

# The Examination of Mechanical Stress in Mouse Models of Imiquimod-induced Psoriasis

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**INTRODUCTION:** Psoriasis is a skin disorder that can be complicated by nail deformity, arthritis, and enthesitis. Recent studies highlight the importance of the inflammatory cytokine pathways in the pathogenesis of psoriasis. Especially, IL-17, IL-23, and tumor necrosis factor (TNF)- $\alpha$  were reported as the key effector cytokines of psoriasis. Additionally, gamma delta T cells that respond to IL-23 augment inflammation by producing some inflammatory cytokines such as IL-17 and TNF- $\alpha$ . Though it was known that mechanical stress is one of the factors that cause psoriatic arthritis and enthesitis, the detailed mechanism between pathogenesis and mechanical stress remains unclear. The aim of this study was that the effects of mechanical stress on the pathological condition of psoriasis using mouse models of imiquimod-induced psoriasis.

**METHODS:** Twelve mice were randomly divided into IMQ-TRED- group (control mice), IMQ-TRED+ group (treadmill running mice), IMQ+TRED- group (5% imiquimod (IMQ) treated mice), and IMQ+TRED+ group (IMQ treated and treadmill running mice). IMQ cream was topically applied to the shaved back skin of the mice in IMQ+TRED- group and IMQ+TRED+ group, respectively. The mice in IMQ-TRED+ group and IMQ+TRED+ group underwent downhill treadmill running for one hour a day. IMQ treatment and treadmill running were performed for 2 weeks. The severity of skin inflammation was monitored and graded using a modified clinical psoriasis area and severity index (PASI) score. Body weights and spleen weights were compared between all groups. Flow cytometry detected gamma delta+ T cell percentage in the spleen. The serum level of TNF- $\alpha$  was measured using an ELISA kit. For histopathology, the spleen and thymus tissue sections were immunostained with antibodies against IL-17 and IL-23. The number of IL-17 and IL-23-positive cells in representative high-power fields was counted in five areas.

**RESULTS:** The modified PASI scores were exacerbated in IMQ+TRED- group and IMQ+TRED+ group from Day 3 to 4. The body weights of mice in IMQ+TRED- group and IMQ+TRED+ group were generally decreased compared to those in IMQ-TRED- group and IMQ-TRED+ group (Figure 1). On the other hand, the mice in IMQ+TRED- group and IMQ+TRED+ had greater spleen than IMQ- groups (Figure 2). Also, the frequency of gamma delta+ T cells in the spleen significantly increased in IMQ+TRED+ group than IMQ- groups (Figure 3). TNF- $\alpha$  was markedly increased in IMQ+TRED+ group. Furthermore, the numbers of IL-17 and IL-23-positive cells in the spleen and thymus were significantly higher in IMQ+TRED+ group than in other groups ( $P < 0.01$  and  $P < 0.001$ , respectively).

**DISCUSSION:** This study revealed that IMQ treatment caused the pathological condition of psoriasis and that the mechanical stress aggravated the condition via increasing gamma delta+ T cells, IL-17, IL-23, and TNF- $\alpha$ . The effect of mechanical stress on the condition of psoriasis has been unclear so far. Thus, the outcome of this study will help examine the precise pathogenesis of psoriasis and treat it.

## SIGNIFICANCE/CLINICAL RELEVANCE:

This study revealed the effect of mechanical stress in mouse models of Imiquimod-induced psoriasis.

## IMAGES AND TABLES:

Figure1

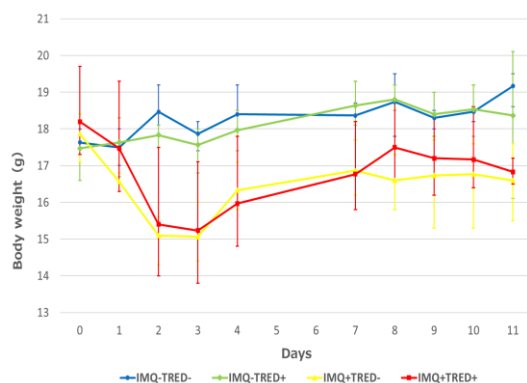


Figure2

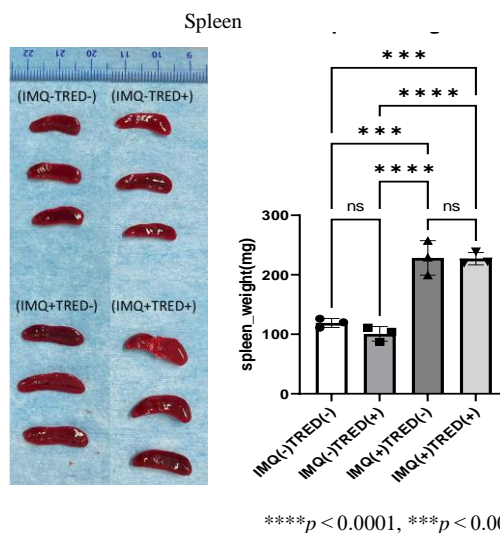


Figure3

