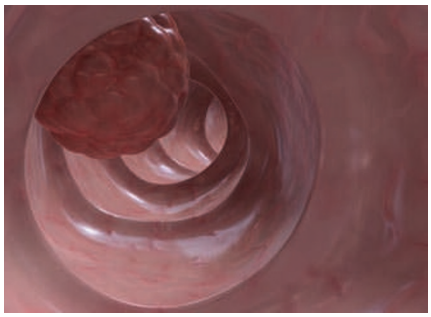
GENETICS

BRAF but not *KRAS* is prognostic in colon cancer

Around 35–42% of colorectal cancers (CRC) harbor mutations in *KRAS,* which occur early in the course of the disease. Patients with metastatic CRC who have *KRAS* mutations derive no benefit from anti-EGFR antibodies, and the *BRAF* V600E mutation also confers resistance to such therapies. Roth *et al*. prospectively examined the prognostic role of *BRAF* and *KRAS* mutations in a large randomized study, and found that *BRAF* mutations are a strong prognostic factor for overall survival particularly in patients with stage II disease who have either low or no microsatellite instability.



DNA was collected from 1,404 patients with stage II or III adenocarcinoma of the colon. *KRAS* and *BRAF* V600E mutations were identified in 37% and 7.9% of samples, respectively. These mutation rates did not differ significantly between stage II and III tumors. Multivariate analysis revealed that *KRAS* mutation was significantly associated with tumor grade, and right-sided tumors. The *BRAF* V600E mutation was significantly associated with female sex, tumor grade, age over 60 years, high levels of MSI, and right-sided tumors.

In multivariate analysis, mutated *KRAS* did not have prognostic value in determining relapse-free survival or overall survival. The *BRAF* V600E mutation was not prognostic for relapse-free survival; however, it did predict an overall survival benefit, especially in patients with low levels of MSI or stable MSI tumors.

Roth and his team conclude *KRAS* has no prognostic value in CRC but their evidence suggests that *BRAF* is prognostic for overall survival, despite both proteins functioning in the same pathway.

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Original article Roth, A. D. *et al*. Prognostic role of *KRAS* and *BRAF* in stage II and III resected colon cancer: results of the translational study on the PETACC-3, EORTC 40993, SAKK 60-00 trial. *J. Clin. Oncol.* **28**, 466–474 (2010)