

Genetic association of gastric cancer with miRNA clusters including the cancer-related genes MIR29, MIR25, MIR93 and MIR106: Results from the EPIC-EURGAST study

Espinosa-Parrilla, Yolanda

Muñoz, Xavier

Bonet, Catalina

Garcia, Nadia

Venceslá, Adoración

Yiannakouris, Nikos

Naccarati, Alessio

Sieri, Sabina

Panico, Salvatore

Huerta, José M.

Barricarte, Aurelio

Menéndez, Virginia

Sánchez-Cantalejo, Emilio

Dorransoro,

MicroRNAs (miRNAs) are post-transcriptional gene regulators involved in a wide range of biological processes including tumorigenesis. Deregulation of miRNA pathways has been associated with cancer but the contribution of their genetic variability to this disorder is poorly known. We analyzed the genetic association of gastric cancer (GC) and its anatomical and histological subtypes, with 133 single-nucleotide polymorphisms (SNPs) tagging 15 isolated miRNAs and 24 miRNA clusters potentially involved in cancer, in 365 GC cases and 1,284 matched controls within the European Prospective Investigation into Cancer and Nutrition cohort. Various SNPs were associated with GC under the log-additive model. Furthermore, several of these miRNAs passed the gene-based permutation test when analyzed according to GC subtypes: three tagSNPs of the

miR-29a/miR-29b-1 cluster were associated with diffuse subtype (minimum p-value= 1.7×10^{-4} ; odds ratio, OR=1.72; 95% confidence interval, CI=1.30-2.28), two t