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Oligopeptide-based polymers targeting human antigen R (HuR) for the treatment of psoriasis

Ai-Li Shiau

National Cheng Kung University, Taiwan

Psoriasis is a common chronic inflammatory skin disease, characterized by abnormal differentiation and proliferation of keratinocytes, angiogenesis and infiltration of inflammatory cells that secrete Th1 and Th17 associated cytokines in the skin lesion, such as TNF-α, IL-17 and IL-20. Although mRNAs that encode cytokines are short-lived mRNAs in eukaryotes, the premRNAs, which contain AU-Rich Elements (AREs) in their 3'-untranslated regions, are recognized and stabilized by Human Antigen R (HuR), an RNA-binding protein, for post-transcription. Previous studies have suggested that HuR is involved in the stabilization of mRNAs in the psoriatic skin. HuR binds to and regulates IL-20 mRNA and relocalizes to the cytoplasm of psoriatic keratinocytes. Furthermore, HuR can bind numerous transcripts involved in the pathogenesis of psoriasis. Therefore, HuR may be a potential therapeutic target for psoriasis. In the present study, we tested several novel oligopeptides that targeted the RNA binding site of HuR as therapeutic agents for psoriasis. A mouse model of imiquimod (IMQ)-induced psoriasis-like dermatitis was generated in BALB/c mice by daily topical application of IMQ cream on the ear from days 0 to 9. The mice were treated with oligopeptides from days 5 to 10. The pathological features of psoriasis were scored daily using the thickness gauge and clinical Psoriasis Area and Severity Index (PASI). We found that the oligopeptide JS-1 could significantly ameliorate psoriasis pathogenesis in a dose-dependent manner. The oligopeptide affected the HuR downstream signaling pathway. Collectively, this study may provide an alternative therapeutic strategy for psoriasis.

Biography

Ai-Li Shiau is a Distinguished Professor of the Department of Microbiology and Immunology and Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Taiwan. She currently serves as the Head of the Department of Microbiology and Immunology, NCKU. She has received her PhD in Molecular Biology from University of Edinburgh. She has expertise in viral vectors for gene therapy and vaccine applications and published more than 100 papers in peer-reviewed international journals.

alshiau@mail.ncku.edu.tw

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