

Abstract

Biol Reprod. 2008 Nov 12. [Epub ahead of print]

Vitamin D Induces Innate Antibacterial Responses in Human Trophoblasts via an Intracrine Pathway.

Liu N, Kaplan AT, Low J, Nguyen L, Liu GY, Equils O, Hewison M.

BACKGROUND: The active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)₂D) is a potent inducer of the antimicrobial protein cathelicidin, CAMP (LL37). In macrophages this response is dependent on intracrine synthesis of 1,25(OH)₂D from precursor 25-hydroxyvitamin D (25OHD), catalyzed by the enzyme 25-hydroxyvitamin D-1α-hydroxylase (CYP27B1).

OBJECTIVE: In view of the fact that trophoblastic cells also express abundant CYP27B1, we postulated a similar intracrine pathway for induction of CAMP in the placenta.

METHODS AND RESULTS: Analysis of placenta explants, primary cultures of human trophoblast, and the 3A trophoblastic cell line treated with 1,25(OH)₂D (1-100 nM) revealed dose-dependent induction of CAMP similar to that observed with primary cultures of human macrophages. Also consistent with macrophages, induction of trophoblastic CAMP was enhanced via intracrine conversion of 25OHD to 1,25(OH)₂D. However, in contrast to macrophages, induction of CAMP by vitamin D in trophoblasts was not enhanced by co-stimulation with toll-like receptor ligands such as lipopolysaccharide. Despite this, exposure to vitamin D metabolites significantly enhanced antibacterial responses in trophoblastic cells: 3A cells infected with *Escherichia coli* (*E. coli*) showed decreased numbers of bacterial colony-forming units compared to vehicle-treated controls when treated with 25OHD (49.6 ± 10.9 %) or 1,25(OH)₂D (45.4 ± 9.2 %), both *P* < 0.001. Treatment with 25OHD (1-100 nM) or 1,25(OH)₂D (0.1-10 nM) also protected 3A cells against cell death following infection with *E. coli* (13.6-26.9 and 22.3-40.2% protection respectively).

CONCLUSION: These observations indicate that 1,25(OH)₂D can function as an intracrine regulator of CAMP in trophoblasts, and may thus provide a novel mechanism for activation of innate immune responses in the placenta.

PMID: 19005165

FREE FULL TEXT