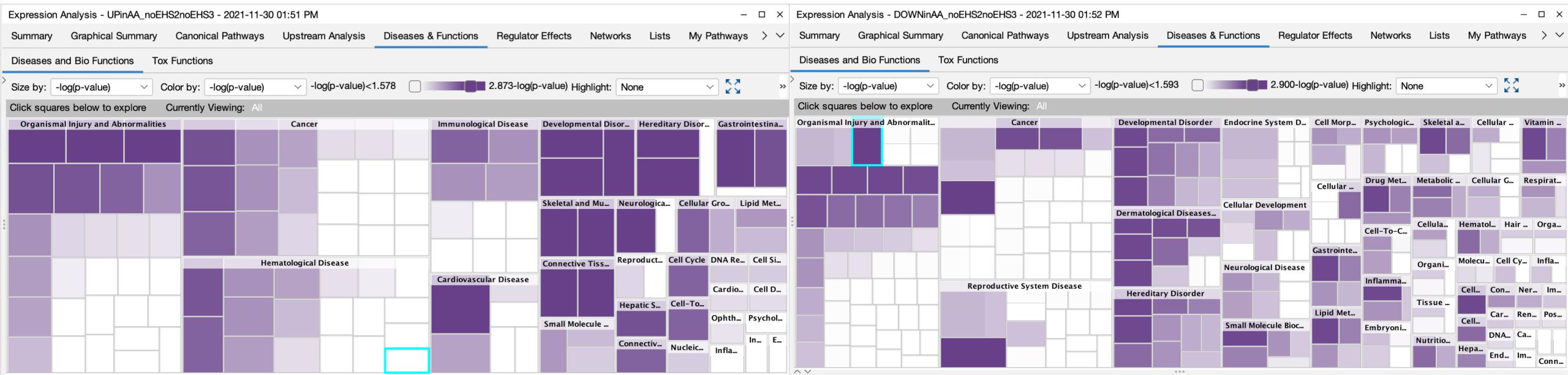


# Pathway analysis

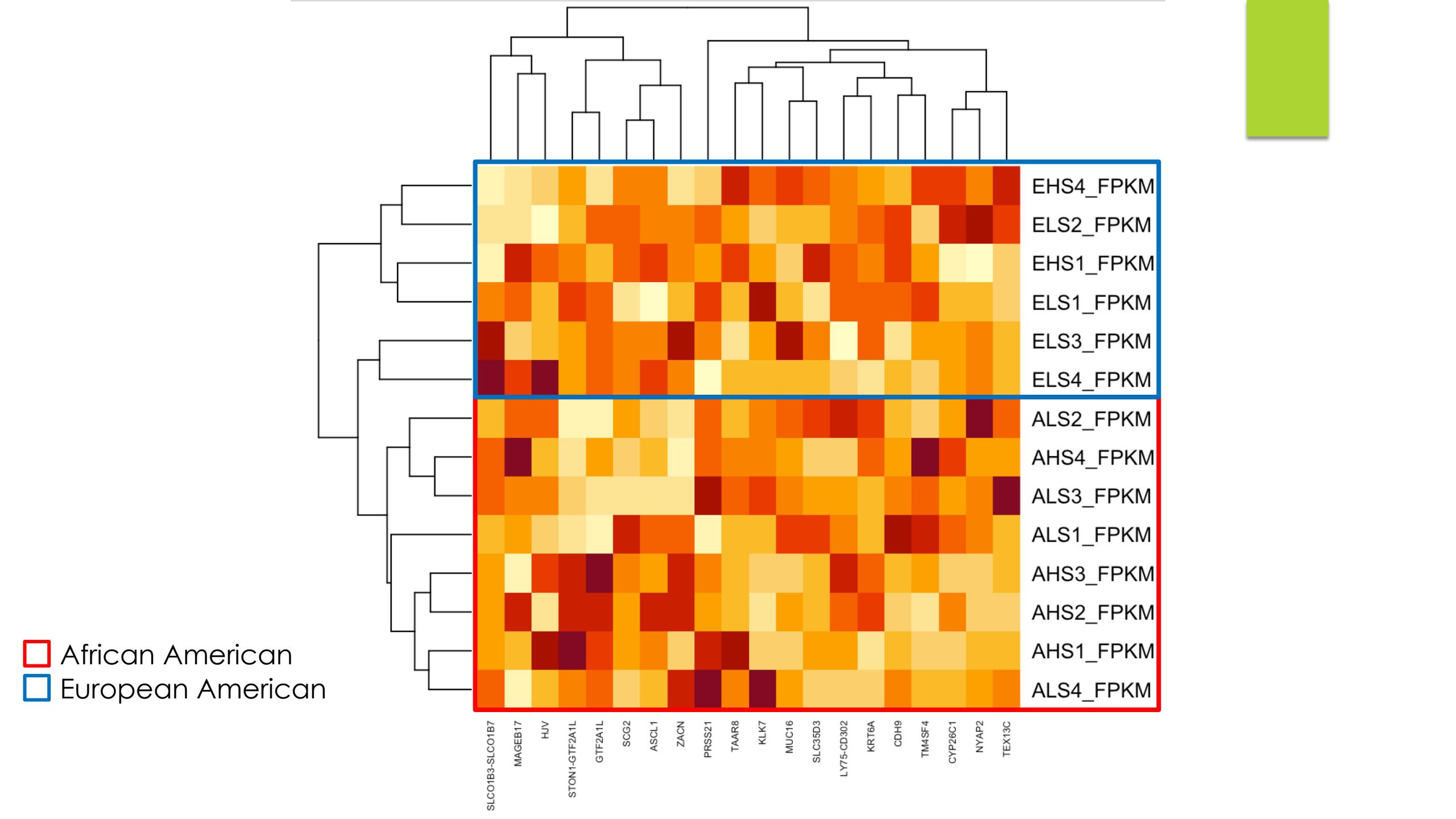
- ▶ Put in upregulated and downregulated genes list separately.
  - ▶ Upregulated genes : 51
  - ▶ Downregulated genes : 113



