

# The role of skin-specific genes in skin cancer

## Project Proposal

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# Background

Skin cancer -> Most common type of cancer in humans

- **Melanoma** (Only 2% of all skin cancers, but most deaths!)
- **Non-melanoma**

## Risk factors:

- ☐ Moles
- ☐ UV exposure
- ☐ Genetic background





# Background

Problem : Cancer escaping immune surveillance

How?

- Tissue restricted antigens (TRA) are upregulated in cancer cells

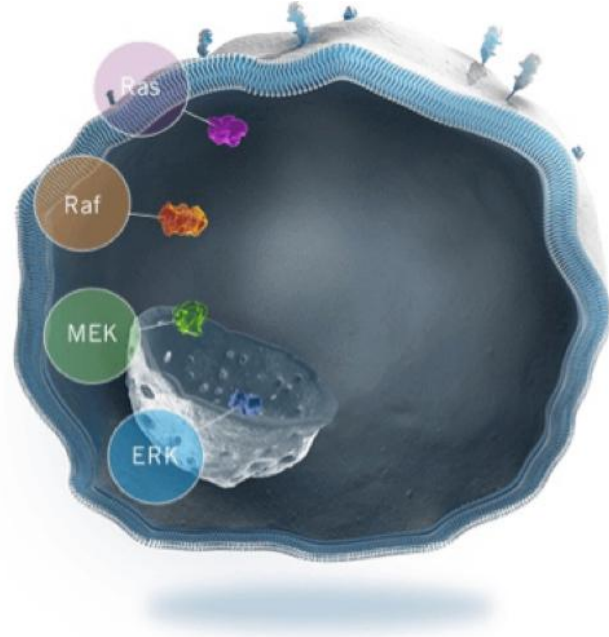
What can be done:

- TRA as drug targets (**Cancer immunotherapy!**)

# Background

The significance of MAPK-pathway in melanoma development:

- Mutated BRAF can lead to abnormal MAPK-signaling  
→ 50% of all melanoma cases



<https://www.genetechonology.com/pathways/cancer-tumor-targets/mapk.html#:~:text=The%20mitogen%20activated%20protein%20kinase,%2C%20cellular%20growth%2C%20and%20survival.&text=Abnormal%20MAPK%20signaling%20may%20lead,proliferation%20and%20resistance%20to%20apoptosis.&text=Research%20into%20the%20MAPK%20pathway,be%20important%20in%20some%20cancers.>



# What are we working with?

WM266-4 human melanoma cell line with the genotype BRAF V600D

Treatment with:

- Trametinib: MEK-Inhibitor
- ERK1/2-Inhibitor
- doxycycline-shERK1: silencing ERK1

Extracted mRNA from cells ->->-> labeled fragmented cRNA, hybridized on microarrays



# Data Description

NUMERICAL DATA: Expression Dataframe

Microarrays, Skin Cancer and Breast Cancer GSE27830

Quantification of the gene expression levels

CATEGORICAL DATA: TRA Vector

Nominal values

-> skin specific TRA gene names

```
[1] "SCGB2A2"      "SCGB1D2"      "KRT1"          "KRT10"         "LOR"
[11] "ALS2CL"       "AP001267.1"   "APCDD1"        "ARHGEF19"      "ARHGEF37"
[21] "CAMSAP3"      "CD44"         "CDC42BPG"      "CENPP"         "CXCL14"
[31] "FAM110A"      "FAM57A"       "FAM83H"        "FBX027"        "FBXW7"
```



# Our Main Objective

Identify **upregulated genes in skin cancer**, compare with TRA data to find out if any **TRA genes match** with our results and has the potential to be a drug target.



## Further questions to answer along the way

After identifying upregulated genes:

- Are our identified genes **mostly from the sun exposure data**?
- In **which chromosome** are the identified upregulated genes mostly localised?
- Are there any **non-skin specific genes** that are upregulated in skin cancer?

Do the **efficacy of the drugs** vary? Comparing the expression intensity from our dataset, connecting our information with the duration and type of therapy used in each chip.





