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A Phase Ib Dose-Escalation Study of Encorafenib and Cetuximab with or without Alpelisib in Metastatic BRAF-Mutant Colorectal Cancer

Epigenomic Promoter Alterations Amplify Gene Isoform and Immunogenic Diversity in Gastric Adenocarcinoma

Qamra and colleagues characterized epigenetic promoter alterations in gastric cancer and identified unaltered promoters, somatic tumor-specific promoters gained in tumors, and normal-specific promoters lost in tumors. Overall, 18% of the gastric cancer somatic promoters were alternative promoters that resulted in overexpression of alternative transcript isoforms as well as proteins with altered N-terminal peptide sequences, which may allow for increased proteomic diversity in gastric cancer. Further, alternative somatic promoter usage was linked to decreased tumor immunity. The N-terminal peptides downregulated by gastric cancer somatic promoters elicited immune responses, suggesting that the tumor-specific promoters may decrease tumor immunogenicity. Altogether, these findings identify tumor-specific alternative promoters in gastric cancer that may produce tumor-specific isoforms to promote tumor immune evasion. For details, please see the article by Qamra and colleagues on page 630.