

# What are the genetic differences between cancers that metastasize to the brain vs those that do not?

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ANGSD 2020, WCMC

# What is a *brain metastasis*?

The **most common form** of tumors found in the CNS

**40-50%** of these cerebral metastases arise from primary lung tumors

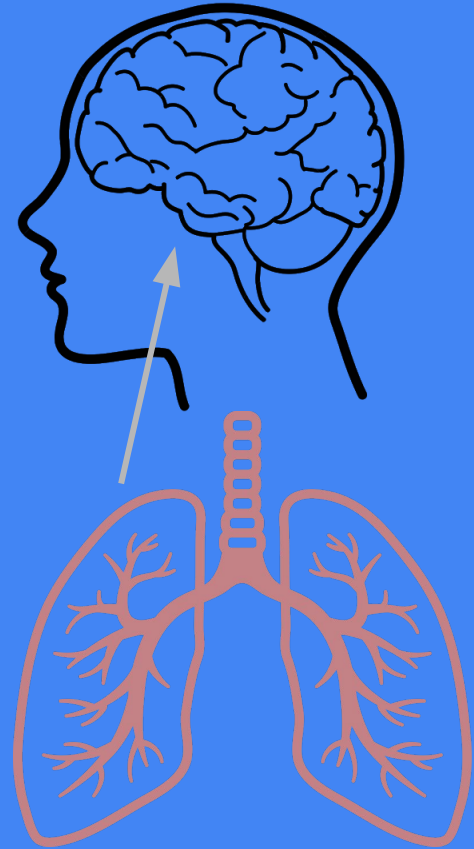
Often detected during times of **relapse**, offering bleak prognosis

**Prevention** of brain metastasis is a critical concern in order to improve survival among lung cancer patients

# Is there a difference in the genetic profiles of lung cancers that have metastasized to the brain?

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I hypothesize downregulation of genes involved with cell-cell adhesion and an upregulation of genes involved with cell proliferation



# Potential signaling pathways and gene signatures associated with brain metastases in NSCLC patients

*With total of 6 lung adenocarcinoma samples: 3 patients with brain metastasis (BM+) and other 3 without brain metastasis (BM-), they were able to identify a total of 566 differentially expressed genes.*



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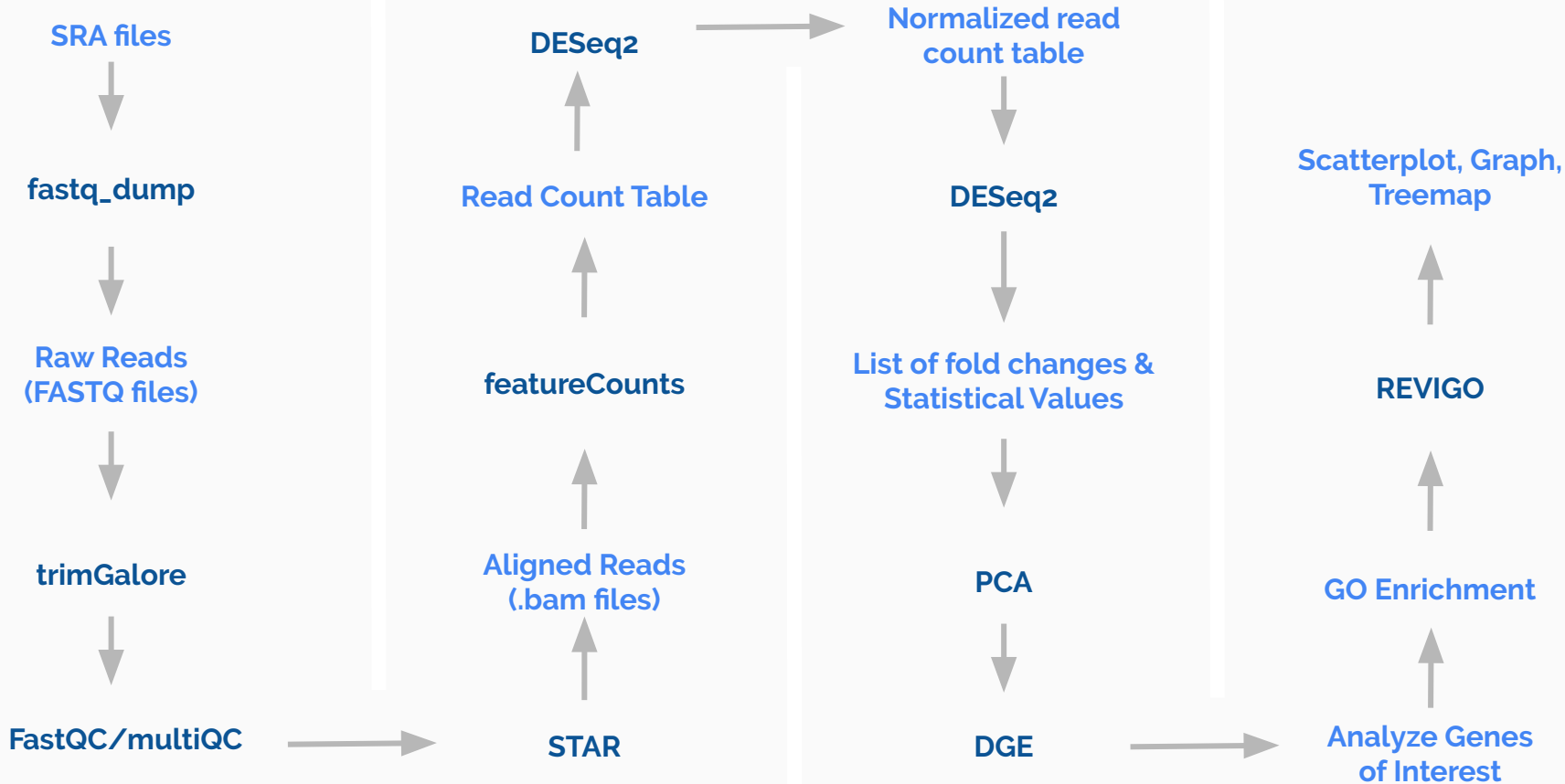
NCBI > GEO > Accession Display

