



Vitamin D metabolism and Th17-related parameters in patients with colorectal cancer

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Introduction

➤ In addition to its role in phosphocalcic metabolism, the vitamin D (vitD) seems to have **anti-carcinogenic** effects, particularly in **colorectal cancer (CRC)**.

➤ The active metabolite of vitD [1,25(OH)₂D₃], converted by the enzyme **CYP27B1**, inhibits proliferation and promotes differentiation of CRC cells which express **vitamin D receptor (VDR)** via the regulation of a high number of genes.

➤ The vitD metabolism seems also to regulate **inflammatory processes** involved in **CRC development and progression**, including the **CD4⁺ T cells** differentiation and the **cytokines production** through the regulation of **genes** implicated in these processes.

Objective

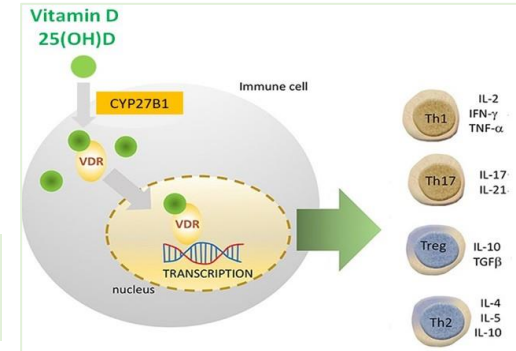
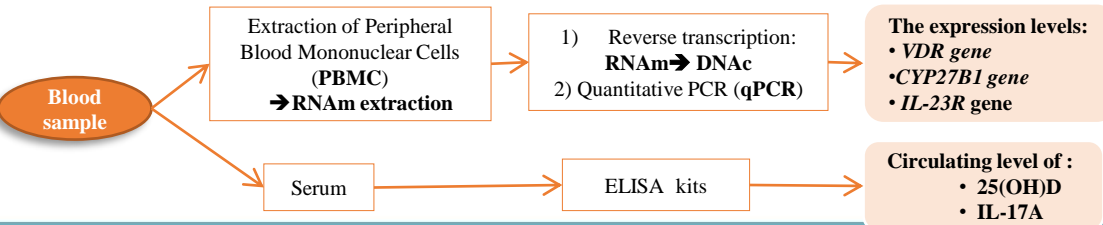
This study investigated in **Tunisian CRC patients in comparison with controls**:

✓ **VitD related parameters** : Circulating level of VitD (**25(OH)D**) ; Gene expression levels of **VDR** and **CYP27B1**

✓ **Th17-related parameters**: Circulating level of **IL-17A** ; Gene expression level of Interleukin 23 receptor (**IL-23R**)

Patients and Methods

➤ **Case-control study** : **32 untreated CRC patients** (newly diagnosed) + **32 healthy controls**



Cyprian F *et al.* Immunomodulatory Effects of Vitamin D .Front Immunol. 2019

Table 1: Choice of primer sequences

Gene	Primer sequences used in qPCR	Tm	Transcript length(pb)
VDR	F : ATCTGCATCGTCTCCCCAGAT	60.76	100
	R AGCGGATGTACGTCTGCAGTG	62.73	
CYP27B1	F : GTCCAGACAGCACTCCACTC	60.04	137
	R:ACCACAGGGTACAGTCTTAGC	59.10	
IL-23R	F : AAAAGGTACTGGCAGCCTTG	58.38	107
	R : AGCCGAGAATTCATGTGTC	57.87	

Results

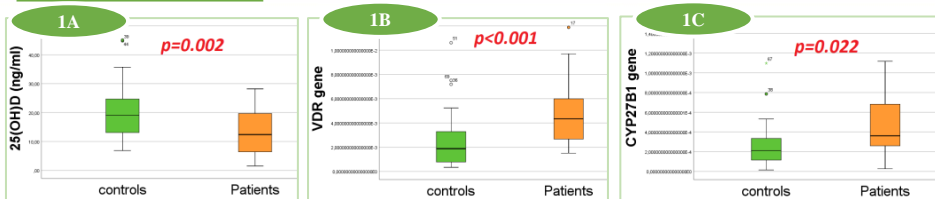


Figure 1: Distribution of Vit D related parameters :

25(OH)D Circulating level (1A) ; VDR gene expression (1B); CYP27B1 gene expression (1C)

A significant association between :
VitD deficiency (25(OH)D < 20 ng/mL)
and risk of CRC
(OR=3.18 ;IC 95% = 1.13 et 8.93 ;
 $p=0.025$).

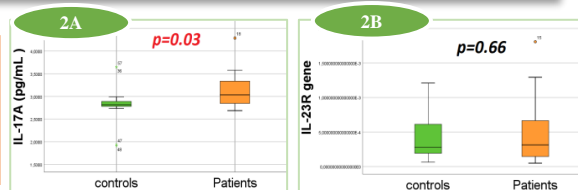


Figure 2: Distribution of Th17-related parameters:

IL-17A Circulating level (2A) ; IL-23R gene expression (2B)

Table 2: Correlation study of the studied the parameters

		25(OH)D	VDR	CYP27B1	IL-23R
VDR	Correlation	-0.15	-	0.29	0.10
	P value	0.2	-	0.01	0.41
CYP27B1	Correlation	0.06	0.29	-	0.43
	P value	0.61	0.01	-	<0.001
IL-23R	Correlation	0.21	0.01	0.43	-
	P value	0.08	0.41	<0.001	-
IL-17A	Correlation	-0.34	0.38	0.33	-0.16
	P value	0.03	0.02	0.04	0.34



Figure 3: Correlation between :

25(OH)D and IL17-A Circulating levels(3A); VDR gene expression and IL17-A circulating level (3B)

Discussion

- VitD is reported to have several chemopreventive effects on CRC including **direct anti-tumor mechanisms**, the effects on the **immune system**, and **gut microbiota modulation** (E.Rinninella *et al.*2021).
- The high expression of the VDR and CYP27B1 genes in patients may be explained by **the activation of CD4+ and CD8+ T cells** (M.Bendix *et al.*2015).
- Regarding **Th17 axis**, the elevation of its parameters (IL17A levels + IL23R gene expression) in patients with CRC seems to be related to **the inflammatory process** in the tumor microenvironment (N.West *et al.*2015).
- In agreement with our results, Bai Chen *et al.* found that decreased 25(OH)D level in CRC correlated with increased IL-17 level and Th17 cell ratio in peripheral blood (Bai Chen *et al.*2022).
- Our results are also in line with the findings of an experimental study which suggested that **1,25(OH)₂D₃ downregulates IL-17A expression in T cells** (S.Joshi *et al.*2011).

Conclusion

- The **vitD**, by binding to its receptor (**VDR**), seems to regulate the expression of a high number of genes involved in CRC cell proliferation as well as T helper cell differentiation.
- Further clinical studies are required to confirm the close interplay between vitD, anti-tumor immunity, and CRC, suggesting a possible role of **vitD** as a potential agent in CRC prevention and therapy.