

# Ancestry informative eQTLs in prostate tumor tissue: implications for observed cancer disparities

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## Introduction and Objectives

African-American men (AAM) are 1.6 times more likely to be diagnosed and 2.4 times more likely to die of prostate cancer (PCa) than European-American men (EAM). Most biomarker research is performed utilizing samples from EAM, and, due to a dearth of data in AAM, it is largely unclear to what extent molecular correlates of PCa initiation and outcomes may be race-specific. This project explores genome-wide differences by race in the distribution of expression quantitative trait loci (eQTLs) in PCa tumor tissues, with specific analytic attention given to SNPs that are known to diverge in ancestral populations.

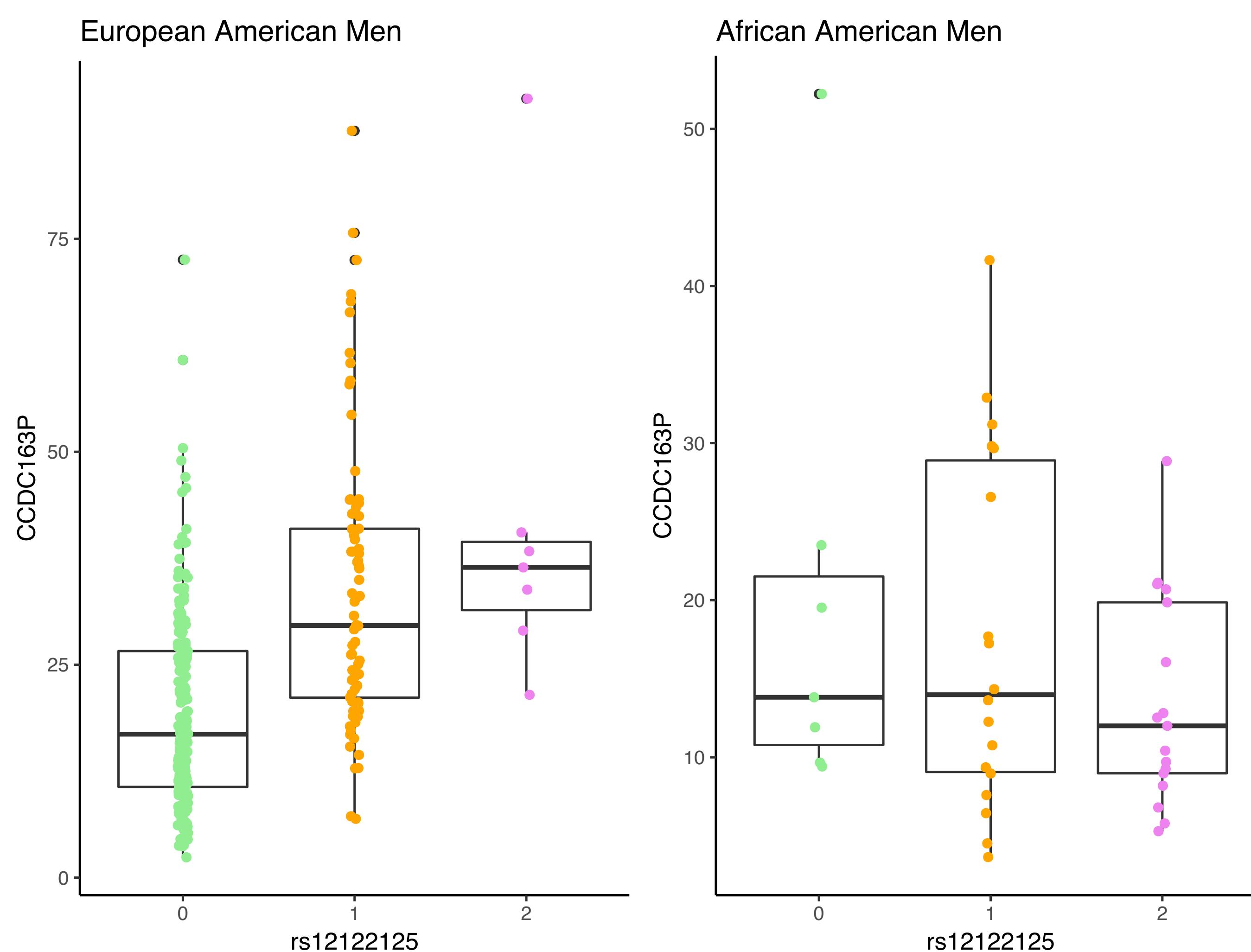


Figure 1: In EAM, ancestry informative SNP rs12122125 is significantly associated with CCDC163P expression, making it an eQTL in EAM, but not preserved in AAM.

