A CIRC RNA SIGNATURE PREDICTS POSTOPERATIVE RECURRENCE IN STAGE II/III COLON CANCER

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Background Current staging methods seem to have only a limited role in predicting the risk of disease recurrence and benefit of adjuvant chemotherapy for patients with stage II/III colon cancer. Circular RNA is a novel type of noncoding RNA with a potential use as biomarkers; however, whether circRNA-based signatures could serve as novel prognostic biomarkers for stage II/III colon cancer is unknown.

Methods 20 paired of frozen tumor tissues and adjacent normal tissues of stage II/III colon cancer were collected and conducted an RNA-sequencing study and profiled circRNAs by a series of bioinformatics analyses to identify the significant circRNA markers. QPCR assay was used to test those markers on the samples from the training and validation cohorts. LASSO-bagging procedure was used to select the top four markers to build the regression model. The cell migration assay in vitro and metastasis study in vivo were performed to detect the function of the top four markers.

Results Dysregulated circRNAs showed strong classification properties in distinguishing the recurrent and nonrecurrent colon cancer patients. A novel prognostic tool (cirScore) based on four circRNAs (i.e., hsa_circ_0122319, hsa_circ_0087391, hsa_circ_0079480 and hsa_circ_0008039) is developed and validated to improve the prognostic stratification for patients with radically resected stage II/III colon cancer. The proposed cirScore can effectively classify patients with stage II/III colon cancer into groups with low and high risks of disease recurrence. Loss-of-function assays indicated that the representative circRNAs plays functional roles in the sophisticated regulation of colon cancer progression.

Conclusions Our current study addresses an important gap, which is the refinement of our prognostic tools for stage II/III colon cancer, by using a novel approach that takes into consideration the circular RNA. The proposed cirScore might be used in the future to guide better and more personalized treatment decisions for patients with stage II/III colon cancer.