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Perspective

PREDICTION OF DRUGS FOR HUMAN CANCER

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INTRODUCTION

The disruption of immune-related pathways has the potential to significantly contribute to cancer. However, the extent to which tumorigenesis is affected by immune-related pathways as a result of aging is largely unknown. Methods: Using genomic and transcriptomic data, we examined the immune-related genes and pathways of 25 different types of cancer in depth here. Based on our findings, we discovered a number of pathways with aging-related characteristics in a variety of cancers, which were further supported by conventional aging-related gene sets. In a variety of cancers, a strong correlation between aging and mutation burdens in cytokines and cytokines receptor pathways was found through genomic analysis.

DISCUSSION

In addition, immune-related pathways were found to improve melanoma prognosis. In addition, melanoma and non-small cell lung cancer patients' responses to immune checkpoint blockade therapy were strongly correlated with these pathways' expression levels. We predicted immune- and aging-related genes in pan-cancer using a network-based approach and used these genes for the discovery of potential immunotherapy drugs. Potential drug targets, FYN, JUN, and SRC, were identified by mapping drug target data to our top-ranked genes. Conclusions: Our comprehensive research contributed to the understanding of the associations between cancer, aging, and immune-related pathways and may be a resource for promoting clinical treatment. Numerous studies have established that aging is one of the most important causes of a wide range of cancers. People get older, their risk of dying from cancer and developing tumors skyrockets. The disruption of the immune system is another well-known characteristic of cancer. The body's innate and adaptive immune processes become impaired as the immune system ages, which can lead to an inflammatory environment. As a result, an enflamed tumor microenvironment may alter the immune landscape [1].

Immunotherapy has proven to be a promising treatment option for a variety of cancers, with impressive outcomes. Immune checkpoint blockade (ICB) therapies have provided patients with long-term benefits by inhibiting checkpoint molecules like programmed cell death, programmed cell death 1 ligand 1 (PD-L1), and cytotoxic T-lymphocyte associated protein 4 (CTLA-4). T cells,

which are capable of constructing and maintaining the immune landscape, are the primary targets of ICB therapy. T cell dysfunction may result from the aging process's decline in the immune system; as a result, ICB therapy does not work for patients. The expression of PD-L/PD-L1 has been identified as a biomarker for immunotherapy response in current multi-omics studies. However, when they function, genes frequently interact closely with one another rather than being isolated from one another. It is still unclear what role the immune-related pathway plays in cancer and aging. Immunotherapy resistance mechanisms may be better understood if the immune-related pathway's role in aging and cancer is fully characterized [2-4].

To further refine these gaps, we combined genomic and transcriptomic data from 25 different types of cancer. In this study, we systematically investigated the differences in immune-related pathways in pan-cancer that are influenced by age and cancer. Cancer-specific characteristics were observed when immune-related pathways were altered as cells grew older, as we discovered. In addition, the patterns of alteration of these pathways with age were investigated. In melanoma and non-small cell lung cancer, we found several immune-related pathways that may be able to predict a patient's response to immunotherapy. Using a network-based approach, potential drug targets for ICB therapies were predicted. As a whole, our findings have the potential to shed light on the age-related roles that immune-related pathways play in tumorigenesis and provide guidance for immunotherapy options. Ipilimumab, pembrolizumab, nivolumab, and atezolimumab are among the checkpoint inhibitor drug combinations that have been approved following ongoing clinical trials. The goal of our study was to anticipate possible drug combinations that would improve immunotherapy response. In pan-cancer, we used a restart method and a random walk to find genes associated with aging and cancer; DGIdb was able to suggest a number of potential drugs by utilizing these 136 genes as input. Dasatinib is an SRC family kinase inhibitor; Dasatinib has been successfully used to target SRC inhibition in a variety of cancers. Additionally, FYN has been confirmed as one of dasatinib's kinase targets. Gemcitabine, which has the potential to rewire immune-related pathways in the tumor microenvironment, is a first-line treatment for pancreatic cancer. Gemcitabine and anti-PD-1 increased the activity of CD8+ T cells and M1 macrophages. As a result, more preclinical options may be available for patients to benefit from immunotherapy. Our work could provide candidates for future studies, and future experimental validation would improve our results [3,4]

Only 17 genesets from Immport, which curate immunologically relevant gene lists related to specific immune functions, were utilized in this study. Research in related fields will get even better in the future if more datasets from other sources are used. Our systematic analysis of immune-related pathways in pan-cancer revealed the aging and tumor-related characteristics of these pathways and suggested that a number of pathways may assist in enhancing the response to cancer immunotherapy. With the help of our findings, we were able to fully comprehend the role that immune-related pathways can play in cancer immunity and develop practical strategies for expanding clinical tumor therapy [5,6].

CONCLUSION

By applying transcriptomic and genomic analysis to immune-related genes and pathways, our research concluded that aging, immunity, and cancer are connected. In human cancer, this study discovered an aging-like perturbation in the expression and mutation pattern of immune pathways. It's possible that these pathways could be used as biomarkers for cancer immunotherapy. The significance of immune-related genes and pathways that play oncogenic roles in aging was brought to light by our research, which has the potential to further illuminate immunotherapy for patients.

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