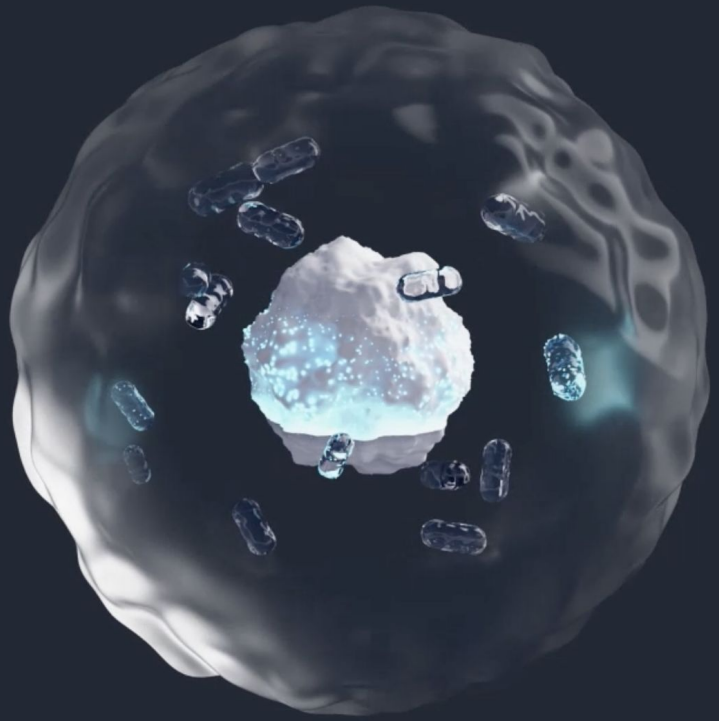
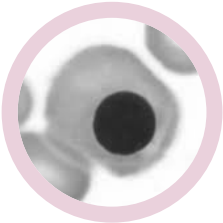
deepcell

Enrichment of Single Cells Using Deep Learning Based Classification and Sorting

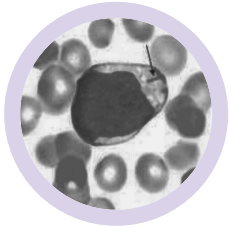
ABRF Annual Meeting,
2021-03-11



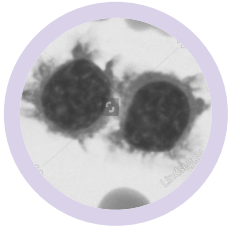
Unique cell morphology correlates to diseases and conditions



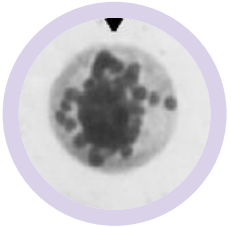
Fetal cell



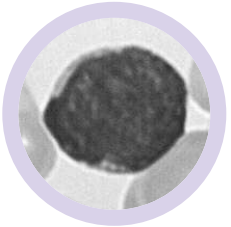
Acute myeloid leukemia



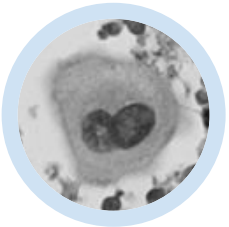
Hairy cell leukemia



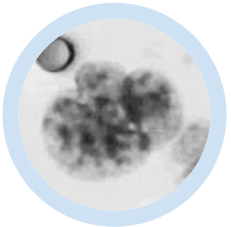
Myelodysplastic Syndrome



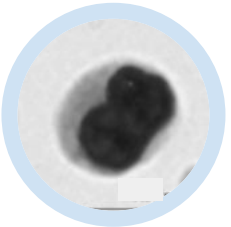
Acute lymphoblastic leukemia



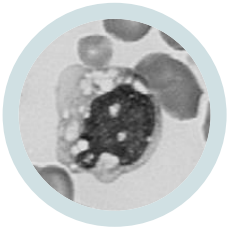
Lung cancer (NSCLC)



