



# PARADIGM, Tumor Map

Yulia Newton  
TGCT Update  
July 2, 2015



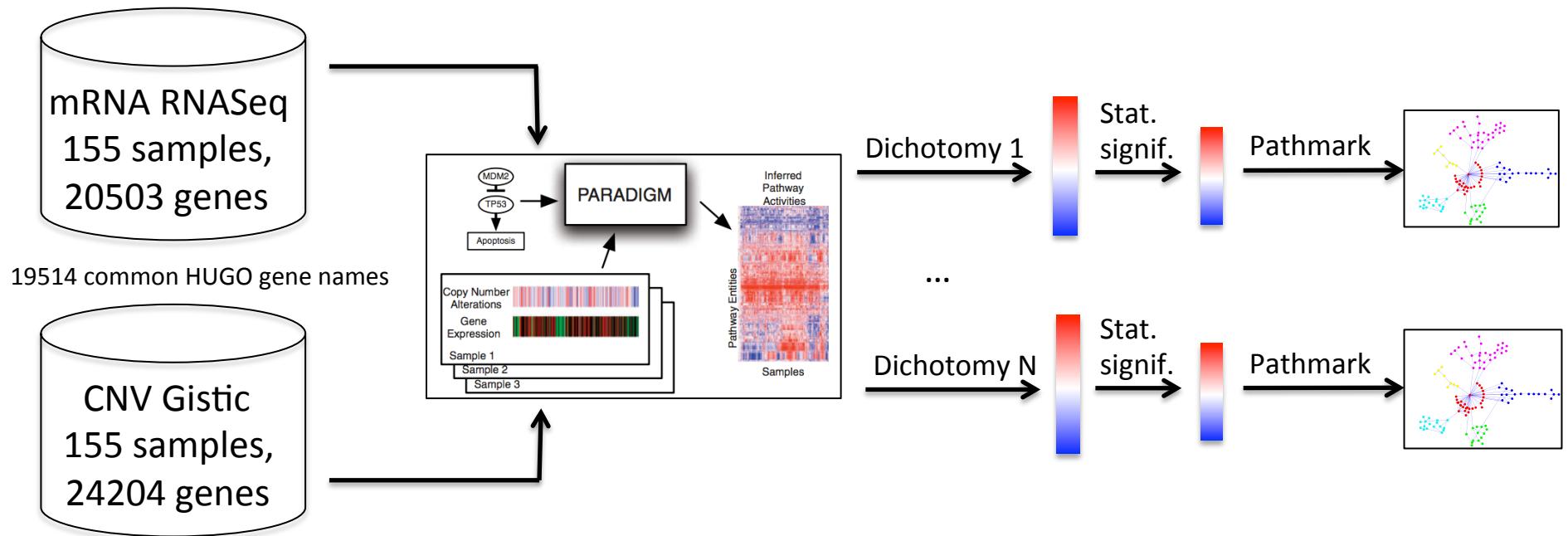
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*promoting discovery and invention for human health and well-being*



# Agenda

- PARADIGM
- Tumor Map

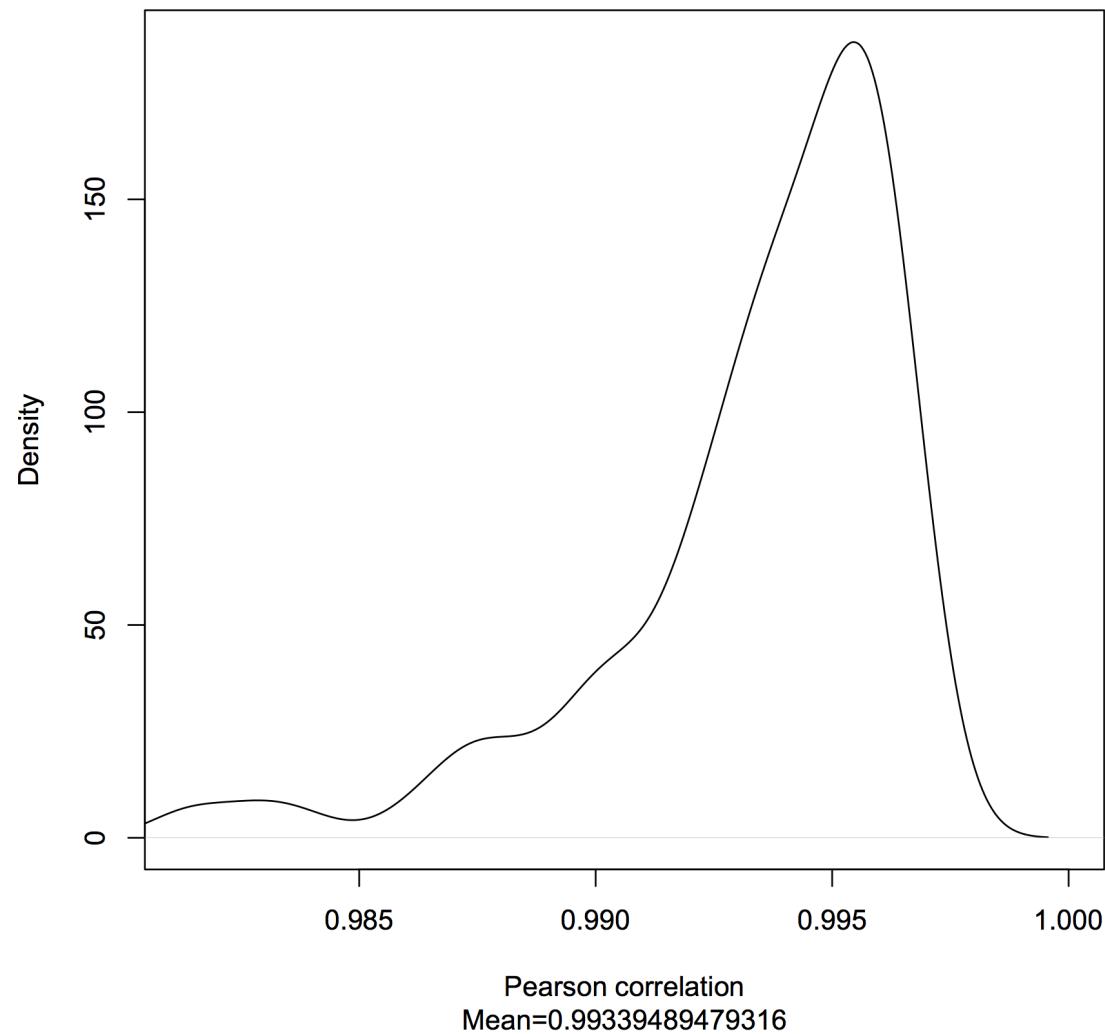
# PARADIGM Pipeline Overview



# mRNA Data Is More Informative Than CNV In Pathway Space

Correlation of IPLs between PARADIGM runs

Correlation between  
the results of  
PARADIGM based on  
mRNA only and  
PARADIGM based on  
mRNA+CNV:



# Note About Histology Calls

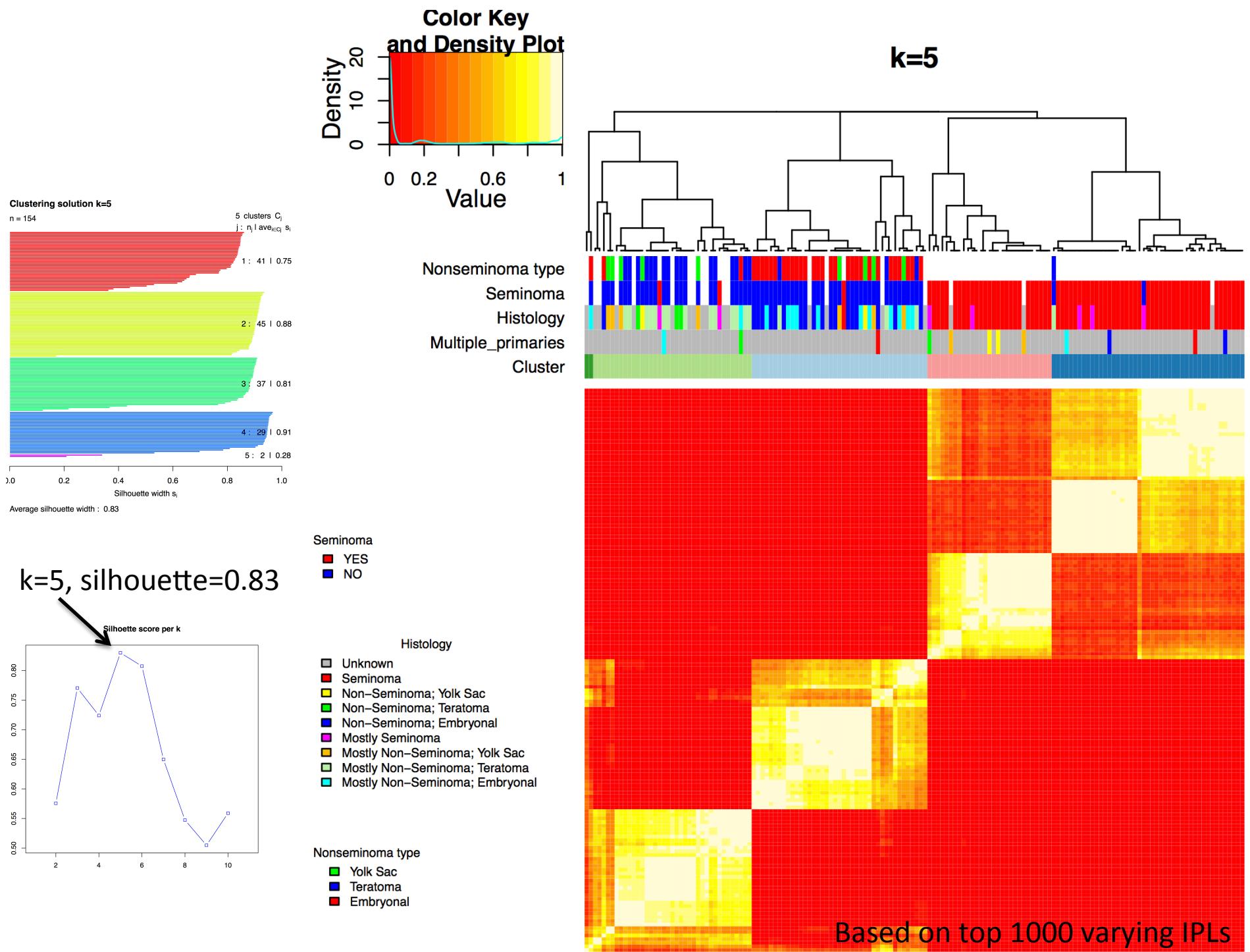
Histology diagnosis:

