

1536-DRUG-seq: Transcriptomics Platform for Ultra-Scalable Phenotypic Screening

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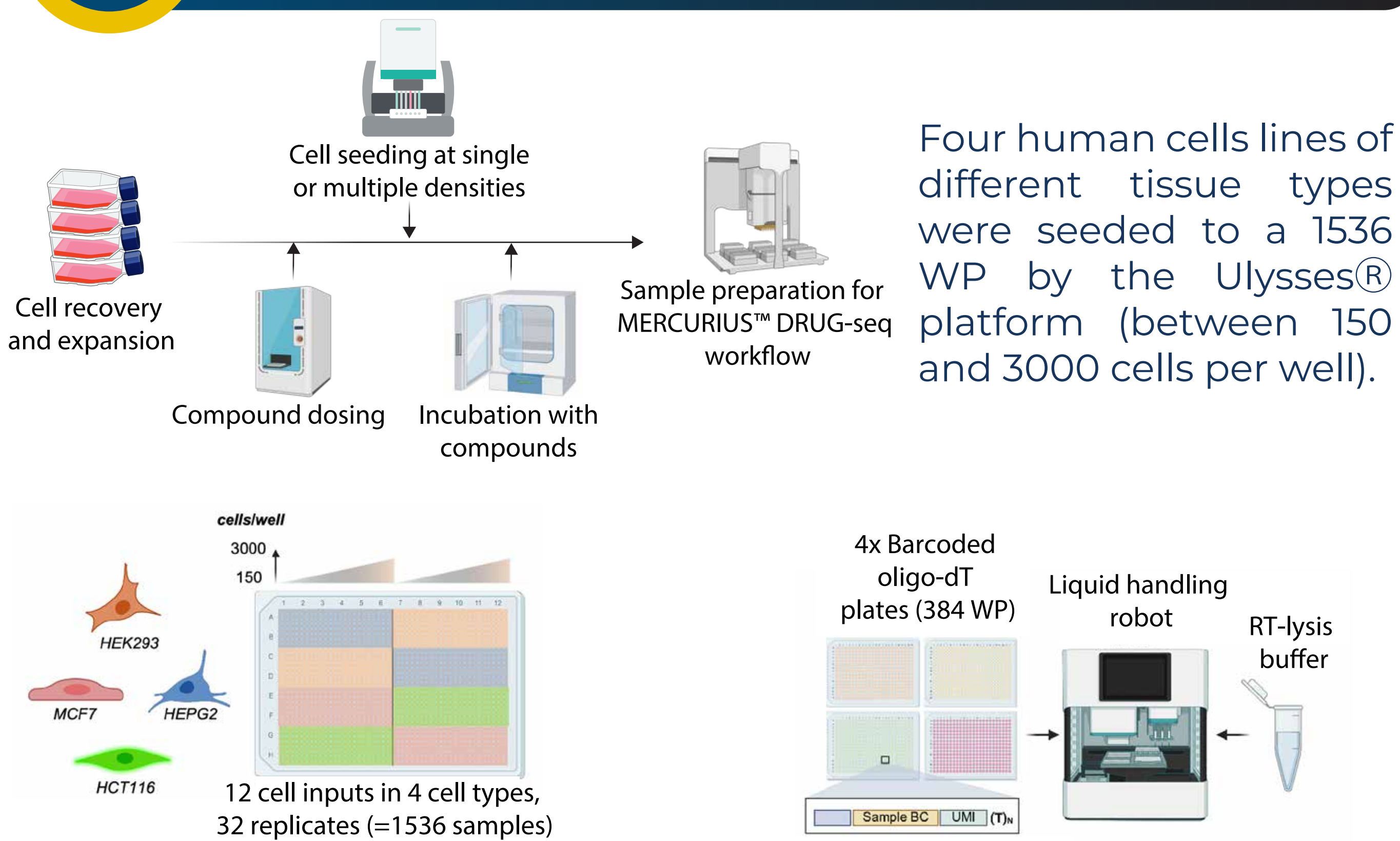
1 Abstract

Scalable drug discovery requires high-quality phenotypic data compatible with AI/ML-driven analysis. While transcriptomic profiling provides strong mechanistic insight, conventional RNA-seq lacks the scalability needed for ultra-high-throughput screening.

