Adiponectin Signaling Regulates Lipid Production in Human Sebocytes

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Introduction

- Adiponectin, an adipokine expressed specifically in adipose tissue, has been implicated in various diseases, such as diabetes, obesity and cardiovascular disease.
- The sebaceous gland plays a vital role in skin homeostasis by producing sebum.
- Sebaceous glands express both adiponectin receptors (AdipoR)1 and AdipoR2, and this finding suggested a role of adiponectin in sebum production.
- However, no reports have shown that adiponectin signaling directly influences lipid production. The potential roles of adiponectin and its mechanisms of action in human sebaceous glands require clarification.

Purpose of this study

- In this study, we investigated the effects of adiponectin on sebum production in the sebaceous glands in vitro.
- Our findings provide compelling evidence that adiponectin plays a significant role in human sebocyte biology.

Expression of adiponectin receptors in human sebaceous glands and sebocytes

(A) Human sebaceous glands were assayed for adiponectin receptor (AdipoR)1 and AdipoR2 by immunohistochemistry. Inset, isotype control. (B) Immunofluorescence labeling of AdipoR1 and AdipoR2 (green) in human sebocytes. Nuclei were counterstained with DAPI (blue). Inset, isotype control. (C, D) Western blotting and RT-PCR of sebocyte lysates. Human keratinocytes and fibroblasts expressing AdipoR1 and AdipoR2 were used as positive controls. Scale bars = 20 μ m. Sebo, sebocytes; KC, keratinocytes; FB, fibroblasts.

Effects of adiponectin on cell proliferation in human sebocytes

(A) The effects of adiponectin on sebocyte viability were examined by MTT assay. (B) Rate of [³H]-thymidine incorporation into sebocytes treated with various doses of adiponectin, calculated as a percentage of the value in untreated cells. (c) Dose-dependent effects of adiponectin on sebocyte proliferation were examined using microscopy from low cell seeding assays. Scale bars = 400 μ m. Data represent means $\pm$ SEM (n = 6). Data were analyzed using Student's ttest (*P < 0.05).

Effects of adiponectin on lipid production in human sebocytes

(A) Detection of intracellular lipids in sebocytes treated with adiponectin using microscopy after Oil Red O and Nile red staining. (B) Lipid levels in sebocytes treated with various doses of adiponectin. (C) Relative abundance of major lipid classes determined by thin-layer chromatography. (D) The effect of adiponectin in three-dimensional (3D) culture of human sebocytes. Organoid structures in 3D culture of sebocytes were stained with hematoxylin and eosin (H&E), Nile red, SREBP and epithelial membrane antigen (EMA).

Induction of lipid synthesis by adiponectin in human sebocytes by activating APPL1-AMP activated protein kinase (AMPK) signaling

(A) After sebocytes were treated with adiponectin, whole cell lysates were prepared and analyzed by Western blotting. (B) Sebocytes were transfected with control, AdipoR1 or AdipoR2-targeting siRNA and the intracellular protein levels of each signals were determined by Western blotting. (C) Sebocytes were incubated with different concentrations of compound C and protein signals were determined by Western blotting and intracellular lipid levels were measured by Oil Red O staining.

Summary

- We demonstrated that human sebaceous glands in vivo and sebocytes in vitro express adiponectin receptor and that adiponectin increased cell proliferation.
- Moreover, based on a lipogenesis study using Oil Red O, Nile red staining and thin layer chromatography, adiponectin strongly upregulated lipid production in sebocytes.
- In three-dimensional culture of sebocytes, lipid synthesis was markedly enhanced in sebocytes treated with adiponectin.
- This study suggested that adiponectin plays a significant role in human sebaceous gland biology.
- Adiponectin signaling is a promising target in the clinical management of barrier disorders in which sebum production is decreased, such as in atopic dermatitis and aged skin.