Histology %:

Seminoma; NOS	
Non-Seminoma; Embryonal Carcinoma   Non-Seminoma; Yolk Sac Tumor	95 5
Non-Seminoma; Teratoma (Mature)   Non-Seminoma; Yolk Sac Tumor	95 5
Non-Seminoma; Embryonal Carcinoma	
Non-Seminoma; Yolk Sac Tumor	
Non-Seminoma; Embryonal Carcinoma	
Non-Seminoma; Teratoma (Immature)   Non-Seminoma; Yolk Sac Tumor   Non-Seminoma; Embryonal Carcinoma	40 30 20 10
Non-Seminoma; Embryonal Carcinoma   Non-Seminoma; Yolk Sac Tumor   Non-Seminoma; Teratoma (Mature)	80 10 10
Non-Seminoma; Teratoma (Mature)   Seminoma; NOS   Non-Seminoma; Embryonal Carcinoma	35 50 10 5
Non-Seminoma; Teratoma (Mature)	
Non-Seminoma; Teratoma (Mature)   Non-Seminoma; Yolk Sac Tumor	95 5
Non-Seminoma; Embryonal Carcinoma   Non-Seminoma; Teratoma (Mature)   Non-Seminoma; Yolk Sac Tumor	40 20 20 20
Non-Seminoma; Embryonal Carcinoma	

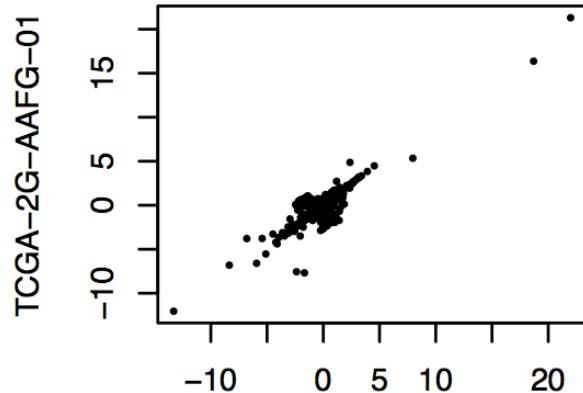
Histology

- Unknown
- Seminoma
- Non-Seminoma; Yolk Sac
- Non-Seminoma; Teratoma
- Non-Seminoma; Embryonal
- Mostly Seminoma
- Mostly Non-Seminoma; Yolk Sac
- Mostly Non-Seminoma; Teratoma
- Mostly Non-Seminoma; Embryonal



