Poster nr. 7

Vitamin D receptor expression in cutaneous melanoma tissue

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Background and Aims

Vitamin D (VD) has anticancer properties, which is mediated by the vitamin D receptor (VDR). A reduction of the VDR expression is proposed as a negative prognostic marker, since reduced expression is observed in cutaneous melanoma (CM) in comparison to normal skin and melanocytic nevi (1). Limited research is done to explore genetic factors influencing VDR expression in CM tissue.
The aim of the study is *to* investigate a correlation of genetic variants of *VDR* with VDR expression (nuclear and cytoplasmic) in primary CM tissue and to assess the prognostic significance of VDR by correlating its expression with pathology of the primary tumor.

Methods

In primary CM tissue of a prospectively recruited cohort of 407 CM patients, we determined VDR expression both in the nucleus and in the cytoplasma by semi-quantitative assessment using histochemistry. Scoring was expressed in percentage and histoscore (H-score). Thirteen *VDR* single nucleotide polymorphisms (SNPs) were genotyped using TaqMan. VDR expression was correlated with *VDR* SNPs, and pathology parameters of primary CM tissue in univariate analyses.

Results

A statistical significant correlation between the absence of mitosis and increased nuclear VDR expression was found (p-value: 0.0023;KW-Test). For perineural invasion a statistically significant association with decreased nuclear VDR expression was established (p-value 0.0358; KW-Test) (Table 1) . In addition we found a negative correlation between nuclear and cytoplasmic VDR expression and Clark level, Breslow thickness and TNM staging, but the results were statistically not significant (results not shown).

Table 1 Correlation of VDR expression with pathology of CM tissue

	VDR % nucleus		VDR % cytoplasm		VDR H score	
Mitosis	*n*	*Median (Q1, Q3)*	*n*	*Median (Q1, Q3)*	*n*	*Median (Q1, Q3)*
No presence	21	70 (40;90)	21	100 (70;100)	21	100 (85;130)
Presence	251	35 (15;70)	252	80 (30;100)	251	95 (30;130)
Kruskal-Wallis Test	**p= 0.0023**		p= 0.0637		p= 0.2886	
Perineural invasion	*n*	*Median (Q1, Q3)*	*n*	*Median (Q1, Q3)*	*n*	*Median (Q1, Q3)*
No presence	96	40 (20;70)	97	80 (35;100)	96	90 (40;120)
Presence	6	5 (5;30)	6	20 (10;60)	6	25 (10;60)
Kruskal-Wallis Test	**p= 0.0358**		p= 0.0631		p= 0.0796	

Linear regression analysis of thirteen *VDR* SNPs with VDR expression showed a significant association of 2 SNPs with VDR protein expression in the cytoplasm. We indeed found a significant association between SNP rs1544410 (Bsm1) and cytoplasmic VDR expression, expressed as percentage (p = 0.014) with the A allele being associated with reduced cytoplasmic VDR expression. For SNP rs2228570 (Fok1) presence of the A allele was associated with a higher expression of the VDR in the cytoplasm (p = 0.001), see Table 2 In contrast to the cytoplasmatic expression, no statistically significant association between the *VDR* SNPs and nuclear VDR expression was found.

Table 2 Correlation of VDR SNPS with cytoplasmatic VDR expression

SNP	Reference Allele	N	BETA	SE	L95U	U95	P-value
Rs1544410 (Bsm1)	A	57	-3,11	4,01	-10,97	4,74	**0.014**
Rs2228570 (Fok1)	A	220	11,39	3,47	4,60	18,18	**0.001**

Conclusion

Genetic variants of the VDR have an influence on the VDR expression in CM tissue.

- The A allele of the genetic *VDR* polymorphism Fok1 was associated with a higher expression of the VDR in the cytoplasm
- The A allele for the genetic *VDR* polymorphism Bsm1 was associated with a reduced cytoplasmatic VDR expression

This study also indicates a prognostic property of VDR in CM

- High mitotic rate is correlated with a reduced nuclear VDR expression

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