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Abstract 4323: 1,25-Dihydroxyvitamin D3 inhibits oral squamous cell carcinoma cell growth via microRNA regulation

Heba Said Ismail Hussein, Wei Wang, Liang Shan, Karl Thompson, Kareem Washington, Gihane Madkour, and Xinbin Gu

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Article

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Abstract

Objective: Oral squamous cell carcinomas (OSCC) is one of top ten cancers lead to death in USA. This study focused on the impacts of 1,25-dihydroxyvitamin D3 (1,25(OH)₂D3) treatment on the inhibition of OSCC growth *in vitro* and the alteration of microRNA (miRNA) expression profile by the treatment.

Materials and Methods: 1,25(OH)₂D3-associated apoptosis, cell cycle arrest, and proliferative effect in cultured OSCC cells were assessed using flow cytometry and western blotting methods. miRNA expression profiles were measured using nanoString Sprint Profiler and the Nanostring human miRNA panel. More miRNAs functional pathways were retrieved through bioinformatics using Qiagen IPA system.

Results: 1,25(OH)₂D3 was found to inhibit the growth of human JHU-22 OSCC cells in a dose-dependent manner with IC₅₀ of 1.56 x 10⁻⁶ M. High levels of apoptotic cells and related biomarkers were obtained when the cells were treated with 1,25(OH)₂D3. Over 20 miRNAs were upregulated and 23 downregulated by more than two folds, in 1,25(OH)₂D3 treated versus untreated JHU-22 cells. Bioinformatics analysis showed molecular functions of most dysregulated miRNAs. For example, MiR-125b-5p upregulated caspases number 2, 6, 7 in addition to upregulating apoptosis facilitator like BCL-2, BIM, and AIF.

Conclusion: Our data suggested that 1,25(OH)₂D₃ function as a OSCC inhibitor is through regulating miRNA expression profile and miRNA function directly or indirectly. 1,25(OH)₂D₃ has potential to be an anticancer agent for OSCC prevention and treatment.

miRNA	Control (C9)	Vitamin D (D9)	C9/D9
hsa-miR-624-3p	8	28	3.5
hsa-miR-521	10	27	2.7
hsa-miR-221-5p	11	29	2.64
hsa-miR-1301-3p	7	18	2.57
hsa-miR-520a-3p	8	20	2.5
hsa-miR-153-3p	12	28	2.33
hsa-miR-122-5p	16	37	2.31
hsa-miR-1206	15	34	2.27
hsa-miR-125b-5p	686	1547	2.26
hsa-miR-450b-3p	4	9	2.25
hsa-miR-613	21	9	-2.33
hsa-miR-147b	26	11	-2.36
hsa-miR-525-3p	12	5	-2.40
hsa-miR-5196-3p+hsa-miR-6732-3p	18	7	-2.57
hsa-miR-181b-5p+hsa-miR-181d-5p	21	8	-2.63
hsa-miR-182-3p	32	12	-2.67
hsa-miR-941	22	8	-2.75
hsa-miR-671-3p	17	6	-2.83
hsa-miR-944	18	6	-3.00
hsa-miR-1245b-3p	24	6	-4.00

Fold change of top ten unregulated and down regulated miRNAs at nine hour treatment.

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