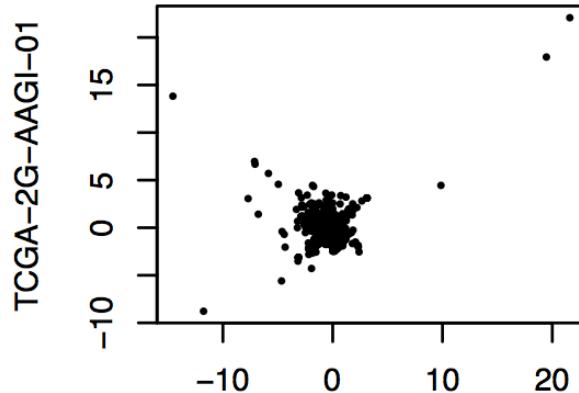
# Match Primaries

**TCGA-2G-AAFG**



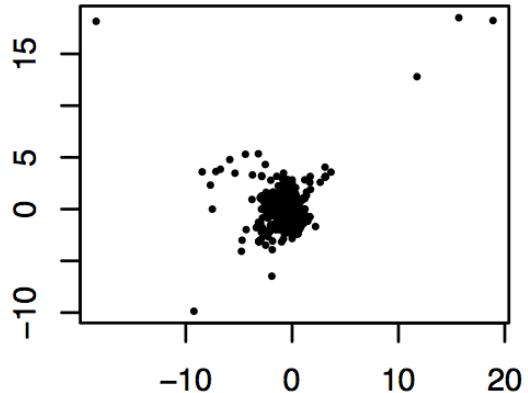
TCGA-2G-AAFG-05

**TCGA-2G-AAGI**



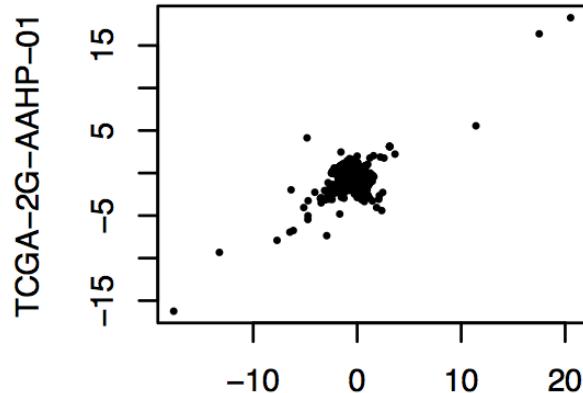
TCGA-2G-AAGI-05

**TCGA-2G-AAGY**



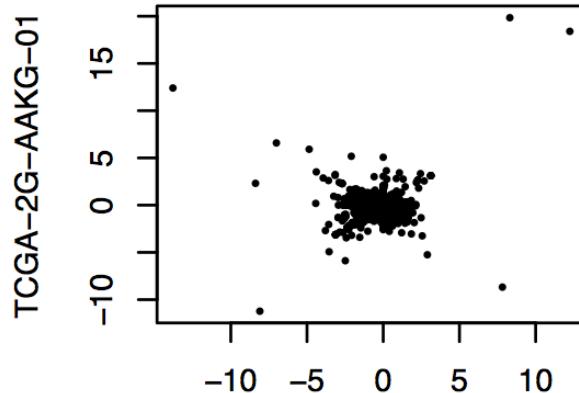
TCGA-2G-AAGY-05

**TCGA-2G-AAHP**



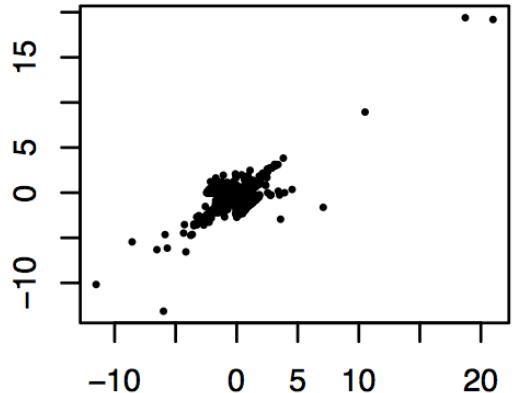
TCGA-2G-AAHP-05

**TCGA-2G-AAKG**



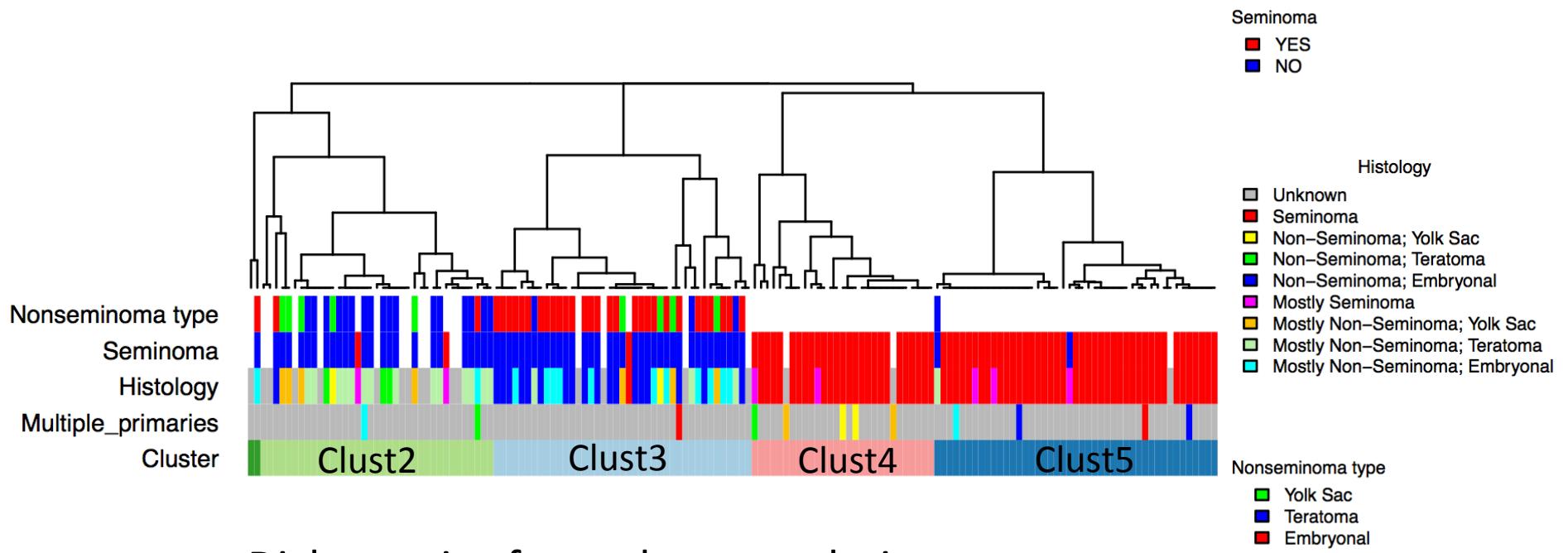
TCGA-2G-AAKG-05

**TCGA-2G-AAKO**



TCGA-2G-AAKO-05

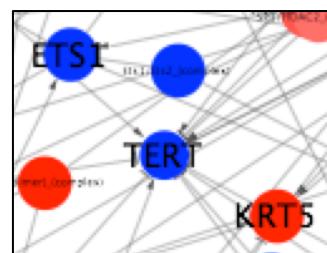
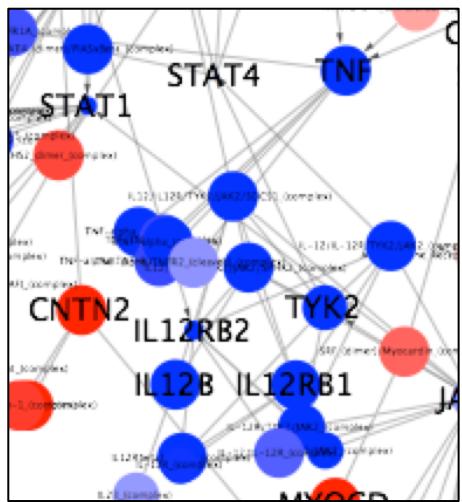
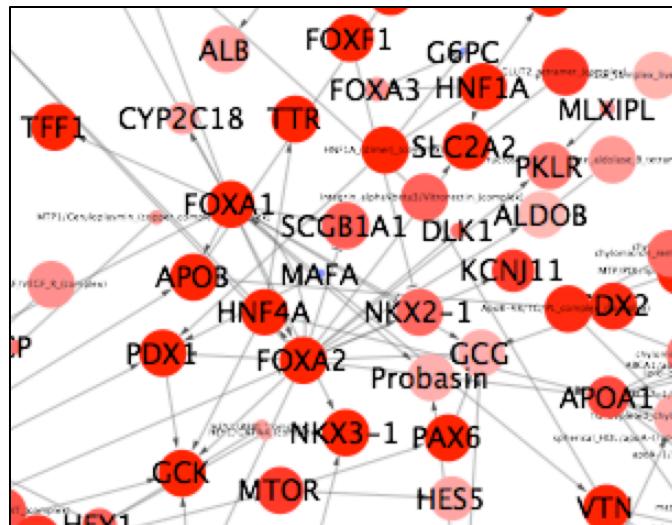
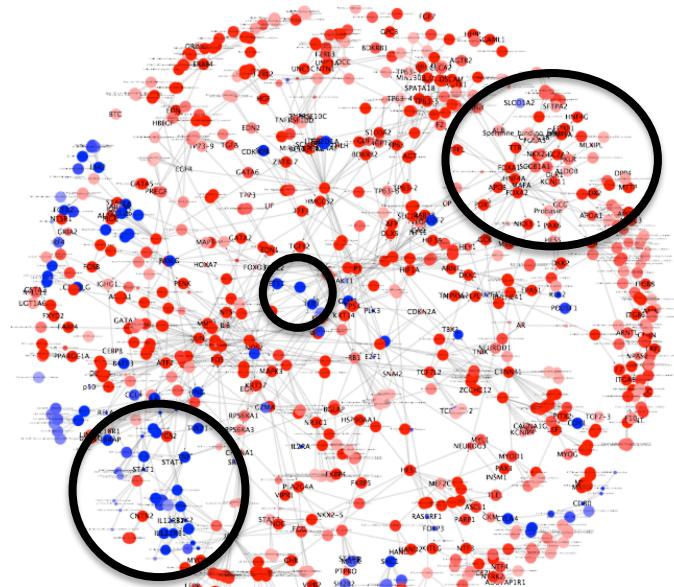
# Interesting Dichotomies



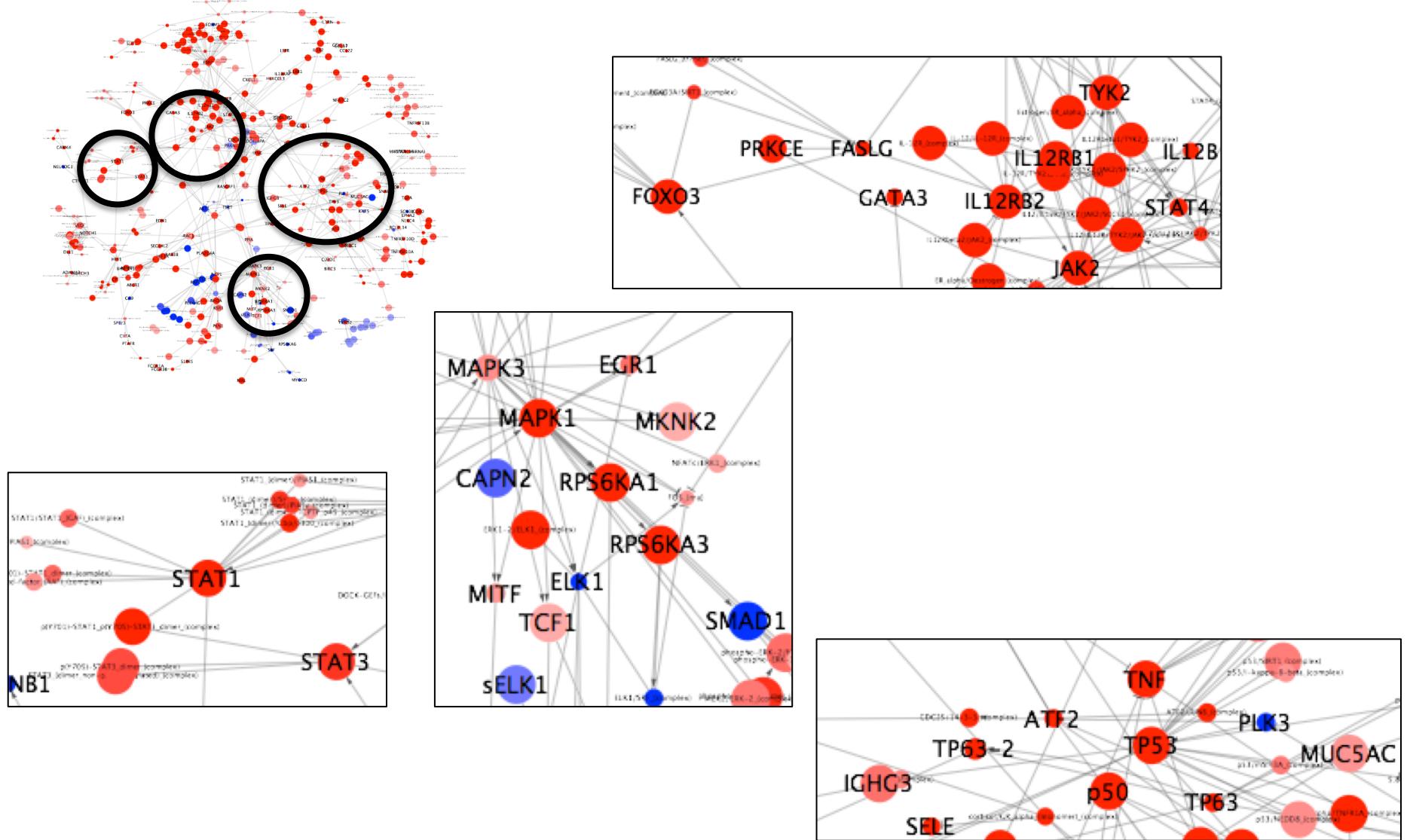
Dichotomies for pathway analysis:

