DATA-DRIVEN PRECISION MEDICINE APPROACHES TO CANCER: TUMOR DORMANCY

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Tumor Cell Dormancy

- **Pre-invasive stage**
  - Premalignant or undetectable lesion
  - Years?

- **Invasive stage**
  - Treatment
  - Years

- **Minimal residual disease and metastatic stage**
  - Months
  - Years
  - Decades

**Cell of origin**
- in non-diseased tissue

**Primary tumor**

**Pre-malignant cell**

**DTC**

**Metastasis**

**Dissemination**

**Reawakening**
Tumor Cell Dormancy in Pancreatic Cancer

Pancreatic adenocarcinoma
Tumor Cell Dormancy in Pancreatic Cancer

Pancreatic cancer generally has short survival.

High neo-antigen burden in tumors and abundant CD8+ T-cell infiltrates predict long survival.

Balachandran et al. Nature, 2017
Workflow: Isolation and characterization of DTCs in human

- Florescence Activated Cell Sorting (FACS)
- Single Cell RNA Seq
- Single Cell Gene Expression Estimates Achieved
  - Microfluidic Partitioning
  - Barcoding techniques
Seurat Single Cell Genomics

- Normalization: Feature counts for each cell are divided by the total counts for that cell and multiplied by the scale factor. This is then natural-log transformed.

- Find Variable Features: Learn a statistical model of technical noise directly from the data, and remove this without dampening biological heterogeneity.

- Anchors Between Datasets: Take into account neighbors (k). Features identified in both samples are compared.
Clustering Visualization
Gene Specific Results
Copy Number Variation (CNV)

Structural Variation

Amplifications
Deletions

-> Implications

Copy Number Variation

Segment of DNA in which copy number differences have been found.
The segment may range from one kilobase to several megabases in size.

Next Generation Sequencing
HoneyBADGER

- Hidden Markov Model integrated Bayesian approach for detecting CNV and LOH events from single-cell RNA-seq data.

- Data must be filtered for highly expressed shared genes and scaled for library size differences.

- Inputted gene expression matrix is normalized using reference data. We expect large-scale deviations in expression from the reference on average to be indicative of underlying CNVs.

- HMM identifies a number of candidate CNVs to test.
Heatmap Visualization

Red = higher avg expression compared to reference
Blue = lower avg expression compared to reference
Continued Investigation
- Data Handling within functions
- Com 0 vs. Com 1

Connection with overall goal
- Greater Understand Dormancy
- Use Dormancy for Cancer Treatment Improvements
- Personal Experience
THANK YOU

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REFERENCES


• Normalization and variance stabilization of single-cell RNA-seq data using regularized negative binomial regression Christoph Hafemeister, Rahul Satija bioRxiv 576827; DOI: https://doi.org/10.1101/576827