Differential Gene Expression Caused by Cisplatin in Ovarian Cancer Cell Lines

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ABSTRACT

Ovarian cancers often become resistant to cisplatin, a chemotherapy drug. It has been hypothesized that the epithelial-mesenchymal transition(EMT) contributes to the resistance of cisplatin in cancer cells. The EMT is a physiological process that is involved in cancer cell invasion and metastasis. When cells lose their epithelial characteristics and gain mesenchymal properties, it is believed that this causes invasion and metastasis. Thus, we compared an epithelial ovarian cancer cell line OVCA 420 and a mesenchymal cancer cell line OV90, to determine which biological processes and cellular components showed differences in gene expression.

BACKGROUND

Cisplatin is an anti-cancer chemotherapy drug that works by stopping the cancer cells from multiplying. It binds together the strands of the cells' genetic material, DNA. Cisplatin damages the DNA inside the cancer cells and so prevents them from multiplying. Ovarian cancer is a type of cancer that begins in the ovaries and forms tumors in the cells covering the ovaries.

MATERIALS

DATA SOURCE:
NCBI (National Center for Biotechnology Information)
After extracting the data from NCBI, two particular cell lines were selected for comparison. These selected cell lines included both treated and untreated cisplatin cells.
OVCA 420-epithelial
OV90-mesenchymal

```
gset@phenoData@data[,  c("characteristics_ch1", "characteristics_ch1.2")]
```

```
          characteristics_ch1 characteristics_ch1.2
GSM1160772     cell line: OV90       treatment: none
GSM1160773     cell line: OV90       treatment: none
GSM1160774     cell line: OV90       treatment: none
GSM1160775     cell line: OV90  treatment: Cisplatin
GSM1160776     cell line: OV90  treatment: Cisplatin
GSM1160777     cell line: OV90  treatment: Cisplatin
```

