A disease network-based deep learning approach for characterizing melanoma

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INTRODUCTION

Multiple types of genomic aberrations occur in cutaneous melanoma, and some can impact the prognosis of the disease. Hence, the integration of genomics data with clinical outcome could facilitate the identification of the most relevant genomic features for melanoma progression.

METHOD

We developed an approach that integrates genomics data with a disease network and deep learning model for the prognostic classification of melanoma patients and assessed the impact of different genomic features (**Fig. 1**).

RESULTS

The deep learning model utilizes clusters (“communities”) identified in the network to effectively reduce the dimensionality of genomics data into a patient score profile (**Fig. 2**). Using this profile, we identified three disease subtypes that differ in survival time (**Fig. 3**). Subsequently, we quantified and ranked the impact of genomic features on the patient score profile using a machine-learning technique. Follow-up analysis of the top-ranking features provided us with a biological interpretation at both pathway and molecular levels, such as their mutation and interactome profiles in melanoma and their involvement in signal transduction, immune response, and cell cycle pathways (**Fig. 4**). Taken together, we demonstrated the power of network-based artificial intelligence to provide personalized prognostic assessment for melanoma patients.

REFERENCE

Lai X, Zhou JF, Wessely A, Heppt M, Maier A, Berking C, Vera J, Zhang L. International Journal of Cancer. 2022; 150(6): 1029-1044. DOI: 10.1002/ijc.33860.

Characterize **genomic heterogeneity** of **melanoma** using **a deep learning model** driven by **multi-omics data** and **a disease network**.

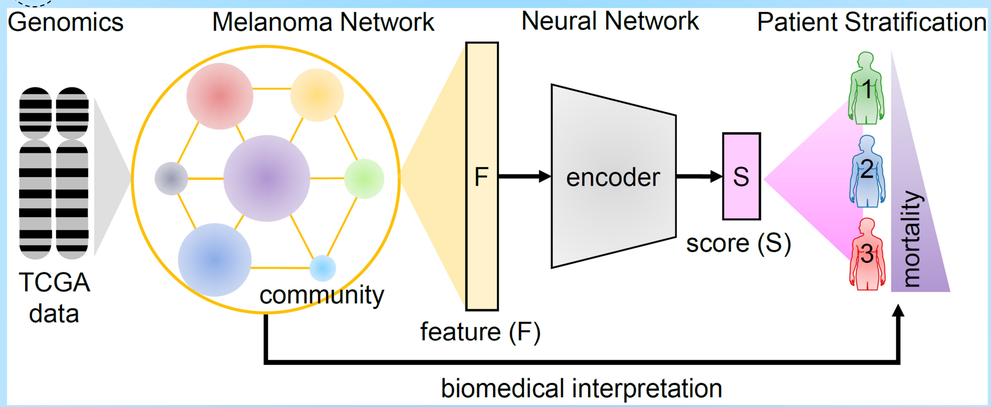

Fig. 1 The workflow used in the study. We first integrated the genomics data from TCGA into a melanoma network and performed network modularization. Next, we used the genomic data in the identified network communities as the input for an autoencoder model. The model transformed the genomics profiles of patients into a network community-based score. Then, we used the scoring profile of patients to classify patients and analyzed the survival rate of the identified patient clusters. Finally, we combined Shapley additive explanations (SHAP) analysis, gene set enrichment analysis, and the melanoma network to provide biomedical interpretation to the model.