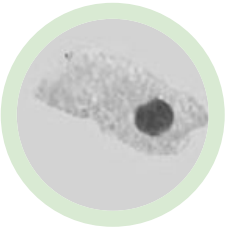
Breast cancer



Colorectal cancer



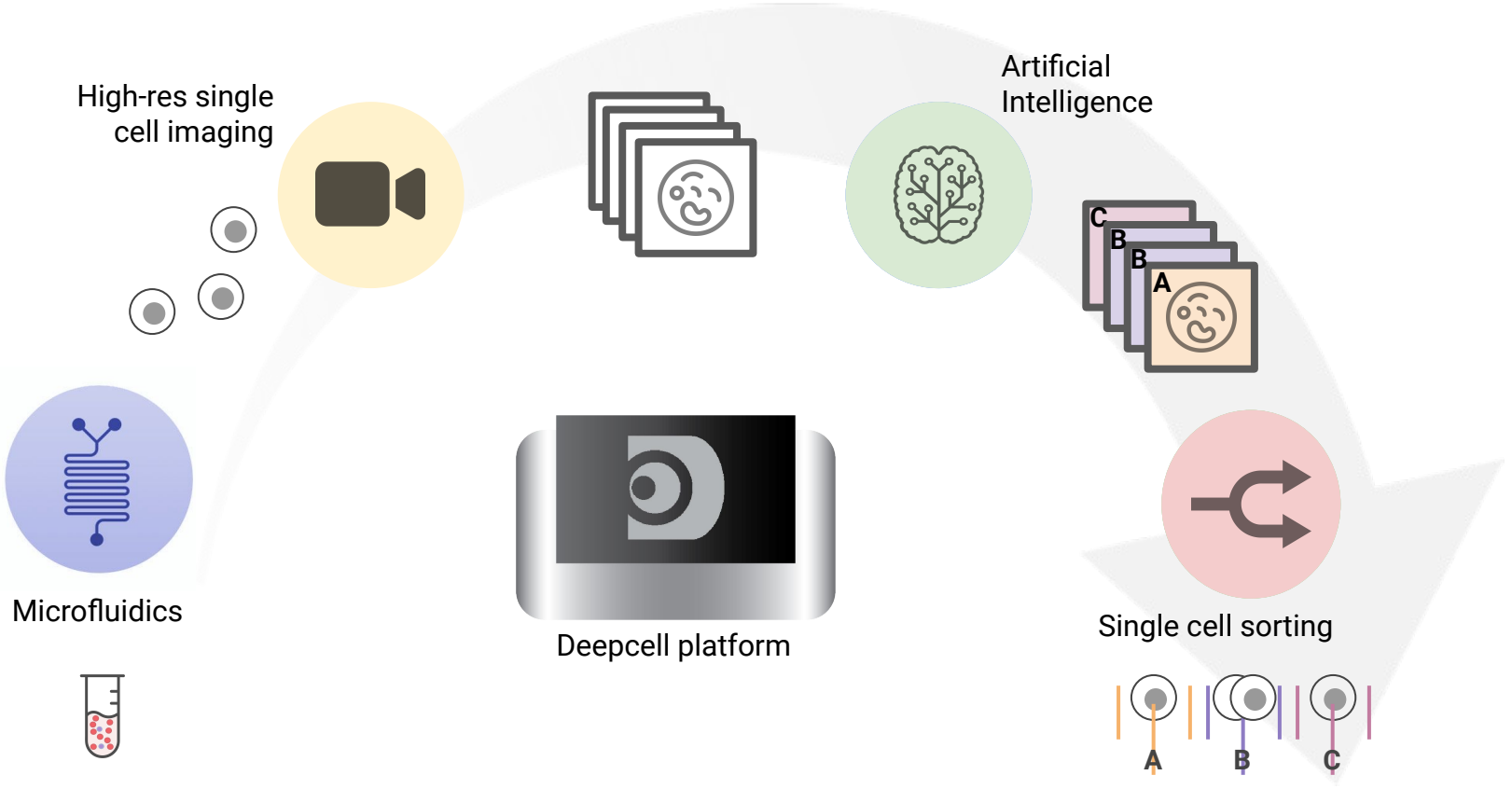
Sepsis



Kidney fibrosis

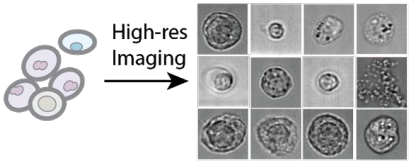
- Prenatal
- Liquid Tumour
- Solid Tumour
- Infectious disease
- Fibrosis

Deepcell is an AI-powered platform that identifies and isolates viable, morphologically distinct cells