- Clust2 vs. all
- Clust3 vs. all
- Clust4+Clust5 vs. all
- Clust4 vs. Clust5
- Clust2 vs. Clust3

# Cluster 2 vs. All



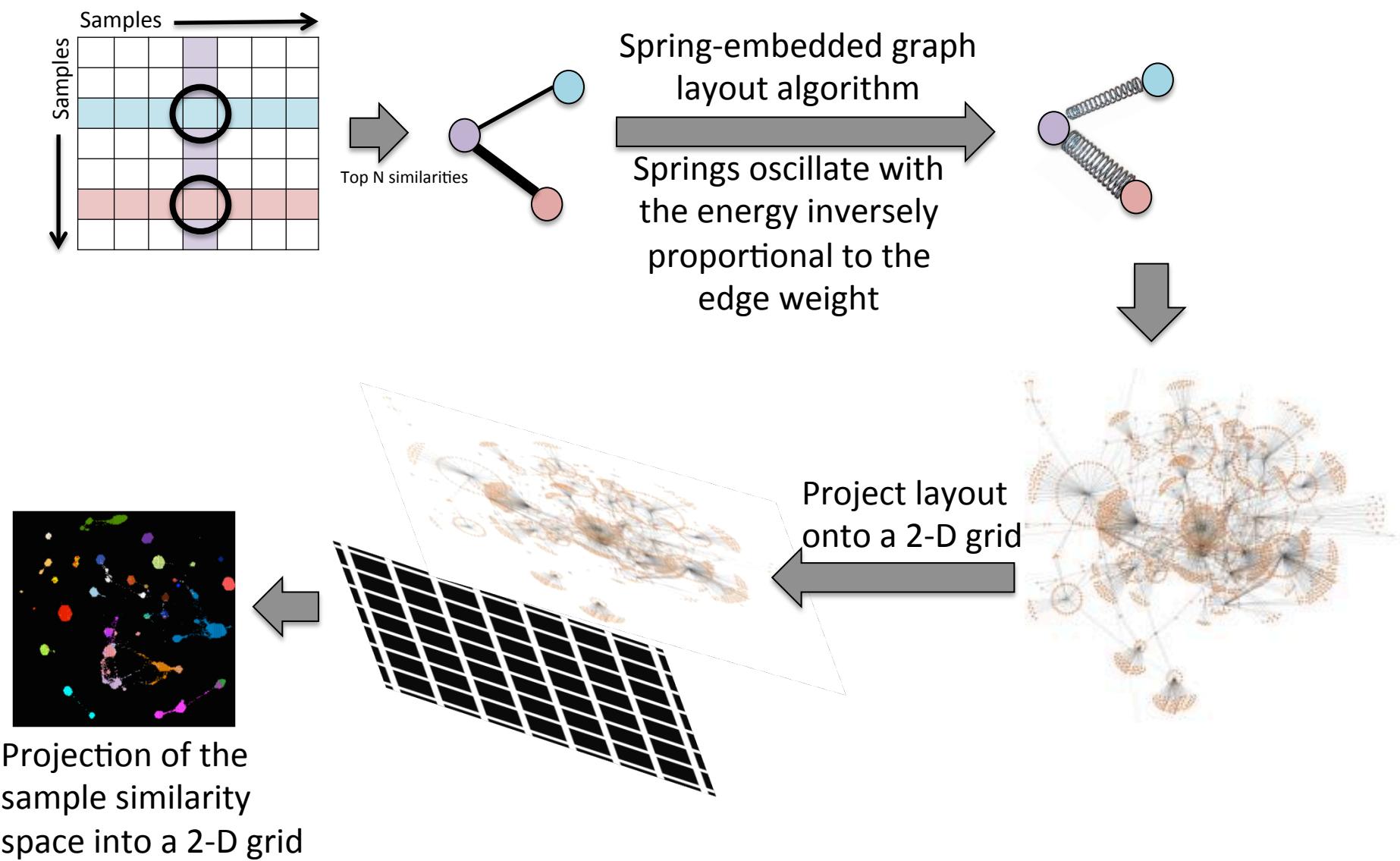
# Cluster 4 vs. Cluster 5



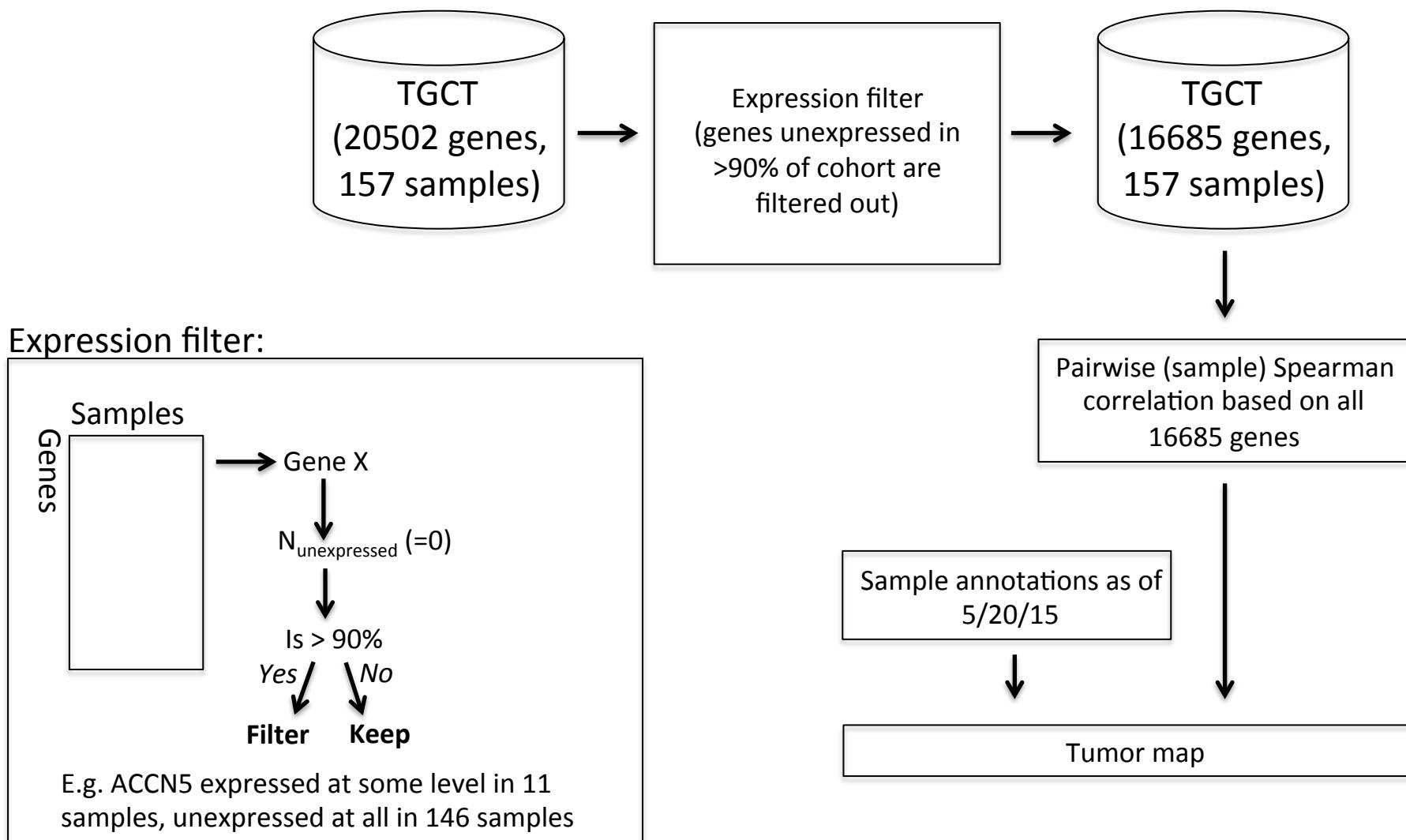
# Tumor Map Method

- Manuscript in progress
  - Based on published pancan12
- Part of the manuscript for the joint gliomas paper (GBM+LGG)
- Projecting similarity space
- Analyzing data in the space of a single data type (e.g. mRNA, methylation, etc.) or combined data types (e.g. mRNA +methylation, mut+CNV)

