Specific racial CYP2R1 correlation with circadian rhythm genes in prostate adenocarcinoma

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Abstract

Introduction: Vitamin D in its hormonal form, 1α,25-dihydroxyvitamin D3 (1,25(OH)2D3) binds to the vitamin D receptor (VDR) to regulate genes, for example, in skeletal mineralization. However, it also has other potent biological functions in regulating apoptosis, proliferation, and inflammation. In carcinogenesis, 1,25(OH)2D3 may be exploited to regulate these crucial pathways. It is also clear that a frequent cancer disparity exists amongst African American (AA) men with prostate cancer compared to European Americans (EA). AA men show a higher incidence rate and two to three times increased risk of mortality than EA counterparts. Various groups have suggested that 1,25(OH)2D3 levels and/or VDR functions are risk factors linked with increased prostate cancer incidence in AA men. Incidentally, reports showed that VD plays a crucial role in regulating circadian rhythm (CR). There is, therefore, a need to understand and evaluate 1,25(OH)2D3-dependent CR regulation and the association with racial disparity in prostate cancer. This study aimed to determine if there are differentially expressed VD metabolic enzymes in AA and EA and evaluate if the differential expression correlates with CR genes.

Methods: The Cancer Genome Atlas Research Network (TCGA), 2015 database was queried for expression of VD metabolizing enzymes and CR genes. The search was carried out on prostate adenocarcinoma expressions of AA and EA. VD metabolizing enzymes queried are CYP2R1, CYP24A1, CYP27B1, CYP27A1, while CR genes queried include ARNTL, CLOCK, CRY1, CRY2, CSNK1E, NPAS2, PER1, PER2, PER3, and TIMELESS. Prostate adenocarcinoma racial differential expressions of AA and EA were evaluated, and a correlation study was done using the Pearson correlation.

Results: VD metabolic enzyme, CYP2R1, and CR gene, ARNTL were significantly upregulated in AA compared to EA counterparts. Although CYPR1 correlates negatively with CLOCK, CRY2, and PER3 in both races, CYPR1 specifically showed a positive correlation with CR gene CRY1 in EA and negative correlations with CR genes NPAS2 and CSNK1E in AA. However, a significant correlation between CYP2R1 and ARNTL in EA and AA was not observed.

Conclusion: The data suggest a relationship between racial influence and prostate cancer associated with VD metabolism and CR regulation. Hence, it is crucial to elucidate CYP2R1 regulation in prostate cancer related to VD levels and CR regulation, especially with a focus on racial disparities.