

## 論 文 要 旨

### 〔 Cleaved CD147 Shed from the Surface of Malignant Melanoma Cells 〕 Activates MMP2 Produced by Fibroblasts

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Background: Cluster of differentiation 147 (CD147)/basigin on the malignant tumor cell surface is critical for tumor proliferation, invasiveness, metastasis, and angiogenesis. CD147 expressed on malignant melanoma cells can induce tumor cell invasion by stimulating the production of matrix metalloproteinases (MMPs) by surrounding fibroblasts. Membrane vesicles, microvesicles and exosomes have attracted attention, as vehicles of functional molecules and their association with CD147 has been reported. Cleaved CD147 fragments released from tumor cells were reported to interact with fibroblasts. We investigated the intercellular mechanisms by which CD147 stimulates fibroblasts to induce MMP2 activity. Materials and Methods: CD147 was knocked-down using short hairpin RNA (shRNA). The stimulatory effect of CD147 in cell culture supernatants, microvesicles, and exosomes on the enzymatic activity of MMP2 was examined by gelatin zymography. Results: Supernatants from A375 control cells induced increased enzymatic activity of fibroblasts; such activity was significantly lower in CD147 knock-down cells. Conclusion: Cleaved CD147 plays a pivotal role in stimulating fibroblasts to induce MMP2 activity.