Symposium 16: Optimization of molecular targeting therapy for colorectal cancer using genome based analysis

Development of the new biomarker of colorectal cancer using the comprehensive molecular analyses

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From the end of 20th century, many molecular target drugs were introduced into cancer therapy. The treatment outcome of metastatic colorectal cancer improves steadily by the induction of the molecular target drug, and the median survival time in the representative phase III study reaches for 30 months. However, all molecular target drugs are expensive, and some of them are inferior in cost effectiveness as compared with conventional chemotherapeutic drugs. Therefore, the stratification of the patients by biomarker predicting treatment sensitivity is important to improve the cost effectiveness of the molecular target drugs. To date, in colorectal cancer treatment, the drug that biomarker was established is only anti-EGFR antibody. Recently, the biomarker of the anti-EGFR antibody was expanded for any mutation of the RAS gene by exon 2 mutation of KRAS gene. As a result, cost effectiveness is thought to be improved by the increase of the specificity for patient selection. In addition, the mutation of PIK3CA gene and the BRAF gene, and loss of PTEN expression are regarded as candidates of the biomarker, but the medical evidence about the utility is still poor.

We have developed the new biomarker using comprehensive molecular analyses with the goal of optimization of colorectal cancer treatment. The cohort of 100 metastatic colorectal cancers treated with standard chemotherapy was used for comprehensive gene expression analysis. Also, the cohort of 97 metastatic colorectal cancers treated for anti-EGFR antibody was used for comprehensive DNA methylation and whole exome sequence analysis. From results of the analyses, we found methods to classify metastatic colorectal cancer in subtypes based on a molecular biologic characteristic. Also, association of the molecular subtype and the effect of treatment with anticancer drug were examined. In this symposium, we focus on the association of the subtype and the effects of the anti-EGFR antibody.

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