# Pathway analysis with downregulated genes

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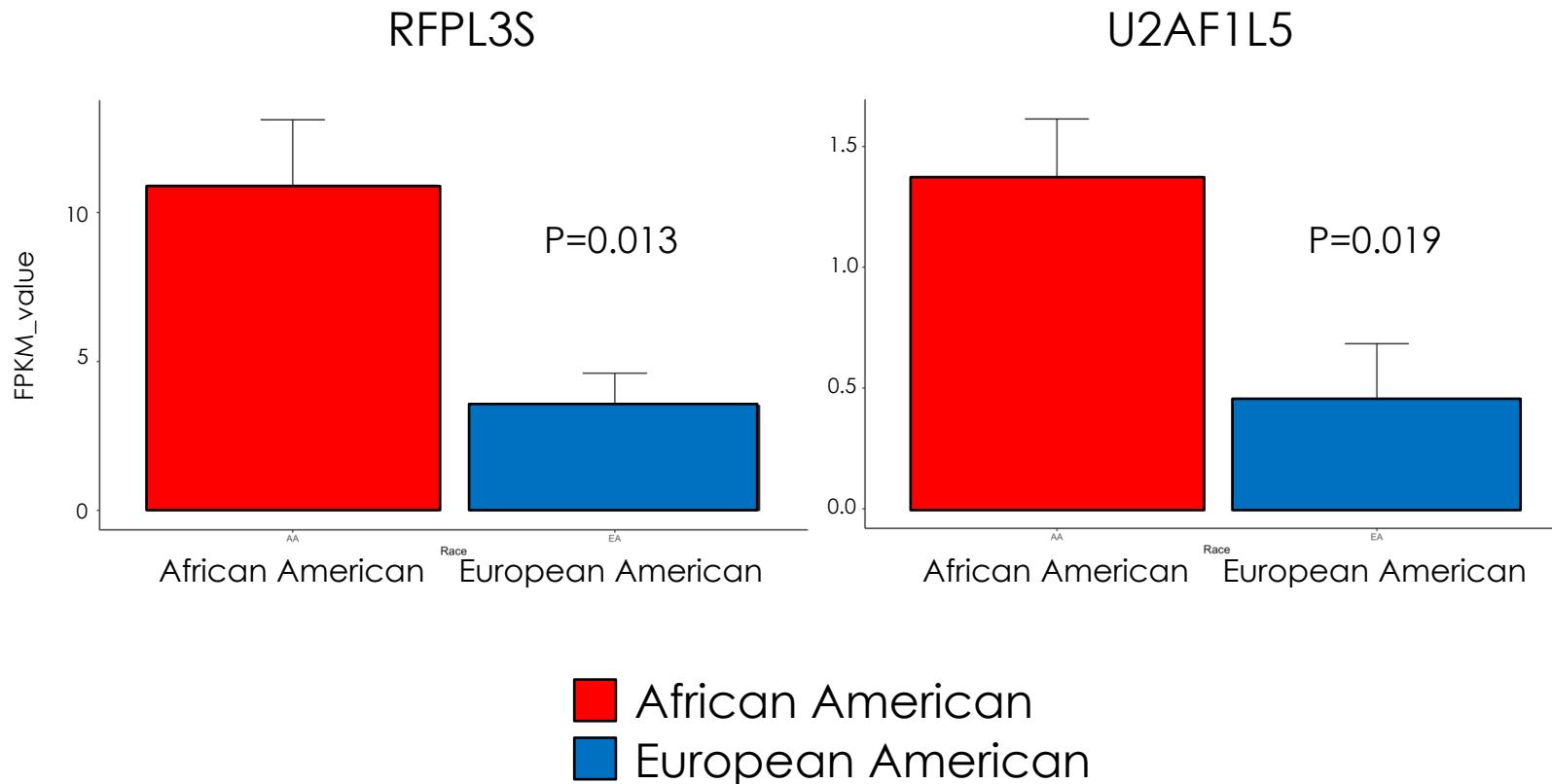
Cate	Diseases or Functions Annotation	p-value	Molecules	# Molecules
Cancer	Penis squamous cell carcinoma	0.000661	GTF2A1L,LY75-CD302,STON1-GTF2A1L	3
Cancer	Skin squamous cell carcinoma	0.00168	CDH9,GTF2A1L,MUC16,NYAP2,SLCO1B3-SLCO1B7,STON1-GTF2A1L,TAAR8	7
Cancer	Desmoplastic melanoma	0.00194	MUC16,SLCO1B3-SLCO1B7	2
Cancer	Stage 1A primary serous ovarian carcinoma	0.0108	MUC16	1
Cancer	Stage 3c primary serous ovarian carcinoma	0.0108	MUC16	1
Cancer	Primary clear cell ovarian carcinoma	0.0124	MUC16	1
Cancer	Grade 3 primary serous ovarian carcinoma	0.0124	MUC16	1
Cancer	Bladder carcinoma	0.0181	CYP26C1,HJV,MAGEB17,MUC16,SCG2,SLC35D3,STON1-GTF2A1L,TAAR8,TM4SF4	9
Cancer	Mucosal melanoma	0.0181	CYP26C1,KLK7,MUC16,NYAP2	4
Cancer	Pulmonary blastoma in lung pleura	0.0185	CDH9	1
Cancer	FIGO stage III-IV peritoneal endometrioid adenocarcinoma	0.0246	MUC16	1
Cancer	FIGO stage III-IV ovarian endometrioid carcinoma	0.0246	MUC16	1
Cancer	Nonfunctional neuroendocrine tumor	0.0246	ASCL1	1
Cancer	FIGO stage III-IV serous ovarian adenocarcinoma	0.0246	MUC16	1
Cancer	FIGO stage III-IV fallopian tube clear cell adenocarcinoma	0.0246	MUC16	1
