Deep transfer learning for single-cell drug response prediction

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Background: drug response prediction at the bulk level

Examples of computational tools for bulk data:

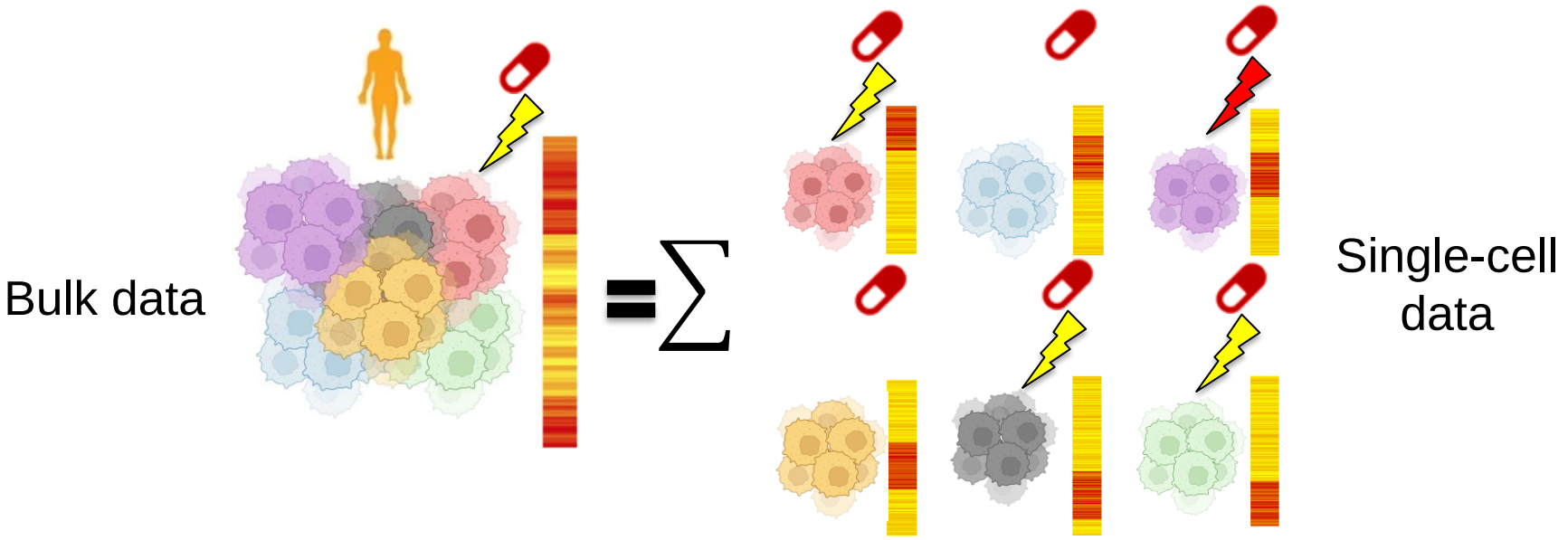
deepDR (Zeng, Xiangxiang, et al. "deepDR: a network-based deep learning approach to in silico drug repositioning." Bioinformatics 35.24 (2019): 5191-5198.) Dr. Zhongming Zhao

VAEN (Jia, Peilin, et al. "Deep generative neural network for accurate drug response imputation." Nature Communications 12.1 (2021): 1740.) Dr. Zhongming Zhao

DeepDR (Chiu, Yu-Chiao, et al. "Predicting drug response of tumors from integrated genomic profiles by deep neural networks." BMC Medical Genomics 12.1 (2019): 143-155.) Dr. Yidong Chen

DeepDep (Chiu, Yu-Chiao, et al. "Predicting and characterizing a cancer dependency map of tumors with deep learning." Science Advances 7.34 (2021): eabh1275.) Dr. Yidong Chen

Challenges in predicting drug response at the single-cell level



How to predict single-cell level drug response?

- High heterogeneity -- cannot directly apply tools designed for bulk data
- Not enough single-cell data with drug response labels for model training/validation

scDEAL: deep transfer learning for single-cell drug response prediction

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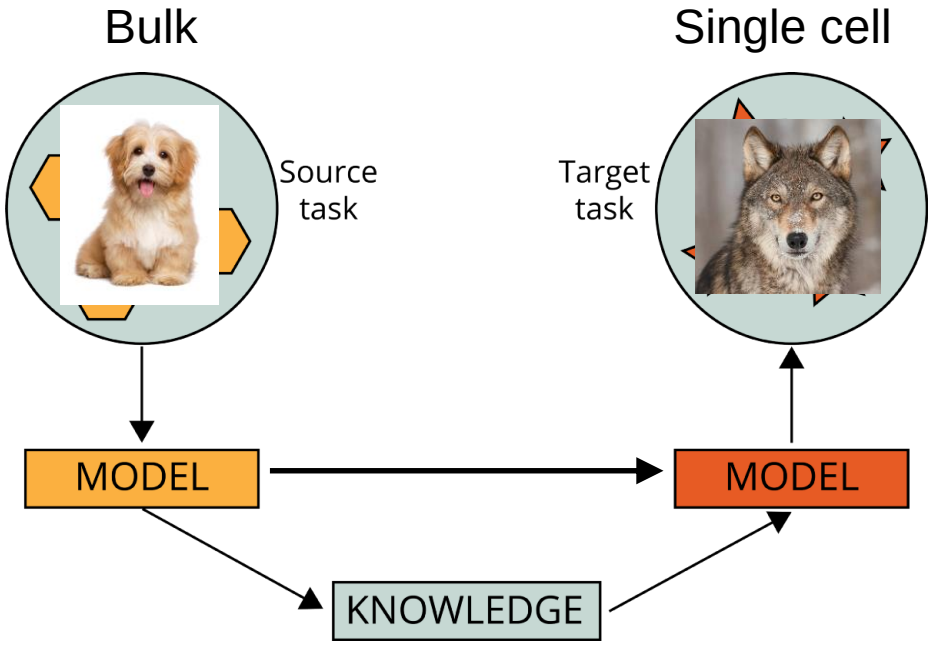
Deep transfer learning



