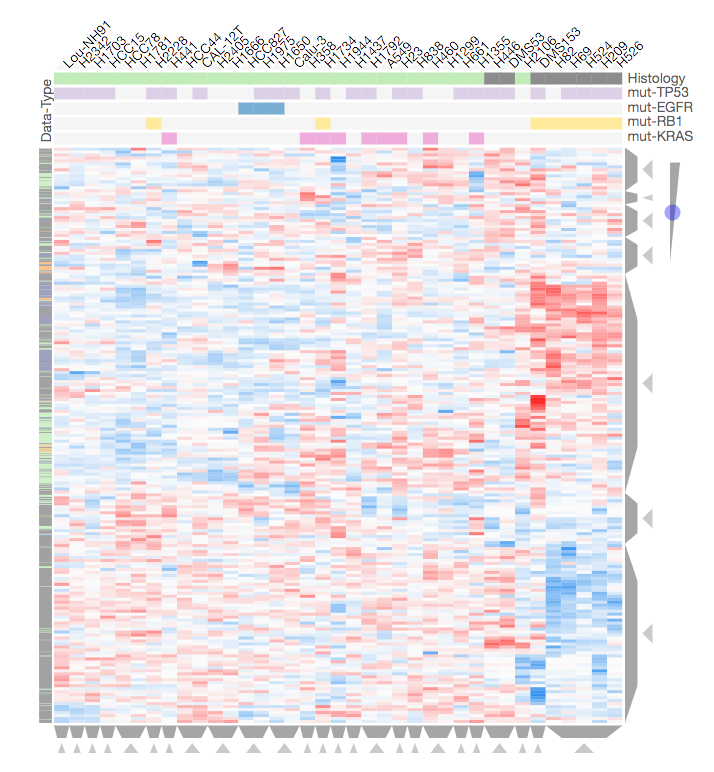
# CST PTM Data



This is a combination of all types of PTM data. I excluded PTMs that had too many missing values (details in processing notebook). I will focus on the two large clusters with high and low PTM values in SCLE and vice versa in NSCLC.

## GO Bio Process

### Up-regulated SCLC PTMs:

mRNA processing, gene expression, splicing, …

### Down-regulated SCLC PTMs:

neurotrophin TRK receptor signaling, mRNA processing response to peptide, … (PTMs were mostly phosphorylation)

## KEGG 2016

### Up-regulated SCLC PTMs:

Spliceosome, mRNA surbeilance, …

### Down-regulated SCLC PTMS:

Neurotrophin signaling pathway

### MGI Mammalian Phenotype Level 4:

Abnormal embryo for both clusters.

# Gene Expression Data CCLE

# ../../../Desktop/Screen%20Shot%202017-04-10%20at%202.54.47%20PM.png

This includes the top ~1000 variably expressed genes across the lung cancer cell lines. I’ll focus on the three largest clusters.

## GO Biological Process

### Up-regulated SCLC Genes:

neuronal differentiation

Refs: Neuronal Characteristics of small-cell lung cancer [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2361510/). Markers of small cell lung cancer [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC441408/).

### Down-regulated SCLC Genes:

Wounding, cell migration, cell component movement, cell motility, adhesion, ECM, …

Ref: An adherent subline of a unique small-cell lung cancer cell line downregulates antigens of the neural cell adhesion molecule [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC329817/): “Small-cell lung cancer (SCLC) lines are distinguished from non-small-cell lung cancer (NSCLC) lines by their growth in gloating aggregates, in contrast to the adherent monolayers formed by NSCLC cells in culture,”.

### Mixed-regulated Genes (bottom cluster):

No strong enrichments, endopepsidase, single cell adhesion

## ChEA

### Up-regulated SCLC Genes:

SUZ12, BMI1

Refs: SUZ12 is involved in progression on NSCLC by promoting cell proliferation and metastasis [link](https://www.ncbi.nlm.nih.gov/pubmed/24633887). BMI1 expression modulates non-small cell lung cancer progression [link](https://www.ncbi.nlm.nih.gov/pubmed/25880371).

### Down-regulated SCLC Genes:

SOX2, CJUN, ERLA, SMAD2/3

Refs: The role of SOX2 in small cell lung cancer [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4367598/).

### Mixed-regulated Genes (bottom cluster):

SOX2 enrichment

### Down-regulated SCLC:

Focal adhesion, proteoglycans in cancer, influenza A, TNF signaling

## Disesase Perturbatiosn from GEO Up (expression sig comparisons)

### Up-regulated SCLC Genes:

**Multiple sclerosis**, spinal muscular atrophy, **large cell neuroendocrine carcinoma,** multiple scletosis, **oligodendroglioma**, anterior horn cell disease, squamous cell carcinoma of the mouth, astrocytoma,

Summary: there is similarity between the up-regulated genes in SCLC cell lines and the up-regulated genes in several neuronal-related diseases and cancers.

Refs:

Multiple associations between a broad spectrum of autoimmune diseases, chronic inflammatory diseases and cancer [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3349285/).

Large cell neuroendocrine carcinoma: an aggressive form of non-small cell lung cancer [link](https://www.ncbi.nlm.nih.gov/pubmed/15999058). Large-cell neuroendocrine carcinoma (LCNEC) of the lung displays morphologic and immunohistochemical characteristics common to neuronendocrine tumors and morphogenic features of large cell carcinomas [link](http://www.medscape.com/viewarticle/550291_1).

Oligodendrogliomas come from oligodendrocytes, one of the types of cells that make up the supportive, or glial, tissue of the brain,

### Down-regulated SCLC Genes:

**Pancreatic ductal adenocarcinoma**, papillary carcinoma, ulcerative colitis, pancreatic …

Summary: pancreatic cancer is also caused by smoking. Pancreatic cancer can metastasize to the lung and cause confusion in diagnosis.