Cancer	FIGO stage III-IV fallopian tube endometrioid adenocarcinoma	0.0246	MUC16	1
Cancer	FIGO stage III-IV peritoneal clear cell adenocarcinoma	0.0246	MUC16	1
Cancer	FIGO stage III-IV clear-cell ovarian carcinoma	0.0246	MUC16	1
Cancer	Brain oligodendrogloma	0.0258	CDH9,GTF2A1L,KRT6A,MUC16,PRSS21,SLCO1B3-SLCO1B7,STON1-GTF2A1L,TEX13C	8
Cancer	Grade 3 malignant glioma	0.0274	CDH9,GTF2A1L,KRT6A,MUC16,PRSS21,SLCO1B3-SLCO1B7,STON1-GTF2A1L,TEX13C	8
Cancer	Genitourinary squamous cell carcinoma	0.0297	GTF2A1L,LY75-CD302,NYAP2,STON1-GTF2A1L	4
Cancer	BRCA1 mutation negative BRCA2 mutation negative serous ova	0.0307	MUC16	1
Cancer	BRCA1 mutation negative BRCA2 mutation negative peritoneal	0.0322	MUC16	1
Cancer	BRCA1 mutation negative BRCA2 mutation negative fallopian tu	0.0322	MUC16	1
Cancer	Peritoneal mixed carcinoma	0.0427	MUC16	1
Cancer	High grade peritoneal endometrioid adenocarcinoma	0.0427	MUC16	1
Cancer	High grade fallopian tube endometrioid adenocarcinoma	0.0427	MUC16	1
Cancer	High grade ovarian endometrioid carcinoma	0.0442	MUC16	1
Cancer	Humerus osteosarcoma	0.0442	ZACN	1
Cancer	Fallopian tube mixed carcinoma	0.0442	MUC16	1
Cancer	Peritoneal undifferentiated carcinoma	0.0471	MUC16	1
Cancer	Undifferentiated ovarian carcinoma	0.0486	MUC16	1
Cancer	Undifferentiated fallopian tube carcinoma	0.0486	MUC16	1