Gene expression – drug response

- **Train a model** that can learn gene expression-drug response relation at the **bulk level**;
- Transfer the trained model to **predict single-cell** drug response

scDEAL:

nature communications

Article

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Deep transfer learning of cancer drug responses by integrating bulk and single-cell RNA-seq data

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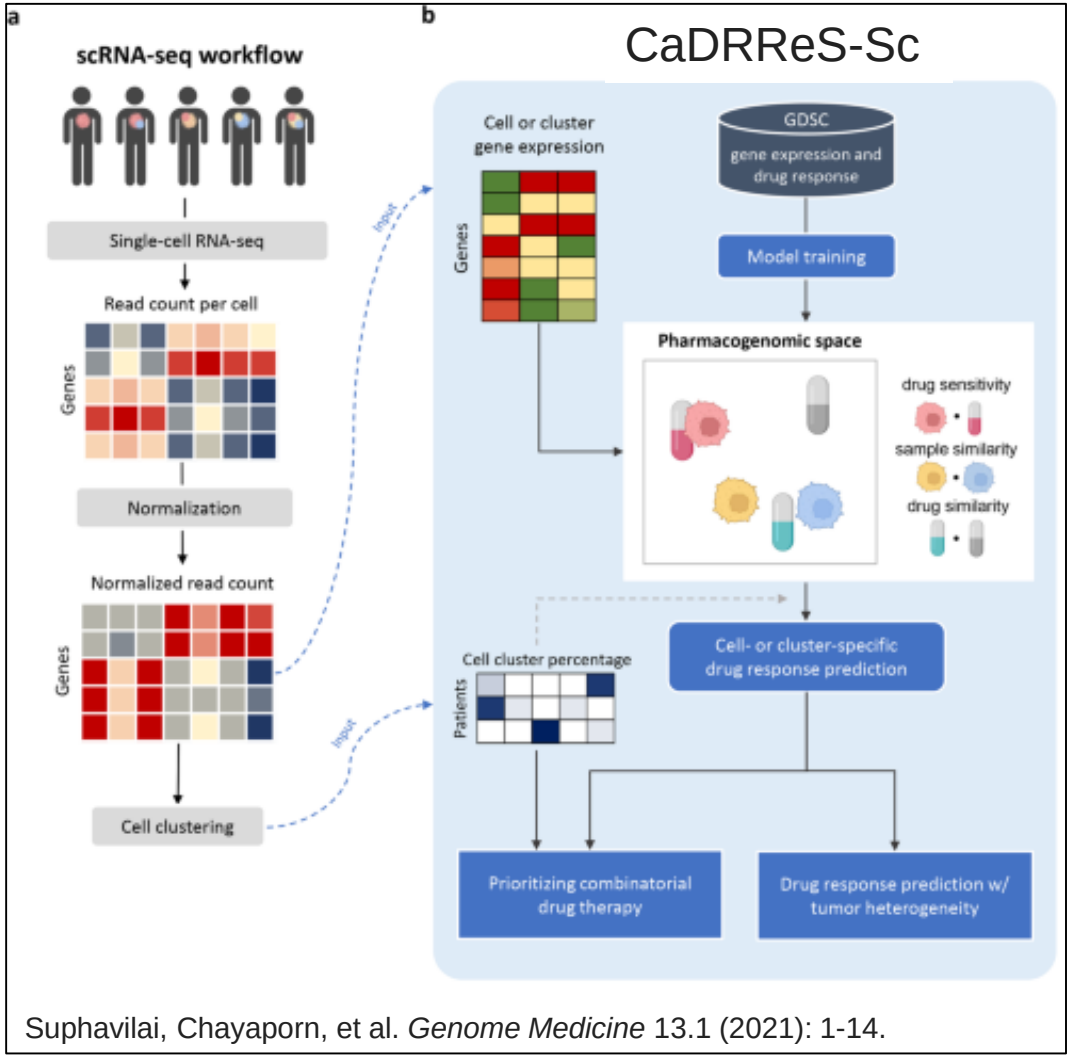
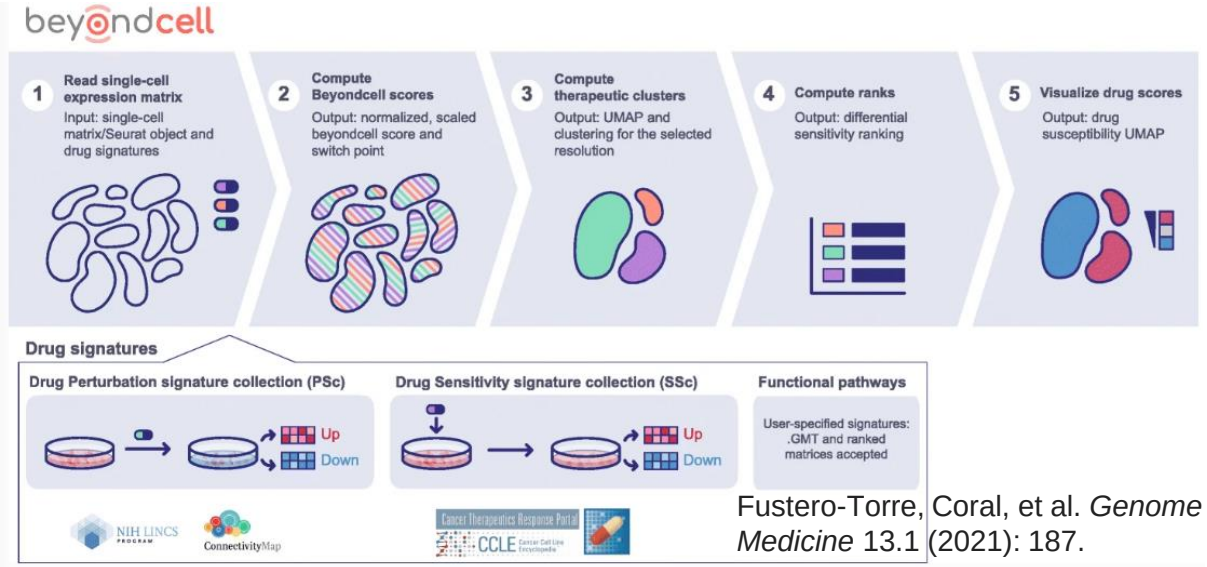
Prof. Qin Ma

