World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:17, No:01, 2023

Ramification of Pemphigus Vulgaris Sera and the Monoclonal Antibody Against Desmoglein-3 on Nrf2 Expression in Keratinocyte Cultures

Authors : Faris Mohsin Alabeedi

Abstract : Pemphigus Vulgaris (PV) is a life-threatening autoimmune blistering disease characterized by the presence of autoantibodies directed against the epidermis's surface proteins. There are two forms of PV, mucocutaneous and mucosal-dominant PV. Disruption of the cell junctions is a hallmark of PV due to the autoantibodies targeting the desmosomal cadherins, desmoglein-3 (Dsg3) and desmoglein-1, leading to acantholysis in the skin and mucous membrane. Although the pathogenesis of PV is known, the detailed molecular events remain not fully understood. Our recent study has shown that both the PV sera and pathogenic anti-Dsg3 antibody AK23 can induce ROS and cause oxidative stress in cultured keratinocytes. In line with our finding, other independent studies also demonstrate oxidative stress in PV. Since Nrf2 plays a crucial role in cellular anti-oxidative stress response, we hypothesize that the expression of Nrf2 may alter in PV. Thus, treatment of cells with PV sera or AK23 may cause changes in Nrf2 expression and distribution. The purpose of this study was to examine the effect of AK23 and PV sera on Nrf2 in a normal human keratinocyte cell line, such as NTERT cells. Both a time-course and dose-dependent experiments with AK23, alongside the matched isotype control IgG, were performed in keratinocyte cultures and analysed by immunofluorescence for Nrf2 and Dsg3. Additionally, the same approach was conducted with the sera from PV patients and healthy individuals that served as a control in this study. All the fluorescent images were analysed using ImageJ software. Each experiment was repeated twice. In general, variations were observed throughout this study. In the dose-response experiments, although enhanced Dsg3 expression was consistently detected in AK23 treated cells, the expression of Nrf2 showed no consistent findings between the experiments, although changes in its expression were noticeable in cells treated with AK23. In the time-course study, a trend with induction of Nrf2 over time was shown in control cells treated with mouse isotype IgG. Treatment with AK23 showed a reduction of Nrf2 in a time-dependent manner, especially at the 24-hour time point. However, the earlier time points, such as 2 hours and 6 hours with AK23 treatments, detected somewhat variations. Finally, PV sera caused a decrease of Dsg3, but on the other hand, variations were observed in Nrf2 expression in PV sera treated cells. In general, PV sera seemed to cause a reduction of Nrf2 in the majority of PV sera treated samples. In addition, more pronounced cytoplasmic expression of Nrf2 has been observed in PV sera treated cells than those treated with AK23, suggesting that polyclonal and monoclonal IgG might induce a different effect on Nrf2 expression and distribution. Further experimental studies are crucial to obtain a more coincide global view of Nrf2-mediated gene regulation. In particular, Pemphigus Voulgaris studies assessing how the Nrf2-dependent network changes from a physiological to a pathological condition can provide insight into disease mechanisms and perhaps initiate further treatment approaches.

Keywords : pemphigus vulgaris, monoclonal antibody against desmoglein-3, Nrf2 oxidative stress, keratinocyte cultures
Conference Title : ICODOP 2023 : International Conference on Oral Dermatology and Oral Pathology
Conference Location : Rome, Italy
Conference Dates : January 16-17, 2023