FINAL PRESENTATION

-Drug Sensitivity in Cancer Cell Lines-

Ovarian Cancer

- 07/22/2021 -

Data Statistics SS 21

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AIM OF THE PROJECT

1. Determine how the applied drugs affect the cancer cell lines - particularly the ovarian cell lines
2. Finding the most effective drugs
3. Investigate drug dosage dependency
4. Relation between drug sensitivity in ovarian cancer cell lines and gene expression patterns

GENERAL OVERVIEW

- Obtain data to work with ➡ **Data Filtering, Exploration, Reorganization**

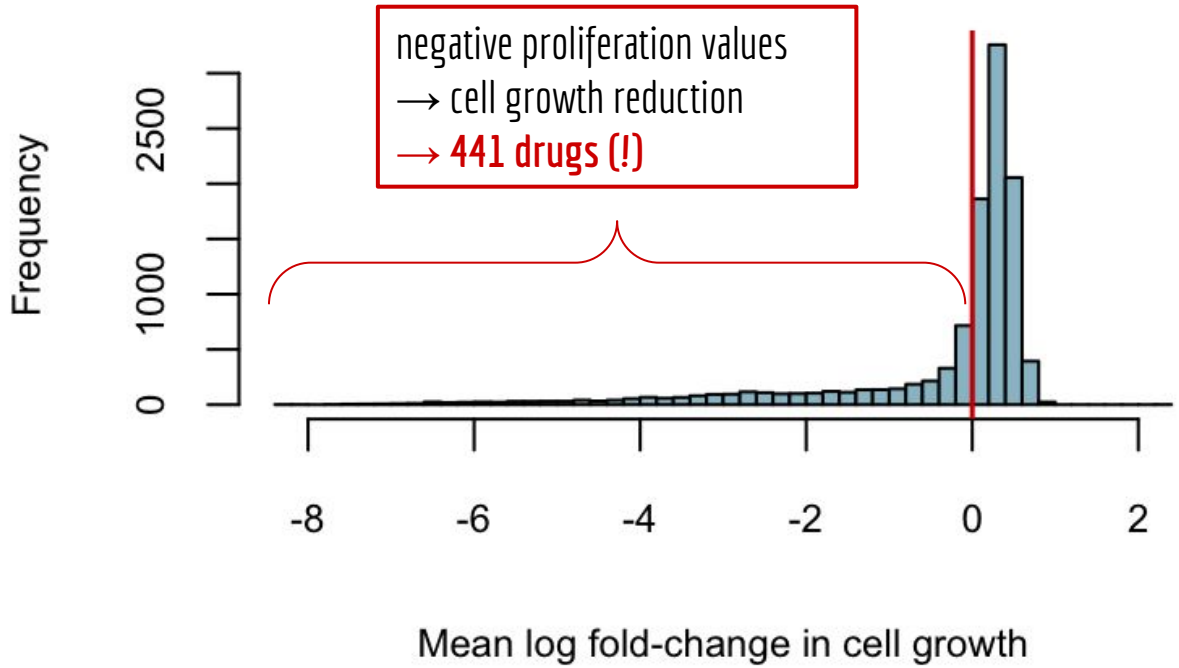
- Analysis of drug influence on proliferation rates
- Identification of most effective drugs (MOA)

