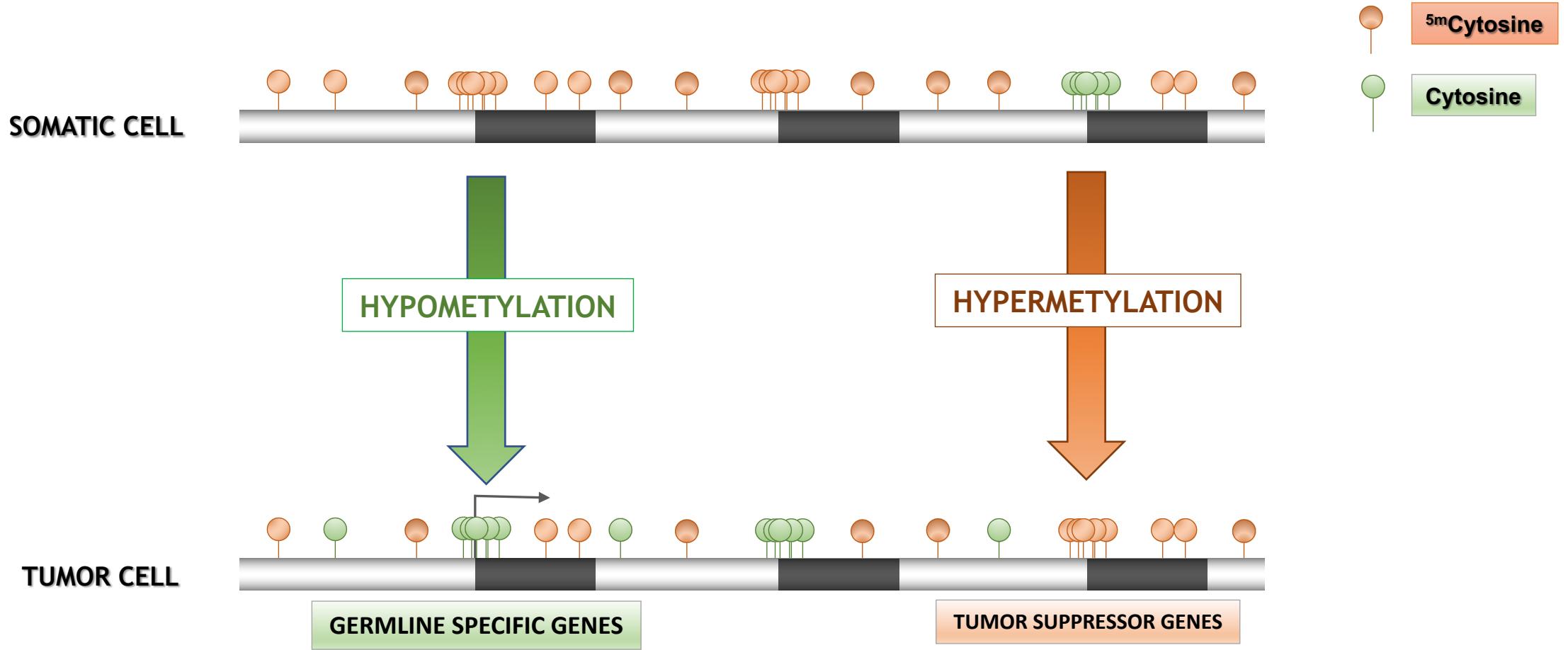


# Genome-wide approach to identify transcripts induced by DNA demethylation in tumor cells

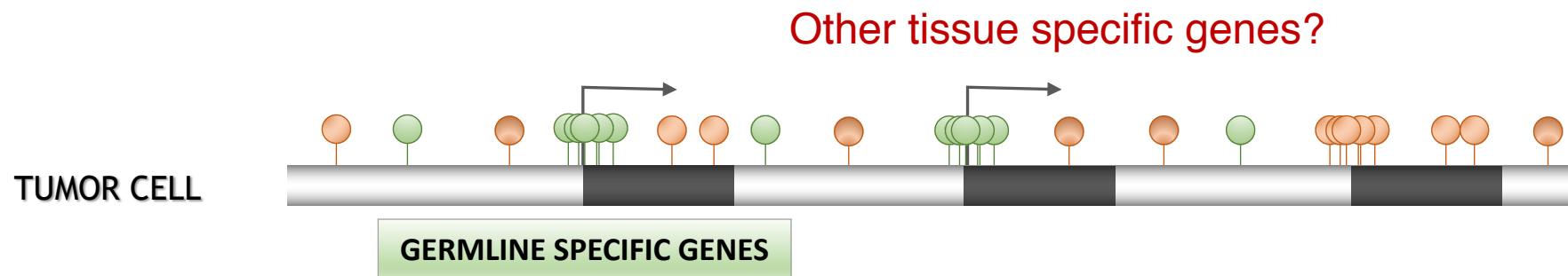
Axelle Loriot  
Computational Biology and Bioinformatics  
de Duve Institute

# Methylation profiles are profoundly altered in cancer cells

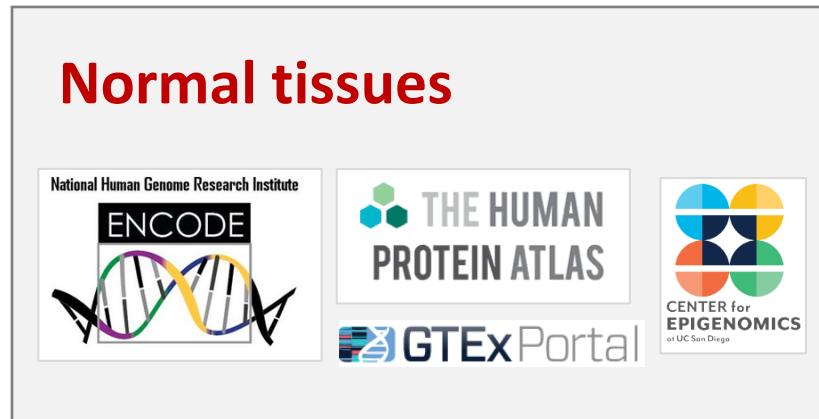
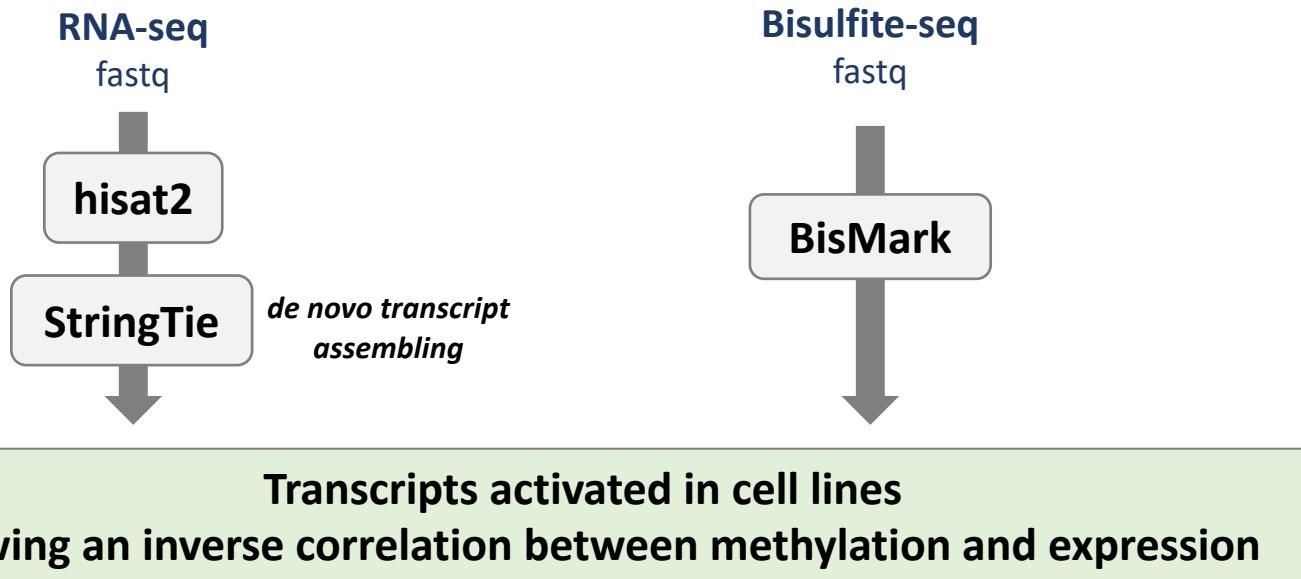
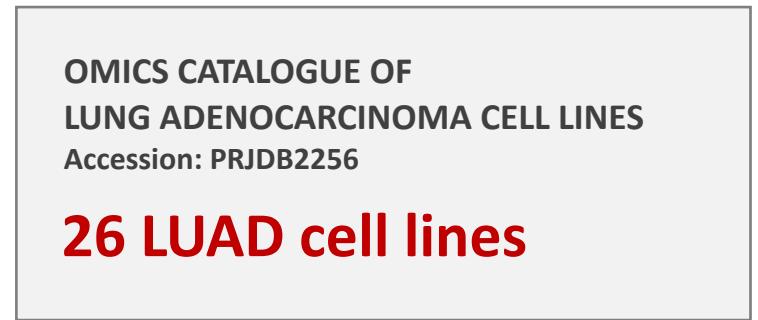


## Genome-wide approach to uncover the set of transcripts activated by DNA demethylation in tumors

- Other tissue specific genes reactivated by demethylation in tumors ?
- Tumor specific transcripts could be isoforms using demethylated alternative promoters