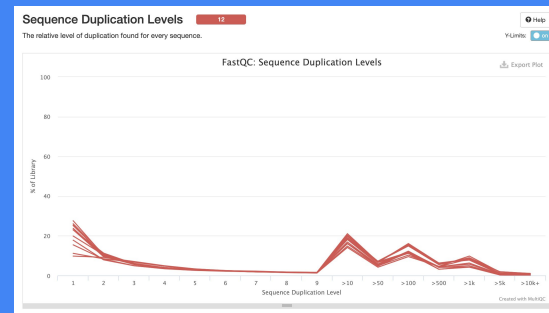
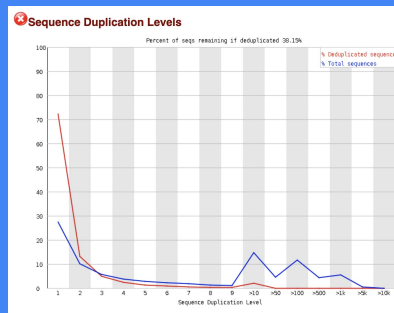
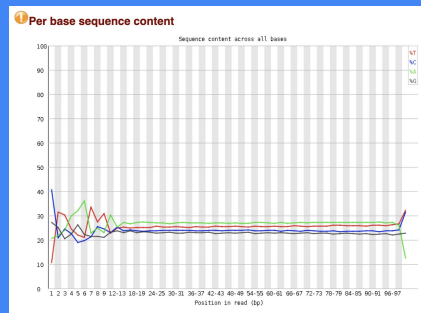
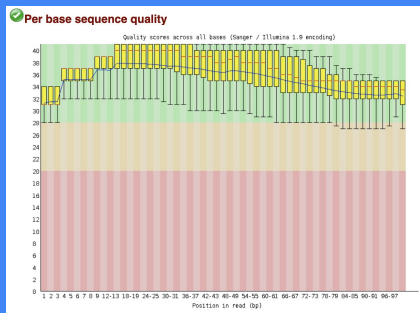
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Scope: Self Format: HTML Amount: Quick GEO accession: GSE126548