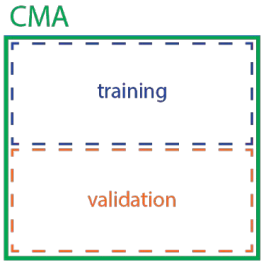


The AI brain

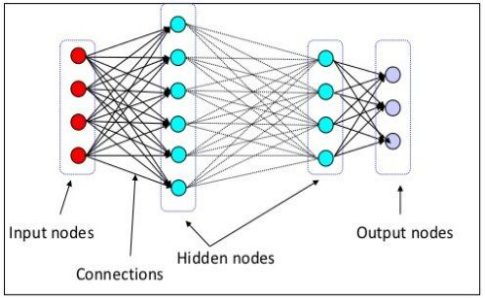
High resolution bright-field imaging



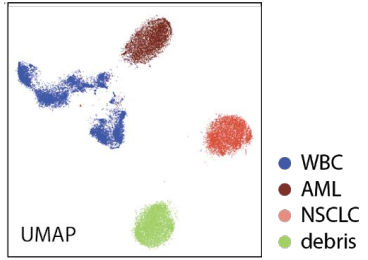
Integration into Cell Morphology Atlas

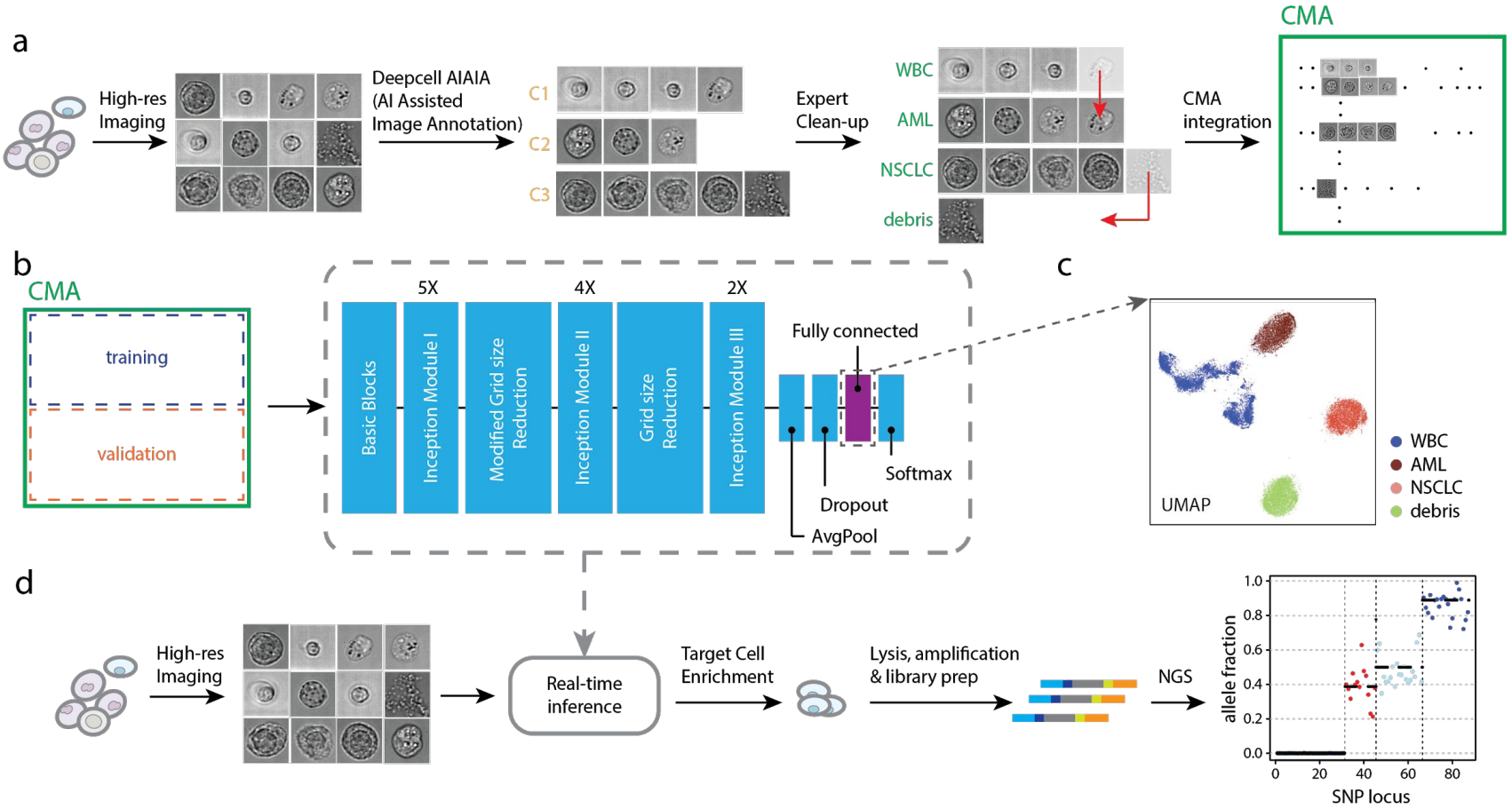


Deep Neural Network



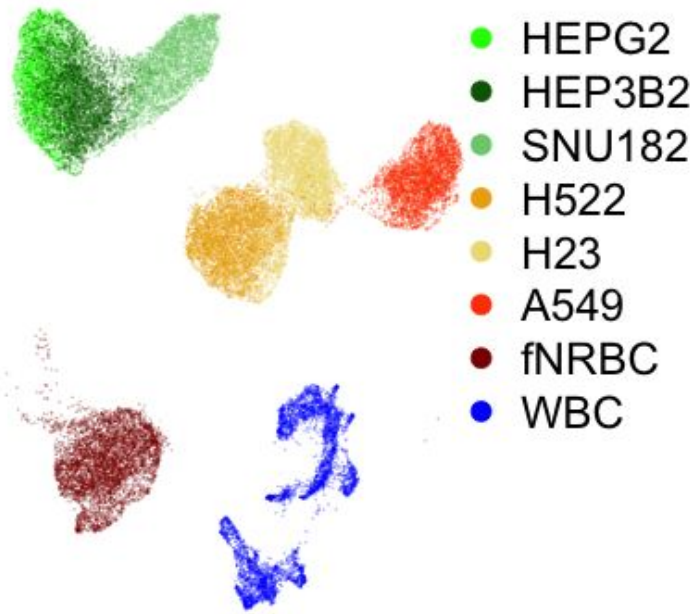
Quantitative Morphology Analysis

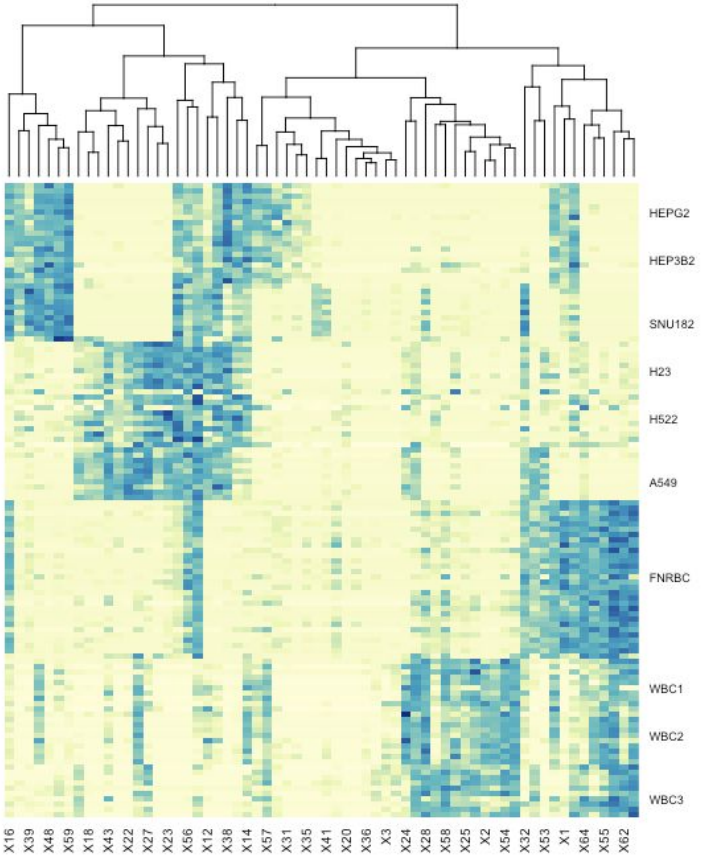



a
High-res Imaging
Deepcell AIAIA (AI Assisted Image Annotation)
C1
C2
C3
Expert Clean-up
WBC
AML
NSCLC
debris
CMA integration
CMA
b
CMA
training
validation
5X
4X
2X
Basic Blocks
Inception Module I
Modified Grid size Reduction
Inception Module II
Grid size Reduction
Inception Module III
Fully connected
Softmax
Dropout
AvgPool
c
UMAP
WBC
AML
NSCLC
debris
d
High-res Imaging
Real-time inference
Target Cell Enrichment
Lysis, amplification & library prep
NGS
allele fraction
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
80
SNP locus