# Tumor Map Method

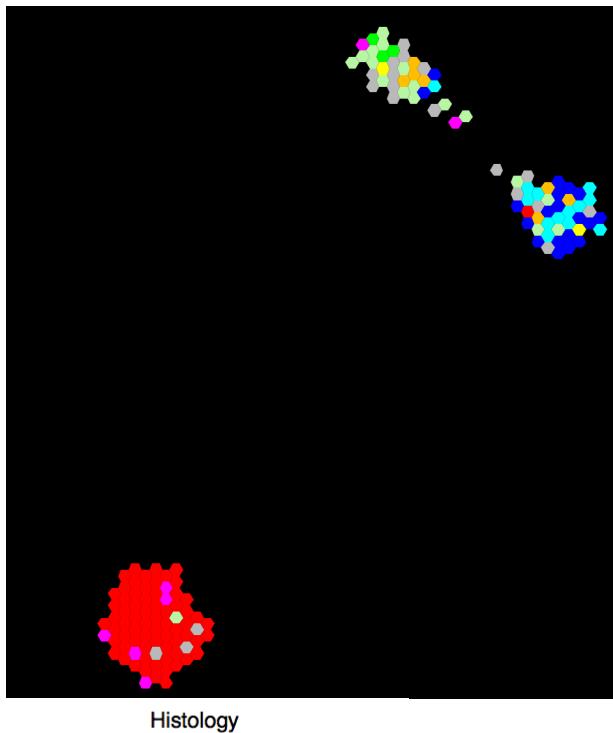


# Tumor Map Analysis of TGCT mRNA



# mRNA Space Recapitulates Histology

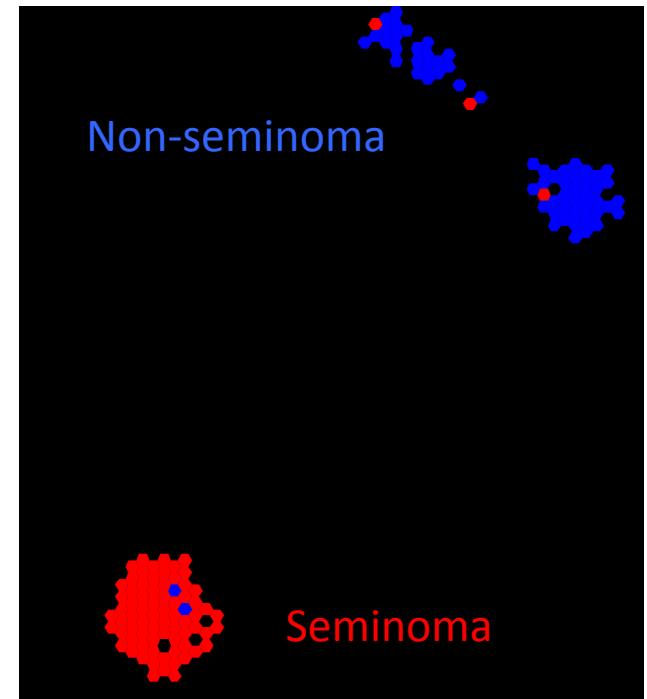
Colored by histology:



Histology

- Unknown
- Seminoma
- Non-Seminoma; Yolk Sac
- Non-Seminoma; Teratoma
- Non-Seminoma; Embryonal
- Mostly Seminoma
- Mostly Non-Seminoma; Yolk Sac
- Mostly Non-Seminoma; Teratoma
- Mostly Non-Seminoma; Embryonal

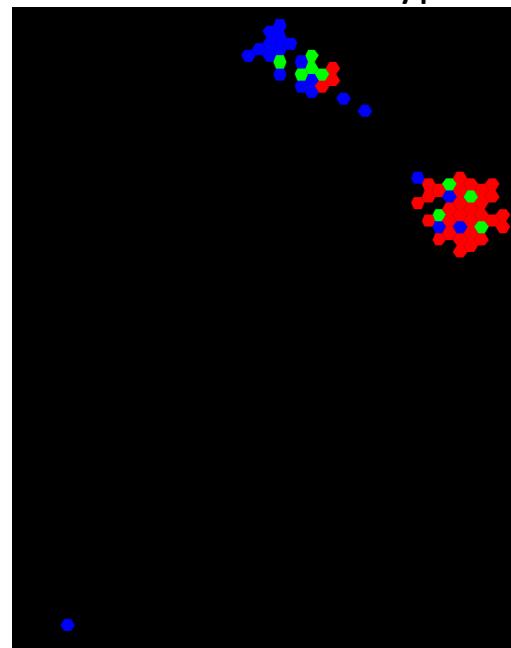
Colored by seminoma/not:



Non-seminoma

Seminoma

Colored by  
non-seminoma type:

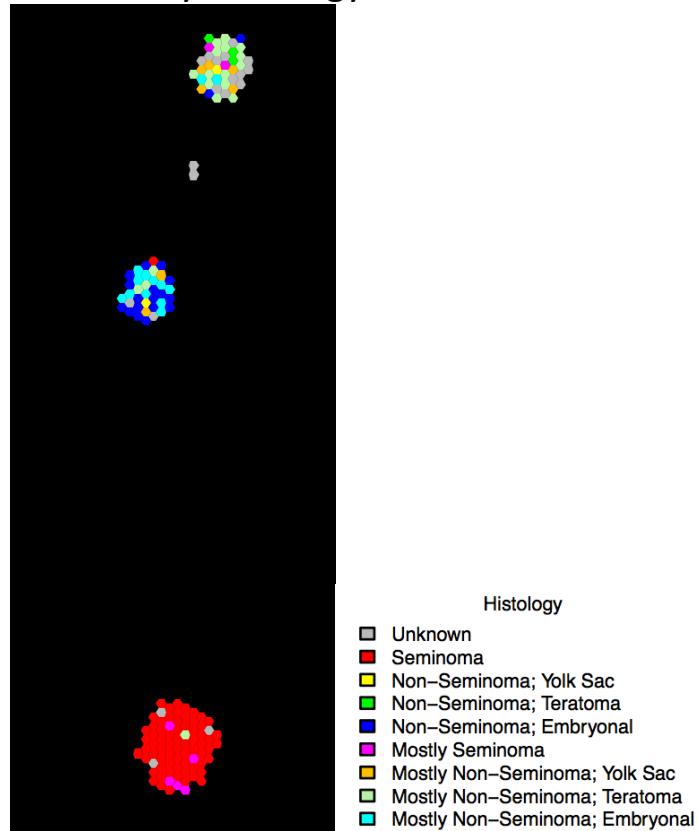


Nonseminoma type

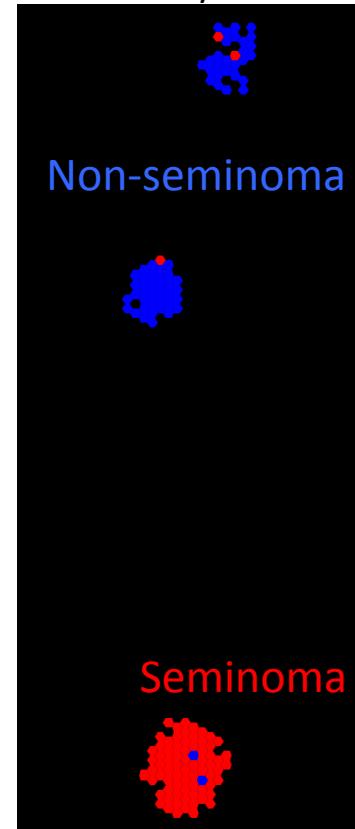
- Yolk Sac
- Teratoma
- Embryonal

# miRNA Space Correlates With mRNA Space

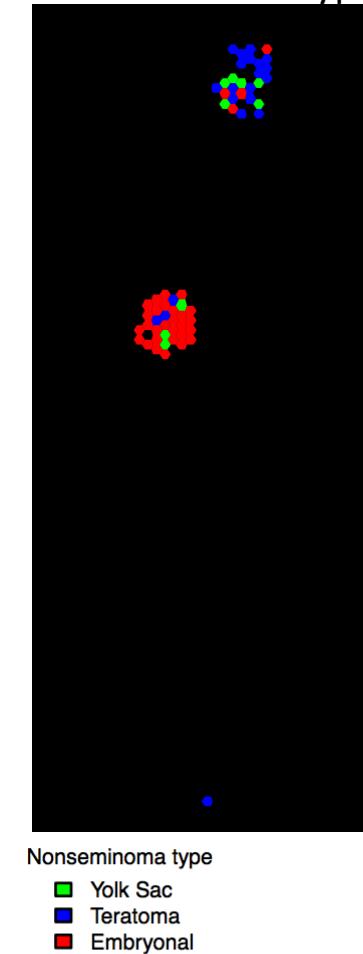
Colored by histology:



Colored by seminoma/not:



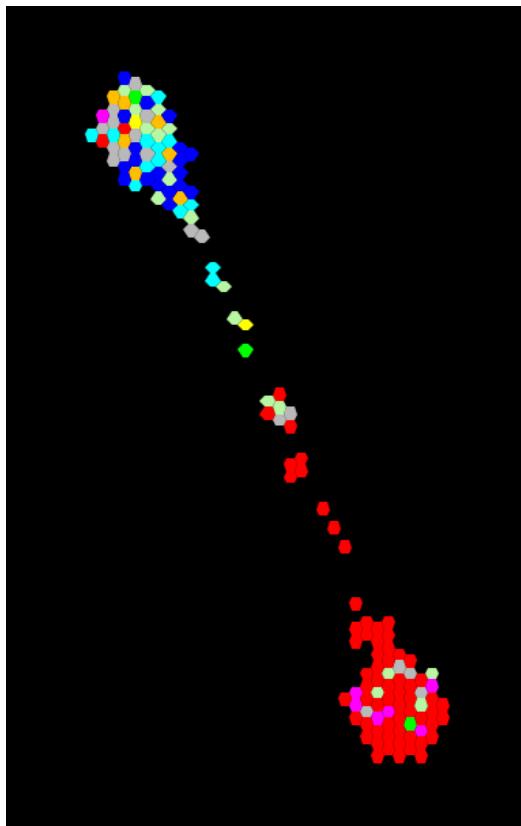
Colored by non-seminoma type:



Those miRNA's that had expression levels  $\leq 50$  in more than 50% of cohort were filtered out. 199 features left after the filter.