## TCGA Data

- Cohort of 332 primary prostate cancer patients with high quality RNA expression and genotype data
- RNA-seq expression was obtained from prostate tumor tissue
- Germline genotypes were obtained from blood or normal prostate tissue

## Methods

### Admixture:

- Ancestry estimates for 3 ancestral populations calculated from genotypes using Admixture software
- Dominant population (>50%) was used to determine race

### Ancestry Informative Markers:

- 2,076 SNPs
- Based on variation in minor allele frequencies between AAM and EAM

### eQTL Analysis:

- Additive model based on tumor gene expression and number of minor alleles for each genotype
- 42 million association tests
- Bonferroni-adjusted p-value threshold of  $1.17^{-8}$

## Results

- 43 AAM and 282 EAM
- 39 eQTLs in AAM and 40 in EAM
- Multiple SNPs on Chromosome X were part of eQTLs in both AAM and EAM, however only one gene on Chromosome X was part of an eQTLs in EAM
- Both AAM and EAM had eQTLs with multiple genes in the KRTAP (Keratin associated proteins) family
- No overlap between any of the genes or SNPs involved in the AAM and EAM eQTLs

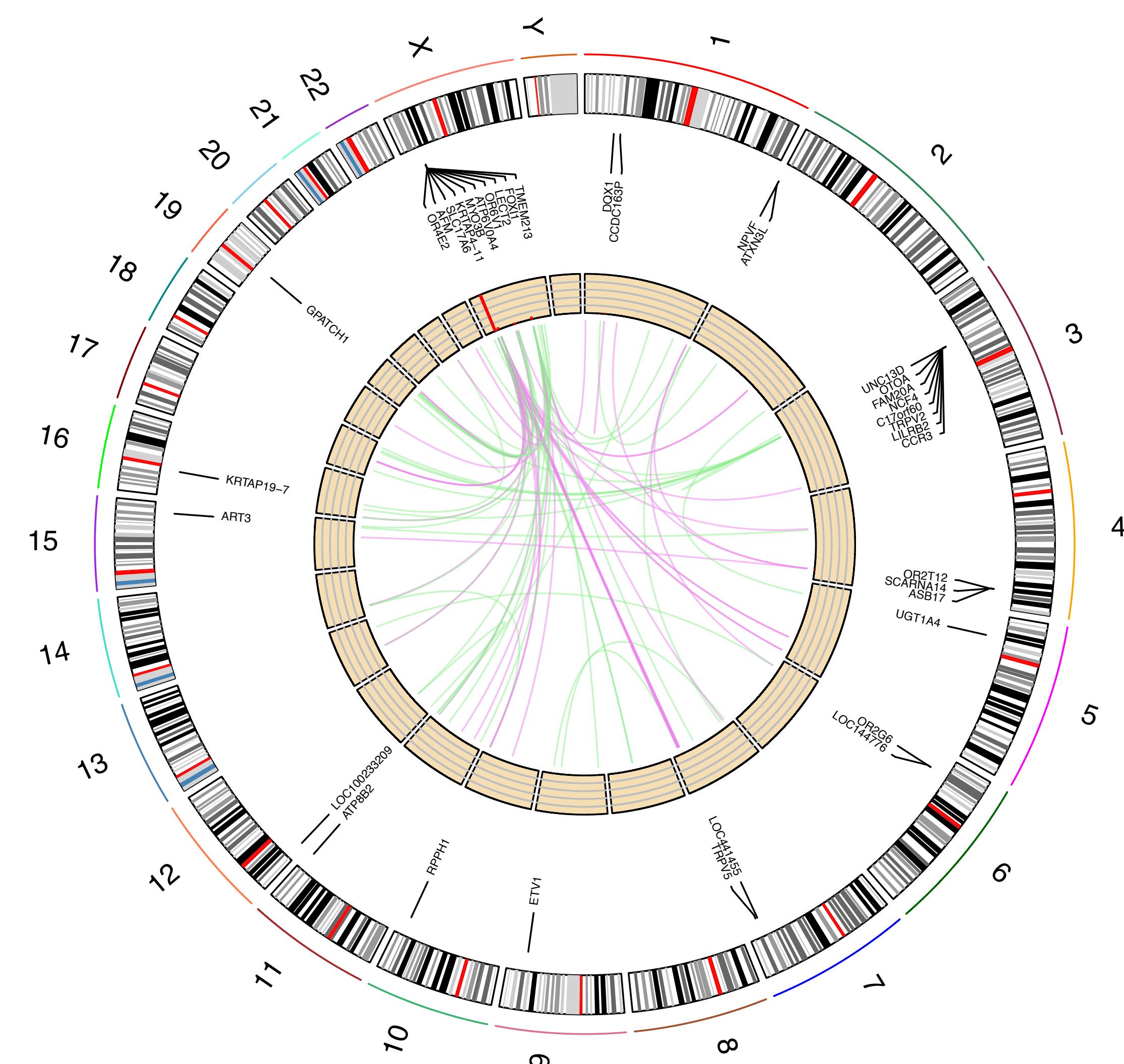


Figure 2: Circos plot of significant eQTLs in each cohort. Those from AAM are in green and EAM are in pink.

## Conclusions

- Divergent SNP-gene relationships in prostate tumor tissue exist between EAM and AAM, providing further evidence that the biologic properties of prostate tumors may differ by race
- Future work will examine the relationship between race-specific eQTLs and observed PCa outcomes
- Validation in additional cohorts, particularly GTEx, is planned