The feasible approach to monitor the MRD for recurrence after the radical treatment for stage III colorectal cancer cases.

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Background & objectives

Cancer genome medicine has begun recommending therapies based on comprehensive genome profiling (CGP) for solid tumors. However, considering the cost-effectiveness and invasiveness in monitoring postoperative minimum residual disease (MRD) of colorectal cancer, we developed an approach to detect methylated ctDNA as the most feasible assay to detect MRD compared to other conventional measures.

Methods

Analyzing the public database of the methylation array could identify methylated promoter regions of three genes. They were colorectal cancer-specific, cancer-specific, non-expression in healthy tissues nor blood, the inverse association between the expression of target transcripts and methylated β-value, and independent poor prognostic factors. Using digital PCR assay, we quantified and defined “the amplicon of methylated sites using a methylated site-specific enzyme (AMUSE)" as the value of each sample.

Results

We examined chronologic 180 and 114 time points plasma samples from 28 recurrence and 19 relapse-free cases. The results showed 22 AMUSE-positive cases (sensitivity 78.6%) out of 28 recurrence cases and 17 AMUSE-negative cases (specificity 89.5%) out of 19 recurrence-free cases. The time to recurrence diagnosed by AMUSE was an average of 208 days shorter than by the conventional diagnosis CT. In addition, the positive value for AMUSE at either the second or third sampling blood in 19 cases indicated a significantly poorer prognosis than the other 28 cases (p=9E-04).

Conclusion

In conclusion, the AMUSE assay fulfills clinical needs regarding inter-case universal accuracy, minimized invasiveness, and cost-effectiveness for monitoring MRD toward recurrence. This

assay can evaluate the effectiveness of the ACT after the curative operation on stage III colorectal cancer cases.