

Drug screening data from massive bulk gene expression databases can be analyzed to determine the optimal clinical application of cancer drugs. The growing amount of single-cell RNA sequencing (scRNA-seq) data also provides insights into improving therapeutic effectiveness by helping to study the heterogeneity of drug responses for cancer cell subpopulations. Developing computational approaches to predict and interpret cancer drug response in single-cell data collected from clinical samples can be very useful. We propose scDEAL, a deep transfer learning framework for cancer drug response prediction at the single-cell level by integrating large-scale bulk cell-line data. The highlight in scDEAL involves harmonizing drug-related bulk RNA-seq data with scRNA-seq data and transferring the model trained on bulk RNA-seq data to predict drug responses in scRNA-seq. Another feature of scDEAL is the integrated gradient feature interpretation to infer the signature genes of drug resistance mechanisms. We benchmark scDEAL on six scRNA-seq datasets and demonstrate its model interpretability via three case studies focusing on drug response label prediction, gene signature identification, and pseudotime analysis. We believe that scDEAL could help study cell reprogramming, drug selection, and repurposing for improving therapeutic efficacy.