# Pathway analysis with upregulated genes

Cate	Diseases or Functions Annotation	p-value	Molecules	# Molec
Cancer, Gallbladder adenocarcinoma		0.00196	CSMD1,U2AF1/U2AF1L5	2
Cancer, Refractory cytopenia with multilineage dysplasia and ringed sideroblasts		0.00212	U2AF1/U2AF1L5	1
Cancer, Leukemic transformation of essential thrombocythemia		0.00283	U2AF1/U2AF1L5	1
Cancer, Leukemic transformation of myelofibrosis		0.00635	U2AF1/U2AF1L5	1
Cancer, Systemic mastocytosis with associated clonal hematological non-mast cell lineage disease		0.00635	U2AF1/U2AF1L5	1
Cancer, Leukemic transformation of myelodysplastic myeloproliferative disease		0.00775	U2AF1/U2AF1L5	1
Cancer, Refractory anemia with excess blasts type 1		0.00845	U2AF1/U2AF1L5	1
Cellular Accumulation of cervical cancer cell lines		0.00986	U2AF1/U2AF1L5	1
Cancer, Myelodysplastic syndrome with multilineage dysplasia		0.012	U2AF1/U2AF1L5	1
Cardiov: Cell viability of endothelial cell lines		0.0182	U2AF1/U2AF1L5	1
Cancer, Refractory anemia with excess of blasts type 2		0.0182	U2AF1/U2AF1L5	1
Cancer, Blastic plasmacytoid dendritic cell neoplasm		0.0189	U2AF1/U2AF1L5	1
Cancer, Type M0 acute myeloid leukemia		0.0217	U2AF1/U2AF1L5	1
Cancer, High-risk myelodysplastic syndrome		0.0293	U2AF1/U2AF1L5	1
Infectio: Replication of Infectious bronchitis virus		0.03	U2AF1/U2AF1L5	1
Cancer, Acute myeloid leukemia associated with myelodysplastic syndrome		0.0327	U2AF1/U2AF1L5	1
Cancer, Myelodysplastic syndrome with ring sideroblasts		0.0341	U2AF1/U2AF1L5	1
Cancer, Treatment-related acute myeloid leukemia		0.0382	U2AF1/U2AF1L5	1
Cancer, Polycythemia vera		0.0436	U2AF1/U2AF1L5	1
Cancer, Type M2 acute myeloid leukemia		0.0436	U2AF1/U2AF1L5	1
Cancer, Type M1 acute myeloid leukemia		0.0484	U2AF1/U2AF1L5	1
Cancer, Type M4 acute myeloid leukemia		0.0491	U2AF1/U2AF1L5	1

