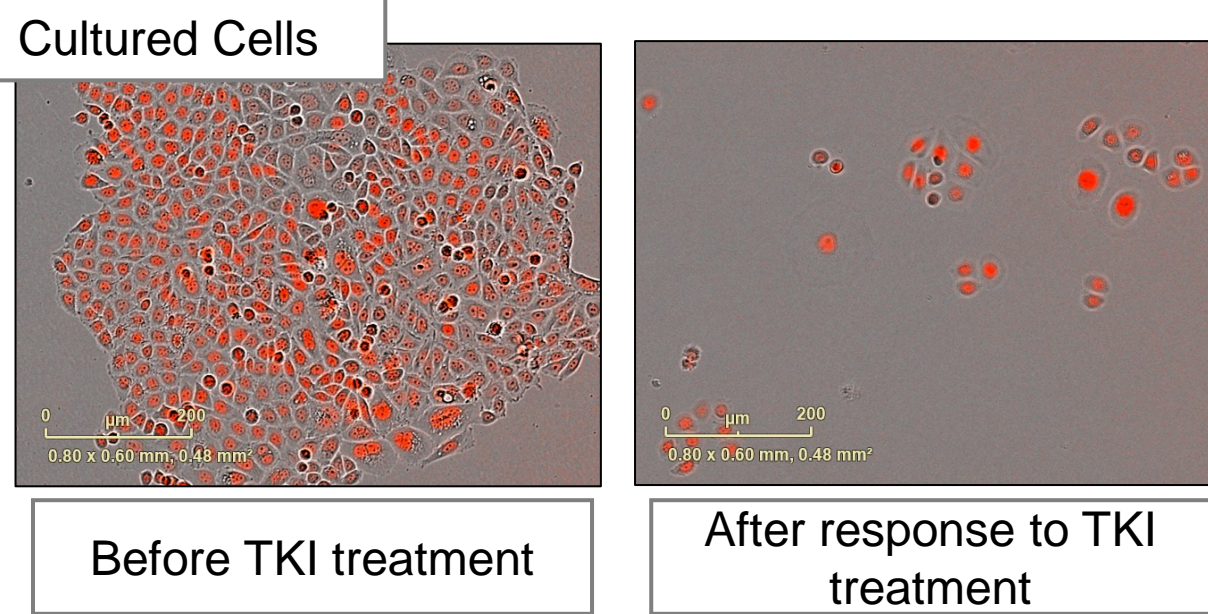
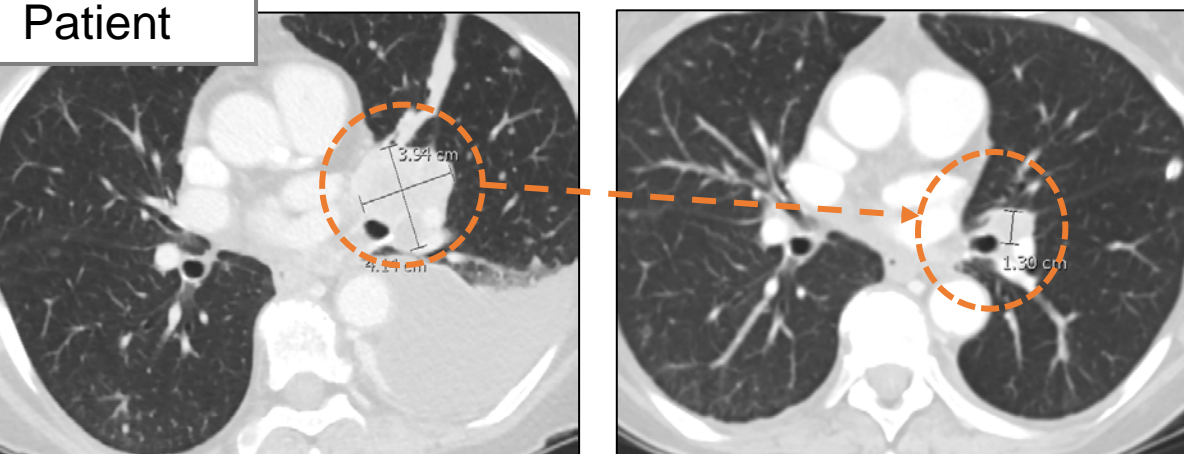


# Identify, characterize and develop strategies to combat the drug-tolerant persister cells (DTPCs) before development of acquired resistance in *EGFR*-mutant NSCLC

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## Backgrounds



- Anti-tumor response?  
**- Yes! BUT it is partial (incomplete) response.**  
**There are residual 'persisters'.**