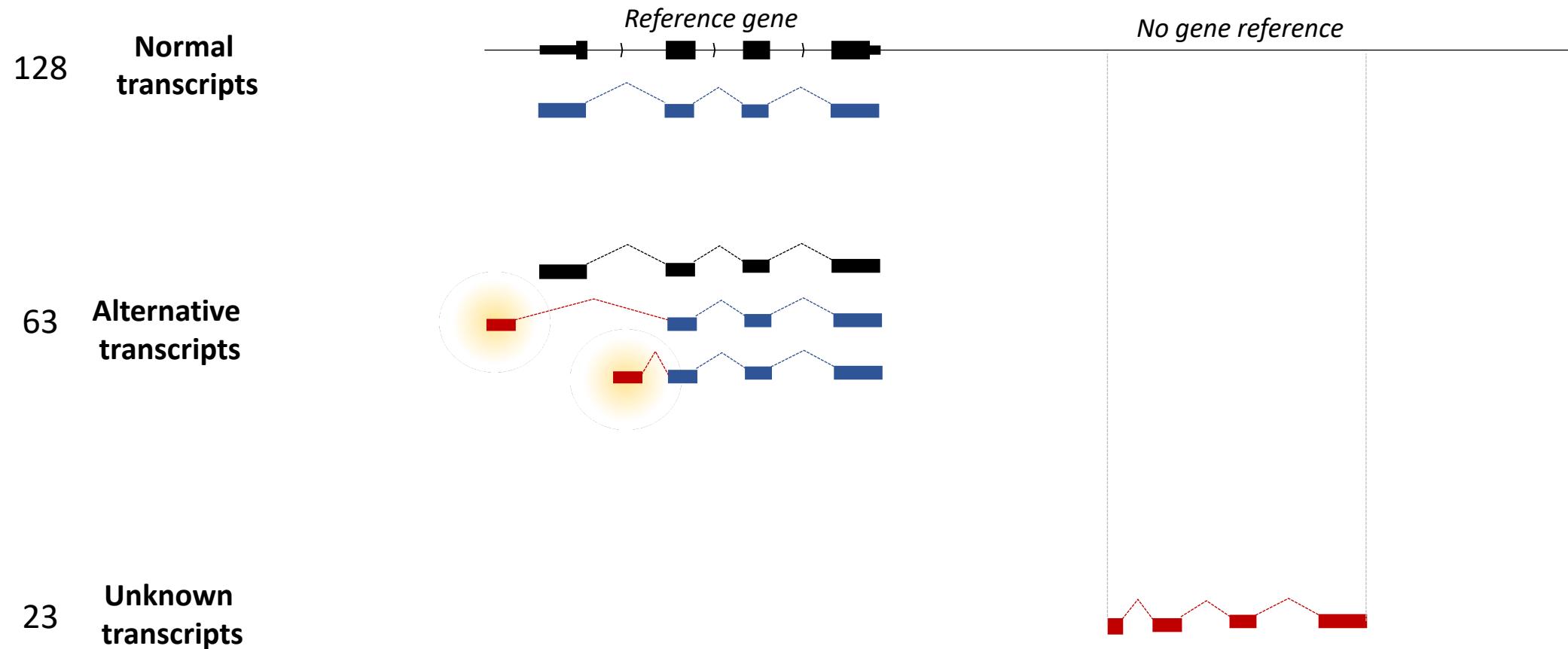


# METHODOLOGY



- Tissue specificity analysis
- Methylation profile analysis

# 214 transcripts identified



# AGO1: an example of alternative transcript activated by demethylation

128

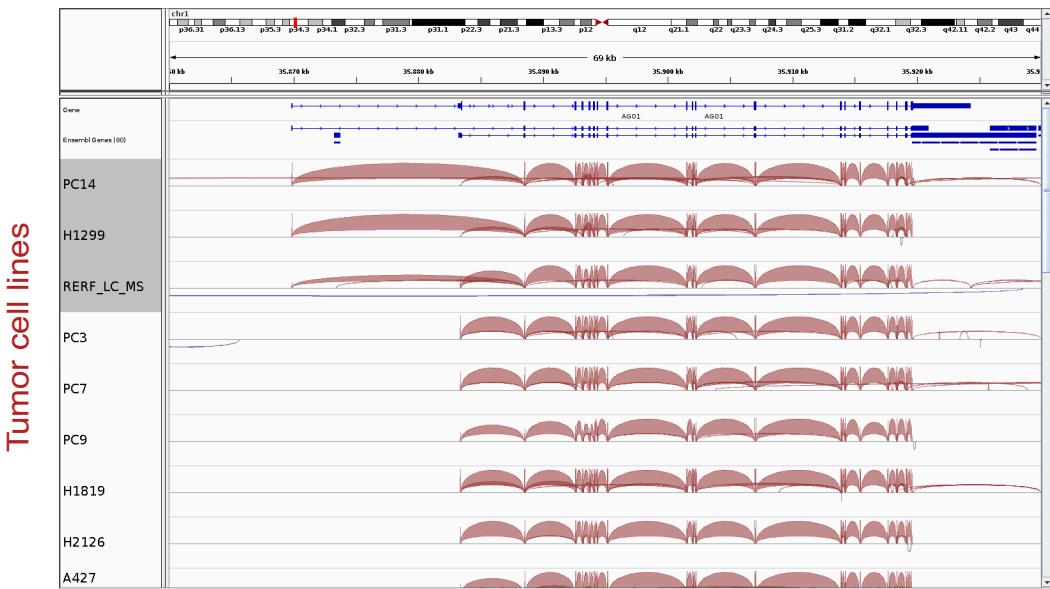
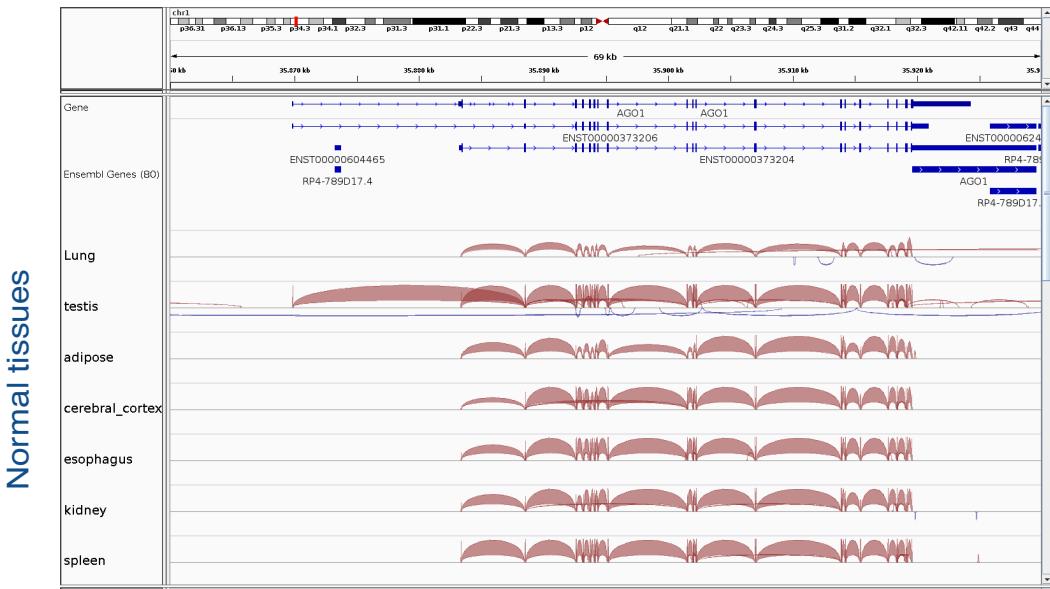
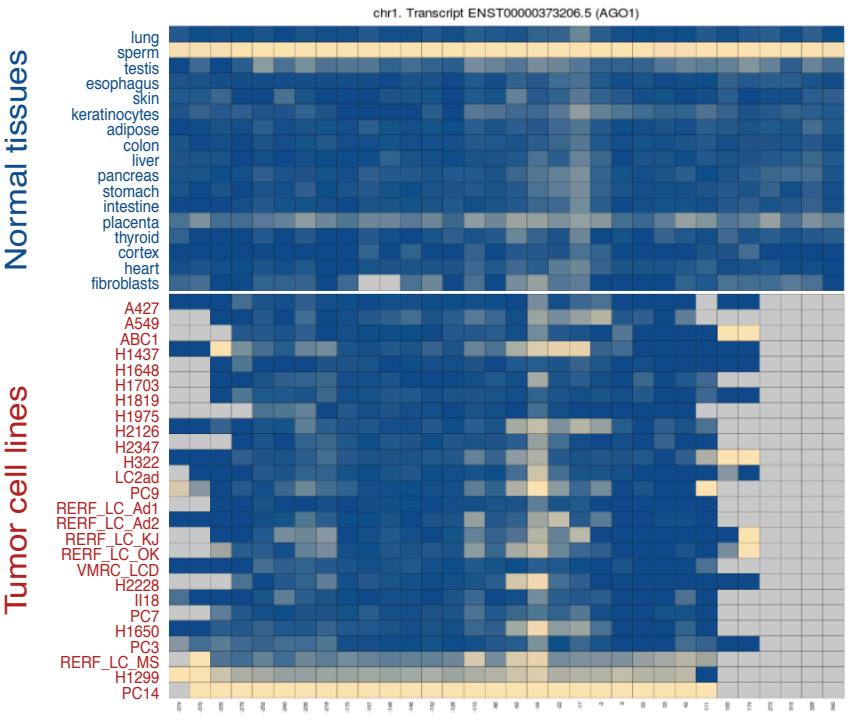
Normal transcripts