**Series GSE126548** Query DataSets for GSE126548

Status	Public on Feb 19, 2019
Title	Potential signaling pathways and gene signatures associated with brain metastases in NSCLC patients
Organism	<a href="#">Homo sapiens</a>
Experiment type	Expression profiling by high throughput sequencing
Summary	RNA-Seq analyses of various cancers have identified thousands of target genes that help guide clinical treatment. By using RNA-Seq analysis, we examined primary lung tumors from NSCLC patients with and without BM to identify differentially-expressed genes and potential signaling pathways in two groups. A total of 6 patients with histopathologically confirmed NSCLC (against AJCC criteria) were enrolled in the RNA-Seq study, 3 patients with BM and other 3 without BM. All the cancer tissues used in this study were taken from surgical specimens and biopsies, and preserved immediately in liquid nitrogen after surgery. Totally, 566 differentially-expressed genes between BM+ and BM- samples were identified by DESeq2 with log2Fold Change being more than 2 and P value of statistical test less than 0.05, 326 genes were significantly down-regulated and 240 genes were up-regulated in BM+ group.
Overall design	RNA isolation and RNA sequencing were performed in 6 NSCLC patients, 3 patients with BM and other 3 without BM. All libraries were sequenced on the Illumina Hiseq 2500 Sequencer.
Contributor(s)	<a href="#">Dong X, Dong X</a>
Citation missing	Has this study been published? Please <a href="#">login</a> to update or <a href="#">notify</a> GEO.
Submission date	Feb 13, 2019
Last update date	Mar 27, 2019
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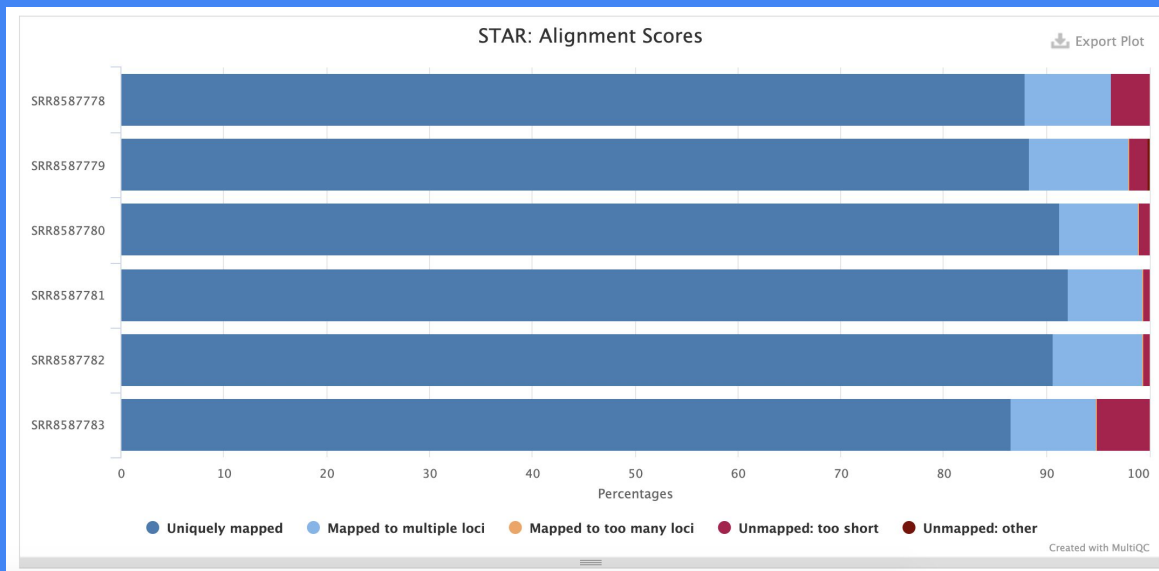
# FastQC/MultiQC

Per base sequence quality shows the aggregated quality score at each position along all the reads

Expected increase of variability in the end since the adapters were trimmed (--minOverlap = 1 by default)

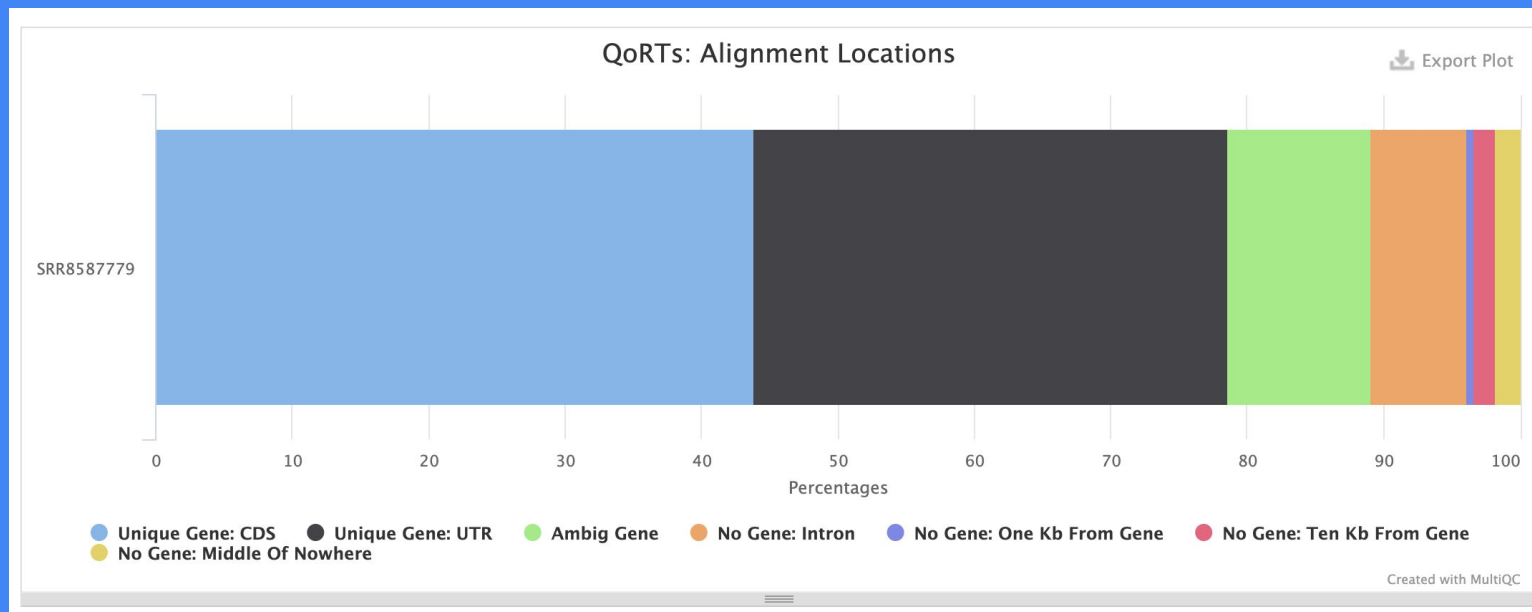
A high level of duplication can be due to either higher gene expression or indicating some kind of enrichment bias (PCR over amplification)

