Identification of the signaling pathway mediating the anti-inflammatory effect of cannabidiol on human sebocytes

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Cannabidiol (CBD), the major non-psychotropic phytocannabinoid of Cannabis sativa, was found to suppress unstimulated sebocytes lipolysis and expression of anti-inflammatory cytokines. We have also described that the lipostatic and growth-inhibitory effects of CBD are mediated by the activation of transient receptor potential vanilloid 4 (TRPV4) channels; however, the molecular mechanism of its anti-inflammatory action is still unknown. Since the anti-inflammatory effect of CBD in a mouse lung injury model was dependent on the C_{56}5 protein-coupled A2a adenosine receptor, in our current study, we first analyzed the expression of A2a on human SZ95 sebocytes. Using quantitative “real-time” PCR (Q-PCR), immunity/chemistry and Western blot, A2a receptors were identified on sebocytes. Moreover, CBD treatment elevated the intracellular cAMP concentration suggesting the activation of the receptor. We also demonstrated that CBD increased tribbles protein-coupled receptor, in our current study, we first analyzed the expression of A2a on human SZ95 sebocytes. Of further importance, the activation of “A2a receptor antagonist (ZM241385) was able to prevent the up-regulation of TRIB3 by CBD. Of further importance, ZM241385 also suppressed the CBD-evoked inhibition of bacterial lipopolysaccharide-induced NF-κB activation. Our results collectively suggest that CBD exerts its anti-inflammatory effect by the activation of “A2a receptor → cAMP → TRIB3 NF-κB” axis.

Propionibacterium acne activates the NLRP3 inflammasome in human SZ95 sebocytes

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Propionibacterium acne (P. acne) in sebaceous glands are considered to play an important role in the development of acne. However, information regarding the activation of innate immunity by P. acne in the sebaceous gland is limited. In this study, we investigated whether P. acne activates the inflammasome in human sebaceous glands in vivo and vitro. We found that IL-1β expression was upregulated in sebaceous glands of acne lesions. After stimulation of human SZ95 sebocytes with P. acne, the activation of caspase-1 and secretion of IL-1β were enhanced significantly. Moreover, knocking down the expression of NLRP3 (but not AIM2) abolished P. acne-induced IL-1β production in SZ95 sebocytes. The activation of the NLRP3 inflammasome by P. acne was dependent on protease activity and ROS generation. Finally, we found that NALP1-deficient mice displayed reduced inflammatory responses to P. acne. These results suggest that human sebocytes are important immunocompetent cells that induce the NLRP3 inflammasome, and that P. acne-induced IL-1β activation in sebaceous glands plays an important role in acne pathogenesis.