



ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

THE EFFECT AND IRRITATION OF ADAPALENE ON CUTIBACTERIUM ACNES VIA HTS

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Introduction: Cutibacterium acnes is involved in acne as an opportunistic pathogen. Contrary to what was previously thought, proliferation of C. acnes is not the crucial pathogenic factor. Instead, activation of the innate immunity induced by C. acnes might lead to this chronic inflammatory condition.

Objective: To establish the screening platform of acne by nematodes, and detect the anti-inflammatory activity and stimulation of adapalene.

Materials and Methods: The high throughput liquid screening assay was developed here to identify effective anti-infective compounds in 96-well assay plates of worms. Tetracycline was as positive control to save worms in the liquid assay. Minimum inhibitory concentration was presented as the lowest concentration of an antimicrobial that inhibited the visible growth of C. acnes. The membrane permeability of C. acnes was detected by monitoring the uptake of SYTOX Green after treating with compounds.

Results: We provided results from HTS in nematodes Caenorhabditis elegans that led to better characterization of adapalene treating acne. Compared to tetracycline, adapalene inhibited the growth of C. acnes while adapalene didn't show anti-C. acnes effect, even under high concentration. Then we found that adapalene reduced the production of pro-inflammatory cytokines, such as IL-6 and IL-8 on PMA stimulated human epidermoid carcinoma cells. But when exposure of human keratinocytes to adapalene, it result in the activation of the cells and secretion of IL-6 and IL-8.

Conclusion: The liquid C. elegans - C. acnes assay established here allows screening for anti-acne compounds that are not toxic to the host. We confirm the utility of C. elegans as a screening platform for acne treatment, and adapalene can rescue C. acnes infected worms. Although it has anti-inflammation effects, adapalene changes the expression of IL-6 and IL-8 depending on the host inflammation conditions. Normal human keratinocytes could be triggered inflammatory responses by the stimulation of adapalene.

