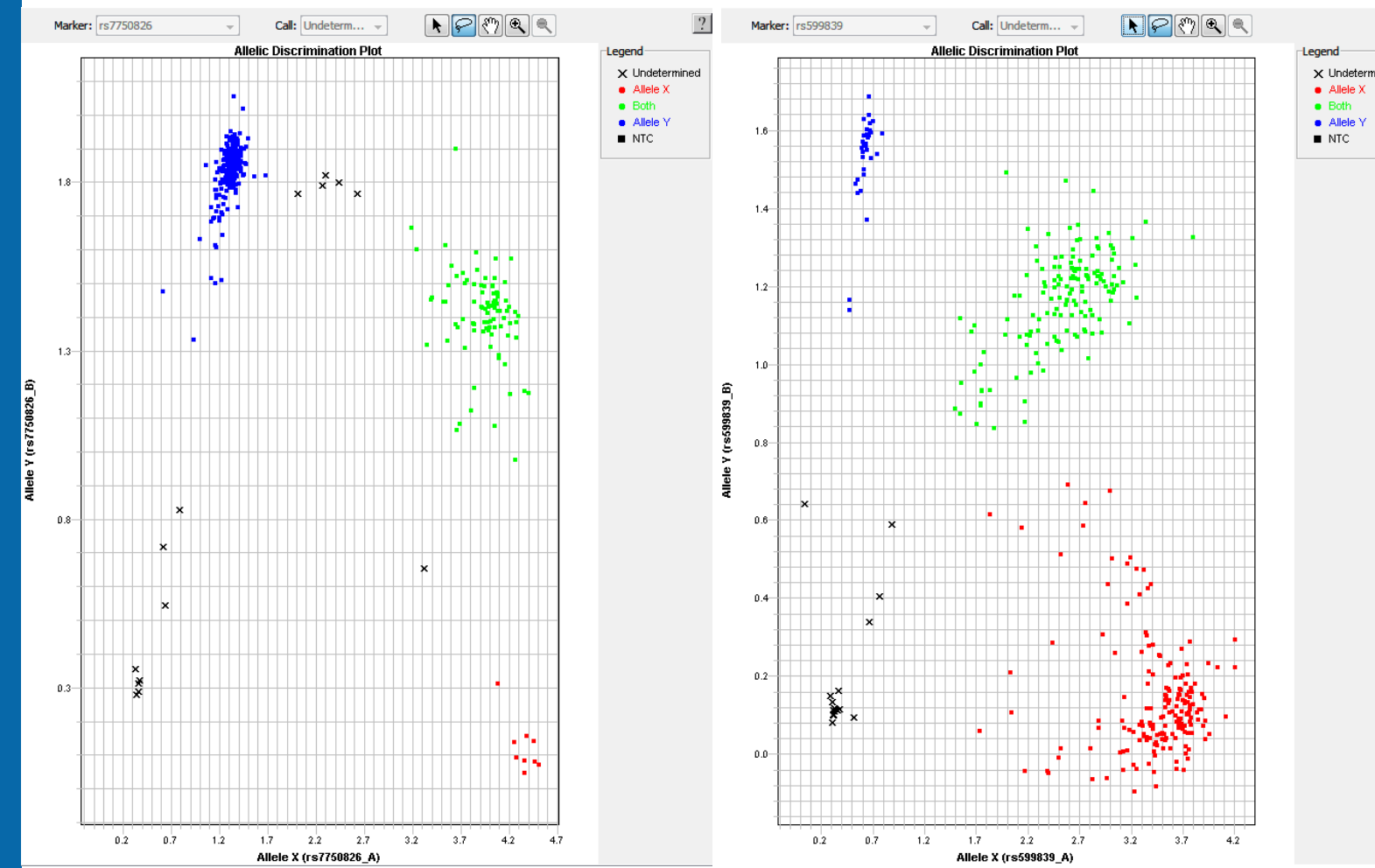
- Coronary artery disease (CAD) is the most common type of heart disease and leading cause of death, with heritability estimated at 50% to 60%.
- This suggests that a genetic variant is a potential risk factor of the disease
- We selected 5 single nucleotide polymorphisms (SNPs) based on previous association to CAD or pathologically related diseases such as stroke and atrial fibrillation (AF).
- Failure to replicate successful genome-wide association studies (GWAS) in European populations in African American populations led us to evaluate the association of SNPs formerly associated with stroke and AF to CAD using Taqman Assay.
- We hypothesized that some genes associated with CAD or CAD-related phenotypes in European samples may contribute to the risk of CAD in African Americans.