Recently published tools

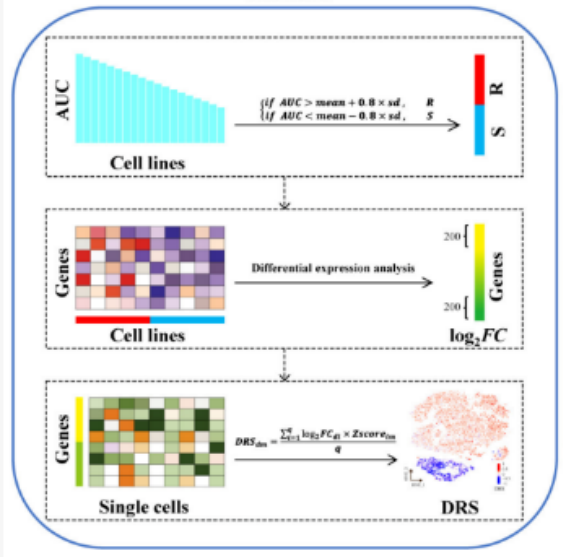


Suphavilai, Chayaporn, et al. *Genome Medicine* 13.1 (2021): 1-14.



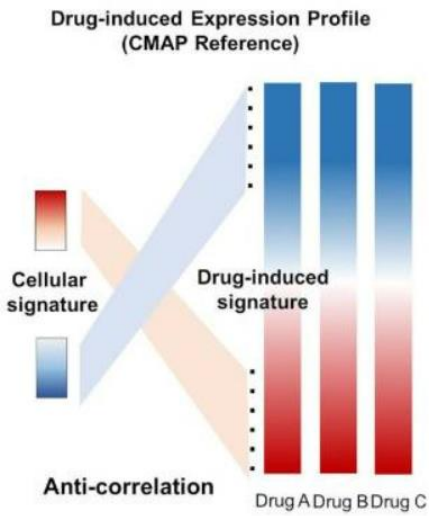
Fustero-Torre, Coral, et al. *Genome Medicine* 13.1 (2021): 187.

scDR



Lei, Wanyue, et al. *Genes* 14.2 (2023): 268.

CeDR Atlas

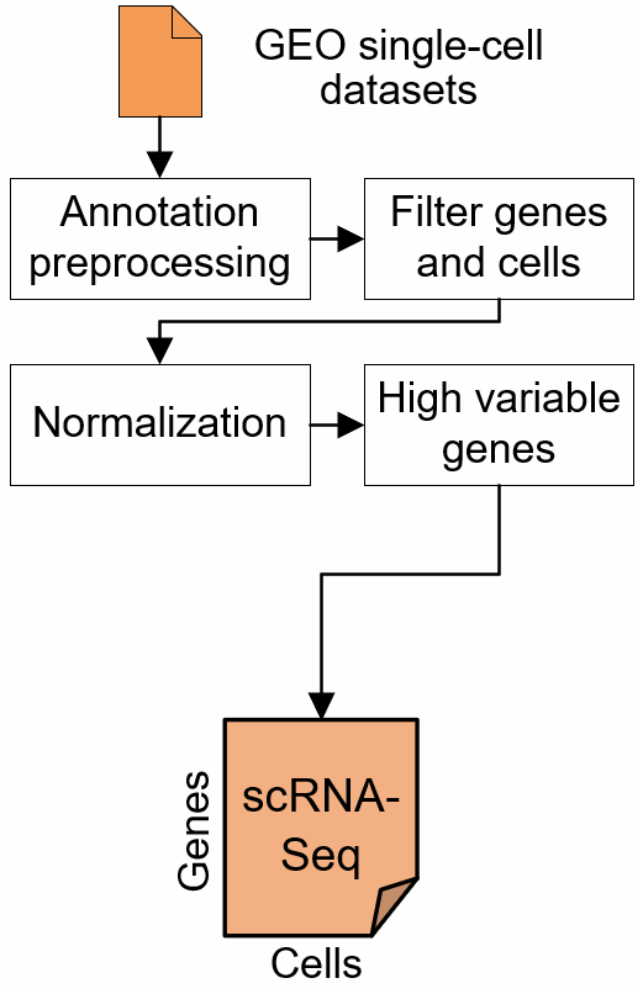


Wang, Yin-Ying, et al. *Nucleic acids research* 50.D1 (2022): D1164-D1171.

