学位論文の要旨

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主論文の題名

Combination of *RERG* and *ZNF671* methylation rates in circulating cell-free DNA: A novel biomarker for screening of nasopharyngeal carcinoma

主論文の要旨

Nasopharyngeal carcinoma (NPC) is a prevalent malignancy in Southeast Asia, hence, identifying easily detectable biomarkers for NPC screening is essential for better diagnosis and prognosis. Using genome-wide and targeted analyses based on next-generation sequencing approaches, we previously showed that gene promoters are hypermethylated in NPC tissues. To confirm whether DNA methylation rates of genes could be used as biomarkers for NPC screening, 79 histologically diagnosed NPC patients and 29 noncancer patients were recruited. A convenient quantitative analysis of DNA methylation using real-time PCR (qAMP) was carried out, involving pretreatment of tissue DNA, and circulating cell-free DNA (ccfDNA) from nonhemolytic plasma, with methylation-sensitive and/or methylation-dependent restriction enzymes. The qAMP analyses revealed that methylation rates of *RERG*, *ZNF671*, *ITGA4*, and *SHISA3* were significantly higher in NPC primary tumor tissues compared to noncancerous tissues, with sufficient diagnostic accuracy of the area under receiver operating characteristic curves (AUC). Interestingly, higher methylation rates of *RERG* in ccfDNA were statistically significant and yielded a very good AUC; however, those of *ZNF671*, *ITGA4*, and *SHISA3* were not significant. Furthermore, the combination of methylation rates of *RERG* and *ZNF671* in ccfDNA showed higher diagnostic accuracy than either of them individually. In conclusion, the methylation rates of specific genes in ccfDNA can serve as novel biomarkers for early detection and screening of NPC.