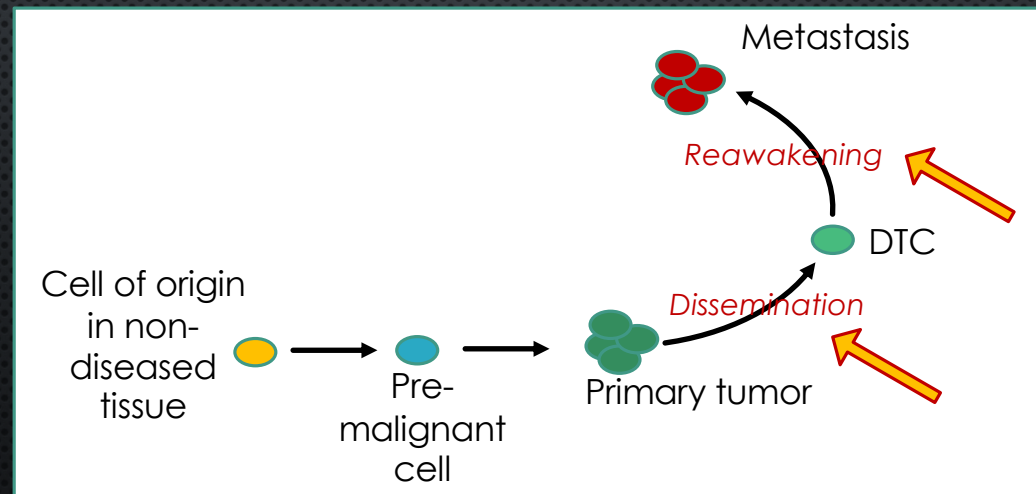
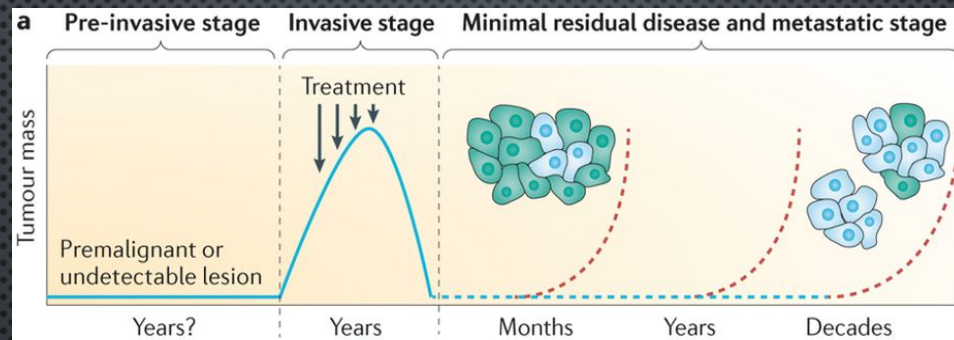


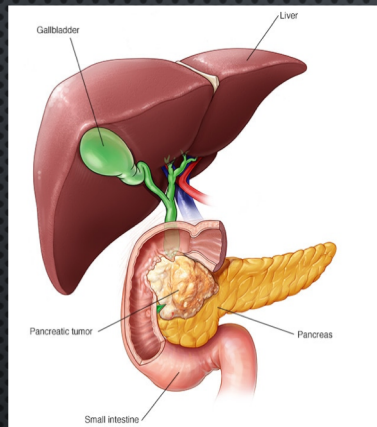
DATA-DRIVEN PRECISION MEDICINE
APPROACHES TO CANCER:
TUMOR DORMANCY

BY ERIN DAHL
DR. SUBHAJYOTI DE, PHD

Tumor Cell Dormancy



Tumor Cell Dormancy in Pancreatic Cancer



Pancreatic adenocarcinoma

CANCER RESEARCH UK Together we will beat cancer

Search

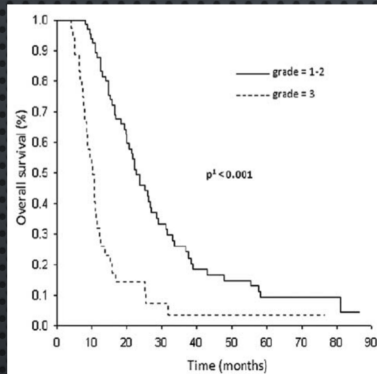
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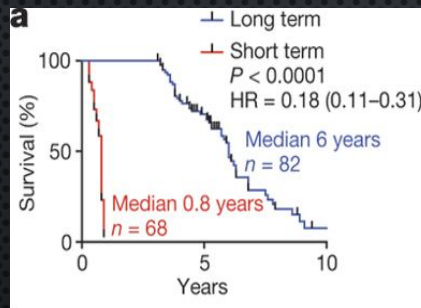
Pancreatic cancer survival statistics

