Project Proposal

-Drug Sensitivity in Cancer Cell Lines-

Ovarian Cancer

Data Statistics SS 21

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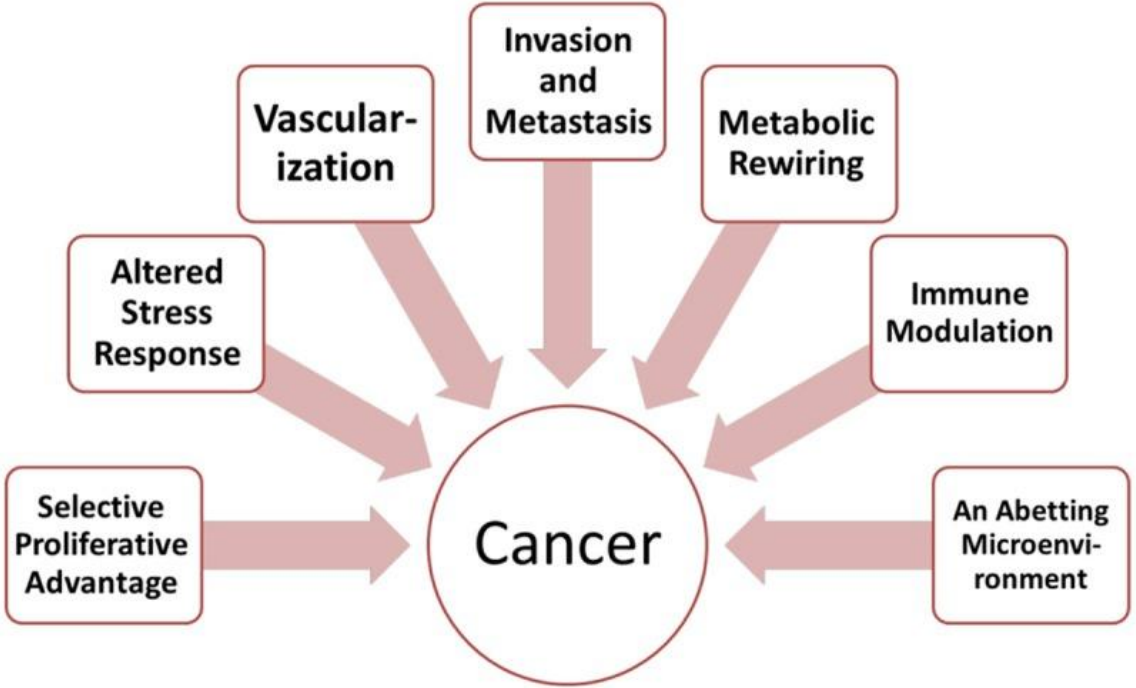
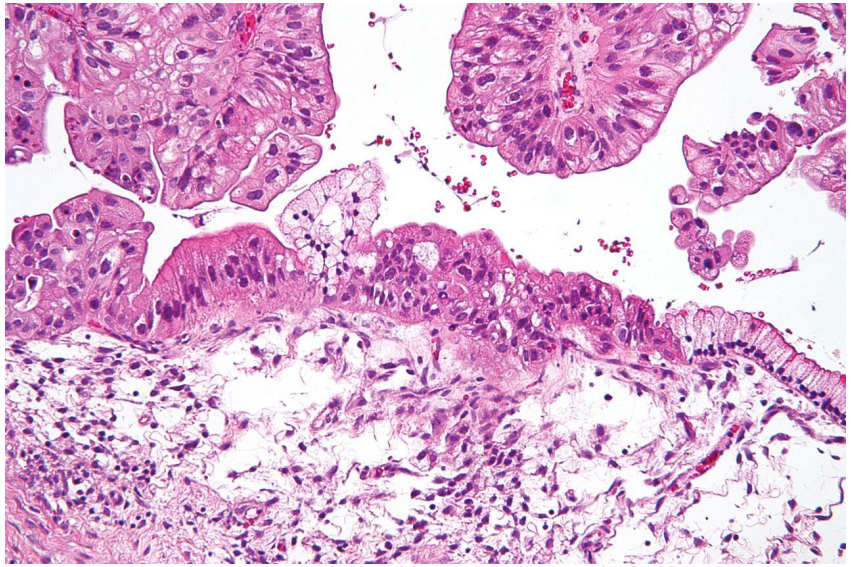
Cancer Hallmarks



