A PAN-CANCER ANALYSIS OF FERROPTOSIS-RELATED GENE ARACHIDONIC ACID 15-LIPOXYGENASE-1 (ALOX15): ITS PROGNOSTIC AND IMMUNOTHERAPEUTIC VALUES

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Emerging research has identified ferroptosis as a novel form of programmed cell death, and Arachidonic acid 15-lipoxygenase-1 (ALOX15) stands out as a pivotal gene in mediating this process. Nonetheless, the role of ALOX15 in human tumors remains elusive. We utilized TIMER 2.0 to investigate the differential expression profiles of ALOX15 between pan-cancer and normal tissues. Further data from the TCGA, GEPIA, UALCAN, HPA, and CPTAC databases were analyzed to verify the levels of mRNA, protein expression, and promoter methylation across various cancer types. The survival prognosis, clinical features, and genetic alterations of ALOX15 were also evaluated. GO/KEGG enrichment analyses and single-cell transcriptome sequencing were employed for functional enrichment analysis. The gene mutation of ALOX15 and its prognostic value were analyzed using the cBioPortal platform. Finally, the relationship between ALOX15 and immune cell infiltration, Immune Checkpoints (ICKs), genomic instability, and drug sensitivity was further explored using GSCA. Our findings revealed that the transcription and protein expression of ALOX15 were significantly reduced in HNSC, LUAD, LUSC, SKCM, KICH, and THCA, while they were up-regulated in ESCA, LIHC, PRAD, and UCEC. Notably, the expression of ALOX15 had prognostic value for certain cancers, including LUAD, LUSC, LIHC, KIRC, HNSC, THCA, and LGG. Additionally, ALOX15 expression was markedly correlated with clinical characteristics, immune cell infiltration, ICKs, genomic instability, and antitumor drug sensitivity in various tumors. Gene mutations of ALOX15 and their prognostic value were discovered in pan-cancers. Furthermore, GO/KEGG analysis and single-cell transcriptome sequencing indicated that ALOX15 was significantly associated with cancer-related pathways. Our comprehensive pan-cancer analysis shed light on the role and significance of ALOX15, suggesting its potential as a prognostic and immunotherapeutic marker for pan-cancer. These findings may provide new directions and evidence for cancer therapeutics.

Key words: *ferroptosis, bioinformatics, prognosis, pan-cancer, ALOX15, biological functions, immune.*

ПАНРАКОВИЙ АНАЛІЗ ГЕНУ АРАХІДОНАТ-15-ЛІПОКСИГЕНАЗИ-1 (ALOX15), ПОВ'ЯЗАНОГО З ФЕРРОПТОЗОМ: ЙОГО ПРОГНОСТИЧНА ТА ІМУНОТЕРАПЕВТИЧНА ЦІННІСТЬ

Під час нового дослідження було виявлено ферроптоз як новітню форму програмованої смерті клітин. Арахідонат-15-ліпоксигеназа-1 (ALOX15) виступає основним геном-посередником у цьому процесі. Однак, роль ALOX15 у розвитку пухлин людини залишається недостатньо вивченою. Ми використали TIMER 2.0 для дослідження профілів диференційної експресії ALOX15 у панракових і нормальних тканинах. Було проаналізовано подальші дані з баз даних TCGA, GEPIA, UALCAN, HPA та CPTAC і верифіковано рівні мРНК, експресії білків і метилювання промотерів для різних онкологічних захворювань. Також було проведено оцінку прогнозу виживання, клінічних рис і генетичних змін ALOX15. Для аналізу подальшого збагачення було використано аналіз збагачення за шляхами GO/KEGG та одноклітинне секвенування транскриптома. Генна мутація ALOX15 та її прогностична цінність були проаналізовані за допомогою платформи cBioPortal. Згодом було проведено подальше дослідження відносин між ALOX15 та інфільтрацією імунних клітин, імунними контрольними точками (ІКТ), нестабільністю геному і чутливістю до препаратів за використання GSCA. Ми виявили, що транскрипція і експресія білку ALOX15 були значно зниженими в HNSC, LUAD, LUSC, SKCM, KICH та THCA, але залишалися підвищеними в ESCA, LIHC, PRAD та UCEC. Зокрема, експресія ALOX15 мала прогностичну цінність для певних видів онкологічних захворювань, зокрема LUAD, LUSC, LIHC, KIRC, HNSC, THCA та LGG. Крім того, експресія ALOX15 перебувала в чіткій кореляції з клінічними характеристиками, інфільтрацією імунних клітин, ІКТ, нестабільністю геному і чутливістю різних пухлин до протипухлинних препаратів. Панраковий аналіз виявив генні мутації ALOX15 та їхню прогностичну цінність. Крім того, аналіз GO/KEGG та секвенування одноклітинного транскриптома продемонстрували суттєвий асоціативний зв'язок між ALOX15 та онкошляхами. Наш комплексний панраковий аналіз пролив світло на роль і значимість ALOX15, припускаючи його

потенційну роль прогностичного та імунотерапевтичного маркера для панракового аналізу. Ці результати можуть надати онкотерапії нових доказів і задати їй нового напрямку.

Ключові слова: ферроптоз, біоінформатика, прогноз, панраковий, ALOX15, біологічні функції, інфільтрація імунних клітин.

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Received June 22, 2023
Received December 29, 2023
Accepted September 18, 2024