63

Alternative transcripts

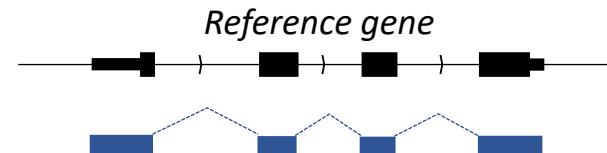
23

Unknown transcripts

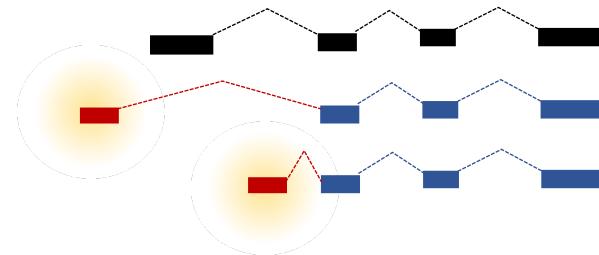


# Tissue specificity

128      **Normal transcripts**



63      **Alternative transcripts**



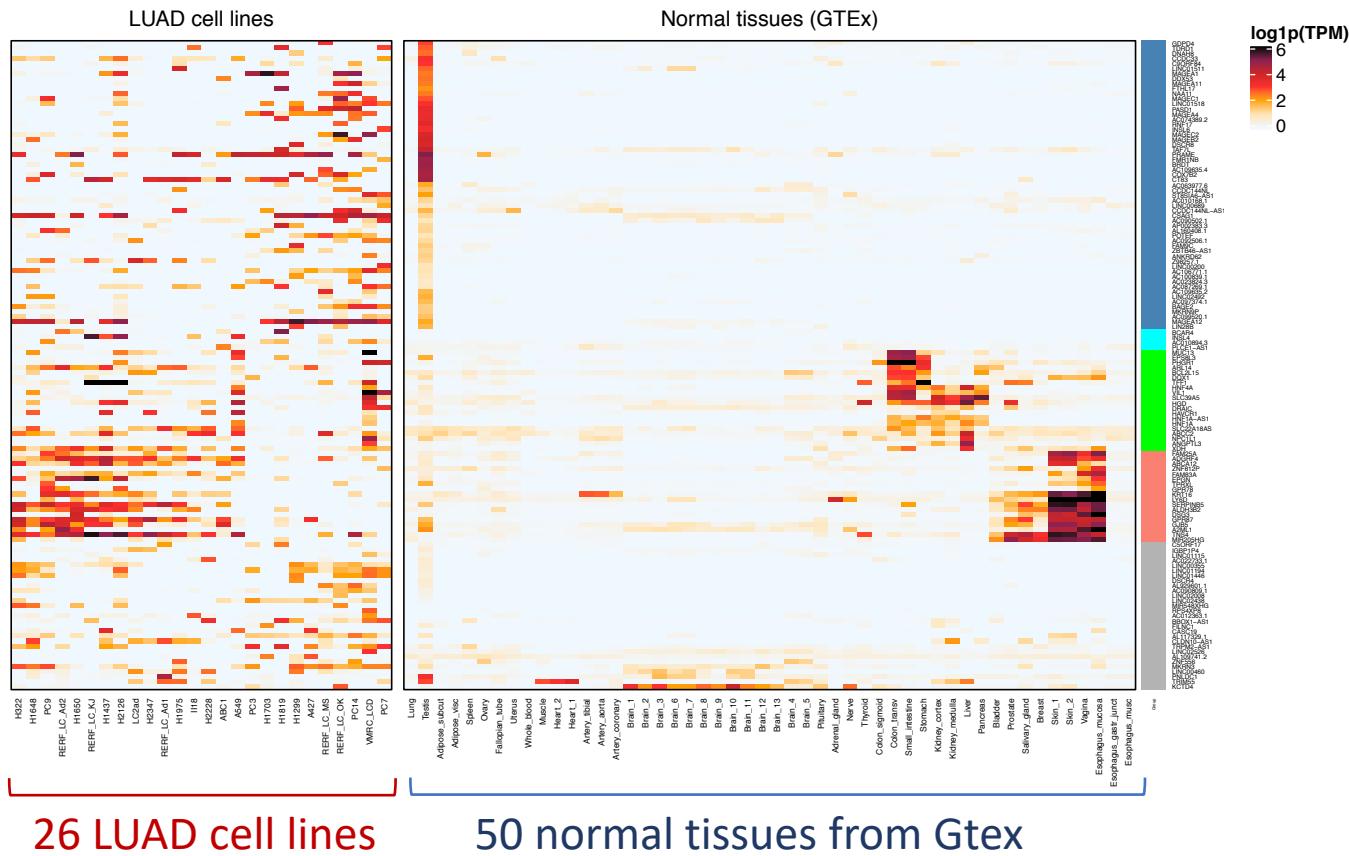
23      **Unknown transcripts**



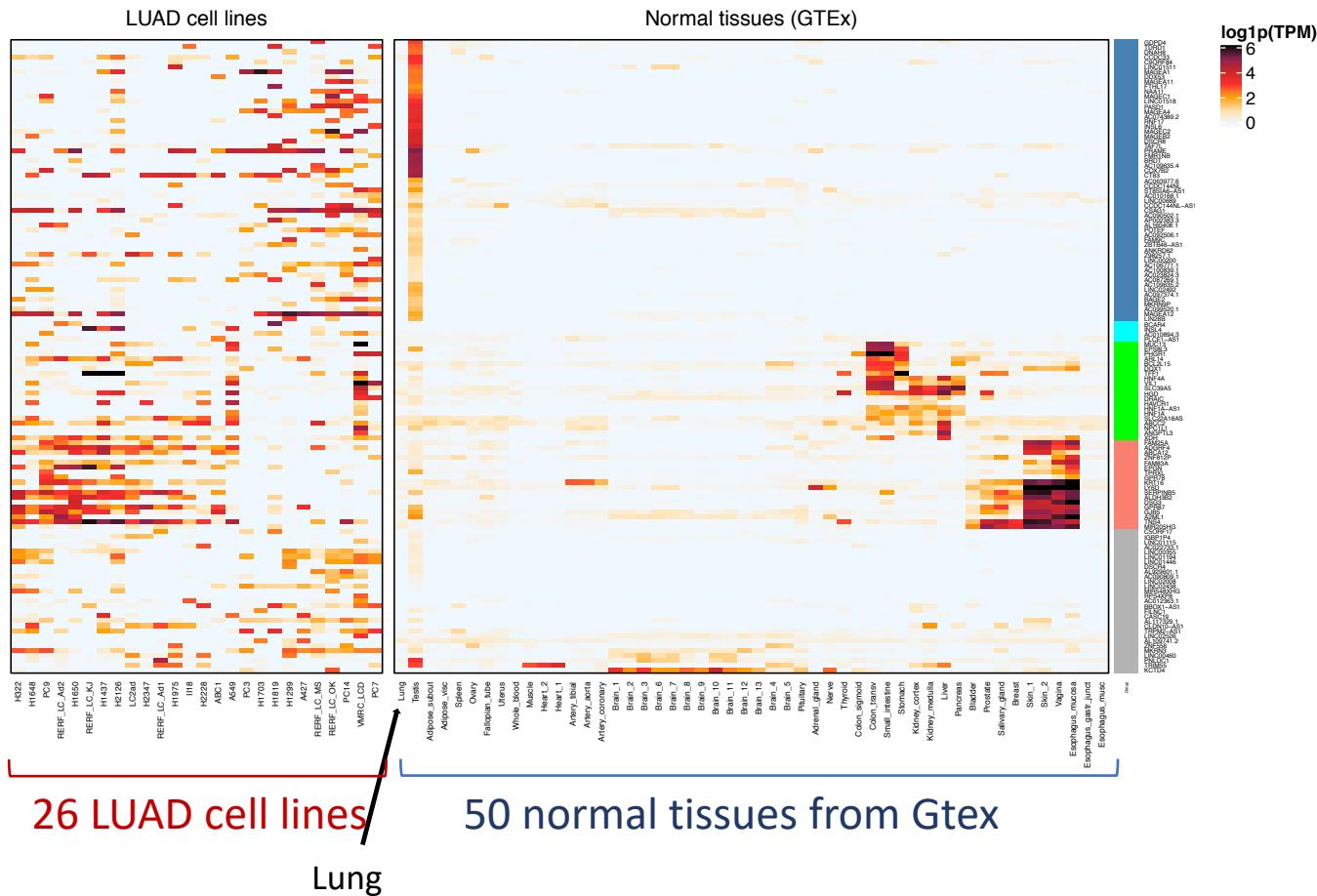
RNAseq of 53 normal tissues  
Multiple samples per tissues  
Processed data only