- With RNA-Seq data, it is more likely that there are certain genes that are overly expressed and thus have more “duplicates”.

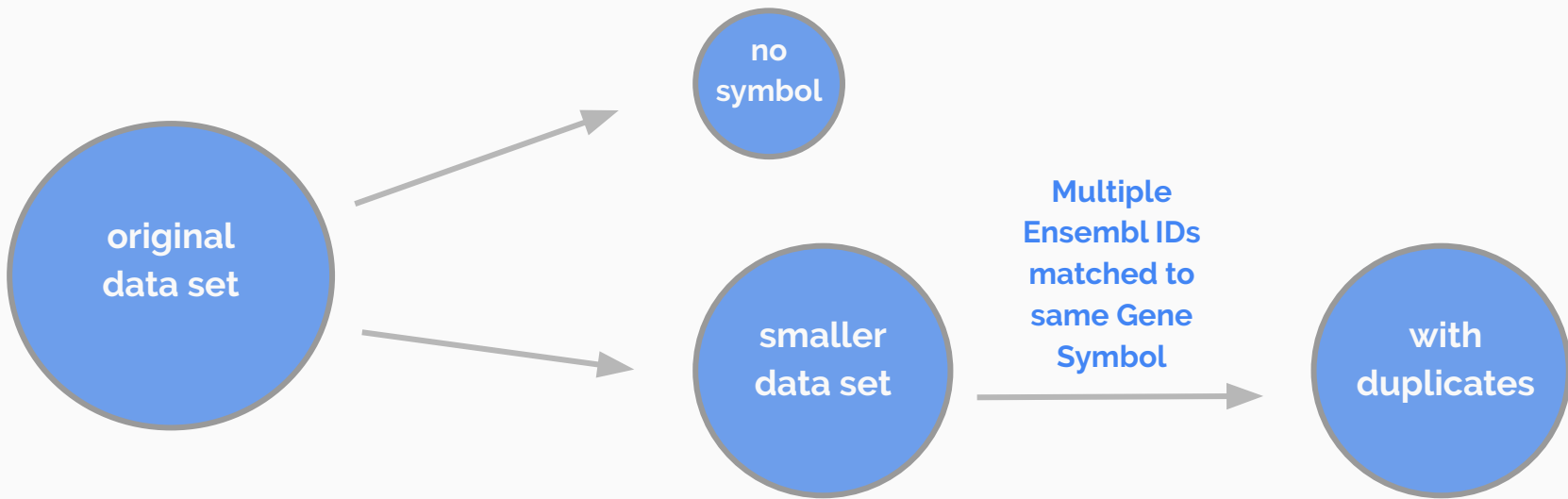


The **STAR Alignment** mostly mapped to unique reads in the genome. Above, uniquely mapped, unmapped, and multi mapped regions add up to 100%

**QORTS Analysis** offers more information on gene diversity  
Plot below shows that we captured a lot of exonic RNA. CDS (coding sequence) region in an mRNA is flanked by the UTRs (untranslated regions).