We present an updated MERCURIUS™ DRUG-seq workflow, an RNA-extraction-free, cells-to-library method compatible with 1536-well plate (WP) formats paired with fully automated cell preparation and treatment using Arctoris' Ulysses® modular automation platform. Profiling across four human cell lines demonstrates robust, reproducible transcriptomic readouts with reduced reagent use, hands-on time, and cost while maintaining gene detection sensitivity. Automated execution ensures consistency across thousands of conditions, generating standardized, high-quality datasets suitable for downstream AI/ML analysis.

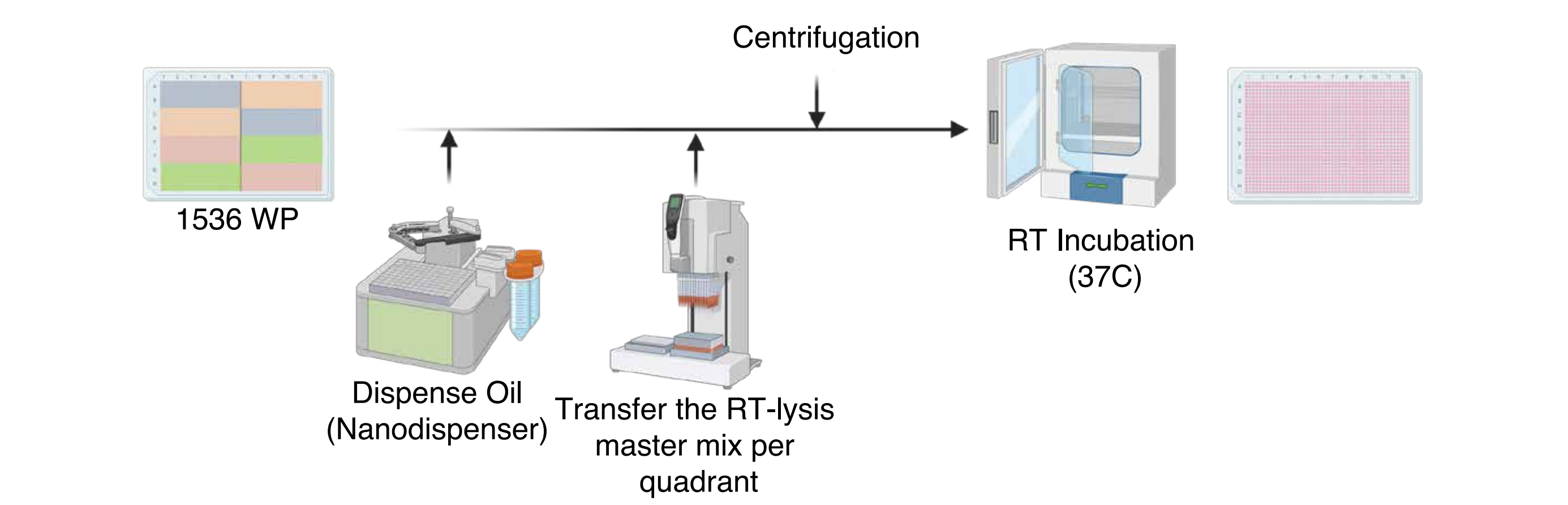
MERCURIUS™ DRUG-seq enables whole-transcriptome screening at scale, supporting compound MoA studies, safety assessment, and genetic perturbation screens to generate standardized datasets for AI-driven drug discovery.

