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POSTER ABSTRACTS

621.LYMPHOMAS: TRANSLATIONAL-MOLECULAR AND GENETIC

Predicting CAR-T Response in Mantle Cell Lymphoma Using Deep Neural Network Models on Single-Cell RNA Sequencing Data

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Introduction

The approval of CD19 chimeric antigen receptor (CAR) T therapy by the FDA for relapsed mantle cell lymphoma (MCL) represents a significant advancement. However, patients are resistant or experience relapse after receiving CAR T therapy. High degree of transcriptomic heterogeneities among MCL tumor cells makes it challenging to predict response to CAR-T therapy. In this study, we employed deep learning models in conjunction with single-cell RNA sequencing data to predict the response to CAR-T therapy in MCL patients.

Methods

In this study, we collected and analyzed 39 patient samples treated with CAR-T therapy, of which 30 were sensitive and 9 were resistant to the treatment. Single-cell RNA sequencing was performed on these samples, and downstream analysis was conducted using the Seurat R package (version 4.3.0.1), including dimension reduction and cell type annotation. B cells were isolated *in-silico*, followed by differential gene expression analysis using the Wixcoxon rank sum test. The identified differentially expressed genes were then used as inputs for deep learning neural networks to predict the response to CAR-T therapy (Figure 1A).

We applied a multilayer perceptron (MLP) network as the binary classifier for response prediction. The model consists of four fully connected layers, including one input layer, two intermediate hidden layers, and one output layer. The number of neurons in the input layer corresponds to that of the differentially expressed genes. The two hidden layers have 64 and 16 neurons, respectively, each followed by one activation layer using rectified linear unit (ReLU) and one dropout layer with dropout rate of 0.4. The features from the latter hidden layer were extracted for embedding plots. The output layer has two neurons with activation function of Softmax, each neuron representing the probability of categorical patient response labels. A leave-one-sample-out approach was employed to calculate the prediction accuracy.

Results

A total of 49,112 cells passed the quality control criteria, with 15,322 identified as tumor B cells (31.19%, Figure 1B). We observed a high level of transcriptomic heterogeneity among tumor cells in patients. Differential expression analysis revealed 1,236 genes with significantly different expression between sensitive and resistant samples (adjusted p-value < 0.05).

To evaluate the predictive performance of our model, we employed a leave-one-sample-out approach and achieved an average accuracy of 90.07%. For instance, when sample K0 was used as the test dataset and all other samples were used as the training dataset, 91.49% of cells from sample K0 were accurately predicted to be sensitive (Figure 1C). Further, visualization of the hidden layer using the Uniform Manifold Approximation (UMAP) embedding plot demonstrated that sample K0 fell into the same area as other sensitive samples.

Conclusion

In conclusion, our study highlights the potential of deep learning models and single-cell RNA sequencing data in predicting the response to CAR-T therapy in MCL. These findings hold promise for clinical applications and may contribute to the development of personalized treatment strategies for MCL patients.

Disclosures Jain: *AstraZeneca:* Consultancy, Honoraria.

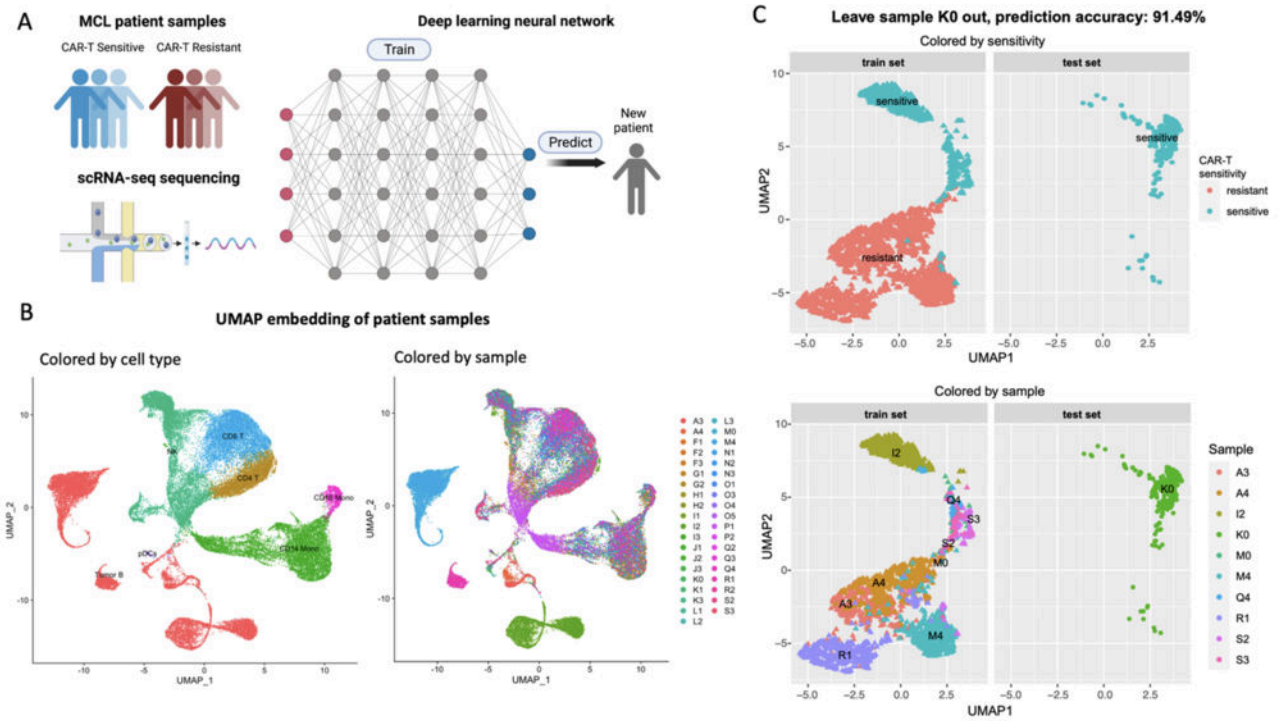

Figure 1. Leveraging single-cell RNA-seq and deep learning models in CAR-T response prediction. (A) Workflow shows experimental design. CAR-T sensitive and resistant MCL patient samples were collected and subject to scRNA-seq. The gene expression profile at single cell resolution were used as input for deep learning neural network. **(B)** UMAP embedding of scRNA-seq datasets colored by cell type (left) or sample (right). Each dot represents a cell. **(C)** UMAP embedding of intermediate hidden layer of neural network colored by CAR-T sensitivity (top) or sample (bottom). Patient sample K0, the test set, was accurately predicted to be CAR-T sensitive.

Figure 1

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