PROJECT PROPOSAL

The role of tissue-specific antigens in different cancer entities
KALLIKREIN GENES

Anouk Dupé, Dustin Schilling, David Eckey, Maria Yemane
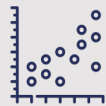
Supervisor: Dr. Maria Dinkelacker
Tutor: Nils Mechtel

Agenda

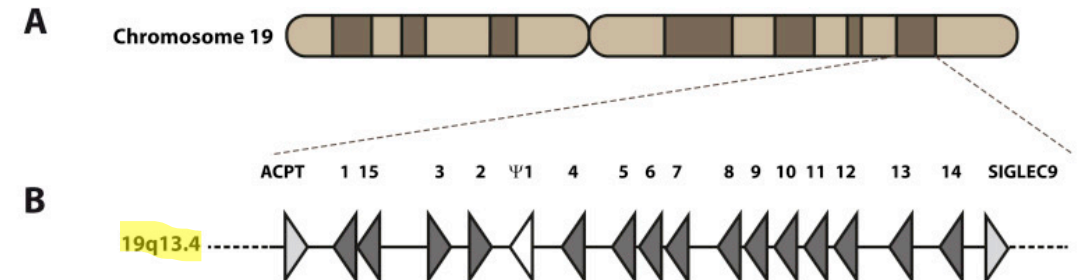|		
	Biological background	01
	Data sets and plot example	02
	Milestones	03
	Team organization	04

Introduction to kallikreins

- Family of trypsin-like serine proteases

- Cluster of 15 genes → Coexpressed

- Expression regulated by steroid hormones

- Secreted proteases
  - Involved in regulation of blood pressure, tissue remodelling, etc.

Kalinska et al. 2015

Role of kallikreins in cancer

- Expression altered in hormone-related cancer
  - Up- and Downregulation

- hK proteins promote or inhibit cacogenesis
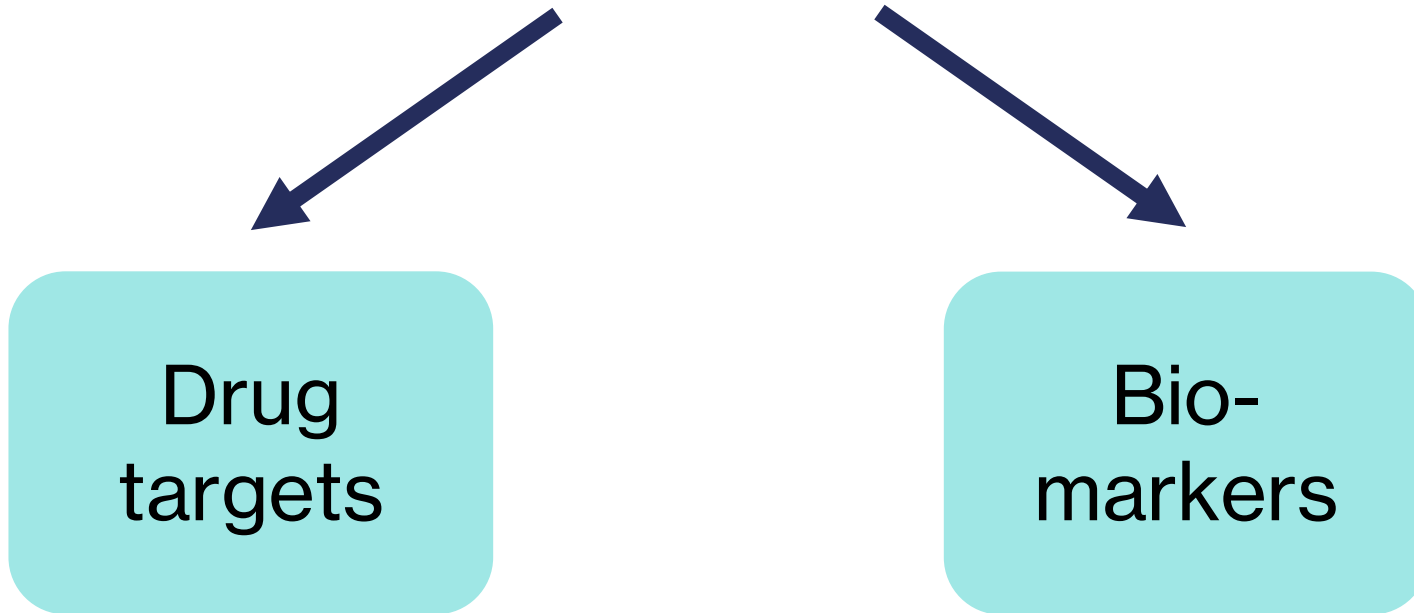
Drug targets

Bio-markers

Cancer data sets

small cell lung cancer
GSE149507

breast cancer
GSE65216

primary breast cancer
GSE27830

6 patients:
-> carcinoma tissue
-> normal tissue
=> 12 samples

=> 20 samples
Her2, LumA,
LumB, TNBC

=> 10 samples

(1) Cai et al. 2021
(2) Maire et al. 2013
(3) Nagel et al. 2012

Cancer data sets

**small cell
lung cancer**
GSE149507

**breast
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GSE65216

**primary
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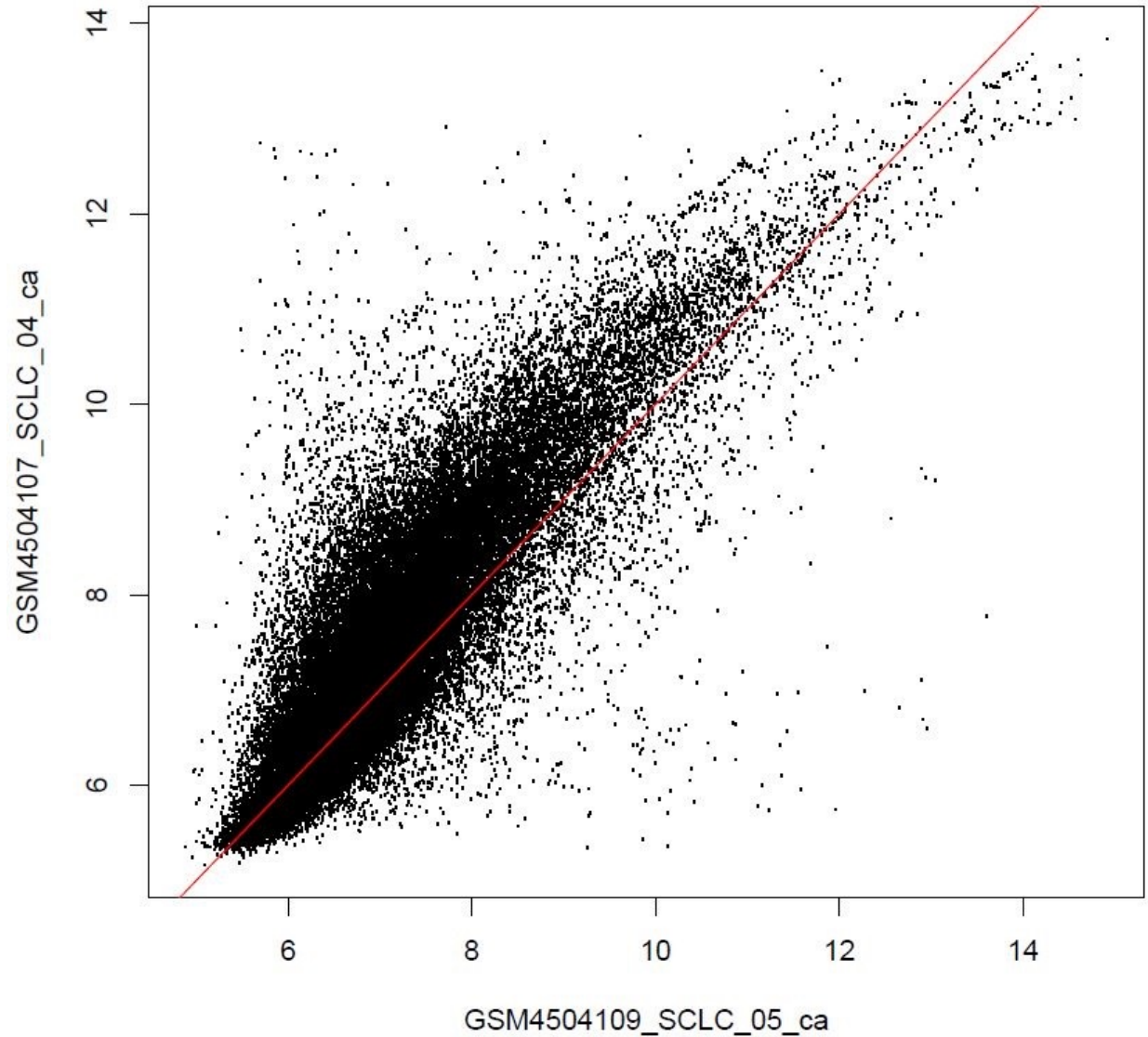**overall 73 unique KLK transcripts**
➡ TRAs: 27 KLK transcripts

