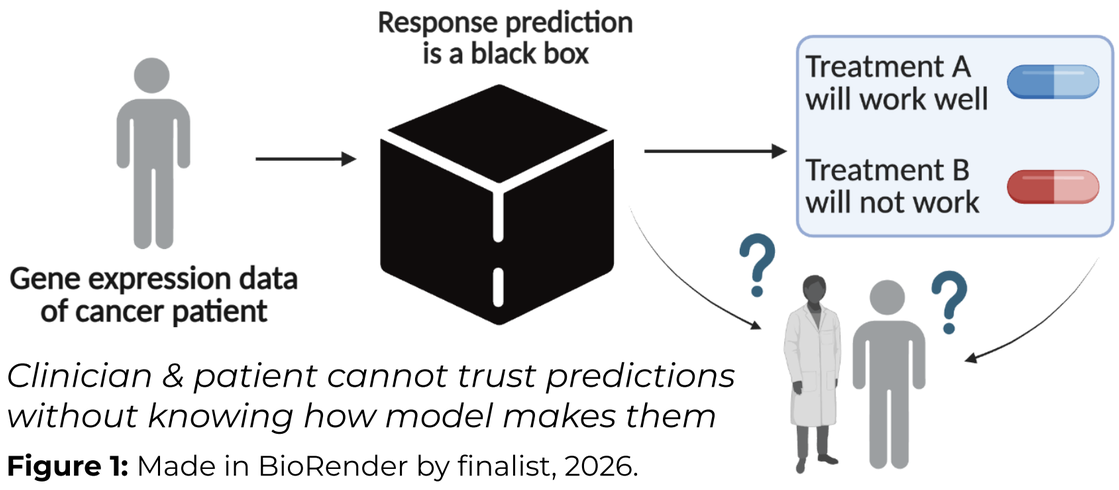
I2-CISSP: An Interpretable Machine Learning Framework for Robust and Practical Prediction of Cisplatin Response in Human Tumors

Introduction

- AI models can *personalize cancer treatment* by predicting whether a chemotherapy will work well for a patient [1, 2]
- BUT, **most current models are black boxes:** clinicians and patients cannot understand how they make predictions [3,4]
- **Lack of transparency reduces trust & usability** [5-6]



Clinician & patient cannot trust predictions without knowing how model makes them

Figure 1: Made in BioRender by finalist, 2026.

I2-CISSP integrates tumor and cell line data sources to ***more accurately predict human tumor response*** *to cisplatin, while* ***allowing clinicians and patients to understand its predictions*** *through* ***two distinct forms of interpretation.***

