Propionibacterium acnes stimulates cytokines, antimicrobial peptides, and matrix metalloproteinases expression through activation of protease-activated receptor-2 in keratinocytes and sebocytes.

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Propionibacterium acnes (P. acnes) has been implicated in the pathogenesis of inflammatory acne by stimulating keratinocytes and sebocytes to produce proinflammatory cytokines. P. acnes induces delayed type hypersensitivity response by producing lipases, proteases, hyaluronidases, and chemotactic factors. Recent reports demonstrated that protease-activated receptor-2 (PAR-2) activation has proinflammatory effects and plays a pathogenic role in the various inflammatory diseases. The purpose of our study was to investigate whether protease from P. acnes can activate PAR-2, and whether P. acnes induces the expression of cytokines, antimicrobial peptides (AMPs), and matrix metalloproteinases (MMPs) in keratinocytes and sebocytes via the pathway involving PAR-2 activation. We found that 2.5uM PAR2 agonist peptide (AP) or 24hr P. acnes supernatant (P. acnes) induced calcium signals which was dose dependently inhibited by PAR-2 antagonist in immortalized keratinocytes (HaCaT cells) and SZ95 sebocytes (SZ95). Desensitization of PAR-2 by repetitive AP or P. acnes stimulation suggested that P. acnes-mediated calcium signals were mediated by PAR-2 activation. In addition, AP or P. acnes treatment resulted in the increased mRNA expression of proinflammatory cytokines, such as IL-1α, IL-6, IL-8 and TNF-α, and AMPs such as human β-defensin-2 and LL-37 in HaCaT cells and SZ95. AP or P. acnes also increased MMP-1, 2, 3, 9, 13 in HaCaT cells and MMP-1, 3, 9 in SZ95. Inhibition of PAR-2 by PAR-2 antagonist and the inhibition of protease activity by serine protease inhibitor resulted in a partially decreased P. acnes-induced expression of cytokines, AMPs, and MMPs in HaCaT cells and SZ95. From these results, we suggest that protease/PAR-2 signal is one of the factors that contributes to the acne pathogenesis.

Key words: Propionibacterium acnes, Protease-activated receptor 2

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