(1) Cai et al. 2021
(2) Maire et al. 2013
(3) Nagel et al. 2012

Quality control

lung cancer data set:
-> broken chip

scatterplot of probe GSM4504109_SCLC_05_ca and GSM4504107_SCLC_04_ca
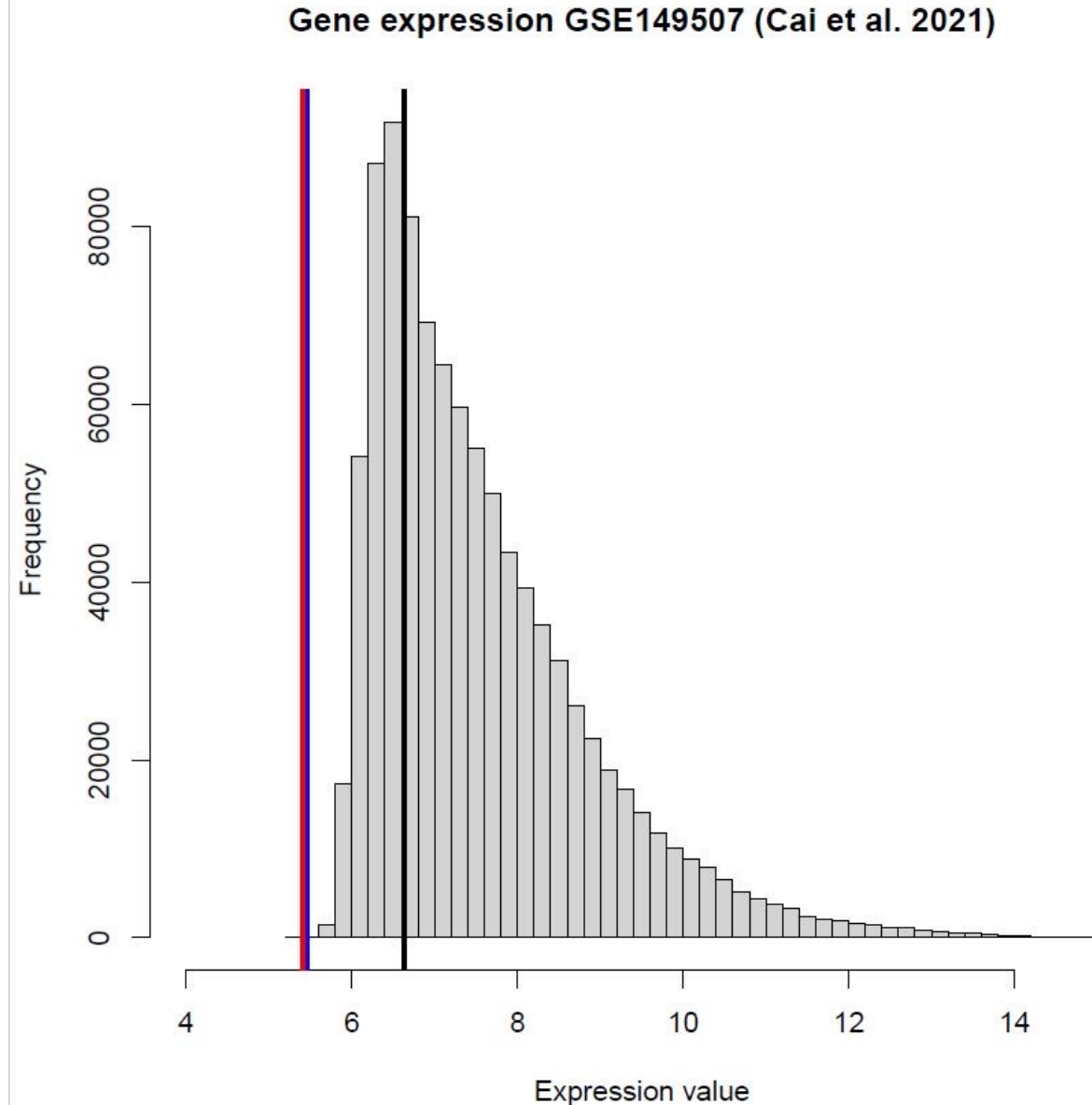
Small cell lung cancer
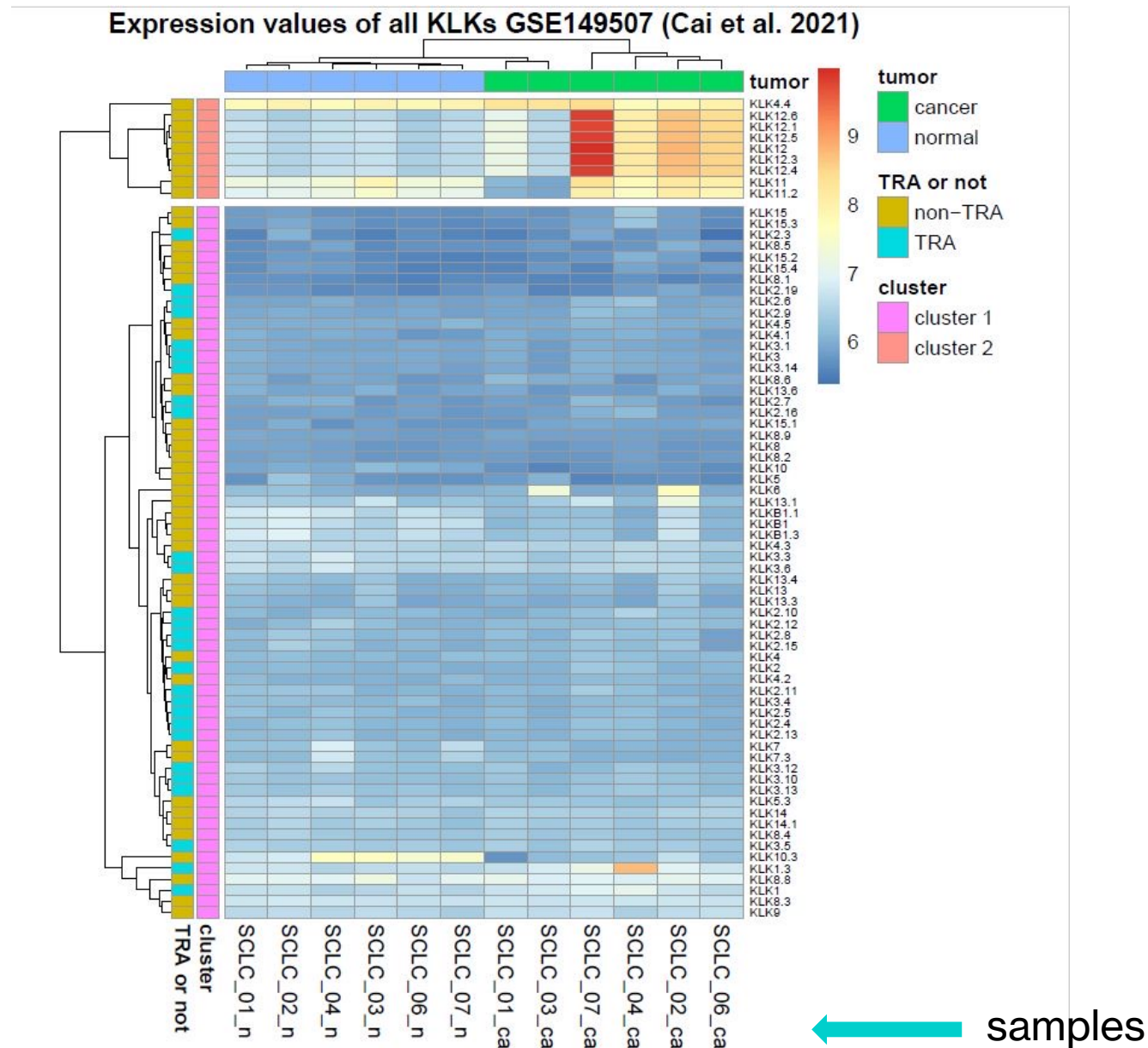
Black: Median all genes
Blue: Median all KLKs
Red: Median TRA KLKs

