19 May, 2022

Prof. Dr. Fukumi Furukawa  
Chief Editor   
Trends in Immunotherapy

Dear Prof. Dr. Fukumi Furukawa,

We are pleased to submit our manuscript titled “Activation of proteinase-activated receptor-2 (PAR-2) simultaneously induces and suppresses inflammation in HaCaT cells” for consideration as an Original Research Article in the Trends in Immunotherapy.

In this study, we investigated the induction and suppression of inflammation by pattern recognition receptors (PRRs) activation *in vitro* using the epidermal keratinocyte cell line HaCaT cells. In particular, we focused on PAR-2 activation because of conflicting reports of its induction and suppression of inflammation.

What is noteworthy about this study is that PAR-2 activation has the opposing effects of simultaneously inducing and suppressing inflammation. That is, RAR-2 activation in HaCaT cells induces IL-6 and IL-8 in an agonist concentration-dependent manner, but suppresses MCP-1. Although the mechanism needs further investigation, we would like to report our interesting findings.

In this study, collaborative research group was made between Wakayama Medical University, Jabara Laboratory, and Osaka Medical and Pharmaceutical University, and Takatsuki Red Cross Hospital. YM and SA took part in planning and executing cell experiments. FF provided guidance and advice in the design and execution of the experiment. KB and MT supported for the execution of these experiments.

Research expenses of this study was partially supported by the grant“Research and development support project for pioneering industrial technology by Wakayama Prefectural Government”. After planning of our collaborative research project, Jabara Laboratory applied for this grant. This grant was distributed to Wakayama Medical University and Osaka Medical and Pharmaceutical University from Jabara Laboratory.

This manuscript has not been previously published and is not under consideration in the same or similar form for any other publication. All authors listed contributed sufficiently to the project to be included as authors.

We believe that this paper will be of great interest to your readers and we hope that you find it acceptable for publication in the Trends in Immunotherapy.

Sincerely yours,

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