### Mixed-regulated Genes (bottom cluster):

**Pancreatic ductal adenocarcinoma**, prostate cancer …

## MGI Mammalian Phenotype Level 4

### Up-regulated SCLC Genes:

Abrormal neuronal morphology, abnormal neuronal physiology, brain nervous system, etc…

### Down-regulated SCLC Genes:

Abnormal innate immunity, blood vessel, inflammatory reponse, abnormal response to injury

### Mixed-regulated Genes (bottom cluster):

Abnormal extraembryonic tissue, impared skin barrier, abnormal skin appearance, abnormal epidermal layer, abnormal skin physiology,

# Merge PTM and Gene Expression Data (~2500 rows)

# ../../../Desktop/Screen%20Shot%202017-04-10%20at%203.17.37%20PM.png

## GO Biological Processes

### Up-regulated SCLC:

mRNA processing, mRNA splicing, gene expression,

Ref: Aberrant RNA splicing and its functional consequences in cancer cells [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2561970/).

### Down-regulated SCLC:

Cellular component movement, cell motility, cell migration, locomotion, response to wounding, response to virus/organism, cell adhesion, cell junction, coagulation

Ref: See above: An adherent subline…

## ChEA (may not make sense since this is mix of data types)

### Up-regulated SCLC:

KDM5B, FOXM1, E2F1

### Down-regulated SCLC:

SOX2, SMAD3, SMAD3, RELA, …

Ref:

Comprehensive genomic analysis identifies SOX2 as a frequently amplified gene in small-cell lung cancer [link](http://www.nature.com/ng/journal/v44/n10/full/ng.2405.html).

The role of SOX2 in small cell lung cancer, lung adenocarcinoma and sqyamous cell carcinoma of the lung [link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4367598/).

## KEGG 2016

### Up-regulated SCLC:

RNA transport, spliceosome, mRNA surveillance, mTOR signaling

### Down-regulated SCLC:

Focal adhesion, proteoglycans in cancer, influenza A, TNF signaling

## MGI Mammalian Phenotype Level 4

### Up-regulated SCLC:

Prenatal lethality, abnormal neuron morphology

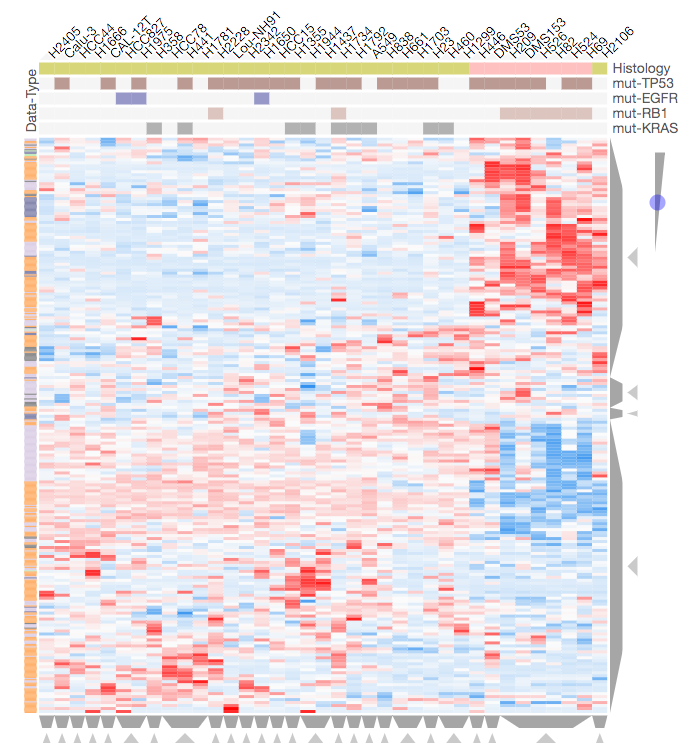
### Down-regulated SCLC:

Abnormal immunity, abnormal epidermal layer, embryogenesis, cardiovascular

### Is there a relationship between GO enrichment cell motility and ChEA enrichment SOX2/SMAD2/etc.. ?

This reference seems to imply that loss of SOX2 leads to cell motility [link](https://www.ncbi.nlm.nih.gov/pubmed/26040981)

# Merge PTM and Gene Expression Data Filtered (~700 rows, two large clusters)



## GO Biological Processes

### Up-regulated SCLC:

mRNA splicing, mRNA processing, lung epithelian cell differentiation, lung cell differentiation, epithelial cell differentiation, neuron fate specification,

### Down-regulated SCLC:

Single organism cell adhesion, response to inorganic substances, cell-substrate adhesion, cell-cell adhesion, nitrogen compound, substrate adhesion dependent cell spreading

## ChEA

### Up-regulated SCLC:

BMI1, RNF2, SUZ12

### Down-regulated SCLC:

CJUN, KLF4, RARG, ..

## KEGG

### Up-regulated SCLC:

Low enrichment: Thyroid hormone signaling, viral carcinogenesis

### Down-regulated SCLC:

Proteoglycans in cancer, viral myocarditis, focal adhesion, leishmaniasis, complement and coagulation cascades, platelet activation,

## MGI Mammalian Phenotype level 4

### Up-regulated SCLC:

Abnormal pancreas morphology, abnormal neuron physiology, abnormal neuron morphology, abnormal nervous system, brain morphology, prenatal lethality, maternal imprinting

### Down-regulated SCLC:

Abnormal dermal layer, abnormal response to injury, abnormal innate immunity, abnormal cell adhesion, pre/post weaning lethality