# Differential Gene Expression in Cisplatin-Resistant and FOLFOX-Resistant Cancer Cells

Group 7 BIOL 6150 Group Project

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# Contents

# Cancer Treatments


Use of cytotoxic chemicals

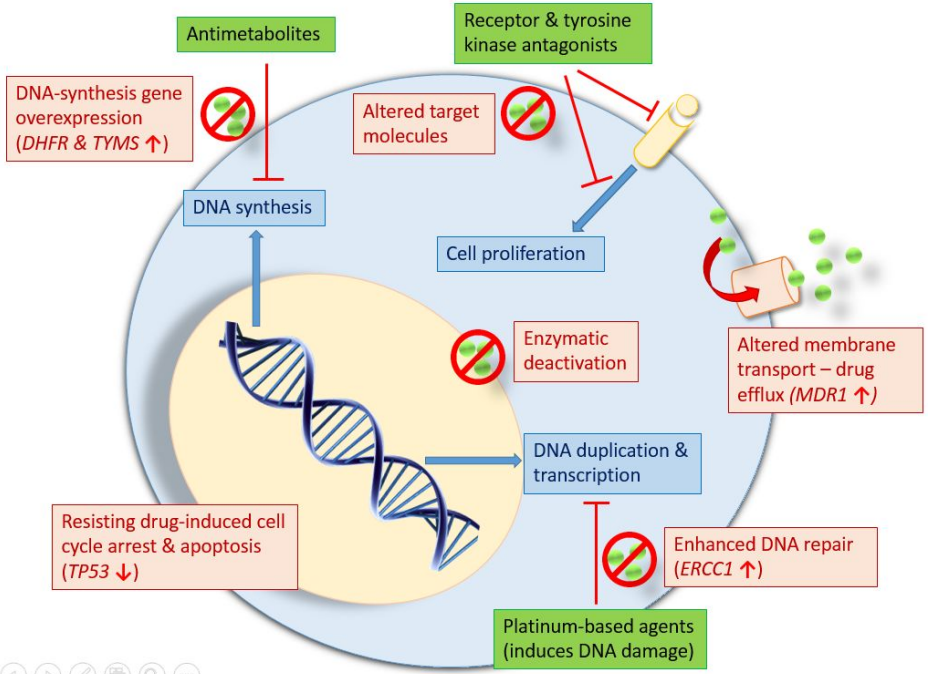
https://www.houstonmethodist.org/cancer/treatment-options/
National Cancer Institute

# Chemotherapy Drug Resistance

- Drug-sensitive cells do not survive, therefore, drug-resistant cells are enriched and propagated
- A variety of mechanisms are altered in resistant cancer cells

How does this resistance occur?

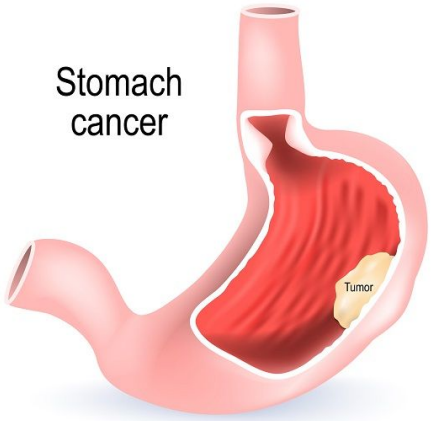
How do different therapies elicit resistance?




https://en.wikipedia.org/wiki/Antineoplastic_resistance#/media/File:Antineoplastic_resistances.png

# Gastric Cancer and Chemotherapy Drugs

- Develops in the stomach lining.
- Third most common cause of cancer-related death.




https://www.singhealth.com.sg/patient-care/conditions-treatments/stomach-cancer/overview

What genes are differentially expressed between cisplatin-resistant and FOLFOX-resistant gastric cancer cells?