# Barplot of RFPL3S and U2AF1L5



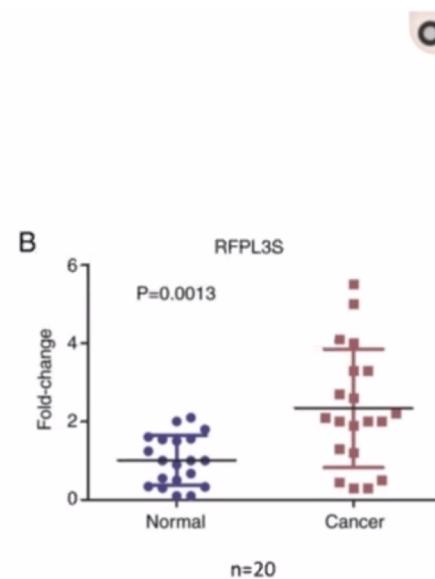
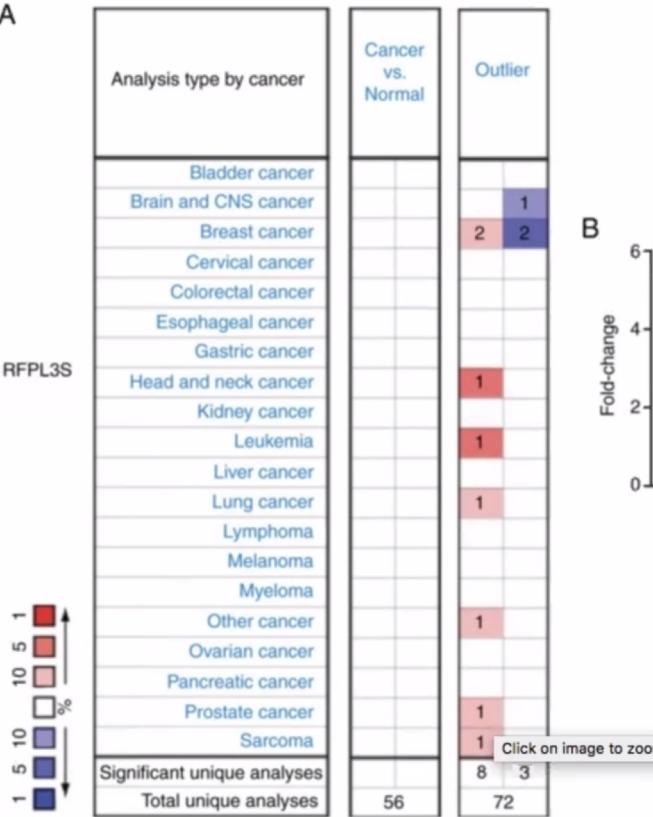
# Previous study of genes RFPL3S

- ▶ RFPL3S was first described in 1999 (Seroussi et al, *Genome Research*) and is a non-coding, antisense transcript of RFPL3 and is located on chr 22. This non-coding gene was produced during evolution from intrachromosomal duplications within the 22q12–13 region, and share an ancestral origin with the highly-variable MHC locus on chr 6.
- ▶ There is very limited information about RFPL3S function or its role in cancer (there are only three papers on Pubmed).
- ▶ However, a recent paper (Liu et al, *Oncology Letters* 2020) showed RFPL3S “was highly expressed in lung cancer tissues when compared with normal tissues and was significantly associated with pN factor, pTNM stage and Ki-67 labeling index.” In addition, “increased RFPL3S expression was associated with poor survival and was inversely associated with first progression in all patients.”