=> Expression values are given at **Gene level**

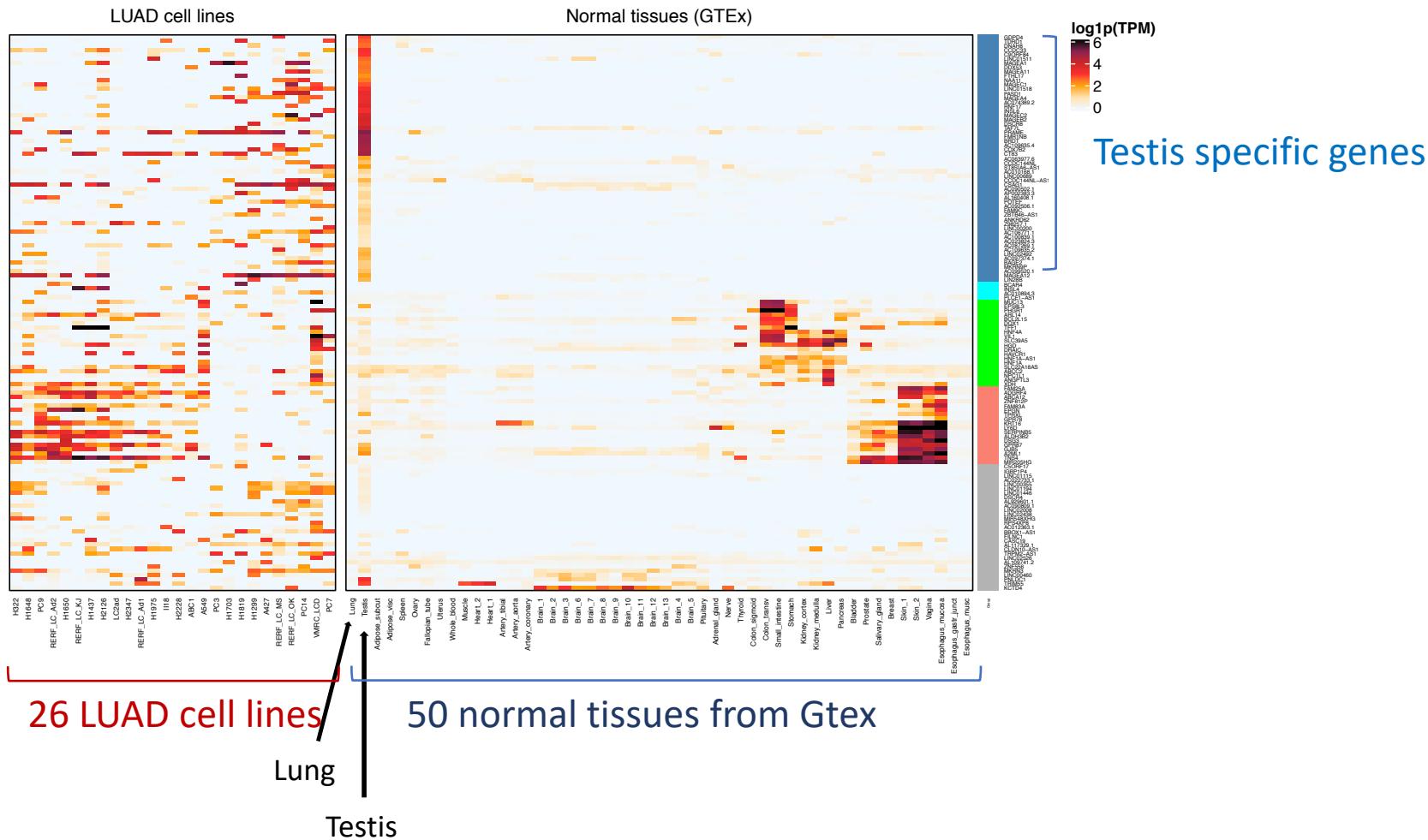
# Tissue specificity



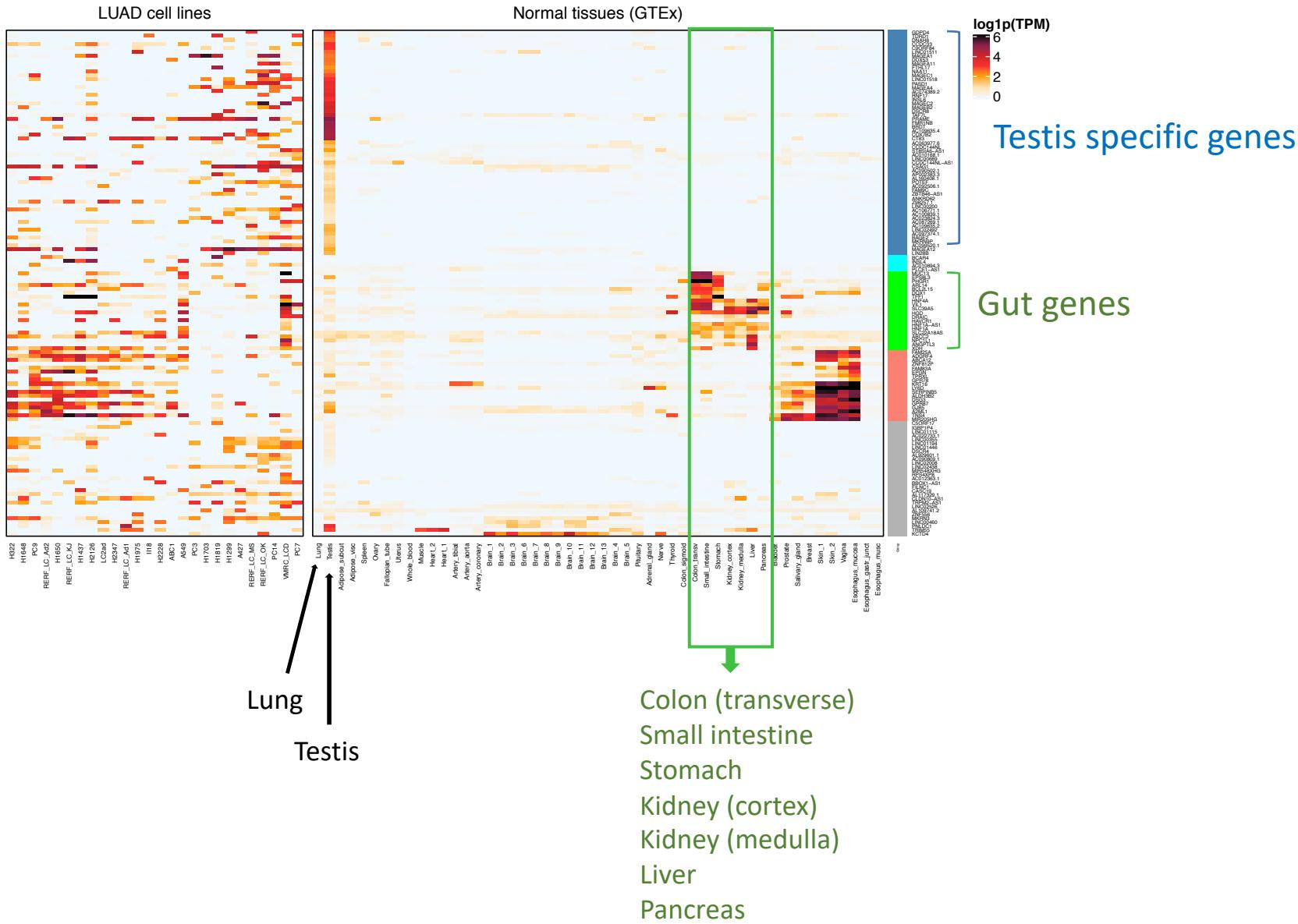
# Tissue specificity



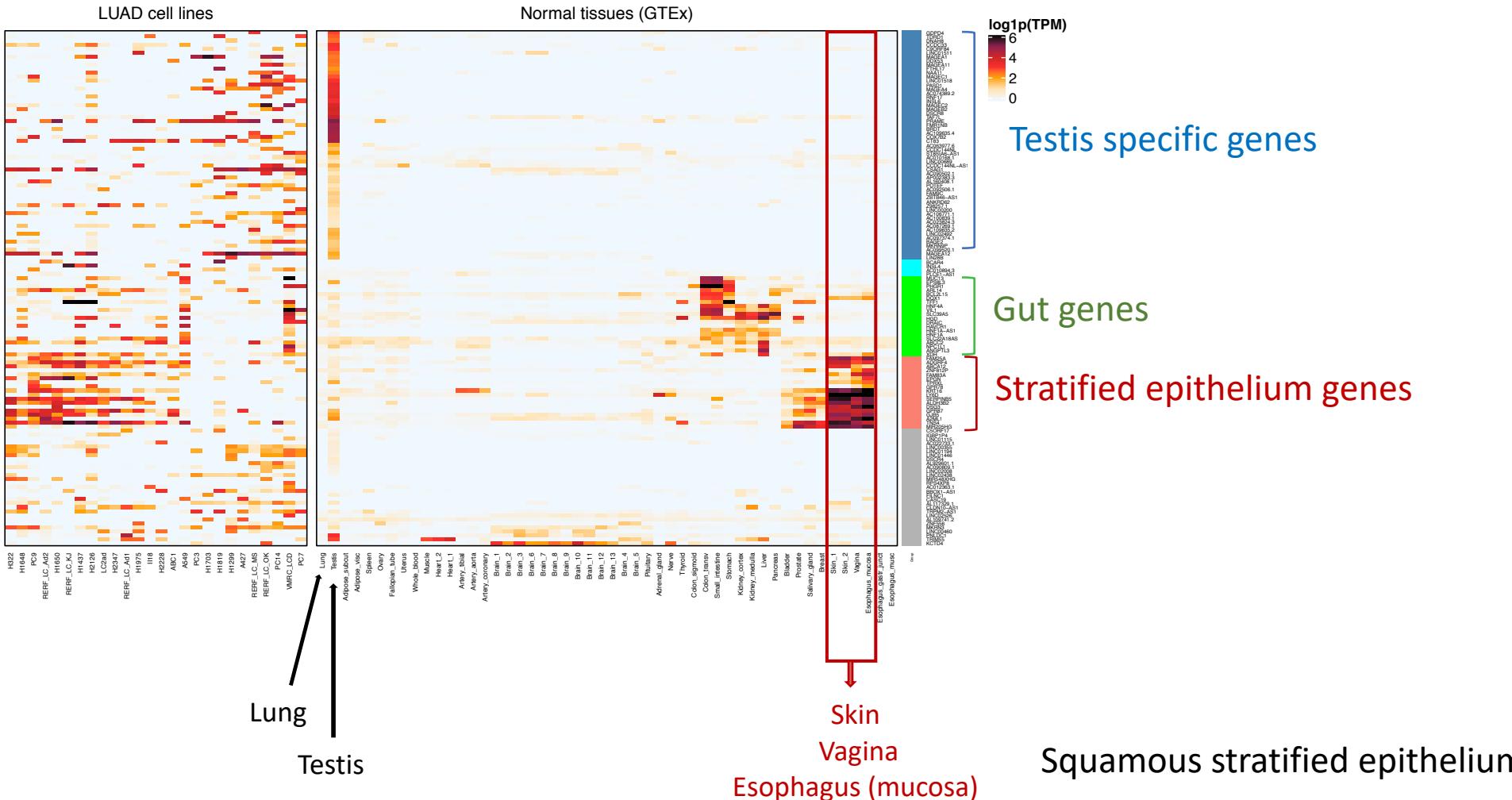
