

Title	Tumorigenic Role of Podoplanin in Esophageal Squamous-Cell Carcinoma
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論文審査の結果の要旨

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学位論文名	Tumorigenic Role of Podoplanin in Esophageal Squamous-Cell Carcinoma (食道扁平上皮癌におけるポドプランニンの造腫瘍効果)
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論文内容の要旨

〔 目 的 〕

The objectives of the present study were to examine the role of podoplanin in esophageal squamous-cell carcinoma (ESCC).

〔 方法ならびに成績 〕

METHODS: Expression of podoplanin was examined immunohistochemically in 61 cases of ESCC that had not been treated with chemotherapy or radiotherapy before surgery. Because cancer stem-cell quantities have been reported to increase with chemotherapy and radiotherapy, cases in patients who did not receive such prior therapies were included in this study. Cases with >10% tumor cells showing signals for podoplanin were categorized as podoplanin high, and the others were classified as podoplanin low. The effects of podoplanin on the behavior of cancer cells were evaluated in ESCC cell lines in which podoplanin expression was knocked down.

RESULTS: To examine whether podoplanin could be used as a cancer stem cell marker for ESCC, podoplanin-positive and podoplanin-negative fractions were sorted separately from the ESCC cell line and cultured. Podoplanin-positive ESCC cells yielded both podoplanin-positive and podoplanin-negative cells, whereas few cells were obtained from podoplanin-negative ESCC cells. When podoplanin expression was knocked down, ESCC cell lines became vulnerable to anticancer drugs and showed defective invasion and tumorigenic activities. Nineteen (31.1%) of 61 cases were categorized as podoplanin high. Podoplanin-high cases were correlated with T category, stage of disease, lymphatic and vascular invasion, recurrence, and prognosis of patients. Podoplanin-low cases showed better overall and disease-free survival.

〔 総 括 〕

Role of podoplanin, which is supposed to be one of the cancer stem cell markers, was examined. Podoplanin played a role for tumorigenesis and malignant progression in esophageal squamous cell carcinoma, and its high expression could be a poor prognostic factor.

BACKGROUND: Podoplanin, a mucin-type transmembrane glycoprotein, is thought to be one of the cancer stem cell markers for squamous-cell carcinoma of the vulva. The objectives of the present study were to examine the role of podoplanin in esophageal squamous-cell carcinoma (ESCC).

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METHODS: Expression of podoplanin was examined immunohistochemically in 61 cases of ESCC that had not been treated with chemotherapy or radiotherapy before surgery. Because cancer stem-cell quantities have been reported to increase with chemotherapy and radiotherapy, cases in patients who did not receive such prior therapies were included in this study. Cases with >10% tumor cells showing signals for podoplanin were categorized as podoplanin high, and the others were classified as podoplanin low. The effects of podoplanin on the behavior of cancer cells were evaluated in ESCC cell lines in which podoplanin expression was knocked down.

RESULTS: To examine whether podoplanin could be used as a cancer stem cell marker for ESCC, podoplanin-positive and podoplanin-negative fractions were sorted separately from the ESCC cell line and cultured. Podoplanin-positive ESCC cells yielded both podoplanin-positive and podoplanin-negative cells, whereas few cells were obtained from podoplanin-negative ESCC cells. When podoplanin expression was knocked down, ESCC cell lines became vulnerable to anticancer drugs and showed defective invasion and tumorigenic activities. Nineteen (31.1%) of 61 cases were categorized as podoplanin high. Podoplanin-high cases were correlated with T category, stage of disease, lymphatic and vascular invasion, recurrence, and prognosis of patients. Podoplanin-low cases showed better overall and disease-free survival. **CONCLUSIONS:** There is a role for podoplanin in tumorigenesis and malignant progression in ESCC

CONCLUSION: Role of podoplanin, which is supposed to be one of the cancer stem cell markers, was examined. Podoplanin played a role for tumorigenesis and malignant progression in esophageal squamous cell carcinoma, and its high expression could be a poor prognostic factor.