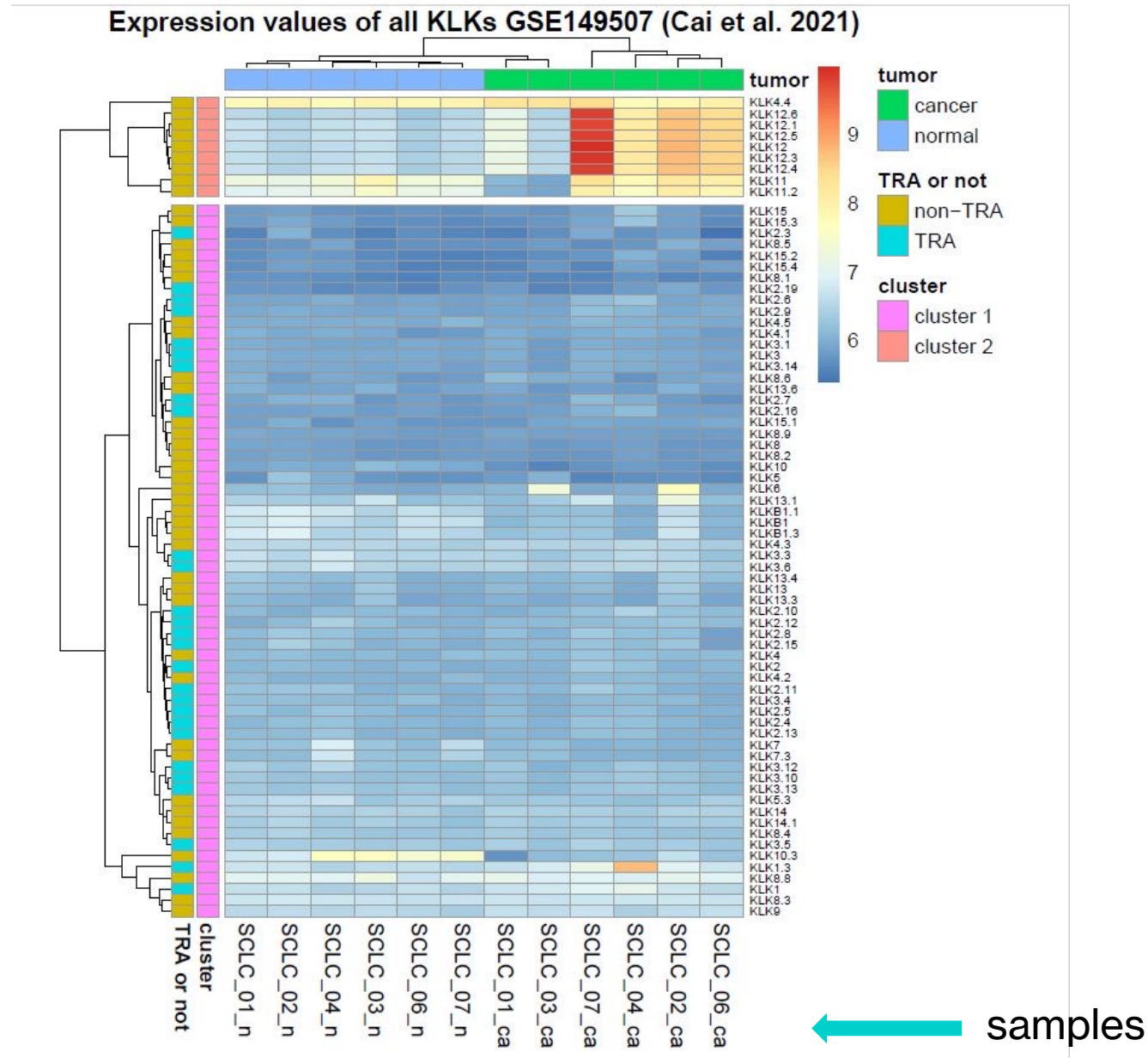Log2 gene expression value

Low expression of (TRA) KLKs

Gene expression GSE149507 (Cai et al. 2021)

Exploratory analysis

Expression values of all KLKs GSE149507 (Cai et al. 2021)

samples

Exploratory analysis

Cluster

→ starting point

for further analysis

Expression values of all KLKs GSE149507 (Cai et al. 2021)

samples

Main goal

-> which kallikrein genes are TRAs?
-> gene expression clusters specific for
cancer type?
-> target for cancer therapy?

Milestones

MILESTONE 01

Filter lung- , breast- and rawdataset for kallikrein genes and determine which of them are TRAs

PCA
K means

20.06.21

MILESTONE 03

Provide statistical prove by testing for significance in obtained values from MS 02.

29.05.21   Scan

MILESTONE 02

Screening for expression patterns in datasets - KLKs, TRAs – PCA to determine most relevant genes in different entities.

30.06.21   T Test

Gantt Chart

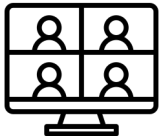|	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Project start		▲ 21.04.2021												
Exploratory analysis														
Project proposal					▲ 12.05.2021									
Scan														
PCA & K means														
Statistical test														
Final presentation														
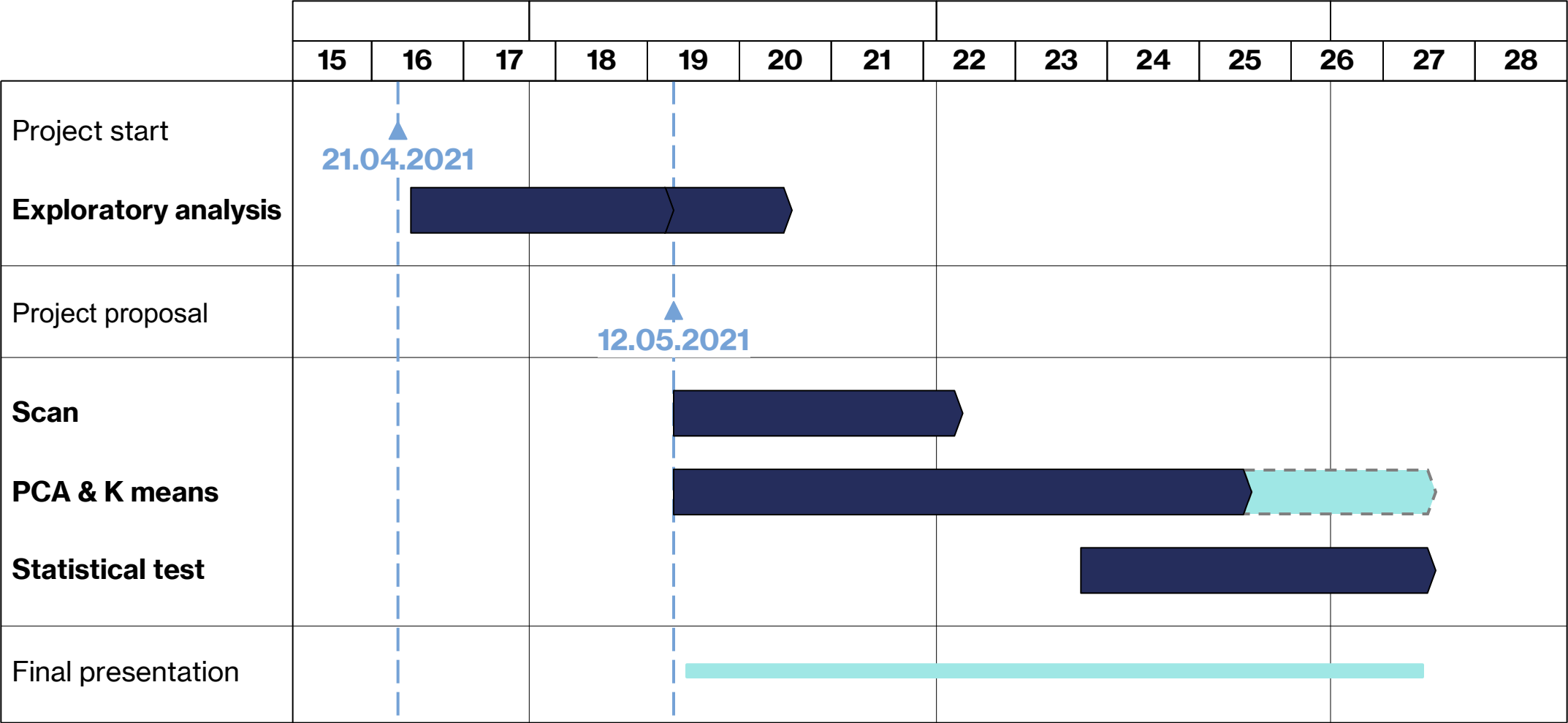
Teamwork aspect