# Tissue specificity



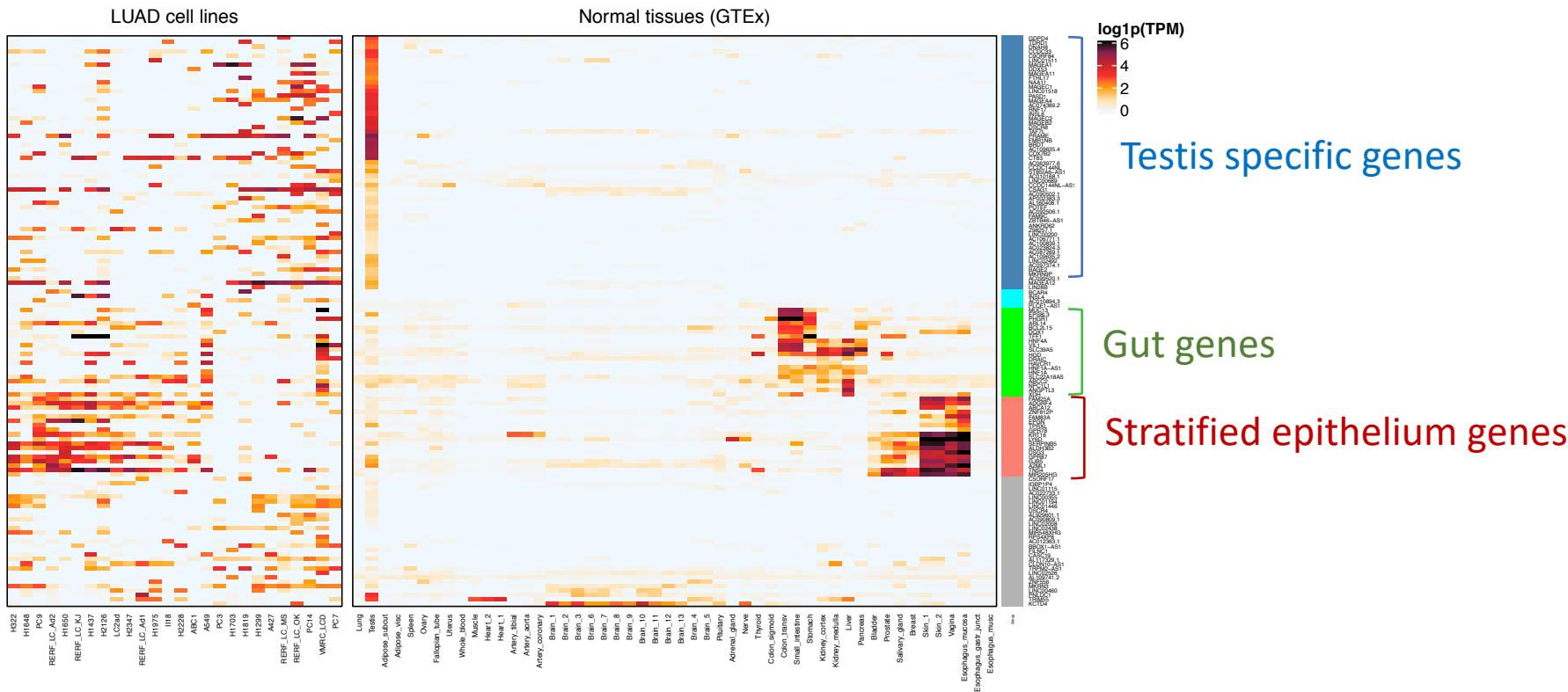
# Tissue specificity



# Tissue specificity



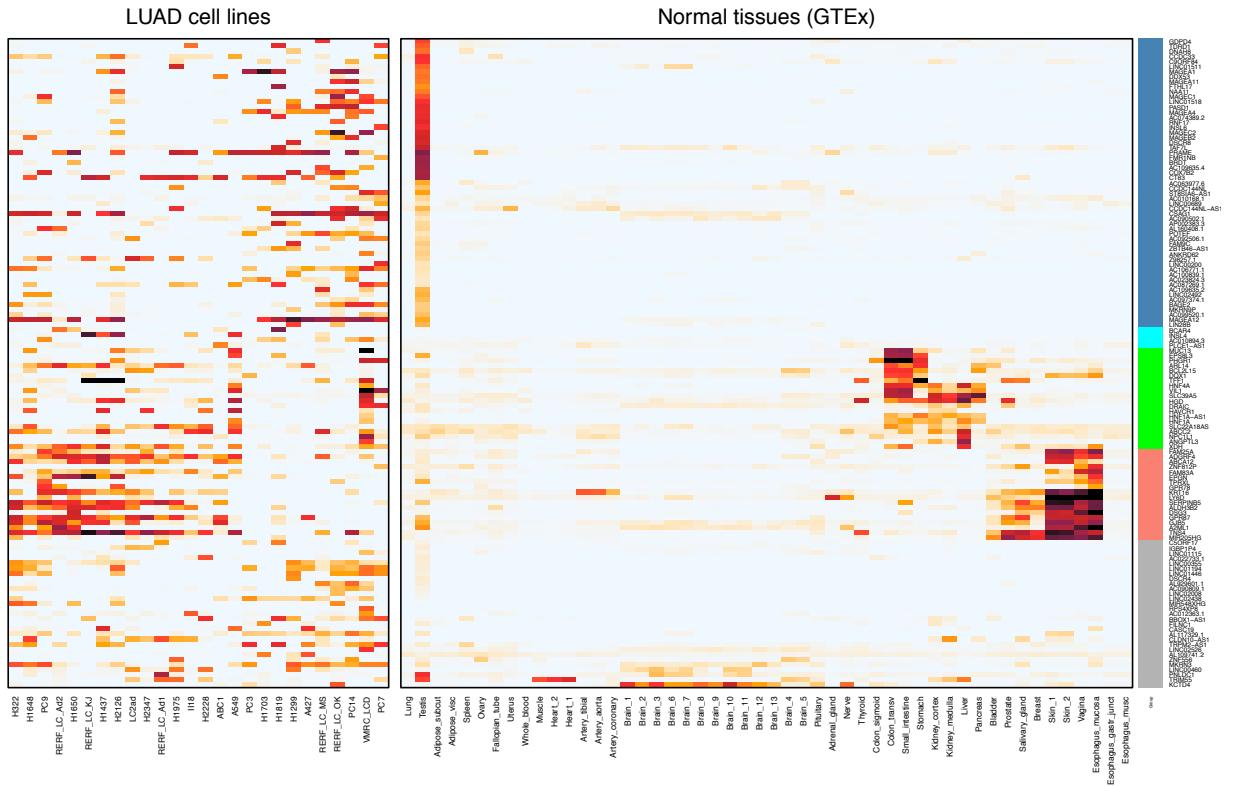
# Survival analyses



Is the activation of these genes in LUAD tumors  
associated to particular clinical features ?

