Novel drug combination prediction Case study: PTCL patient tumors

First we provide a proof of concept for the applicability of DeepPTCL for precision medicine settings. Second we implemented our model to identify customized synergistic combinations for individual cancer patients.

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Leave-one-cell-out procedure validates the proof of concept of DeepPTCL model in simulating a new patient tumor

To simulate a case of new patient tumor, we additionally tested our model in the most challenging leave cell out to validate cell line specific performance when the cell line was not part of the training set. In this way, the cell lines in the test dataset are the most different from those in the training dataset. The leave cell out is a robust method to test the generalization of the our model.

We compared to the tw0 public state-of-art models based on the metric of Aera Under ROC (AUROC) and Precision Under ROC (PRAUC). Our model **DeepPTCL** has obtained **best performance** (**AUROC= 0.82, PRAUC =0.43**) compared to Transynergy (AUROC = 0.80 , PRAUC = 0.37), DeepSynergy(AUROC = 0.80 , PRAUC = 0.36).

To see how well our model predicted the synergy ranking if different combinations of drugs within cell lines, we also calculated he Spearman correlation between DeepPTCL predictions and the actual synergy scores by cell lines. We observed the ranking of drug combinations were fairly consistent across all cell lines, predominantly between 0.6 and 0.75.

The identified selective synergies among approved drugs may offer novel drug repurposing opportunities for treating PTCL in a precision medicine setting

As shown in the previous section, combination predictions were successfully carried out with DeepPTCL platform in the pan-cancer cell lines with varying genetic characteristics. We implemented the trained model to predict synergy in the patient's transcriptional data. The model predictions were ranked according to their predicted synergy scores. The following subsections detail the synergistic predictions for each patient case.

