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Identification of age- associated genes as prognostic factors in non-small cell lung cancer

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INTRODUCTION

The inevitability of a time-dependent decline in physiological organ performance as we age is a major risk factor for cancer development. Life expectancy is increasing in most industrialized countries as a consequence of advancements in health-care delivery, sanitation management, and food availability. As a result, the population is changing, with a growing number of people at risk of acquiring cancer. Cell senescence is one of the hallmarks where cancer and aging are fundamentally different as accumulating DNA damage usually will cause an upregulation of cell cycle inhibitors leading to senescence or apoptosis while malignant cells avoid this by generating additional mutations such as deletion of tumor suppressors.(1-3)

METHODS AND MATERIALS

The inevitability of a time-dependent decline in physiological organ performance as we age is a major risk factor for cancer development. Life expectancy is increasing in most industrialized countries as a consequence of advancements in health-care delivery, sanitation management, and food availability. As a result, the population is changing, with a growing number of people at risk of acquiring cancer. Cell senescence is one of the hallmarks where cancer and aging are fundamentally different as accumulating DNA damage usually will cause an upregulation of cell cycle inhibitors leading to senescence or apoptosis while malignant cells avoid this by generating additional mutations such as deletion of tumor suppressors. Our study reveal new ageing genes model for non-small cell lung cancer NSCLC patients. Researchers from the Genomic Data Commons (GDC, accessible via the portal:<https://portal.gdc.cancer.gov/>) managed to collect gene expression data from NCLC tissues third level. Transcriptomic analysis from The Cancer Genome Atlas TCGA and matching ageing genes to find new ageing genes signature for both lung squamous cell cancer LUSC and lung adenocarcinoma LUAD. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) were conducted by using <https://biit.cs.ut.ee/gprofiler/gost>.

RESULTS

Known variables from 486 LUSC patients and 450 LUAD cases were collected and analyzed . For LUSC, ANKLE1, and LRRK2, and SMC6, and KRT16 with AUC =96% .For LUAD type TERT, HMGA2, CAV1, KRT16 and CDK1 with AUC =84 %. These signature model was consistently showed significant by Cox regression in overall survival for LUSC and LUAD (P= 0.003, HR= 1.53, CI = 1.15-2.05) and (P= 0.008, HR= 1.56, CI = 1.12—2.17) respectively. The LUSC gene signature was connected with the biological process of aging, cell aging, cellular senescence, and cell aging regulation, whilst KEGG pathways were largely associated with cellular senescence and cell cycle. Furthermore, LUAD biological activities include enzyme binding, transcription factor binding, and catalytic activity on DNA, whereas the gene signature model is significantly associated with cell cycle and cellular senescence on KEGG pathways.

CONCLUSIONS

This novel signature model proposed showed significant effectiveness against several non-small cell lung cancer subgroups. Future research is needed to determine the therapeutic use of biomarkers in personalized NSCLC care with monotherapy or in combination with chemotherapy.

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