# Previous study of genes RFPL3S

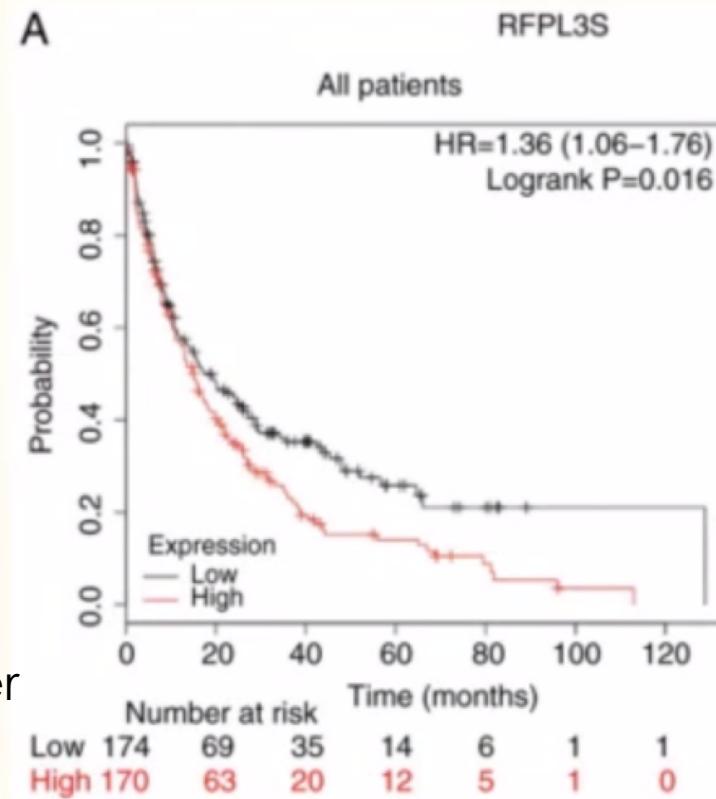
Oncol Lett. 2020 Aug; 20(2).

A



RFPL3S had significantly higher expression in lung cancer than normal lung tissue.

A



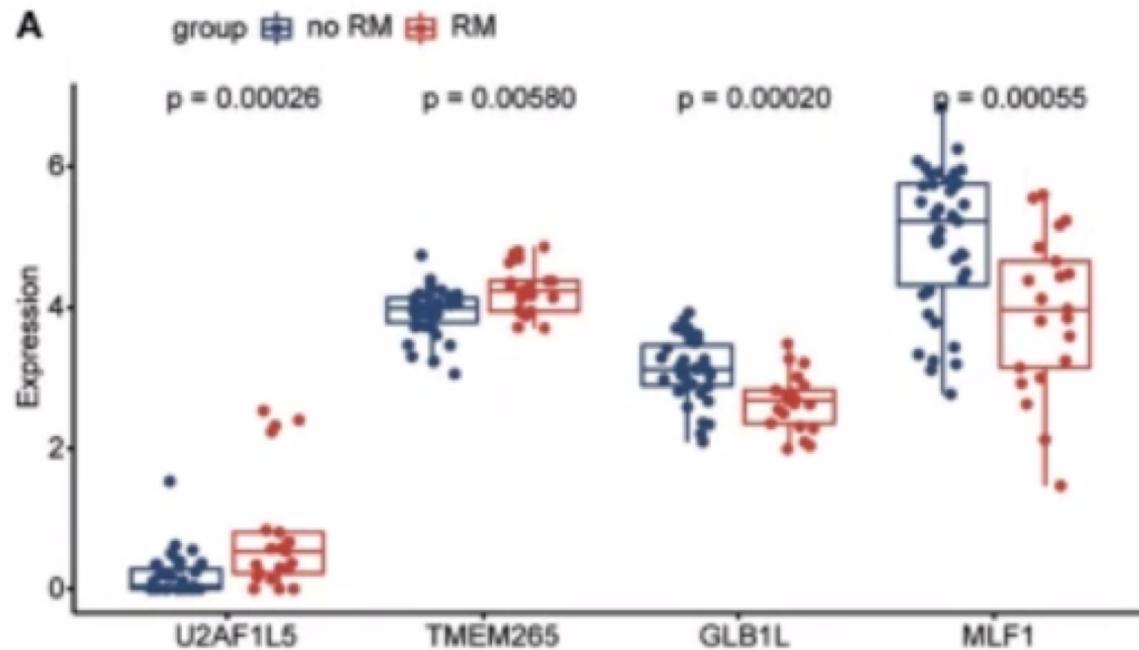
High RFPL3S expression is associated with poor survival in lung cancer.