Separability of cells and understanding heterogeneity of morphology

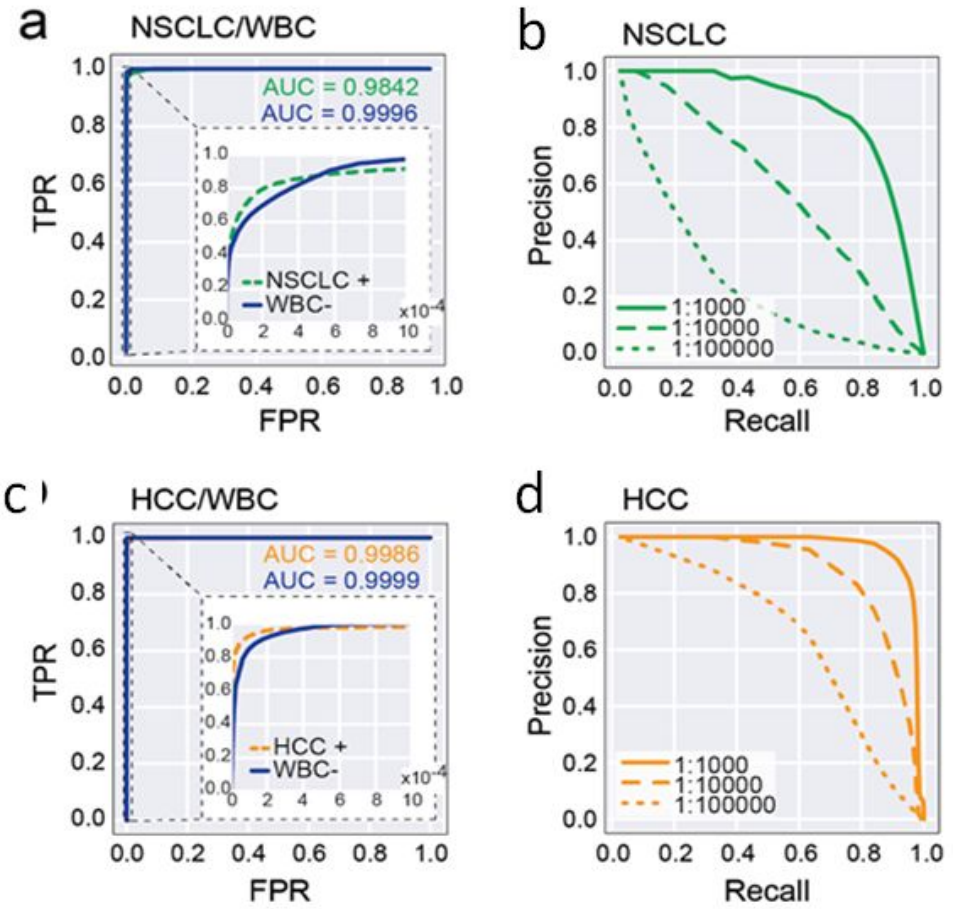
Morphology UMAP of multiple cell lines





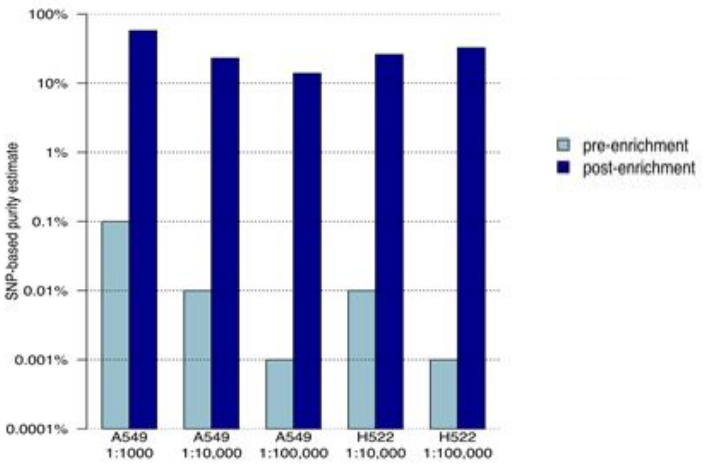
Real-time classification and label-free sorting beyond single markers