Study Workflow

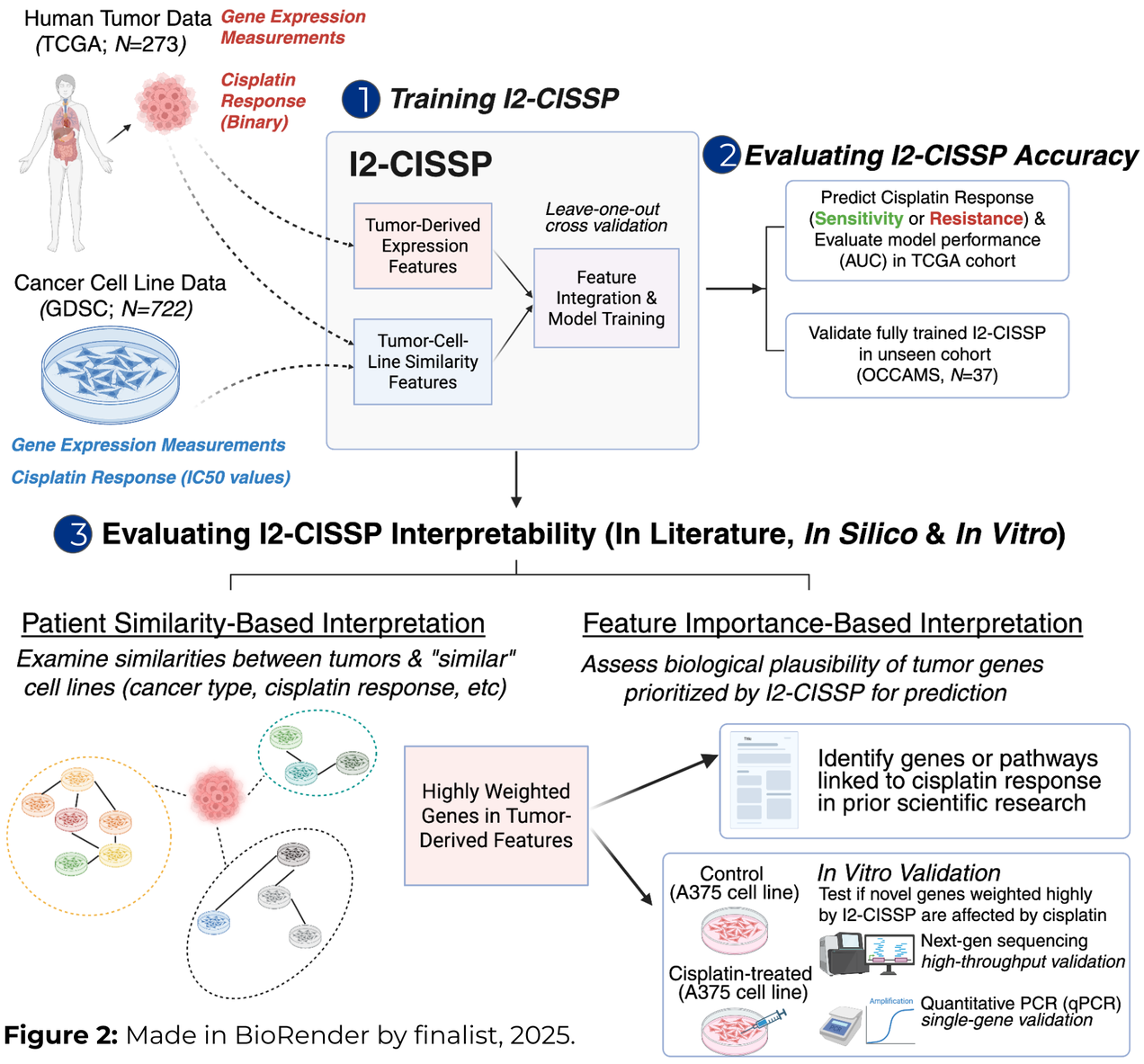


Figure 2: Made in BioRender by finalist, 2025.

Key Results: I2-CISSP Displays High Predictive Accuracy and Dual Interpretability

I2-CISSP significantly outperforms other interpretable baselines and illustrates the importance of tumor & cell line data integration