➡ **Descriptive Statistics**
Dimension Reduction

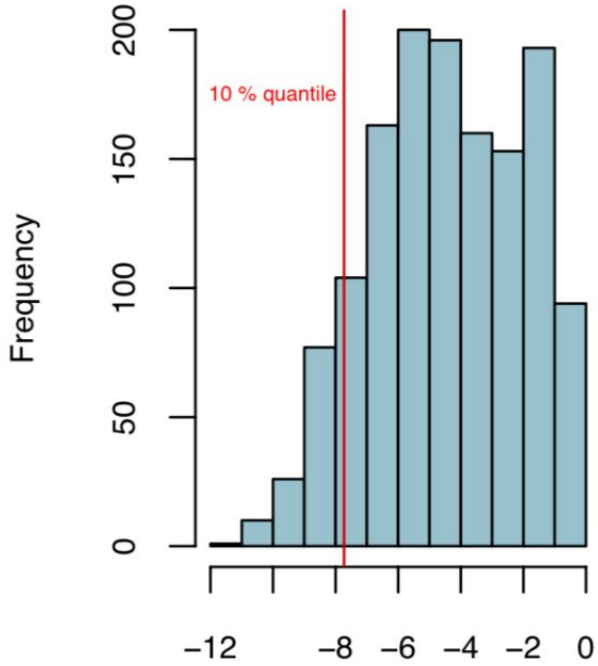
GENERAL OVERVIEW

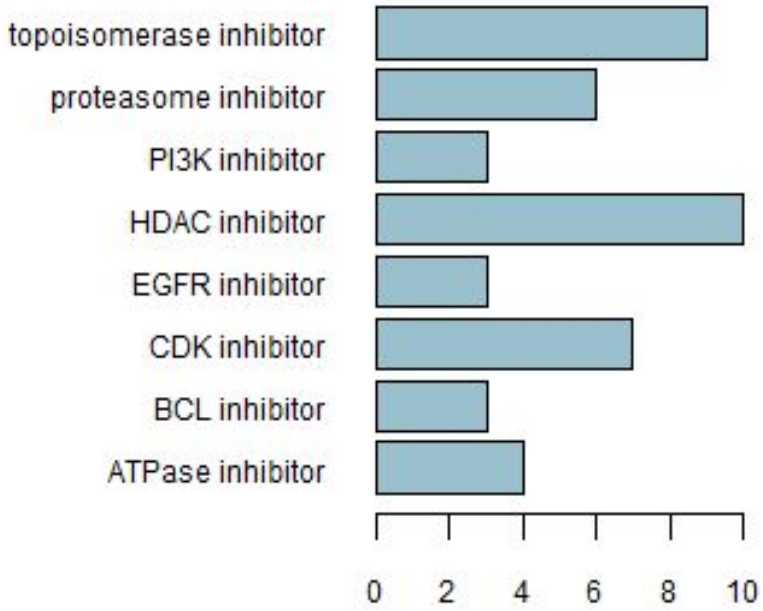
- Test the effect of drug dosage on proliferation values → **Descriptive Statistics**
- Correlation between drug response and specific gene expression patterns → **Statistical Tests**
- Prediction of drug efficiency from gene expressions/mutations → **Multivariate Linear Regression Analysis**

GENERAL OVERVIEW



MOST EFFECTIVE DRUGS



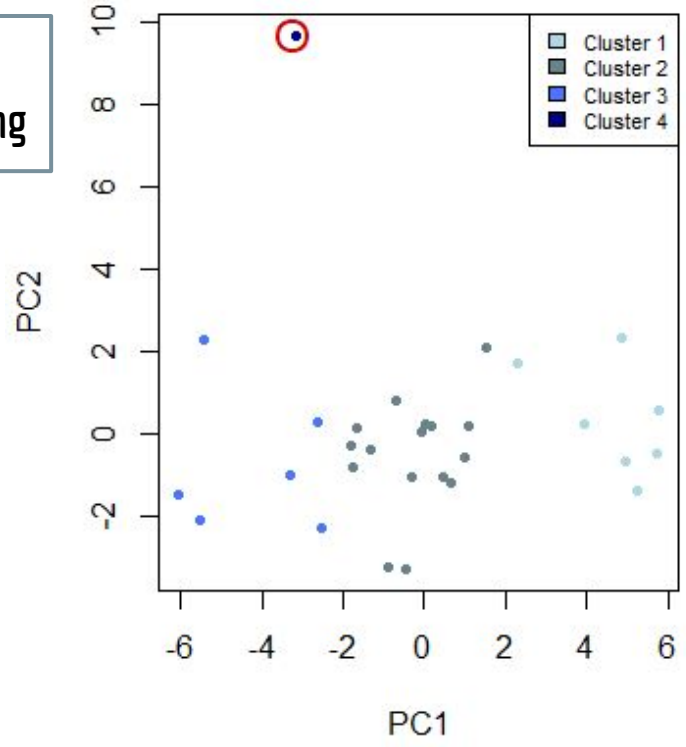


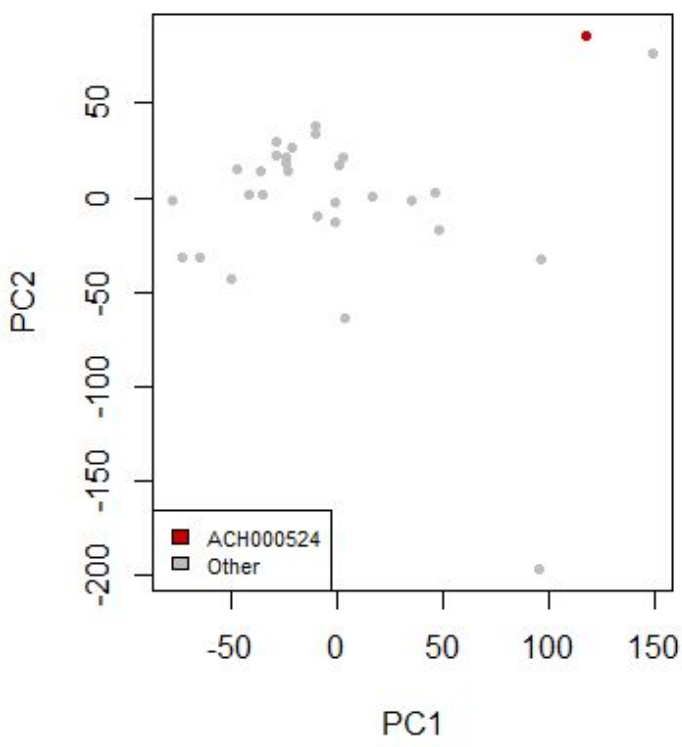
→ focus on the 45 most common MOAs that caused the lowest negative proliferation values