- tumor Stage
- Tumor grade
- Survival

# Survival analyses

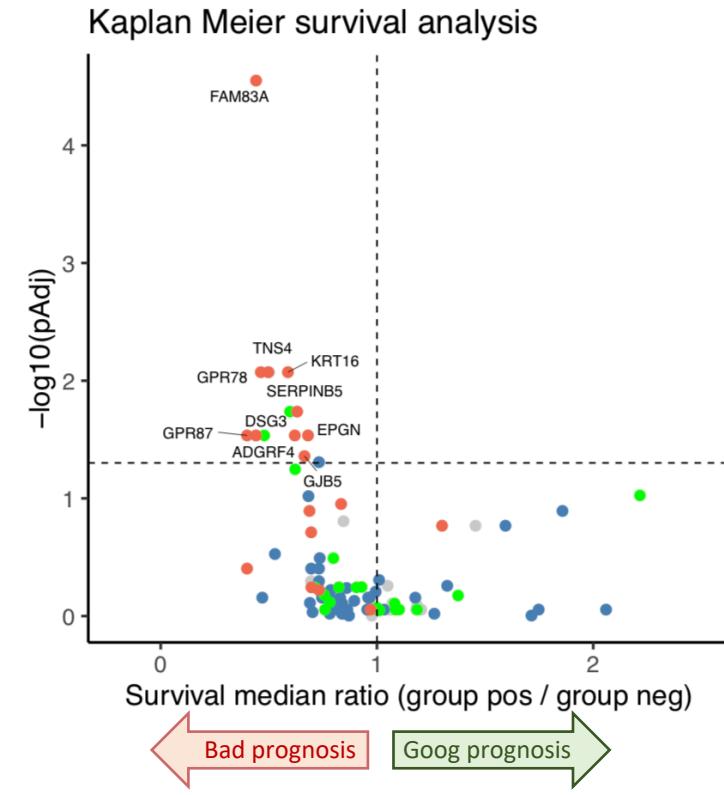


Stratified  
epithelium  
genes

Is the activation of these genes in LUAD tumors  
associated to particular clinical features ?

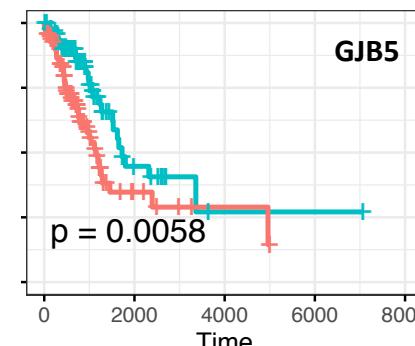
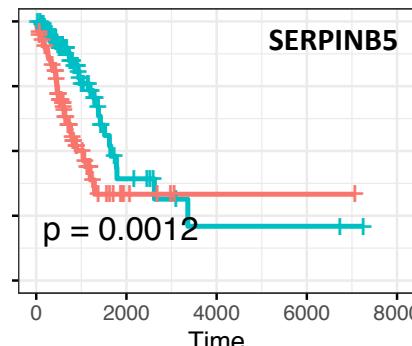
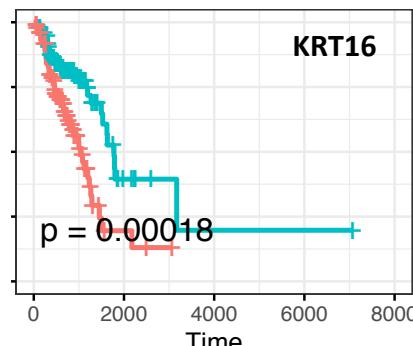
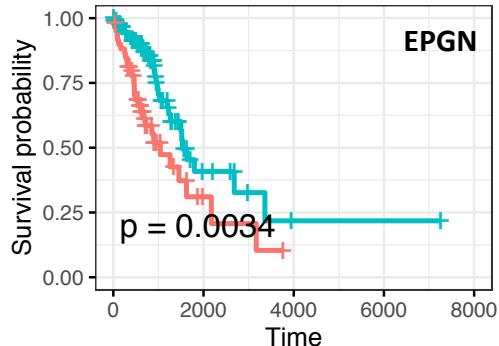
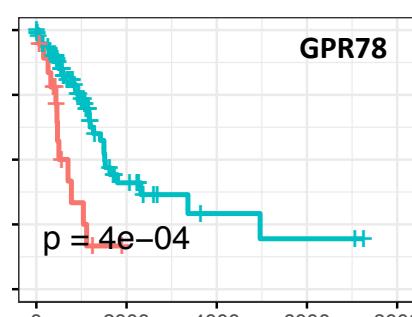
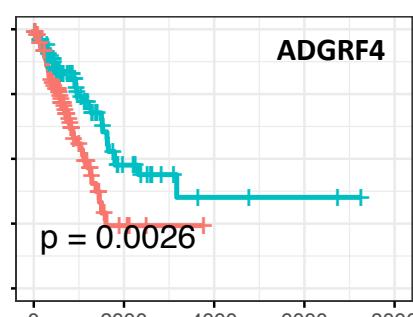
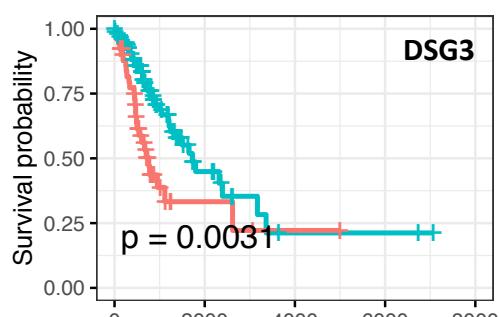
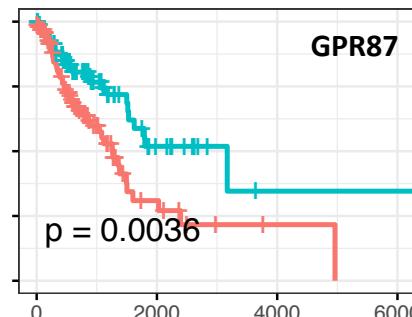
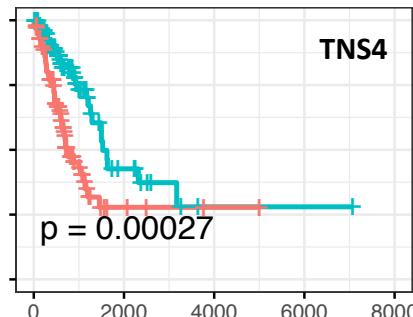
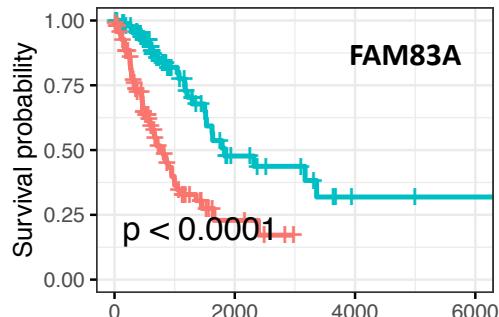
**THE CANCER GENOME ATLAS**  
National Cancer Institute  
National Human Genome Research Institute