Classifier performance on NSCLC, hepatocarcinoma against WBC

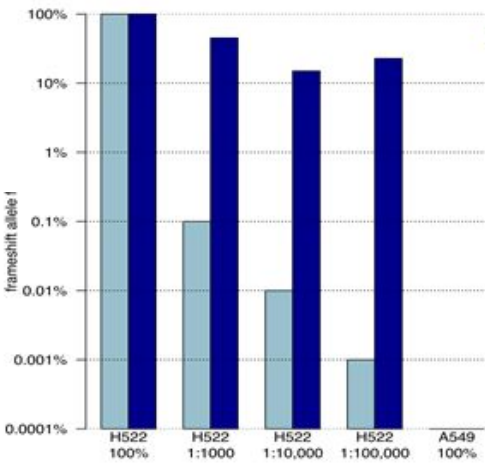


Rare cell enrichment with sorting: NSCLC spiked into WBC and whole blood

A549 or H522 spiked into WBC



SNP-based purity and enrichment estimate



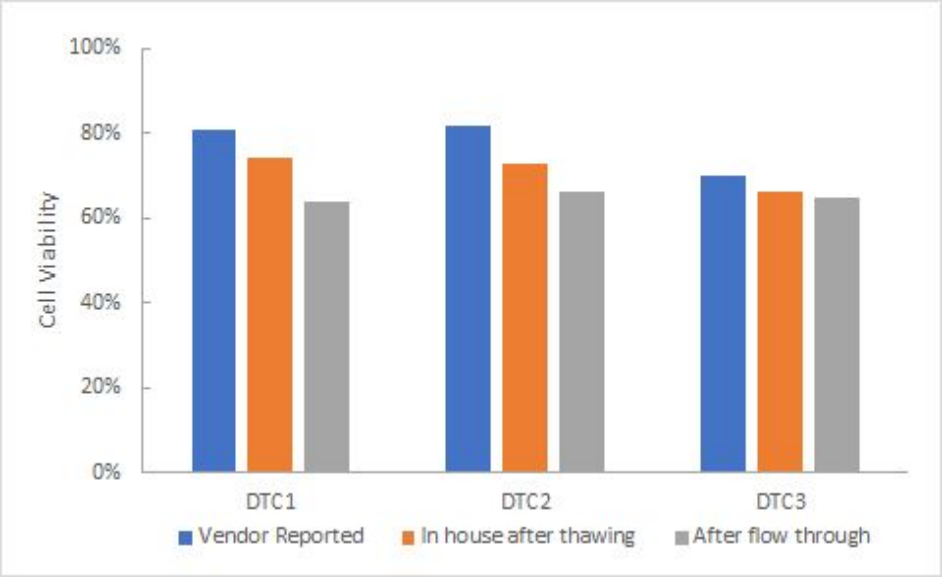
Detecting a frame-shift TP53 mutation in H522

A549 Spiked into whole blood

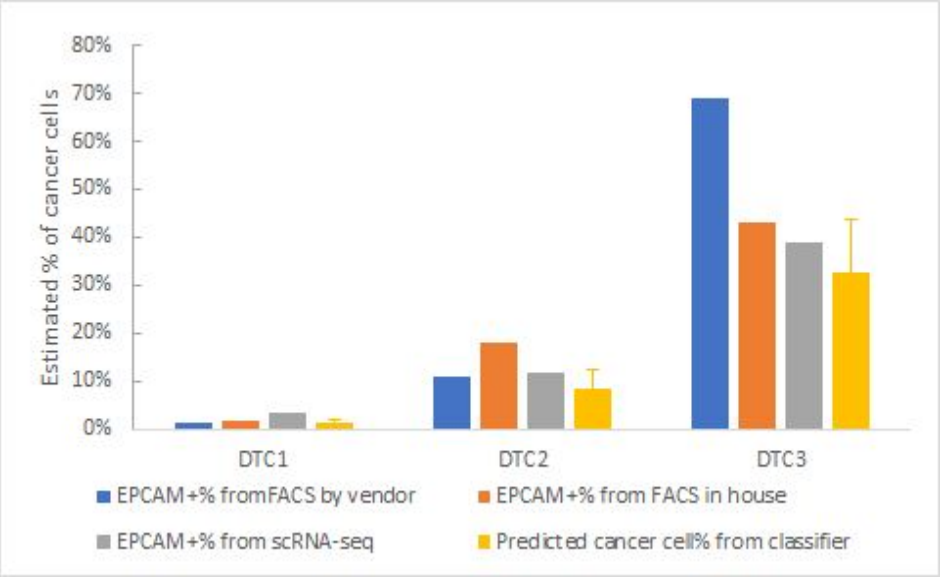
Spike-in concentration	Sorted cell purity	Fold enrichment by CD45 depletion	Overall fold enrichment
400/ml	55%	13	10,900
400/ml	80%	16.2	29,000
40/ml	43%	11	33,500
40/ml	35%	6.7	27,800

Profiling of patient dissociated tumor cells with AI morphological classifier

Cell viability

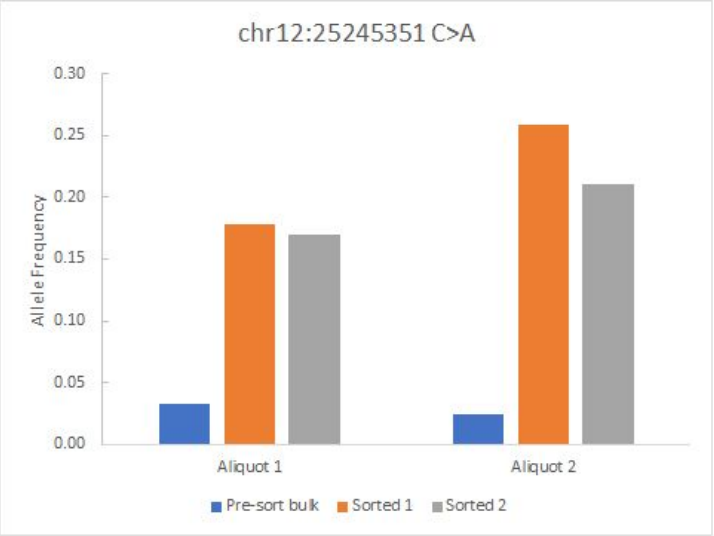


Estimated tumor content



Enrichment of cancer cells from DTCs: oncogene mutations

chr12:25245351 C>A KRAS G12C



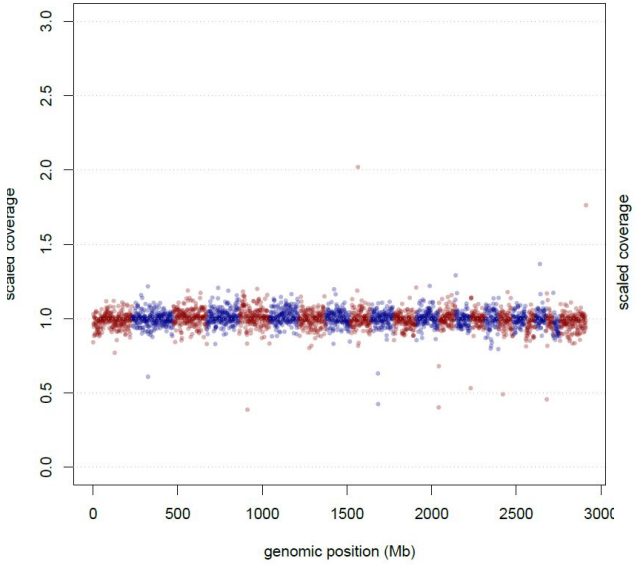
Heterogeneity of Mutations from different aliquots