2 Workflow design

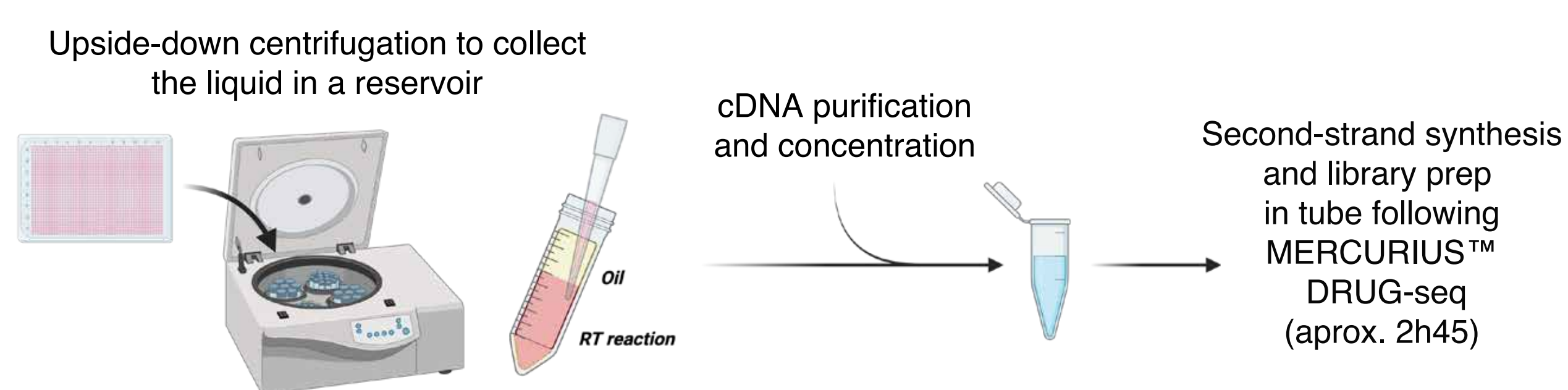


Experimental design for the 1536 WP across multiple input conditions.

Four 384 WP containing 1536 barcoded oligo-dT primers were mixed with the RT and lysis buffer. Each 384 WP fills one quadrant across four 1536 WP; in this experiment, only one 1536 WP was processed.