- tumor Stage
- Tumor grade
- Survival

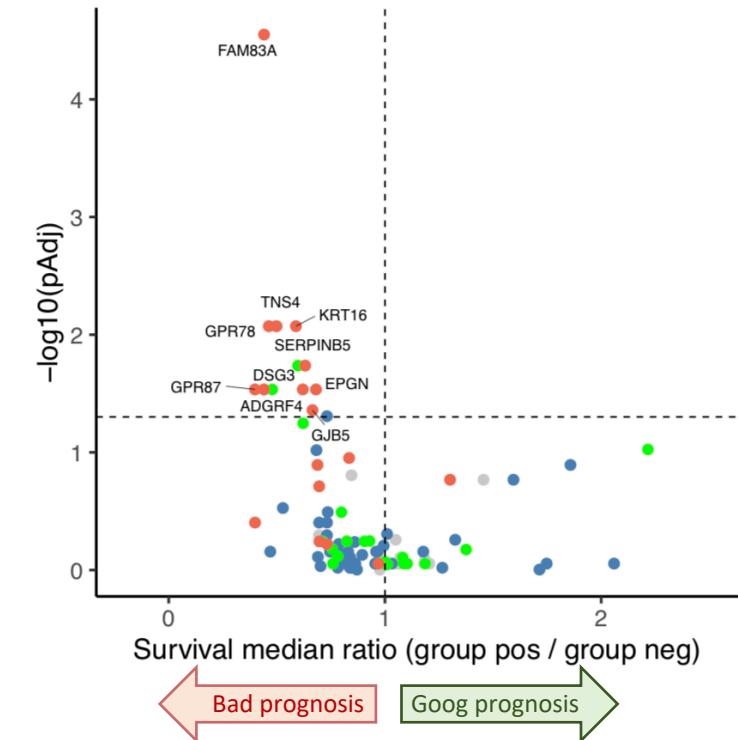


# Survival analyses

Strata + group=neg - group=pos

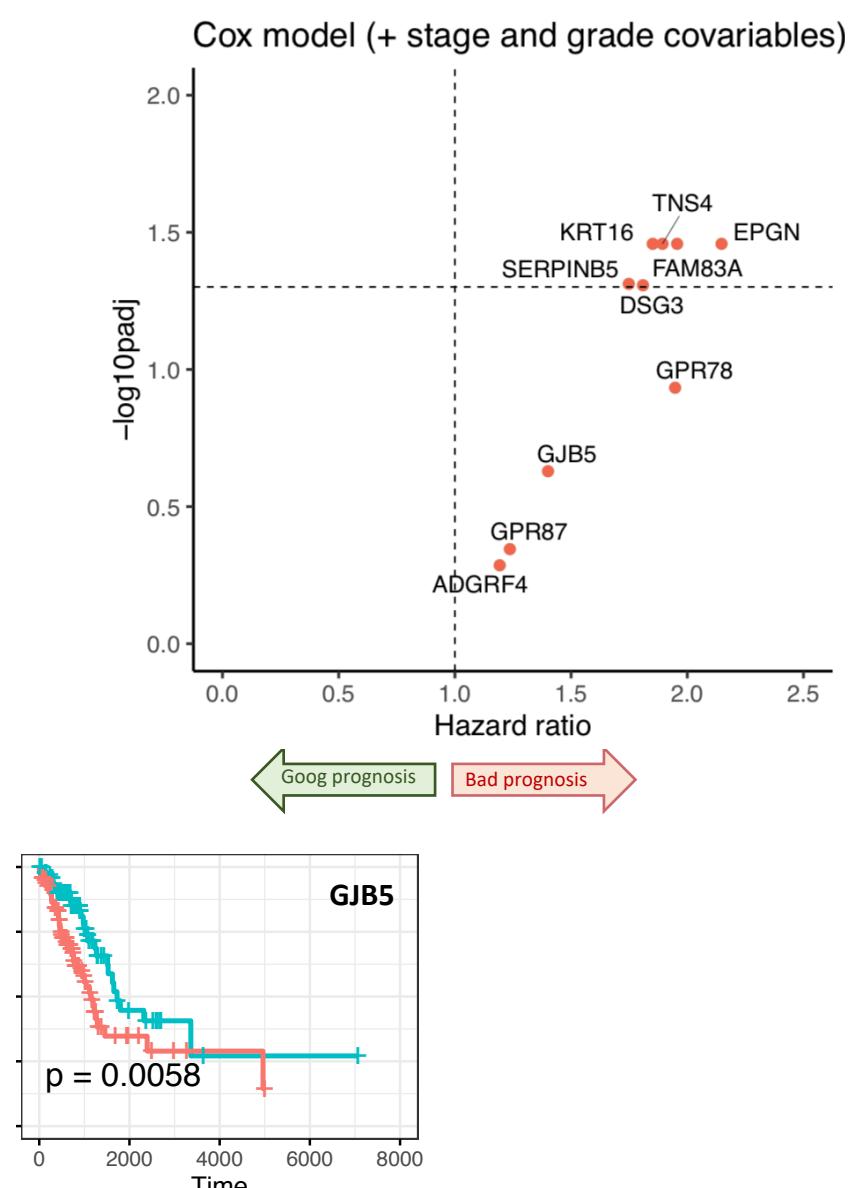
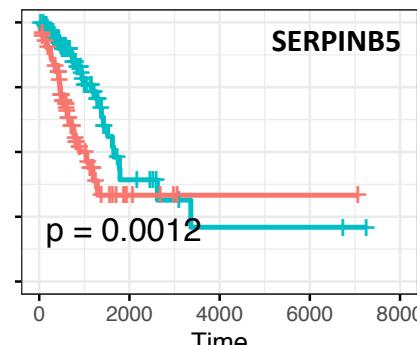
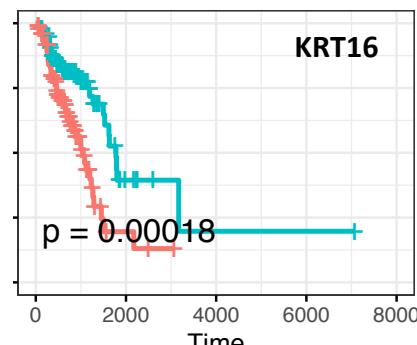
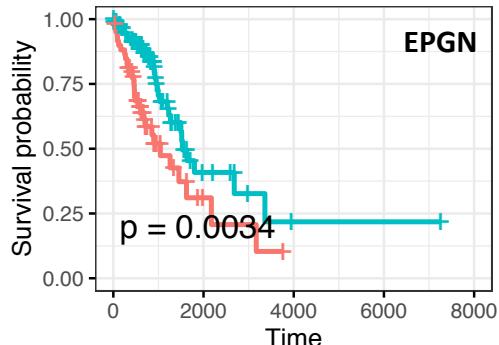
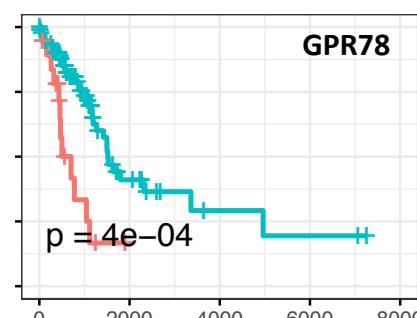
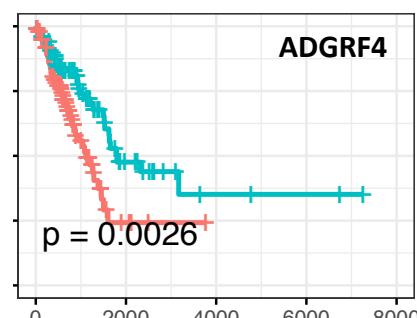
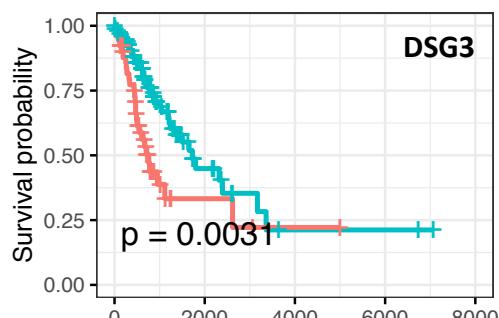
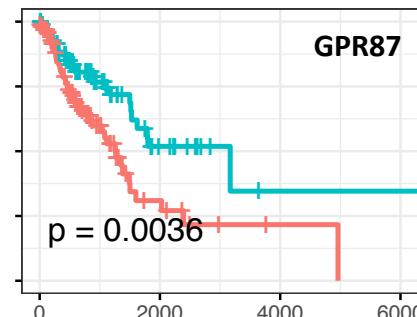
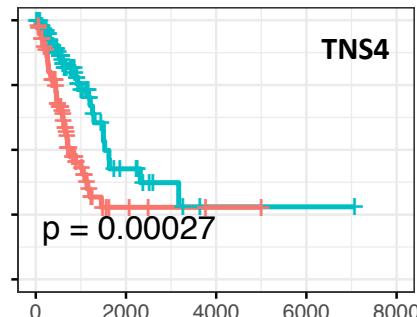
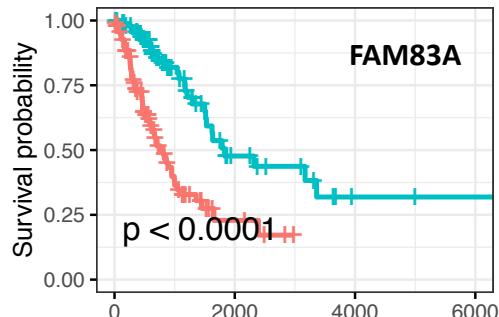


