Aberrant Methylation of HLT Gene in Human Esophageal Cancer

Liang Wang¹,², Xiaojing Zhang³, Peng Yin¹, Yan Gao⁴, Yuan Zhang¹, Xianling Feng¹, Si Chen¹, Huimin Yu¹, Weiling Huang¹, Yong Huang¹, Qianhe Jian¹, Zhenfu Zhao¹, Xinmin Fan¹ and Zhe Jin²,³,⁴

¹Department of Pathology, The Shenzhen University School of Medicine, Shenzhen, Guangdong, People’s Republic of China, 518 060
²Shenzhen Key Laboratory of Micromolecule Innovatal Drugs, The Shenzhen University School of Medicine, Shenzhen, Guangdong, People’s Republic of China, 518 060
³Shenzhen Key Laboratory of translational Medicine of Tumor, School of Medicine, Shenzhen University, Shenzhen, Guangdong, People’s Republic of China, 518 060
⁴Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University Shenzhen Graduate School, Shenzhen, Guangdong, P.R. of China, 518 055
⁵Nanshan Hospital, Guangdong Medical College, Shenzhen, Guangdong, P.R. of China, 518 052

KEYWORDS Alcohol, EAC, ESCC, HLT, Hypermethylation

ABSTRACT The aim of this study was to investigate whether and at which neoplastic stage promoter hypermethylation of Helicase-like Transcription Factor (HLTF) is involved in human esophageal carcinogenesis. The researchers examined HLT promoter hypermethylation using real-time quantitative methylation-specific PCR in 229 primary human esophageal tissues of contrasting histological types. Both HLT mean normalized methylation value (NMV) and hypermethylation frequency were significantly higher in dysplastic Barrett’s esophagus (Dy: 0.0303 and 10.0%), and esophageal adenocarcinomas (EAC, 0.0079 and 10.4%) than in normal esophagus (NE, 0.0006 and 0.0%; p<0.05 and p<0.05, respectively). Incremental increases in the frequency of HLT hypermethylation were observed during progression from NE (0.0%) to Barrett’s esophagus (BE, 3.3%), D (10.0%), and EAC (10.4%). Meanwhile, HLT mean NMV was significantly higher in esophageal squamous cell carcinoma (ESCC, 0.0102) than in NE (p<0.05). Also, HLT was hypermethylated in 7.7% ESCCs. Furthermore, mean NMV of HLT was significantly higher in current alcohol drinking EAC patients (0.0194) than in non-current ones (0.0066, p<0.05). HLT hypermethylation is an uncommon event in human esophageal cancer, but occurs early in a subset of EAC, and is related to the alcohol drinking status of EAC patients.