Increased methylation levels at cytosines proximal to guanines (CpG) in the promoter regions of tumor suppressor genes has been reported to play an important role in the development and progression of bladder cancer. In this study, we conducted a genome-wide analysis using data from The Cancer Genome Atlas to better characterize CpG methylation and mRNA expression patterns in urothelial carcinomas and to identify new epigenetic biomarkers of survival. 223 genes displayed significant relationships between CpG methylation and mRNA expression levels. Hypermethylation proximal to the transcription start site and hypomethylation within the 3' untranslated region and body region were associated with gene silencing. These 223 genes were functionally enriched for their role in glutamate receptor signaling and among them was a novel, tumor-stage-independent epigenetic biomarker of overall mortality for patients with basal-like urothelial carcinomas, GRIA1. This research highlights glutamate receptors as targets for investigation in the development of urothelial cancer.

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