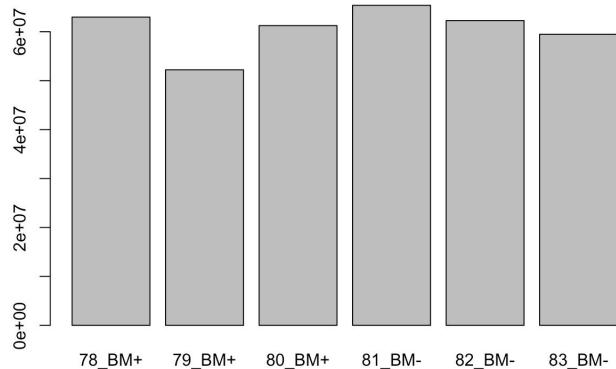




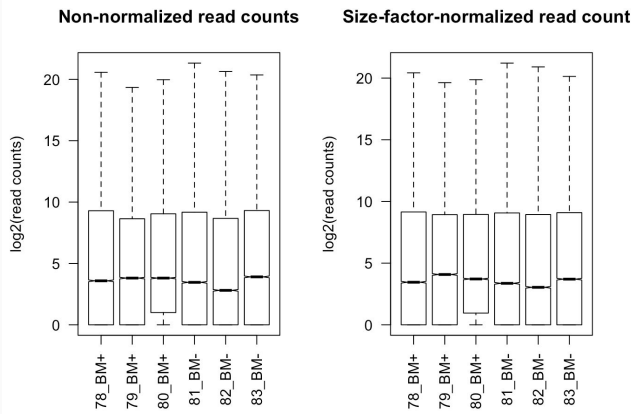
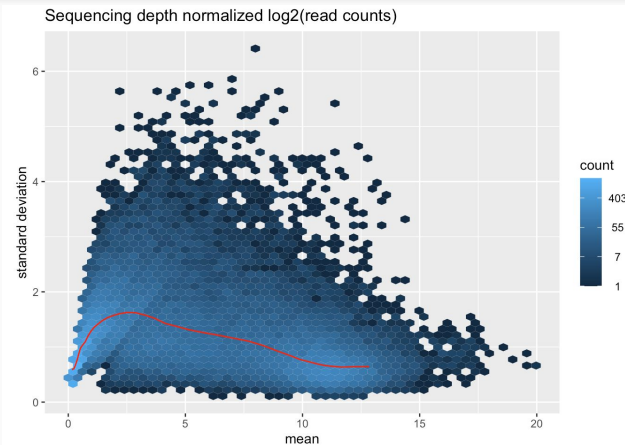
### **featureCounts *Obstacles***

I was given all of my information with Ensembl IDs.  
Had to convert to Gene Symbols to make them valuable  
Lost chunks of data

