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

主論文の要旨
Rac GTPase activating protein (RacGAP) 1 plays a key role in controlling various cellular phenomena including cytokinesis, transformation, invasive migration, and metastasis. This study investigated the function and clinical significance of RacGAP1 expression in colorectal cancer (CRC). The intrinsic functions of RacGAP1 in CRC cells were analyzed using small interfering RNA (siRNA). We analyzed RacGAP1 mRNA expression in surgical specimens from 193 CRC patients (Cohort 1) by real-time polymerase chain reaction. Finally, we validated RacGAP1 protein expression using formalin-fixed paraffin-embedded samples from 298 CRC patients (Cohort 2) by immunohistochemistry. Reduced RacGAP1 expression by siRNA in CRC cell lines showed significantly decreased cellular proliferation, migration, and invasion. In Cohort 1, RacGAP1 expression in CRC was significantly higher than in adjacent normal mucosa, and increased according to TNM stage progression. High RacGAP1 expression in tumors was significantly associated with progression and prognosis. In Cohort 2, RacGAP1 protein was overexpressed mainly in the nuclei of CRC cells; however, its expression was scarcely observed in normal colorectal mucosa. 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. Our data provide novel evidence for the biological and clinical significance of RacGAP1 as a potential biomarker for identifying patients with lymph node metastasis and poor prognosis in CRC.