Data availability and preprocessing

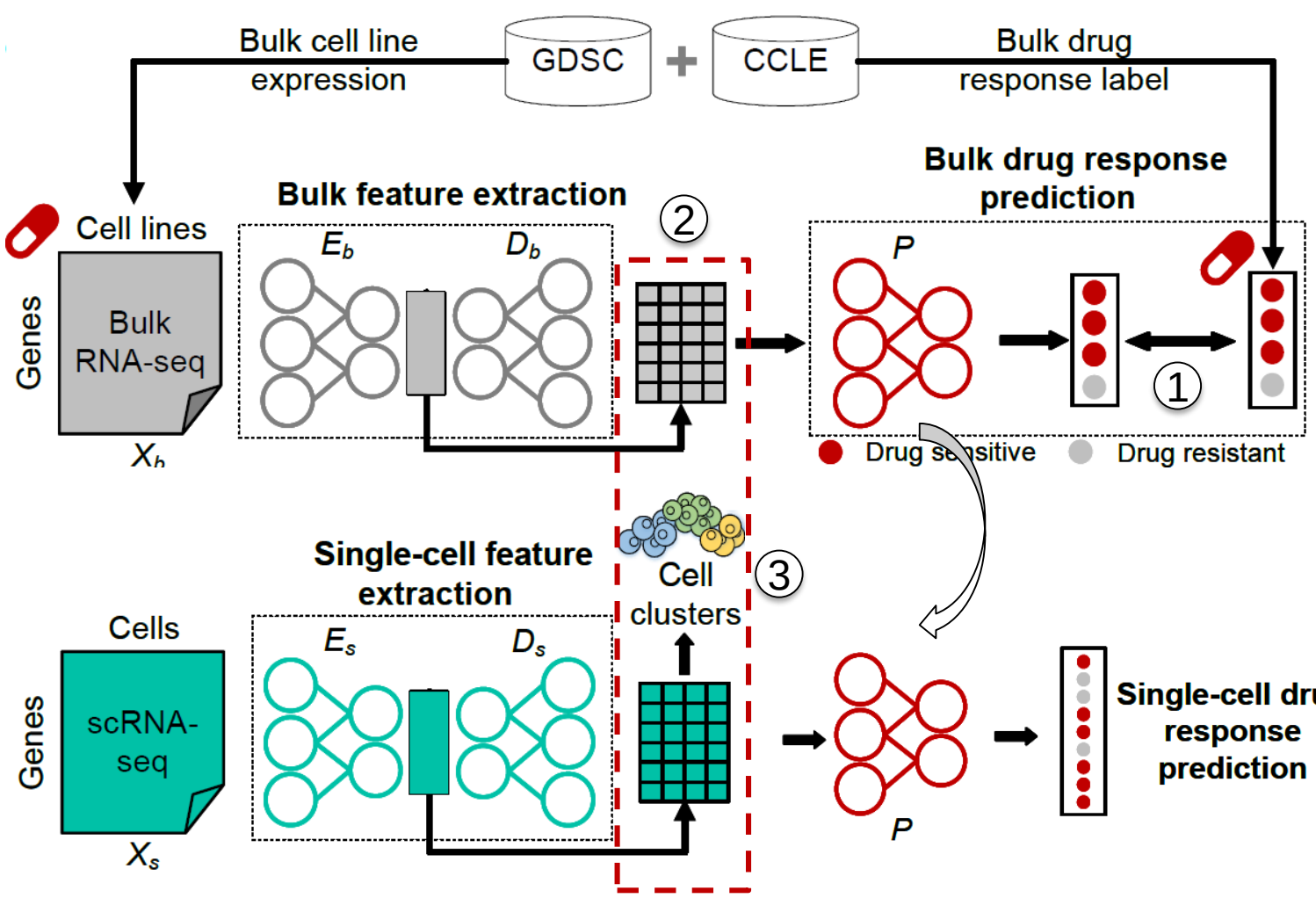
	# cell lines	# drugs	# genes
GDSC	804	192	17,419
CCLE	476	1,448	19,177
GDSC+CCLE	1,280	1,557	15,962

	Drug	GEO access	Cells	Cancer type
Data 1	Cisplatin	GSE117872	548	Oral squamous cell carcinomas
Data 2			568	
Data 3	Gefitinib	GSE112274	507	Lung cancer
Data 4	Docetaxel	GSE140440	324	Prostate Cancer
Data 5	Erlotinib	GSE149383	1,496	Lung cancer
Data 6	I-BET-762	GSE110894	1,419	Acute myeloid leukemia



Chen, Junyi, et al. *Nature Communications* 13.1 (2022): 6494.