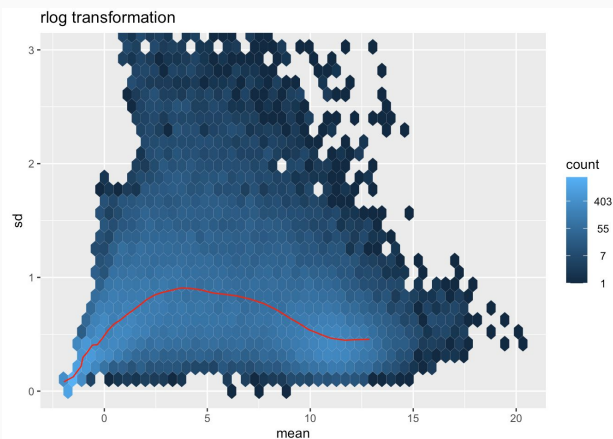
# DESeq Analysis

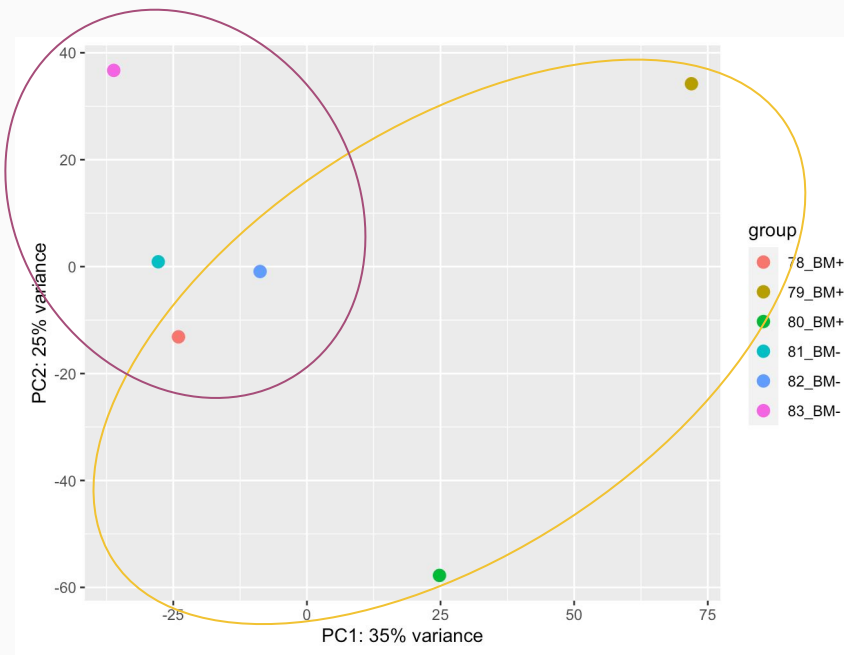


**normalizing data**  
account for sequencing  
depth

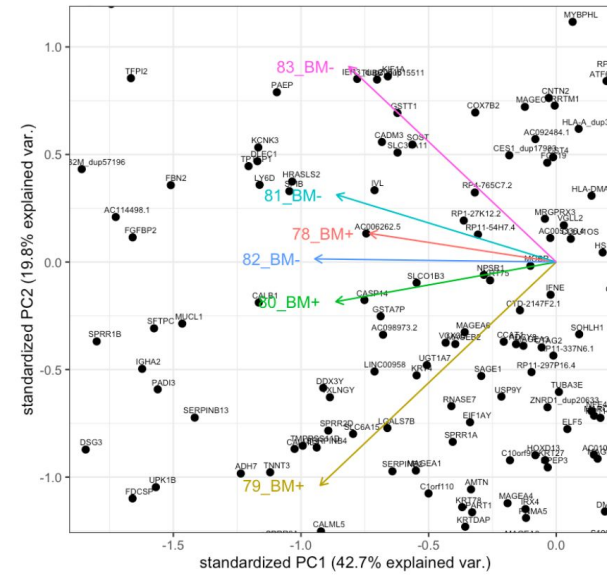


**rlog transformation**  
reduce the dependence  
of the variance on the  
mean





Zoomed window

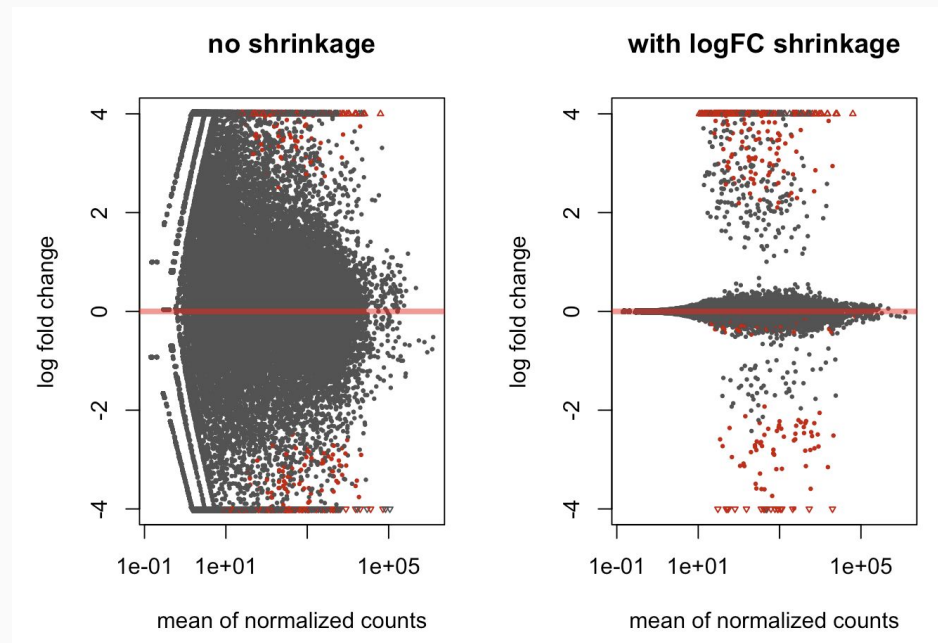


## PCA & PCAExplorer

genespca plot - computes and plots the principal components of the genes and displays the samples as in a typical biplot visualization

# logFC shrinkage & Volcano plot

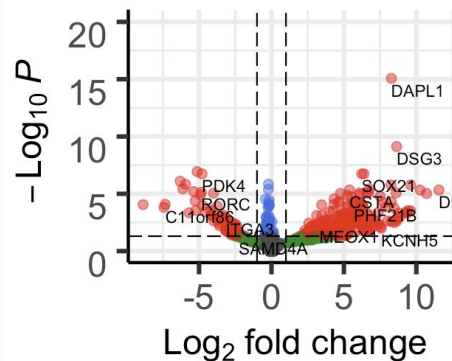
shrinkage reduce the importance of those genes that are lowly and noisily expressed  
volcano plot shows the larger values are more significant



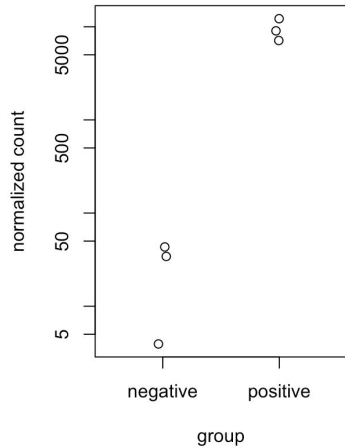
## with logFC shrinkage

EnhancedVolcano

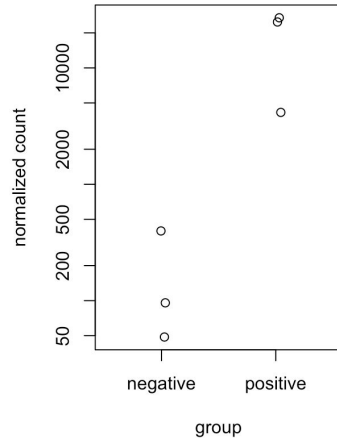
● Log<sub>2</sub> FC ● p-value ● p - value