Kaplan Meier survival analysis

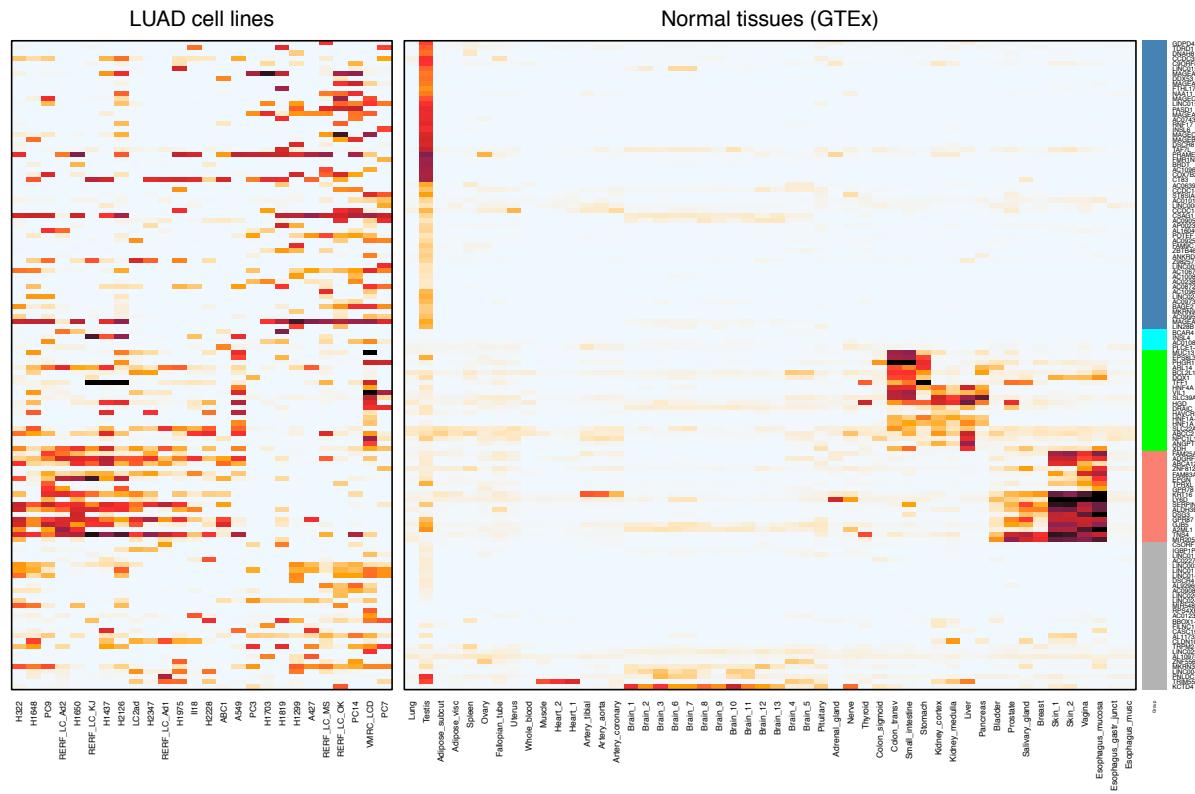


# Survival analyses

Strata + group=neg - group=pos



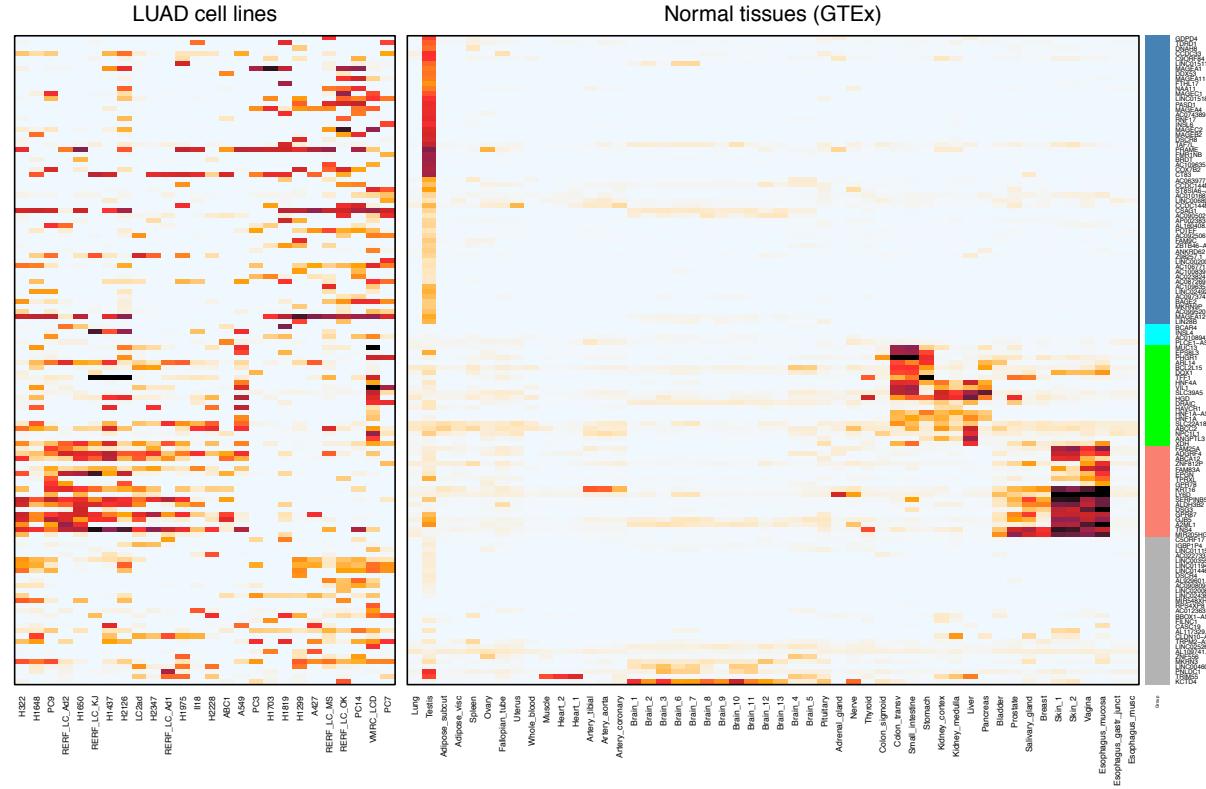
# CONCLUSION



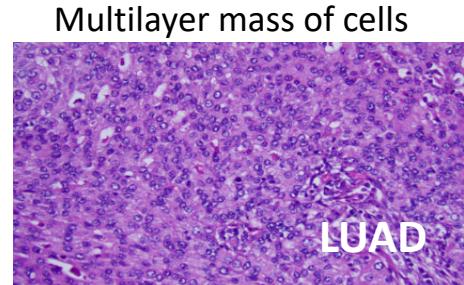
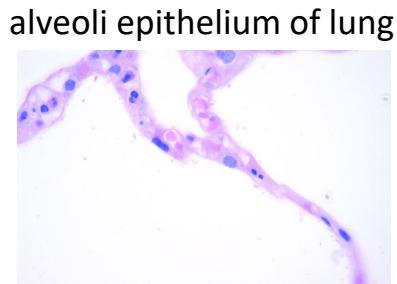
Stratified epithelium genes

- Associated to bad prognosis
- Prognosis biomarkers
- Oncogenic functions ?

# CONCLUSION



Activation of “stratification” genes ?



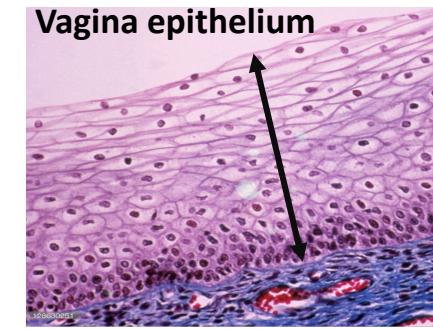
Stratified epithelium genes

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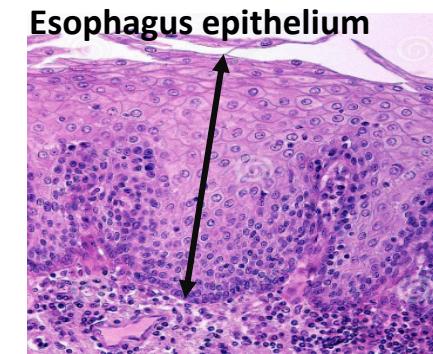
Skin epithelium



Vagina epithelium

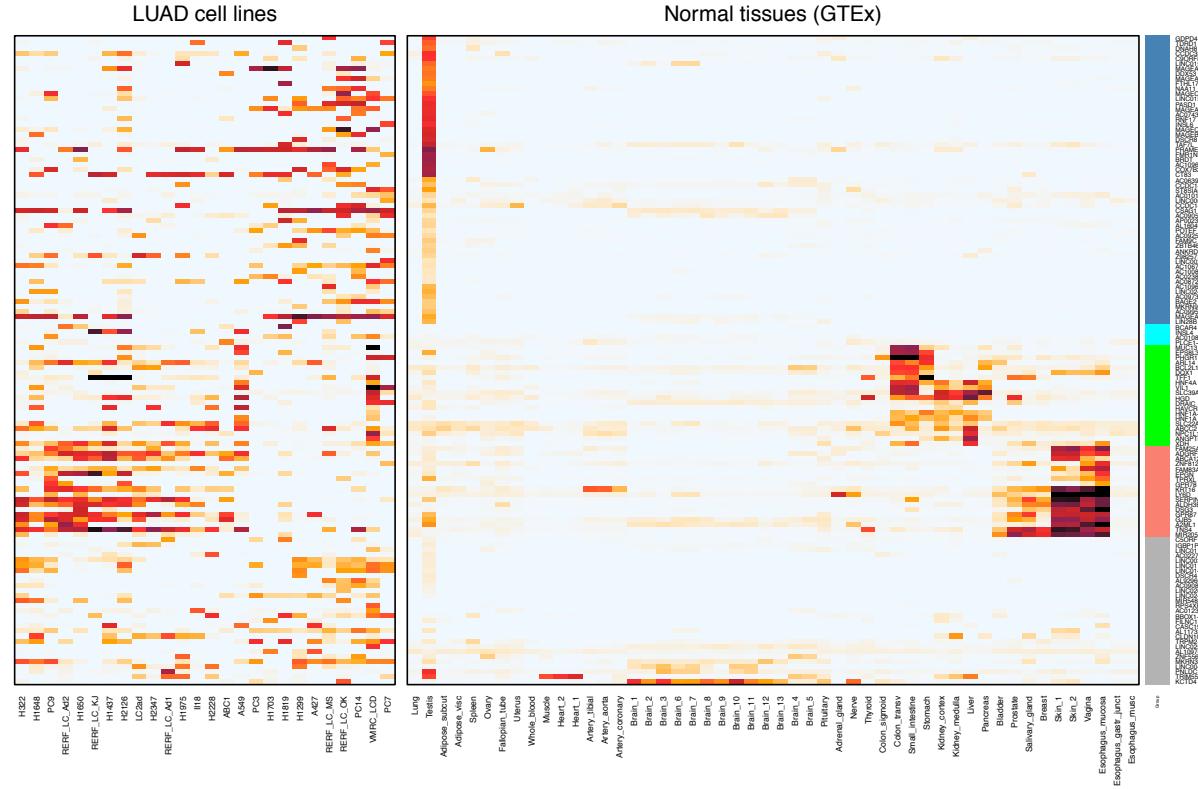


Esophagus epithelium

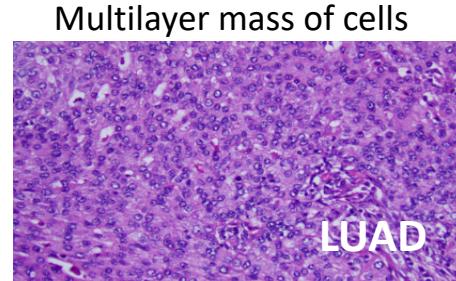


squamous stratified epithelium

# CONCLUSION



Activation of “stratification” genes ?



Stratified epithelium genes

- Associated to bad prognosis
- Prognosis biomarkers
- Oncogenic functions ?

Preliminary results:

Other epithelium stratified genes are also activated in LUAD tumors by a mechanism independent of DNA methylation

- « Stratification » gene signature in LUAD tumors ?



Pr Charles De Smet  
Anna Diacofotakis

**Genetics and Epigenetics Unit**  
De Duve Institute  
belgium

Pr Laurent Gatto  
**Computational Biology and Bioinformatics**  
de Duve Institute



Actions de Recherches concertées

