学位論文審査結果の要旨

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（学位論文審査結果の要旨）

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

【主論文審査結果の要旨】

著者らは論文において下記の内容を述べている。

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.

上咽頭癌におけるスクリーニングバイオマーカーを探索し、癌組織において、4 つの候補遺伝子はいずれも非癌組織に比べ、早期の癌でもメチル化率が有意に高いことを明らかにし、スクリーニングに応用できる科学的根拠を得た。さらに、侵襲性の低い血液試料を用い、ccfDNA メチル化率は 4 つの候補遺伝子のうち RERG と ZNF671 の 2 つを組み合わせることで高い正診率を示し、上咽頭癌の早期診断スクリーニングのバイオマーカーに資する可能性を示した論文であり、学術上極めて 有益であり、学位論文として価値あるものと認めた。

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