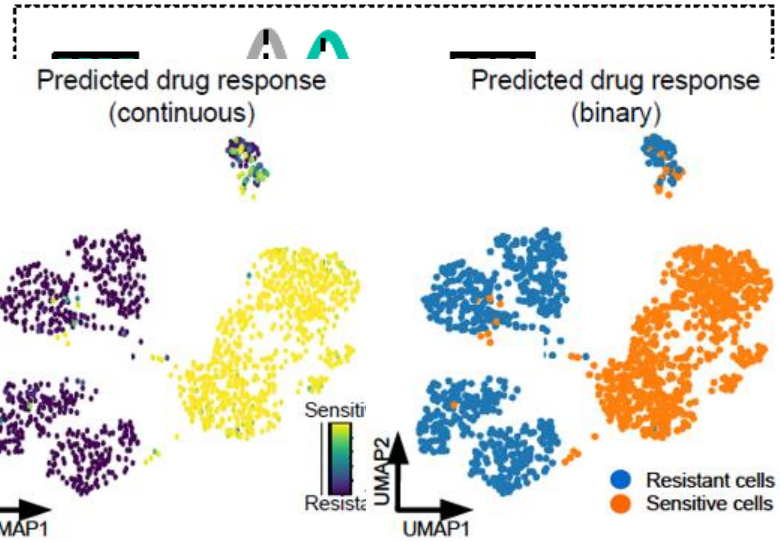
The design of the scDEAL framework



1 $loss_{class}(P, Y_b, Y_b^0) = min(Cross\ Entropy\ (Y_b, Y_b^0))$

2 $loss_{MMD}(E_b(X_b), E_s(X_s)) = |\frac{1}{n}\sum_{i=1}^{n}\phi(x_b^i) - \frac{1}{m}\sum_{j=1}^{m}\phi(x_s^j)|_H$

3 $regulizer = \sum_{CC} cosine_{similarity}(X_s)$



$loss_{class} + \alpha * loss_{MMD} + \beta * regulizer$

- **The prediction is for one drug at a time**
- **scDEAL is label free – no cell cluster or experimental labels required**

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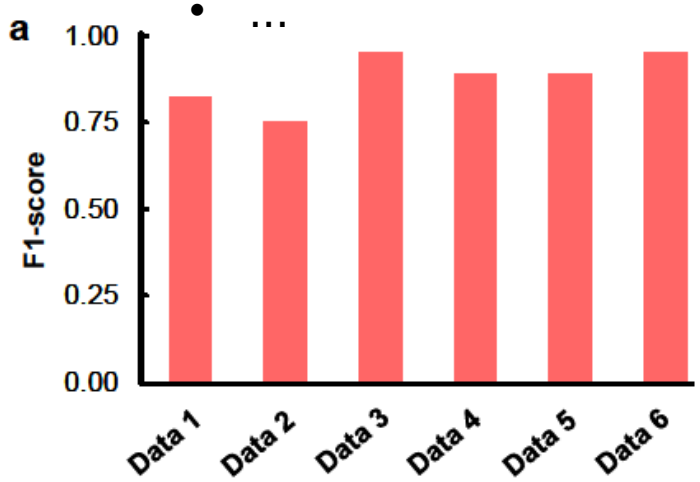
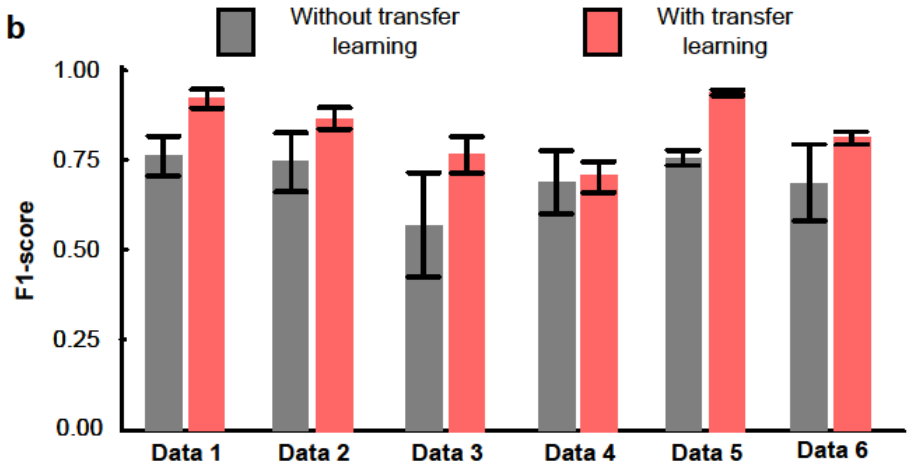
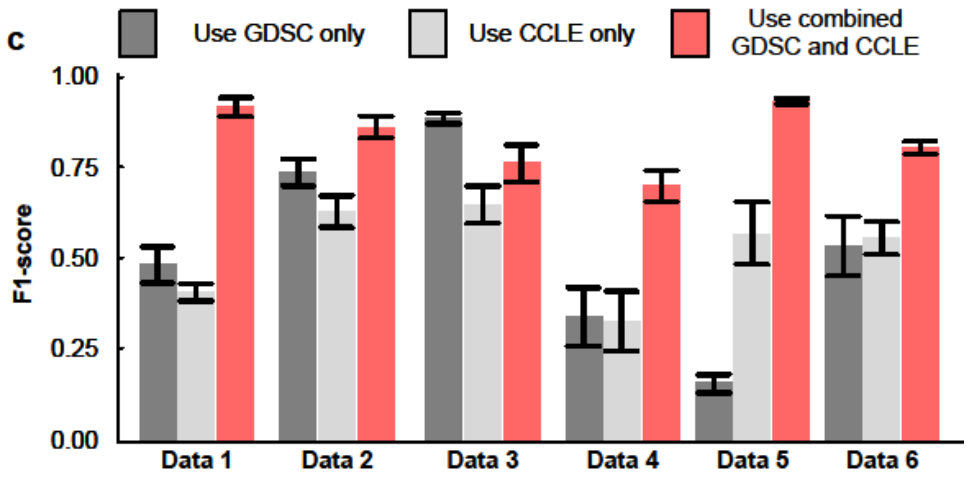
Benchmark evaluation and model validation

