PROPIONIC ACID SECRETED BY PROPIONIBACTERIUM ACNES MAY MODIFY THE CELLULAR PROPERTIES OF KERATINOCYTES

Gábor Tax1

Edit Urbán2, Róbert Puskás3, Zoltán Kónya3,4, Lajos Kemény1,5 and Kornélia Szabó5

1. Department of Dermatology and Allergology, University of Szeged, Hungary

2. Institute of Clinical Microbiology, University of Szeged, Hungary

3. Department of Applied and Environmental Chemistry, University of Szeged, Hungary

4. Reaction Kinetics and Surface Chemistry Research Group of the Hungarian Academy of Sciences, Szeged, Hungary

5. MTA-SZTE Dermatological Research Group, Szeged, Hungary

Propionibacterium acnes (P. acnes) bacterium is a member of the skin microflora, but may also serve as an opportunistic pathogen contributing to the pathogenesis of acne vulgaris. Earlier we have shown that various P. acnes strains (889, 6609, ATCC 11828) belonging to different phylogroups differentially affect the cellular properties of cultured human keratinocytes in a strain-specific and dose-dependent manner. High doses of the pathogenic 889 and ATCC 11828 strains also resulted characteristic morphological changes and membrane damage, which lead to the cytotoxicity of human in vitro cultures keratinocytes (HPV-KER).

Our aim was to further analyze the interaction of human in vitro cultured keratinocytes and identify bacterially-derived factors that may mediate the previously observed effects.
In order to systematically quantify the *P. acnes*-induced cytotoxicity we performed spectrophotometric lactate dehydrogenase (LDH) and hemoglobin (HgB) assays using supernatant samples of bacterial treated HPV-KER cells and erythrocytes. The amount of released free LDH and HgB exhibited strain- and dose-dependent differences. We also noted the differential acidification of the pH in the culture supernatants. *P. acnes* is known to secrete propionic acid (PA), a characteristic, acidic end-product of bacterial fermentation in these species. In order to analyze whether *P. acnes*-derived PA has any role in the observed cellular changes we treated HPV-KER cells with the acid and analyzed the cell morphology. Microscopic analysis of the PA treated cultures revealed cells with similar irregular membrane morphologies observed earlier upon high dose *P. acnes* 889 and ATCC 11828 treatments. Finally, we measured the amount of secreted short chain fatty acids (SCFA) in the *P. acnes* 889, 6609 and ATCC 11828-treated HPV-KER supernatant samples by mass spectrometry. These studies revealed marked differences in the amount of secreted PA; high dose treatment of the 889 and ATCC 11828 strains leading to higher levels.

*P. acnes*-induced cellular changes depend on the type and amount of the applied bacterial strains. The observed differences may be due to variations of the amount of a secreted metabolic end-product, PA. Together with other bacterially-derived molecules it may be an active contributor of the *P. acnes*-induced cellular changes.

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