The anti-inflammatory effects of stress hormones on lipopolysaccharide-stimulated macrophages

Y.L. Hung[1] and K. Suzuki ,[2] [1]Graduate School of Sport Sciences, Waseda University 2-579-15, Mikajima, Tokorozawa, Saitama, 359-1192 Japan and [2]Faculty of Sport Sciences, Waseda University 2-579-15, Mikajima, Tokorozawa, Saitama, 359-1192 Japan.

Innate immune responses are involved in the development of several chronic diseases, including atherosclerosis, type 2 diabetes and cancer. Indeed, the inflammatory responses of macrophages *via* activation of Toll-like receptor 4 (TLR4) play an important role in innate immune responses to pathogenesis of chronic diseases. On the other hand, exercise training suppresses production of pro-inflammatory cytokines and down-regulates TLR4 expression. The several bioactive substances such as stress hormones (catecholamines and glucocorticoids) and cytokines are induced during exercise, and are involved in the exercise-induced immunoregulation. It has been found that the stress hormones contribute to the anti-inflammatory effects of exercise. However, the mechanisms underlying the exercise-induced immunoregulation are not well understood. Especially, the effects of stress hormones on TLR4 signaling pathway of macrophages are still unclear.

Macrophage cell line RAW cells were incubated in a 96-well plate, and induced TLR4 signaling pathway by treatment with TLR4 ligand lipopolysaccharide (LPS). To investigate the anti-inflammatory effects of stress hormones, LPS-stimulated RAW cells were treated with different concentration of catecholamines (adrenaline and noradrenaline) and glucocorticoids receptor ligand (dexamethasone). The different final concentrations of adrenaline and noradrenaline were 1, 10 and 100μM, and the different final concentrations of dexamethasone were 0.1, 1 and 10μM. After 24 hour incubation, cell supernatant was harvested for measurement of pro-inflammatory cytokine production (tumor necrosis factor-alpha, TNF-α) by enzyme-linked immunosorbent assay (ELISA). Both noradrenaline and dexamethasone significantly suppressed TLR4-induced TNF-α production in LPS-stimulated RAW cells, and exerted the concentration-dependent responses. The production of TNF-α in 1, 10 and 100uM noradrenaline treatment was significantly decreased. The treatment of 0.1, 1 and 10μM dexamethasone significantly suppressed the production of TNF-α. The production of TNF-α in 1μM adrenaline treatment was decreased. In this study, both noradrenaline and dexamethasone exerted anti-inflammatory effect in LPS-stimulated RAW cells, and suppressed TNF-α production from TLR4-induced signaling pathway.