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Commentary

A new immune-based prognostic scoring system for multiple myeloma

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In the US, multiple myeloma (MM) accounts for around 2% of all cancer-related fatalities and is the second most frequent hematologic malignancy.[1] Developing new treatments and medication regimens has significantly increased survival rates.[2] Even in groups participating in uniformly treated clinical trials, survival rates continue to vary widely despite significant advancements in therapy.[3,4] This discrepancy emphasizes how crucial risk stratification is for prognostication at diagnosis and for patient selection in treatment trials.[5,6]

Improved risk characterization in MM has been the goal of proposed modifications to the International Staging System (ISS) based on fluorescence *in situ* hybridization (FISH).[7–9] Despite notable advancements, several issues have prevented these models from being widely used in clinical practice. For example, established risk groupings still carry significant patient variability. Moreover, these models ignore several prognostically relevant and time-dependent features and are, therefore, unable to predict the outcomes of individual patients. Furthermore, they largely ignore several prognostically relevant genomic and time-dependent features.

The treatment must also be included, limiting their ability to inform therapeutic decisions. Finally, they define the relative risk of either progression or death for a group of patients with only similar features. A new comprehensive scoring system that enhances comprehension of a multihit disease's prognostic implications is still needed.

In a recent study published in Molecular Therapy – Nucleic Acids in 2022, Jian et al. created the first neoantigen immune system response score, dubbed NAIRscore, that predicts overall survival in MM patients.[10] They used 516 paired outcomes in each tumor (i.e., mutation annotation format (Maf) and fragments per kilobase of transcript per million mapped reads (FPKM) data) of 478 patients with MM downloaded from the the Multiple Myeloma Research Foundation's clinical outcomes in multiple myeloma personal assessment (MMRF-CoMMpass) project to establish this score. This score represents the most complete pipeline identifying and predicting neoantigens in MM tumors. It then combines the neoantigen load, the cytolytic score, and the human leukocyte antigen I (HLA-I) score to indicate the quality of the immune response to immunotherapy and to predict overall survival (OS). In addition to developing NAIRscore to stratify MM samples with high and low NAIRscore samples and predict OS, they developed a friendly web-based tool (http://www.biostatistics.online/MMPrgognosis/)[10] that allows quick searching, browsing, and downloading of detailed information about MM neoantigens.

For instance, users need to provide two text files from the same patient with MM: a Maf file to reflect somatic mutations in the tumor and an FPKM file to represent the expression levels of genes in the tumor. After uploading the two files, those neoantigens in the tumor can be identified within minutes, and users can directly download results for further exploration, such as personalized neoantigen vaccines. In the meantime, users can also obtain the predictive OS table and risk curve.

NAIRscore also provides efficient analysis tools to infer differentially expressed genes (DEGs) and cytolytic scores for individual MM tumors. It offers detailed and diverse significant biology processes (BPs) about immune response, including T cell activation, immune response-activating cell-surface receptor signaling pathways, regulation of T cell activation, and antigen receptor-mediated signaling pathways. It also provides the cell component (CC) and molecular function (MF) of the T cell receptor (TCR) complex, antigen binding, TCR binding, and major histocompatibility complex (MHC) class I protein binding, enabling users to identify neoantigens in tumors in a precise manner.

Finally, thanks to the elegant web server MMprognosis, researchers needing an intensive bioinformatics background can comprehend the largely unexplored roles of neoantigens in MM patients.

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AUTHOR CONTRIBUTIONS

M.H. and H.M.A. conceptualized, designed, and wrote the commentary.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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