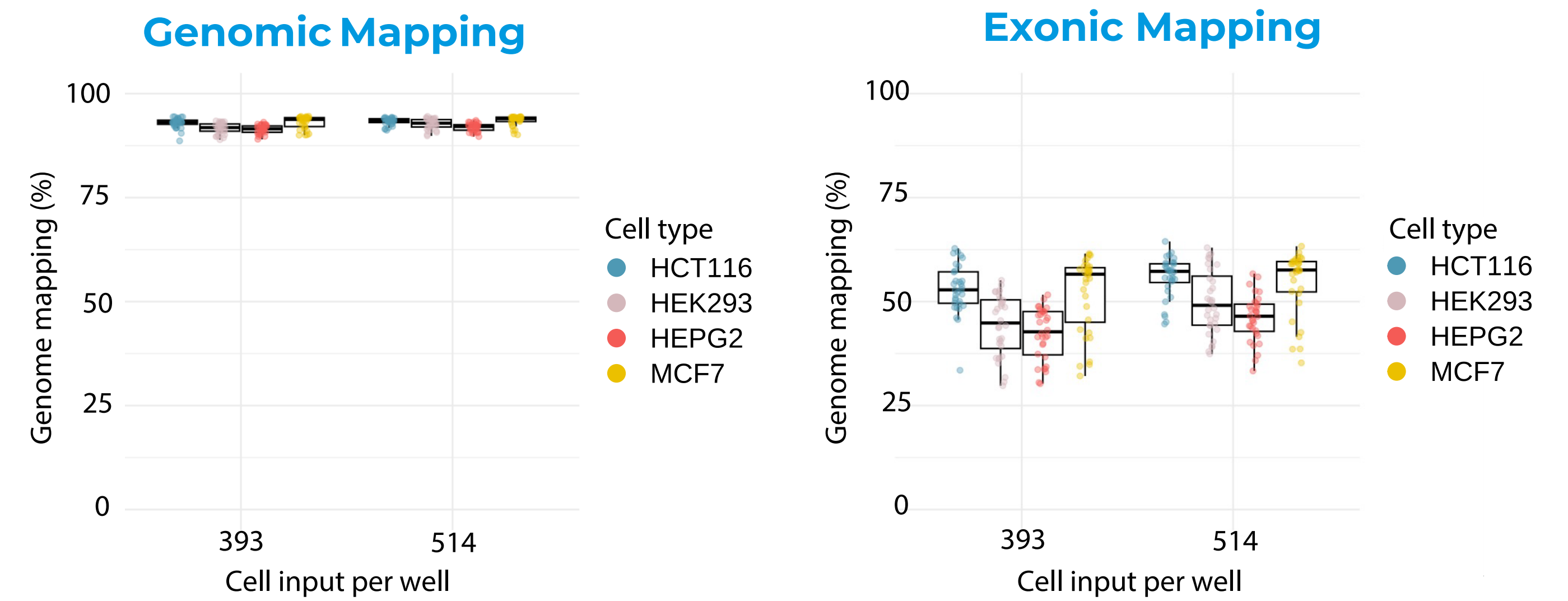


An oil overlay is applied to the cells prior to adding the RT-lysis master mix to prevent evaporation. The reaction is then incubated at 37°C in a standard incubator, enabling easy scaling for simultaneous processing of dozens of plates.

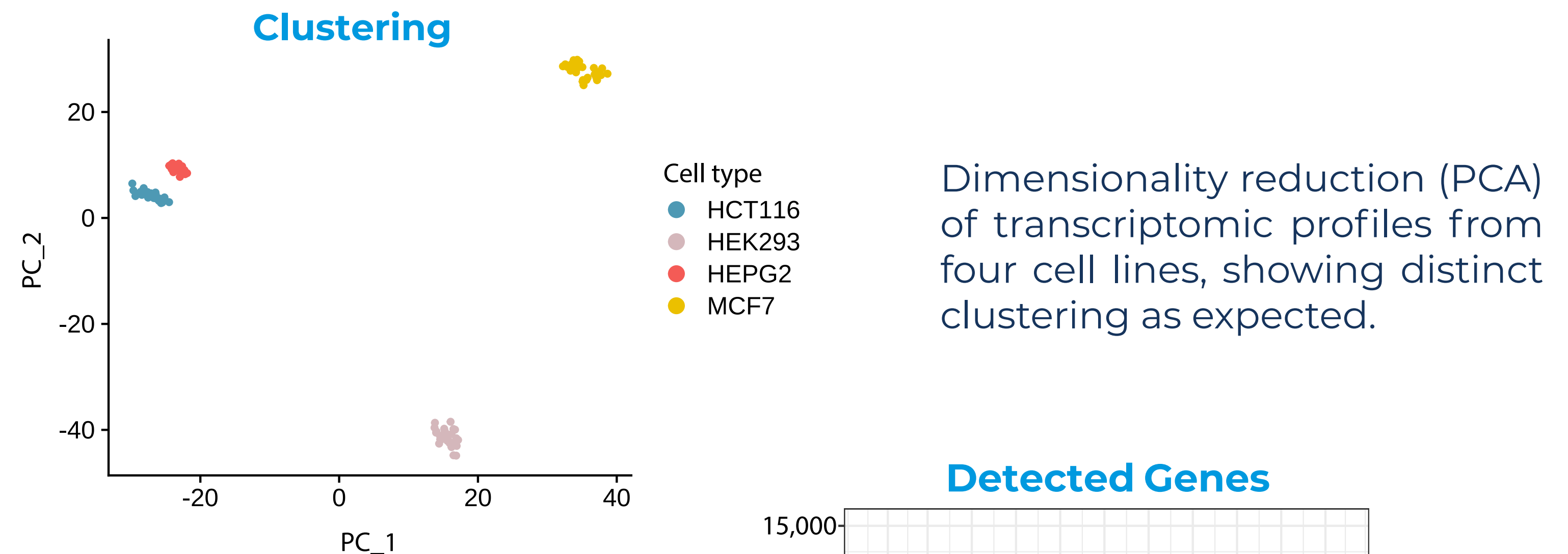


cDNA is collected by centrifugation, followed by purification and pooling of all 1536 samples into a single tube. Subsequent processing is performed with all samples maintained in the pooled tube.