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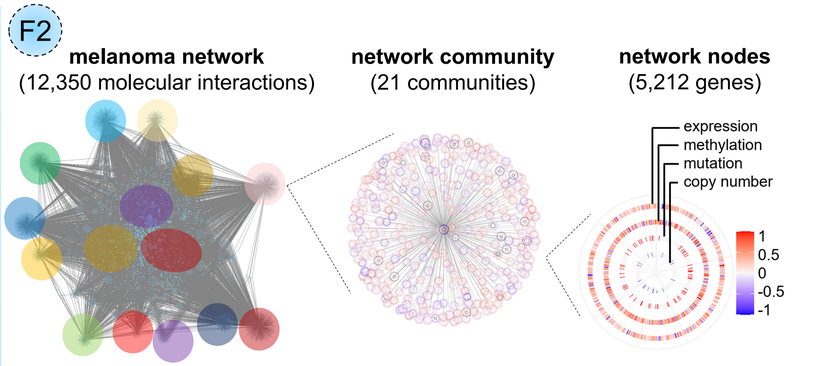

Fig. 2 The melanoma network. We used a simulated annealing algorithm to partition the melanoma network and identified 21 communities with a modularity score of 0.485. Each community represents a group of functionally relevant genes. We integrated the genomics data into the network for follow-up analysis.

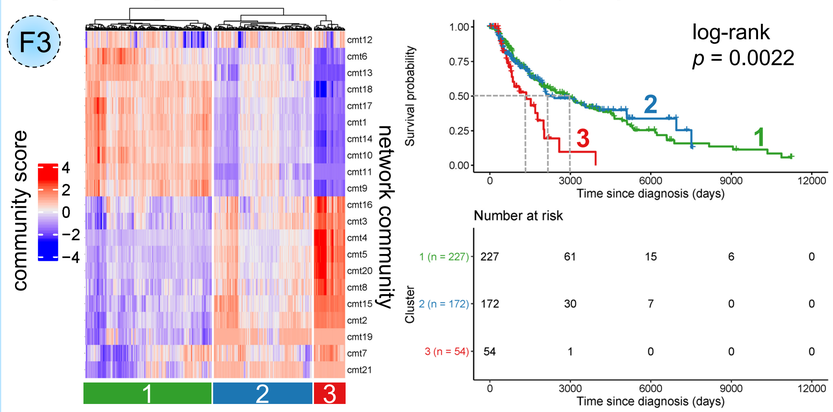

Fig. 3 Patient classification. We identified three patient clusters using the network-community score that represents a low-dimensional embedding of patients’ gene expression and methylation profiles. The patient clusters show significantly different survival rates. We obtained the score from an unsupervised neural network model with one input layer, three hidden layers, and one reconstructed layer. We used Bayesian optimization to find the model’s best hyper-parameters, such as mini-batch size, learning rate, and sparse penalty parameters. We trained the model with a maximum of 1,000 epochs and used early stopping to prevent overfitting.

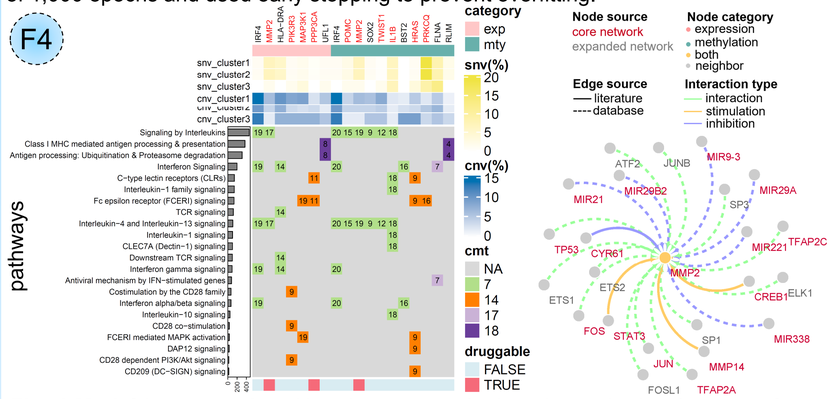

Fig. 4 Model interpretation. Here is an example that shows the involvement of top-ranking features in signal transduction pathways and their copy number variation (CNV) and simple nucleotide variation (SNV) in the patient clusters and druggability. In addition, we can trace the interactions of the features in the melanoma network.