Abstract

iMedPub Journals
http://www.imedpub.com

Journal of Medical Oncology

2022
Vol 5. No. 3

Induction of epigenetic alterations in gastric epithelium and their contribution to gastric tumorigenesis

Atsushi Kaneda
Chiba University, Japan

Abstract

Cancer arises through accumulation of epigenetic and genetic alterations and therefore is stratified into several molecular subtypes using comprehensive epigenomic and genomic information. We showed that accumulated epigenomic alteration could causally modify tumor risk. We also comprehensively stratified gastric cancer into 4-5 DNA methylation epigenotypes, depending on pathogens. While the majority of gastric cancer is associated with Helicobacter pylori infection, a subset of gastric cancer, ranging 7-15%, is associated with Epstein-Barr virus (EBV) infection. EBV+ gastric cancer exhibits most severe DNA hypermethylation and EBV itself was shown to cause the extensive hypermethylation phenotype when infected into gastric epithelial cells, involving increased expression of DNMT1. Demethylating enzyme TET2 was found to function as a resistant factor against DNA methylation induction and hMeDIP-seq and MeDIP-seq analyses revealed that target regions of hydroxy methylation by TET2 significantly overlapped with target regions of de novo DNA methylation by EBV infection. The repression of TET2 due to viral transcripts or up-regulated human miRNAs significantly contributes to de novo methylation acquisition. Other epigenomic alterations are also involved in promoter regions, enhancer regions, etc., during EBV infection and cause aberrant regulation of critical genes e.g. proliferative genes or tumor suppressor genes. Another cancer subtype with DNA hypermethylation phenotype involves aberrant methylation of mismatch repair gene MLH1, leading to microsatellite instability (MSI) and gene hypermutation in gastric cancer. These subsets of gastric cancer with hypermethylation phenotype, i.e., EBV+ subtype and MSI-high subtype, showed unique gene mutation patterns, which contribute to gastric tumorigenesis synergistically with DNA hypermethylation.

Received: May 08, 2022; **Accepted:** May 16, 2022; **Published:** May 25, 2022

Biography

Atsushi Kaneda has obtained his MD degree from University of Tokyo and became Assistant Professor at the Department of Gastrointestinal Surgery, University of Tokyo where he conducted genome-wide DNA methylation analysis in gastric cancer and acquired PhD degree. He has also studied at Johns Hopkins University and showed that accumulated epigenetic alteration could modify intestinal tumor risk using mouse model of IGF2 LOI. As an Associate Professor at University of Tokyo and as Professor at Department of Molecular Oncology, Chiba University since 2013, he has conducted projects to clarify epigenomic mechanisms in gastrointestinal carcinogenesis.