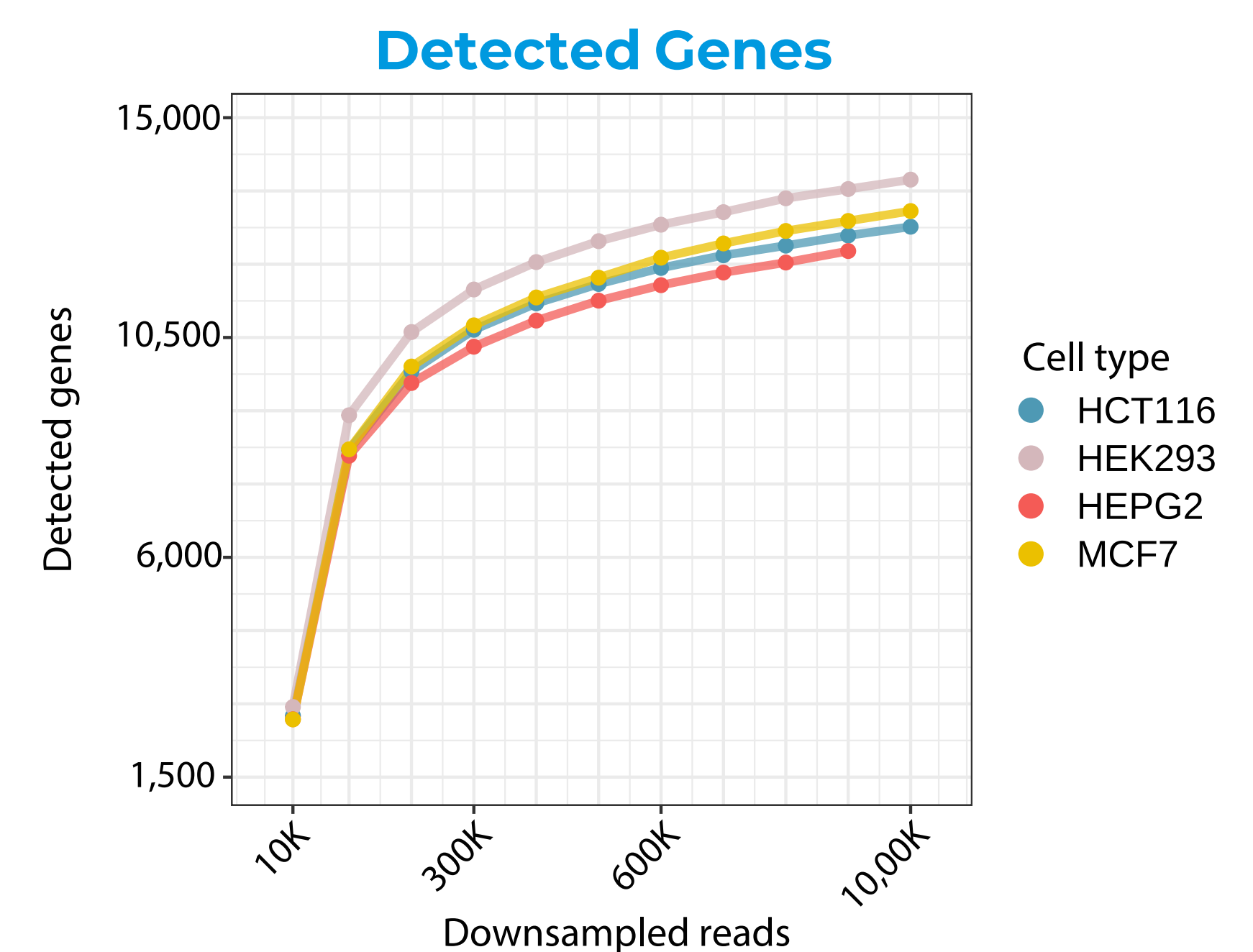
3 Results



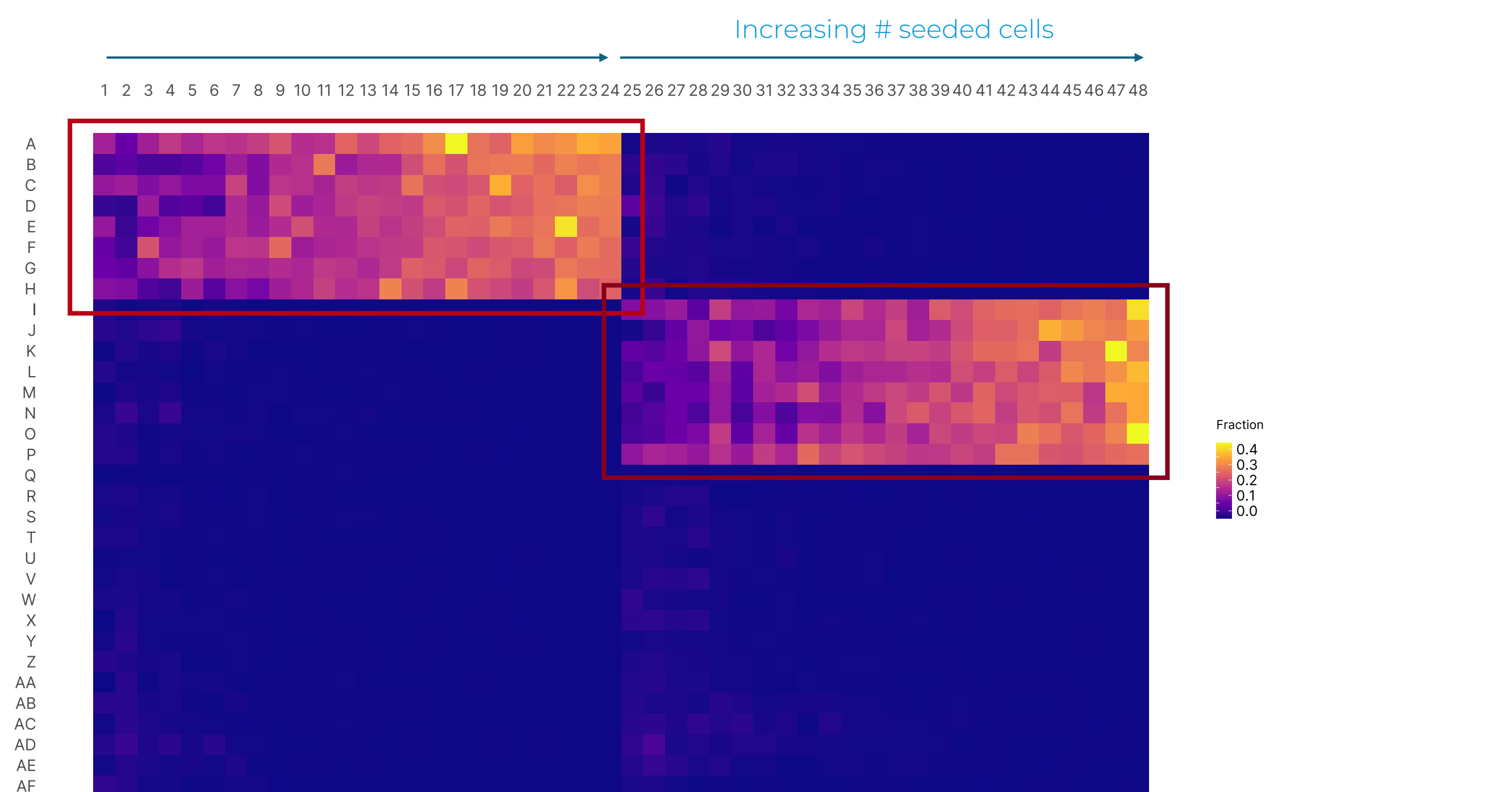
All cell types exhibited a high proportion of reads mapping to the genome, with the majority aligning to exonic features. These values are consistent with our results obtained using the 384 WP format. Although only two representative conditions are shown, the results were consistent across all seeded input cell numbers.



Gene detection per cell line (~1,000 seeded cells) as a function of sequencing depth after downsampling, demonstrating consistently high detection levels across



Cell type specific expression



Fraction of reads associated with the Albumin (ALB) gene, which is expected to be expressed in liver-derived cells such as HepG2. The positions of HepG2 cells on the plate are highlighted with red square boxes.

4 Conclusions

The new MERCURIUS™ 1536 WP DRUG-seq workflow demonstrates unprecedented potential for large-scale, high-throughput transcriptomic screening, delivering consistent, high-quality results with a high number of detected genes, while ensuring reproducibility at scale, to enable the generation of standardized datasets optimized for AI/ML-driven drug discovery.

Presentation Details

Date and Time: Wed, Feb 11, 1:00 PM - 1:20 PM

Room: Solutions Spotlight Theater

Booth #2539

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