Survival	Age	Improvement
Less than 1% Survive pancreatic cancer for 10 or more years, 2010-11, England and Wales	15-49 YEARS Age that pancreatic cancer survival is highest, 2009-2013, England	NO INCREASE Pancreatic cancer survival in the UK has not changed in the last 40 years

Tumor Cell Dormancy in Pancreatic Cancer

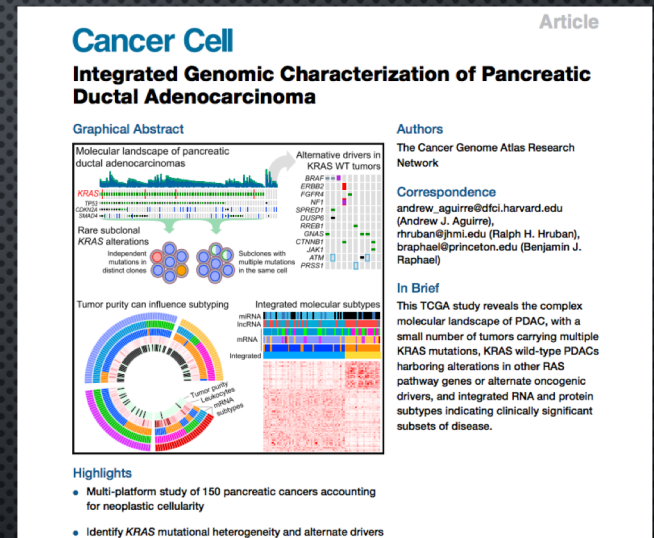


Pancreatic cancer generally has short survival

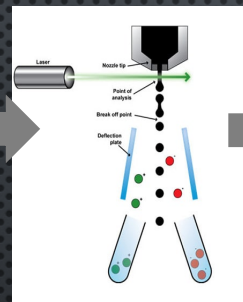
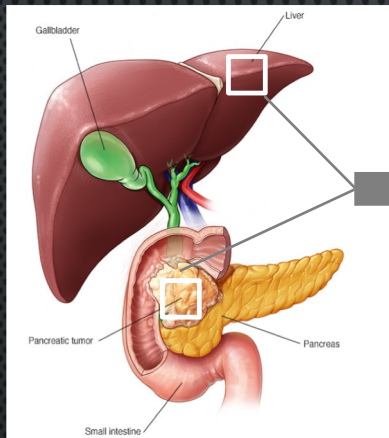


High neo-antigen burden in tumors and abundant CD8+ T-cell infiltrates predict long survival.

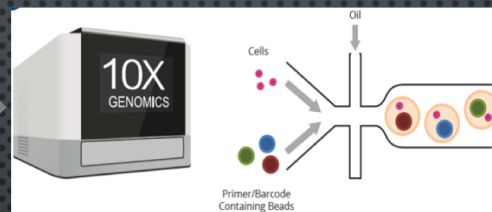
Balachandran et al. Nature, 2017



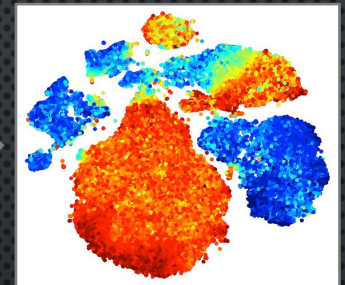
Workflow: Isolation and characterization of DTCs in human



Fluorescence
Activated
Cell Sorting
(FACS)



