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Integrating Machine Learning (ML) methods in single-cell experimental workflow increases throughput and accuracy for target identification in immuno-oncology

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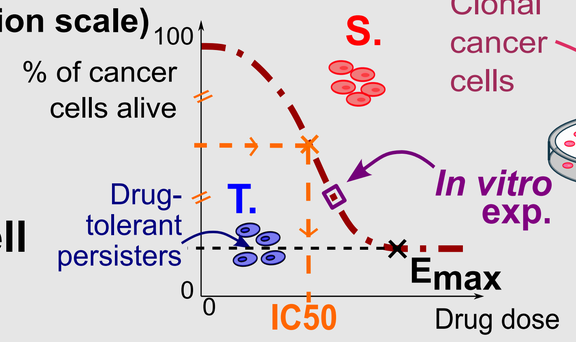
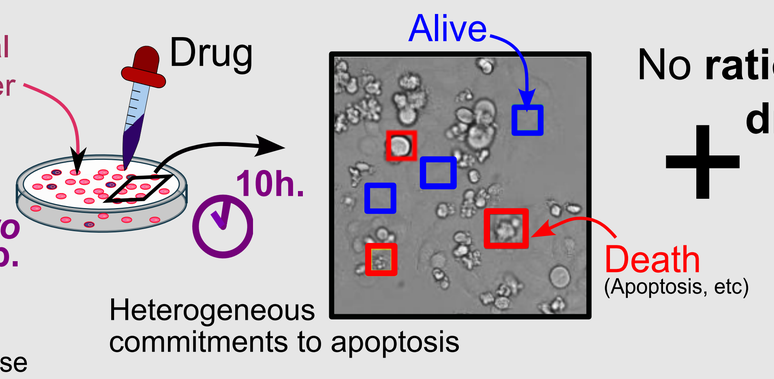
Problems

Methods to evaluates **drug-efficacy** are **static** and don't consider **single-cell heterogeneity**

Pharmacological profile (population scale)





No **rational way** to find **biomarkers** of **drug-tolerance** and **therapeutic targets** for drug-combination

+

Therapeutic failure

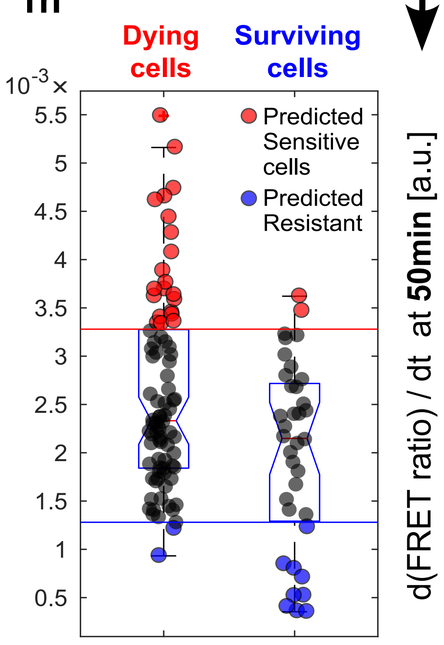
Our technical solution

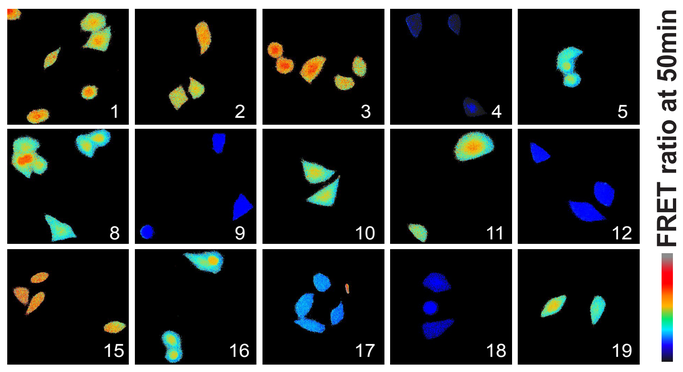
FATE-SEQ

Drawback: Only 4% of the cells were isolated for profiling during proof of concept with the death-ligand TRAIL[1,3]

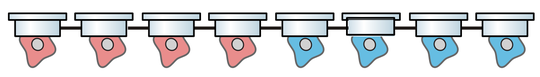
A **Single-cell drug response dynamics** by live-cell microscopy (1)

Cell drug response forecasting before 1h

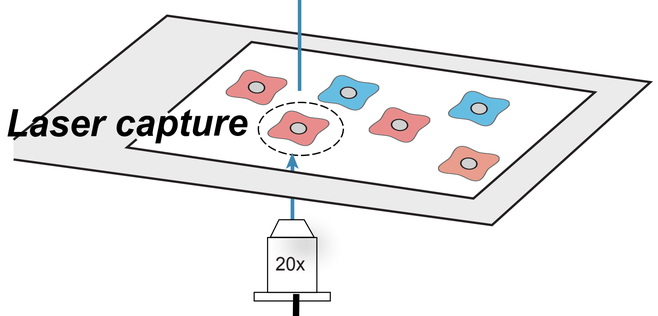




(2)