# Some Teratomas Track With Seminomas In CNV Space

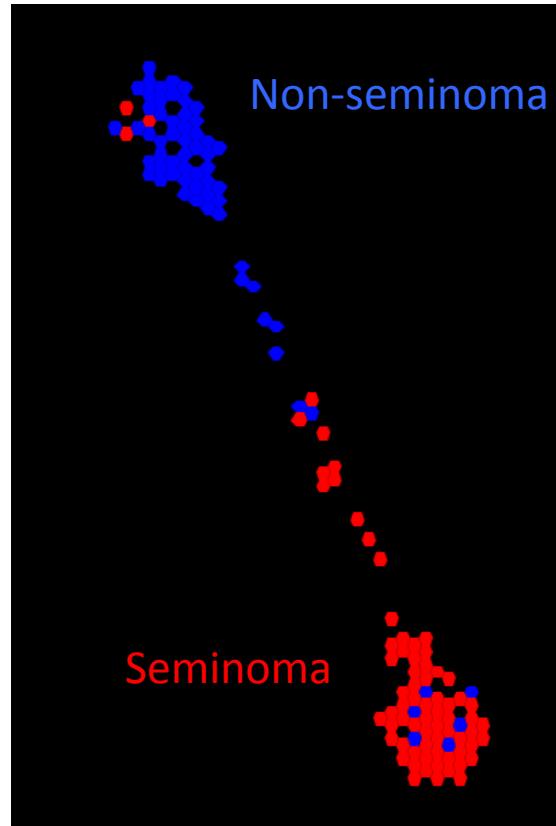
Colored by histology:



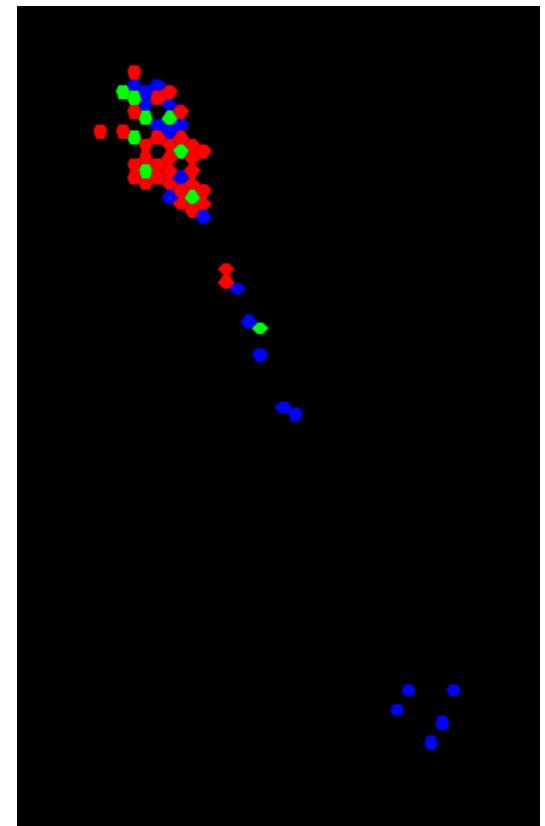
Histology

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Colored by seminoma/not:



Colored by non-seminoma type:

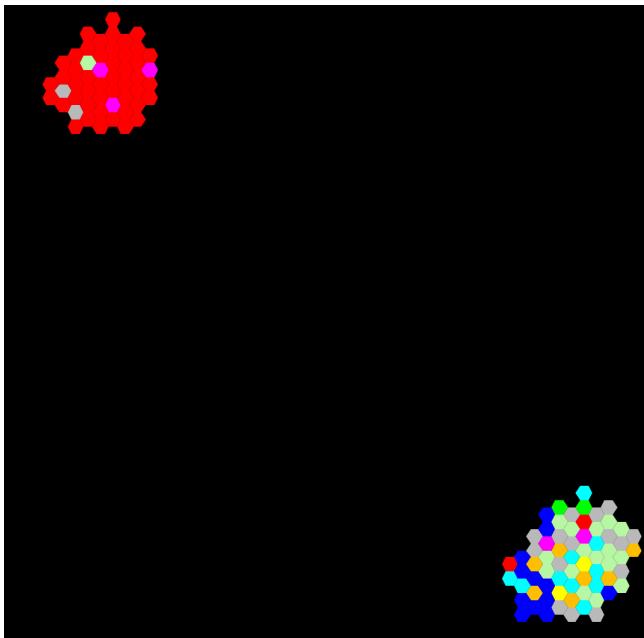


Nonseminoma type

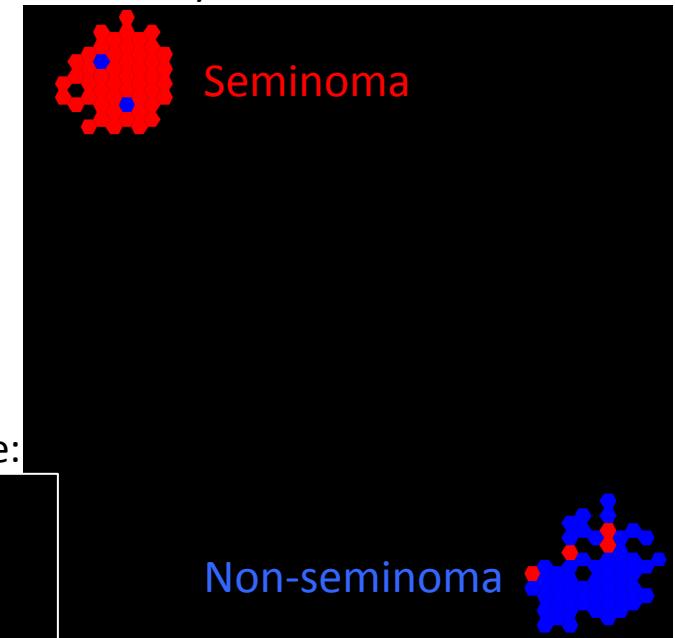
- Yolk Sac
- Teratoma
- Embryonal

# Seminomas and Non-seminomas Are Two Distinct Groups In RPPA Space

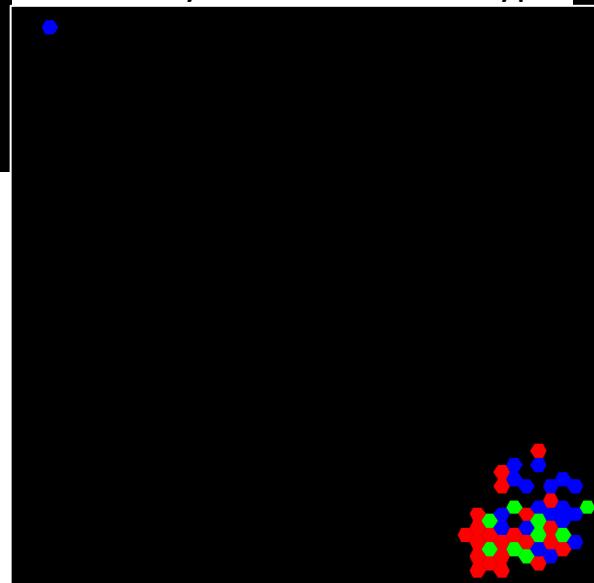
Colored by histology:



Colored by seminoma/not:



Colored by non-seminoma type:

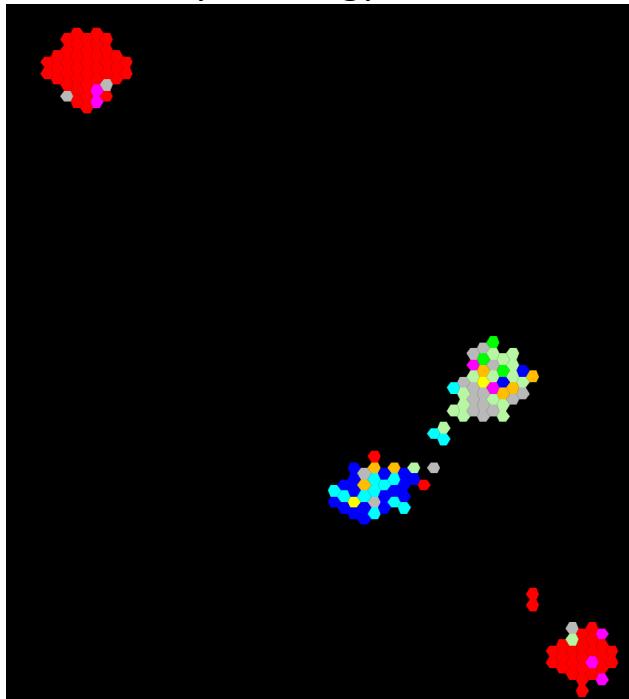


- Histology
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  - Non-Seminoma; Embryonal
  - Mostly Seminoma
  - Mostly Non-Seminoma; Yolk Sac
  - Mostly Non-Seminoma; Teratoma
  - Mostly Non-Seminoma; Embryonal

- Nonseminoma type
- Yolk Sac
  - Teratoma
  - Embryonal

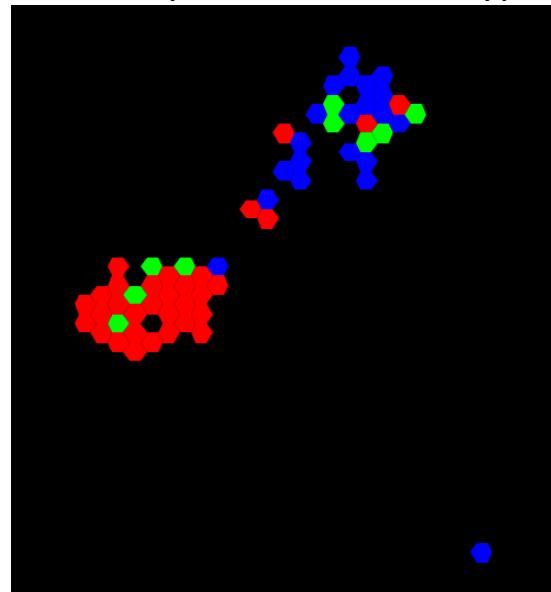
# Two Possible Seminoma Subtypes In Methylation Space

Colored by histology:

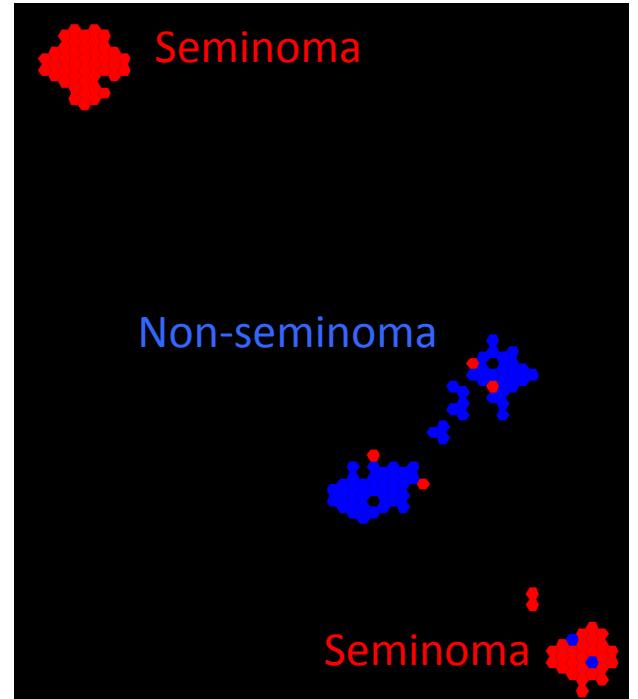


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- Mostly Non-Seminoma; Teratoma
- Mostly Non-Seminoma; Embryonal

Colored by non-seminoma type:



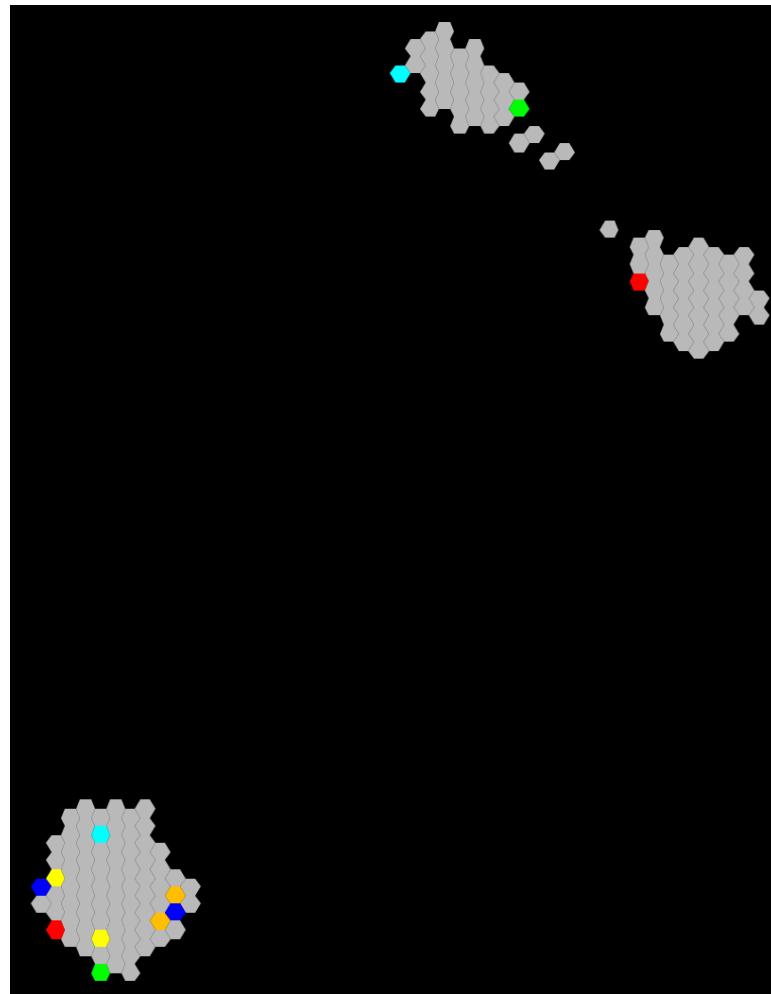
Colored by seminoma/not:



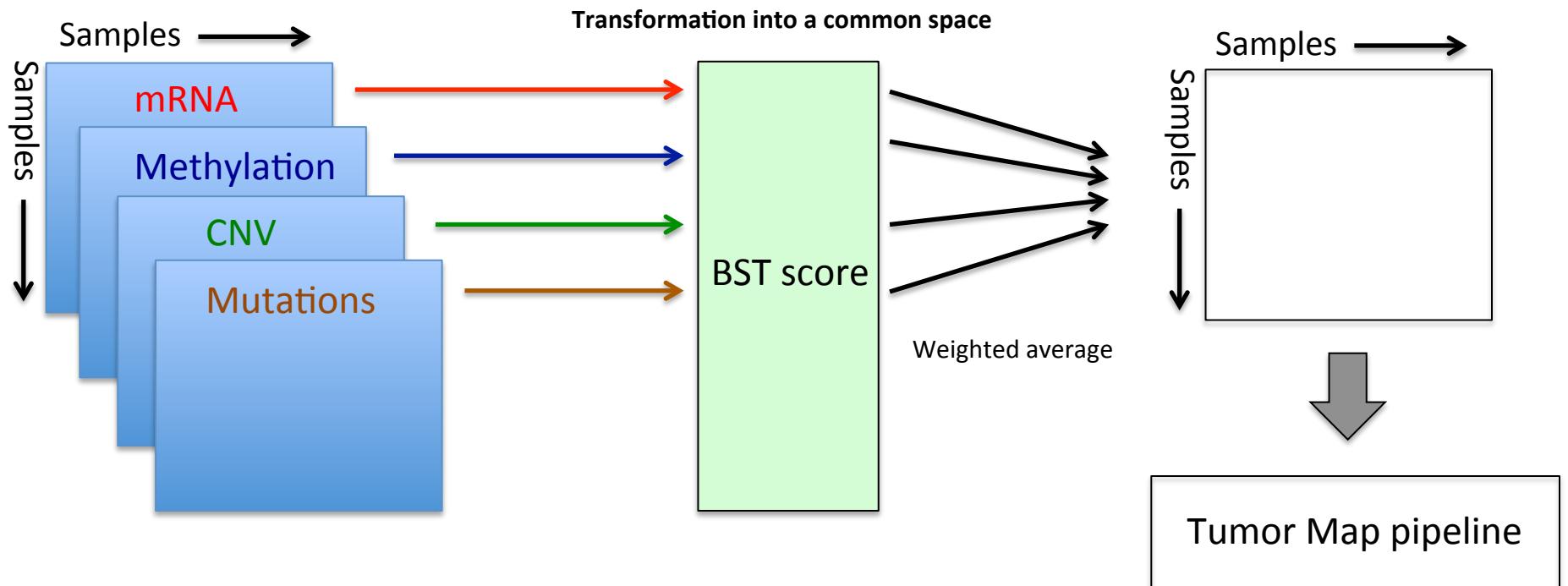
- Yolk Sac
- Teratoma
- Embryonal

Those probes that had methylation levels  $\leq 0.05$  in more than 90% of cohort were filtered out. 264143 probes left after the filter.