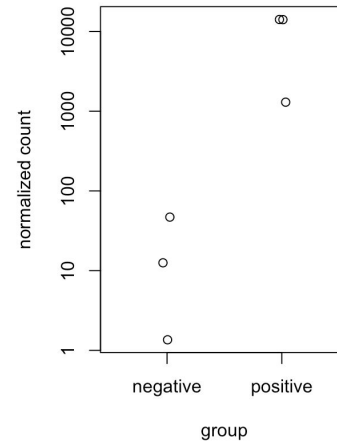
Total = 40876 variables

**DAPL1**

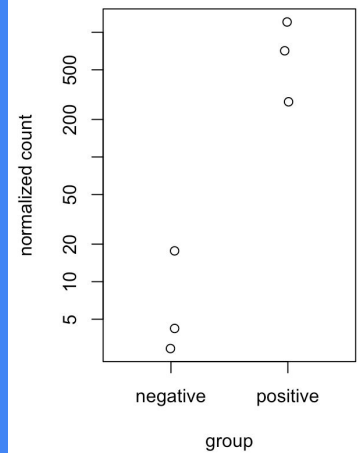
commonly enriched gene in cervical cancer, head and neck cancer, lung cancer, ovarian cancer, or thyroid cancer

**NTRK2**

receptor tyrosine kinase that is involved in the development and the maturation of the central and the peripheral nervous systems

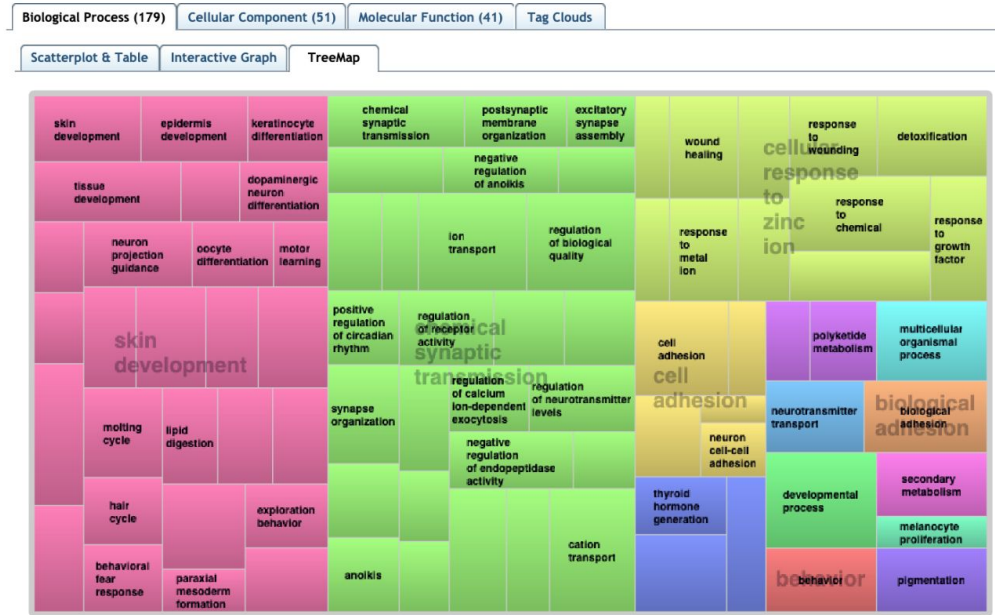
**DSG3**

DSG3 has also been shown in several cancers including skin, prostate, lung and head-neck cancer

**SOX21**

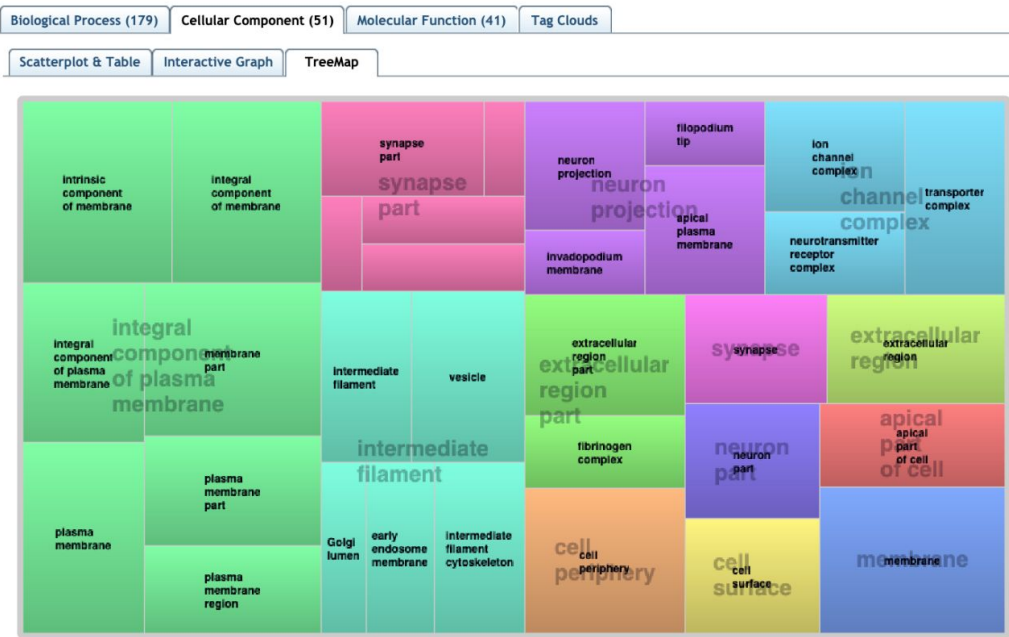
Sox21 promotes neuronal cellular differentiation by counteracting the activity of Sox1, Sox2, and Sox3