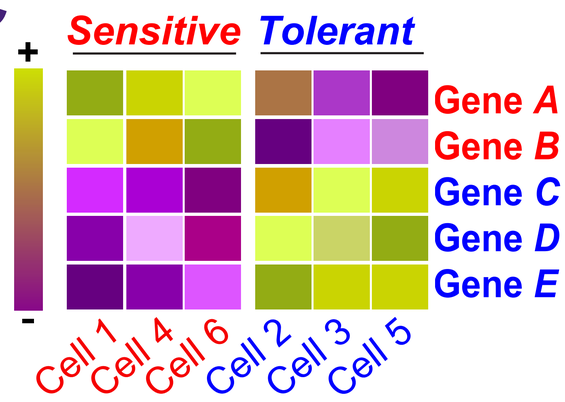
B



Same-cell isolation by laser-capture microdissection

Single-cell transcriptomic profile by single-cell RNA sequencing

C



(3) **GENetRank** Gene prioritization[4]

Therapeutic targets + **Molecular profile of drug efficacy** + **Cell-based assay validation**

Our improvements with ML

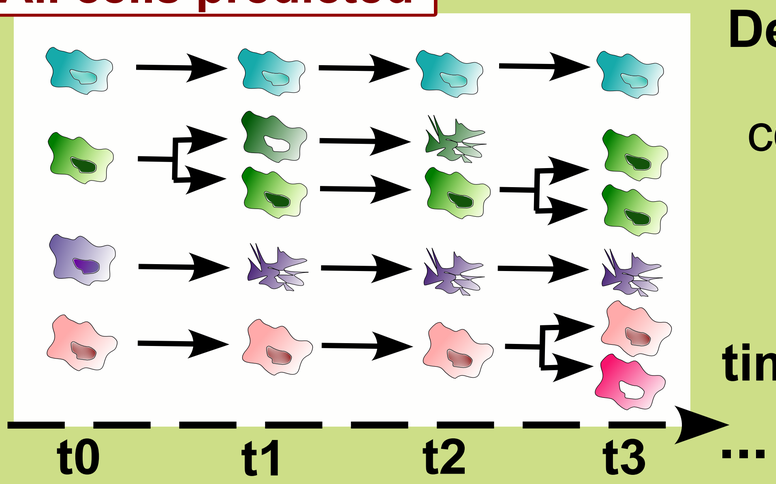
Cell tracking (1)

Cell Segmentation + Tracking with U-Net

+ **Automatic Detection of cell lineage** with correlation filters

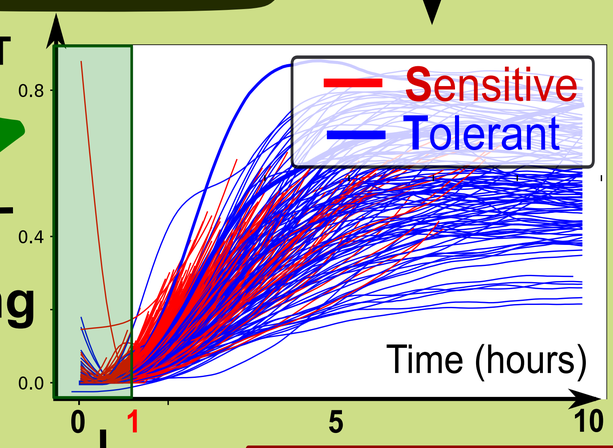
+ **Fluorescent time-trajectories extraction**

Accuracy = 97%
All cells predicted



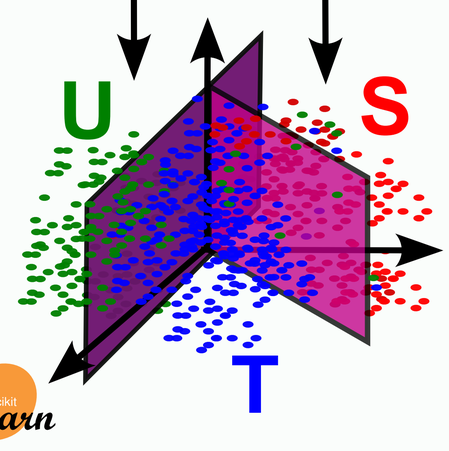
Cell-fate forecasting (2)

Sparse & short time-trajectories



Mathematical modeling of **apoptosis**[2] fitted for **each cell**

eDRUG
early Drug Response UpGraded ML classifier



Augmented feature input space

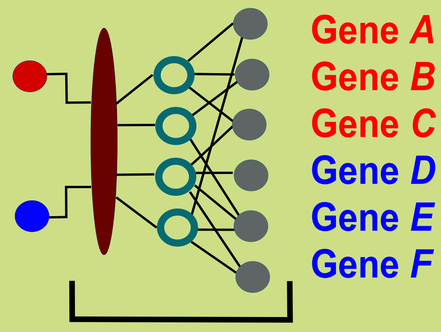
2 x more cells isolated with the same precision

Gene prioritization (3)

data from **scRNAseq**

Attribution scores = gene rank

Gene A	80%
Gene C	74%
Gene D	99%
Gene E	45%



Explainable ML: DeepLIFT[5]

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