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

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## Background and Hypothesis

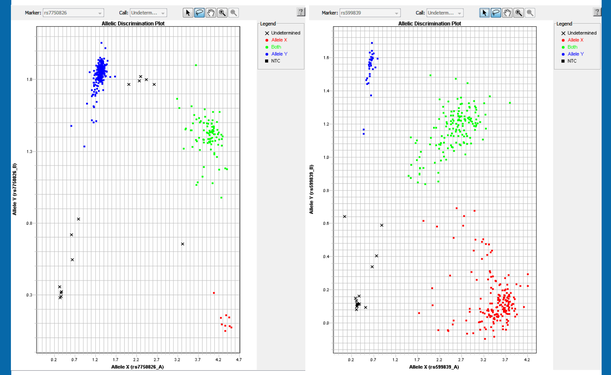
- Coronary artery disease (CAD) is the most common type of heart disease and leading cause of death, with heritability estimated at 50% to 60%.
- This suggests that a genetic variant is a potential risk factor of the disease
- We selected 5 single nucleotide polymorphisms (SNPs) based on previous association 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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