1439 NOVEL CANCER-ASSOCIATED FIBROBLAST-RELATED MARKERS MEDIATE ANTITUMOR IMMUNITY IN COLON CANCER

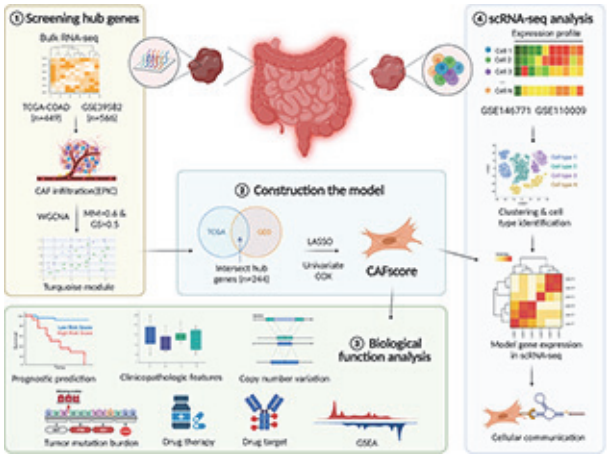
[1]Leqian Ying*, [2]Lin Liu. [1]*Southeast University, Nanjing, Jiangsu, China*; [2]*The Affiliated Zhong-Da Hospital of Southeast University, Nanjing, Jiangsu, China*

Background Cancer-associated fibroblast (CAF) is closely linked to cellular dysfunction, metabolic disorder, cancer progression, and treatment resistance in colon cancer (CC). In short, the research of CAF in CC has made progress, but related fields still need to be further explored. Our study further expands the function of CAF in CC from the perspective of bulk RNA-sequencing (RNA-seq) and single cell RNA-seq (scRNA-seq).

Methods CAF infiltrations based on mRNA expression data from the TCGA-COAD and GSE39582 cohorts were assessed using the estimate the proportion of immune and cancer cells (EPIC), microenvironment cell populations-counter (MCP-counter), xCell, and ESTIMATE algorithms. CAF hub genes that strongly associated with EPIC-quantified CAF infiltrations were filtrated by weighted gene co-expression network analysis. Data for scRNA-seq were obtained from the GSE146771 and GSE110009 cohorts. A practical CAF risk score (CAFscore) was successfully built to evaluate the clinical outcome, somatic hypermutation, biological processes and potential effective drugs (figure 1).

Results The CAFscore was built from three prognostic-related CAF hub genes chosen using univariate Cox and LASSO regression analysis, including CRIP2, FSTL3 and SLC2A3. By taking the optimal cutoff values of CAFscore, high CAFscore was closely related to malignant biological behavior. And CAFscore did excellently in both the training and external validation cohorts. Furthermore, high CAFscore was connected to somatic hypermutation, immunological evasion and treatment resistance. The half maximum inhibitory concentration (IC50) of first-line therapeutic agents in low CAFscore subgroup was lower than high subgroup. As for biomedical function, aerobic respiration and substance metabolism were enriched in the low CAFscore subgroup, and ECM receptor interaction, focal adhesion, pathway in cancer, TGFb signaling pathway were significantly positively correlated with CAFscore. In addition, CRIP2 and FSTL3 were highly expressed in stromal cells of GSE146771 and GSE110009, especially in CAF. TGFb pathway related ligands and receptors are generally highly expressed in CAF, and play their biological functions by cellular communication.

Conclusions We identified high CAFscore to be associated with the adverse prognosis, malignant biological behavior, somatic hypermutation, drug insensitivity and cellular communication of CC patients. The crucial biomedical function of key genes of CAFscore was multidimensionally validated based on bulk RNA-seq and scRNA-seq.



Abstract 1439 Figure 1

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1439