High EPHB2 mutation rate in gastric but not endometrial tumors with microsatellite instability.

The EPH/EFN family of receptor tyrosine kinases regulates cell adhesion and migration and has an important role in controlling cell positioning in the normal intestinal epithelium. Inactivation of EPHB2 has recently been shown to accelerate tumorigenesis in the colon and rectum, and we have previously demonstrated frequent frameshift mutations (41%) in an A9 coding microsatellite repeat in exon 17 of EPHB2 in colorectal tumors with microsatellite instability (MSI). In this study, we extended these analyses to extracolonic MSI cancers, and found frameshift EPHB2 mutations in 39% (25/64) of gastric tumors and 14% (8/56) of endometrial tumors. Regression analysis of these EPHB2 mutation data on the basis of our previously proposed statistical model identified EPHB2 as a selective target of frameshift mutations in MSI gastric cancers but not in MSI endometrial carcinomas. These results suggest a functional role for EPHB2 in gastric tumor progression, and emphasize the differences between the tumorigenic processes in MSI gastrointestinal and endometrial cancer.