Communication tool: WhatsApp

Jour Fix: monday, 5 pm

Debrief meeting after tutorial

Calls via Discord

Project manangement tool: Notion

BioInfo Project

Jour Fix: montags, 17 Uhr (Discord)

Project proposal: **12.05.21**

Programm: **R Studio**

📎 Aufgabenübersicht.pdf 61.7KB

Carl: Data Analysis – MoBi SS2021

Dropbox Dinkelacker (TRA Übersicht+Paper)

Dropbox Dinkelacker (TRA Daten)

Dropbox Dinkelacker (R Course)

Type '/' for commands

🍇 Paper Zusammenfassung

🥩 Plan Präsentation

🎬 Fragen fürs Tut

🏅 Fragestellungen
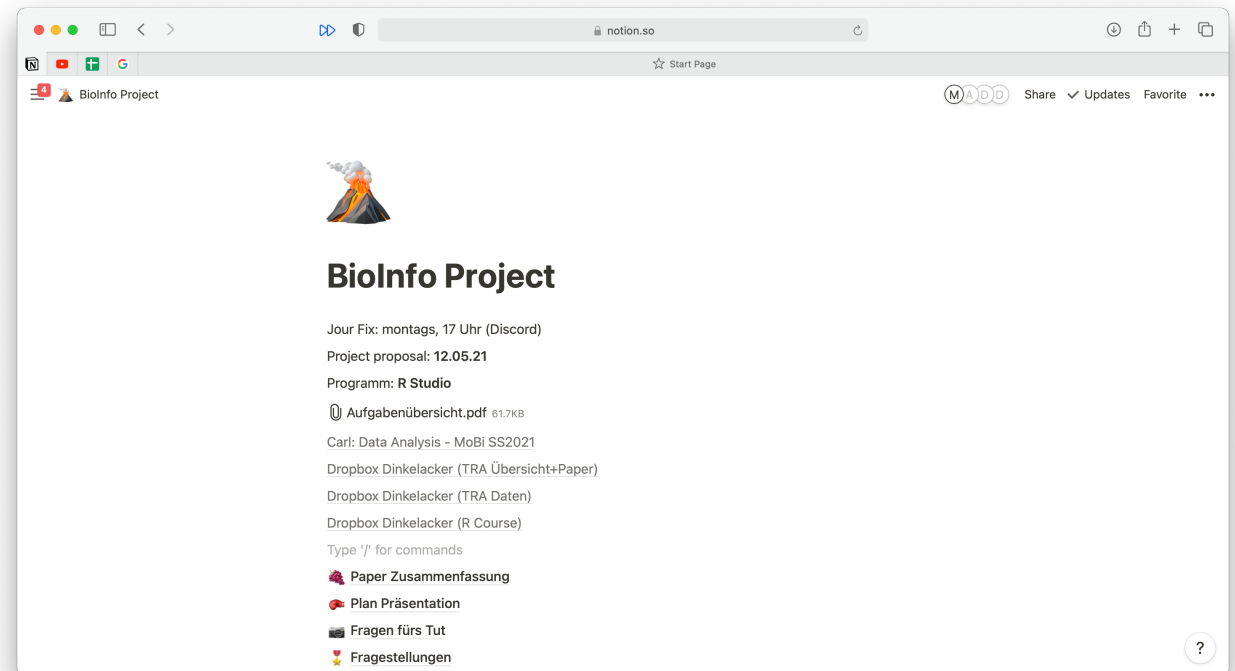
Questions?