Yousef Ahmed Fouad and Carmen Aanei, 2017

Ovarian cancer

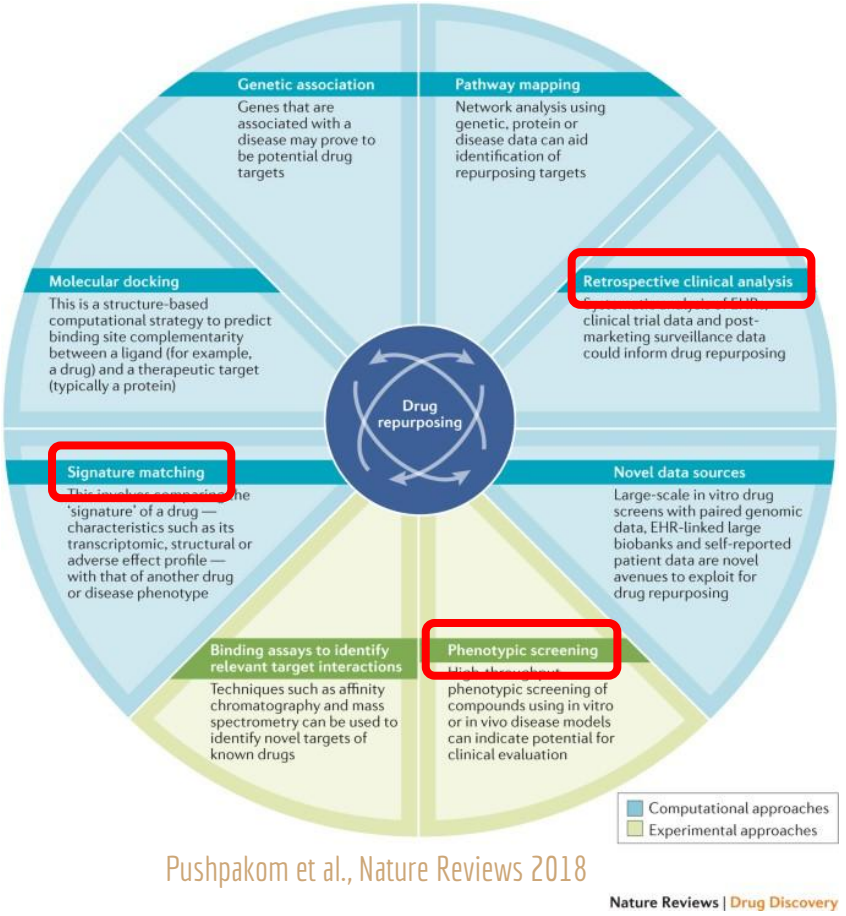


https://en.wikipedia.org/wiki/Ovarian_cancer

- Most lethal gynecological malignant tumor in the developed world
- Significant genetic heterogeneity
- Concerning female patients mainly over the age of 50
- Molecular defects: TP53, KRAS, BRCA1 or BRCA2 mutations

Drug repurposing

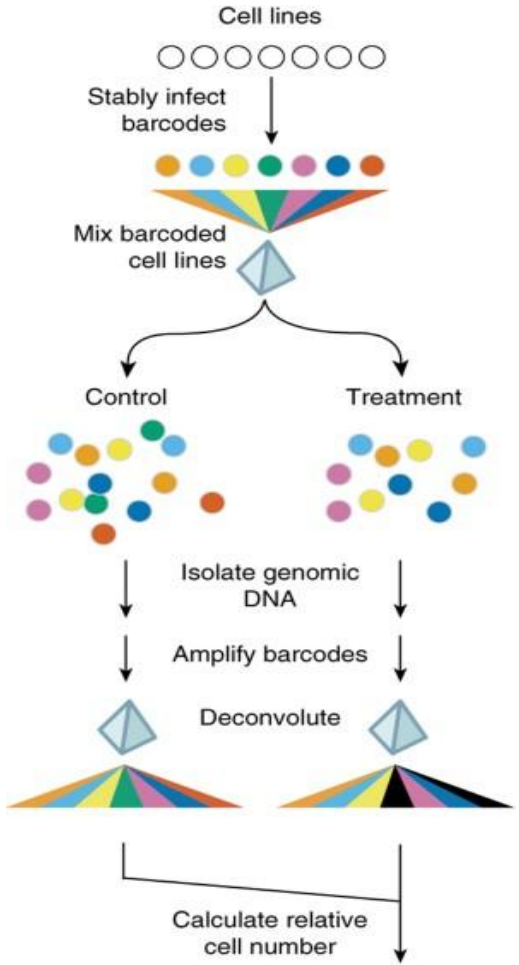
- New usage for existing drugs outside of traditional medical indication
- Signature matching
- Clinical data analysis
- Phenotypic screen



