INTRODUCTION

Men diagnosed with metastatic prostate cancer (PCA) have 71% lower 5-year survival rate compared to men with local/regional disease (29% versus 100%). Once the cancer spreads to other organs, the disease becomes less responsive to conventional treatment strategies. Moreover, there is a 25% disease recurrence rate among PCA patients who undergo a radical prostatectomy.

Consequently, new biomarkers are needed to: distinguish between responsive to conventional treatment strategies, and whole body homeostasis. Failure to undergo this process permits survival of transformed cells, leading to genetic alteration, genomic instability, and a more severe cancer phenotype.

Several studies have evaluated the link between apoptosis-related sequence variants and cancer outcomes. Apoptosis (aka, programmed cell death) is a biological process that leads to genetic alteration, genomic instability, and a more severe cancer phenotype.

HYPOTHESIS

Apoptosis-signing Sequence Variants (SNPs) in Apoptosis-related Genes may be related to PCA susceptibility and aggressive disease (29% versus 100%).

RESEARCH OBJECTIVE

Evaluate the joint modifying effects of 10,878 single nucleotide polymorphism (SNP) pairs in relation to PCA susceptibility and aggressive disease among European-American men.

METHODS

- Assess differences in the genotype frequency comparing cases and controls using Chi-square and Fisher’s Exact Test
- Logistic Regression Analysis
- Calculated risk estimates and corresponding 95% Confidence Intervals
- Adjusted for potential confounders [Prostate-Specific Antigen (PSA) and family history of prostate cancer]
- HWE p-value >0.05, genotype call rate ≥95%
- PLINK & Statistical Analysis Software (SAS) 9.4
- Individual Apoptosis-related Sequence Variants on Prostate Cancer among PLCO study participants.

RESULTS

Approximately 1% of the apoptosis SNP pairs were significantly associated with PCA risk (n = 121) and aggressive disease (n = 117) under the overall dominant, recessive and additive genetic models using PLINK & SAS.

CONCLUSIONS

- Identified genetic markers may help to improve or replace prostate cancer prognostication and treatment strategies.
- Additional studies are needed to assess whether our 4 apoptosis-related SNP pairs are predictive of aggressive PCA on the multiplicative scale. For example, the MAPK14-BRE SNP was significantly associated with aggressive prostate cancer even after adjusting for confounders and multiple comparison bias.
- Inheritance of at least 3 minor alleles detected within the CASP5-TNFRSF1B axes was linked to a 1.8 fold increase in the risk of developing aggressive prostate cancer.

ACKNOWLEDGEMENTS

- Additional studies are needed to assess whether our 4 apoptosis-related SNP pairs are predictive of aggressive disease above and beyond standard clinic-pathological parameters.
- Validated genetic markers may help to improve or replace prostate cancer prognostic and treatment strategies.
- These research findings may help to identify new genetic signatures beyond standard clinic-pathological parameters.

STUDY DESIGN

- Cancer Genetics & Markers of Susceptibility (CGEMS) study
- Genome wide association study (GWAS) database
- Access SNP data from CGEMS study period
- Phylogenetic analysis
- Analyzed >10,878 pair-wise interactions
- All p-values were adjusted for confounders and multiple comparison bias.

FUTURE DIRECTIONS

- These research findings may help to identify new genetic signatures beyond standard clinic-pathological parameters.
- Validated genetic markers may help to improve or replace prostate cancer prognostic and treatment strategies.
- Additional studies are needed to assess whether our 4 apoptosis-related SNP pairs are predictive of aggressive disease above and beyond standard clinic-pathological parameters.

CONCLUSION