# Learning and actioning general principles of cancer cell drug sensitivity

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**Presenter**: Yu, Sun **Date/Time**: 2025/10/16, 15:20-16:10

**Commentator**: Asst.Prof. Hsiang-Chi Huang **Location**: Room 601, Med College Building

**Background:**

Large-scale pharmacogenomic screenings such as GDSC and PRISM have enabled systematic exploration of cancer cell line (CCL) drug sensitivities, offering opportunities for precision oncology. However, translating these findings into clinically actionable insights remains challenging, as current predictive models often lack interpretability and fail to generalize from cell line transcriptomes to patient-derived data. To address these limitations, integrating biologically meaningful representations of drug mechanisms of action (MOAs) and patient-specific transcriptional programs is essential for improving prediction accuracy and translational potential.

**Objective:**

This study aims to develop an interpretable machine learning framework (CellHit) that predicts cancer drug sensitivity from transcriptomic data while enhancing biological interpretability and clinical applicability.

**Results:**

Using GDSC and PRISM datasets, CellHit trained XGBoost-based drug-specific models that achieved high prediction accuracy (Pearson's ρ up to 0.89). The models recovered known drug targets (e.g., BCL2 for Venetoclax) and correctly identified MOA-related pathways. Incorporating LLM-curated MOA genes further improved predictive performance. When applied to TCGA data, CellHit successfully retrieved drugs aligned with approved cancer therapies and proposed new repurposing or combination opportunities. Experimental validations in pancreatic and glioblastoma samples confirmed the accuracy and biological relevance of predictions.

**Conclusions:**

CellHit effectively bridges cancer cell line pharmacogenomics and patient tumor data, providing an explainable and scalable tool for drug response prediction and personalized treatment discovery.