

STUDYING THE NEGATIVE REGULATORY FACTORS OF THE
PROPIONIBACTERIUM ACNES-INDUCED SIGNALING PATHWAYS IN *IN VITRO*
CULTURED IMMORTALIZED KERATINOCYTES

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Propionibacterium acnes (*P. acnes*) is a resident microbe of the healthy human skin microbiome, but also know to simulate immune and inflammatory events via the activation of Toll-like receptors (TLRs). These molecular pathways are well characterized, but little is known about the endogen negative regulatory mechanisms in the keratinocytes that counteract the bacterium-induced signaling events and thus may protect the host from the prolonged, uncontrolled and often destructive inflammation.

In our studies we aimed to characterize the keratinocyte expression of endogen negative regulators of TLR signaling pathways previously identified in other cell types, and to analyze their possible role in the attenuation of the *P. acnes*-induced molecular events. For that, we studied the basal mRNA and protein expression of selected genes (SIGIRR, TOLLIP, TNFAIP3, TNIP1) in a human, *in vitro* cultured immortalized keratinocyte cell line (HPV-KER) by real time RT-PCR and western blot analysis.

Our results suggest that all the investigated negative regulators are expressed in HPV-KER cells and the TNFAIP3 and TNIP1 mRNA expressions significantly and dose dependently increase in response to the bacterium. At the protein level, we found increased TNFAIP3 and decreased SIGIRR expressions following the bacterial treatment, and these events also appeared to be dose dependent. Next, we compared the effect of two *P. acnes* strains (889, 6609) belonging to different phylogenetic groups within the species (IA and IB, respectively), but no major differences have been observed in the induced expression changes.

Our study suggests that in our *in vitro* model system *P. acnes* causes a dose-dependent activation of downstream TLR signaling processes. However, parallel to that specialized, endogen negative regulators are also expressed in these cells, which may control the bacterial-induced molecular events, and thus can be important for the maintenance of epidermal homeostasis.

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