# Organisation

skin cancer and breast cancer parallel

Normalization of  
microarray data

2nd Week of May

Descriptive statistics  
analysis of expression  
levels

3rd-4th Week of May

Building a regression  
model

1st Week of June

Preparing the  
presentation

4th Week of June

1st Week of May

Identify skin-specific  
genes from TRA data

2nd Week of May

Quality control of  
microarrays

4th Week of May

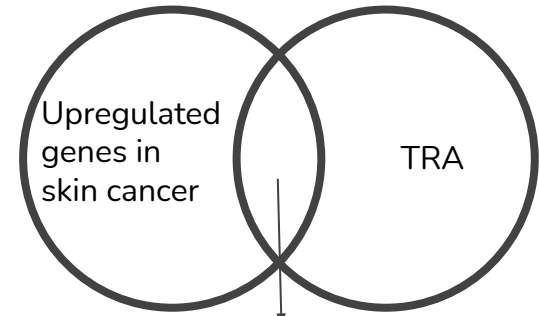
Clustering

2nd- 3rd Week of June

Finishing the report



# Methods



## 1) Analysis with descriptive statistics:

- Heatmaps (Visualization of skin-specific gene expression)
- Barplot (Distribution in chromosomes)
- Venn diagram
- Box plots (Expression of skin-specific genes in skin cancer):
  - Grouped by different treatments & on different time periods
  - Sun VS no sun exposure

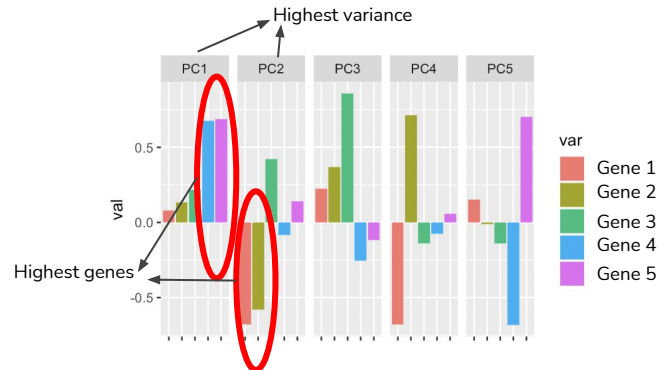
Potential drug targets  
(skin- and **non** skin-specific)

## 2) Clustering: k-means

- Elbow method, silhouette → Optimal amount of clusters
- Observe patterns



# Methods



## 3) Dimension reduction: PCA

- Find the principal components that explain most of the variance of our skin cancer dataset
- Identify genes from these PCs that contribute the most to the variance

## 4) Linear modeling:

- Regression Model
  - Predict relationship of identified genes with drug target genes (ERK, etc.)
  - Example: Expression of non-skin-specific gene used to predict ERK expression
- F-test → Best prediction model



# What did we do until now?

Melanoma microarray  
chip names



- Filter TRA tables -> Human skin-specific TRAs



Normalization of melanoma microarray  
data set



Gene Expression melanoma data frame



Filtering skin-specific TRAs in  
the gene expression melanoma  
data frame

Gene names



	GSM1387513_sherk1- D3a	GSM1387514_sherk1- D3b	GSM1387515_sherk1- D3c	GSM1387525_sherk1- D7a	GSM1387527_sherk1- D7c
A2ML1	5.712456	5.840425	5.822129	5.624177	5.757851
AACS	9.700679	9.577292	9.493689	9.584939	9.575073
AADACL2	5.121151	5.200550	5.171339	5.215717	5.208109
ABCA12	5.758000	5.651394	5.800670	5.742912	5.720462
ABHD12B	5.500152	5.595327	5.463102	5.655431	5.693763
ABHD5	8.863773	8.782844	8.585597	9.031559	8.810857
ACAP3	7.086765	7.164285	7.056074	7.039174	7.282637
ACER1	6.375048	6.443568	6.299403	6.277664	6.364174
ACVR2A	9.783693	10.078800	9.801101	9.907579	9.795192
ADAM15	8.243245	8.344145	8.270667	8.240065	8.204795
ADGRF2	5.942704	5.845375	5.860404	5.860404	5.829077
ADGRF4	5.806937	5.718587	5.629339	5.829695	5.662445
ADRB2	6.913961	7.224369	6.972564	7.592311	7.701687
AHNAK	8.234221	8.214370	8.047431	8.293025	8.129481
AJUBA	8.668198	8.668334	8.826362	8.897877	8.956261





# Breast cancer data set

**Question:** Are there any up-regulated skin specific genes in breast cancer?

→ Possible drug target

**Plan:**

- Normalize data
- Skin specific TRAs in breast cancer vs melanoma
  - Examine overall (di)similarity of gene expression patterns
    - Box plots
    - Heatmaps
    - Distributions
    - Clustering etc.



# Literature

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