Mutation: chr12:25245351 C>A, Protein: KRAS G12C

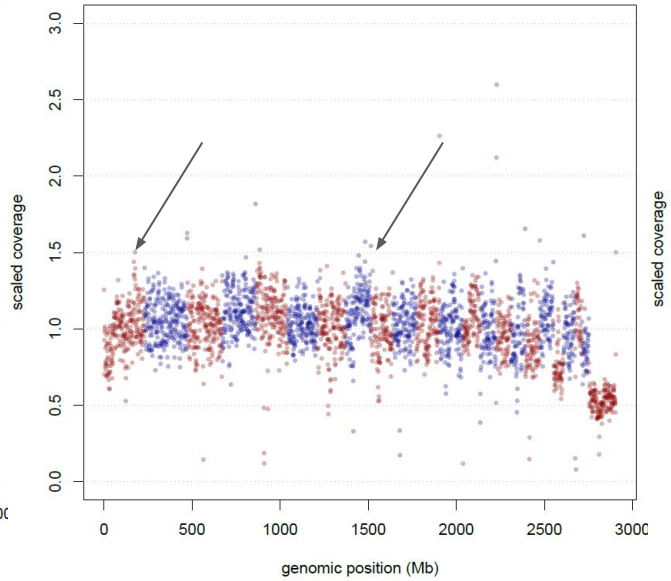
- KRAS G12C mutation occurs in about 13% of NSCLC patients, and 1%-3% of colorectal and other solid tumors - known to decrease likelihood of survival and associated with high likelihood of brain metastases.
- Candidate drugs in clinical trials: sotorasib (Amgen), adagrasib (Mirati Therapeutics), JNJ-74699157 (JNJ)

Enrichment of cancer cells from DTC: copy number variations

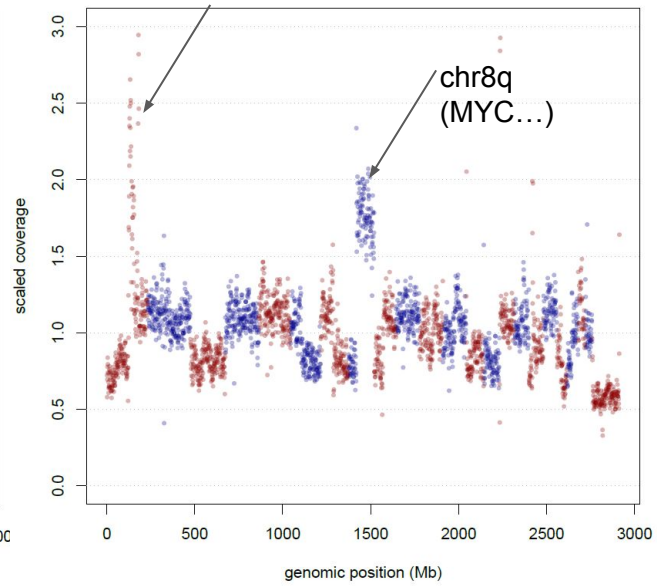
GM12878 (control cell)



