学 位 論 文 の 要 約

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主論文の題名

RacGAP1 expression, increasing tumor malignant potential, as a predictive biomarker for lymph node metastasis and poor prognosis in colorectal cancer

（腫瘍悪性度を亢進させるRacGAP1発現は、大腸癌におけるリンパ節転移および予後不良予測のためのバイオマーカーとなる）

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主論文の要約

Background:
Rac GTPase activating protein (RacGAP) 1 plays a key role in controlling various cellular phenomena including cytokinesis, transformation, invasive migration, and metastasis. This study aimed to clarify the clinical significance of RacGAP1 expression in colorectal cancer (CRC).
Methods:
The intrinsic functions of RacGAP1 in CRC cells were analyzed using small interfering RNA (siRNA). We analyzed RacGAP1 expression in surgical specimens from CRC patients by real-time polymerase chain reaction (Cohort 1) and immunohistochemistry (Cohort 2).
Results:
Reduced RacGAP1 expression by siRNA in CRC cell lines showed significantly decreased cellular proliferation, migration, and invasion. In Cohort 1, high RacGAP1 expression in tumors was significantly associated with tumor progression and prognosis. In Cohort 2,

RacGAP1 protein expression was significantly higher in CRC patients with higher T stage, vessel invasion, and lymph node and distant metastasis. Increased expression of RacGAP1 protein was significantly associated with poor disease-free and overall survival. Multivariate analyses revealed that high RacGAP1 expression was an independent predictive marker for lymph node metastasis, recurrence, and poor prognosis in CRC.

Conclusion:

We demonstrated novel evidence of RacGAP1 expression in CRC. CRC patients with high expression of RacGAP1 had worse OS and DFS, which highlights that identification of RacGAP1 expression is potentially helpful in identifying patients who have a high risk of recurrence and need adjuvant chemotherapy and strict surveillance. We verified the clinical significance of RacGAP1 as a novel predictive biomarker of lymph node metastasis, which can help reduce CRC-related mortality and morbidity by practicing minimally invasive and curative treatment during earlier stages of CRC.