Pushpakom et al., Nature Reviews 2018

Methods - PRISM

- DNA barcoding
  ⟶ screening drugs against cell lines in pools
- DMSO = negative control
- Incubation period of 5 days
- Amplification of barcode sequences
- Luminex detection
- Establish a ratio between the quantity of treated cell lines and the negative control cell lines



Yu, C. et al., Nature 2016

Data Sets

- Data frame *prism*:

  ⟶ effect of medical treatments on cell growth of different cell lines

- Additional data sets:

  ⟶ *prism.treat* (drugs)

  ⟶ *prism.cl* (cell lines)

drug name::dosage::assay name

DepMap_IDs of cell lines

	BRD-A00077618-236-07-6::0.00061034::HTS002	BRD-A00077618-236-07-6::0.0024414::HTS002	BRD-A00077618-236-07-6::0.00976562::HTS002
ACH-000007	0.155930785	0.019270857	-0.325728482
ACH-000008	0.184595649	0.225428031	0.514571347
ACH-000011	-0.129951554	0.082021548	-0.465501527
ACH-000012	0.264334776	0.343490487	-0.156107708
ACH-000013	0.284201840	0.717880776	0.098727706

Data Sets

- Data frame *prism.achilles*:

  ⟶ gene knockdown scores

  ⟶ smaller values:
  = gene has a higher essentiality

- Additional data sets:

  ⟶ *prism.exp* (TPM values)

  ⟶ *prism.cnv* (CN values)

  ⟶ *prism.snv* (observed mutations)

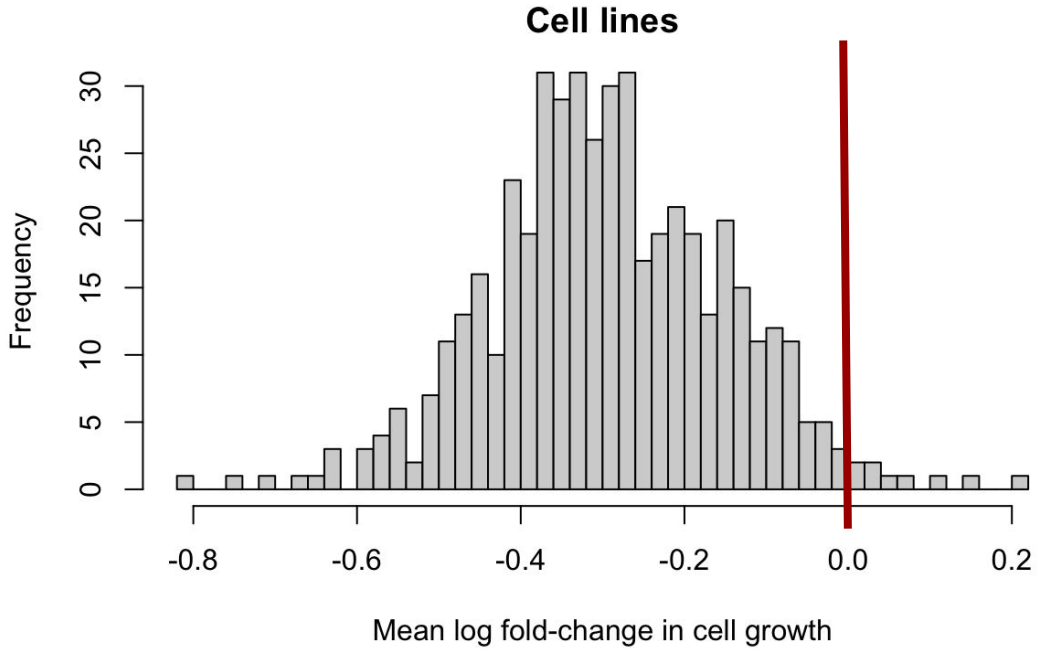
gene names

DepMap_IDs of cell lines

	A1BG	A1CF	A2M	A2ML1	A3GALT2	A4GALT
ACH-000007	0.066211918	0.073849767	-0.065866962	0.156037564	0.100957813	0.1409968606
ACH-000011	0.270231724	0.072104660	0.014604614	0.433243290	-0.030273403	-0.2390799522
ACH-000012	0.015445134	0.173129613	0.104252319	0.305781945	0.058204201	-0.1900014664
ACH-000013	0.062819955	0.038241805	-0.030842945	0.210707395	-0.065721722	-0.0796803284
ACH-000014	0.137092353	-0.054472837	0.012998483	0.187520545	-0.018819321	-0.1307547147
ACH-000015	-0.068873122	-0.005479247	-0.167313092	0.144660178	-0.022596340	-0.1073700152