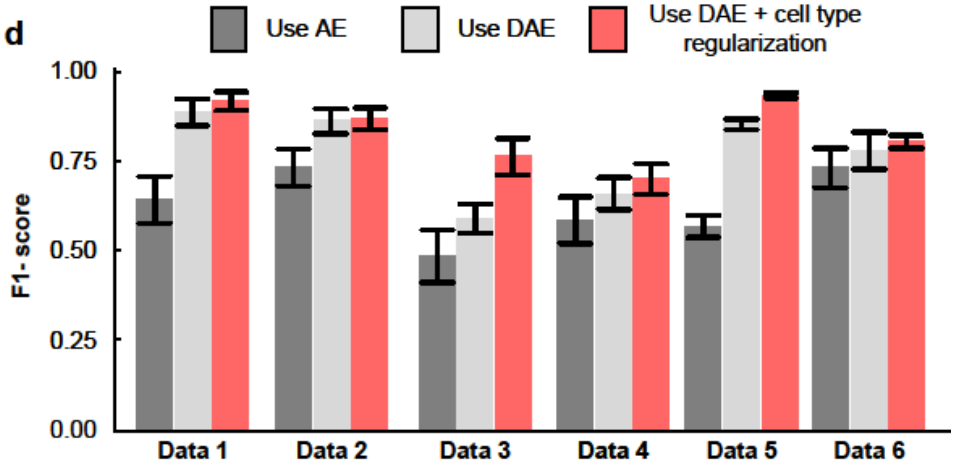
Define single-cell drug response labels based on sample information, e.g.:

- Without treatment/DMSO – all sensitive
- Treatment after a short time – all sensitive
- Treatment after a long time – all resistant
- …









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scDEAL accurately predicted Cisplatin response in OSCC and identify critical genes related to drug response