### Major barrier in clinic:

- Ultimately drives tumor recurrence
- Difficult to get clinical biopsy

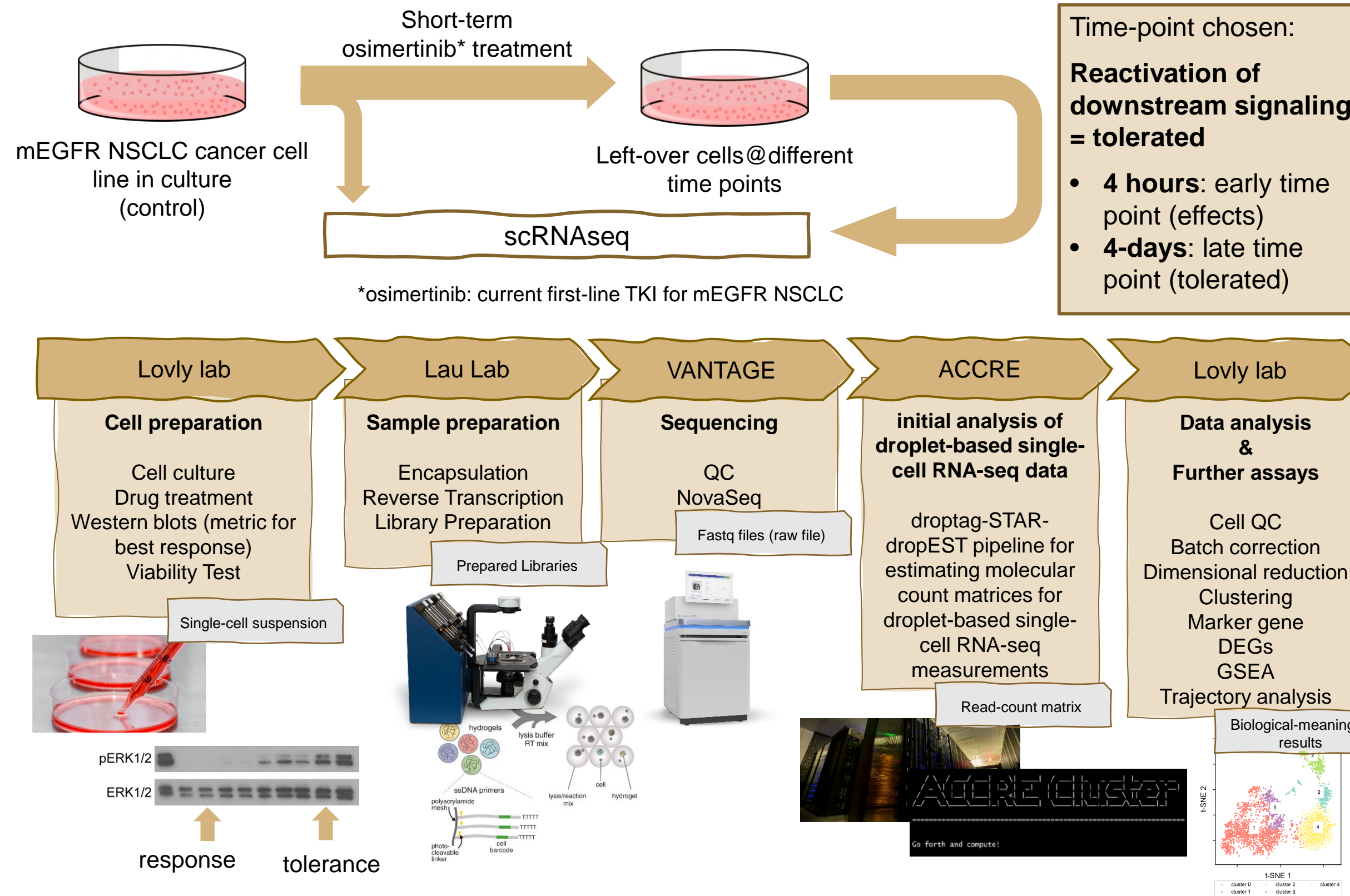
### What we don't know:

- Why didn't these cells respond to the therapy?
- What is the difference in these persisters?
- How do we go from the partial tumor shrinkage to more complete tumor shrinkage?

## Hypothesis

*EGFR*-mutant lung cancers have inherent diversity in tumor cell populations with different genomic features leading to differences in drug response, the **drug-induced drug-tolerant persister cells (DTPCs)** population formed rapidly after the initial exposure to TKI, and is the main reason for incomplete response and a critical step of development of permanent acquired resistance.

## Approaches



## Conclusions

- Our preliminary data show that *EGFR*-mutant lung cancer cells are heterogeneous and contain multiple sub-populations of cells, even in the absence of drug treatment.
- Our results represent an initial step for the rationale to identify genes and pathways that are required for DTPC survival. We have identified several potential key targets (e.g. CD74) and key pathways (e.g. EMT pathways)

## Future directions

- Perform further bioinformatics analysis (e.g. trajectory analysis) on the scRNAseq database
- Expand and compare the study to more treatment and more cell lines
- Perform protein level verification of the key targets and pathways identified in scRNAseq
- Reveal novel therapeutic vulnerabilities that can be targeted to eradicate DTPCs and enhance anti-tumor response for patients with *EGFR*-mutant lung cancer

## Results