Distribution of mean sensitivity across all cell lines

```r
```{r Distribution of mean sensitivity across all cell lines}
hist(apply(prism, 1, function(x){mean(x,na.rm=TRUE)}), breaks = 50, main = "Cell lines",
xlab = "Mean log fold-change in cell growth")
```
```



General Methods

1. **Data Filtering and Reorganization**
2. **Descriptive Statistics**
3. **Dimension Reduction**
   a. PCA
   b. Clustering (k-means)
4. **Statistical Test**
   a. T-test
5. **Linear Regression Analysis**

Predicting the effect of drug treatments on ovarian cancer cell lines

1. How do different drugs influence ovary cancer cell lines and which are particularly noticeable? How do these specific drugs affect the other cell lines?

2. Is the sensitivity of different drugs on ovary cancer cell lines connected to specific cancer-related genes or gene knock-outs?

Milestones

1.1 Do certain drugs have a specific positive or negative influence on the proliferation of the ovary cancer cell lines?

1.2 Are the medical effects on cell lines independent of the cancer cell line types?

1.3 How does the dosage of the medical treatment affect the treatment results?

1. How do different drugs influence our ovary cancer cell lines and which are particularly noticeable? How do these specific drugs affect the other cell lines?

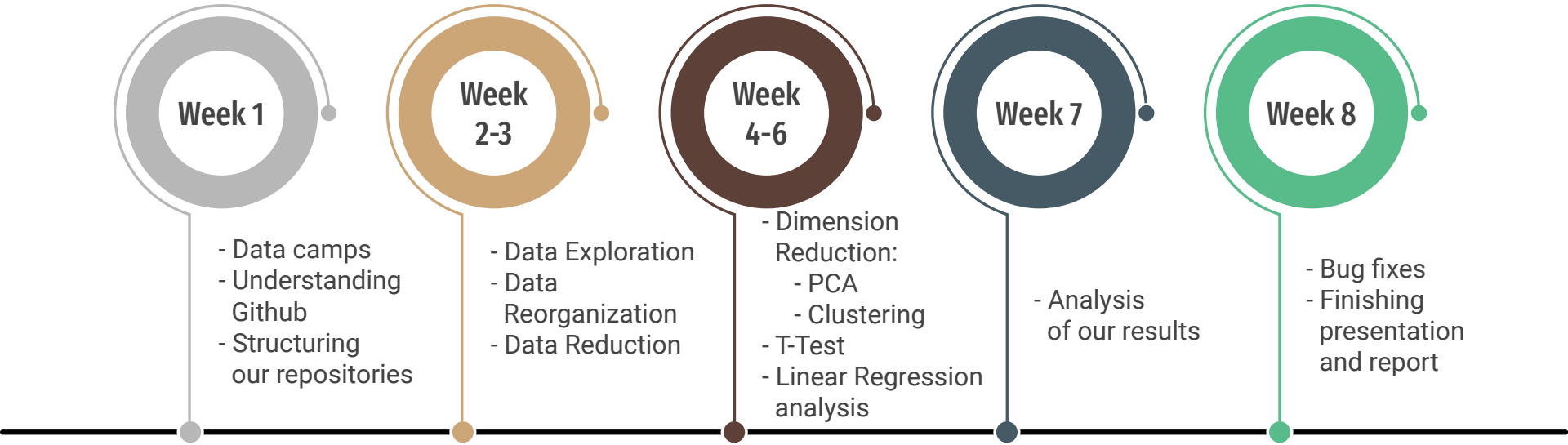
2. Is the sensitivity of different drugs on ovary cancer cell lines connected to specific cancer-related genes or gene knockdowns?

2.1 Do the ovarian cancer cell lines show a different response to similar drugs according to their specific mutations (KRAS, BRCA1/2,...)?

2.3 How well can we predict the drug efficiency from certain gene mutations or expressions?

2.2 Does the drug response depend on the gene expression patterns/knockdown scores in ovary cancer cell lines?

Timeline


Week 1
- Data camps
- Understanding Github
- Structuring our repositories
Week 2-3
- Data Exploration
- Data Reorganization
- Data Reduction
Week 4-6
- Dimension Reduction:
- PCA
- Clustering
- T-Test
- Linear Regression analysis
Week 7
- Analysis of our results
Week 8
- Bug fixes
- Finishing presentation and report

References

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