Single Cell RNA Seq



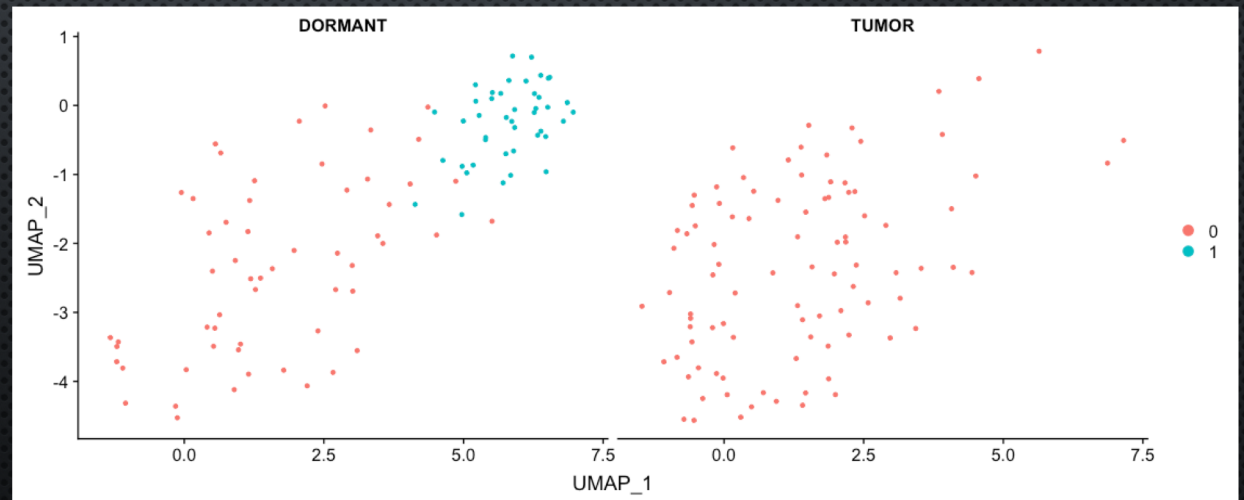
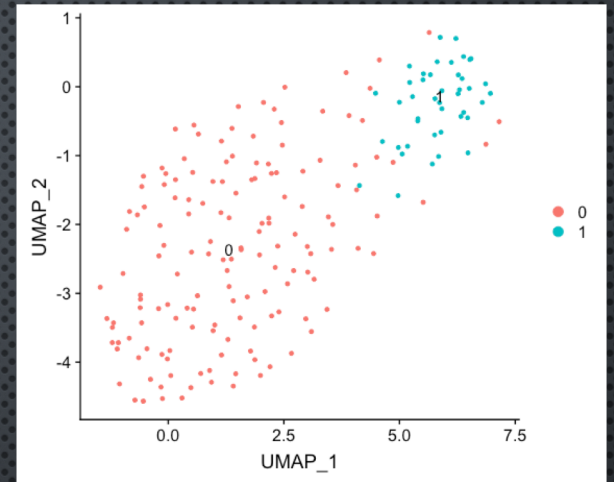
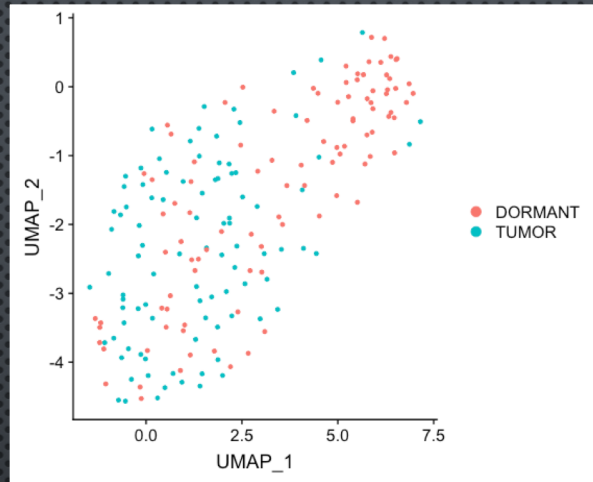
Single Cell Gene Expression Estimates Achieved

- Microfluidic Partitioning
- Barcoding techniques

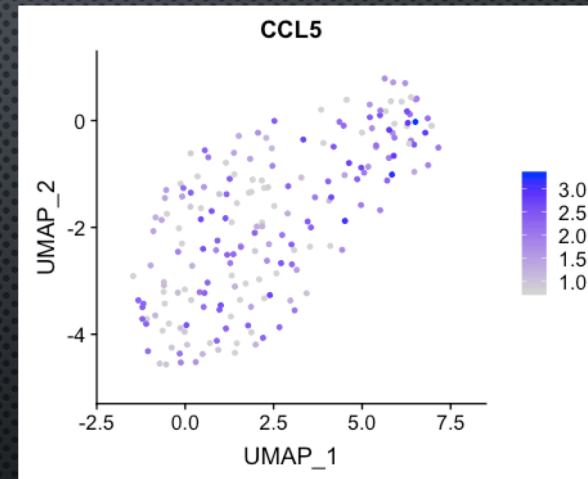
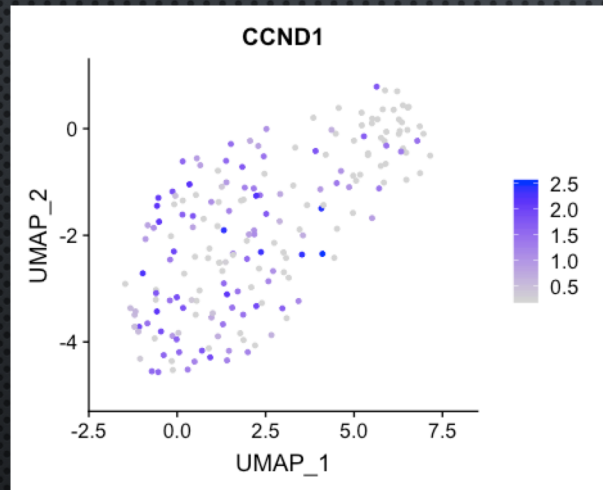
Seurat Single Cell Genomics