DTC bulk

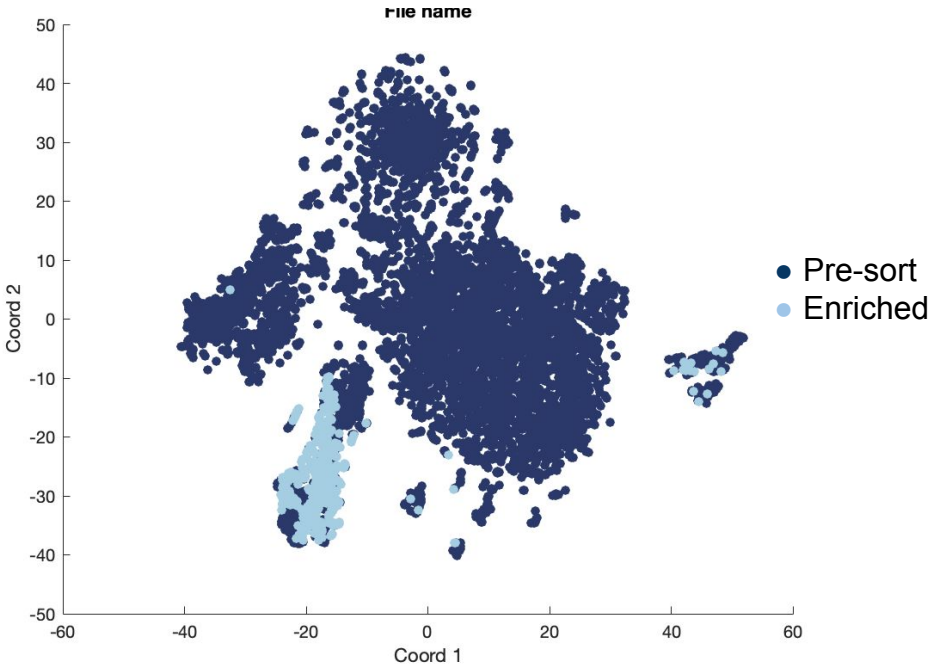


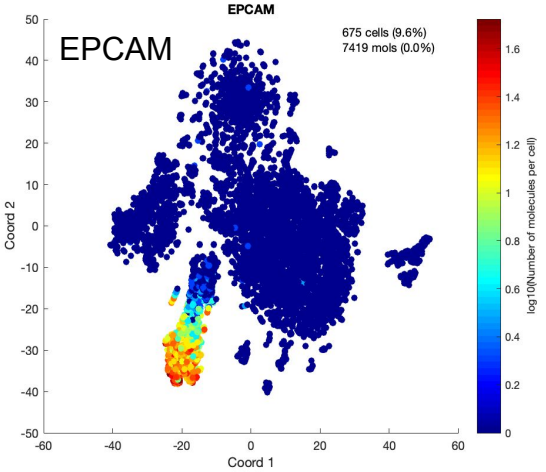
DTC enriched

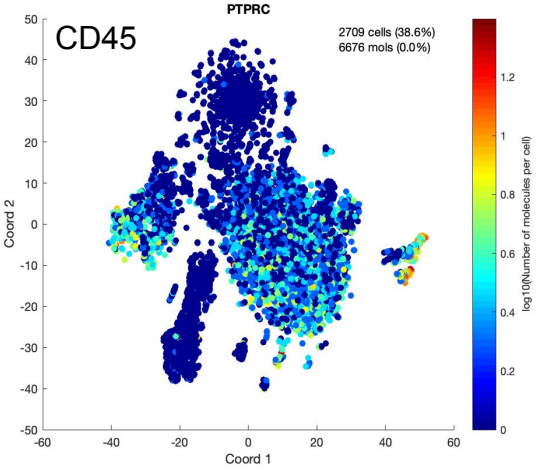


Enrichment of cancer cells from DTC: scRNA-seq (whole transcriptome)

UMAP of DTC Pre-sort vs Enriched

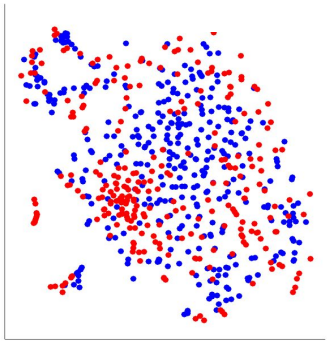


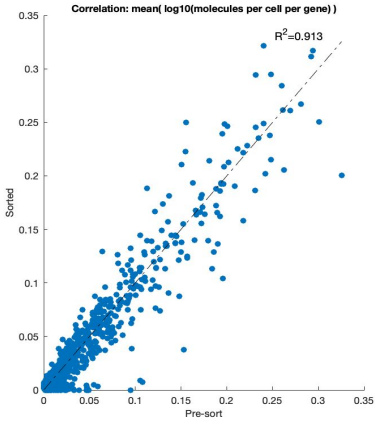


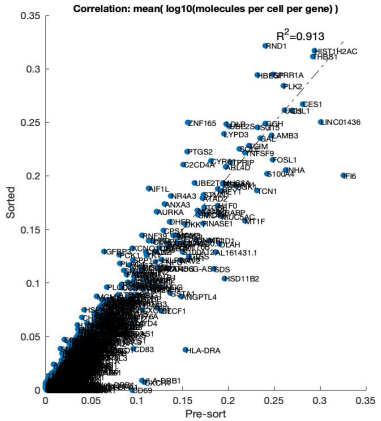


Gene correlation in EPCAM+ cluster (after further subclustering)

Feature selected genes (920)

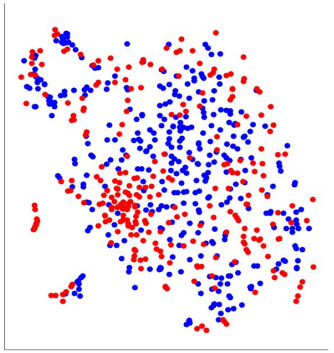


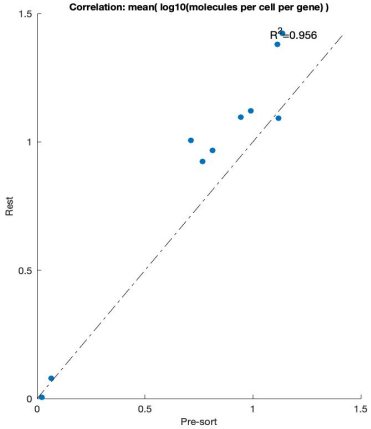


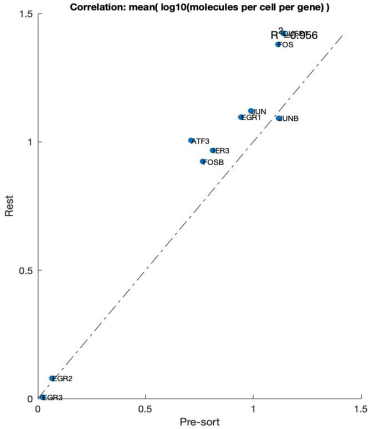


- Pre-sort
- Enriched

Stress response genes (10)