# Datasets

A Therapeutic Strategy for Chemotherapy-Resistant Gastric Cancer via Destabilization of Both β-Catenin and RAS. *Cancers (Basel)* 2019

- Series GSE122130
- Expression profiling by high throughput sequencing
- Illumina HiSeq 2500 (Homo sapiens)

| Sample ID | Sample Types |
|---|---|
| GSM3689265 -GSM3689271 | FOLFOX-treated (7 replicates) |
| GSM3689272 -GSM3689275 | FOLFOX-untreated (4 replicates) |

Next-Generation Sequencing Analysis of mRNA Profile in Cisplatin-Resistant Gastric Cancer Cell Line SGC7901. *Med Sci Monit* 2019

- Series GSE128967
- Expression profiling by high throughput sequencing
- BGISEQ-500 (Homo sapiens)

| Sample ID | Sample Types |
|---|---|
| GSM3455901 | Cisplatin-resistant |
| GSM3455902 | Cisplatin-sensitive |

# Results

A Therapeutic Strategy for Chemotherapy-Resistant Gastric Cancer via Destabilization of Both β-Catenin and RAS. *Cancers (Basel)* 2019

Results obtained:

- Overexpression of CD44 and S100A4.
- Relationship between Wnt/-catenin and RAS/ERK pathways.

Next-Generation Sequencing Analysis of mRNA Profile in Cisplatin-Resistant Gastric Cancer Cell Line SGC7901. *Med Sci Monit* 2019

Results obtained:

- 3165 DEGs(2014 upregulated and 1151 downregulated)
- Top 5 genes: CBSL, GAGE12B, SORBS2, LOC101927345 and RBM14-RBM4.

# Cisplatin-Resistance vs FOLFOX Resistance

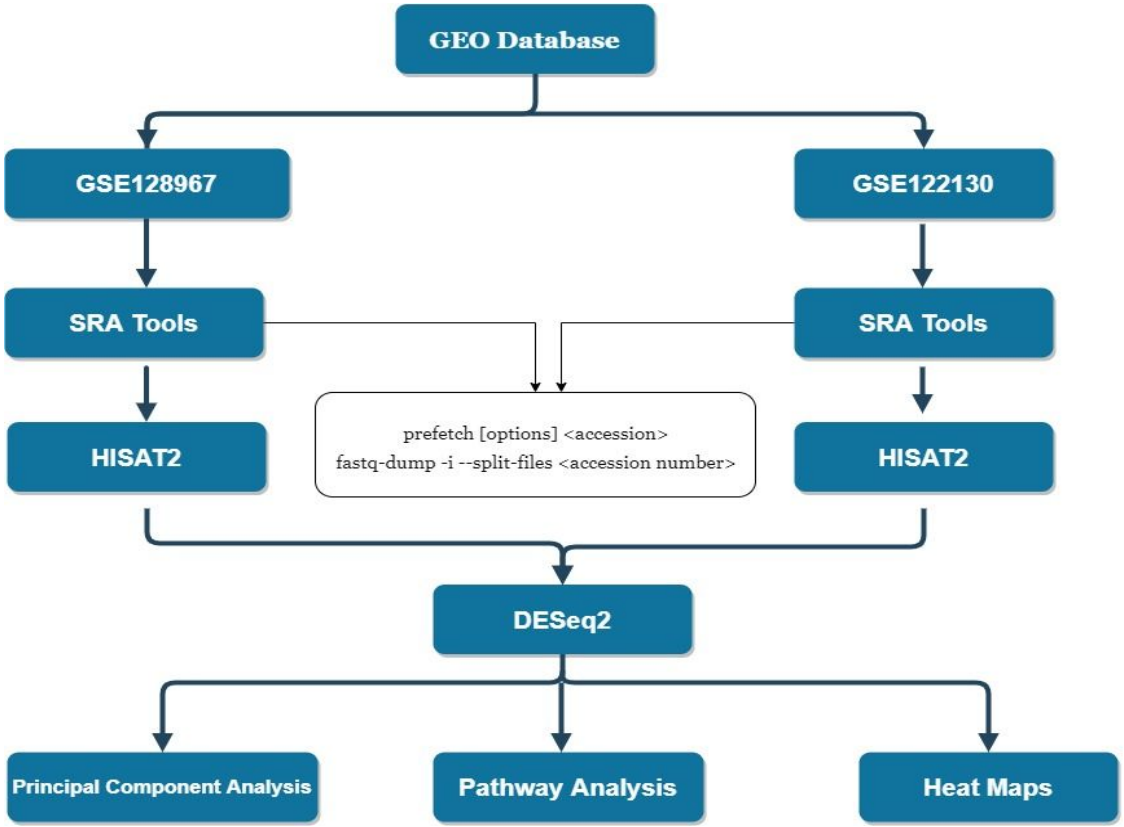
Our Hypothesis:

Are the genes which cause the resistance in Cisplatin treated Samples , cause the same resistance in Folfox treated Samples?