# Previous study of gene U2AF1L5

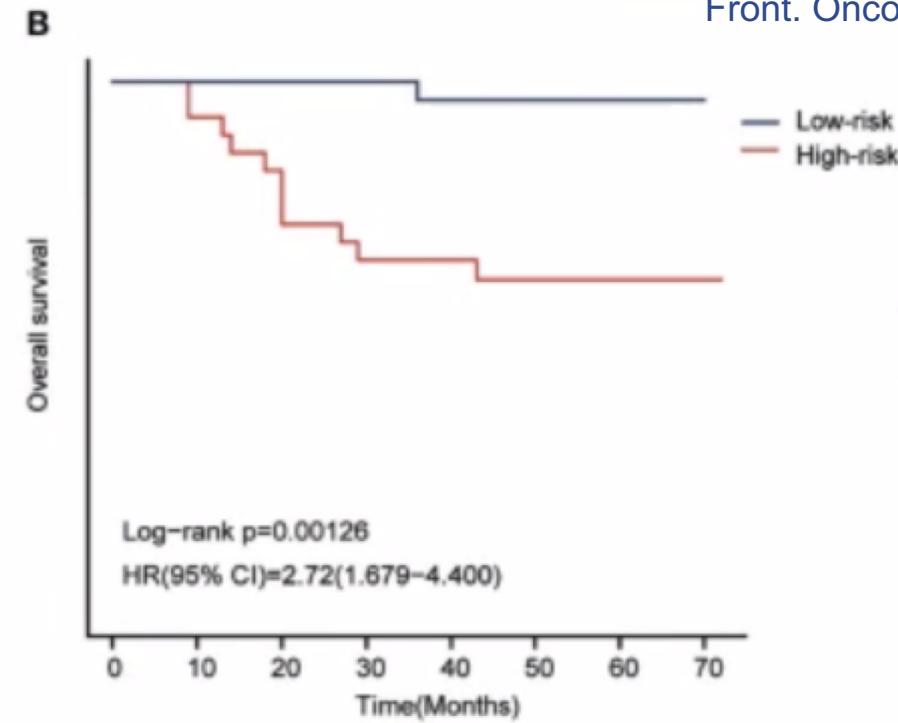
- ▶ U2AF1L5 (U2 Small Nuclear RNA Auxiliary Factor 1 Like 5) is a Protein Coding gene and plays a critical role in RNA splicing and is located on chr 21. (<https://www.genecards.org/cgi-bin/carddisp.pl?gene=U2AF1L5>)
- ▶ There is very limited information about U2AF1L5 function or its role in cancer (there are only two papers on Pubmed).
- ▶ However, a recent paper (Zhao et al, *Frontiers in Oncology* 2021) using machine learning from Nasopharyngeal carcinoma (NPC) RNA-Seq data identified U2AF1L5 as one of four genes able to predict NPC recurrence/metastasis. “Of the four mRNAs, two were protective mRNAs (GLB1L and MLF1) whose high expression was associated with better prognosis. In contrast, high expression of the remaining two mRNAs (**U2AF1L5** and TMEM265) was associated with poor outcomes.”

# Previous study of genes U2AF1L5

Front. Oncol. 2021 August 07.



U2AF1L5 was expressed higher in NPC that had recurrence/metastasis (RM) compared to NPC with no RM.



A 4-gene machine learning model that includes U2A51LF was associated with NPC patient survival.