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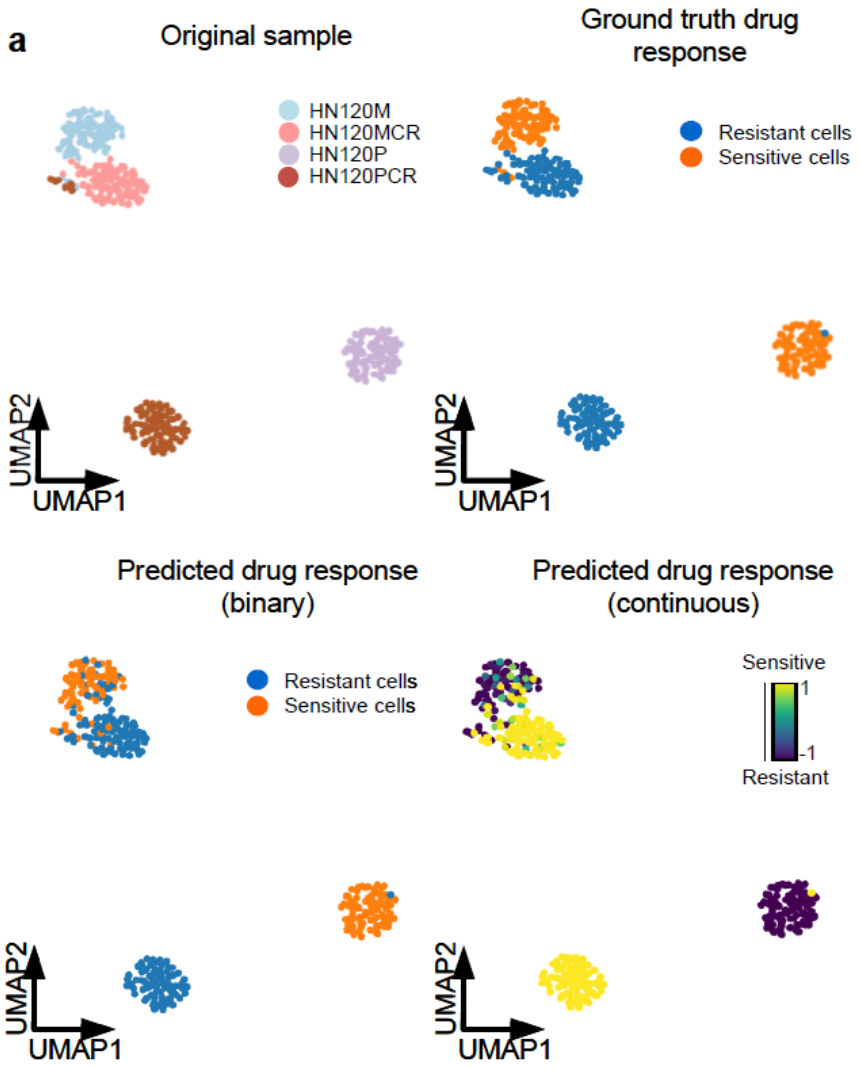
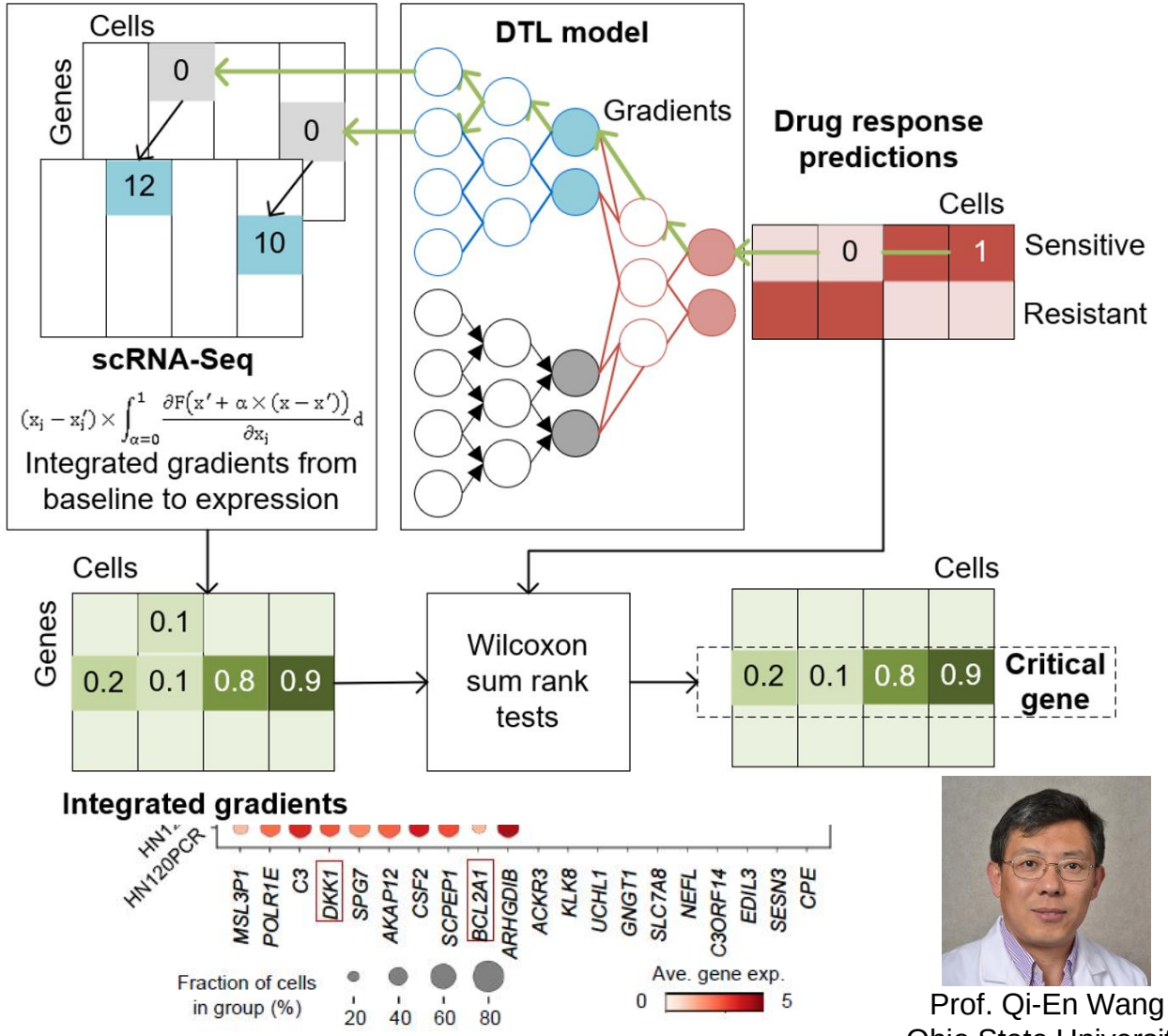
Sample: Oral squamous cell carcinoma (OSCC) (Data 1; 548 cells)
Treatment: Cisplatin





