

(Form: Century 11 point, A4 size)

Report of "Research Award of Oral Sciences"

Major : Oral Sciences
Grade : 4th
Department : Prosthodontics and Oral Rehabilitation
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Title: Metal Allergy Mediates the Development of Oral Lichen Planus via
TSLP-TSLPR Signaling

1. Aim of research and results obtained (Approximately 400 words):

The purpose of this study was to analyze the histopathology of patients diagnosed with oral lichen planus (OLP) and to clarify whether TSLP-TSLPR signaling was associated with the pathogenesis of both metal allergy and OLP.

In the beginning, I screened and analyzed the secretion of cytokines on the Human keratinocyte cell line (HaCaT) that was stimulated by Nickel (II) chloride hexahydrate. The purpose of this study model was to mimic the microenvironment of OLP that was induced by metal ions. In vitro study, the result of PCR showed that human keratinocytes induced by NiCl₂ expressed pro-inflammatory cytokines of IL-6, IL-12, IL-1 β , TNF- α , and thymic stromal lymphopoietin (TSLP) in 0, 24, 48, and 72 h. Subsequently, I performed qRT-PCR that showed significantly upregulated on the expression of TNF- α , IL-1 β , IL-6, and TSLP in 72 h after nickel stimulation. Similarly, the production of TNF- α and IL-1 β in cultured keratinocytes was increased significantly after stimulation with NiCl₂ using ELISA. These results might be concluded that metal ions affected the secretion of cytokines in keratinocytes.

In situ study, I screened and compared the cytokine expressions and immune cells in OLP samples between metal allergy-positive and metal allergy-negative patients by immunohistochemistry staining. The result exhibited that T cells and Langerhans cells/dendritic cells infiltration in the epithelium were higher in the metal-allergy positive than metal-allergy negative patients in OLP lesion.

This result indicated that metal allergy influenced the accumulation of T cells and Langerhans cells/dendritic cells in the epithelial layer of OLP samples. Moreover, the expression of TSLP, TSLPR, and TNF- α was produced at significantly higher quantities in the mucosal epithelium of metal allergy-positive patients. Subsequently, I investigated the cytokine secretion in keratinocytes of OLP samples by immunofluorescence staining. The result showed that TSLP secretion was increased in keratinocytes, particularly in the basal epithelium of metal-allergy positive patients. Furthermore, TNF- α production was also widely appeared in the epithelial tissue of metal-allergy positive patients. These results could be concluded that metal allergy upregulated the secretion of TSLP and TNF- α by keratinocytes in epithelial tissue of OLP. Meanwhile, the expression of TSLPR increased in the epithelial layer of metal allergy-positive sample. I suspected that TSLPR was expressed by T cells or Dendritic cells, which also increased in the epithelial layer of metal allergy-positive samples. Thus, the interaction of TSLP-TSLPR signaling might occur between keratinocytes and T cells or keratinocytes and dendritic cells. However, this hypothesis mechanism requires more investigation in future studies.

2. Self-evaluation of research achievement:

- This research achievement is good to encourage the doctoral students to improve their knowledge and skill in research
- The funding could be used to support the research of doctoral student
- I hope in the future, the research award of oral sciences also gives feedback or advice to doctoral students who submitted the research proposal

3. Meeting presentation:

* Title, conference, venue, date, co-author, presentation (oral/ poster).

(Underline the speaker.)

1. The Pathogenesis of Oral Lichen Planus Related to Metal Allergy Reaction, 2021 Tokushima Biosciences Retreat, Virtual Meeting, 2021 September 17-18, Mohammad Fadyl Yunizar, Megumi Watanabe, Lipei Liu, Norikazu Minami, Tetsuo Ichikawa, Oral Presentation.

2. The Pathogenesis of Oral Lichen Planus Related to Metal Allergy Reaction, International College of Prosthodontist Conference, Virtual Meeting, 2021 September 22-25, Mohammad Fadyl Yunizar, Megumi Watanabe, Lipei Liu, Tetsuo Ichikawa, Poster Presentation.

The meeting presentations were supported by research award to purchase the research equipment.

4. Journal publication:

* Title, journal, volume, number, paragraph, date, co-author.

(Underline the speaker.)

Metal Allergy Mediated the Development of Oral Lichen Planus via TSLP-TSLPR Signaling, Journal of Clinical Medicine, 11, 3, 519, 20 January 2022, Mohammad Fadyl Yunizar, Megumi Watanabe, Lipei Liu, Norikazu Minami, Tetsuo Ichikawa.

The journal publication was supported by research award to purchase the research equipment.