MOST EFFECTIVE DRUGS

Dimension Reduction → Principal Component Analysis; Outlier Cell Line

MOA Clustering



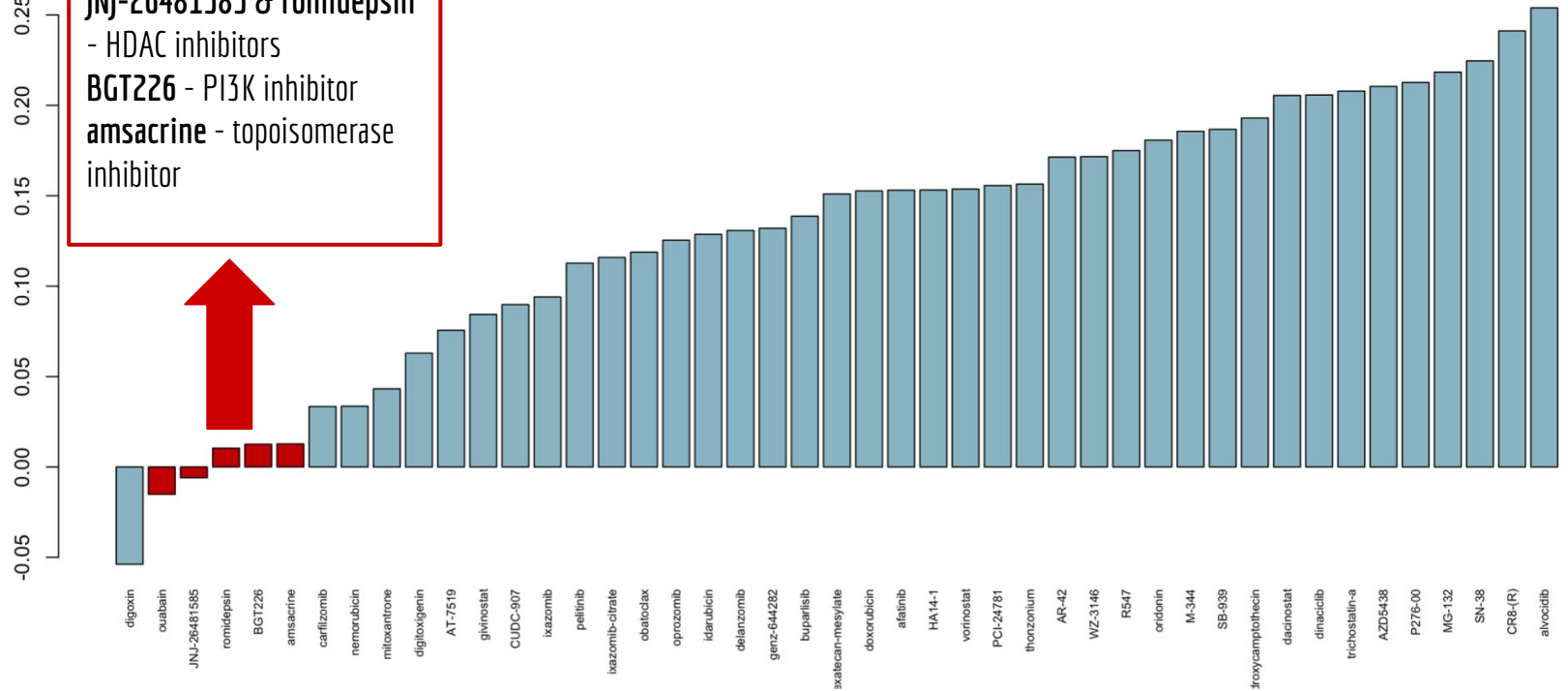


CNV Clustering

GENERALLY EFFECTIVE DRUGS

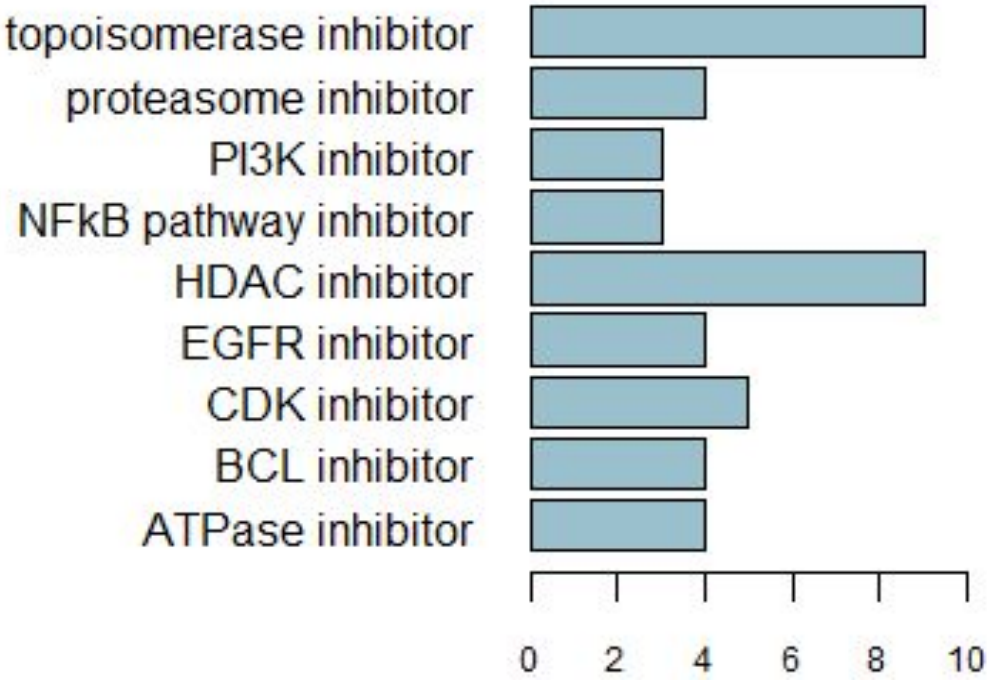
values close to zero show a similar effect on the proliferation among all cell lines

ouabain - ATPase inhibitor
JNJ-26481585 & romidepsin - HDAC inhibitors
BGT226 - PI3K inhibitor
amsacrine - topoisomerase inhibitor