Literature

- Cai et al., 2021: Cell-autonomous immune gene expression is repressed in pulmonary neuroendocrine cells and small cell lung cancer.
- Maire et al., 2013: Polo-like kinase 1: a potential therapeutic option in combination with conventional chemotherapy for the management of patients with triple-negative breast cancer.
- Nagel et al., 2012: Gene expression profiling assigns CHEK2 1100delC breast cancers to the luminal intrinsic subtypes.
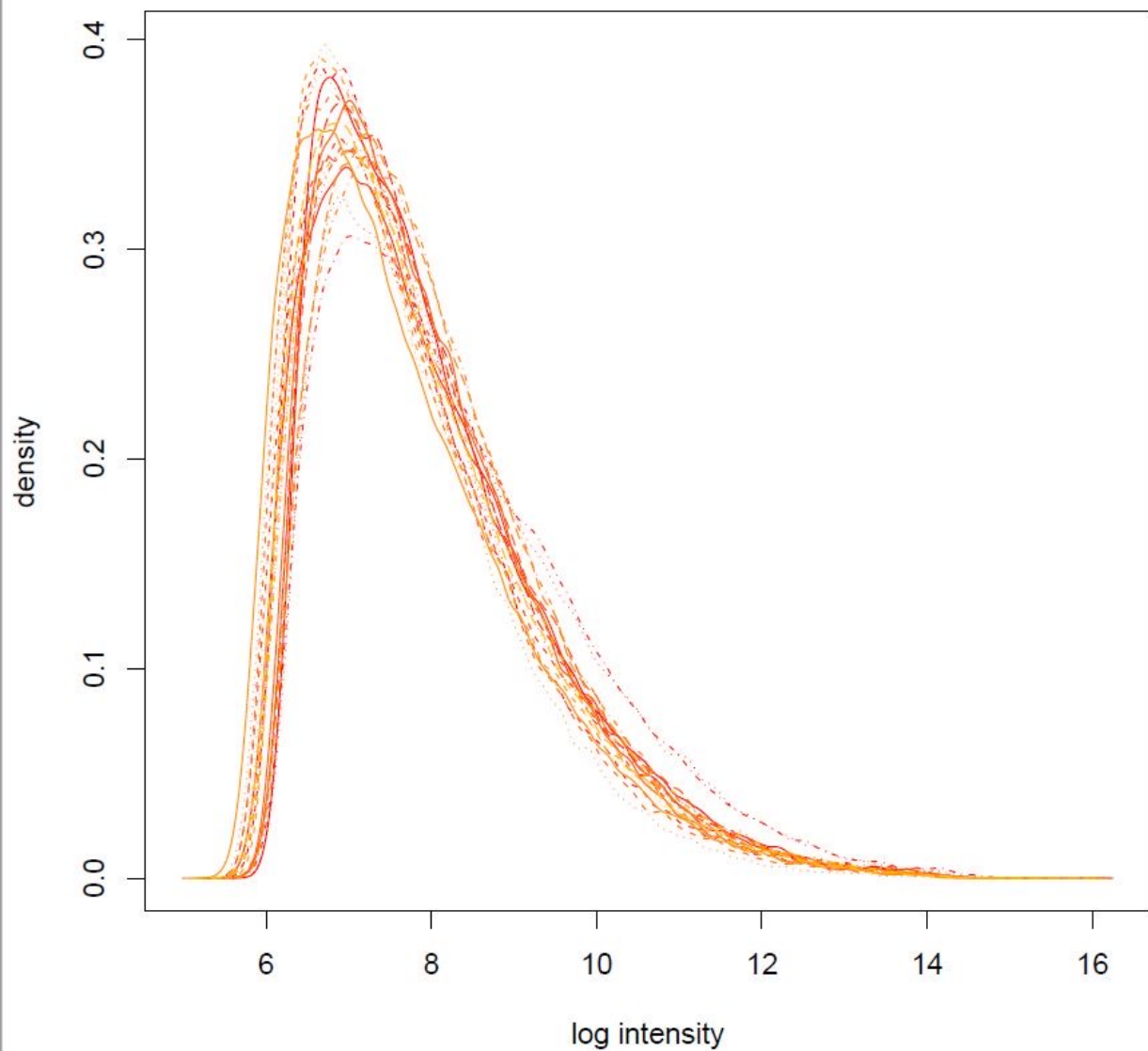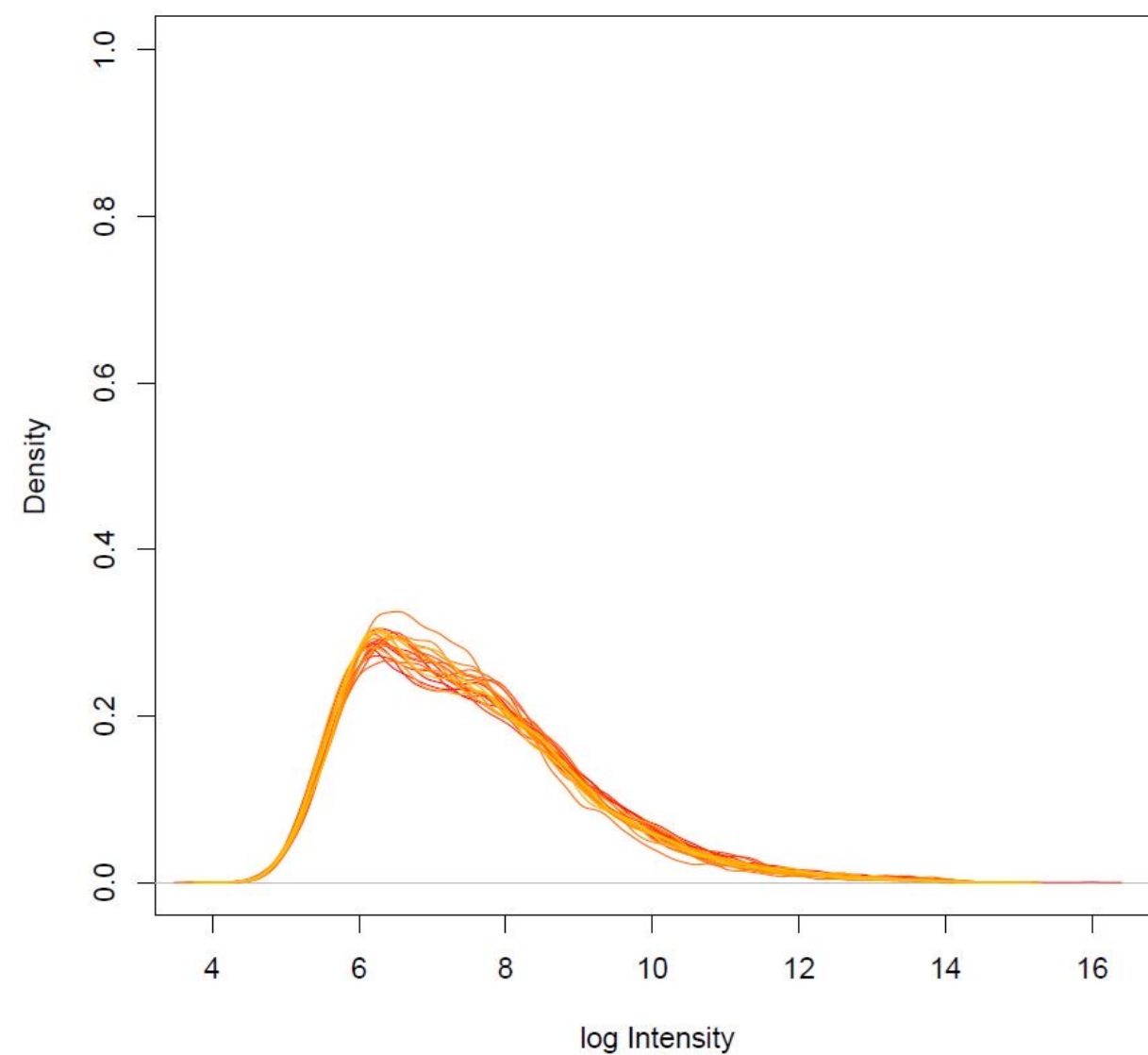
Gene expression GSE149507 (Cai et al. 2021)
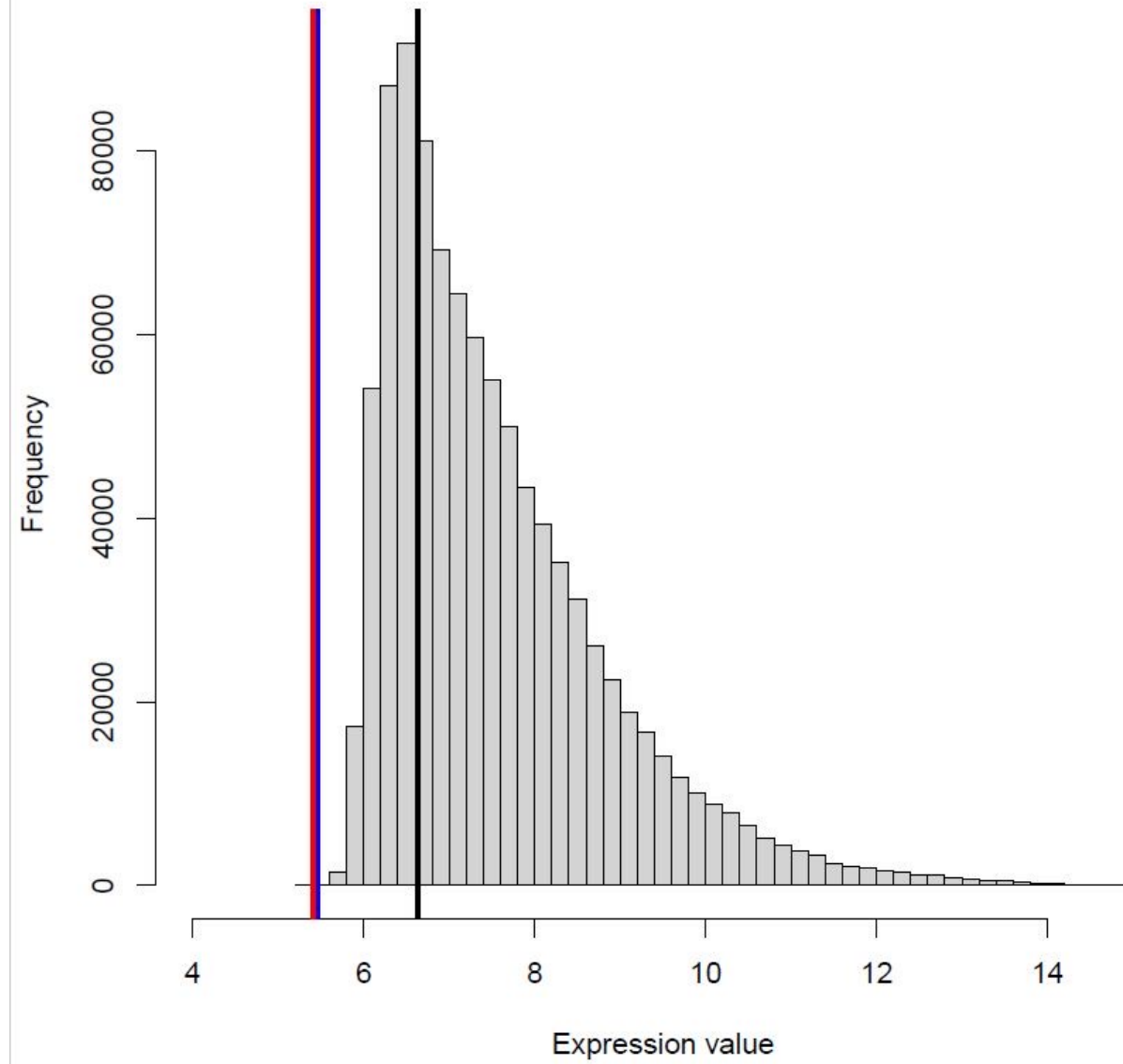
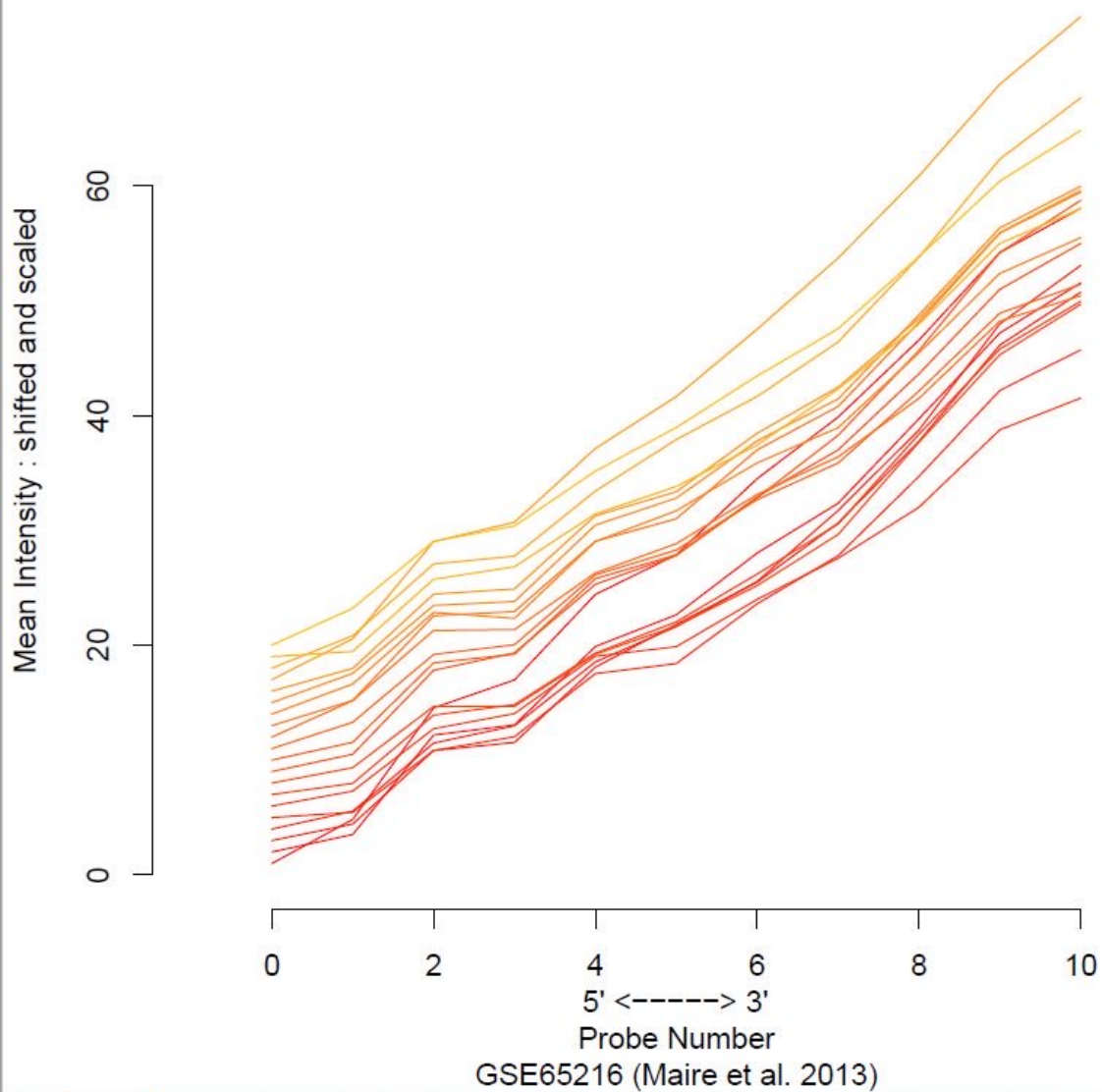**Gene expression GSE27830 (Nagel et al. 2021)**
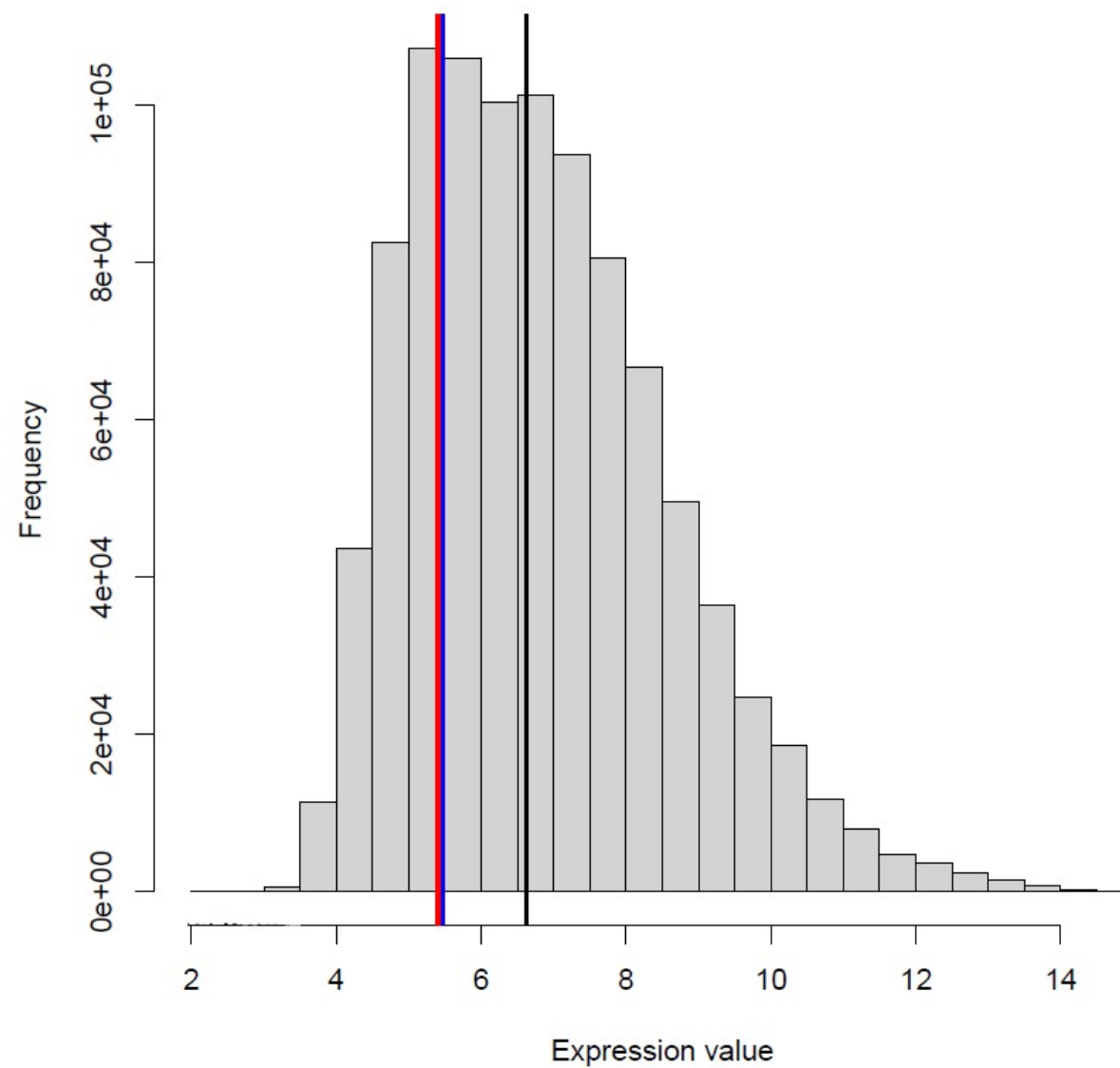
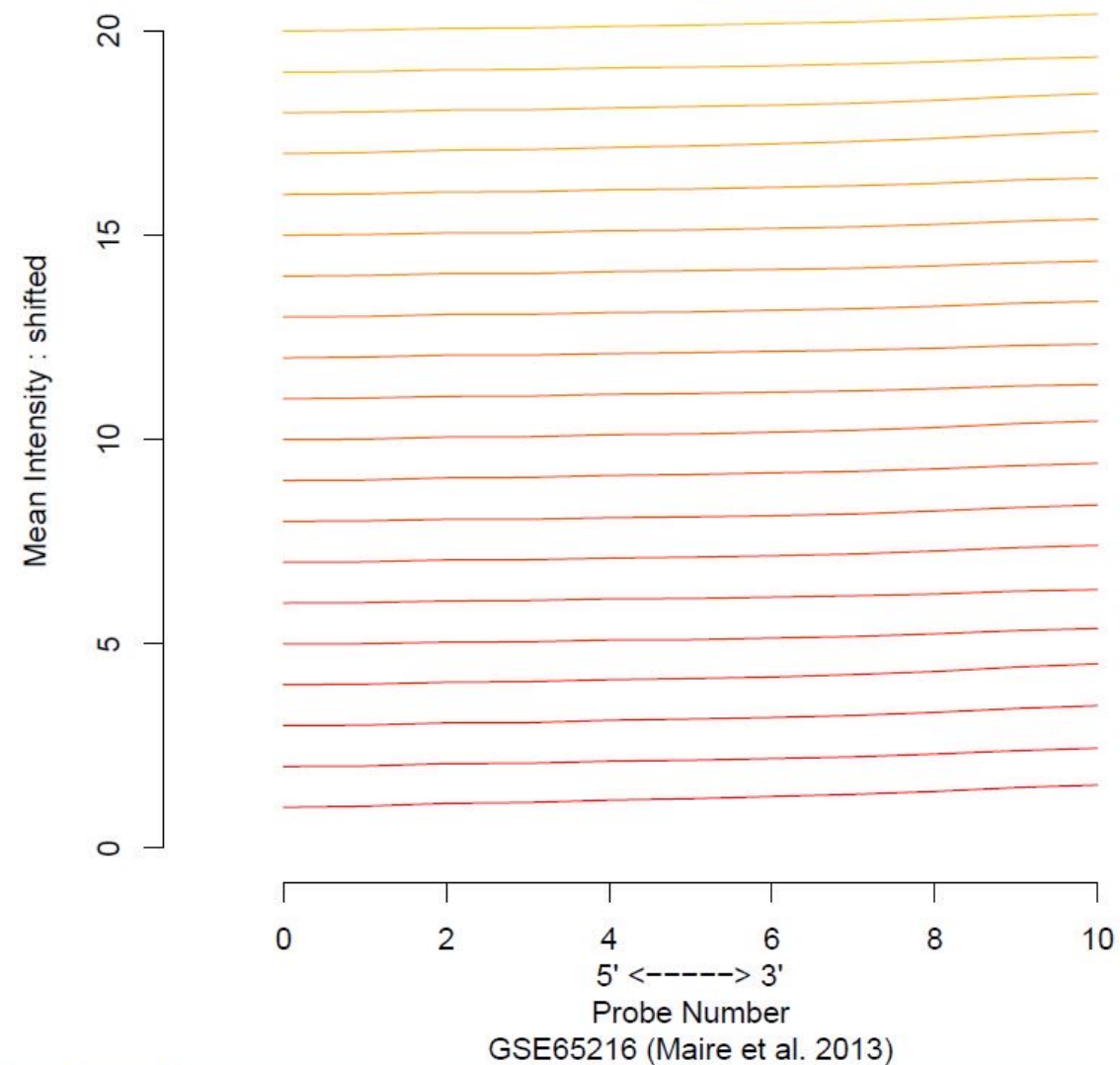GSE65216 (Maire et al. 2013) density function before normalization