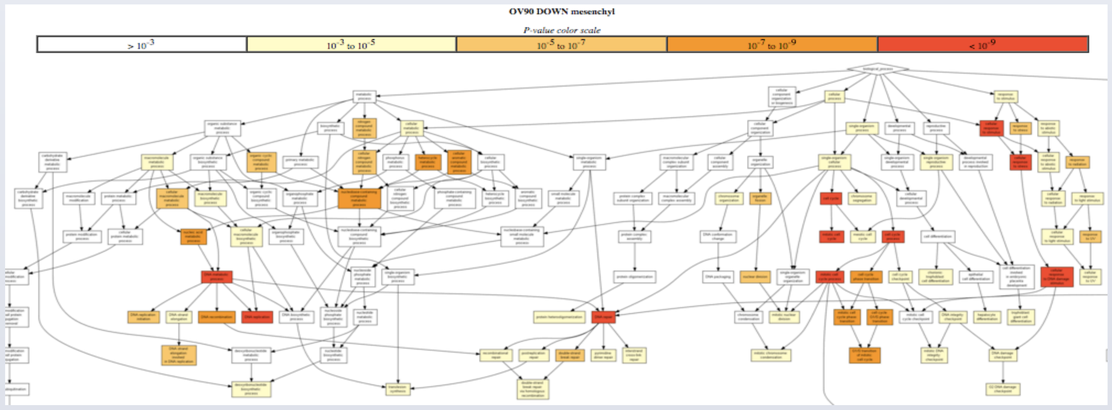
METHODS

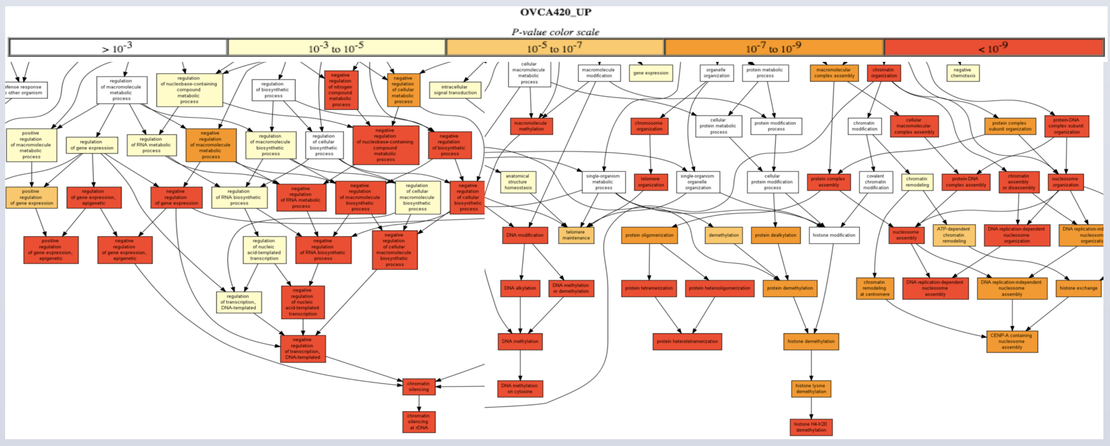
R limma package
Performs analysis of expression profiles in terms of co-regulated sets of genes or in terms of higher-order expression signatures, which provides enhanced possibilities for biological interpretation of gene expression differences between the cancer cell lines

Pathway Analysis
Identifies specific differences contributing to the resistance of particular cancer cells versus others

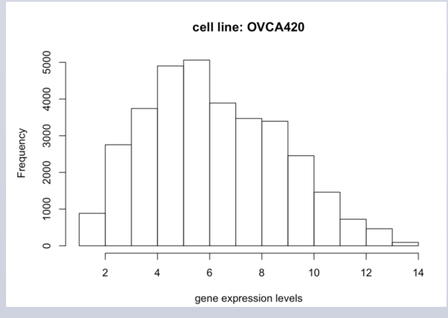
Network Clustering Analysis
This type of analysis measures the similarity of genes and their expression patterns. These measures of similarity can be measured in various ways that are problem dependent, for example, by the correlation coefficient between the selected genes.

RESULTS






```
#   Differential expression analysis with limma
# rm(list=ls())
setwd("~/github/MJ_RISE2016/project2.GSE47856")
library(Biobase)
library(GEOquery)
library(limma)
```



CONCLUSION

We found that cisplatin significantly up-regulated cell cycle pathways in the epithelial-like cancer cell line of OVCA 420. On the contrast, cisplatin significantly down-regulated cell cycle pathways in mesenchymal-like cancer cell line of OV90. Our results suggest that mesenchymal-like cancer cells are more resistant to cisplatin by down-regulation through its cell proliferation process. This research is the beginning for identifying which part in the cell cycle is affecting patients' resistance to chemotherapy treatments. In the future this research will be transferred to actual treated and untreated cells versus untreated and treated cell lines.

REFERENCES

Kalluri, Raghu, and Robert A. Weinberg. "The Basics of Epithelial-mesenchymal Transition." *JCI - The Basics of Epithelial-mesenchymal Transition*. The Journal of Clinical Investigation, June 2009. Web. 04 Feb. 2016.

Katabuchi, H. "Cell Biology of Human Ovarian Surface Epithelial Cells and Ovarian Carcinogenesis." *National Center for Biotechnology Information*. U.S. National Library of Medicine, June 2003. Web. 04 Feb. 2016.

Sharan, R., R. Elkon, and R. Shamir. "Correction: Cluster Analysis and Display of Genome-Wide Expression Patterns." *Proceedings of the National Academy of Sciences of the United States of America* 96.19 (1999): 10943. Department of Human Genetics and Molecular Medicine. Web.

QH Miow TZ Tan J Ye , JA Lau , T Yokomizo , J-P Thiery and S Mori. Epithelial–mesenchymal status renders differential responses to cisplatin in ovarian cancer.

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