The role of sphingosine-1 phosphate in keloid formation.

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Background

The formation of keloid may involve a complex cascade of pathogenic processes, including proliferation, apoptosis, and other processes in skin-related cells. Altered growth factor modulation, abnormal collagen turnover, genes, immune system, and sebum reaction is assumed theories.[1)] The precise mechanism underlying keloid formation is complex and has not yet been established. When the human body is injured or under stress, the platelet secretes various growth factors and stress relief substances. One of these is the S1P (Sphingosine-1 phosphate). Sphingosine-1-phosphate (S1P) plays an important role in the regulation of cell proliferation, wound healing, survival and cell death[.2, 3)] In this study, we identified sphingolipid expressed differentially between normal skin and keloid scar tissues and examined their function in keloid formation using fibroblasts.

Method

5 normal and 5 keloid volunteers were enrolled. To check the expression of S1P receptor level, real time PCR, Western blotting and immunohistochemistry test done. By performing Western blotting, relationship between Rho activity, MAP kinase, S1PR and fibroblast was analyzed. S1P antagonist was used to analyzing connection between S1PR and amount of collagen by Western blot. Collagen level in the tissues was analyzed by immunohistochemistry and ELISA. To find a method of signaling process of keloid, MAP kinase and Rho activation pathway were tested.

Result

Increase in S1PR1 and S1PR2 level was observed in the keloid tissues compared to the healthy tissues.(Figure 1) We have examined the relationship between S1P concentrations to the quantity of collagen expression via Western blotting, as a result we have observed that the quantity of collagen expression increases with the concentration of S1P.(Figure 2) When we used inhibitors to suppress S1PR1 and S1PR2 the quantity of collagen expression have decreased. MAP kinase system and Rho activity were activated in keloid samples. Expression of JNK and ERK were elevated in Western blot.

Discussion

The properties of S1P accelerate the production of collagen, inhibits apoptosis of cells could contribute to the production of keloid.[4, 5)] The results of this study showed that S1P was elevated in keloid scar tissue, S1P was markedly related with Rho activity and MAP kinase. And Collagen production was inhibited by S1P antagonist. These results suggest that S1P may participate in keloid formation by collagen production and can be valuable therapeutic target for keloid lesions.

Reference

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Figure 1. The percentage of S1PR expression in normal and keloid tissue. Above is measured by real time PCR, below is measured by western blot. Expression of S1PR is elevated in keloid tissues. The level of expressed protein was measured, higher in keloid tissues.

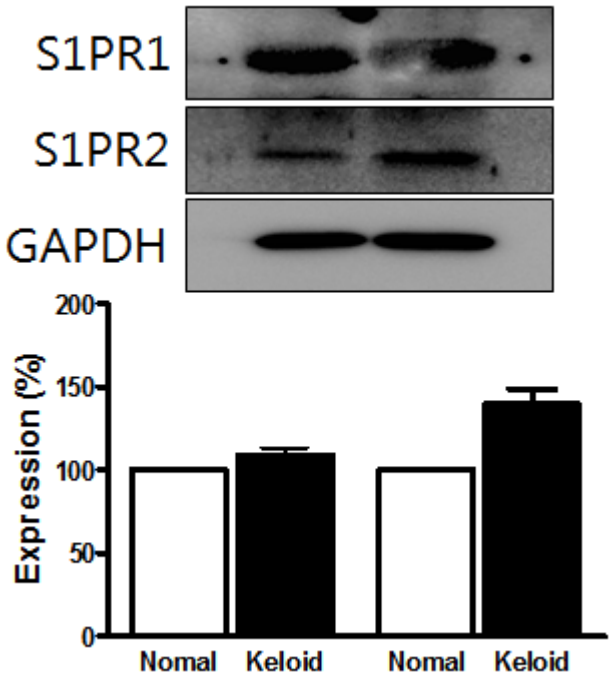

Figure 2. The relationship of collagen expression and S1P concentration measured by Western blot. The more concentrated S1P, the more collagen expression observed.