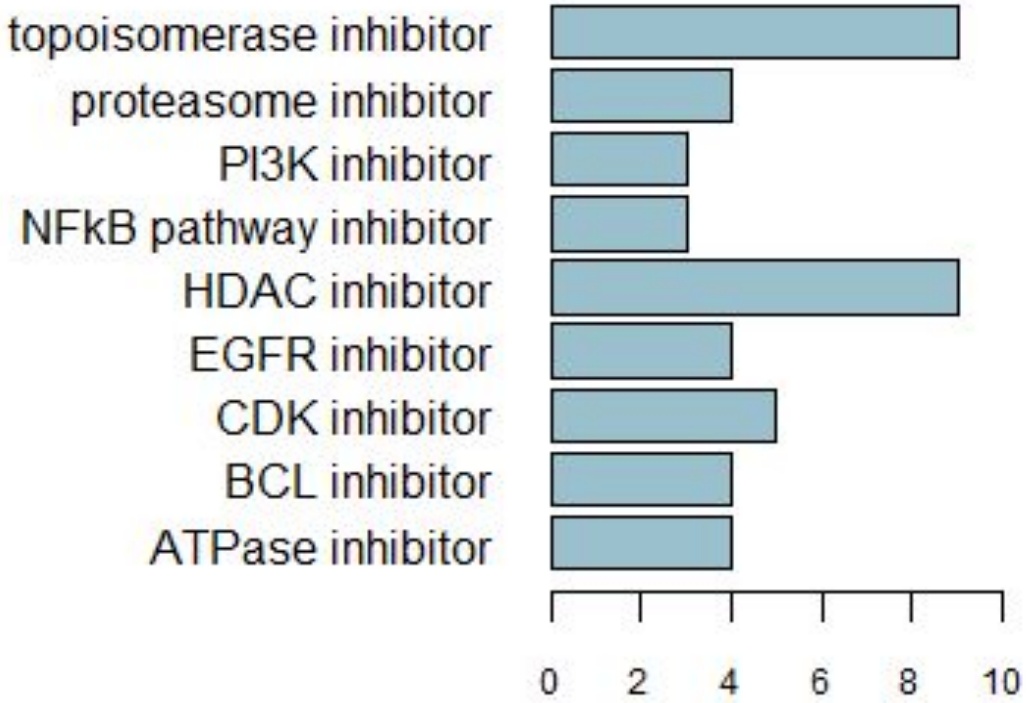
DRUG EFFECT ON TYPES OF CELL LINES

Mechanism of Action - non-ovarian cancer cell lines

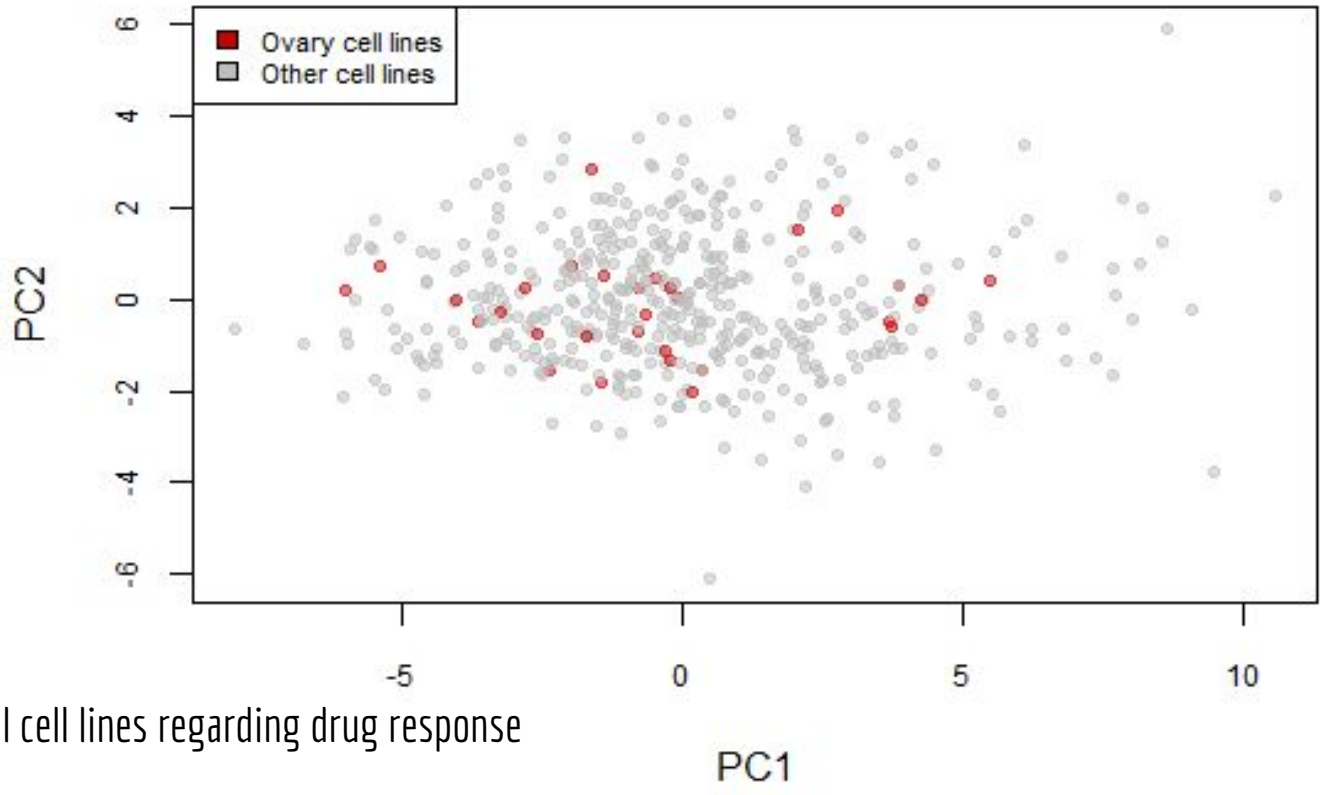


FISHER'S EXACT TEST

H0-Hypothesis: There is no association between the occurence of specific MOAs and the cell line type (either ovary or non-ovary)



DIMENSION REDUCTION



→ PCA on all cell lines regarding drug response

UNPAIRED TWO-SIDED WELCH'S T-TEST

	p_value <dbl>	Bonferroni <dbl>
TAK-733	0.0002778925	0.3873821
tyloxapol	0.4544301001	1.0000000

