Endoglin enhances the progression of angiosarcoma through the regulation of non-Smad TGF-B signaling

Ryoko Sakamoto¹, Ikko Kajihara¹, Saki Maeda-Otsuka¹, Saori Yamada-Kanazawa¹, Mamiko Masuzawa², Mikio Masuzawa³, Yasuyuki Amoh², Daichi Hoshina⁴, Riichiro Abe⁵, Hironobu Ihn¹



- 1: Department of Dermatology and Plastic Surgery, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan
- 2: Department of Dermatology, Kitasato University School of Medicine, Kanagawa, Japan
- 3: Department of Molecular Diagnostics, School of Allied Health Sciences, Kitasato University, Kanagawa, Japan
- 4: Department of Dermatology, Hokkaido University Graduate School of Medicine, Hokkaido, Japan
- 5: Department of Dermatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

BACKGROUND OBJECTIVE

extracellular acidification rate (ECAR)

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OCR/ECAR

EC

Angiosarcoma is a rare malignant tumor derived from endothelial cells and its prognosis is poor because advanced angiosarcoma is resistant to standard chemotherapy, and new therapies are urgently needed. Endoglin (CD105) is a membrane glycoprotein that acts as a coreceptor for transforming growth factor- β (TGF- β) signaling. Endoglin is overexpressed in the tumor-associated endothelial cells, and it enhances angiogenesis. Numerous clinical trials are testing the effectiveness of anti-endoglin antibody in various types of malignancies. Here, we investigated the role of endoglin in the pathogenesis of angiosarcoma and whether the inhibition of endoglin may have anti-tumor activity.

Overexpression of endoglin in angiosarcoma Regulatory molecular mechanism of endoglin RESULT in angiosarcoma ISO-HAS HAMON **ISO-HAS** Normal EC **HAMON** Endoglin Ctrl **ENG** Ctrl **ENG** Ctrl **ENG** β-actin siRNA siRNA siRNA siRNA Endoglin Relative Endoglin protein levels Senile Survivin angioma p-VE cadherin VE cadherin Angiosarcoma p-paxillin paxillin ISO-HAS HAMON β-actin **Knock-down of endoglin promoted apoptosis** and suppressed migration, invasion, and the Warburg effect EC **ISO-HAS HAMON** in angiosarcoma cells Relative caspase 3/7 **ISO-HAS** EC **HAMON Apoptosis** Ctrl siRNA Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA Overexpression of endoglin in angiosarcoma TβR-II TBR-II HAMON ENGSI /P16.3% Endoglin ALK1 16% ISOHAS E / E1 2.3% ≘ Q4-1 0.25% **ENG** siRNA Non-Smad signaling Smad signaling Survivin Warburg effect Paxillin. Migration assay **HAMON** EC **ISO-HAS** Smad VE cadherin Relative cell number Caspase 3/7 Tube formation Invasion 4 **Apoptosis** Migration ... Regulation of gene Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA transcription Invasion assay **Anti-tumor effects** Relative cell number Inhibition of endoglin CONCLUSION Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA Ctrl siRNA ENG siRNA OCR/ECAR Knock-down of endoglin promoted apoptosis and Warburg effect: anaerobic glycolysis in cancer cells suppressed migration, invasion, and the Warburg cellular oxygen consumption rate (OCR)

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effect in angiosarcoma cells.

non-Smad TGF-β signaling.

angiosarcoma.

Anti-tumor effect of endoglin for angiosarcoma was

not based on the regulation of Smad signaling, but

Endoglin could be a novel therapeutic target for