

Transcriptome expression of vitamin D genes in tumors and risk of lethal prostate cancer

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Introduction

- Prostate cancer has the highest incidence of all cancers in men in the United States.
- Vitamin D has been found to have several anticancer properties in other cancer sites, including cell cycle arrest, apoptosis, and inhibition of angiogenesis.
- In this study, we investigated:
 - the burden of prostate cancer in the United States
 - the relationship between expression of 11 genes in the vitamin D pathway and risk of lethal prostate cancer
 - somatic genetic alterations in 11 vitamin D-related genes in prostate tumors

Methods

- To describe the burden of prostate cancer in the United States, we leveraged the IARC's Global Cancer Observatory, the NIH's State Cancer Profile, and the SEER Program's databases.
- Using data from 251 patients in the Health Professionals' Follow-up Study (HPFS), we calculated odds ratios for the association between mRNA expression of 11 vitamin D-related genes and lethal prostate cancer.
- We examined data from the Cancer Genome Atlas (n=290) in cBioPortal to study somatic genetic alterations in 11 vitamin D-related genes in prostate tumors by Gleason score.

Results

Race	Incidence (per 100,000)
All Races	109.8
White	102.3
Black	175.2
Asian/Pacific Islander	56.7
American Indian/Alaska Native	54.6
Hispanic	92.0
Non-Hispanic	112.6

Figure 1. Prostate Cancer Incidence by Race (per 100,000)

Race	Mortality (per 100,000)
All Races	19.0
White	17.9
Black	37.4
Asian/Pacific Islander	8.8
American Indian/Alaska Native	18.5
Hispanic	15.6
Non-Hispanic	19.3

Figure 2. Prostate Cancer Mortality by Race (per 100,000)

Gene	Odds Ratio	Lower 95% CI	Upper 95% CI
VDR	1.14	0.67	1.93
RXRA	0.96	0.57	1.63
GC*	0.59	0.35	1.01
DHCR7	0.88	0.52	1.48
CYP27A1*	1.45	0.86	2.46
CYP2R1	0.85	0.51	1.45
CYP27B1	1.06	0.63	1.80
CYP24A1	1.04	0.61	1.77
LRP2	0.69	0.41	1.17
CUBN	1.23	0.72	2.08
CASR*	0.58	0.34	0.99

*indicates significance

Figure 4. Odds Ratios (OR) and 95% Confidence Intervals (CI) for the Association Between mRNA Expression for 11 Vitamin D Genes and Risk of Lethal Prostate Cancer



Figure 5. Somatic Changes in Prostate Cancer Tumors Associated With Altered Gene Expression for Vitamin D Pathway Genes

Characteristic	Category	Count	Frequency
Year of Diagnosis	1980-1989	22	8.76%
	1990-1999	205	81.67%
	2000-2009	24	9.56%
BMI Category	<25 kg/m ²	124	49.40%
	≥25 kg/m ²	127	50.60%
Gleason Grade	Gleason 2-6	25	9.96%
	Gleason 7	163	64.94%
	Gleason 8-10	63	25.10%
TNM Stage	T1/T2	202	80.48%
	T3	23	9.16%
	T4/N1/M1	17	6.77%
	missing	9	3.59%
Lethality	Non-lethal	167	66.53%
	Lethal	84	33.47%

Figure 3. Demographic Characteristics of Men Diagnosed with Prostate Cancer in Health Professionals Follow-Up Study

Conclusion

- Somatic changes related to mRNA expression of certain genes in the Vitamin D pathway may be associated with risk of lethal prostate cancer.
- Understanding the interaction of genes in the vitamin D pathway with lethal prostate cancer may help inform prevention and treatment strategies.