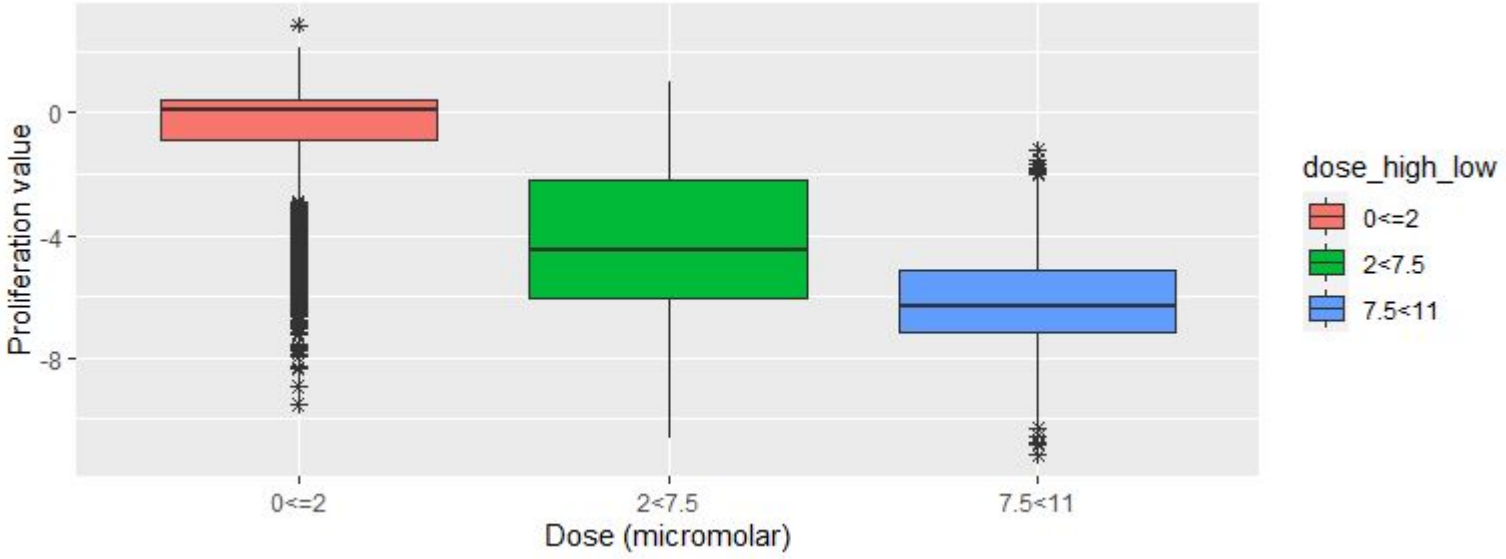
⟶ no relation between drug response and cell line type regarding ovarian and non-ovarian cancer cell lines

