

ABSTRACT OF DISSERTATION

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| Title | Metal Allergy Mediates the Development of Oral Lichen Planus via TSLP-TSLPR Signaling (金属アレルギーは TSLP-TSLPR シグナルを介して口腔扁平苔癬の発症に関与する) |
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| <p>Background: Metal allergy is classified as a delayed-type hypersensitive reaction of type-IV and mediated by hapten-specific T cells. However, the molecular mechanisms of pathogenesis on the allergy are still investigated. Oral lichen planus (OLP) has been reported as clinical manifestation of metal allergy, wherein T cell also has a critical role in the pathogenesis of OLP. In addition, thymic stromal lymphopoietin (TSLP) and its receptor (TSLPR) are the potential keys in both mechanism roles. Nevertheless, the immunological studies to elucidate their relationship have not been performed.</p> <p>Objective: To compare differences in the histopathology of OLP patients diagnosed by biopsy as metal allergy-positive and metal allergy-negative and investigate the interaction cells in epithelial layer induced by TSLP and TSLPR.</p> <p>Methodology: The histopathological examination was conducted by comparing distinguishes between metal allergy-positive and -negative groups diagnosed by biopsy of OLP patients. TSLP and TSLPR expression were interpreted to analyse the interaction between epidermal keratinocytes and T cells. In vitro study, human keratinocyte cell line HaCaT cells were stimulated with NiCl₂ for 24, 48, and 72 hours to assess inflammatory cytokine expression using qRT-PCR and ELISA.</p> <p>Result: T cell infiltration in the epithelium was higher in the metal-allergy positive patients than metal-allergy negative patients of the OLP lesion. Moreover,</p> | |

TSLP-TSLPR signaling, and TNF- α secretion were higher in the metal allergy-positive epithelial tissue samples than those in the metal-allergy negative. Simultaneously, the qRT-PCR assay showed that the mRNA expression of TNF- α , interleukin 1-beta (IL-1 β), IL-6, TSLP, and IL-12 was significantly increased after 72 hours of stimulation HaCaT cells induced with NiCl₂. The secretion of TNF- α level in HaCaT stimulated with NiCl₂ was up-regulated in 24 h, 48 h, and 72 h, and IL-1 β level was increased in 72 h by ELISA.

Conclusion:

Metal allergy is associated with increased TSLP expression in keratinocytes and elevated TNF- α levels in the epithelium. The accumulation of T cells at the lesion site would enhance to development of diseases. These findings imply that metal allergy may play a role in the pathogenesis of OLP.