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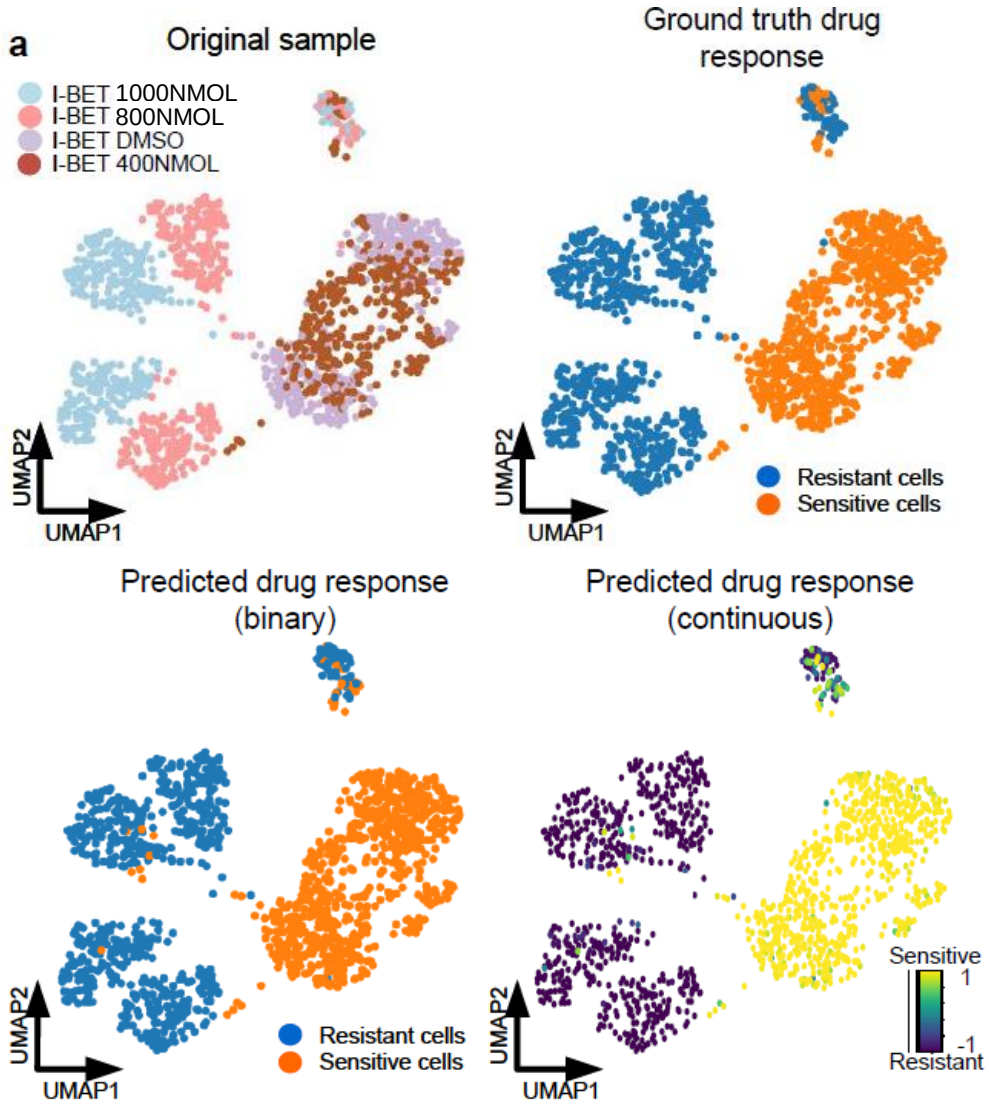
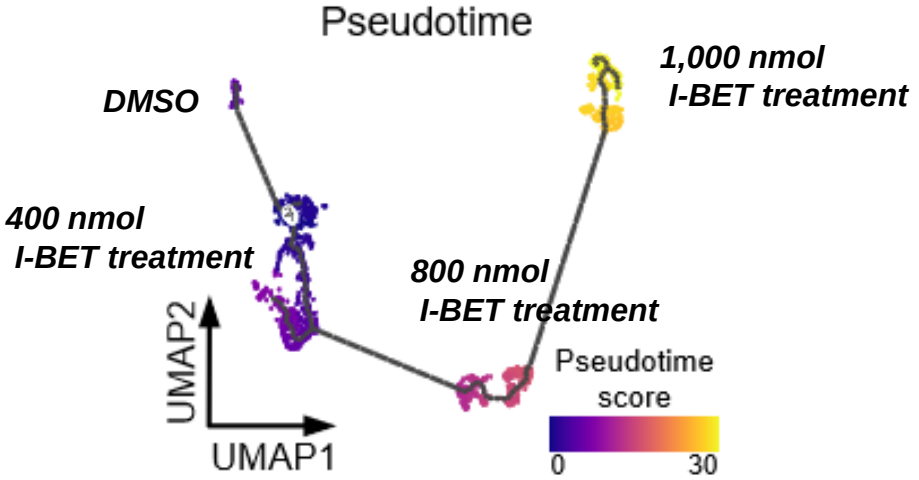
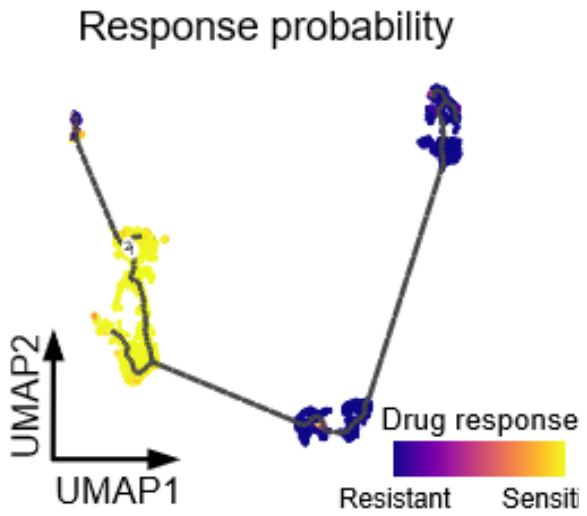
scDEAL predicted drug response align with treatment dosage

Sample: Acute myeloid leukemia (1,419 cells)
Treatment: BET inhibitor (I-BET)







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Summary and discussion

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What did we do?

- We developed scDEAL, adapting a deep transfer learning model, for single-cell drug response prediction.
- scDEAL can accurately predict drug responses on different scRNA-seq data and identify critical genes responsible for drug response.

What's next?

- Optimization for cross-patient and cross-species prediction
- Include more single-cell modalities (e.g., DNA mutation and metabolites)
- Predict combinatory drug responses
- and more…

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