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Vitamin D_3–Induced Promotor Dissociation of PU.1 and YY1 Results in FcεRI Reduction on Dendritic Cells in Atopic Dermatitis

Nadine Herrmann, Tim J. Nümm, Kazumasa Iwamoto, Nicole Leib, Susanne Koch, Yasmin Majlesain, Laura Maintz, Helene Kirins, Sylvia Schnautz and Thomas Bieber

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KEY POINTS

- Vitamin D_3 reduces FcεRI expression on epidermal DC in atopic dermatitis.
- This is independent of activation and results in impaired FcεRI-mediated function.
- Vitamin D_3 causes dissociation of PU.1 and YY1 from the FcεRI α-chain promotor.

Abstract

Atopic dermatitis (AD) is a severe inflammatory skin disease. Langerhans cells and inflammatory dendritic epidermal cells (IDEC) are located in the epidermis of AD patients and contribute to the inflammatory processes. Both express robustly the high-affinity receptor for IgE, FcεRI, and thereby sense allergens. A beneficial role of vitamin D_3 in AD is discussed to be important especially in patients with allergic sensitization. We hypothesized that vitamin D_3 impacts FcεRI expression and addressed this in human ex vivo skin, in vitro Langerhans cells, and IDEC models generated from primary human precursor cells. We show in this article that biologically active vitamin D_3 [$1,25(OH)_2$-D_3] significantly downregulated FcεRI at the protein and mRNA levels of the receptor's α-chain, analyzed by flow cytometry and quantitative RT-PCR. We also describe the expression of a functional vitamin D receptor in IDEC. $1,25(OH)_2$-D_3–mediated FcεRI reduction was direct and resulted in impaired activation of IDEC upon FcεRI engagement as monitored by CD83 expression. FcεRI regulation by $1,25(OH)_2$-D_3 was independent of maturation and expression levels of microRNA-155 and PU.1 (as upstream