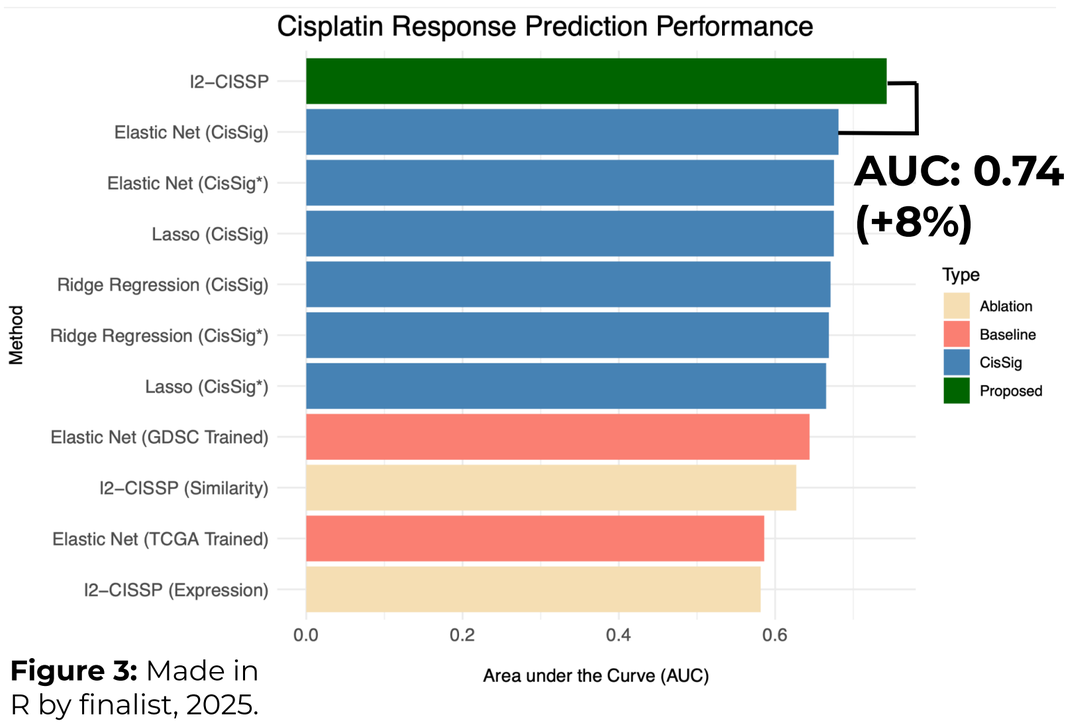


Figure 3: Made in R by finalist, 2025.

Patient-similarity based interpretation: Comparing the cancer type of a patient tumor to the cell lines I2-CISSP matches it with during prediction can **validate correct classifications & flag incorrect ones**

