学位論文抄録

Tsukushi controls cell differentiation during the hair cycle and wound healing by regulating TGF-β1

(Tsukushiは毛周期および創傷治癒においてTGF-β1を
制御しながら細胞分化を調節する)

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Abstract of the Thesis

Background and Purpose

The hair follicle is a complex mini-organ, that supplies the stem/progenitor cells during both wound healing and skin development. Several signaling molecules belonging to the Wnt, shh, and transforming growth factor β (TGF-β) signaling cascades are involved in normal hair follicle cycling and wound healing. However, the systemic mechanism of how these humoral factors are controlled remains largely unknown. Previously, we reported that Tsukushi (TSK), a member of the small leucine-rich repeat proteoglycan family, functions extracellularly as a key coordinator of multiple signaling networks.In this study, we analyzed TSK function during hair development and wound healing.

Methods

We used the TSK knockout mice and investigate the TSK expression pattern during hair development and wound healing. Next, we compared the hair cycle and wound healing between Wild type mice and TSK knockout mice. To study the interaction with TSK, we examined mRNA expression level of several molecules during hair cycle and wound healing. In addition, we used NIH3T3 cells for TSK gain of function in vitro.

Results

TSK was expressed in developing hair cells and sebaceous glands during hair follicle morphogenesis. Targeted disruption of the TSK gene causes the hair cycle to be delayed with low TGF-β1. After wounding, TSK expression is sequentially observed in macrophages, myofibroblasts, regenerated epidermis, and granulation tissue during wound healing. In mice lacking TSK, the levels of inflammatory related cytokines such as TGF-β1 are upregulated during wound healing. Biochemical analysis indicates that TSK binds directly to TGF-β1. Furthermore, TSK inhibits the myofibroblasts differentiation induced by TGF-β1 in vitro.

Conclusions

TSK controls cell differentiation during the hair cycle and wound healing by regulating TGF-β1.