- 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

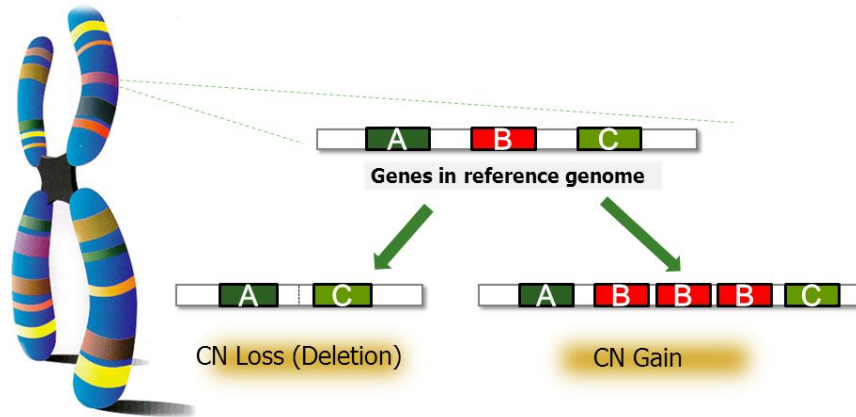


Gene Specific Results



Copy Number Variation (CNV)

Structural Variation



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

MACROGEN

Amplifications
Deletions

-> Implications

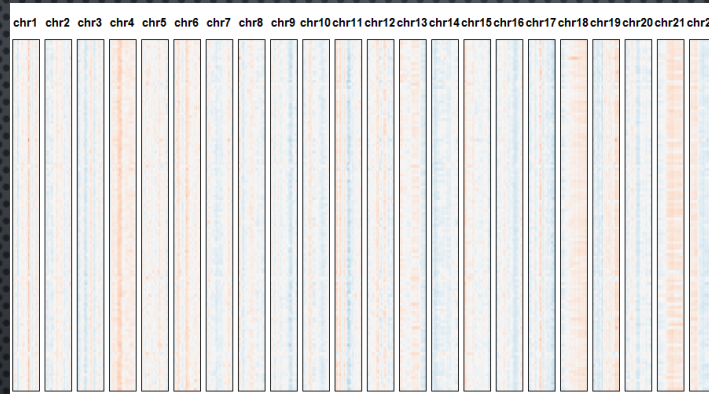
HoneyBADGER

- 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

HMM
statistical model that can be used to describe the evolution of observable events that depend on internal factors, which are not directly observable.

Heatmap Visualization

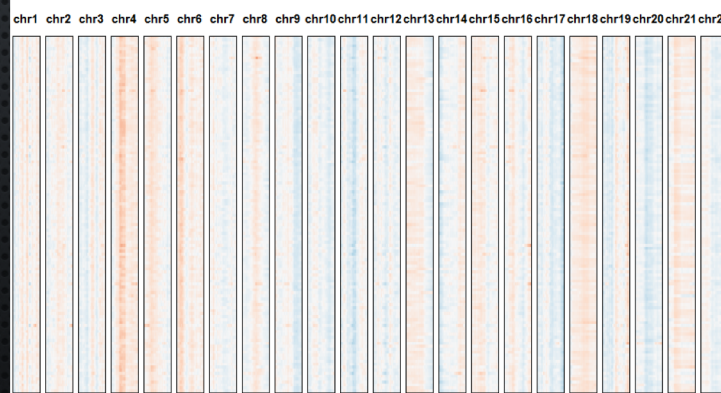
TUMOR



Red = higher avg expression compared to reference

Blue = lower avg expression compared to reference

DORMANT



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

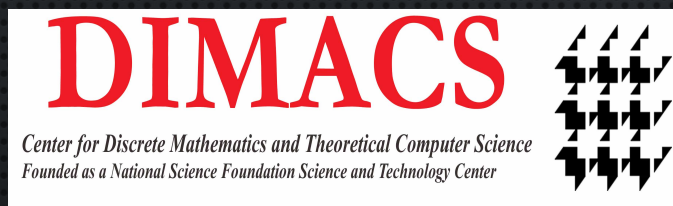
THANK YOU

MENTOR: DR. SUBHAJYOTI DE

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DIMACS PROGRAM

RUTGERS CANCER INSTITUTE



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- 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](https://doi.org/10.1101/576827)
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