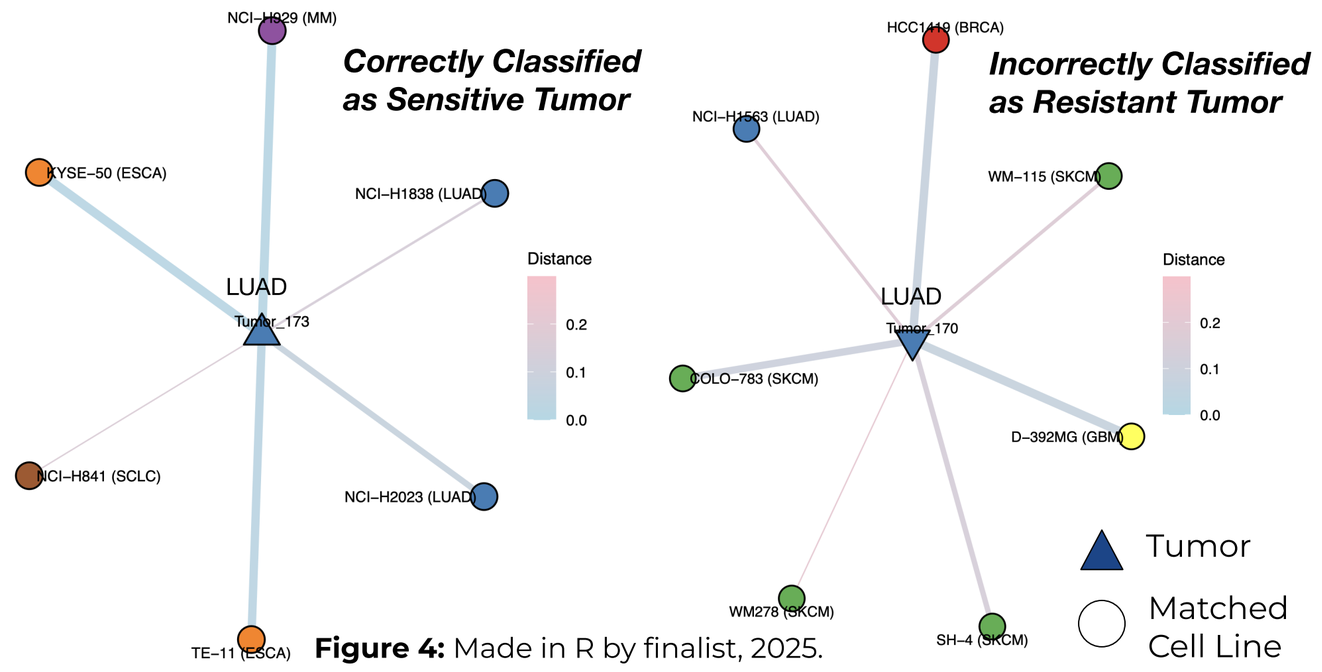


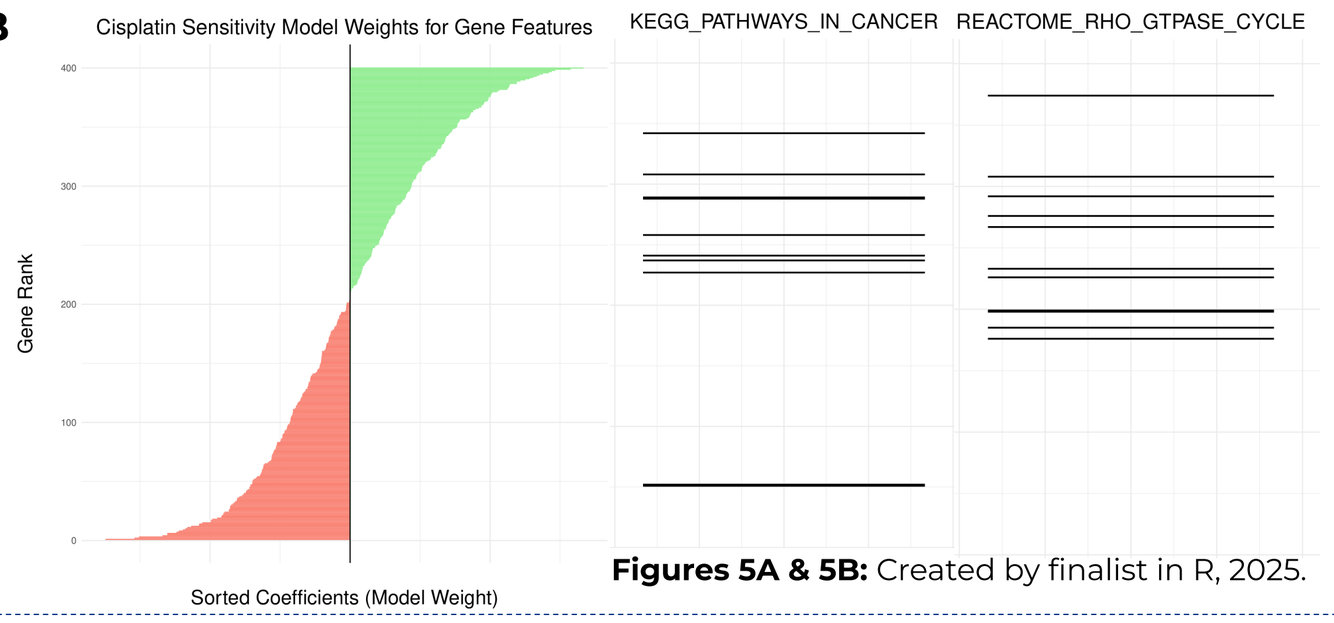
Figure 4: Made in R by finalist, 2025.

Feature-importance based interpretation: Gene-weight analysis & *in vitro* validation show I2-CISSP prioritizes genes known to affect cisplatin response and points to new genes that may influence resistance.

A

Gene Name	Previous Cisplatin Link?	Prior Evidence & Potential Mechanisms	Validated In Vitro in this Study
ZFP36	Partially, in two cancers	Downregulates BCL2, degrades oncogenic mRNAs [7]	Yes (quantitative PCR)
MT1G	Yes	Binds to heavy metals, inactivating cisplatin [8]	Yes (next-generation sequencing)
C4A	No	N/A	Yes (next-generation sequencing)
PTPRF	Partially	Cisplatin damages PTPs via covalent adducts [9]	No
ZNF853	Partially	Cisplatin alters ZNF853 expr. in cell lines [10]	Yes (next-generation sequencing)

B



Figures 5A & 5B: Created by finalist in R, 2025.

Discussion & Conclusions

I2-CISSP **robustly predicts cisplatin response** in human tumor cohorts with significantly higher accuracy than other interpretable baselines

I2-CISSP helps clinicians & patients **understand its predictions via two forms of interpretation**, enabling informed decision-making & providing insights into cisplatin resistance in cancer

Future work will address study limitations by (1) ranking multiple treatment options per patient rather than predicting single-drug response, (2) conducting more rigorous *in vitro* validation, and (3) exploring rule-based ("glass-box") models.

Icons sourced (top to bottom) from: freepik.com/icon/accuracy_8596602, flaticon.com/free-icon/trust_5465755, flaticon.com/free-icon/future_6020262

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