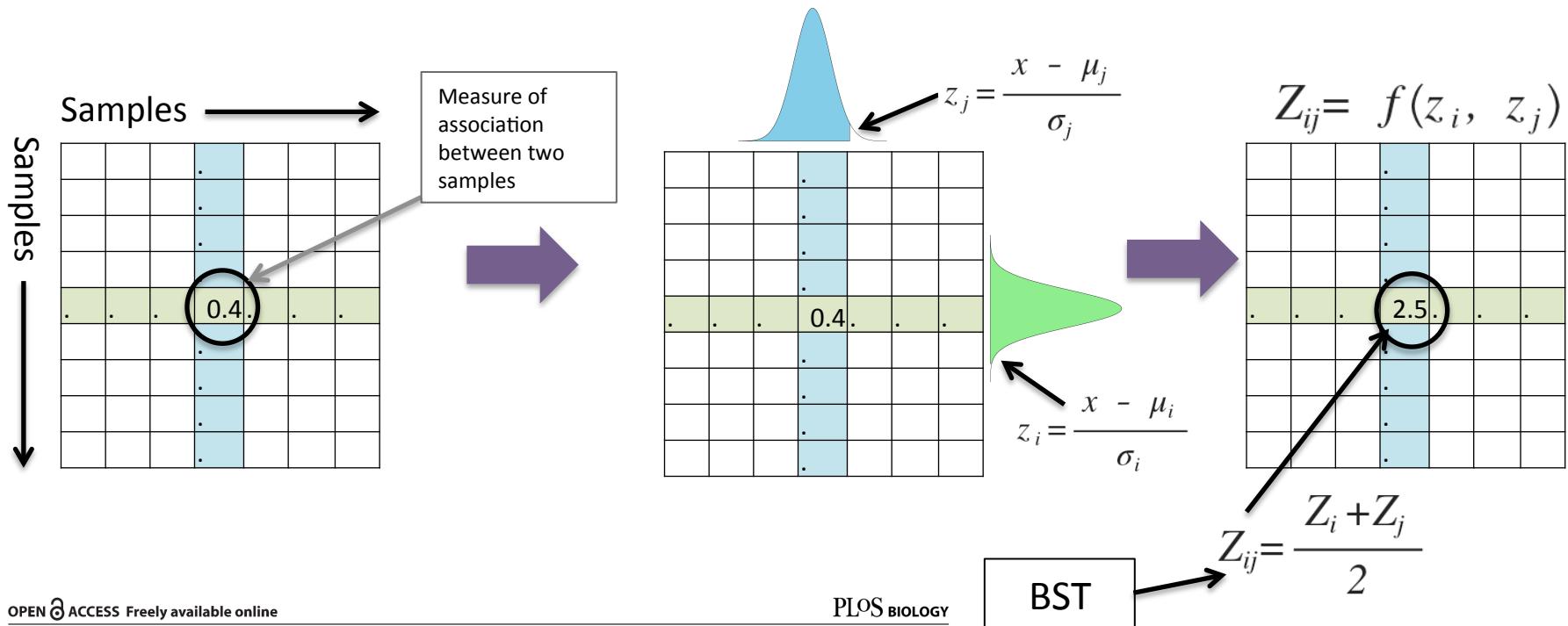
# Multiple Primaries In mRNA Space



# Combined Tumor Maps



# Transformation Into a Common Space (Bivariate Standardization Transformation)



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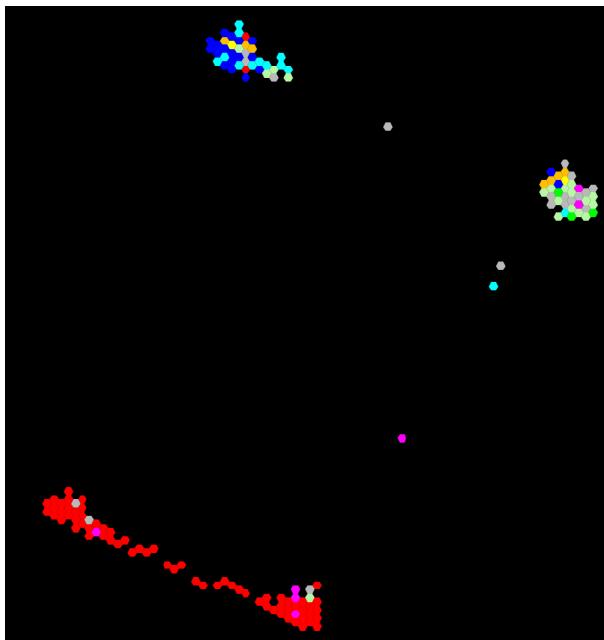
## Large-Scale Mapping and Validation of *Escherichia coli* Transcriptional Regulation from a Compendium of Expression Profiles

Jeremiah J. Faith<sup>1,2</sup>\*, Boris Hayete<sup>1</sup>\*, Joshua T. Thaden<sup>2,3</sup>, Ilaria Mogno<sup>2,4</sup>, Jamey Wierzbowski<sup>2,5</sup>, Guillaume Cottarel<sup>2,5</sup>,  
Simon Kasif<sup>1,2</sup>, James J. Collins<sup>1,2</sup>, Timothy S. Gardner<sup>1,2\*</sup>

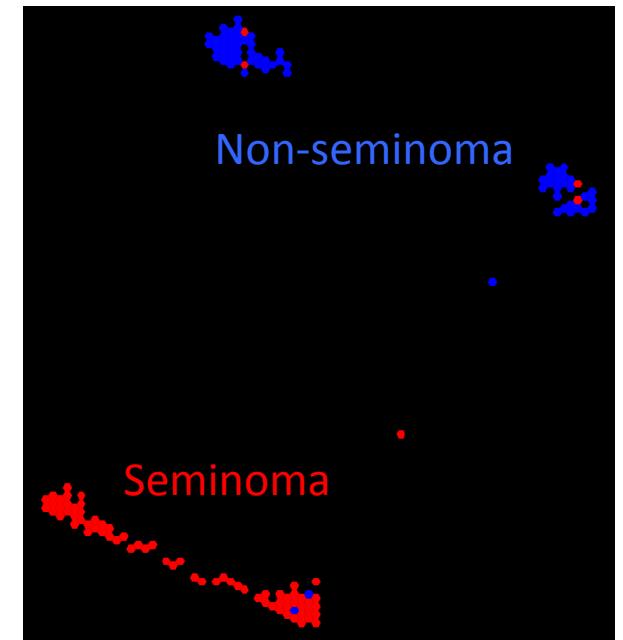
1 Bioinformatics Program, Boston University, Boston, Massachusetts, United States of America, 2 Department of Biomedical Engineering, Boston University, Boston, Massachusetts, United States of America, 3 Boston University School of Medicine, Boston, Massachusetts, United States of America, 4 Department of Computer and Systems Science A. Ruberti, University of Rome, La Sapienza, Rome, Italy, 5 Cellicon Biotechnologies, Boston, Massachusetts, United States of America

# Combined tumor maps

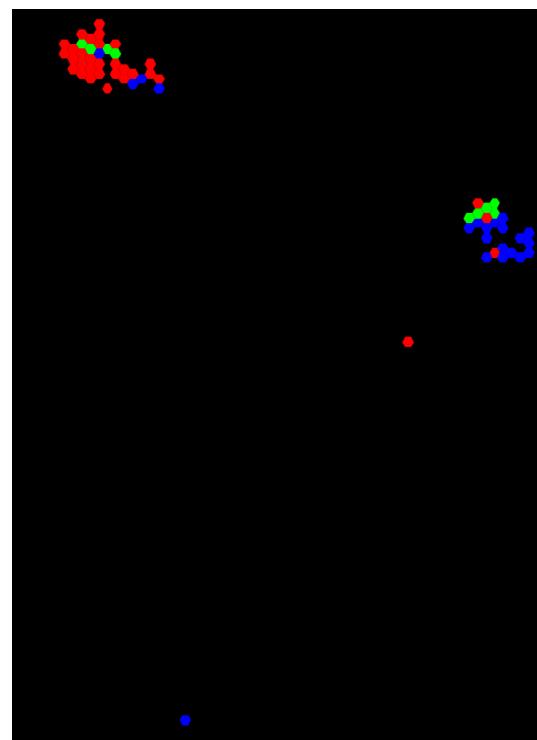
Colored by histology:



Colored by seminoma/not:



Colored by non-seminoma type:



# Next Steps

- PARADIGM
  - Further analysis and refining of the pathways
  - Survival analysis of PARADIGM subtypes
  - Analysis with additional pathway databases (e.g. STRING)
  - Additional dichotomies
- Tumor Map
  - Mutation data
  - Investigate map islands/subtypes
  - TGCT in the context of pancan12 dataset
- Need
  - Survival data