Medical University of Graz

Therapeutic potential of antimicrobial peptides in atopic dermatitis

Summary

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Supervisor:	Prof. Dr. Peter Wolf
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between August 14, 2020 00:00 and October 10, 2020 23:59 (Europe/Zurich)

Description

Background:

Atopic dermatitis (AD) is a common inflammatory skin disease with complex etiopathology linked to abnormal inflammatory pathways, and dysbiotic colonization by *Staphylococcus aureus* (*S. aureus*).[1] The microbial dysbiosis is related to failure in expressing antimicrobial peptides (AMPs; small peptides bearing microbiocidal and immunomodulatory functions) in the skin.[2] Phototherapy (using different wavebands of UV radiation) is a widely used treatment for moderate to severe AD and is known to decrease cutaneous inflammation with minimal or no systemic side effects. Intriguingly, UV is known to modulate microbial communities and induce certain AMPs in the skin.[3, 4]

Hypothesis and Objectives:

We hypothesize that the efficacy of phototherapy in AD patients depends on the capacity of UV to (re)induce the expression of AMPs from the host skin or microbe, which can normalize the dysbiotic *S. aureus* colonization. Furthermore, we hypothesize that such AMPs could be used therapeutically to target *S. aureus* and improve AD symptoms.[5] The primary objectives of the proposed work are to (i) screen the diversity of host- and microbe-associated AMPs and (ii) investigate impact of UV radiation on *S. aureus* biology in AD patients undergoing phototherapy; (iii) decipher the complex interplay between *S. aureus* colonization, UV exposure, and AMP expression; (iv) to establish novel therapeutic strategies by reducing the dysbiotic microbiome/colonization with certain AMPs in an *S. aureus*-induced AD-like mouse models.[6]

Methodology:

Overall, the multidisciplinary and translational nature of this proposed work will involve a combination of microbiology, immunology, bioinformatics, and molecular biology. The PhD candidate will utilize state-of-the-art techniques such as *de novo* peptide sequencing using mass spectrometry (to detect AMPs), whole genome shotgun sequencing, RNA sequencing, bioinformatics (for AMP database, microbiome analysis and statistics) and biologic samples from patients and pre-clinical models to achieve the objectives.

The PhD candidate will be given the opportunity to design and conduct experiments and to present research results at international scientific meetings.

References:

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6. Gamradt, P., L. Laoubi, A. Nosbaum, V. Mutez, V. Lenief, S. Grande, D. Redoules, A. M. Schmitt, J. F. Nicolas, and M. Vocanson. "Inhibitory Checkpoint Receptors Control Cd8(+) Resident Memory T Cells to Prevent Skin Allergy." *J Allergy Clin Immunol* 143, no. 6 (2019): 2147-57 e9.

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