# Biological Processes



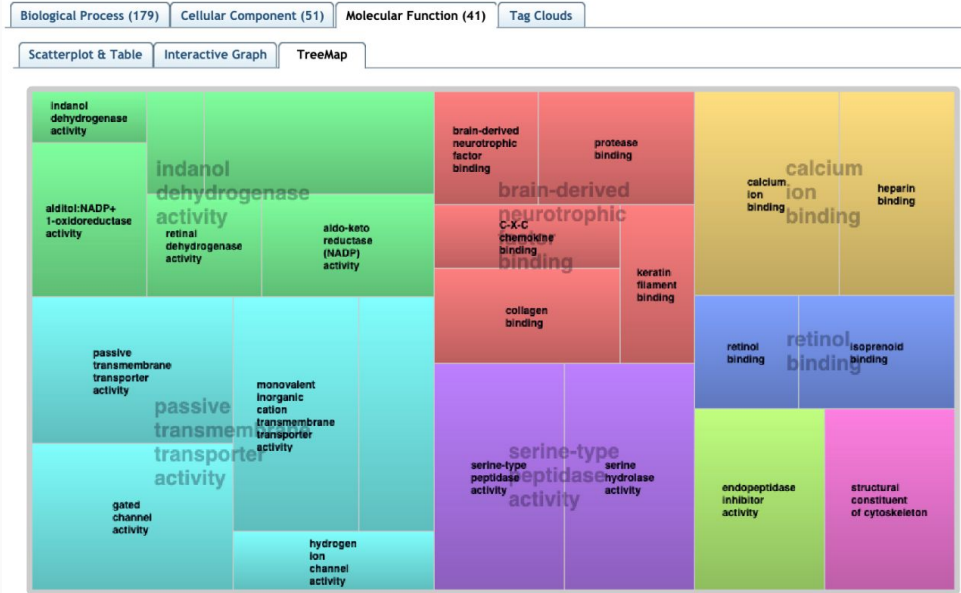
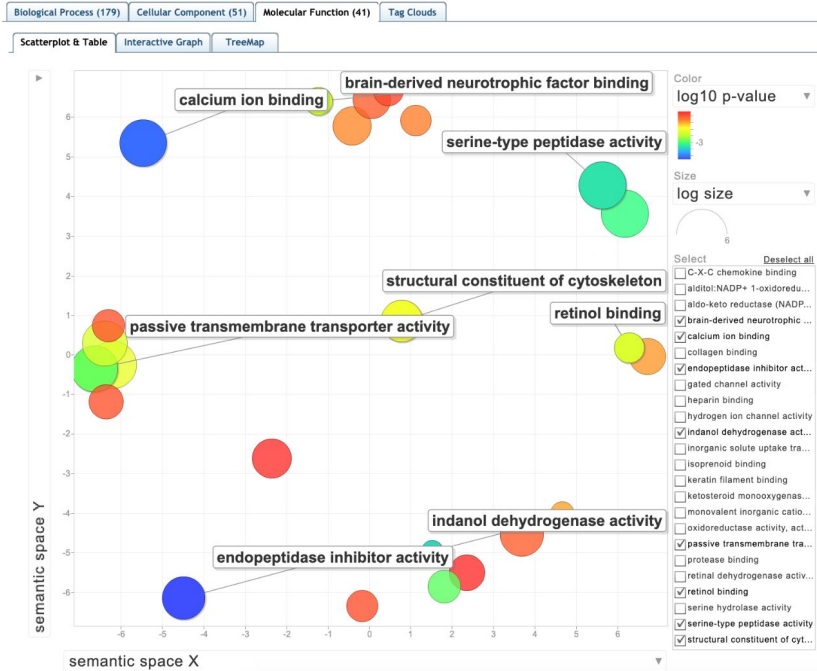
*biological processes: skin development, synaptic transmission, cellular response to the zinc ion, cell adhesion, and biological adhesion*

# Cellular Component



*cellular component: many genes are involved in the membrane and synapse region of the cells*

# Molecular Function



*many genes were involved in transmembrane transport activity and neurotrophic factor binding*



**Thank you.**