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

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.

The paper reports that RacGAP1 is a predictor of poor prognosis in CRC, and its presence is associated with lymph node metastasis. The authors note that RacGAP1 has the potential to be a valuable biomarker for evaluating disease progression and predicting survival outcomes in CRC patients.

Carcinogenesis
Published: January 7, 2015
doi: 10.1093/carcin/bgu327

著者名
Hiroki Imaoka, Yuji Toiyama, Susumu Saigusa, Mikio Kawamura, Aya Kawamoto, Yoshinaga Okugawa, Junichiro Hiro, Koji Tanaka, Yasuhiro Inoue, Yasuhiko Mohri, Masato Kusunoki