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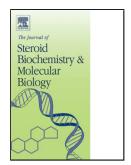
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### ACCEPTED MANUSCRIPT

# Regulation of vitamin D receptor expression by retinoic acid receptor alpha in acute myeloid leukemia cells.

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#### **Highlights**

- We show that RAR $\alpha$  is responsible for regulating *VDR* transcription in AML cells.
- We show that the *VDR* transcriptional 1a variant is regulated by RAR $\alpha$  in AML cells.
- *VDR* gene expression is low in the absence of RARα agonist in KG1 cells.
- We identify a *VDR* transcript variant originating from a new exon 1g.
- The *cis*-regulatory element, used by RARα, is located in the promoter region of exon 1a.

#### Abstract

Acute myeloid leukemia (AML) is the predominant acute leukemia among adults, characterized by an accumulation of malignant immature myeloid precursors. A very promising way to treat AML is differentiation therapy using either all-trans-retinoic acid (ATRA) or 1,25-dihydroxyvitamin  $D_3$  (1,25D), or the use of both these differentiation-inducing agents. However, the effect of combination treatment varies in different AML cell lines, and this is due to ATRA either down- or up-regulating transcription of vitamin D receptor (VDR) in the cells examined. The mechanism of transcriptional regulation of VDR in response to ATRA has not been fully elucidated. Here, we show that the retinoic acid receptor  $\alpha$  (RAR $\alpha$ ) is responsible for regulating VDR

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