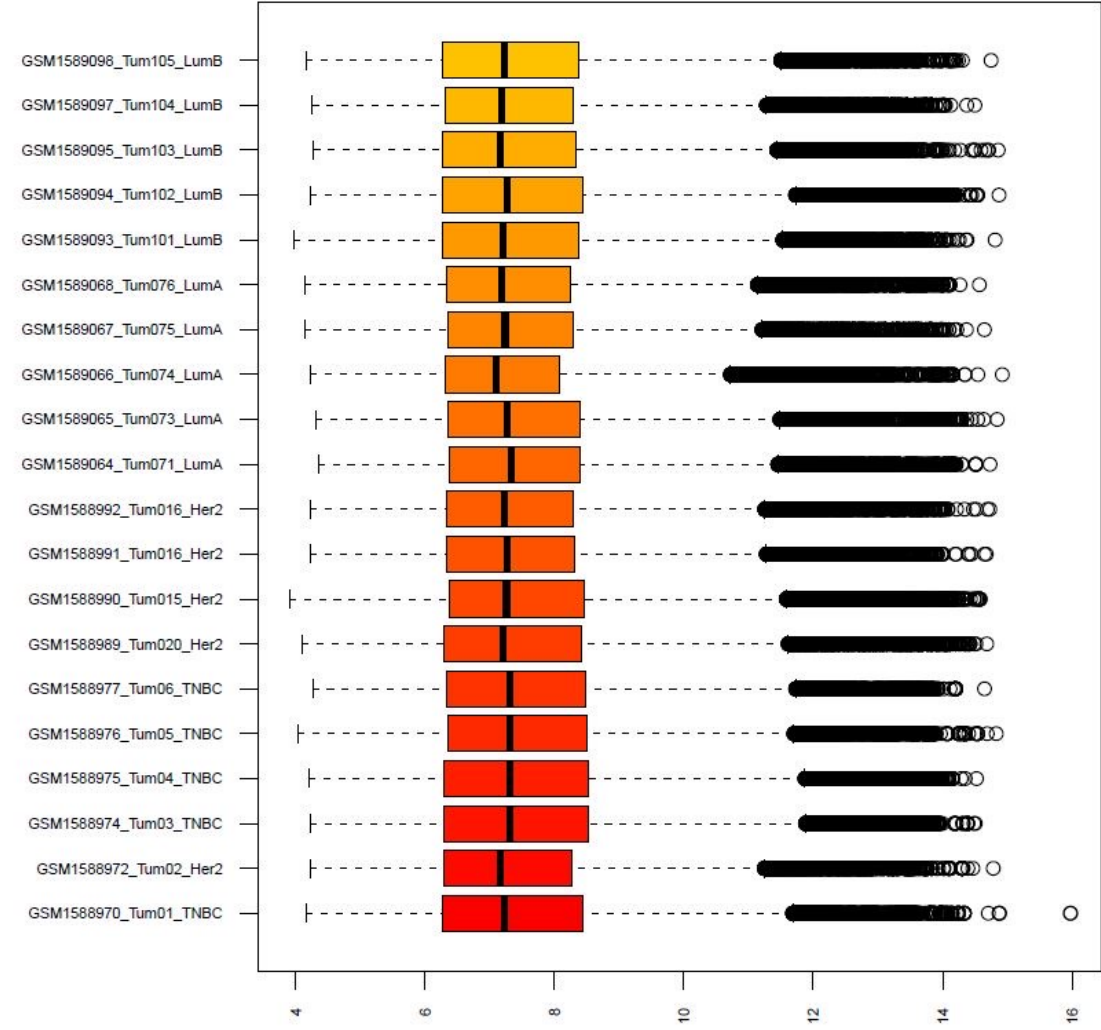GSE65216 (Maire et al. 2013) density function after normalization