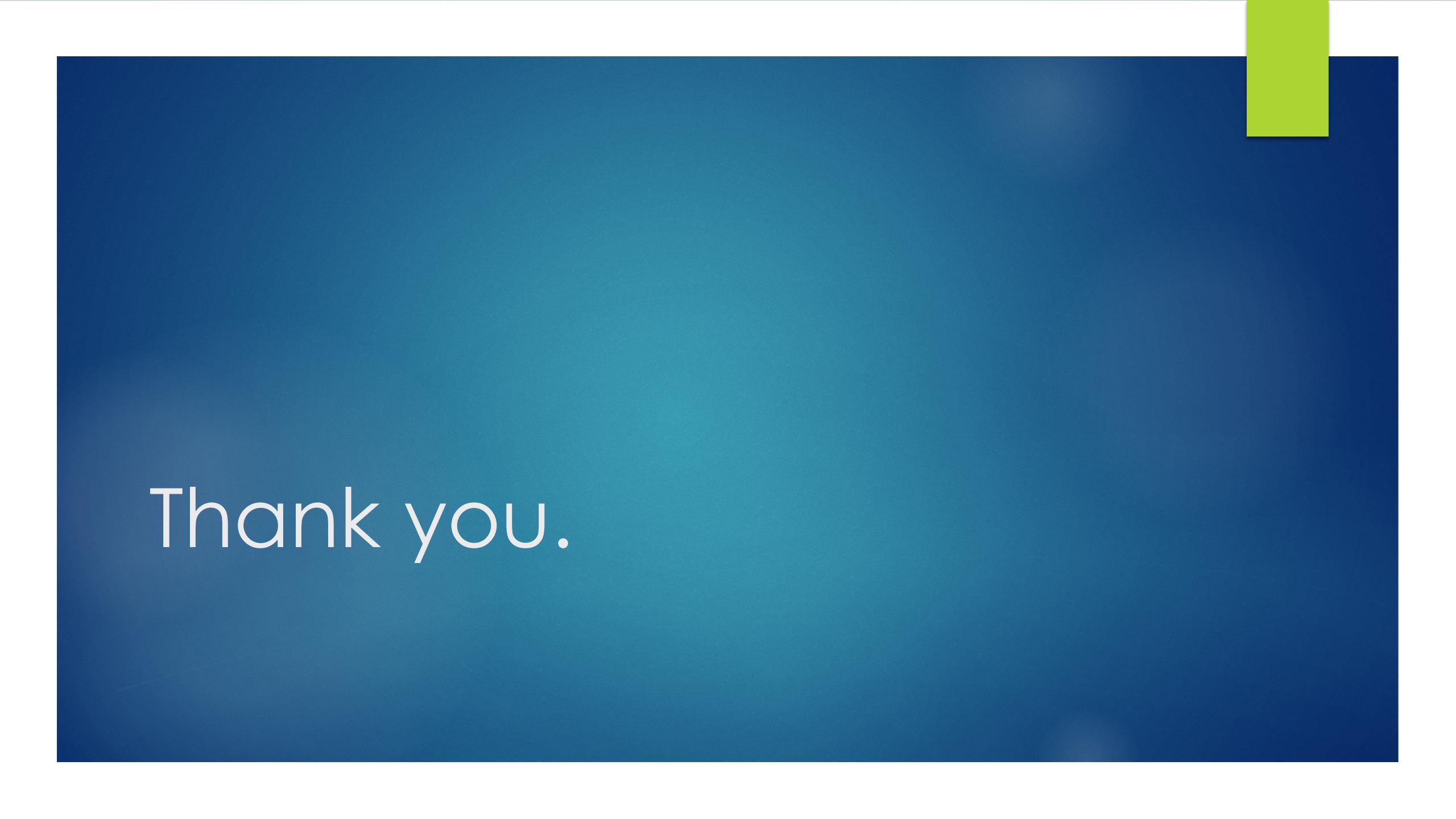
# Conclusions & future studies

## ► Conclusions

- ▶ RFPL3S and U2AF1L5 were expressed significantly higher in the African American group than the European American group.
- ▶ Limited information is available about these genes' function.
- ▶ However, two recent studies in lung cancer and Nasopharyngeal carcinoma (NPC) support the hypothesis that increased the expression of these genes is associated with recurrence, metastasis, and poor survival.
- ▶ I hypothesize that the health disparity observed in African American men with prostate cancer may be due to higher expression of these genes, and that they may be useful markers for prostate cancer prognosis and/or may served as novel drug-treatment targets. This data suggests that differential gene expression between African American men and European American men may influence the severity and survival of prostate cancer.

## ► Future studies

- ▶ Assess RFPL3S and U2AF1L5 expression in additional samples or independent datasets.
- ▶ Perform laboratory studies in cancer cell lines or animal models to determine the effect of RFPL3S and U2AF1L5 overexpression.
- ▶ Evaluate if RFPL3S and U2AF1L5 expression is related to vitamin D levels (another part of this dataset that was not analyzed for my project).



Thank you.