Proinflammatory cytokines and CD4+ T cells increase the expression of IL-6 by keloid fibroblasts

Naoki Murao[1], Munezumi Fujita[1,2], Toshihiko Hayashi[1], Ken-ichiro Seino[3], Masaaki Murakami[4], Yuhei Yamamoto[1]

[1]Department of Plastic and Reconstructive Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Hokkaido, Japan

[2]Department of Plastic and Reconstructive Surgery, Fukushima Medical University, Fukushima, Japan

[3]Division of Immunobiology, Institute for Genetic Medicine, Hokkaido University, Hokkaido, Japan

[4]Division of Molecular Psychoimmunology, Institute for Genetic Medicine, Hokkaido University, Hokkaido, Japan

Keloid is an inflammatory and fibrotic disease with an unknown pathogenesis. Keloid tissue contains high numbers of many inflammatory cells, including macrophages and CD4+ T cells. Moreover, proinflammatory cytokines, such as interleukin (IL)-1ß, IL-6, and tumor necrosis factor-α, are overexpressed by keloid fibroblasts and keloid tissues. Therefore, keloids are often thought to be the result of an excessive wound healing response. We investigated the IL-6 expression in keloid fibroblasts after stimulating them with proinflammatory cytokines. We also examined the interaction between CD4+ T cells and keloid fibroblasts by using a coculture system. Stimulated keloid fibroblasts expressed higher levels of IL-6. In addition, CD4+ T cells increased the expression of IL-6 by keloid fibroblasts. Our findings suggest that autocrine and paracrine signaling activates keloid fibroblasts to secrete proinflammatory cytokines. This supports the notion that a prolonged or abnormal inflammatory response may lead to keloid formation.