# Analytical Tools

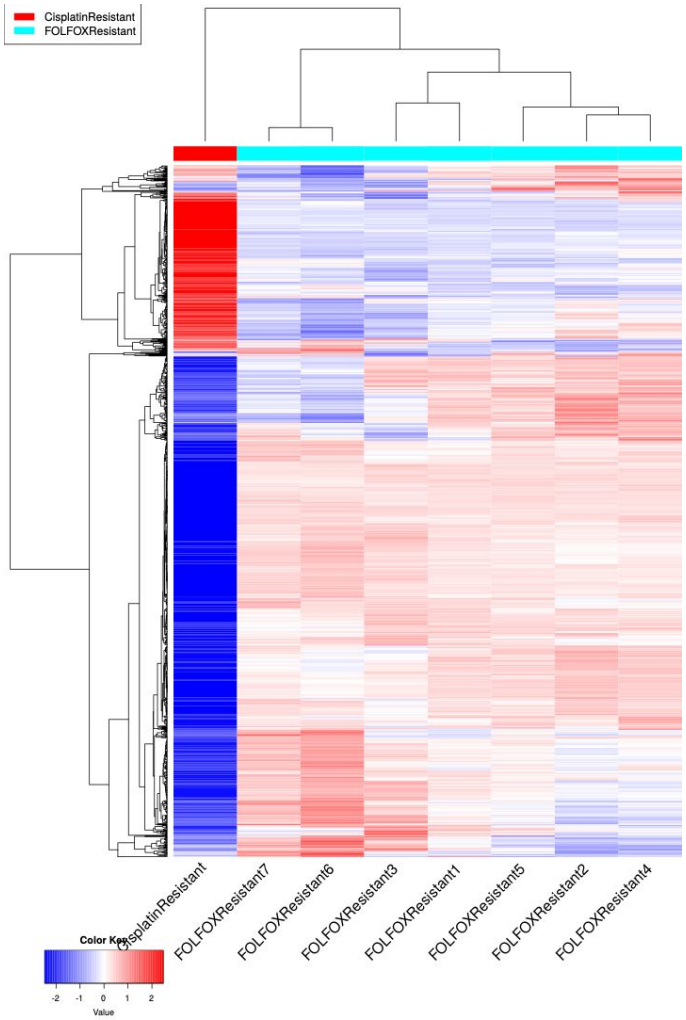
1. HISTAT : RNA-seq qualification(processing the reads)
2. DESeq2 : differential gene expression analysis
3. IDEP : PCA, heatmap
4. ShinyGo : Local pathway analysis
5. Reactome : Global pathway analysis

# Workflow


GEO Database
GSE128967
GSE122130
SRA Tools
SRA Tools
prefetch [options] <accession>
fastq-dump -i --split-files <accession number>
HISAT2
HISAT2
DESeq2
Principal Component Analysis
Pathway Analysis
Heat Maps