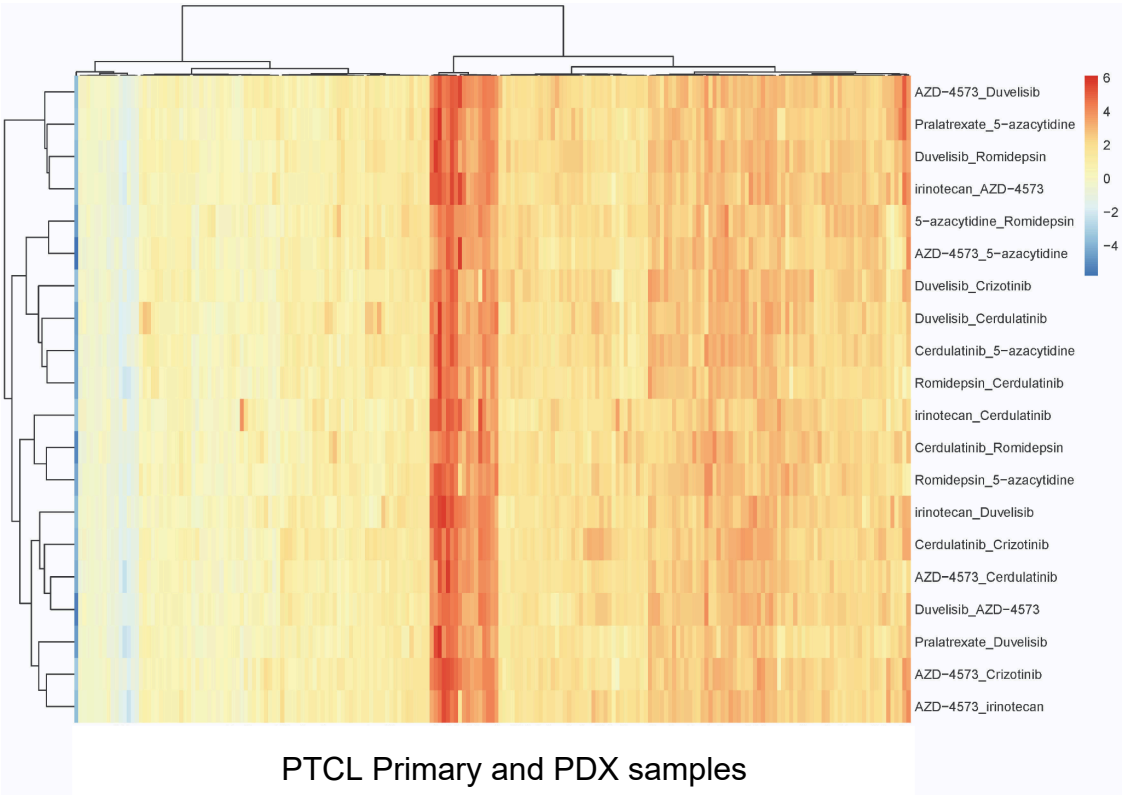

Figure1 . Top 20 shared combinations predicted to have synergy. The numbers on the color bar correspond to the ZIP synergy score, separately for each patient sample and combination.

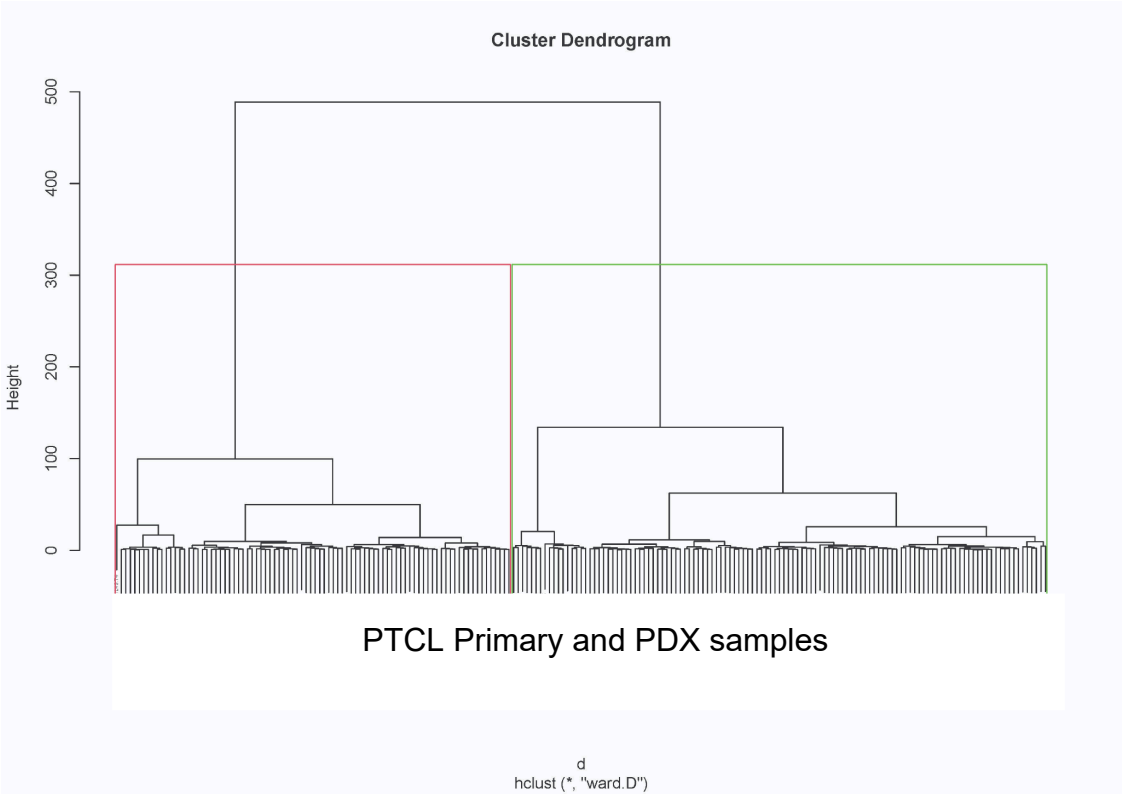

Figure2. Based on the predicted synergy scores, we plotted all combinations with synergy across at least two profiles. We find some combinations of drugs tend to have higher synergy in green block, and that some combinations of drugs tend to have lower synergy in red blocks.

