Title

Translational single-cell research enabled by Singleron's end-to-end research platform

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Abstract

We describe Singleron's integrated single-cell platform spanning wet-lab, sequencing, and analytics and show, via a multiple myeloma (MM) case study, how interpretable machine learning on single-cell profiles can generate therapy-specific response predictions and compact prognostic signatures suitable for downstream clinical assay development.

1. Introduction

Single-cell profiling resolves intratumoral heterogeneity and tumor microenvironment (TME) states that impact therapy response and prognosis, but clinical translation requires reproducible wet-lab workflows, scalable analytics, and interpretable models. Singleron provides an end-to-end solution: tissue processing, single-cell capture and library construction, and analysis pipelines designed for translational research. We summarize these offerings and present a focused MM example predicting response to daratumumab and deriving prognostic signatures amenable to bulk assays.

2. Singleron platform overview

2.1 Wet-lab technologies

- Tissue and single-cell preparation: Optimized dissociation protocols across challenging tissues and low-input samples; high viability and recovery.
- Single-cell partitioning: SCOPE-chip SD (≈10k cells/chip) and HD (≈30k cells/chip) formats for flexible throughput.
- RNA capture and library construction:
    - GEXSCOPE for high-sensitivity mRNA profiling with UMI barcoding.
- Targeted modules:
    - V(D)J repertoire: GEXSCOPE V(D)J for CDR3 capture; sCircle for full-length immunoreceptors.
    - FocuSCOPE: customized detection of SNVs, fusions, rare and non-polyA transcripts.
- QC checkpoints: Cell viability, cDNA yield, library complexity, and sequencing metrics standardized across runs.

2.2 Data analysis ecosystem

- Primary processing: Alignment, UMI deduplication, cell calling, doublet removal, feature quantification.
- Interpretable ML: Cell-level prediction models with SHAP-based feature attributions to identify gene drivers and reduce models to compact signatures.

- Reference resources: Synecosys database for standardized, curated single-cell datasets with metadata and automated analytics to contextualize new studies.

3. Case study: Multiple myeloma

3.1 Cohorts and objective

- Data sources: Combined public (e.g., Cohen et al.) and in-house scRNA-seq datasets of malignant plasma cells and TME from pre-treatment bone marrow samples.
- Clinical task: Predict response to daratumumab-containing regimens and identify features enabling simplified wet lab assays. Independent cohorts were used for validation.

3.2 Modeling approach

- Cell-level response scoring: Supervised ML model predicts response propensity per cell; patient-level prediction uses the median cell score as a decision statistic.
- Confound handling: Curated training to balance responder/non-responder classes; harmonization across data capture modalities.
- Interpretability: SHAP to rank features and support model reduction to small gene sets.

3.3 Results

- Therapy specificity: Accurate patient-level predictions for daratumumab regimens; substantially lower concordance in non-daratumumab cohorts, indicating mechanism-specific signal rather than generic prognosis.
- Model reduction: Comparable performance achievable with tens of genes, supporting transfer to bulk RNA-based assays (e.g., qPCR/RNA-seq panels).
- Prognosis from single-cell to bulk: Signatures derived from single-cell models improved stratification when combined with R-ISS in bulk datasets, increasing hazard ratios versus R-ISS alone.

4. Practical clinical translation path

- From single-cell discovery to deployable assays:
    1. Discover therapy-specific cell states and gene features via single-cell + interpretable ML.
    2. Reduce to small gene panels or protein markers.
    3. Implement in bulk RNA panels, qPCR, or flow cytometry/imaging for cost-effective clinical workflows.
- Singleron's offerings cover sample-to-result: wet-lab execution, targeted capture (including TCR/BCR, non-polyA), model interpretation, and report generation for translational programs.

5. Discussion

This workflow demonstrates a practical route from high-content single-cell data to actionable clinical predictions, emphasizing reproducible wet-lab processes, rare-signal preservation, and interpretable modeling. While MM/daratumumab is presented as a single example, the

approach is generalizable to other therapies and indications, facilitating companion diagnostics and risk stratification pipelines.

6. Conclusion

Singleron's end-to-end platform, tissue dissociation through targeted capture to interpretable ML, supports development of therapy-specific prediction models and compact prognostic signatures that can be deployed in simpler bulk assays. These capabilities enable translational studies at scale and accelerate movement from discovery to practical clinical tools.

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References

- Cohen et al., Nature Medicine (2021) – daratumumab cohort (plate-based scRNA-seq).