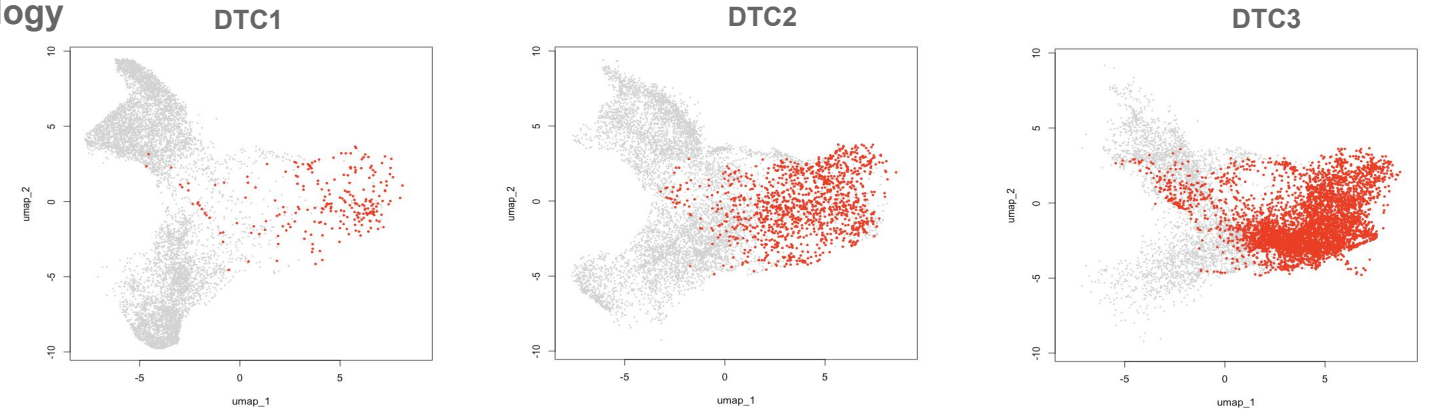




Studying single cell heterogeneity with morphology and gene expression

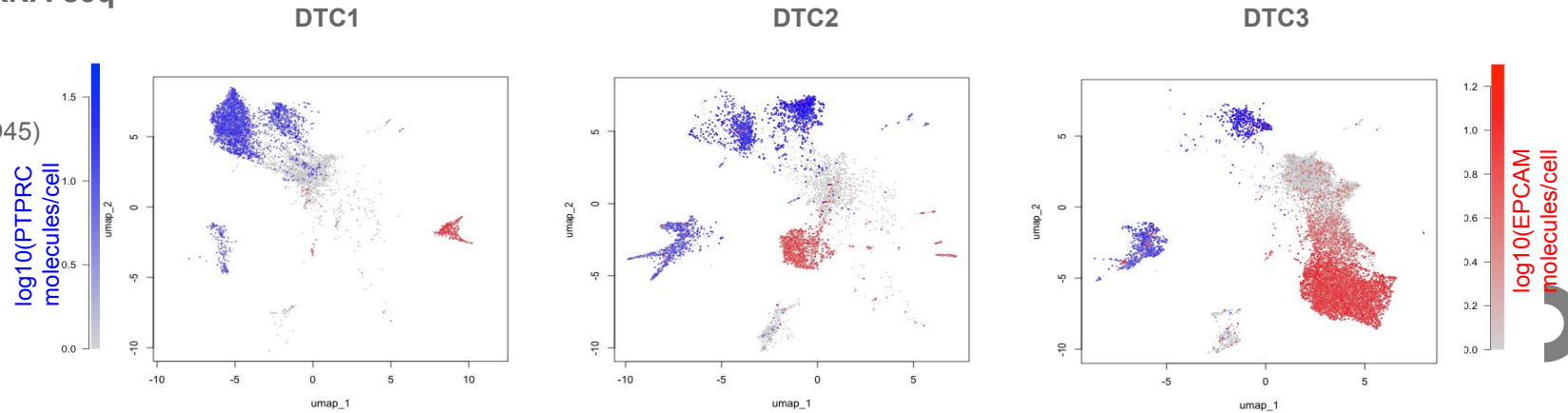
UMAP of Morphology

- malignant
- other

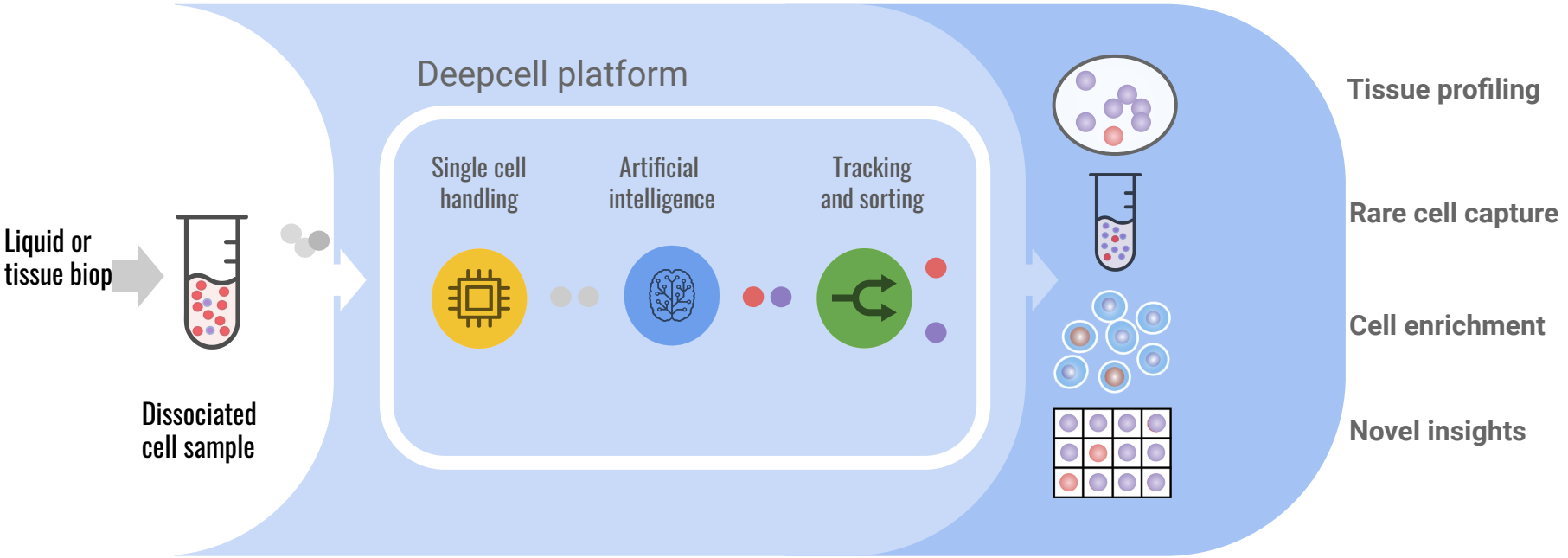


UMAP of scRNA-seq

- EPCAM
- PTPRC(CD45)



Conclusion: **AI**-powered analysis and **label-free** single cell sorting



Deepcell's platform integrates cell morphology into our multi-omic view of biology, thus paving the path that connects the genome to the patient.