RNA degradation plot

Mean Intensity : shifted and scaled

5' <-----> 3'
Probe Number
GSE65216 (Maire et al. 2013)

RNA degradation plot

Mean Intensity : shifted

5' <-----> 3'
Probe Number
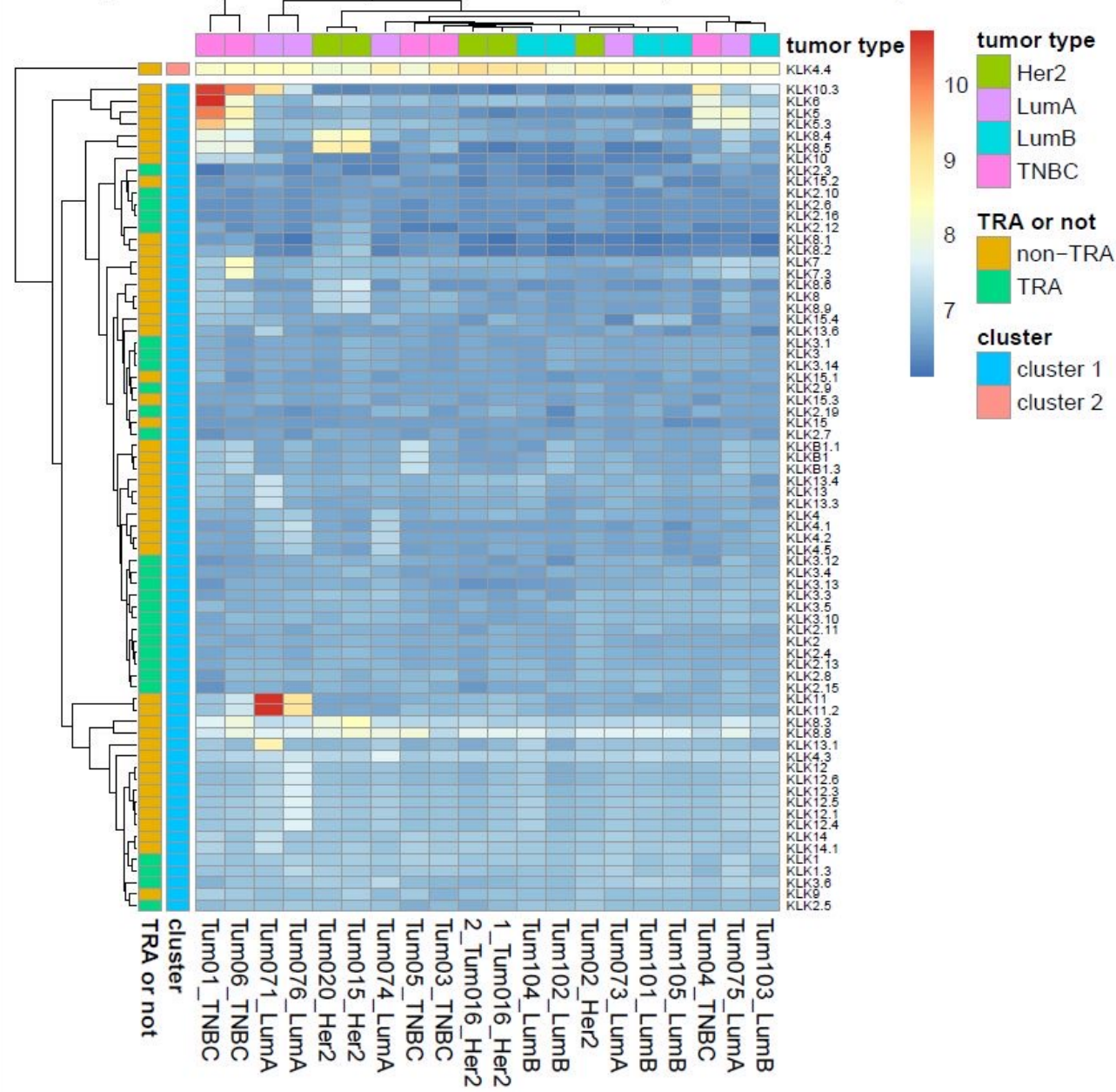GSE65216 (Maire et al. 2013)

GSE65216 (Maire et al. 2013) gene expression after normalization

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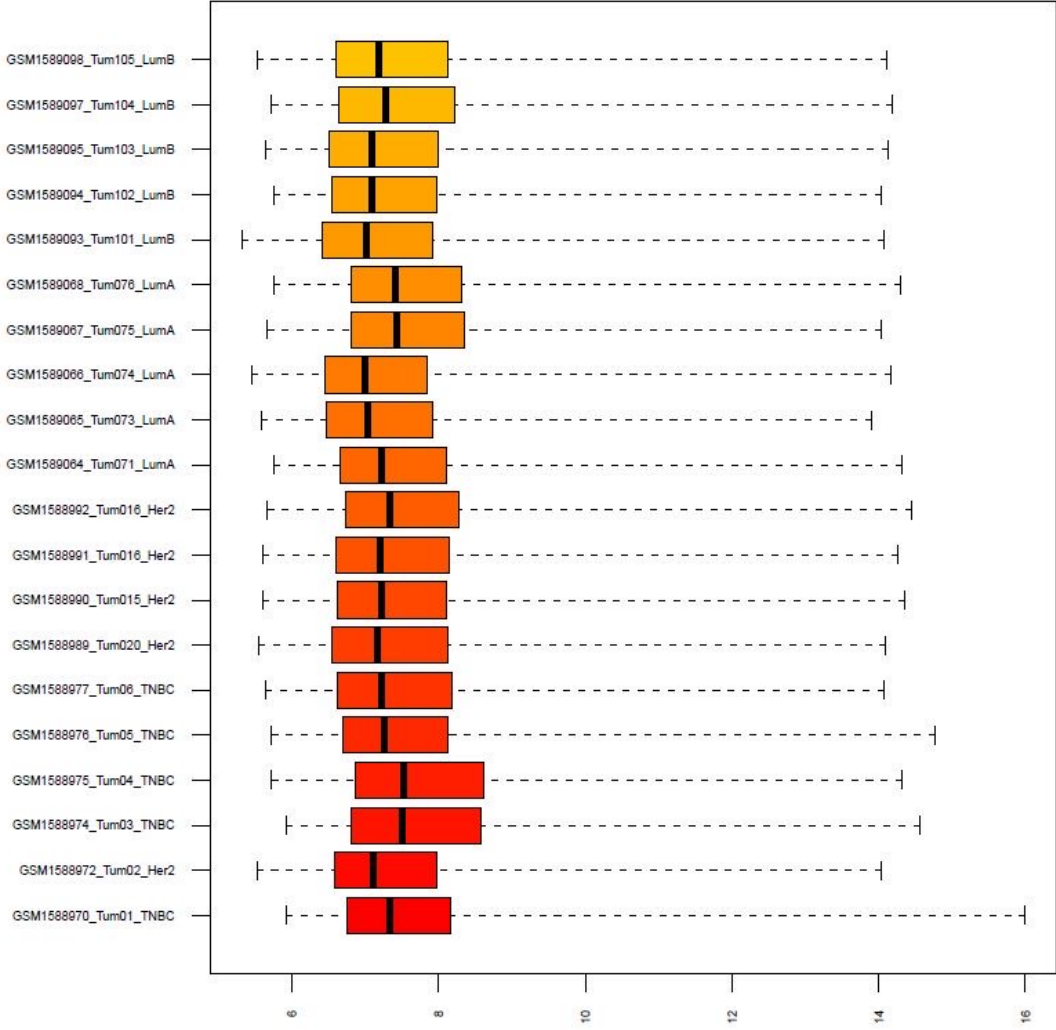
Expression values of all KLKs GSE65216 (Maire et al. 2013)

Expression values of all KLKs GSE27830 (Nagel et al. 2012)