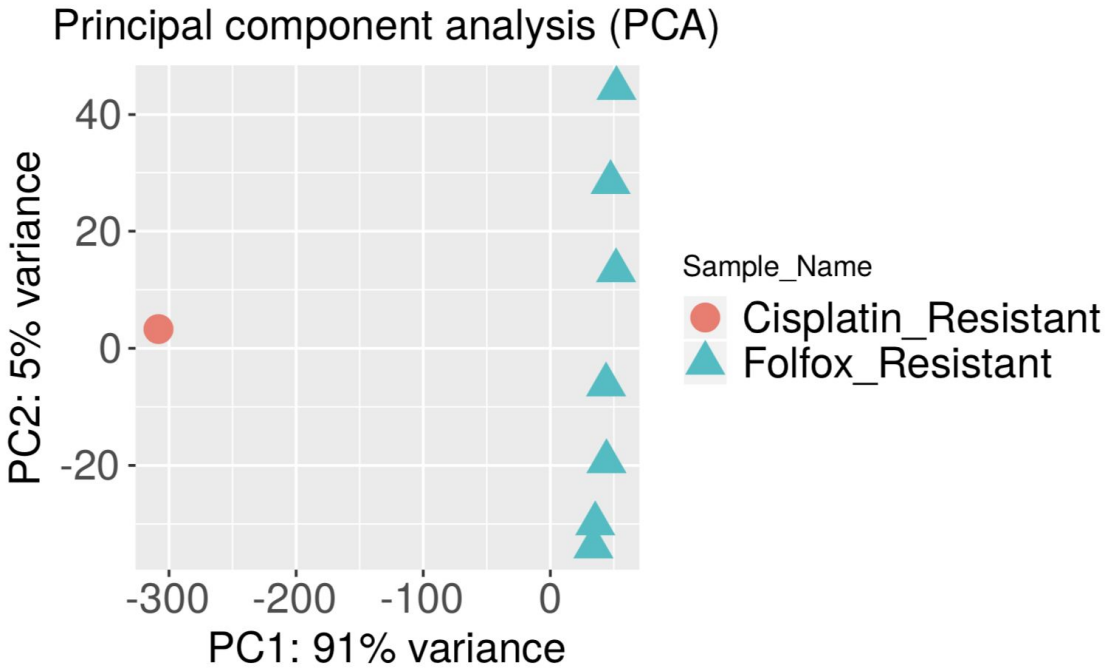
# Heatmap - IDEP

1. The rows represent the number of genes being analysed.
2. The columns represent the samples.
3. The heatmap brings all the similar rows and columns nearer to each other in the plot.
4. Hierarchical clustering was used here, it generates dendrograms to the side of the plot.
5. Hierarchical clustering calculates the pairwise distance between all data points and joins the data points that are the least distance apart.

