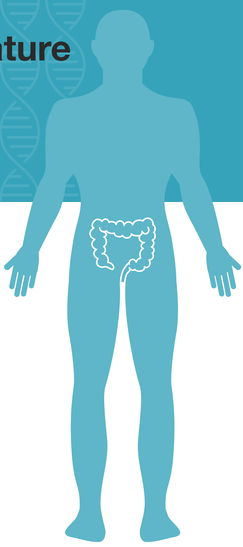
Establishment of a 12-gene expression signature to predict colon cancer prognosis



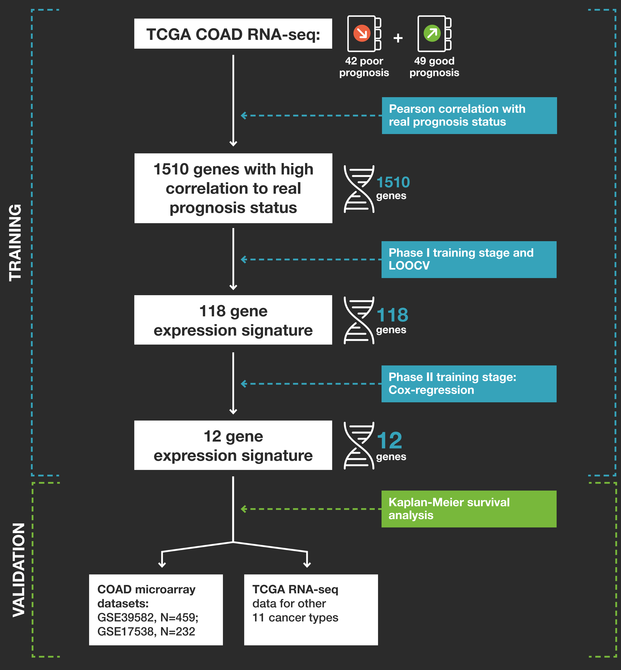
INTRODUCTION

Robust and accurate gene expression signature is essential to assist oncologists to determine which subset of patients at similar Tumor-Lymph Node-Metastasis (TNM) stage has high recurrence risk and could benefit from adjuvant therapies.

Here we applied a two-step supervised machine-learning method and established a 12-gene expression signature to precisely predict colon adenocarcinoma (COAD) prognosis by using COAD RNA-seq transcriptome data from The Cancer Genome Atlas (TCGA).

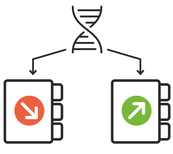
METHODOLOGY

The predictive performance of the 12-gene signature was validated with two independent gene expression microarray datasets: GSE39582 and GSE17538.



RESULTS

The signature could effectively separate poor prognosis patients from the good prognosis group in GSE17538. For patients with proficient mismatch repair system (pMMR) in GSE39582, the signature could also effectively distinguish the high risk group from the low risk group.



Interestingly, advanced stage patients were significantly enriched in the high 12-gene score group. After stage stratification, the signature could still distinguish poor prognosis patients in GSE17538 from good prognosis within stage II and stage II&III in the outcome of DFS. Within stage III or II / III pMMR patients treated with Adjuvant Chemotherapies (ACT), patients with higher 12-gene score showed poorer prognosis. Among stage II/III pMMR patients with lower 12-gene scores in GSE39582, the subgroup receiving ACT showed significantly longer OS time compared with those who received no ACT, while there is no obvious difference between counterparts among patients with higher 12-gene scores.

Besides COAD, **our 12-gene signature is multifunctional in several other cancer types** including kidney cancer, lung cancer, uveal and skin melanoma, brain cancer, and pancreatic cancer. Functional classification showed that seven of the twelve genes are involved in immune system function and regulation.

CONCLUSION

Our 12-gene signature could potentially be used to guide decisions about adjuvant therapy for patients with stage II/III and pMMR COAD.

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