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Meta-analysis of the mutational status of circulation tumor cells and paired primary tumor tissues from colorectal cancer patients

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As predictive markers for anti-EGFR therapy, KRAS and BRAF mutations are routinely detected in primary and metastatic colorectal cancer (CRC) cells, but seldom in circulating tumor cells (CTCs). Detecting mutations in CTCs could help explain mutational differences between tumor cells at local sites and distant metastases, thereby improving treatment outcomes. Here, we conducted a systematic review and meta-analysis to compare KRAS and BRAF mutations in paired CTCs and primary tumors from CRC patients, to detect any possible discordance. A total of 244 CRC patients from nine studies were included. Our subgroup meta-analysis demonstrated that the total odds ratio for mutations in CTCs was only 55% of that in primary tumors in the stage IV subgroup. We also found low heterogeneity among studies and differences in mutations between CTCs and primary tumors in the stage IV subgroup (I 2 = 0%, P = 0.01). We observed a higher frequency of KRAS mutations in CTCs than in primary tumors at early stages (I + II), a similar frequency in stage III, and a lower frequency in stage IV. There were also differences among the Epcam-targeted CTC enrichment, PCR-based mutation profiling, and ≥ 3 CTCs enriched (I 2 = 0%, P = 0.03) subgroups. These finding indicate mutational discordance between CTCs and primary CRCs, particularly in the stage IV and KRAS subgroups. We suggest large-sample studies stratified by clinical stage and KRAS subtype are urgently warranted to accurately evaluate mutational variations in CTCs compared to primary and metastatic CRC cells.

Biography

Yong Liu is currently working at Surgical Department of Colorectal Cancer, Zhejiang Cancer Hospital, Hangzhou, Zhejiang Province, China.

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