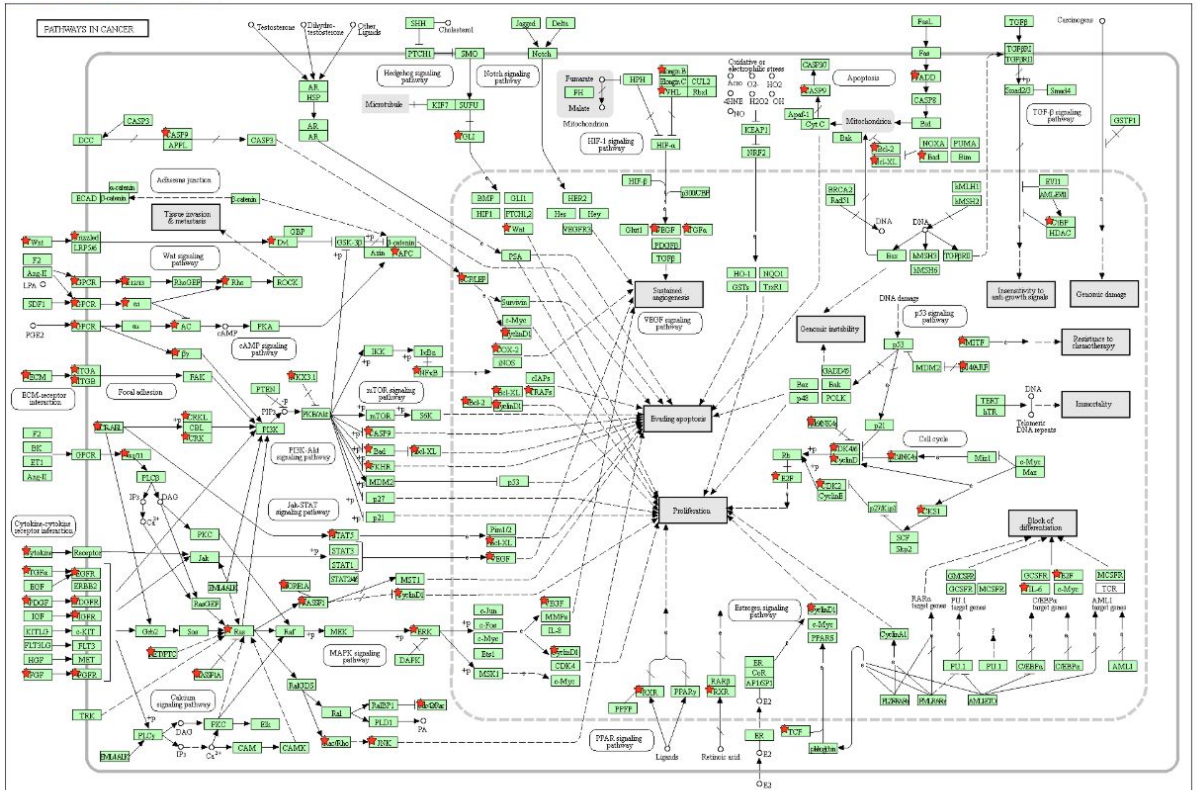



Cisplatin Resistant
vs
FOLFOX Resistant

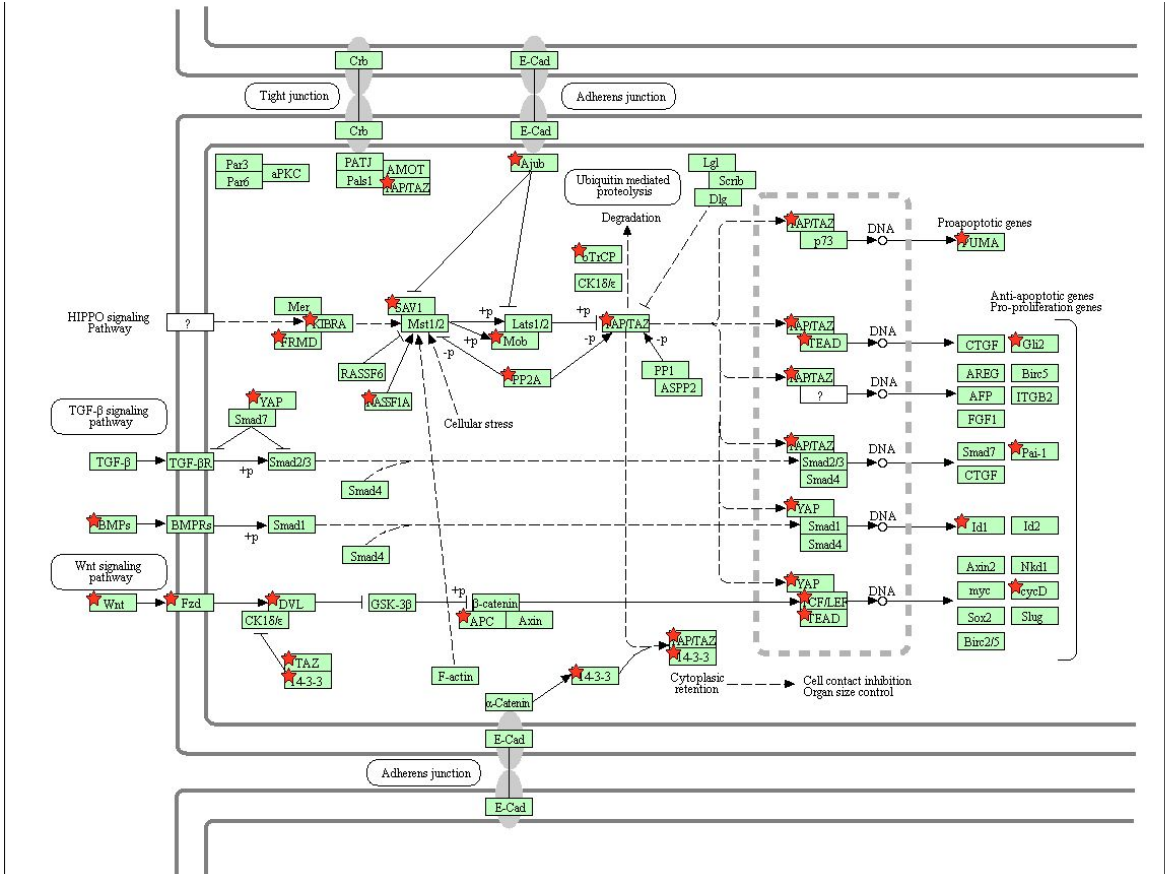
# Principal Component Analysis (PCA) - IDEP