Methodology

- 5µL Polymerase Chain Reaction Mix:
 - 2x Taqman Master Mix
 - 40x Taqman Assay
 - DNA templates and water
- Dual 384-well PE 9700 systems
- Taqman Genotyping was done to analyze the genotype of the case and control samples.
- By running tests comparing the occurrence of each SNP in these samples, we determined the significance of our data.
- Statistical Analysis:
 - Hardy-Weinberg Equilibrium Test
 - Allelic association, 2 by 2 Chi-squared test
 - Genotypic analysis under 3 genetic models
 - Adjusted genotypic analysis under additive model
- PLINK was used to run these tests.

Data

Two Examples of Taqman Genotyping Cluster Plots



Summary of 5 SNPs

SNP ID	Gene/Locus	Alleles A/B	Case AA/AB/BB	Control AA/AB/BB	Missing (%)	P_{HWE}
rs599839	SORT1	A/G	51/191/231	83/285/380	0.06149	0.009279
rs3135506	APOA5	C/G	3/67/424	1/83/690	0.02537	0.7226
rs12646447	PTIX2	C/T	12/90/375	6/171/575	0.05534	0.08844
rs7750826	FOXF2	G/A	17/133/342	24/237/504	0.03382	0.6333
rs35033432	15q21.3	A/G	10/91/378	10/134/600	0.05995	0.4268

Result of Allelic Association of 5 SNPs With CAD

SNP ID	Minor	Freq (Case)	Freq (Control)	OR (95%CI)	P Value
rs599839	A	0.3047	0.1785	1.04	0.6659
rs12646447	C	0.1208	0.1210	1.37	0.05384
rs7750826	G	0.1798	0.1747	0.98	0.8717
rs3135506	C	0.0623	0.0673	0.89	0.2913
rs35022432	G	0.1083	0.0961	1.14	0.3366

There were no statistically significant P-values from the results of the allelic association Chi-squared test.

Results

Results of Genotypic Association of 5 SNPs With CAD

SNP ID	Model	Case	Control	Chi Sq.	DF	P-value
rs599839	Add	51/191/231	83/285/380	0.6356	2	0.7277
	Dom	242/231	368/380	0.4475	1	0.5035
	Rec	51/422	83/665	0.02924	1	0.8642
rs12646447	Add	12/90/375	6/171/575	8.116	2	0.0173
	Dom	102/375	177/575	0.7714	1	0.3798
	Rec	12/465	6/746	5.968	1	0.0146
rs7750826	Add	17/133/342	24/237/504	2.264	2	0.3223
	Dom	150/342	261/504	1.793	1	0.1806
	Rec	17/475	24/741	0.09598	1	0.7567
rs3135506	Add	3/67/424	1/83/690	NA	NA	NA
	Dom	70/424	84/690	NA	NA	NA
	Rec	3/491	1/773	NA	NA	NA
rs35022432	Add	10/91/378	10/134/600	1.249	2	0.5356
	Dom	101/378	144/600	0.5449	1	0.4604
	Rec	10/469	10/734	1.002	1	0.3169

- SNP 12646447 showed statistically significant P-values in the Additive ($P = .0173$) and Recessive ($P = .0146$) models, as well as an Odd Ratio value of 1.37.

Conclusions

- We found that SNP rs12646447 in gene PTIX2 contributed significantly to the risk of CAD in African Americans.
- Our results suggest a pleiotropy effect of gene PTIX2 on multiple diseases. Gene PTIX2 might be involved in the shared pathway that leads to increased risk of stroke, AF, and CAD.

Recommendations

- In future studies, replication across independent/larger African American samples should be done to confirm the results of this study on the gene PTIX2.
- More covariates should be adjusted for using the logistic regression model.

References

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