⟶ clusters 2 and 4

⟶ p-value › confidence level α = 0.05

DRUG DOSAGE DEPENDENCY

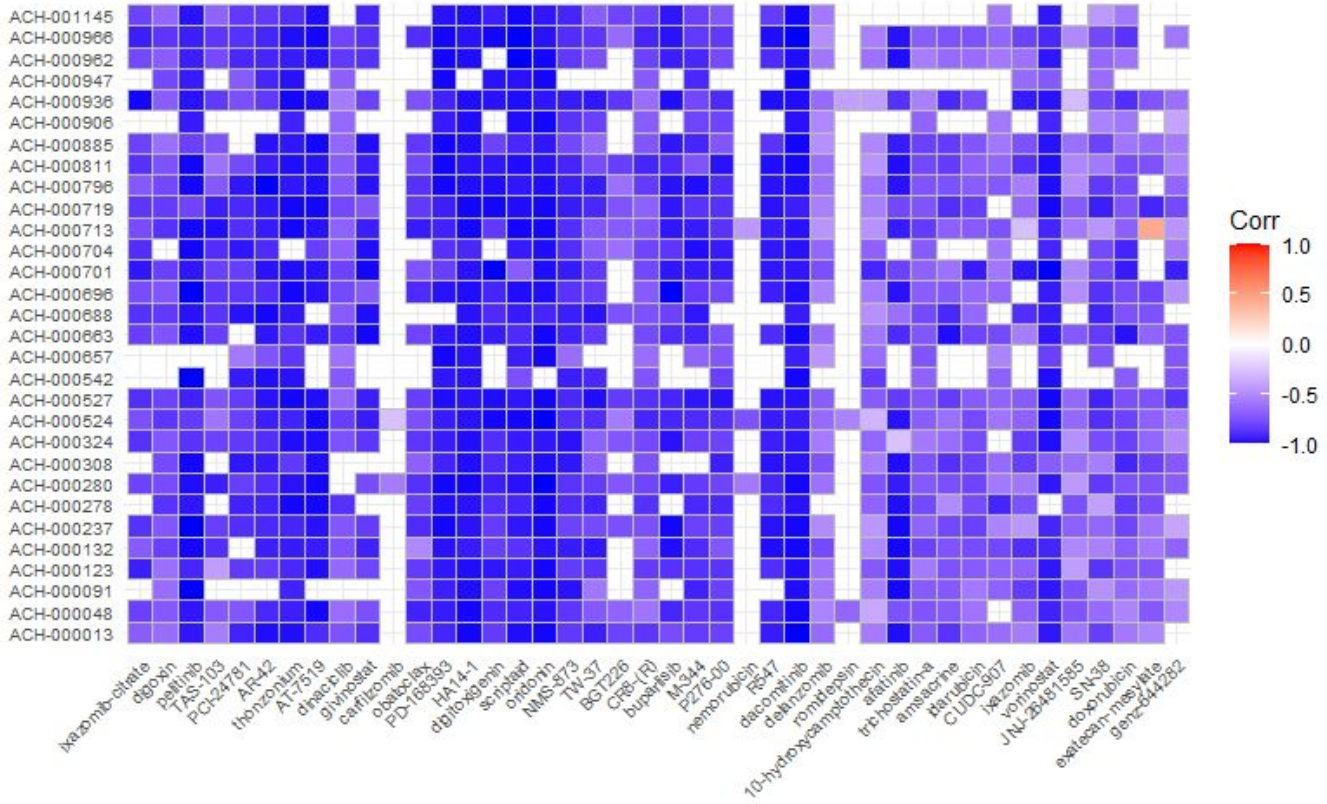
Boxplot



⟶ 3 stages: low, medium, high dose

⟶ inverse correlation - **Increased drug dose leads to reduction of proliferation rates!**

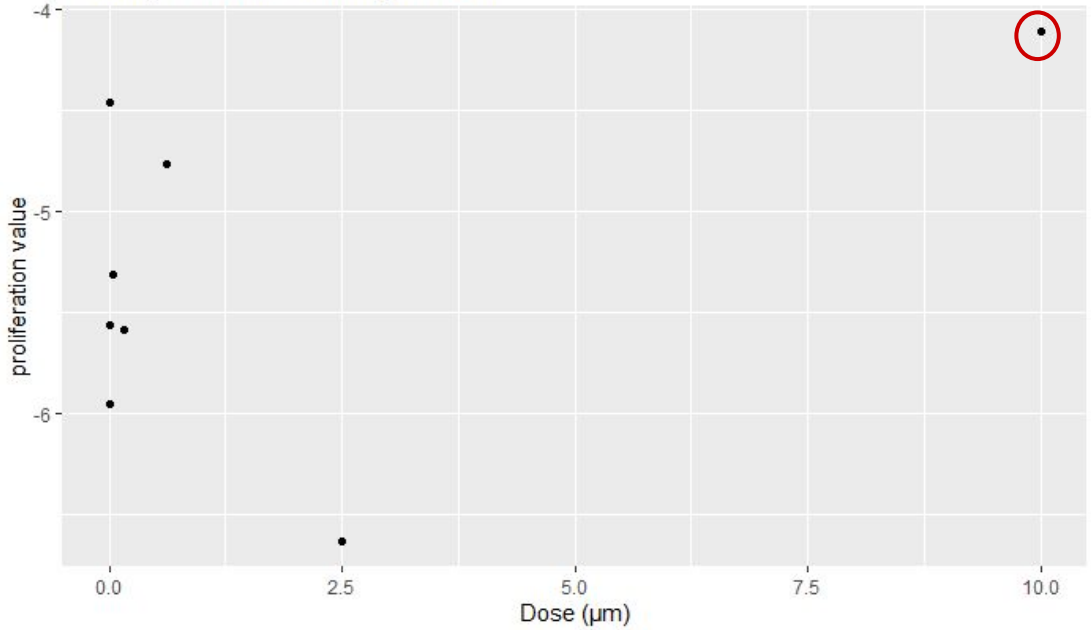
DRUG DOSAGE DEPENDENCY



Pearson Correlation

DRUG DOSAGE DEPENDENCY

```
ggplot_dose_proliferationvalues_red<-ggplot(df_ovary_prism_treat_effective_reduced, aes(x=dose,
y=df_ovary_prism_treat_effective_reduced$`ACH-000713`)) +
  geom_point()+
  labs(title="Plot of proliferation value per dose",x="Dose (µm)", y = "proliferation value")
ggplot_dose_proliferationvalues_red
```



COMPARISON OF GENE EXPRESSION PATTERNS

Unpaired two-sided Welch's T-Test, Bonferroni Correction

	p_value	Bonferroni	target	disease_area
trichostatin-a	1.27e-05	0.0176843	HDAC inhibitor	Oncology
semaxanib	1.43e-05	0.0198872	VEGFR inhibitor	Oncology
alvocidib	2.45e-05	0.0342022	CDK inhibitor	Oncology

