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
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
Separability of cells and understanding heterogeneity of morphology

Morphology UMAP of multiple cell lines

- HEPG2
- HEP3B2
- SNU182
- H522
- H23
- A549
- fNRBC
- WBC
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

<table>
<thead>
<tr>
<th>Spike-in concentration</th>
<th>Sorted cell purity</th>
<th>Fold enrichment by CD45 depletion</th>
<th>Overall fold enrichment</th>
</tr>
</thead>
<tbody>
<tr>
<td>400/ml</td>
<td>55%</td>
<td>13</td>
<td>10,900</td>
</tr>
<tr>
<td>400/ml</td>
<td>80%</td>
<td>16.2</td>
<td>29,000</td>
</tr>
<tr>
<td>40/ml</td>
<td>43%</td>
<td>11</td>
<td>33,500</td>
</tr>
<tr>
<td>40/ml</td>
<td>35%</td>
<td>6.7</td>
<td>27,800</td>
</tr>
</tbody>
</table>
Profiling of patient dissociated tumor cells with AI morphological classifier

Cell viability

Estimated tumor content
Enrichment of cancer cells from DTCs: oncogene mutations

- **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)

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

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**Heterogeneity of Mutations from different aliquots**

**chr12:25245351 C>A**

![Graph showing allele frequency for chr12:25245351 C>A in Aliquot 1 and 2](image)

**Aliquot 2 TP53**

![Graph showing allele frequency for chr17:7675783 C>A and chr17:7675208 C>T in Aliquot 2](image)
Enrichment of cancer cells from DTC: copy number variations

GM12878 (control cell)  DTC bulk  DTC enriched

chr8q (MYC...)
Enrichment of cancer cells from DTC: scRNA-seq (whole transcriptome)
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)

log₁₀(EPCAM molecules/cell)
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.