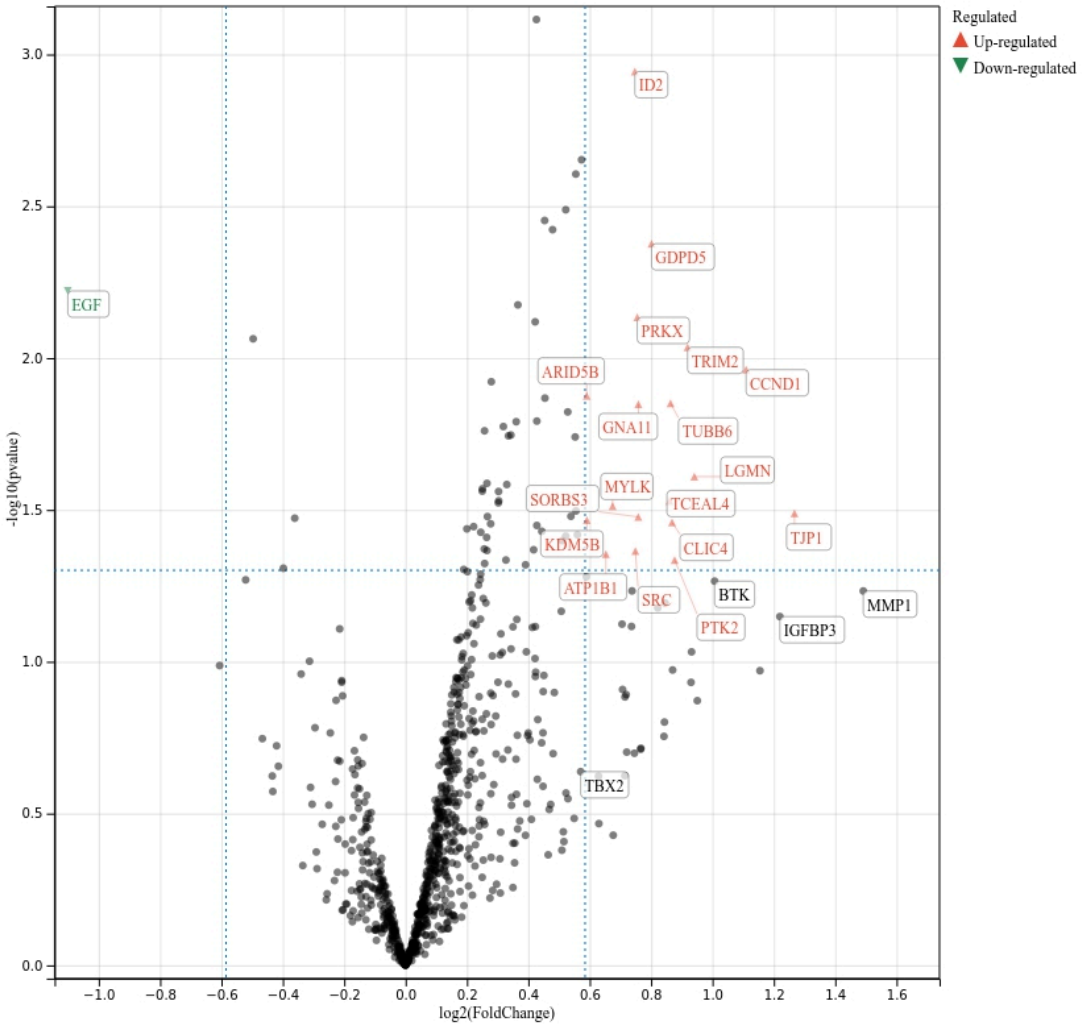

Figure 3. Differential genes between transcriptional context of two profiles (higher synergy group v.s. lower synergy group) using the R package Limma.

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https://wandb.ai/chloexyz123/giorgio/reports/Novel-drug-combination-prediction-Case-study-PTCL-patient-tumors--Vmlldzo2MzcxNzMy?accessToken=5xio4zmle5tb9z5swg38nnku3n74avnqo4eush6tvtdj29y842sf8qb7tpr8s4dw