IDENTIFICATION OF NEGATIVE REGULATORY ELEMENTS COUNTERACTING THE *PROPIONIBACTERIUM ACNES*-INDUCED SIGNALING PATHWAYS IN *IN VITRO* CULTURED IMMORTALIZED KERATONICYTES

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Introduction: Acne is the most common dermatological disease affecting a large percentage of the adolescent population. Under special circumstances the otherwise skin commensal *Propionibacterium acnes* (*P. acnes)* bacterium plays a key role in lesion development. The bacterium has been shown to induce immune and inflammatory events by the activation of pathogen recognition receptors (e.g Toll-like receptors 2 and 4; TLR2-4) in human epidermal keratinocytes. Little is known, however, about the negative regulatory mechanism that counteracts TLR activation, thus protects the host from the prolonged, often destructive, uncontrolled inflammation.

Methods: In order to identify and analyze factors playing a key role in the attenuation of the *P. acnes*–induced TLR activation processes, we analyzed the mRNA expression of selected wellknown negative regulators of these signaling events (SIGIRR, TOLLIP, TNFAIP3, TNIP1). Cultured human immortalized keratinocytes (HPV-KER) were treated with *P. acnes 889* strain and the gene expression changes were followed by real time RT-PCR.

Results: Our results show that all the investigated negative regulators are expressed in HPV-KER cells. Moreover, the TNFAIP3 and TNIP1 mRNS expression exhibited transient changes, reaching a maximum at 6-12 hours after the bacterial treatment. These processes seem to be dose-dependent, as parallel with the increase of the applied *P. acnes* dose, the mRNA expressions of TNFAIP3 and TNIP1 also increased, which may be the result of a growing rate of NF-kB activation.

Conclusions: Our study suggests that in our *in vitro* model system *P. acnes* causes the dose-dependent activation of the TLR signaling processes. Special negative regulators do exist, which can control these events, and can be important for the maintenance of epidermal homeostasis. Based on our results we propose that the net ratio of positive and negative regulatory processes can be important determinants of the intensity of *P. acnes* driven innate, and inflammatory events, and thus also the severity of induced acne symptoms.