P33 Chondromodulin-I derived from the inner meniscus inhibits VEGF-mediated endothelial cell proliferation

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Objective Anti-angiogenic factors, such as chondromodulin-I (ChM-I) and endostatin, have important roles in preserving the avascularity of cartilage. Another aspect, angiogenic factor vascular endothelial growth factor (VEGF) can promote vascularization. However, the relationship between ChM-I and VEGF is unclear in the meniscus. We hypothesized that the inner meniscus might prevent VEGF-mediated angiogenesis by inducing ChM-I.

Methods Macroscopically intact lateral menisci were obtained at total knee arthroplasty in patients with knee osteoarthritis. The deposition of ChM-I, endostatin, and VEGF was evaluated by immunohistochemical analyses. RNA samples were obtained from meniscal tissues and cultured meniscus cells. The concentration of ChM-I, endostatin, and VEGF in conditioned media was measured by ELISA, respectively. The effects of ChM-I derived from the inner meniscus was evaluated by endothelial cell proliferation.

Results ChM-I was mainly detected in the inner and superficial zones of meniscus. On the other hand, distribution of endostatin and VEGF were similar between the inner and outer meniscus. In Western blot, ChM-I was detected only in the inner meniscus, whereas endostatin was equally observed in both inner and outer meniscus. In addition, ChM-I concentration of the inner meniscus-derived conditioned medium was higher than that of the outer meniscus-derived medium. ChM-I removal from the inner meniscus-derived medium and functional blocking of ChM-I significantly increased endothelial cell proliferation.

Conclusion We revealed that the inner meniscus contained larger amounts of ChM-I. The inner meniscus-derived ChM-I inhibited VEGF-mediated endothelial cell proliferation. Our results suggest that ChM-I may be a key anti-angiogenic factor for maintaining the avascularity of the inner meniscus.