⟶ clusters 1 and 3, prism

COMPARISON OF GENE EXPRESSION PATTERNS

	p_value	Bonferroni
torin-1	1.629024e-05	0.02270859
AVN-944	1.744655e-05	0.02432050

→ significant drugs for clusters 2 and 3 (prism.treat)

	p_value	Bonferroni
BMS-387032	0.0001512419	0.2108312
alvocidib	0.0004119957	0.5743220

→ no significant drugs for clusters 1 and 2 (prism.treat)

COMPARISON OF GENE EXPRESSION PATTERNS

Unpaired two-sided Welch's T-Test, Bonferroni Correction

	p_value	Bonferroni
UCHL1	0.0002004211	1
UACA	0.0004426973	1
BEX4	0.0007019719	1

→ prism.exp

	p_value	Bonferroni
OPHN1	0.002237303	1
YIPF6	0.002237303	1
STARD8	0.002237303	1

→ prism.cnv

	p_value	Bonferroni
OR4C11	0.0001866203	1
KLRK1	0.0001895998	1
KRT36	0.0002972446	1

→ prism.achilles

MULTIPLE REGRESSION MODEL

```r
learning_celllines = sample(1:nrow(regression_data_no_nas), 13, replace = F)
learning_regression <- regression_data_no_nas[learning_celllines,]
check_regression <- regression_data_no_nas[-learning_celllines,]
```

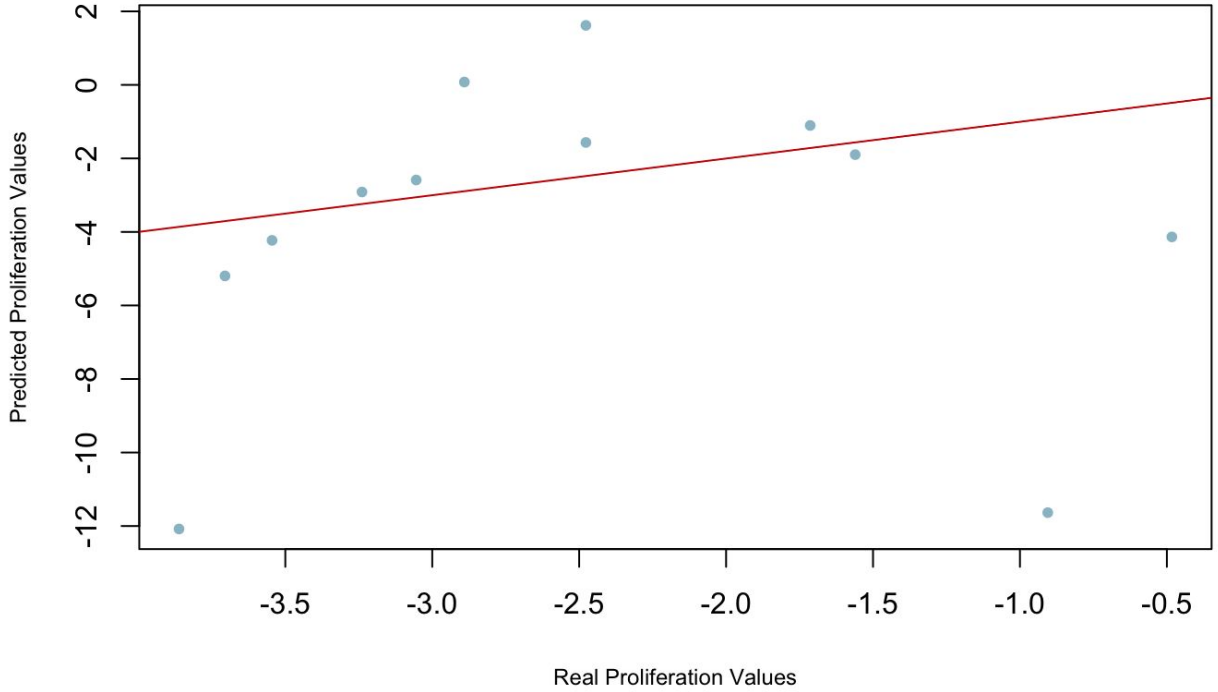
```r
regression_model <- lm(formula = (disulfiram) ~  .,data=learning_regression)
```

summary(regression_model):

⟶ relevant values:

- R^2 -Value
- Adjusted R^2 -Value
- p-value of F-statistic

PREDICTED VALUES VS. REAL VALUES



CONCLUSIONS

HDAC-, topoisomerase- and CDK-inhibitors successfully reduce the proliferation of ovarian cancer cell lines

These are the most common MOAs regarding all the other cell lines

No significant difference of their effect regarding the cell line type

Certain drugs show different effects on various cell lines

Thank you for your attention!

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