# Pathway Analysis

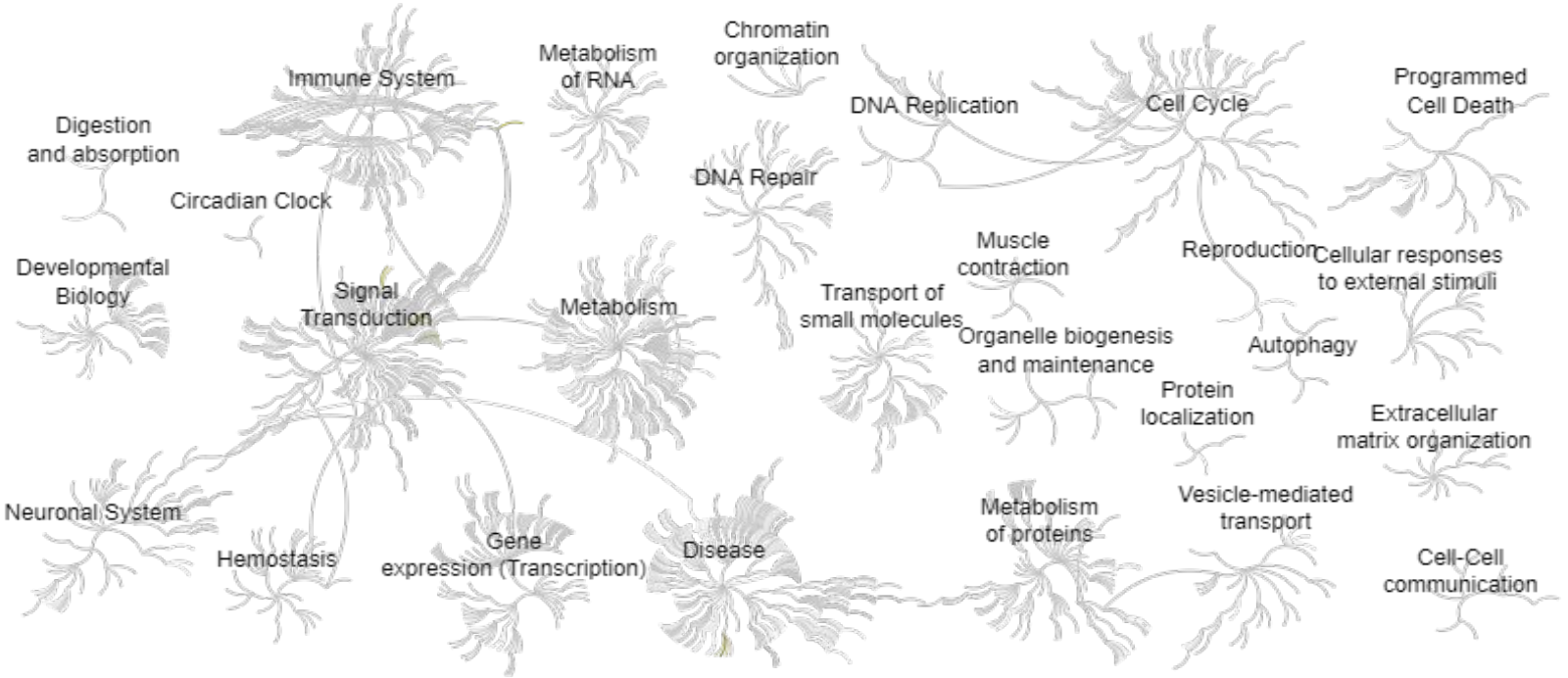



Pathways in Cancer



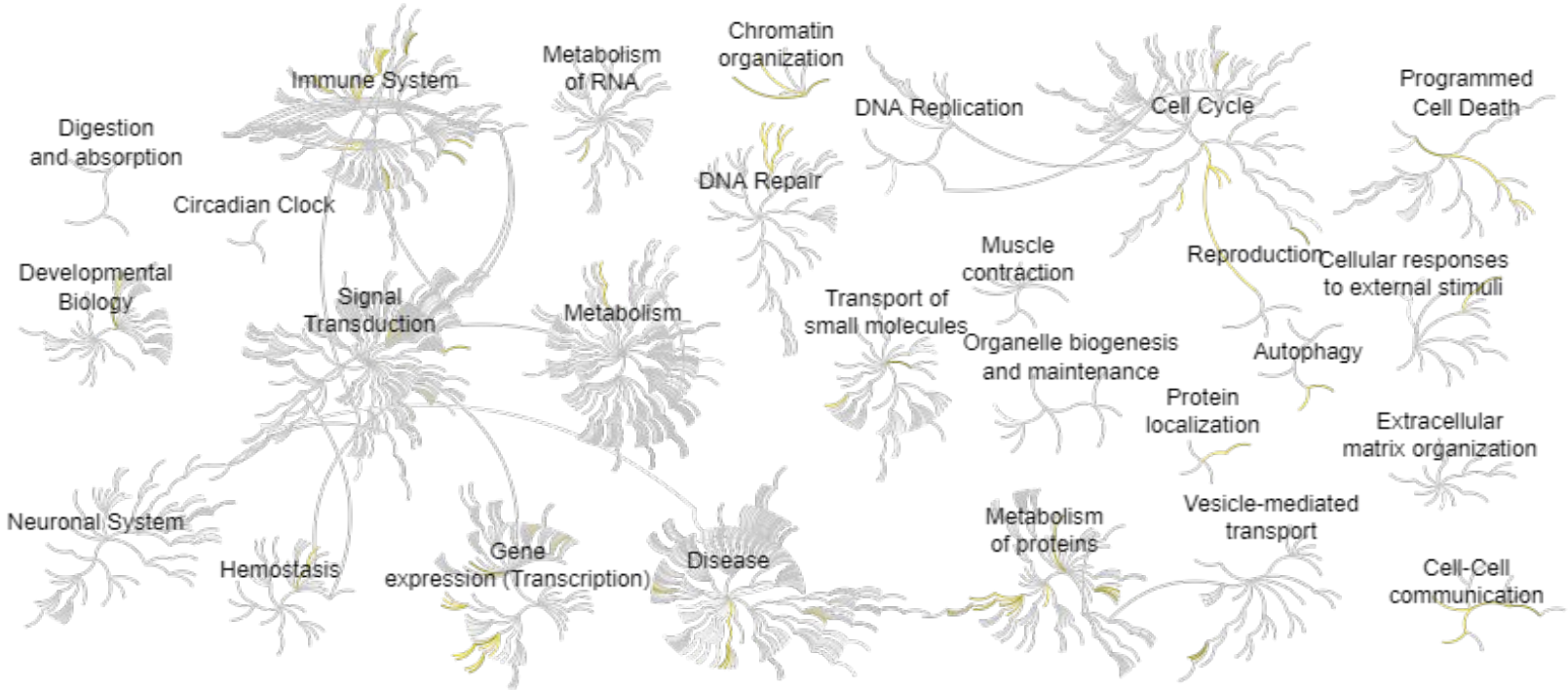

# Hippo Signaling Pathway

# Pathway Analysis - Global Pathway




**Under-expressed genes** (adjusted p-value < 0.001 & log2FC < 0)

# Pathway Analysis - Global Pathway




**Over-expressed genes** (adjusted p-value < 0.001 & log2FC > 0)

# Conclusion

- The differentially expressed genes between the Cisplatin-resistant and FOLFOX-resistant samples were analysed and compared.
- On further analysis we found that CBSL, SORBS2, LOC101927345 and RBM14-RBM4 weren’t being differentially expressed between the two resistant datasets.

Future Goals:

- To further analyse the FOLFOX resistance characteristics and to look whether the genes CBSL, SORBS2, LOC101927345 and RBM14-RBM4 are also responsible for it.

# References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